Surfing on protein waves: proteophoresis as a mechanism for bacterial genome partitioning

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Outline

1. Bacterial DNA segregation: the ParABS system

2. Dynamics: complexes surfing on protein waves
Segregation of bacterial DNA

How is the bacterial genome segregated?

Credit: J. Rech

2 μm

Replication → Segregation → Division

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**Bacterial genome partitioning**

**Bacterial DNA segregation: the ParABS system**

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**The ParABS operon**

- **ParA**: “motor” protein (ATPase, Walker-type)
- **ParB**: binding protein (specific or non-specific binding)
- **parS**: centromere-like DNA sequence
Bacterial DNA segregation: experimental facts

Le Gall et al, Nat. Comm. '16

Bouet's team, LMGM, unpublished

Single cell

Average

N=5,843

Axial position, nm

Le Gall et al, Nat. Comm. '16
How does ParABS work?

**Step 1.** Formation of the partition complex

**Step 2.** Separation of the copies of DNA

**Step 3.** Positioning

### 3 components:

- 2 proteins (ParA & ParB)
- Specific binding sites (parS)

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Bacterial genome partitioning
Bacterial genome partitioning
Dynamics: complexes surfing on protein waves

Bacterial DNA segregation: interactions of ParAB

ParA-slow (ATP)
ParA-fast (ADP)
nucleoid DNA
ParBS

1/4 3/4
catalytic
"cargo" scaffolding equipositioning

k2
substrate

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Dynamical steps: Reaction-Diffusion equations

ParA-fast: \[
\frac{\partial u}{\partial t} = D_1 \Delta u - k_1 u(r, t) + k_2 v(r, t) \sum_i S(r - r_i(t))
\]

ParA-slow: \[
\frac{\partial v}{\partial t} = D_2 \Delta v + k_1 u(r, t) - k_2 v(r, t) \sum_i S(r - r_i(t))
\]

\[
m\gamma \frac{dr_i}{dt}(t) = \varepsilon \int_V \nabla v(r', t) S(r' - r_i(t)) \, d^3r'
\]

- Feedback between the partition complexes and ParA densities
  \rightarrow Non-linear system with dynamical instability
Dynamical instability
Threshold of dynamical stability obtained with Traveling Waves (TW) ansatz:
\[ u(x, t) = u(\xi); \quad v(x, t) = v(\xi), \text{ where } \xi = x - c_{TW} t \]

\[ |c_{TW}| \quad \alpha = \frac{\varepsilon}{m \gamma D^2} \]

Stability TW-like
Static solution unstable

\[ \alpha_c = N_{ParA}^{-1} \]
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Quasistatic hypothesis: calculation of the profiles

\[ \alpha < \alpha_c \]

\[ \alpha = \alpha_c \]

\[ \alpha > \alpha_c \]
Comparison with experiments

Single cell

Average

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Minimal reaction-diffusion system:
→ sufficient to explain segregation and positioning in ParABS

Non-linear coupling between ParBS and ParA densities:
→ Self-consistent description of the 3 protein species

Analytical analysis:
→ dynamical transition (stable/unstable regime)

arXiv:1702.07372 [q-bio.SC]
Physical modeling

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

Molecular biology

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

Super-resolution microscopy

D. Cattoni
A. Le Gall
M. Nollmann
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Screening length

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Infinite system (left) Supercritical pitchfork bifurcation diagram of reduced system in the $(K, \nu)$ space. (right) Dynamical phase diagram in the plane $(K, \sigma)$ where $K = \frac{\alpha m_0}{4D\ell}$ and $\sigma$ is the dimensionless width of a gaussian source. The red curve represents the boundary (critical value $K_c$ vs. $\sigma$).
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Supercritical pitchfork bifurcation

Periodic Boundary Conditions (left) Dynamical phase diagram in the plane \((K, \mu)\) where \(K = \frac{\alpha m_0}{4D\ell}\) and \(\mu = \frac{L}{\ell}\) 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 \(K = \frac{\alpha m_0}{4D\ell}\) for different values of \(\mu = \frac{L}{\ell}\) 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.)