Self-organization mechanisms in *Myxococcus xanthus* swarms

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Myxococcus xanthus **is a model bacteria famous for its coordinated multicellular behavior resulting in formation of various dynamical patterns. Examples of these patterns include fruiting bodies - aggregates in which tens of thousands of bacteria self-organize to sporulate under starvation conditions and ripples - dynamical bacterial density waves propagating through the colony during predation. Relating these complex self-organization patterns in *M. xanthus* swarms to motility of individual cells is a complex-reverse engineering problem that cannot be solved solely by traditional experimental research. Our group addresses this problem with a complementary approach - a combination of biostatistical image quantification of the experimental data with agent-based modeling.**

***Keywords — Myxococcus xanthus*, Ripples, fruiting bodies, aggregation.**

I. BACKGROUND

Myxococcus xanthus has been long studied for its unique life cycle and ability to dynamically self-organize. During their growth phase cells move in large swarms preying on other microorganisms. When faced with nutritional stress at high density on a solid surface, cells aggregate into a fruiting body and differentiate dormant myxospores. During starvation-induced aggregation and during predation *M. xanthus* cells are known to self-organize into periodic bands of traveling waves, termed ripples. Despite extensive use of microcinematography and molecular genetics to examine aggregation and ripples – the biophysical basis of these behaviors is not completely understood. A quantitative metric is essential to assess the agreement of experimentally observed aggregation patterns with those produced by mathematical models aiming to reproduce the morphogenesis *in silico*. While various groups identified overlapping but distinct sets of model ingredients that lead to aggregation in computational simulations further quantification of experimental data is essential to refine these models.

II. RESULTS

To better understand the aggregation dynamics we develop high-throughput image quantification and statistical analysis methods. A quantitative metric of features characterizing each aggregate is used to deduce the properties of the aggregates correlated with each fate. The analysis shows that small aggregate size but not neighbor related parameters correlate with aggregate dispersal. Furthermore, close proximity is necessary but not sufficient for aggregate merging. Finally, splitting occurs for those aggregates that are unusually large and elongated. These observations place severe constraints on the underlying aggregation mechanisms and present strong evidence against the role of long-range morphogenic gradients or biased cell exchange in the dispersal, merging, or splitting of transient aggregates.

To extend our earlier model to explain predatory ripples we have constructed a mathematical agent-based model that demonstrates that three ingredients are sufficient to generate rippling behavior: (1) side-to-side signaling between two cells that causes one or both of cells to reverse, (2) a minimal refractory time-period after each reversal during which cells can not reverse and therefore are not sensitive to signaling, and (3) physical interactions that cause the cells to locally align. Furthermore, we hypothesize that the presence of prey induces ripples by stimulating side-by-side signaling. This model leads to experimentally confirmed predictions of the relation between the wavelength and reversal time and suggests several physiological benefits to rippling when prey is present. First, when swarming over prey *M. xanthus* cells will spread faster when subject to side-by-side signaling. Second, when prey is covered individual *M. xanthus* cells within waves are subject to more periodic motion patterns and as a result drift will be reduced. Thus, rippling behavior allows *M. xanthus* cells to cover its prey faster and stay over it for longer. These modeling predictions were also tested experimentally by observing ripples over *E. coli* prey with fluorescence microscopy quantifying the images with Fourier and wavelet transforms.

III. CONCLUSION

With combination of agent-based modeling, time-lapse microcinematography experiments and image quantification we have gained new insights on the mechanisms of *M. xanthus* self-organization.

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