

Decision-Making in Bacteriophage Lambda: A View from the Single Phage

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Short Abstract — Upon infection of *E. coli* by bacteriophage lambda, a decision is made between the lytic pathway, leading to cell death and the release of new phages; and the lysogenic pathway, in which the phage genome integrates into the bacterial chromosome. In this study, we use live fluorescence microscopy to follow lambda infection and the resulting cell fate at the level of individual cells and phages, with the aim of elucidating the different parameters affecting decision-making. In addition, we follow phage trajectories in space to learn how a single phage finds its target on the host cell.

Keywords — Single cell, single phage, decision-making, fluorescently-labeled phage, phage trajectory.

THE post-infection decision process between lytic and lysogenic pathways serves as a paradigm for an environmentally-regulated genetic switch. A key “control parameter” in the system is believed to be the number of phages infecting each cell (the “multiplicity of infection”, or MOI). The MOI-dependence of cell fate has been studied in population-based assays [1]. Beyond MOI dependence, a recent study demonstrated the effect of cell volume on cell fate [2]. However, such population-based assays coarse-grain potentially critical information such as the actual number of phages infecting an individual cell and the position of the infecting phages on the cell surface. In this study, we follow lambda infection and the resulting cell fate under the microscope, at the level of individual cells and phages. Fluorescently-labeled phages and fluorescent reporters for key promoters are used to detect the two different pathways. The fluorescently-labeled phage (based on λ eyfp [3]) allows us to track the exact phage number and location [4] on the host cell during infection and follow the lytic pathway as time goes on. In the same cells, a reporter plasmid (based on pE-gfp [5]) is used to detect the lysogenic pathway. Our aim is to create a spatiotemporal map linking the microscopic infection parameters—number and position of infecting phages, cell age and growth rate, etc.—with the eventual decision made.

In addition, we are investigating the way a single phage

finds its target on the host cell for injecting its DNA. We use Total Internal Reflection Fluorescence (TIRF) Microscopy to follow the motion of fluorescently-labeled phages on the cell surface, and characterize their interaction with their target, the LamB receptor (labeled with a different color).

REFERENCES

- [1] Kourilsky P (1973) Lysogenization by Bacteriophage Lambda I. Multiple Infection and the Lysogenic Response. *Mol Gen Genet* **122**, 183-195.
- [2] St-Pierre F, Endy D (2008) Determination of cell fate selection during phage lambda infection. *PNAS* **105**, 20705-20710.
- [3] Alvarez LJ, Thomen P, Makushok T, Chatenay D (2007) Propagation of Fluorescent Viruses in Growing Plaques. *Biotechnol Bioeng* **96**, 615-621.
- [4] Edgar R, Rokney A, Feeney M, Semsey S, Kessel M, Goldberg MB, Adhya S, Oppenheim AB (2008) Bacteriophage infection is targeted to cellular poles. *Mol Microbiol* **68**, 1107-1116.
- [5] Kobiler O, Rokney A, Friedman N, Court D, Stavans J, Oppenheim AB (2005) Quantitative Kinetic Analysis of the Bacteriophage λ genetic network. *PNAS* **102**, 4470-4475.

Acknowledgements: This work was funded by NIH grant R01GM082837-01A1.

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