

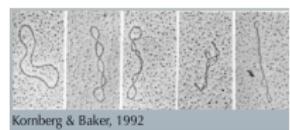
Biophysical modeling of bacterial DNA segregation

Jean-Charles WALTER

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CNRS & Université de Montpellier*

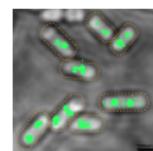
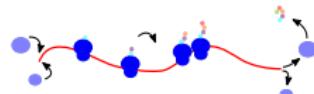
SPLDS22
Pont-à-Mousson, France
May 2022

Physics meets Biology



New paradigm of Matter

Self-organized & regulated systems



Microscopy
Molecular Biology

Biology

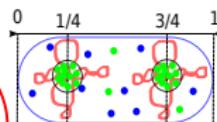


Physics

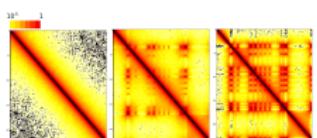
Polymers

Active Matter

Colloids



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

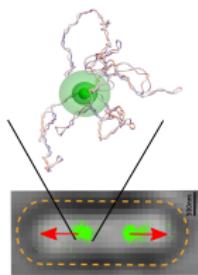


Structural interconnectivity



$$\sigma = -0.06$$

Genomic physics



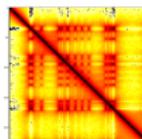
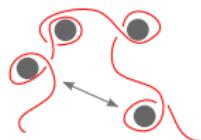
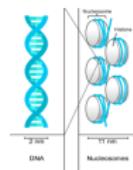
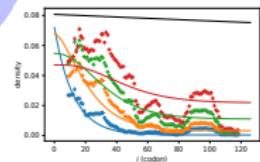
Bacterial DNA organization & segregation

genomic
physics

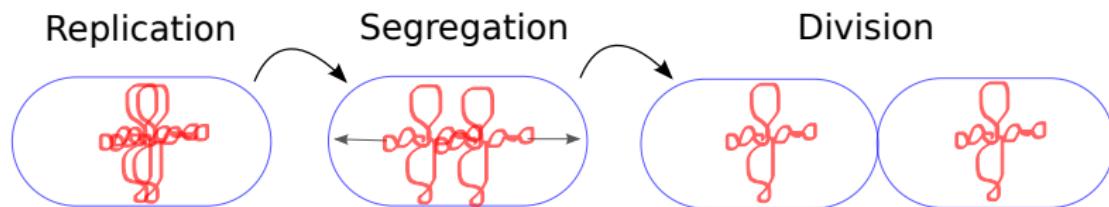
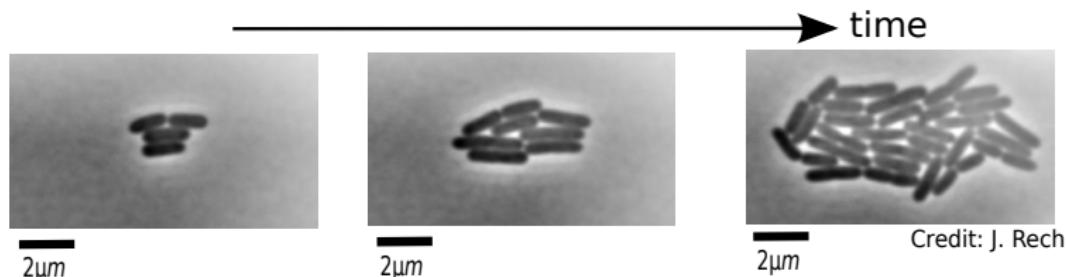


Translation of messenger RNA by ribosomes

Epigenetic regulation of eukaryotic chromatin

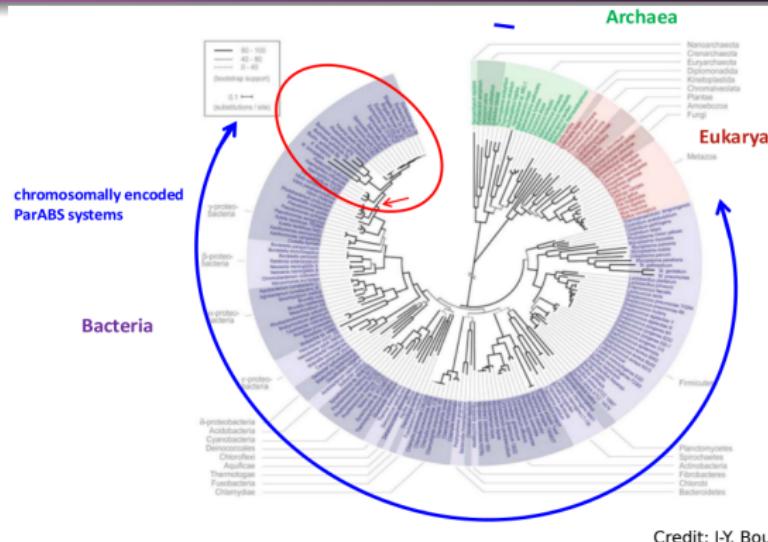


Bacterial DNA segregation



How is the bacterial genome segregated ?

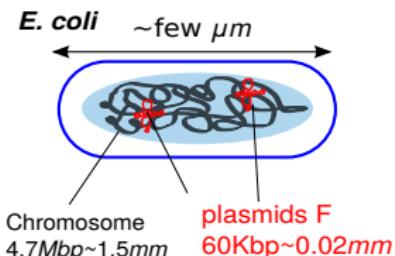
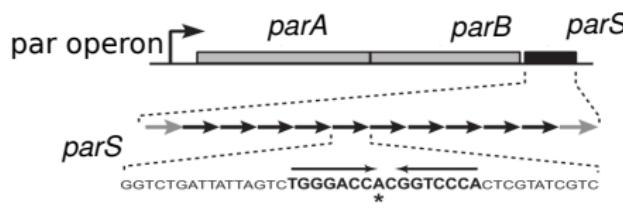
Bacterial DNA segregation: the ParABS system



Credit: J-Y. Bouet

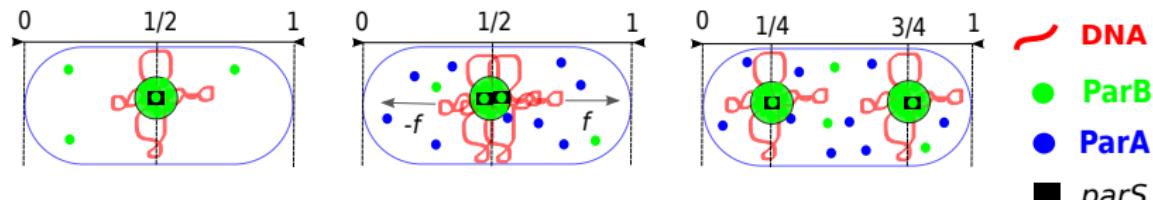
- ParABS is strongly conserved
- Ancient mechanism of liquid-liquid phase separation (LLPS)

The ParABS system: the molecular actors



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

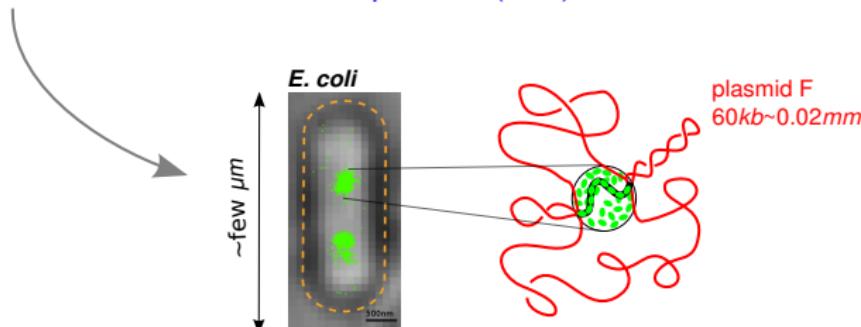
Bacterial DNA segregation: the ParABS system



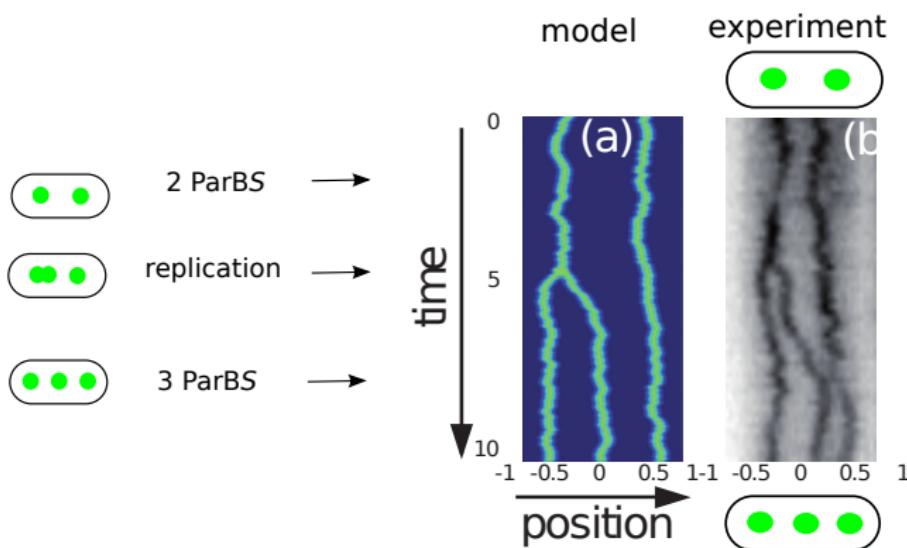
Step 1. Formation of ParBS
Equilibrium LLPS ?

Step 2. Separation of DNA copies
Non-eq. phase separation (ATP)

Step 3.
Equipoiontoring

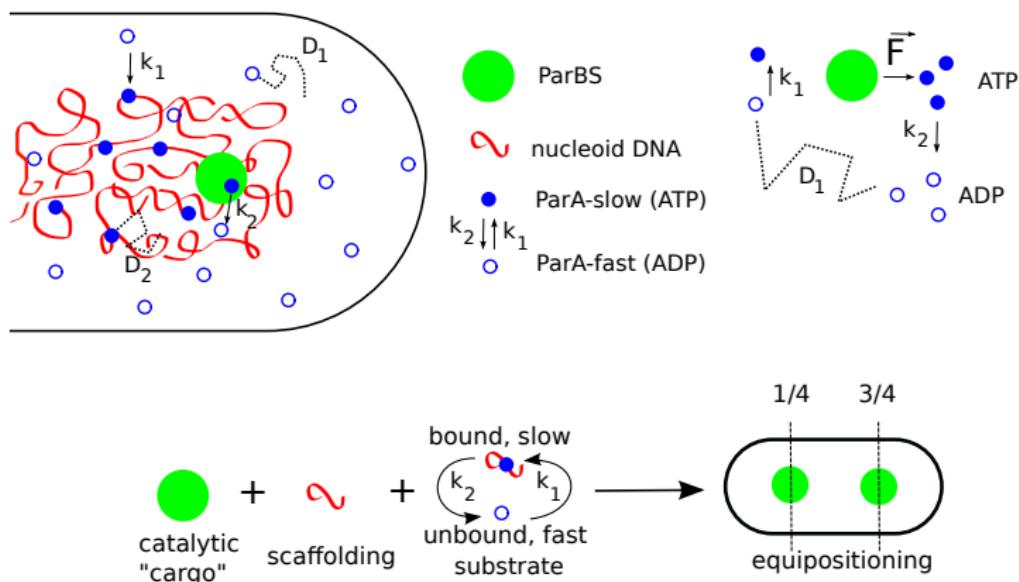


Equipositioning along the cell axis



What are the main physical actors of DNA segregation ?

Reaction-diffusion process: Molecular interactions



Reaction-Diffusion equations

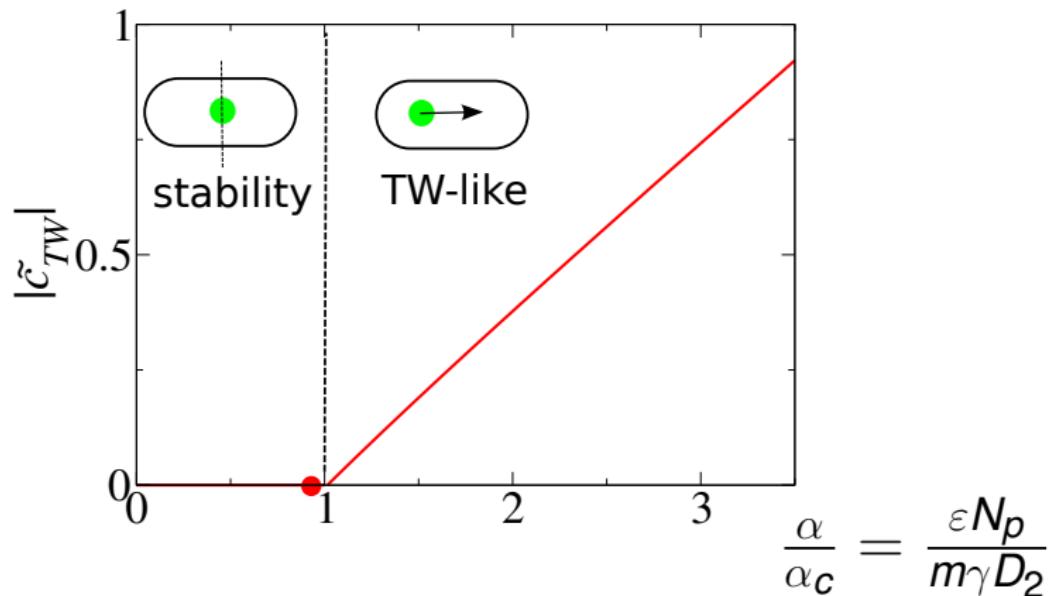
$$\text{ParA-slow (ATP): } \frac{\partial \textcolor{red}{v}}{\partial t} = D_2 \Delta \textcolor{red}{v} + k_1 \textcolor{blue}{u}(\mathbf{r}, t) - k_2 \textcolor{red}{v}(\mathbf{r}, t) \sum_i \textcolor{green}{S}(\mathbf{r} - \mathbf{r}_i(t))$$

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

$$\text{ParBS: } m\gamma \frac{d\mathbf{r}_i}{dt}(t) = \varepsilon \int_V \nabla \textcolor{red}{v}(\mathbf{r}', t) \textcolor{green}{S}(\mathbf{r}' - \mathbf{r}_i(t)) d^3\mathbf{r}'$$

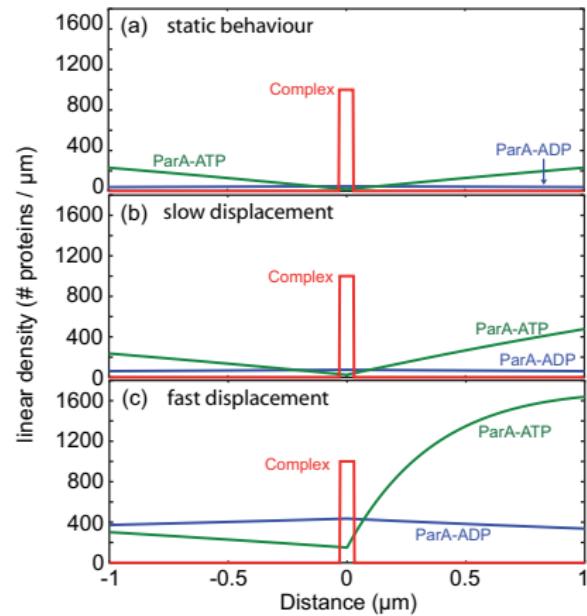
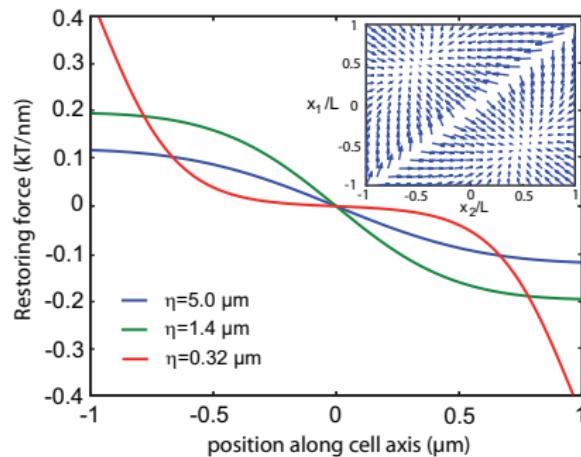
- **Feedback** between the partition complexes and ParA densities
→ Non-linear system with **dynamical instability**

Dynamical instability: bifurcation obtained with Traveling Wave ansatz

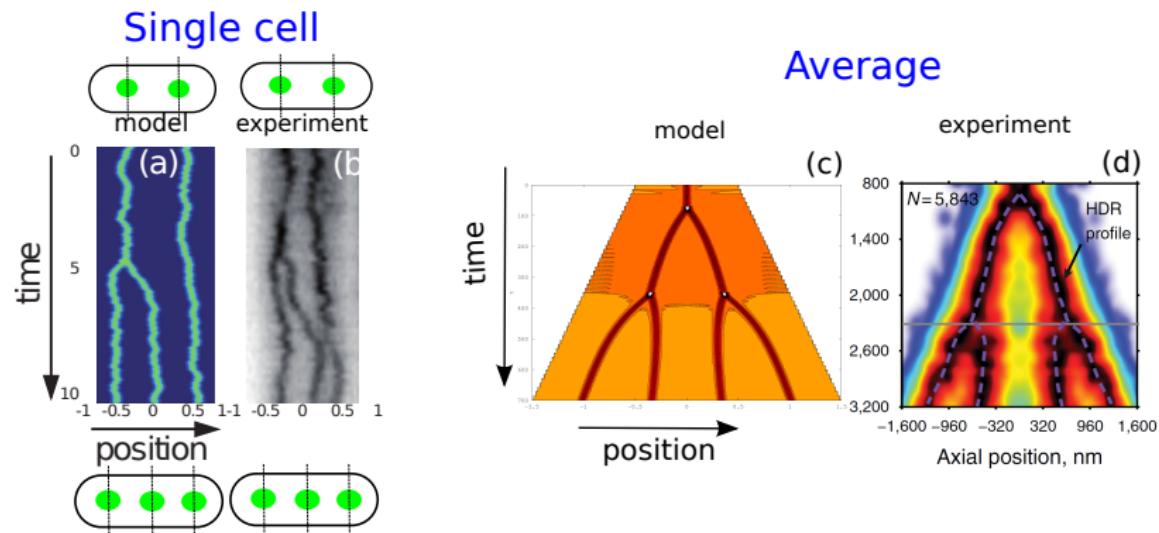


Restoring force & gradient of ParA-ATP

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

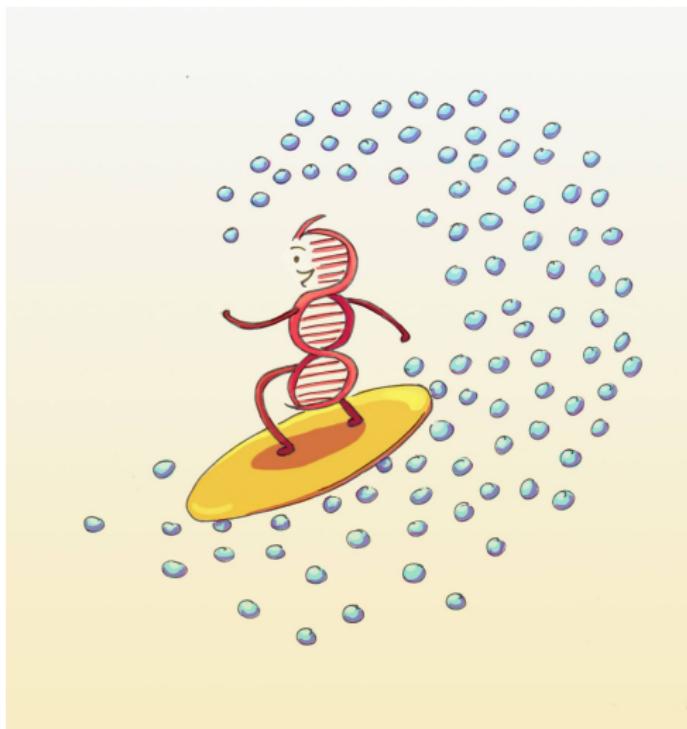


Comparison with experiments

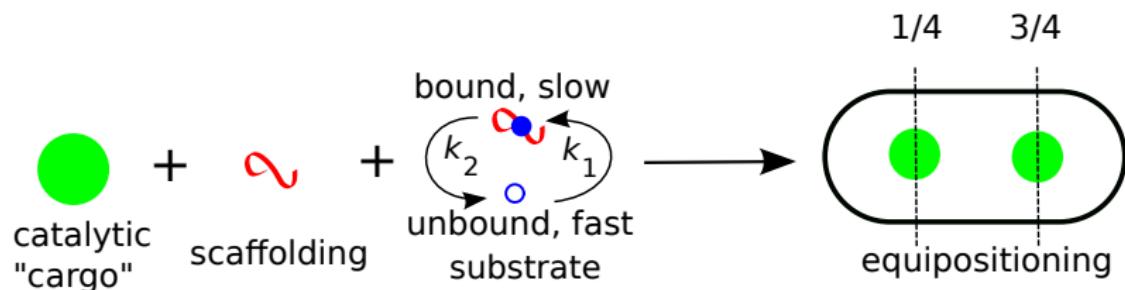


Fluorescence microscopy & Superresolution microscopy

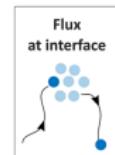
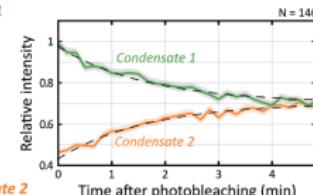
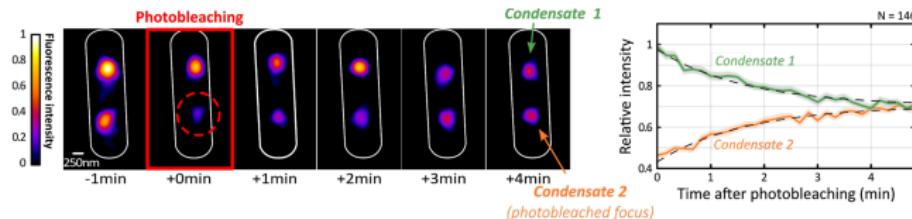
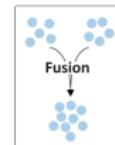
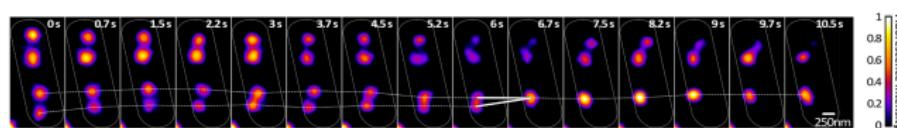
Conclusion



Conclusion



Liquid-like behaviour of ParBS complexes

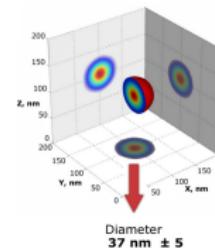


Baptiste Guilhas



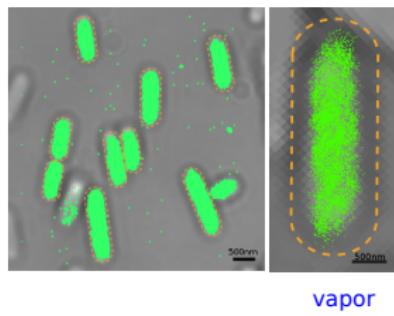
Antoine Le Gall

Nollmann's Lab, CBS, Montpellier

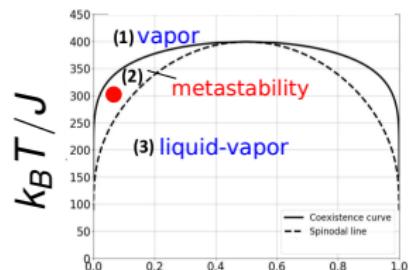
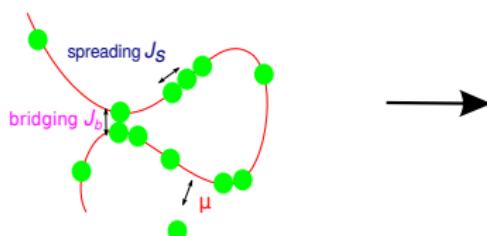
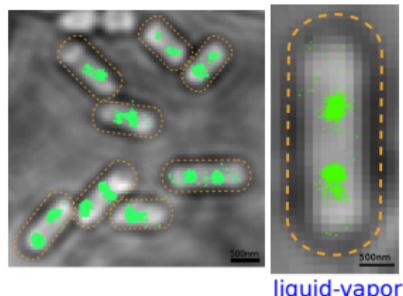


Guilhas, JCW,...Le Gall, Nollmann **ATP-driven separation of liquid phase condensates in bacteria** Mol. Cell '20

Liquid-like behaviour of ParBS complexes



specific binding
→
ParB/parS



Thank you for your attention!

J Dorignac
F Geniet
J Palmeri
A Parmeggiani
N-O Walliser
Biophysical modeling

C Chevalier
G David
P Soudon

A David
A Choquet

Molecular biology

B Guilhas
D Cattoni
A Le Gall
M Nollmann
Super resolution microscopy

Bioinformatics
E Rivals

N Wingreen

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C Mathieu-Demazière
J Rech
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Université Grenoble Alpes

TiMC

I Junier
T Lepage

Numerical Simulations

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