Agent-based Model for Developmental Aggregation in *Myxococcus xanthus* Bacteria

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Using a mechanistic agent-based model, we uncover the physical basis of behaviors that control aggregation of *M. xanthus* cells into multicellular mounds. The observed bias in reversal times with respect to cell's direction relative to the aggregates can be explained by chemotaxis but not by contact-dependent signaling model. On the other hand, a combination of local alignment by steric interactions and the ability of cells to lay and follow slime trails explains observed patterns of cell orientation. Incorporating these effects in our model leads to the formation of stable aggregates in quantitative agreement with the experiments.

I. BACKGROUND

SPATIAL multicellular self-organization is widely studied due to its biological significance across all kingdoms of life. *Myxococcus xanthus* is a rod-shaped soil bacterium that serves as a simple model system to study self-organization. Under different environmental conditions, *M. xanthus* cells self-organize into distinct dynamical patterns [1]. For example, starving cells execute a complex multicellular developmental program by aggregating into multicellular mounds, termed fruiting bodies [1,2]. Despite decades of research, the mechanistic basis of self-organization in *M. xanthus* is not yet fully understood. In particular, how cells aggregate into fruiting bodies is still not clear.

Recently, an approach that combined fluorescence microscopy with data-driven modeling uncovered the set of cellular behaviors required for aggregation: decreased cell motility inside the aggregates, a biased walk toward aggregate centroids, and alignment among neighboring cells and in a radial direction to the nearest aggregate [3]. Here we use a mechanistic agent-based model to test possible biological mechanisms of these behaviors.

II. RESULTS

To test aggregation mechanisms, we developed an agent-based model. In this model, each cell is represented by a point-agent characterized by its position and moving direction. Each agent actively aligns its direction with nearby agents and secrete slime trails. Other agents can sense and follow these trails by turning towards high slime density regions. At low cell density, our model matches the patterns of collective alignment observed in experiments [3] and reproduced by detailed biophysical model [4]. At high cell density, the model can efficiently simulate alternative hypotheses on cell behaviors.

A. A contact signaling based model does not lead to stable aggregation.

In the first model, we assumed that the reversal period of each cells is dependent on a contact dependent signal that conveys the direction of the surrounding cells. The model using this contact-based signal is unable to form stable aggregates, even if the parameters in this mechanism are fitted to the bias data [3].

B. A chemotaxis model produces biased movement similar to the experiment and helps with aggregation.

In the second model, we assumed a chemotaxis mechanism, i.e. cells produce a diffusible chemical signal that affects the reversal period via an intracellular chemotaxis network with adaptation. Applying this mechanism into our model, we find that the resulting model can replicate the experimentally observed bias and aggregation patterns [3].

C. Local cell alignment and slime-trail following can explain observed cell-orientation patterns.

Using our chemotaxis model with local cell alignment and slime-trail following, we compare the simulated distributions of agents' orientation with those observed in experiments [3]. The results are in qualitative agreement: near aggregate boundaries, cells move in circumferential direction rotating around aggregates whereas further away cells align radially to aggregate centers. These patterns are partially driven by cell alignment and slime trails prior to aggregation initiation.

III. CONCLUSION

We propose that *M. xanthus* cells use a chemotaxis mechanism to form aggregates. Combined with local alignment and slime-trail following, these mechanisms are sufficient to explain the observed aggregation patterns.

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