The Red Blood Cell Membrane

Nir Gov *

Thorsten Auth

*** in collaboration with Prof. Sam Safran**

The red blood cell is a biological system of importance and remarkable in its ability to function under a wide variety of conditions. Its lifetime in the human vascular system is about 120 days, during which it experiences numerous deformations in flow and strong shape changes while it is squeezed through narrow capillaries (Skalak and Branemark, 1969). In vitro studies reveal intriguing mechanical properties that are not yet completely understood from a theoretical point of view. On the one hand, static deformation experiments have been performed using optical tweezers or the micropipette aspiration technique (Svetina et al., 2004). In these experiments, the cell membrane appears to be very stiff. On the other hand it is possible with light scattering or interference contrast experiments to observe the motion of the membrane while the cell is attached to a surface (Brochard and Lennon, 1975; Zilker et al., 1987). The results suggest that the cell membrane shows strong, but transient shape fluctuations. In addition to these seemingly contradictory results, depletion or addition of ATP changes the magnitude of the fluctuations which are observed with light scattering as well as the average cell structure (Gov and Safran, 2005).

Shape fluctuations of simple, lipid membranes have been well studied using the concepts of soft-matter physics. The membrane can be described as a mathematical surface whose energy is a function of the shape (or of the local curvature). The transient shape changes that are observed are attributed to entropy-driven, thermal fluctuations of the membrane around some average shape. The lipid membrane is usually in the fluid state and does not have any restoring force to shear deformations; only curvature deformations are relevant. However, this description cannot be simply applied to the observations of the red blood cell shape fluctuations because the lipid membrane is coupled to a spectrin cytoskeleton. Electron micrographs show that this cytoskeleton consists of a hexagonal network of flexible filaments that are sparsely attached to the lipid bilayer. The coupling is an important element in resolving the apparent contradiction between the results of static deformation and light scattering experiments mentioned above. While the static deformation experiments suggest that the membrane possesses a large shear modulus, the light scattering experiments can only be explained if the shear modulus is very small.

We have studied more realistic models that take into account the composite structure of the red blood cell membrane. Recent phenomenological models demonstrate that statics and dynamics can be explained by considering the bilayer membrane to be both, under tension and confined by the spectrin network [see Fig. 1] (Gov, 2004; Gov et al., 2003). In a more microscopic model, we couple the thermal fluctuations of the lipid, fluid bilayer with those of a nearby solid-like, polymerized membrane that represents the cytoskeleton

Department of Chemical Physics

972 8 934 3323

nir.gov@weizmann.ac.il

www.weizmann.ac.il/oc/facday2005/gov-abs.html

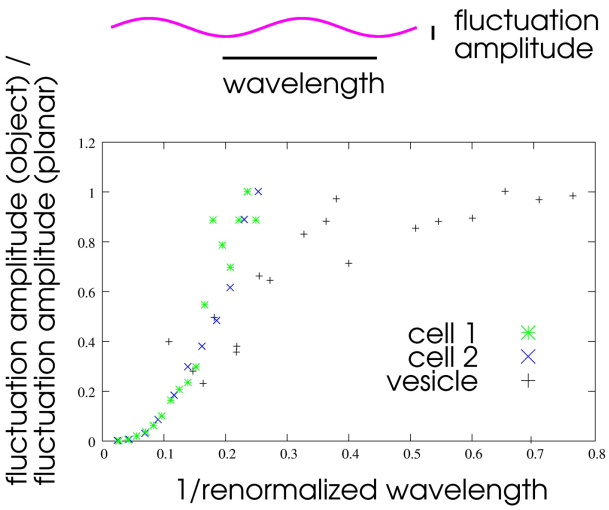

Fig. 1 *The fluctuation spectrum of cell membranes and of a vesicle (modified from Gov et al., 2003). The fluctuation amplitudes are renormalized by the fluctuation amplitudes of a free, planar bilayer while the wavelength is renormalized by an average distance between spectrin and bilayer.*

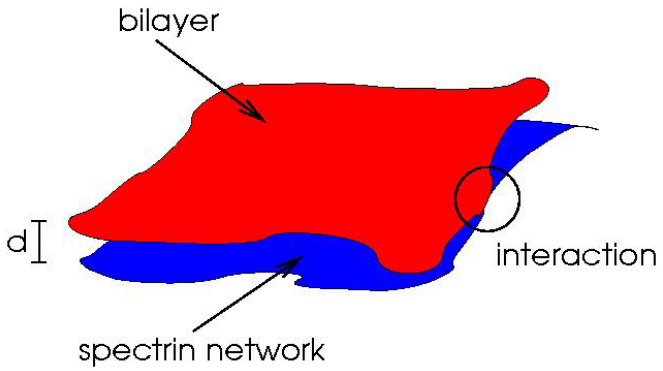

Fig. 2 *The model of two fluctuating surfaces used to describe the cell membrane. Both surfaces are kept at distance d due to the anchors in a real cell. The fluctuations of the bilayer surface are determined by its bending modulus while the fluctuations of the spectrin network are governed by shear. Both surfaces interact if the hit each other.*

In addition, we are investigating the effects of the ATP concentration on the coupling and the resulting fluctuations of the coupled lipid and spectrin membranes. These studies are motivated by the fact that changes in the ATP concentration can lead to a significant increase of the fluctuation spectrum.

Selected publications

Brochard, F. and Lennon, J.F. (1975) Frequency Spectrum of Flicker Phenomenon in Erythrocytes. Journal De Physique, 36, 1035-1047.

Skalak, R. and Branemark, P. (1969) Deformation Of Red Blood Cells In Capillaries. Science, 164, 717-&.

Zilker, A., Engelhardt, H. and Sackmann, E. (1987) Dynamic Reflection Interference Contrast (Ric-) Microscopy - a New Method to Study Surface Excitations of Cells and to Measure Membrane Bending Elastic-Moduli. Journal De Physique, 48, 2139-2151.

Evans, E. and Rawicz, W. (1997) Elasticity of ‘‘fuzzy’’ biomembranes. Physical Review Letters, 79, 2379-2382.

Gov, N., Zilman, A.G. and Safran, S. (2003) Cytoskeleton confinement and tension of red blood cell membranes. Physical Review Letters, 90, -.

Svetina, S., Kuzman, D., Waugh, R.E., Ziherl, P. and Zeks, B. (2004) The cooperative role of membrane skeleton and bilayer in the mechanical behaviour of red blood cells. Bioelectrochemistry, 62, 107-113.

Gov, N. (2004) Membrane undulations driven by force fluctuations of active proteins. Physical Review Letters, 93, -.

Gov, N. and Safran, S. (2005) Red blood cell shape and fluctuations: Cytoskeleton confinement and ATP activity. Journal of Biological Physics, 31, 453-464.

Acknowledgements

T. A. thanks the Minerva foundation for support through a postdoctoral fellowship.