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Research paper

Computation of the effective mechanical response of biological networks accounting for large configuration changes

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ABSTRACT

The asymptotic homogenization technique is involved to derive the effective elastic response of biological membranes viewed as repetitive beam networks. Thereby, a systematic methodology is established, allowing the prediction of the overall mechanical properties of biological membranes in the nonlinear regime, reflecting the influence of the geometrical and mechanical micro-parameters of the network structure on the overall response of the equivalent continuum. Biomembranes networks are classified based on nodal connectivity, so that we analyze in this work 3, 4 and 6-connectivity networks, which are representative of most biological networks. The individual filaments of the network are described as undulated beams prone to entropic elasticity, with tensile moduli determined from their persistence length. The effective micropolar continuum evaluated as a continuum substitute of the biological network has a kinematics reflecting the discrete network deformation modes, involving a nodal displacement and a microrotation. The statics involves the classical Cauchy stress and internal moments encapsulated into couple stresses, which develop internal work in duality to microcurvatures reflecting local network undulations. The relative ratio of the characteristic bending length of the effective micropolar continuum to the unit cell size determines the relevant choice of the equivalent medium. In most cases, the Cauchy continuum is sufficient to model biomembranes. The peptidoglycan network may exhibit a re-entrant hexagonal configuration due to thermal or pressure fluctuations, for which micropolar effects become important. The homogenized responses are in good agreement with FE simulations performed over the whole network. The predictive nature of the employed homogenization technique allows the identification of a strain energy density of a hyperelastic model, for the purpose of performing structural calculations of the shape evolutions of biomembranes.

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1. Introduction

The membrane of biological cells is made of the assembly of filaments which are linked together as part of a network or are associated with the cell membrane to build a two-dimensional thin sheet. Two-dimensional biological networks may be wrapped around a cell as its wall or be attached to its plasma or nuclear membrane. Structural elements of biological cells are soft and responsible of the large deformability and easy motion of the cell, contrary to most of the engineered man made thin structural materials used in sheet industries. The mechanics of biological membranes is clearly related to the network architecture and to the entropic like elasticity of the filaments. The development of predictive nanomechanical models aiming at understanding the impact of the network architecture and micromechanical properties on the continuum scale is important, as the experimental determination of the mechanical properties of biological membranes is delicate, and the membrane anisotropy and large deformability have to be accounted for.

The experimental determination of the mechanical properties of biomembranes has raised many works in the literature since the early 1970. Various techniques have been developed in the last two decades to access the mechanical properties of cells, vesicles and biological membranes in a broad sense, which are shortly reviewed in the sequel for the red blood cells (RBC) more specifically. An overview of these techniques is presented in Kim et al. (2012). The deformability of RBC plays a crucial role in its main function, especially oxygen transport through blood circulation within the body. RBC's have the ability to withstand large deformations in order to modify their shape during their circulation trough the microvasculature. The deformability of RBC can be altered by diverse pathophysiological conditions, which in turn will modify the pathophysiology. For instance, such interactions are reflected by the fact that RBC deformability determines blood viscosity and hence blood circulation. Experimental techniques of various types have developed over the past years to measure the mechanical response of RBCs in order to better understand the correlations between these properties and RBC related diseases. We shortly review the panel of available techniques for measuring the deformability of RBCs, through the viscoelastic properties of the RBC membrane cortex structure. Elastic properties of the highly complex RBC membrane can be explained by the area expansion modulus, the shear modulus, and the bending modulus, corresponding to the three fundamental deformation modes (area expansion, shear, and bending respectively). Micropipette aspiration consists in the application of a negative pressure onto the RBC membrane using a glass micropipette of micrometric diameter (smaller by a factor 2–3 in comparison to the RBC diameter). The amount of aspiration of the RBC into the micropipette reflects the viscoelastic properties of the RBC membrane (Evans and La Celle, 1975; Shiga and Maeda, 1990; Hochmuth, 2000). Both the area expansion modulus, the shear modulus and bending modulus can be measured by this technique; their respective value was obtained as $K = 450$ nM/m (Evans and Waugh, 1977), $\mu = 9 \pm 1.7$ μN/m (Evans and Mohandas, 1984), and $B = 43.5 k_B T$. At a much lower scale, atomic force microscopy (AFM) images the topography of diverse materials at atomic or molecular scale using a cantilever with a sharp tip to probe the surface of the tested solids. The vertical motion of the tip into contact with the surface of the probed samples is monitored by photodiodes which detect small changes of the laser beam position reflected from the tip. Not only images of the RBC membrane can be obtained with high spatial resolution, but also the cytoskeleton structure can be visualized. Young's moduli of RBCs can be measured considering that the tip modulus is much higher in comparison to the Young modulus of tested sample. Optical tweezers is another technique using highly focused laser beams transferring the linear or angular momentum of light, which due to refraction at the tested surface of spherical particles (nm- and μm-sized), induces a change of linear momentum exerting trapping forces. Optical tweezers have been used in biophysics and soft matter sciences to measure forces of the order of a few pN (Ashkin, 1970; Lee and Grier, 2007); The deformability and thus mechanical properties of RBCs can be measured by optical tweezers by applying optical force to two silica beads attached to opposite sides of the membrane (Henon and Lenormand, 1999), or by stretching RBCs using two diverging laser beams from opposite directions (Guck and Ananthakrishnan, 2001).The shear modulus can then be measured from the recorded change of RBC diameter in combination with membrane models. The detection of membrane fluctuations due to thermal agitation can also be accessed by the same technique by imposing a deformation (Yoon and Kotar, 2011). Magnetic twisting cytometry applies torques, by imposing static and oscillating magnetic fields exerted on microbeads attached to the surface of the cell membrane. The stiffness and loss moduli of the membrane are determined at different frequencies from the recorded displacement of the beads. The torsional stiffness modulus does not depend on frequency and is of the order of 10^{-3} Pa/nm, and the bending and shear moduli are found respectively in the range $0.2-0.8$ pN · μm and $6-12$ μN/m (Puig-De-Morales-Marinkovic et al., 2007). Quantitative phase imaging techniques like diffraction phase microscopy have been widely used to measure the RBC deformation; they rely on the principle of laser interference to measure the dynamic membrane fluctuations at the submicron level. The shear modulus, area expansion modulus and effective viscoelastic properties of RBCs can be measured (Popescu and Ikeda, 2006; Wang and Ding, 2011). Alterations in the deformability of RBCs can further be related to the occurrence of cell disease (Kim et al., 2012). Dynamic light scattering access to the rheology of RBCs but provides poor information related to RBC deformability since the signals are collected from a large collection of cells instead from individual cells. Fourier transform light scattering is able to test individual cells in their morphology and rheology (membrane surface tension and viscosity) by recording both amplitude and phase information. It has been used to analyze pathological effects on the deformability of RBCs, such as malaria infection (Park and Best, 2010) or sickle cell disease (Kim et al., 2012).

Mechanical models for cells can be derived using either micro/nanostructural or continuum approaches (Lim et al., 2006). The first category includes microscopic molecular