# Origins of Multicellularity

Presentation for Seminar 19548: Major Evolutionary Trasitions

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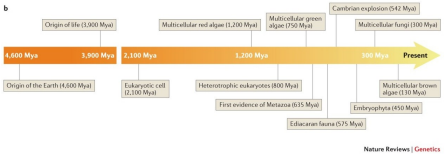
# Multicellularity as Definition

Evolution has had at least 20 separate attempts at forming multicellular organisms.

Plants, Animals and Fungi



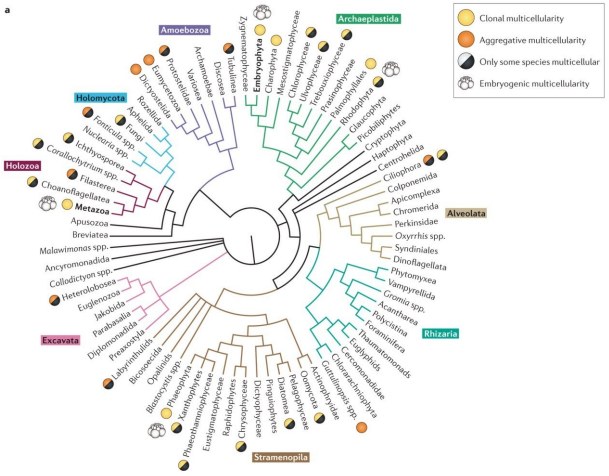




Figure: Phylogenetic tree of all life types. Shows the clades of multicellular organisms, Sebé-Pedrós et al. (2017)

# What is multicellularity?

Two ways to make a simple multicellular entity out of single cells:

- a single cell divides and its offspring stick together
- several solitary cells aggregate to form a colony

Division and adhesion is characteristic of multicellular forms of aquatic origin, whereas aggregation is typical in terrestrially derived colonies.

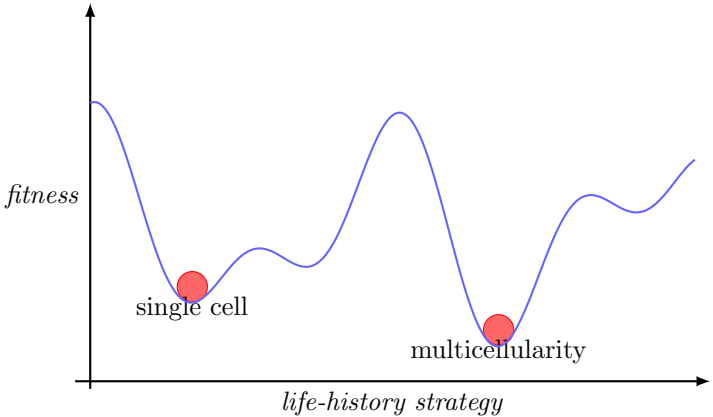
# What is multicellularity?

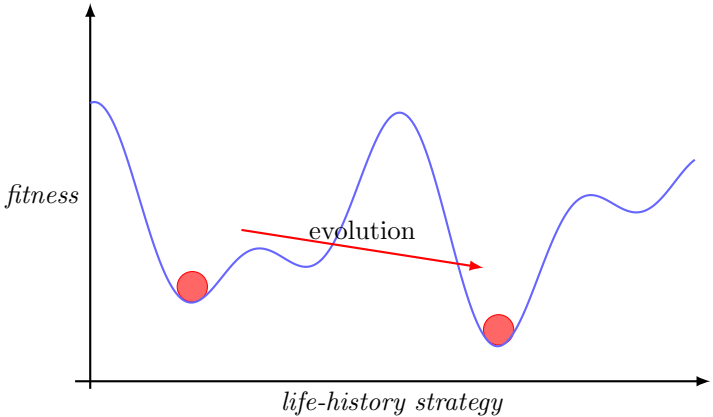
An overall coordination of at least some key function is a necessary and sufficient condition for a colony of cells to qualify as multicellular.
It is the presence of developmentally differentiated cell types in a colony that makes it truly multicellular. Szathmáry and Wolpert (2003)

# Why is multicellularity possible?

> “If stars did not exist, it would be easy to prove that this is what we expect.”
>
> —— Geoffrey Burbidge, Director, Kitt Peak National Observatory

So is multicellularity (~~as well as ecological system~~).


fitness
single cell
multicellularity
life-history strategy


fitness
evolution
life-history strategy

## What makes the transition from single cells to multicellularity?

We focus on two perspective of the question:

- How could the transition happened: the biological basis of multicellularity
- Why is it happened: the advantage of multicellularity

# The Biological Basis of Multicellularity

Although the question of how animals evolved from their protozoan ancestors has at times seemed intractable, developments in phylogenetics and comparative genomics have paved the way for new insights.

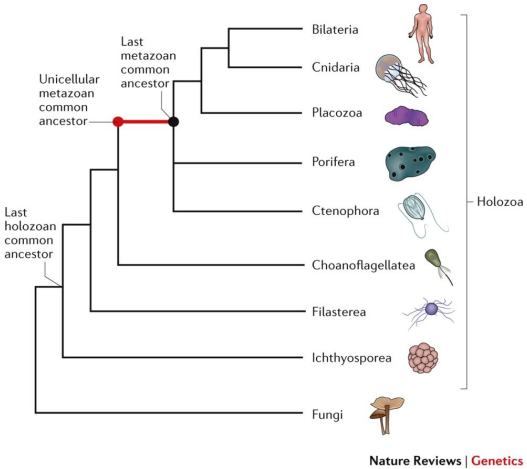



Figure: Phylogenetics of animal. There are three independent unicellular holozoan lineages that are closely related to animals: namely, *Ichthyosporea*, *Filasterea* and *Choanoflagellatea*.

The integrity of multicellular organisms requires **stable adhesion** between neighboring cells, coordination of cellular behavior (e.g., the cell cycle and cell migration) through **cell-cell signaling**, and fine-scale **regulation of gene activity** to control the identity and spatial distribution of **differentiated cells** (King (2004)).

- cellular adhesion between animal cells may derive from protein families previously used by heterotrophic flagellates to recognize and capture select bacterial and protozoan prey.
- the ability of protozoa to monitor and respond to cues from their changing environments means that metazoan signal transduction has many potential antecedents from the life histories of free-living protozoa.
- unicellular eukaryotes are also capable of differentiation; in their case, differentiation occurs temporally rather than spatially, often in response to environmental cues or biotic signals.
- Richter et al. (2018)

# Advantages of Multicellularity

Fitness of A New Kind of Life-Cycle

- trade-off between cell division and motility
  motility and mitosis compete for the same cellular machinery.
  Initially, the division of labor between cell fission and motility may have been temporal, with colonies composed of multipotent cells each of which took turns either dividing or providing flagellar activity. For each cell in a colony, a benefit of cooperation would be the maintenance of motility during cell division.
- cooperation and large size
  With the origin of predation, and particularly the ability to engulf prey through phagocytosis, came selection for multicellularity among normally unicellular prey.
  - The first heterotrophs probably targeted small bacteria and particles of detritus, with the ability to ingest larger cells (e.g., algae and other heterotrophic protozoa) evolving later;
  - By assembling as a multicelled organism, prey could escape the upper limits of a predator's capacity to ingest foreign objects (Herron et al. (2019)).

The fitness of any evolutionary unit can be understood in terms of its two basic components: fecundity (reproduction) and viability (survival) (On the transfer of fitness from the cell to the multicellular organism) (Michod (2005)).

Populations can improve survival in response to the stress by evolving multicellularity or cell differentiation—or both; however, these responses have associated costs when the stress is absent.

# A Simple Model of Multicellularity

Isaksson et al. (2025) studied the evolutionary trajectory from unicellularity toward an early multicellular life cycle with differentiation in a selective environment where populations experience repeated bouts of abiotic stress.

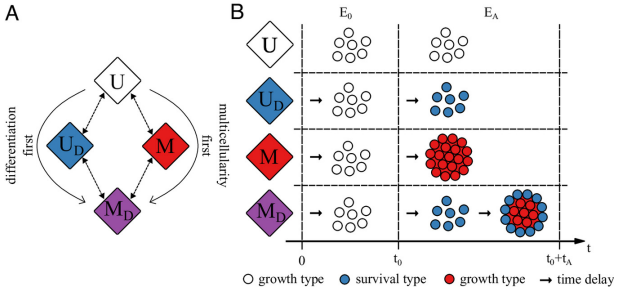



Figure: A. For possible life circles; B. Populations undergo growth in $E_0$ (where population grows exponentially according to a rate $b$) and survival in $E_A$ (causes the population to die at a rate $d$)

fitness of $\mathbf{U}$ and $\mathbf{U_D}$:

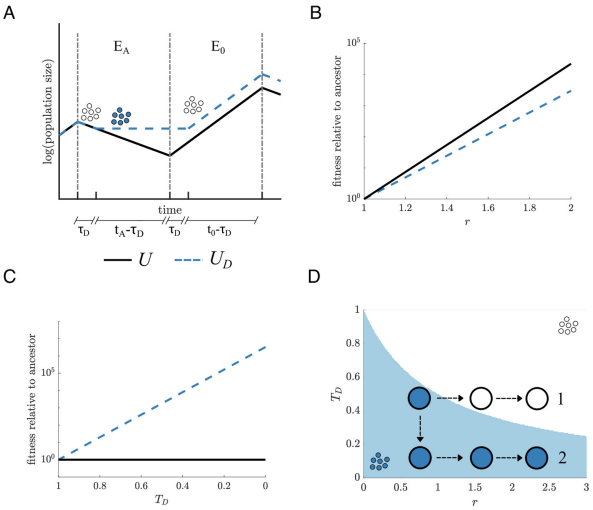
$$U = e^{bt_0 - dt_A} \quad (1)$$

$$U_D = e^{b(t_0 - \tau_D) - d\tau_D} \quad (2)$$

when $\mathbf{U_D} > \mathbf{U}$, we have:

$$T_D < \frac{1}{1+r} \quad (3)$$

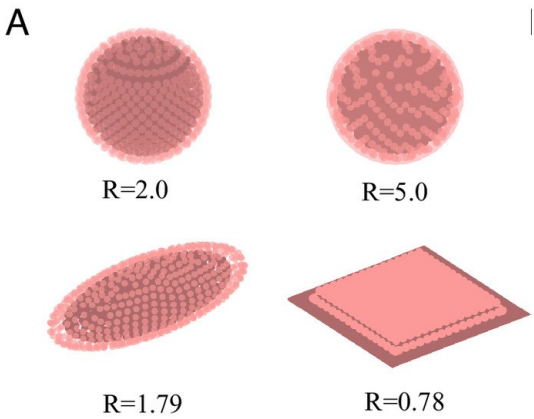
where $T_D = \frac{\tau_D}{t_A}$, $r = \frac{b}{d}$.



## fitness of **M**:

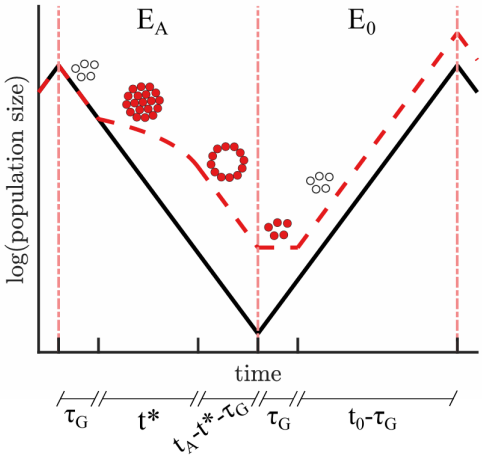
The fitness advantage of **M** depends on how much protection is afforded to inner cells, which in turn depends on the structure of the group as well as the length of time spent in the stressful ($\mathbf{E_A}$) environment.
Introduced a parameter **R** to characteristic the structure,

$$R = \frac{\text{interior cells}}{\text{exterior cells}}$$



## fitness of **M**:

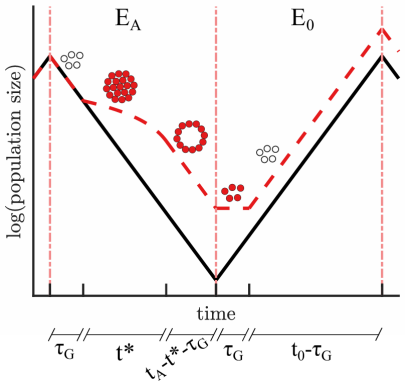
As the outer cells of groups die and get replaced, the inner pool of cells will eventually be emptied. This happens at some time $t^*$ in $\mathbf{E_A}$, and after this, the surface structure starts to collapse.
We mainly focus on the condition where $t_A - \tau_G < t^*$ ($\mathbf{M_2}$). (because of the cost of dissociation)



fitness of **M**:

$$\begin{cases} M_1 = e^{b_G} g_1(t_A - \tau_G) & t_A - \tau_G < t^* \\ M_2 = e^{b_G} g_1(t^*) g_2(t_A - \tau_G - t^*) & t_A - \tau_G < t^* \end{cases}$$

where $e^{b_G} = e^{b(t_0 - \tau_G) - d\tau_G}$.
The form of $g_2$ is simple:
$g_2(t_A - \tau_G - t^*) = e^{-d(t_A - \tau_G - t^*)}$



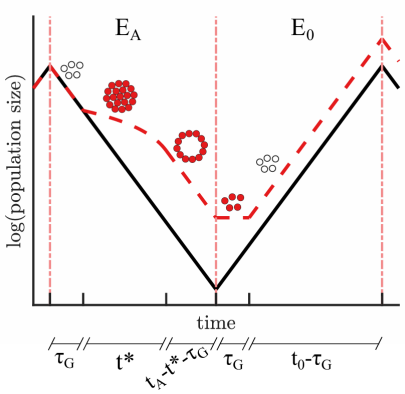
# fitness of $\mathbf{M}$:$g_1$

$$\begin{cases} \frac{\mathrm{d}M_{1,o}}{\mathrm{t}} = 0 \\ \frac{\mathrm{d}M_{1,i}}{\mathrm{t}} = -dM_{1,o}(t) \end{cases}$$

$$\begin{aligned} g_1(t) &= \frac{(1-dt)M_{1,o} + M_{1,i}}{M_{1,i} + M_{1,o}} \\ &= \frac{(1-dt) + R}{1+R} \end{aligned}$$

Also,

$$M_{1,i}(t) = 0 \Rightarrow t^* = \frac{R}{d}$$

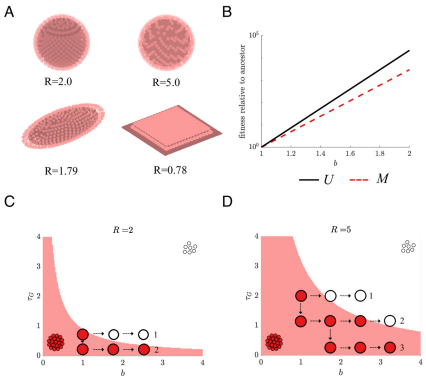


fitness of **M**:

$$\begin{cases} M_1 = \frac{(1-d(t_A-\tau_G))+R}{1+R} e^{b(t_0-\tau_G)-d\tau_G} & t_A - \tau_G < t^* \\ M_2 = \frac{e^R}{1+R} e^{b(t_0-\tau_G)-dt_A} & t_A - \tau_G < t^* \end{cases} \tag{4}$$

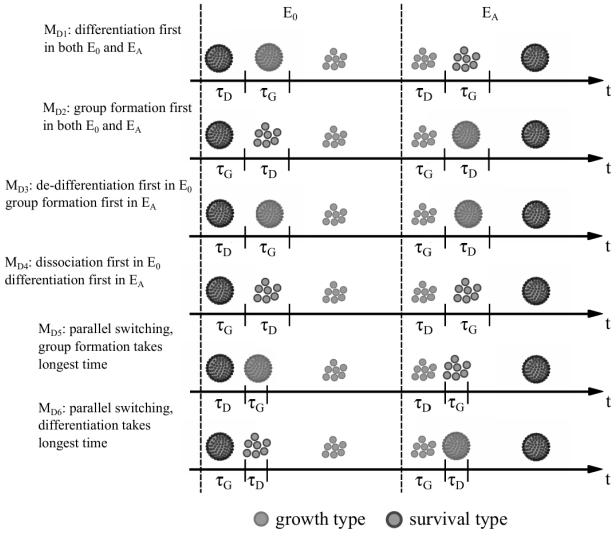
where $R$ is is the ratio of the number of interior cells to exterior cells.
when $\mathbf{M_2} > \mathbf{U}$, we have:

$$b\tau_G < R - \ln(1+R) \tag{5}$$

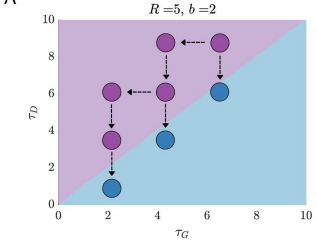


When it comes to $\mathbf{M_D}$, the sequence of differentiation and aggregation is important. As a result, there is more than one case of it. Taking case 4 as an example:

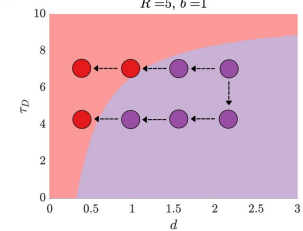
$$M_{D4} = \frac{Re^{b\tau_D} + 1}{1 + R} e^{b(t_0 - \tau_G - \tau_D) - d\tau_D} \tag{6}$$



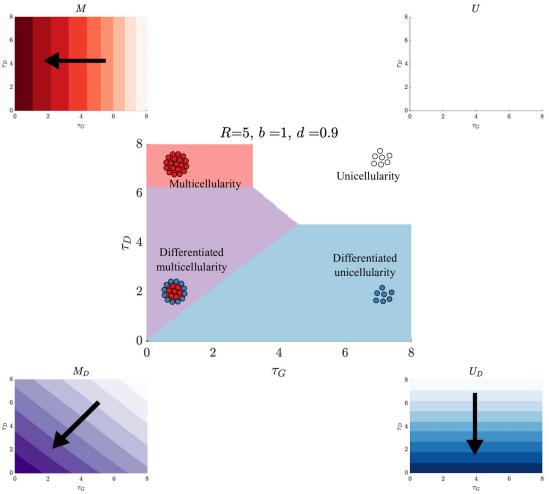
A


$R=5,\ b=2$
$\tau_D$
$\tau_G$

B


$R=5,\ b=1$
$\tau_D$
$d$

C


$M$
$U$
$R=5,\ b=1,\ d=0.9$
Multicellularity
Unicellularity
Differentiated multicellularity
Differentiated unicellularity
$\tau_D$
$\tau_G$
$M_D$
$U_D$

To map possible adaptive trajectories in the higher dimensional parameter space, Isaksson et al. (2025) performed evolutionary simulations that allow mutations in the defining traits of the life cycles (Evolutionary Simulations).

- Mutations in: the birth and death rates ($b$, $d$), the time delay for differentiation ($\tau_d$), and the time delay for group formation/dissociation ($\tau_g$).
- allow mutations to alter whether populations differentiate or form multicellular groups.

Compute the fitness effect on the population and assume it fixes based on the extent to which it increases relative fitness (Evolutionary Simulations).

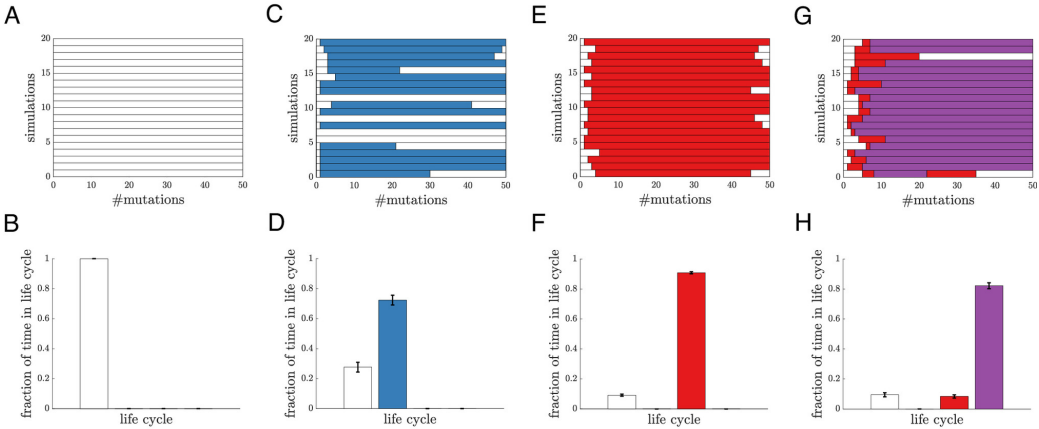



Figure: Above: A plot shows 20 sample evolutionary simulations. All mutations are adaptive and a mutation is accepted with a probability based on its relative fitness; Below: A histogram shows the fraction of time spent in each life cycle.

# A possible improvement

In the Isaksson et al. (2025) model, the cost of both differentiation and aggregation is determined by the time required for these processes.
We introduce an generalized constraint: total energy availability.
Energy is consumed during the following biological processes: growth, defense/resistance, differentiation (particularly toward more resistant traits), and maintaining cell associations. As a result:

$$E_0 = E_b + E_d + E_D + E_G \tag{7}$$

# Relate mathematical constraints to parameters

$$\begin{cases} b = k_1 \cdot \mathbf{E_b} \\ d_0 = k_2 \cdot (1 - \mathbf{E_d}) \\ d_D = f(\mathbf{E_D}) \\ d = d_0 \cdot d_D \\ R = k_4 \cdot \mathbf{E_g} \end{cases}$$

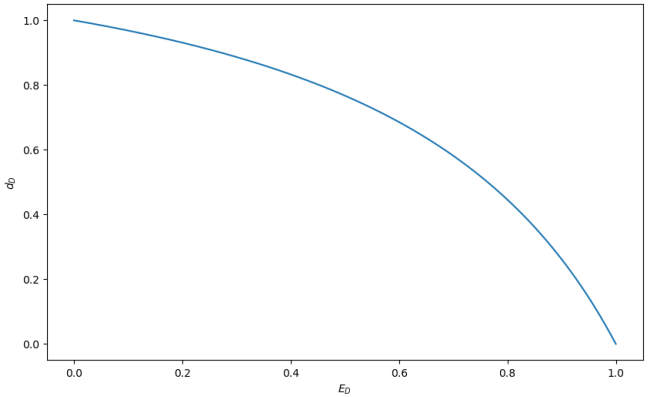



Figure: The diagram of $f(E_D)$

Then the fitness of each strategy is given as following (without the time cost ($\tau$)):

$$\begin{cases} U = e^{bt_0 - d_0 t_A} \\ U_D = e^{bt_0 - dt_A} \\ M = \begin{cases} \frac{(1-d_0 t_A)+R}{1+R} e^{bt_0} & t_A < R/d \\ \frac{e^R}{1+R} e^{bt_0 - d_0 t_A} & t_A > R/d \end{cases} \\ M_{D4} = \begin{cases} \frac{(1-dt_A)+R}{1+R} e^{bt_0} & t_A < R/d \\ \frac{e^R}{1+R} e^{bt_0 - dt_A} & t_A > R/d \end{cases} \end{cases}$$

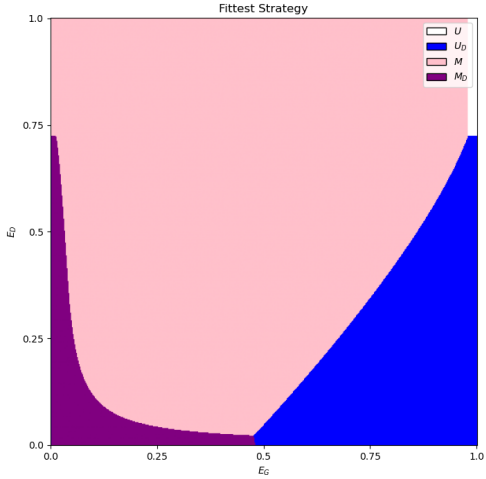



Figure: $t_0 = 1, t_A = 1$

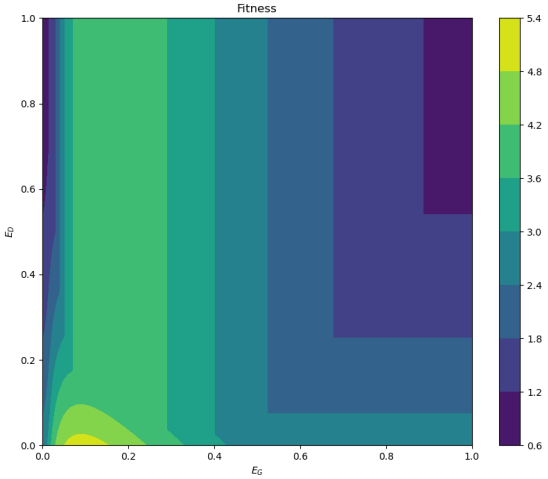



Figure: fitness of the left phase diagram

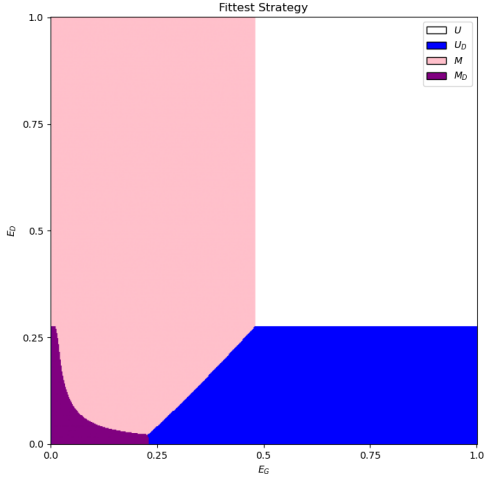



Figure: $t_0 = 1, t_A = 2$

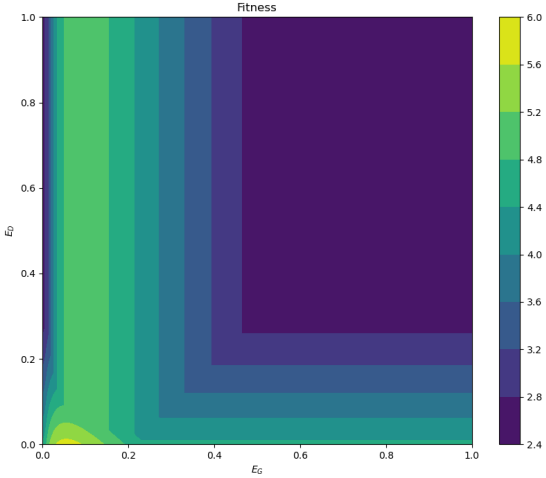



Figure: fitness of the left phase diagram

# Selective Advantages of Multicellularity:

Two dimensions: individual and cells
The division of labor lead to the problem that fitness of some cells decrease.
Considering the classic cooperation model, it is always easy for cheaters to invade a interacting group, which lead to the collapse of group. Mutations will even strengthen the tendency.

Table: An illustration of a cooperation game

| interest | N | C |
|---|---|---|
| N | 1 | 5 |
| C | 0.5 | 0.1 |

## The advantages of egg

It is advantageous for the unit of reproduction (the propagule) to be as small as possible (that is, a single cell), as the uniformity thus created will reduce the likelihood of conflict between cells.
Development from a single cell — an egg — may have been essential for multicellular organisms to have evolved, as they have, into such an enormous variety of different forms.
Wolpert and Szathmáry (2002)

# Why Eukaryotes

Clonal Multicellularity Reduces $N_e$.
Prokaryotes and Eukaryotes Show Opposite Genomic Responses to Low $N_e$.

Szathmáry (2024)
In nascent multicellular eukaryotes, the lowered $N_e$ imposed by reproductive bottlenecks would have driven expansions of genomic content. This drift-induced increase in genetic material could provide fodder for evolutionary innovation through emergence of new genes, regulatory elements, and splice variants.

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