Cell nucleus visualization with phenotypic characteristics

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Abstract

In order to elucidate the developmental mechanism of multicellular organisms, it is important to quantify the spatiotemporal features (phenotypic characteristics) of cells appearing during cell division and to analyze their relationship (correlation). Furthermore, in order to analyze whether phenotypic characteristics correlate, it is necessary to observe shapes of cell nuclei having a phenotypic characteristic. We proposed a system that visualizes phenotypic characteristics and three-dimensional cell nucleus shapes before, but there were problems that cell nucleus shapes cannot be observed individually and information such as cell nuclear position or movement distance was insufficient. In order to solve such problems, we have improved visualization methods of several cell nuclei and phenotypic characteristics. In the experiments, we performed user evaluation for experts who research the developmental dynamics of the cells. This system enabled them to analyze them smoothly and come up with new ideas.

**Keywords**: Phenotypic characteristics, Cell nuclear shape, Semi-transparent rendering.

**Index Terms**: K.6.1 [Management of Computing and Information Systems]: Project and People Management—Life Cycle; K.7.m [The Computing Profession]: Miscellaneous—Ethics

# Introduction

In the field of life sciences, research for elucidating the developmental mechanism of multicellular organism using nematode (*C.elegans*), which is one of representative model organisms, is actively carried out. To elucidate it, which phenotypic characteristics affect other ones have been studied. We previously developed a system that narrows down pairs with high correlation between phenotypic characteristics up to the 8 cell stage and visualizes the three dimensional shape of cell nuclei having the selected characteristic. [1]

　When phenotypic characteristics expressed over multiple time steps are chosen, an average shape was visualized so that the outline of cell nuclei could be observed at a glance. However, since the average shape is not an actual cell nucleus shape, it is necessary to observe an individual shape. In addition, in the case of phenotypic characteristics of position and distance, it is difficult to grasp them only from a cell nucleus shape, so it is necessary to visualize them.

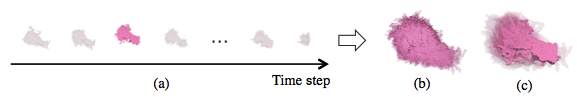
In this study, we propose methods to visualize cell nuclei having a phenotypic characteristic appearing over multiple time steps and to show information of position and distance.

# METHOD

In this chapter, we propose two visualization methods of cell nucleus having a phenotypic characteristic.

## Visualization of 3D cell nuclei

In this section, we describe a method to visualize both the approximate form of cell nuclei and an individual cell nucleus when a phenotypic characteristic exists over multiple time steps. Figure 1(a) shows how shapes of several cell nuclei with a phenotypic characteristic change over time. First, in order to display an outline of them, all the cell nuclei are overlapped and displayed as shown in Figure 1(b). When you want to observe a specific cell nucleus shape, it changes opaque and the other ones are translucently drawn. When rendering semitransparent cell nuclei simultaneously, polygon sort processing is necessary, so we performed the stochastic rendering technique[2].



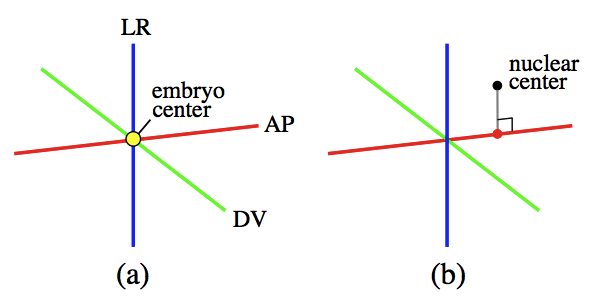
1. (a) A time change of the cell nucleus shape. (b) The result of overlapping all of them. (c) The result of highlighting a specific cell nucleus shape.

## Visualization of phenotypic characteristic

In this section, we describe how to visualize the phenotypic characteristics, a cell nuclear position, a distance between a cell nucleus center and an embryo center, and a movement distance of a cell nucleus.

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2.2.1 Nuclear position

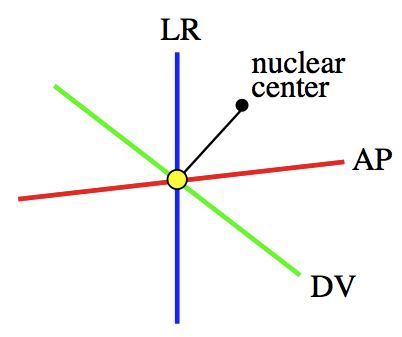


1. (a) The anterior-posterior axis (AP), dorso-ventral axis (DV), left-right axis (LR) of a *C.elegans* embryo and the embryo center (b) The result of subtracting a vertical line from the cell nuclear center to the AP axis

In order to show a cell nuclear position relative to the AP, DV, LR axis, we visualized these axes and the cell nuclear position. In the *C.elegans* embryo, anterior-posterior(AP) axis, dorso-ventral(DV) axis and left-right(LR) axis[3] are defined, and they are orthogonal each other. As shown in Figure 2 (a), red line is AP axis, green one is DV axis, blue one is LR axis and the yellow sphere is the embryo center. We drew the cell nuclear center with the black sphere and the foot of the perpendicular to the axis where the feature value was measured (AP axis in Fig. 2 (b)) with a sphere of the same color as the axis.

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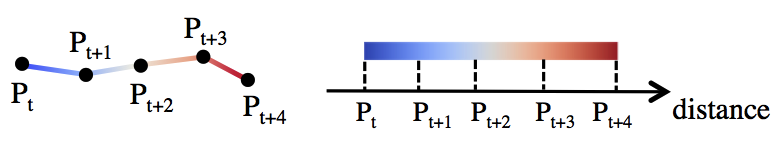
2.2.2 Distance between nuclear center and embryo center

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1. Results of connecting a cell nuclear center to a embryo center

To show a phenotypic characteristic of the distance between an embryo center and a cell nuclear center, we connected them by a black line.

2.2.3 Distance of nuclear movement

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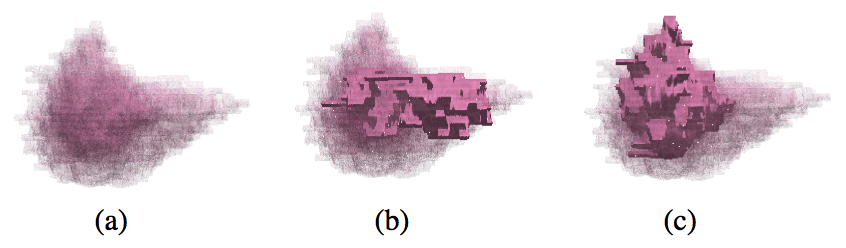
1. Cell nucleus migration distance. The colors of the line segments were colored with a divergence chromaticity diagram.

In order to show the phenotypic characteristics of cell nucleus migration distance, we visualized the centroid of the cell nucleus for the time step in which the feature appears and connected it with a line. Pt in Figure 4 calculates the distance between the position points of the cell nucleus at the time step t and color the line corresponding to the distance from the starting point with the diverging color map[4]. It means that the cell nucleus moves in the direction from blue to red as time goes on.

# Experimental result

In order to show the usefulness of the proposed method, the results using the method of Chapter 2 and the evaluation of the two domain experts are described. We used the BDML data of nematode embryo in Section 3.1 [5], the data on the time of onset of phenotypic features, and in Section 3.2 these two data and the centroid data of the cell nucleus, the centroid data of the embryo, AP, DV, LR axis data It was used.

## Visualization of several 3D cell nucleus shapes

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When selecting the phenotype characteristic "AB cell migration distance at 2 cell stage", AB cells having that characteristic exist over 27 time steps. Figure 5 (a) shows the results of visualizing 27 cells simultaneously. Figure 5 (b) shows the cell nucleus at the 5th step, and Figure 5 (c) shows the result of selecting the cell nucleus at the 22nd step, showing that the cell nucleus at the specified time step is highlighted. Previously, as shown in Figure 5 (a), only the result of overlapping of multiple cells could be observed,評価

## 表現型特徴の可視化

Figure 6は表現型特徴「」を選択した結果である。

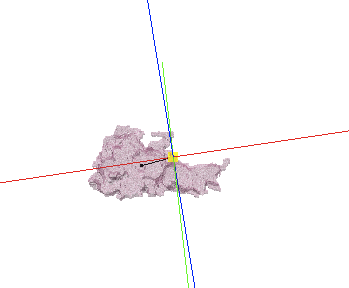
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Figure 7は表現型特徴「」を選択した結果である。

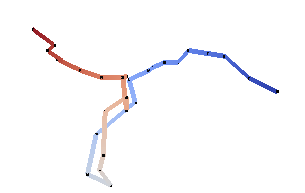
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Figure 8は表現型特徴「細胞核ABaの移動距離」を可視化した結果である。

# Conclusion

本研究では

表現型特徴間の相関を計算するために、33個の線虫胚の特徴量が計測されているが、指定した表現型特徴を持つ細胞核を表示する際、今は1つの胚の細胞核と特徴の表示しか可視化していない。将来、全ての胚の細胞核と特徴の表示を可視化することで、特徴量が増加または減少していく様子を表せるだろう。

References

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