Games of multicellularity

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H I G H L I G H T S

- Simple multicellular organisms arise by cells staying together after division.
- Staying together generates a particular population structure.
- We study deterministic evolutionary dynamics in that population structure.
- We derive conditions for natural selection to favor one strategy over another.
- Simple multicellularity promotes cooperation among cells.

A R T I C L E   I N F O

A B S T R A C T

Evolutionary game dynamics are often studied in the context of different population structures. Here we propose a new population structure that is inspired by simple multicellular life forms. In our model, cells reproduce but can stay together after reproduction. They reach complexes of a certain size, n, before producing single cells again. The cells within a complex derive payoff from an evolutionary game by interacting with each other. The reproductive rate of cells is proportional to their payoff. We consider all two-strategy games. We study deterministic evolutionary dynamics with mutations, and derive exact conditions for selection to favor one strategy over another. Our main result has the same symmetry as the well-known sigma condition, which has been proven for stochastic game dynamics and weak selection. For a maximum complex size of $n=2$ our result holds for any intensity of selection. For $n \geq 3$ it holds for weak selection. As specific examples we study the prisoner's dilemma and hawk-dove games. Our model advances theoretical work on multicellularity by allowing for frequency-dependent interactions within groups.

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1. Introduction

The emergence of multicellular life forms is an important step in the evolutionary history of life on earth (Grosberg and Strathmann, 2007; Bell and Mooers, 1997; Knoll, 2011; Bonner, 1998, 2009a, 2009b; Rokas, 2008; Carroll, 2001; Rainey, 2007; Michod, 1997, 1996; Michod and Roze, 2001; Hanschen et al., 2015). Multicellularity arose numerous times in prokaryotes, including in cyanobacteria, actinomycetes, and myxobacteria (Grosberg and Strathmann, 2007; Bell and Mooers, 1997; Schirrmeister et al., 2011). Complex multicellular organisms evolved in six eukaryotic groups: animals, plants, fungi as well as brown, green and red algae.

A comparison between simple multicellular and their relative unicellular organisms indicates multiple evolutionary transitions. These include increase in genetic complexity, cell differentiation, cell adhesion and cell-to-cell communication (Rokas, 2008). Division of labor, efficient dispersal, improved metabolic efficiency, and limiting interaction with non-cooperative individuals have been suggested as advantageous traits offered by multicellularity (Michod and Roze, 2001; Michod, 2007; Bonner, 1998; Pfeiffer et al., 2001; Pfeiffer and Bonhoeffer, 2003; Kirk, 2005; Mora Van Cauwelaert et al., 2015) (see also Grosberg and Strathmann, 2007 and references therein.)

Multicellular organisms are usually formed by single cells whose daughter cells stay together after division (Bonner, 1998; Koschwanez et al., 2011; Maliet et al., 2015; Rossetti et al., 2011). In contrast, multicellular organisms via aggregation are formed by separate cells coming together. Staying together and coming

together lead to very different evolutionary dynamics (Tarnita et al., 2013), and pose different challenges for the problem of evolution of cooperation (Nowak, 2006b; Nowak et al., 2010a; Olejarz and Nowak, 2014). The same two modes for the evolution of complexity are also observed in the context of eusociality among insects (Wilson, 1971; Gadagkar and Bonner, 1994; Gadagkar, 2001; Hunt, 2007). A common route to eusociality is daughters staying with their mothers (Nowak et al., 2010b), but there is also the coming together of different individuals in the formation of new colonies (Wilson, 1971; Gadagkar, 2001).

Here, we carry out a theoretical study of the dynamics underlying the evolution of multicellularity. Previous studies of such dynamics, both theoretical and experimental, have often been carried out under the assumption that within-group fitnesses derive from a simple, additive cooperative dilemma. For example, cells producing ATP from an external energy resource might do so with high yield but low rate, or with low yield but high rate (Pfeiffer et al., 2001). In the context of a group of cells trying to make use of an energy resource, the former behavior characterizes cooperators, and the latter defectors, because the benefits of a high rate of resource use accrue to the individual cell, while the costs of inefficient resource use accrue more broadly within the group (Pfeiffer and Bonhoeffer, 2003). If the costs accrue equally to all group members, the strategic problem within the group can be conceptualized as an additive public goods game. Many other models of the evolution of multicellularity can be conceptualized in the same way (Penn et al., 2012). For example, the aggregation of biofilms in *Pseudomonas* bacteria involves the production, costly to individual providers, of the components of an extracellular matrix and other substances (Davies and Geesey, 1995; Matsukawa and Greenberg, 2004; Diggle et al., 2006).

This assumption reduces the strategic conflicts within each multicellular unit to a very simple, frequency-independent form (Michod, 1999). Because a group's reproductive success is shared equally among its constituents (no matter their type), the only within-group conflict involves the constant cost to cooperation.

This is not realistic in many scenarios. In the example of ATP production described above, if the benefits of efficient resource use accrue more locally than to the whole group (for example, to pairs of interacting cells within the group), then the strategic interactions among cells are more complicated than a linear public goods game (Fig. 1). Without taking this into account (i.e., assuming that the benefits produced by cooperators are shared evenly among group members), it would seem that defectors should always be at an advantage within the group. But once the strategic complexity of local interactions is taken into account, then cooperators can have a within-group advantage if most of their interactions within the group are with fellow cooperators (Fig. 1).

Another example where strategic interaction within the group is important is when certain cell types are preferentially found in the reproductive propagules emitted by the group. Thus, in multicellular clusters of the yeast *Saccharomyces cerevisiae*, experimentally selected for by gravity-based methods, some cells (cooperators) undergo apoptosis to destabilise the multicellular unit and create new propagules; having apoptosed, they cannot themselves be in these propagules (Ratcliff et al., 2012; Pentz et al., 2015).

Another example involves cells that either aggressively or passively try to sequester resources for themselves; if the presence of many aggressive types involves a destructive cost to them, then the within-group conflict resembles a hawk-dove game. Because the within-group conflicts are frequency-independent in this example, their effects in the context of the evolution of multicellularity cannot be understood under a linear public goods conceptualization.
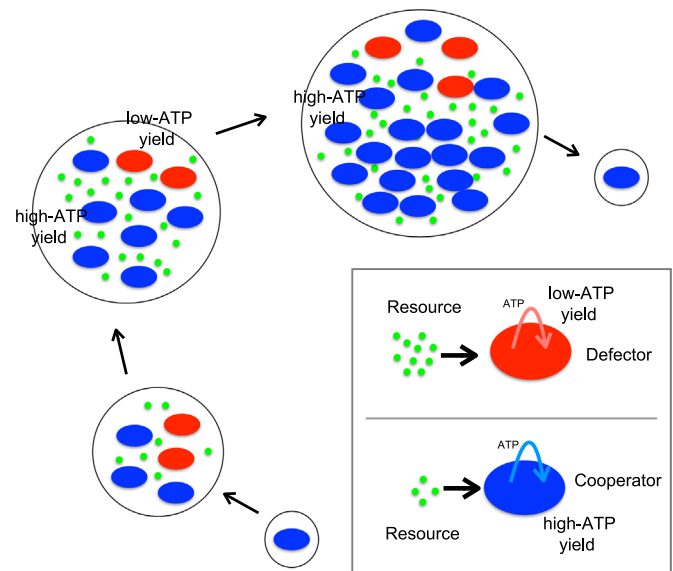
Fig. 1. Growth of a simple multicellular complex containing two competing metabolic phenotypes (Pfeiffer et al., 2001). The cooperator phenotype (blue) uses the limited food resource to produce ATP with high efficiency but low rate; the defector phenotype produces ATP with low efficiency but high rate. If the benefits of efficient resource use are shared equitably among the whole group, and the benefits of a high rate of resource use are enjoyed by individual cells, then the within-group conflict is a linear public goods game. In this case, the results of interactions within the group are frequency-independent, and defectors always grow as a proportion of the group. On the other hand, if the benefit of efficient resource use is shared more locally, then within-group strategic interactions are more complex. Now, cooperators can increase as a proportion of the group if they typically interact with cooperators, which can occur, for example, if a viscous spatial structure governs interactions (pictured). (For interpretation of the references to color in this figure caption, the reader is referred to the web version of this paper.)

To put it concisely, the evolution of multicellularity is often studied in a framework that does not adequately account for the *interactions* of cells within a group. In this paper, we place the evolution of multicellularity into an explicitly game-theoretic framework. Evolutionary game dynamics is the study of frequency dependent selection (Maynard Smith, 1982; Hofbauer and Sigmund, 1998; Nowak, 2006a). The success of a genotype (or phenotype or strategy) depends on the frequency of different genotypes in the population. Evolutionary game dynamics was initially studied in well-mixed and infinitely large populations using deterministic differential (Hofbauer and Sigmund, 1998; Maynard Smith, 1982; Weibull, 1997). More recently it has moved to finite population sizes using stochastic dynamics (Nowak, 2006a; Taylor et al., 2004; Traulsen and Hauert, 2009). Evolutionary games are also studied in structured populations (Nowak and May, 1992; Page et al., 2000; Hauert and Doebeli, 2004; Ohtsuki et al., 2006; Szabó et al., 2000; Tarnita et al., 2009a, 2009b; Hauert and Imhof, 2012; Langer et al., 2008; Antal et al., 2009b; Allen and Nowak, 2015; Cooney et al., 2016).

A game-theoretic approach to the evolution of multicellularity allows us to generalize the traditional framework by accounting for frequency-dependent competition within multicellular units.

The primary goal of our paper is to understand how the population structure of simple multicellularity affects the outcome of biological games. Previous studies have explored the evolutionary emergence of staying together (Tarnita et al., 2013) in the context of diffusible public goods (Olejarz and Nowak, 2014) and in stochastic dynamics (Ghang and Nowak, 2014). Here we study deterministic evolutionary dynamics in a population where staying together has already evolved.

In our model, single cells divide, but the two daughter cells can stay together after cell division. These cells may undergo further