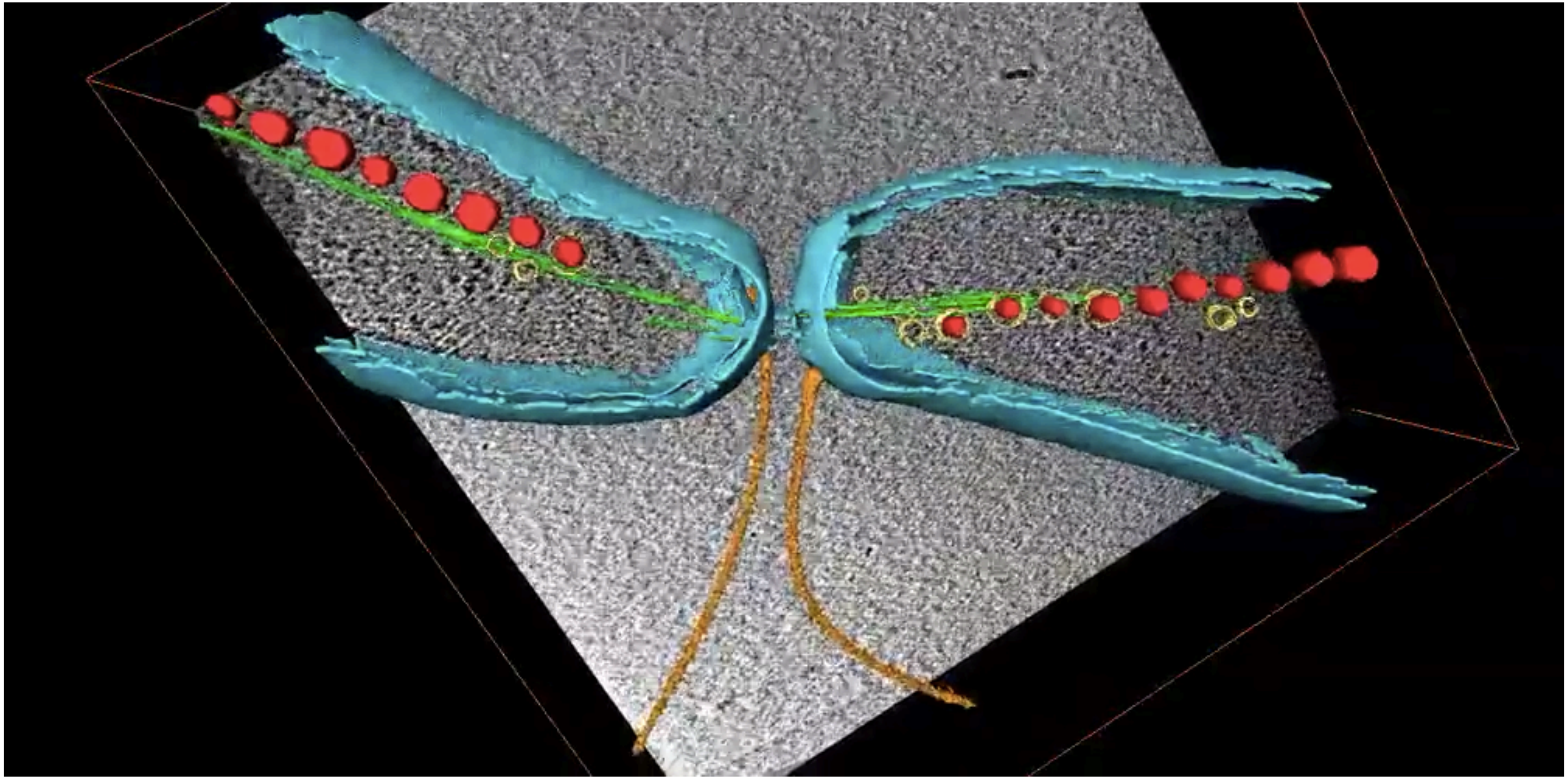
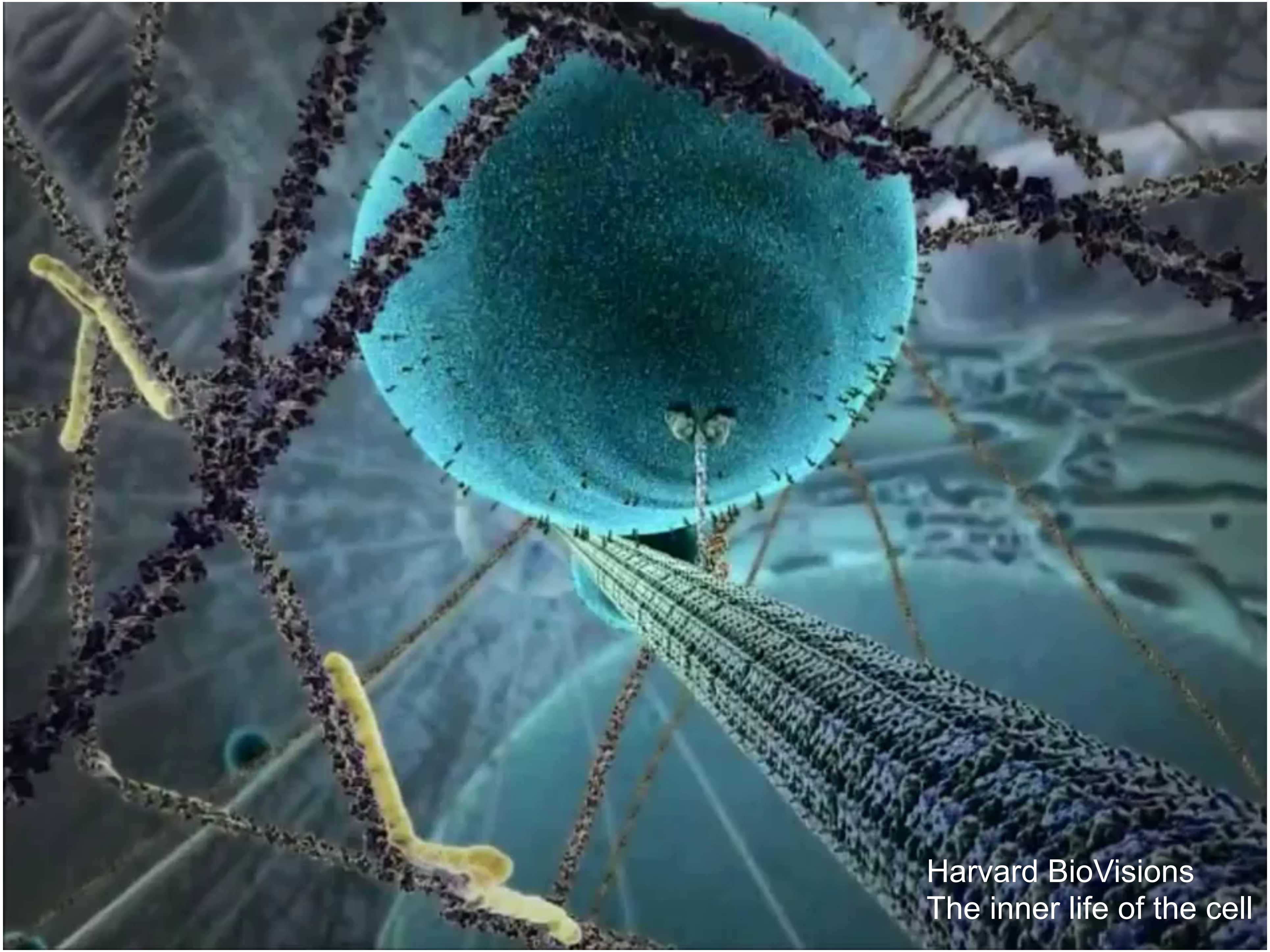
Traffic on filaments: molecular motors in difficult conditions

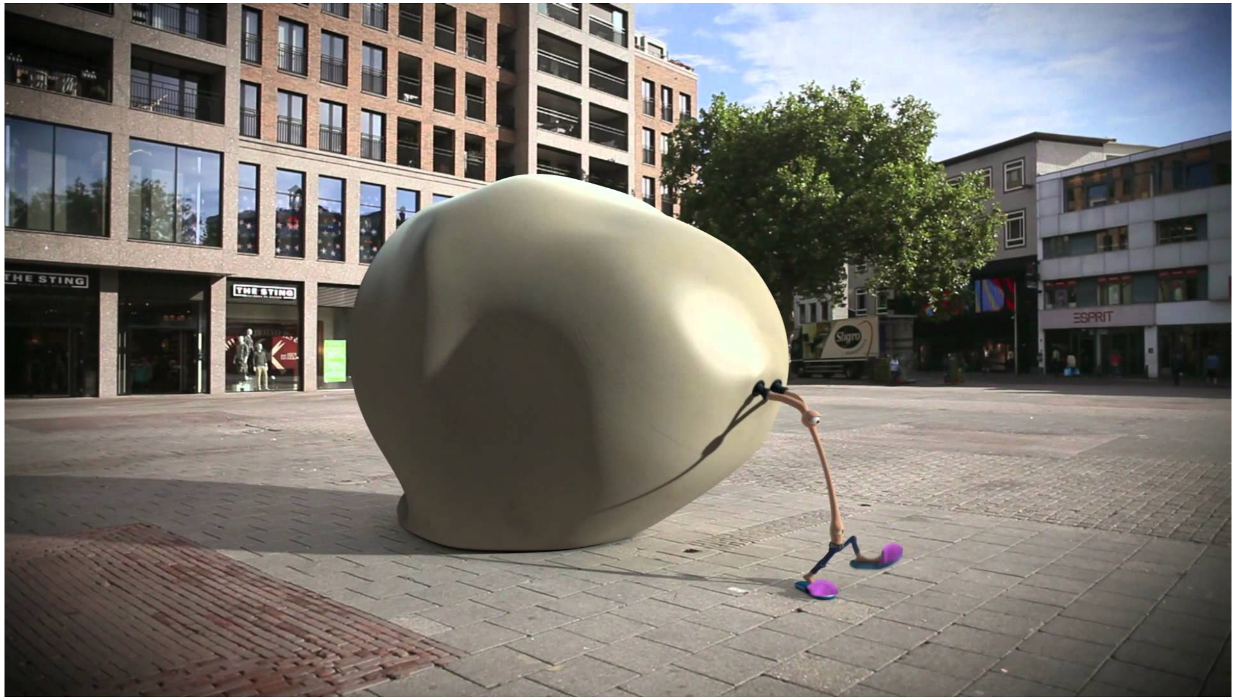


Stefan Klumpp

GEORG-AUGUST-UNIVERSITÄT GÖTTINGEN

Max-Planck-Institut für Kolloid- und Grenzflächenforschung


Harvard BioVisions
The inner life of the cell

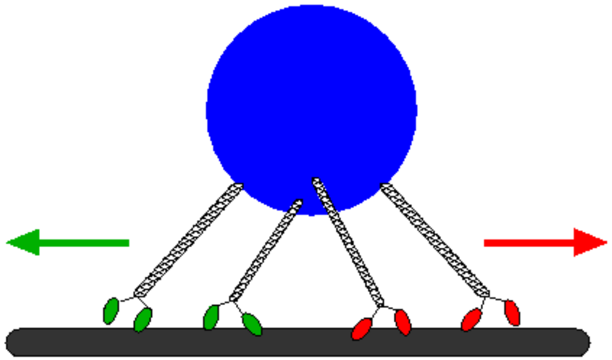


Hoogenraad lab
A day in the life of a motor protein

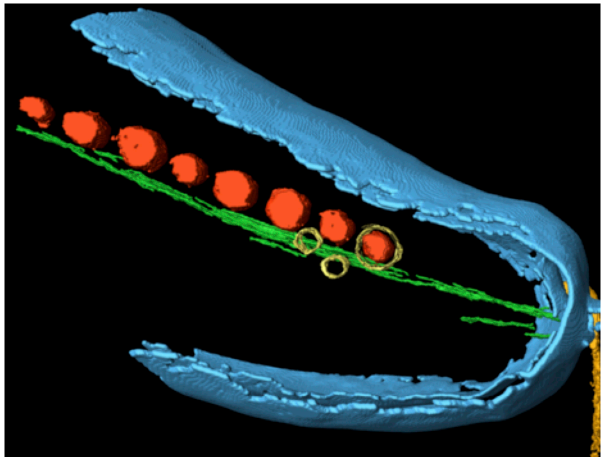
www.youtube.com/watch?v=tMKlPDBRJ1E

- stochasticity
- opposing force
    - other motors
    - external forces
- crowded conditions on filament/ in cytoplasm
- dynamic tracks

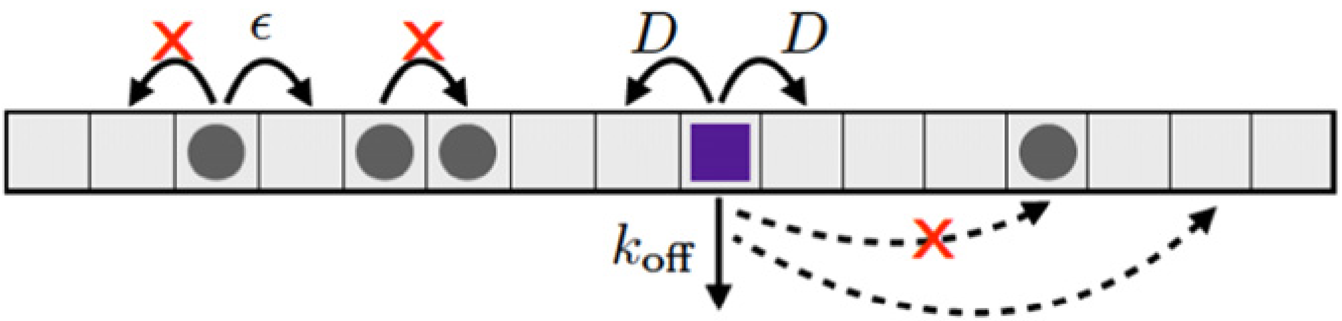
tug of war between teams of cytoskeletal motors



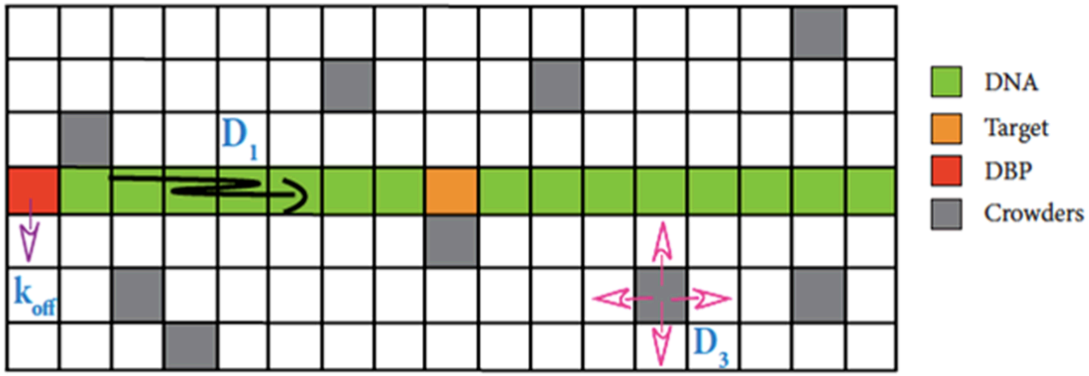
magnetosome filament in magnetotactic bacteria

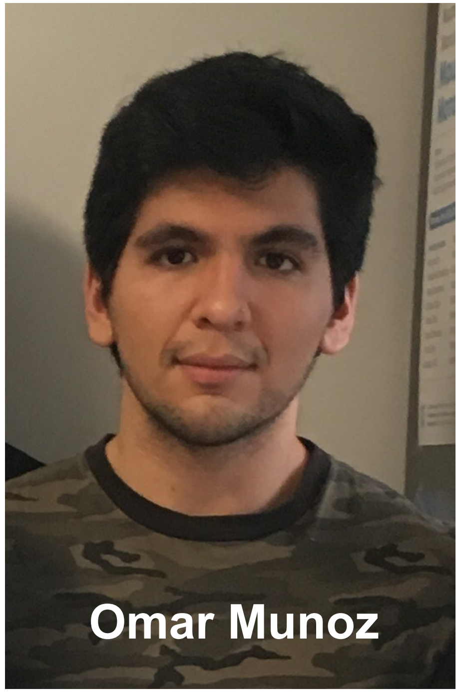


Roadblocks in exclusion processes
(static or dynamic)



DNA binding in crowded conditions
(obstacles on DNA, in cytoplasm)

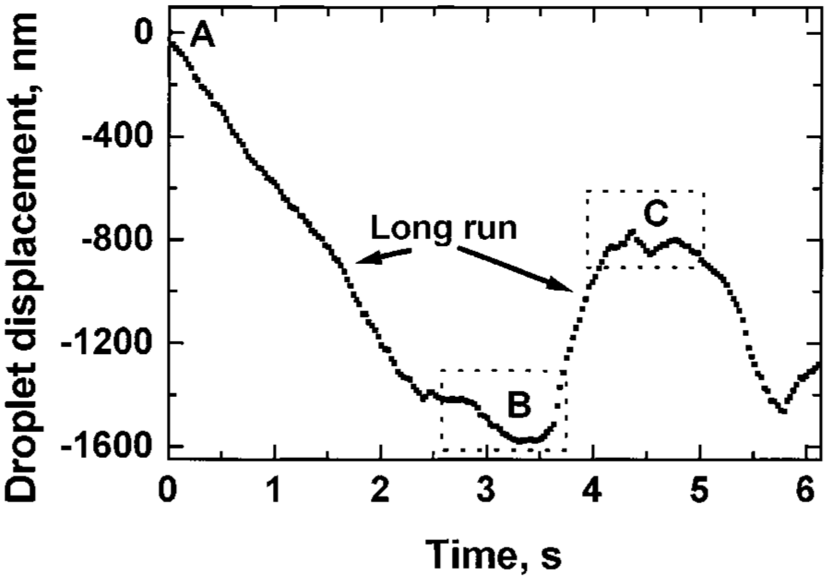


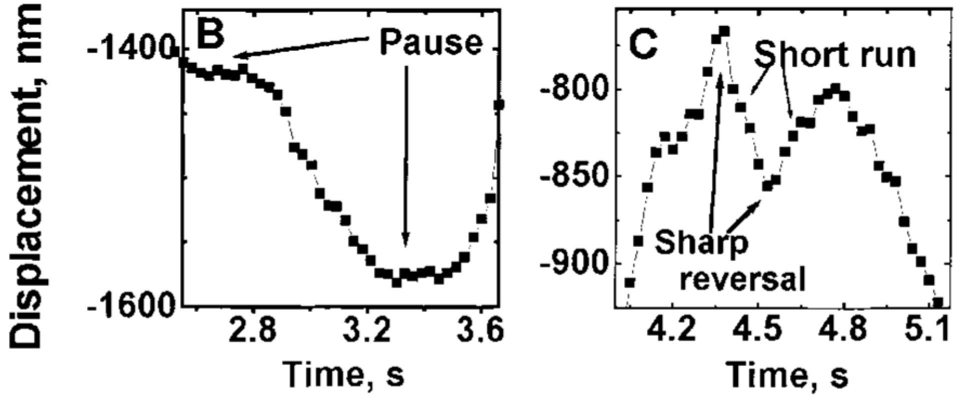


Traffic on the cytoskeleton

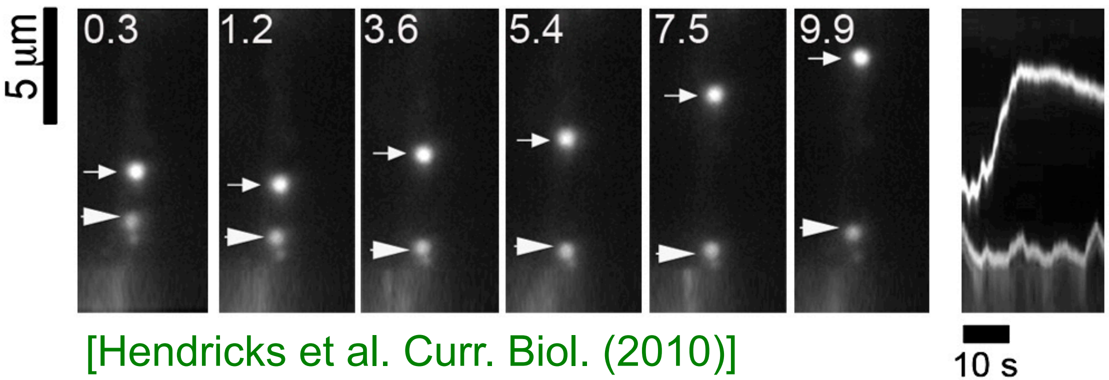
TUG OF WAR AND ALL THAT

Bidirectional transport: Tug of war and all that...

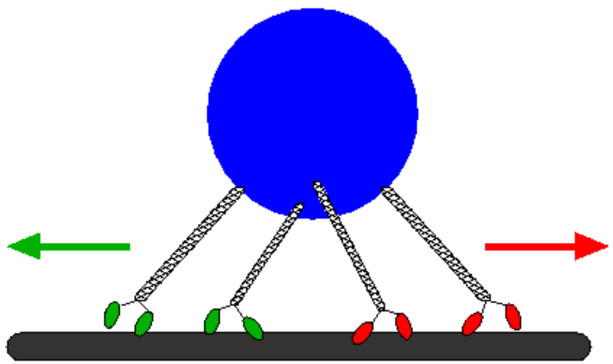




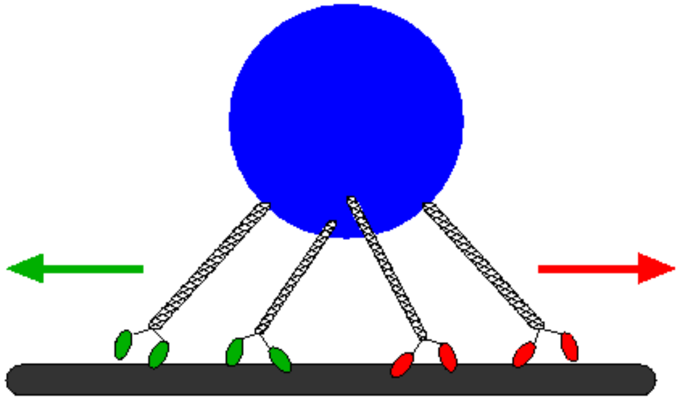
[Gross et al. J. Cell Biol. (2000)]

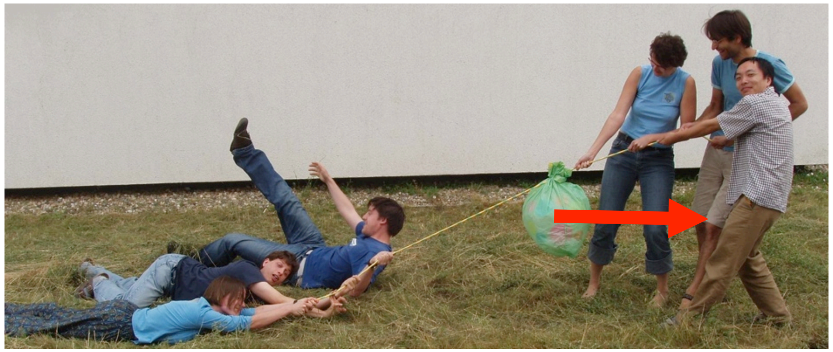


[Hendricks et al. Curr. Biol. (2010)]



Bidirectional transport: Tug of war and all that...



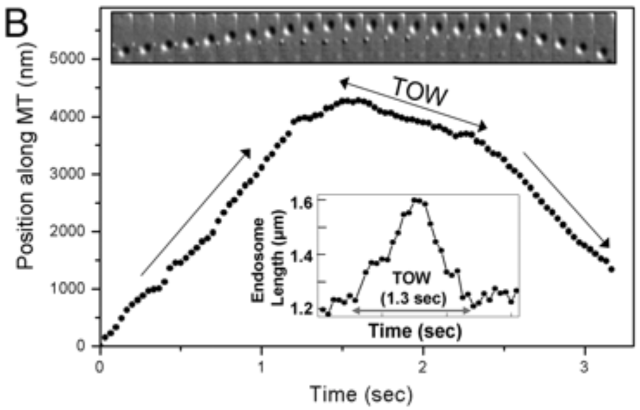


Tug-of-war model:
mechanical forces coordinate
opposite-direction motors

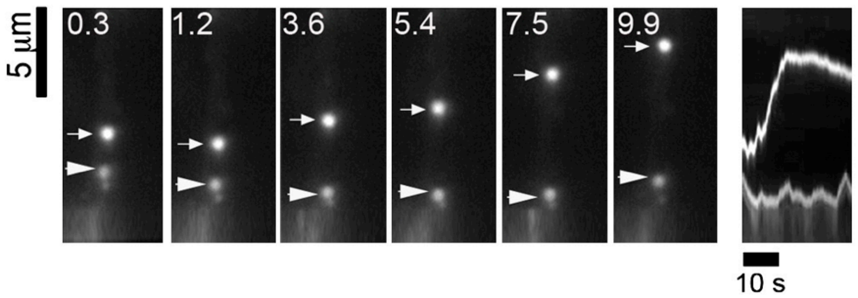
instability due to force-induced
unbinding

Müller, Klumpp, Lipowsky, PNAS **105**, 4609 (2008)

Experimental evidence for a tug-of-war



endosomes in Dictyostelium cells:
endosome elongates during slow phase
Soppina et al., PNAS (2009)



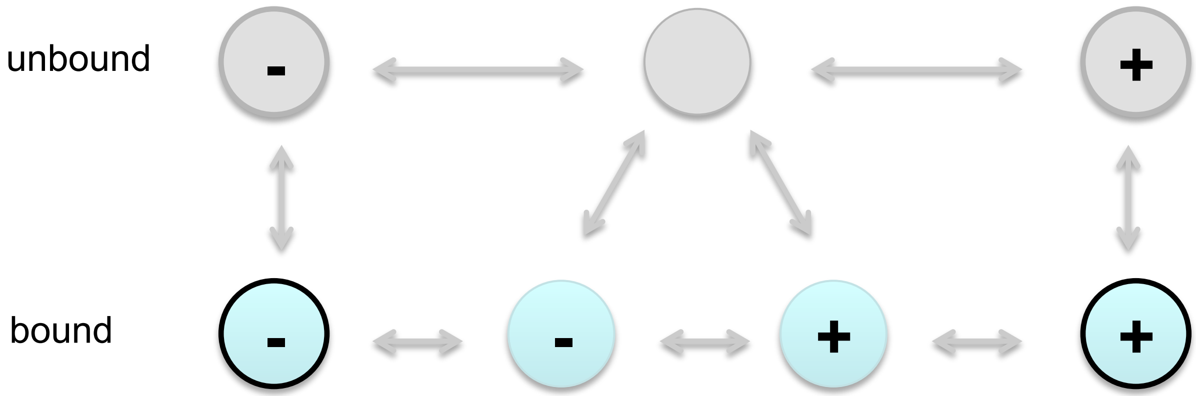
neuronal vesicles:
observed motion quantitatively
in agreement with tug-of-war model
Hendricks et al., Curr Biol (2010)

but also: some observations point to additional biochem. regulation

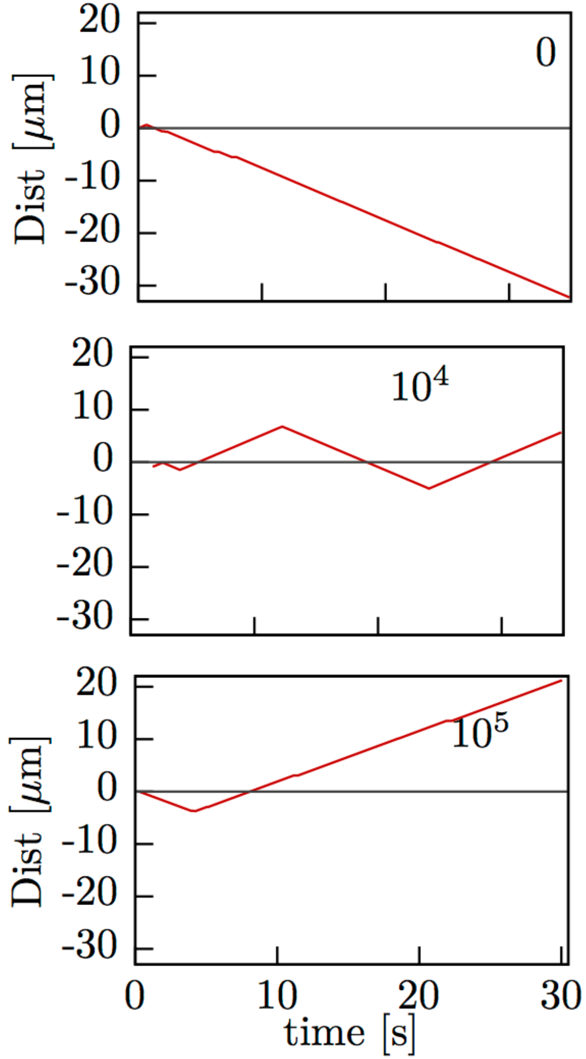
- lipid droplets: long pauses Kunwar et al. PNAS 2012
- lipid droplets: same direction after unbinding Leidel et al. Biophys J 2012
- known regulator JIP1 Fu & Holzbaur 2013

→ control by generic mechanics + specific biochemistry

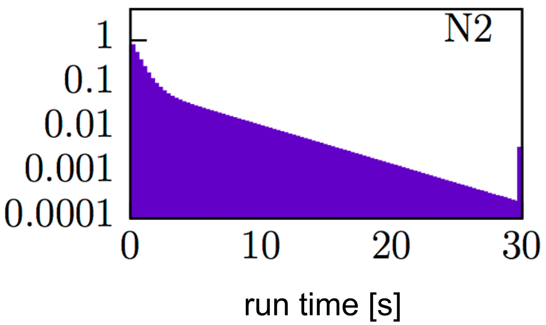
Toy model: bidirectional transport with regulation



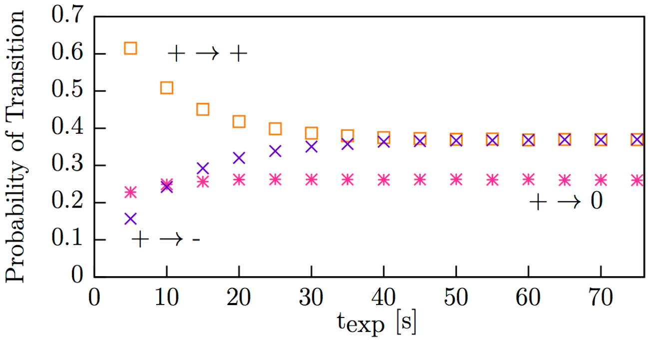
bidirectional transport
+ „locked-in“ states due to regulation



rare very long runs

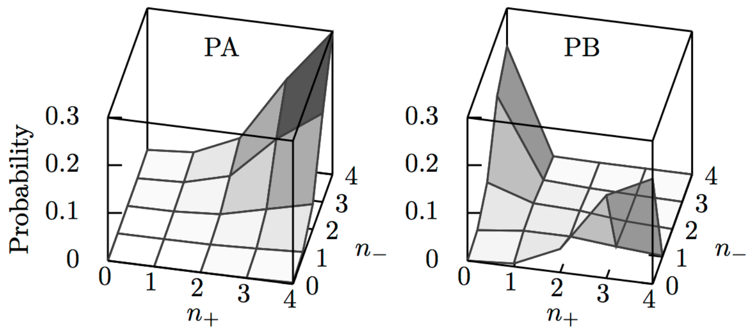


Memory upon unbinding

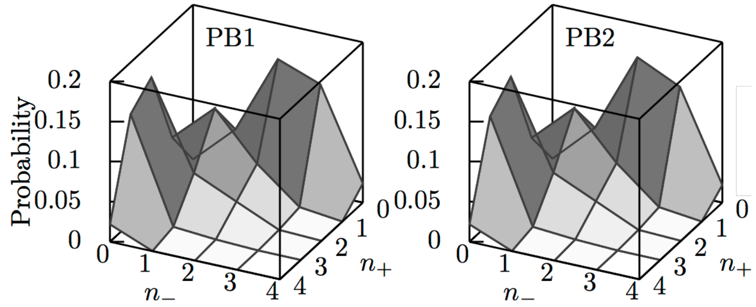


Omar Munoz

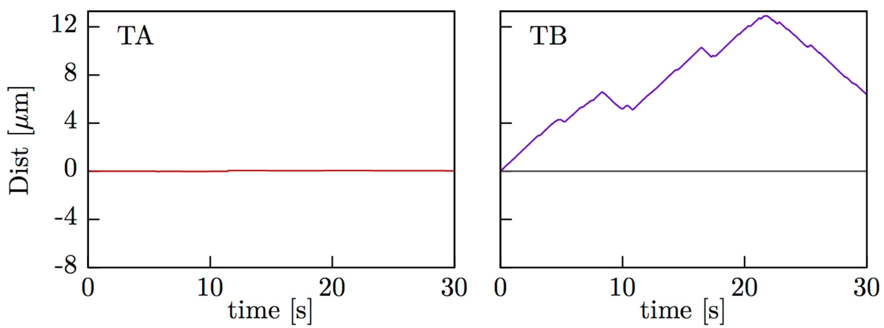
Tug-of-war with activation/inactivation

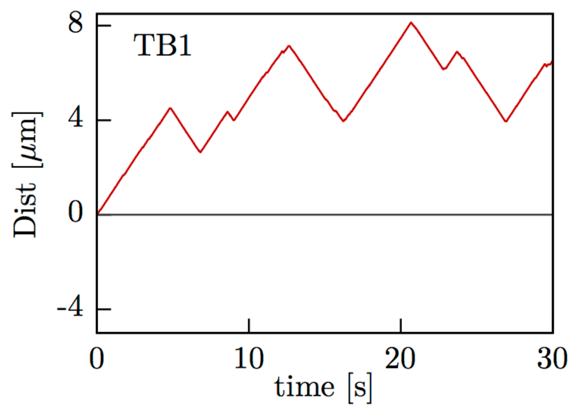


tug-of-war model



with motor activation



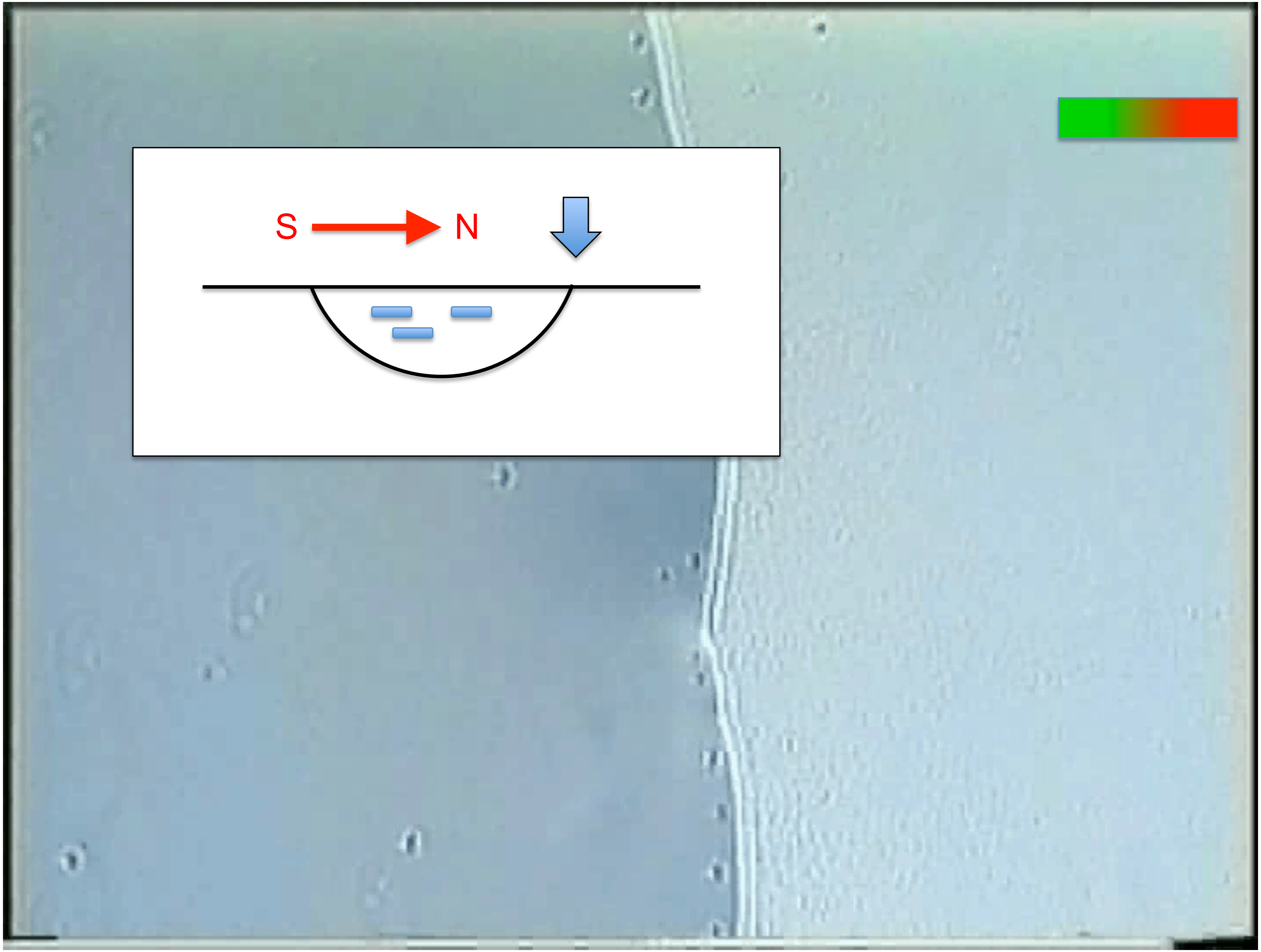


activation provides a mechanism for lock-in of direction
abolishes parameter dependence

Omar Munoz

Traffic on a bacterial cytoskeleton

FILAMENTS IN MAGNETOTACTIC BACTERIA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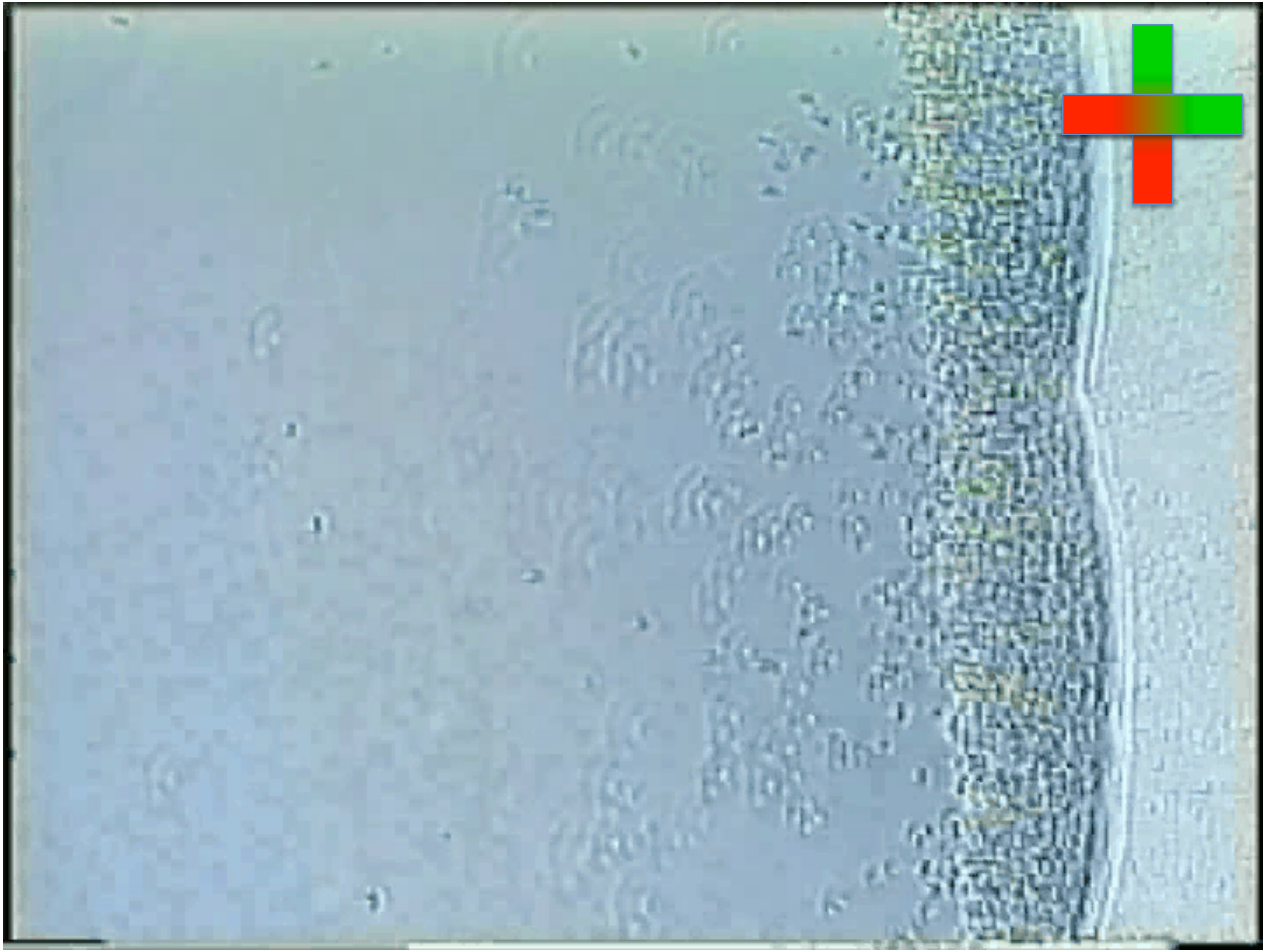

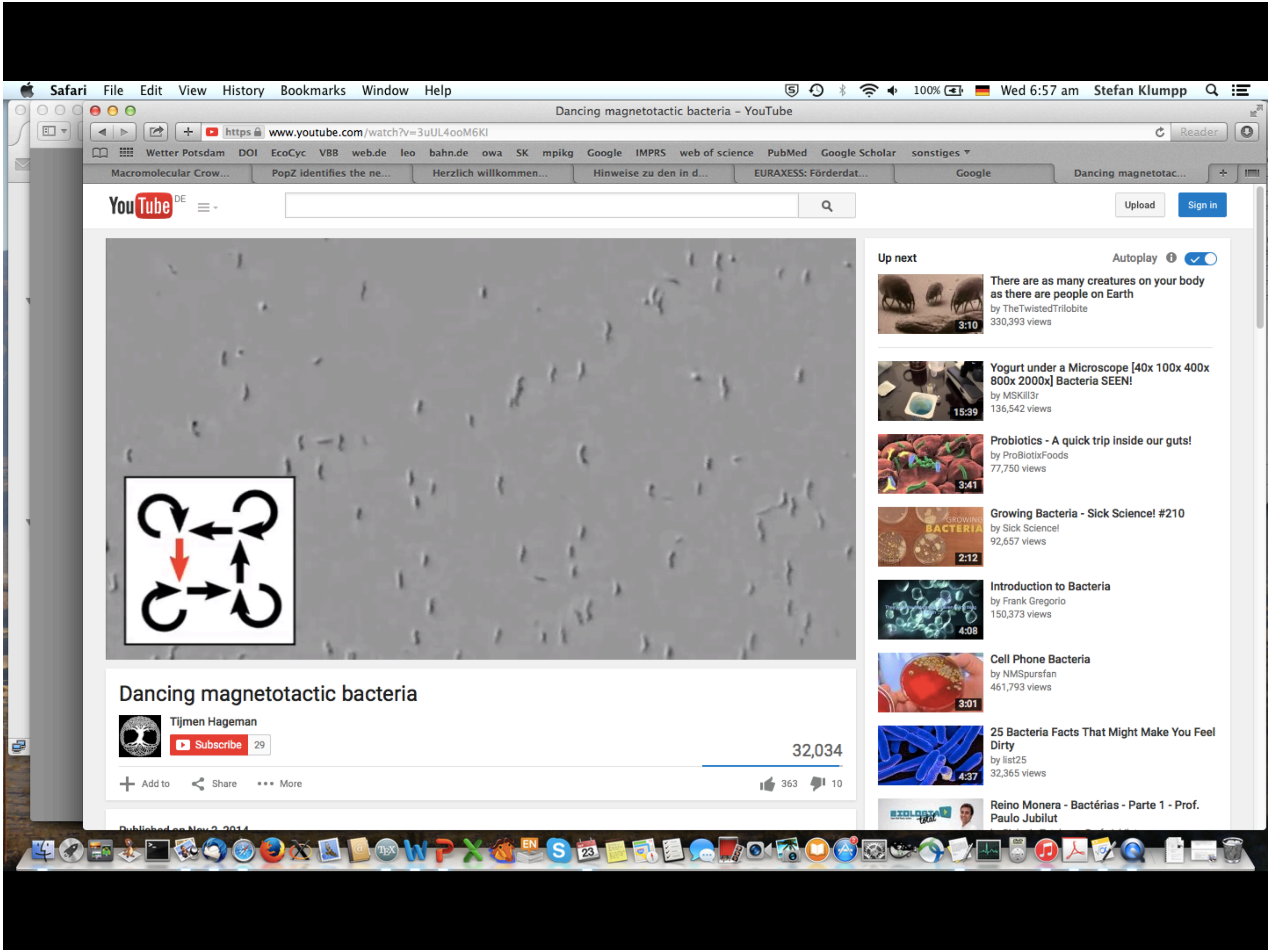

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100% Wed 6:57 am Stefan Klumpp
Dancing magnetotactic bacteria - YouTube
https www.youtube.com/watch?v=3uUL4ooM6KI
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Macromolecular Crow... PopZ identifies the ne... Herzlich willkommen... Hinweise zu den in d... EURAXESS: Förderdat... Google Dancing magnetotac...
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Dancing magnetotactic bacteria
Tijmen Hageman
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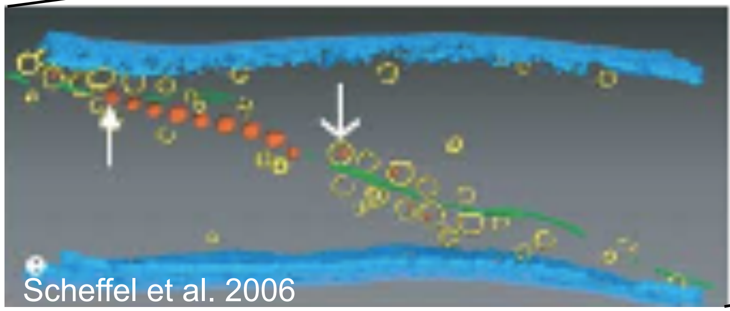
Magnetotactic bacteria

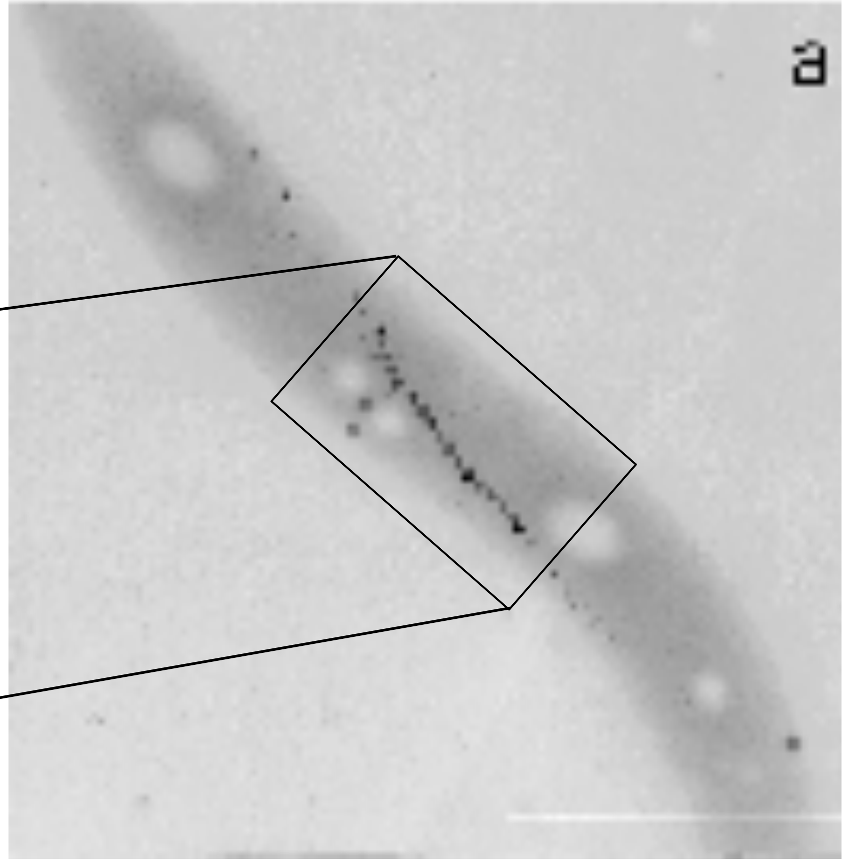
• form a chain of magnetic organelles (magnetosomes)
→ compass needle

• orient and navigate in magn. field of the earth



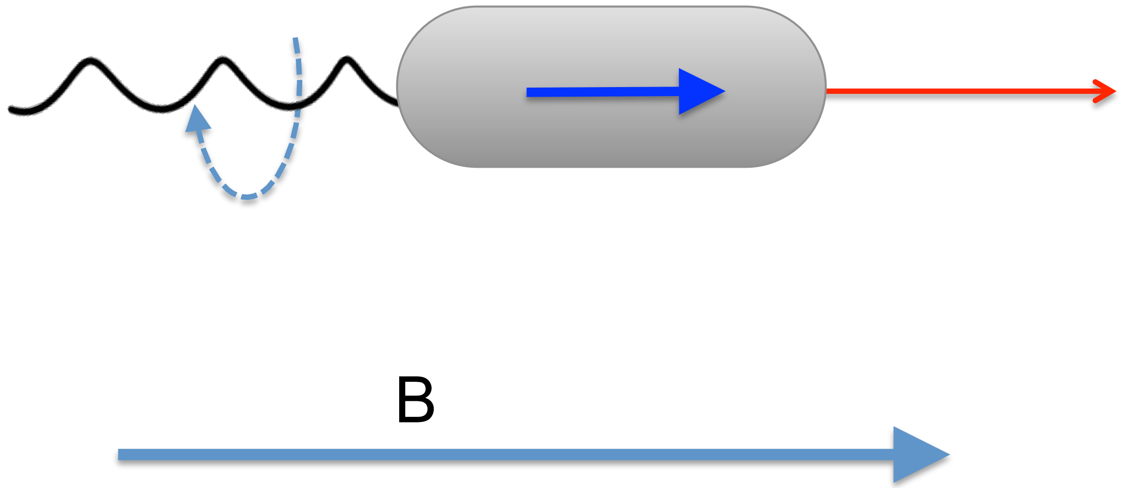
• ~40nm Fe_3O_4 crystals in vesicles, aligned on filament (MamK)

• permanent magnets, single-domain particles



Magnetospirillum gryphiswaldense
MSR-1

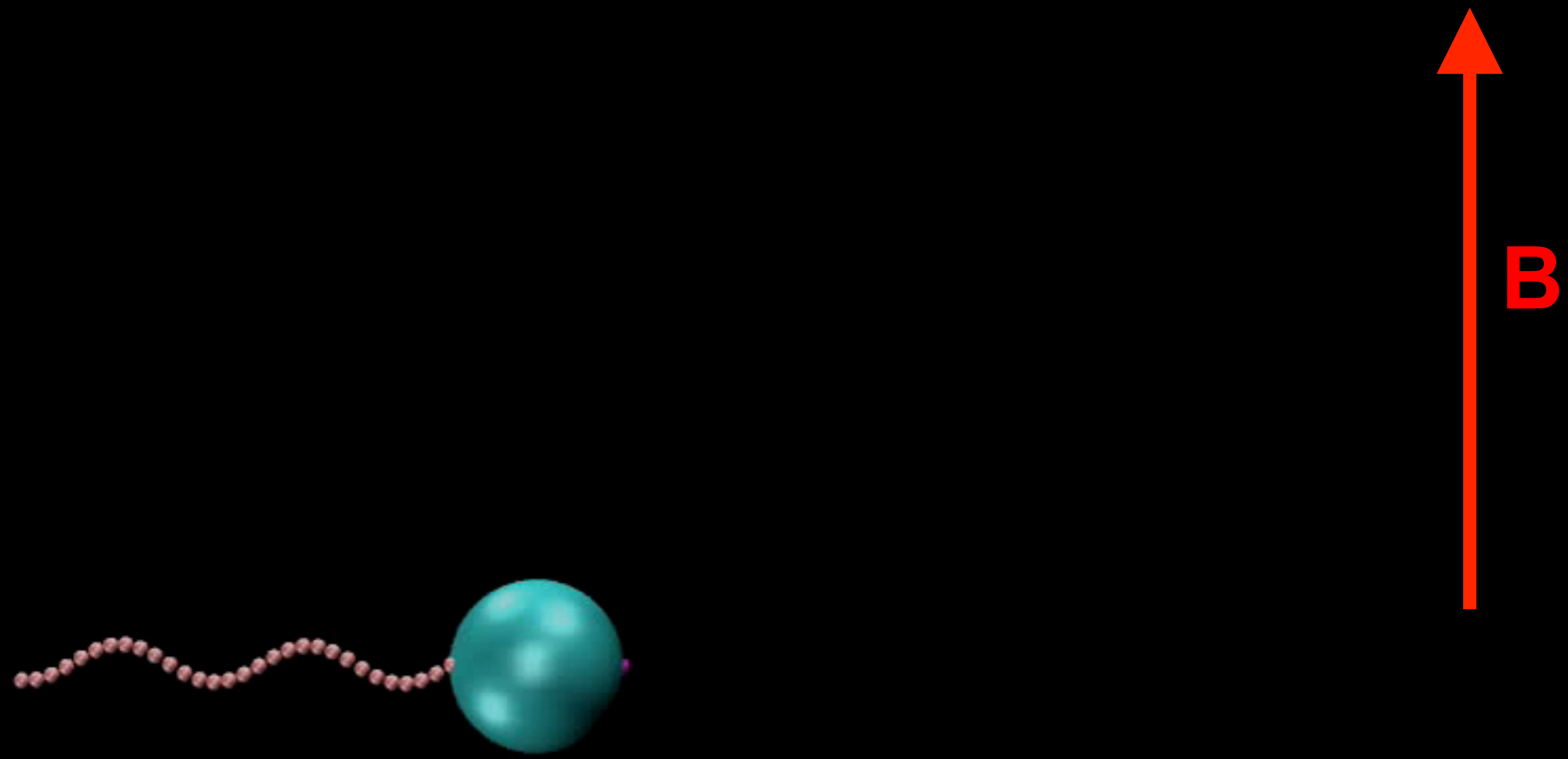
Passive alignment + active propulsion



„Self-propelled compass needle“

Homogeneous field: alignment but no attraction

Passive alignment + active propulsion



Sarah Mohammadinejad

Compass needle: structural requirement

Straight chain for high magnetic moment

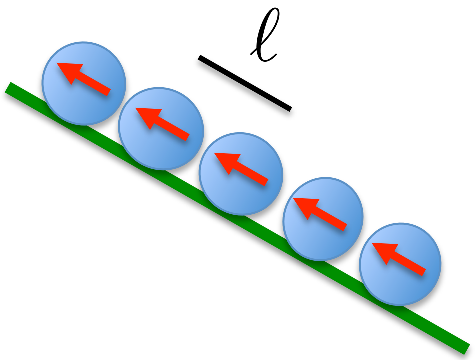
Bending rigidity $\kappa = \kappa_{\mathrm{fil}} + \kappa_{\mathrm{magn}}$

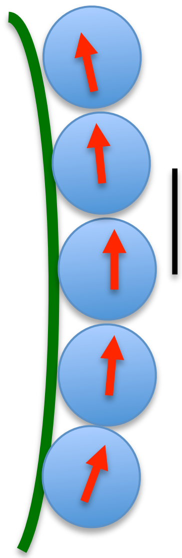
$$E_{\mathrm{magn}} \approx E_{\mathrm{lin}} + \frac{1}{2} N \frac{\kappa_{\mathrm{magn}}}{\ell} \left(\frac{\ell}{R} \right)^2$$

$$\kappa_{\mathrm{magn}} \approx \epsilon \ell \frac{\zeta(3)}{4}$$

persistence length: $L_p = \frac{\kappa}{k_B T}$

$L_{p,\mathrm{magn}} = \frac{\kappa_{\mathrm{magn}}}{k_B T}$ ~ 3-4 μm ~ cell length





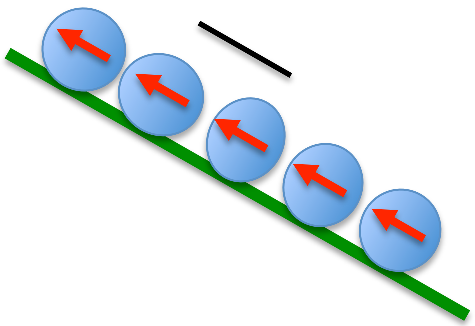
Kiani, Faivre, Klumpp, New J Phys 2015

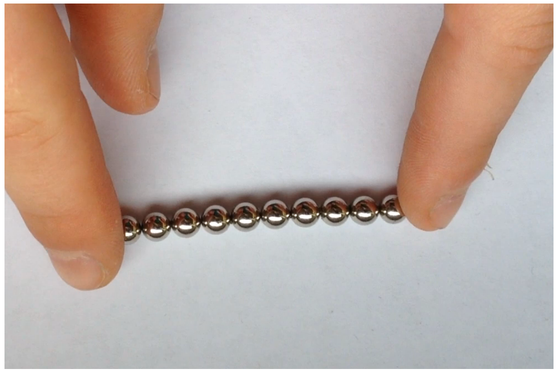
Compass needle: structural requirement

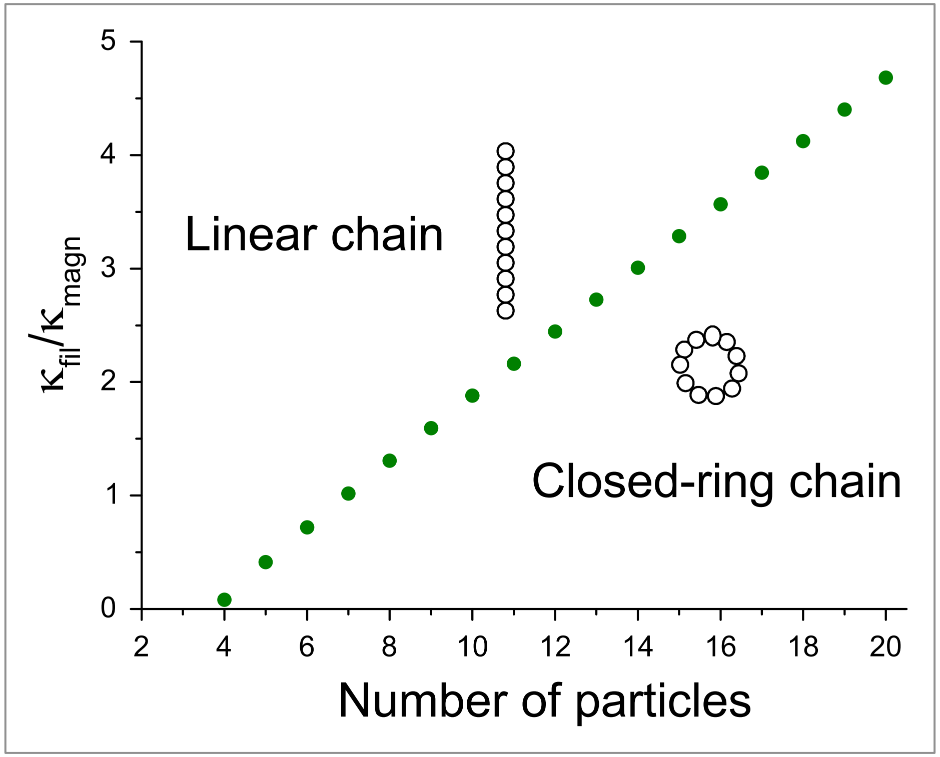
persistence length:

$$L_{p,\mathrm{magn}} = \frac{\kappa_{\mathrm{magn}}}{k_B T}$$

~ 3-4 μm ~ cell length







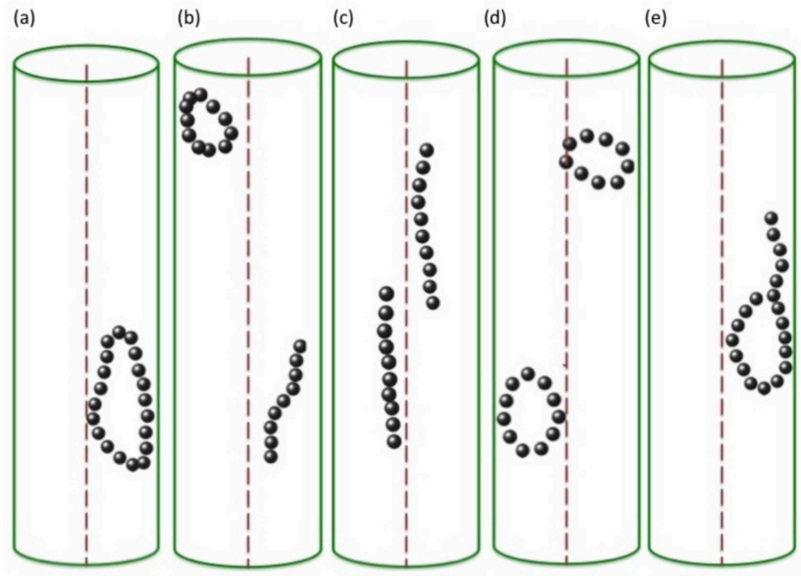
straight magnetic chain is metastable

➔ stabilized by filament

Kiani, Faivre, Klumpp, New J Phys 2015

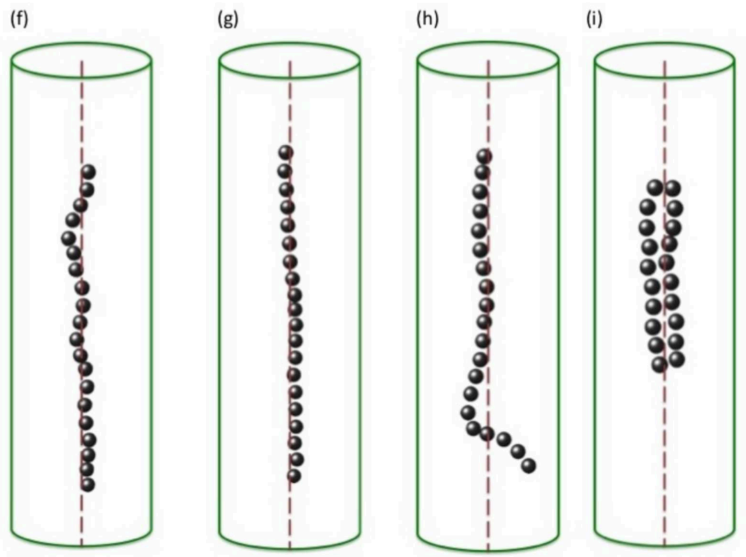
Compass needle: structural requirement

without binding to filament



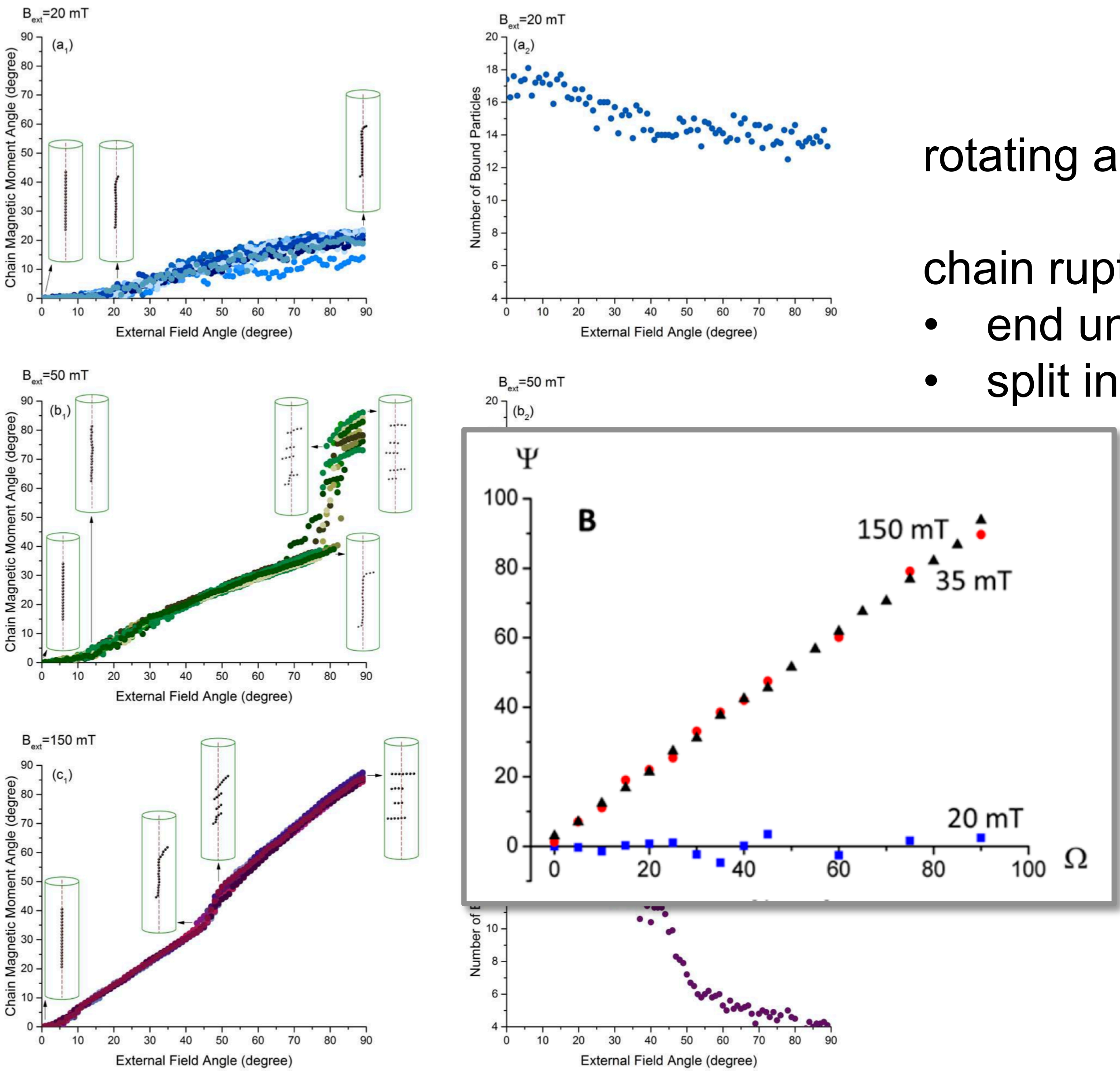
filament stabilizes chain: MC simulations

with binding to filament



Bahareh Kiani

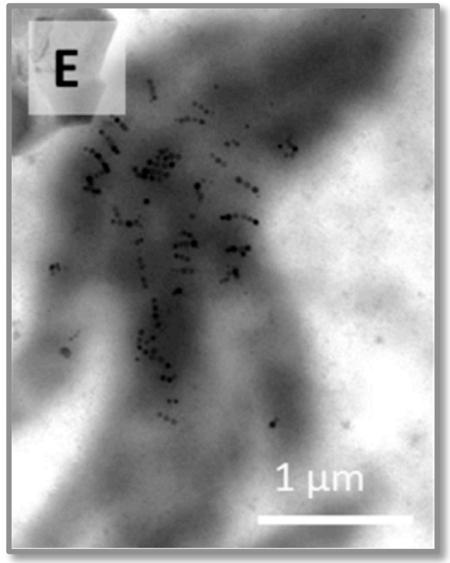
Probing mechanical stability



rotating a magnetic field

chain ruptures in 2 steps

- end unbinding
- split into short chains



A. Körning et al.
Nano Lett. 2014

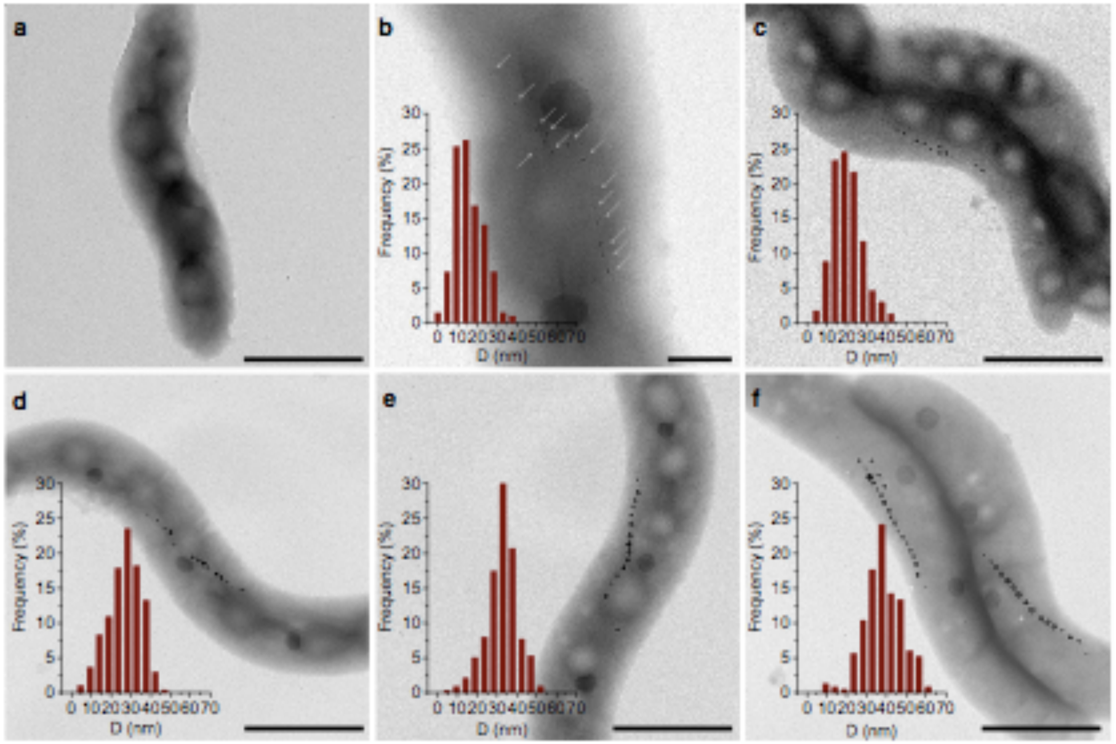
Positioning of magnetosomes, chain formation, cell division

AN ACTIVE FILAMENT

Formation of magnetosome chains

• experiment: iron-starved cells shifted to medium with iron, but no nutrients
• form magnetosome chains over 5-10 hours

110 min 280 min



330 min 420 min 1320 min

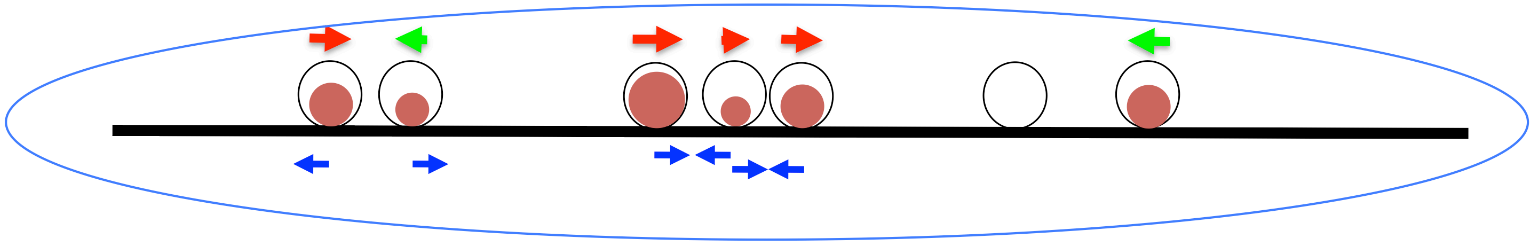
→ role of magnetic interactions?
(interplay of physics and biology)

→ diffusion + magn. interactions sufficient for chain formation?
→ role of MamK,J proteins?

→ idea: in-silico mutants defective in processes

[Faivre et al. Biophys. J. 2010]

Model for chain formation



- hybrid Langevin dynamics–Monte Carlo simulation

- 3 degrees of freedom:
  - position (1d) → Langevin eq.
  - crystal volume → stoch. nucleation, determinist. growth
  - direction of magnetization (1d) → MC spin flip, hysteresis for crystals > crit. size

- simulate ~10 hours of dynamics

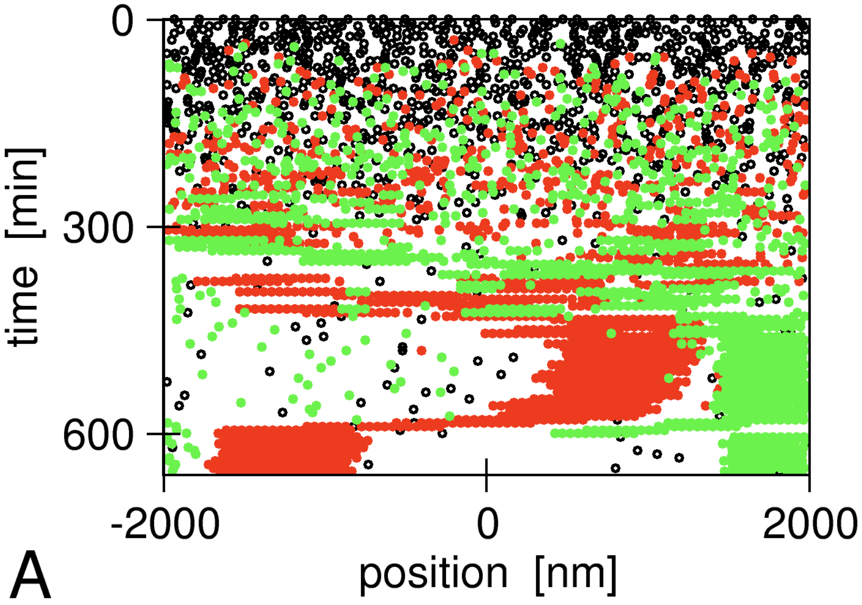
- most parameters known, diffusion coeff. varied over wide range

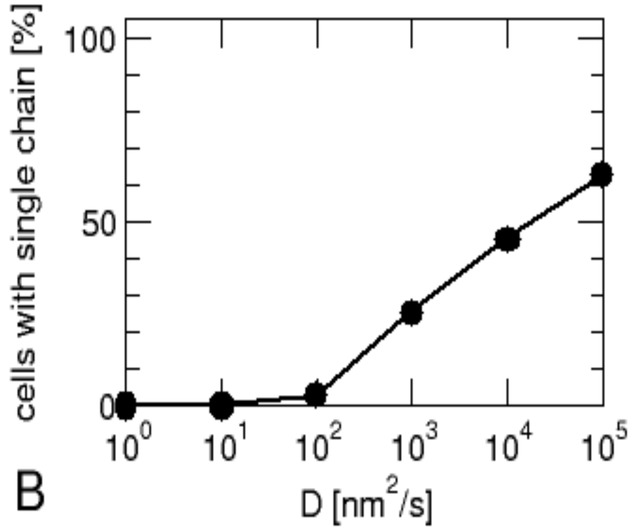
Klumpp & Faivre, PLoS One 7, e33562 (2012)

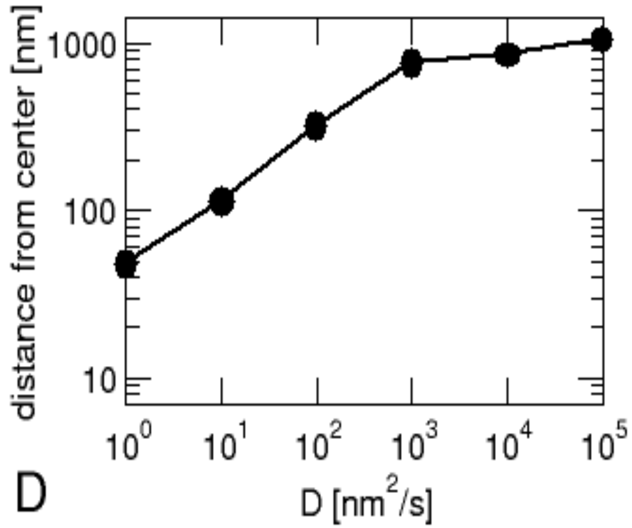
Diffusion + magn. interactions

diffusion + magn. interactions sufficient for chain formation?

analyze simulated cells 10 hours after induction



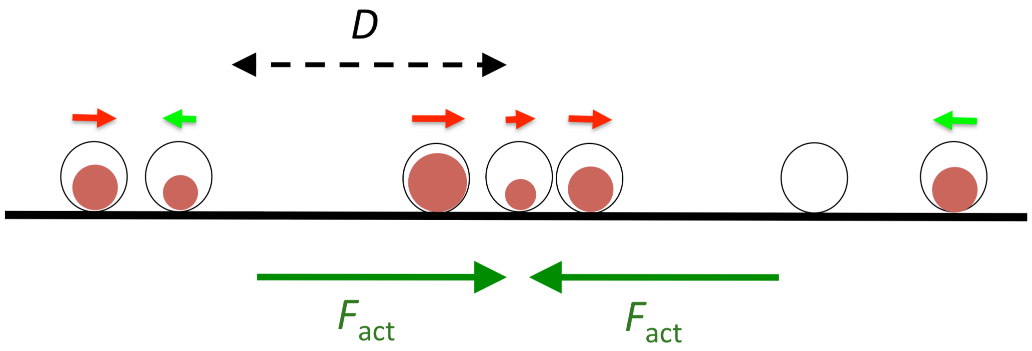


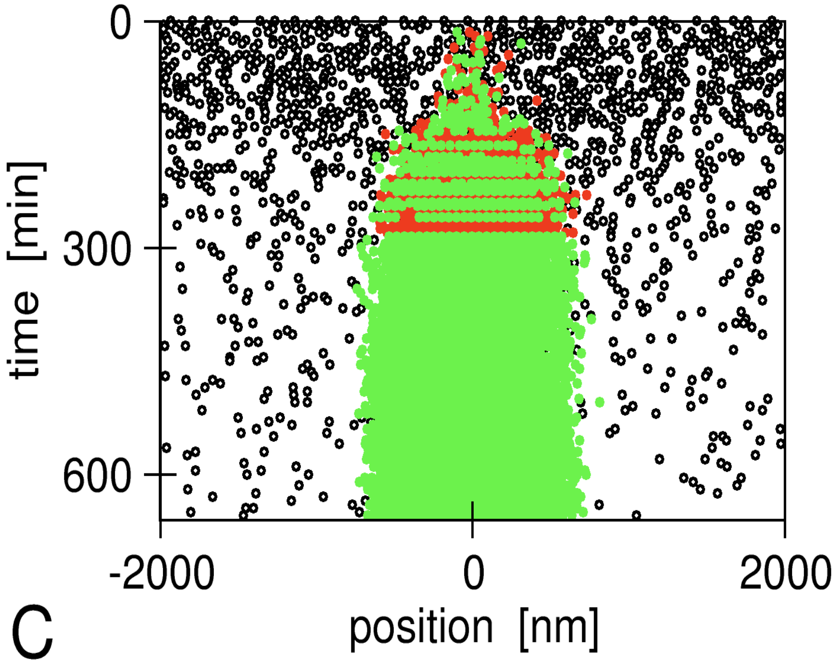


- substantial fraction of cells form ≥2 chains
- chains not centered
- onset of magnetization later than in expt.

Active transport to cell center

active transport,
driven by (de)polymerization
of cytoskeletal filaments?
(MamK, FtsZ-like, others?)





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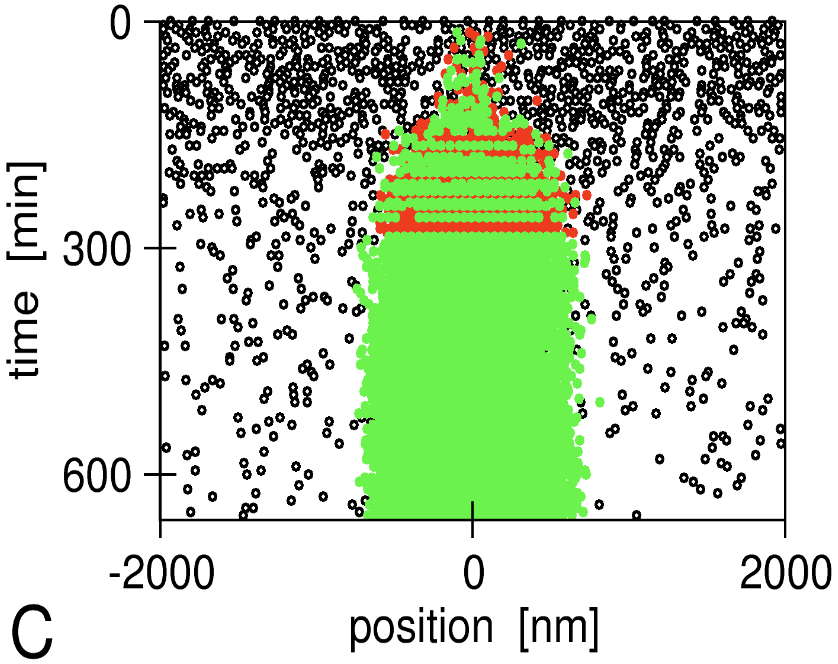
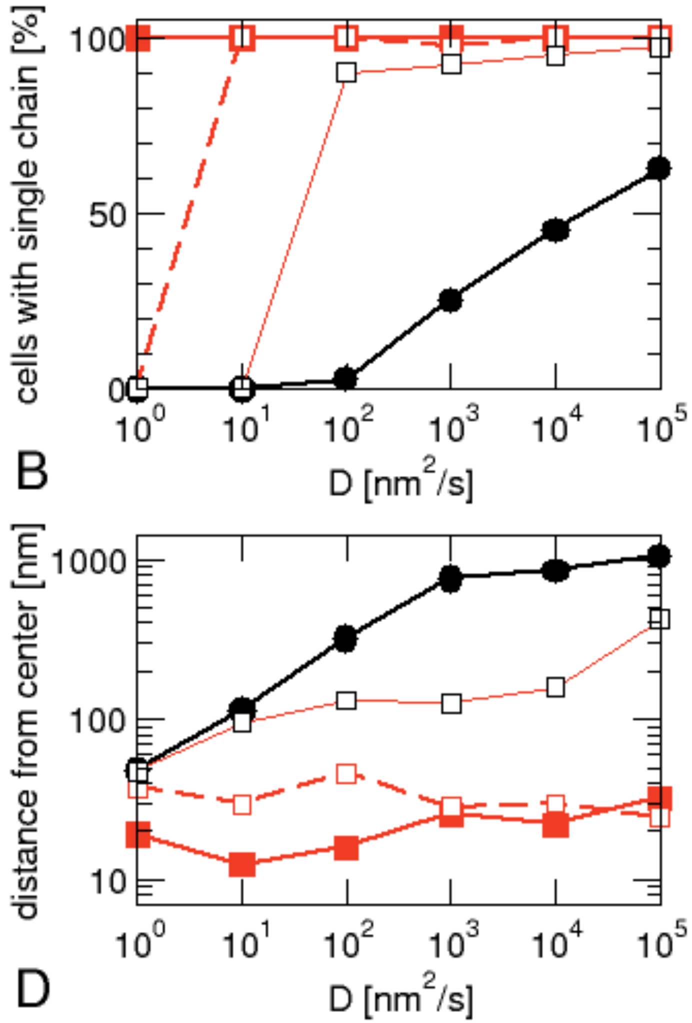


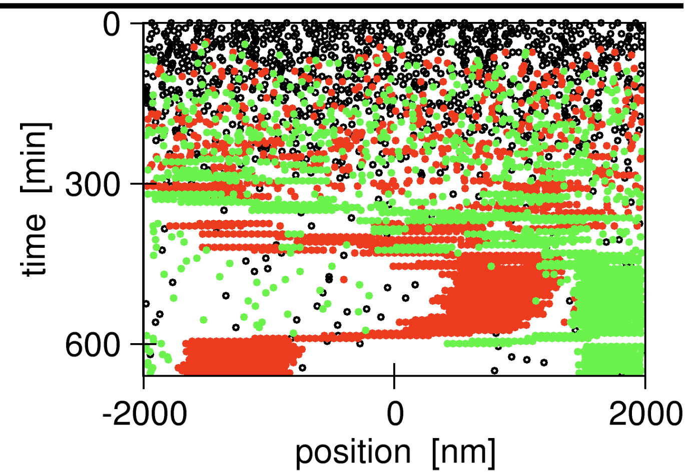


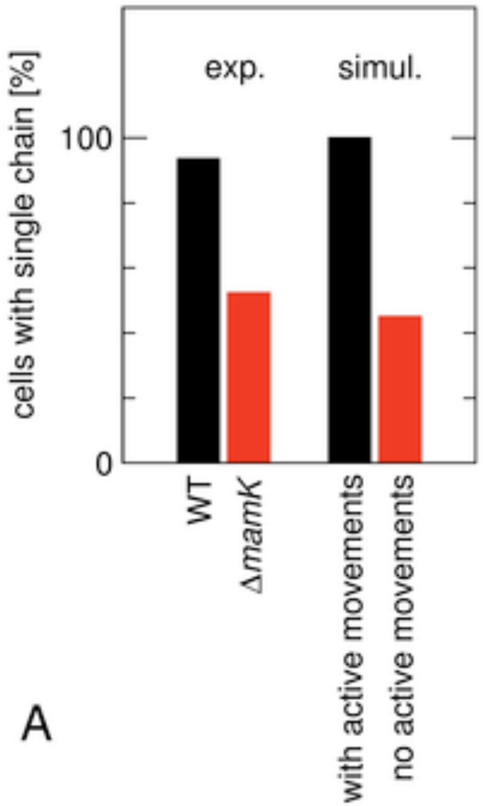
→ robust chain formation above velocity threshold v=$DF_{act}/(kT)$ ≈ 15 nm/min
→ competition with local chain formation
→ forces/velocities in range for (de-)polymerization motors

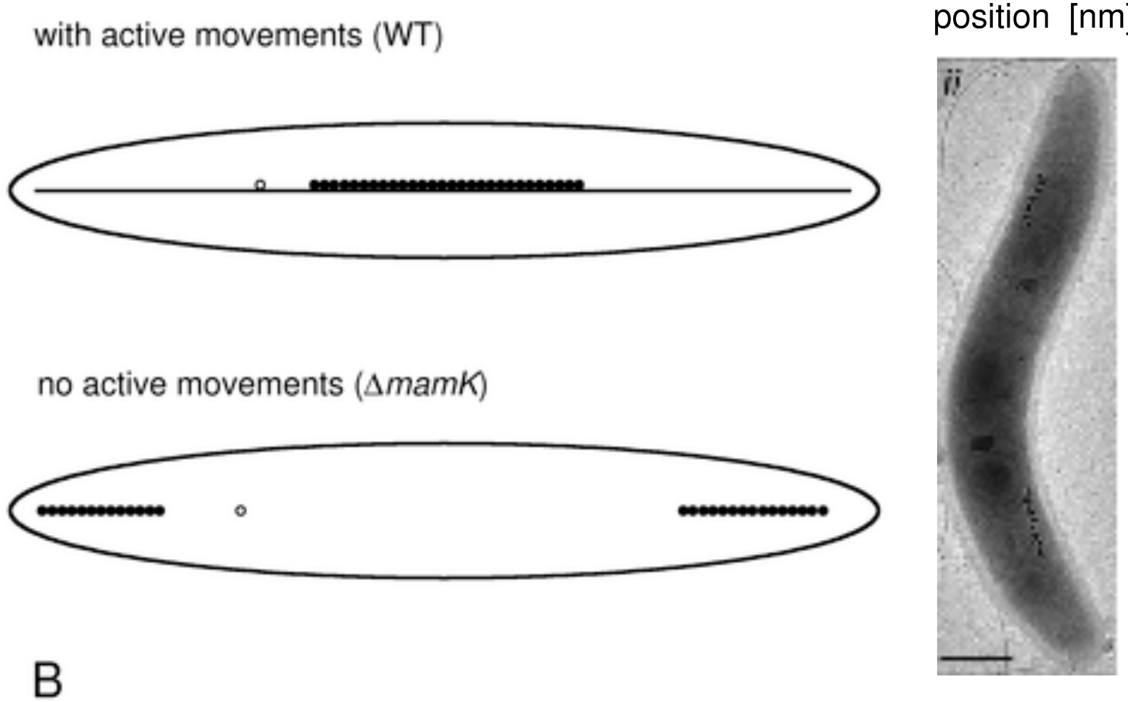
mamK deletion mutant

- MamK discovered as main protein of filaments

- *mamK* deletion in *M. gryphiswaldense*:
shorter chains, cells with multiple chains
[Katzmann et al. Mol. Micro 2010]





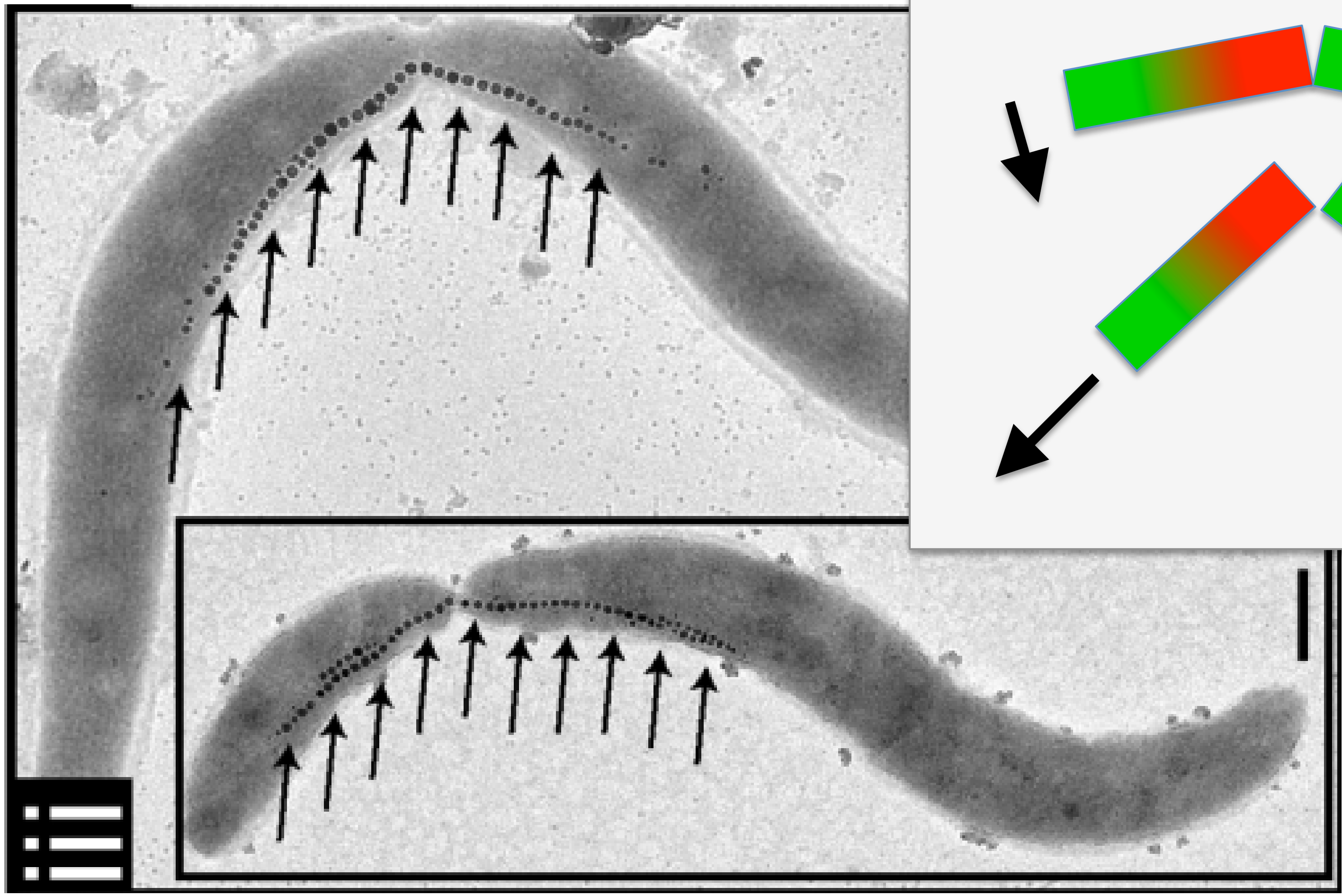


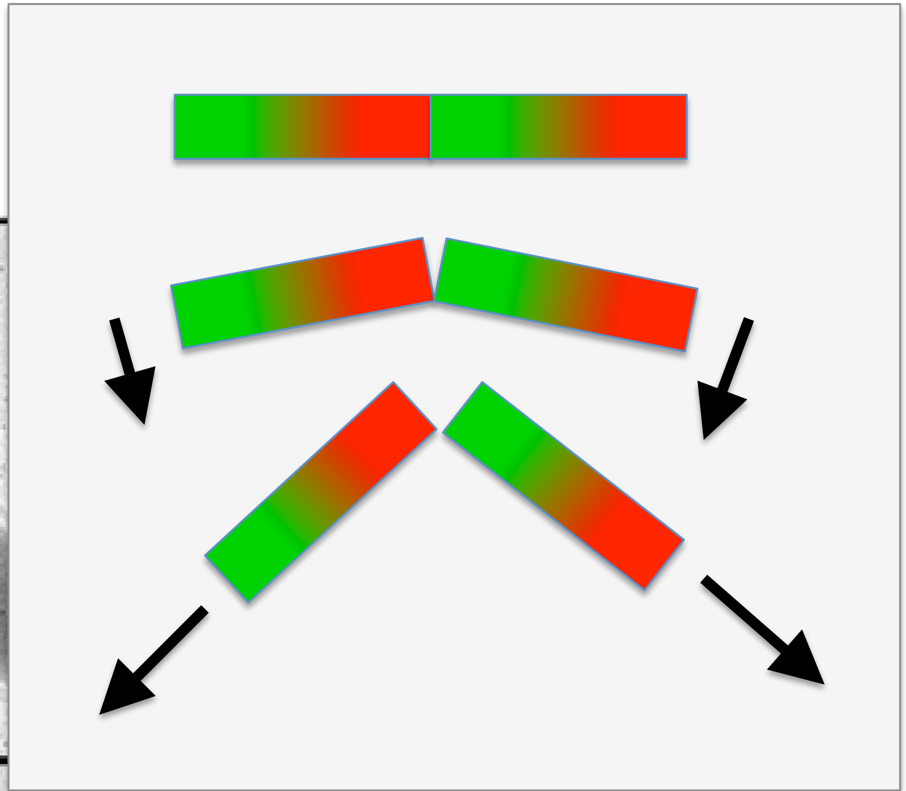
→ role for *mamK* in active transport (motor?)

Klumpp & Faivre, PLoS One 7, e33562 (2012)

Cell division in magnetotactic bacteria

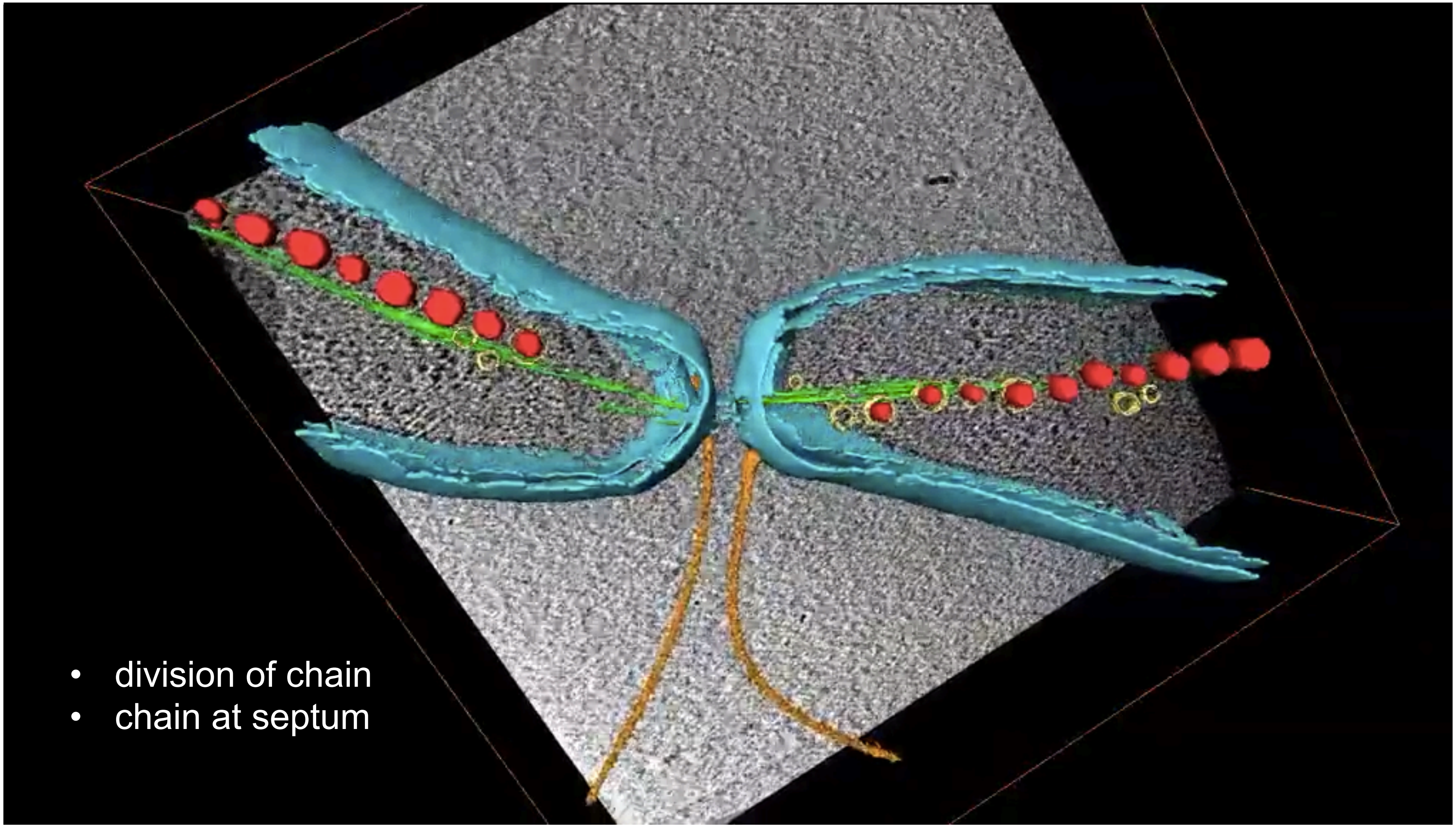
- magnetosome chain is divided
  → magnetic polarity inherited





Katzmann et al. 2011,
Staniland et al. 2010

Repositioning of the chain



➡ chain posittioned in cell center before division
chain repositioned to cell center after division

Mauricio Toro-Nahuelpan

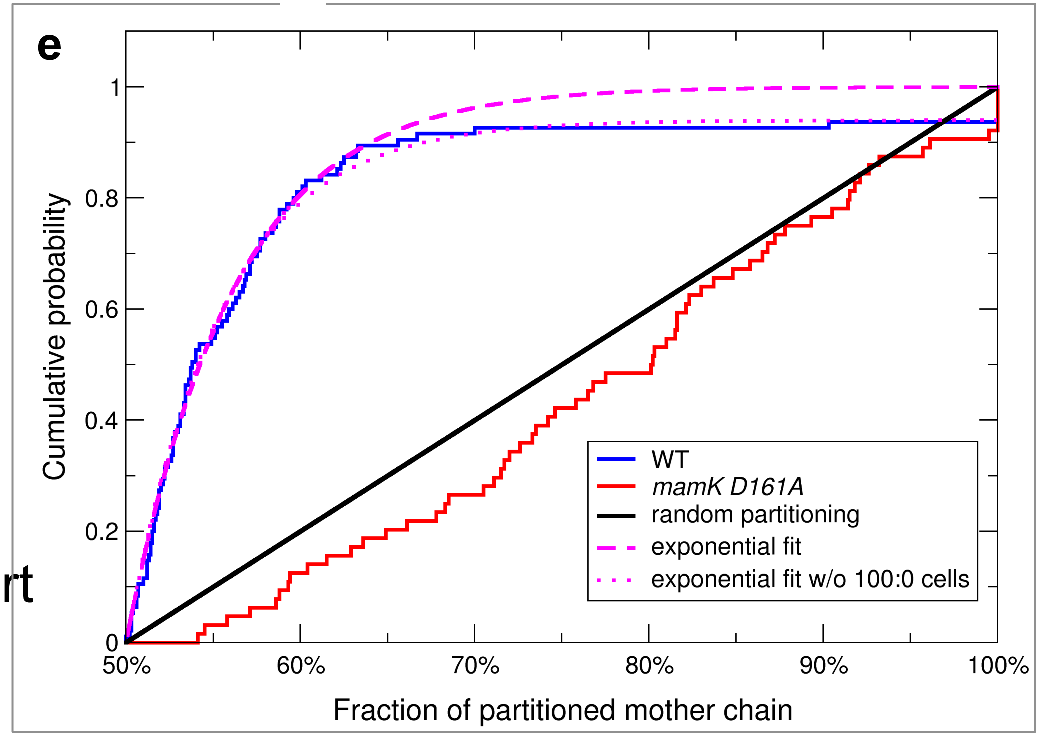
Before division: positioning in the cell center

quantitative analysis of chain partitioning:

- WT: precise partitioning
  (~6 % or ~1 magnetosome)
- *mamK* D161A: approx. random

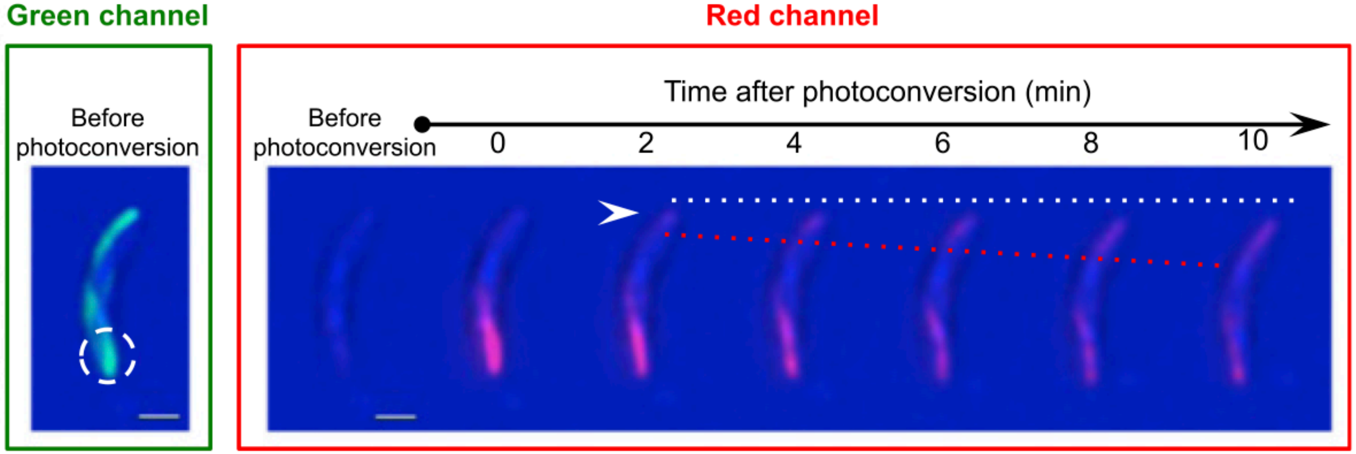
→ active positioning due to active filament

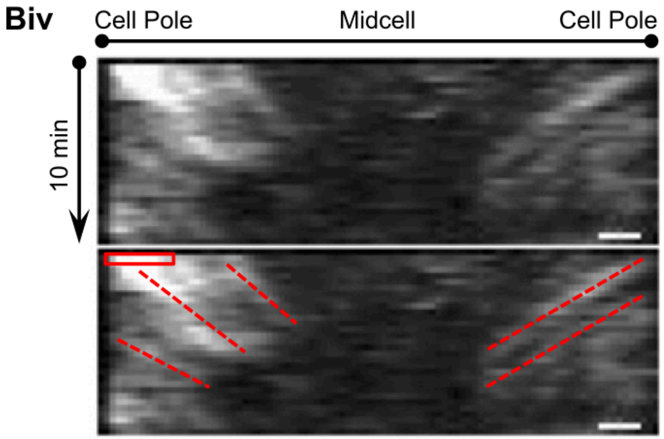
→ exp. fit: balance of active transport and diffusion



Toro-Nahuelpan et al. BMC Biol. 2016

Active filament

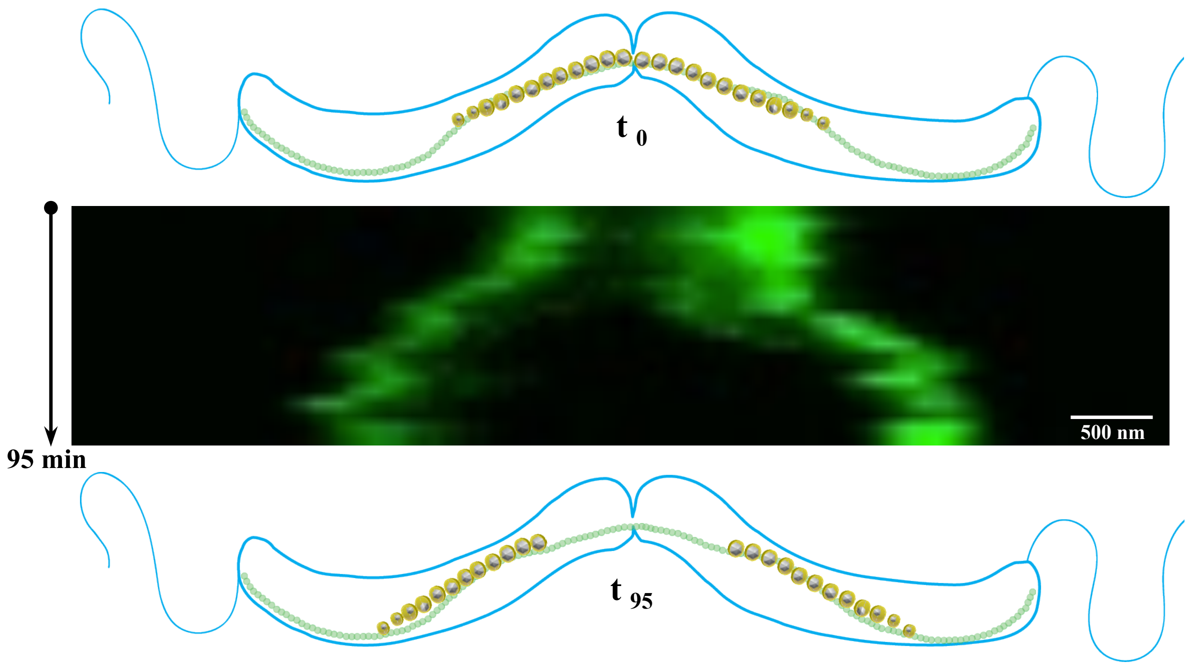


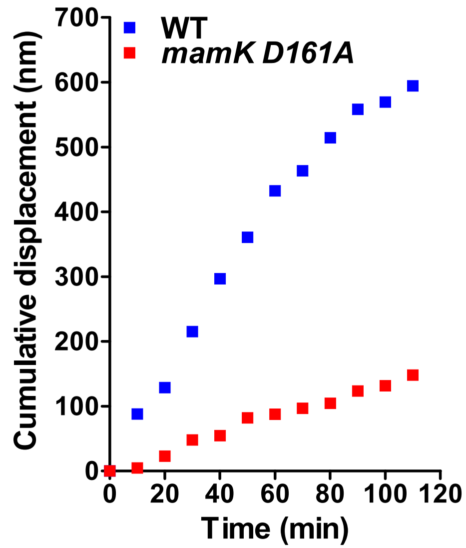


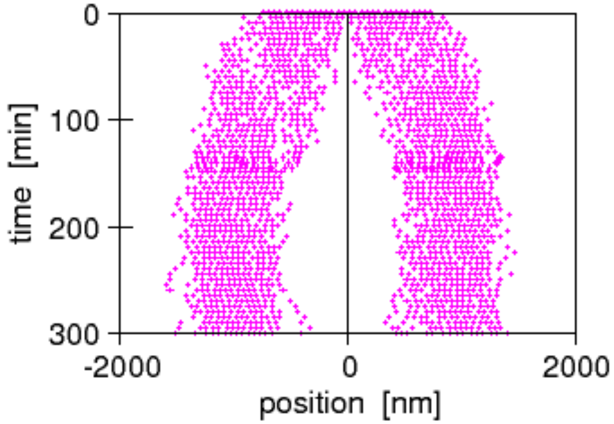
- labeled MamK travels to center from both poles
- speed 0.3 μm/min

Mauricio Toro-Nahuelpan

Repositioning after cell division







→ active movement to cell center
→ labeled magnetosomes slower than filament 7 nm/min
→ dependent on hydrolysis by filament

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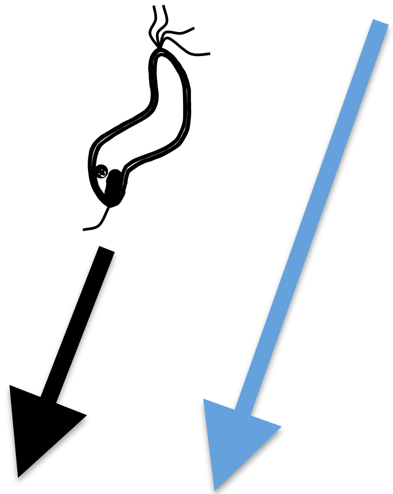
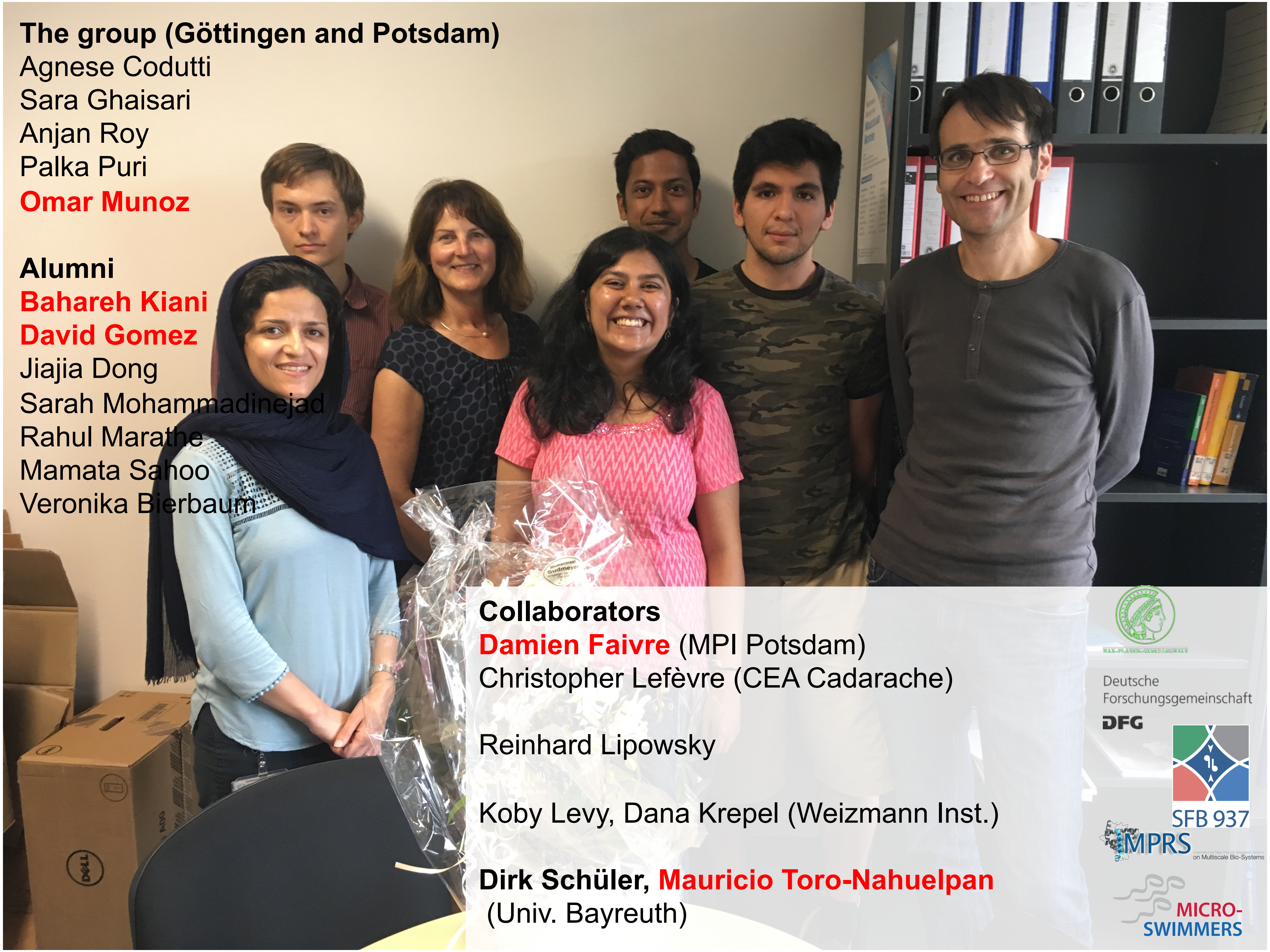
Summary

magnetotactic bacteria: model system to study role of physics in biology



- magnetism: new functions + constraints
- many interesting problems to be studied
- key role of active processes
- challenge: generic physical forces and specific signals (chemotactic signaling etc.)



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