RELAXATION OF A SIMULATED LIPID BILAYER VESICLE COMPRESSED BY AN AFM

Ben Barlow, Martine Bertrand & Béla Joós

Department of Physics, University of Ottawa

ABSTRACT

As model physical systems, lipid bilayer vesicles (vesicles) have been an attractive starting point for theoretical work, simulations and experiments. Vesicles serve as prototypes of simple cells and knowledge of their mechanical properties is important to understanding living cells.

- Using Coarse-Grained Molecular Dynamics simulations[1], we study the relaxation of bilayer vesicles, uniaxially compressed by an Atomic Force Microscope (AFM) cantilever.
- **The relaxation time exhibits a strong force-dependence.**
- **We explain this in terms of thermal undulations present in lipid bilayers.**[2]
- Force-compression curves are very similar to recent experiments[3] wherein giant unilamellar vesicles were compressed in a nearly identical manner.

AFM APPARATUS

Parallel Plate Compression:

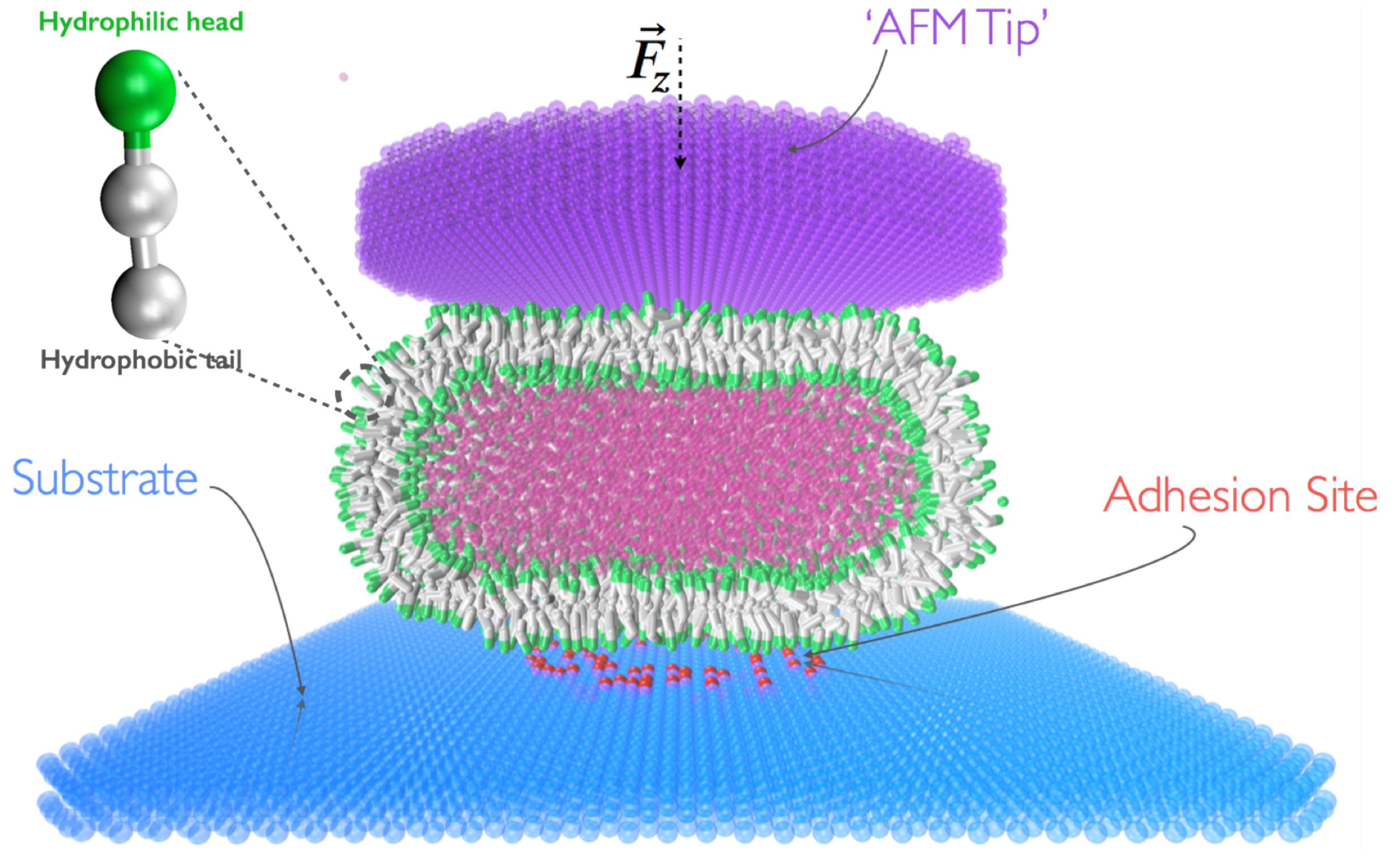


Figure 1: Simulated vesicle undergoing parallel plate compression. In addition to the ordinary substrate particles, a bullseye of randomly distributed 'sticky' particles was placed at the centre of the substrate to ensure adhesion. Without this *adhesion site*, the vesicle would slip out from underneath the AFM Tip. Coarse-grained lipid shown at upper left.

SUMMARY

- The relaxation time depends on the magnitude of the applied stress, increasing sharply in the limit of low stress.
- This result is connected to entropic undulations in the bilayer via Equation 5, which we derive out of the Helfrich and Servuss Model[2] (Equation 4).
- Our derivation predicts a *finite* maximum relaxation time, proportional to the membrane's surface area.
- Moreover, since undulations have been observed in real vesicles and cells, the force-dependence should be present in them as well.
- **The connection between our vesicle's relaxation time, entropic undulations and the applied stress may help to explain the wide variability of relaxation (and recovery) times reported for cells.**

REFERENCES

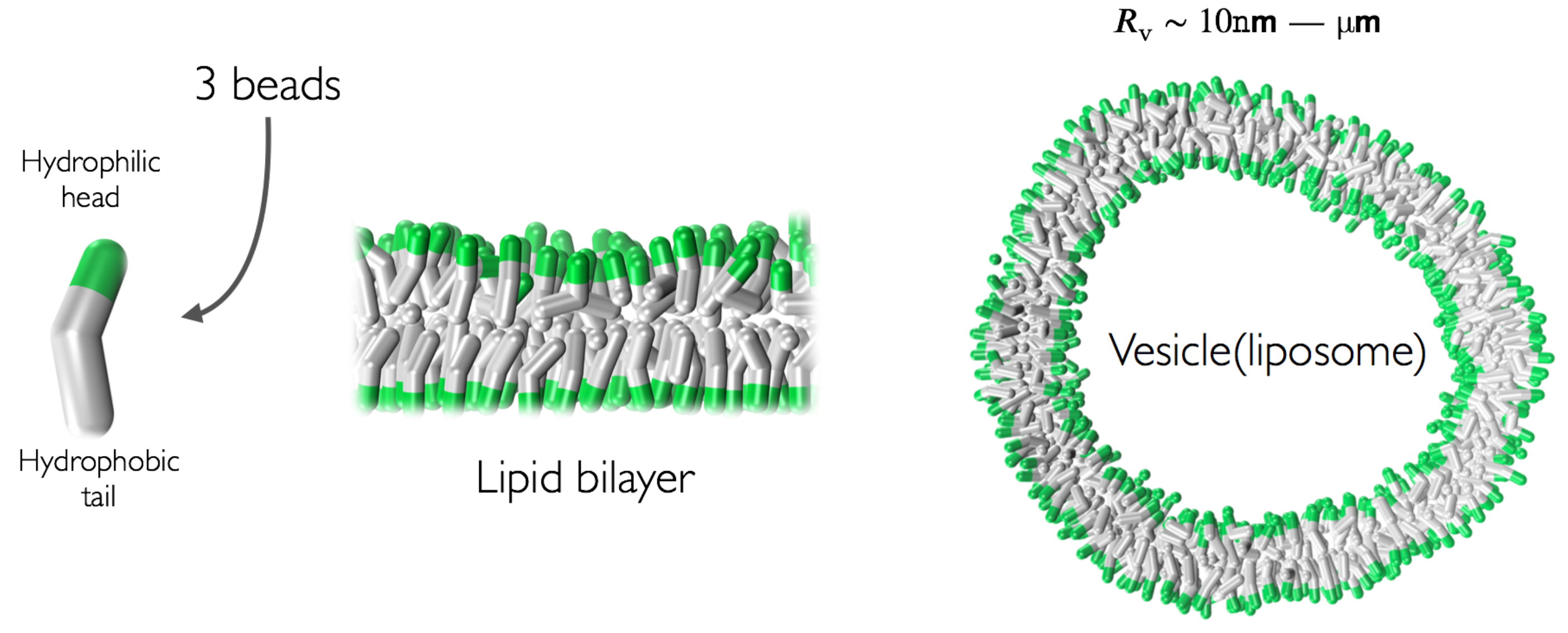
[1] Joshua A. Anderson, Chris D. Lorenz, and A. Travesset. General purpose molecular dynamics simulations fully implemented on graphics processing units. *J. Comput. Phys.*, 227(10):5342–5359, May 2008.

[2] W. Helfrich and R.-M. Servuss. Undulations, steric interaction and cohesion of fluid membranes. *Il Nuovo Cimento D*, 3(1):137–151, January 1984.

[3] Edith Schäfer, Torben-Tobias Kliesch, and Andreas Janshoff. Mechanical Properties of Giant Liposomes Compressed between Two Parallel Plates: Impact of Artificial Actin Shells. *Langmuir*, 29(33):10463–10474, August 2013.

LIPID BILAYER VESICLES

- In aqueous solution, phospholipids self-assemble to form closed membranes called *lipid bilayer vesicles.*



WHAT WE MEASURE

- Membrane area expansion (equilibrium)

$$\alpha \equiv \left(\frac{\Delta A}{A}\right) \tag{1}$$

- Relaxation time τ, of the area expansion following a step-force (F_z)

$$\alpha(t) \sim \left(1 - e^{-t/\tau}\right) \tag{2}$$

- Vertical compression (equilibrium)

$$\Delta z_{Tip}(F_z) = z(F_z) - z_\circ \tag{3}$$

DYNAMICS: STRESS RELAXATION $\alpha(t) \longrightarrow \tau$

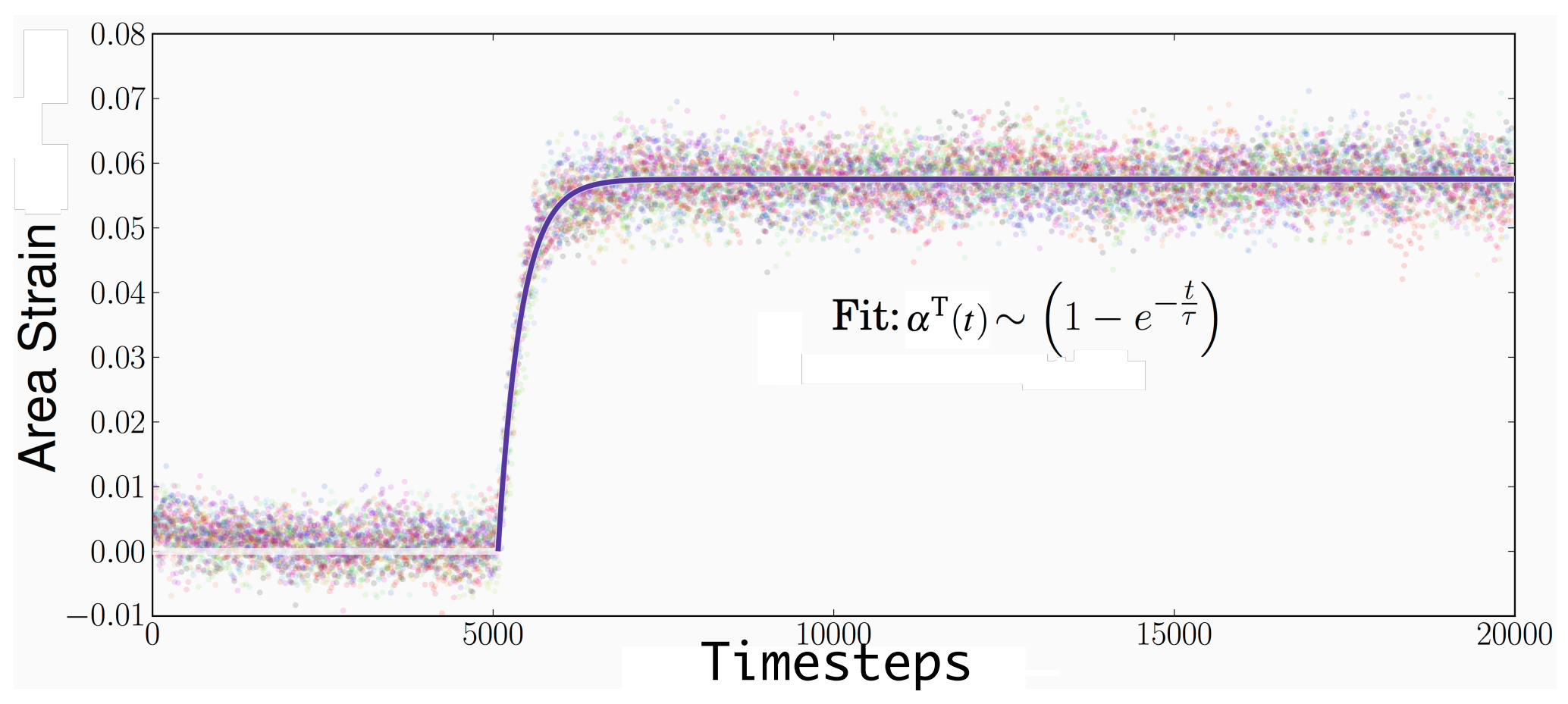


Figure 2: Ensemble fit to creep response of the bilayer's triangulated area at $F_z = -100\text{F}$. For each value of the applied force, data from multiple simulations are fit as one timeseries. This helps to reduce the uncertainty on the relaxation time, by reducing the influence of noise from any particular simulation on the fit.

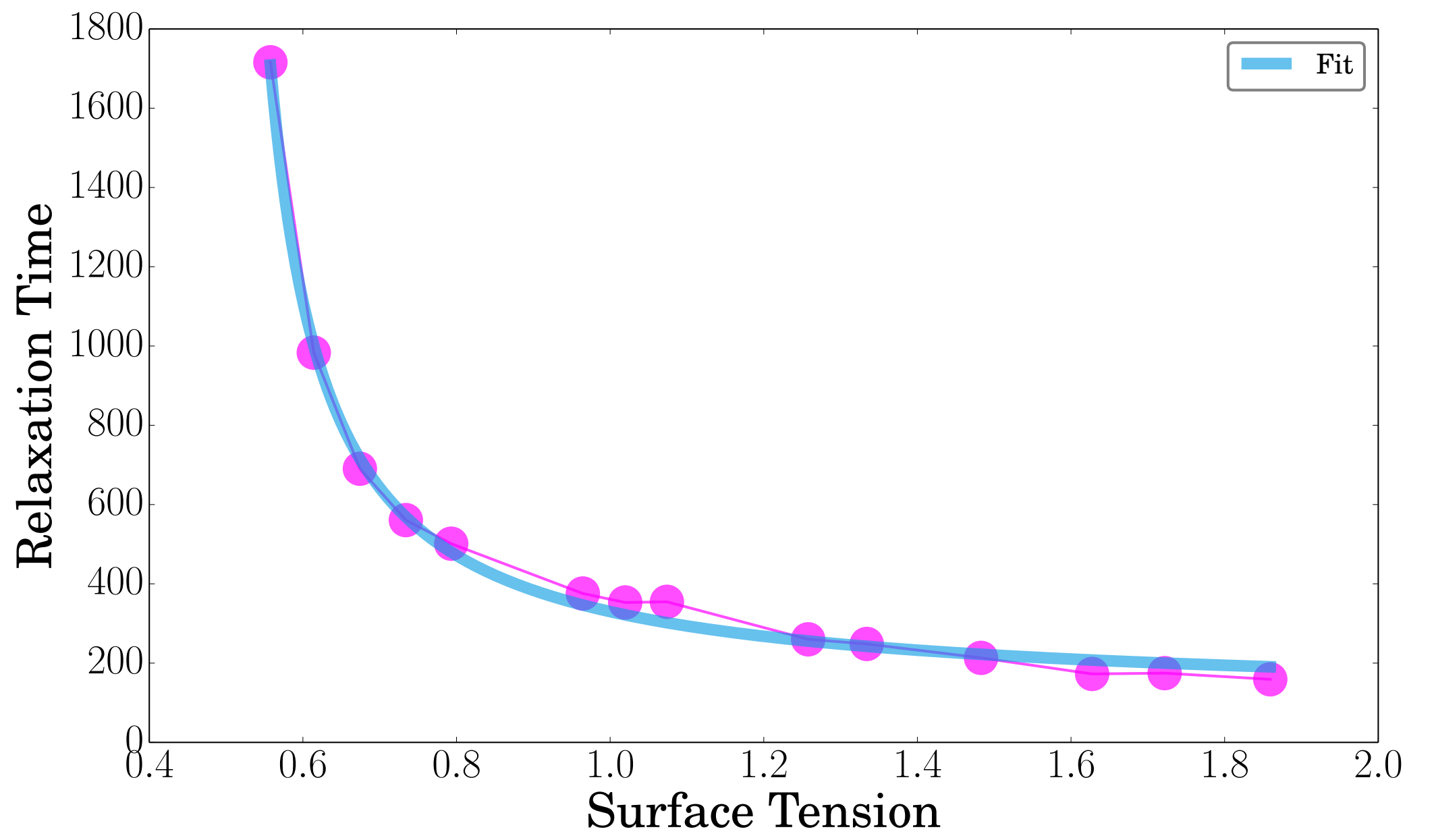


Figure 3: Relaxation time versus surface tension. Equation 5 leads to a correct description of the force dependence of the relaxation time $\tau(\gamma)$.

THEORY

- Area expansion α as a function of surface tension γ (HS model)[2]

$$\alpha(\gamma) = \underbrace{\frac{k_B T}{8\pi\kappa} \ln\left(\frac{\frac{\zeta\kappa}{A} + \gamma}{\frac{\zeta\kappa}{a} + \gamma}\right)}_{entropic} + \underbrace{\frac{\gamma}{K_A}}_{direct}. \tag{4}$$

- From HS model, we derive the relaxation time

$$\tau(\gamma) \sim \eta \frac{\partial \alpha}{\partial \gamma} \approx \eta \left(\frac{1}{K_A} + \frac{\frac{k_B T}{8\pi\kappa}}{\frac{\zeta\kappa}{A} + \gamma}\right). \tag{5}$$

EQUILIBRIUM: PROJECTED AREA, TRIANGULATED AREA, VERTICAL COMPRESSION

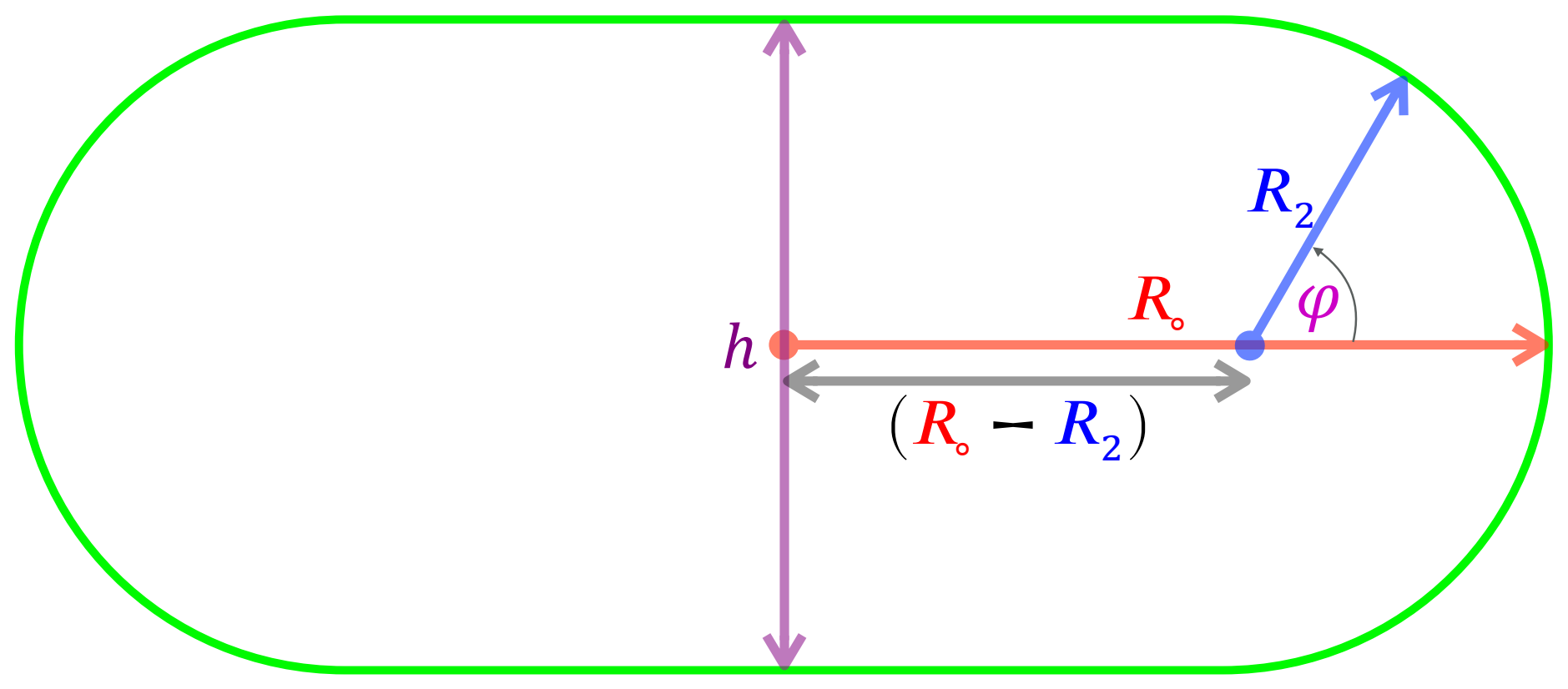


Figure 4: Parametrization of a compressed vesicle. In the context of projected area and membrane undulations, this profile delineates the apparent surface of the vesicle. The shape of the compressed vesicle is well approximated by a "filled torus" —a doughnut without a hole. Coordinates: In this figure, h lies along the z-axis. ϕ lies in the xy-plane. $\varphi = \arctan(z/R_2)$.

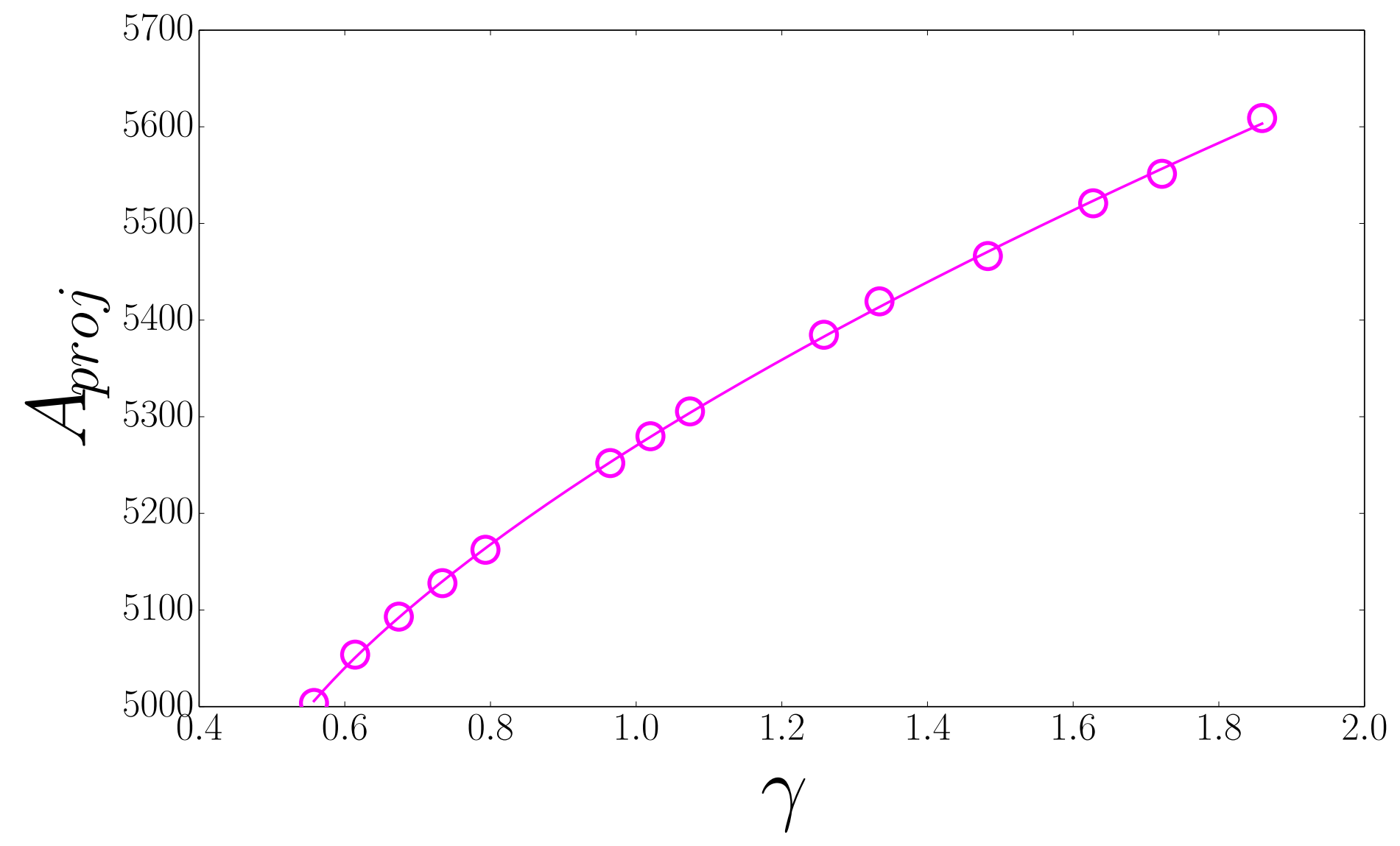


Figure 5: Projected area versus surface tension. The tension (x-axis) has been estimated via the work done compressing the vesicle.

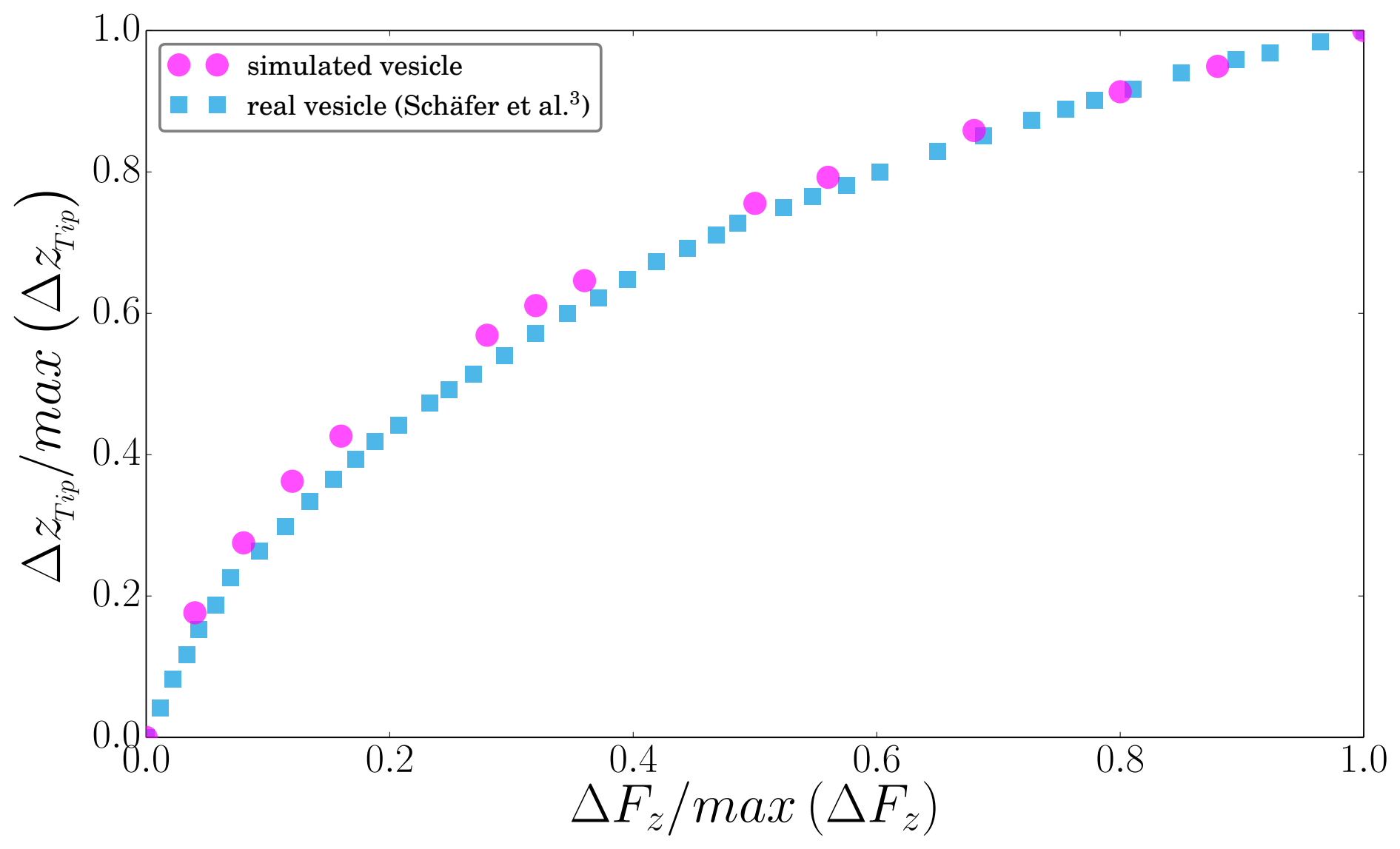


Figure 6: Vertical compression: Relative height change as a function of applied force. The similarity between simulation and experimental data (modified from Schäfer et al. 2013) is striking.

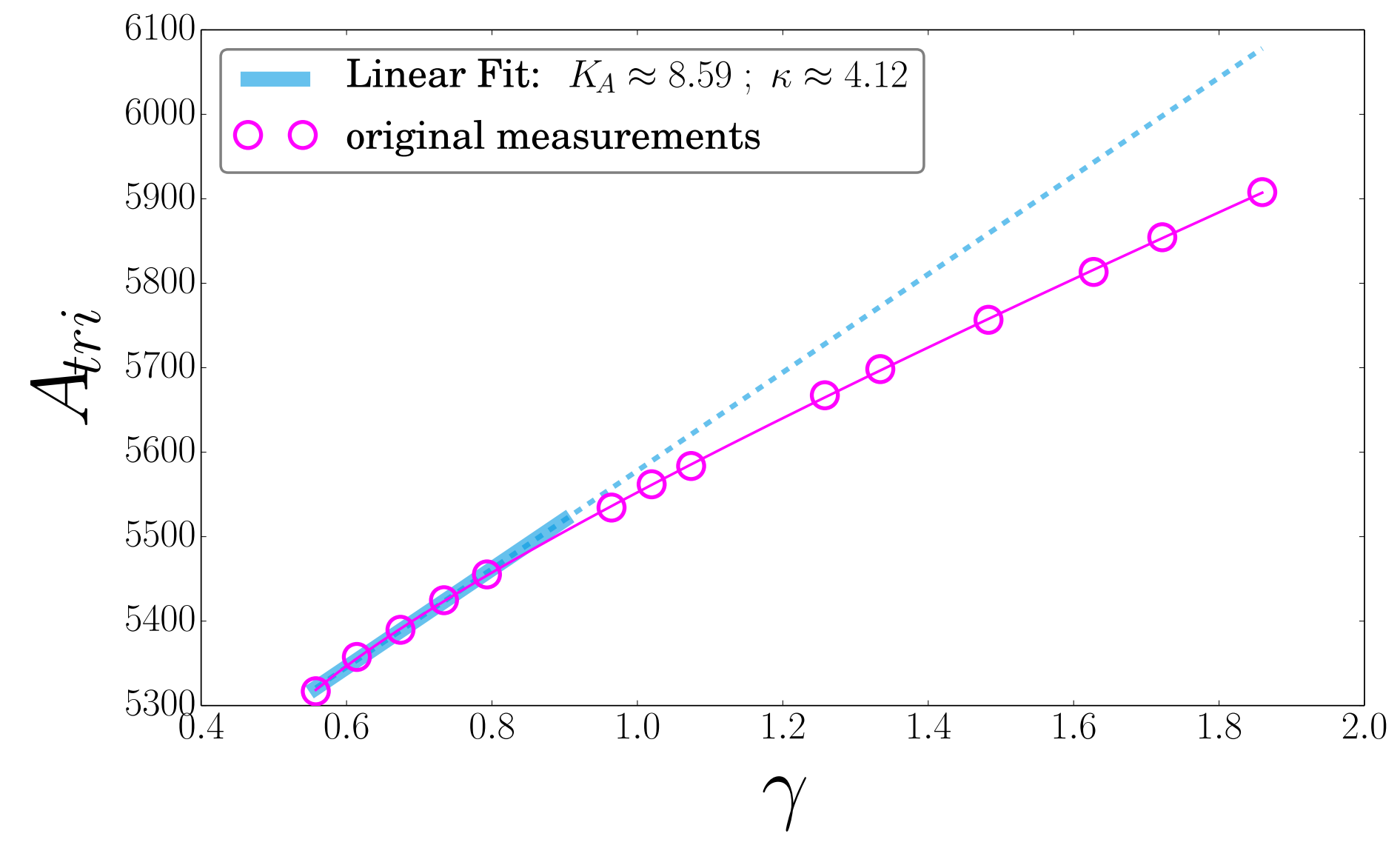


Figure 7: Triangulated area versus surface tension. The tension (x-axis) has been estimated via the work done compressing the vesicle. K_A is estimated using a linear fit to the low tension regime. The bending rigidity is $\kappa = K_A l^2/48$, where l is the bilayer thickness.