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Study of budding yeast colony formation and its characterizations by using circular granular cell

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Abstract. Budding yeast can exhibit colony formation in solid substrate. The colony of pathogenic budding yeast can colonize various surfaces of the human body and medical devices. Furthermore, it can form biofilm that resists drug effective therapy. The formation of the colony is affected by the interaction between cells and with its growth media. The cell budding pattern holds an important role in colony expansion. To study this colony growth, the molecular dynamic method was chosen to simulate the interaction between budding yeast cells. Every cell was modelled by circular granular cells, which can grow and produce buds. Cohesion force, contact force, and Stokes force govern this model to mimic the interaction between cells and with the growth substrate. Characterization was determined by the maximum (L_{max}) and minimum (L_{min}) distances between two cells within the colony and whether two lines that connect the two cells in the maximum and minimum distances intersect each other. Therefore, it can be recognized the colony shape in circular, oval, and irregular shapes. Simulation resulted that colony formation are mostly in oval shape with little branch. It also shows that greater cohesion strength obtains more compact colony formation.

1. Introduction

Yeast is a well-known unicellular organism that becomes a model to study many biological processes, such as cancer and cell cycle in multicellular organism [1, 2]. The yeast cell grows by increasing its volume until reaching a critical size. This growth undergoes in a cycle. Some species of yeast can divide by forming bud at the periphery of the mother cell, called budding yeast such as the popular baker's yeast *Saccharomycess cerevisiae*. The cell division occurs after the DNA replication. Bud of a mother yeast cell can emerge at a place in mother cell circumference. It will stick to its mother cell until it is ready to produce new cells. Cell division of budding yeast will occur until reaching its lifespan limit.

Budding yeast can exhibit some multicellular properties such as colony formation. The colony formation of pathogenic budding yeast, such as *Candida sp*, can colonize in the human body or some medical devices [3]. Moreover, it can form biofilm that considered as a major cause of human infection and can resist drug therapy. This work aims to study the early formation of the budding yeast colony by taking account some parameters, especially cell cohesion and cell budding pattern.

2. Method

Cell growth can be modelled by using several approaches which can be classified into two main categories, continuum approach and discrete approach. Those methods are used based on how the cell is defined. By using the discrete approach, a cell can be defined by its biophysical or biological parameters and approximated by simpler shape such as sphere [4].

Budding yeast's cell actual shape is ovoid. Due to the assumption that colony formation is seen from above, the cell is modelled and simulated in two-dimension. The cell is modelled by using circular granular cell, neglected its internal properties. Cell growth is defined by increasing in cell diameter. After reaching its maximum size, cell will divide by producing buds at its periphery. The new cell will go through a period of diameter growth (t_G) before it has ability to produce bud while the mother cell can directly produce another bud after a delay time. The time interval between two buds birth in a mother cell is defined by t_B.

The site of new bud emergence is considered to affect colony spreading. In this work, simulation is limited by maximum number of cells (N) and four cell budding patterns (θ) which expected to represent a possible pattern in budding yeast colony growth. New cell that occupy some spaces will interact with existed cells and its growth medium. All the interaction is simulated using molecular dynamic method.
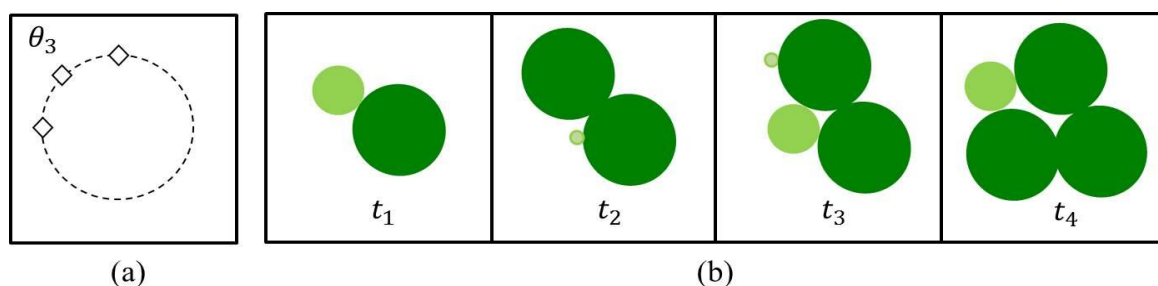
Figure 1. (a) Possible sites of new bud (θ_3); (b) Illustrations of colony formation with budding pattern θ_3.

Cell-cell interactions are represented by two forces, cohesion force and contact force. Medium or growth substrate is assumed to affect the colony formation. Due to this assumption, the movement of cell is also depended by the viscosity of substrate (η). The interaction between cells and growth substrate is represented by Stokes force. Formulation of all forces and their explanation are already provided in previous work. [5].

At the initial condition, there are already three cells in the system. One of them has the ability to produce new cells while others are still growing. Parameter values of simulation are chosen so that it does not need a huge amount of computation time. Most of simulation parameters are provided in table 1.

Table 1. Simulation parameters.

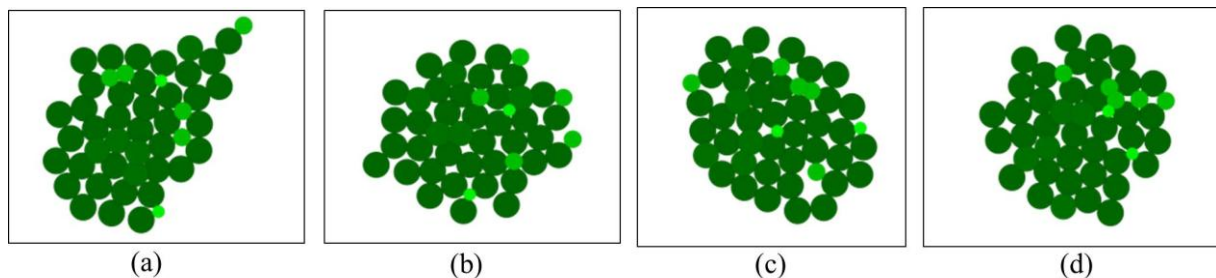| Parameter	Values
η	15.0
m	1.0
Δt	10^{-5}
t_B	15.0
t_G	3.0
N	50

3. Results and discussion

Characterization of the colony was determined by the maximum and minimum distances between two cells within the colony and whether two lines that connect the two cells in the maximum and minimum distances intersect each other. Therefore, it can be recognized the shape of the colony. Colony

formation that has the same maximum and minimum distance value will be considered as circular. If the values are different and the intersection line within the colony, then the shape is considered as oval, else the colony is defined as in irregular shape.

Two parameters are varied in this simulation: cohesion strength (G) and budding pattern (θ). The variation of parameter simulation is provided in table 2. Every combination of G and θ values are simulated until five repetitions, since the alteration of the angle in the budding pattern occurs randomly. Figure 2 and 3 show some simulation results.

Table 2. Parameter variations in simulation.

| Variation	Cohesion Strength (G)	Budding pattern (θ)
Value	$G = 2.0$ $G = 5.0$	$\theta_1 = \frac{\pi}{4}$ $\theta_2 = 0, \frac{\pi}{4}$ $\theta_3 = \frac{\pi}{2}, \frac{5\pi}{4}, \pi$ $\theta_4 = 0, \frac{\pi}{2}, \pi, \frac{3\pi}{2}$

(a)   (b)   (c)   (d)

Figure 2. Simulation result of every cell budding pattern (a) θ_1, (b) θ_2, (c) θ_3, (d) θ_4 and cohesion strength G = 5.

(a)   (b)   (c)   (d)
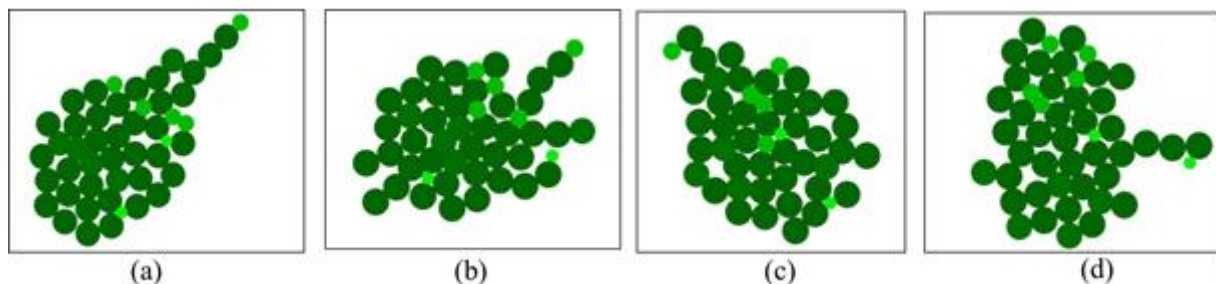
Figure 3. Simulation result of every cell budding pattern (a) θ_1, (b) θ_2, (c) θ_3, (d) θ_4 and cohesion strength G = 2.

Different values of cohesion strength give significant differences in colony formation. Greater cohesion strength result more compact colony formation. It is caused by cells in a colony tend to adhere each other and leaving it birth-site. It is also shown in figure 4, the difference distance between L_{max} and L_{min} for G = 2 are wider that G=5. Besides, branching structure is found in G = 2 for almost all budding patterns. The average graph shows that the average colony formation is in oval shapes.
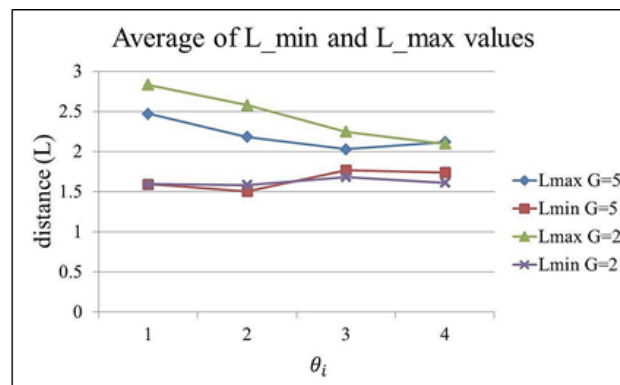
Figure 4. The average of maximum and minimum distances values, L_{min} and L_{max} of a colony for two different values of G = 2, 5.

4. Conclusion

A model for two dimensional colony formation based on the circular granular cell has been presented. It was found out that the strength of cohesion between cells and cell budding pattern has a significant role in determining colony expansion that determined by the maximum and minimum distances of the cell within the colony. The greater cohesion strength value will produce more compact colony formation.

References

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