Mitochondria cristae dynamics: an active membrane model

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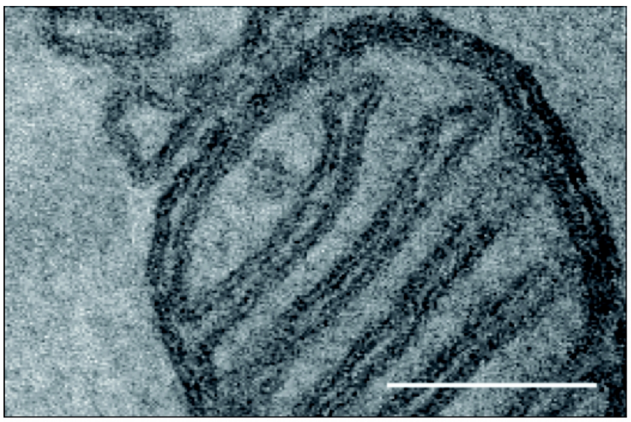
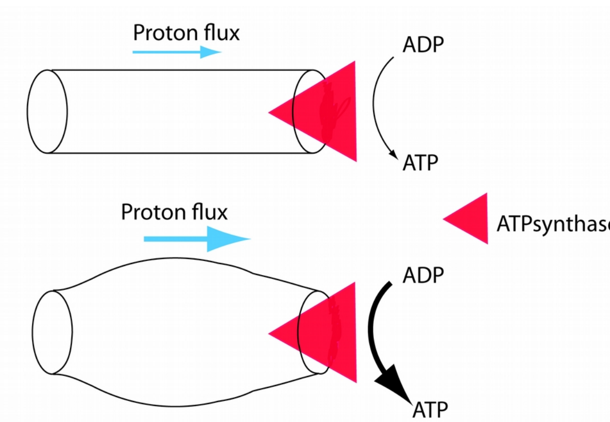
Biological context

Mitochondria are the place of production of ATP in eukaryotic cell. These organelles are composed of dozens of dynamical tubular invaginations of nanometric size: the cristae. The ATPasynthases, which are the proteins that synthesize 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 depends upon stimuli and conditions and in particular on the rate of ATP production[1]. The mitochondrial membrane is enriched in specific lipids, the cardiolipins, whose acid-basic properties are coupled with interesting mechanical properties, since the spontaneous curvature of the bilipid membrane they form is a 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 the mechanical properties of the cristae membrane and the proton flux inside the invaginations could lead to an increase of the ATP production rate.



Electron microscopy photo of mitochondria. Scale bar 100nm.



Sketch of coupling between cristae shape and proton flux.

Modeling

We model the cristae as a tube of membrane described with a Helfrich Hamiltonian (an elastic energy penalizing deformations) and assume that the paramaters of this 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 with mechanical and chemical boundary conditions that model those of the real biological system, and study the deformation driven by increasing 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

<u>References:</u>

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).