Simulation of Cell Group Formation Regulated by Coordination Number, Cell Cycle and Duplication Frequency

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ABSTRACT

The effects of coordination number, a cell cycle and duplication frequency on cell-group formation have been investigated in a computer simulation. In the simulation, multiplication occurs in the last three steps of a cell cycle with a probability function to give variations in the interval. Each cell has a constant coordination number: four or six. When a cell gets surrounded by adjacent cells, its status changes from an active stage to a resting stage. Each cell repeats multiplication, and disappears when the times of multiplication reach to the limit. Variation was made in the coordination number, in the interval of multiplication and in the limited times of multiplication. The cells of the colony, which have the larger number of coordination, have reached the larger maximum population and disappeared earlier.

Keywords: Simulation, Biological Cell, Group Formation, Coordination, Number, Duplication Frequency, Cell Cycle and Population

1. INTRODUCTION

In biological tissue, mitosis is regulated not only by a cell cycle and duplication frequency, but also by the adjacent cells [1]. A cell enters mitosis after a certain period. The duration of the cycle scatters in a certain range. The times of multiplication cannot exceed the programmed limit except cancerous cells or generative cells. Mitosis of the normal cell is controlled by the contact of adjacent cells. When a cell is surrounded by others, it enters a resting stage and stops the multiplication process except cancerous cells.

The previous simulation shows that both the cell cycle and the duplication frequency control the life span of the colony, the maximum population of cells, the stability in population, and the interaction between colonies [2].

The arrangement of cells varies with tissue [3]. The number of surrounding cells in a colony has been fixed as a coordination number in the present study. The effects of the coordination number, the cell cycle and the duplication frequency on the group formation of cells have been investigated in the computer simulation.

2. METHODS

The simulation consists of the following processes. Each loop-step of calculation corresponds to time. The parameters of the coordination number, the cell cycle and the duplication frequency were set at the beginning of the calculation process.

Cell cycle
The phase of the cell cycle in each cell progresses with time. To give variations in the interval, the multiplication occurs in the last three steps of the cell cycle with the probability function (Fig. 1). Their multiplication probabilities are 25 percent in the third step before last, 50 percent in the step before last and 100 percent in the last step, respectively.

Cell contact
A plane is divided into square or hexagonal elements: seats. That makes the plane, in which each seat is surrounded by four or six adjacent seats, respectively. Each cell occupies one seat. The seats of 100 times 100 spread in the plane. A central seat is selected for the initial location of a cell at the beginning of the simulation. After the multiplication, two duplicated cells occupy two seats: one is the original seat and the other is the adjacent seat to the original (Fig. 2).

When a cell gets surrounded by adjacent cells, the cell changes its status from the active stage to the resting stage (Fig. 3). In the resting stage the cell stops the multiplication process.

Duplication frequency
The cell repeats multiplication, and disappears, when the times of multiplication reaches to the limit. When the seat adjacent to the cell in the resting stage becomes vacant, the cell returns from the resting stage to the active stage and follows the previous process.

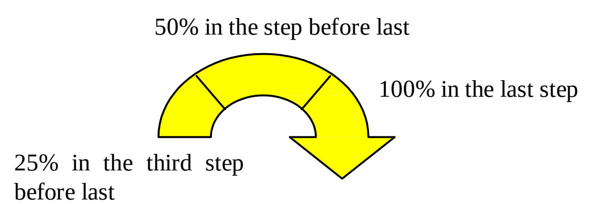

Fig. 1: Multiplication probabilities in the cell cycle.

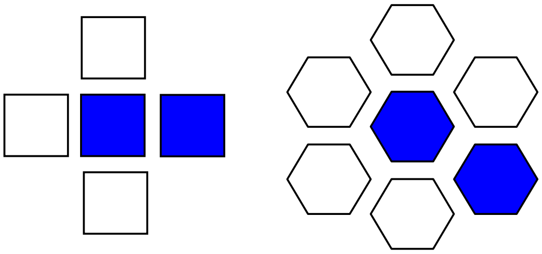

Fig. 2: Each seat is surrounded by four (left) or six (right) adjacent seats.

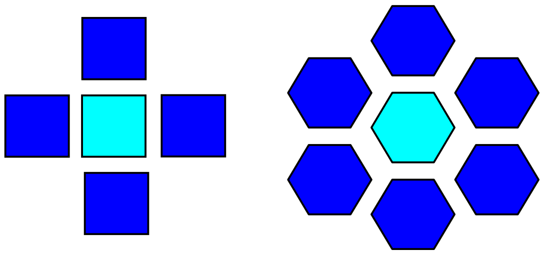

Fig. 3: A cell surrounded by adjacent cells changes its status from the active stage to the resting stage.

Life span and population
When the calculation finishes about every cell existing in the plane, the step advances to the next and the time count increases by one. The life span of the colony corresponds to the step when all cells of the colony disappear. Population of cells is counted at each step.

Display
All seats are displayed in the window at each step. The change of the stage from active to resting is displayed with the change of the color of cells. Figures 4 & 5 exemplify the colony with the coordination number of four and six, respectively. The colored cells at the rim show their active stages in Figs. 4(b) & 5(b). These processes were programmed in "C" language and operated on "Microsoft Windows".

3. RESULTS

In the simulation, variation has been made in three parameters: the coordination number, the interval of multiplication and the limited times of multiplication. Cells repeated multiplication (Figs. 4(a) & 5(a)), increased in the number (Figs. 4(b) & 5(b)), and then decreased to extinction (Figs. 4(c) & 5(c)).

When the simulation starts from one cell located in the central location of the plane, results have been as follows.

In Figs. 6-9, the data points of triangle and of circle show the coordination number of four and of six, respectively. Each data point shows the mean value of five trials. The scatter range of each trial was below ten percent of the mean value.

Fig. 4(a): Cells repeat multiplication.

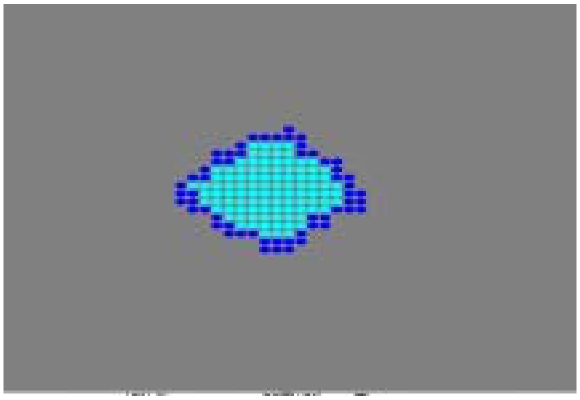

Fig. 4(b): Cells increase in the number. Cells in the center part of the colony are in the resting stage with the changed color.

Fig. 4(c): Cells decrease to extinction.

When the times of multiplication is limited in the constant value of ten steps, the life span of the colony increases in proportion to the interval of multiplication; cell cycle (Fig. 6(a)). The maximum population of cells is saturated, when the cell cycle is longer than ten steps (Fig. 6(b)). The maximum population of cells scatters, when the cell cycle is shorter than ten steps. The life span in coordination number of four is longer than that of six, although the maximum population in coordination number of four is smaller than that of six. The tendency has been similar, when the times of multiplication is limited in the constant value of twenty steps (Fig. 7).

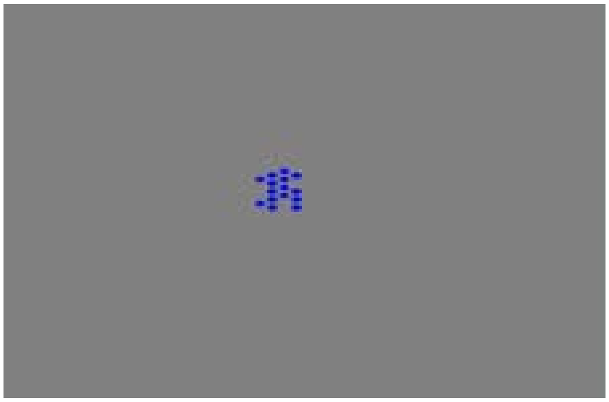

Fig. 5(a): Cells repeat multiplication.

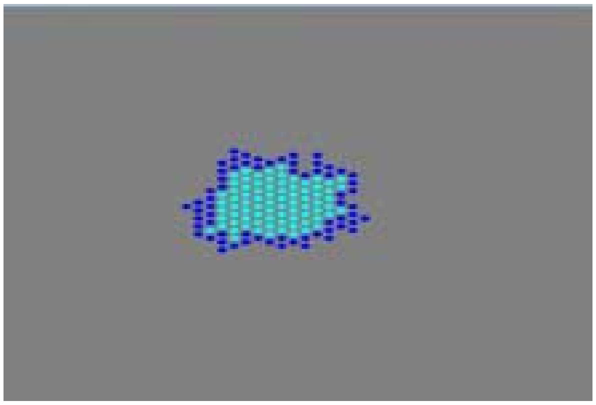

Fig. 5(b): Cells increase in the number. Cells in the center part of the colony are in the resting stage with the changed color.

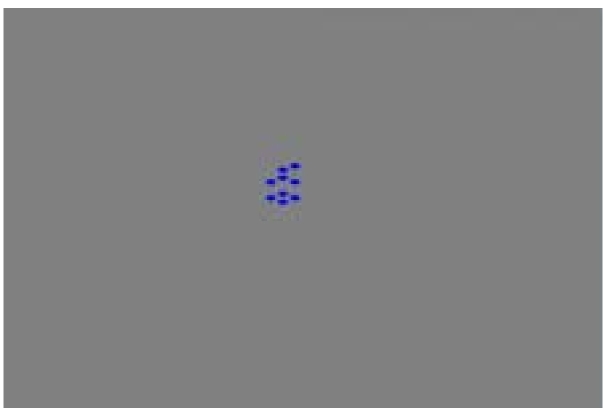

Fig. 5(c): Cells decrease to extinction.

When the cell cycle keeps in the constant value of ten steps, both the life span of the colony and the maximum population of cells have increased exponentially with the limited times of multiplication (Fig. 8). The life span in coordination number of four is longer than that of six, although the maximum population in coordination number of four is smaller than that of six. The tendency has been similar, when the cell cycle keeps in the constant value of twenty steps (Fig. 9).

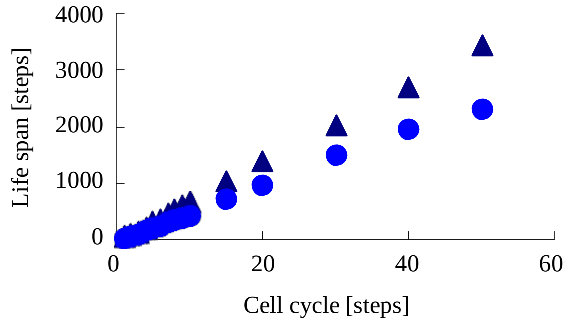

Fig. 6(a): Life span vs. cell cycle at times of multiplication of 10.

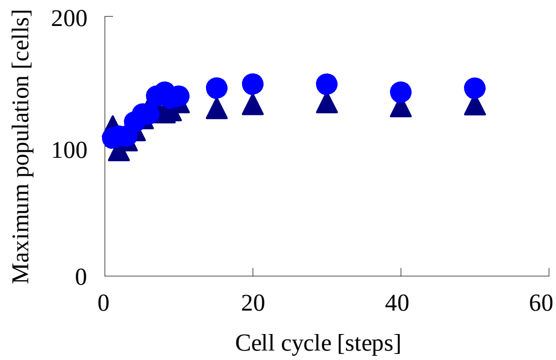

Fig. 6(b): Maximum population vs. cell cycle at times of multiplication of 10.

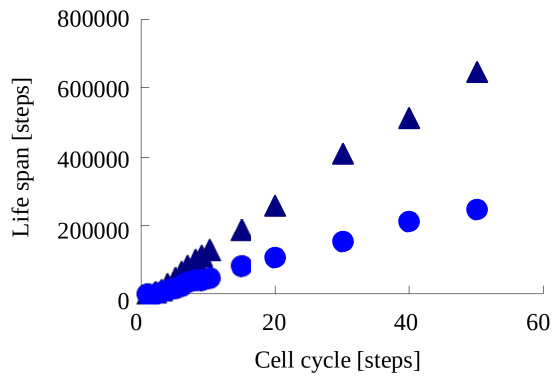

Fig. 7(a): Life span vs. cell cycle at limited times of multiplication of 20.

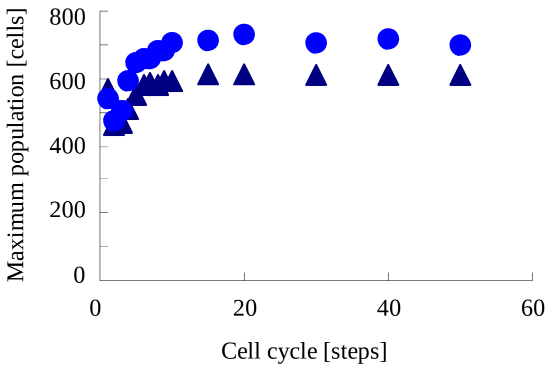

Fig. 7(b): Maximum population vs. cell cycle at limited times of multiplication of 20.

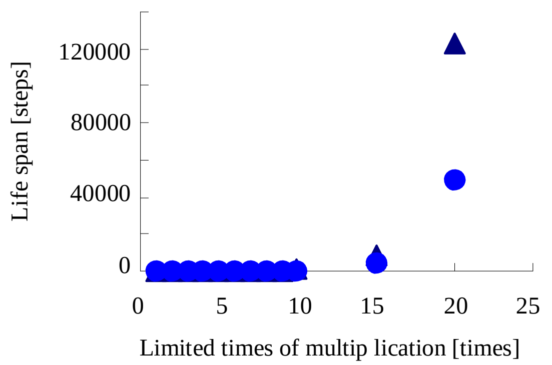

Fig. 8(a): Life span vs. limited times of multiplication at cell cycle of 10.

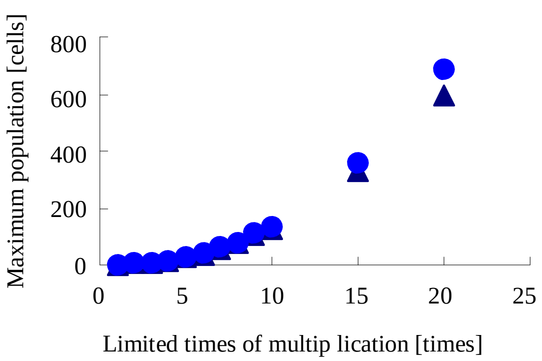

Fig. 8(b): Maximum population vs. limited times of multiplication at cell cycle of 10.

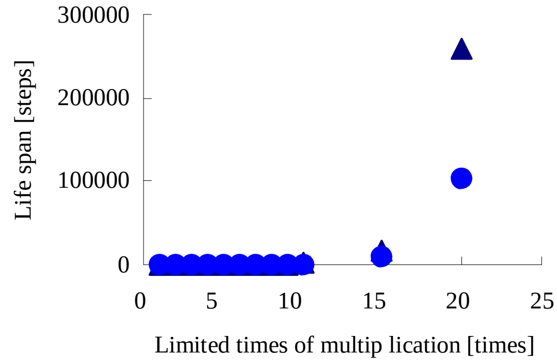

Fig. 9(a): Life span vs. limited times of multiplication at cell cycle of 20.

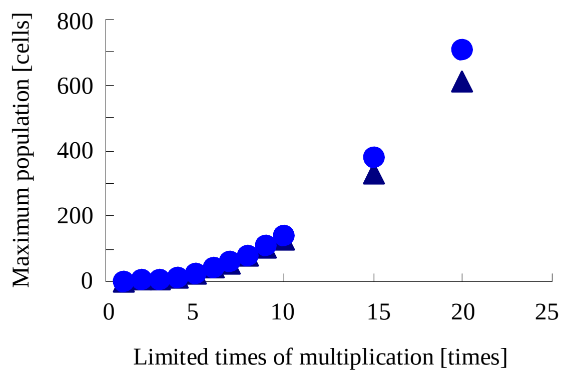

Fig. 9(b): Maximum population vs. limited times of multiplication at cell cycle of 20.

4. DISCUSSION

Many communication routes among biological cells have been discovered by recent studies [1]. The cell culture provides a method to study about the society of cells [4, 5]. The behavior of group of cells has also been studied in the research field of "Artificial Life" [6]. The computer simulation provides a method to analyze the system.

Multiplication is one of the typical characters of cells. The programmed rules to regulate multiplication of cells may govern the life span of the organs. Many factors might control multiplication.

Three factors have been highlighted in the present study: coordination number, cell cycle and duplication frequency. When the cell gets surrounded by adjacent cells, the cell changes its status from the active stage to the resting stage, and stops the multiplication process. The effects of them on the group formation have been evaluated by counting population and steps.

The life span of the colony has increased in proportion to the cell cycle. The life span of the colony has increased exponentially with the limited duplication frequency. The cell cycle longer than ten steps has stabilized the maximum population (Figs. 6(b) & 7(b)).

When the limited times of multiplication is longer than five steps, the data of the maximum population of cells have separated from the calculated line of exponential function [2]. The difference means that the multiplication has been controlled by the effect of cell contact.

The arrangement of cells varies with biological tissue [6]. The coordination number in the simulation represents the number of adjacent cells. The larger coordination number accelerates duplication frequency, which makes the larger number of population of the colony. The larger coordination number, however, reduces the resting cells, which shortens the life span of the colony.

The coordination number, the cell cycle and the duplication frequency programmed in the colony have governed the group formation.

Simplification of the rules enables the accelerated simulation. It causes, however, some conflicts in the simulation. For example, the simultaneous calculation in each step causes the conflict as two independently duplicated cells occupy the same seat. The last one occupies the seat in the present simulation, although the conflict does not occur frequently. A lot of calculation loops are necessary to solve the conflict. That extends the calculation time.

5. CONCLUSION

The simulation shows that both the life span of the colony and the maximum population of cells vary with the cell cycle and the duplication frequency. The simulation also shows that the coordination number controls the life span of the colony and the maximum population of cells.

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