Mechanomicrobiology: From Single Cells to Biofilms

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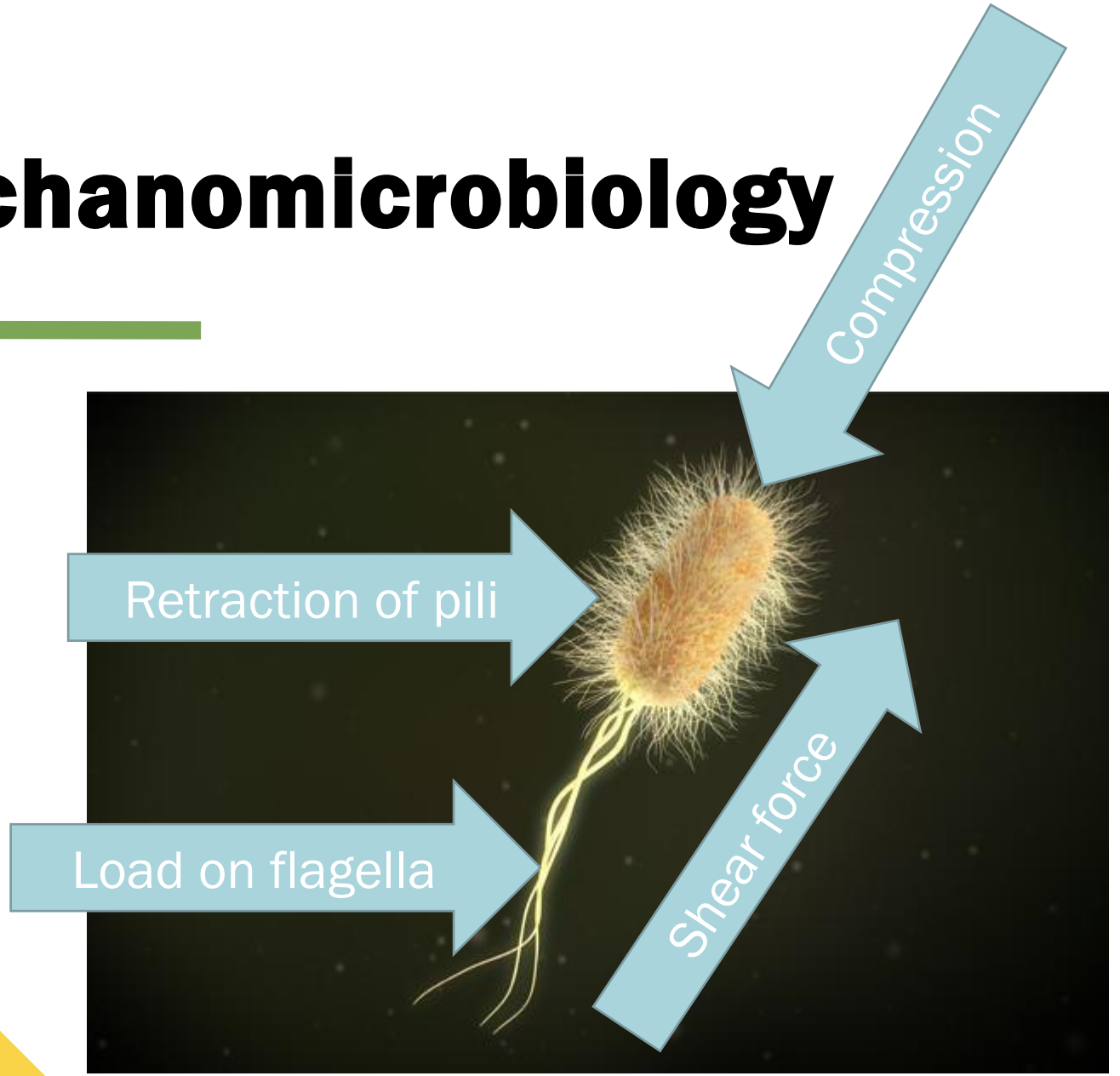
6 Dec 2022

Outlines

- Mechanical forces on bacteria
- Mechanosensing
- Mechanotransduction
- Mechanical forces generation during biofilm growth
- Discussion
- Summary

Mechanical forces on bacteria

Mechanomicrobiology



Forces

Sense

Respond

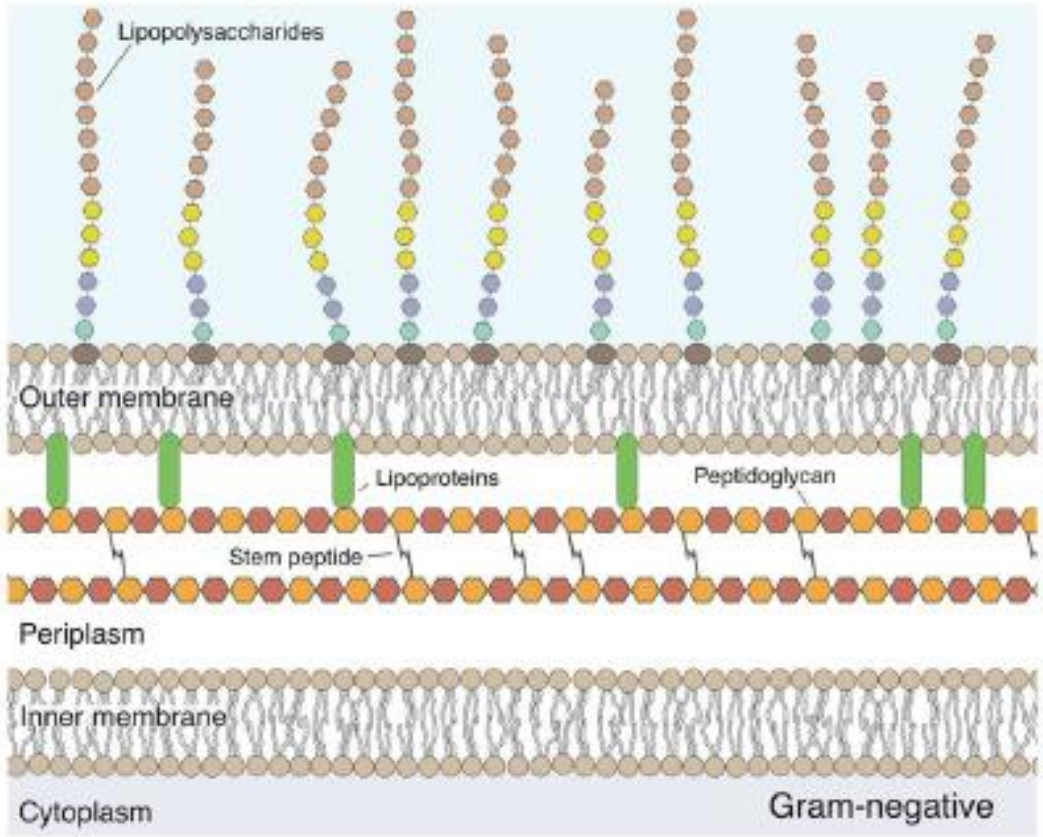
(Dufrene & Persat, 2020)

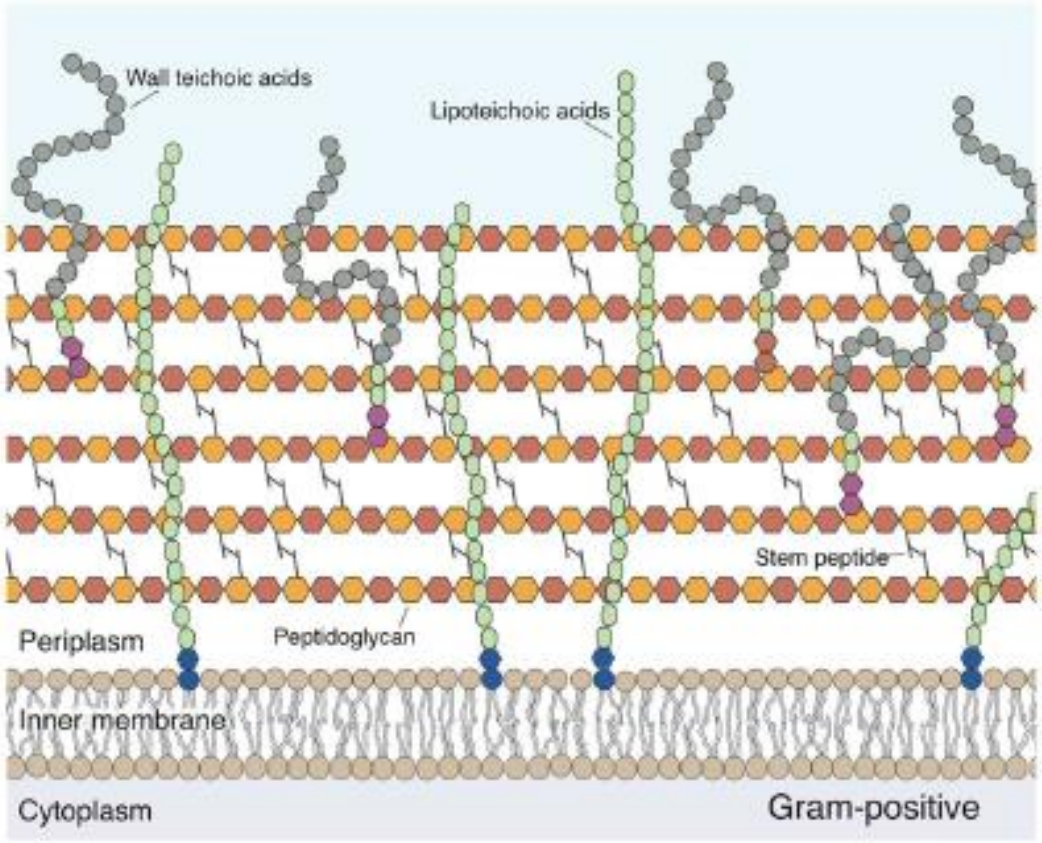
“

Architecture is
the adaptation of form
to resist force.

(John Ruskin, 1874, as cited in Young, 2003)

Peptidoglycan

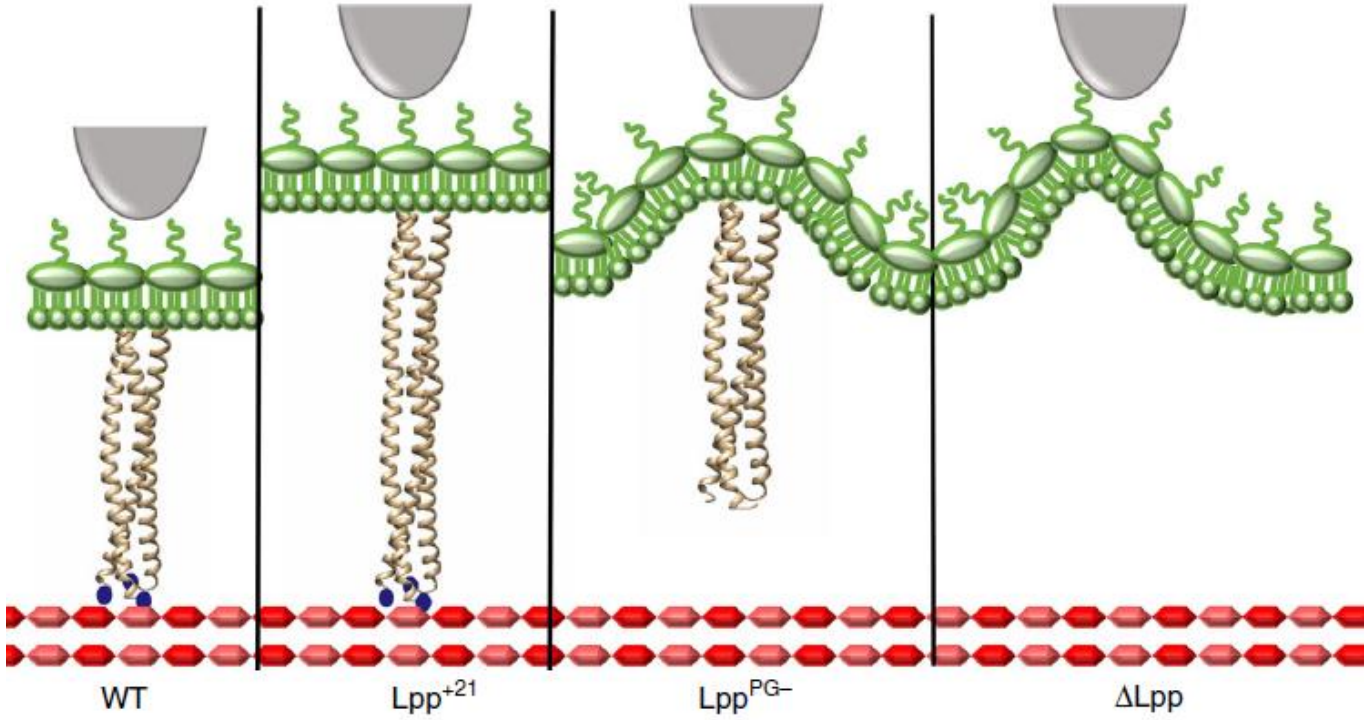


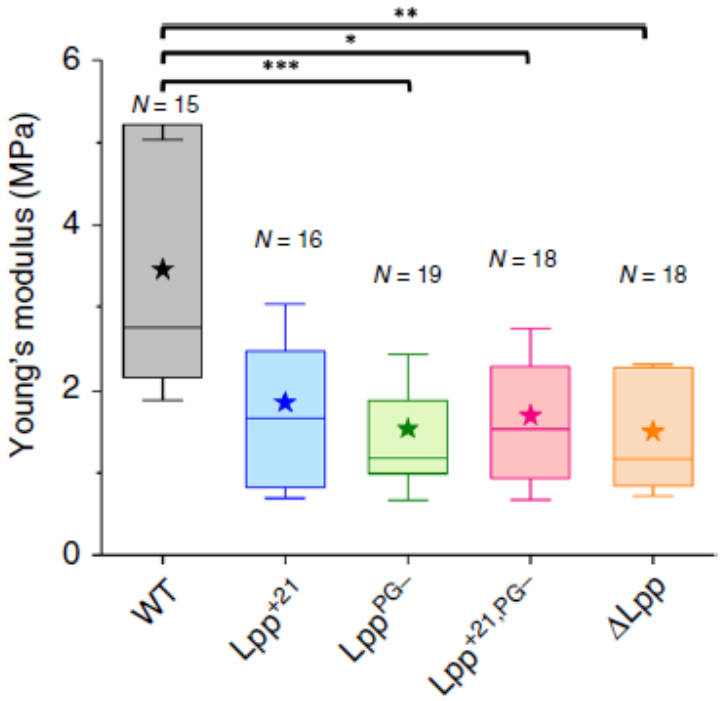


(Auer & Weibel, 2017)

Lipoprotein Lpp

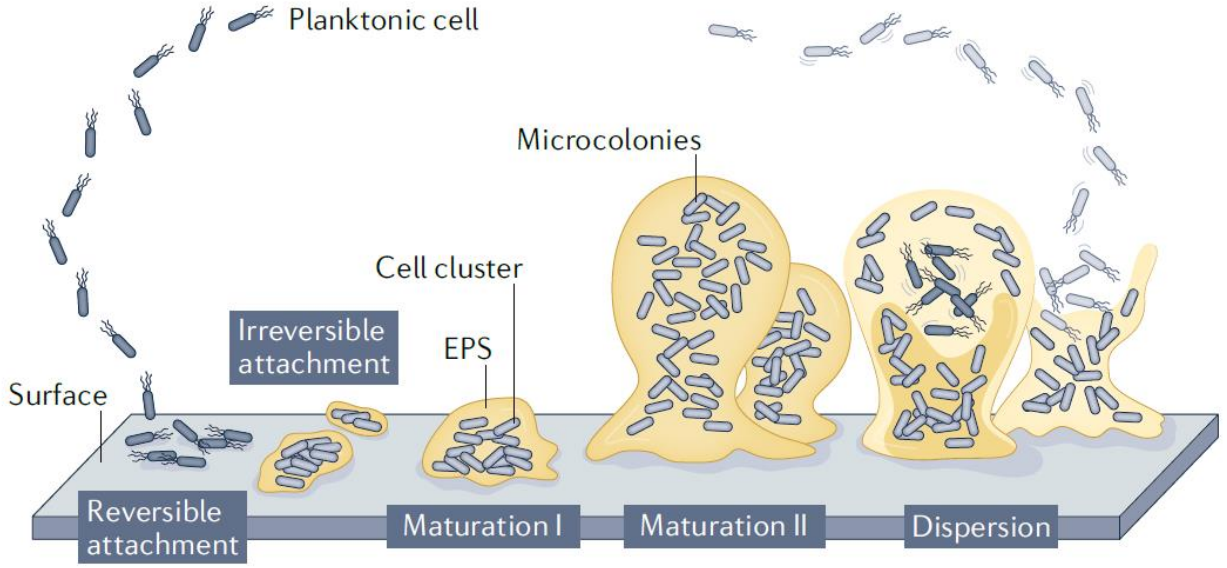
Provides only covalent crosslink between outer membrane and peptidoglycan of *Escherichia coli*





(Mathelie-Guinlet *et al.*, 2020)

Biofilm development

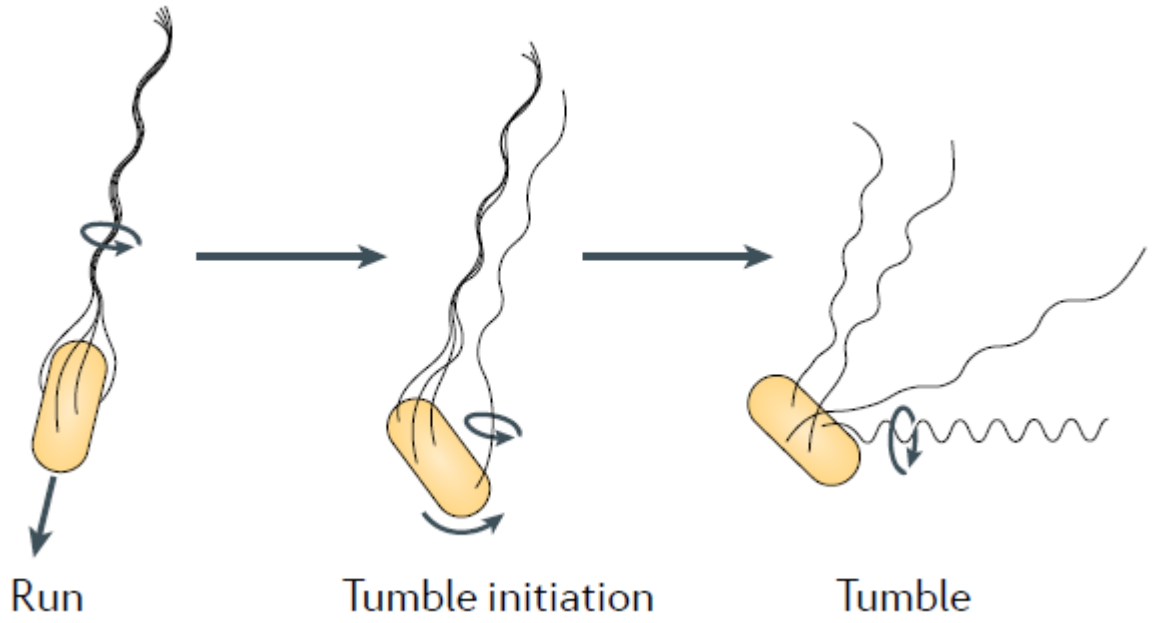


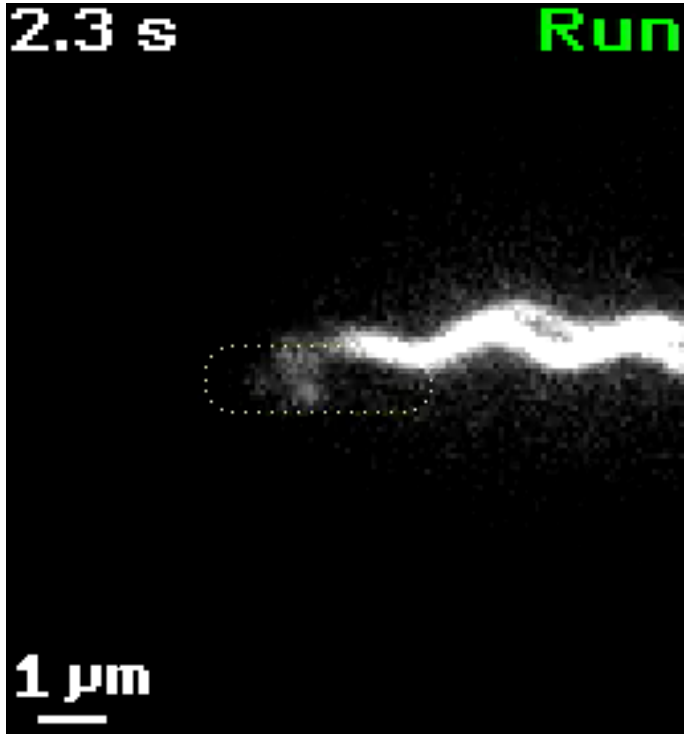
Motility → Mechanosensing → Mechanotransduction → Mechanical forces generation during biofilm growth

(Sauer *et al.*, 2022)

Motility

Swimming of *E.coli*





(Mears et al., 2014; Wadhwa & Berg, 2022)

Mechanosensing

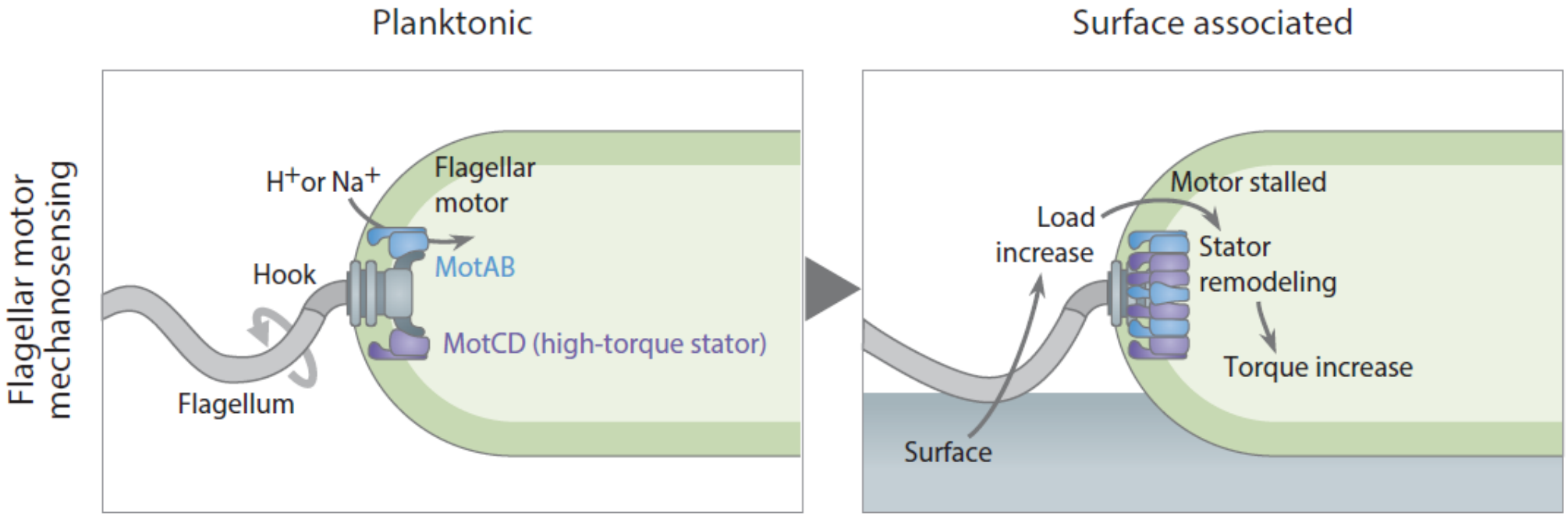
- Surface sensing
- Flow sensing

Surface sensing

- Surface appendages (Flagella, Type IV pili)
- Envelop stress/deformation

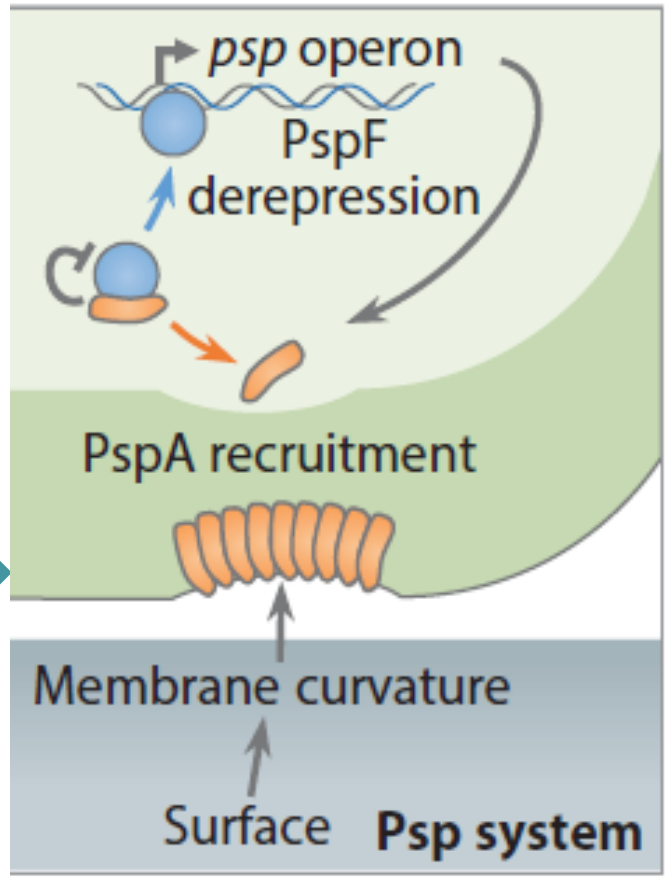
(Kimkes & Heinemann, 2020; Laventie & Jenal, 2020)

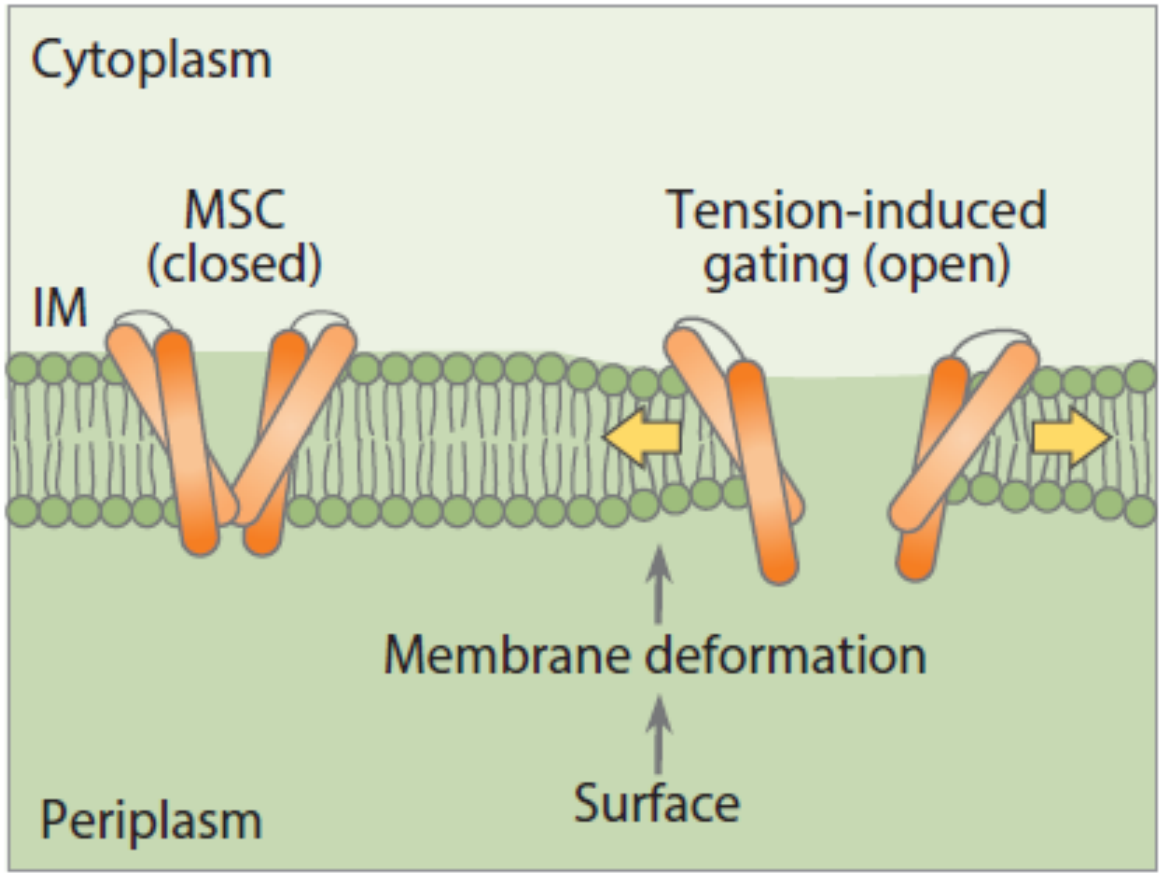
Surface sensing of rotor stalling/remodeling



(Laventie & Jenal, 2020)

Surface sensing of envelop stress/deformation





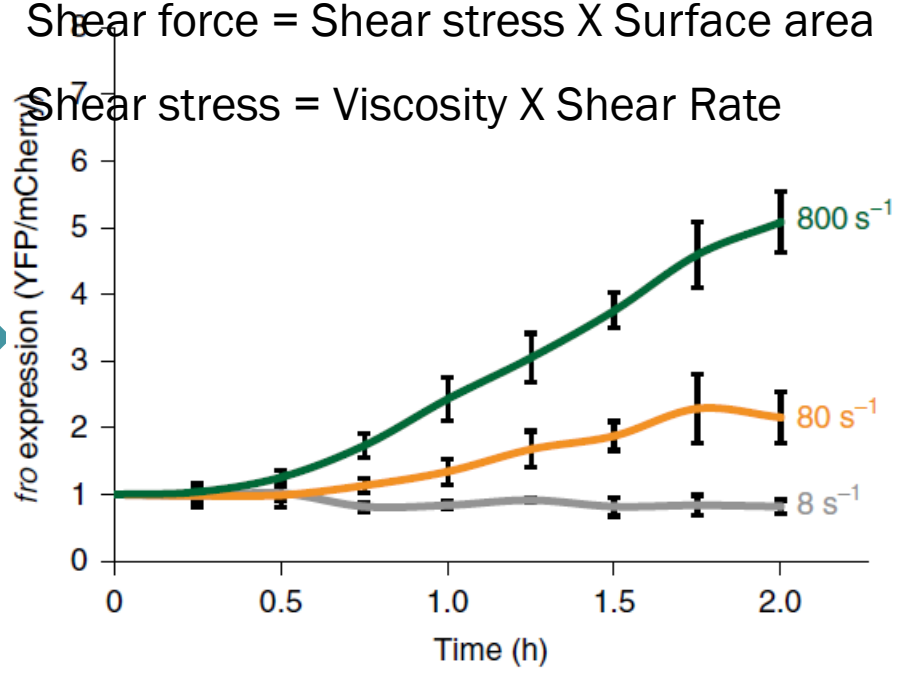
(Laventie & Jenal, 2020)

Rheosensing: flow sensing

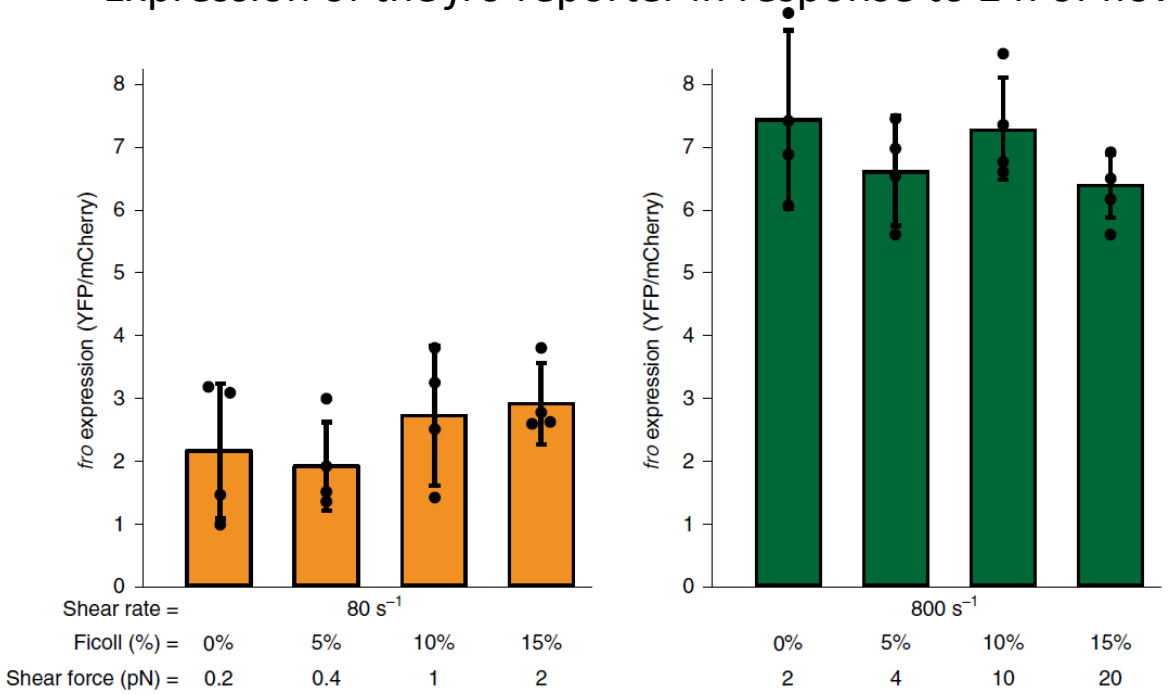
- Shear rate (the kinematic component of flow), in unit of time^{-1}
- Shear stress (the force-related component of flow), in unit of force/area

Shear force = Shear stress X Surface area

Shear stress = Viscosity X Shear Rate



Expression of the *fro* reporter in response to 2 h of flow



(Sanfilippo *et al.*, 2019)

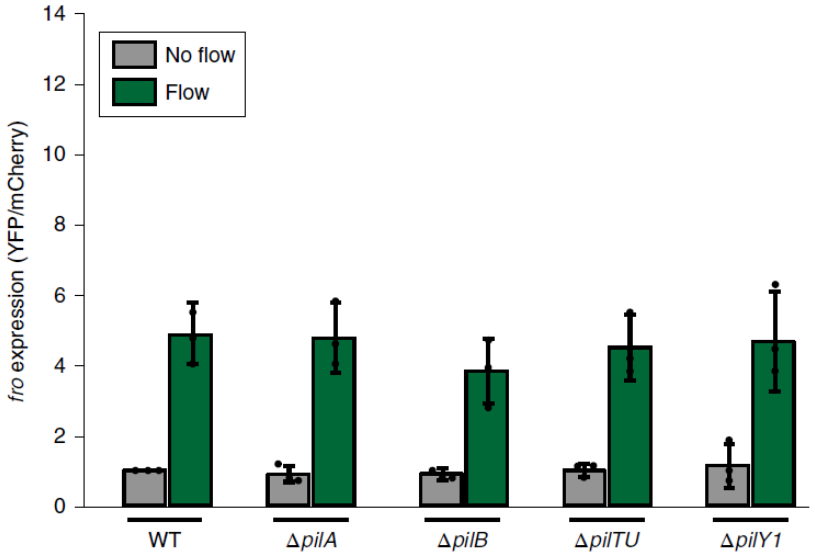
Induction of *fro* does not require surface sensors but σ factor and anti-σ factor

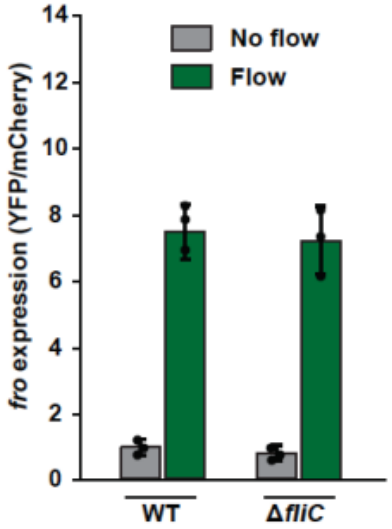
Surface sensors

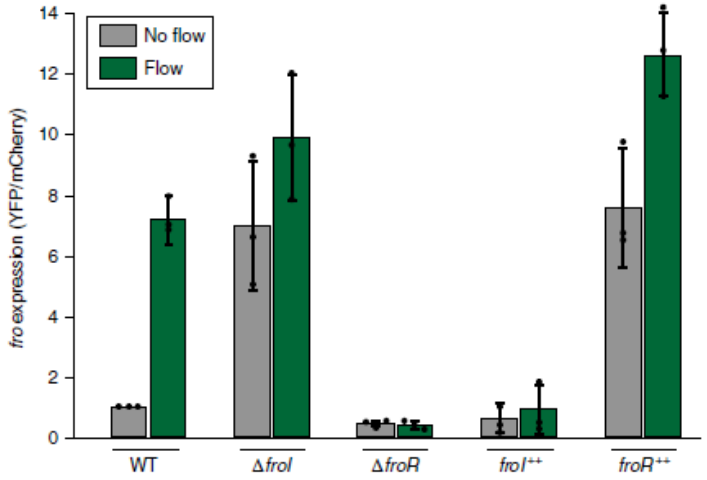
- type IV pili: *pilA* (pilus fibre), *pilB* (pilus extension) and *pilTU* (pilus retraction)
- PilY1: *pilY1* is required for surface-activated virulence in *P. aeruginosa*
- Flagella: *filC* (Flagellin is the subunit protein which polymerizes to form the filaments of bacterial flagella)

σ factors and anti-σ factor

- *froR*++: overexpression of σ factor
- *froI*++: overexpression of anti-σ factor





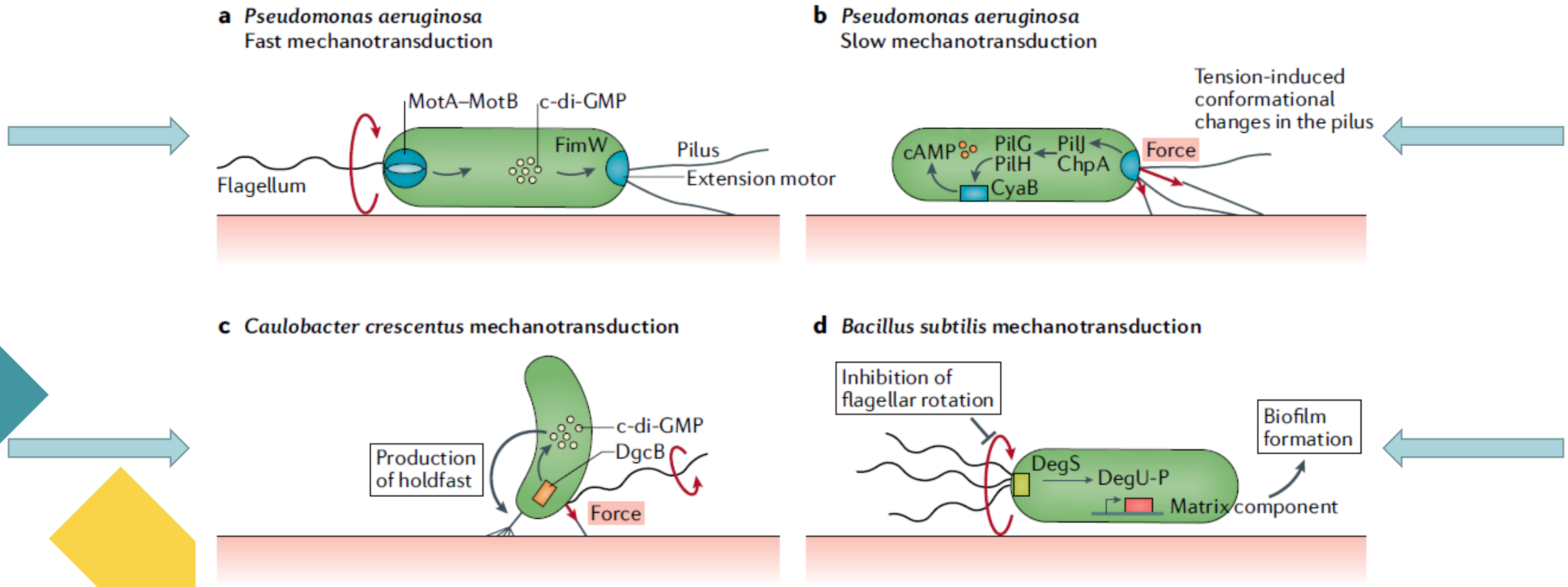


(Sanfilippo *et al.*, 2019)

Mechanotransduction

Converting mechanical inputs to cellular responses

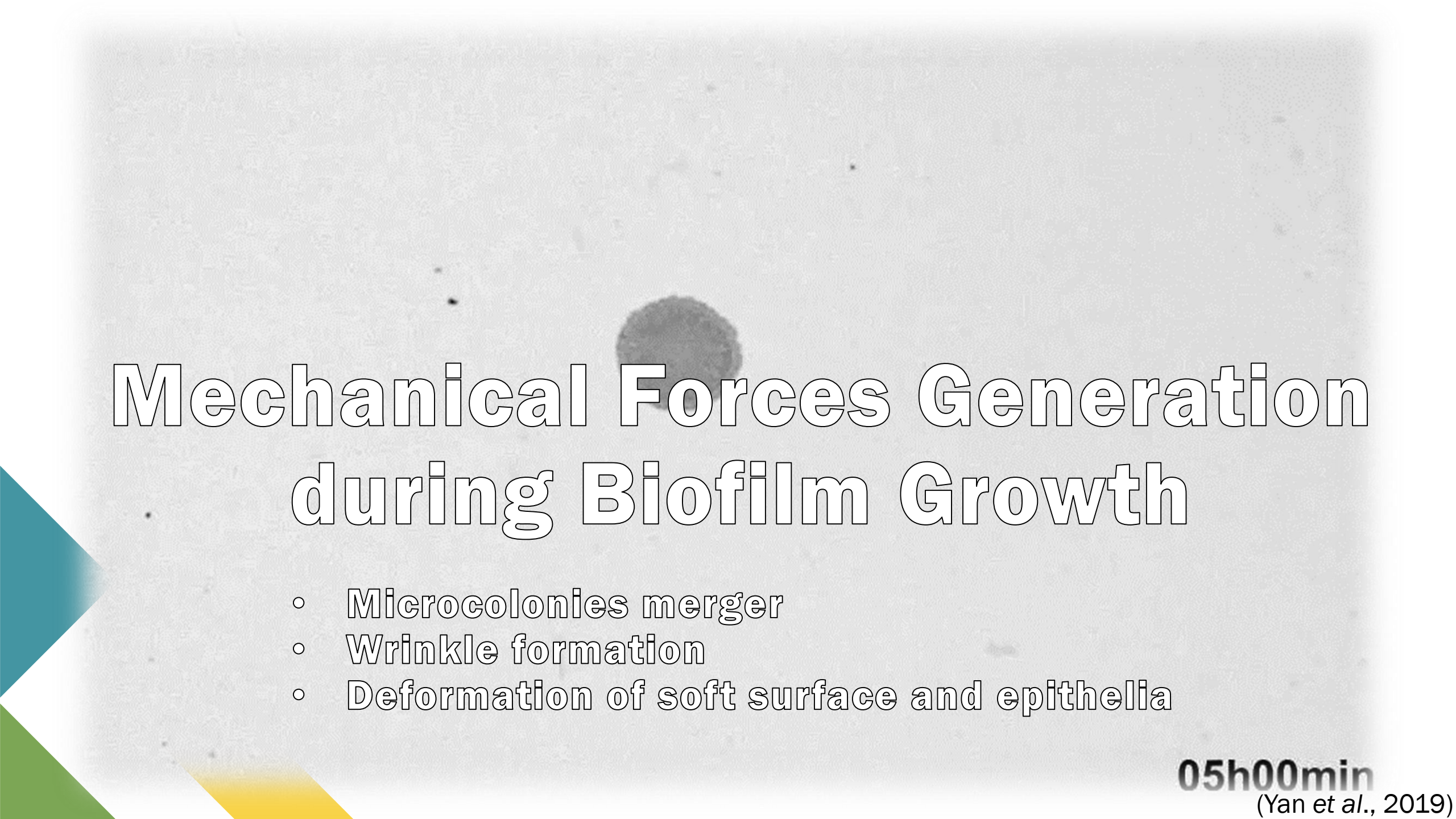
Mechanotransduction



(Dufrene & Persat, 2020)

Mechanical Forces Generation during Biofilm Growth

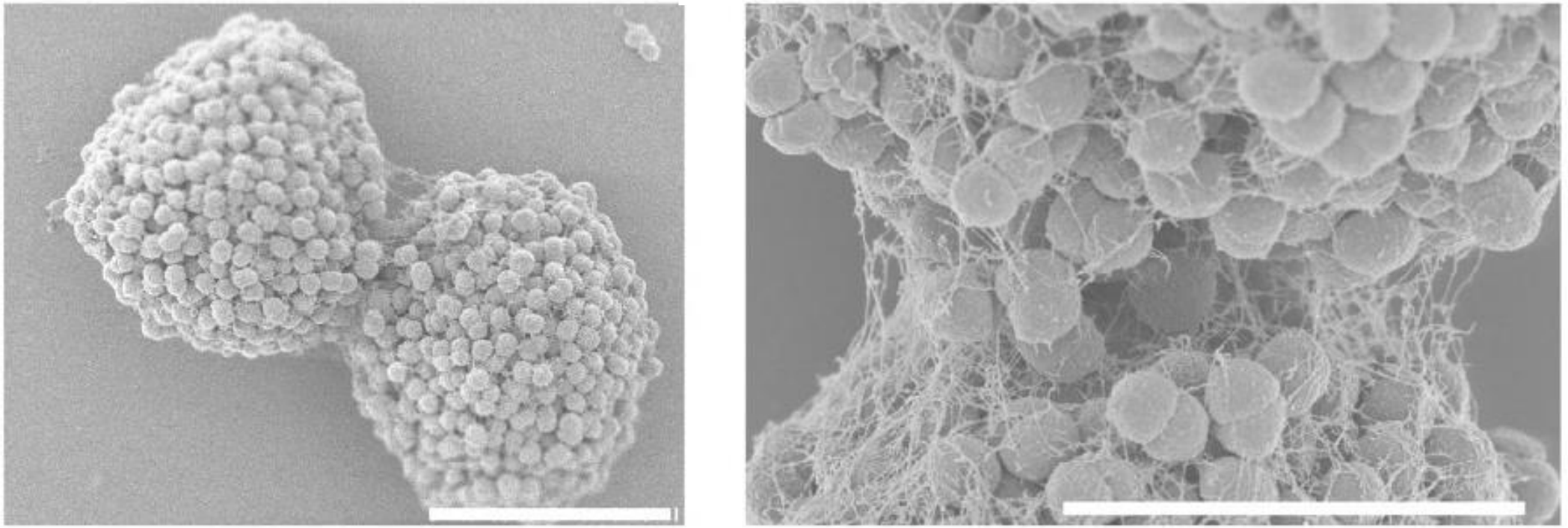
- Microcolonies merger
- Wrinkle formation
- Deformation of soft surface and epithelia



(Yan *et al.*, 2019)

Microcolonies Merger

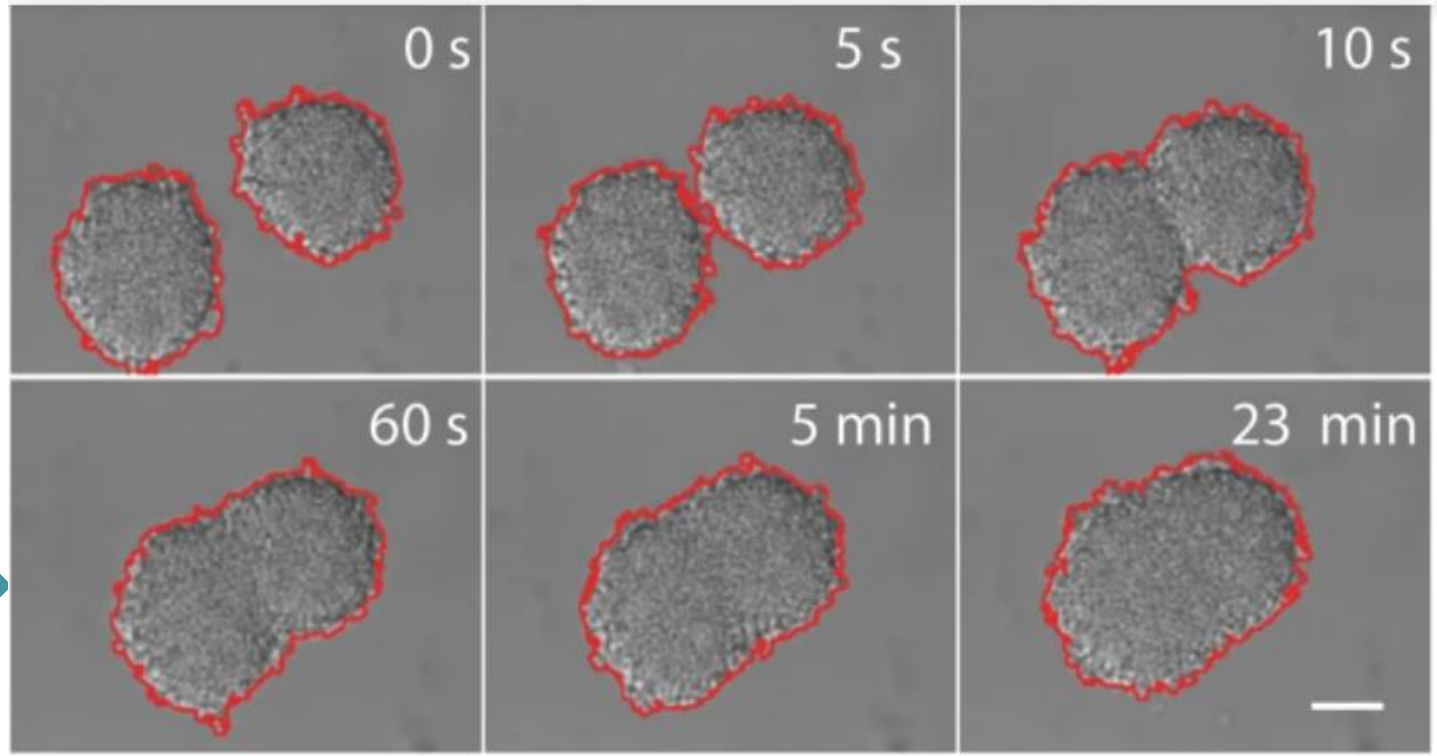
Microcolonies merger

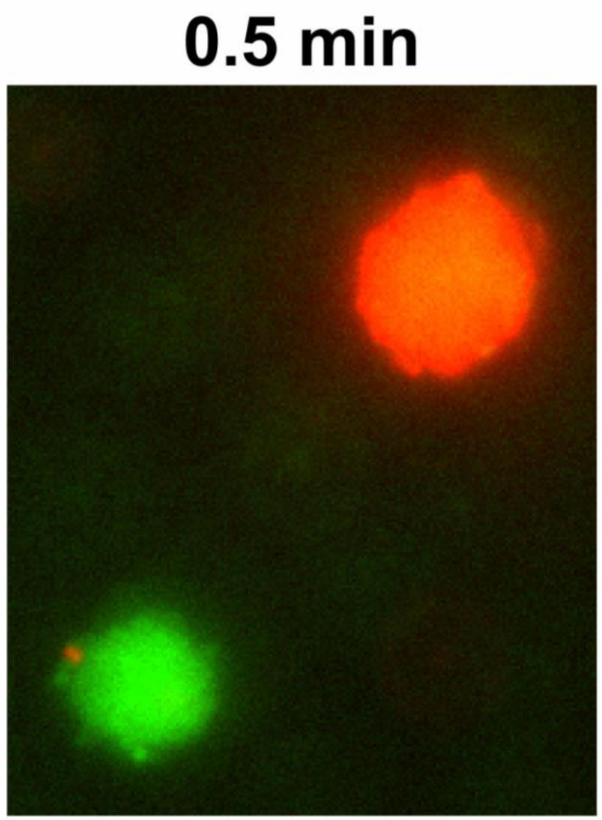


Scanning Electron Micrograph of two emerging *Neisseria gonorrhoeae* microcolonies. Scale bar = 8 µM (left). Scale bar = 4 µM (right).

(Ponisch *et al*., 2018)

Microcolonies merger

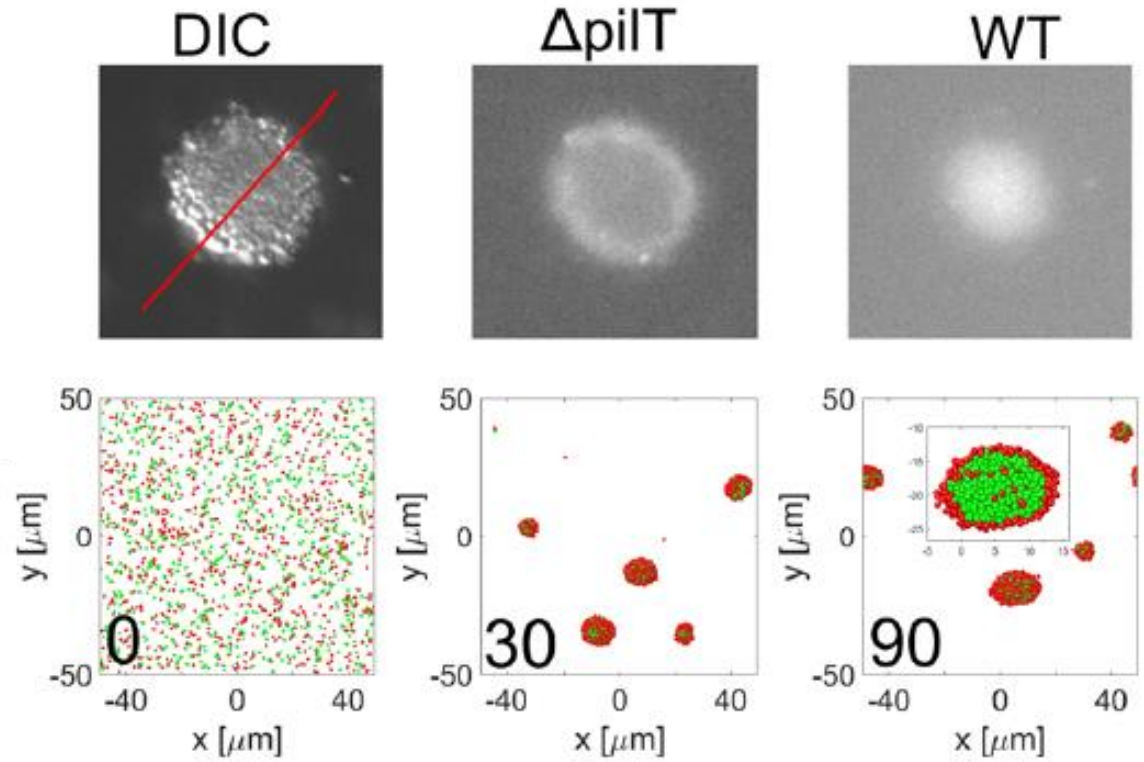




Two emerging *Neisseria gonorrhoeae* microcolonies. Scale bar = 10 µM.

(Ponisch *et al*., 2018)

Differential behavior within microcolonies

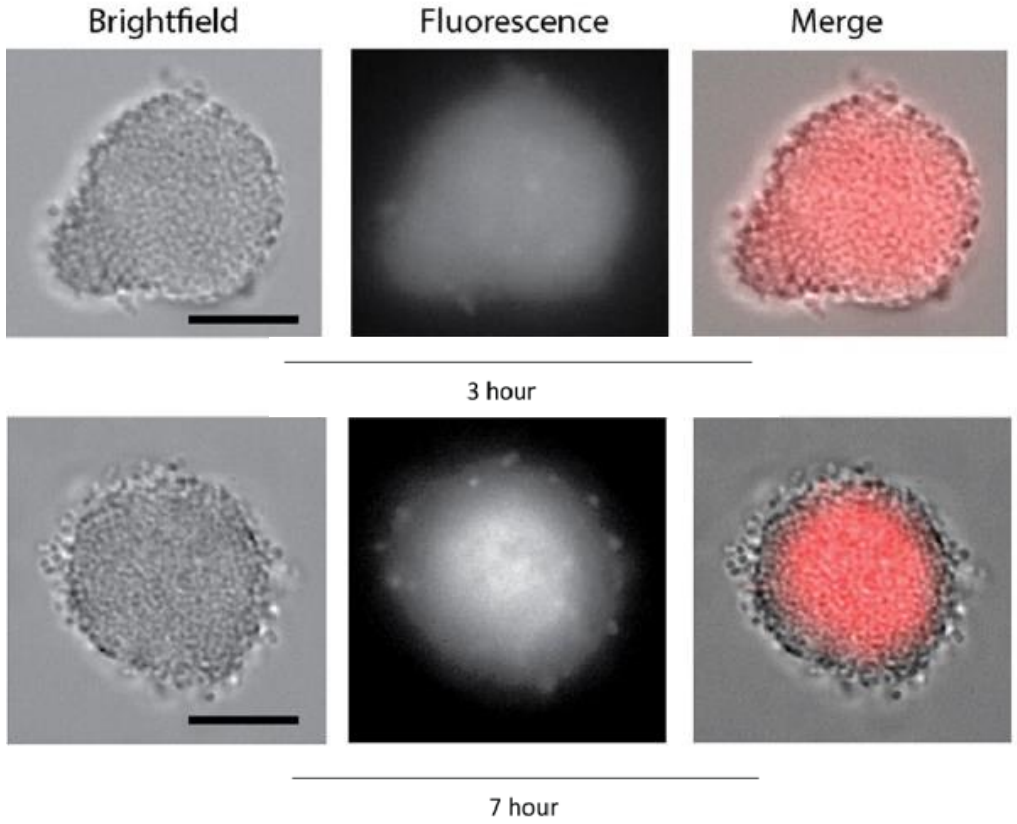


Demixing of Ng microcolonies of WT and ΔpilT mutant cells.

- Cells closer to the surface have higher motility
- Cells in the core have lower motility due to higher re-binding rate of Type IV pili
- The forces generated by retracting of Type IV pili contribute to the shaping of microcolonies

(Ponisch *et al.*, 2018)

Heterogeneous motility behavior induces heterogeneous gene expression



Heterogeneous genetic expression within a microcolony. Scale bar = 10 μM

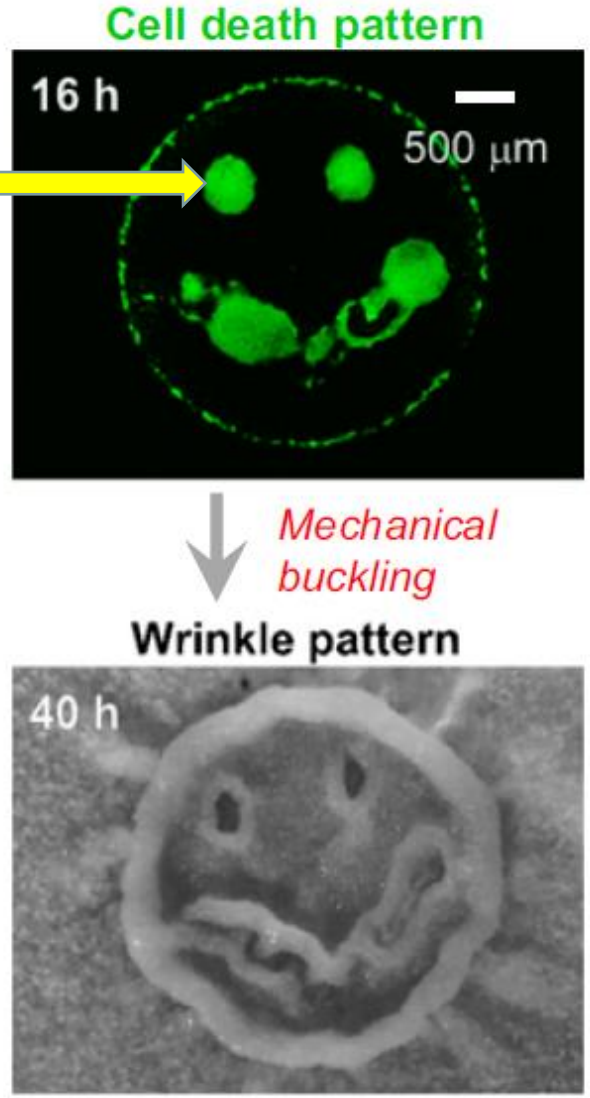
(Ponisch *et al.*, 2018)

Wrinkle Formation

Wrinkle formation

- Cell death and wrinkle structure correlate in space
- Cell death occurs first, followed by convergence directed towards the center of the preceding region of cell death
- Localized cell death focuses lateral forces which initiate wrinkle formation

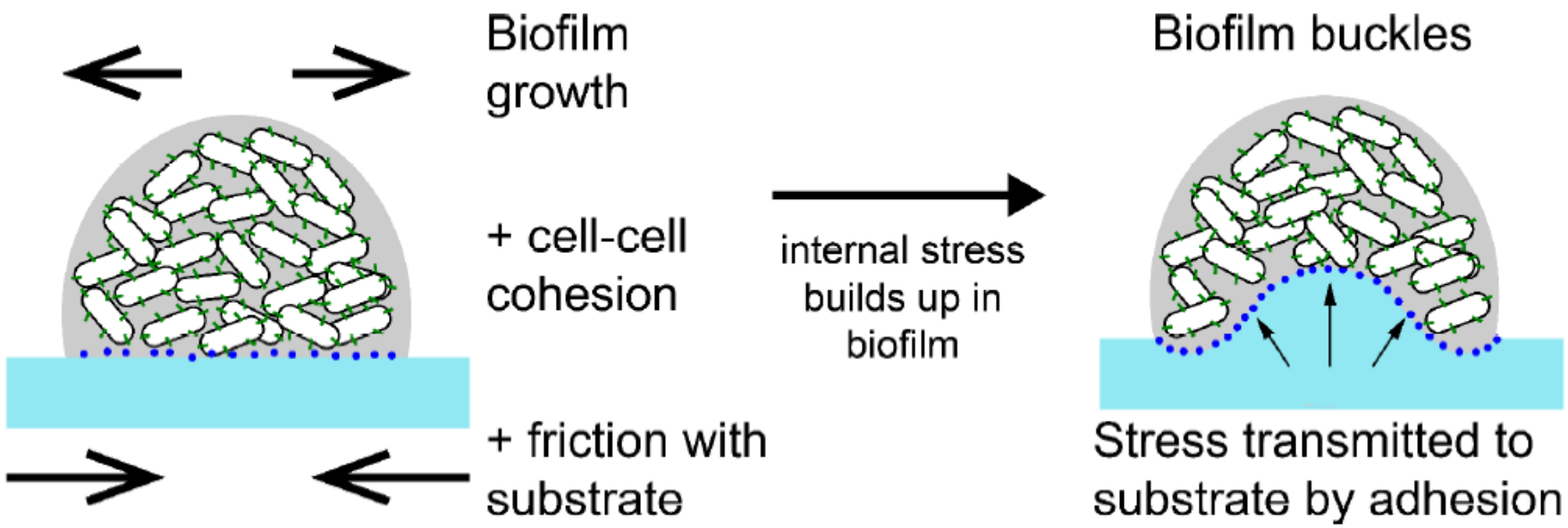
Higher cell density



(Asally *et al.*, 2012)

Deformation of Soft Surface and Epithelia

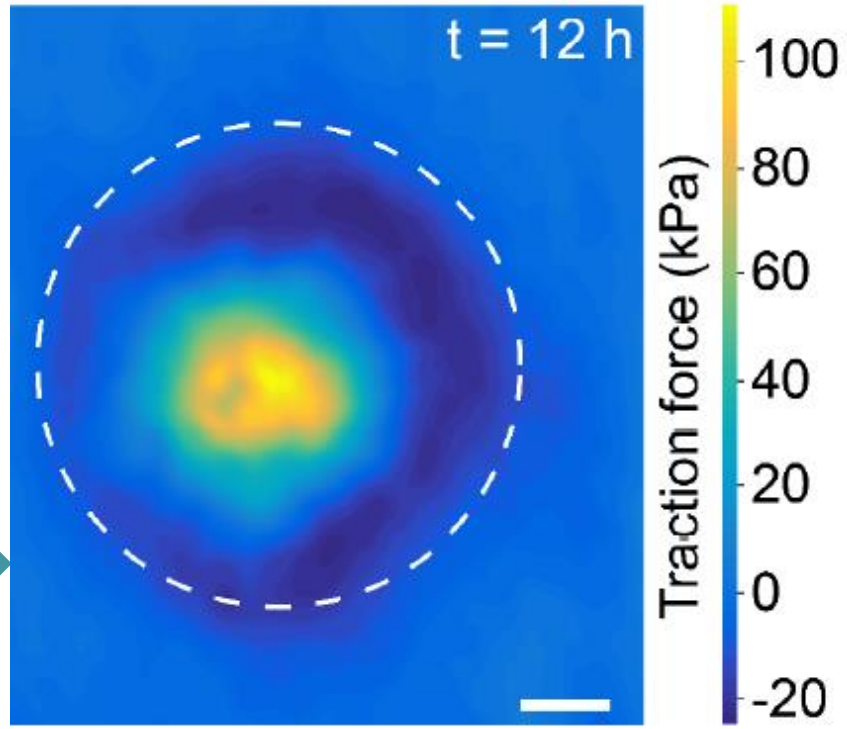
Deformation of soft surface



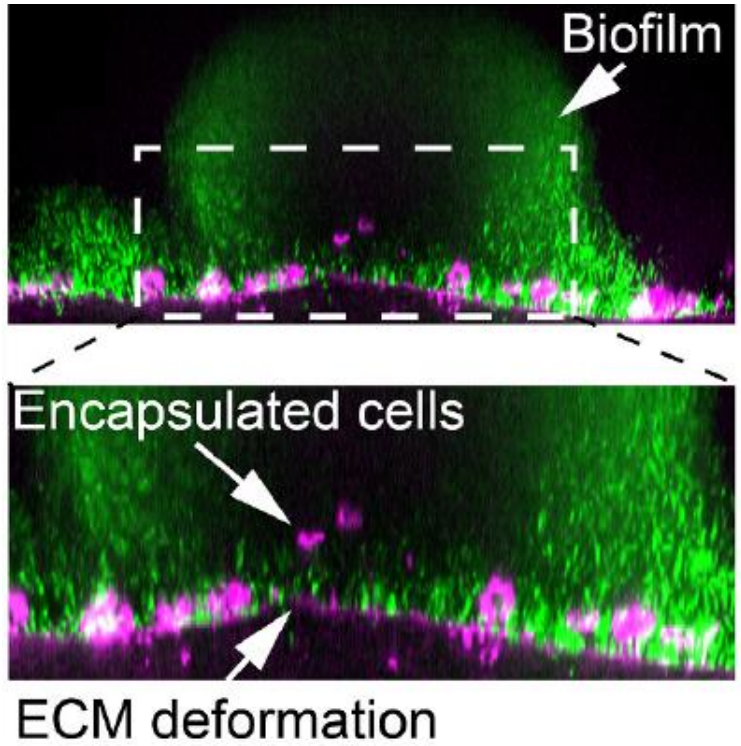
A model for the mechanism of biofilm deformation of soft substrates.

(Cont *et al*., 2020)

Deformation of epithelia



Traction force microscopy measurements at the hydrogel-biofilm interface.
Scale bar = 20 μM



Confocal images monolayers of CMT-93 cells at the surface of extracellular matrix (ECM).
Scale bar = 20 μM

(Cont *et al.*, 2020)

Discussion

Experimental settings

Growth media

The mechanical properties varies significantly with growth media, including the properties of the fluid and fluid dynamics

Properties of surface

The forces vary widely with properties of different surfaces

Molecular mechanisms

Mechanisms are unknown
Conformations are unclear

Theory construction & model building

Combination of different aspects

Molecular, cellular, microbiological, biophysical and computational techniques

Inadequate data

Data is not yet enough to compare measurements

(Auer & Weibel, 2017; Dufrene & Persat, 2020; Laventie & Jenal, 2020; Sauer et al., 2022)

Summary

Mechanomicrobiology studies how bacteria sense and respond to mechanical forces, and how bacteria resist and generate mechanical forces.

Mechanical signals play an important role in influencing bacterial phenotype.

By further study, we will be able to solve the mystery of how bacteria adapt to the environment, and develop strategies for bacterial growth inhibition.

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Thank you