

Mechanobiology of microbes

ME-480

Alex Persat

Bacteria



Pseudomonas aeruginosa

Lecture outline

- Bacteria: what are they and what do they do?
- Adhesion
- Swimming
- Crawling
- Sense of touch

Quizz

Bacteria

why do we care about them?

Present in oceans, soil, humans, plants, air

$> 10^{30}$ bacteria in the biosphere

$\sim 10^{14}$ bacteria in a human body

$\times 10^2$ more bacterial than human genes in our body

Photosynthesis	(oxygen)
Industry	(fuel, food, waste management)
Pathogenicity	(infection, food poisoning)
Symbiosis	(immune system, digestion)
Biotechnology	(CRISPR, cell-based therapies, natural products)



cyanobacteria



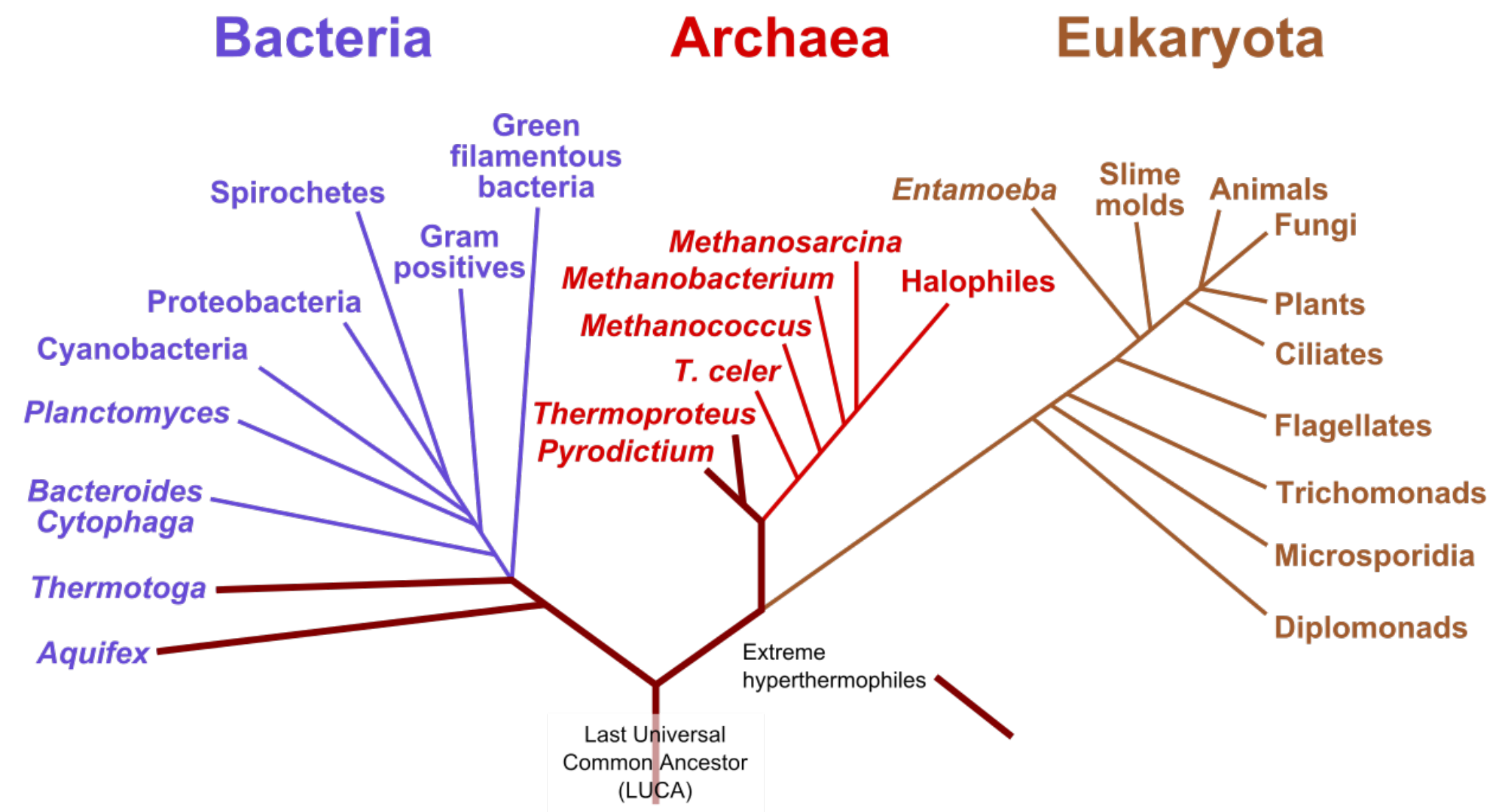
Propionibacterium freundenreichii



Wolbachia against dengue and Zika

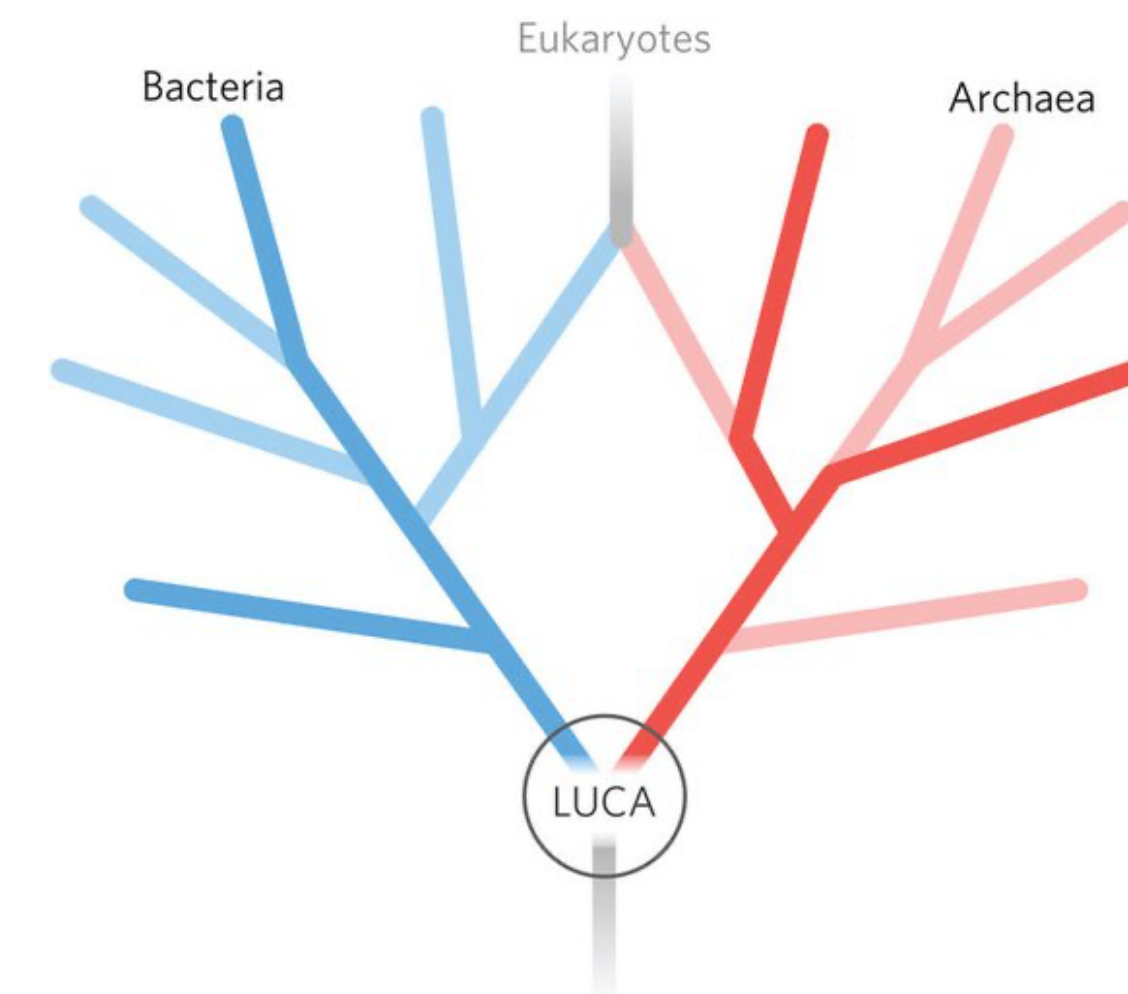
The origin of bacteria is the origin of life

Phylogenetic Tree of Life



wikipedia

LUCA was a prokaryote
(3.8×10^9 years)

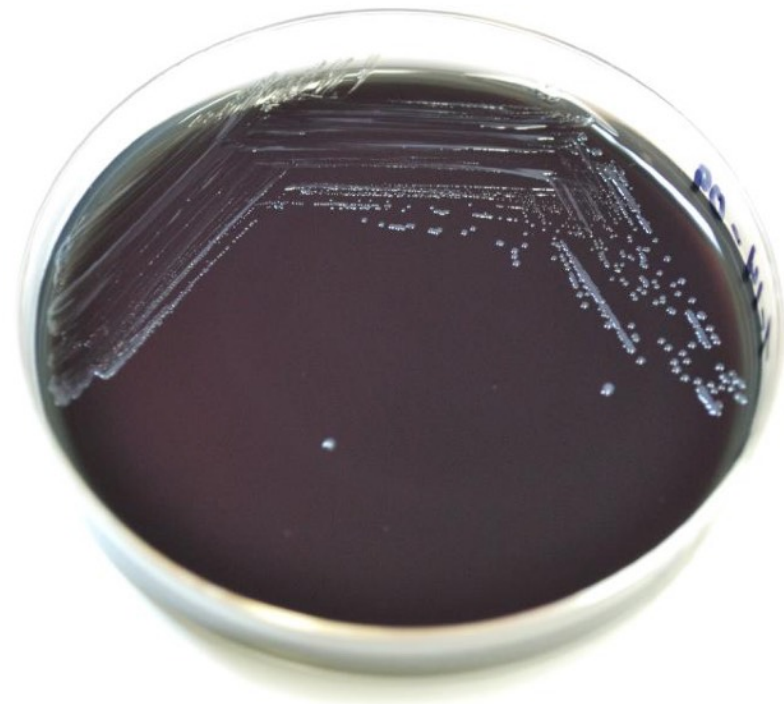


astrobiology.nasa.gov

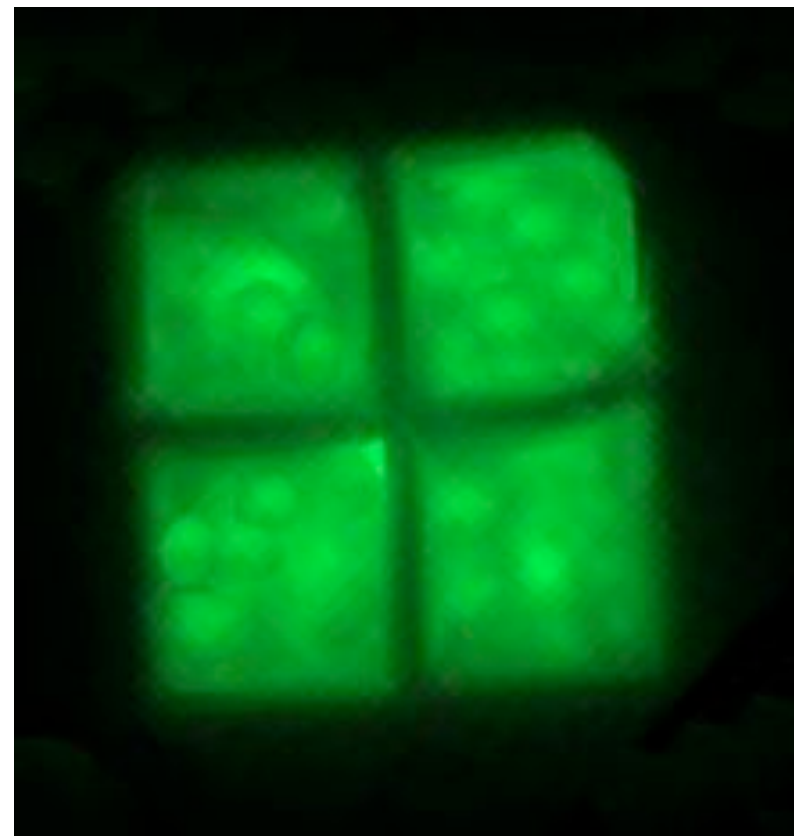
origin of eukaryotes likely from
endosymbiosis of a bacterium by
archaeal host

The environments of bacteria

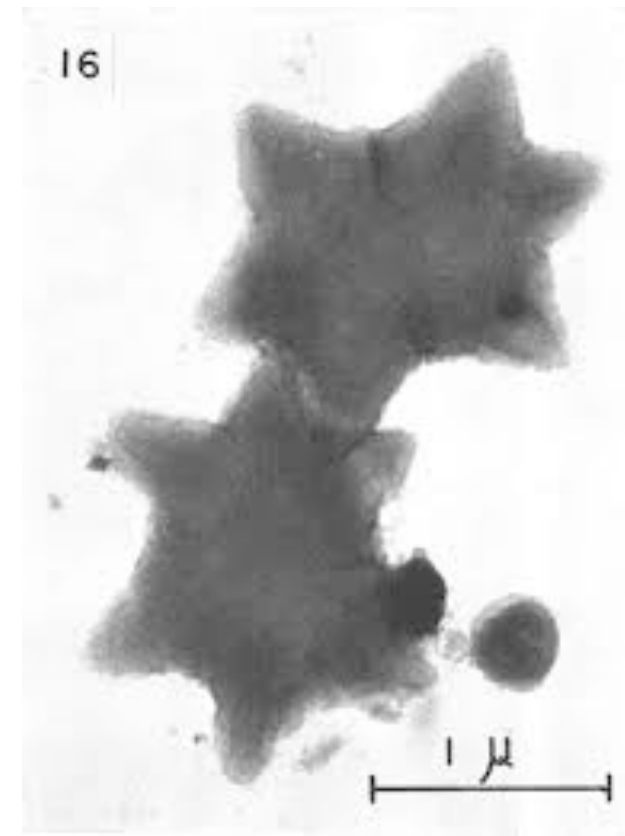
- many environments generate many types of stresses
- bacteria must (rapidly) adapt to these conditions



The many shapes of bacteria

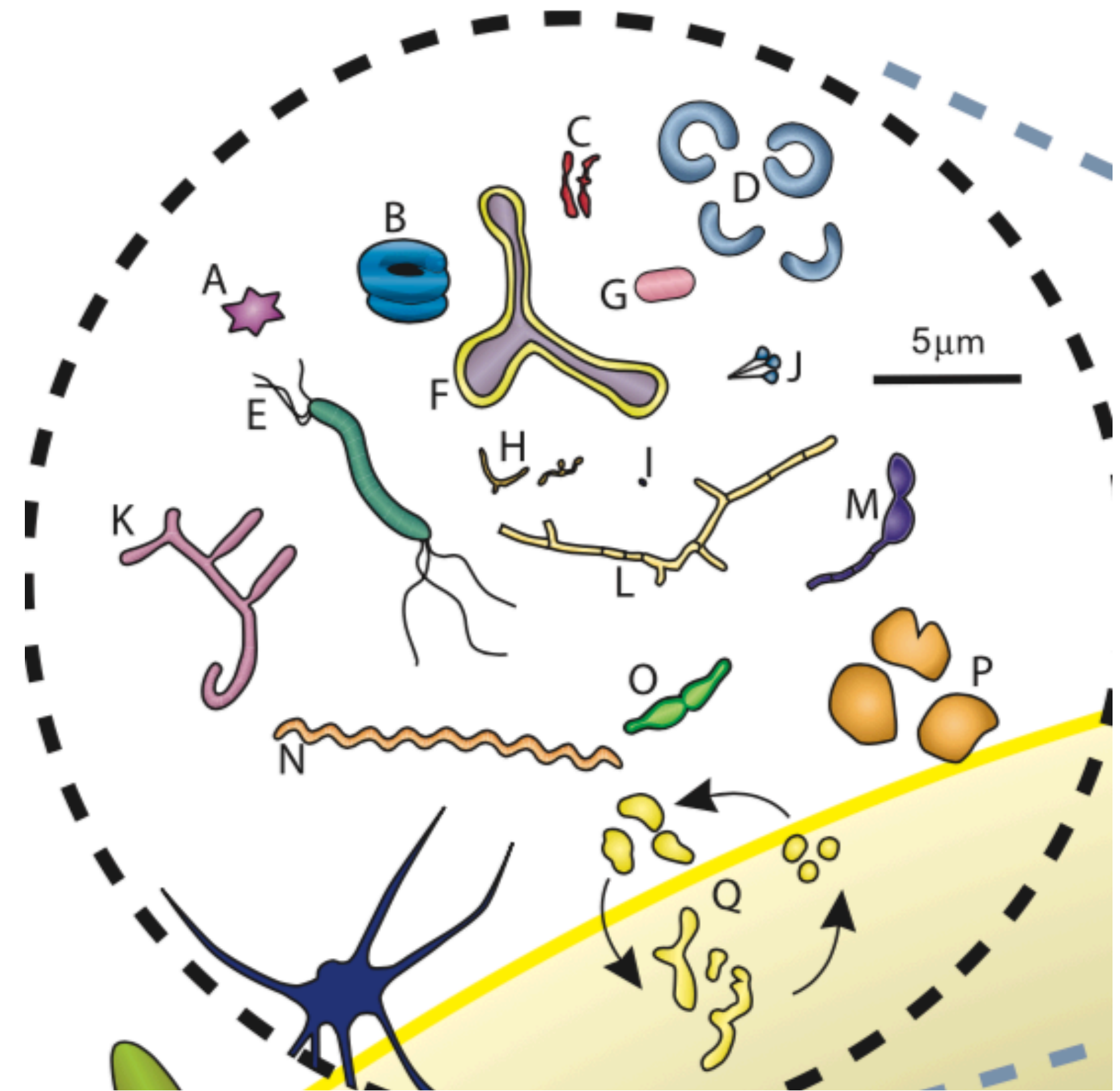


Haloquadratum



Prosthecomicrobium

- How do they maintain their shapes?
- Why these shapes?

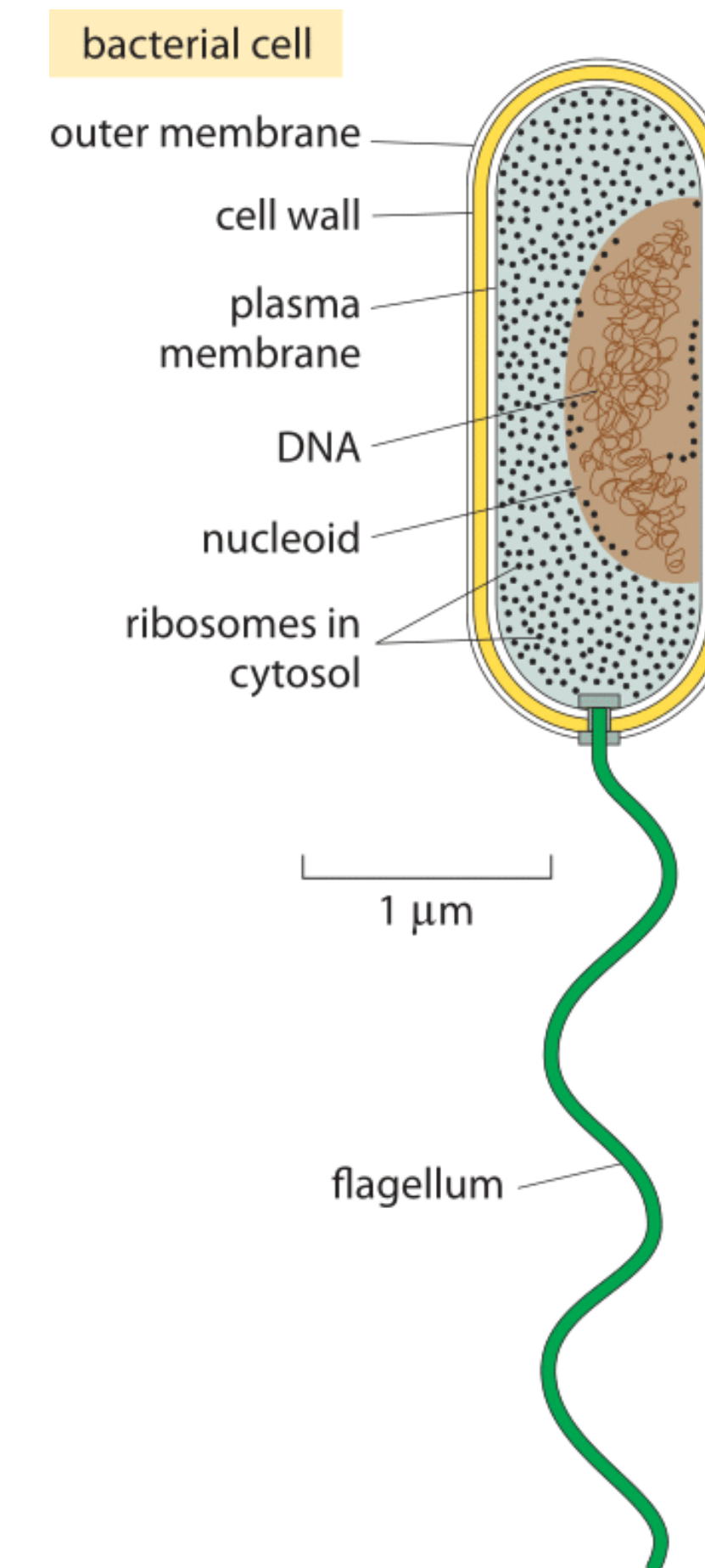


The cell wall maintains cellular integrity

The bacterial cell wall is:

- mechanically robust
- maintains cell shape
- dynamic

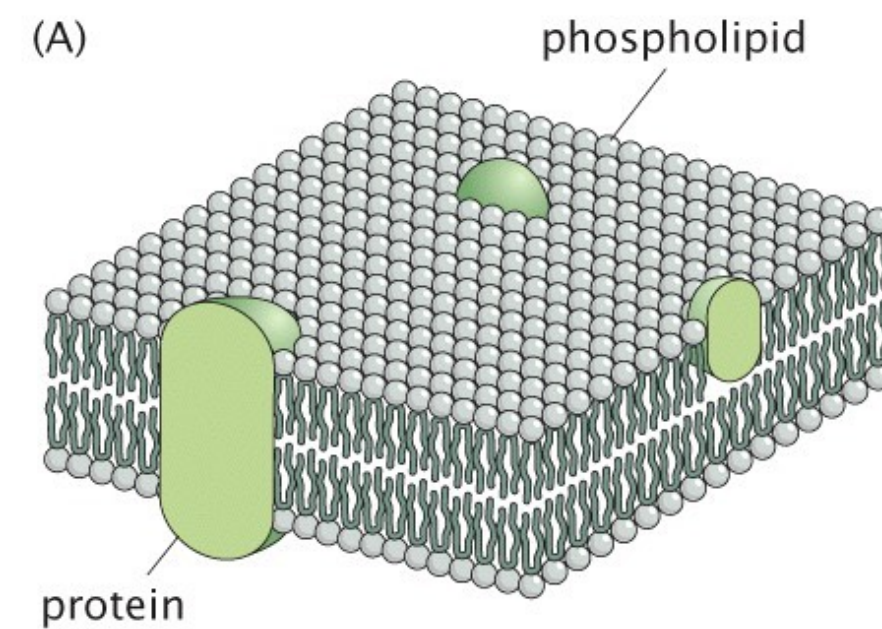
Synthesis is guided by cytoskeletal proteins



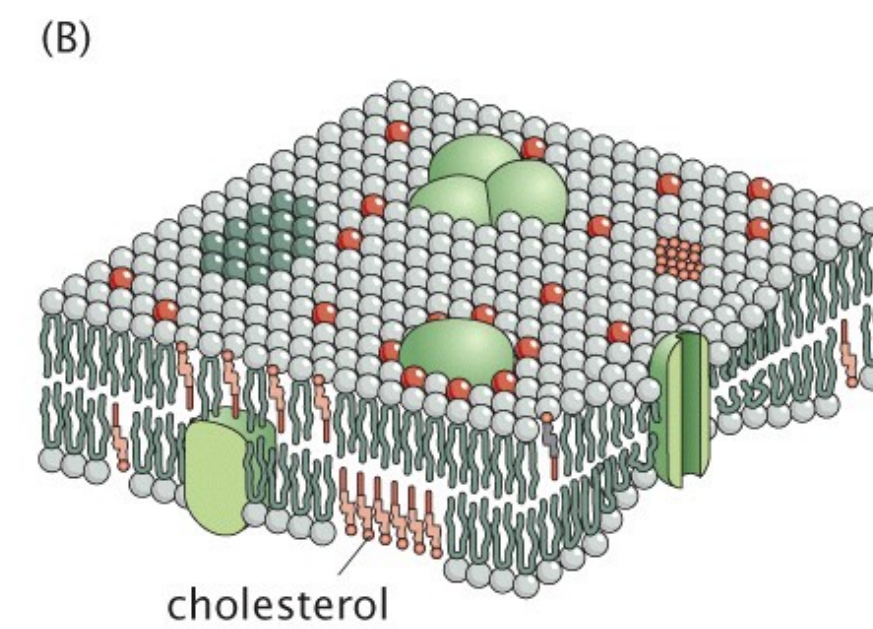
The cell envelope is complex

Surface components interface a cell with its environment

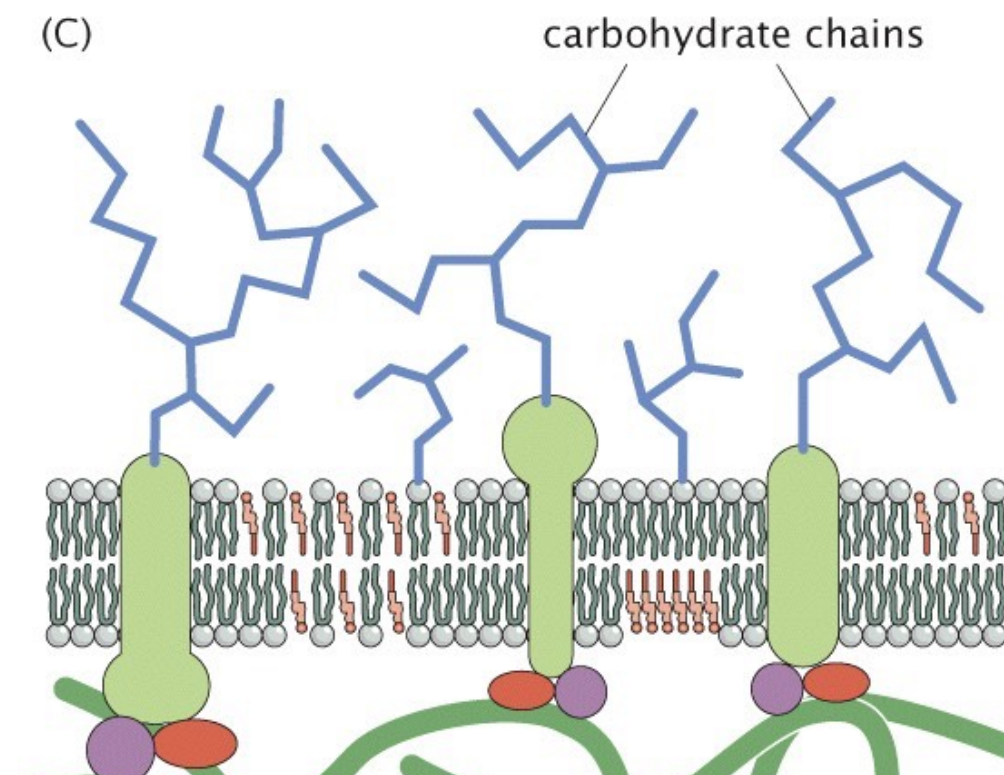
For all cells (prokaryotes and eukaryotes)



Simple lipid bilayer



Heterogeneous membranes with microdomains

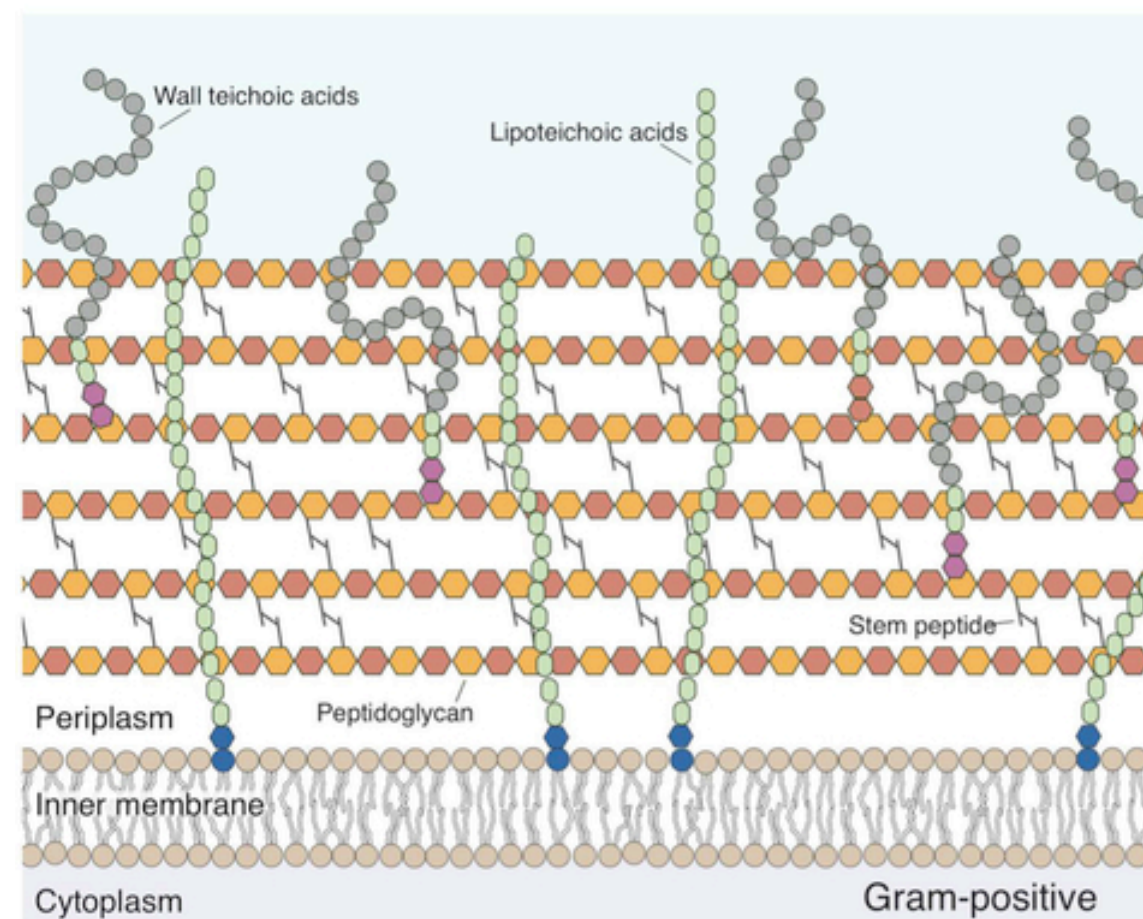
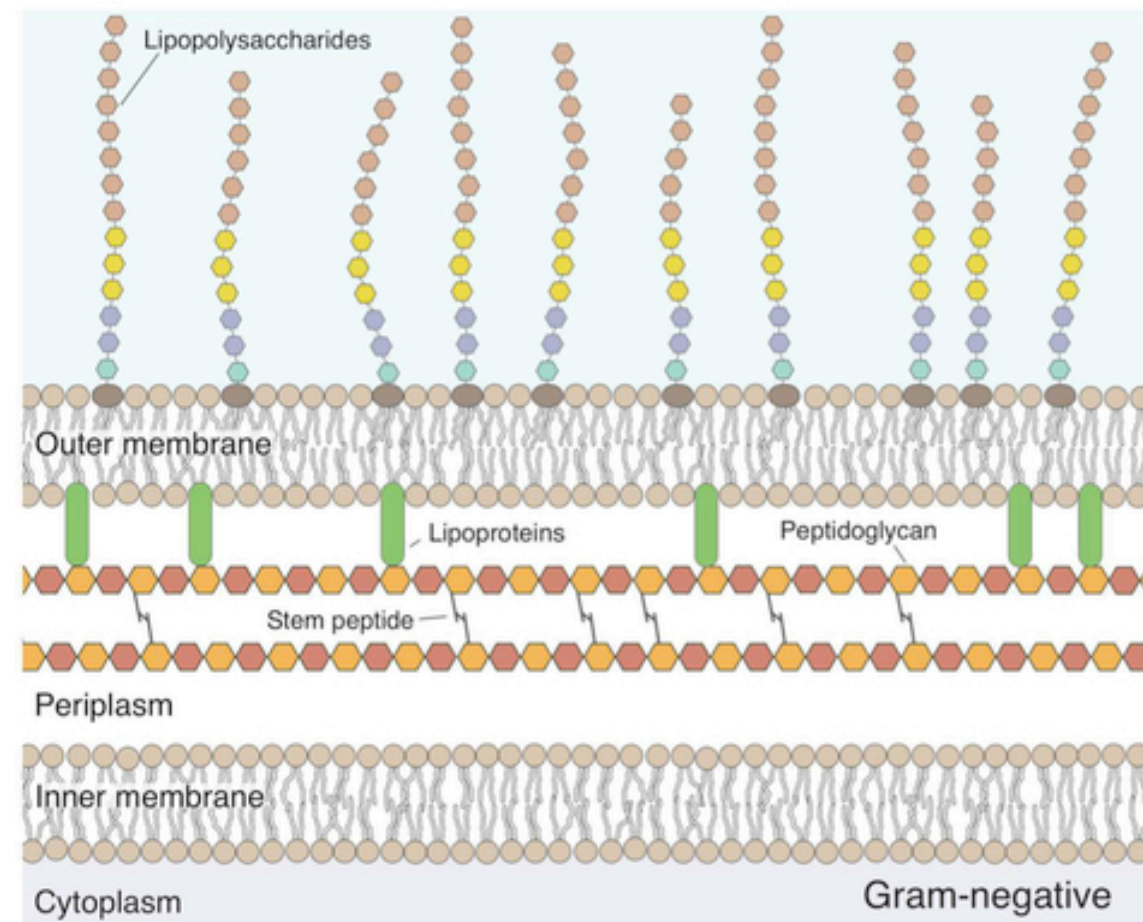


Additional structures extend in the third dimension:

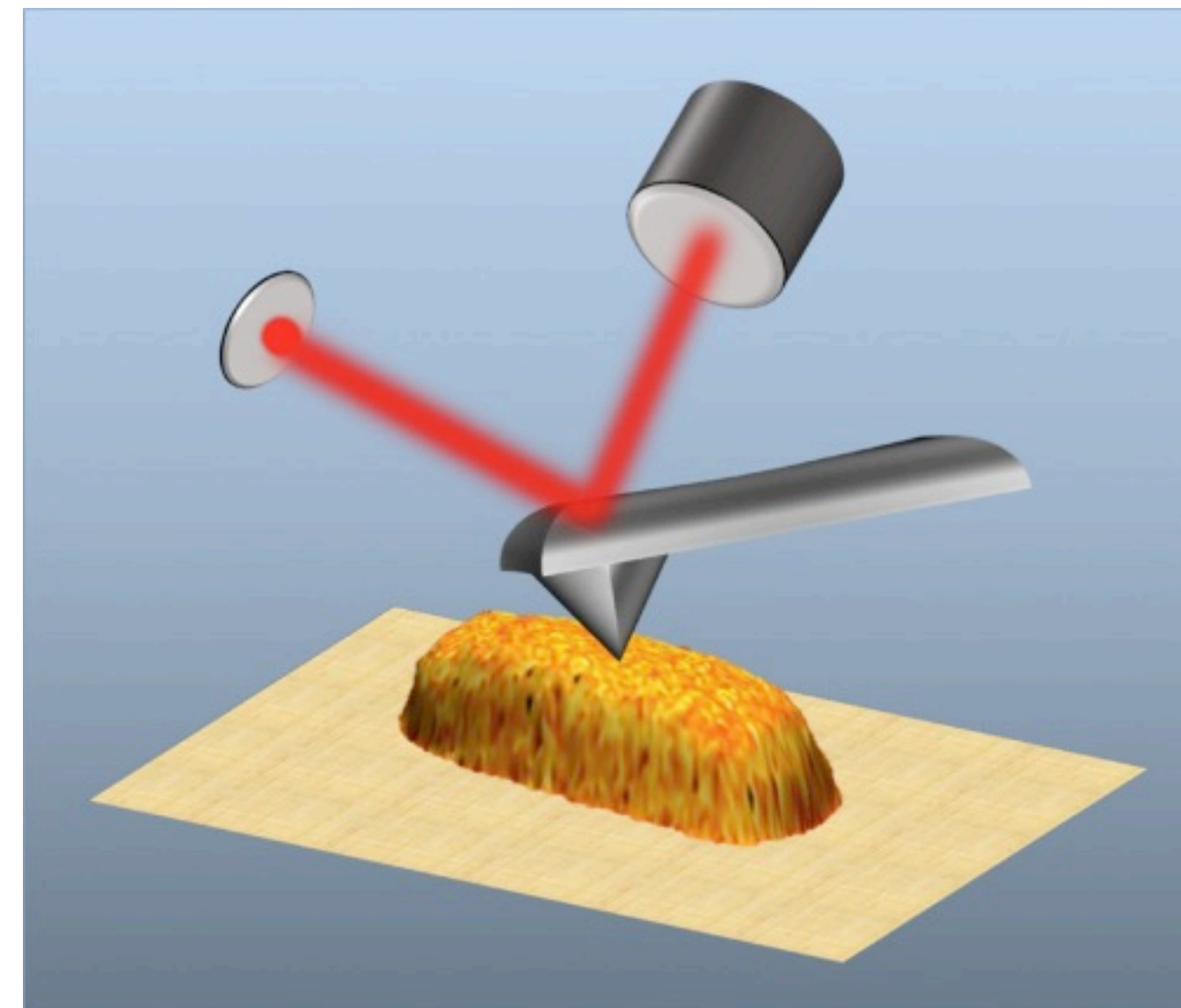
- sugars
- proteins

The cell wall maintains bacterial integrity

A major distinctive feature from eukaryotes



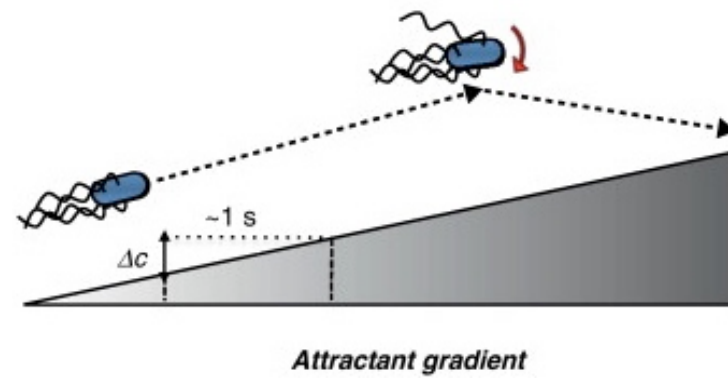
AFM measurements on
single bacteria



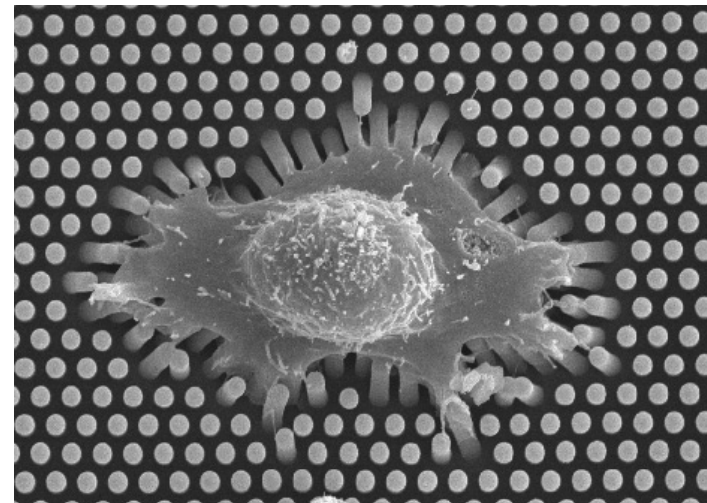
Trends in Microbiology

**Cell wall stiffness
10-50 MPa**

Mechanical sensing



Sourjik, Curr Opin Cell Bio 2012



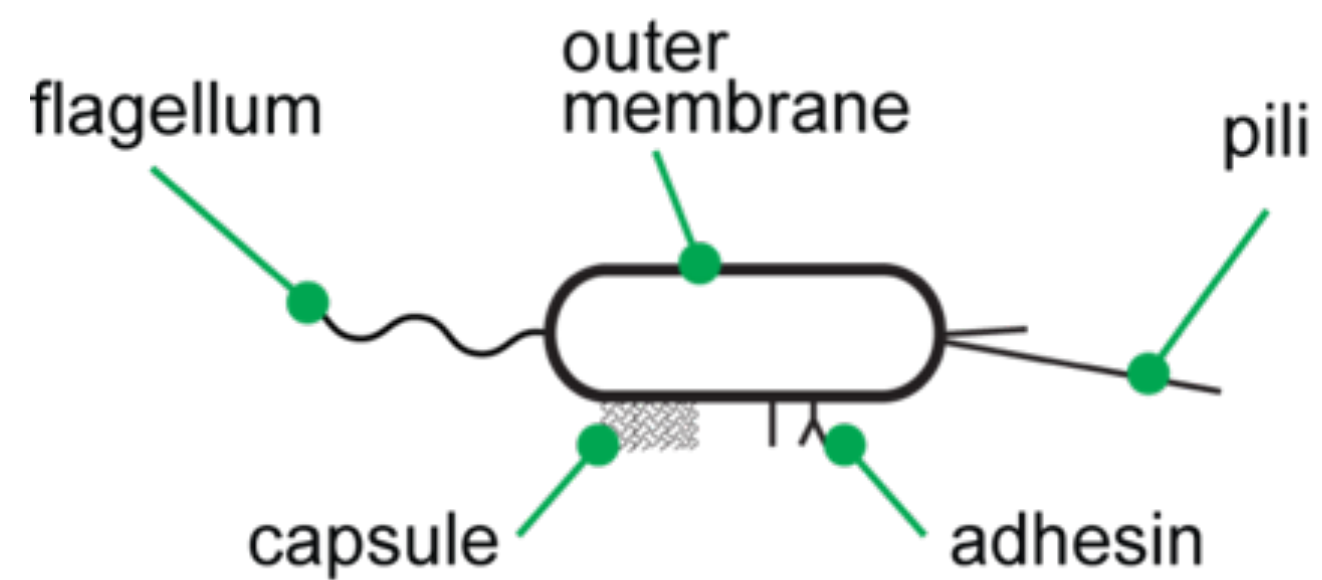
Trichet, PNAS 2012

Can bacteria actively transduce mechanical stimulation into cellular responses?

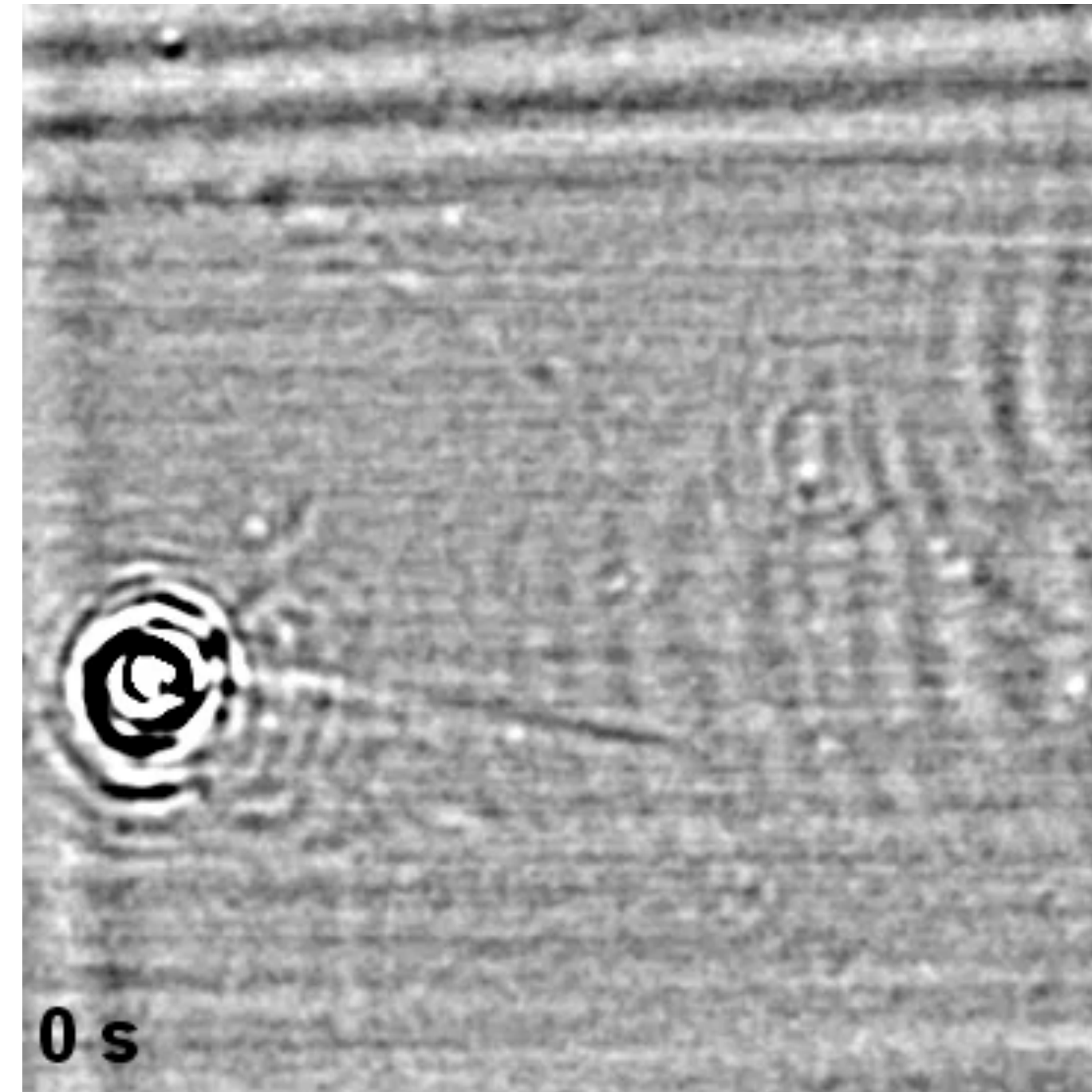


Single cell mechanical interactions

Single cells mechanically interact with their environments through surface structures



Persat, Curr. Op. Micro. 2017



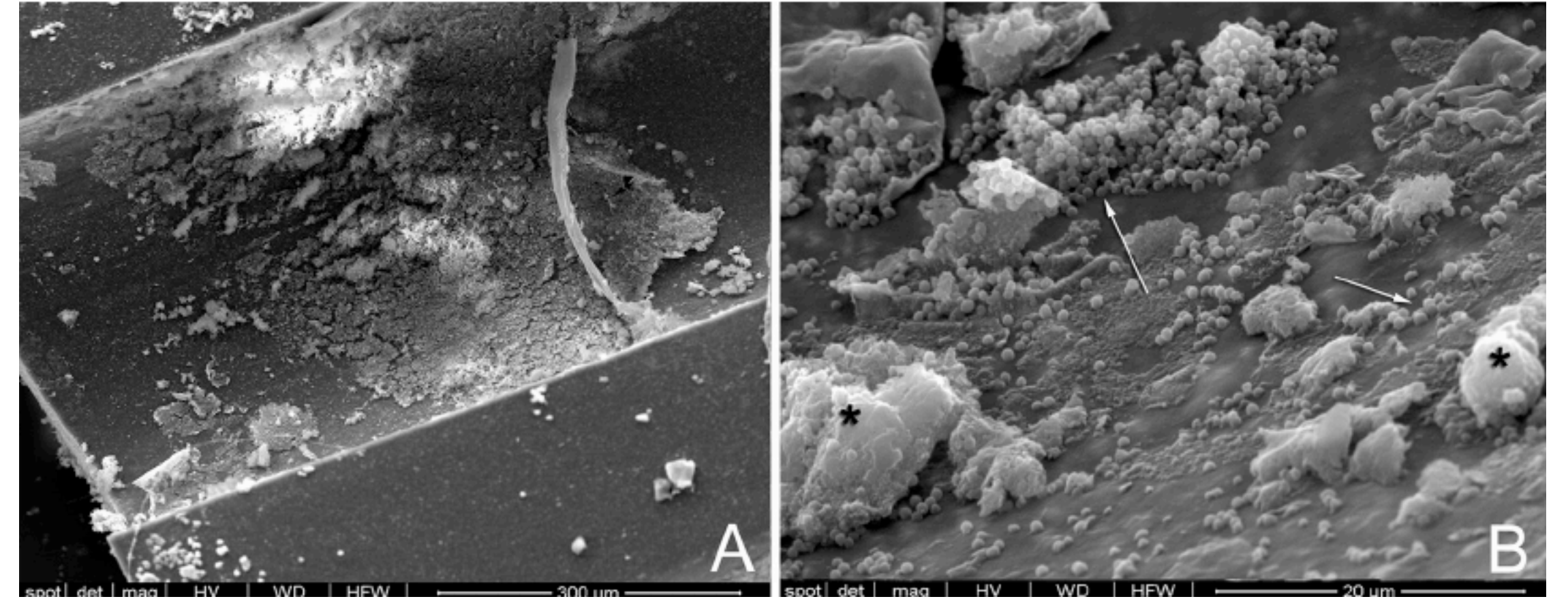
Tala, Nature Microbiology 2019

Adhesion

Bacterial adhesion in industry

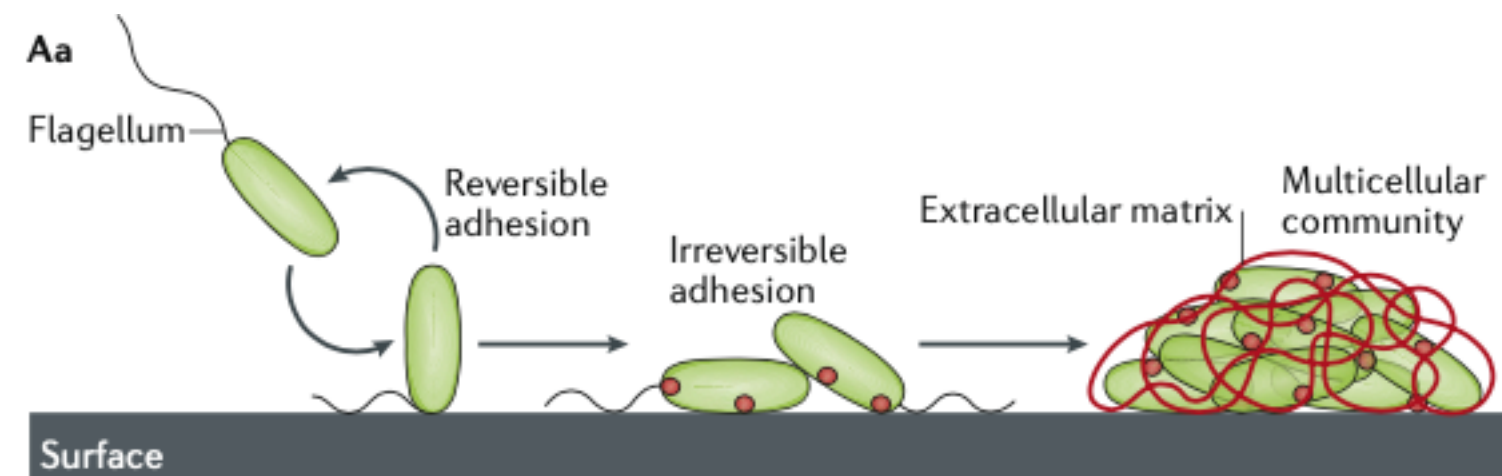
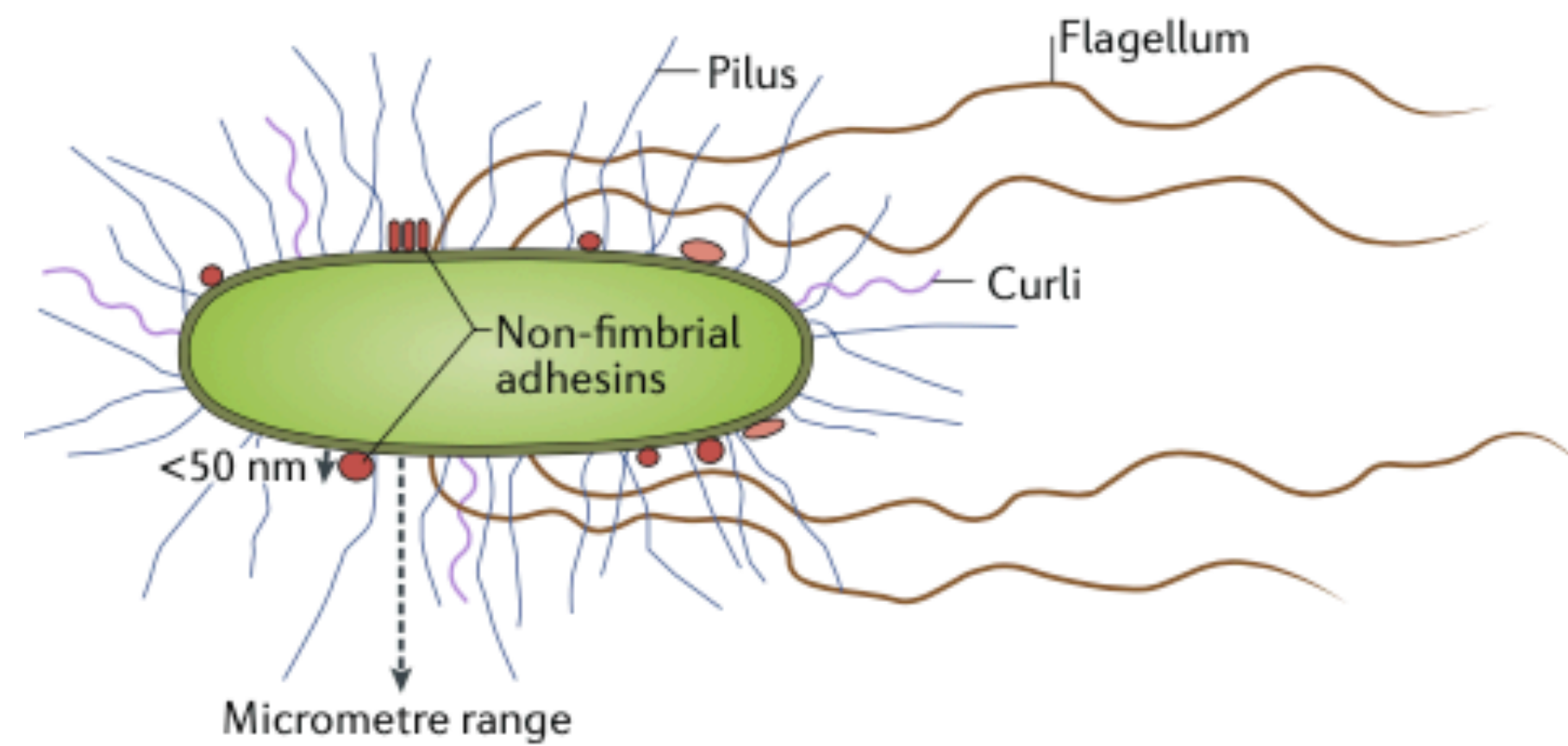


Bacteria adhesion in health and disease

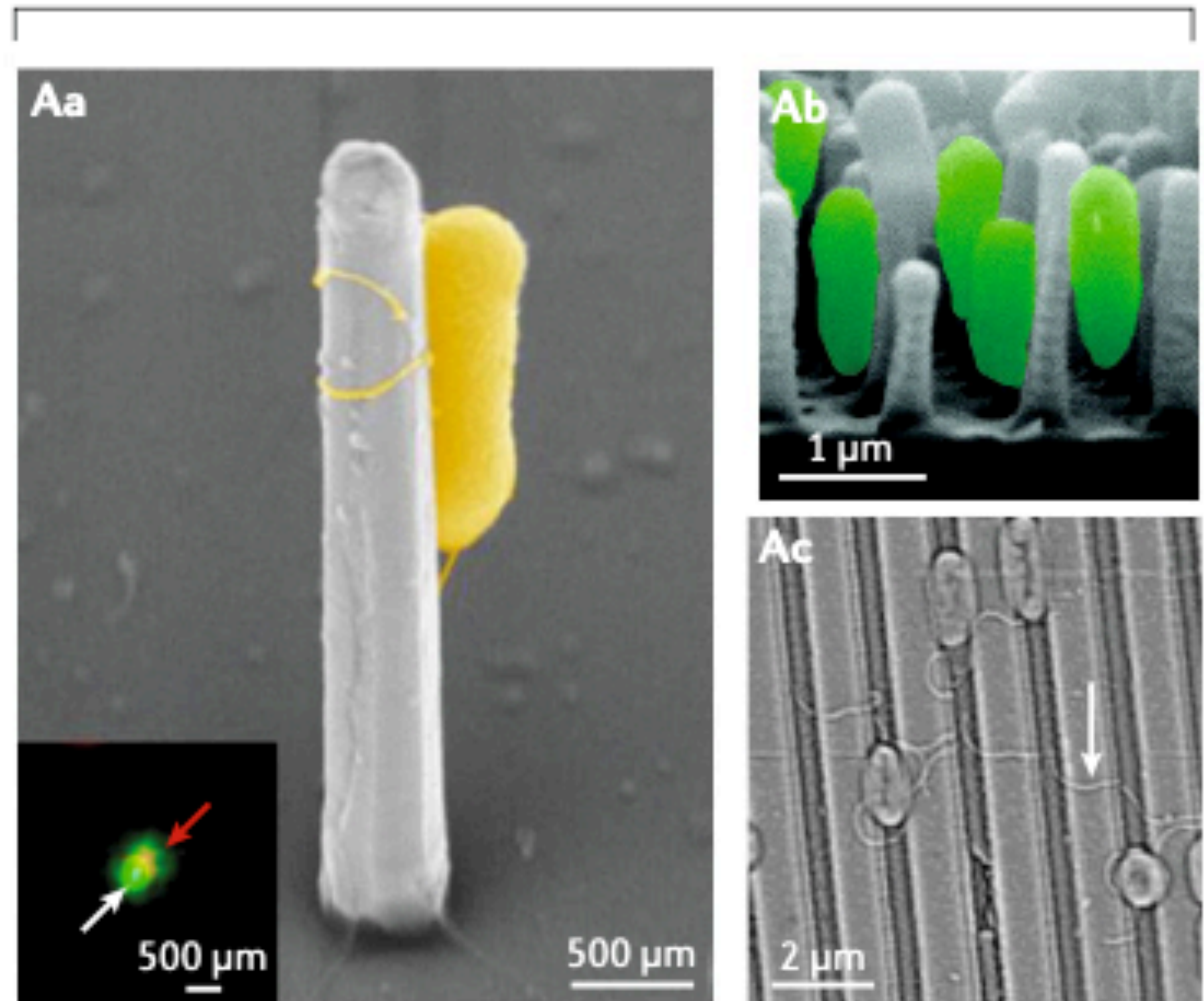


Mechanisms of adhesion

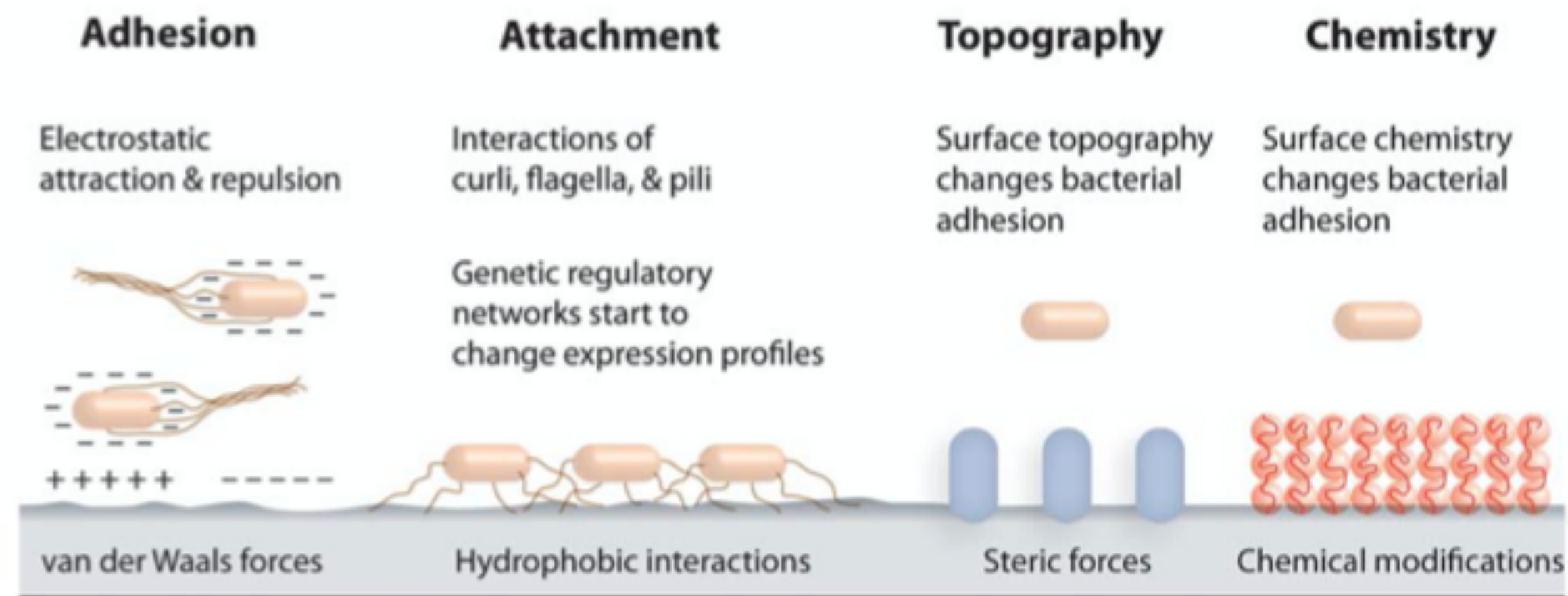
bacteria attach using adhesins



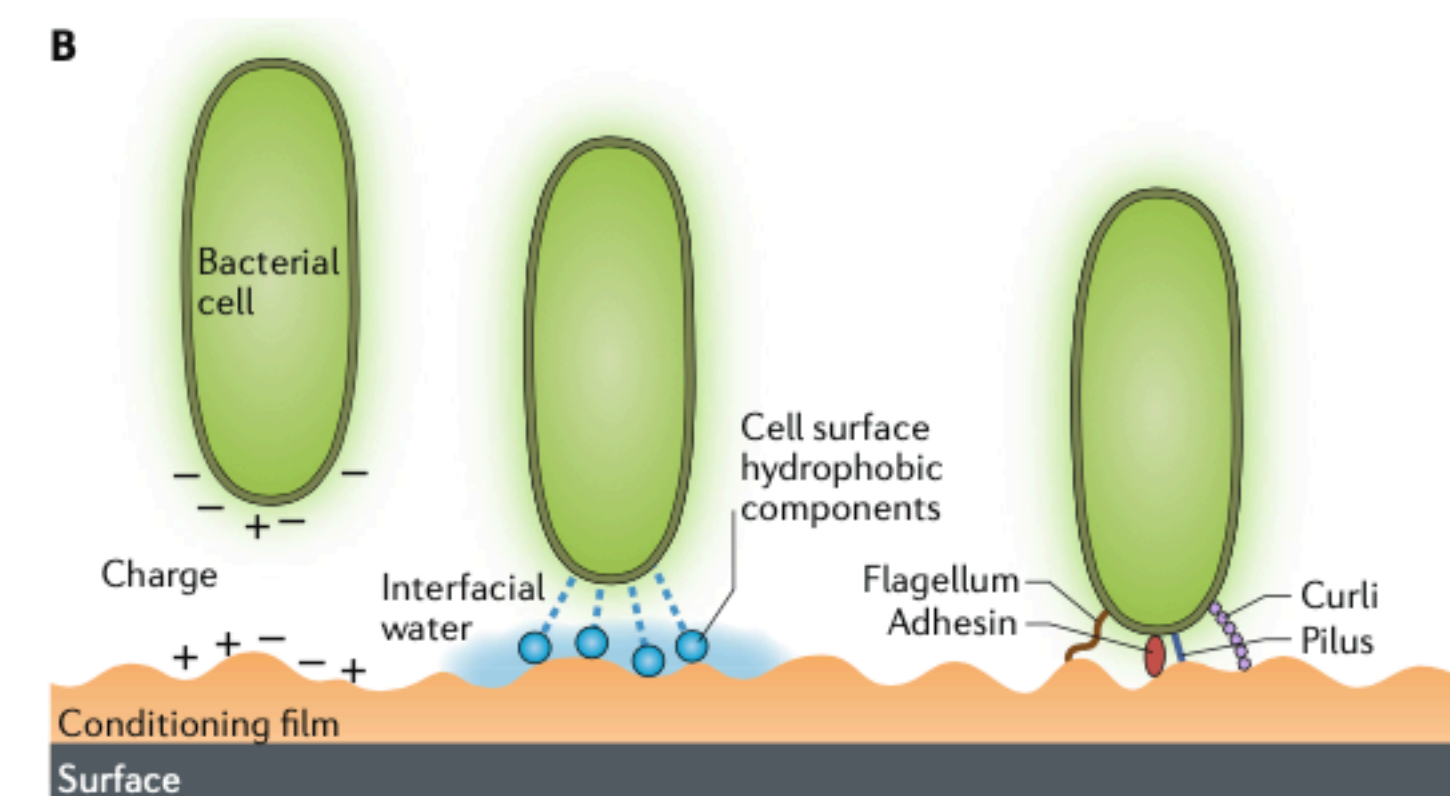
Micropatterned surfaces



Physicochemical basis of adhesion



Weibel and Tuson, Soft Matter

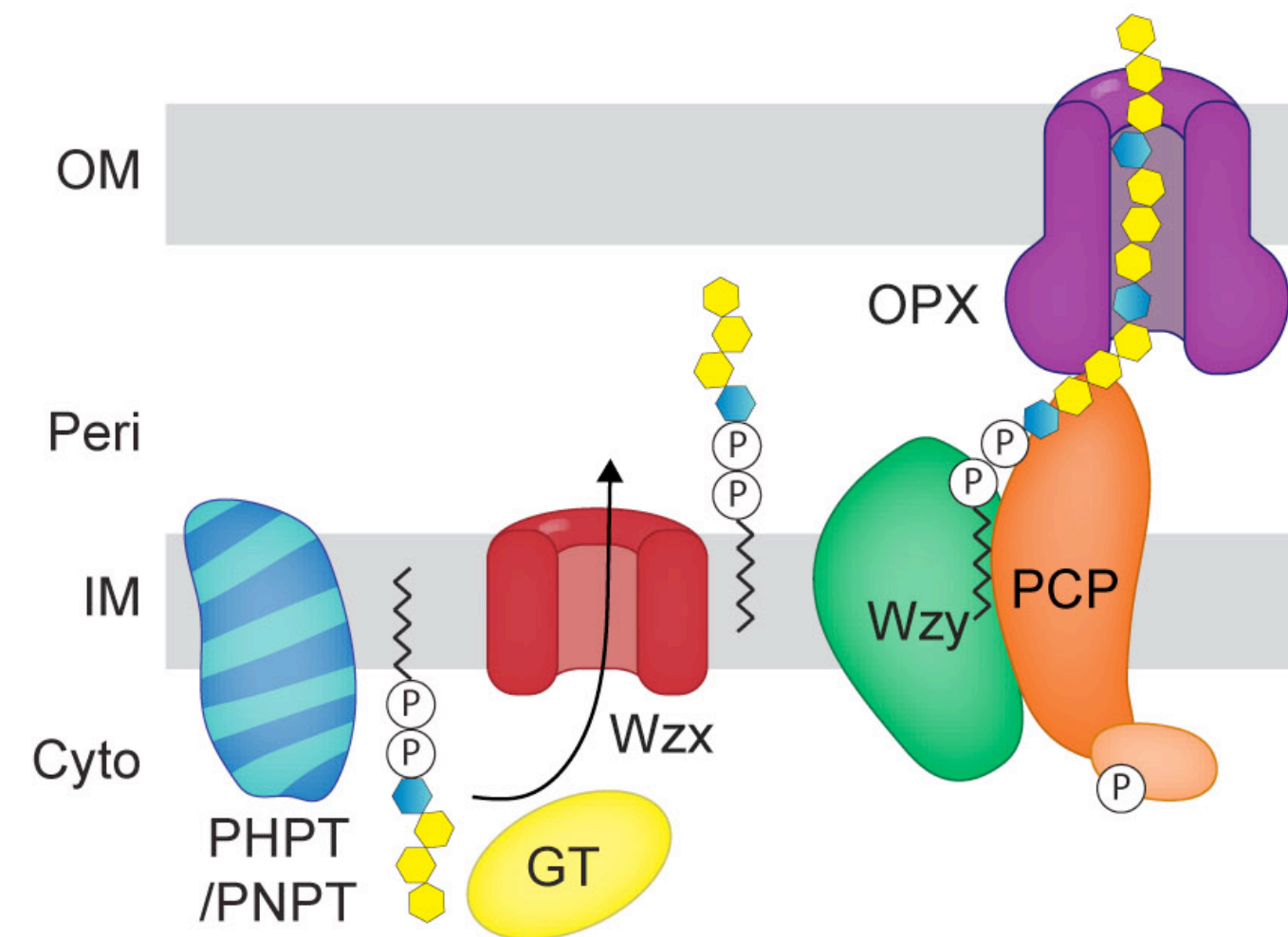


Berne and Brun, Nat. Rev. Micro.

Non-specific adhesion

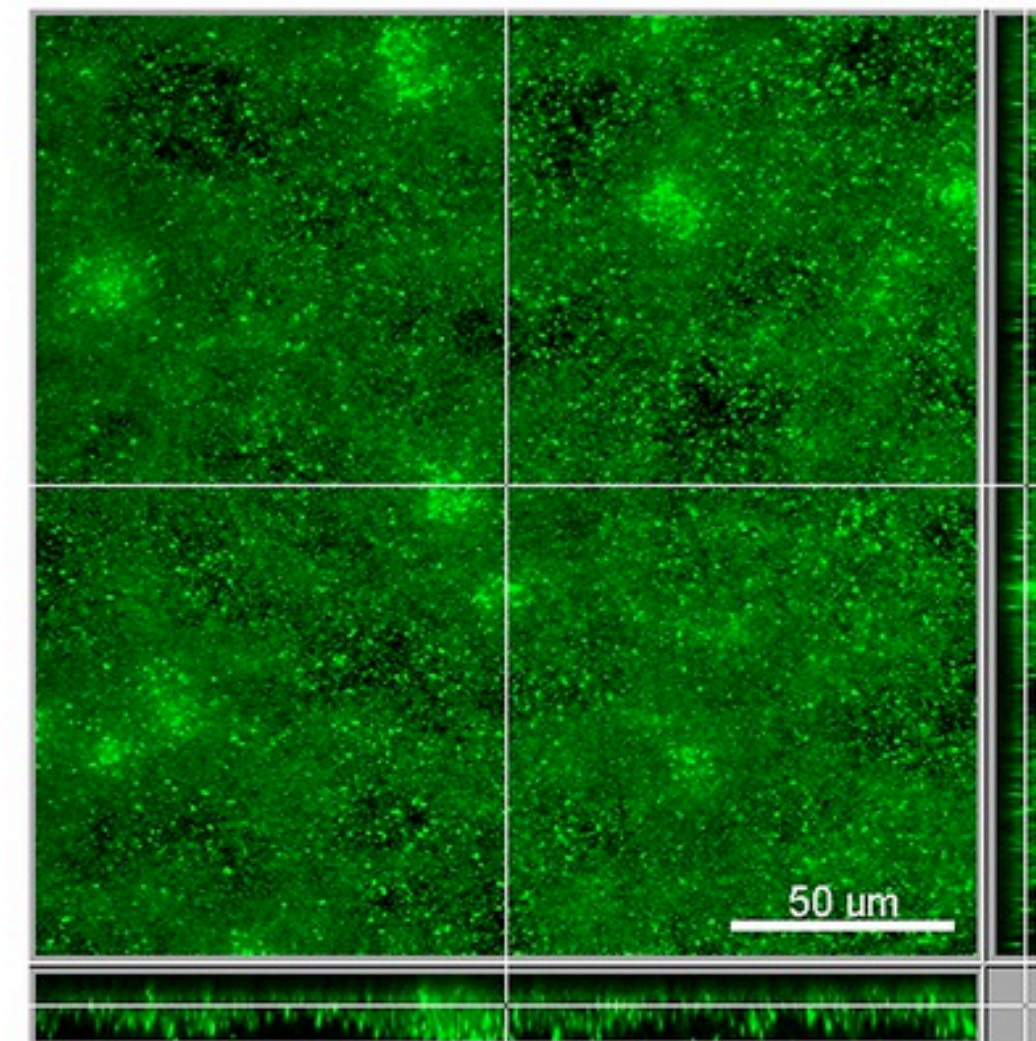
Cells attach to surfaces independently of precise chemistry

Bacteria secrete polysaccharides which function as “glue”

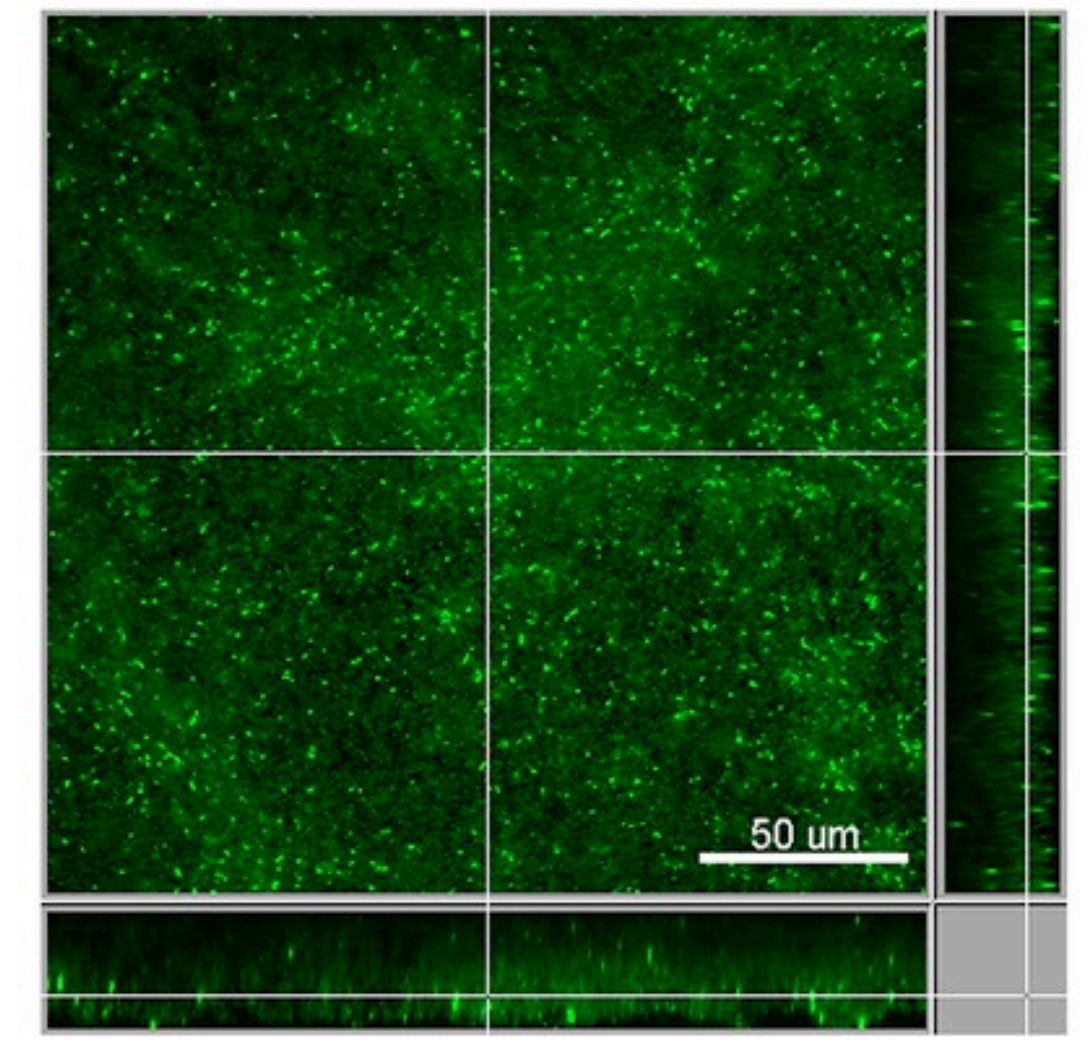


Example of *Pseudomonas aeruginosa*
Psl is a polysaccharide glue

PAO1



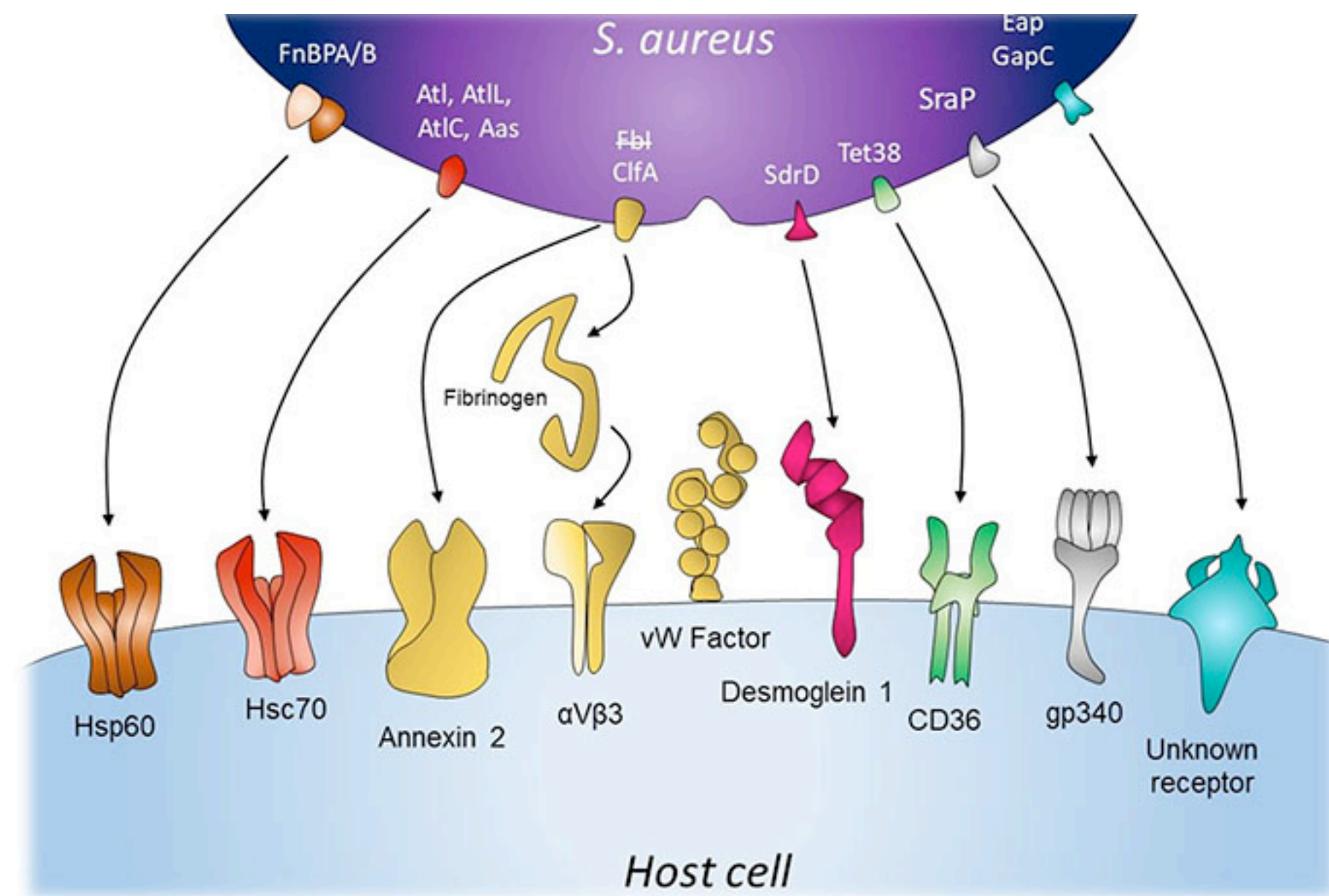
$\Delta\text{psl/G}$



Specific adhesion

cells attach to specific receptors using specific adhesins

Staphylococcus aureus displays many adhesins



Enteropathogenic *E. coli* injects the host with a receptor

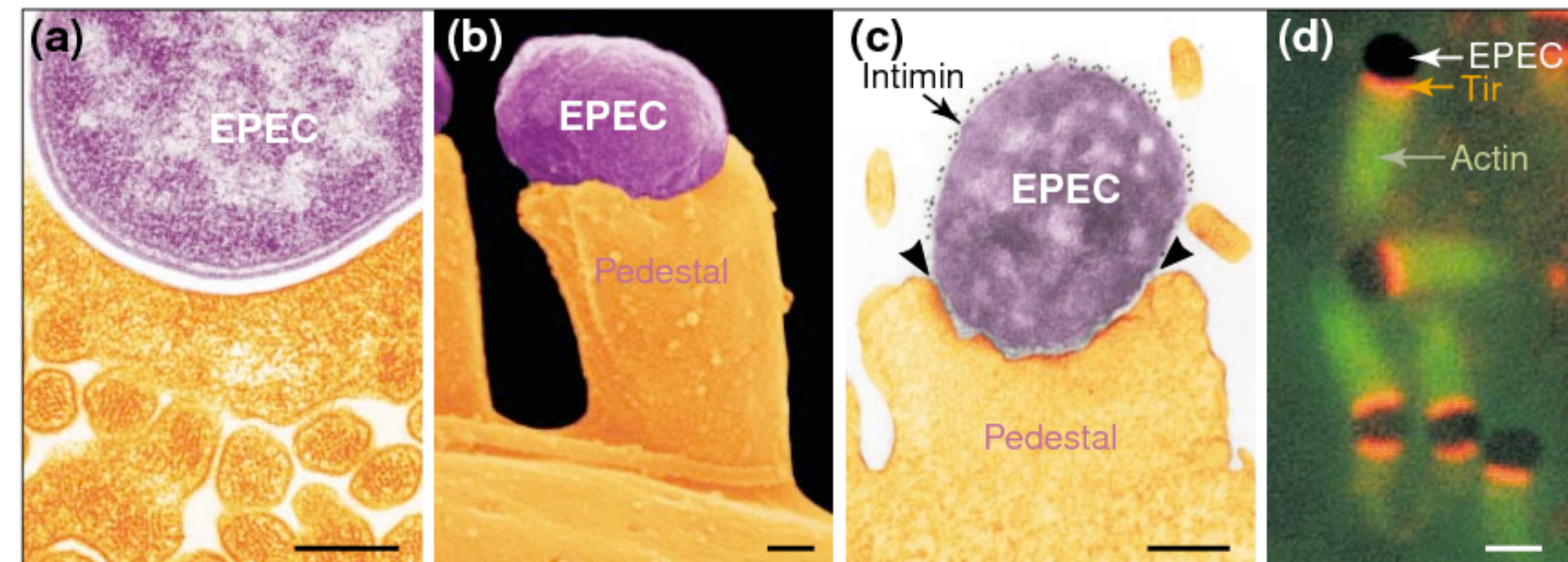
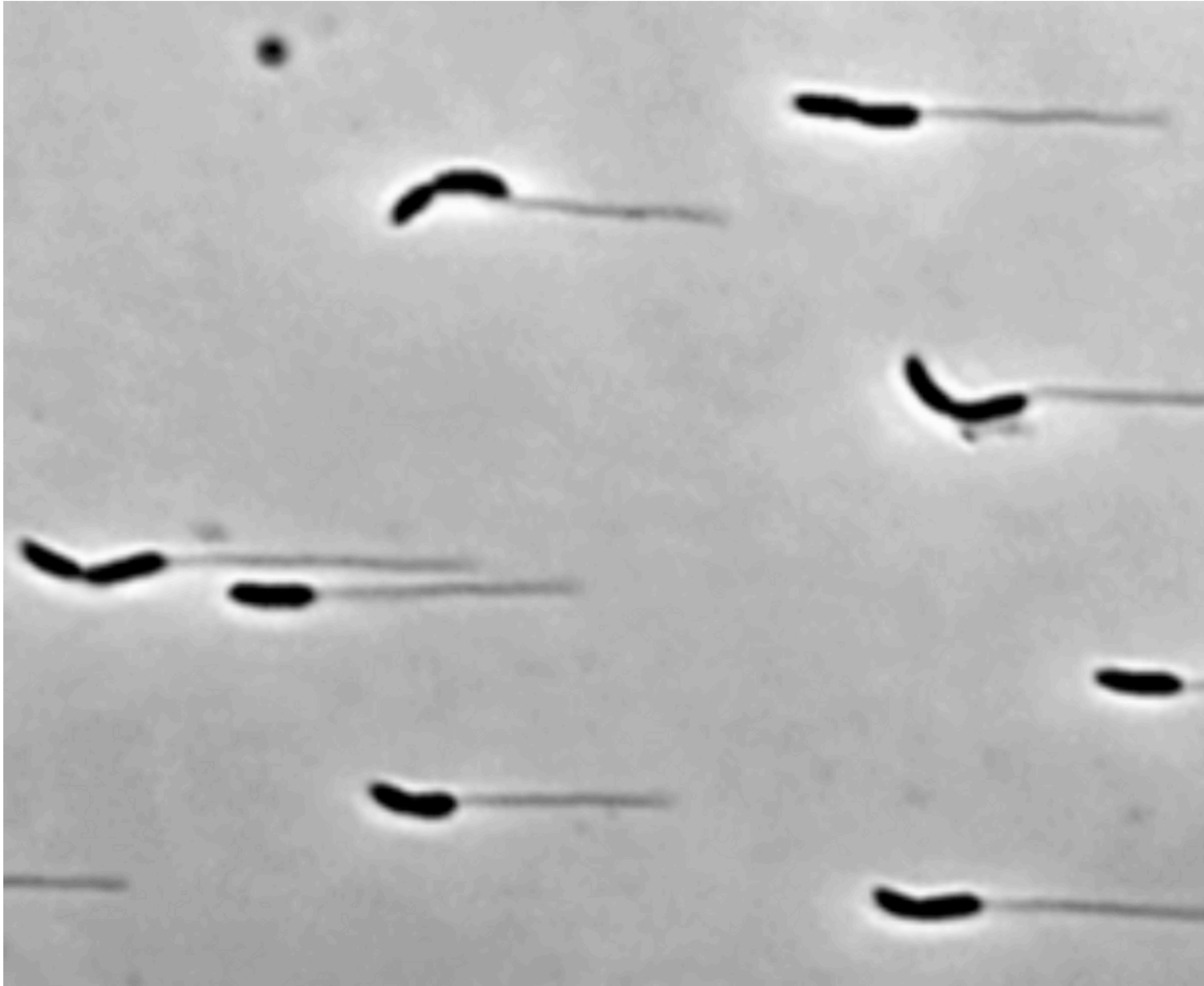


Fig. 1. Attaching/effacing (A/E) lesion formation by enteropathogenic *Escherichia coli* (EPEC).

■ Mechanics of adhesion

cells resist detachment



WHO
CAULOBACTER CRESCENTUS

WHERE
UNITED STATES

WHEN
2006

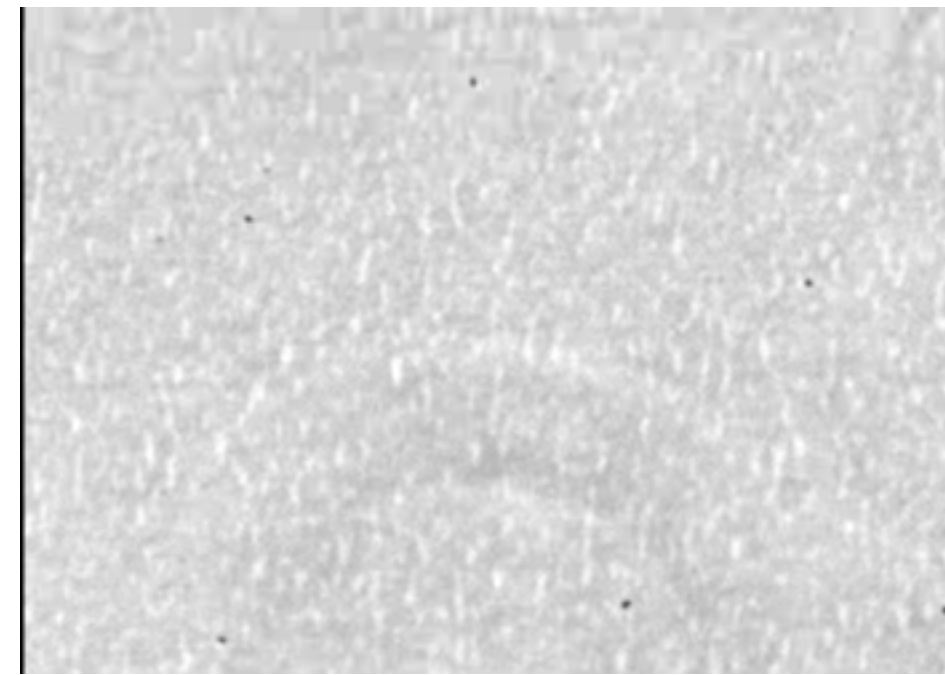
In 2006, researchers at Indiana University, USA, found that the bacterium *Caulobacter crescentus* produced a sticky substance that allowed it to attach to virtually any surface and even under water. The bacteria produced a mixture of long sugar-based molecules called polysaccharides that are around 7 times stronger than a Gecko's sticky foot! The scientists measured 14 bacteria attaching themselves to a borosilicate substrate (glass-like base) and found it took a force between 0.11 to 2.26 micro-Newtons, averaging 0.59 ± 0.62 micro-Newtons, to detach the microbe. This equates to a ripping force of around 70 Newtons per square millimetre (10,153 pound-force per square inch) force over all compared to commercial 'super' glue (cyanoacrylate) that fails at around 25 newtons per square millimetre (3,626 pound-force per square inch). The report on the research appeared in the Proceedings of the National Academy of Science.

Some bacteria attach better under load

E. coli in flow



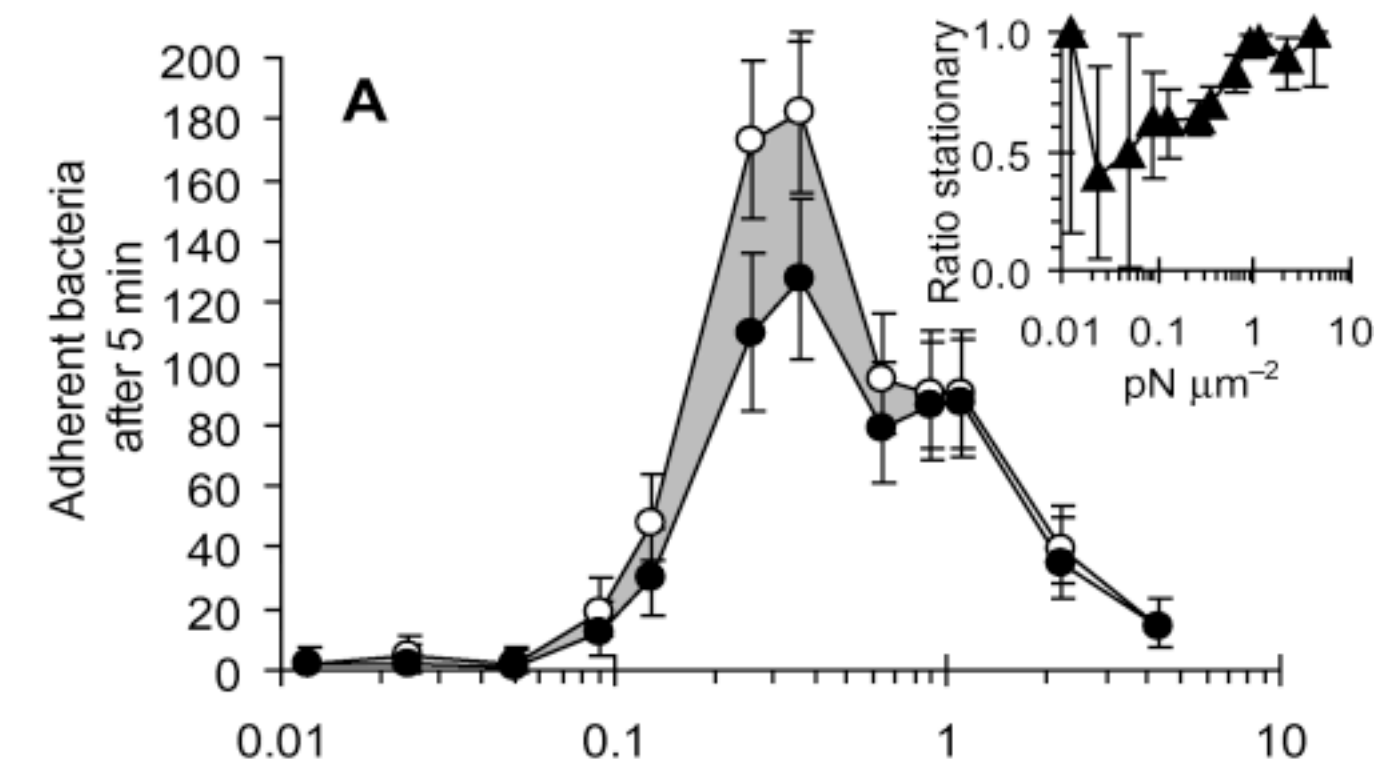
Weak flow



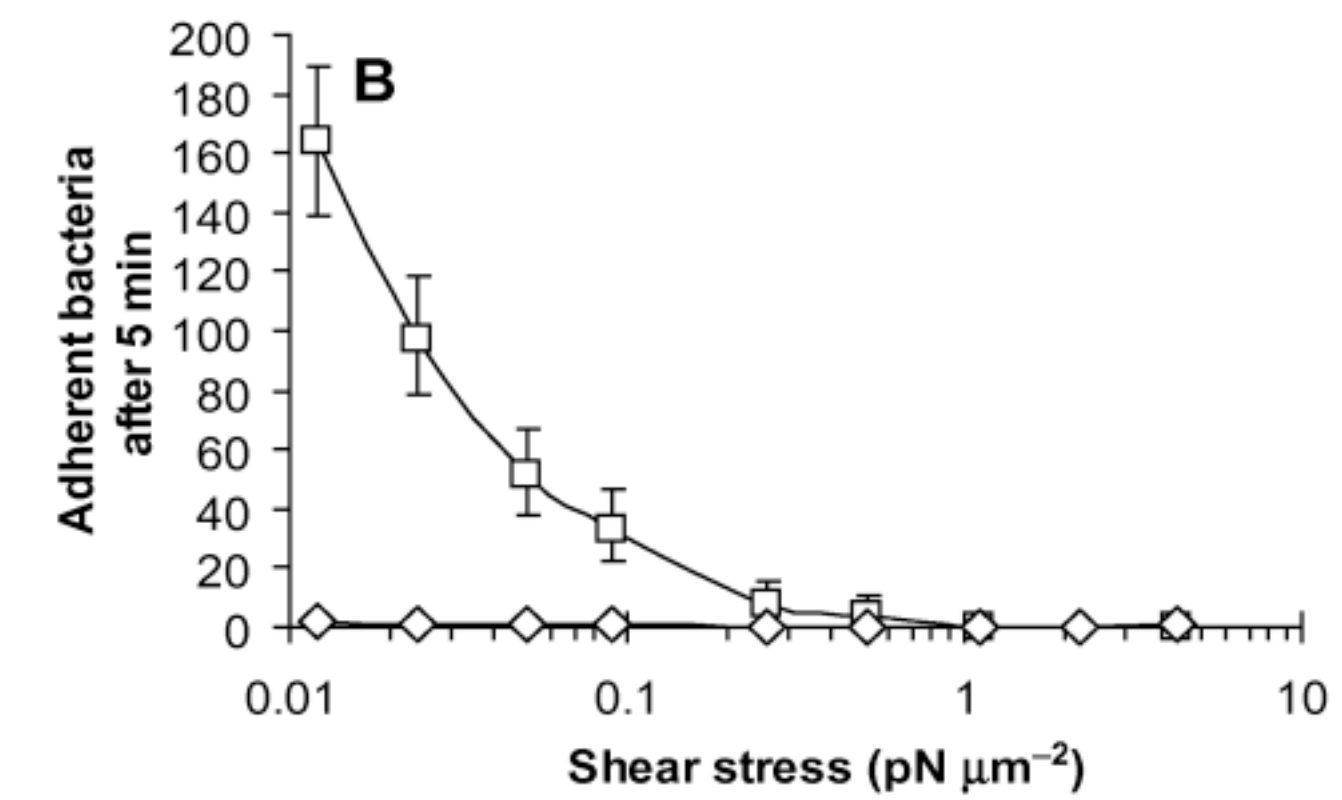
Moderate flow



Moderate flow
at high imaging speed



“catch bond”



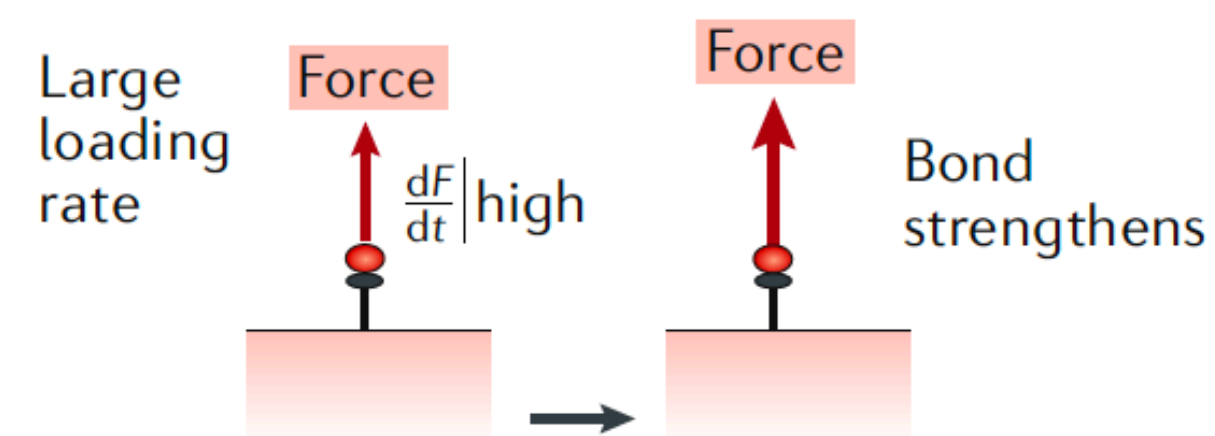
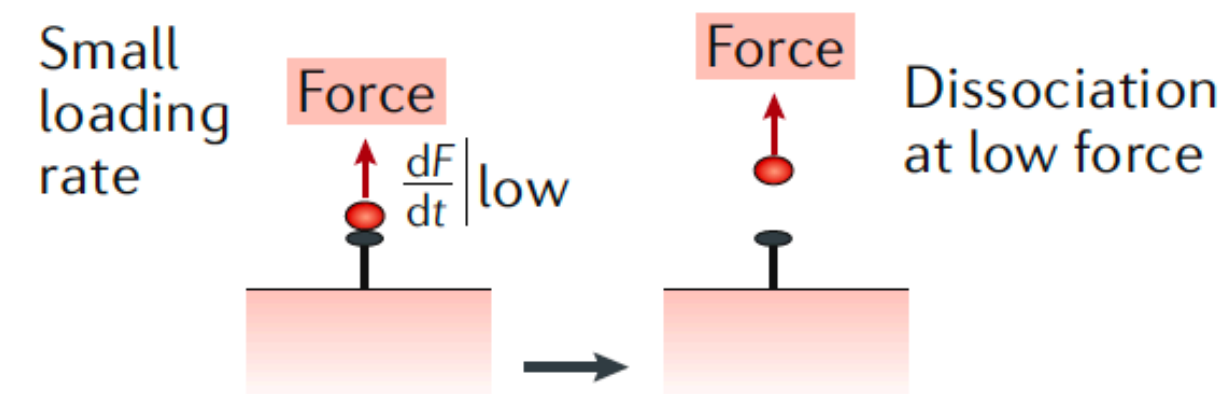
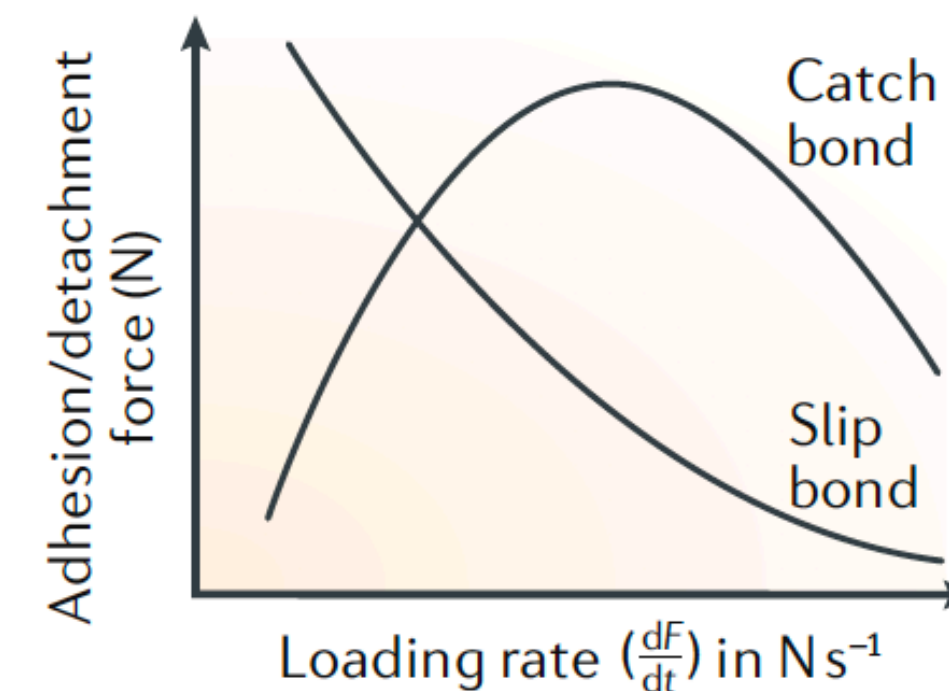
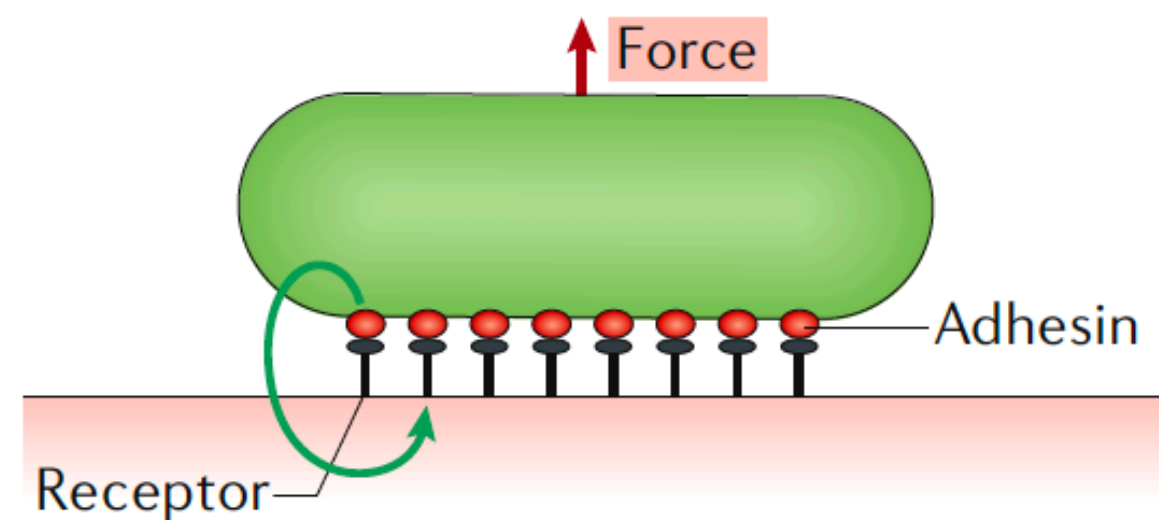
negative control
“slip bond”

Catch bonds

the molecular adhesion senses force

c Mechanosensation in adhesion

Catch bond

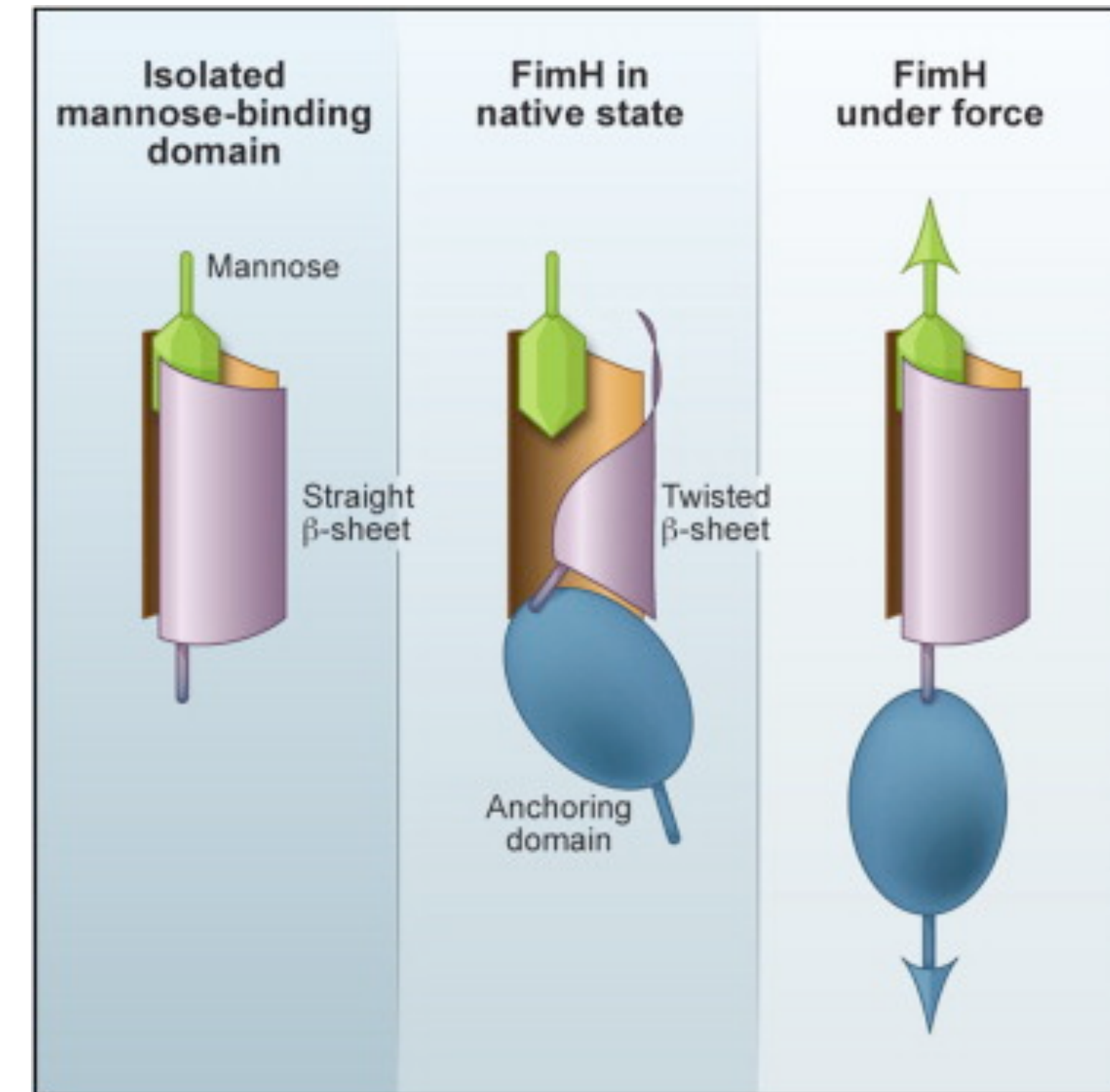
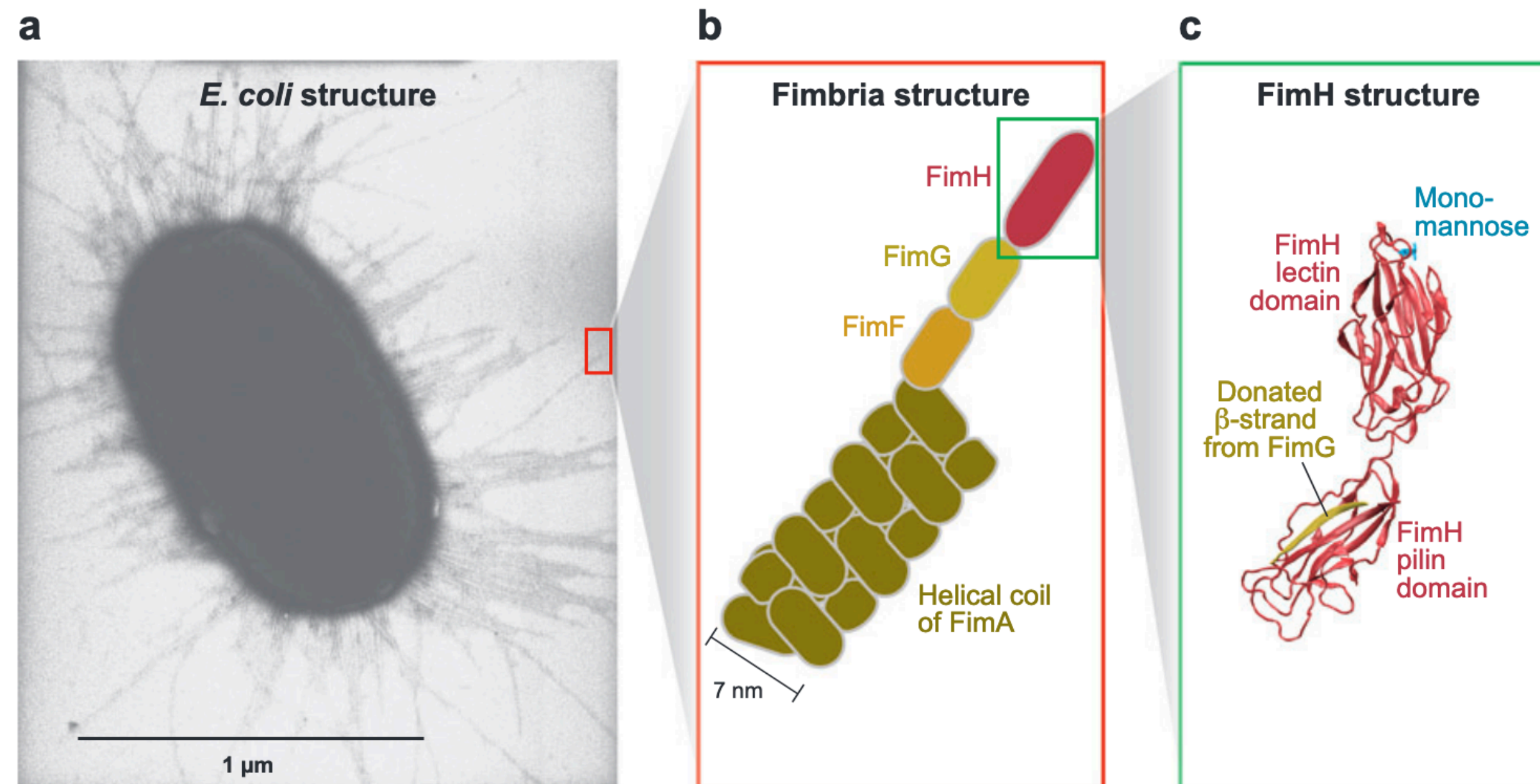


Catch bonds are common in pathogens that experience flow environments

(urinary tract infections, bloodstream infection)

Structural basis for catch bonds

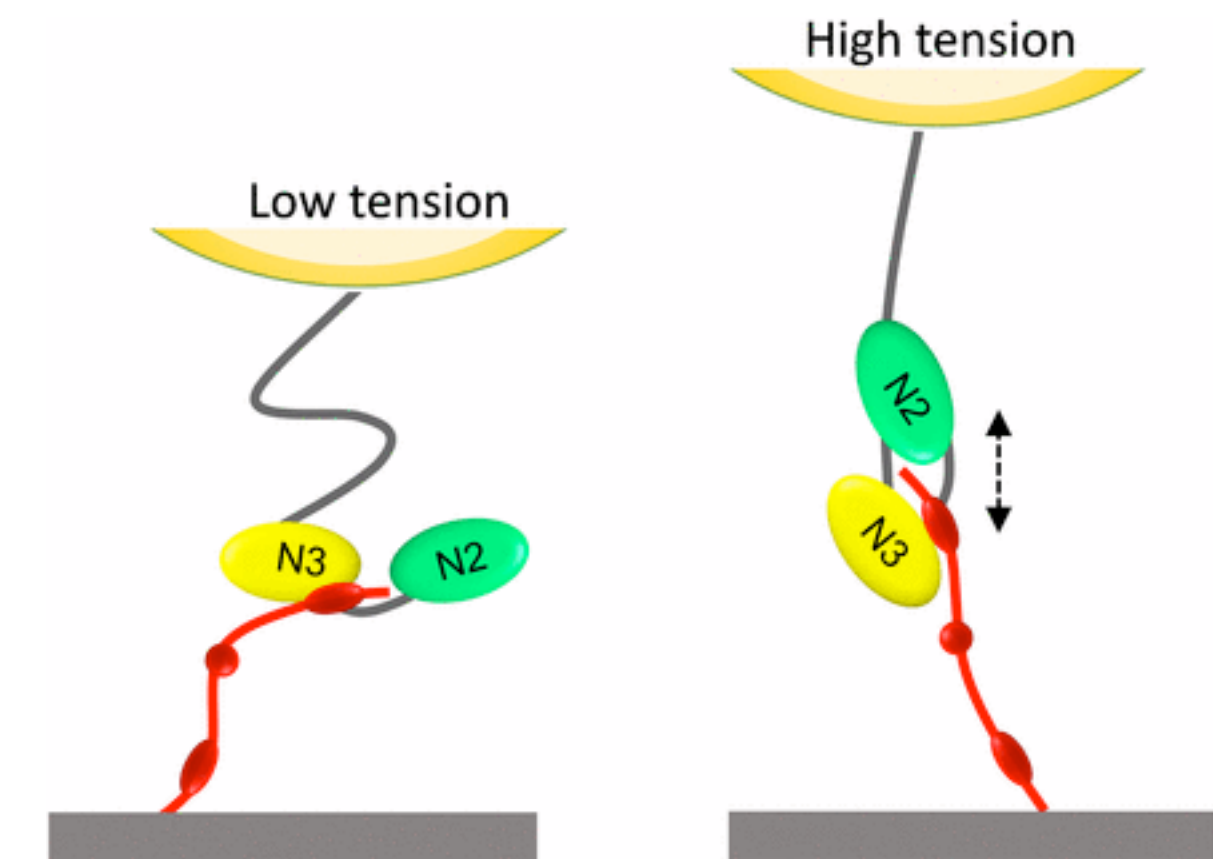
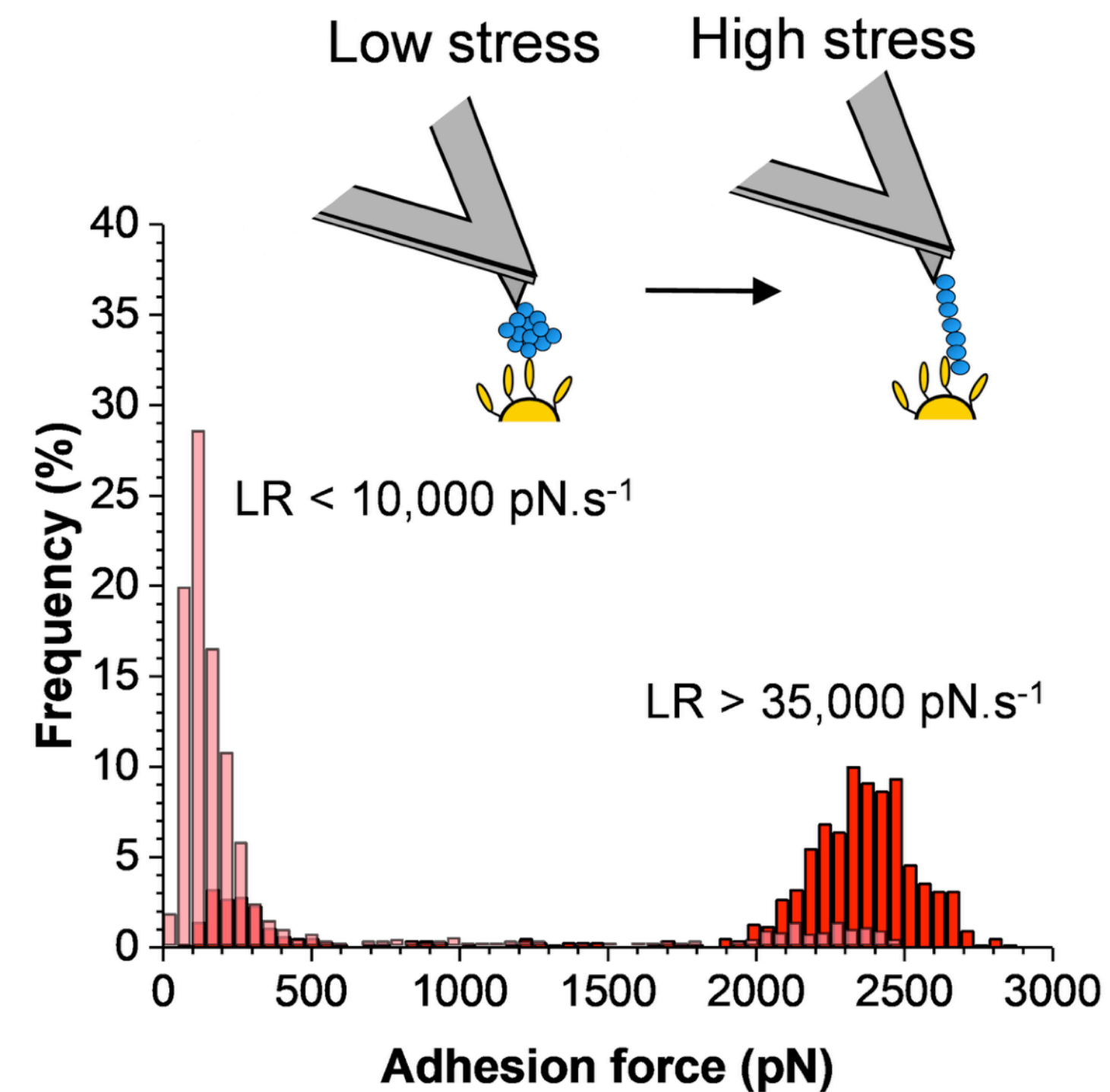
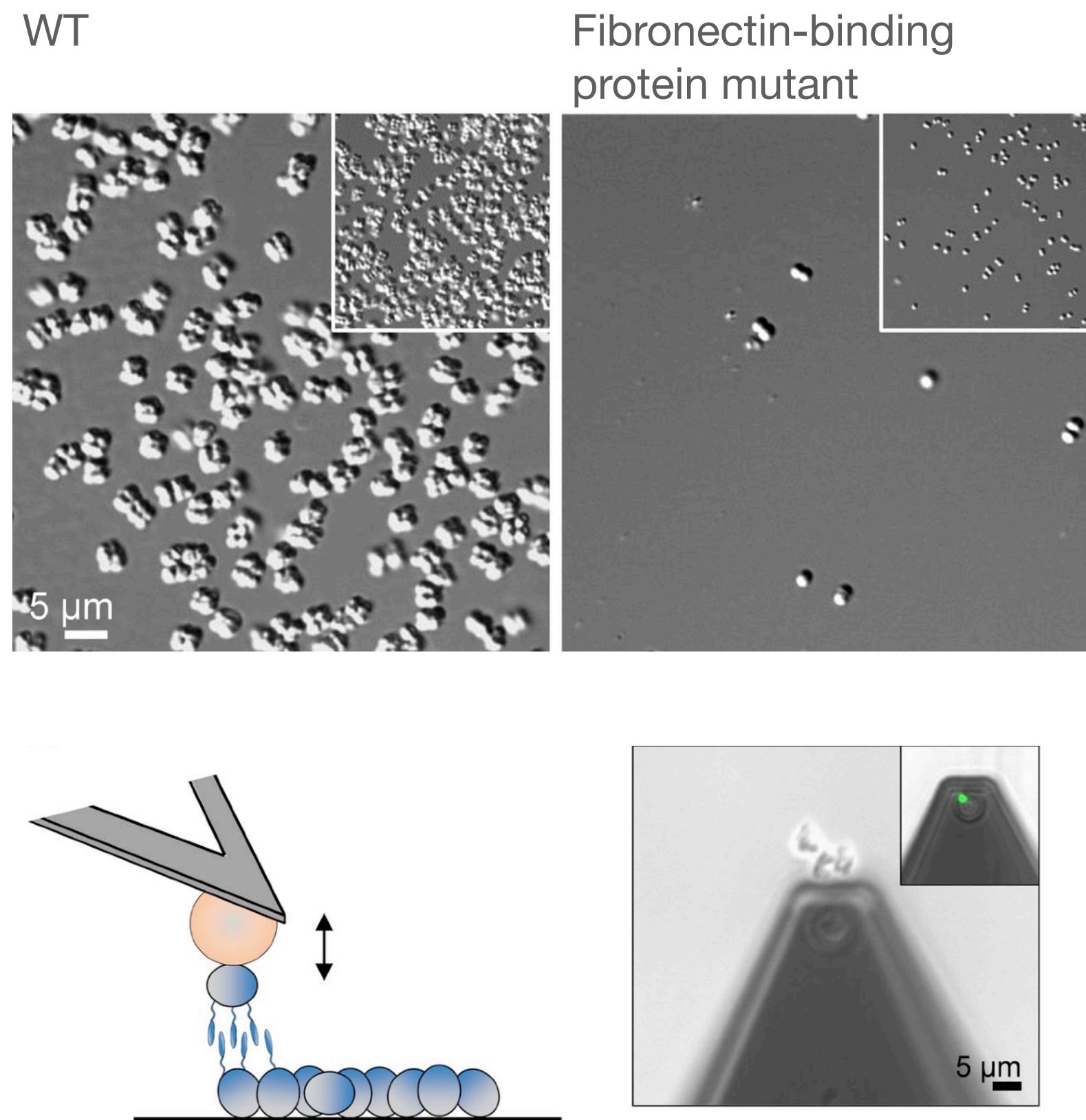
Uropathogenic *E. coli* (UPEC)



Other catch bond examples

Staphylococcus aureus binds to the blood plasma fibrinogen

Attachment to fibronectin-coated surfaces



Summary: slip vs catch bonds

biomechanics vs mechanobiology

Moving

Review Article | [Published: 21 September 2021](#)

Bacterial motility: machinery and mechanisms

[Navish Wadhwa](#)  & [Howard C. Berg](#) 

[Nature Reviews Microbiology](#) **20**, 161–173 (2022) | [Cite this article](#)

“No more pleasant sight has ever yet come before my eye than these many thousands of living creatures seen all alive in a little drop of water ... each several creature having its own proper motion.”

Antonie van Leeuwenhoek's 18th letter to the Royal Society on observations made on 6 August 1676 of “little eels”



Bacterial motility

Swimming



Living at the microscale

- How does it feel to live at the scale of a few micrometers?
- How did microorganisms evolve to adapt to these different conditions?
- What are the consequences of small scales on biological microflows?

Life at low Reynolds number

E. M. Purcell

Lyman Laboratory, Harvard University, Cambridge, Massachusetts 02138

(Received 12 June 1976)

The hydrodynamics of swimming microorganisms

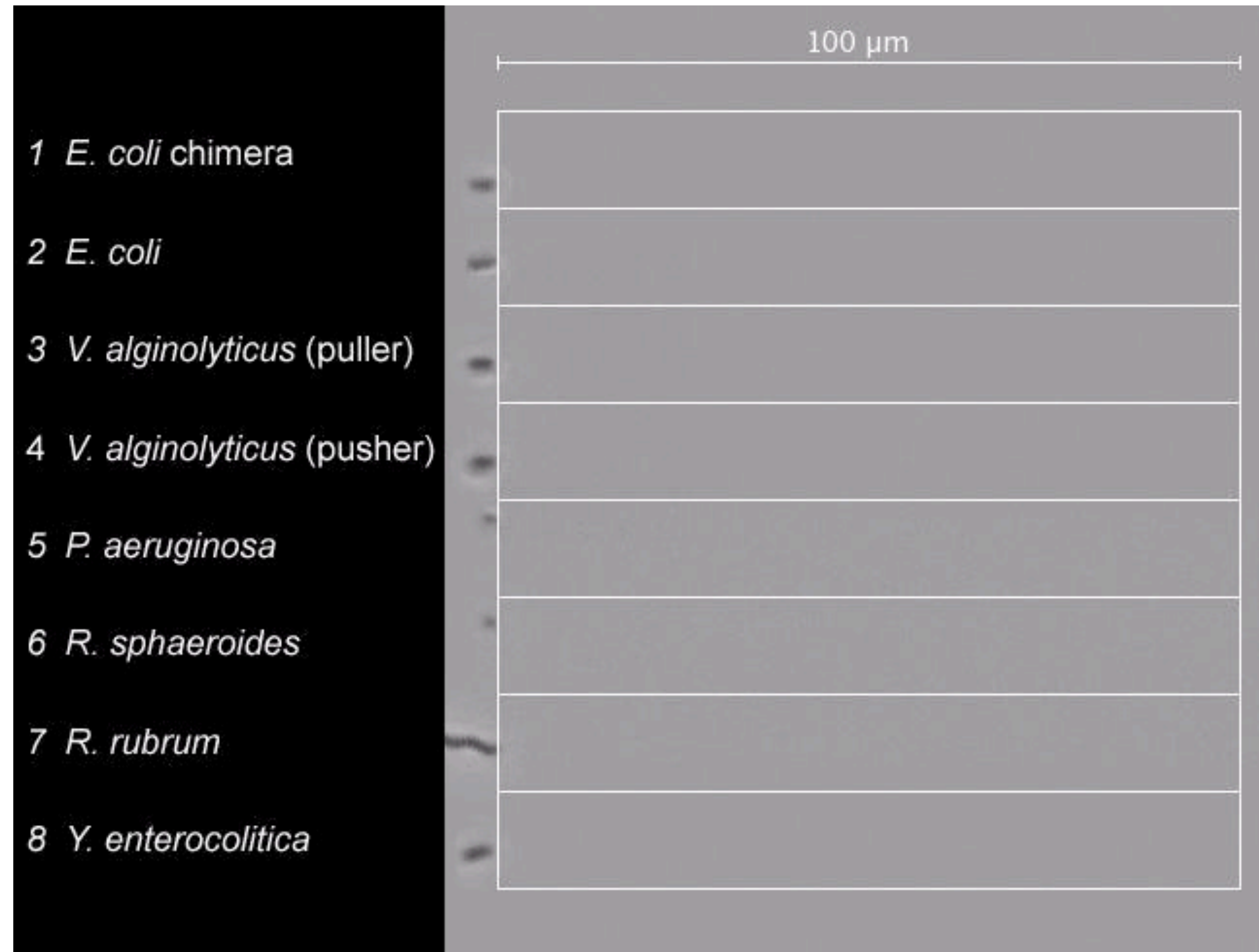
Eric Lauga¹ and Thomas R Powers²

The Scallop Theorem



Bacterial swimming

Ready, set, go!



Bacterial flagellum

a rotating filament

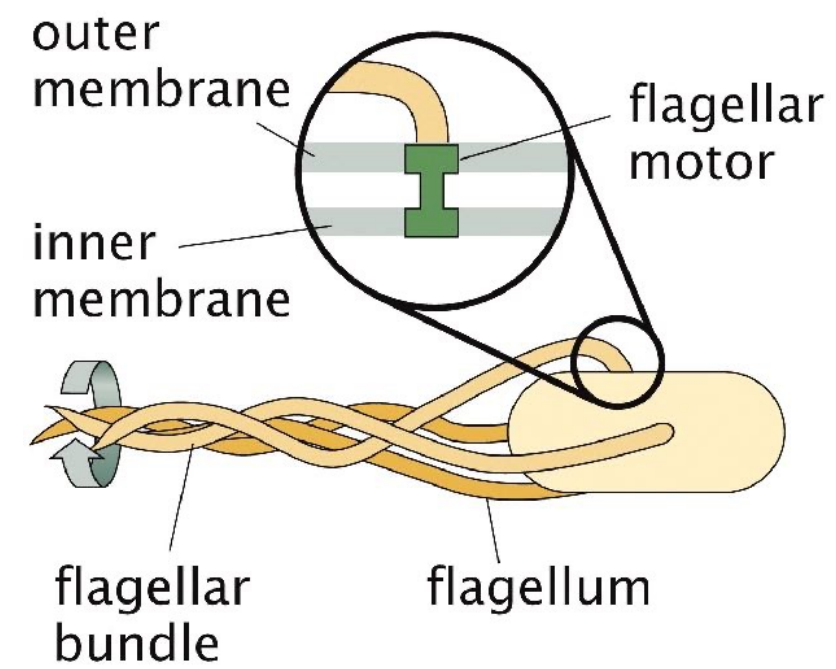
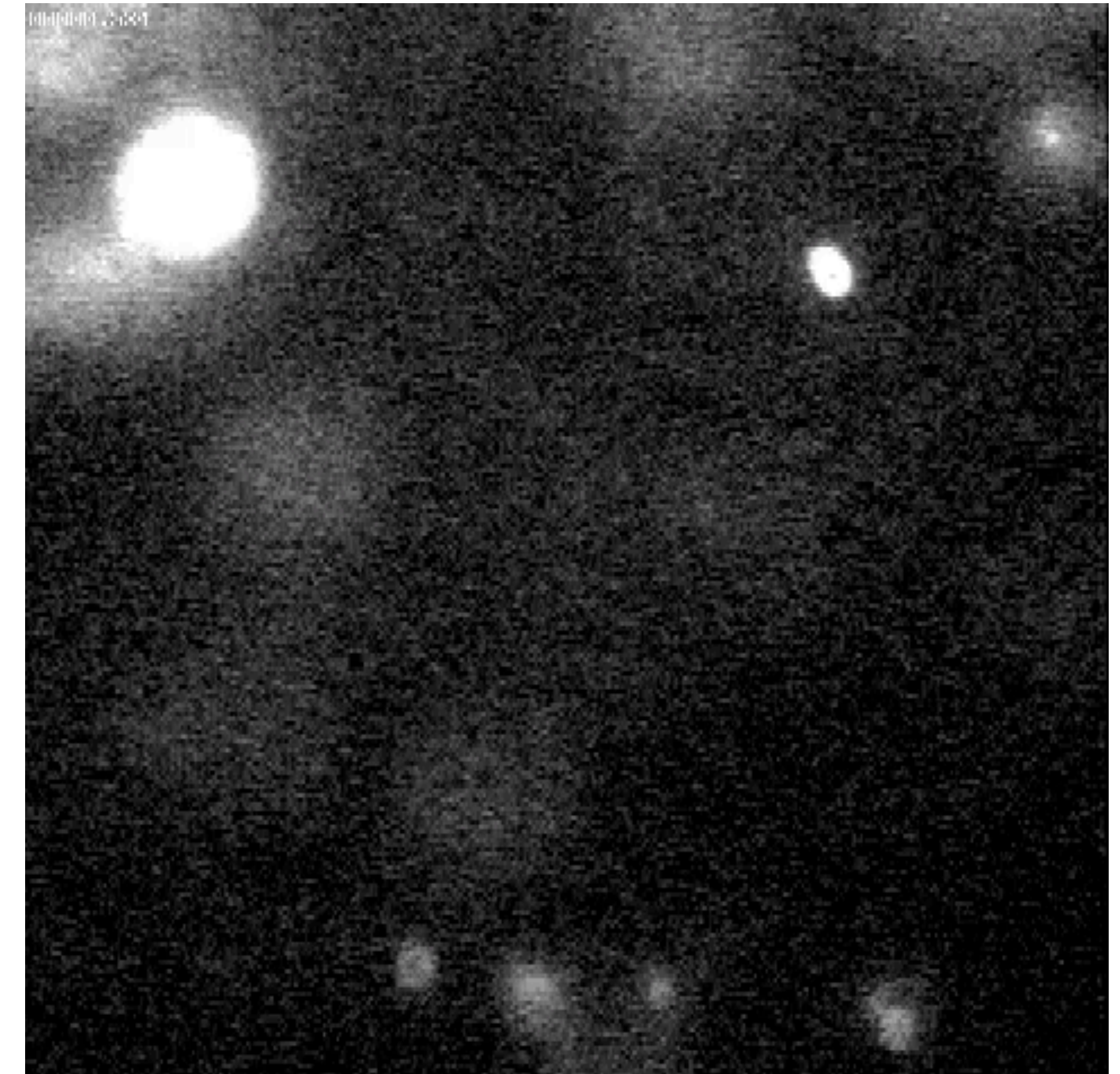
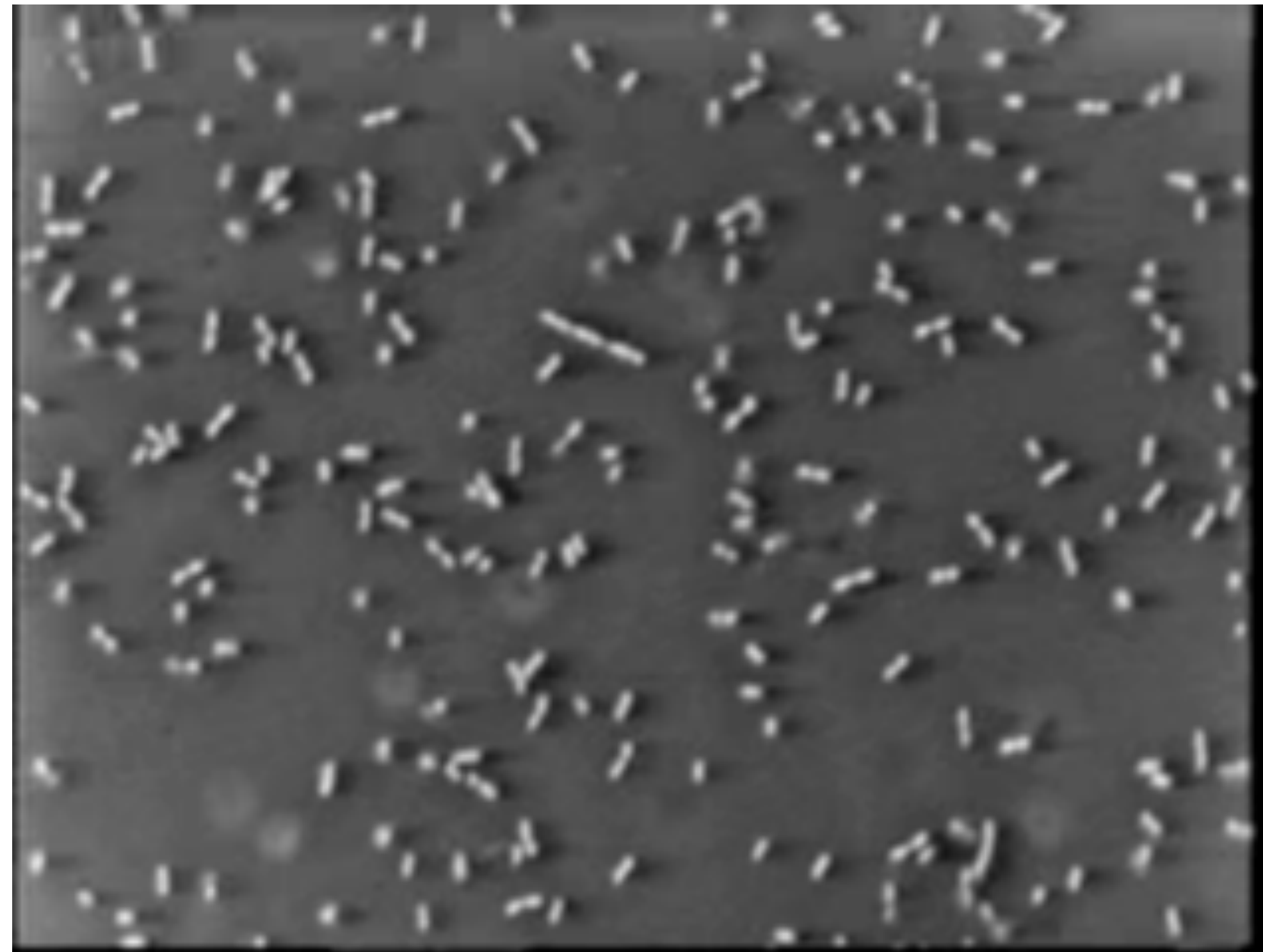
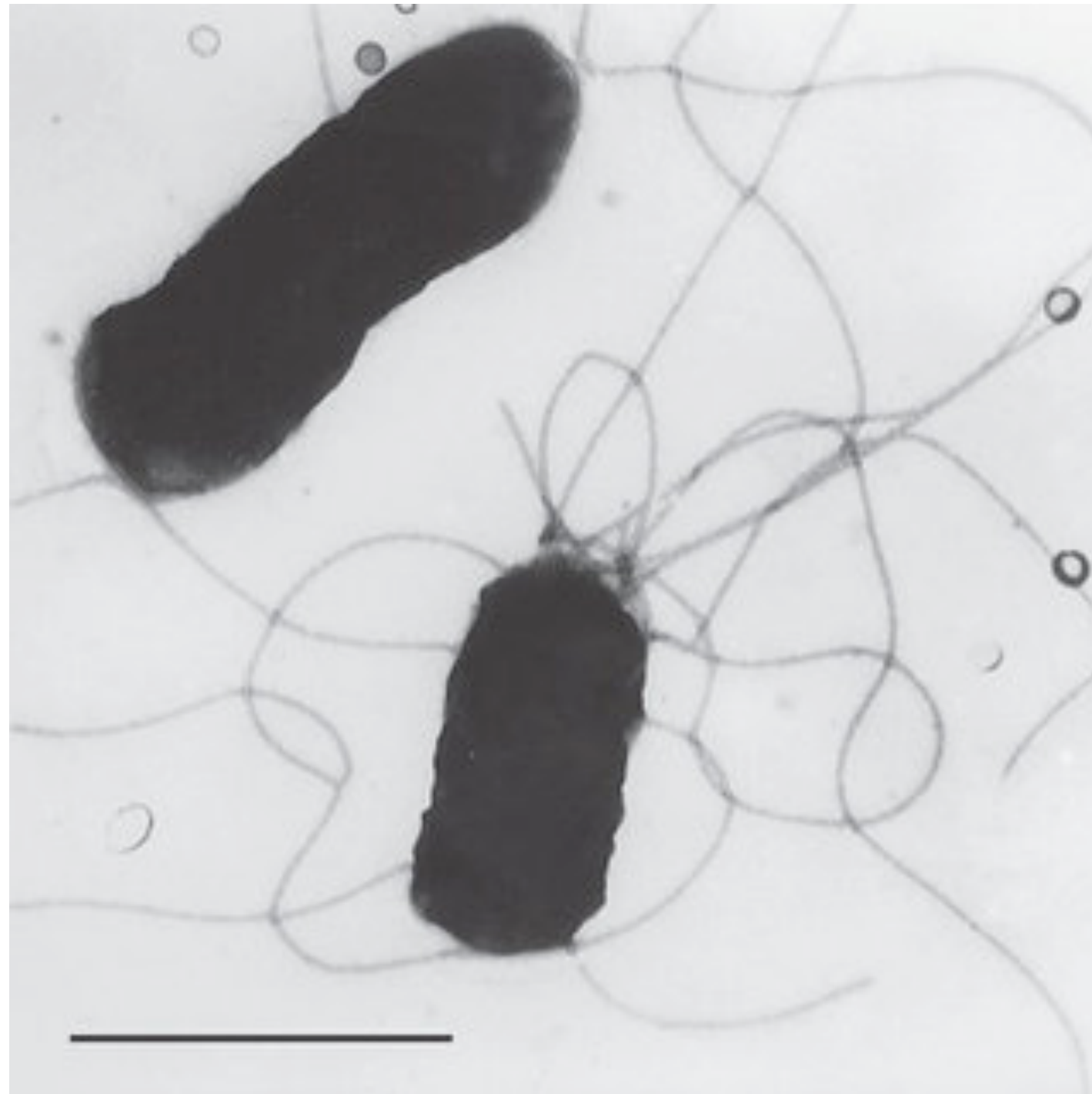


Figure 4.16a Physical Biology of the Cell, 2ed. (© Garland Science 2012)



Bacterial flagellum



transmitted electron
microscopy of *E. coli*

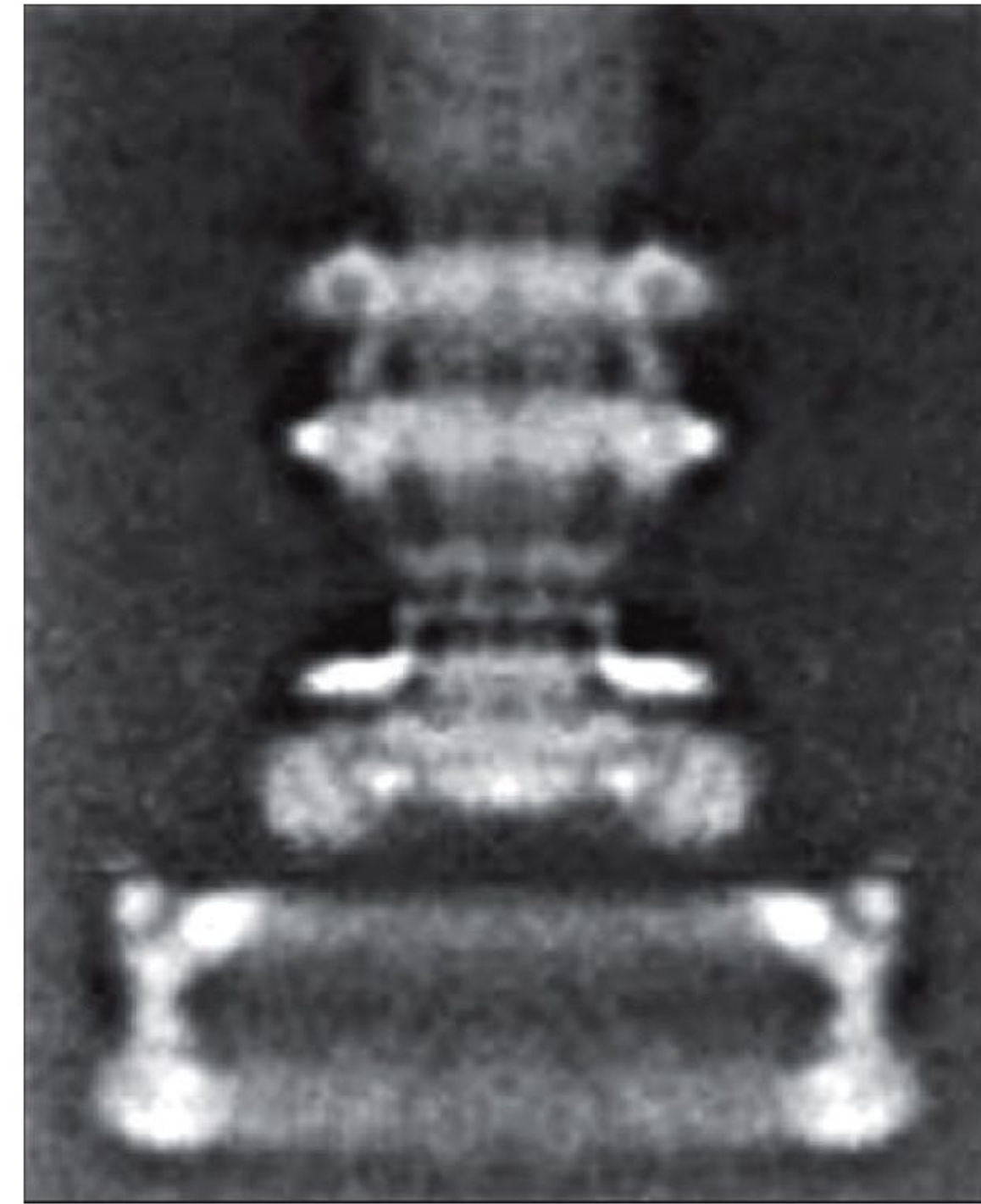
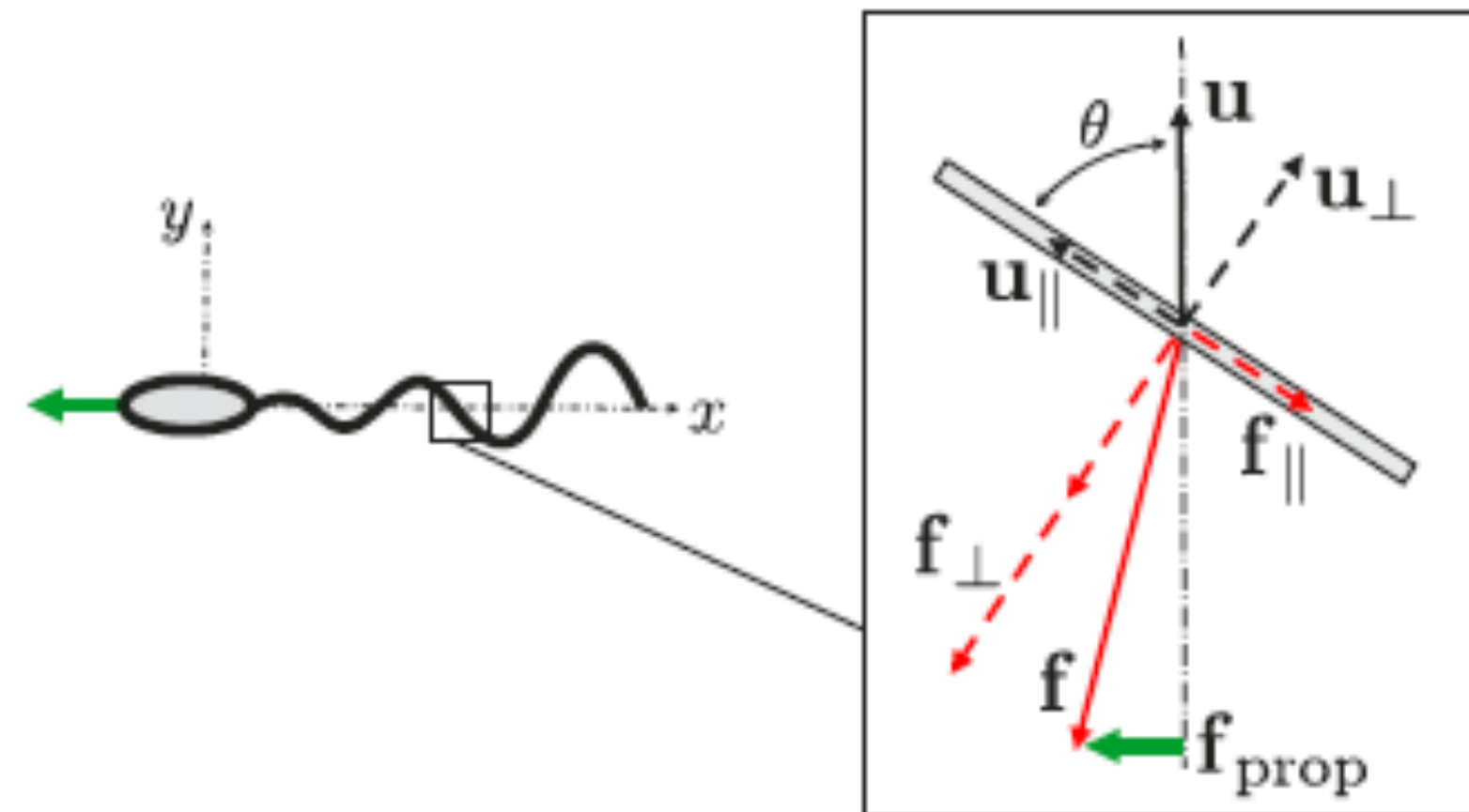
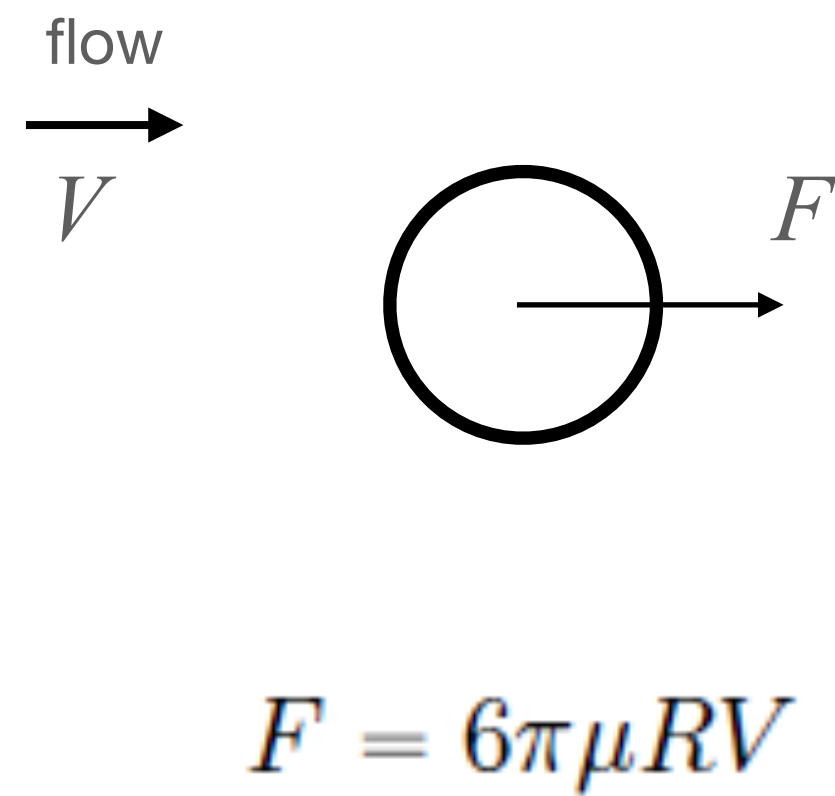


Figure 3.24b Physical Biology of the Cell, 2ed. (© Garland Science 2013)

cryo electron microscopy
of a bacterial flagellum

Hydrodynamics of flagellar propulsion

Drag anisotropy generates thrust



$$f_\perp = \gamma_\perp v_\perp \simeq 4\pi\mu L v_\perp$$

$$f_\parallel = \gamma_\parallel v_\parallel \simeq 2\pi\mu L v_\parallel$$

$$\gamma_\perp = 2\gamma_\parallel \text{ (from "resistive theory")}$$

Bacterial flagellar motor

- Works on H^+ gradient (not ATP!)
- Can rotate both directions
- $f \sim 100$ Hz

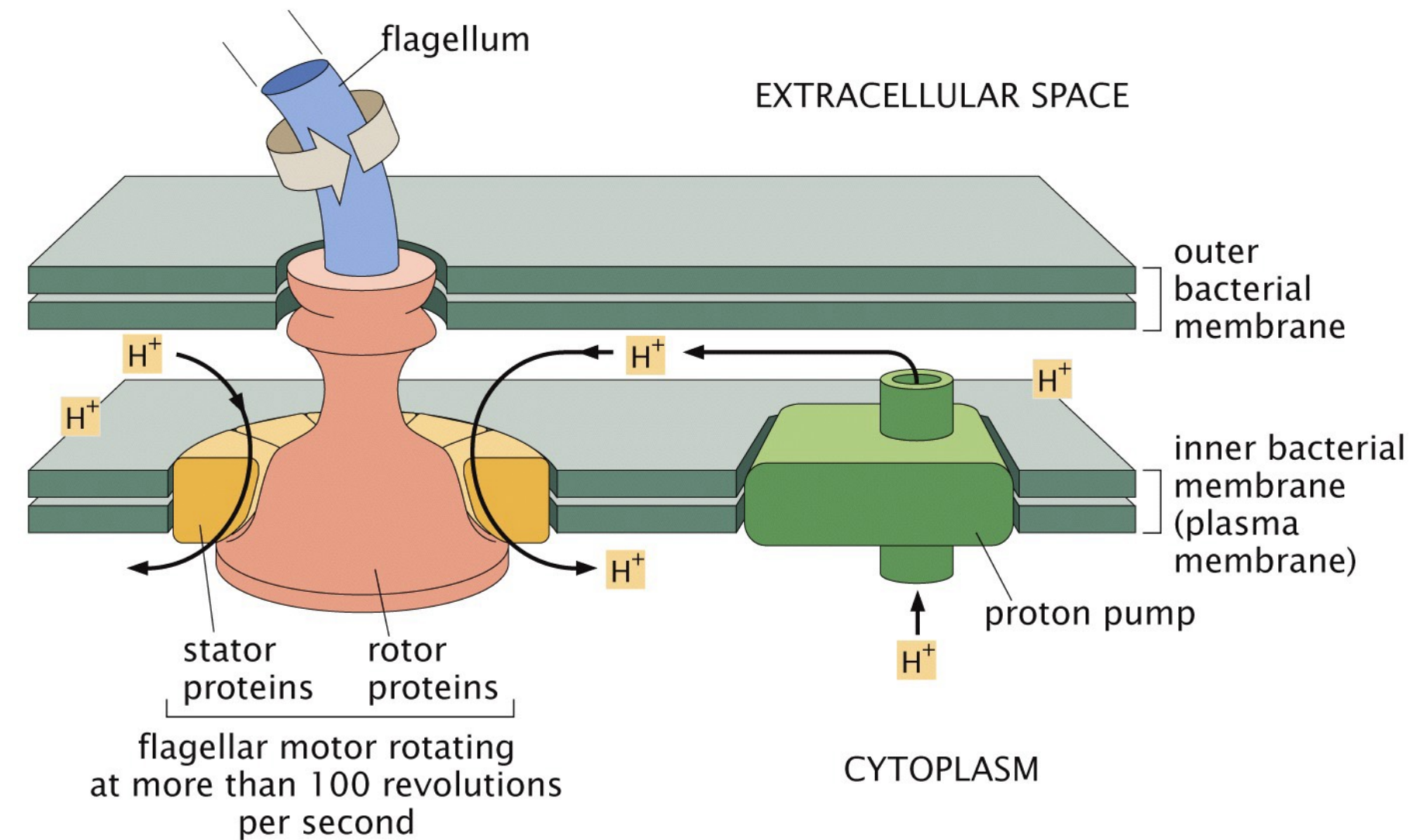
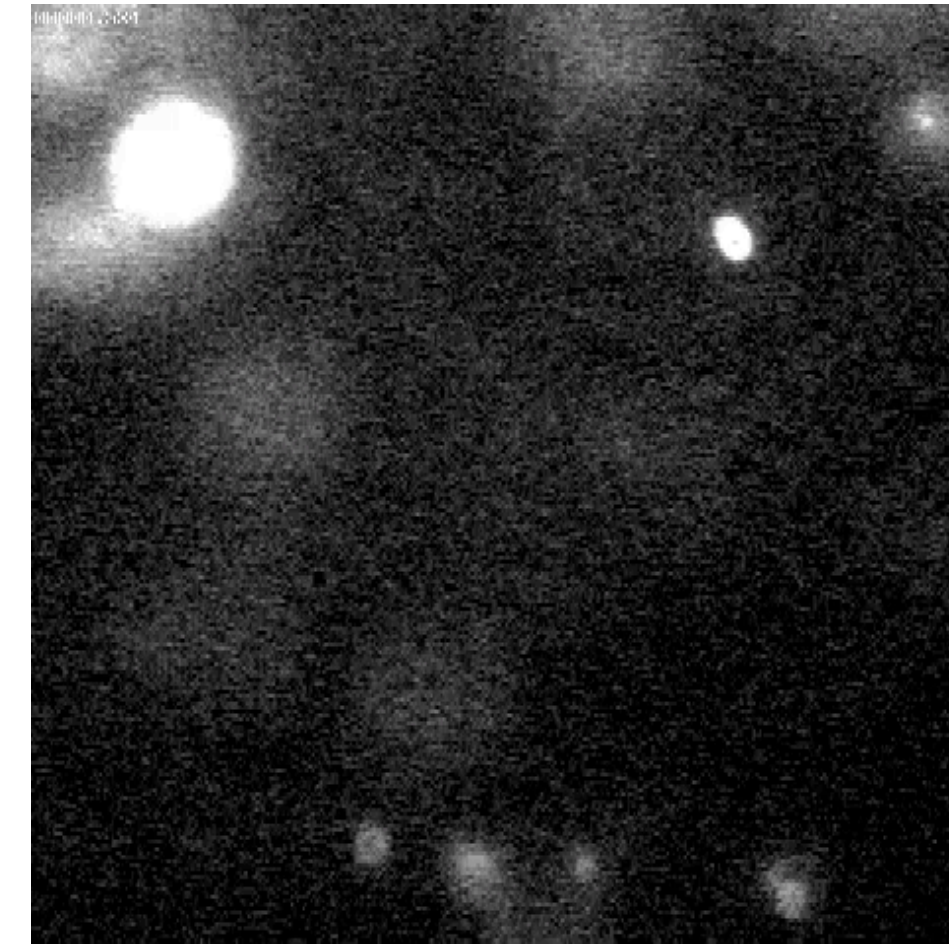


Figure 16.14a Physical Biology of the Cell, 2ed. (© Garland Science 2013)

The flagellum is a rotating protein machine

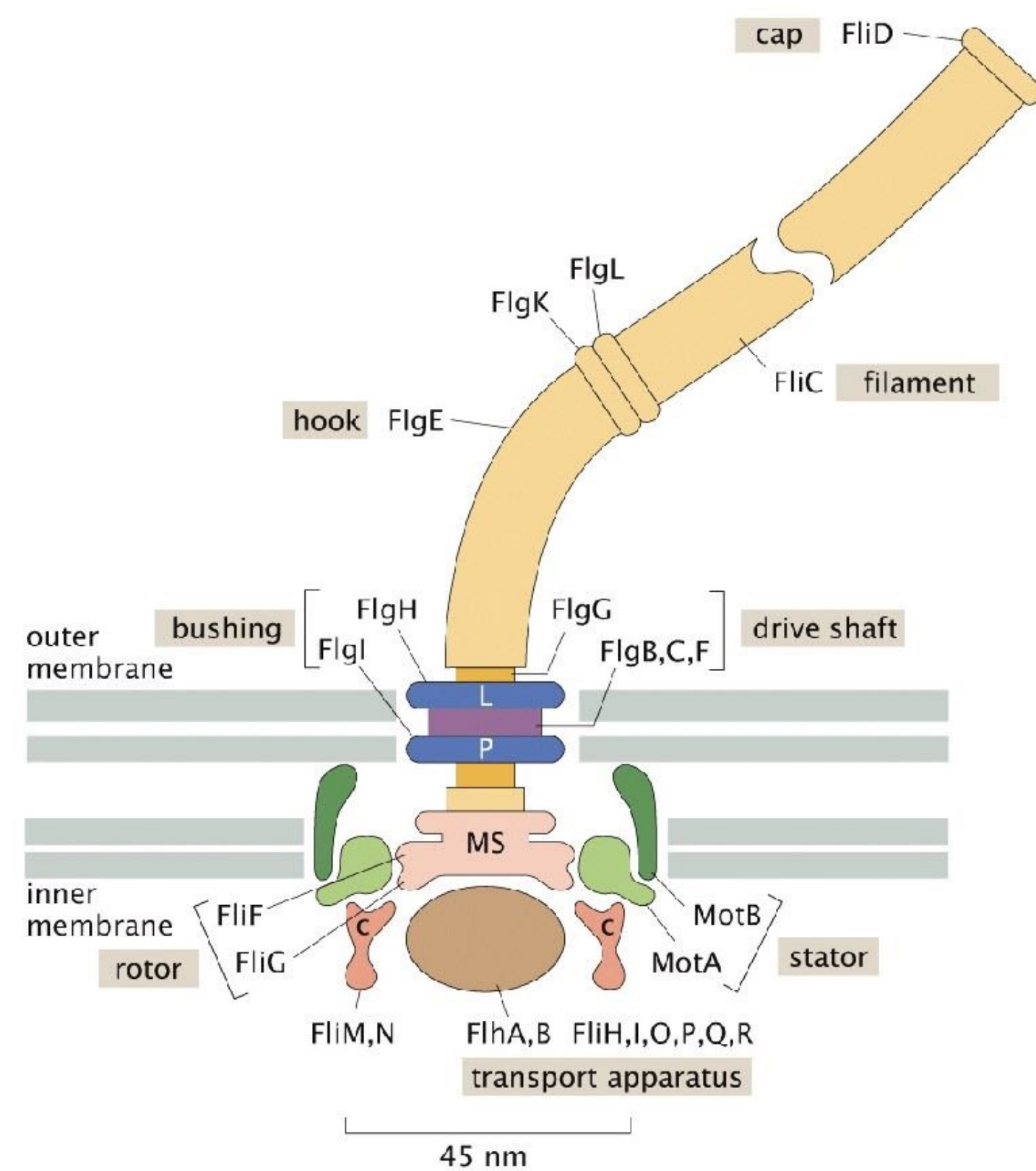
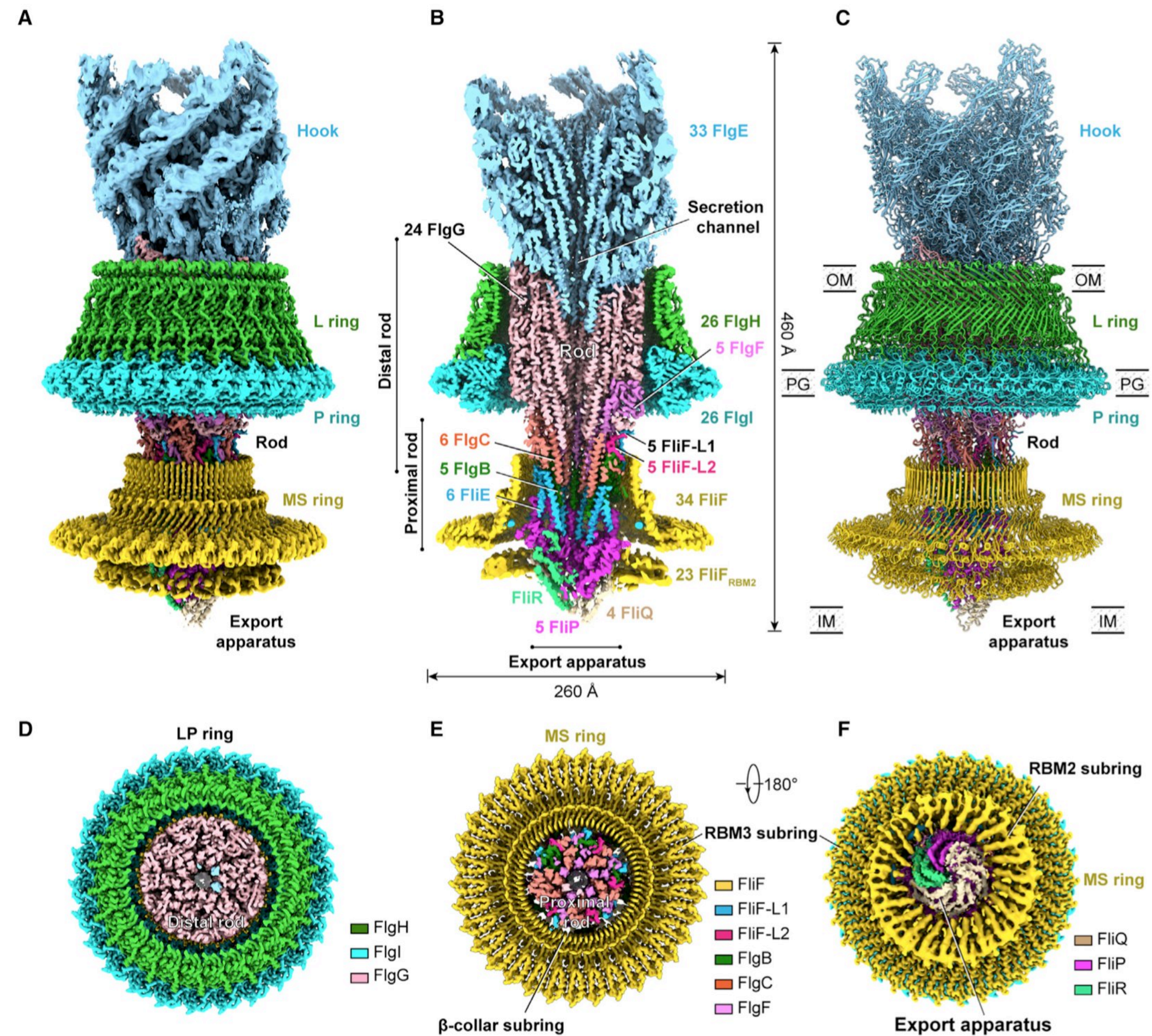
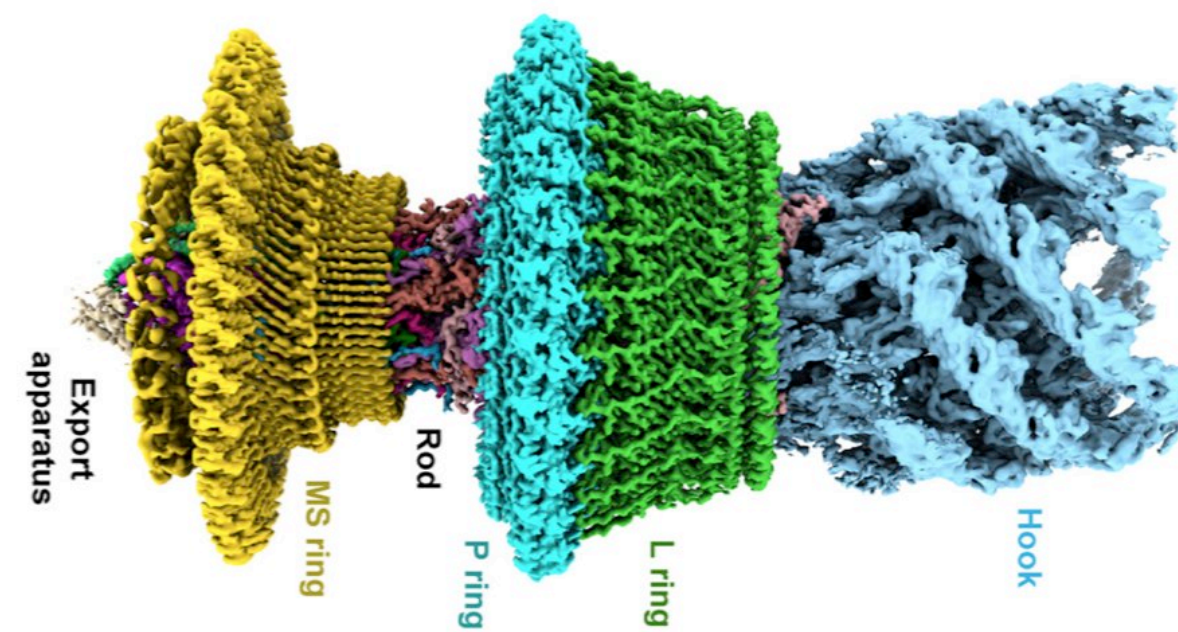
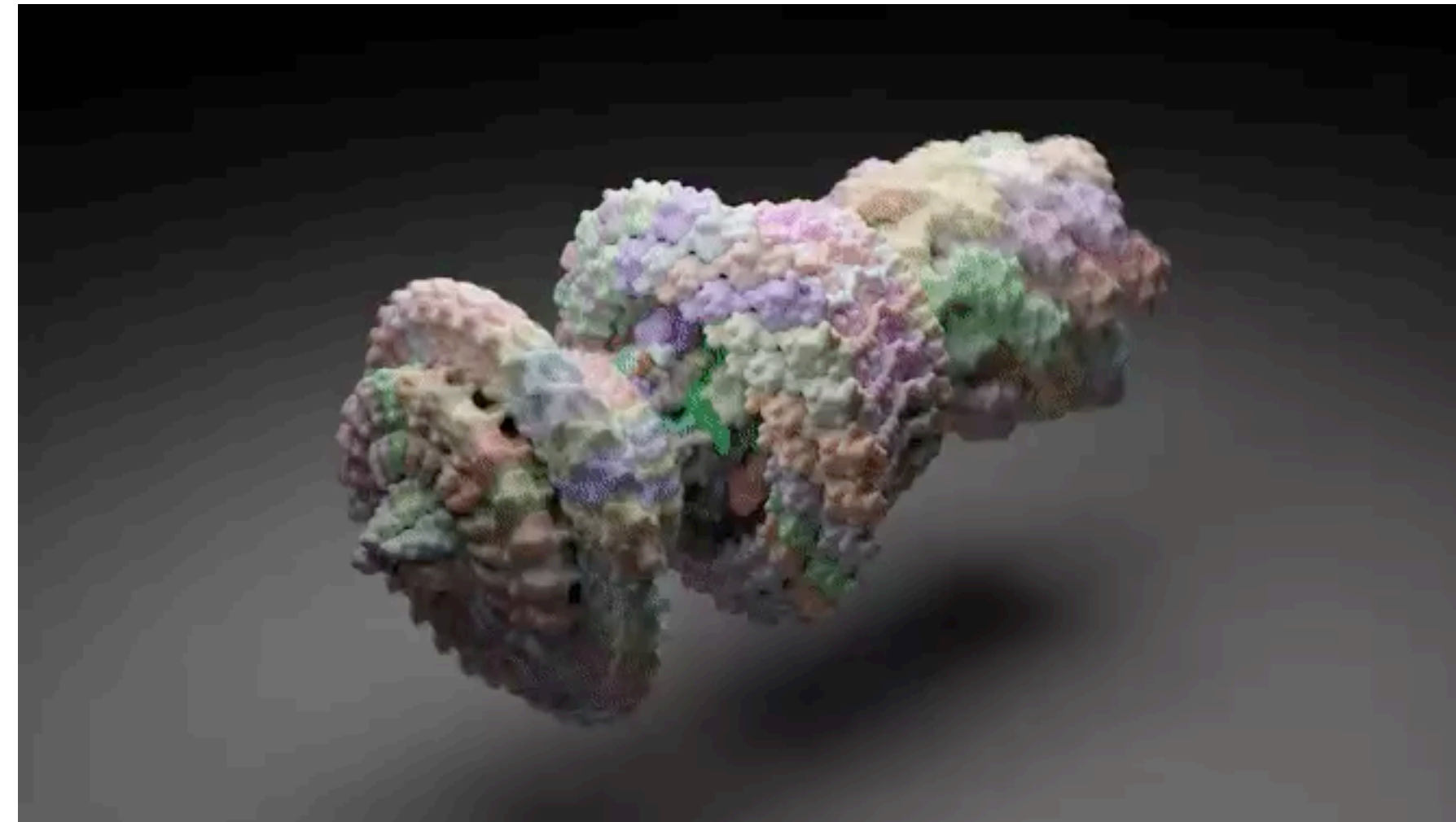


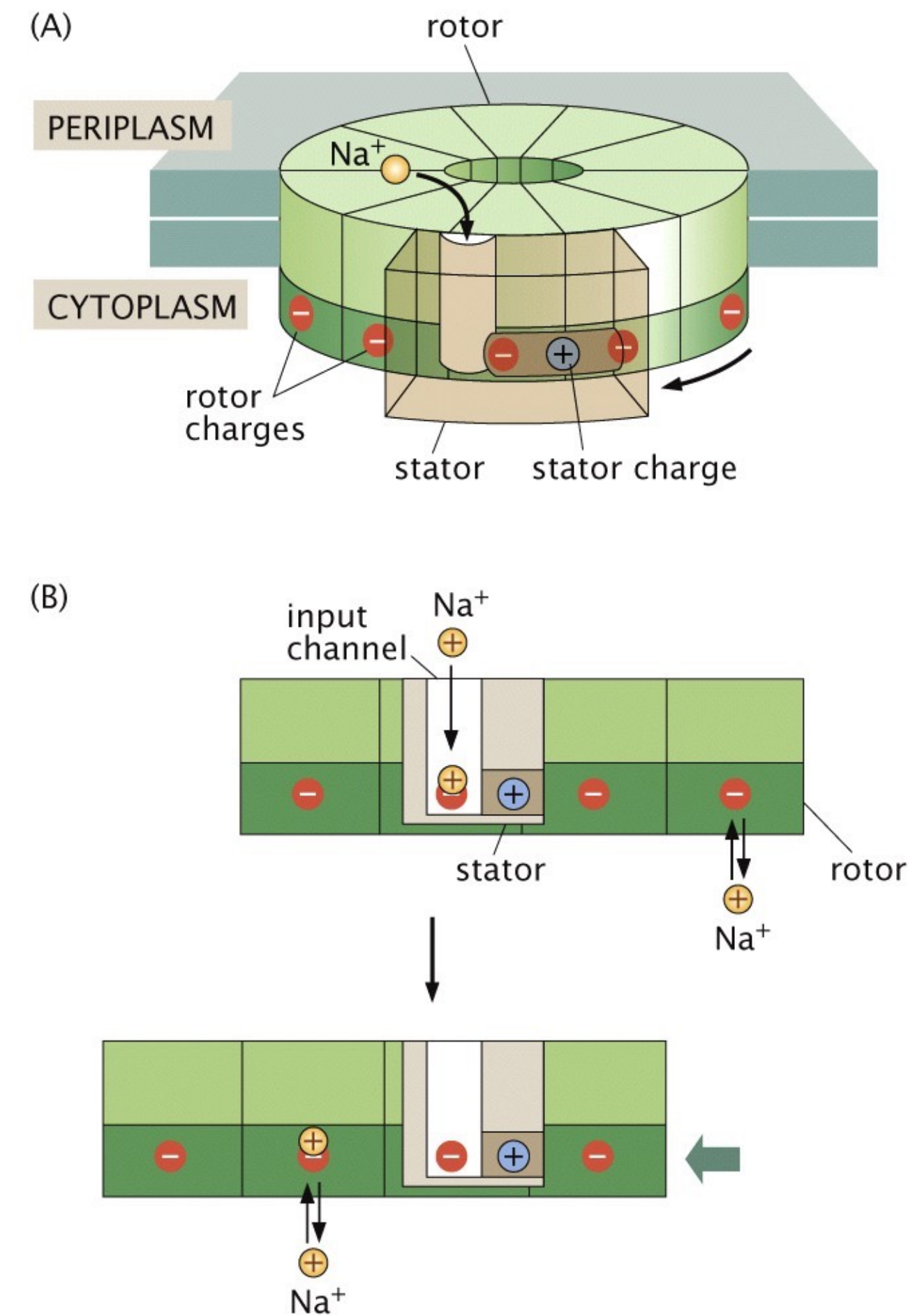
Figure 3.24a Physical Biology of the Cell, 2ed. (© Garland Science 2013)



Rotating protein assembly



Molecular mechanism of rotation



**Ion transport
-> charge screening**

**Rotation and ion
release**

Figure 16.42 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Where do bacteria swim?

Bacteria use a reversal strategy

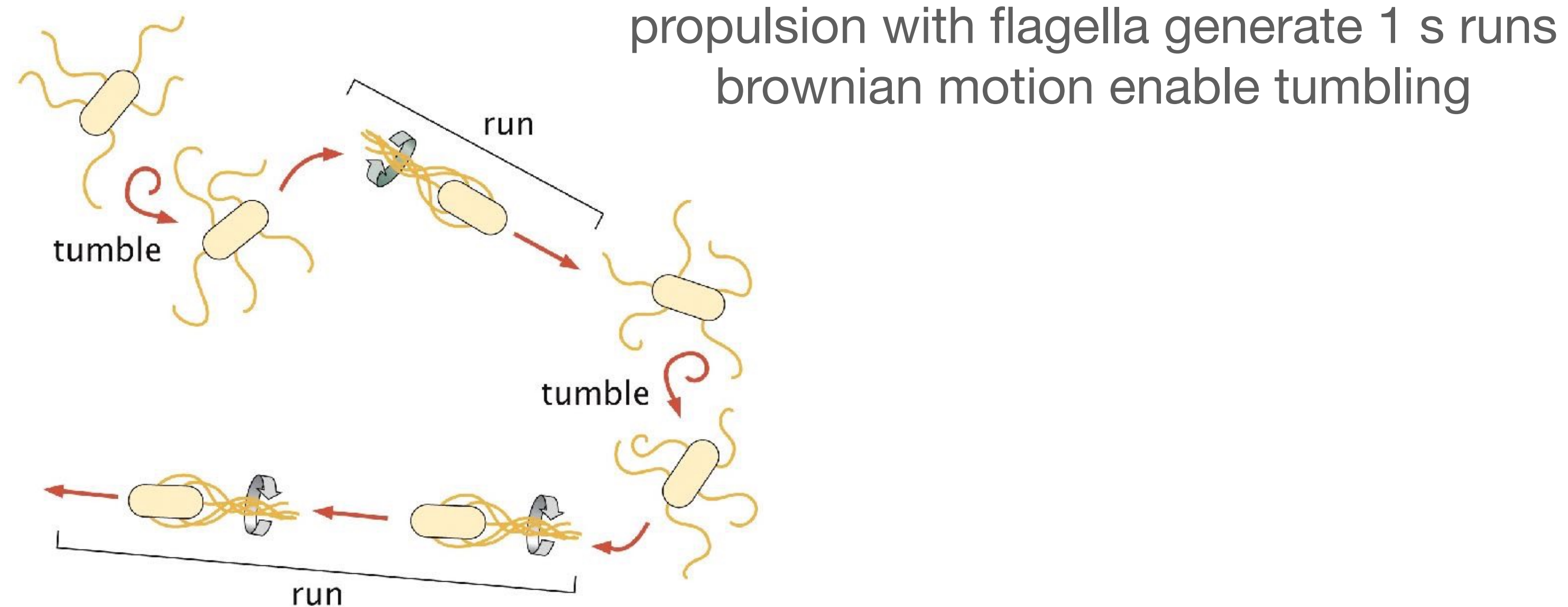


Figure 4.16b Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Tumbling allows single cells to change direction

Chemotaxis

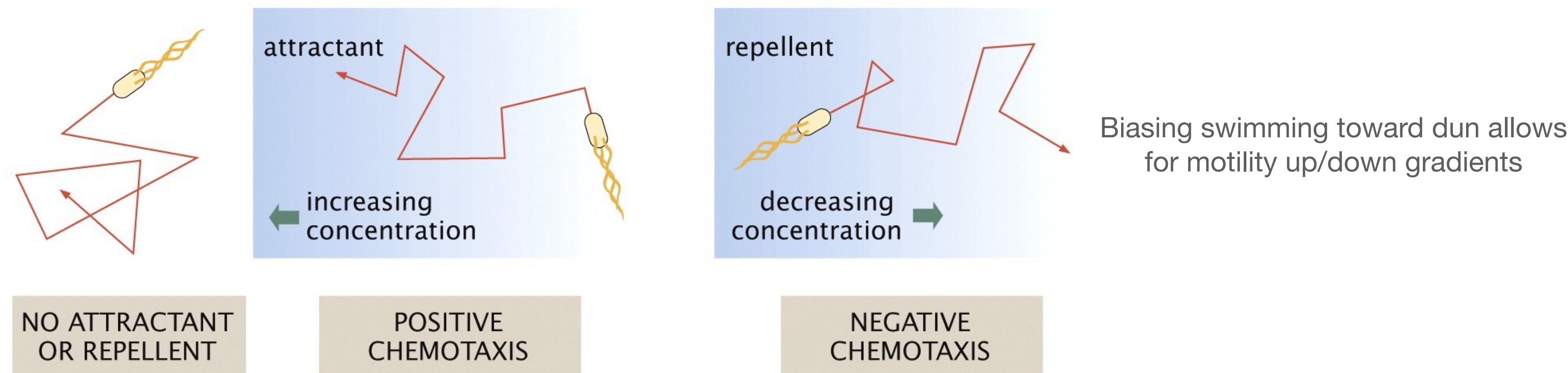


Figure 4.16d Physical Biology of the Cell, 2ed. (© Garland Science 2013)

At the molecular level:
chemotaxis system connects ligand
sensing to motor activity

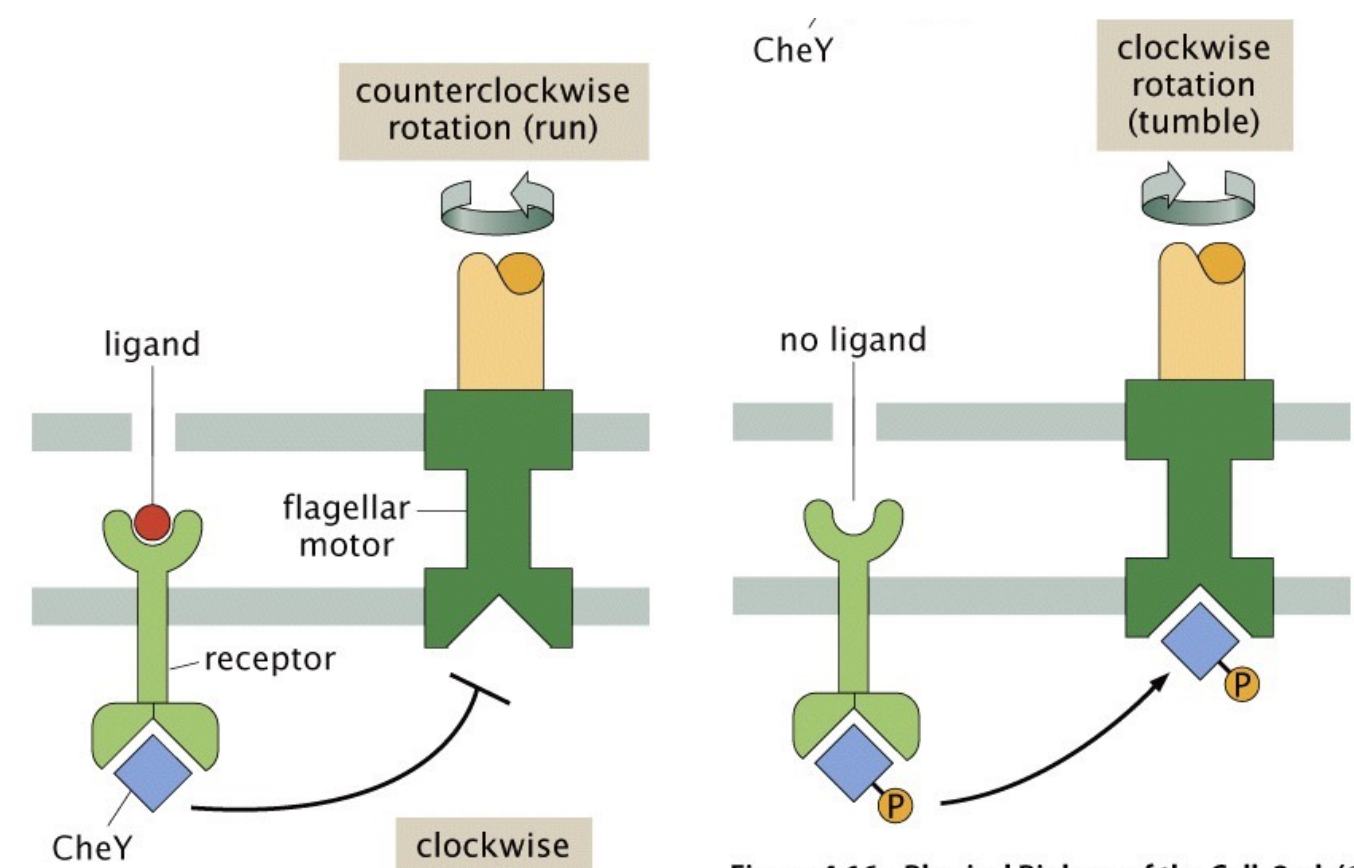
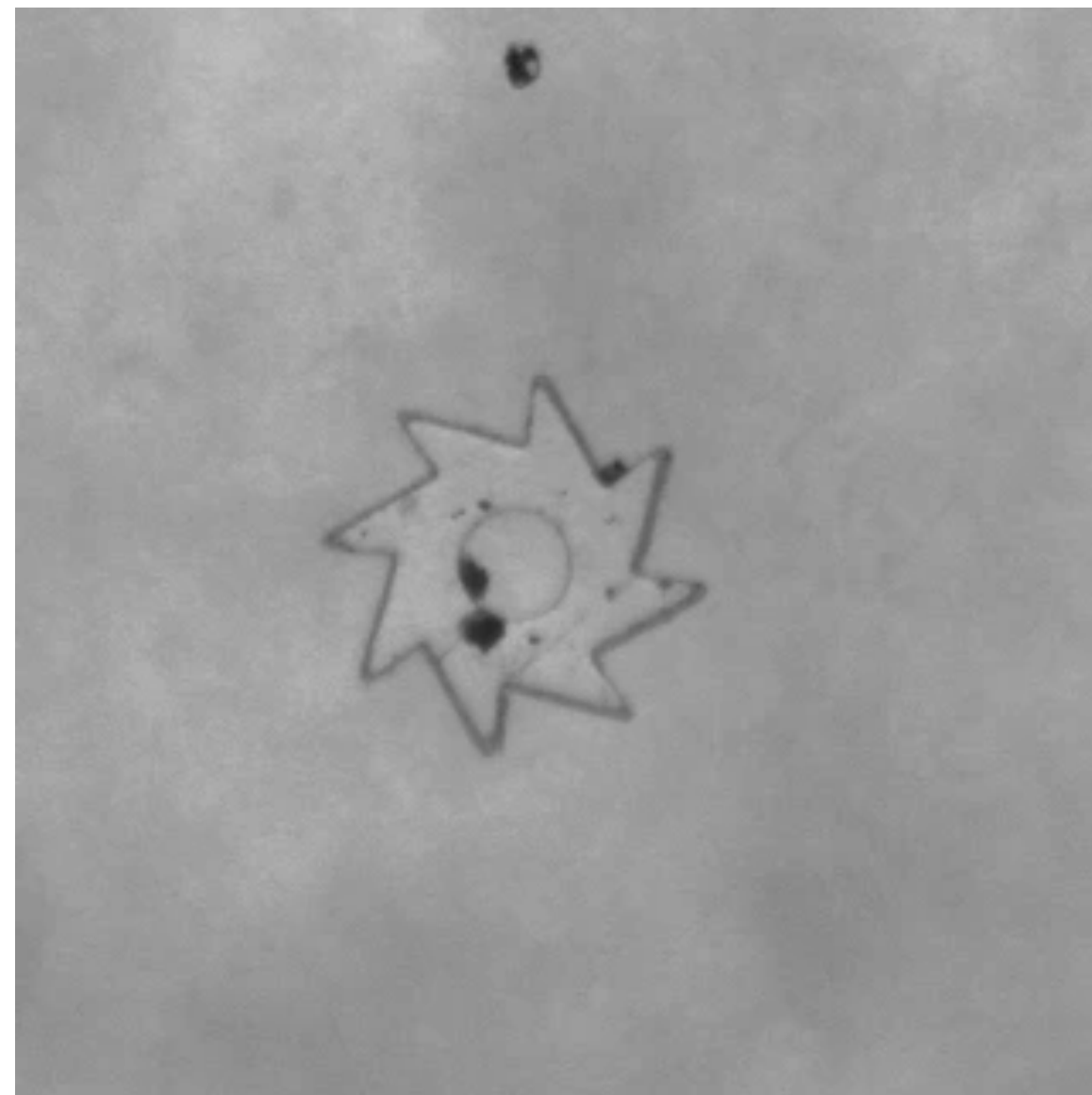


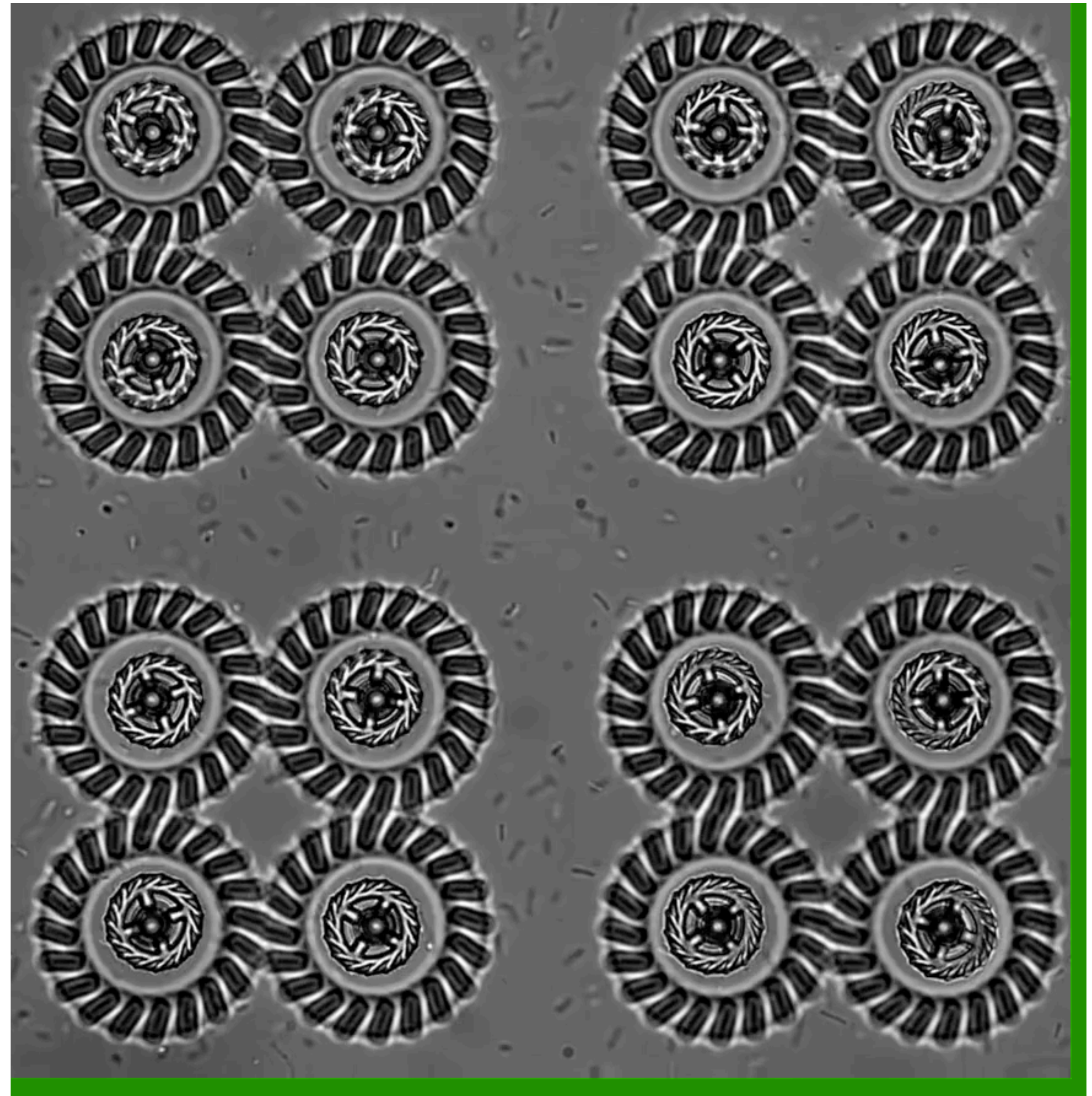
Figure 4.16c Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Harnessing motility

Bacteria can power machines



Sokolov, PNAS 2010



Vizsnyiczai, Nat Com. 2017

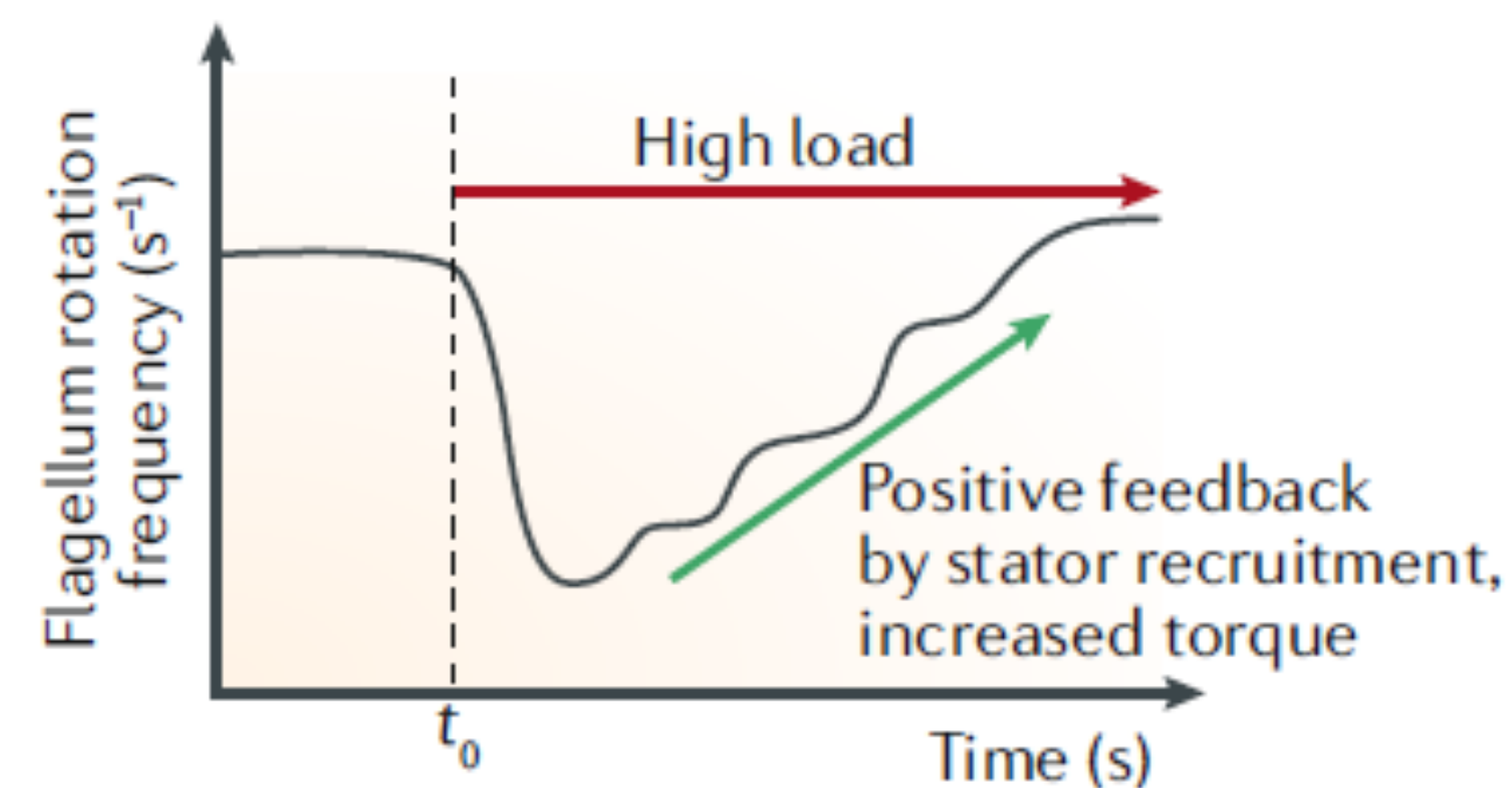
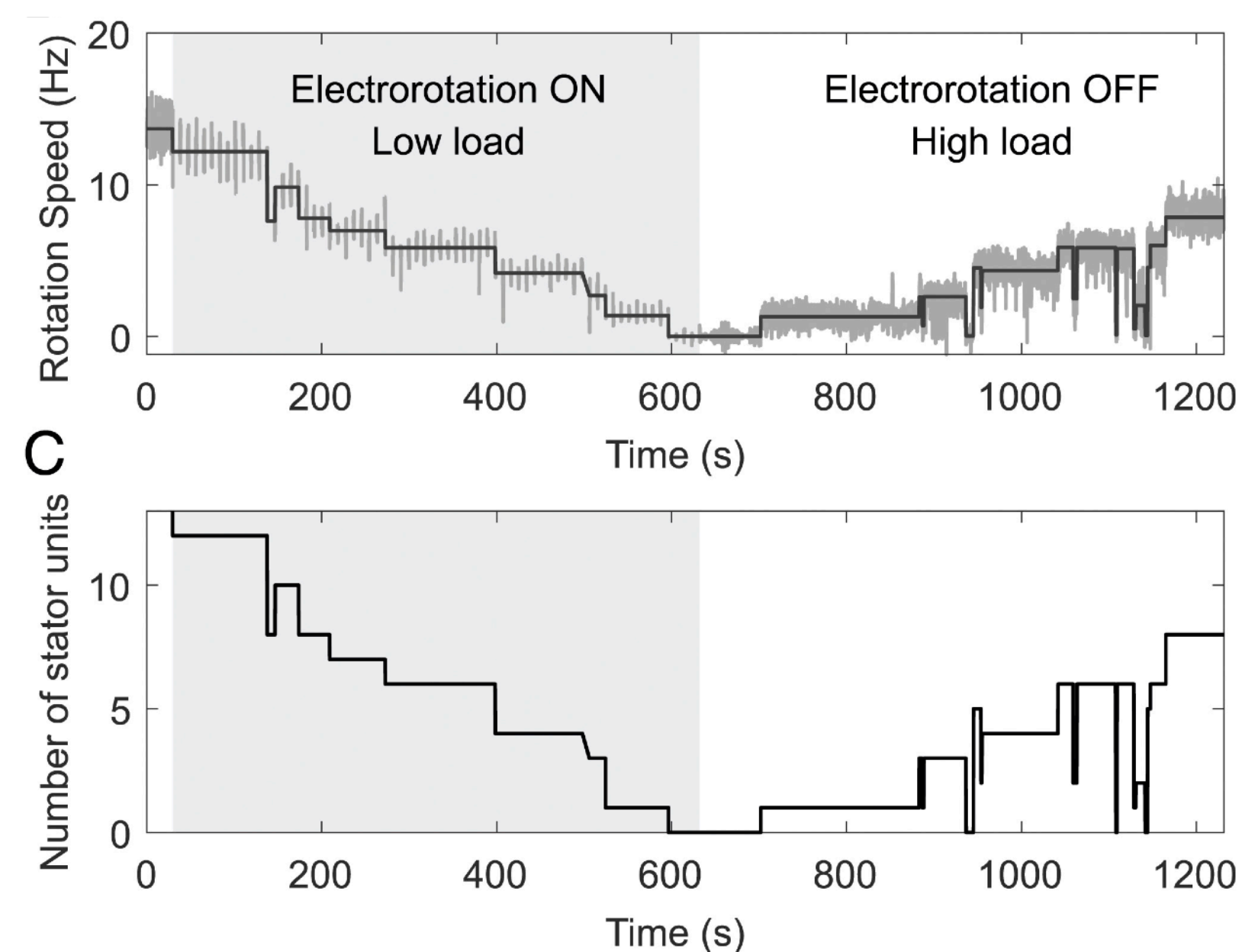
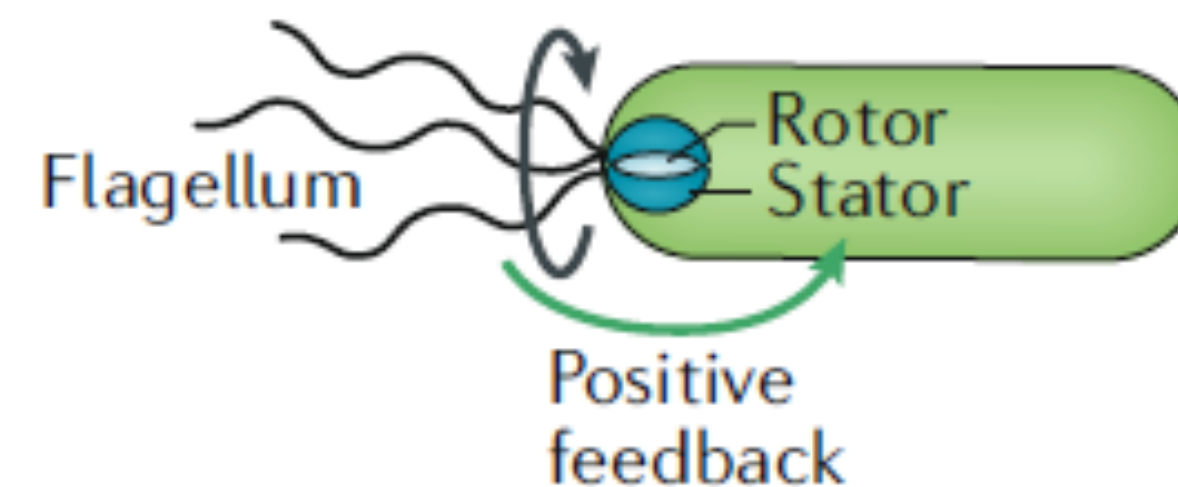
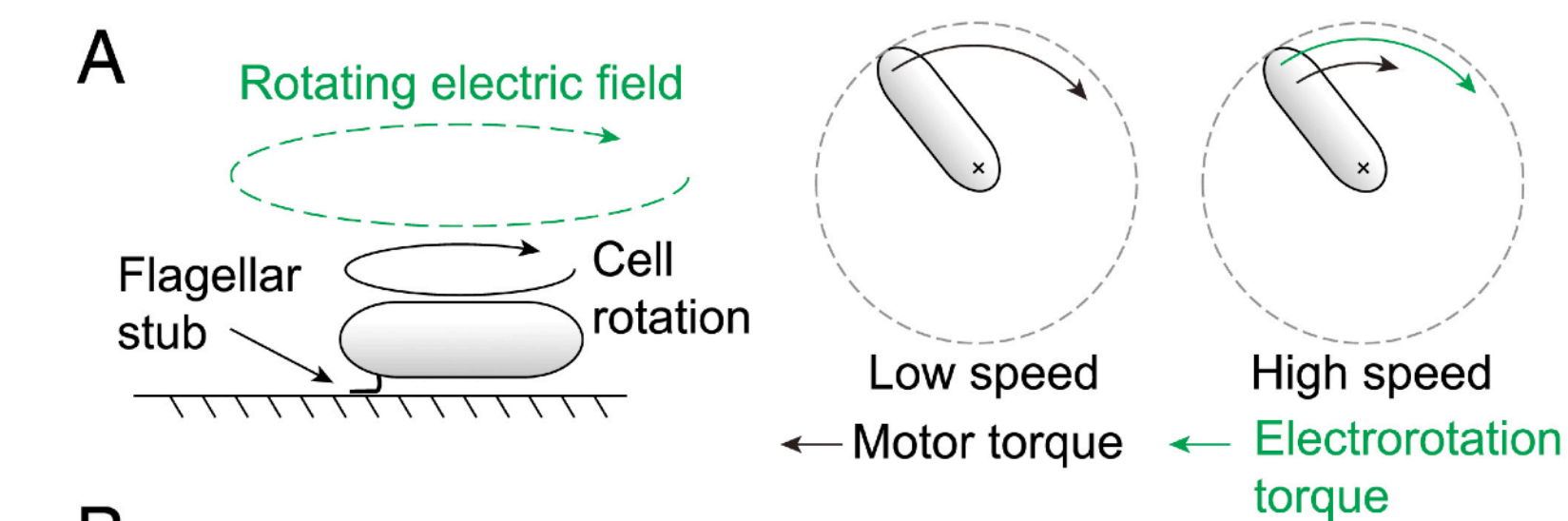
Tethering flagella

A tool to perturb flagellum rotation



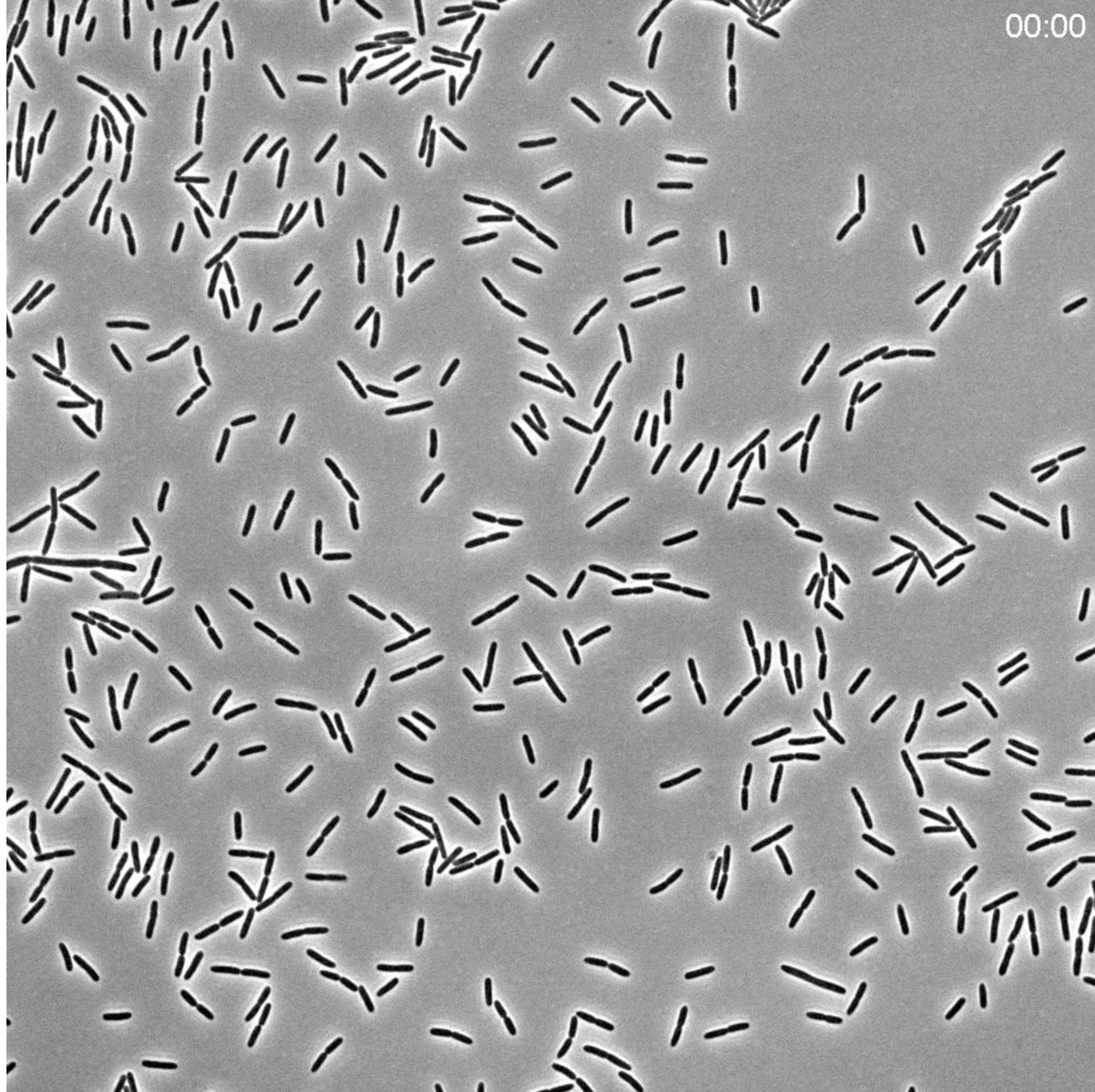
Nesper, eLife 2017

Bacteria can change gears

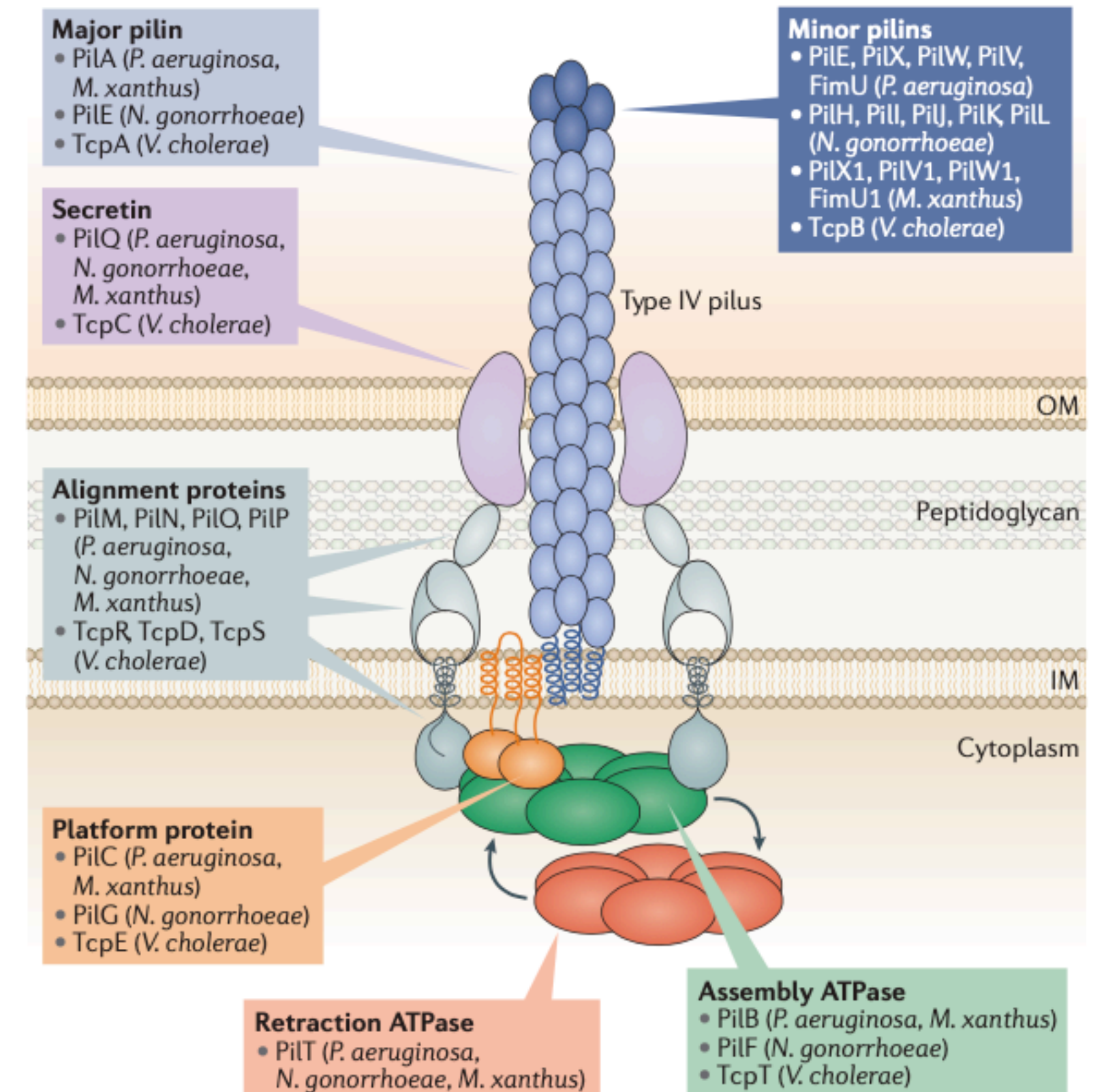
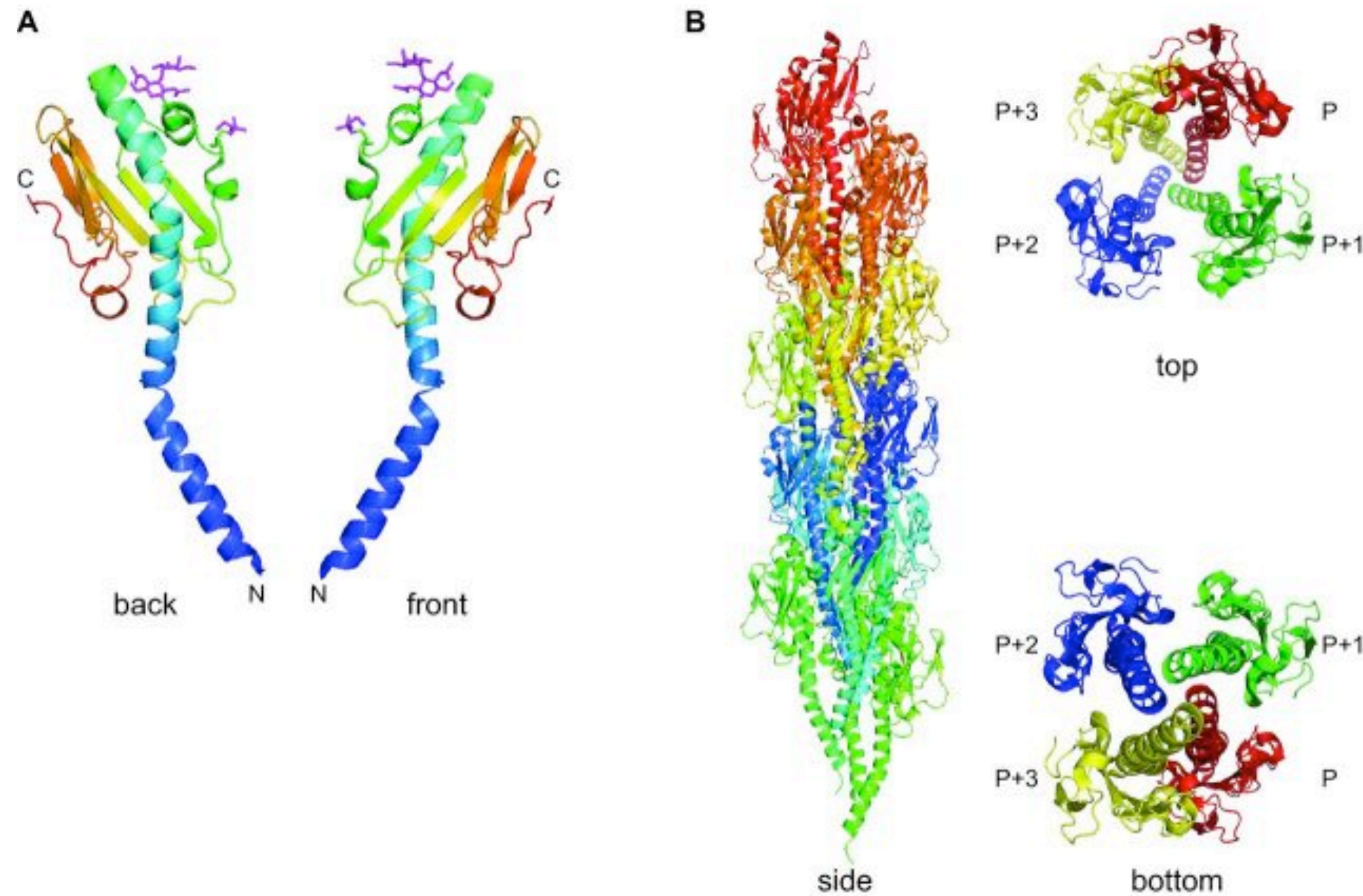


Twitching motility

Bacteria can crawl

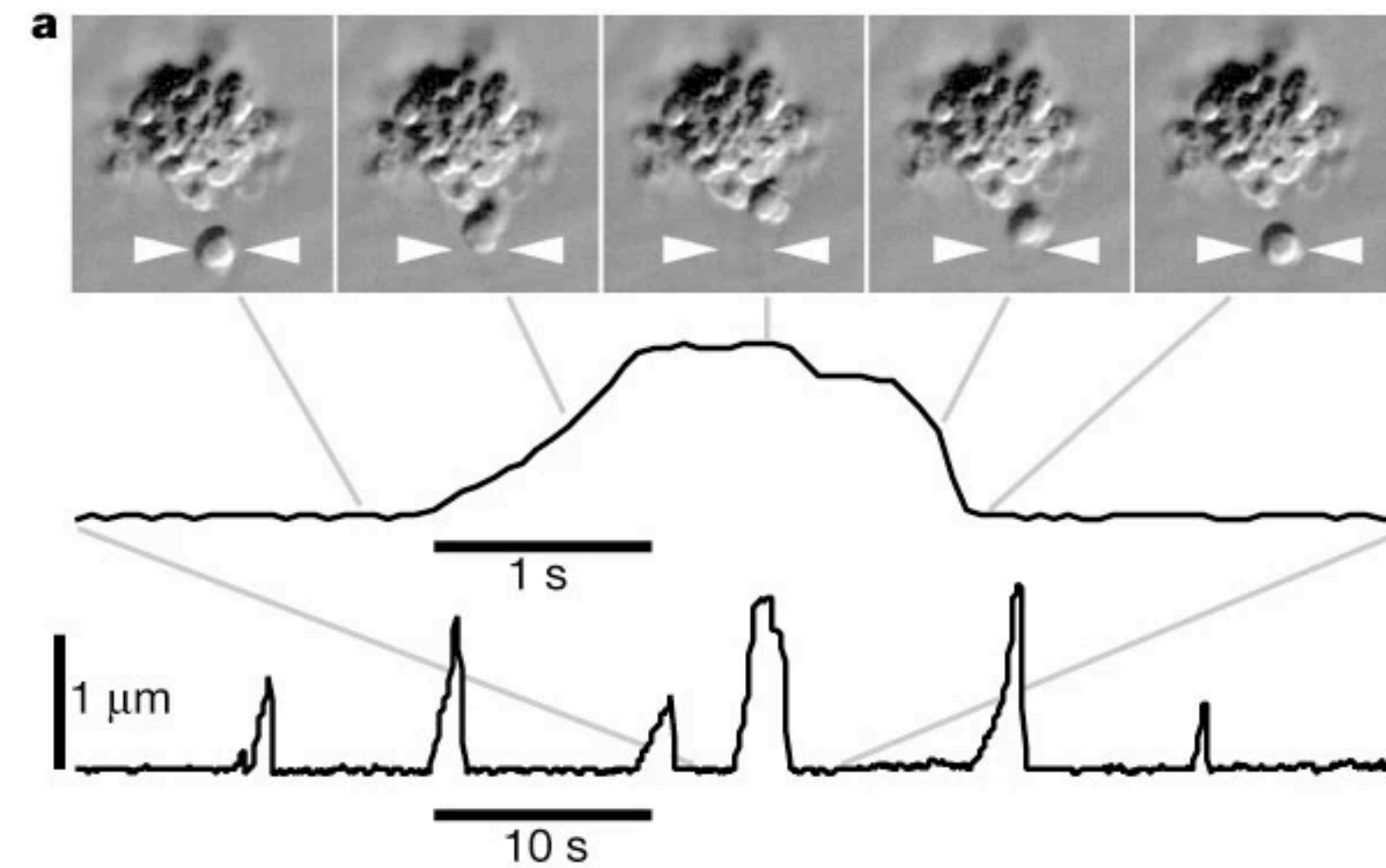
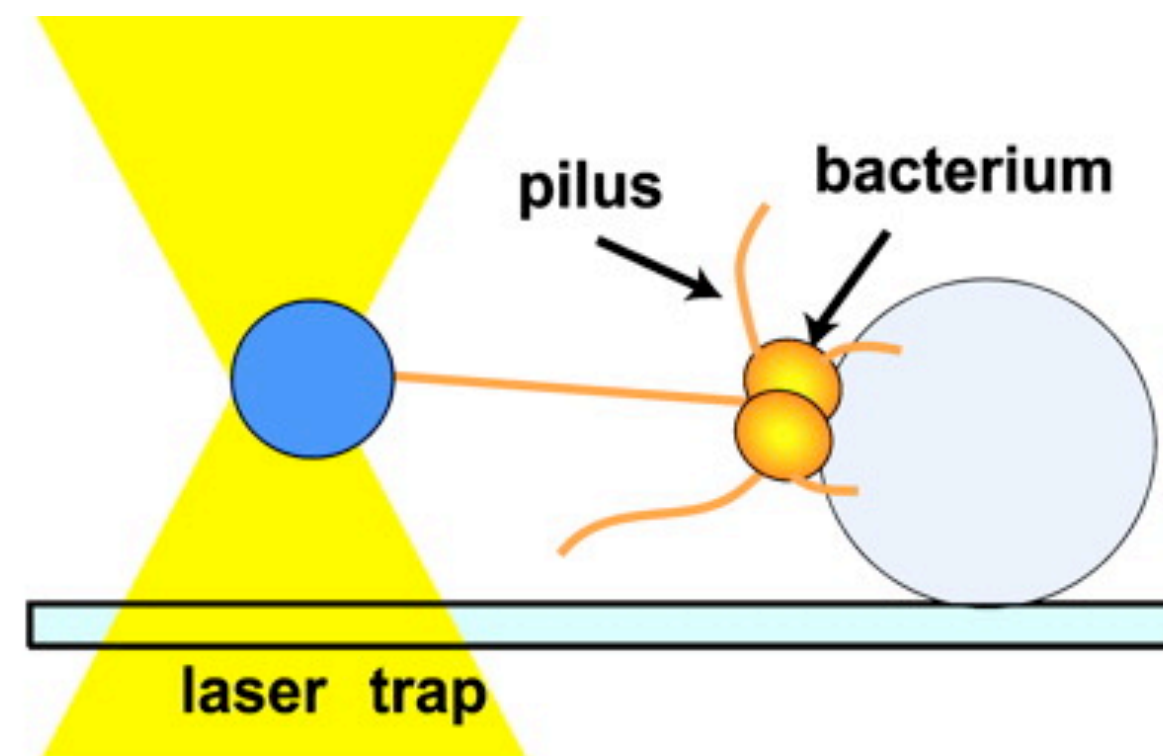


Type IV pili are protein polymers



Type IV pili are motorized

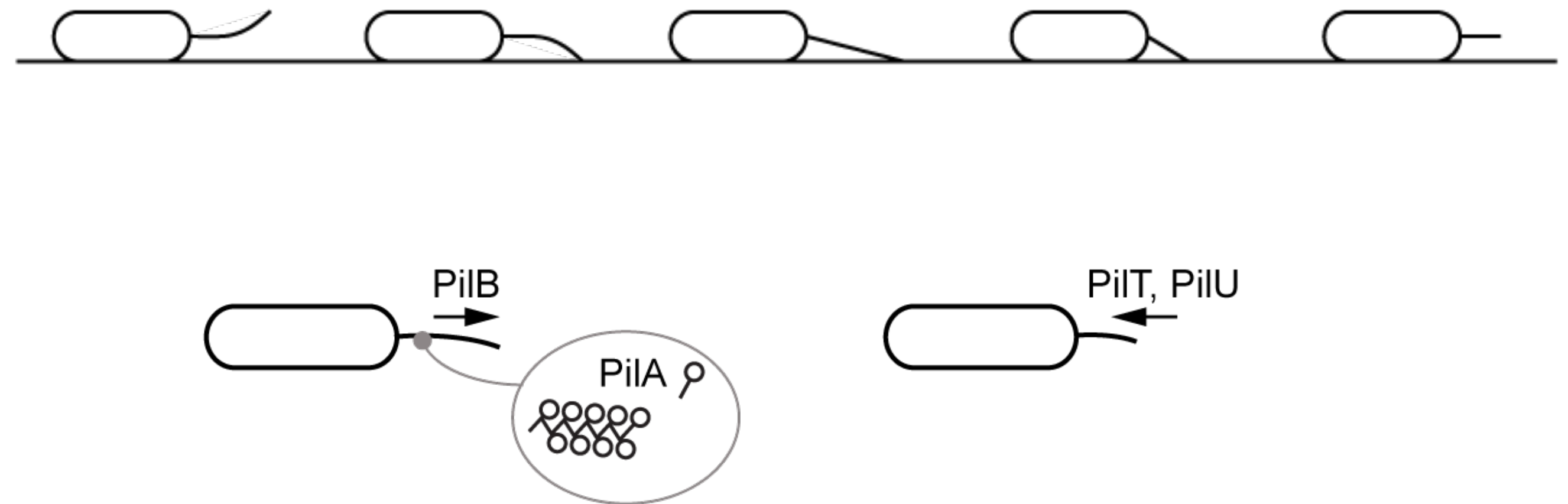
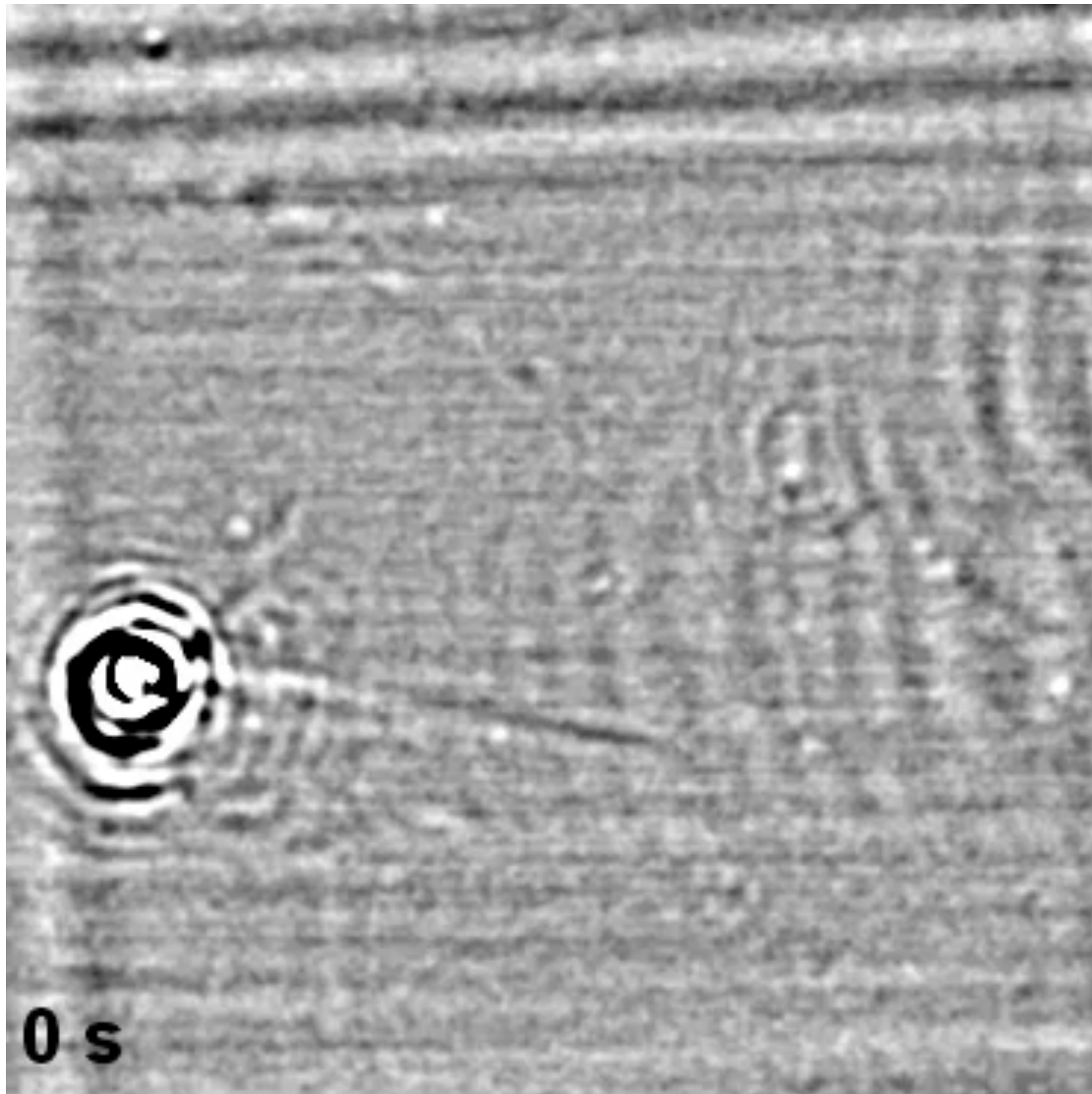
Early measurements with optical tweezers



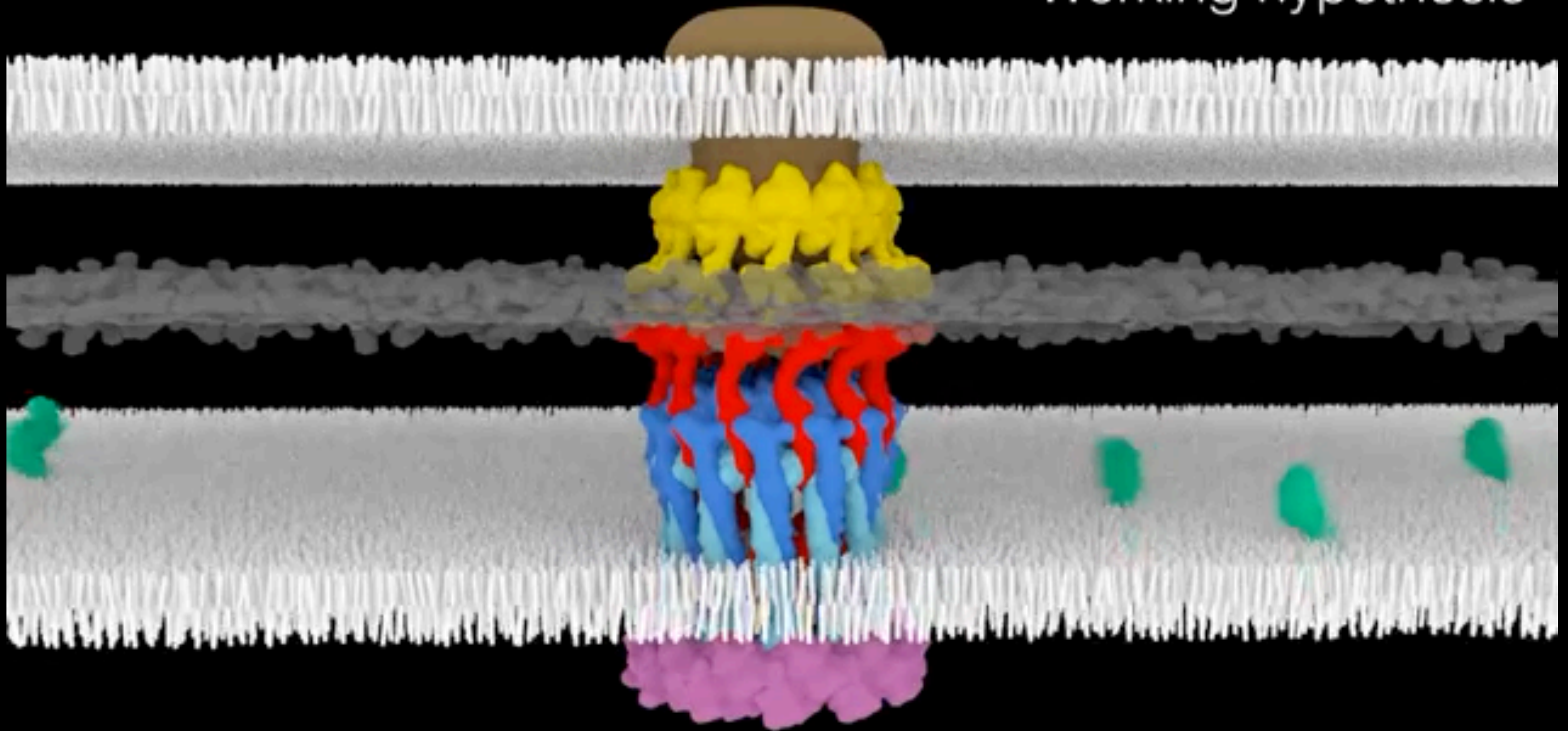
Mike Sheetz and Berenike Meier

Bacteria twitch using motorized filaments

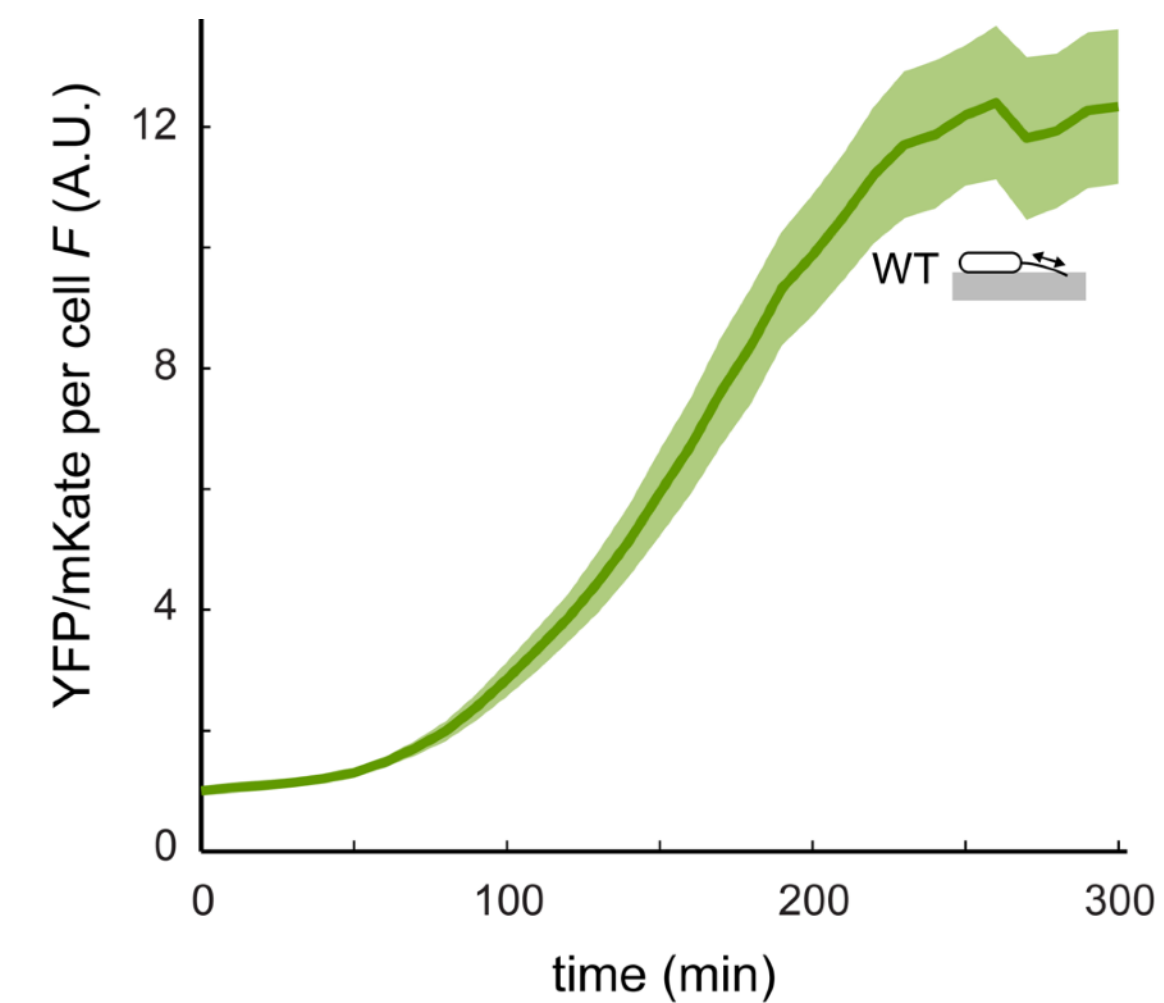
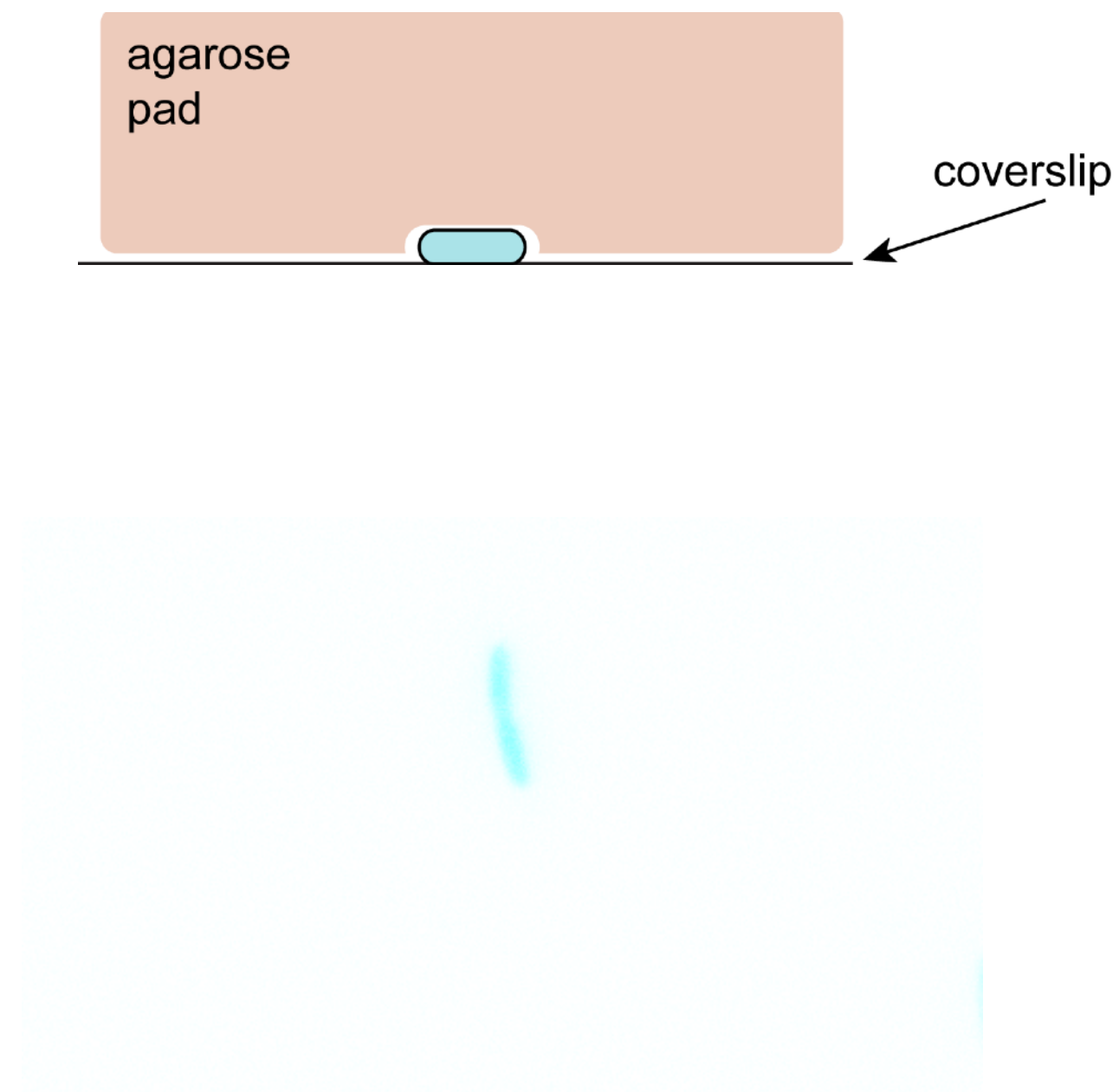
“type IV pili” extend and retract from the cell surface



Working hypothesis



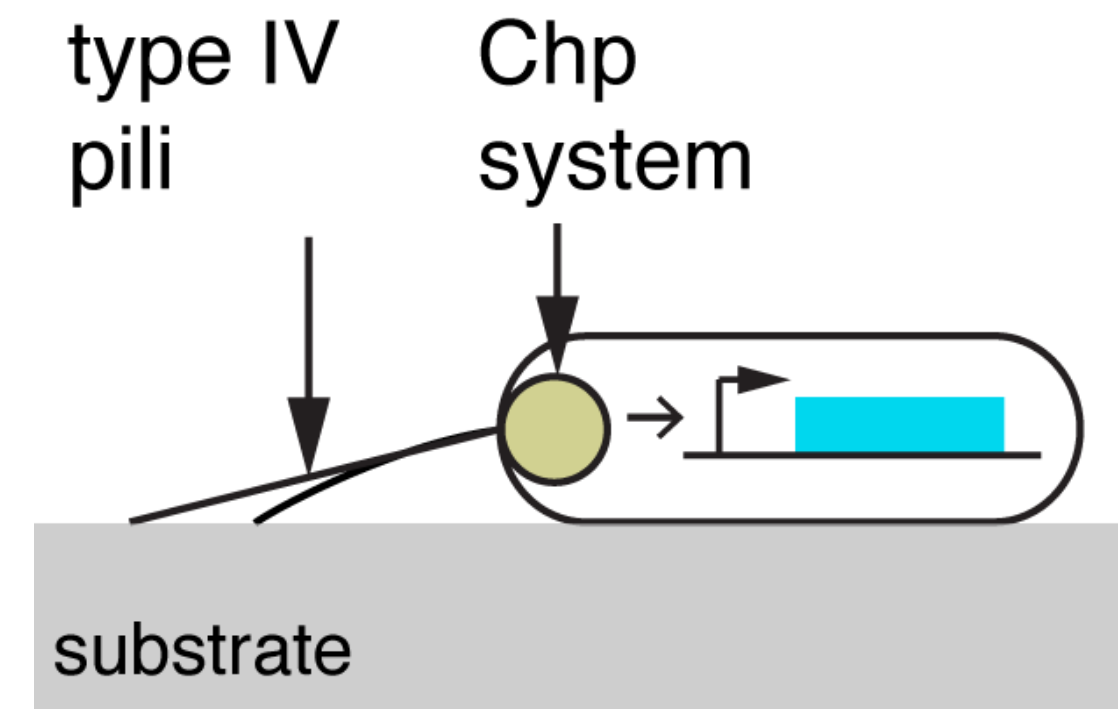
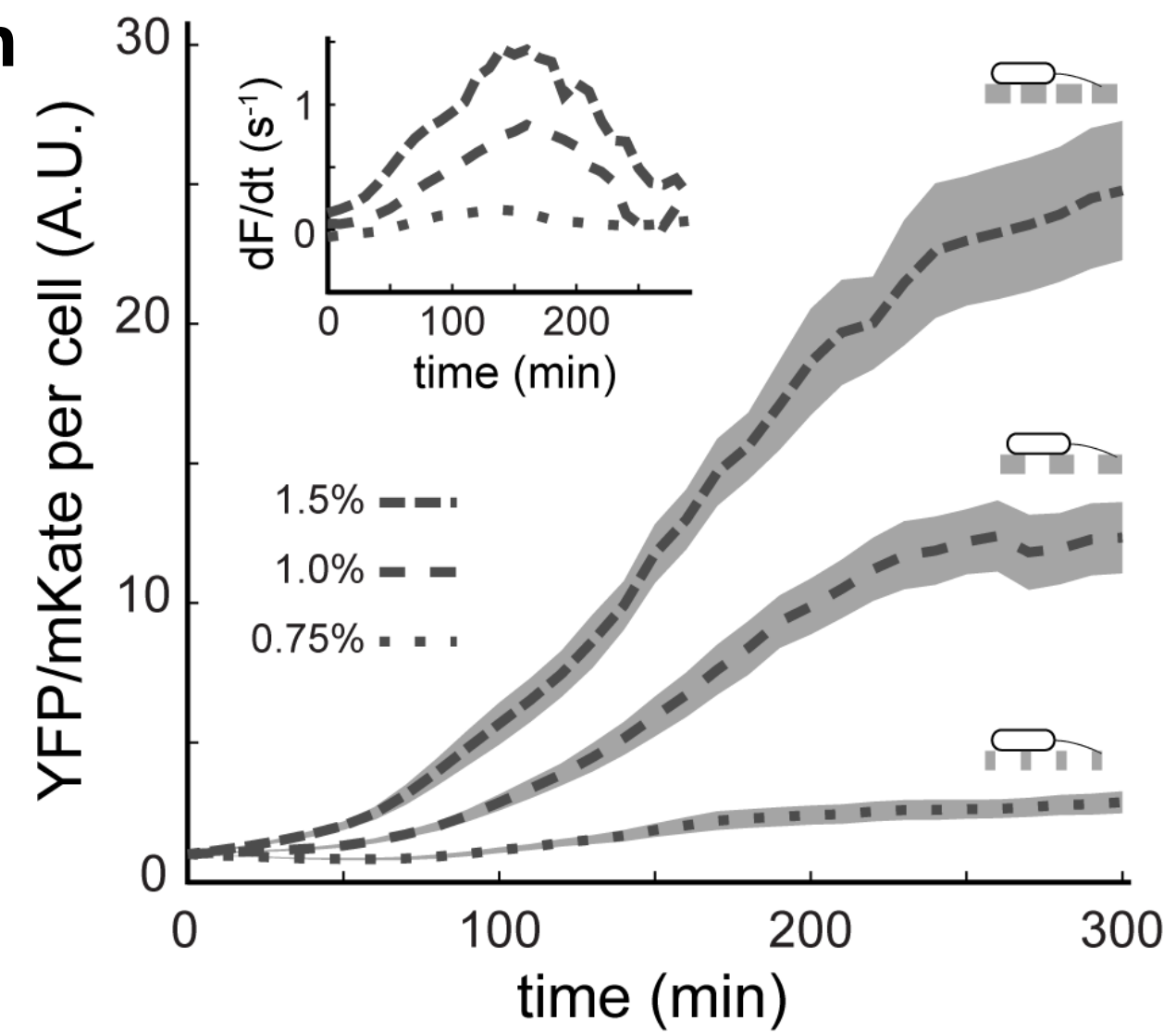
Dynamics measurements of response to surface



Persat, PNAS 2015

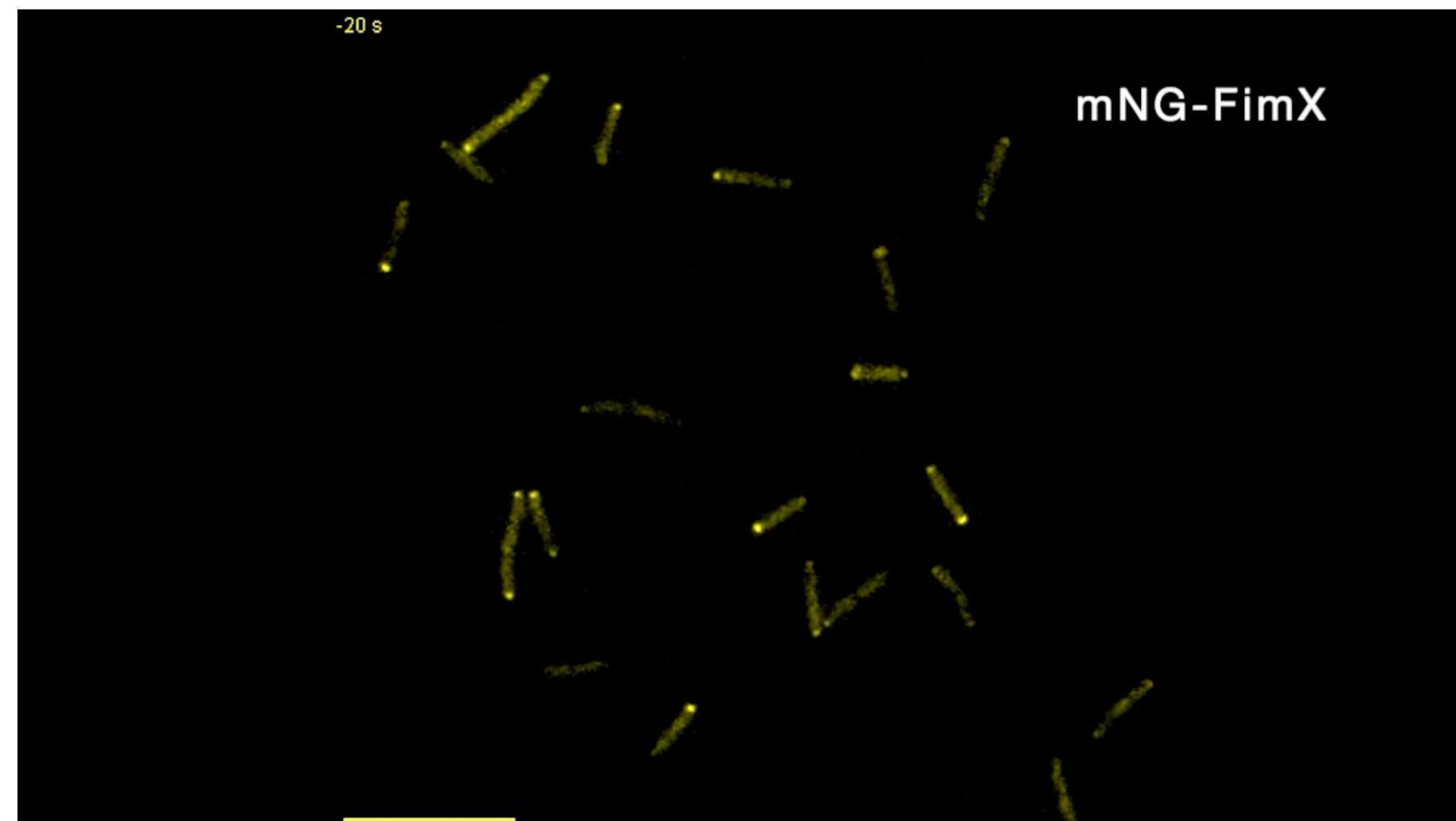
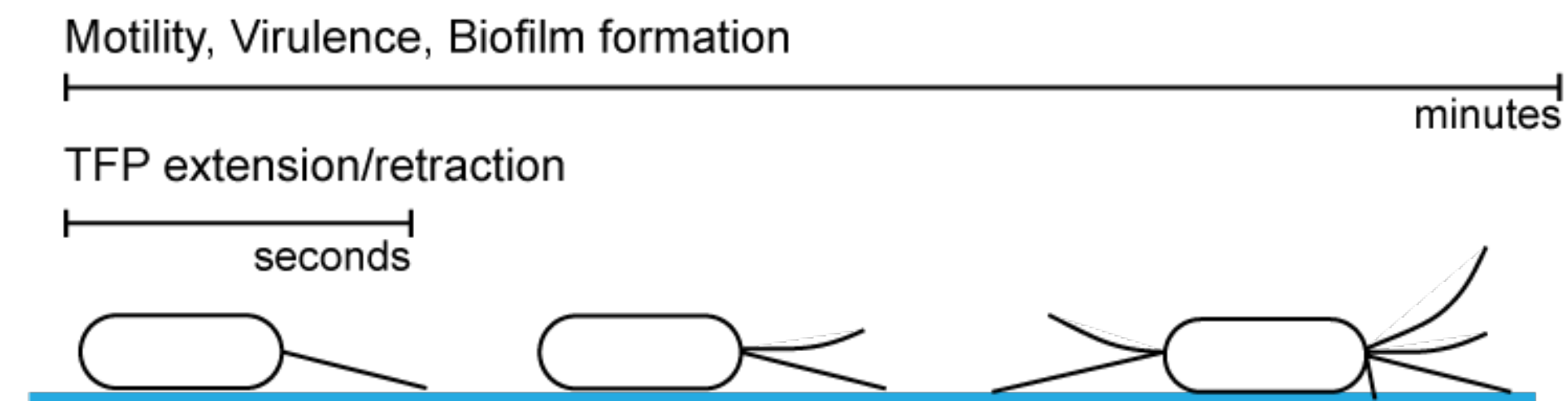
Mechanosensing with pili

response depends on
substrate stiffness

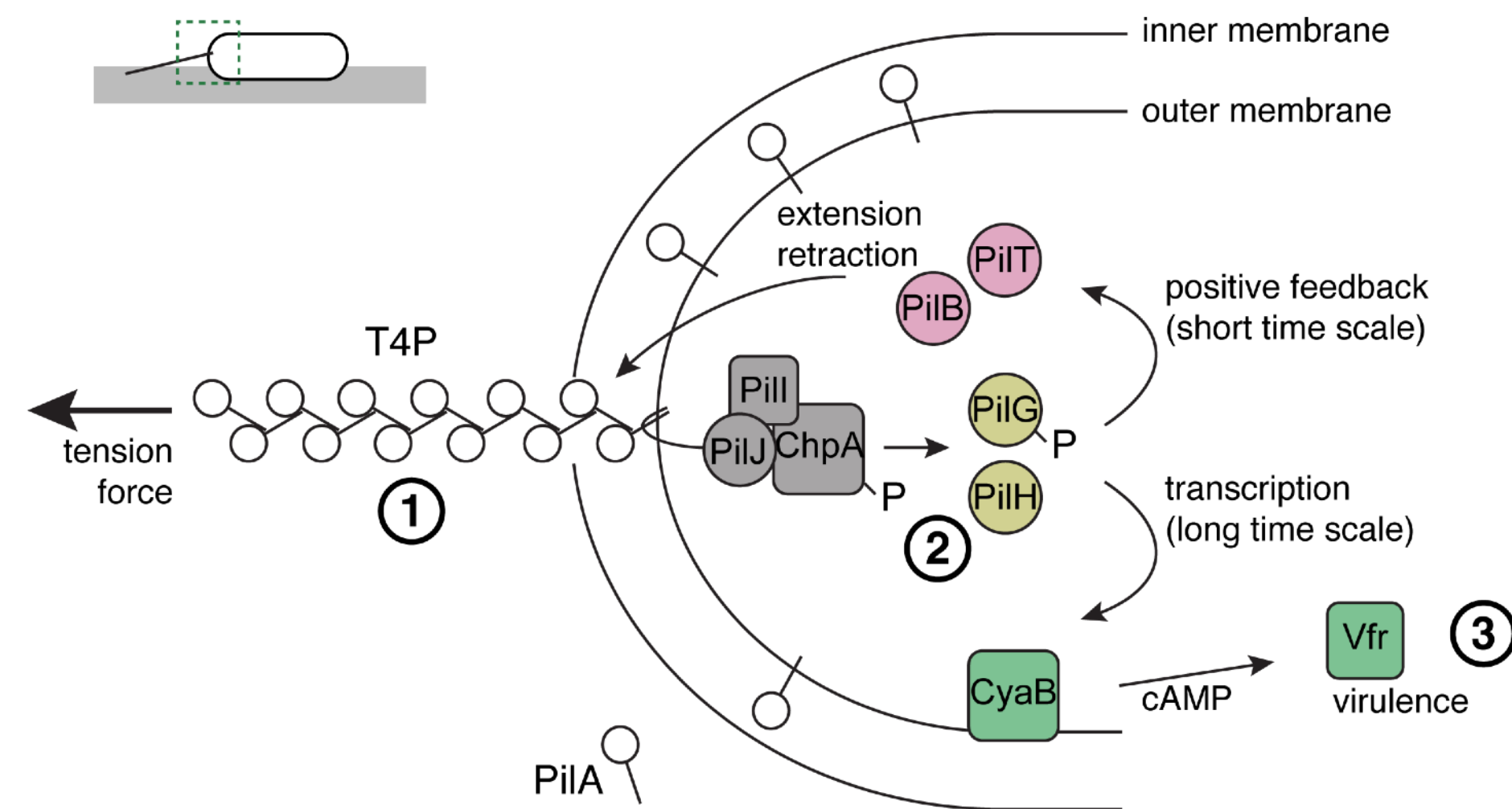


PNAS 2015

Mechanotaxis with pili

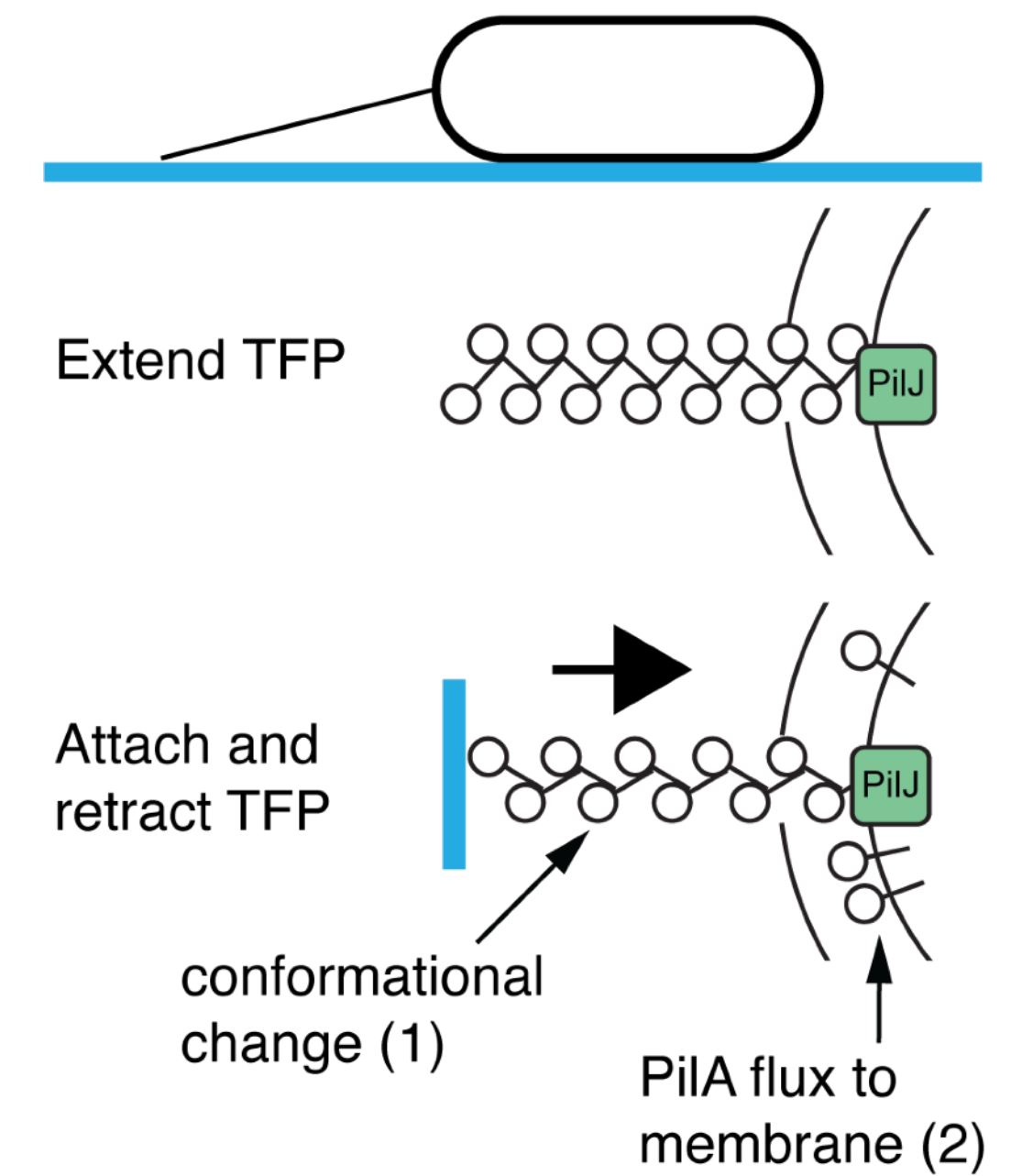
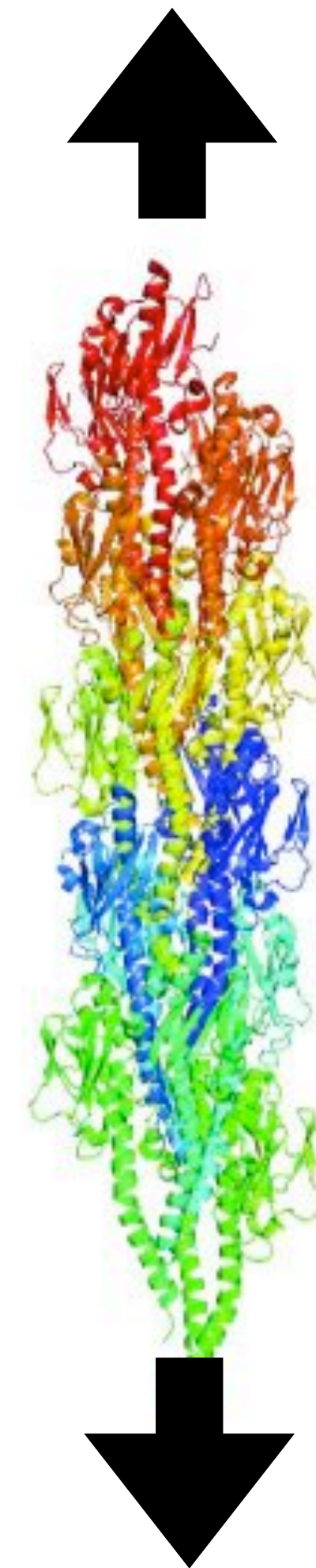
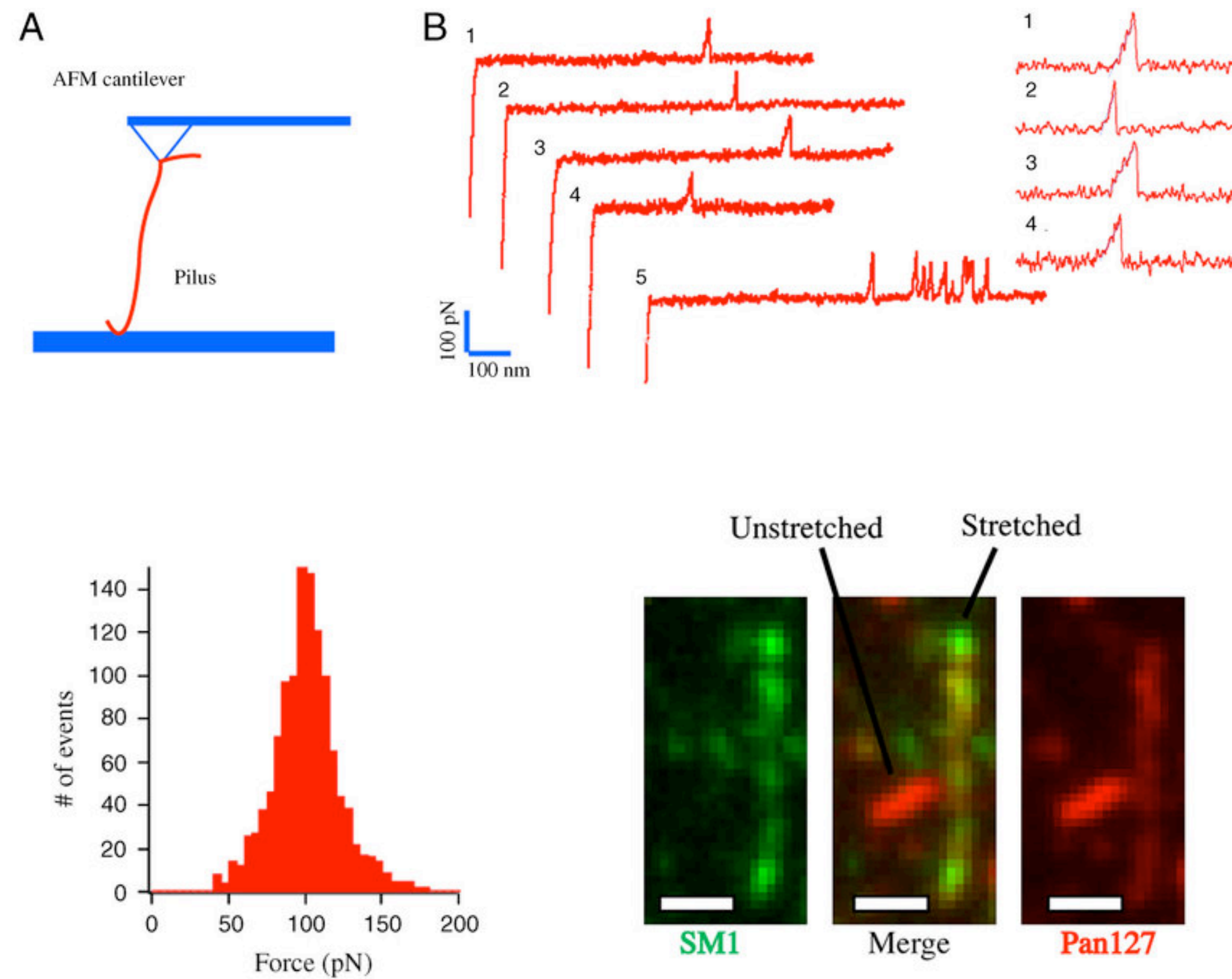


Mechanotransduction in *Pseudomonas aeruginosa*



How do pili sense force?

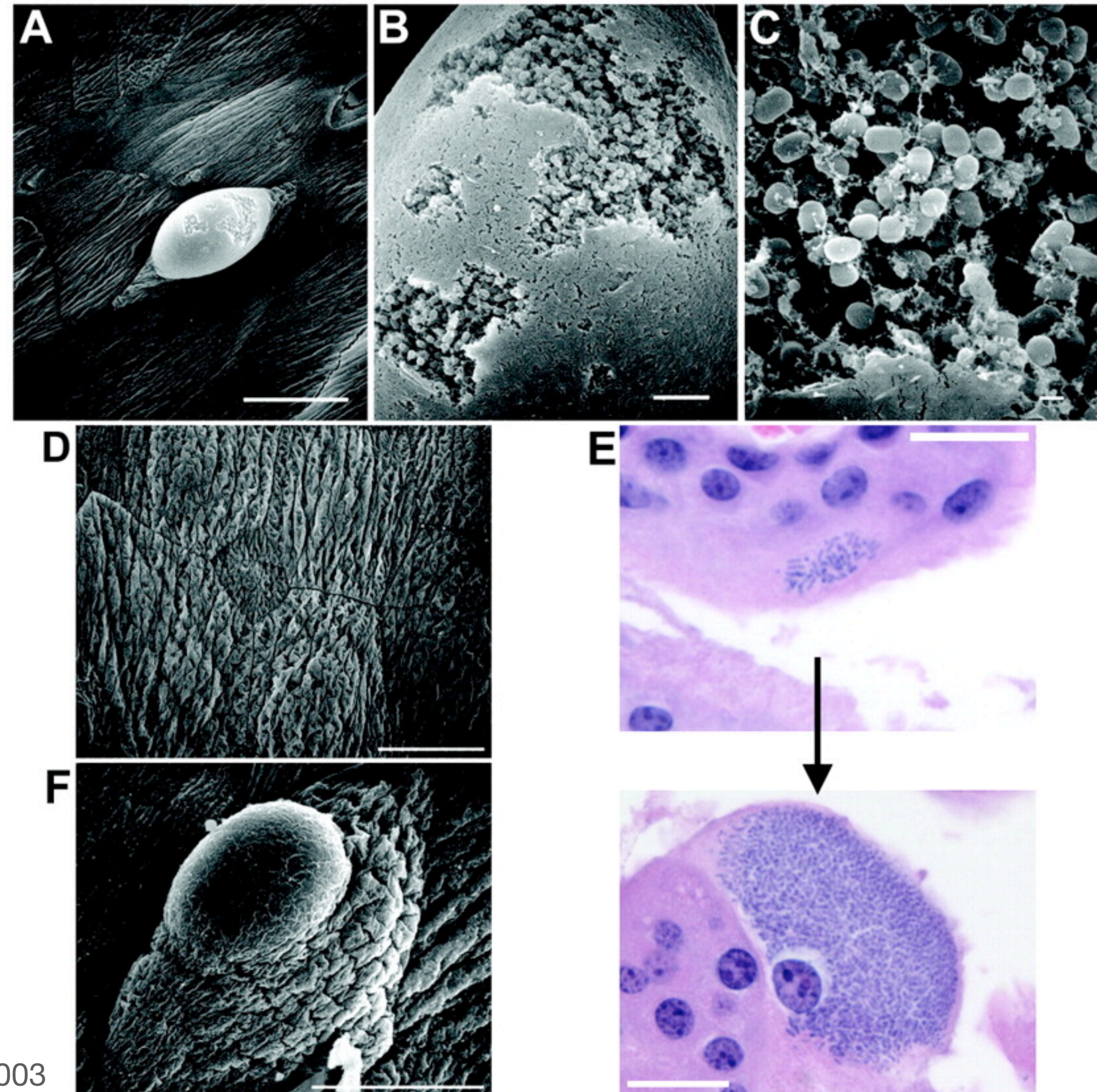
Pili (and any protein) behave as springs



Bacteria often grow in confinement

E. coli commonly infects the urinary tract

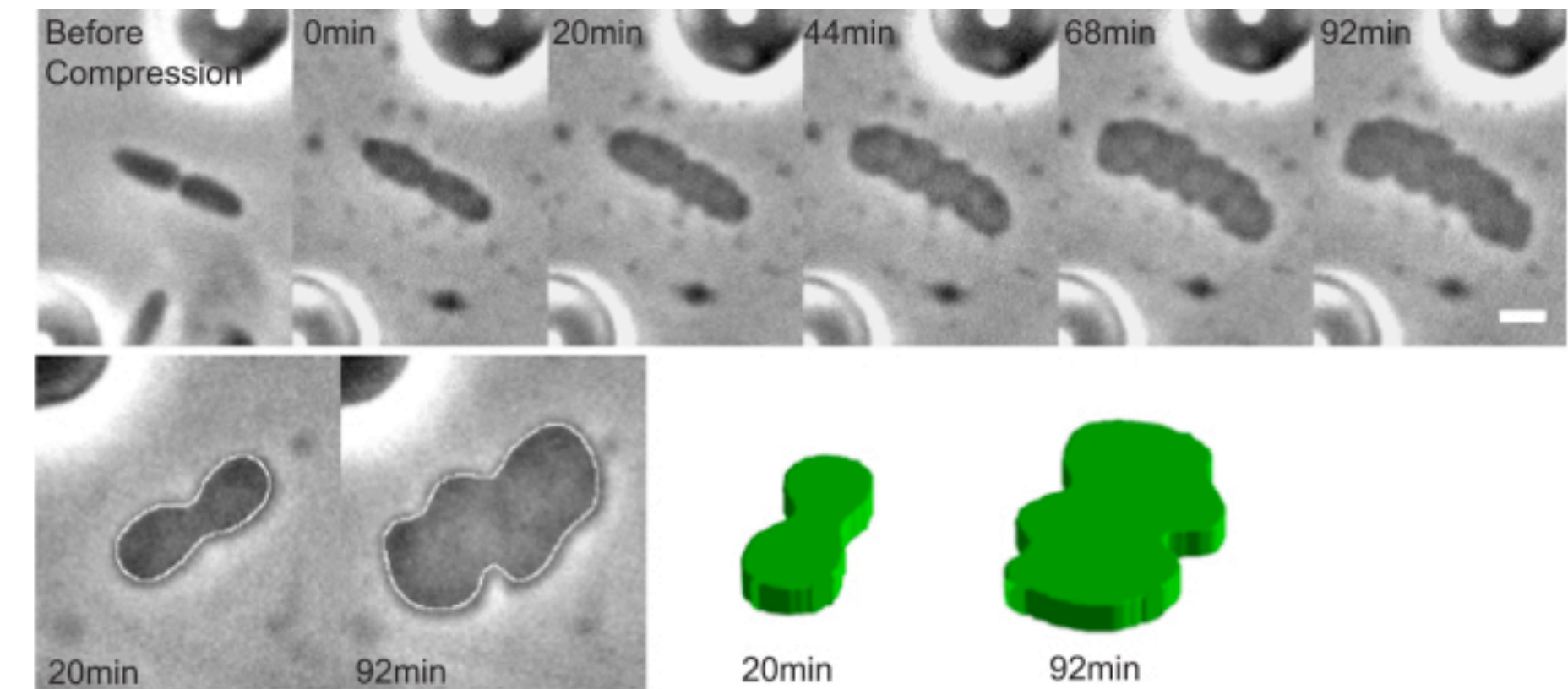
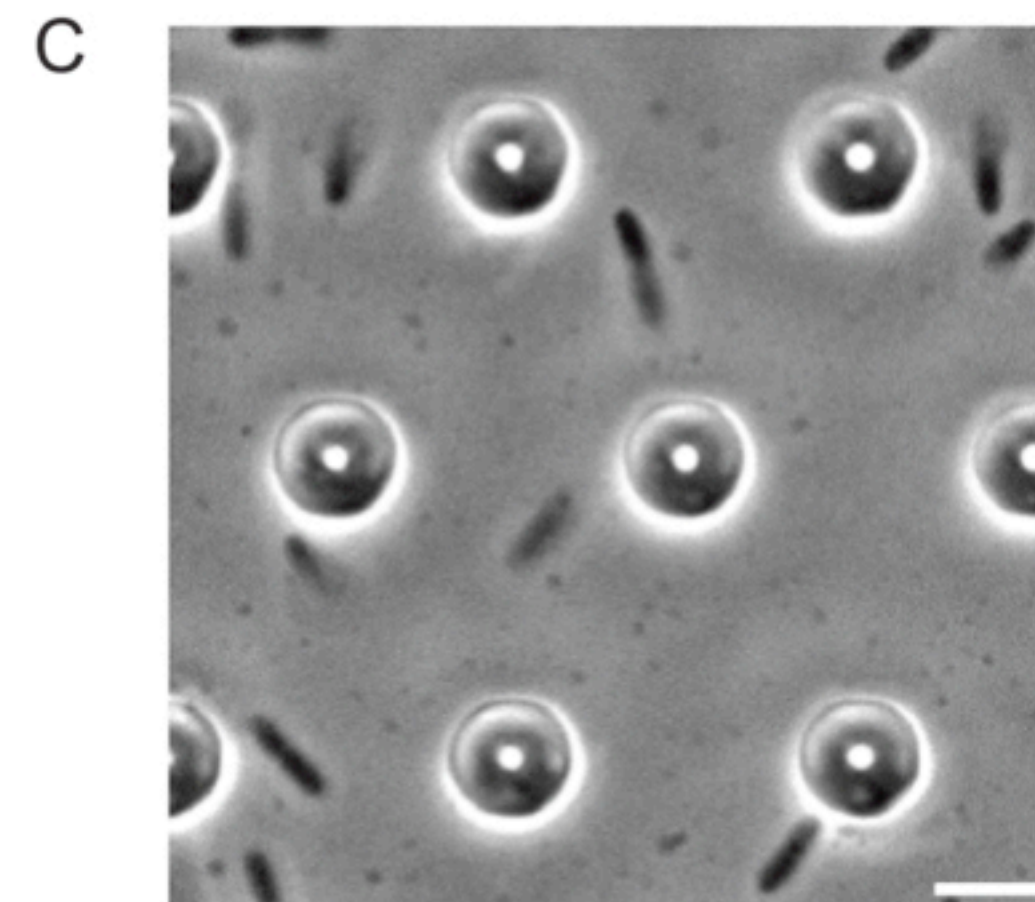
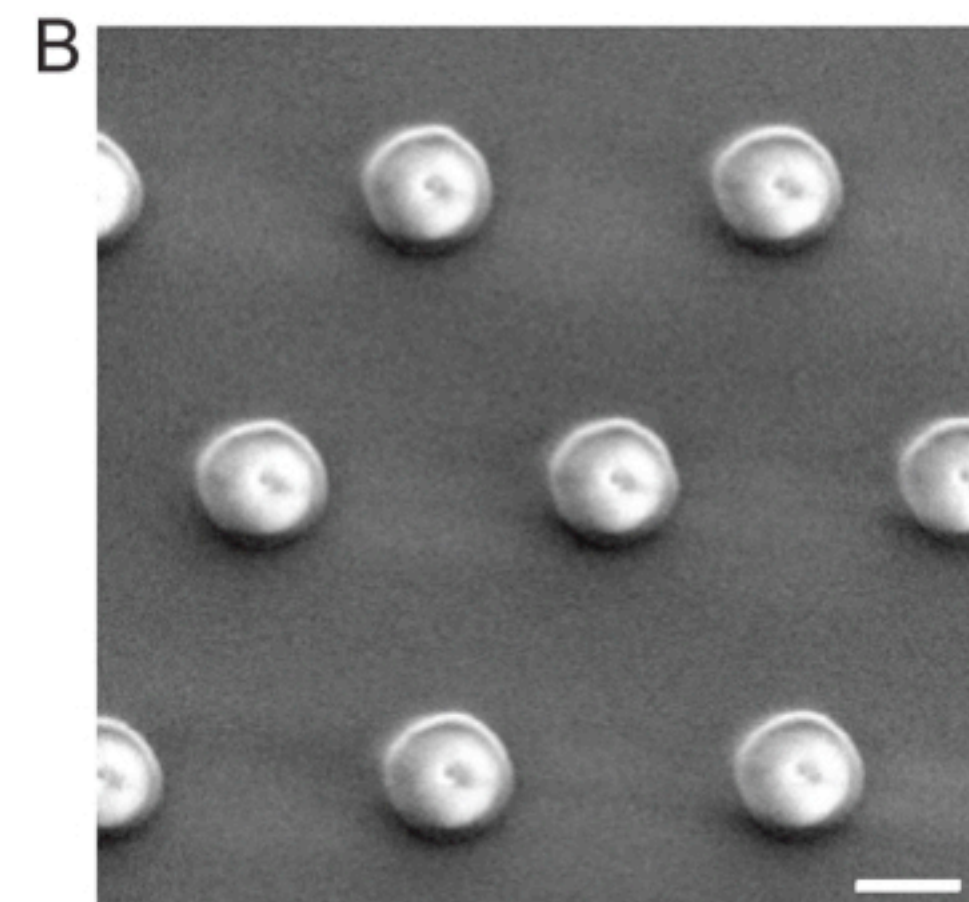
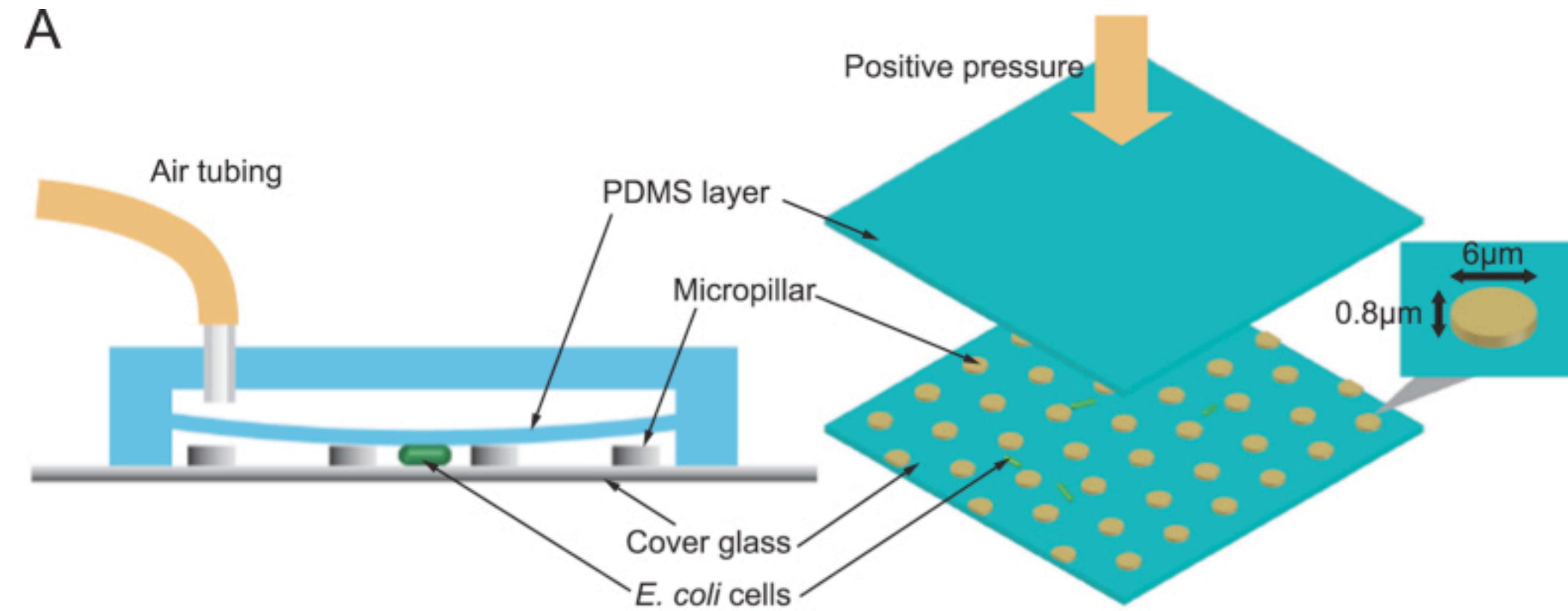
Forms cell-embedded “pods” that are compressing the community



the end?

Squeezing bacteria

It's not so simple



Bacterial growth under compression

Bacteria sense and respond to cell envelop perturbations

