Study of Signal Processing in Quorum Sensing at Single-Cell Level

Tao Long[1], Bonnie L. Bassler[2], and Ned S. Wingreen[3]

***Short Abstract* — Accurate and faithful signal processing is essential for living cells to make correct adjustments in response to various extracellular cues. Quorum sensing is a process in which bacteria produce and respond to autoinducers to regulate cell density dependent gene expression. To investigate the problem of information processing in quorum sensing circuit, fluorescent protein reporters and single-cell microscopy are applied to quantitatively measure the intracellular response in a quorum-sensing bacterium – *Vibrio harveyi*. Combined with modeling, we explored features such as integration and disentanglement of multiple signals, sensitivity of signal response and fidelity of signal propagation in presence of inevitable noise.**

***Keywords* — Signal Processing, Quorum Sensing, Single Cell**

BACTERIA respond to their environment and to each other and accordingly adjust their gene-expression levels. Accurate signal detection and faithful signal transduction are important for bacteria to make correct responsive decisions to survive in a complicated changing environment. To better understand this information processing by living bacteria, we studied a model system – the quorum-sensing system in *Vibrio harveyi*. Quorum sensing is a process in which bacteria communicate with each other by diffusible chemical molecules, termed "autoinducers", to commit to community-wide coordinated gene expression [1]. Autoinducers (AIs) are produced by the quorum-sensing bacteria themselves and secreted outside of cell. At low cell density, in the absence of appreciable amounts of autoinducers, signal cannot be detected and bacteria act as individuals. At high cell density, with accumulation of autoinducers, bacteria respond to detected signals and synchronize gene expression within the population to allow the group of bacteria to act in unison. Three types of autoinducers – AI-1, AI-2, and CAI-1 – are detected coincidently by their cognate receptors – LuxN, LuxPQ, and CqsS. Information from all three receptors is then integrated and transduced via phosphorelay to the response regulator LuxO, with LuxU acting as intermediate. When LuxO is phosphorylated, it activates the expression of five small RNAs that destabilize the mRNA encoding the master quorum-sensing transcriptional regulator LuxR [2].

To quantitatively study cellular information processing of quorum sensing circuit, we constructed strains with green fluorescent protein (GFP) reporter fused to one of the small RNA promoters. In order to parse individual signaling pathways and address the problem of integration and disentanglement of multiple signals, we also constructed strains having only AI-1 sensing pathway, AI-2 sensing pathway, and both AI-1 and AI-2 sensing pathways. Synthases of autoinducers are also disrupted in all strains to achieve precise control over autoinducer concentrations.

By single-cell microscopy [3], we obtained dose-response curves of GFP concentrations in response to various combinations and concentrations of AI-1 and AI-2. A model describing the system is established based on current biochemical knowledge from literature [4,5] and experimental data from this work. Problems such as information disentanglement, response sensitivity and noise propagation are investigated using this model.

Acknowledgements: T.L. acknowledges support from Burroughs Wellcome Fund.

[1]Department of Physics, Princeton University, NJ 08544, USA. E-mail: taolong@princeton.edu

[2]Howard Hughes Medical Institute and Department of Molecular Biology, Princeton University, NJ 08544, USA. E-mail: bbassler@princeton.edu

[3]Department of Molecular Biology, Princeton University, NJ 08544, USA. E-mail: wingreen@princeton.edu

REFERENCES

[1] Waters CM, Bassler BL (2005) Quorum sensing: cell-to-cell communication in bacteria. *Annu. Rev. Cell Dev. Biol*. **21**, 319-346

[2] Tu KC, Bassler BL (2007) Multiple small RNAs act additively to integrate sensory information and control quorum sensing in *Vibrio harveyi*. *Genes & Development* **21**, 221-233

[3] Rosenfeld N, Young JW, Alon U, Swain PS, Elowitz MB (2005) Gene regulation at the single-cell level. *Science* **307**, 1962-1965

[4] Timmen M, Bassler BL, Jung K (2006) AI-1 influences the kinase activity but not the phosphatase activity of LuxN of *Vibrio harveyi*. *J Biol. Chem.* **281**, 24398-24404

[5] Neiditch MB, Federle MJ, Pompeani AJ, Kelly RC, et al (2006) Ligand-induced asymmetry in histidine sensor kinase complex regulates quorum sensing. *Cell* **126**, 1095-11