Mitochondria cristae dynamics: an active membrane model

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Biological context

Mitochondria are the place of production of ATP in eukaryotic cells. These organelles are composed of dozens of dynamical tubular invaginations of nanometric size: the cristae. The ATPaze, protein synthesizing the ATP are located in the curved regions of the invaginations and use a proton gradient generated inside the cristae by the respiratory complex chain to produce ATP. The shape of the cristae modifies upon stimuli and condition and in particular with the rate of ATP production[1]. The mitochondrial membrane is enriched in lipids, the cardiolipins, which acid-basic properties are coupled with interesting mechanical properties as the spontaneous curvature of the bilipid membrane they form is function of the pH[2,3]. Moreover, the cardiolipin knock-out mutants possess altered and dysfunctional mitochondria. We would like to test the hypothesis that a coupling between mechanical properties of the cristae membrane and proton flux inside the invagination could lead to an increase of the ATP production rate.

Modeling

We model the cristae as tube of membrane described with an Helfrich Hamiltonian and assume that the paramaters of the Hamiltonian depend on the local pH. We will first consider an infinite cylinder submitted to a pH gradient and study the stability of the system as a function of the pH dependence of the different parameters. We will then consider a finite cylinder which mechanical and chemical boundary conditions will model the biological system ones and study the deformation driven by growing values of proton flux. Finally, we will study the dynamics of the deformation.

This internship is a theoretical internship but regular discussions with biologists are planed.

The techniques used are: mechanical description of membranes, differential geometry, Green's functions.

Possibility of thesis after the intership: Yes

References:

1. Review Mitochondrial Cristae: Where Beauty Meets Functionality, Cogliati et al., *Trends in Biochemical Sciences*, 41 (2016).

2. Membrane Deformation under Local pH Gradient: Mimicking Mitochondrial Cristae Dynamics, Khalifat et al., *Biophysical Journal*, 95 (2008).

3. Lipid membrane deformation in response to a local pH modification: theory and experiments, Bitbol et al., *Soft Matter*, 8 (2012).