Evolution of Regulatory Complexity Through Genome Organization

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Evolution of complexity

Homo sapiens

Caulobacter crescentus
Evolution of complexity in gene regulation.
Modelling evolution of gene regulation

Advantages:

Study **general patterns** of evolution:
   N>1; independent of biochemistry.
Record the entire **evolutionary history**.
Uncover the precise **regulatory mechanisms**.
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Crombach & Hogeweg (2008)
Modelling evolution of gene regulation

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Crombach & Hogeweg (2008)
A model of cell-cycle regulation
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Caulobacter crescentus

Sanchez-Osorio et al. (2017)
A model of cell-cycle regulation

*Caulobacter crescentus*

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Caulobacter crescentus

Network

 Sanchez-Osorio et al. (2017)

Cell-cycle
A model of cell-cycle regulation

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division death

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Caulobacter crescentus

Network

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Mutations
- small (e.g. bitstrings)
- large (e.g. organization)

Genome structure

Cell-cycle

division death

4/10
A model of cell-cycle regulation

Caulobacter crescentus

Network

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Genome structure

Stochastic binding

\[ p_i = \frac{k_0 \cdot e^{\epsilon \cdot H_i}}{1 + \sum_j k_0 \cdot e^{\epsilon \cdot H_j}} \]
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Network

Sanchez-Osorio et al. (2017)

Mutations
- small (e.g., bitstrings)
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Genome structure

Mutation impacts regulation

Stochastic binding

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A model of cell-cycle regulation

**Caulobacter crescentus**

- **Network**
- **Sanchez-Osorio et al. (2017)**
- **Genome structure**
- **Stochastic binding**

- **Mutations**
  - small (e.a. bitstrings)
  - large (e.a. organization)

- **Replication** impacts regulation

**Cell-cycle**

- division
- death

**Nutrient gradient sets replication speed**

\[ p_i = \frac{k_0 \cdot e^{\epsilon \cdot H_i}}{1 + \sum_j k_0 \cdot e^{\epsilon \cdot H_j}} \]
Rich evolutionary dynamics in replicate experiments

Range expansion coincides with genome expansion

Genome size ($L$): 60 90 120
Density ($N$): 0.0 1.0

Replicate

$T_n = 0.683$
Rich evolutionary dynamics in replicate experiments
Rich evolutionary dynamics in replicate experiments

→ Range expansion coincides with genome expansion
Rich evolutionary dynamics in replicate experiments

→ Range expansion coincides with genome expansion
Cell-cycle adaptation to poor conditions

![Graph showing cell-cycle duration vs. nutrient abundance]

- Ancestor
- Evolved:
  - Sector 3
  - Sector 5
  - Sector 7
  - Sector 9

Cell-cycle duration ($\tau$, in $t$) vs. Nutrient abundance ($n$)

Limit
Cell-cycle adaptation to poor conditions

![Graph showing cell-cycle duration (τ, in t) vs. nutrient abundance (n)]
Cell-cycle adaptation to poor conditions

![Graph showing cell-cycle duration vs. nutrient abundance](image)
Cell-cycle adaptation to poor conditions

Slower cell-cycles to deal with low nutrient abundance
Cell-cycle adaptation to poor conditions

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Cell-cycle adaptation to poor conditions

Slower cell-cycles to deal with low nutrient abundance

Low quality cell-cycle

High quality cell-cycle: more efficient
Network expansion enhances cell-cycle
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High quality (R2)

- More efficient replication
Network expansion enhances cell-cycle

High quality (R2)

- More efficient replication
- Network expansion & rewiring at the core
Network expansion enhances cell-cycle

High quality (R2)

- More efficient replication
- Network expansion & rewiring at the core

Low quality (R10)

- Exploits ancestral S-loop
Specialist and generalist strategies evolve
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Specialists: Adaptation to local conditions

Generalists: Individual plasticity

Cell-cycle duration ($\tau$, in $t$)

Nutrient abundance ($n$)
Specialist and generalist strategies evolve

- **10**: Evolution of strategies with different nutrient abundance (n).
- **3**: Lines indicating n observed in sector and R_0 values.
- **2**: Graph showing cell-cycle duration (τ, in t) for different sectors.
- **8**: Further analysis of nutrient abundance and cell-cycle duration.

Legend:
- Ancestor
- Evolved:
  - Sector 3
  - Sector 5
  - Sector 7
  - Sector 9
Regulation depends on network & genome

Emergence of cell-cycle checkpoint
Multiple innovations required for generalism

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Emergence of cell-cycle checkpoint

1. Activation

2. AND-gate
Multiple innovations required for generalism

Cell-cycle

3. Time integration

Network

1. Activation

Genome

2. AND-gate

Emergence of cell-cycle checkpoint
Range expansion coincides with genome expansion
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Extra complexity:

generalism ← emergent genome organisation
Summary

- Range expansion coincides with genome expansion
- Extra complexity:
  - generalism ← emergent genome organisation
- Regulation = network + genome + ...
  - → Caulobacter
Acknowledgements

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Supplementary Figures (1)

- Figures labeled 1, 2, 3, and 8 depict graphs showing the relationship between cell-cycle duration ($\tau$) and nutrient abundance ($n$).
- Figures 1 and 2 likely compare ancestral and evolved conditions.
- Figures 3 and 8 highlight different scenarios of $R_0$, with $R_0 > 1$ and $R_0 < 1$.
- The graph shows a limit in sector 3, indicating a threshold effect.
Supplementary Figures (4)