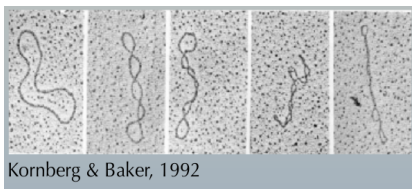
Biophysical modeling of bacterial DNA segregation

Jean-Charles WALTER

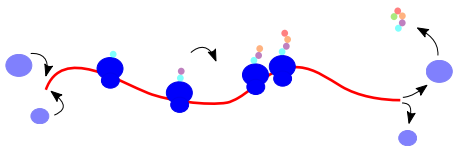
Laboratoire Charles Coulomb (L2C)
CNRS & Université de Montpellier

Institute for Condensed Matter Physics (NAS)
Lviv, Ukraine
2nd of March 2023

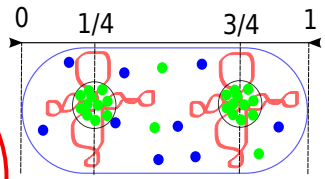
Physics meets Biology

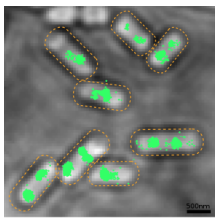


New paradigm of Matter



Self-organized & regulated systems





Micro scopy

Molecular Biology

Biology

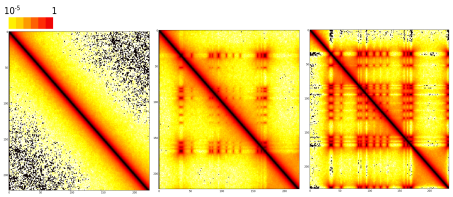
Polymers

Physics

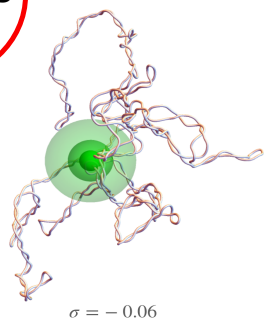
Active Matter

Colloids

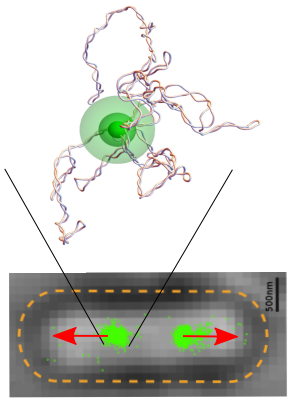
- Storage of information
- Variability of gene expression
- Membraneless compartments

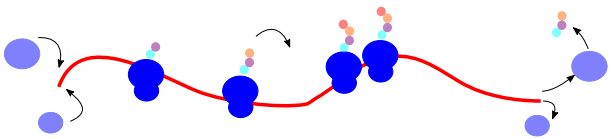


Structural interconnectivity



Genomic physics

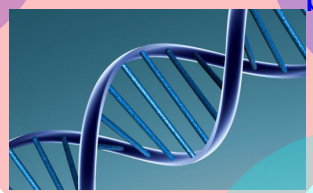


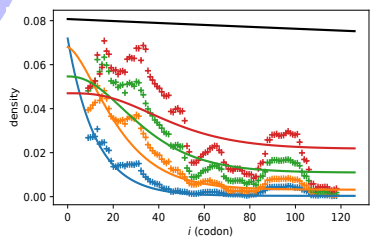


Bacterial DNA organization & segregation

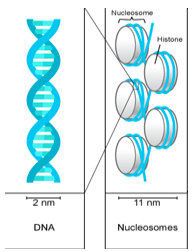
genomic physics

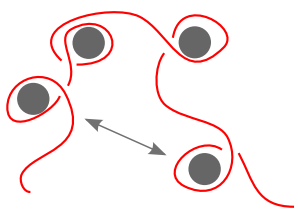
Translation of messenger RNA by ribosomes

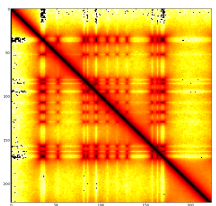




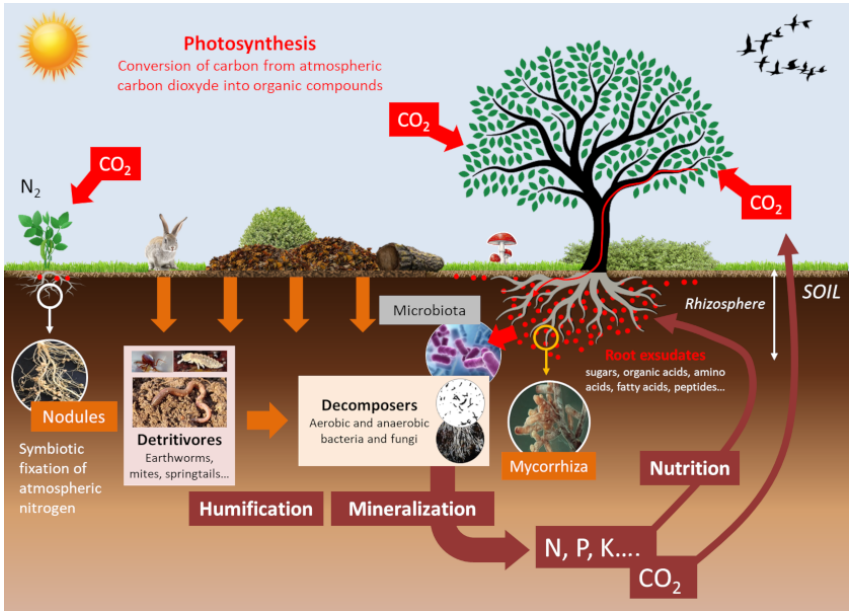
Epigenetic regulation of eukaryotic chromatin





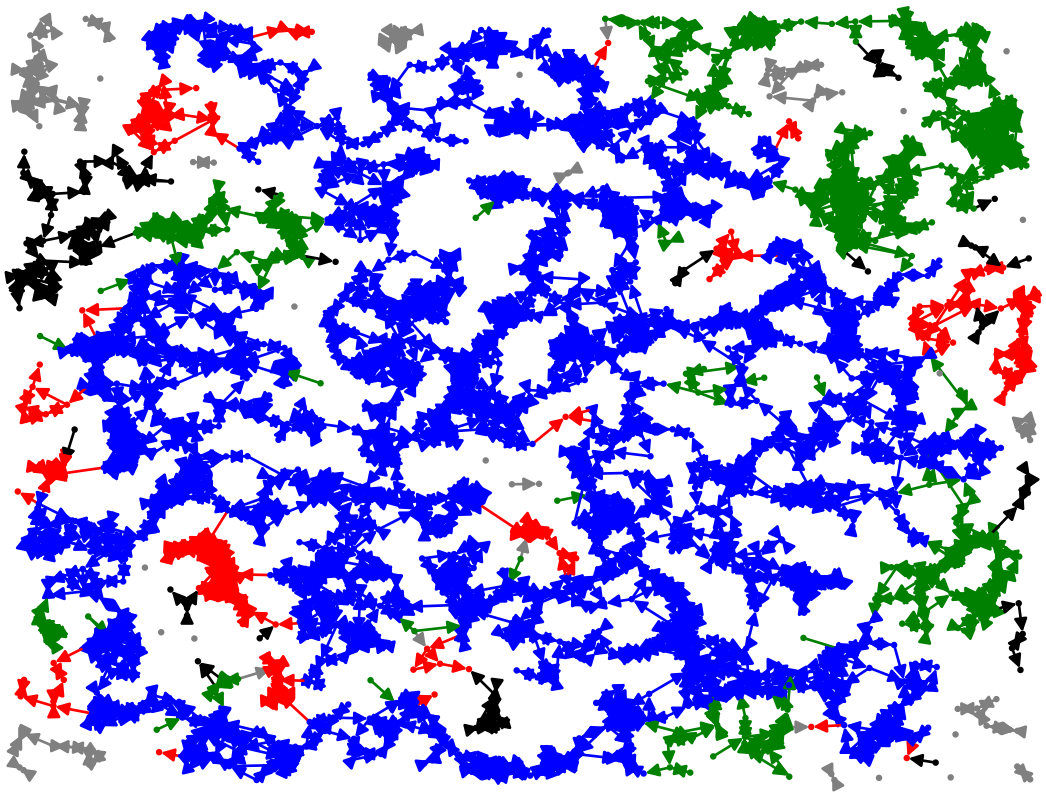


Plant-microbiote interactions



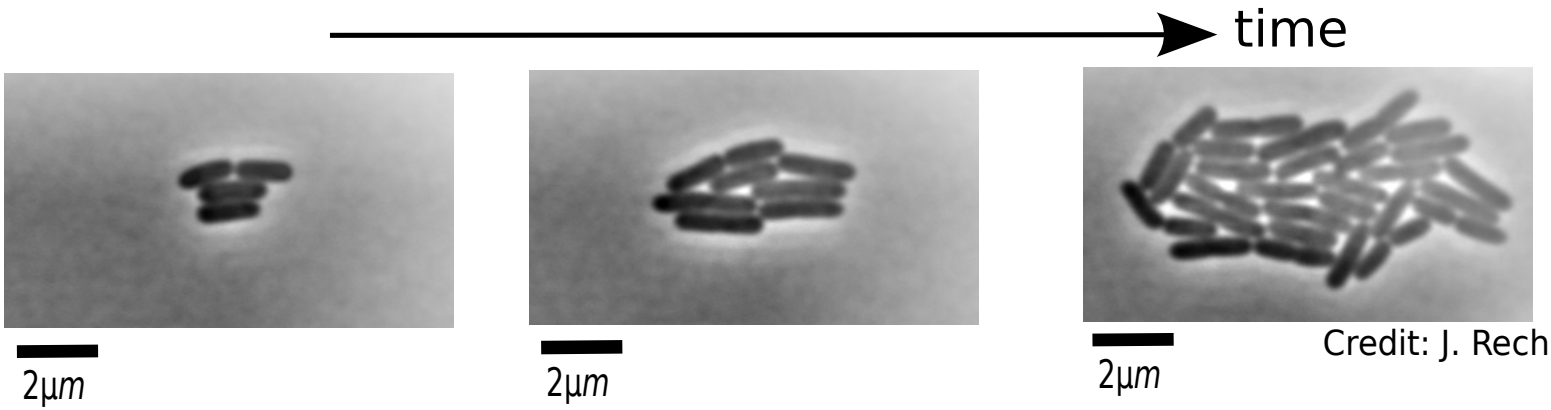
- Lotka-Volerra-like modeling of microbial population dynamics

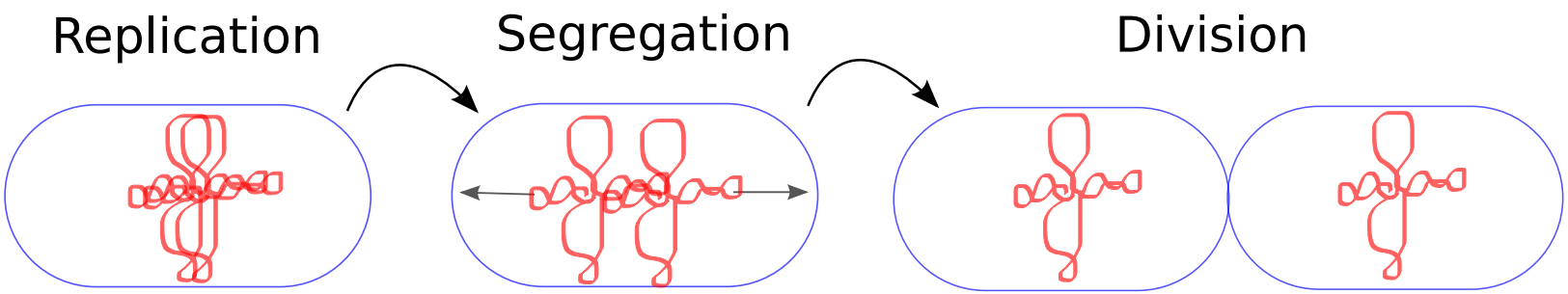
Directed random geometric graphs



- Effect of directedness on the critical properties at percolation

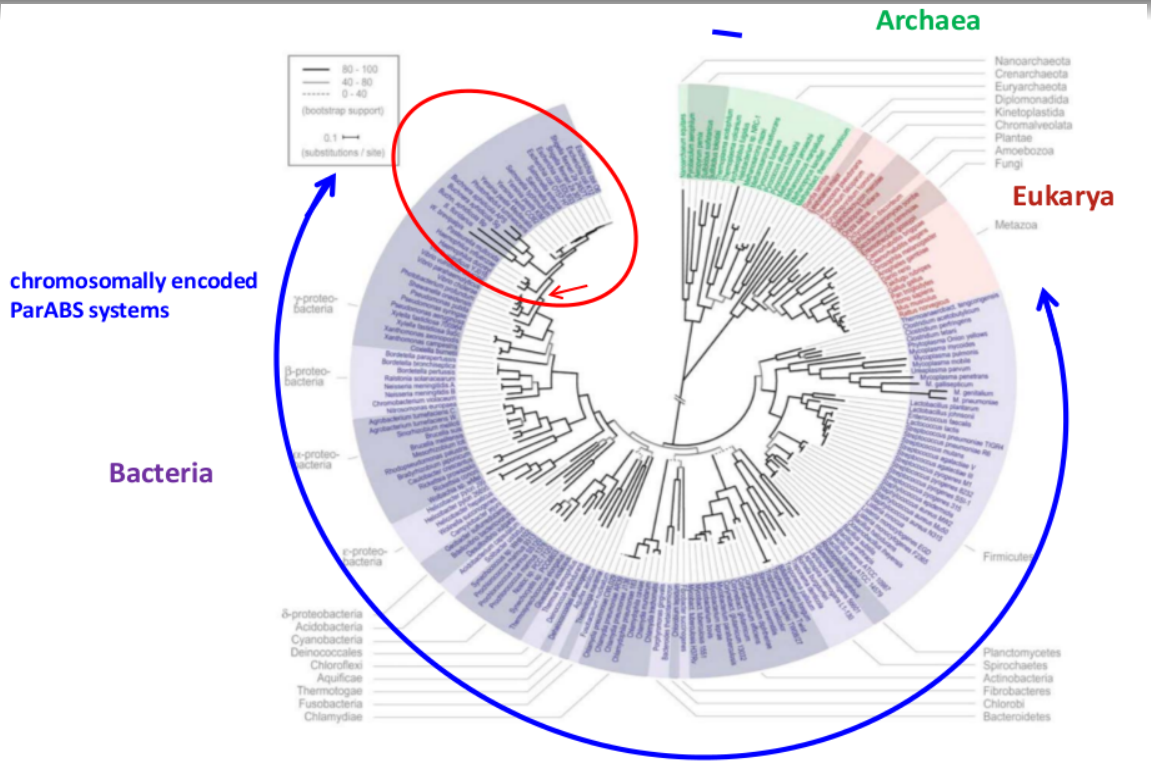
Bacterial DNA segregation





How is the bacterial genome segregated ?

Bacterial DNA segregation: the ParAB*S* system

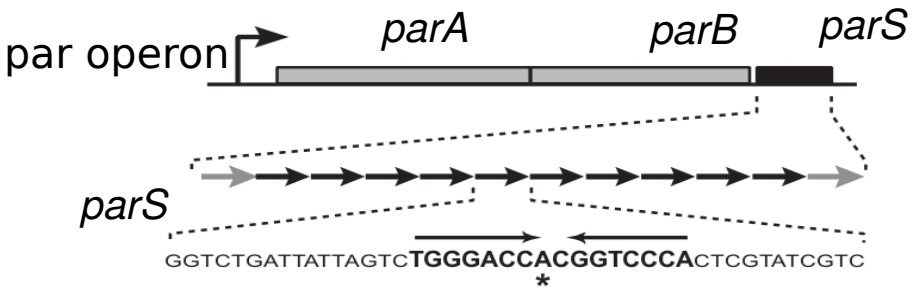


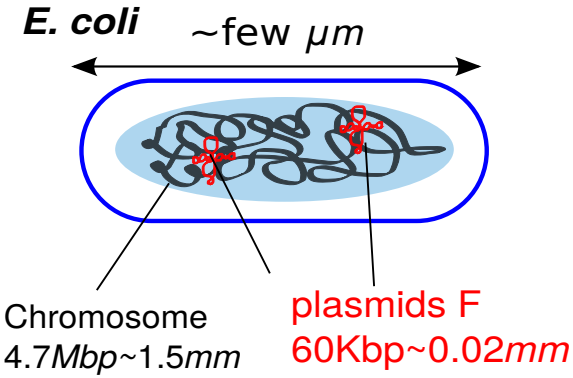
Credit: J-Y. Bouet

→ ParAB*S* is strongly conserved

→ Ancient mechanism of liquid-liquid phase separation (**LLPS**)

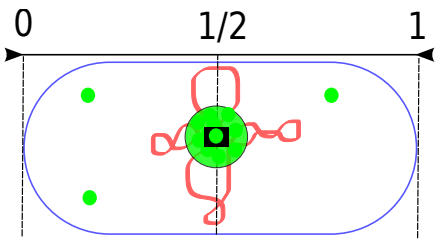
The ParAB*S* system: the molecular actors





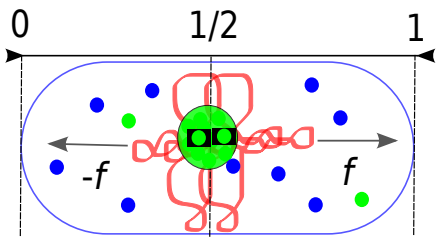
- ParA: “motor” protein (ATPase)
- ParB: binding protein (specific or non-specific binding)
- *parS*: specific DNA sequence

Bacterial DNA segregation: the ParAB*S* system



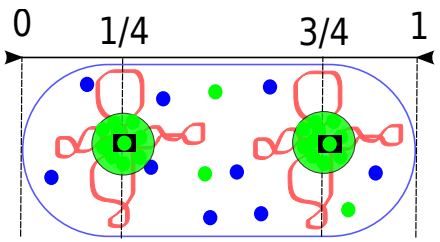
Step 1. Formation of ParB*S*

Equilibrium LLPS ?

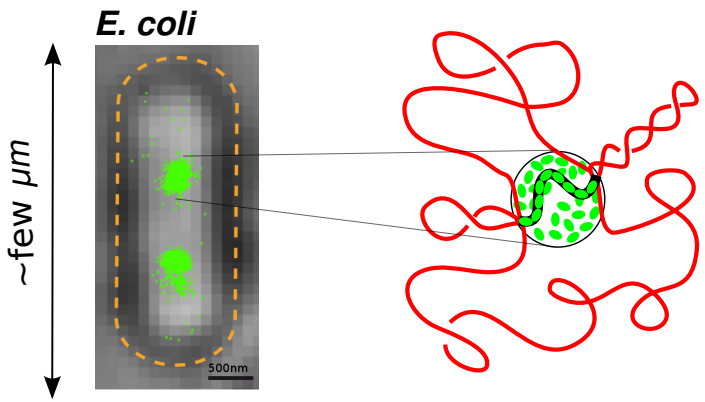


Step 2. Separation of DNA copies

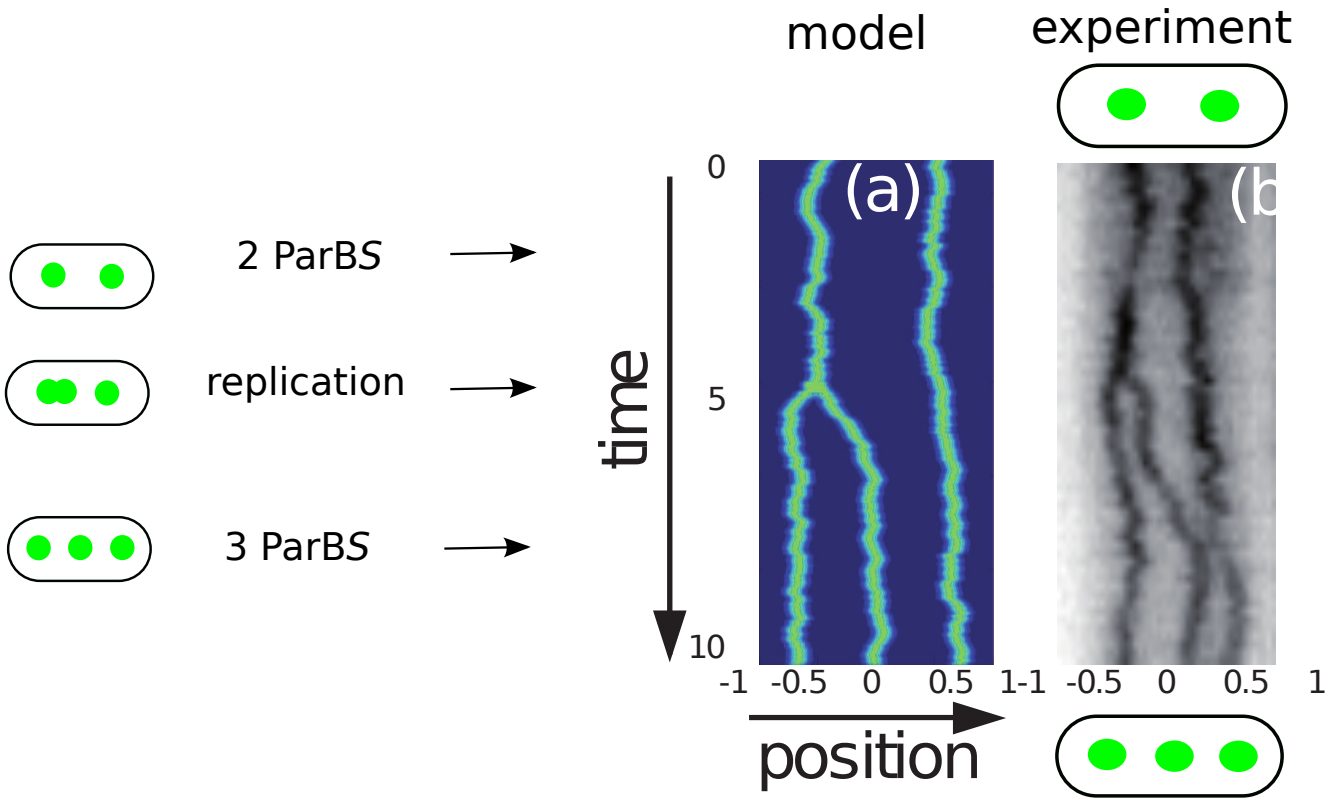
Non-eq. phase separation (ATP)



Step 3. Equipositioning

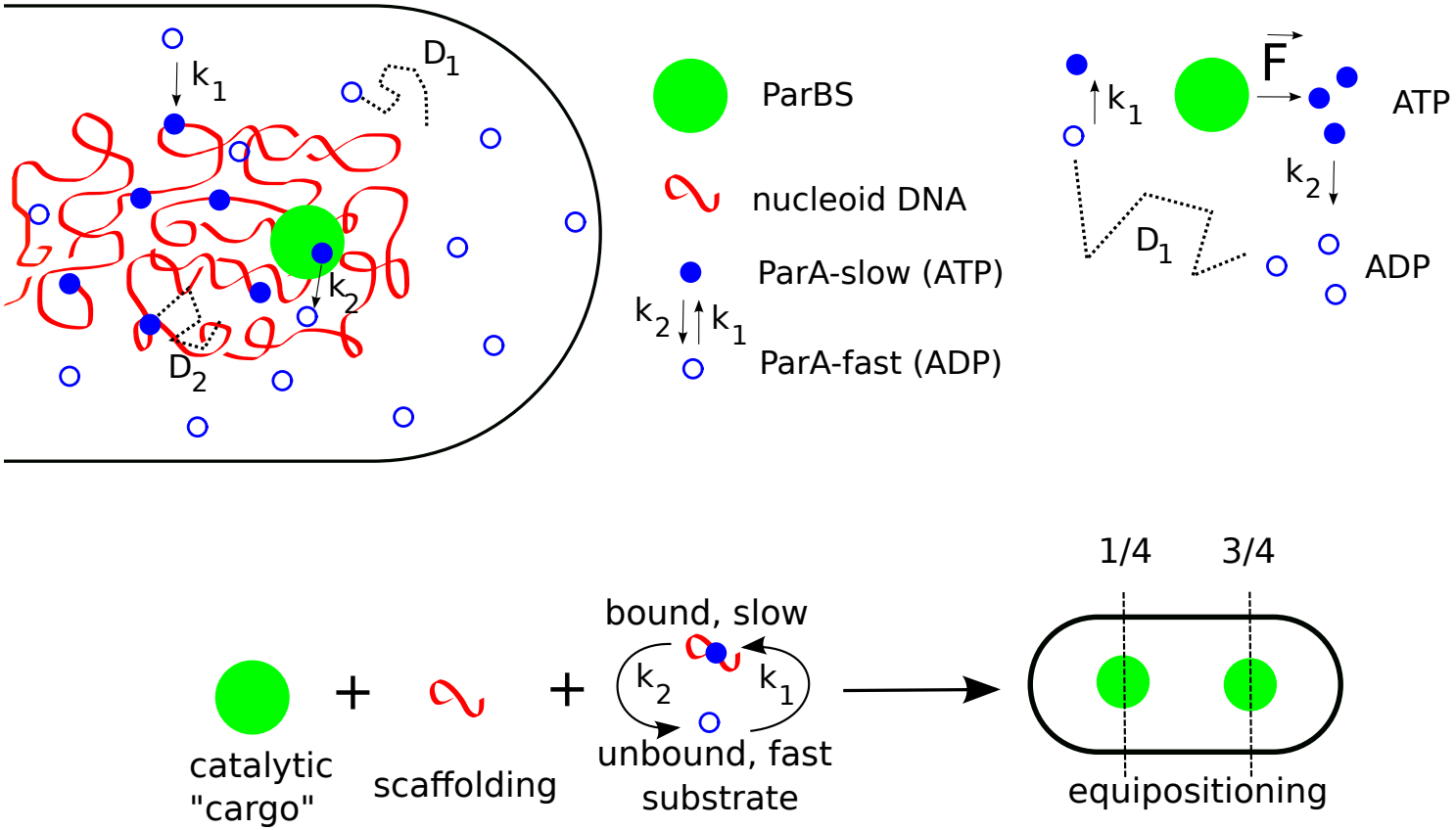


Equipositioning along the cell axis



What are the main physical actors of DNA segregation ?

Reaction-diffusion process: Molecular interactions



Reaction-Diffusion equations

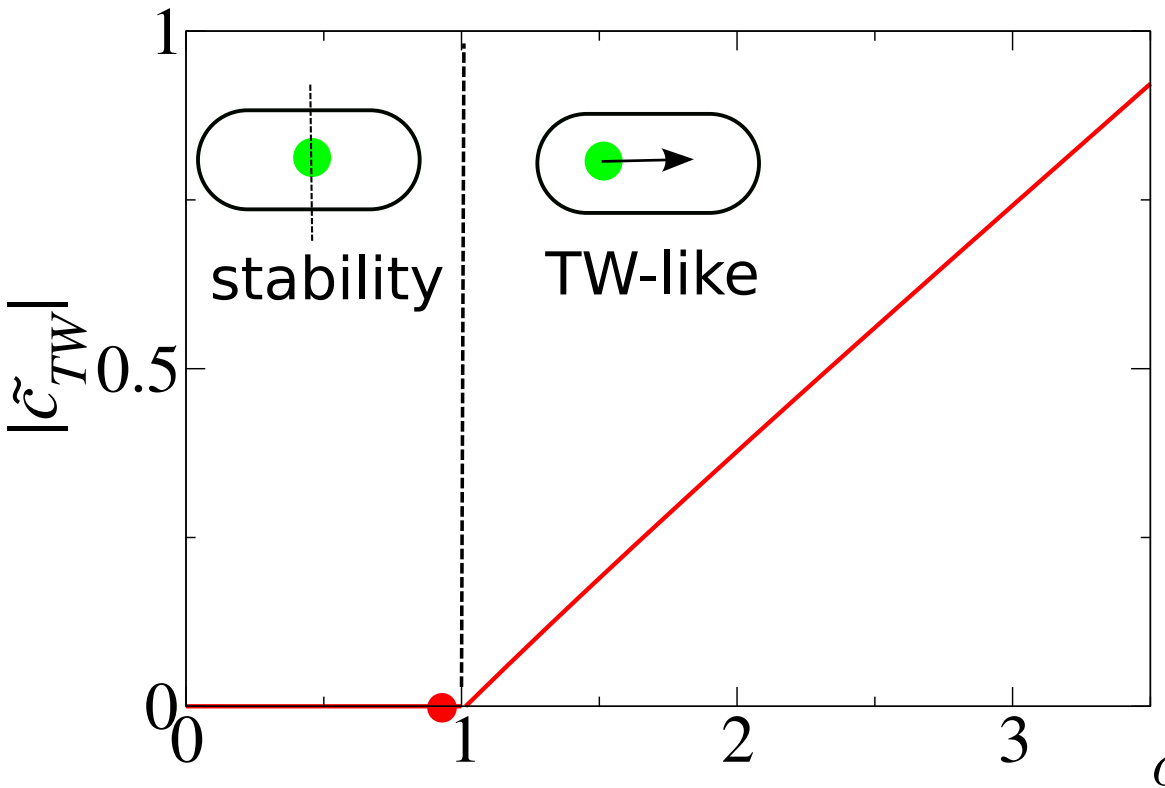
ParA-slow (ATP): $$\frac{\partial v}{\partial t} = D_2\,\Delta v + k_1\,u(\mathbf{r},t) - k_2\,v(\mathbf{r},t)\sum_i S(\mathbf{r}-\mathbf{r}_i(t))$$

ParA-fast (ADP): $$\frac{\partial u}{\partial t} = D_1\,\Delta u - k_1\,u(\mathbf{r},t) + k_2\,v(\mathbf{r},t)\sum_i S(\mathbf{r}-\mathbf{r}_i(t))$$

ParB*S*: $$m\gamma\frac{d\mathbf{r}_i}{dt}(t) = \varepsilon\int_V \nabla v(\mathbf{r}',t)\,S(\mathbf{r}'-\mathbf{r}_i(t))\,d^3\mathbf{r}'$$

- Feedback between the partition complexes and ParA densities
  $\rightarrow$ Non-linear system with dynamical instability

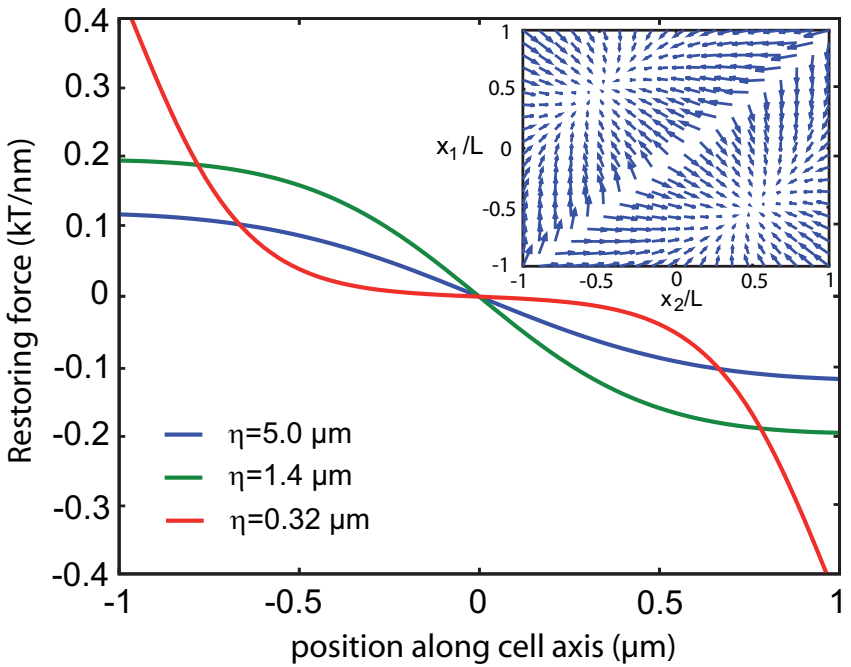
Dynamical instability: bifurcation obtained with Traveling Wave ansatz

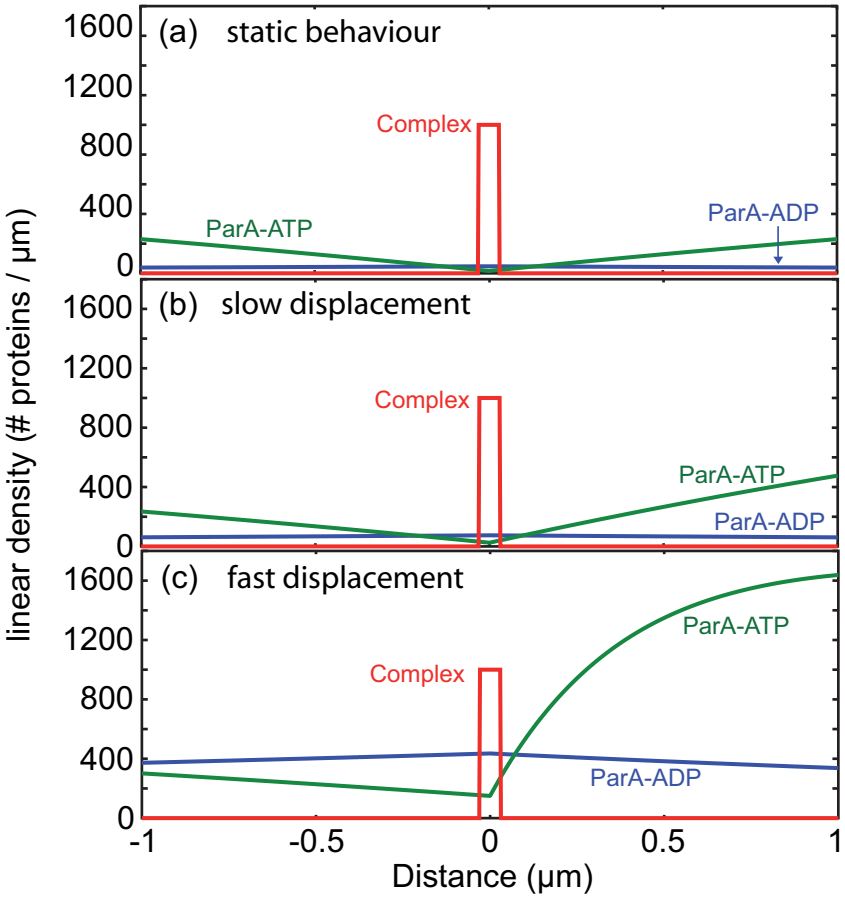


$$\frac{\alpha}{\alpha_c} = \frac{\varepsilon N_p}{m\gamma D_2}$$

Restoring force & gradient of ParA-ATP

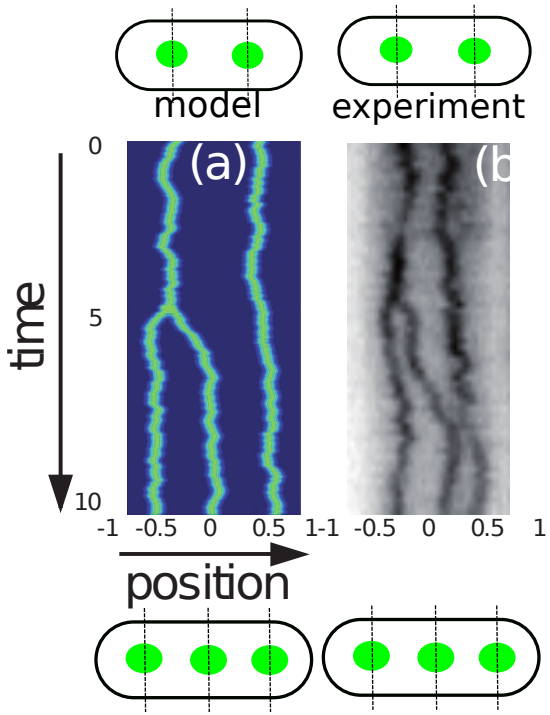
$$\eta = \sqrt{\frac{D_1}{k_1}}$$



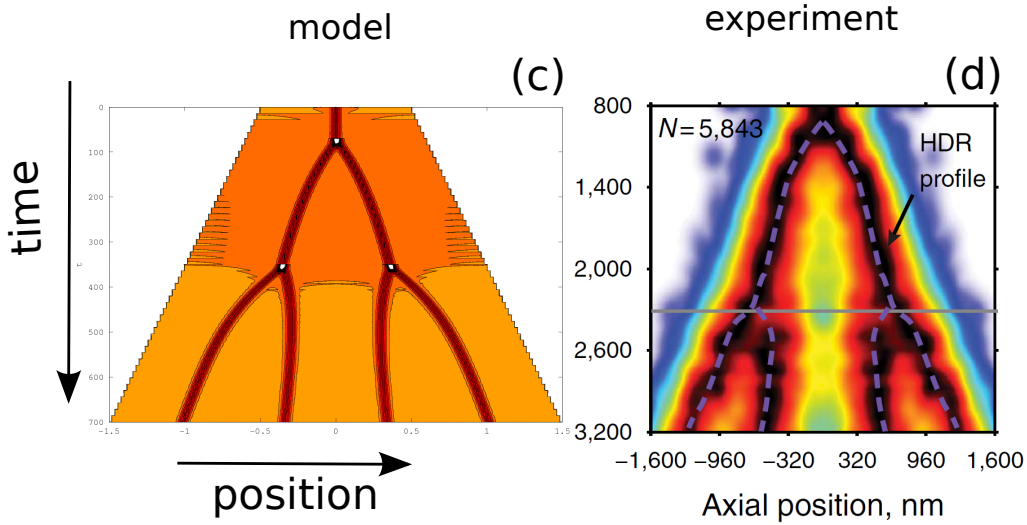


Comparison with experiments

Single cell

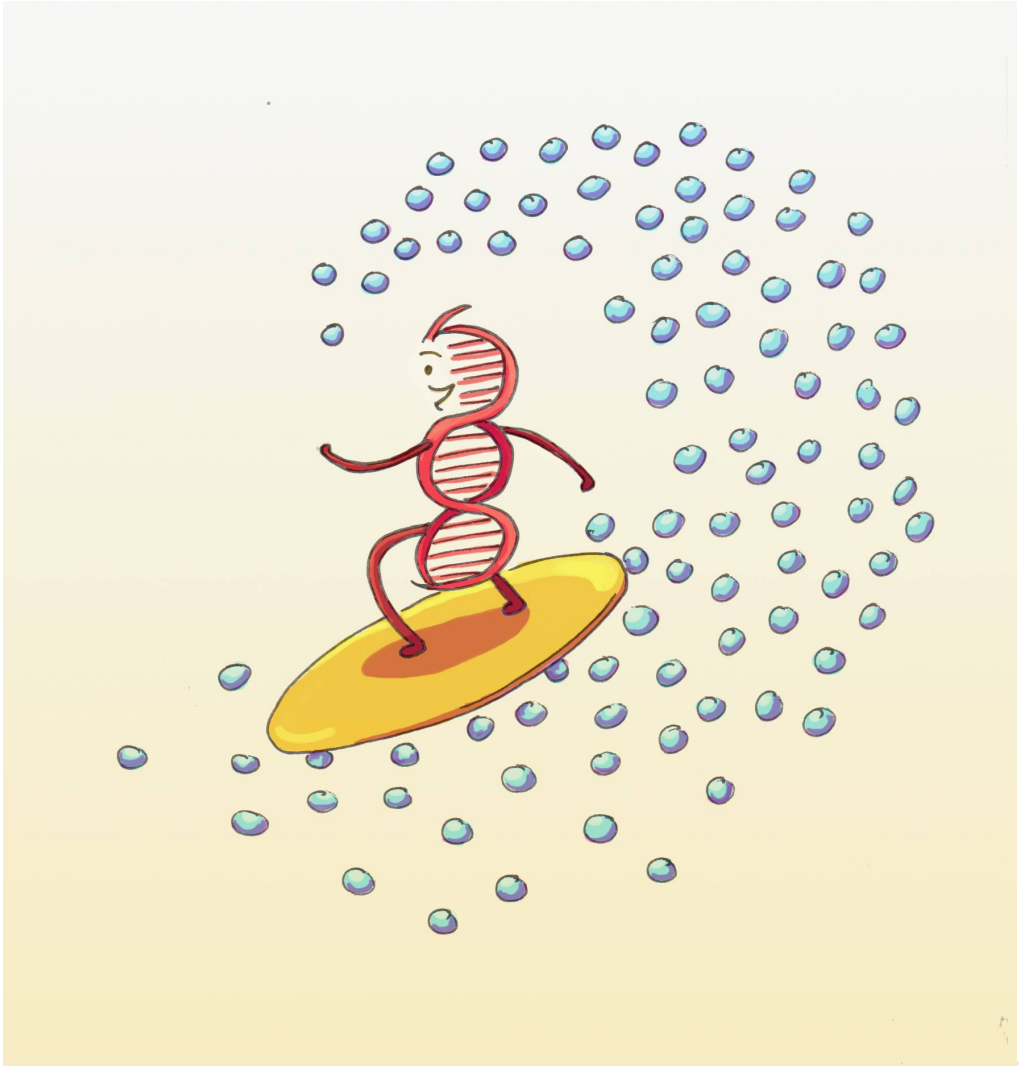


Average

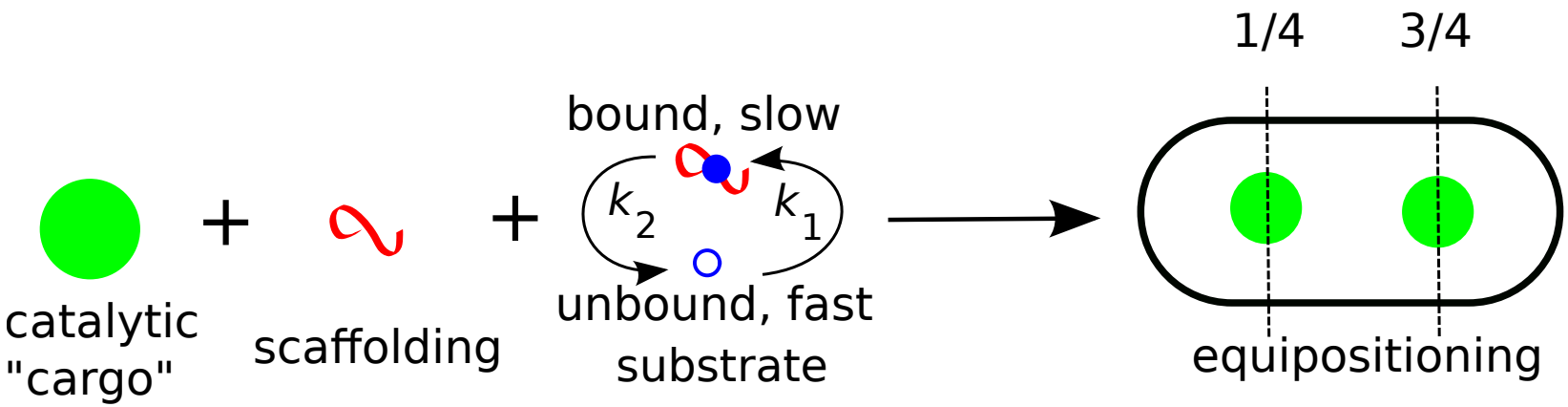


Fluorescence microscopy & Superresolution microscopy

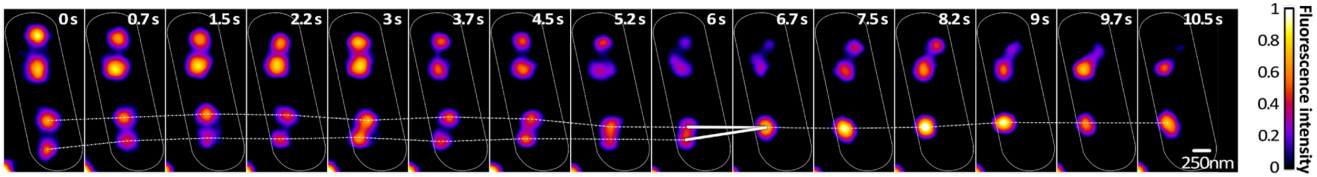
Conclusion

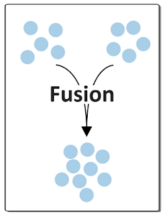


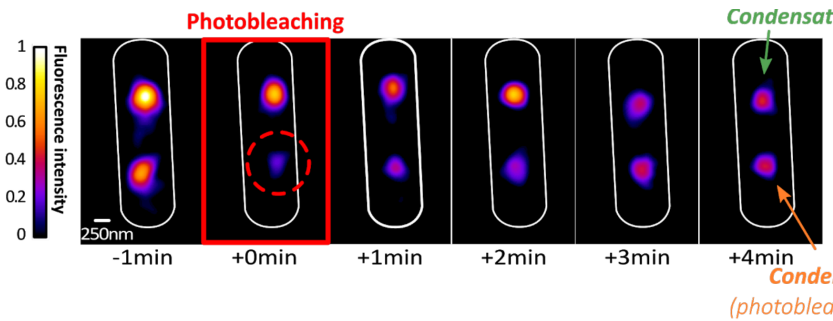
Conclusion

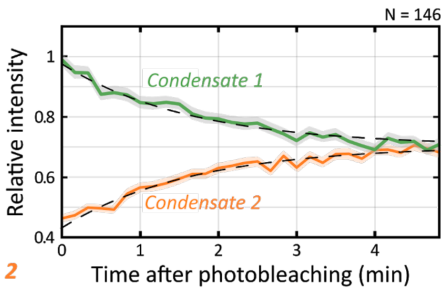

bound, slow
k_2
k_1
unbound, fast
substrate
catalytic
"cargo"
scaffolding
1/4
3/4
equipositioning

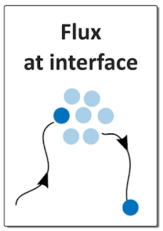
Liquid-like behaviour of ParB*S* complexes



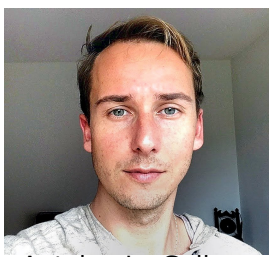






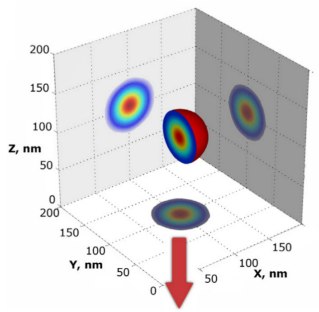


Baptiste Guilhas



Antoine Le Gall

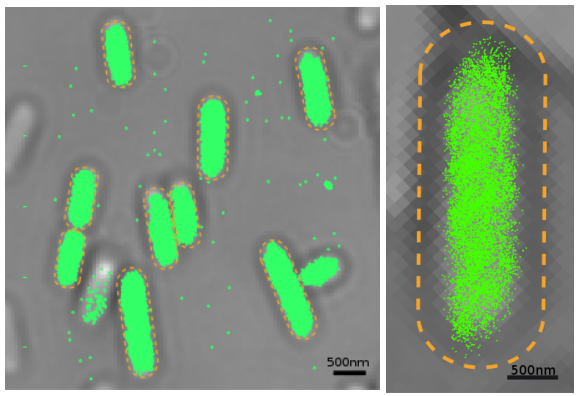
Nollmann's Lab, CBS, Montpellier



Diameter
37 nm ± 5

Guilhas, JCW,...Le Gall, Nollmann **ATP-driven separation of liquid phase condensates in bacteria** *Mol. Cell* '20

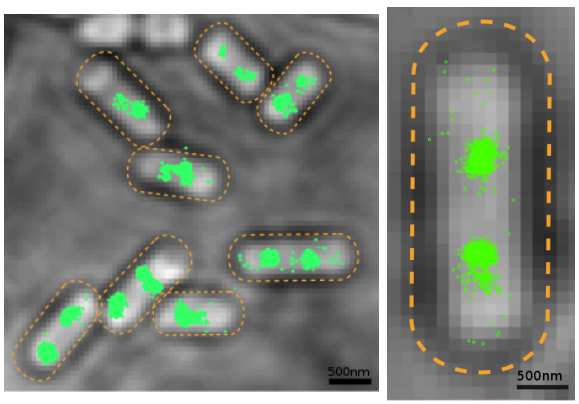
Liquid-like behaviour of ParB*S* complexes



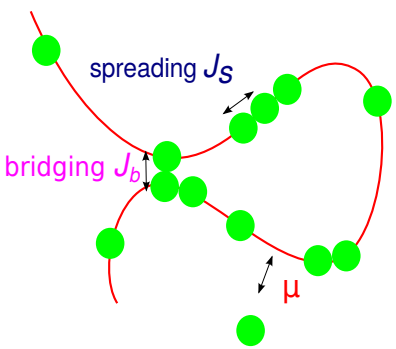
vapor

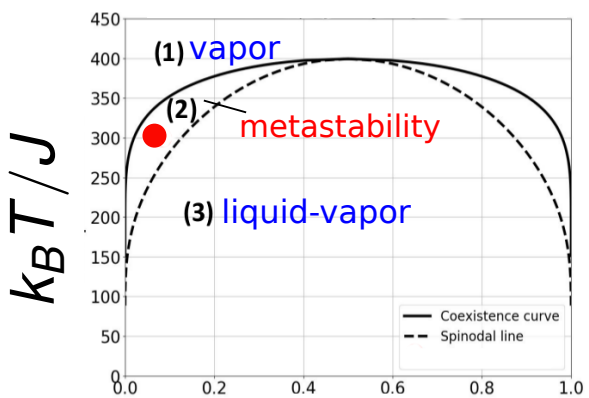
specific binding

ParB/*parS*



liquid-vapor





Thank you for your attention!