Surfing on protein waves: modeling the bacterial genome partitioning

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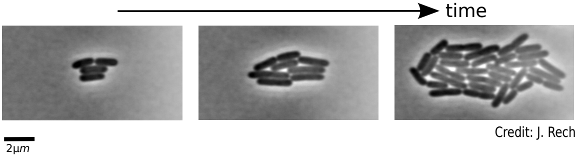
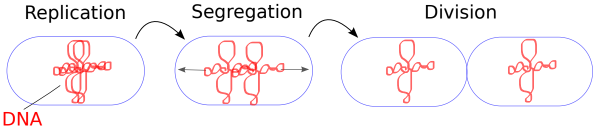
Outline

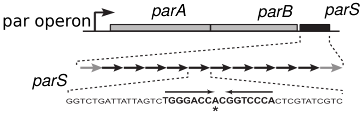
Segregation of bacterial DNA

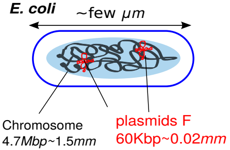




How is the bacterial genome segregated ?

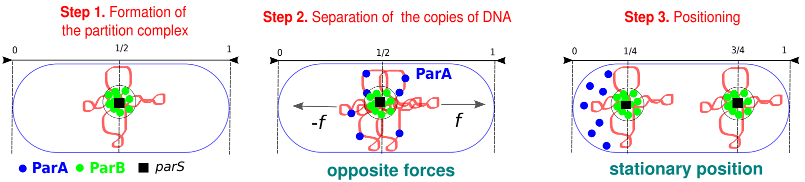
The ParABS operon





- ParA: "motor" protein (ATPase, Walker-type)
- ParB: binding protein (specific or non-specific binding)
- *parS*: centromere-like DNA sequence

The ParABS segregation system: molecular actors



ParBS: Liquid-Liquid phase separation

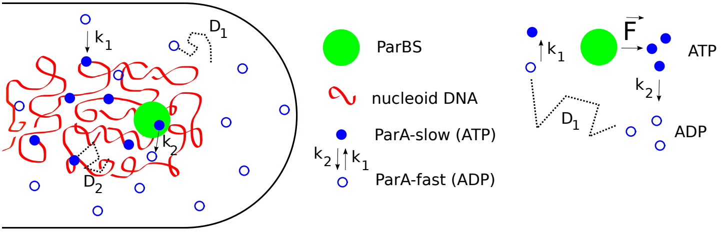
David, JCW, ..., Palmeri (2019) submitted

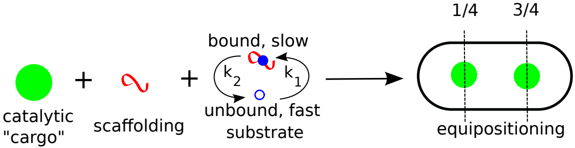
Guilhas, JCW, ..., Nollmann (2019) submitted

3 components: 2 proteins (ParA & ParB) + specific binding sites (*parS*)

How to describe both segregation and positioning of macromolecular assembly in a fluid phase ?

Molecular interactions and diffusion





Reaction-Diffusion equations (ParA) coupled to Brownian motion (ParBS)

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

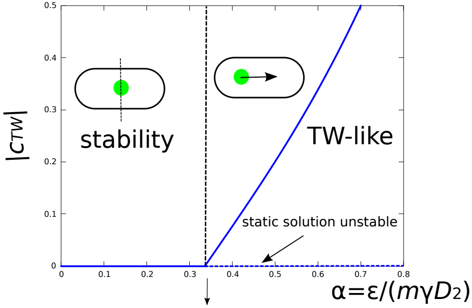
ParA-fast (ADP): $$\frac{\partial u}{\partial t} = D_1\,\Delta u - k_1\,u(\mathbf{r},t) + k_2\,v(\mathbf{r},t)\sum_i S(\mathbf{r}-\mathbf{r}_i(t))$$

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

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

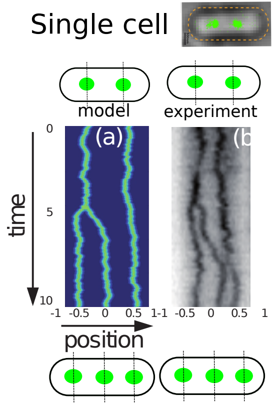
Dynamical instability: supercritical pitchfork bifurcation

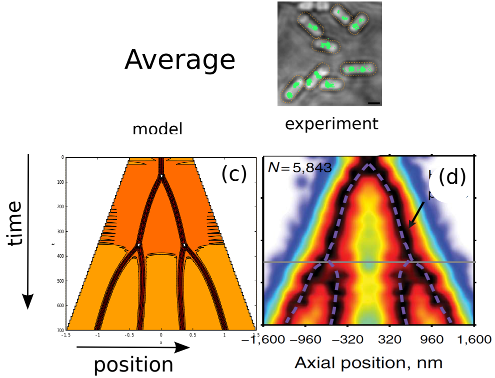
Threshold of dynamical stability obtained with Traveling Waves (TW) *ansatz*: $u(x,t) = u(\xi)$; $v(x,t) = v(\xi)$, where $\xi = x - c_{TW}\, t$



$$\alpha_c = N^{-1}_{ParA \in \mathcal{C}}$$

Comparison with experiments





Summary

- Minimal reaction-diffusion system:
  $\rightarrow$ sufficient to explain segregation and positioning in ParAB*S*
- Non-linear coupling between ParB*S* and ParA densities:
  $\rightarrow$ Self-consistent description of the 3 protein species
- Analytical analysis:
  $\rightarrow$ dynamical transition (stable/unstable regime)

JCW, Dorignac J., Lorman V., Rech J., Bouet J.-Y., Nollmann M., Palmeri J., Parmeggiani A. & Geniet F., *Surfing on protein waves: proteophoresis as a mechanism for bacterial genome partitioning*, *Phys. Rev. Lett.* **119**, 028101.

`arXiv:1702.07372 [q-bio.SC]`

Physical modeling

G. David
J. Dorignac
F. Geniet
V. Lorman
J. Palmeri
A. Parmeggiani

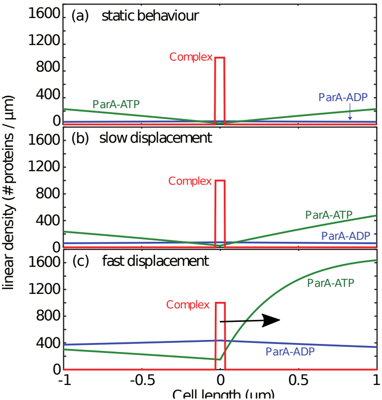
Molecular biology

R. Diaz
A. Sanchez
J. Rech
J-Y. Bouet

Super-resolution microscopy

D. Cattoni
A. Le Gall
M. Nollmann

Density profiles obtained with biological paramaters

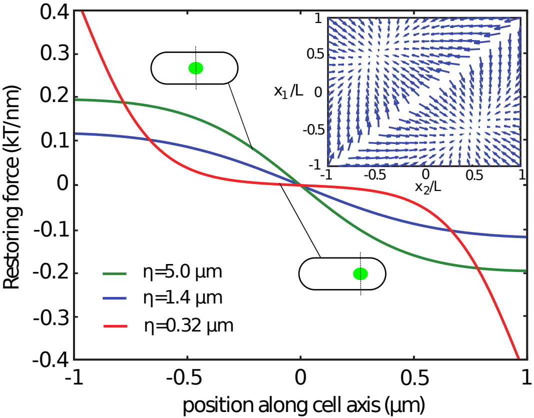


$\alpha < \alpha_c$

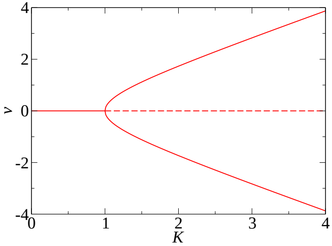
$\alpha = \alpha_c$

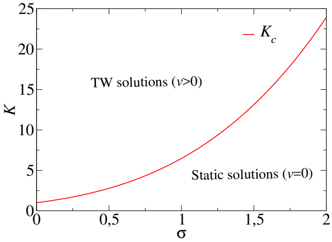
$\alpha > \alpha_c$

Screening length



Supercritical pitchfork bifurcation

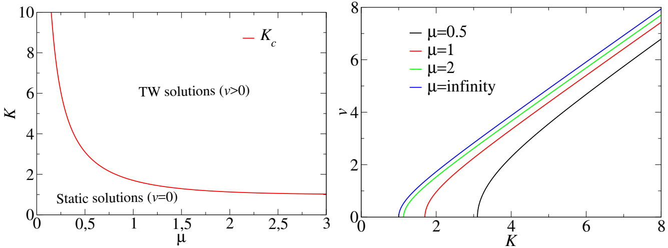




Infinite system (left) Supercritical pitchfork bifurcation diagram of reduced system in the (K, v) space.

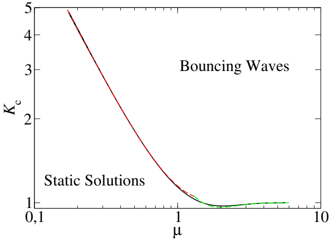
(right) Dynamical phase diagram in the plane (K, σ) where $K = \alpha m_0/(4D\ell)$ and σ is the dimensionless width of a gaussian source. The red curve represents the boundary (critical value K_c vs. σ).

Supercritical pitchfork bifurcation



Periodic Boundary Conditions (left) Dynamical phase diagram in the plane (K, μ) where $K = \alpha m_0/(4D\ell)$ and $\mu = L/\ell$ is the dimensionless ratio between L (size domain $2L$) and the screening length $\ell = \sqrt{D/k}$. (right) TW dimensionless velocity v (positive) vs. parameter $K = \alpha m_0/(4D\ell)$ for different values of $\mu = L/\ell$ from 0.5 to 2 and for $\mu \to \infty$. The blue curve is the same as the upper part for infinite system, thus the right limit is recovered.

Supercritical pitchfork bifurcation



No-Flux Boundary Conditions (Log-log plot of the instability threshold $K_c(\mu)$ versus the system size to screening length ratio $\mu = L/\ell$ for a Dirac source.