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Microbial Growth Modeling and Simulation Based on Cellular Automata

Hong Men and Xiaojuan Zhao
School of Automation Engineering, Northeast Dianli University, Jilin 132012, China

Abstract: In order to simulate the micro-evolutionary process of the microbial growth, [Methods] in this study, we adopt two-dimensional cellular automata as its growth space. Based on evolutionary mechanism of microbial and cell-cell interactions, we adopt Moore neighborhood and make the transition rules. Finally, we construct the microbial growth model. [Results] It can describe the relationships among the cell growth, division and death. And also can effectively reflect spatial inhibition effect and substrate limitation effect. [Conclusions] The simulation results show that CA model is not only consistent with the classic microbial kinetic model, but also be able to simulate the microbial growth and evolution.

Keywords: Cellular automata model, substrate limitation effect, space inhibition effect, transition rules

INTRODUCTION

The research of the evolution and the growth process of microbial individual cells have a certain effect on improving the microbial production and optimize microbial culture conditions. The mathematical model is a powerful tool for microbial growth simulation.

Classic microbial kinetics model (Chunrong, 2004) utilizes continuous differential equations, microbial growth utilizes Monod equation. Assumed microbial growth rate is proportional to the substrate consumption rate which can describe microbial growth and substrate removal kinetics from a macro point of view. Once the growth of microorganisms involves micro issues, such as mechanisms of microbial evolution, microbial characteristics (diversity, randomness, sensitivity) in complex systems, we must consider it from microscopic aspect. But currently, the existed computer models focus on the analysis from microscopic perspective, such as discrete models (Saadia and Marie, 2002), communications walking model (Fogedby, 1991) which based on the nutrient diffusion-controlled growth. They consider less factors and the research scope is limited. CA model (Heiko *et al*., 1998) is based on a very limited set of rules but it shows the diversity of microbial growth behavior (microbial cell growth, decline and fall off, etc.). It bases on qualitative conclusions of the biology to design simple local evolution rules to examine the characteristics of micro-organisms, which offers a theoretical CA model for the modeling and simulation of the complex system. At the same time, it has special meaning for the research of the micro evolution process of micro-organisms in the complex system.

This study establishes the CA model of microbial growth and simulates the process of microbial growth evolution. It also makes a research on the influence of the substrate limit effect and space inhibition effect to the evolution process.

THE COMPOSITION OF CA MODEL

This study proposes two-dimensional cellular automata space (Picioreanu *et al*., 2000) as CA model growth space and every cell is with different state. Microbial evolution process is conversion process that the cell state value changes constantly. Microbial growth model contains five elements:

$$A = \{t, Cell, Cellspace, Neighborhoods, Rules\}$$

t	=	Discrete time
Cell	=	The cells
Cellspace	=	Set of all cells in model
Neighborhoods	=	Neighborhood of model cells
Rules	=	The evolving rules of cells

The discrete time of CA model: Microbial growth cycle T needs to be discretized, each Discrete time $t = kT_0$, $k = \{0,1,2.....\}$ is discrete time sequence, T_0 is discrete time interval.

The cell and the cell space of CA model: Two-dimensional CA model of cell space is plane which constitutes a two-dimensional coordinate system $O(i, j)$, $Cell(i, j)$ is located in the (i, j), It is $Cellspace = \{Cell(i, j) \mid i, j \in \{0,1,2....\}\}$.

Corresponding Author: Men Hong, School of Automation Engineering, Northeast Dianli University, Jilin 132012, China, Tel.: +86-432-64807283

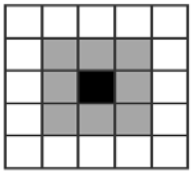


Fig. 1: Moore neighborhood

The cell -neighborhood Of CA model: The cell-neighborhood of CA model is $V(Cell(i, j))$, which shows the evolution range of model evolution rules. The study adopts the *Moore* neighborhood. There are eight cell-neighborhoods for two dimensional spaces, as Fig. 1 shows.

The cell state Of CA model: Each cell in CA model has different states. In the simulation, make sure that $Cell(i, j)$ is in the state of $S_{ij}(t)$ at t and $S_{ij}(t)$ has three different state values: $S_{ij}(t)$ = 1denotes empty or cell death state, $S_{ij}(t)$ = 1 denotes dividing state, $S_{ij}(t)$ = 2 denotes growth state.

THE MODELING OF MICROBIAL CA

In the process of Microbial growth and reproduction, system has rich substance in the beginning, as the time going on; the substance in the system begins to decrease. Due to the competition for substance which leads to microorganisms grow slowly, and this phenomenon is called substrate limitation effect. At the same time, as the cell growth and division, the available area decreases that result in the reduction of the whole growth region (De Beer *et al*., 1994). When the entire surface area is occupied, the growth and division will stop, this phenomenon is called spatial inhibition effect (Lacasta *et al*., 1999). The two-dimensional CA model that this study proposes mainly considers the substrate limitation effect and spatial inhibition effect on the process of microbial evolution.

The growth of microbial is arranged in a two-dimensional grid named $(L_i \times L_j)$, the cell is represented by the cellular in the grid. Its location shows by coordinate (i, j) and the state of the cell in position (i, j) shows by $S_{ij}(t)$. The state space of the system is: (0, 1, 2)-(empty, division, growth). The neighborhood of cells selects *Moore* neighborhood when $r = 1$. According to certain rules, cells in the grid grow, divide, death.

Substrate limitation effect: Abstract the substance to be particles that only has quality but no volume. At the location of coordinate (i, j), there are $x_{ij}(t)$ substrate particle. The diffusion of substance within a grid equivalent to many particle random walks. This study uses a discrete lattice gas automata HPP model (Feng and Tao, 2001) to describe. In order to make each particle can select new direction that is allowed by the grid, the model adds a random motion to describe the diffusion of matrix.

Growth cell changes into a division cell after it takes in a matrix. If the division cell neighbor is not occupied completely by cells, the cell will randomly select one empty cell to divide. After the division, the division cell changes into growth cell. Every growth cell has a certain survival time.

Microbial evolution rules:

$$S_{ij}(t+1) = \begin{cases} 2 & (S_{ij}(t) = 1) \,\&\, [\exists V(Cell(i, j)) = 0] \\ 1 & S_{ij}(t) = 2 \,\&\, x_{ij}(t) \geq 1 \\ 0 & S_{ij}(t) = 0 \,||\, [S_{ij}(t) = 2 \,\&\, t_c = 0] \end{cases} \quad (1)$$

Spatial inhibition effect: Spatial inhibition effect is due to the competition of microbial cell growth space. In order to grow and divide, a microorganism must stick to a plane. Once it does, the cells begin to divide, several divisions later; they will form a small colony. This result leads to the decrease of the available space as the division and growth of the cell. Eventually, the whole microorganisms' growth begins to decrease. When the entire surface area is occupied, growth and division will stop.

Microbial state is divided into division and growth, the cell in division state will respond differently according to the neighborhood circumstances. If the cell number in neighborhood is greater than a certain threshold, the spatial inhabitation effect makes the division cell no longer divide, but change into the growth state. When the cell number in neighborhood is less than the threshold, the cell in division state begin to divide with certain probability. The reason that this study proposes probabilistic mechanism is under ideal state, there are still complex interactions between individual. Probability mechanism can not only reflect the microbial evolution microscopic mechanism, but also make the model have better adaptability.

In two dimensional spaces, microbial growth is influenced by Moore neighborhood's 8 lattices. $N_{(i, j)1}(t)$ represents the number of cells when neighborhood state is 1 at t, N (i, j) = 2 represents the number of cells when neighborhood state is 2 at t. N_0 is the threshold, which reflects the inhibition effect of microbial growth. According to the above description, this study designs the following CA model partial evolution rules:

If $S_{ij}(t) = 0,\ N_{(i,j)1}(t) > 0$ and $N_{(i,j)1}(t) + N_{(i,j)2}(t) \leq N_0$, $N_{(i,j)1}(t) + N_{(i,j)2}(t) = j$

then the probability of $S_{ij}(t) = 2$ is P_j;

If $S_{ij}(t) = 1,$ and $N_{(i,j)1}(t) + N_{(i,j)2}(t) > N_0$, then $S_{ij}(t) = 2;$

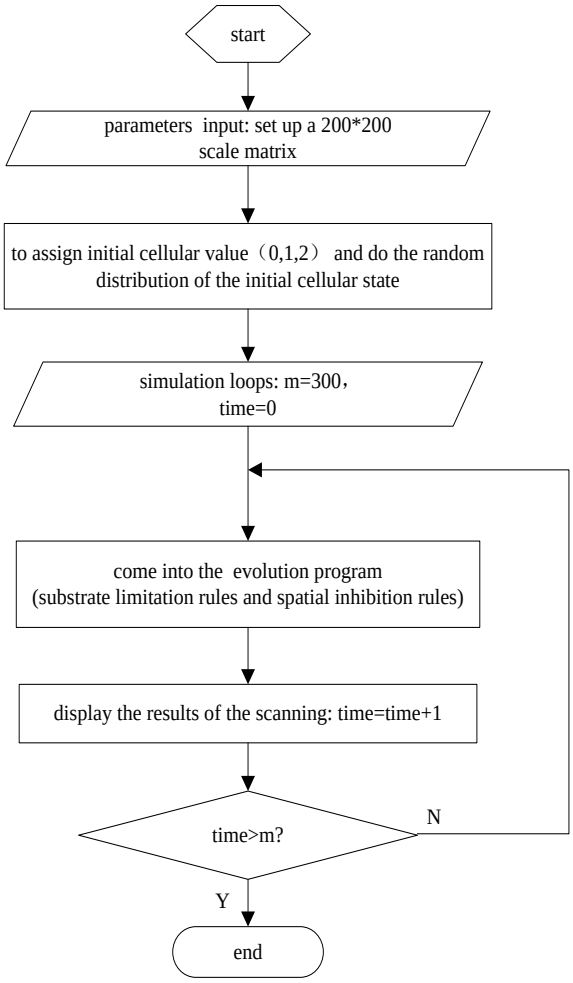


Fig. 2: The simulation flow chart of CA model

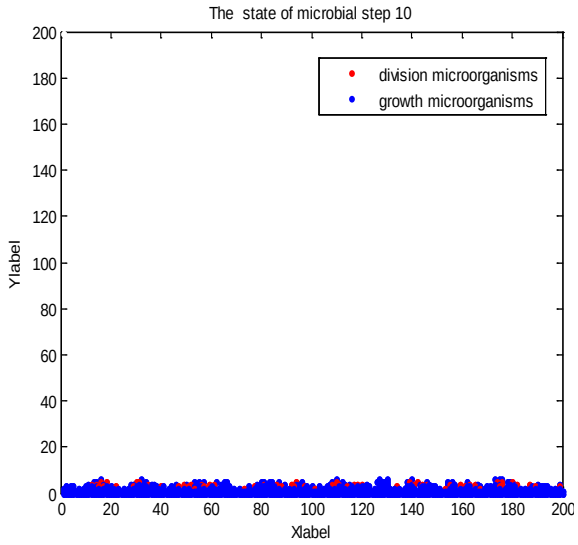
If $S_{ij}(t) = 2$, and $N_{(i, j)1}(t)\ N_{(i, j)2}(t) + N_{(i, j)1}(t) \leq N_0$, $N_{(i,j)1}(t) + N_{(i,j)2}(t) = j$;

then the probability of $S_{ij}(t) = 1$, is P_j.

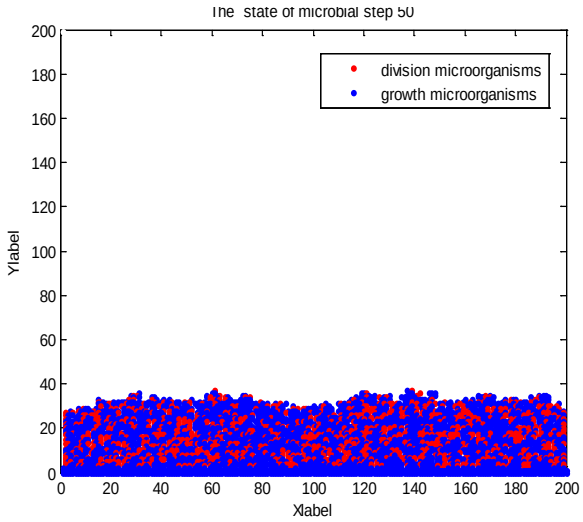
The simulation flow chart Of CA model: In the simulation of two dimensional CA model, comprehensively consider the influence of substrate limitation effect and spatial inhibition effect to the microbial evolution, the Fig. 2 shows the established flow chart:

SIMULATION RESULTS AND DISCUSSION

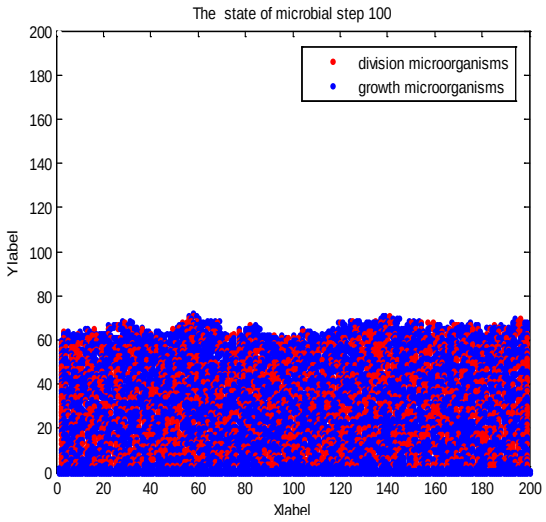
According to references and experiences, combined with mechanism of the microbial growth the initial parameters (Naigong and Ruan, 2004a) are set as: the initial concentration of substance is $s(0) = 60g/L$, the microbial initial concentration is $x(0) = 6g/L$. According to "the simulation flow chart



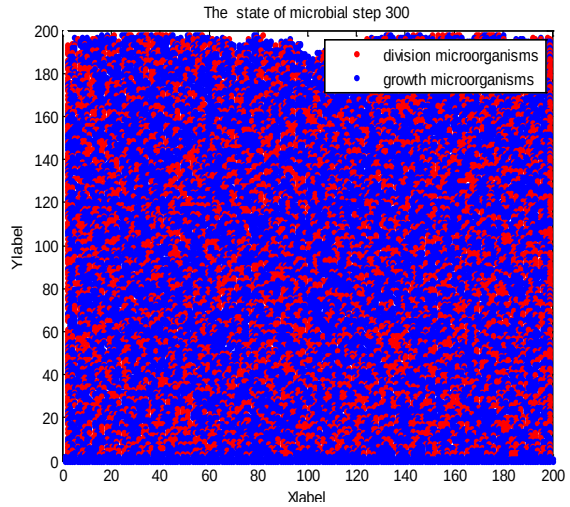
T = 1h



t = 5h



t = 10h



t = 30h

Fig. 3: The result of microbial evolution process with time changing

of CA model", we will write program and manipulate simulation experiment.

The process of microbial evolution: Figure 3 is the result of microbial evolution process with time changing.

From Fig. 3, we can see that microbial distribution become more and more wider and microbial concentration gradually increase with time changing, which illustrates that microorganisms are growing and reproducing unceasingly. Because of the spatial inhibition effect, the increasing speed of blue areas (division cell) is obviously higher than the red areas (growth cell); Because of the substrate limitation effect, the growth rate of microbial evolution in the prior period is obviously slower than that of the later period. When $t = 30h$, microorganisms are filled with the two-dimensional space of CA model that illustrate the microbial concentration has reached its maximum. From Fig. 3, we can see that CA model can better simulate the growth of microorganism and evolution process.

Microbial spatial inhibition effect: In the simulation experiments, this study takes different N_0 and probability combination to research spatial inhibition effect of microbial growth, with the increase of N_0, the spatial inhibition effect between cells is weakened gradually; when $N_0 = 2$, spatial inhibition effect is very strong and microbial growth is slow; when $N_0 = 3$ $N_0 = 3$, the spatial inhibition effect is weakened gradually, when $N_0 \geq 4$,the effect is more weak. Figure 4 shows microbial concentration curve with time changing when probability take P1= 0.5, P2 = 0.25, P3 = 0.125 and

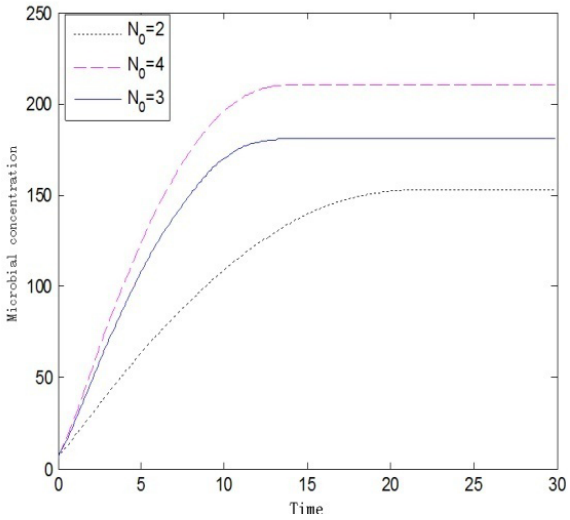


Fig. 4: Microbial concentration curve

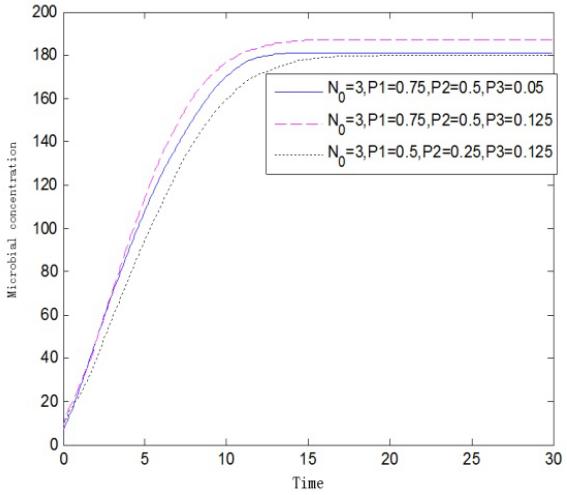


Fig. 5: The microbial concentration changes with time under three different probabilities

different N_0. From Fig. 4 we can see that as N_0 increase gradually, the spatial inhibition effect becomes less, the microbial growth process becomes faster, the microbial concentration increases.

Figure 5 shows the microbial concentration changes with time under three different probability when $N_0 = 3$. From Fig. 5, we can see if we select the same N_0, but different probability, there is still difference in the microbial growth process. Probability mechanism is not only representing the micro mechanism of microbial evolution, but also makes the model more adaptive. Only combine with the real biology experiment, we can get more progress.

Microbial substrate limitation effect: In the simulation experience, the study selects material

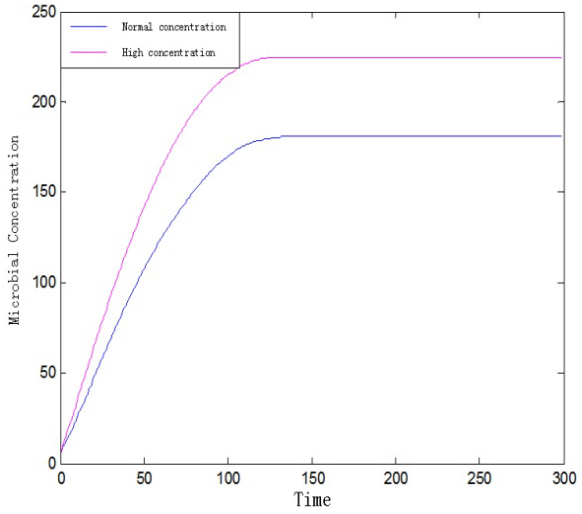


Fig. 6: The analysis chart of substrate limitation effect

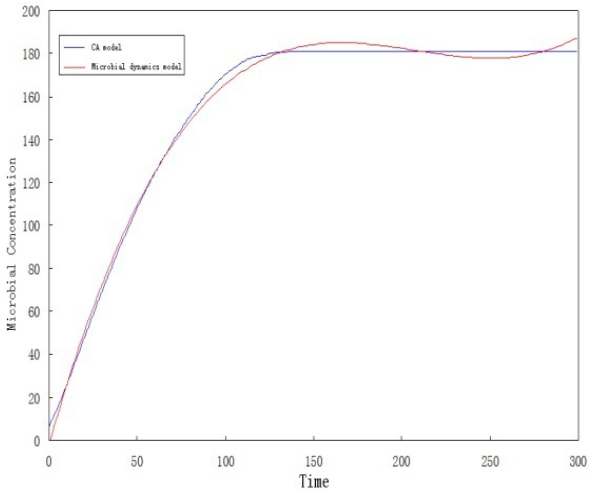


Fig. 7: Comparison of microbial CA model simulation results and kinetic model simulation results

Concentrationas $s_1(0) = 60g/L$ and $s_2(0) = 70g/L$, microbial initial concentration as $x(0) = 6g/L$, the result is showed in Fig. 6.

We can see from Fig. 6, because of the substrate limitation effect, the higher the material concentration, the faster the colony growth, the closer the microbial densification.

COMPARISONS BETWEEN CA MODEL AND KINETIC MODEL

Classic microbial kinetics formula (Ngqin, 2006):

$$m = m_0 + \pi x h(\mu t)^2 + 2\pi x h \mu r_0 t + kt^3 \quad (2)$$

m = Microbial biomass
m_0 = Initial biomass
t = Time
x = Microbial concentration
h = Colony height
μ = Microbial growth rate
r_0 = Initial microbial radiu
k = Random factor

The main parameters of kinetic model refer to Hardy *et al*. (1976) and Naigong and Ruan (2004b), as formula:

$$m = 6 - 1.458t^2 + 29.24t + 0.0223t^3 \quad (3)$$

Make comparison between microbial CA model simulation results and microbial kinetic model simulation results, the results are shown in Fig. 7.

This study uses correlation coefficient to study the two models' similarity. The formula as:

$$R = \frac{\sum (x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum (x_i - \bar{x})^2 \sum (y_i - \bar{y})^2}} \quad (4)$$

$R = 0.9965$, it illustrates the two kinds of model result with high similarity and consistency.

CONCLUSION

This study builds a microorganism growth model based on CA; the main conclusions are as follows:

- The CA model can simulate the evolution process of microbial growth by express the relationship among cell growth, division and death.
- The CA model can reflect the spatial inhibition effect of microbial growth process effectively. The smaller the spatial inhibition effect, the faster the microbial growth speed.
- The CA model can reflect the substrate limitation effect of microbial growth process effectively. The growth rate in the early period of the evolution is higher than the later period. That is the higher the microbial substrate concentration, the faster the microbial propagation.

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