MARGULIS' THEORY ON DIVISION OF LABOUR IN CELLS REVISITED

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ABSTRACT

Division of labour is a marked feature of multicellular organisms. Margulis proposed that the ancestors of metazoans had only one microtubule organizing center (MTOC), so they could not move and divide simultaneously. Selection for simultaneous movement and cell division had driven the division of labour between cells. However, no evidence or explanation for this assumption was provided. Why could the unicellular ancestors not have multiple MTOCs? The gain and loss of three possible strategies are discussed. It was found that the advantage of one or two MTOC per cell is environment-dependent. Unicellular organisms with only one MTOC per cell are favored only in resource-limited environments without strong predatory pressure. If division of labour occurring in a bicellular organism just makes simultaneous movement and cell division possible, the possibility of its fixation by natural selection is very low because a somatic cell performing the function of an MTOC is obviously wasting resources. Evolutionary biologists should search for other selective forces for division of labour in cells.

1. INTRODUCTION

The origin of multicellular organisms is one of the major transitions in evolution (Maynard Smith and Szathmáry, 1995). As division of labour in cells is the marked feature of multicellular organisms, its origin and evolution are very important in the origin and evolution of multicellular organisms.

Margulis (1981) proposed a hypothesis on division of labour between cells in the origin of metazoans. Later, Buss (1987) enlightened it in detail. Mitotic spindles, cilia and flagella are all depending on the microtubule organizing center (MTOC). If unicellular organisms have only one MTOC per cell, they can either move or divide. However, they cannot do both simultaneously. There are some ways to meet the need for simultaneous movement and cell division, e.g. possessing multiple MTOCs in one cell (Buss, 1987). Margulis (1981) and Buss (1987) believe that some protist mutants, including the ancestors of metazoans, had never resolved the problem. Cilia or flagella have to be resorbed and redifferentiated as spindles before the initiation of mitosis. Ciliation reappears only after the spindle has disappeared after cell division. Both Margulis and Buss argued that selection would favor a division of labour between two

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unseparated sister cells, with one using its MTOC to move and the other using it to divide. This interesting idea is cited by biologists (e.g. Jablonka and Lamb, 1995) in their publications.

As an alternative to the Margulis-Buss theory, Bell (1989) supposed that the ancestor of metazoans had two types of MTOCs, one of which preferentially functions as the basal bodies of cilia or flagella while the other functions in the spindle. The former MTOCs would be present in fully differentiated somatic cells of metazoans, and the latter would be present in the germ line. That is, the possession of a single MTOC was viewed as the consequence of being a metazoan, rather than a constraint on metazoan evolution.

The theory of Margulis depends on the assumption that the unicellular ancestors of metazoans could not have more than one MTOC per cell. Why? Neither Margulis nor Buss provided further explanation or support for their assumption. There were two possible reasons. The frequency of the appearance of those mutants with more than one MTOC per cell was extremely low. So their appearance was very unlikely, or even impossible. The second was that although they appeared at a high frequency, they were not favored by natural selection.

From the fact that many other protists have more than one MTOC per cell (Buss, 1987), it can be seen that the presence of multiple MTOCs in one cell is not impossible and there were at least no strong negative forces to eliminate them. Selective forces for simultaneous movement and cell division favors both mutants producing multiple MTOCs and mutants with the division of labour proposed by Margulis and Buss. For the division of labour to occur, at least two steps are required: The daughter cells do not separate after cell division; they should differentiate and cooperate. The frequency for the division of labour to occur seems not to be higher than producing multiple MTOCs in one cell.

We cannot agree with the interesting ideas of Margulis and Buss, if no selective forces are found favoring a single MTOC per cell in combination with the division of labour between unseparated daughter cells.

2. ONE OR TWO MTOCS IN UNICELLULAR ORGANISMS

Suppose two protist mutants (*A* and *B*) exist that are genetically and biologically identical except the number of MTOC per cell. Mutant *A* with just one MTOC per cell performs the functions of movement and cell division at different times, while mutant *B* with two MTOCs in one cell can move and divide simultaneously.

To finish cell division, a certain amount of energy and materials are needed, e.g. synthesizing DNA and various proteins. The cells cannot divide before accumulating enough materials and energy. The cells of mutant *A* cannot move and divide simultaneously, so they cannot search for food in the *M* (mitotic) phase of cell cycle. By contrast, the cells of mutants *B* can search for food at all times during cell cycle: $M + S + G$, where *S* and *G* are the DNA synthesis phase and the gap phase, respectively. Provided that there is no difference in the efficiency in searching for food between the cells of mutants *A* and *B*, $S + G$ and $M + S + G$ may be respectively designated to the rates of the cells of mutant *A* and *B* in accumulating materials and energy.

The cells of mutant *B* can accumulate more materials and energy in a certain time period which corresponds with one cell cycle. But they need more materials and energy to synthesize more tubulin which is needed for building the additional MTOCs. If we assume certain amounts (*E*) of materials and energy are needed for a cell of

mutant *A* to divide once, then a little more materials and energy, $(1 + r)E$, are needed for the cells of mutant *B*.

At equilibrium, where mutant *A* and *B* coexist, one or two MTOCs does not change the relative growth rate,

$$(S + G)/E = (M + S + G)/(1 + r)E \quad (1)$$

Then, $(1 + r)(S + G) = M + S + G$. So,

$$G = M/r - S \quad (2)$$

It is obvious that preparation is easy for organisms growing in optimal environments, but difficult for organisms growing in adverse environments. Many workers have examined the cell cycle of various cells under different growing conditions. It was found that the cell cycle length can be altered by changing the richness of necessary nutrients. The variation is mainly due to variation in the length of gap phase (G_1 or $G_1 + G_2$), with the duration of *S* (DNA synthetic) phase and *M* (mitotic) phase being relatively constant (Clowes, 1965; Barford and Hall, 1976; Cornell and Horwitz, 1980; Guiguet *et al*., 1984 and references therein). Sometimes, the G_1 is too short to be detectable (Nygaard *et al*., 1960; Robbins and Scharff, 1967). While in some other cases, G_1 phase can be extremely elongated. Even the quiescent G_0 state was viewed to be a greatly extended G_1 phase by some authors (Pardee *et al*., 1978 and references therein). So it can be assumed that *M* and *S* are constant.

In an optimal environment, $G < M/r - S$. So, $(S + G)/E < (M + S + G)/(1 + r)E$, the cells of mutant *B* would grow better than those of mutant *A*.

In an adverse environment, $G > M/r - S$. So, $(S + G)/E > (M + S + G)/(1 + r)E$, the cells of mutant *A* would grow better than those of mutant *B*.

These results are fairly easy to see intuitively. The cells with just one MTOC face the problem of unable-to-move while dividing. The frequency of the problem depends on the relative length of mitotic phase to the whole cell cycle, i.e. the rate of cell reproduction. If resource supply is enough for the cells to divide continuously, the problem is critical. On the contrary, the problem is not so serious for the cells growing in adverse environments. That is, the necessity of an MTOC specified for cell division depends on the rate of cell reproduction. As the cells growing in adverse environments are expected to have a long cell cycle, possessing an additional MTOC is apparently wasting materials and energy.

We prefer a sentence from a book of Nesse and Williams (1994): "Like any engineer, evolution must constantly compromise". If the cells take the advantage of simultaneous movement and division, they must waste some materials and energy, more or less depending on the quality of the environment. To save resources, they cannot move while dividing. They must compromise. Only starved cells are more likely to have just one MTOC per cell.

Other negative effects of just one MTOC per cell may change the point of equilibrium quantitatively, but not qualitatively. Besides being unable to search for food, cells possessing only one MTOC have an increase in the risk of being preyed upon. The danger (*D*) of being preyed upon is apparently correlated to the duration of the mitotic phase: $D = dM$, where *d* is the risk coefficient. If we integrate the risk into the above model, equation (1) changes into:

$$(S + G)/E - D = (M + S + G)/(1 + r)E.$$

That is $(S + G)/E - dM = (M + S + G)/(1 + r)E$, Then,

$$G = (1 + 1/r)EMd + M/r - S \quad (3)$$

It is not difficult to see that $(1 + 1/r)EM$ is always above zero. Predatory selection thus pushes the equilibrium point to more adverse environments.

Just roughly imagine the value of r and the normal value of cell cycle (M, S and G), we can obtain the following conclusion from the equilibrium point: Unicellular organisms with just one MTOC per cell should have existed in very special habitat, if they had ever existed.

3. SEGREGATION OF MOVEMENT AND CELL DIVISION

If division of labour occurred between two unseparated sister cells, with one using its MTOC to move and the other using it to divide, the somatic cells of this bicellular organism would fulfill the function of one MTOC. The materials and energy required to reproduce are doubled, r in the above equations should be replaced by the value of one. The point of equilibrium in resource-limited environments changes into:

$$G = M - S \tag{4}$$

And that with predatory pressure changes into:

$$G = 2EMd + M - S \tag{5}$$

As the M phase is usually shorter than the S phase (Darnell *et al.*, 1990), such division of labour in bicellular organisms becomes possible only when predatory selection and abundant resources exist. But, in contrast with the cells of mutant B, it is obviously wasting materials and energy.

Although, division of labour may result in other advantages, like protecting DNA (Niu and Chen, 1997), no evidence suggests that the costs can be outweighed. Many biologists believe that division of labour increases the efficiency of relevant functions (Maynard Smith and Szathmáry, 1995; Szathmáry and Maynard Smith, 1995). We confuted that opinion in our previous paper (Niu and Chen, 1997). If division of labour means simply to regroup the functions, any advantage should be accompanied by some disadvantages. Many biological processes are mutually incompatible when they are run at a high level (Gerhart and Kirschner, 1997, Ch. 6). Although division of labour, by itself, does not necessarily result in any net advantage, it opens the way to run those processes in the same individual by departmentalization of different functions. This does not mean that the proposition of Margulis and Buss cannot take place. Schuster (1996) pointed out that the disadvantage will be small when resources are cheap. Meanwhile random drift may also contribute to the maintenance of the division of labour. But for fixation of the division of labour, another hypothesis is necessary.

We assume that the movement of protist cells is also one of such processes as proposed by Gerhart and Kirschner (1997), it will be incompatible with other cellular processes when it is run at a high level. The power of a cilium or flagellum in unicellular organisms is thus the compromise between the reduction of intracellular conflict and escape from predators. The segregation of cell movement and cell division in different cells will release the limit for the power of cilia and flagella to increase. When predatory pressure increases, a more powerful cilium or flagellum is required and bicellular mutants with the division of labour will be fixed in the population.

The cost of a somatic cell to perform the function of a flagellum can be reduced by reducing the size of the somatic cells like that of *Volvox* (Kirk, 1998).

4. DISCUSSION AND CONCLUSION

Our results show that such unicellular organisms should have existed in a very special habitat, if they have ever existed. So the difficulty of Margulis' theory on division of labour in cells lies in its premise that the ancestor of metazoans had only one MTOC per cell. Even if such organisms have ever existed, they had two ways to solve the problem of simultaneous movement and cell division: Possessing multiple MTOCs per cell, or multicellularity and division of labour. In resource-limited environments, division of labour would never be favored. Even if the resources are abundant, strong predatory pressure is required for the division of labour to happen.

But in nature, essential resources are finite in quantity, so conditions with abundant resources seldom last for very long. The unicellular ancestors were surely often starved. Kerszberg and Wolpert (1998) proposed that starvation might have initiated multicellularity in evolution. Although their discussion was mainly focussed on the multicellularity of metazoans, the theory can be extended to the multicellularity of metaphytes and prokaryotes (like *Myxococcus xanthus*) without any difficulties. We prefer their idea.

The reason for Buss (1987) to adopt Margulis' theory on division of labour in cells is that most metazoan cells have only one MTOC. Bell (1989) proposed an alternate hypothesis that it might be the consequence of the evolution of metazoans. Although there are still some possibilities for division of labour to have occurred in the way that Margulis proposed, it is more likely to result from another selective force than simultaneous movement and cell division. As division of labour in cells makes it possible to express fewer genes in individual cells, Niu and Chen (1997) proposed that nuclear DNA might be protected. In addition, Gerhart and Kirschner (1997) pointed out that mutually incompatible biological processes could run in the same individual after division of labour in cells. A familiar example is photosynthesis and nitrogen fixation in cyanobacteria. The enzyme responsible for nitrogen fixation cannot operate in the presence of oxygen, which is the product of photosynthesis. Division of labour in cells solved this problem by running the two functions in different cells.

One marked feature of *Volvox* is the division of labour between somatic cells and germ cells. All the cells of *Volvox* have only one MTOC, the somatic cells use it to move and the germ cells use it to divide (Kirk, 1998). Koufopanou (1994) also proposed that the multicellularity of *Volvox* was to move and divide simultaneously in aquatic environments. However, Koufopanou's hypothesis depends on the special cytological features of the green flagellates, which have no counterparts in metazoans and unicellular ancestors.

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