

Modeling viral copy number dynamics during infection by bacteriophage lambda

Seth Coleman^{1,2,3}, Oleg Igoshin^{1,2,3}, and Ido Golding^{3,4}

Short Abstract — Infection of an *E. coli* cell by the bacteriophage (virus) lambda results in a cell-fate decision between two outcomes: cell death following rampant viral replication, or viral dormancy and integration into the host genome. While much attention has been focused on the effect of the initial number of co-infecting viruses on the decision, the role and regulation of post-infection replication is still poorly understood. We are developing a model of the post-infection decision focusing on regulation of replication, with the goal of achieving a clearer understanding of the role of viral copy number in the decision.

Keywords — Cell-fate decision, replication, viral copy number

THE infection of *E. coli* by the bacteriophage lambda is a paradigm for cell-fate decisions [1]. During infection, a choice is made between two pathways: rampant viral replication leading to cell death (lysis), or dormancy and passive viral replication (lysogeny) [2].

While the decision outcome is influenced by many factors [3], the number of simultaneously infecting viruses (multiplicity of infection, or MOI) was one of the first identified [4] and remains the one of the most studied [5]. During infection, high MOI biases the decision towards lysogeny, whereas low MOI biases it towards lysis — a curious reversal of the relative viral copy number levels at the end of the decision for each fate. However, the mechanism by which viral copy number is sensed and integrated into the decision is not well understood [6]. More broadly, the mapping of copy number to expression dynamics in gene regulatory networks remains an active area of research [7].

We are currently developing a kinetic model to explore the role of viral copy number in the lambda cell-fate decision. The model consists of a deterministic system of ordinary differential equations describing a simplified lambda gene regulatory network, focusing on the regulation

of replication by key proteins, and is able to describe infection both in wild type and replication-deficient mutants. After calibrating the model with experimental data describing viral replication kinetics, we will make testable predictions and elucidate the mechanism by which viral copy number biases the decision. The knowledge we gain from the lambda system may provide additional insights into how gene copy number affects network dynamics.

REFERENCES

- [1] Golding I (2011) Decision Making in Living Cells: Lessons from a Simple System. *Annu Rev Biophys* **40**, 63-80.
- [2] Ptashne M (2004) *A Genetic Switch*. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY.
- [3] Oppenheim AB, Kobiler O, Stavans J, Court DL, Adhya S (2005) Switches in Bacteriophage Lambda Development. *Annu Rev Genet* **39**, 409-429.
- [4] Kourilsky P (1973) Lysogenization by Bacteriophage Lambda I. Multiple Infection and the Lysogenic Response. *Mol Gen Genet* **122**, 183-195.
- [5] Zeng L, Skinner SO, Zong C, Sippy J, Feiss M, Golding I (2010) Decision Making at a Subcellular Level Determines the Outcome of Bacteriophage Infection. *Cell* **141**, 682-691.
- [6] Semsey S, Campion C, Mohamed A, Svenningsen SO (2015) How long can bacteriophage λ change its mind? *Bacteriophage* **5**, e1012930.
- [7] Song R, Liu P, Acar M (2014) Network-dosage compensation topologies as recurrent network motifs in natural gene networks. *BMC Syst Biol* **8**, 69.

Acknowledgements: This work was funded by the National Science Foundation (PHYS-1427654, PHYS-1430124, PHYS-1147498), the National Institutes of Health (R01GM082837), the Welch Foundation (Q-1759) and the John S. Dunn Foundation (Collaborative Research Award).

¹Applied Physics Graduate Program, Rice University, Houston, TX. E-mail: colemans@rice.edu

²Department of Bioengineering, Rice University, Houston, TX. E-mail: igoshin@rice.edu

³Center for Theoretical Biological Physics, Rice University, Houston, TX. E-mail: igolding@illinois.edu

⁴Verna and Marrs McLean Department of Biochemistry and Molecular Biology, Baylor College of Medicine, Houston, TX.