

## Review of “Social conflicts in *Dictyostelium discoideum*: a matter of scales”

### Summary

This paper presents an overview of the social conflicts that can arise in *Dictyostelium discoideum* when multicellular structures are formed by the aggregation of genetically heterogeneous cells. In particular, this work is focused on the causes and consequences of spore bias, or the over/under- representation of certain genotypes in the spore mass relative to their initial frequency in a chimeric group. The authors begin with a brief introduction to aggregative multicellular life cycles, the difficulties associated with measuring differential fitness of co-aggregating genotypes, the problem of ‘cheating’ during multicellular development of the fruiting body, and the question of why the existence of cheaters does not doom collective function altogether. The question of why cheats (specifically, genotypes that exhibit positive spore bias) don’t doom collectives is then addressed from two different conceptual perspectives for understanding social conflicts: the strain-level and the cell-level perspective.

This article provides a comprehensive review of an interesting topic and I think these authors are providing a valuable perspective on how we conceptualize social interactions in microbes. I especially enjoyed the discussion section, in which the authors lay out the key questions they believe must be addressed in order to build adequate predictive evolutionary models. In fact, I would love for the themes introduced in the discussion to be raised much earlier in the manuscript so that they could be carried throughout the text! This could be helpful because it wasn’t always obvious to me how the experimental data being summarized related back to the central themes of the manuscript. For example, while it is true that physiological state and cell cycle phase influence developmental fate, it is unclear whether these factors are expected to have differential effects on the developmental decisions of cells of different genotypes or if cells of all genotypes are influenced similarly by these factors. If there is no differential effect of environment, would the incorporation of these sources of phenotypic heterogeneity change our predictions about how the system will evolve? If so, how? For me, it would be extremely helpful to have a table summarizing the major sources of phenotypic heterogeneity, how they influence cell developmental fate, and how model predictions might change when these sources of variation are incorporated. The fact that “different conceptualizations lead to different predictions” is a key takeaway message of the paper being highlighted in the conclusions section.

Another area I had some difficulty with was the balance of arguments in favor of the strain-level vs. the cell-level perspective. The abstract sets up an expectation that this review will be a balanced comparison two competing conceptual frameworks for understanding (and perhaps modeling) social conflicts in *Dictyostelium discoideum*. However, the cell-level perspective receives a disproportionate amount of attention and seems to be the better supported of the two conceptual frameworks based on the results presented. If this is indeed the perspective of the authors, this argument could be made early on in the manuscript and each consecutive subsection in the “Cell-level strategies” section could serve as further support for the need to consider cell-level properties when performing experiments and building models of

*Dictyostelium* social evolution. If this is not the perspective of the authors, some further consideration could be given to how strain-level models might be able to accommodate some of the relevant sources of phenotypic heterogeneity (as discussed in the stochastic vs. deterministic models subsection of the discussion).

### **Minor comments**

In the abstract where it says, “cheater populations are selectively advantaged,” I might add “when interacting with cooperators”.

The final paragraph of the introduction (pg 4, bottom) seems to be a concatenation of two different versions of the same paragraph. This starts about halfway through the paragraph with: “Here we take a step back...; A fundamental distinction...; We first consider...”. One version, or the other, should definitely be deleted.

In the “Strategies of interacting strains section,” I’m wondering if the conditions for a Prisoner’s dilemma have been fully demonstrated in *Dictyostelium*. If so, pointing readers to the relevant references would be appreciated. If not, perhaps a short explanation of why this is the expectation?

Also on the topic of the Prisoner’s dilemma: the statement that “cheating is always better than cooperating, irrespective of the other player’s strategy” is, of course, accurate. However, could it also be made clear that the Prisoner’s dilemma also requires the condition that mutual cooperation is more beneficial than mutual defection?

Has Simpson’s paradox been invoked to explain the success of cooperators in heterogeneous populations of *Dictyostelium*? The assumption of differential productivity of groups with higher a proportion of cooperators seems like it could be reasonable. This could provide an explanation for how cooperation can persist even without mechanisms for positive assortment.