Lipid composition modulates nanomechanics of transmembrane proteins

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Abstract

There is a need to investigate the increasingly emergent problem of antibiotic resistance because of the social impact and economic consequences [1]. The use of new nanoscale techniques opens new perspectives in the study of the mechanisms involved in the generation of resistances [2]. Particularly, multidrug efflux pumps are under the spotlight to understand the molecular and physicochemical basis of the efflux mechanism to decrease the antibiotic concentration inside the bacterium. We used lactose permease (Lac Y) from *Escherichia coli* as a paradigm for the secondary transport proteins that couple the energy stored in an electrochemical ion gradient to a concentration gradient (ß-galactoside/H+ symport) to study the effect of the lipid matrix in its nanostructure. Firstly we characterized with the Atomic Force Microscope (AFM) the nanomechanics of the lipids in Supported Lipid Bilayers (SLBs) mimicking the lipid composition of bacteria (Figure 1). Secondly we incorporate the protein to the lipid bilayers and investigate the changes produced when modifying the lipid environment (Figure 2). We found that proteins were segregated into liquid-crystalline phases (L_α) whilst the forces needed to extend a single protein were higher when the unsaturation in the hydrocarbon chains of the lipids decreased. This fact could be related to the lateral pressure on the protein in the lipid bilayer evidenced during the unfolding of a single protein when pulling it with the AFM tip.

References

[1] Alanis, A.J., Archives of Medical Research, **36** (2005) 697.
[2] Longo, G., Alonso-Sarduy, L., Marques Rio, L., Bizzini, A., Trampuz, A., Notz, J., Dietler, G., Kasas, S. Nature Nanotechnology, **8** (2013) 522.

Figures

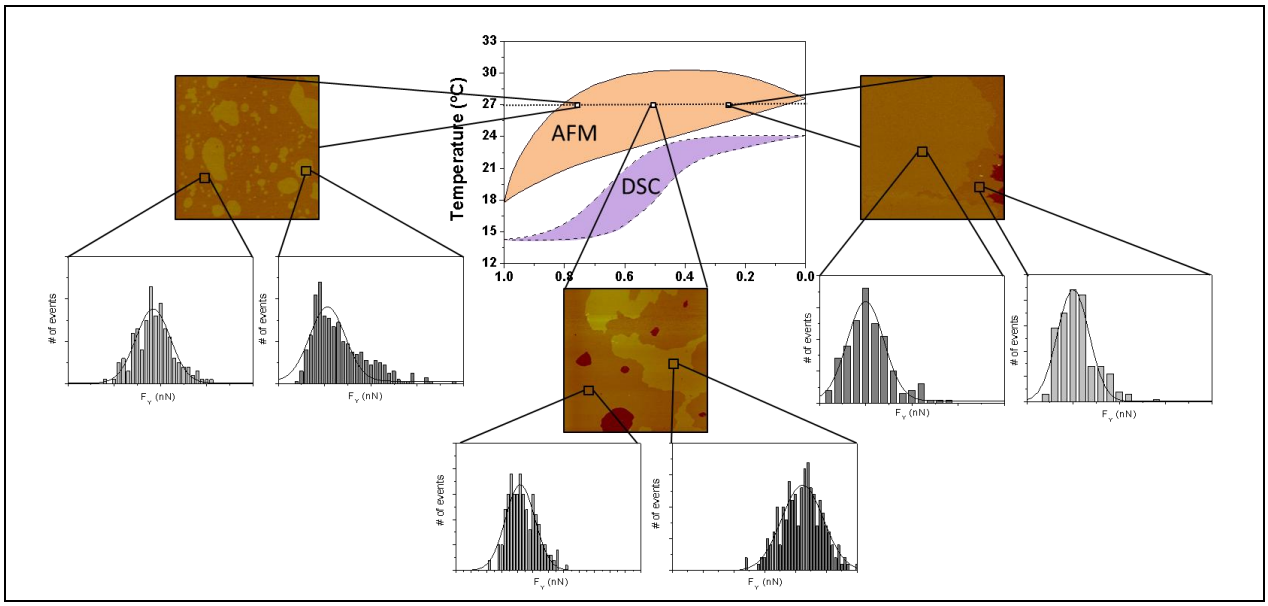

Figure 1. Nanomechanics of lipids forming SLBs mimicking *E. coli* inner membrane. Comparative of the phase diagram obtained with DSC and AFM.

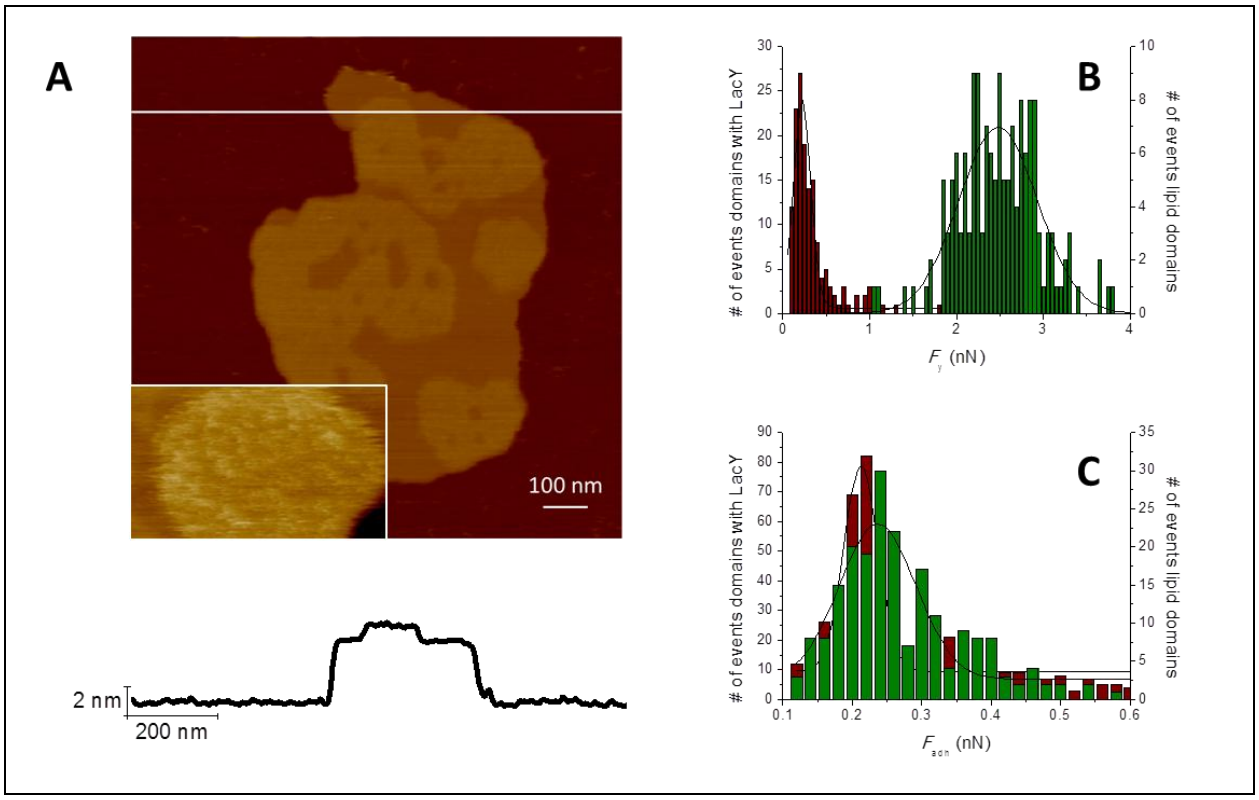

Figure 2. AFM topographic image and height profile analysis of a SLB composed of POPE:POPG (3:1,mol/mol) with LacY at a LPR (w/w) of 0.5 (Z scale = 15 nm) (A). Insert in A presents a magnified image (470 × 280 nm, Z = 3 nm) where domains with LacY can be distinguished from domains without LacY. Histograms present the distribution of forces of domains with LacY (red) and domains without LacY (green) for Fy (B) and Fadh (C). Fittings to a Gaussian distribution are represented in solid lines.