Transitions in individuality

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SUMMARY

The evolution of multicellular organisms is the premier example of the integration of lower levels into a single, higher-level individual. Explaining the evolutionary transition from single cells to multicellular organisms is a major challenge for evolutionary theory. We provide an explicit two locus genetic framework for understanding this transition in terms of the increase of cooperation among cells and the regulation of conflict within the emerging organism. Heritability of fitness and individuality at the new level emerge as a result of the evolution of organismal functions that restrict the opportunity for conflict within and ensure cooperation among cells. Conflict leads, through the evolution of adaptations that reduce it, to greater individuality and harmony for the organism.

1. INTRODUCTION

The evolution of multicellular organisms is the premier example of the integration of lower evolutionary levels into a single, higher-level individual. Explaining the transition from single cells to multicellular organisms is a challenge for evolutionary theory. Darwin argued that natural selection requires heritable variations in fitness (Darwin 1859). Levels in the biological hierarchy—genes, chromosomes, cells, organisms, kin groups, groups—possess these properties to varying degrees according to which they may function as evolutionary individuals, or units of selection (Lewontin 1970; Hull 1981). Beginning with Buss (1987) and more recently Maynard Smith and Szathmary (1995; Szathmary & Maynard Smith 1995), attention has focused on understanding transitions between these different levels of individuality.

An organism may be viewed as a group of cooperating cells related by common descent. Selection among cells, below the level of the organism, could weaken this harmony and threaten the organism's individual integrity. Deleterious mutation leads to loss of cell and tissue function leading to the proliferation of non-cooperating cells. The evidence that within-organism mutation and selection among cells threatens the individual integrity of organisms has been discussed elsewhere (Michod 1996, 1997*a*, *b*). For the organism to develop and maintain its integrity and individuality in the face of this internal conflict, ways must have been found to regulate the selfish tendencies of cells and to promote their cooperative interactions. Otherwise the organism could not exist as a unit of selection.

Using multilevel population genetics models, Michod found that the levels of cooperation can be low in organisms that do not have a germ line or do not directly regulate the selfish tendencies of cells, even with the high levels of kinship among cells resulting from reproduction through a single cell zygote stage (Michod 1996, 1997*a*). This suggests that there is a problem in coping with within-organism variation and selection that the zygote stage (and the resulting kinship among cells) does not adequately cope with. Two-locus modifier theory was then used to show that this problem would select for modifiers restricting within-organism change (for example, modifiers that create a germ line or police the selfish tendencies of cells) once within-organism variation reached a critical level (Michod 1996, 1997*b*). Here we use two-locus modifier theory to show how and why heritability of fitness emerges during an evolutionary transition to a new, higher level of organization, the organism.

2. MODEL

Our model for the evolution of multicellular organisms involves the dynamic system of two loci in a haploid organism introduced previously (see tables 1 and 2, and equations 1–4 of Michod (1996), and appendix A of Michod (1997*a*)). These papers should be consulted for a full discussion of the underlying assumptions. Evolution at these two loci involves both within- and between-organism selection in a multilevel context. The first locus determines how cells interact; there are two alleles, cooperate and defect (C, D). The second locus modifies the parameters at the first locus that affect within-organism change; again there are two alleles, either a modifier (M) or no modifier (m). In the case of sex, the model life cycle assumes that gametes unite to form a zygote which develops into the adult form. In the case of asexual reproduction, a zygote is produced directly which then develops into the adult. Development involves cell division during which there is mutation and cellular selection. Within-organism change depends on both mutation and selection during development. Adult fitness (expected number of gametes or zygotes produced) depends upon both adult size and the level of cooperation among cells in the adult form.

Organismal development and fitness at the cell and organism levels are represented in terms of four parameters:

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Table 1. *Equilibria in two-locus modifier model*

(Equilibrium 3 is given in equation (3) of Michod (1996).)

equilibrium	description of equilibrium	interpretation
1	no cooperation, no modifier	single cells, no organism
2	no cooperation, modifier fixed	biologically uninteresting
3	polymorphic for cooperation and defection, no modifier	group of cooperating cells, no higher level functions
4	polymorphic for cooperation and defection, modifier fixed	multicellular organism, integrated group of cooperating cells with higher-level function mediating conflict within

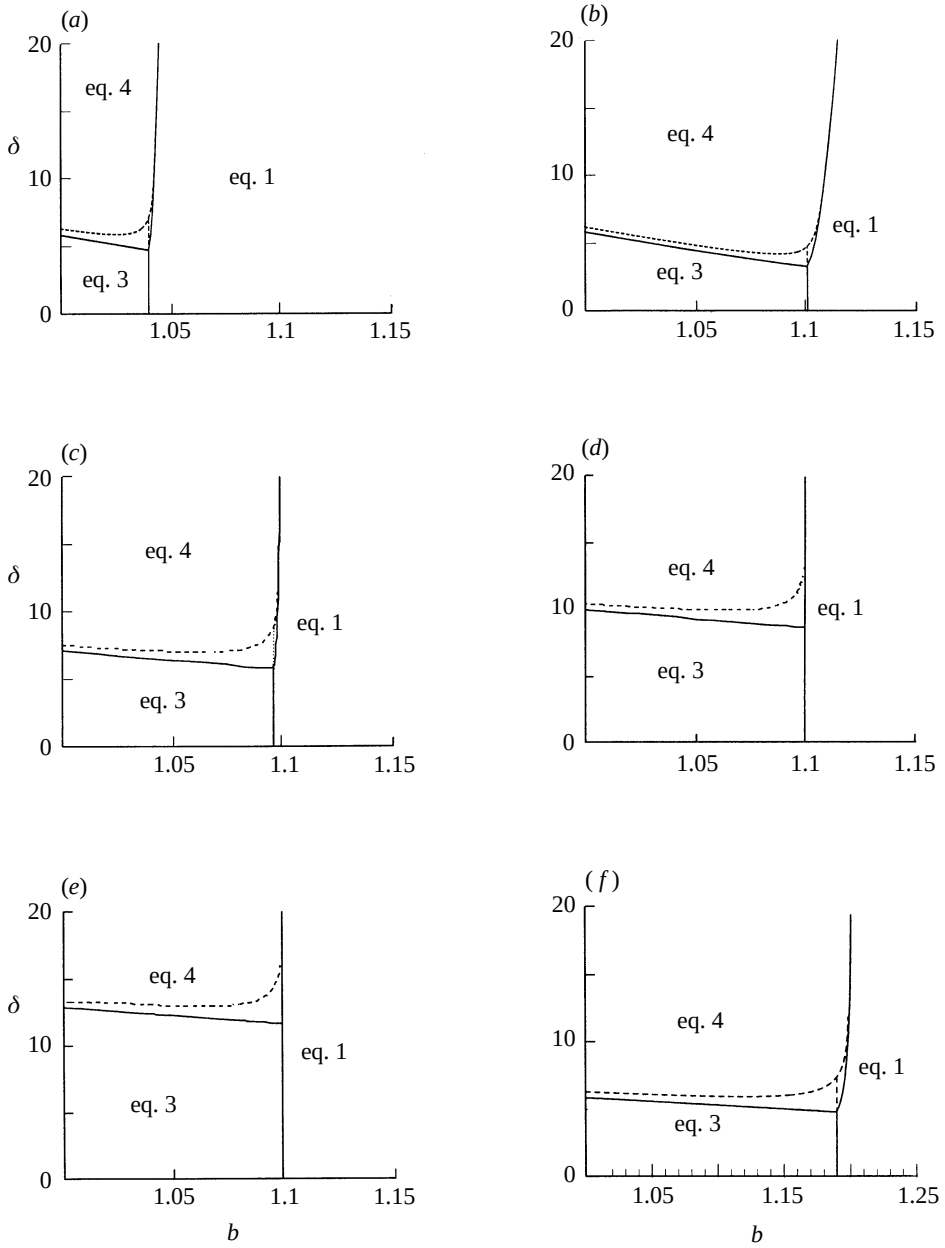

Figure 1. Stability of evolutionary equilibria. The modifier is assumed to decrease the development time for the germ line (when compared to the soma) by amount δ. Regions of stability for the different equilibria described in table 1 are given as a function of the advantage of defection, b, and δ, for different values of the mutation rate, μ, development time, t, and advantage of cooperation, β. Solid curves are for asexual reproduction and dashed curves for sexual reproduction assuming a recombination rate of $r = 0.25$ between the modifier and cooperate/defect locus. Cells sequestered in the germ line are not available for somatic function. The mutation rate is assumed to be the same in the soma and the germ line. See also figure 1 of Michod (1996) for more detailed treatment of the boundary between equilibrium 3 and 4. The parameter values in the panels are: (*a*) $\beta = 3$, $t = 40$, $\mu = 0.003$; (*b*) $\beta = 30$, $t = 40$, $\mu = 0.003$; (*c*) $\beta = 3$, $t = 20$, $\mu = 0.001$; (*d*) $\beta = 3$, $t = 20$, $\mu = 0.0001$; (*e*) $\beta = 3$, $t = 20$, $\mu = 0.00001$; (*f*) $\beta = 3$, $t = 10$, $\mu = 0.003$.

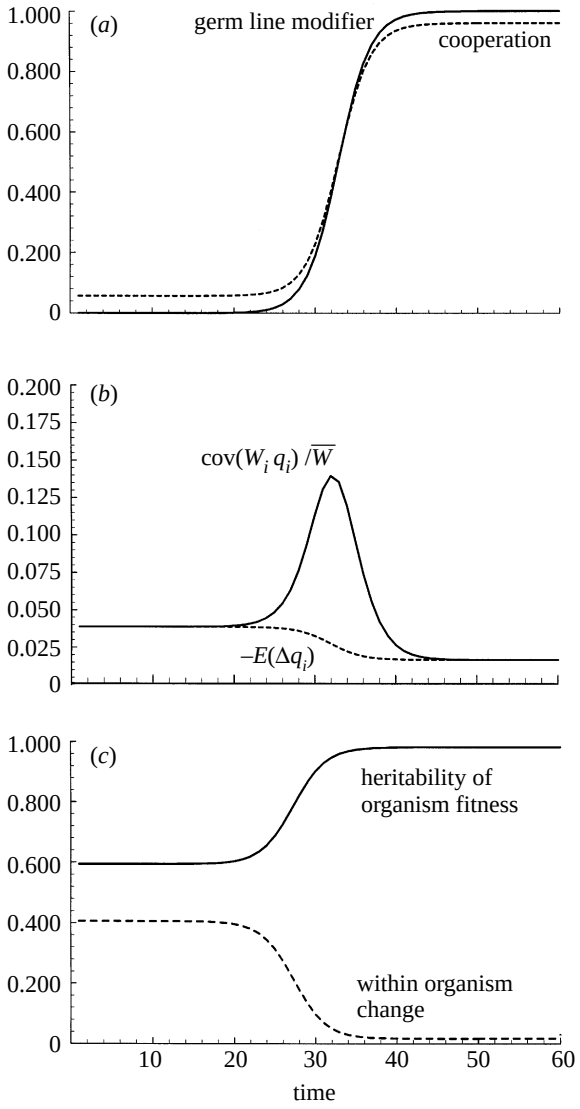

Figure 2. Components of an evolutionary transition. The figure considers the case of a transition between equilibrium 3 and 4 (see table 1) for a costly germ line modifier of within-organism change (discussed in Michod (1996)). The parameter values studied are $\mu = 0.003$, $\beta = 30$, $t = 40$, $\delta = 35$ and $b = 1.1$. The x-axis is time in organism generations. The y-axis in (a) is gene frequency; the y-axis in (b) and (c) correspond to the different curves as labelled. Modifiers increase and sweep through the population as shown by the solid curve in (a) leading to an increase in cooperativity among cells (dashed curve in (a)). As shown in (b), the underlying cause of the modifier's success during the transition is the fact that the heritable covariance in fitness for the organism, $\mathrm{cov}(W_i, q_i)/\bar{W}$ (solid curve), is greater than the average within-organism change, $E(\Delta q_i)$ (dashed curve). Gene frequency dynamics under multilevel selection can be represented by Price's (1970, 1972, 1995) equation $\Delta q = \mathrm{cov}(W_i, q_i)/\bar{W} + E(\Delta q_i)$, with $q_i, \Delta q_i$ being the frequency, and change in frequency, of the C (cooperate) gene within zygotes of type i, and the $q, \Delta q$ frequency, and change in frequency, of the C gene in total population ($i = 1, 2, 3, 4$ for CM, Cm, DM and Dm zygotes respectively). As occurs in (b), the two components of the Price equation must be equal in magnitude before (at equilibrium 3), and after the transition when the population returns to equilibrium (now at equilibrium 4; see Michod (1997*a*) for more analysis of the Price equation in the present context). As a consequence of the modifier's success, the level of cooperation in the population increases dramatically from nearly zero initially to greater than 0.90 after the transition (dashed curve in (a)), and the heritability of fitness at the emerging-organism level increases from approximately 0.6 to close to unity (solid curve in (c)), while the within-organism change in groups with cooperating cells drops from about 0.4 to near zero (dashed curve in (c)). Heritability of fitness is the regression of offspring fitness on fitness of parents. When the population is at equilibrium this definition gives a simple expression for heritability (using the notation of table 1 of Michod (1996) $h^2_W = k_{22}/k_2$ or $h^2_W = K_{11}/K_1$, at equilibrium 3 or 4, respectively. We always have $K_{11}/K_1 > k_{22}/k_2$, so the evolutionary transition always leads to an increase of heritability of fitness). During the transition between equilibrium 3 and 4 all four genotypes are present in the population. During this time it is not possible to simplify the heritability of fitness, however, the expression $h^2_W = \mathrm{cov}(W_P, W_O)/\mathrm{var}(W_P)$ can still be used, where W_P is the fitness of each parent and W_O is average fitness of the offspring.

β, b, μ and t. The parameter β is the benefit to organism fitness of cooperation among its component cells (this benefit is assumed to depend linearly on the frequency of cooperating cells in the organism's adult stage); b is the benefit to cells of their not cooperating (this benefit is assumed to be expressed in terms of the cell's increased rate of replication and is expressed relative to the rate of replication of cooperating cells so that $b > 1$, because cooperation is assumed to be costly at the cell level); μ is the rate of mutation per cell division during development (interpreted here as the genome-wide deleterious mutation rate at all loci leading to a loss of cell function); and t is the time available for development (development allows for within-organism change resulting from mutation, μ, and selection, b, at the cell level). In the case of germ line modifiers, the parameter δ is the decrease in development time for the cells in the germ line (germ line cells divide for fewer cell divisions than do somatic cells). In the case of sexual reproduction, r is the rate of recombination between the cooperate/defect locus and the modifier locus. The complexity of interaction among different cell types and tissue functions is assumed to be represented by two kinds of interactions: cooperate and not cooperate or defect. Heritability of fitness at the organism level is measured by the regression of offspring fitness on adult fitness.

3. EQUILIBRIA AND STABILITY

The transition to individuality involves two steps. First, the increase of cooperation within the group is accompanied by an increase in the level of within-group change as mutation leads to loss of cooperation among cells. Second, modifiers appear that regulate this within-group conflict. Only after the evolution of modifiers of within-group conflict, can we refer to the group of cooperating cells as an 'individual', as the group is now truly indivisible because it possesses higher-level functions that protect its integrity. Here we consider only germline modifiers that reduce the development time of the gamete producing cells by δ. Similar results have been obtained for self-policing modifiers proposed by Frank (1995; see Michod 1996 for results pertaining to policing modifiers).

The equilibria of the system correspond to different evolutionary outcomes. Two alleles at each of two loci give four possible equilibria described qualitatively in table 1 (although only three are of biological interest).

Regions of stability of the different equilibria for different parameter values are given in figure 1 in terms of the reduction of development time caused by the germline modifier, δ, and the advantage of defection at the cell level, b. The transition involving the increase of cooperation (equilibrium 1 to equilibrium 3 in figure 1) has been considered previously (Michod 1997*a*). This transition occurs for parameter values in the regions marked equilibrium 3 in figure 1; cooperation will not increase for parameter values in the equilibrium 1 region. The transition that interests us here involves the increase of modifiers of within-group change and this transition occurs after cooperation increases (equilibrium 3 to equilibrium 4 in figure 1). The conditions under which the population evolves from equilibrium 3 to 4 were first studied in Michod (1996). This transition occurs for parameter values in the equilibrium 4 regions in figure 1. In the next section, we study the components of this transition in terms of the emergence of fitness and the heritability of fitness at the new organism level.

A per cell division mutation rate of $\mu = 0.003$ is assumed in figure 1*a*,*b*,*f*, and in figure 2. We are interpreting this rate as a genome-wide mutation rate, even though only a single locus is explicitly considered in the model. The rate $\mu = 0.003$ is equal to the genome-wide mutation rate in modern DNA-based microbes (bacteria, yeast and a filamentous fungus; see Drake 1991). Because this rate holds for organisms as diverse as bacteria, yeast and a filamentous fungus, we think it is reasonable to assume that a similar rate likely held for those unicells that first formed multicellular groups. Nevertheless, smaller mutation rates may also result in the transition from equilibrium 3 to 4 as shown in figure 1*d*,*e*.

Sex affects the conditions for the transition by requiring slightly larger decreases in development time of the germ line (compare the dashed curves in figure 1 with the solid curves or see figure 2 of Michod 1996). With sex it also takes longer for the transition to occur (results not shown here for reasons of space), because the modifier increases by being more often associated with C alleles in gametes, and recombination breaks apart this association. Nevertheless, we do not see these quantitative differences as presenting any real barriers to the evolution of conflict modification in sexual progenitors.

The parameters have understandable effects on the regions of stability of the different equilibria described in table 1 (see figure 1). For example, as the benefit of cooperation to the group increases from $\beta = 3$ to $\beta = 30$, larger replication benefits of defection at the cell level are tolerated (figure 1*a*,*b*). Likewise, as the size of the organism decreases from $t = 40$ to $t = 20$ to t = 10 (shorter development times), larger benefits of defection at the cell level are tolerated, although the reduction in development time for the germ line to evolve is about the same (figure 1*a*,*c*,*f*). As the mutation rate decreases from 10^{-3} to 10^{-4} to 10^{-5}, it becomes more difficult for germ line modifiers to increase, in the sense that larger reductions in development time are required for there to be a transition from equilibrium 3 to 4 (figure 1*c*,*d*,*e*; see also figure 1 of Michod (1996)).

According to Bell (1985) differentiation between the germ and the soma in the Volvocales results from increasing colony size, with true germ soma differentiation occurring only when colonies reach about 10^3 cells as in the *Volvox* section *Merillosphaera*. Assuming no cell death, this colony size would require a development time of approximately $t = 10$ in our model (in reality, because of cell death, larger t with more risks of within-colony variation would be needed to achieve the same colony size). Although Bell interpreted the dependence of the evolution of the germ line on colony size as an outcome of reproductive specialization driven by resource and energy considerations, this relation is also explained by the need for regulation of within-colony change (see figure 1*f*).

4. EVOLUTIONARY TRANSITION

The transition from cells to multicellular organisms depends on the evolution of functions at the organism level that restrict within-organism change. In figure 2 we give the important components of an evolutionary transition: there is an increase in cooperation and a decrease in conflict among lower-level units (here cells); at the new emerging level (here the multicellular organism) there is an increase in heritability of fitness. These changes are driven by an increased heritable covariance of fitness at the new level which overpowers lower-level change and conflict. As the primary purpose of our model is heuristic, we consider the simplest reproductive and genetic system, that of haploid asexuality, and the parameter values in figure 2 were chosen mainly because they emphasize the different (but interrelated) components of the transition. For this reason, we begin before the transition with a situation in which cooperation can barely be maintained by the processes of group and kin selection (as indicated in figure 2*a* by the fact that cooperation starts out at a very low level initially at equilibrium 3). In this case, the groups of cooperating cells are clearly at risk of extinction before the modifier evolves. The development time of $t = 40$ is at the limit allowed by the other parameters ($\beta = 30$, $b = 1.1$, $\mu = 0.003$) all of which combine to give rise to significant within-organism change in cooperating groups before the transition (as indicated in figure 2*c*). Selection is intense: the 10% advantage of defection at the cell level ($b = 1.1$) requires large benefits of cooperation at the organism level for the linear model of organism fitness assumed here ($\beta = 30$). By assuming a reduction in development time for the germ line of $\delta = 35$, we are well within the equilibrium 4 region of figure 1*b*, so the transition occurs.

We emphasize that even if the initial level of within-organism change is smaller and selection is less intense (as would be the case for smaller β, b, μ and t), the modifier still increases and the transition occurs (assuming δ is in an appropriate region as shown for different parameter values in figure 1 and as discussed further in Michod 1996). For smaller initial levels of within-organism change, the components of the transition are smaller in magnitude than those in figure 2. However, the qualitative points made hold for all cases

we have studied, although the identified effects may be smaller.

Before the evolution of modifiers restricting within-organism change, the 'organism' is just a group of cooperating cells related by common descent from the zygote. Because of high kinship, heritability is significant at the group (organism) level $h^2_W \approx 0.67$, figure 2*c*), but this value is still low for asexual haploidy (heritability at the organism level should equal unity in the case of asexual organisms when there is no environmental variance). Low heritability of fitness at the new level resulting from significant within-organism change poses a threat to continued evolution of the organism. In the case considered in figure 2, development time, and hence organism size, could not increase without the evolution of conflict modifiers. Indeed, as already noted, the continued existence of cell groups at all is highly unlikely, because the cooperation allele is at such a low frequency and stochastic events would likely lead to its extinction. As the modifier begins increasing, the level of within-organism change drops (dashed curve, figure 2*c*) and the level of cooperation among cells increases dramatically (dashed curve, figure 2*a*) as does the heritability of organism fitness (solid curve, figure 2*c*).

In figure 2*b*, the two components of the Price covariance equation are plotted (Price 1970, 1972, 1995). These components partition the total change in gene frequency into heritable fitness effects at the organism level (solid line) and within-organism change (dashed line). In the model studied here, within-organism change is always negative, because defecting cells replicate faster than cooperating cells and there is no back mutation from defection to cooperation. At equilibrium, before and after the transition, the two components of the Price equation must equal one another in magnitude, or else the population could not be in equilibrium (this is shown in figure 2*b*). However, during the transition we see that the covariance of fitness with genotype at the emerging organism level (solid curve, figure 2*b*) is greater than the average change at the cell level (dashed curve, figure 2*b*). This greater heritable covariance in fitness at the higher level forces the modifier into the population.

According to Buss (1987) the individual integrity of complex animal organisms is made possible by the germ line, the sequestered cell lineage set aside early in development for production of gametes. By sequestering a group of cells early in development the opportunity for variation and selection is limited. Maynard Smith and Szathmary disagree with Buss's adaptive explanation of the germ line and argue that kinship among cells in an organism is sufficient to regulate the selfish tendencies of cells (Maynard Smith & Szathmary 1995). By often reproducing through a single cell stage (the zygote), organisms ensure close genetic relatedness among their component cells.

According to the results given here, both kinship and conflict regulation are important to evolutionary transitions. Kinship is necessary for cooperation to evolve in the first place and to generate finite heritability for the emerging organism. Nevertheless, there remains significant within-organism change even in organisms that reproduce through a zygote stage and this variation selects for higher level functions to reduce conflict, such as a germ line or self policing, thereby ensuring high heritability of fitness for the organism.

What happens during an evolutionary transition to a new higher level unit of individuality, in this case the multicellular organism? The evolution of cooperation among related cells sets the stage for the evolution of defection as selfish mutants increase within the proto-organism. The evolution of modifiers restricting within-organism change are the first higher level functions at the emerging organism level. Individuality requires more than just cooperation among a group of related cells, it also depends on the emergence of higher level functions that restrict the opportunity for conflict within and ensure the continued cooperation of the lower-level units. Conflict leads, through the evolution of adaptations that reduce it, to greater individuality and harmony for the organism.

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