Abstract

Using simulation to discuss the deformation of cells is not only efficient, but also inexpensive. In this study, a red blood cell (RBC) model is introduced which is simple but rigorous. This RBC model has been stretched to examine its properties and its results agree well with an experiment which was conducted in 2003. Therefore, the model allows researchers to conduct studies related to deformation of RBCs or investigate properties of RBCs. Moreover, we compare the results using a coarse mesh (270 nodes) to those using a fine mesh (1230 nodes), and it indicates that this approach can imitate the properties of RBCs through a coarse mesh, which means the approach is highly efficient. Based on this RBC model, we can couple it with the computational fluid dynamics to investigate the interaction between cells and flows, as well as mimic other cells with minor modifications in the future.

Introduction

The deformation of cells has been proven related to many diseases. For example, malarial parasites can result in red blood cells with large stiffness [1]. In order to rescue, or even prevent, these diseases, it is important to understand the mechanism of the deformation of cells. Therefore, there is a type of research that is highly efficient and low cost because of the rapidly developed computer technology, especially nowadays. The human red blood cell (RBC) has a complicated structure. The shape of RBC is biconcave with a diameter of about 8.2 – 8.5 μm. In addition, the RBC membrane is composed of three layers: the glycolaxyl on the exterior, the lipid bilayer and the membrane cytoskeleton. The cytoskeleton is actually constructed by a triangular protein network and about 27000 – 45000 junction complexes [2]. The traditional RBC models need an extremely fine mesh whose number of nodes is the same as the number of junction complexes to imitate one single RBC. However, more and more coarse-grained RBC models have been created in the last decade [2,3], which can simulate a RBC using hundreds of nodes. These coarse-grained models enhance the efficiency of computing and boost many studies about RBC. Nonetheless, the validation is important for a simulation model. Dao, Lim and Suresh conducted RBC stretching experiments in 2003 which pointed out the dramatic flexibility of the RBC [4]. Since the setup of the experiments can be easily reconstructed by simulation, the experiments have been widely used to validate the numerical models. Thus, in this study, we compared our simulation results with experiments by Dao et al. to determine if the model in this study was proper to investigate the topics related to deformation and motion of cells.

Methods

There are two steps to create the red blood cell (RBC) model, meshing a membrane and calculating potential energies. First, meshing a membrane means using many particles and triangles to represent an object such as a RBC. Figure 1 shows a meshed RBC model in which the black particles are called nodes, and triangles constituted by three connected nodes are called elements. In this study, the RBC model is meshed through an open source MATLAB code by Per-Olof Persson [5].

Second, in order to mimic the properties of RBCs, four potential energies must be calculated between nodes [2,3]. The four potential energies are the bond energy $U_{\text{bond}}$, the area conservation energy $U_{\text{area}}$, the volume conservation energy $U_{\text{volume}}$, and the bending energy $U_{\text{bending}}$.

The bond energy is a two-body energy which means the energy exists between two nodes as shown in Figure 2 (a). Moreover, the area conservation energy $U_{\text{area}}$ and volume conservation energy $U_{\text{volume}}$ are the three-body energies which occur in a triangle constituted by three neighboring nodes, see Figure 2 (b). Furthermore, the bending energy $U_{\text{bending}}$ exists between two plates, or four nodes, as shown in Figure 2 (c). The position and velocity of each node can be calculated by the potential energies and, therefore, the deformation of RBCs can be simulated. This means the properties of RBCs can be captured by the model.

Conclusion

In summary, a red blood cell model (RBC) has been introduced in this study. A comparison between numerical results and experimental data proves this model can use only hundreds of nodes to express the properties of RBCs. In other words, it is definitely an efficient way to investigate the motion and deformation of RBCs. In the future, the model can be coupled with the computational fluid dynamics to investigate the interaction between blood flows and RBCs, or even other cells.

Reference

6. Parallel Utility for Modeling of Molecular Aggregation (PumMa), the Computational Biology group of the Department of Biomedical Engineering at the Eindhoven University of Technology. http://cbio.bmt.tue.nl/pumma/index.php/Main/HomePage

Results

In order to verify that the red blood cell (RBC) model and our program can deal with the deformation of RBC, a single RBC is stretched by varying external forces $F$ (see Figure 3). The setup of the simulation corresponds to the setup used in the experiments by Dao et al. in 2003 [4].

Some numerical parameters in this model correspond to the membrane Young's module $E_f = 18.9 \times 10^9$ Pa, the membrane shear module $\mu_f = 4.75 \times 10^8$ Pa, and the bending rigidity $k_b = 2.369 \times 10^{-12}$ J.

The longitudinal diameter $D_l$ and the transverse diameter $D_t$ are defined as shown in Figure 4. The numerical results compared to the experiments can be seen in Figure 5.

Figure 1. A meshed membrane. The black particles are called nodes and the triangles constituted by three connected nodes are called elements.

Figure 2. (a) A bond energy $U_{\text{bond}}$ exists between two nodes. (b) A area conservation energy $U_{\text{area}}$ and a volume conservation energy $U_{\text{volume}}$ exist in a triangle constituted by three nodes. (c) A bending energy $U_{\text{bending}}$ exists between two plate, or four nodes. The figures are from PumMa [6].

In summary, a red blood cell model (RBC) has been introduced in this study. A comparison between numerical results and experimental data proves this model can use only hundreds of nodes to express the properties of RBCs. In other words, it is definitely an efficient way to investigate the motion and deformation of RBCs. In the future, the model can be coupled with the computational fluid dynamics to investigate the interaction between blood flows and RBCs, or even other cells.

Figure 3. A sketch of stretching a red blood cell.

Figure 4. Definitions of the longitudinal diameter $D_l$ and the transverse diameter $D_t$.

Figure 5. The longitudinal diameter $D_l$ and the transverse diameter $D_t$ as a function of the external force $F$. The red circle line and the blue triangle line represent the numerical results with $N_p = 270$ and with $N_p = 1230$, respectively. The black diamonds represent the experimental data by Dao et al. [4].

Figure 5 shows that the numerical results agree well with the experimental data. The results between the coarse mesh of $N_p = 270$ and of $N_p = 1230$ do not have a significant difference, where $N_p$ is the number of nodes. It means that the mesh of $N_p = 270$ is enough to imitate the deformation of the RBC. This RBC model has an extreme performance in the time spent. The simulation with $N_p = 270$ required only about 3 minutes for one case.

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