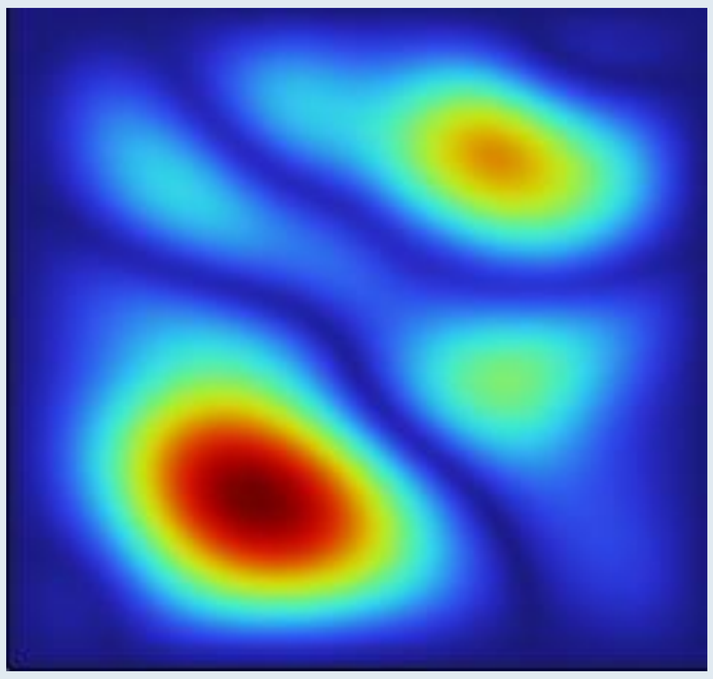

Investigating elastic- and entropic-driven rupture mechanisms of biomembranes

This work focuses on the spontaneous penetration method of the cellular membrane, investigating the role of the thermal forces in the membrane poration, so far unexplained (this is key, for examples, in drug delivery and biochemical detection applications).

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Introduction & Goals

Biomemebranes are characterized by several elastic parameters that appropriately describe the energetics of their deformation under thermal fluctuations [1].

When their structure is quasi-2D several studies [1,2] showed that their disruption, at finite temperature, can be driven either by elastic or entropic forces depending on its size. However, what happens for thicker structures? Using the computational platform COMSOL Multiphysics that allows the coupling between finite element simulations and Brownian motion models, we show that the entropic contribution to the fluctuations and rupture of biomembranes at finite temperature can be the dominant mechanism not only for structures few nanometers thick but also for thicker structures (of the order of 1 um). The results of this work can help shedding light on the dynamic and failure behavior of biomembranes that are key in tissue engineering and drug delivery. The most remarkable advantage of the proposed approach is the possibility of analyzing dynamical processes of bio-structures spanning dimensional and temporal intervals ranging from nanometers to micrometers and from nanoseconds to microseconds, in a computationally very stable and efficient manner. In these spatial and temporal ranges, the Molecular Dynamics (MD) approach is not a viable route.

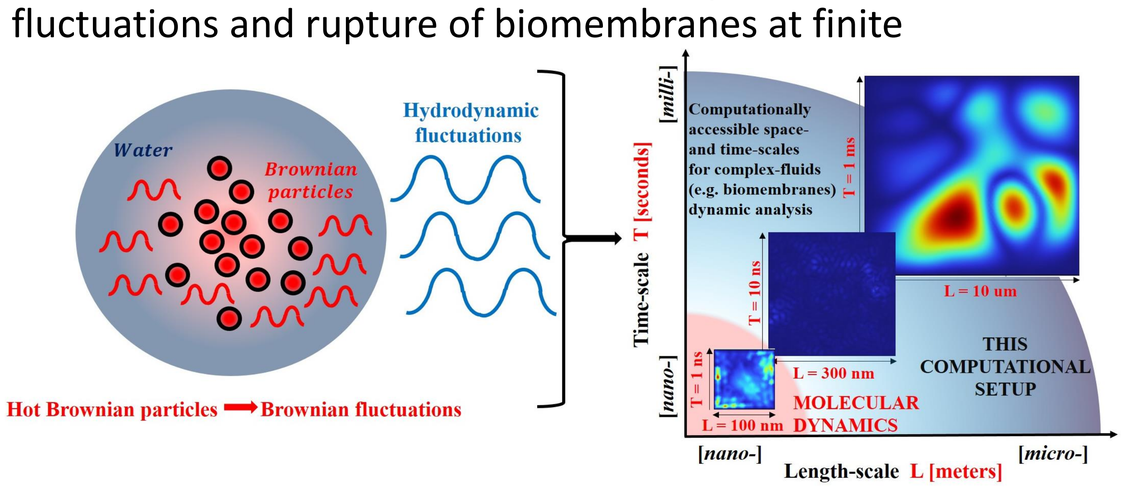

Figure 1. Left: The BIO-membrane fluctuations modeled by using hot Brownian particles. The resulting Brownian motion causes (drag-induced) hydrodynamic fluctuations that act on the membrane thus mimicking entropically-dominated dynamic regimes, currently inaccessible with conventional computational frameworks. Right: The new computational framework allows reliable and efficient dynamic characterizations across space- and time-scales inaccessible to current computational frameworks (e.g. Molecular Dynamics MD).

Methodology

The methodology proposed in this work is based on the use of Brownian particles to introduce thermal fluctuations within a continuum mechanics model. This is a completely novel approach from a technical point of view for studying BIO- systems.

In summary, because the models that simulate the continuum do not have thermal fluctuations and Brownian motion embedded, we designed a way to introduce it. We use Brownian particles at a fixed temperature that move the liquid creating hydrodynamic fluctuations. These fluctuations cause the movement of the membrane, while the membrane is transparent to the Brownian particles.

Results

We started this study by the observation that the models proposed so far were not able to explain why the force required to an indenter to penetrate a biomembrane did not depend on its geometry and particularly the radius of curvature of its tip. This work explains this behavior by identifying the existence of dynamic regimes of the membrane dominated by elastic or entropic forces depending on its length.

To tackle this problem we proposed a continuum mechanics approach (simulating the membrane as an elastic continuum) where the thermal fluctuations are introduced via Brownian particles at fixed temperature. This approach has been validated using analytical predictions, confirms the predictions of MD but overcomes its limits on the temporal and spatial ranges that can be reliably simulated and on the type of phenomena that can be accounted in the model.

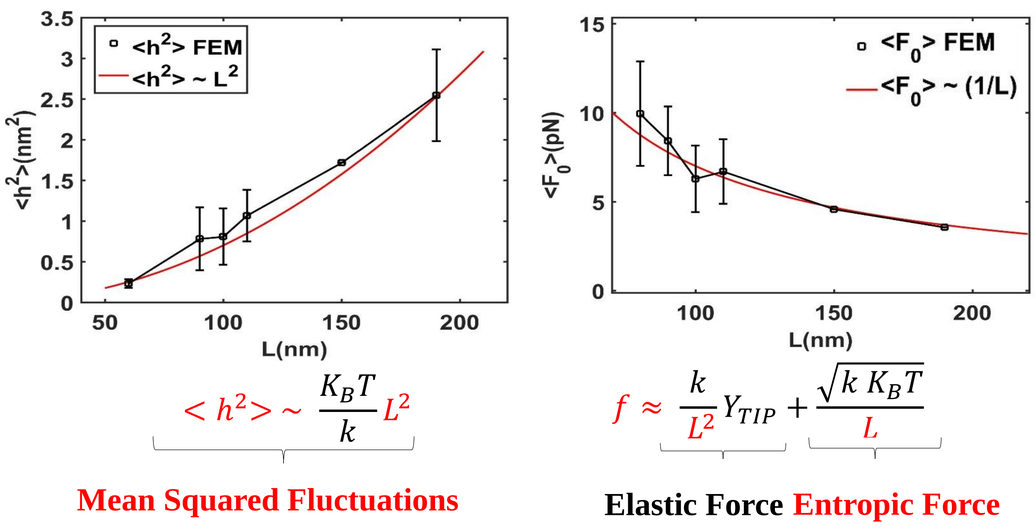

Figure 2. Successful comparison between the theoretical model predictions with FEM simulations for the mean squared fluctuations and the force experienced by the membrane. In particular, the elastic force is expected to scale like 1/L^2 (in this specific case no indenter is considered so the elastic term is 0) and the entropic component like 1/L.

REFERENCES

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