Modeling cytokinesis of eukaryotic cells driven by the actomyosin contractile ring

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SUMMARY

A three-dimensional (3D) hydrodynamic model for cytokinesis of eukaryotic cells is developed, in which we model dynamics of actomyosins in the cell cortex, in particular, along the cytokinetic ring formed in the cortex and in the neighborhood of the cell’s division plane explicitly. Specifically, the active force actuated by the actomyosin’s activity along the cytokinetic ring is modeled by a surface force whose strength is proportional to the actomyosin concentration while the cell morphology is tracked by a phase field model. The model is then solved in 3D space and time using a finite difference method on graphic processing units. Dynamical morphological patterns of eukaryotic cells during cytokinesis are numerically simulated with the model. These simulated morphological patterns agree quantitatively with experimental observations.

1. INTRODUCTION

A cell is the fundamental unit in all living organisms because animals and plants are all made up of cells of a wide range of varieties. The study of cells is therefore an essential part of research in life sciences. Among many functions of a living cell, an important one is the cell’s ability to reproduce. Because of that, all living organisms can grow and continue their lives. Given its unique role played in living organisms, cell study has been the focus of life science research for centuries. With the advancement of experimental technologies today, more cell functions and micro-structural details that regulate the functions have been uncovered, revealing an amazingly complex, microscopic universe of a cell. Many cell functions are being investigated intensively in both theory and experiment. Cell reproduction is one of those functions.

In the cell reproductive cycle, a parent cell undergoes a sequence of intracellular transformations and eventually divides into two or more offspring cells. For prokaryotic cells, the cell proliferation process is called binary division or binary fission. For eukaryotic cells, it is called cell mitotic process or mitosis. The late stage of the cell mitotic process for eukaryotic cells, after the nucleus has been dissolved and chromosomes have been fully separated, is called cytokinesis.

Despite extensive studies on cells over the years, many important mechanisms in living cells remain to be resolved in order to fully understand how a tiny cell works. It has been acknowledged...
that cell division of eukaryotes is determined by many interacting and highly coordinated mechanisms. Any single step goes wrong in a cell cycle may result in a catastrophe or failure, which may then lead to an unwelcome consequence, for instance a cancer or other undesirable cell disfunctions. Thus, a detailed understanding on mitosis of eukaryotes, in particular, cytokinesis is essential to understand many diseases associated with this cell type. For more details about eukaryotic cell’s mitosis, readers are referred to the insightful review article on this topic in [1]. Readers can also find comprehensive review materials for cytokinesis of animal cells in [2, 3] and for cytokinesis of bacteria in [4]. In addition, some works related to mechanical properties of cells during cytokinesis such as material properties of cells and sources of stresses can be found in [5, 6]. The study published in [7] discussed the molecular requirements for cytokinesis, and the work in [8] addressed recent advances in the mechanism of cytokinesis in animal, yeast, and plant cells.

Experimental observations have provide us with a basic phase diagram of cell mitosis (Figure 1). For eukaryotic cells, at the beginning of the mitotic process, the parent cell first duplicates its genetic substances and then forms a mitotic spindle consisting of microtubules [9]. Through a cascade of signaling processes [10], the actin and myosin molecules undergo a self-assembly process to remodel the cell cortex, an intercellular layer rich in actin-filaments and myosin molecules located immediately adjacent to the cell membrane [11]. In sync with the elongation of the mitotic spindle, more actin and myosin molecules ascend to a ring like region in a plane roughly orthogonal to the axis of the mitotic spindle to form the cytokinetic ring or contractile ring in the plane transverse to the axis of the spindle. The plane is called the cleavage plane or division plane [12]. As more actomyosin molecules are accumulated along the cytokinetic ring, a contracting force is generated, which points inward toward the axis of the spindle [11]. The contracting force pushes the membrane inward to create what is known as the cleavage furrow on the membrane [6]. The localized activation of the small GTPase Rho family of proteins at the cell division plane controls the position of the contractile ring [13]. When Rho is specifically activated at the division plane within the cortex, it promotes actin polymerization and myosin-2 activation via Rho effector proteins. Rho-GTP promotes actin filament assembly and myosin-2 assembly [14]. The contractile ring is a dynamic structure within the cortex, in which F-actin and myosin-2 are continuously assembled and disassembled to maintain a roughly constant actomyosin molecular concentration as well as a contracting force to squeeze the cell along the contractile ring. For eukaryotic cells, the positioning of contractile ring and cleavage furrow is regulated by distribution of long astral microtubules [15]. Additional evidence has shown that the cell geometry can influence the position of the cell division plane [16] and ultimately affect the morphology of the offspring cells.

With the vast amount of data from experimental observations, theorists have been trying to come up with testable hypothesis and models to decipher underlying mechanisms that control the mitotic process. In [17], Akiyama et al. proposed a mathematical model for cell cleavage for the sea urchin by considering chemotactic motion of the centrosomes. In [18], Poirier et al. developed a mechanical cell division model by a level-set approach, highlighting the furrow thinning trajectories. In [19], Rejniak et al. formulated an immersed boundary approach for modeling cell division focusing primarily on the mechanical aspect of cell division, which has been extended by [20] to study a single axisymmetric cell growth and division. However, either in the immersed boundary or level-set approach, dynamics of actomyosin were not considered explicitly, instead artificial proxy forces

were employed whose origins were unknown. In [21], Turlier et al. proposed a mechanical model for cytokinesis, providing a physical explanation on the independence of the duration of cytokinesis on the cell size in embryos. In [22, 23], the authors model the contractile ring induced by active forces in the cell cortex. However, these models did not couple the dynamics of cell membrane to the underlying cortex or cytoplasmic dynamics in full three-dimension (3D). Although they can predict the contractile ring dynamics, they cannot do the stress or forces in the mother cell, the flow field of cytoplasm nor the nucleus dynamics. Given the importance of cell mitosis, especially, cytokinesis, it is the time to develop a whole cell model in 3D space and time to study mechanical properties of cells during their cytokinesis. First of all, the stress and force distributions in the mother cell during its cytokinesis are instrumental to determine mechanical properties of the cell. In addition, the coupling between the actomyosin and the cell membrane is essential for cytokinesis. Thus, an artificial proxy force seems to be too simple and too naive to be used in a whole cell model for cytokinesis.

In this paper, we set out to develop a 3D hydrodynamic model to study the cell division process systematically by a phase field approach with a focus on cytokinesis. Phase field models have gained tremendous attention in the last few years, in particular, in the study of interfacial problems in materials science and life science where complex morphological changes need to be resolved. The advantage of the phase field approach, compared with the traditional sharp interface method, including the immersed boundary method, is that the interface is naturally embedded in the model formation such that it does not need to be tracked separately from the actual materials’ components. This can reduce the computational cost tremendously. The phase field model converges to its sharp interface limit [24] as the thickness of the interface approaches zero. For cells, the coarse-grained membrane and other interfaces within a cell do not need to be very sharp, which makes the phase field model a good choice for describing the multiphasic structure in a cell.

Our approach in modeling the cytokinetic process is to develop a mathematical model systematically treating a cell as a multiphasic complex fluid system, where the cytoskeleton, cytoplasm, cell nucleus, and extra-cellular matrix are treated as separate components of a multiphasic, complex fluid mixture. Given the complexity of a cell, a viable model can only be built step-by-step by incorporating finer mechanochemical details incrementally as more detailed cellular mechanisms are uncovered and quantitatively described. The first important step in such a modeling endeavor is therefore to build a framework to simulate the morphological change of the cell membrane in cytokinesis by highlighting the most dominant mechanism during the process. The most dominating factor that one has identified in cytokinesis is the existence of the contractile ring or the cytokinetic ring within the cortex in the neighborhood of the division plane, which is primarily consisted of F-actins and myosins (F-actin polymers inter-digitated by myosin molecules) called collectively as actomyosins in this paper, which are regulated by the Rho family of proteins. Modeling the detail of the cortex as well as the microtubule structures within the cell during cell mitosis remains our ultimate goal for building a mathematical model for the whole cell. However, the effective force that squeezes the cell during cytokinesis is the contractile force exerted by the contractile ring and the surface tension on the membrane. To highlight this mechanism in a simplistic way, we employ a proxy force in lieu of the contractile force generated by the actomyosin dynamics in the cortex in the model and assume the strength of the active force is proportional to the concentration of the actomyosins based on the experimental observation. We are fully committed to develop a more sophisticated model for the cortical layer and the contractile ring within it in the near future.

Given the complexity involved in the nucleus breaking up, migration of replicated chromosomes and reformation of offspring nuclei during cell mitosis, we employ a proxy process in the model to grossly coarse-grain this complex dynamics. In this model, we assume the nucleus has already divided, and new ones have reformed. In the next generation of models for cytokinesis, we would like to replace it by an active polymer model for the spindle formation.

The governing system of equations in the model then consists of the transport equation for each phase variable in the form of volume fractions, continuity equation, and the momentum balance equation for the multiphasic material system. The governing partial differential equations are discretized and solved using a finite difference method on graphic processing units (GPUs) in full 3D.
space and time. Numerical simulations show cytokinetic morphologies that compare well with the experimental observations qualitatively.

We organize the paper into three sections. In Section 2, we present the multi-phase hydrodynamic model for the whole cell in a phase field formulation. It is followed by a brief discussion on the numerical approximation of the governing system of equations. Finally, we present some numerical simulations and discuss the comparison with available experimental observations for cytokinesis of eukaryotes.

2. MATHEMATICAL MODEL FORMULATION

We formulate a one fluid multi-component model to study cytokinesis of an eukaryotic cell. In this model, we treat the cell, cell nucleus along with the extra cellular matrix (ECM) as a three-component fluid mixture in a gross approximation. In the following, we first introduce the notations used in the model, and then, describe its various components. Because we are modeling cytokinesis whose initial configuration is not clearly identified internally, we refer the nucleus in our model either as the cloud of chromosomes together with the necessary amount of cytoplasmic materials to be included in the new nucleus or the actual nucleus after it forms. This allows us to track chromosome dynamics in the model.

2.1. Notations

Consider a fluid mixture in domain $\Omega$ with three bulk phases: cytoplasm, nucleus and, ECM or buffer fluid, whose volume fractions are denoted by $\phi_1$, $\phi_2$, and $\phi_3$, respectively. We assume the fluid mixture is incompressible so that

$$\sum_{i=1}^{3} \phi_i = 1, \quad 0 \leq \phi_i \leq 1, \quad i = 1, 2, 3. \tag{1}$$

To illustrate the idea, we show a two-dimensional (2D) schematic cartoon in Figure 2. This is clearly shown to be a globally three phase but locally two phase model. We use $v_i, \eta_i$ to represent the velocity and viscosity for each phase, $i = 1, 2, 3$, respectively. Then, the volume averaged velocity $\bar{v}$ and viscosity $\bar{\eta}$ are given by

$$\bar{v} = \sum_{i=1}^{3} \phi_i v_i, \quad \bar{\eta} = \sum_{i=1}^{3} \phi_i \eta_i. \tag{2}$$

![Figure 2](image-url)
For interfaces defined by \( \phi_i = 1/2, i = 1, 2 \), their unit normal vectors are denoted by \( \mathbf{n}_1, \mathbf{n}_2 \), and the mean curvatures of the interfaces are denoted by \( \kappa_1, \kappa_2 \), respectively, which can be approximated [25] by

\[
\mathbf{n}_i = -\frac{\nabla \phi_i}{|\nabla \phi_i|}, \quad \kappa_i = \nabla \cdot \mathbf{n}_i \approx \frac{1}{|\nabla \phi_i|} \left( \nabla^2 \phi_i + \frac{2}{\epsilon^2} \phi_i (1 - \phi_i) (2 \phi_i - 1) \right), \quad i = 1, 2,
\]

with \( \epsilon \) representing the thickness of the interfaces in steady state. We note that \( \epsilon \) is a model parameter.

Note that \( \phi_1 \) is the volume fraction of the cytoplasm. \( \{1/2 < \phi_1 \leq 1\} \) represents the cytoplasmic region, and \( \{\phi_1 = 1/2, \phi_2 = 0\} \) (or equivalently \( \{\phi_3 = 1/2, \phi_2 = 0\} \)) represents the cell membrane surface. So, \( \mathbf{n}_1 \) is the external normal of the membrane. \( \{1/2 < \phi_2 \leq 1\} \) represents the two separated regions of nuclei, and \( \{1/2 < \phi_3 \leq 1\} \) represents the region of the buffer.

For eukaryotic cells, cytokinesis begins with the formation of the cytokinetic ring, consisting of actomyosin polymeric networks. The exact location of the cytokinetic ring is believed to be determined by the chromosome spindle during the cell mitotic process. The cytokinetic ring constricts while maintaining roughly a constant density during the final stage of the mitotic process. If the spatial distribution of the actomyosin concentration is not homogeneous, neither is the contractile ring.

In the model, we use \( \mathbf{c}_1, \mathbf{c}_2 \) to represent the position of the two centrosomes at each pole of the cell, respectively, where we assume the poles are located at the opposite end of the cell in this model. Given \( \mathbf{c}_1, \mathbf{c}_2 \), if we denote

\[
\frac{\mathbf{c}_1 + \mathbf{c}_2}{2} = (x_0, y_0, z_0) = \mathbf{x}_0, \quad \frac{\mathbf{c}_1 - \mathbf{c}_2}{2} = (x_1, y_1, z_1).
\]

the division plane is defined as follows:

\[
L = \{(x, y, z) \mid (x_1, y_1, z_1) \cdot (x - x_0, y - y_0, z - z_0) = 0\}. \tag{5}
\]

Then, the distance from any point in the cell to the division plane \( L \) can be calculated by the formula

\[
d(\mathbf{x}) = \min_{\tilde{\mathbf{x}} \in L} \|\mathbf{x} - \tilde{\mathbf{x}}\|_2. \tag{6}
\]

We next introduce the free energy for the fluid mixture system.

### 2.2. Free energies

The total thermodynamic free energy for this mixture system consists of two parts:

\[
F = F_b + F_a, \tag{7}
\]

where \( F_b \) is the free energy due to the interaction among the different phases and \( F_a \) is the free energy due to the actomyosin activity.

For the interaction among the different fluid phases, we adopt the modified Ginzburg–Landau double-well mixing free energy coupled with the conformational entropy, given by

\[
F_b = \int_{\Omega} \left\{ \gamma \left[ \sum_{i=1}^{3} \left( \frac{\epsilon}{2} \|\nabla \phi_i\|^2 + \frac{1}{\epsilon} \phi_i^2 (1 - \phi_i)^2 \right) \right] + \frac{\gamma_0}{2\epsilon} \phi_1^2 \phi_2^2 \phi_3^2 \right\} \, d\mathbf{x}, \tag{8}
\]

where \( \gamma \) is the interfacial tension, \( \gamma_0 > 0 \) is a relatively large constant to penalize the co-existence of phase \( \phi_2 \) and \( \phi_3 \) in case they become adjacent to each other, and \( \epsilon \) is a model parameter proportional to the thickness of the interface. Notice that the choice of interfacial energy is not unique, one might propose a more general case, say...
\[
F_b = \int_{\Omega} \left\{ \gamma \left[ \frac{\varepsilon}{2} \sum_{i=1}^{3} \| \nabla \phi_i \|^2 + \frac{1}{\varepsilon} \left( \phi_1^2 \phi_2^2 + \phi_1^2 \phi_3^2 \right) \right] + \frac{\gamma_0}{2\varepsilon} \phi_2^2 \phi_3^2 \right\} \, dx.
\] (9)

We test both and find that they give the same qualitative result. In the following, we present the results using (8).

For \( F_a \), we propose a chemo-attractive potential for the actomyosin towards the cytoplasm

\[
F_a = \int_{\Omega} \gamma_a \phi_a (\phi_2^2 + \phi_3^2) \, dx,
\] (10)

where \( \gamma_a \) controls chemo-attractive strength. Namely, this potential repels the actomyosin from the buffer fluid phase and the nucleus phase. As the result, the actomyosin is attracted to the cytoplasmic phase.

We further define the chemical potentials \( \mu_i = \frac{\delta F}{\delta \phi_i}, \) \( i = 1, 2, 3 \), and \( \mu_a = \frac{\delta F}{\delta \phi_a} \) for each fluid phase and the actomyosin. Given the specific form of the free energy in (8), we list the chemical potentials as follows:

\[
\begin{align*}
\mu_1 &= \gamma \left( -\varepsilon \nabla^2 \phi_1 + \frac{2}{\varepsilon} \phi_1 (1 - \phi_1) (1 - 2\phi_1) \right), \\
\mu_2 &= \gamma \left( -\varepsilon \nabla^2 \phi_2 + \frac{2}{\varepsilon} \phi_2 (1 - \phi_2) (1 - 2\phi_2) + \frac{\gamma_0}{\varepsilon} \phi_2 \phi_3^2 + 2\gamma_a \phi_a \phi_2 \right), \\
\mu_3 &= \gamma \left( -\varepsilon \nabla^2 \phi_3 + \frac{2}{\varepsilon} \phi_3 (1 - \phi_3) (1 - 2\phi_3) + \frac{\gamma_0}{\varepsilon} \phi_2^2 \phi_3 + 2\gamma_a \phi_a \phi_3 \right), \\
\mu_a &= \gamma_a (\phi_2^2 + \phi_3^2).
\end{align*}
\] (11)

2.3. Transport equations for the phase variables

The transport equation for the volume fraction or the phase variable of each phase is formulated as follows:

\[
\partial_t \phi_i + \nabla \cdot (\mathbf{v} \phi_i) = \nabla \cdot \left( \sum_{j=1}^{3} \alpha_{ij} \nabla \mu_j \right) + g_i, \quad i = 1, 2, 3,
\] (12)

where \( (\alpha_{ij}) \) is the mobility matrix and \( g_i \) is the reactive term for phase \( i \). Note that the volume fractions add up to 1: \( \sum_{i=1}^{3} \phi_i = 1 \) for incompressible mixtures. This along with the Onsager reciprocal relation implies that

\[
\sum_{j=1}^{3} \alpha_{ij} = 0, \quad \alpha_{ij} = \alpha_{ji}.
\] (13)

The off-diagonal mobility coefficients can be obtained from the diagonal coefficients uniquely

\[
\alpha_{12} = \frac{1}{2} (\alpha_{33} - \alpha_{11} - \alpha_{22}), \quad \alpha_{13} = \frac{1}{2} (\alpha_{22} - \alpha_{11} - \alpha_{33}), \quad \alpha_{23} = \frac{1}{2} (\alpha_{11} - \alpha_{22} - \alpha_{33}).
\] (14)

In this model, we assume the diagonal motility parameters have the following forms:

\[
\alpha_{ii} = \lambda \phi_i (1 - \phi_i), \quad i = 1, 2, 3,
\] (15)

with \( \lambda \) represents the strength of the motility parameter. This choice of mobility coefficients renders the transport equations for the volume fractions the singular Cahn–Hilliard type.

It follows from the incompressibility condition that

\[
\sum_{i=1}^{3} g_i = 0.
\] (16)
In the early stage of cell mitosis, the parent cell increases in cytoplasmic and organelle volume (the G1 phase) as well as increases in genetic materials (the G2 phase) right before the replication during the S phase. This involves the change of cell size and shape. This process can be modeled phenomenologically by the following reactive kinetics:

\[
\begin{align*}
    g_1 &= c_1 \phi_1 \phi_3 - c_2 \phi_1 \phi_2, \\
    g_2 &= c_2 \phi_1 \phi_2, \\
    g_3 &= -c_1 \phi_1 \phi_3.
\end{align*}
\] (17)

In this paper, we focus on dynamics of cytokinesis exclusively. So, we assume the G1 and G2 phase have already completed, that is, the cytoplasm and genetic substance have already been doubled, by choosing \( c_1 = c_2 = 0 \). From now on, we assume the volume of the cell will not go through any changes, that is, the total volume is conserved during cytokinesis.

### 2.4. Approximation of chromosome dynamics

We approximate chromosome dynamics during the mitotic process using a simplified strategy bypassing the delicate details about chromosome splitting, microtubule spindle formation, and the reformation of offspring nuclei. Because chromosome dynamics during the mitotic process before the reformation of offspring nuclei is such a complex process, its modeling involves delicate local dynamics and detailed chromosome structures, which warrant a whole new set of studies. We will have it added incrementally in our systematic framework in the future as our modeling endeavor progresses. However, in this paper, we stay focused on the cytokinetic process, in which the membrane of the parent nucleus has already been broken and chromosomes are well-separated near the polarized centrosomes. At the onset of cytokinetic process, the chromosomes are not yet bounded by nucleus walls. But soon after, the offspring nuclei are about to be reformed. Technically, we use phase \( \phi_2 = 1 \) to represent the offspring nuclei as well as the material volumes occupied by the chromosomes together with the necessary cytoplasmic materials to be wrapped in the nuclei after they form. We therefore refer to the chromosome and its neighboring materials to be included in the new nucleus the chromosome cloud.

### 2.5. Transport equation for the actomyosin concentration

For eukaryotic cells, cytokinesis begins with formation of the cytokinetic ring, consisting of actomyosin polymers. The cytokinetic ring constricts while maintaining roughly a constant density during cytokinesis, which is accomplished by a constant remodeling process. This remodeling process is characterized by polymerization of F-actins near the membrane and depolymerization in the cytoplasm.

In this paper, we denote the concentration of actomyosins by \( \phi_a \). We propose that actomyosins are convected and diffused near the cell membrane due to the gradient of chemical potential with a mobility proportional to its concentration. Thus, the transport equation for \( \phi_a \) is proposed as follows:

\[
\frac{\partial \phi_a}{\partial t} + \nabla \cdot (\mathbf{v} \phi_1 \phi_3 \phi_a) = \nabla \cdot (\lambda_4 \nabla \mu_a) + c_a \delta(x, x_0) \phi_1 \phi_3 (\phi_{a0} - \phi_a) - c_b \phi_a,
\] (18)

where \( \lambda_4 \) is the motility parameter for actomyosin and the last two terms are the reactive terms, describing polymerization kinetics near the membrane and depolymerization kinetics in the cytoplasm for actomyosins. To describe various transport effects, we propose the motility parameter as follows:

\[
\lambda_4 = \lambda_a \phi_1 \phi_3 S(\phi_a (\phi_{a0} - \phi_a)),
\] (19)

where \( \lambda_a \) is the motility strength parameter, \( \phi_1 \phi_3 \) is to restrict the diffusion near the cell membrane, \( S(x) \) is the smoothed function, such that \( S(x) = \max(x, 0) \). Here, \( \phi_a (\phi_{a0} - \phi_a) \) is due to the jamming effect (i.e., when the concentration of actomyosins reaches a maximum level \( \phi_{a0} \), no actomyosin transport can take place in the cortex and the maximal transport is achieved at a moderate...
value of actomyosin concentration.). In this model, the cortex is limited to the region where $\phi_a > 0$. The domain of the cortex is determined by the nonzero value of $\phi_a$, which depends strongly on the initial condition. Reactive dynamics in this model are implemented by the second and third terms on the right-hand side in the equation, respectively, where $\delta(x, x_0)$ is a smoothed-delta function. It emphasizes the enhanced polymerization at the cytokinetic ring during cytokinesis. In the numerical study, we use

$$
\delta(x, x_0) = \frac{1}{\sigma \sqrt{2\pi}} e^{-\frac{(x-x_0)^2}{2\sigma^2}}, \quad S(x) = \begin{cases} 
\frac{\varepsilon}{2} (1 + \tanh \frac{x-0.5\varepsilon}{0.01\varepsilon}), & 0 < x < \varepsilon \\
0, & x \geq \varepsilon \end{cases}
$$

(20)

where $d(x)$ is the distance function to the cytokinetic ring centered at $x_0$. This factor $\delta(x_0)\phi_1\phi_3$ for actomyosin remodeling represents the preference of actomyosins in the cytokinetic ring on the division plane near the cell membrane. The term $(\phi_a0 - \phi_a)$ provides a mechanism for actomyosin to grow with a maximum threshold value $\phi_a0$. The two parameters $c_a$ and $c_b$ represent the strength of polymerization and depolymerization process of actomyosins, respectively. The decay rate $c_b$ is assumed a constant in this paper.

2.6. Mass and momentum transport equation

In this model, we assume the fluid mixture is incompressible and very viscous. So, the mass and momentum conservation is given respectively by the Stokes equation and the divergence free condition:

$$
\begin{align*}
-\nabla p + \nabla \cdot (2\eta \mathbf{D}) + \mathbf{F}_e &= 0, \\
\nabla \cdot \mathbf{v} &= 0,
\end{align*}
$$

(21)

with $\eta$ the volume averaged viscosity defined in (2), and $\mathbf{F}_e$ the interfacial force,

$$
\mathbf{F}_e = \mathbf{F}_s + \mathbf{F}_c,
$$

(22)

where $\mathbf{F}_s$ represents the interfacial force due to material’s inhomogeneity and $\mathbf{F}_c$ represents the contractile force induced by actomyosin activities in the cortex, given by

$$
\mathbf{F}_s = \sum_{i=1}^{3} \mu_i \nabla \phi_i,
$$

(23)

$$
\mathbf{F}_c = -4\phi_1\phi_3\gamma d1 \frac{\phi_a}{\phi_a0} \kappa_1 \phi_1 \mathbf{n}_1,
$$

(24)

where $\gamma d1$ controls the strength of the actomyosin induced contractile force, and $4\phi_1\phi_3$ confines the contractile force to the cell membrane. We note there we assume this contractile force is proportional to $\phi_a$ linearly for simplicity. More complex dependence of the contractile fore on myosin and actin concentration [26, 27] would be thoroughly studied in our later research.

2.7. Boundary conditions

We put the cell undergoing mitosis in a large enough box and use periodic boundary conditions in both the x and z direction. In the y direction, we propose the no-flux boundary condition for the phase variables, that is, if we denote $\mathbf{n}$ the unit normal at the boundary in the y direction,

$$
\nabla \phi_i \cdot \mathbf{n}|_{y=0,L_y} = 0, \quad \nabla \mu_i \cdot \mathbf{n}|_{y=0,L_y} = 0, \quad \nabla \phi_a \cdot \mathbf{n}|_{y=0,L_y} = 0.
$$

(25)

For the velocity field $\mathbf{v} = (u, v, w)$, we use the no-slip boundary condition,

$$
\mathbf{v}|_{y=0,L_y} = 0.
$$

(26)
2.8. Non-dimensionalization and dimensionless governing equations

Here, we introduce a characteristic length scale \( h = 4 \times 10^{-5} \) m, time scale \( t_0 = 10s \), density scale \( \rho_0 = 1.0 \times 10^3 \) kg/m\(^3\), as well as the characteristic actomyosin concentration \( \phi_{a0} \), to non-dimensionalize the following variables:

\[
\tilde{t} = \frac{t}{t_0}, \quad \tilde{x} = \frac{x}{h}, \quad \tilde{\phi}_a = \frac{\phi_a}{\phi_{a0}},
\]

(27)

Then, the other variables and parameters are non-dimensionalized as follows:

\[
\begin{align*}
\tilde{v} &= \frac{t_0 v}{h}, \quad \tilde{p} = \frac{\rho_0 t_0^2}{\rho h^2}, \quad \frac{1}{Re_i} \frac{\eta_i t_0}{h^2 \rho_0} \tilde{\lambda}_i = \frac{\lambda_i \rho_0}{t_0}, \quad \tilde{\kappa}_j = \kappa_j h, \quad i = 1, 2, 3, \quad j = 1, 2, \\
\tilde{y} &= \frac{y}{h^2 \rho_0}, \quad \tilde{\phi}_0 = \frac{\phi_{0} h^2}{\rho_0}, \quad \tilde{c}_i = \frac{c_i}{h}, \quad i = 1, 2, \quad \tilde{\lambda}_a = \frac{\lambda_a \phi_{a0}^3}{t_0}, \\
\tilde{y}_{d1} &= \frac{y_{d1} h^2}{\rho_0}, \quad \tilde{c}_a = \frac{c_{a0} t_0}{h}, \quad \tilde{c}_b = \frac{c_{b0} t_0}{h}, \quad \tilde{c}_d = \frac{c_d t_0}{h}, \quad \tilde{\sigma} = \frac{\sigma}{h}, \quad \tilde{\varepsilon} = \frac{\varepsilon}{h}.
\end{align*}
\]

(28)

We will drop the \( \bullet \) in the following. The governing equations in dimensionless form are summarized below:

\[
\begin{align*}
\begin{cases}
-\nabla p + \nabla \cdot \left( \sum_{i=1}^{3} \frac{1}{Re_i} \phi_i \left( \nabla v + \nabla v^T \right) \right) + \sum_{i=1}^{3} \mu_i \nabla \phi_i - 4\gamma_{d1} \phi_{a0}^2 \phi_3 \phi_a \kappa_1 c_1 &= 0, \\
\nabla \cdot v &= 0, \\
\partial_t \phi_i + \nabla \cdot (v \phi_i) &= \nabla \cdot \left( \sum_{j=1}^{3} \alpha_{ij} \nabla \mu_j \right) + g_i, \quad \alpha_{ii} = \lambda_i \phi_i (1 - \phi_i), \quad i = 1, 2, 3, \\
\partial_t \phi_a + \nabla \cdot (v \phi_1 \phi_3 \phi_a) &= \nabla \cdot (\lambda_4 \nabla \mu_a) + c_a \delta(x_0) \phi_1 \phi_3 (1 - \phi_a) - c_b \phi_a.
\end{cases}
\end{align*}
\]

(29)

3. NUMERICAL METHODS

For the coupled equations in this hydrodynamic model, we use extrapolation to decouple them when discretizing in time. That is, for each time step, we solve the momentum equation first using the extrapolated value for various other components. Then, with the updated velocity, we solve the transport equations for the volume fractions and the actomyosin concentration one by one. We note that, in the following, any variable with an overline (\( \bar{v}^{n+1} \)) represents a second-order extrapolation from the \( n \)th and the \((n-1)\)th step, for instance, \( \bar{v}^{n+1} = 2v^n - v^{n-1} \).

3.1. Numerical schemes

The numerical scheme is summarized here. Give the initial profile \( (\phi_1^0, \phi_2^0, \phi_3^0, \phi_a^0, \phi^0, s^0, p^0 = 0) \), and for simplicity of notations, assume \( \phi_i^{-1} = \phi_i^0, \phi_2^{-1} = \phi_2^0, \phi_3^{-1} = \phi_3^0, \phi_a^{-1} = \phi_a^0, \phi^{-1} = \phi^0, s^{-1} = s^0, \) and \( p^{-1} = p^0 \). After having calculated \( (\phi_1^n, \phi_2^n, \phi_3^n, \phi_a^n, \phi^n, s^n, p^n) \), \( n \geq 1 \), we obtain \( (\phi_1^{n+1}, \phi_2^{n+1}, \phi_3^{n+1}, \phi_a^{n+1}, \phi^{n+1}, s^{n+1}, p^{n+1}) \) by the following steps:

1. Predict \( u^{n+1} \):

\[
\begin{align*}
\begin{cases}
C \left( u^{n+1} - \bar{u}^{n+1} \right) + \frac{1}{Re_a} \nabla s^n + \nabla p^n - \frac{1}{Re_a} \nabla^2 u^{n+1} = \\
\nabla \cdot \left( \frac{1}{Re^n + 1} \left( \nabla \phi^{n+1} + \nabla \phi^{n+1}^T \right) \right) + \bar{F}_e^{n+1} + \frac{1}{Re_a} \nabla^2 \phi^{n+1},
\end{cases}
\end{align*}
\]

(30)

\[ u^{n+1}|_{y=0,L_y} = 0, \]

where \( C \) is a stabilizing term [28] (chosen as \( C = 1 \) in this paper), and \( \frac{1}{Re^n + 1} \) is the volume-averaged Reynolds number, \( Re_a \) is the maximum Reynolds number, that is,
Figure 3. Variable locations on the three-dimensional staggered grid.

Figure 4. Two-dimensional schematic of mapping from graphic processing unit threads to mesh elements. This figure shows a two-dimensional schematic on how each thread in graphic processing unit implementation maps into a respective mesh element. Here, we have 16 \times 16 uniform mesh and claim 4 \times 4 blocks in a grid, where each block contains four threads.

\[
\frac{1}{Re_a} = \min \left( \frac{1}{Re_1}, \frac{1}{Re_2}, \frac{1}{Re_3} \right), \quad \frac{1}{Re^{n+1}} = \sum_{i=1}^{3} \frac{1}{Re_i} \phi_i^{n+1},
\]

(31)

with \(Re_i, i = 1, 2, 3,\) are the Reynolds number for the cytoplasm, nucleus, and ECM, respectively.

2. Project \(u^{n+1}:\)

\[
\begin{cases} 
-\Delta \psi^{n+1} = \nabla \cdot u^{n+1}, \\
\frac{\partial \psi^{n+1}}{\partial n}|_{y=0, L_y} = 0.
\end{cases}
\]

(32)

3. Update \((v^{n+1}, s^{n+1}, p^{n+1}):\)

\[
\begin{align*}
   v^{n+1} &= u^{n+1} + \nabla \psi^{n+1}, \\
   s^{n+1} &= s^n - \nabla \cdot u^{n+1}, \\
   p^{n+1} &= p^n - C \psi^n + 1 + \frac{1}{Re_a} s^{n+1}.
\end{align*}
\]

(33)

4. Update \((\phi_2^{n+1}, \phi_3^{n+1}):\)

\[
\begin{cases} 
\frac{3\phi_i^{n+1} - 4\phi_i^n + \phi_i^{n-1}}{2\Delta t} + \nabla \cdot \left( v^{n+1} \phi_i^{n+1} \right) = \nabla \cdot \left[ \sum_{j=2}^{3} \left( \omega_{ij}^{n+1} \nabla \phi_j^{n+1} + \beta_{ij}^{n+1} \nabla^2 \phi_j^{n+1} \right) \right], \\
\nabla \psi^{n+1} \cdot n = 0, \quad \nabla^2 \phi_i^{n+1} \cdot n = 0, \quad i = 2, 3.
\end{cases}
\]

(34)
Table I. Dimensional parameters.

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
<th>Value</th>
<th>Unit</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \eta_1, \eta_3 )</td>
<td>Dynamic viscosity of cytoplasm and ECM</td>
<td>( 10^2 )</td>
<td>Pa \cdot s</td>
<td>[18]</td>
</tr>
<tr>
<td>( \eta_2 )</td>
<td>Dynamics viscosity of nucleus</td>
<td>( 2 \times 10^2 )</td>
<td>Pa \cdot s</td>
<td>Approximation</td>
</tr>
<tr>
<td>( \gamma_0 )</td>
<td>Surface tension strength</td>
<td>( 5.0 \times 10^{-5} )</td>
<td>N/m</td>
<td>[31]</td>
</tr>
<tr>
<td>( \gamma_0 )</td>
<td>Strength for hard core interaction</td>
<td>( 2.5 \times 10^{-8} )</td>
<td>m^2/s^2</td>
<td>Approximation</td>
</tr>
<tr>
<td>( c_a )</td>
<td>Assembly rate of actomyosin</td>
<td>0.1</td>
<td>s^{-1}</td>
<td>[32]</td>
</tr>
<tr>
<td>( c_b )</td>
<td>Disassembly rate of actomyosin</td>
<td>0.2</td>
<td>s^{-1}</td>
<td>[32]</td>
</tr>
<tr>
<td>( \lambda )</td>
<td>Motility parameter for each component</td>
<td>( 2 \times 10^{-15} )</td>
<td>k g^{-1} m^3 s^{-1}</td>
<td></td>
</tr>
<tr>
<td>( \lambda_a )</td>
<td>Motility parameter for actomyosin</td>
<td>( 1.64 \times 10^3 )</td>
<td>k g^{-3} m^9 s^{-2}</td>
<td></td>
</tr>
<tr>
<td>( \gamma_{d1} )</td>
<td>Stimulating strength for cytokinesis</td>
<td>( 7.5 \times 10^{-9} )</td>
<td>k g m^{-2} s^{-2}</td>
<td></td>
</tr>
</tbody>
</table>

ECM, extra cellular matrix.

Figure 5. Three-dimensional view of cell morphology at different stages of cytokinesis. The pink surface shows the cell membrane, and the yellow spheres show the nucleus. The parent cell splits into two offspring cells. After the splitting, the offspring cells round up under the influence of surface tension. (a) The morphology of the parent cell at the onset of cytokinesis. (b–d) The morphology of the parent cell during cytokinesis. (e) The morphology of the dividing cell near the end of cytokinesis. (f) The morphology of the two newly created offspring cells at the end of cytokinesis.

where \( \omega_{ij} \) and \( \beta_{ij} \) are functions of \( \phi_i, \phi_j \) obtained from (12), whose specific forms are omitted here.

5. Update \( \phi_i^{n+1} \):

\[
\phi_i^{n+1} = 1 - \phi_2^{n+1} - \phi_3^{n+1}. \tag{35}
\]

6. Update \( \phi_a^{n+1} \):

\[
\begin{align*}
\phi_a^{(1)} &= \phi_a^n + \Delta t \left( \frac{L}{2} \left( \frac{\phi_n}{\phi_a}, \frac{\phi_n}{\phi_a} \right) + c_a \delta(\mathbf{x}_0) \phi_1^{n+1} \phi_3^{n+1} \left( 1 - \phi_a^n \right) - c_b \phi_a^n \right), \\
\phi_a^{(2)} &= \frac{3}{4} \phi_a^n + \frac{1}{4} \phi_a^{(1)} + \frac{1}{4} \Delta t \left( \frac{L}{2} \left( \phi_a^{(1)}, \frac{\phi_n}{\phi_a^{(1)}} \right) + c_a \delta(\mathbf{x}_0) \phi_1^{n+1} \phi_3^{n+1} \left( 1 - \phi_a^{(1)} \right) - c_b \phi_a^{(1)} \right), \\
\phi_a^{n+1} &= \frac{1}{3} \phi_a^n + \frac{2}{3} \phi_a^{(2)} + \frac{1}{3} \Delta t \left( \frac{L}{2} \left( \phi_a^{(2)}, \phi_a^{n+1} \phi_a^{n+1} \frac{\phi_n}{\phi_a^{n+1}} \right) + c_a \delta(\mathbf{x}_0) \phi_1^{n+1} \phi_3^{n+1} \left( 1 - \phi_a^{(2)} \right) - c_b \phi_a^{(2)} \right).
\end{align*}
\]
where $L(\phi_a, \mathbf{v}_a) \approx -\nabla \cdot (\mathbf{v}_a \phi_a)$ is the advection term evaluated by the third-order WENO scheme [29], with

\[
\begin{align*}
\mathbf{v}^n_a &= \phi_1^n \phi_3^n (\mathbf{v}^n - \lambda_a (1 - \phi_2^n) (\gamma_a \phi_2^n \nabla \phi_2^n + \gamma_{a3} \phi_3^n \nabla \phi_3^n)), \\
\mathbf{v}^{n+1}_a &= \phi_1^{n+1} \phi_3^{n+1} (\mathbf{v}^{n+1} - \lambda_a (1 - \phi_2^{n+1}) (\gamma_a \phi_2^{n+1} \nabla \phi_2^{n+1} + \gamma_{a3} \phi_3^{n+1} \nabla \phi_3^{n+1})).
\end{align*}
\]  

(37)
Figure 8. A comparison between experimental observations and our numerical simulations: (a) Purple urchin zygotes during first mitosis, fixed and stained for DNA (green) and phosphorylated myosin II (magenta; single confocal sections). Top row: interphase, metaphase, and anaphase. Bottom row: early, middle, and late telophase from [34]. (b) Numerical predictions of cell mitotic dynamics: here, red curve represents cell membrane, green curve represents the nucleus membrane, and purple curve represents the contour of the actomyosin distribution.

Remark 1
When solving the Stokes equation, we use the Gauge–Uzawa splitting strategy [30]. If we add Equations (30), (32), and (33), the scheme is

\[
C(v^{n+1} - v^n) + \nabla p^{n+1} + \frac{1}{Re_d} \Delta v^{n+1} = \nabla \left( \frac{1}{Re^{n+1}} \left( \nabla v^{n+1} + \nabla v^{n+1}^T \right) \right) + F_e^{n+1} - \frac{1}{Re_d} \nabla^2 v^{n+1},
\]

which is second-order accuracy in time. In (30), \( s^n, s^{n+1} \) are the Gauge variables [30] introduced in the scheme in order to solve the Stokes equation. Numerically, to avoid the singularity, we compute the unit normal by
\[ \mathbf{n}_i \approx -\frac{\nabla \phi_i}{\sqrt{\|\nabla \phi_i\|^2 + \varepsilon_0}}, \quad i = 1, 2, \quad (39) \]

where we choose \( \varepsilon_0 = 10^{-4} \).

3.2. Spatial discretization and graphic processing unit implementation

For the spatial operators in the scheme, we discretize them using second-order central finite difference method over a uniform spatial grid, where the velocity field is discretized at the center of the mesh surface, and pressure \( p \), phase variables \( \phi_1, \phi_2, \phi_3 \) and actomyosin \( \phi_a \) are discretized at the center, as shown in Figure 3. The boundary conditions are handled by ghost cells.

The fully discretized schemes are implemented on GPUs (graphics processing units) in 3D space for high-performance computing. To better utilize the performance of GPUs, we store all variables in the global memory and store all parameters and mesh information (which do not change the simulation) in the constant memory, such that it reduces the latency of data access.

One advantage of using GPUs is their virtual allocations of processors (we can claim as many threads as we desire, even if it is beyond the existing number of multiprocessors in the physical device). Therefore, in our implementation, we allocate as many processors as the degrees of freedom. A schematic is shown in Figure 4, where we have \( 16 \times 16 \) uniform mesh, so we claim \( 4 \times 4 \) processors per thread.

Figure 9. Two-dimensional and three-dimensional view of actomyosin concentration at various stages of cytokinesis. (a–f) 3D view of the contractile ring at five different time slots; (g–j) two-dimensional view of contractile ring at \( x = 0.75 \) is shown with respect to the first four selected time slots.
blocks with each block containing four threads. In this situation, there is a one-to-one map from the thread to the mesh point, such that each thread calculates the respective component for the matrix vector multiplication. This strategy turns out to be very effective.

4. NUMERICAL RESULTS AND DISCUSSION

We use the numerical solver developed based on the scheme described in the previous section to simulate cytokinesis of eukaryotic cells in 3D space and time. The computational domain is set at $[0, 1.5] \times [0, 1] \times [0, 1]$. The initial cell radius is set at 0.3, and nucleus radius is 0.08, which are $15 \mu m$ and $0.4 \mu m$ in dimensional form, respectively. The parameters used in this model are summarized in Table I, which are obtained either from the literature or based on our best guesses. In addition, we set the model parameters $\varepsilon = \varepsilon_d = 0.01$ h and $\sigma = 0.04$ h. Unless stated otherwise, we will use this set of parameters in the simulations presented in the succeeding text.

We present a 3D numerical result about cytokinesis of an eukaryotic cell in Figure 5 in a series of selected time slots, highlighting representative morphological changes of the cell at different stages. The simulation starts when the cleavage furrow near the division plane starts forming (shown in Figure 5(a)). In Figure 5(c,d), a bridge forms between the two departing offspring cells. The abscission that physically splits the parent cell into two offspring cells takes place after $t = 240$ s. In Figure 5(f), we observe the two newly generated offspring cells reshape into the rounded morphology under the influence of surface tension in their own membranes. This numerical simulation in full 3D uses the hydrodynamic phase field model accounting for actomyosin dynamics without assuming axisymmetry in the cell. This sets the study apart from the available ones.

![Figure 10. Hydrodynamic quantities during cytokinesis.](image)

Figure 10. Hydrodynamic quantities during cytokinesis. This figure shows the hydrodynamic stress $\tau = 2\eta\mathbf{D}$ and cytoplasm velocity field $\phi_1\mathbf{v}$, at a few selected time slots. (a–b) three-dimensional and zoomed view of the stress tensor $\tau$ at $t = 120$ s is shown as ellipsoids; the stress is large in the cytokinetic ring. The unit is $Pa$. As the membrane retreat at the cytokinetic ring, it drags the fluid to the axis of the spindle in the neighborhood of the division plane while pushing the cytoplasmic fluid and fluid in the ECM near the poles outward. (c–e) Two-dimensional slices ($z = 0.5$) of cytosol velocity field $\phi_1\mathbf{v}$ at time $t = 86, 120, 240$ s, respectively, are shown, with unit $\mu m/s$.
This simulation compares well quantitatively with the experimental observation from [33] on dynamics of cytokinetic ring contraction, as shown in Figure 6(a). The distance between two poles of the splitting cell \( |c_1 - c_2| \) is also shown in Figure 6(b).

To better visualize the morphological change of the cell membrane as well as the nucleus during the cell mitotic process, a series of 2D cross-sectional slices at \( x = 0.5 \) are plotted in Figure 7. In particular, the dynamics of nuclei in the offspring cells are shown explicitly.

A comparison with experimental observations of cytokinetic processes with actomyosin distribution is shown in Figure 8. Our numerical results agree qualitatively well with the morphogenetic patterns obtained from the experimental observations shown in Figure 8(a). In particular, the model prediction of actomyosin dynamics in the contractile ring shows qualitatively agreement as well.

The new feature in the hydrodynamic model lies in the integration of actomyosin dynamics. It enables us to show the accumulation of actomyosins along the cytokinetic ring during cytokinesis as well as the decisive role played by the active cytoskeletal structure. Figure 9 depicts the actomyosin concentration at various stages of cell division, in which the 2D slices show the actomyosin concentration in colored maps. The comparison shows that actomyosins are indeed concentrated in the cytokinetic ring and play the instrumental role in forcing and later abscising the membrane to create two offspring cells. In Figure 9, the cytokinetic ring rich in actomyosins is visualized in 3D and its cross-section in 2D in a time series during the cytokinetic process. Specifically, it shows the ring widens and eventually splits into two separate islands inside each offspring cell after cytokinesis. The 2D plots show the projection of the cytokinetic ring onto the division plane.

We note that the advantage of the 3D hydrodynamic model is its capability to couple the interior cytoplasmic fluid flow with the ECM or the ambient fluid through the cell membrane and to predict important hydrodynamic quantities such as stress tensors, normal stress differences, forces, and the

![Figure 11](image_url)

**Figure 11.** The external force distribution. This figure shows the interfacial force (Equation (22)) distributions during cytokinesis. The unit is \( \mu N \). (a–c) shows two-dimensional slice \( (z = 0.5) \) of the interfacial force \( F_s \) at time \( t = 50, 100, \) and 150 s, respectively. The force smooths out the cell surface; (d–f) shows two-dimensional slice \( (z = 0.5) \) of the contractile force \( F_c \) at time \( t = 50, 100 \) and 150 s, respectively. In particular, in (g–j) at the division plane \( (x = 0.75) \), the contractile force \( F_c \) and surface tension force \( F_s \) at time 50 and 100 s are shown, respectively.

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hydrostatic pressure throughout the domain during the cellular morphological transformation. In Figure 10, the detail of the viscous stress $2\eta\mathbf{D}$, average velocity $\mathbf{v}$ at different times, is depicted, respectively. The stress tensor at $(\mathbf{x}, t)$ is visualized as a 3D ellipsoidal object centered at $\mathbf{x}$, whose semiaxes signify the length of the three eigenvalues of the stress tensor. From Figure 10(b), a zoomed view of the stress tensor is shown. The stress is highly inhomogeneous in space near the contractile ring on the division plane, which correlates well with the velocity field shown in Figure 10(c–e), as the cytokinetic ring of the cell is contracting. The velocity field correlates well with the motion of the cell components during this dynamical process.

In addition, the distribution of the active force due to actomyosin activities and the surface tension force are shown in Figure 11, respectively. In Figure 11(d–f), the active forces are mainly distributed in the cortex with much higher values on the division plane than in other places, constricting the cell membrane towards the long axis of the cell (or the axis of the spindle). This is clearly shown in the 2D view of the active force in Figure 11(g–h). As it should be, the active force is distributed on the interfaces near the cytokinetic ring: Whereas surface tension is more evenly distributed along the interfaces, aiming to smooth them out. These two forces oppose to each other on the interface during the cytokinetic process. It is the competition between the surface tension and the active force on the cytokinetic ring that ultimately contributes to the complete of cytokinesis. Figure 11(a–c),(i–j) depicts the surface tension forces respectively from two cross-sections.

5. CONCLUSIONS

In this paper, we develop a multi-phase complex fluid model to study cytokinesis of an eukaryotic cell. Actomyosin dynamics in the cortex is modeled using its concentration coupled completely with hydrodynamics of the entire cell and its surrounding fluid. Dynamical morphological patterns of eukaryotic cells during cytokinesis are numerically simulated with the model. These simulated patterns agree quantitatively with experimental observations. In addition, hydrodynamic variables such as the velocity, hydrostatic pressure, extra stress, and interfacial force field during cytokinesis can be predicted in the simulations. Although some of these measurements are not yet available for cells. Nevertheless, the model is capable of providing the baseline data to be compared with experiments once they become available.

Cell mitosis is a complex process governed by many additional mechano-chemical factors that are not included in the model. Nevertheless, the new model and the accompanying 3D computational tool mark a step forward in developing a full 3D hydrodynamic model for cell mitosis in a hydrodynamically and thermodynamically consistent way. With the modeling framework and numerical tools for cell mitotic dynamics, we can further incorporate additional cellular features or add additional cellular components/microstructures to it.

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REFERENCES


