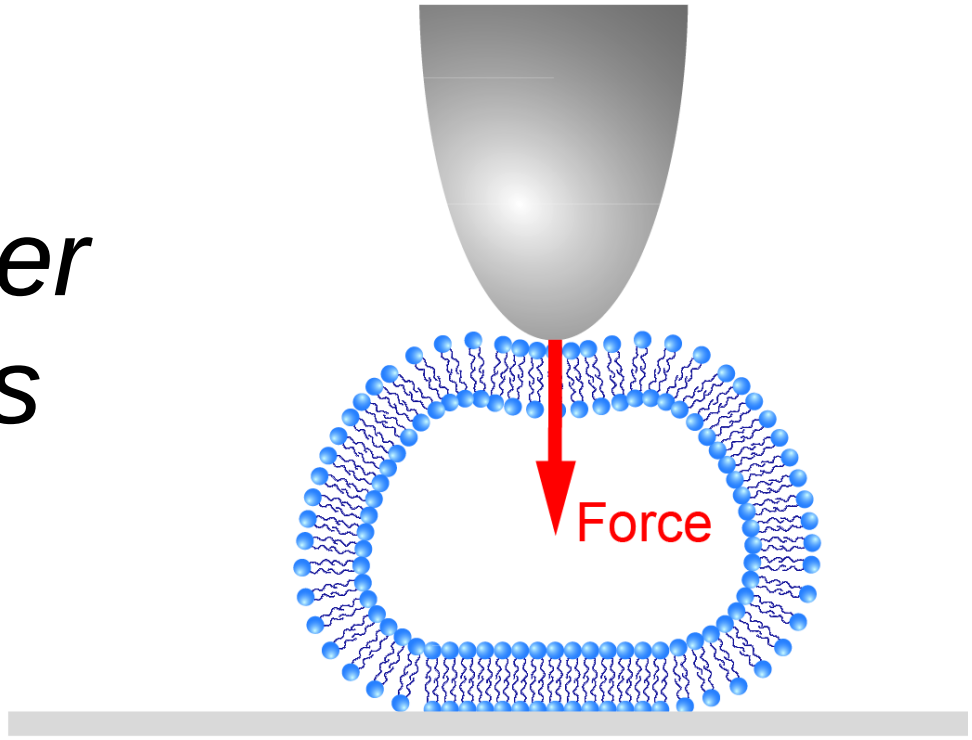
Probing of (Extra-Cellular) Vesicles by Atomic Force Microscopy

Wouter Roos

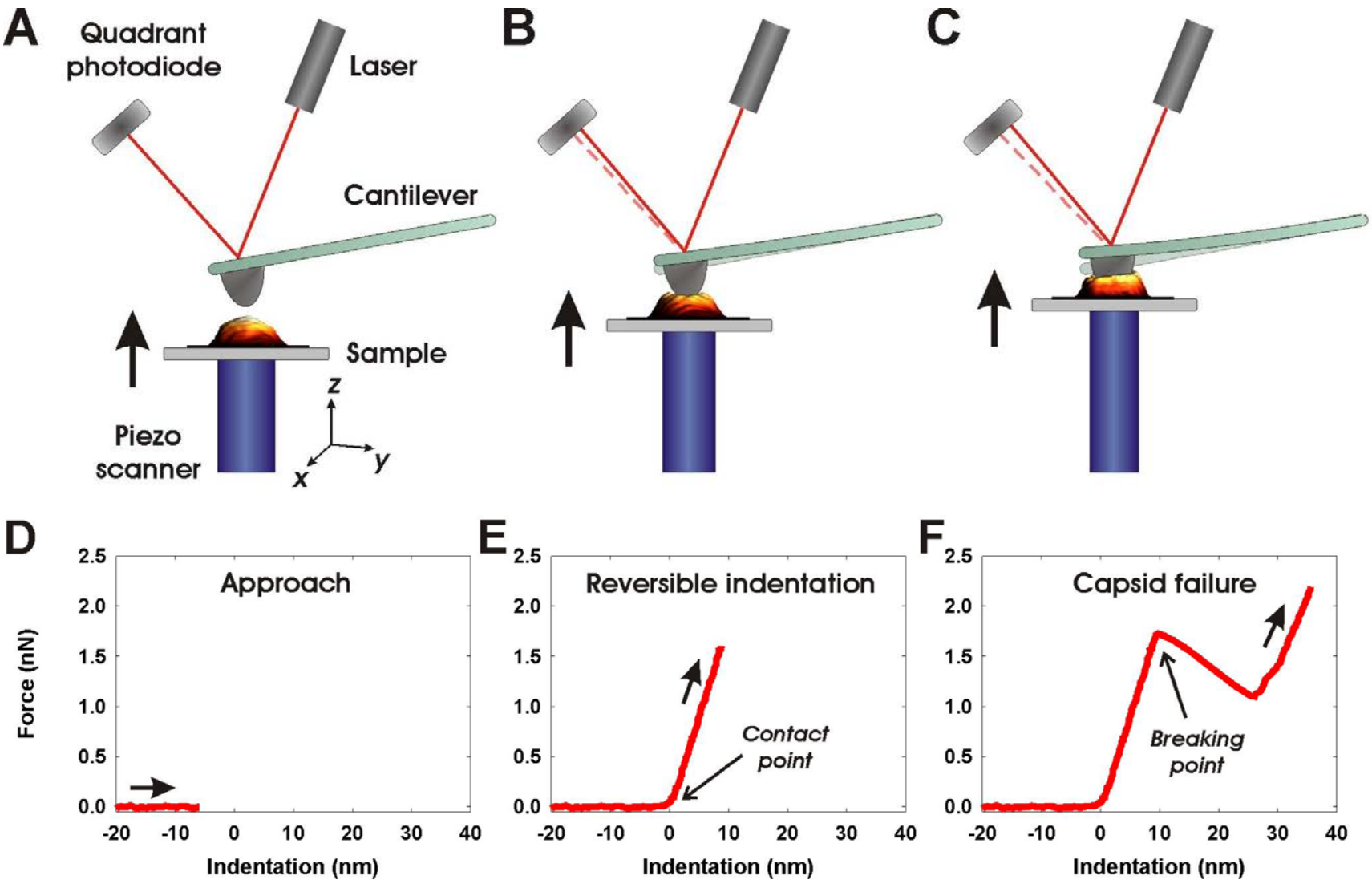


ARBRE MOBIEU
BETWEEN ATOM AND CELL

rijksuniversiteit groningen

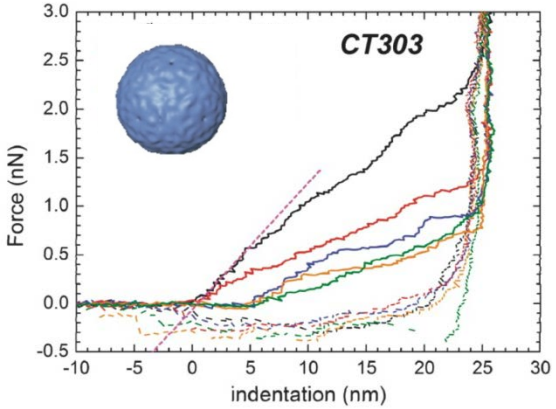
cost

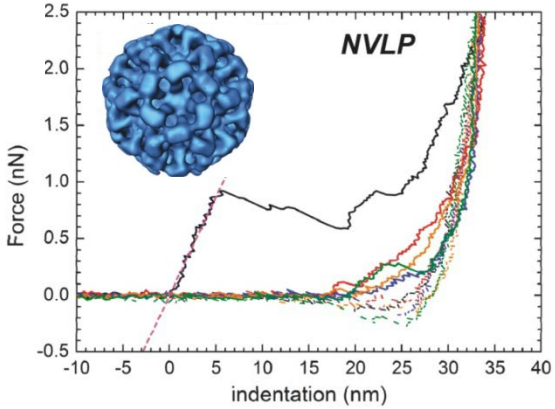
Deforming the shells



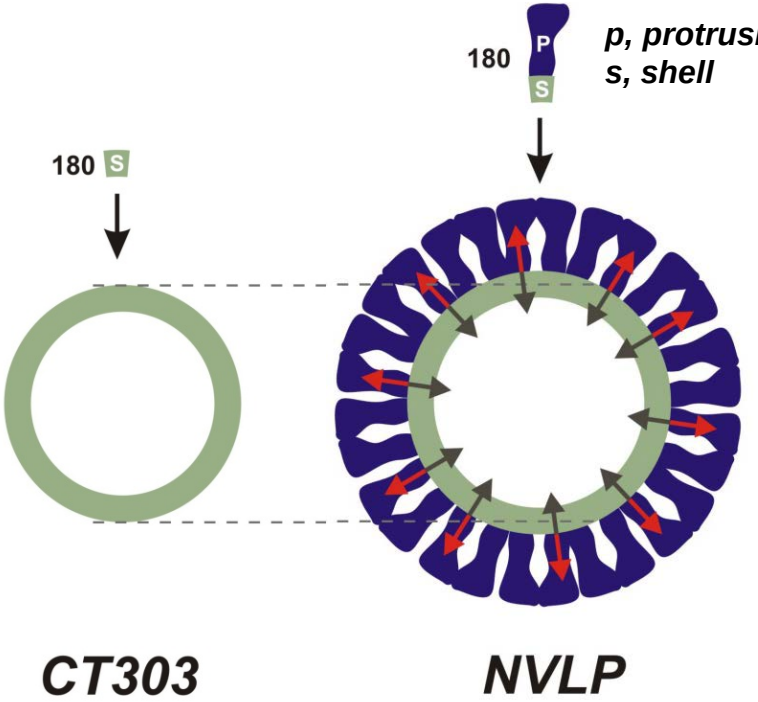
Roos *et al.*, Nature Physics 2010

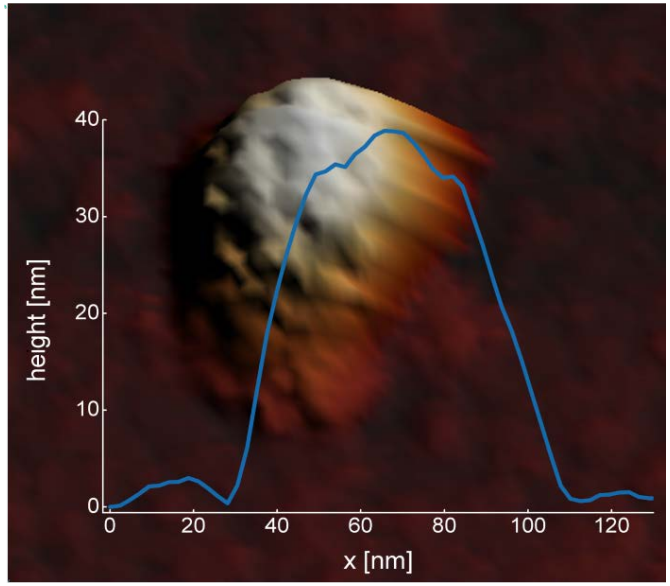
Noro Virus





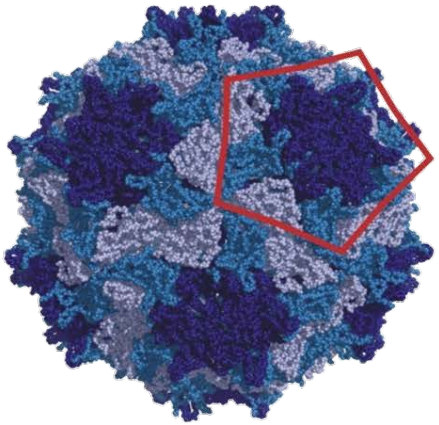
The NVLP's are under an isotropic prestress that strenghtens their structure

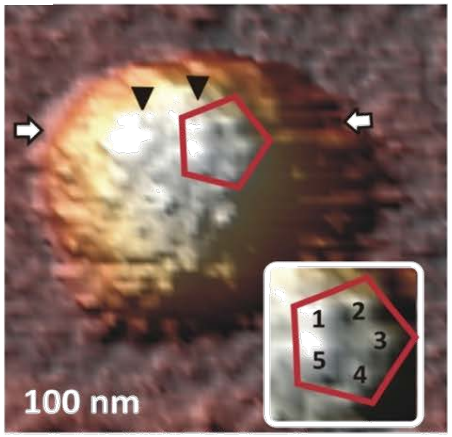


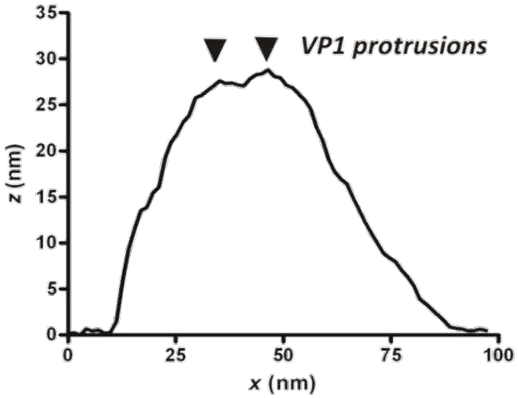


Baclayon *et al.*, Nano Letters (2011)

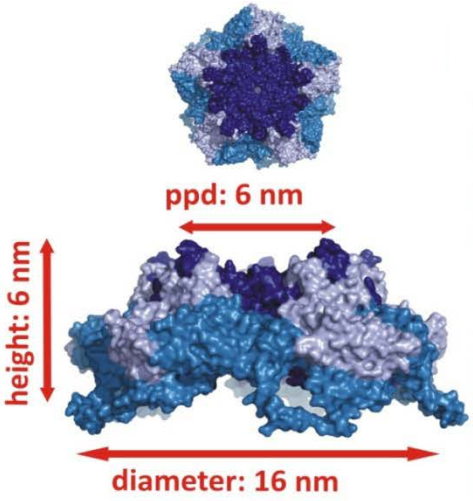
Triatoma Virus

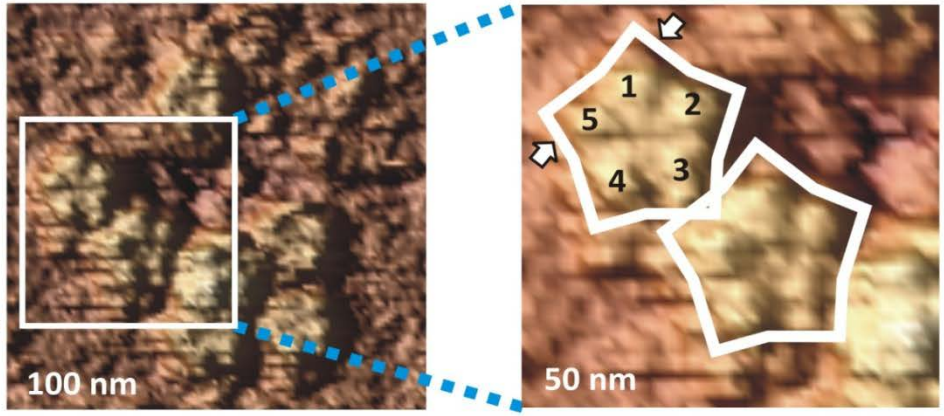






pH dependent stiffness switch





Snijder *et al.*
Nature Chemistry
(2013)

Importance of mechanics of small vesicles

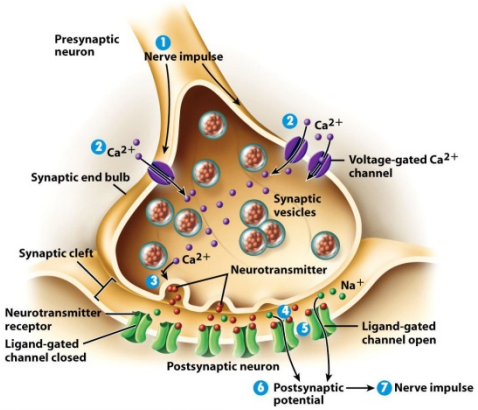
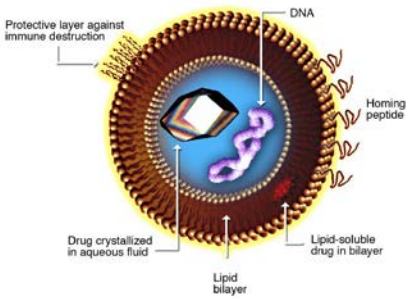


Figure 12-17 Principles of Anatomy and Physiology, 11/e
© 2006 John Wiley & Sons

Synaptic vesicles

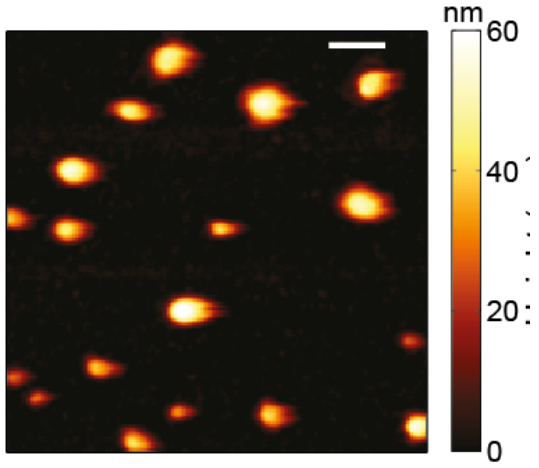
Extracellular vesicles

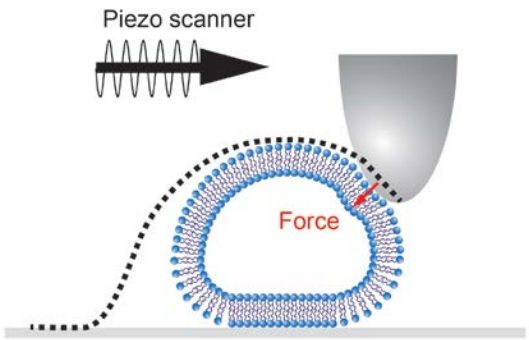


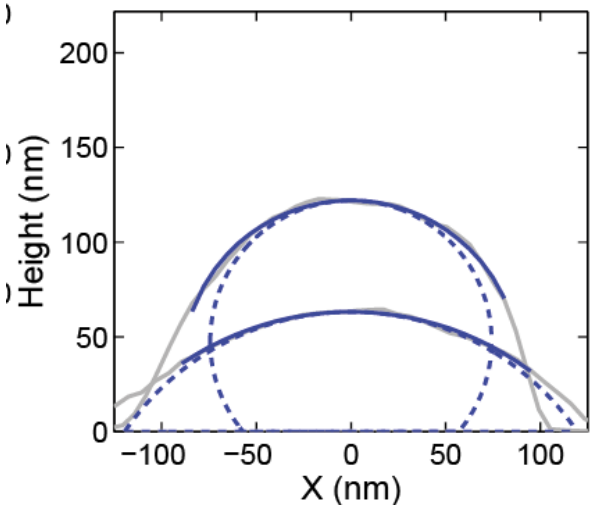
Liposomal drug delivery

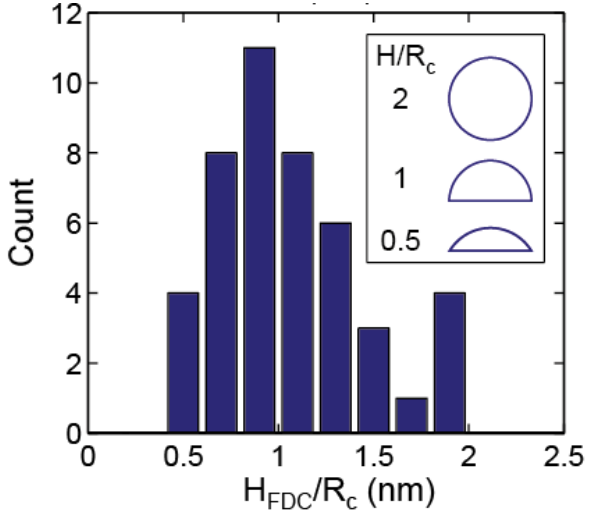
reliawire.com, wikipedia.com

Material properties of vesicles



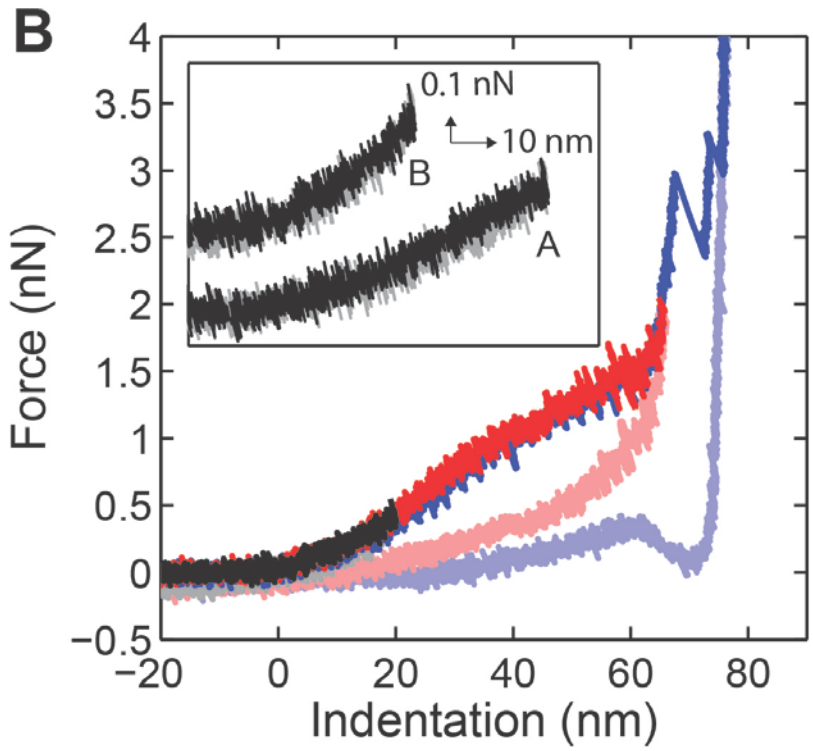






assuming surface area conservation we can determine R_0 (before adhesion)

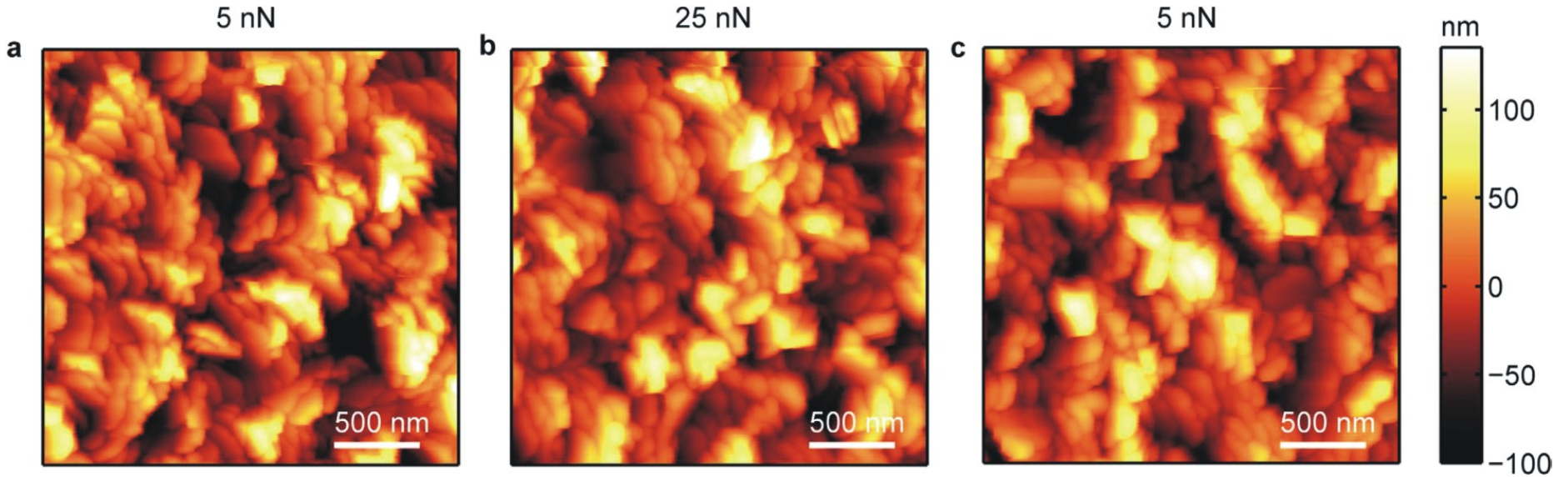
Material properties of vesicles



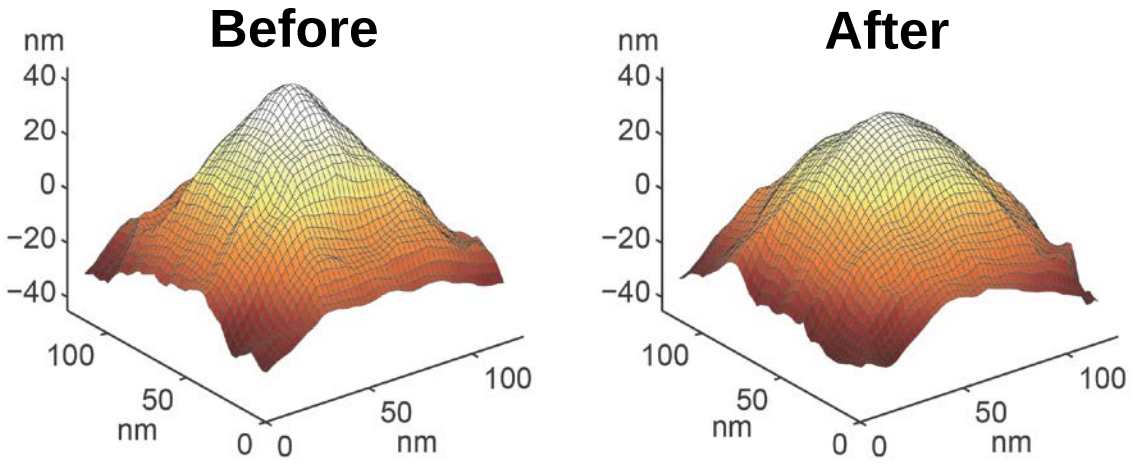
Where does the difference in slope come from?

Tip radius?

Shaping tips

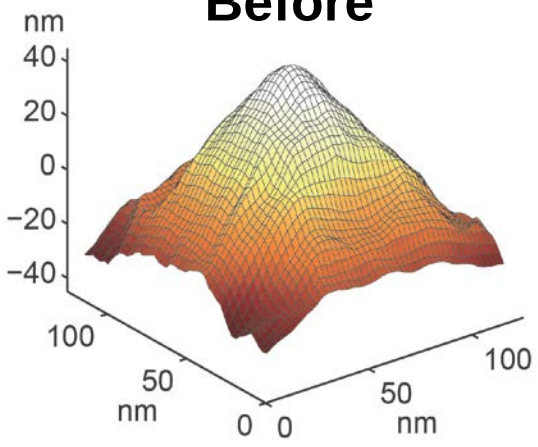


Vorselen *et al.* Sci Reports (2016)



Shaping tips

Before



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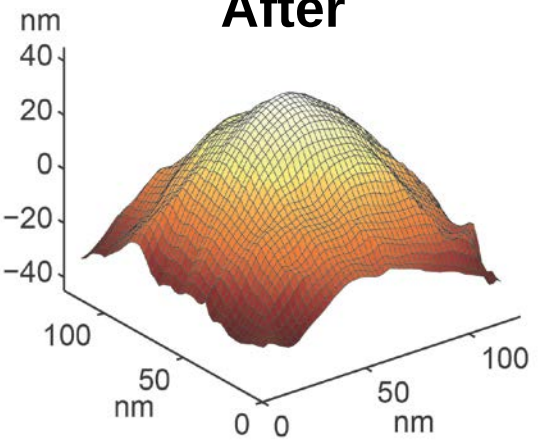
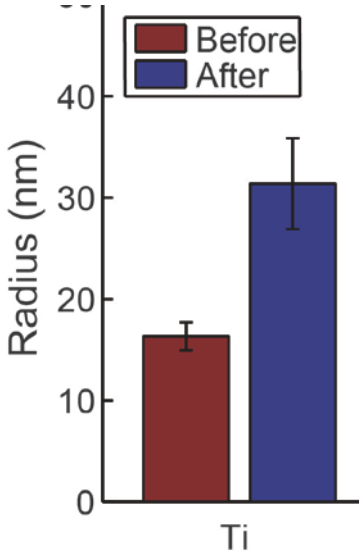
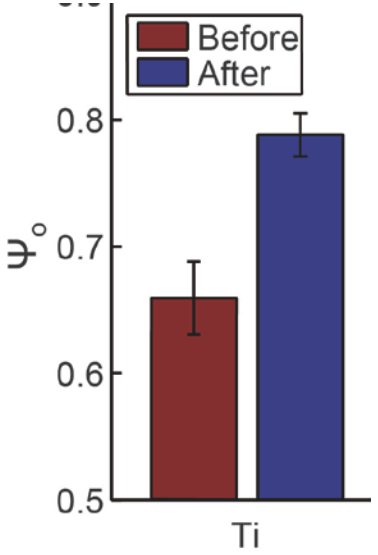
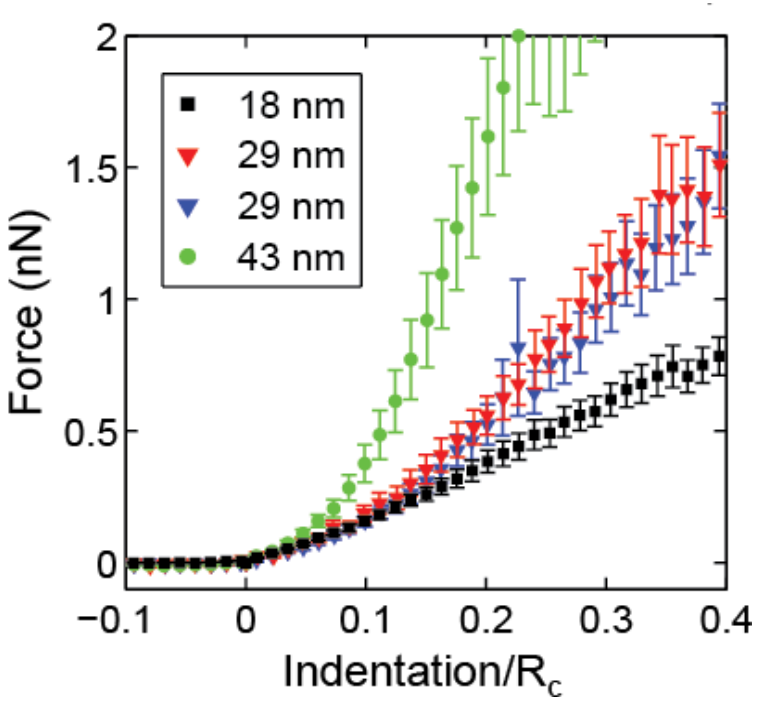






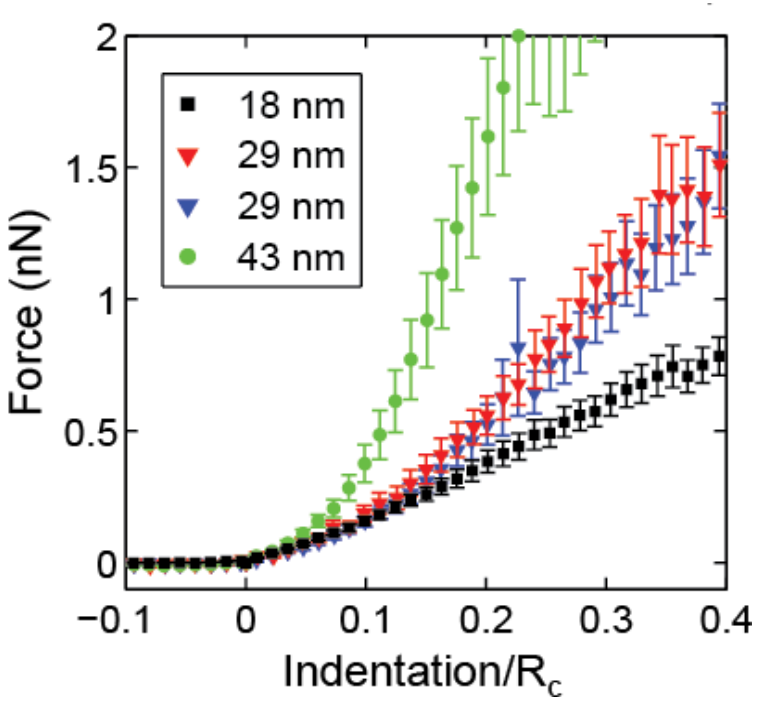
Material properties of vesicles



Vorselen *et al.* ACS Nano (2017)

Tip shape indeed matters!

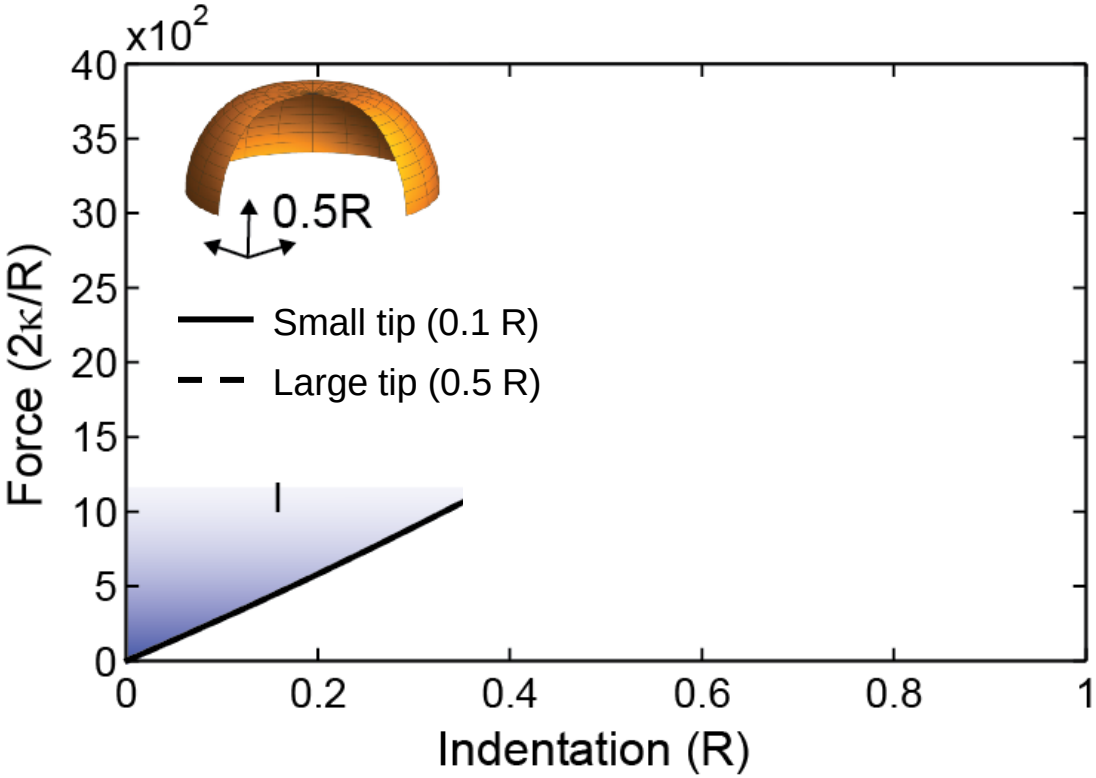
Material properties of vesicles



Vorselen *et al.* ACS Nano (2017)

Tip shape indeed matters!

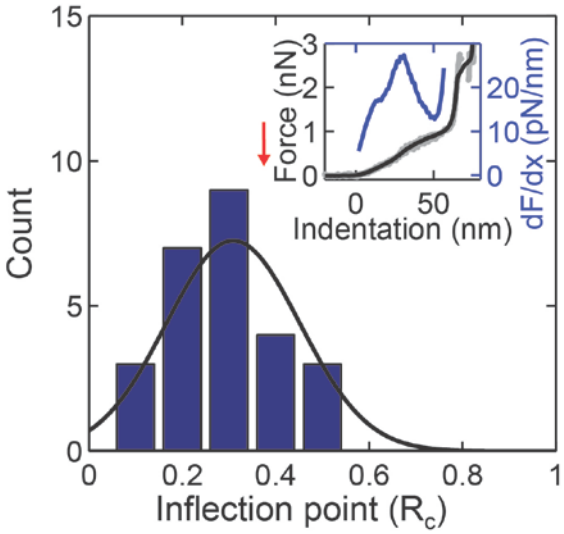
Canham-Helfrich theory (pure bending, no shear)

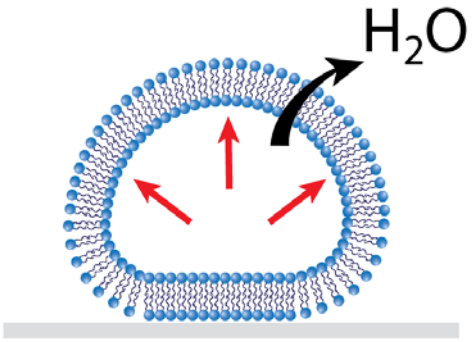


Material properties of vesicles

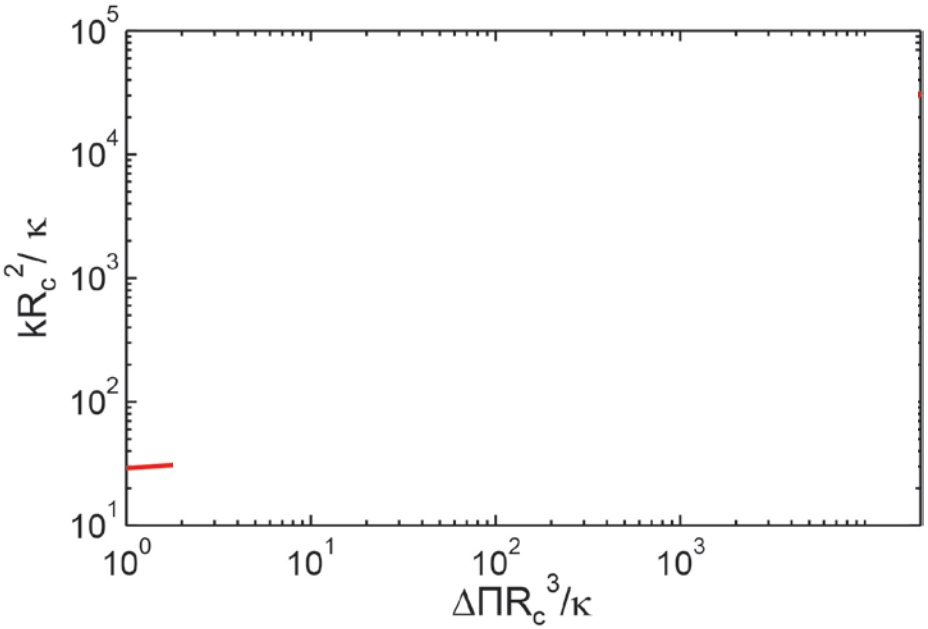
Inflection corresponds well to theoretical prediction

Stiffness is off!



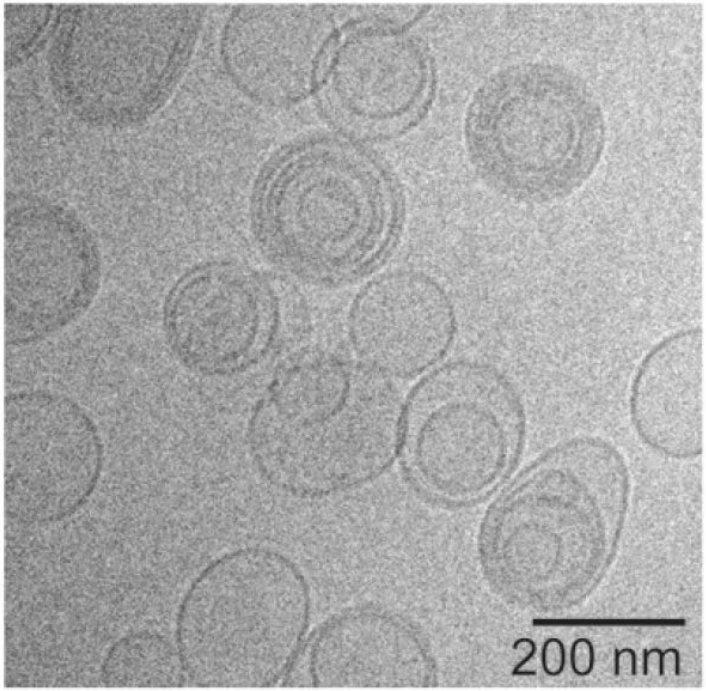


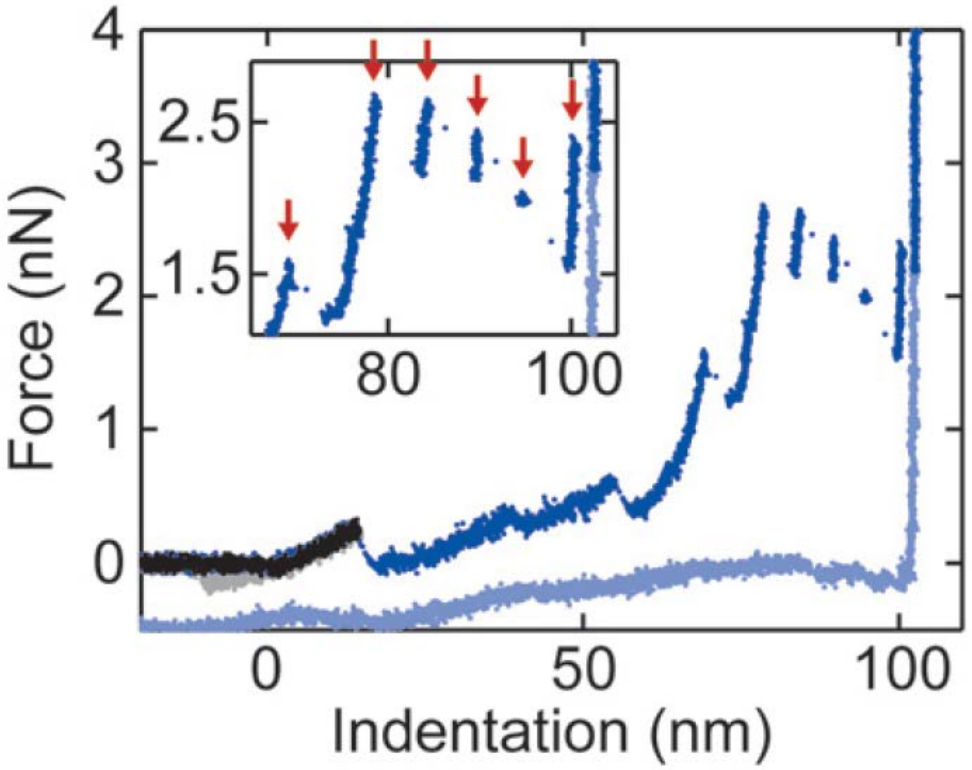
$\kappa = 14 \pm 1\ k_bT$



Correcting for deformation during adhesion and for tip shape and using adapted Canham-Helfrich theory we now determine bending modulus of vesicles.

Multilamellar vesicles

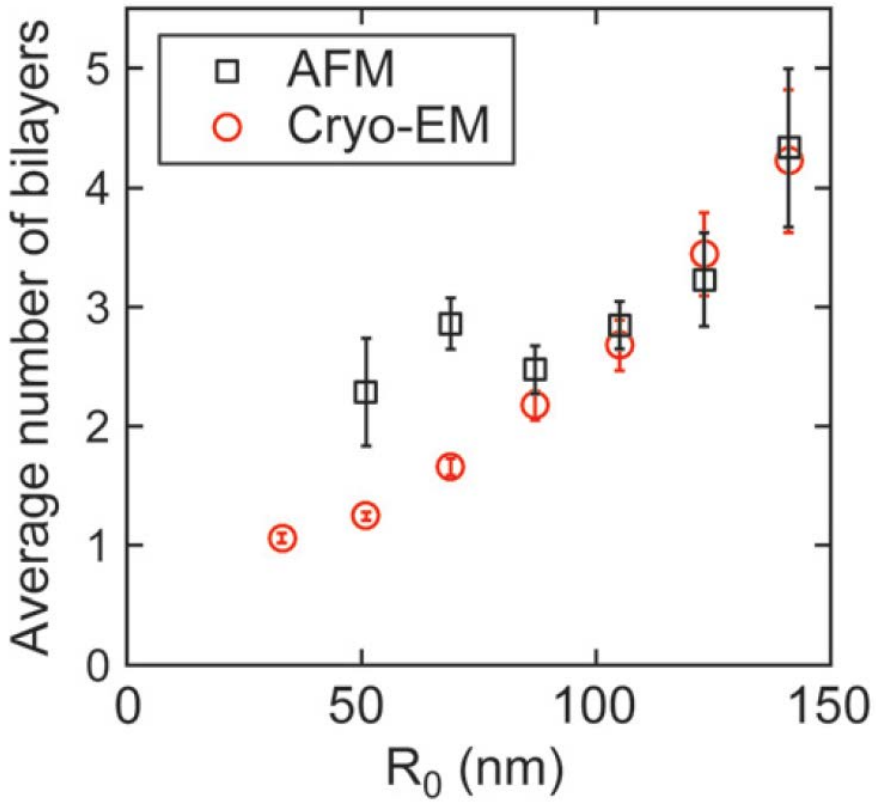




Vorselen *et al.* Nanoscale (2018)

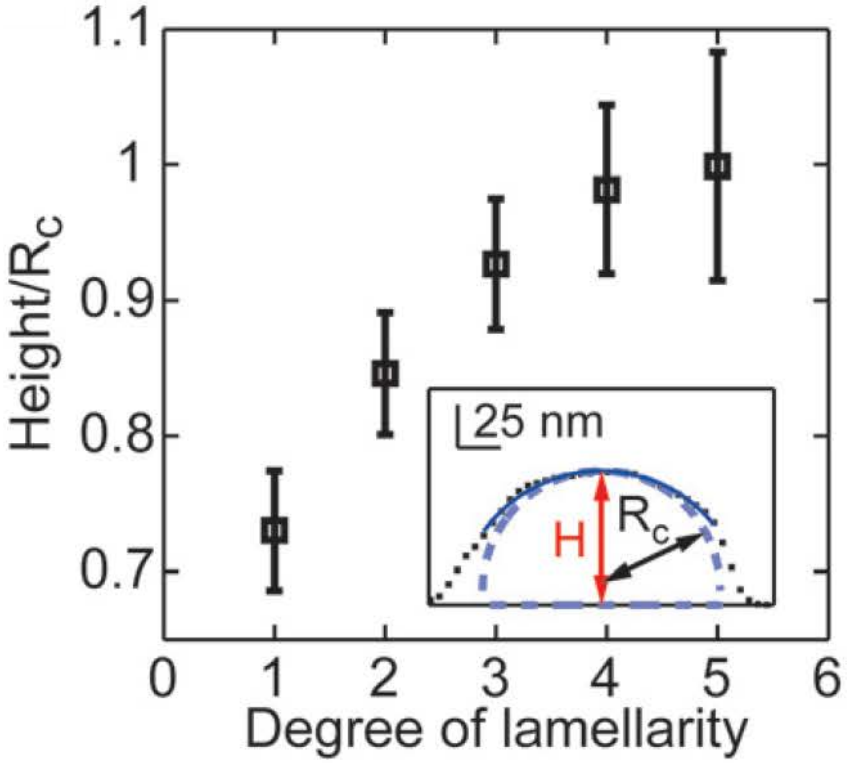
Number of bilayers can be determined by counting
(layers in cryo-EM data and breaks in the AFM data)

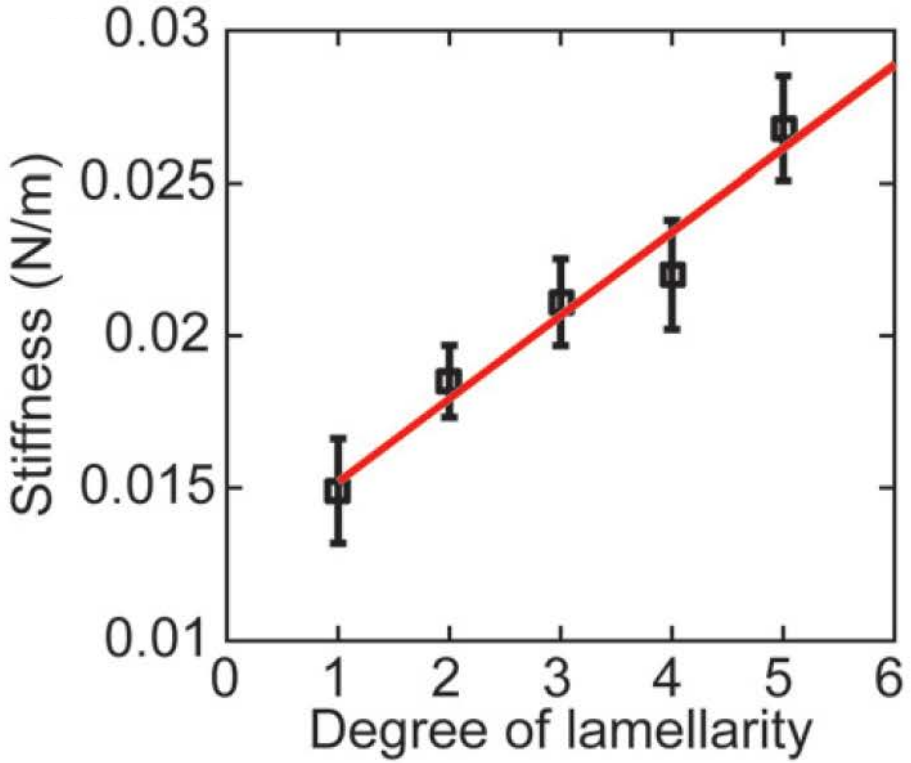
Multilamellar vesicles



Especially for large radii good fit between AFM and cryo-EM

Multilamellar vesicles

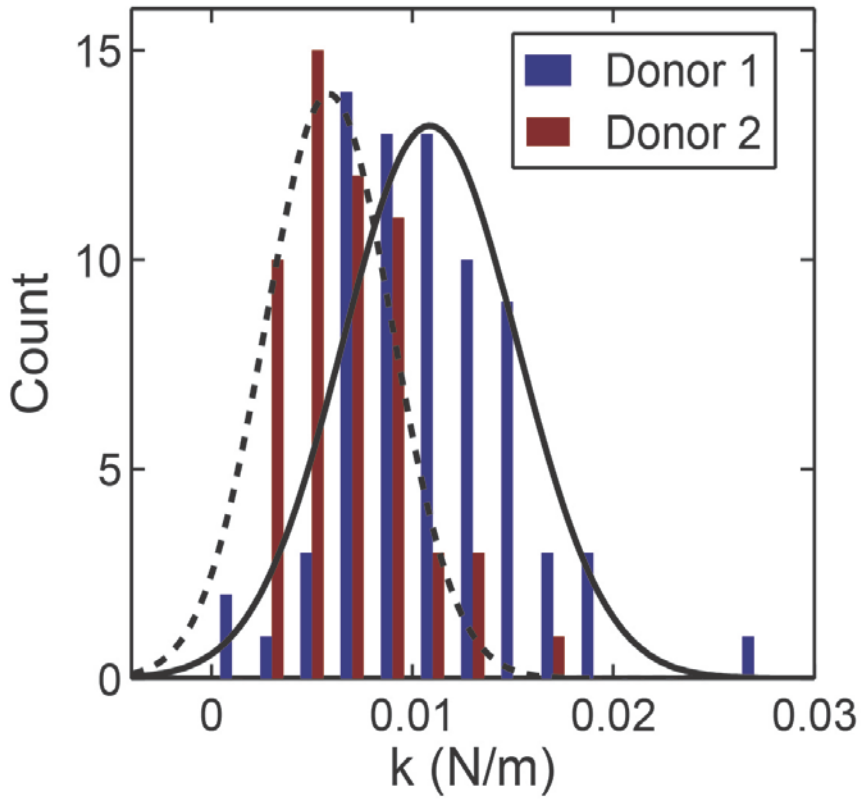


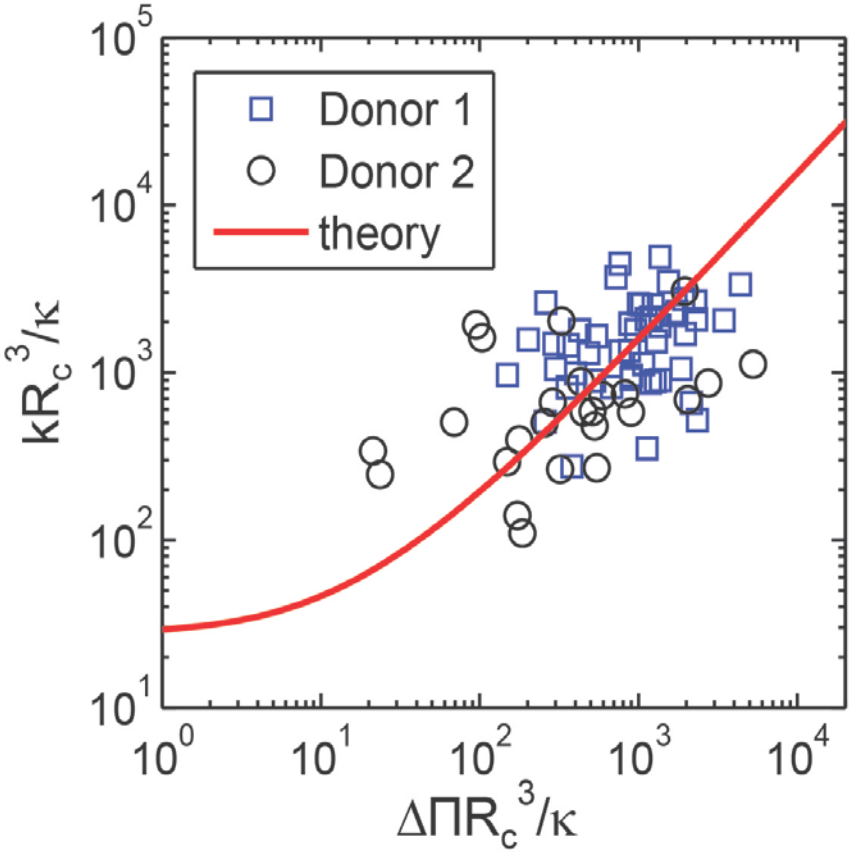


Sphericity increases with lamellarity.

Stiffness scales with lamellarity.

Extracellular vesicles of RBC



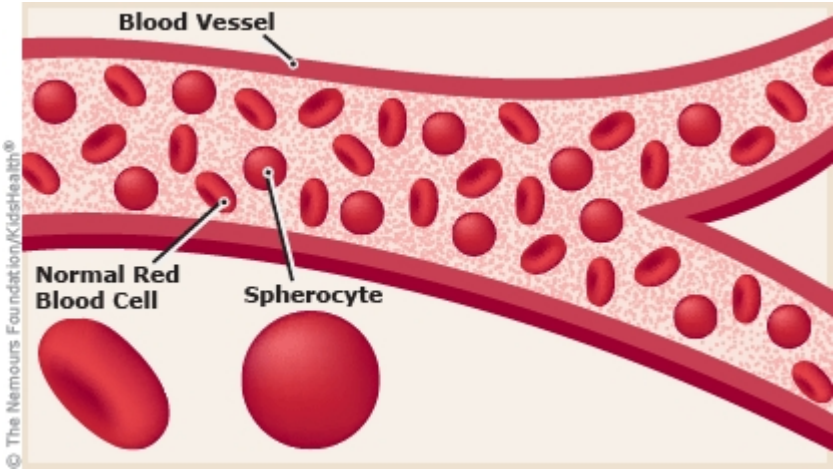


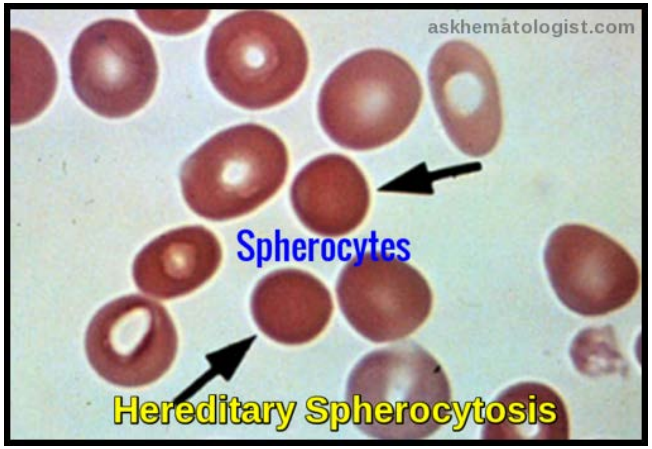
Vorselen *et al.* unpublished

Donor samples have different stiffness, yet similar bending modulus 15 ± 2 k_bT

Mechanics are very comparable to liposomes!

Extracellular vesicles of RBC & Spherocytosis





Weakened link between membrane and cytoskeleton

↓

Increased vesiculation

↓

Rounding and stiffening of RBCs

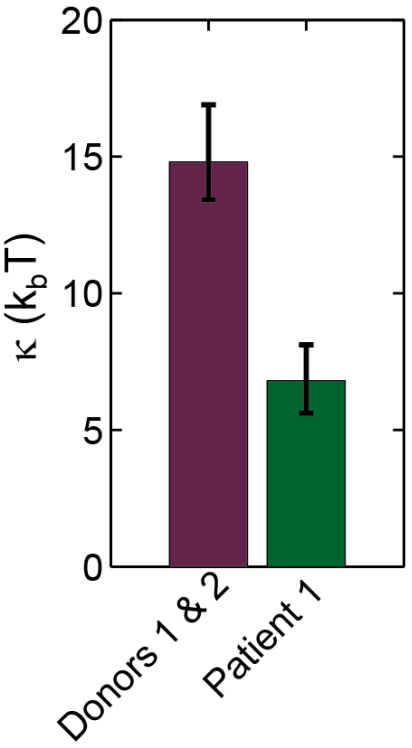
↓

Removal of RBCs in the spleen

↓

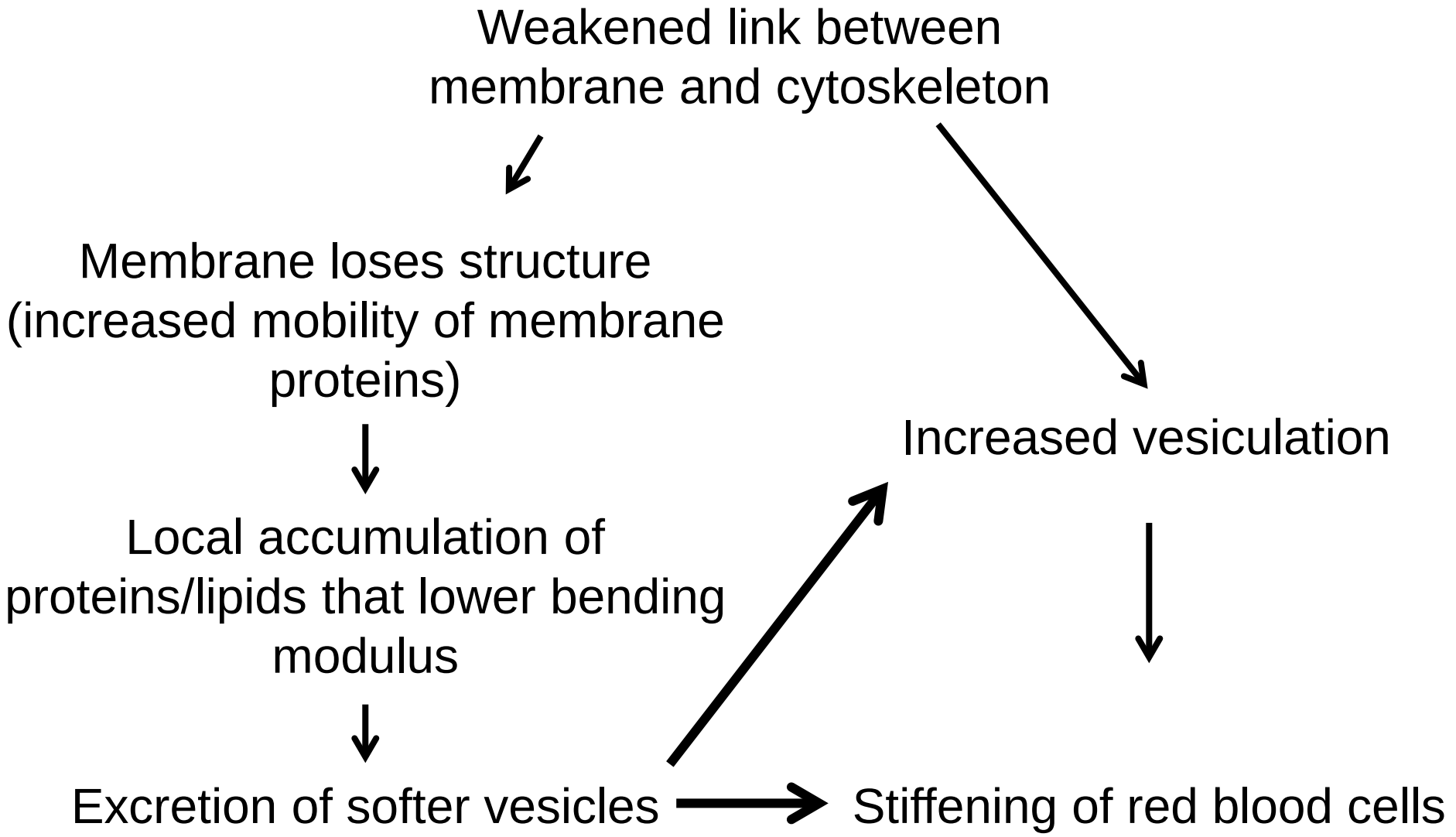
Symptoms like anemia, jaundice and gallstones

Extracellular vesicles of RBC & Spherocytosis

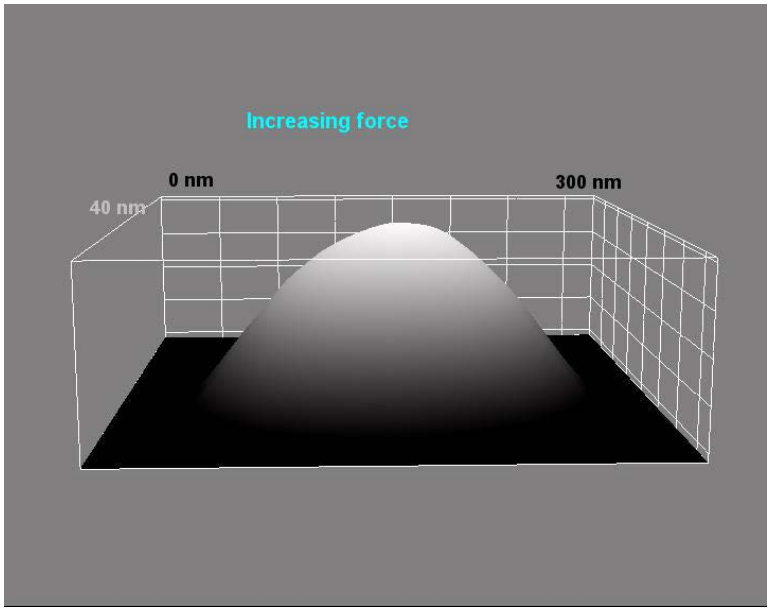


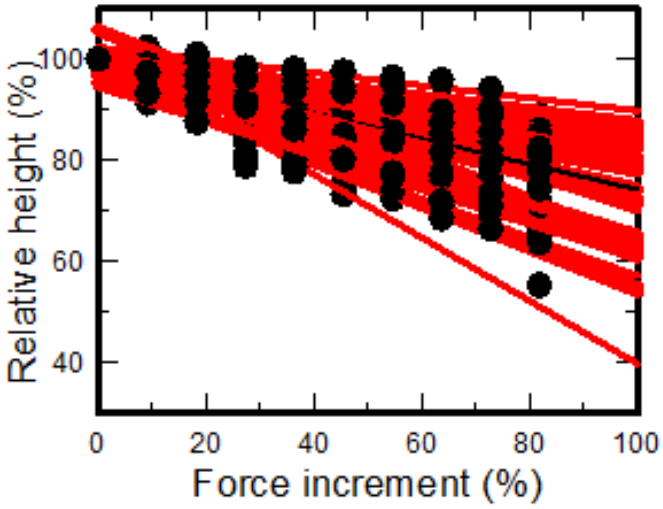
Bending modulus: $7 \pm 2\ k_bT$

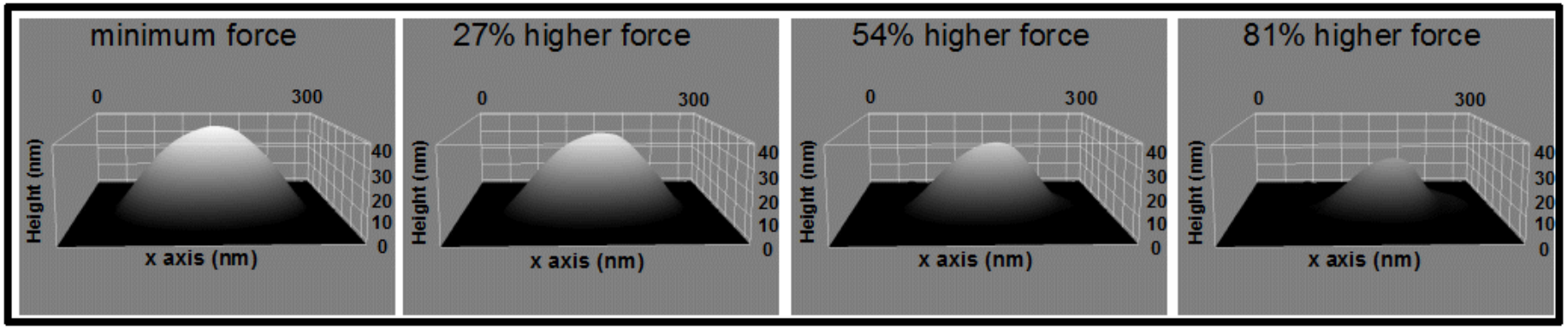
Extracellular vesicles of RBC & Spherocytosis



Dynamic response of vesicles during imaging







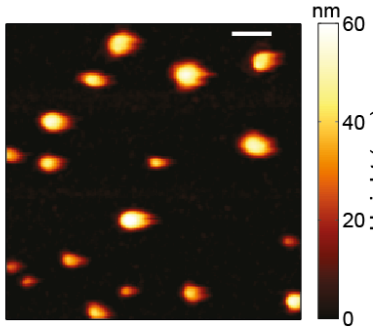
Conclusions

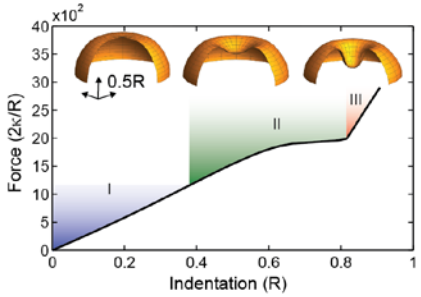
Correspondence between experiment and theory illustrates deep **understanding of mechanics of small vesicles**.

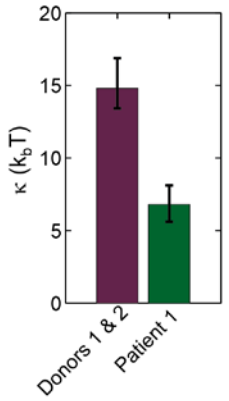
Quantitative model for vesicle indentations based on established theory allows **estimation of bending modulus**.

Approach widely useful for **artificial** and **natural** vesicles

Spherocytosis patient derived vesicles have lower κ, which potentially contributes to the **stiffening and clearance of red blood cells**







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University of Split, Croatia

Aug. 23 - Sept. 01
2018

ABC of physics of life

ASSEMBLING MOLECULAR MACHINES: viruses, ribosomes and other protein-RNA/DNA complexes, quaternary protein structures, DNA, receptors, proteins/ligands, polyelectrolytes

Interactions at **BIOLOGICAL & BIOCOMPATIBLE** interfaces: membranes, adhesion, extracellular matrix, protein-lipid/membrane interactions, biomimetic/hybrid surfaces

CELLS: physical properties of biological and bio-inspired systems






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Fraser MacMillan University of East Anglia, UK
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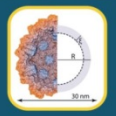


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EBSA&COST grants May 1 Regular registration May 15 Abstracts July 1

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CM1306 MOLECULAR MACHINES
CA15126 MOBIEU

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