# Physical Virology with Atomic Force Microscopy: the interplay between structure and function

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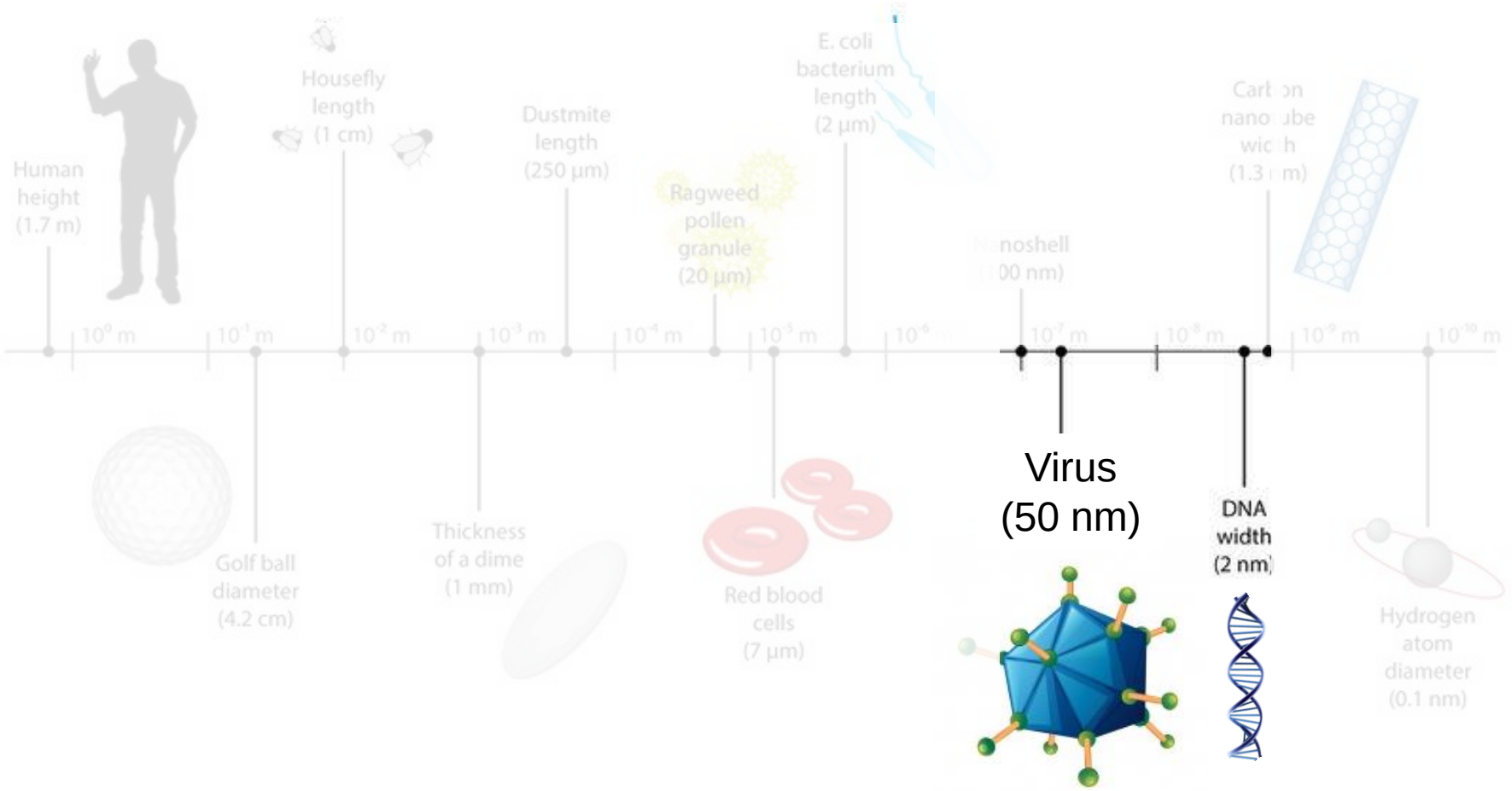
UNIVERSIDAD AUTONOMA DE MADRID

**A CIVIS e-journey into Nano**

# Viruses are nanomachines

# Virus scale


Human height (1.7 m)
Housefly length (1 cm)
Dustmite length (250 µm)
Ragweed pollen granule (20 µm)
E. coli bacterium length (2 µm)
Virus (50 nm)
DNA width (2 nm)
Golf ball diameter (4.2 cm)
Thickness of a dime (1 mm)
Red blood cells (7 µm)
Hydrogen atom diameter (0.1 nm)

# Atomic Force Microscopy

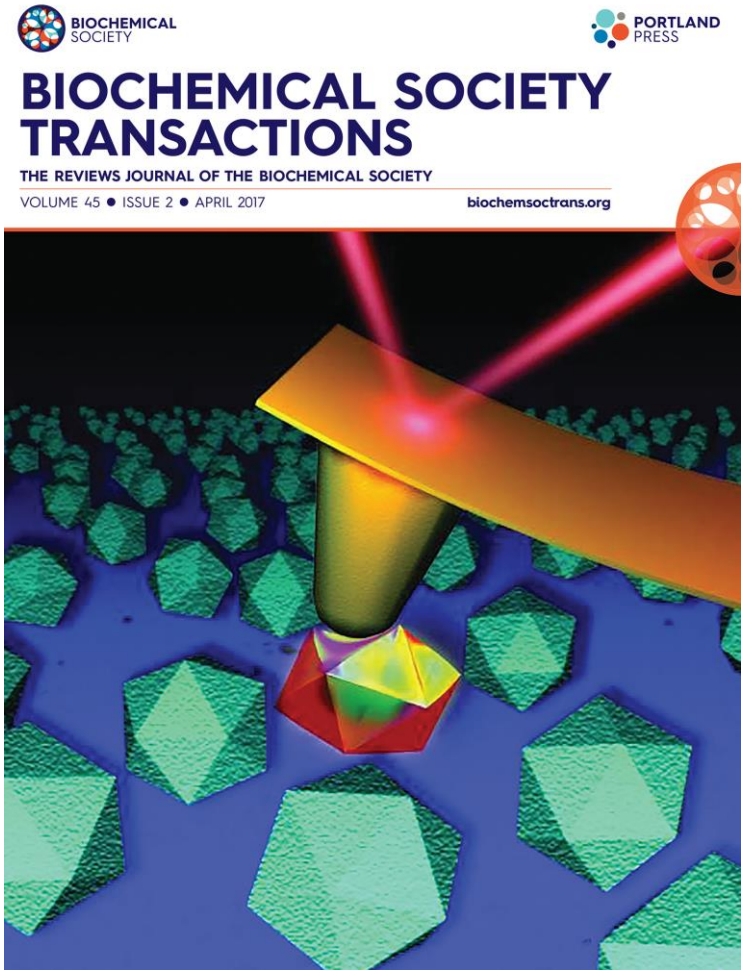
**Physiological conditions**

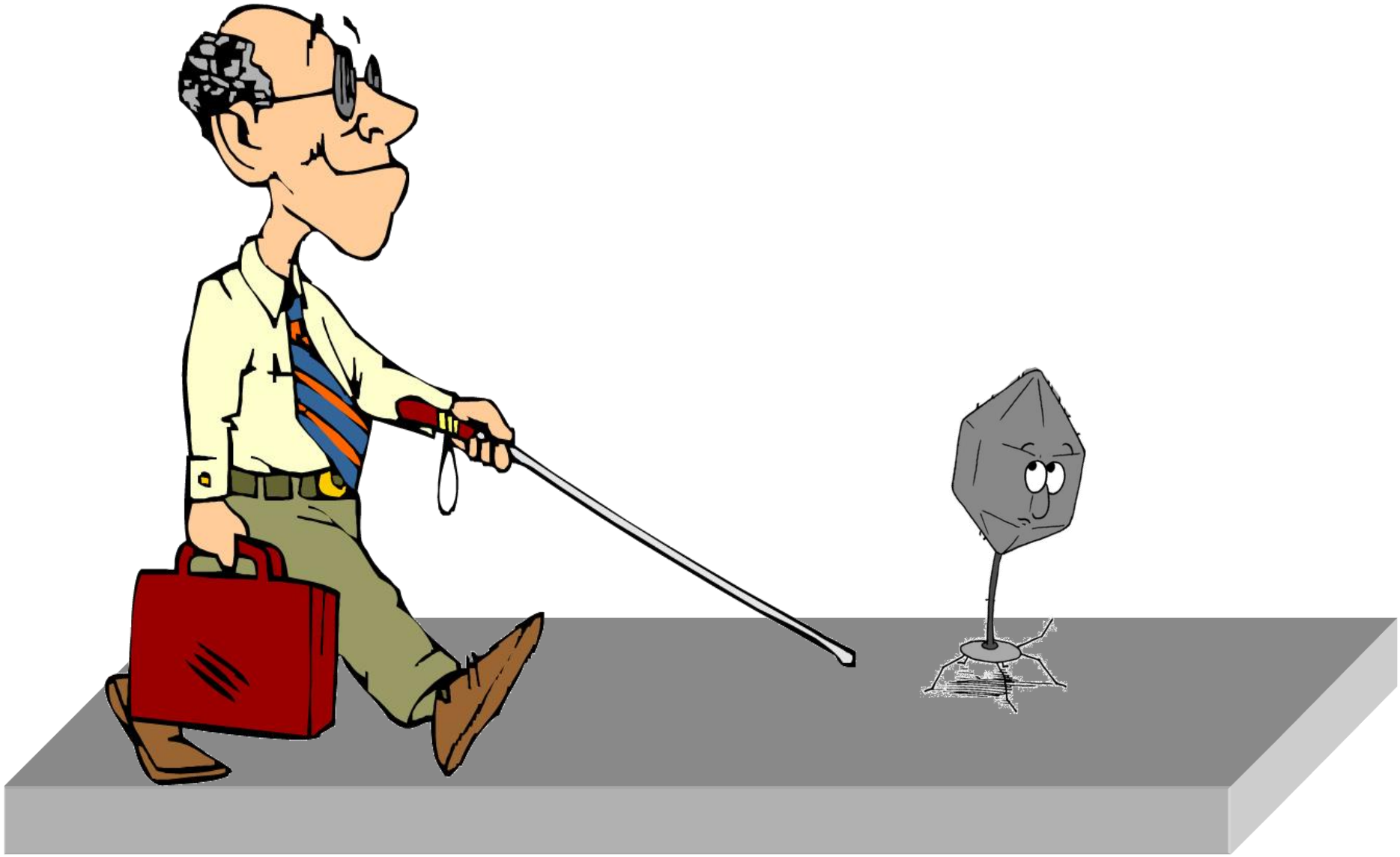
*Functional protein shells*

**Mechanics**

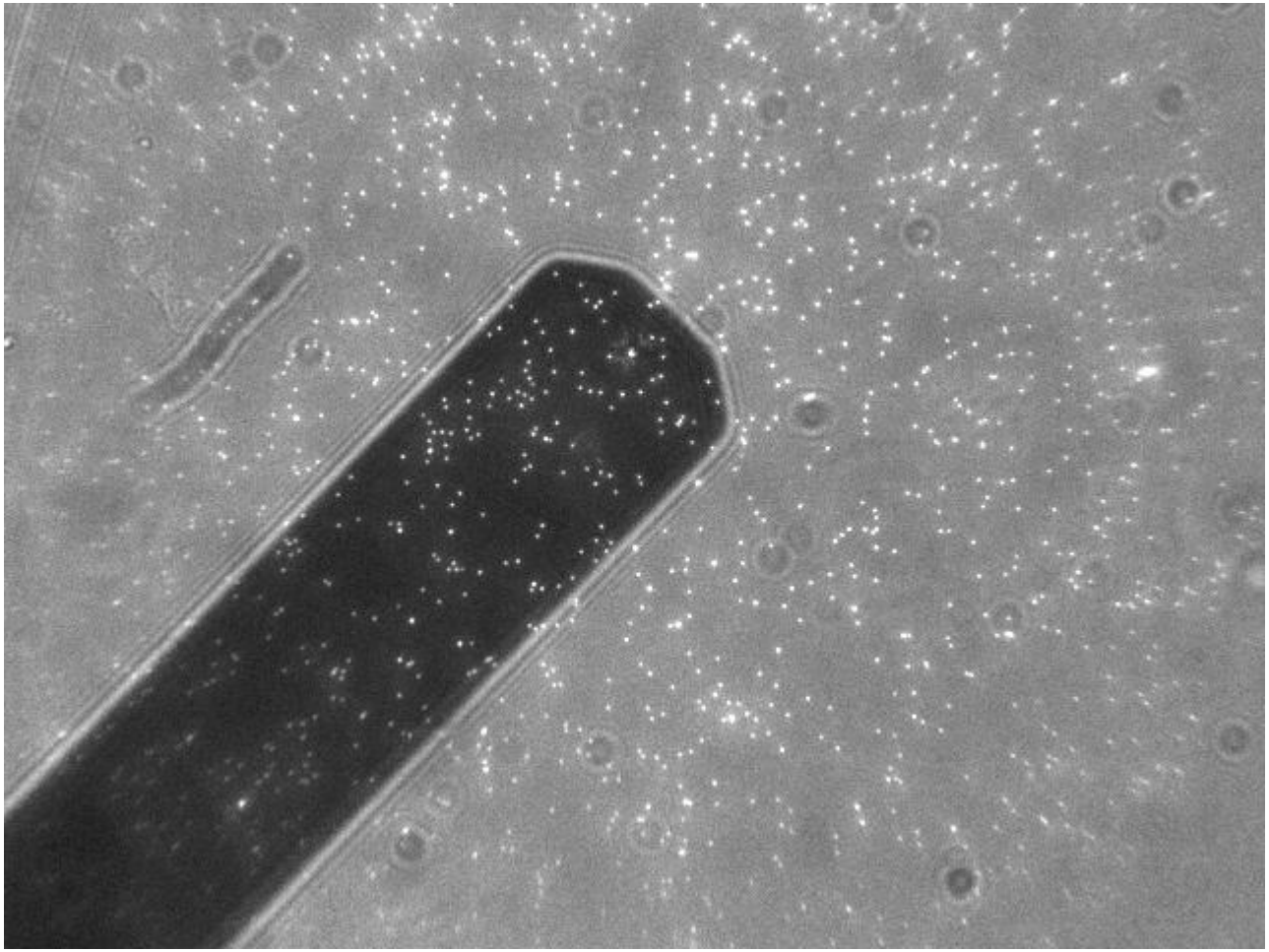
*Manipulation*

*Real time experiments*

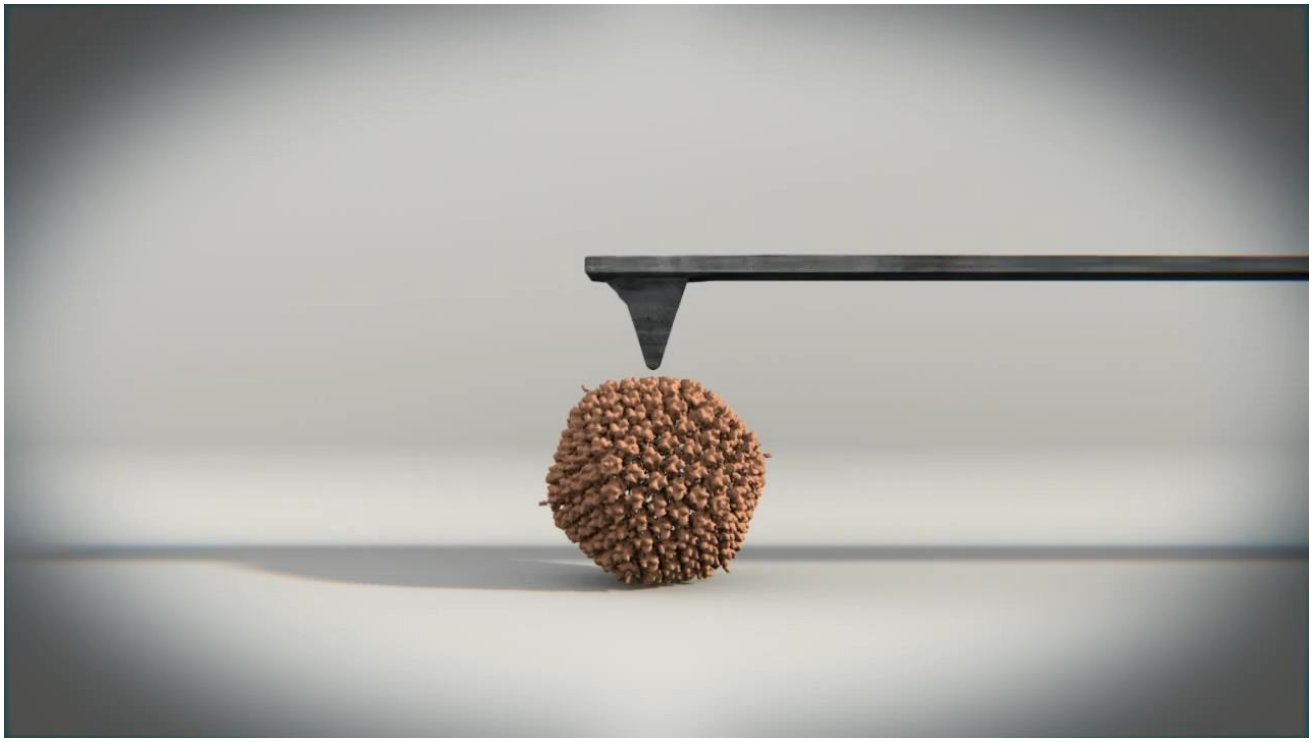




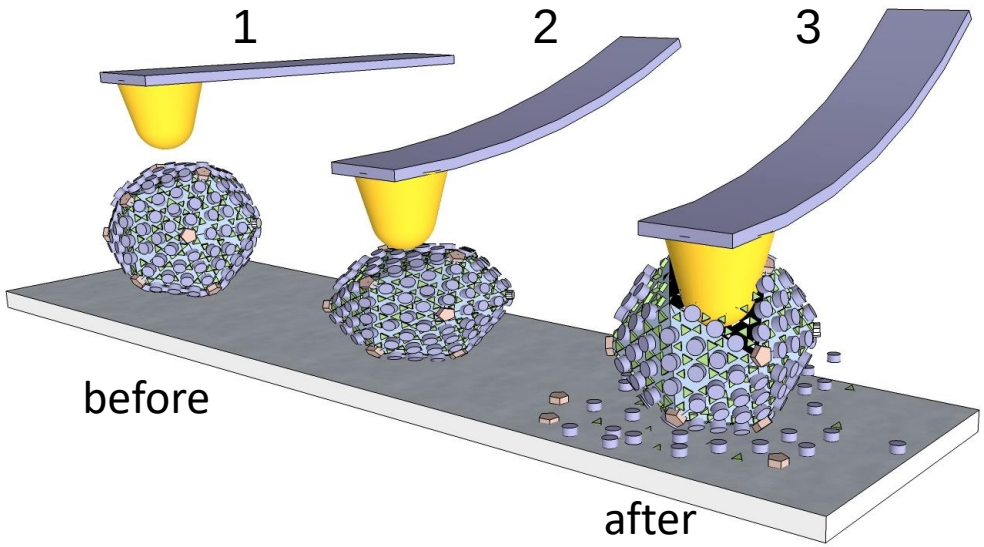
# Cantilever/virus size

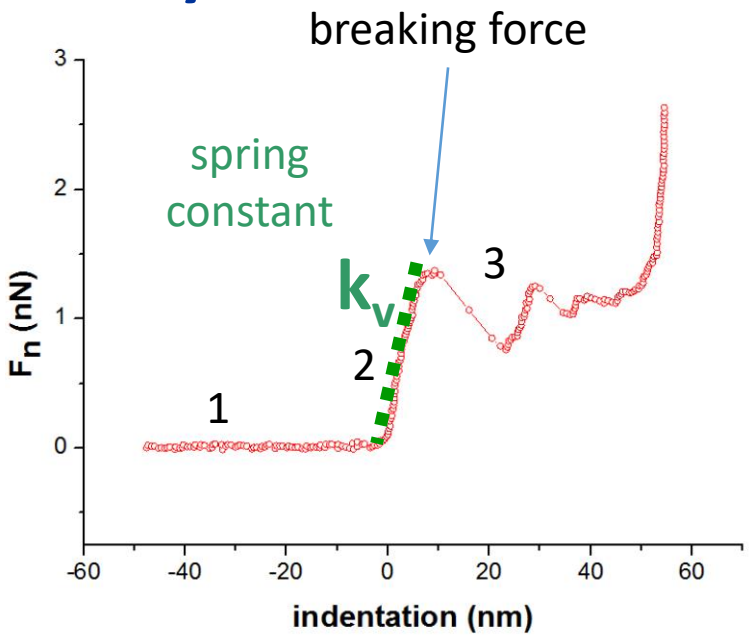


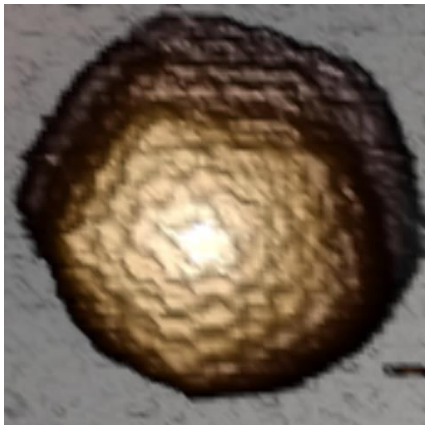
# Single indentation assay



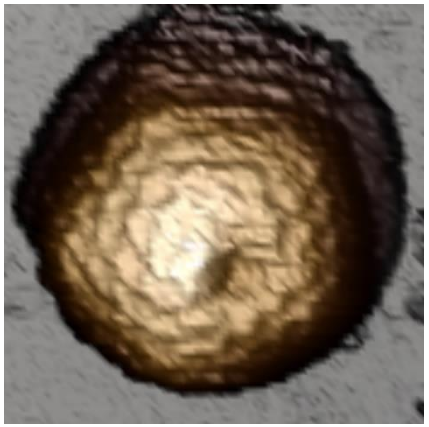
# Single indentation assay



before



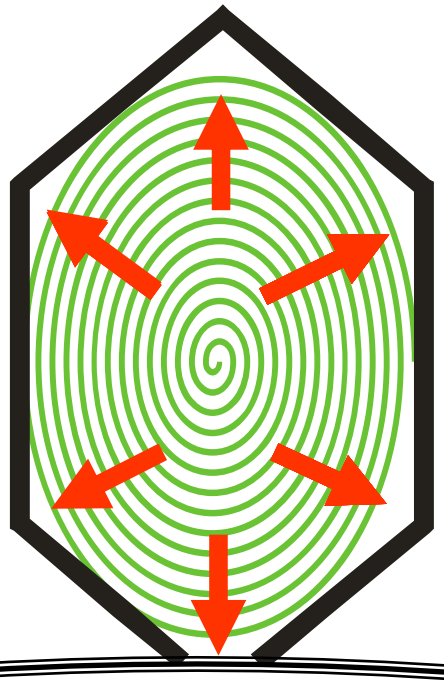
after

# DNA ejection from bacteriophages

**Is DNA confined at high pressures?**

William M. Gelbart and Charles M. Knobler

PERSPECTIVES
27 MARCH 2009 VOL 323 SCIENCE



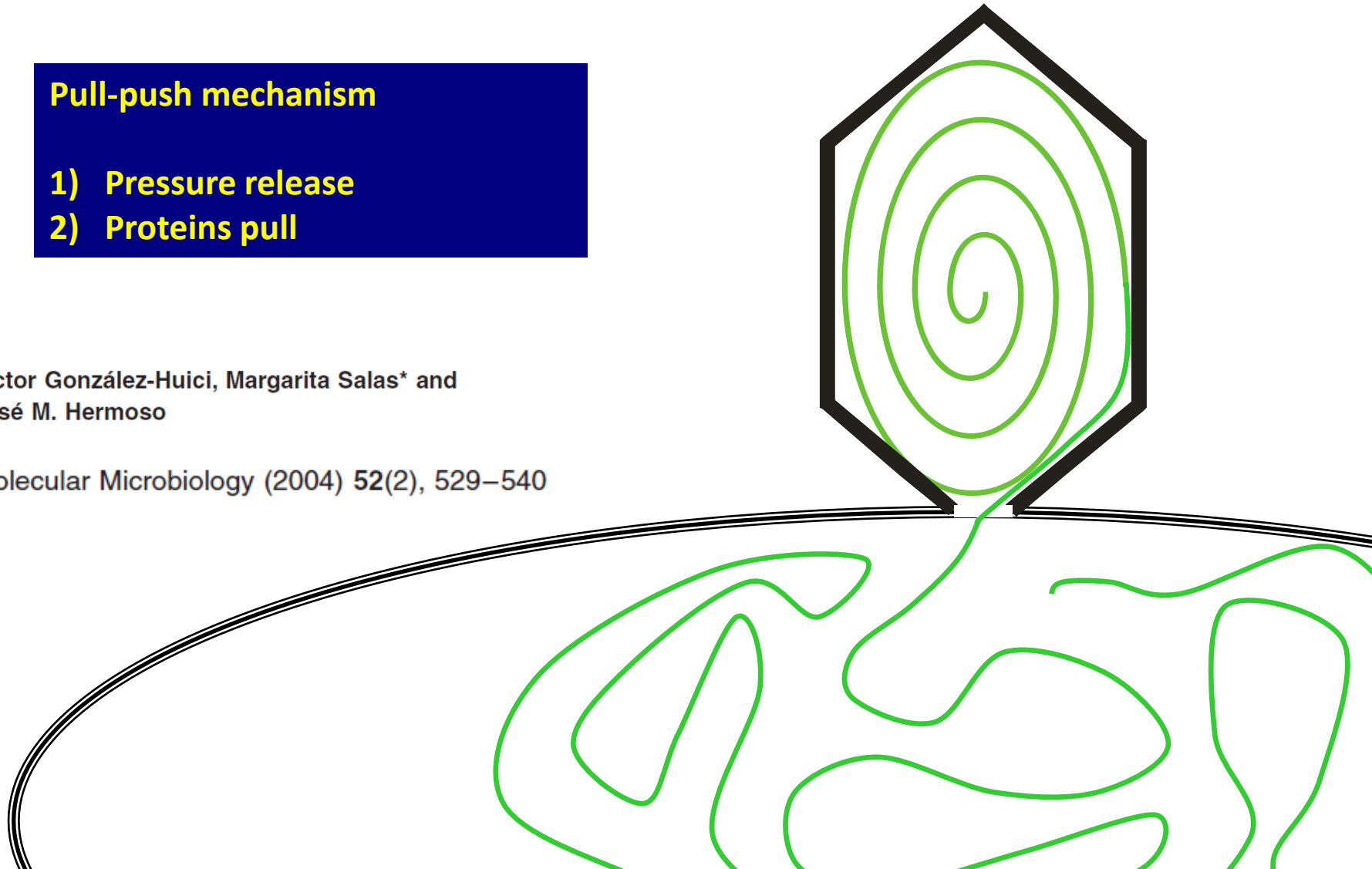
# DNA ejection from bacteriophages

**Pull-push mechanism**

1) **Pressure release**
2) **Proteins pull**

Víctor González-Huici, Margarita Salas* and
José M. Hermoso

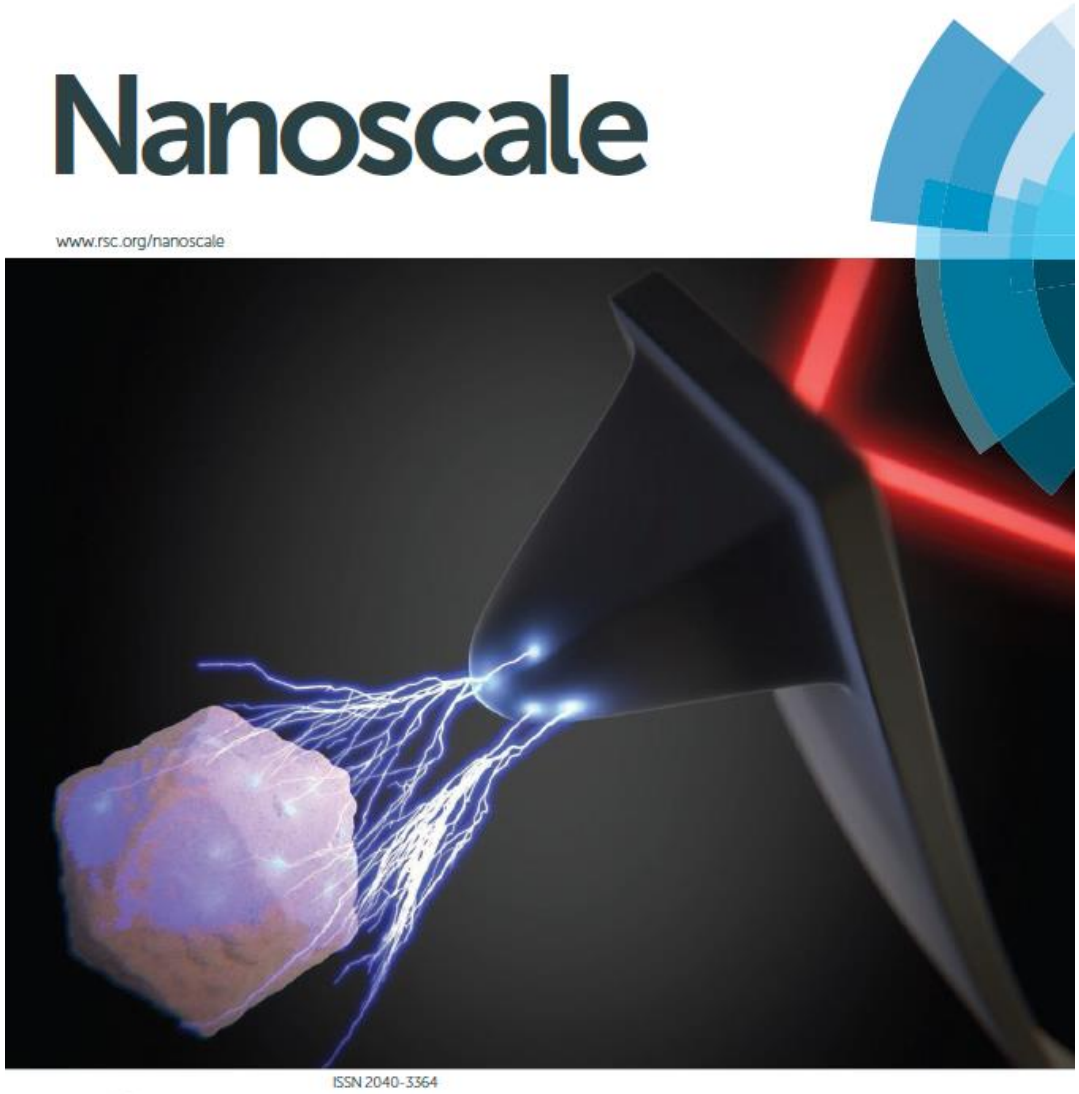
Molecular Microbiology (2004) **52**(2), 529–540



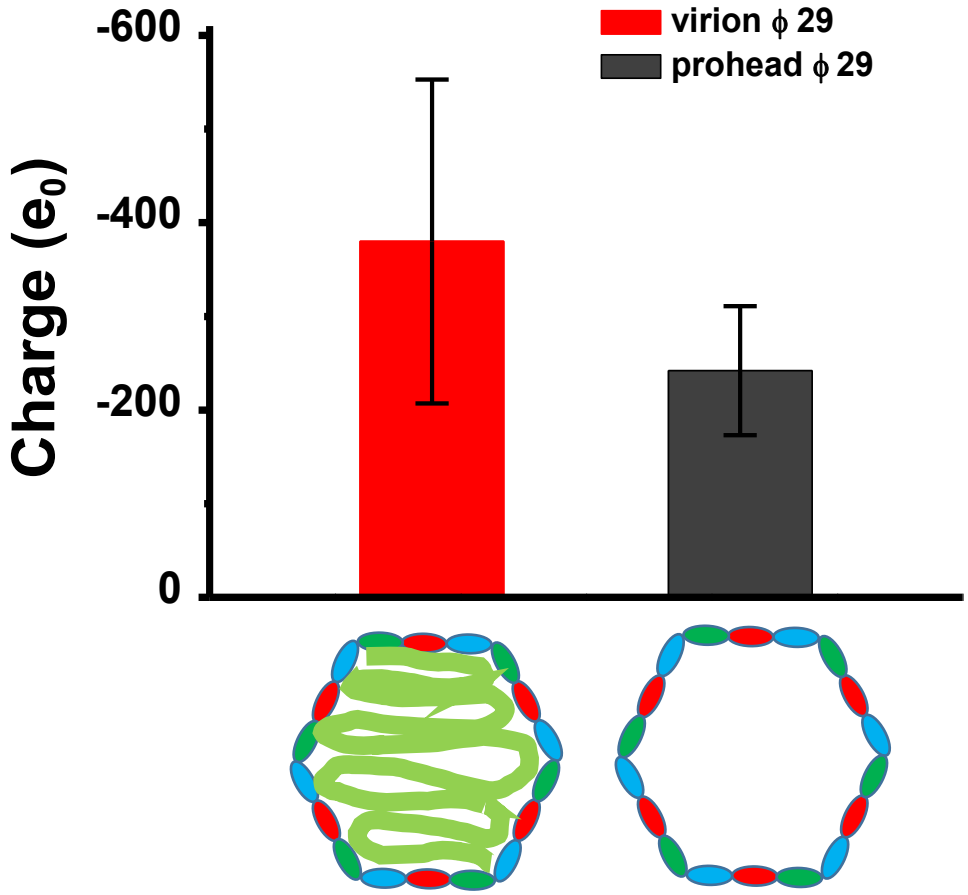

**40 atmospheres (wheel about 2 atmospheres)**

# ELECTROSTATICS

Volume 7 | Number 41 | 7 November 2015 | Pages 17151–17574

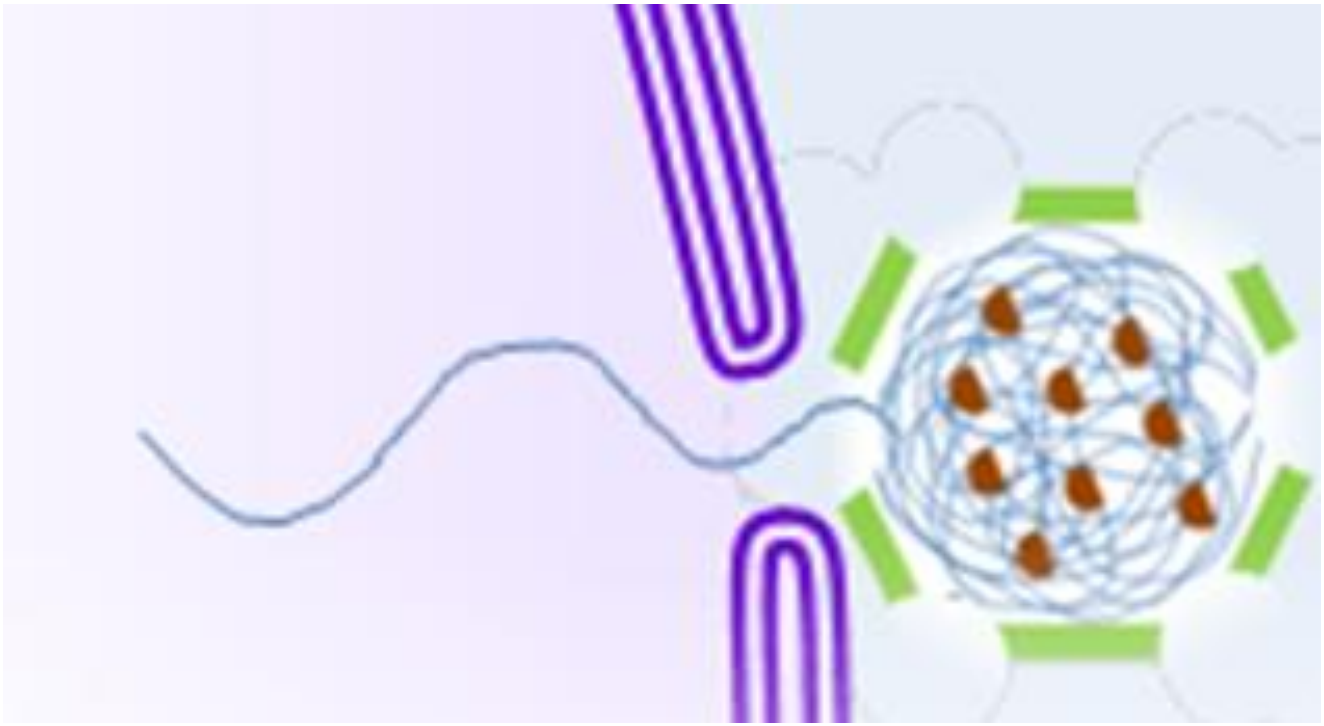


# Phage ϕ29



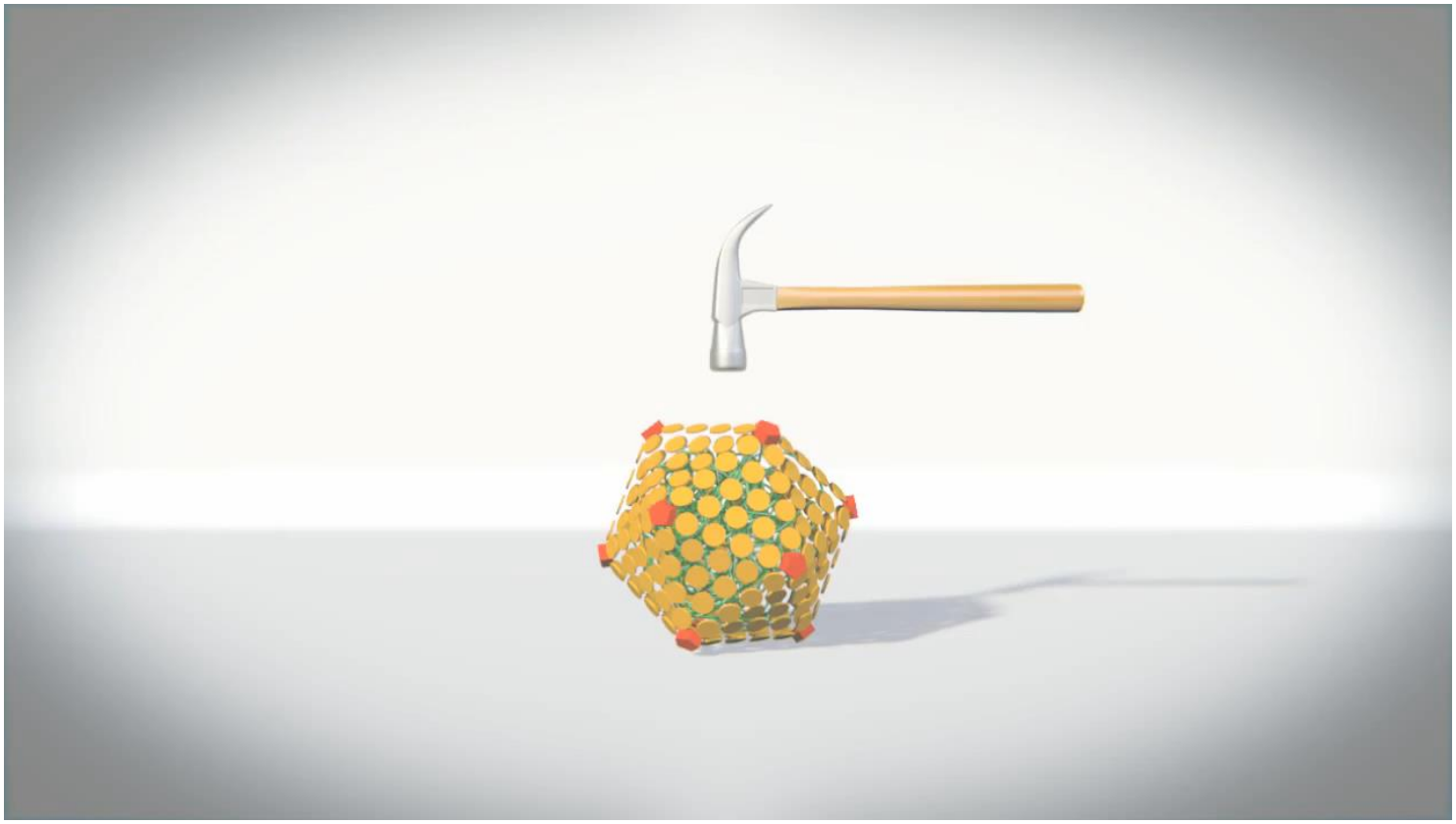

**Viral genome influences on the virus charge**

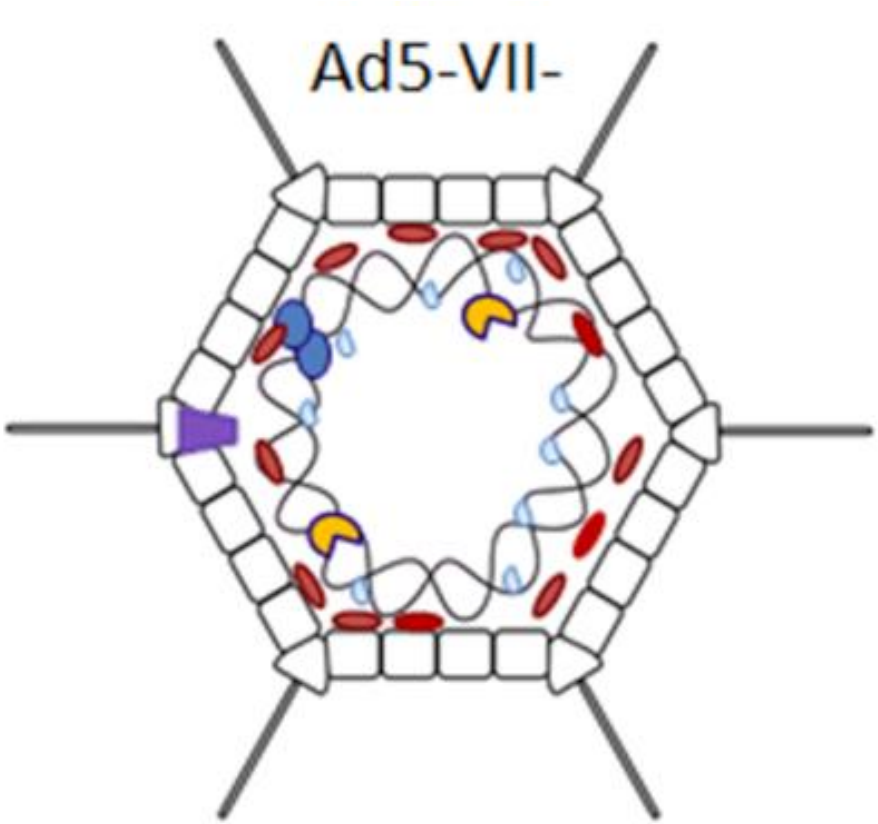
# DNA release human adenovirus

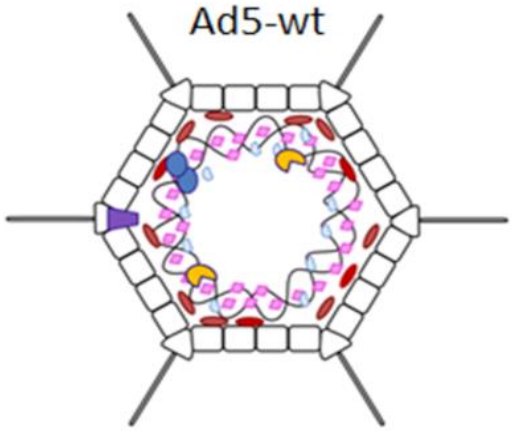


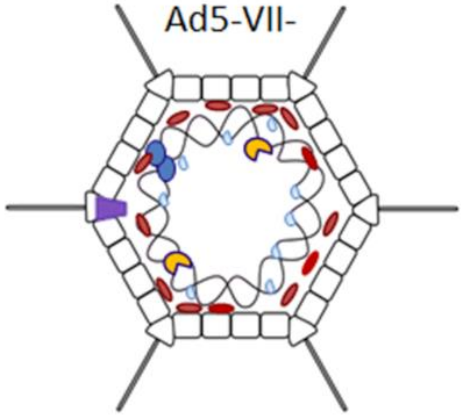
diffusion of DNA from broken particles

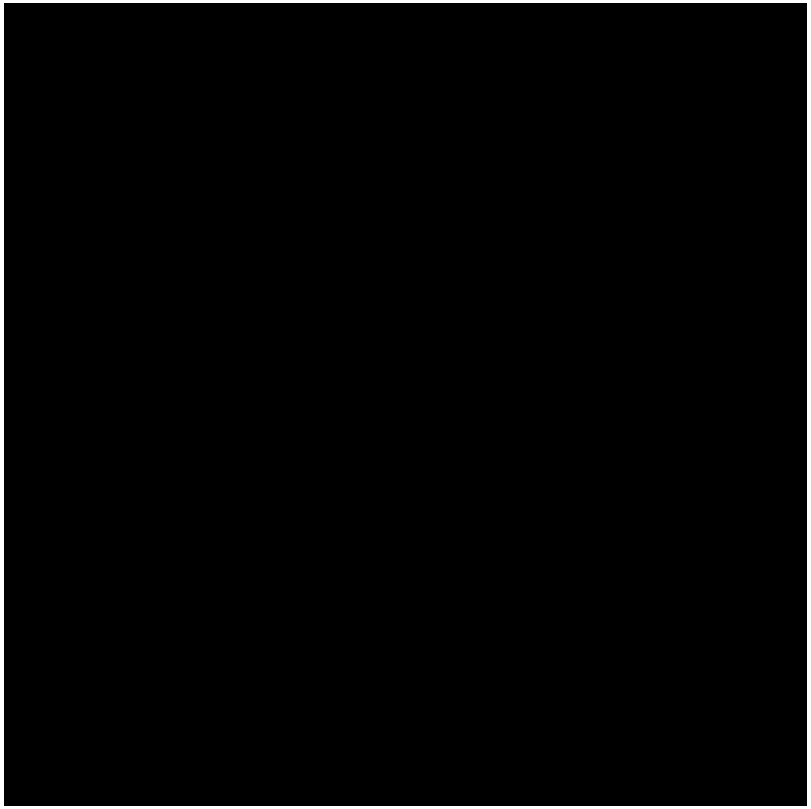
# Mechanical fatigue assay

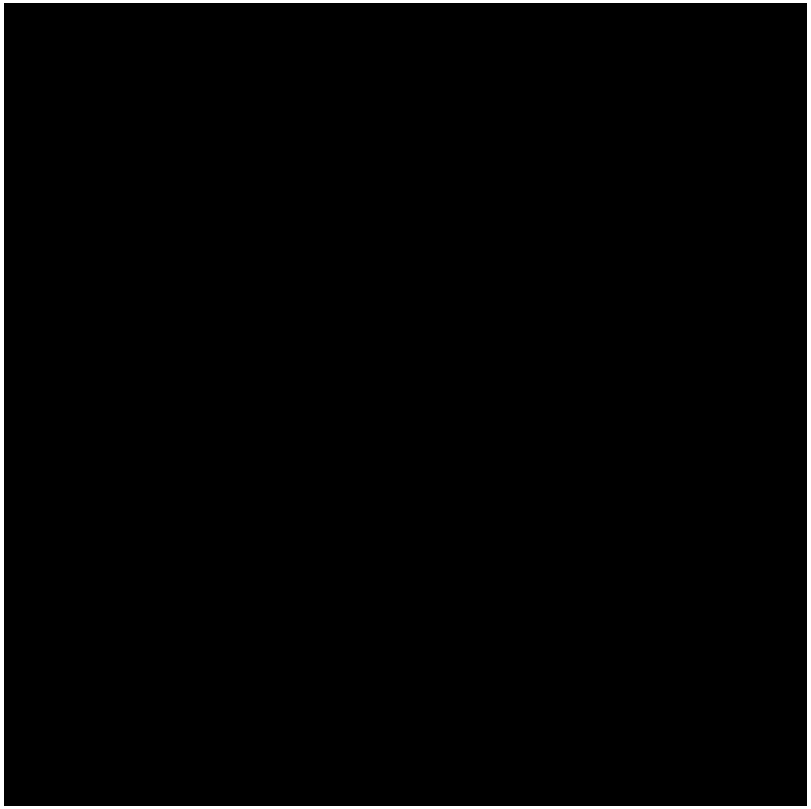



Ad5-VII-

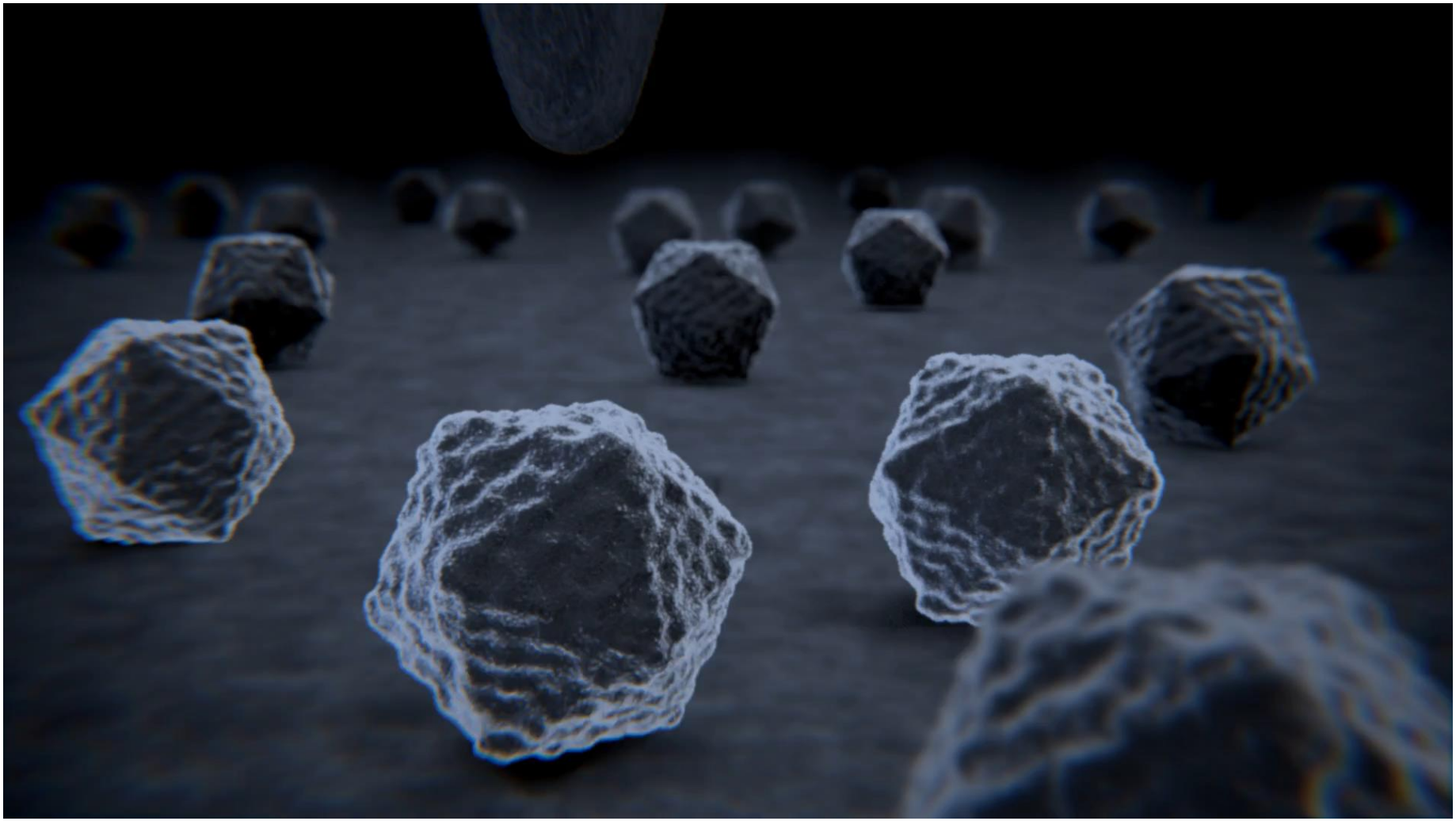

Ad5-wt


Ad5-VII-

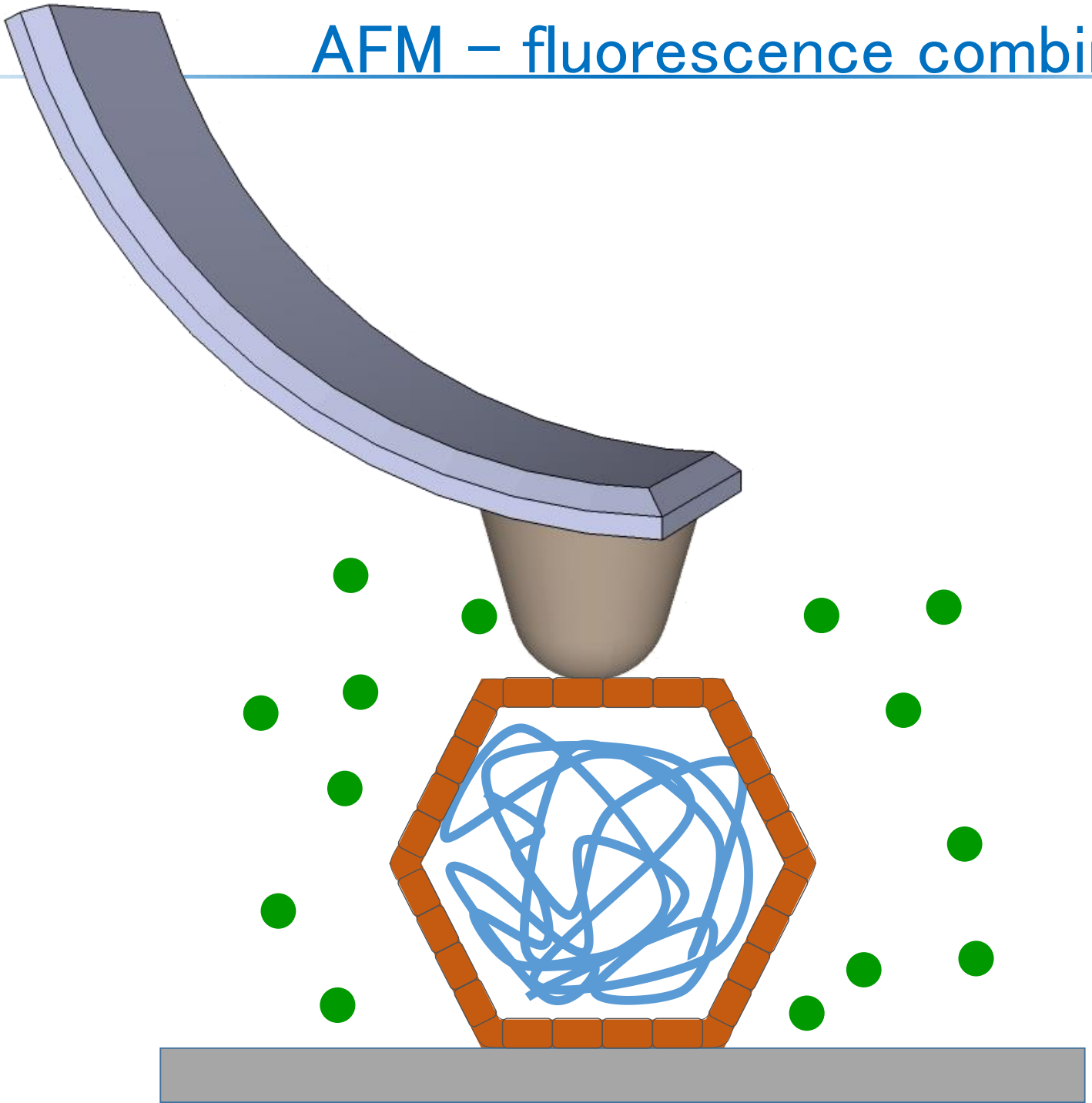




## DNA release: AFM – fluorescence combination



# AFM – fluorescence combination



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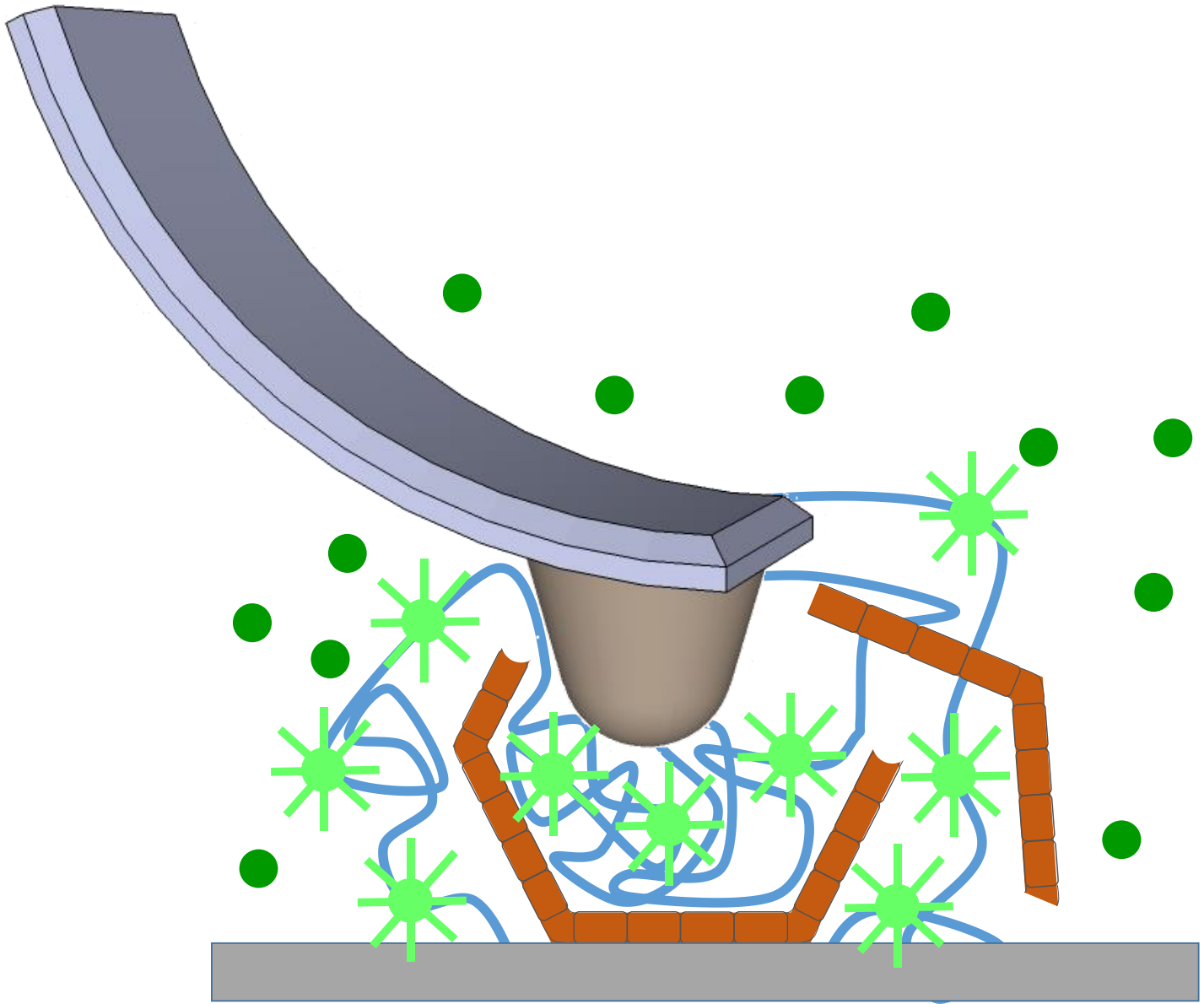
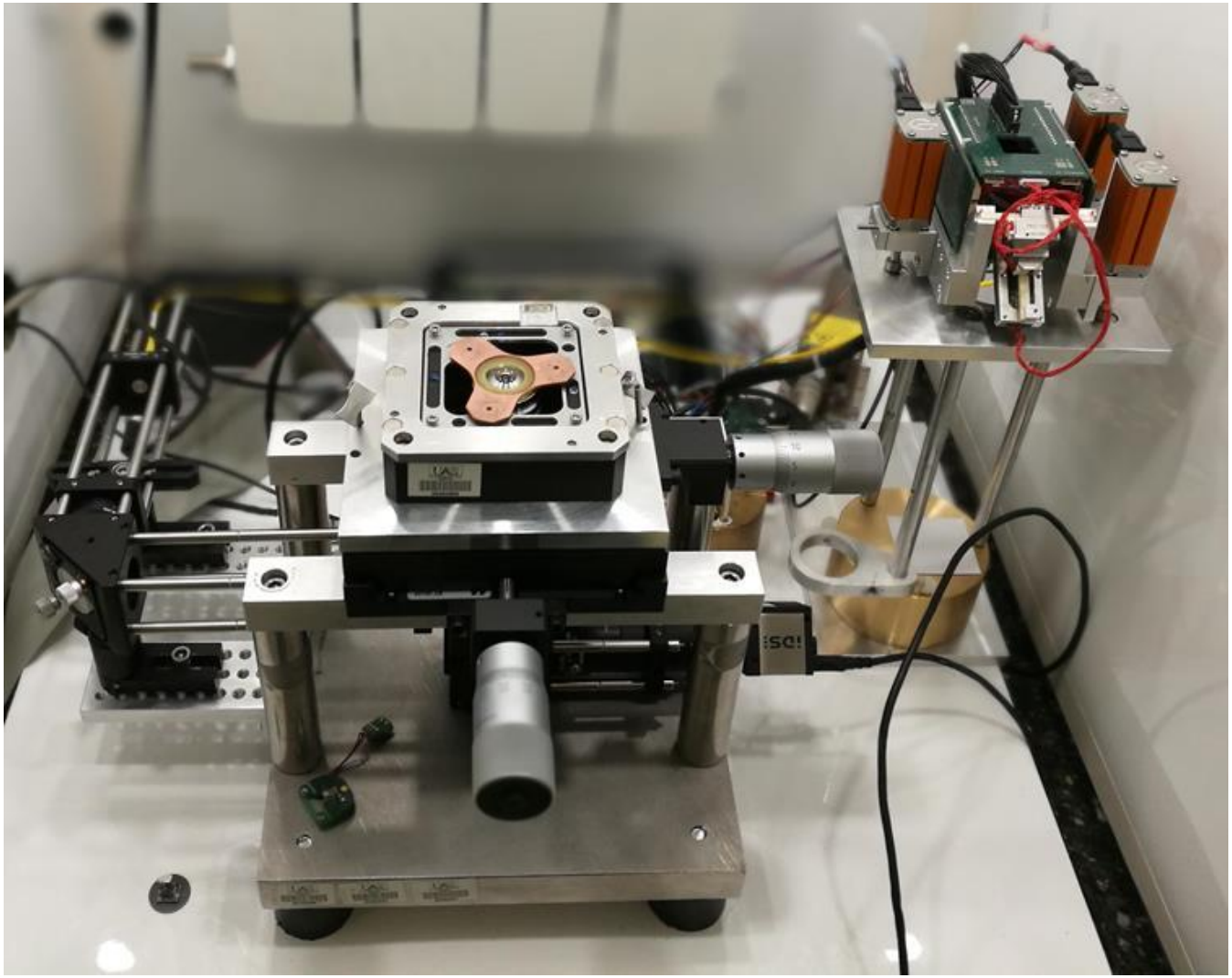
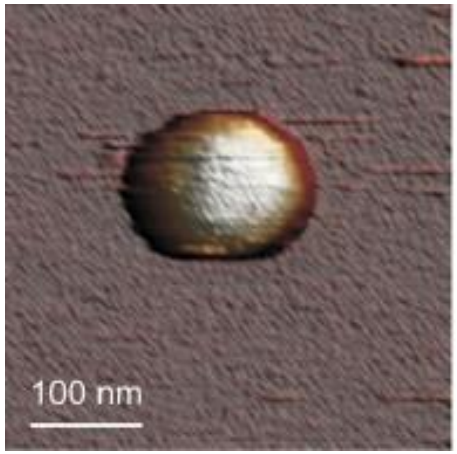
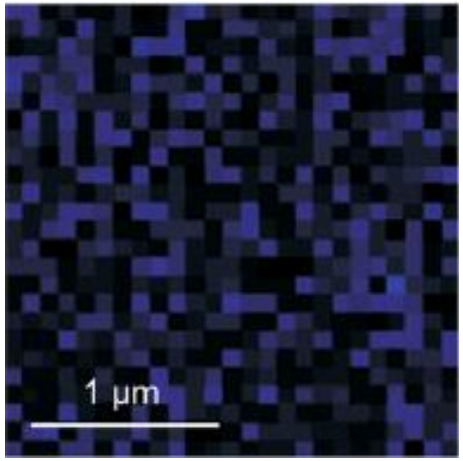


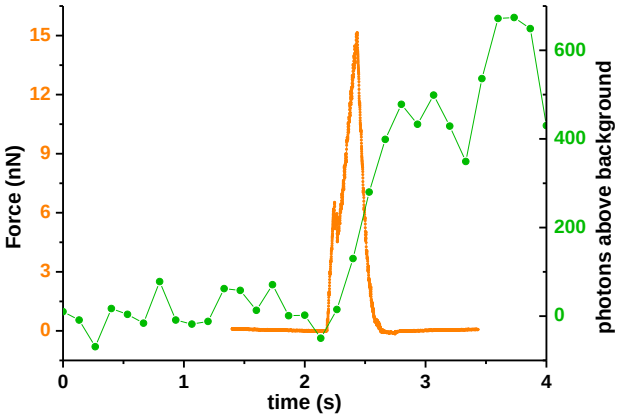
# BUILDING AN AFM/FLUORESCENCE SYSTEM

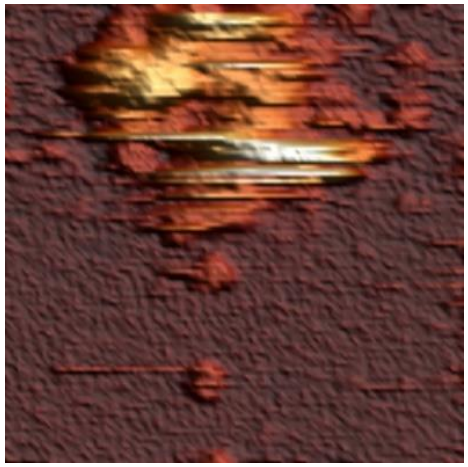


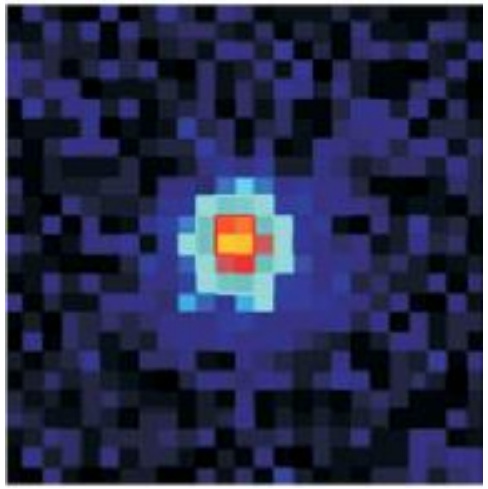
# Mechanical unpacking of Adenovirus



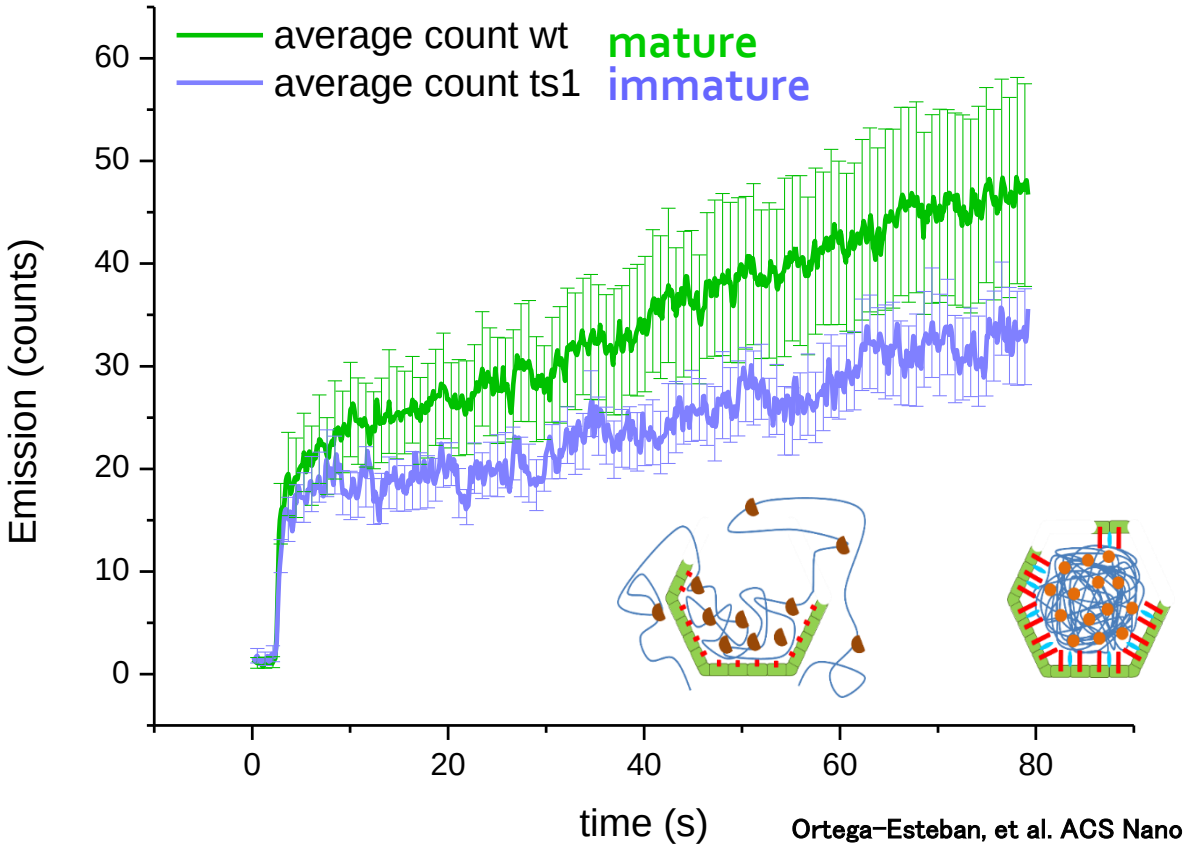





simultaneous single particle fluorescence with AFM

Monitor DNA release with YOYO-1

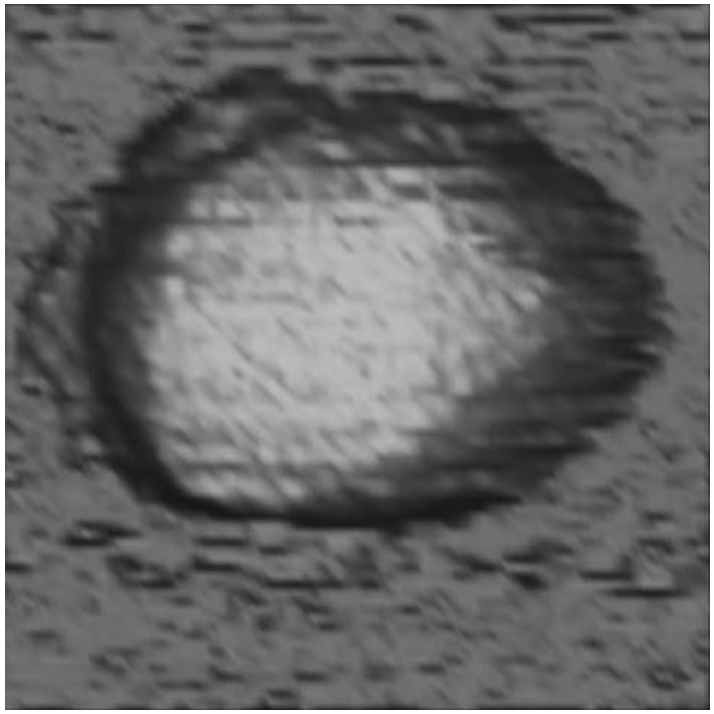
# Quantifying DNA release

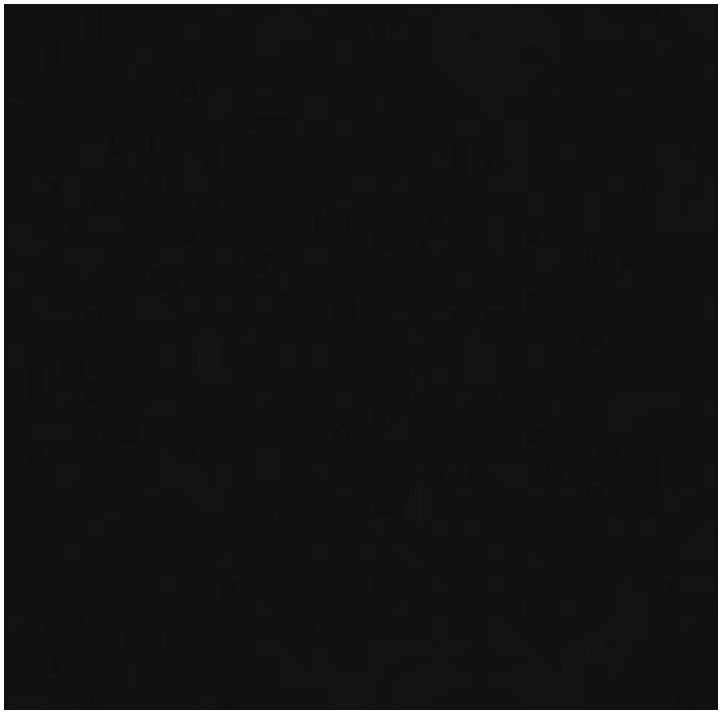



Ortega-Esteban, et al. ACS Nano (1) 2015

Ortega-Esteban, et al. ACS Nano (2) 2015

# Controlled capsid disassembly





## Collaborators

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**Carlos E. Catalano**
**Carmen San Martín**
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**David Reguera**
**Iwan Schaap**
José Ruiz Castón
Mark van Raaij
Mauricio García Mateu
**Nuria Verdaguer**
Rudi Podgornik
Salvatore Cannistraro
**Trevor Douglas**
Urs Greber

## Funding

GOBIERNO DE ESPANA
MINISTERIO DE ECONOMIA Y COMPETITIVIDAD

HFSP

IfiMAC
Condensed Matter Physics Center

Fundación BBVA

**Thank you!**