Stochastic Simulation of Yeast Cells and Its Colony Growth by Using Circular Granular Model for Cases of Growth and Birth Probabilities Depends on Position

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Abstract. Until now, many studies were conducted on microorganisms in order to make the best use of them and prevent the loss. As a type of microorganism that is widely utilized by humans, the yeast has a simple single cell structure that can represent many other complex cell processes and generally has almost elliptical shapes making it easier to model for further investigation. In this study, we model yeast cells with two dimensional circular granular particles and the interaction between them are modeled by the force of gravity, normal force, and Stokes force. The growth and birth factor of yeast cells are modeled stochastic with the simulation is done by using javascript programming language. From the simulation results obtained, showing the growth of yeast cells in the colony has a behavior that is in accordance with the theory, which grows exponentially, as well as the growth of the size of the colony radius whose growth rate is half to the rate of growth of its number of cells.

1. Introduction

Microorganisms, classified as profitable and can be harmful to humans. Because of that, many research has been conducted to study these potential to become more profitable to humans and minimize fatal risk due to those microorganisms. As one of microorganisms that can be profitable to humans and almost elliptical shape, it has a single cell structure that can represent many processes in other cells. It makes yeast has been researched both with experimental and computer modeling.

This research was conducted to model yeast cells with changes of the model from those that have been used before [7] and it has colony growth by only budding or asexual reproduction. Also, qualitatively compare this model with the results that have been obtained before in the research of colony growth of yeast cells [1]. In this research, we use javascript to ease of access by web-browser.

As we know, yeast or often called for Saccharomyces cerevisiae is the member of fungus kingdom with the shape of a circle, elliptical, or cylindrical. But in general can be called almost elliptical shape, has various size between 5 to 10 µm [8]. Yeast cells also have a lifecycle with growth phase at first and then the reproduction phase. When yeast cells has enough mature to reproduce, buds will grow from mature yeast cells with position depends on the genetic of
the cell and the availability of nutrition. On this stage, mother cells will not grow significantly anymore [8]. In this asexual type of reproduction, daughter cells will inherit the same genetic material with the mother cell. After this inheritance of genetic material and daughter cells mature enough, daughter cells can live separately from their mother cell. This lifecycle period can differ between yeast cells.

With the reproduction of yeast cells, the number of cells will increase. The increase in the number of cells in the population has been modeled when nutritional supply is considered infinity as [4]

\[ N = N_0 e^{\lambda t} \]  

(1)

Colony formation of yeast cells can be different because of their nutrition and type of the cell. With enough condition for nutrition, the colony formation can be circular shape [3]. The size of the colony formation has been modeled by [4]

\[ r(t) = r_0 e^{\frac{\lambda t}{2}} \]  

(2)

2. Model of Yeast Cells

2.1. Model of Yeast Cells and Probability of Grow and Cell Birth

In this research, the simulation is done with yeast cells modeled by two-dimensional circle shape and the diameter size as \( D \), the mass of the cells modeled by [6]

\[ m(D) = \pi \rho \left( 0.25D^2 \right) \]  

(3)

Yeast cells growth stochastically with the probability of grow \( P(D+) \) on two condition, homogeneous and not. For conditions of the probability not homogeneous, modeled by only separate by a line placed in \( x \) equal zero for cartesian coordinates with larger than \( x \) equal zero as \( P_1(D+) \) and for \( x \) smaller or equal to zero as \( P_2(D+) \). Where \( P_1(D+) \) larger than \( P_2(D+) \). This condition also applied for the probability of birth \( P(B) \).

2.2. Model of Interaction

Between yeast cells, there are interactions with each other. Its modeled by adhesive force that keeps daughter cells attach with their mother cells [5],

\[ \vec{F}^{AG}_{ij} = -G \frac{m_i m_j}{r_{ij}^3} \hat{e}_{ij} \]  

(4)

The normal force will keep cells from overlapping each other [2],

\[ \vec{F}^{AN}_{ij} = (k \xi_{ij} - k_v \nu_{ij}) \hat{e}_{ij} \]  

(5)

and Stokes force that represent medium viscosity [2],

\[ \vec{F}^S_i = -k_v \ddot{r}_i \]  

(6)

3. Simulation and Data Processing Methods

3.1. Simulation Method

The simulation runs by using the algorithm as follows (Figure 1) from only one cell and limited into a specified number of cells. Positioning the birth of the cells follows,
Figure 1: The algorithm of the program for the simulation.

\[ x_a = x_b + \left( \frac{1}{2} D_b \cos(\theta) \right) \]  
\[ y_a = y_b + \left( \frac{1}{2} D_b \sin(\theta) \right) \]  
with the index of \( a \) for daughter cells and \( b \) index for mother cells. And the \( \theta \) has the same probability between 1 to 360 degrees.

3.2. Data Processing Method
In this study, we processed data for yeast cell size distribution, the number of yeast cell size distribution with the algorithm in Figure 2, distribution of yeast cell size positions with the positions represent into twenty regions where the first ten regions for simulation area \( \leq 0 \) and another ten regions for simulation area \( > 0 \). For colony information, in this study, we processed the colony radius with the algorithm as in Figure 3 and calculated based on

\[ r_C = \max(|\overrightarrow{r_{PM}} - \overrightarrow{r_i}| + \frac{1}{2} D_i) \]  

Also, we map generations of offspring from yeast cells.

4. Results
Parameter used in the simulation presented in the Table 1. Those values obtained from trying various values and comparing them visually. Our simulation, repeated up to 100 times for each probability condition, homogeneous and not.
4.1. The Number of Yeast Cell

From the simulation, whether it is homogeneous or not in Figure 4, we can see at each sample behave almost like which is modeled in theory. Those can be obtained because when all yeast cells have mature enough to reproduce, they all have the same probability to gave birth to a new yeast cell.

\[ P(B, t) = \sum_{i} P(B) \quad (9) \]

then, with the same probability \( P(B) \)

\[ P(B, t) = P(B)N(t) \quad (10) \]

so we can get from the simulation almost like from the theory [4].
4.2. Yeast Cell Size Distribution
As in Figure 5, we can get from the simulation size distribution of yeast cells qualitatively behave like normal distribution. But, because of the number of yeast cells limited to only 100 cells which are too small, so we can only get it qualitatively.

4.3. Yeast Cell Size Position Distribution
In Figure 6, distribution of yeast cell size almost same in all area with probability homogeneous. It can be obtained because in homogeneous probability, all \( P(D+) \) probability to grow has the same value in all the area. So, the size of yeast cells in all area almost same. But, it differs with the not homogeneous type of probability. As we can see, in the area with higher probabilities to grow \( P_1(D+) \) as in the area of \( x > 0 \) is larger than probability to grow \( P_2(D+) \) as in the area of \( x \leq 0 \), the size become bigger too. This can be analogous to the area with enough nutrition for higher probability and lower nutrition for lower probability. Of course in the area with enough nutrition, yeast cells can grow more compared to the area with lower nutrition and even can cause death to the yeast cells.

| Parameter | Value |
|-----------|-------|
| \( N_t \) | 100 |
| \( \rho \) | 7/22 |
| \( P(D+) \) | 1/25 |
| \( P(B) \) | 1/1000 |
| \( P_1(D+) \) | 1/25 |
| \( P_2(D+) \) | 1/35 |
| \( P_1(B) \) | 1/1000 |
| \( P_2(B) \) | 1/2000 |
| max(\text{age}) | 2000 |
| \( G \) | 1000 |
| \( k_\xi \) | \( 10^5 \) |
| \( k_\nu \) | 1 |
| \( k_v \) | \( 10^5 \) |
Figure 5: Size distribution from two sample simulation for type of homogeneous probability (left) and not homogeneous (right).

Figure 6: Size position distribution from two simulation samples for the type of the probability homogeneous (left) and not homogeneous (right).

4.4. The Size of the Colony

From the simulation, we can get the colony size almost same for homogeneous and not homogeneous in Figure 7. This can be obtained because we calculate the colony size from the colony center of mass to the farthest cell. This result, also in accordance with the model of [4] and it has grown rate almost half of the growth rate of the number of yeast cells in the colony. But, if we review from the center of mass of the colony it can be different for the homogeneous type of probability and not (Figure 8). As we can see in the not homogeneous type of probability, the center of mass of the colony tend to be on the area with higher probability. This can be analogous to the area with a higher probability as higher nutritional area. Yeast cells have a tendency to move to the area with higher nutrition even there is no moving mechanism for each yeast cell by itself. Also in the area with higher nutrition, yeast cells can grow more so it sizes bigger than the area with lower nutrition. That is why the center of mass position of the colony in a not homogeneous type of probability tend to be in the area with higher probability.

4.5. Generations of Offspring

In this research, because it only simulate the asexual reproduction on yeast cell model, so the map of generation of offspring is not needed to determine which genetical material inherit to daughter cells. But we can see for the position changes based on the position of the daughter cells and their mothers that interacts with each other in this simulation for further investigation.
5. Conclusions

By using this stochastical model in the simulation, we can model yeast cells and its colony growth and qualitatively shows behavior that is in accordance with both experimental and computational model that has been done before [4, 1]. In the number of yeast cell results, quantitatively shows the behavior of exponential function with the growth rate number almost two times larger than the growth rate of the colony size. This results are compatible with previous experimental results [4]. And by using this model, we also get the results that analogically resemble the state of the yeast cells in the conditions of different regions of nutrition.

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