Keeping it together: 
Organizing the bacterial chromosome for division

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Outline

• The problem of packaging and moving DNA
  - Nucleoid Associated Proteins
  - The ParABS system
• How does ParB condense DNA?
• Lattice model for the ParB-DNA complex
  - Localizing the complex
  - Roadblocks and loops
  - Gene silencing
• Open questions
• Conclusions
Packaging DNA is a challenge

Kavenoff and Bowen, Chromosome (1976)
Chromosomal organization: Nucleoid-associated proteins

Bridging and looping

Bending and coiling

ParABS system: Chromosome segregation in *Caulobacter crescentus*

- How are ~1000 ParB proteins localized on the DNA?
- How do ParBs interact and what is the structure of the ParB-DNA complex?
- What controls formation of the complex?
ParB clusters around *parS* sites in *Bacillus subtilis*

Breier and Grossman, Molecular Microbiology (2007)

Roadblock suppresses spreading

Murray et al. Molecular Microbiology (2006)

ParB clusters around parS sites in *Bacillus subtilis*

"spreading" model


Murray et al. Molecular Microbiology (2006)

Lattice model for DNA-binding proteins

\[ H_{\text{int}} = J_S \sum_{i=1}^{N-1} \phi_i \phi_{i+1} + \frac{J_B}{2} \sum_{|i-j|>1} \phi_i \phi_j \delta_{|\mathbf{r}_i - \mathbf{r}_j|,1} + \sum_{i=1}^{N} \epsilon_i \phi_i. \]
Searching for a minimal model for ParB

Dimer model

Spreading model

Bridging model

Spreading or bridging model

Cluster size distribution

Probability p(n)

- Dimer
- Bridging
- Spreading
- Spreading or bridging
Spreading & bridging model condenses DNA
Can a single *parS* site localize the ParB-DNA complex?

Condensation is essential for localization
How strong a \textit{parS} site is needed for localization?

Entropic “cost” of localization

\[ \Delta \epsilon_{\text{parS}} < k_B T \log \left( \frac{2M_c}{N - 2M_c} \right) \]

In a cell: \( M_c \sim 1000, \ N \sim 130,000 \ \Rightarrow \ \Delta \epsilon_{\text{parS}} < -4.2 \ kT \)
Roadblock experiment is captured by spreading & bridging model

Why doesn’t cluster loop around roadblock?
Statistics of DNA looping

Universal loop-size distribution

\[ p(s) \sim s^{-3\nu} \]

Scaling of loop number

\[ N_{\text{loops}} \sim \exp\left(-\frac{J_s}{k_B T}\right) M_c^\alpha \]

\[ \bar{\rho}_{\text{loops}} \sim M_c^{\alpha-1} \quad \alpha \approx 0.9 \]
Prediction: ParB overexpression should overcome roadblock
ParB silences genes flanking the *parS* site in P1 plasmids

Gene-silencing profiles are captured by the spreading & bridging model

**DNA exposure**

- Increasing parS-distance

**Gene activity**

- Increasing parS-distance
- CAT
- β-Gal

**Collapse of numerical data**

- ParB expression level/(parS distance)

**Collapse of experimental data**

- Remaining activity
- parS distance: 1.2 kbp, 5.4 kbp
Open questions

• Why is parS required for cluster formation?

• How is ParB partitioned between parS sites?


Conclusions

- Bacterial chromosomes/plasmids are organized by DNA-binding proteins
- A minimal “spreading & bridging” model for ParB accounts for:
  - Stability and localization of ParB-DNA complexes at parS sites
  - Roadblock experiments & Gene silencing

Open questions

- Mechanism of nucleation at parS sites?
- Partitioning of ParB (role of DNA supercoiling?)

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Number of \textit{parS} motifs ranges from 1 in \textit{B. burgdorferii} to 24 in \textit{S. coelicolor}

ParB$_2$ (Spo0J$_2$) can bind DNA both specifically and nonspecifically