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Investigation of membrane mechanics using spring networks: Application to red-blood-cell modelling

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ABSTRACT

In recent years a number of red-blood-cell (RBC) models have been proposed using spring networks to represent the RBC membrane. Some results predicted by these models agree well with experimental measurements. However, the suitability of these membrane models has been questioned. The RBC membrane, like a continuum membrane, is mechanically isotropic throughout its surface, but the mechanical properties of a spring network vary on the network surface and change with deformation. In this work spring-network mechanics are investigated in large deformation for the first time via an assessment of the effect of network parameters, i.e. network mesh, spring type and surface constraint. It is found that a spring network is conditionally equivalent to a continuum membrane. In addition, spring networks are employed for RBC modelling to replicate the optical tweezers test. It is found that a spring network is sufficient for modelling the RBC membrane but strain-hardening springs are required. Moreover, the deformation profile of a spring network is presented for the first time via the degree of shear. It is found that spring-network deformation approaches continuous as the mesh density increases.

1. Introduction

Blood is a suspension of cellular elements, including red blood cells (RBCs), white blood cells and platelets. RBCs dominate in terms of population with $5 \times 10^6/\text{mm}^3$ and account for 99% of all suspended elements. A healthy RBC is biconcave in shape with a diameter of 8 μm and a thickness of 2 μm. Structurally, a RBC may be considered as a liquid-core membrane-bounded capsule. The liquid, known as cytoplasm, is generally considered as an incompressible Newtonian fluid. The membrane has a dual-layer structure consisting of a plasma membrane and a cytoskeleton. The plasma membrane is a continuous layer mainly formed by a lipid bilayer while the cytoskeleton is a mesh-like elastic network. Mechanically, the plasma membrane is mainly responsible for the membrane surface incompressibility, bending and viscosity and the cytoskeleton mainly for the in-plane membrane shearing.

Due to the desire to understand microcirculation haemodynamics and RBC disorders, an increasing interest has been shown in RBC mechanics. However, an experiment-based study of RBC mechanics is usually not feasible because of the small RBC dimensions. Thus, numerical modelling emerges as a good alternative. The difficulty with RBC modelling is the accurate representation of the membrane mechanics. Currently, most membrane models are either based on continuum constitutive laws (continuum membrane models) or spring networks (discrete membrane models). A number of continuum membrane models have been proposed for the RBC membrane since the 1970s, e.g. Skalak membrane [1] and neo-Hookean membrane [2]. A continuum membrane model assumes the homogeneity of mechanical properties throughout the membrane surface. Due to the well-established theory of continuum mechanics, continuum RBC models are well developed for the study of cell mechanics [3–5], haemodynamics [6–8] and RBC disorders [9]. Discrete membrane models became popular in the late 1990s [10,11] due to their simplicity and similarity to the cytoskeleton. A number of discrete RBC models yield a good representation of the cell mechanics [12] and capture the characteristics of the cell's response in flow [13–16]. However, discrete RBC models have been criticised for their anisotropic membrane properties [17,18], i.e. spring-network properties.

The study of spring-network mechanics is well reviewed in a number of papers. Gelder [19] showed that a spring network cannot represent a continuum membrane model exactly, but a spring network can accurately represent an isotropic continuum membrane in small deformation if the spring constant is appropriately modified. Hansen et al. reviewed the mechanics of unstructured spring networks [20] and the impact of the networks' topology on their mechanical properties [21]. However, both studies were restricted to small deformation and linear-spring types. Delingette [22] proposed an unusual spring type, i.e. a bi-quadratic spring which includes tensile and angular stiffness, for spring-network simulation. This new spring type showed the great potential of spring networks for accurate 2D membrane and 3D solid simulations [23]. Omori et al. [18] performed a comparison between discrete and continuum membrane models both for 2D and 3D applications. The paper made the important conclusion that a spring network is

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mechanically anisotropic and strain-softening, and thus is not suitable for modelling strain-hardening material, e.g. the RBC membrane.

The objective of this work is to investigate spring-network mechanics, and in particular the effect of network parameters which is frequently neglected in membrane modelling using spring networks. Critically, the suitability of a spring network for RBC modelling is examined. In Section 2, the effect of the network parameters on the mechanics of planar spring networks is investigated. In this work four spring element types are employed to construct spring networks: linear, truss, neo-Hookean (NH) [24] and worm-like-chains (WLC) [11]. In Section 3, these spring networks are used to construct discrete RBC models. The models are subsequently employed to replicate the optical tweezers (OT) test. In this work, membrane fluidity (viscosity) is ignored as we are interested only in the equilibrium state of deformation. Also, the continuum constitutive laws for the continuum membrane models are not discussed in detail here; a detailed description can be found in Barthès-Biesel et al. [25].

2. Spring-network deformation and elasticity

In this section the effect of network parameters, i.e. network mesh, spring element type and surface constraint, on spring-network mechanics is investigated. Meanwhile, the network deformation is compared to deformation predicted using continuum-membrane models, i.e. membrane models created using Hooke's Law (Hooke's), Mooney–Rivlin (MR) material [25] and Skalak (SK) Law [1]. First, a planar membrane is discretised to obtain a mesh representing a spring network with the lines considered the spring elements and the nodes the hinges. Since the membrane shape has no influence on the network properties [20], a square-shaped membrane is chosen. Having obtained a spring network, the network-randomness metric [20] is introduced to measure the deviation of the network from an isotropic topology. Subsequently, the effect of the randomness and mesh density on the network elasticity is discussed. The elasticity of the network with a range of spring-element types is predicted and compared to some continuum membrane models. Finally, the effect of surface constraint is also investigated.

2.1. Construction of a 2D spring network

A square-shaped membrane is discretised using the open-source mesh generator GMSH (GNU General Public License) to obtain an unstructured triangle-based mesh. As mentioned above the mesh represents the spring network with the lines the spring elements and the nodes the frictionless hinges. The network mesh is characterised by four topology parameters [20]: the average spring element length $\overline{L}$, the average node junction functionality $\overline{\varphi}$, i.e. the average number of springs connected to each node, the standard deviation of spring length σ_L and the standard deviation of node junction functionality σ_φ, see Fig. 1. Spring lengths are non-dimensionalised by dividing by the edge length of the discretised square. Therefore, the average spring length $\overline{L}$ is a measure of mesh density of the network. σ_L is the standard deviation of the dimensionless spring length divided by $\overline{L}$, so that σ_L is independent of the mesh density. σ_L and σ_φ together are deemed the network randomness where σ_L is the length randomness and σ_φ is the junction randomness. When the network randomness is zero, i.e. $\sigma_L = 0$ and $\sigma_\varphi = 0$, the network consists of equilateral triangles, i.e. an isotropic topology. All networks employed in this work use an unstructured triangle-based mesh with high network randomness unless otherwise stated. An unstructured mesh is employed in this work for the following reasons:

1. A triangle-based mesh is the most stable topology for a spring network.
2. An isotropic mesh is not feasible for curved surfaces.
3. Among the triangle-based meshes, an unstructured mesh is the most popular in numerical simulations.
4. An unstructured mesh converges towards being isotropic as the network randomness decreases.

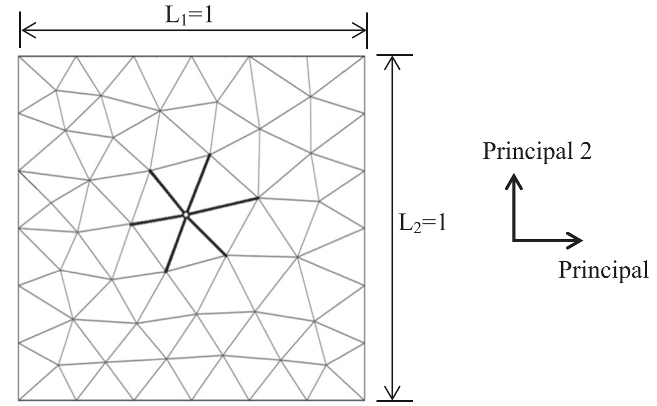

Fig. 1. A square-shaped membrane discretised with an unstructured mesh. All the element lengths are non-dimensionalised by dividing by the edge length; therefore, the square edges have a dimensionless length of one. The node (white dot) in the centre of the network has a junction functionality of six as six springs are connected to this node. For a given network the element connectivity is fixed, i.e. $\overline{\varphi}$ and σ_φ are constant, but $\overline{L}$ and σ_L vary as the network undergoes deformation. Note that in calculating $\overline{\varphi}$, the junction functionalities of the nodes on the boundary are not considered.

2.2. Computation of spring-network deformation

A spring network deforms upon external loading. This deformation is modelled by updating the nodes' position with time. The updating scheme employed is formed using the Taylor series expansion, i.e.

$$p_i(t+\Delta t) = p_i(t) + \Delta t \times p_i{}'(t) + \frac{\Delta t^2}{2} \times p_i{}''(t) + \frac{\Delta t^3}{6} \times p_i{}'''(t) + \ldots \quad (1)$$

where p refers to the position of a node, superscript ′ refers to the derivative with respect to time t, subscript i refers to principal direction 1 or 2, and Δt is the time-step. Viscous damping has to be introduced in Eq. (1) or the spring network oscillates continually. Assuming that each node is associated with a damping which eliminates the node speed, i.e. $p_i{}'(t)$, at each time step and that the high-order differential terms are neglected, Eq. (1) reduces to

$$p_i(t+\Delta t) \approx p_i(t) + \frac{\Delta t^2}{2} \times p_i{}''(t) = p_i(t) + \frac{\Delta t^2}{2} \times \frac{\sum F_{p_i(t)}}{m} = p_i(t) + \sum F_{p_i(t)} \times \Delta T \quad (2)$$

where $\sum F$ is the total force acting on the node, m is the node mass and ΔT is a constant formed by combining Δt and m, i.e. $\Delta T = (\Delta t^2)/(2\ m)$. This modified equation cannot accurately predict the transient motion of a node, but is well suited for the calculation of an equilibrium position [18] subject to a convergence tolerance, e.g. $|\sum F_{pi(t)} \times \Delta T| < 10^{-8}$.

Four spring element types are employed in this work: linear, truss, NH and WLC representing linearly-elastic springs, linearly-elastic springs with varying spring constant, strain-softening springs, and non-linear strain-hardening springs respectively defined as follows:

$$F_{linear} = -kdl \quad (3)$$

$$F_{truss} = -\frac{k}{l_o} dl \quad (4)$$