

**Red blood cell mechanics and membrane fluctuations – passive versus active**

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**Abstract**

Red blood cells (RBCs) are soft and flexible biconcave discs, which are able to pass through capillaries with diameters several times smaller than the RBC size. The RBC deformability also results in noticeable membrane fluctuations, which must be correlated with RBC membrane properties. However, it is still under debate whether RBC membrane fluctuations are simply passive thermal undulations or whether a red cell also experiences active fluctuations which are driven by a metabolic activity or other cell processes. We will present direct evidence that the RBC undulations are not solely passive thermal fluctuations, which has been obtained from a set of different experiments, simulations, and theory. Experimental results show a violation of the fluctuation-dissipation theorem (FDT) for freshly prepared RBCs indicating the existence of active processes. However, the FDT is satisfied for starved cells demonstrating that the membrane fluctuations are passive when the energy supply is absent. Experiments also show a considerable change in the fluctuation amplitudes for fresh and starved cells. Subsequently, we perform simulations which fully mimic and quantify the experiments. We are able to quantitatively extract RBC membrane properties including shear elasticity, bending rigidity, and membrane viscosity. Furthermore, we test a couple of models for active fluctuations, namely force dipoles and monopoles, which may mimic different possible mechanisms including spectrin network remodeling and ion pumps. Simulation results agree well with experimental data and suggest that several processes mentioned above may contribute to active RBC fluctuations.