Coordination of Multiple Flagella in Bacteria through Signaling Noise

Michael W. Sneddon[1,2], William Pontius[1,3], and Thierry Emonet[1,2,3]

Short Abstract **— Molecular noise is an inherent characteristic of signal transduction networks. However, it still remains unclear how cells are generally able to cope with noisy signals and to what extent noise influences cell behavior. Here, we study how molecular noise in bacterial chemotaxis signaling affects the downstream response of multiple flagellar motors by constructing coarse-grained models of the signaling noise, the bacterial flagellar motor, and the interactions of multiple flagella. Interestingly, we find that cells can exploit the upstream signaling noise to coordinate the response of multiple flagella. We also explore some of the consequences of signaling noise and flagella coordination on the search and foraging strategies of bacteria. To build the computational models of the flagellar motor and chemotaxis, we developed a novel, general-purpose, stochastic simulator named NFsim that can efficiently simulate and coarse-grain complex biological systems.**

I. INTRODUCTION

CELLS must continuously cope with noise that arises from small numbers of molecules and stochastic molecular events. A key example of a cellular system that effectively copes with noise is the bacterial chemotaxis signaling network used by bacteria such as *E. coli* to navigate their environment. Although single bacterial cells exhibit an extremely high levels of signaling noise even when unstimulated [1], bacteria are remarkable in their robust ability to track chemical gradients. Here we study how signaling noise in bacterial chemotaxis influences the flagellar motor response to ultimately affect the foraging and tracking capabilities of a cell.

II. RESULTS

We constructed a two-state, coarse-grained model of the flagellar motor where states correspond to clockwise or counterclockwise rotation [2]. We also built a coarse-grained phenomenological model of the interactions and conformational changes of flagella that occur as cells reorient their swimming direction [3]. With the models, we first characterized the typical intra-cellular levels of noise based on experiments. Next, we simulated noisy input signals and presented them to multiple independent flagella in a single cell. With our simulations, we discovered that signaling noise is able to coordinate the response and stochastic switching dynamics of multiple flagella. This result explains a classic study of the coordinated switching dynamics of flagella [4] and provides evidence that noise in bacterial chemotaxis plays a beneficial role in signal processing.

We then extended the model with a cooperative receptor adaptation model and a cell motion model that both reproduce experimental observations [5]. With the extended model, we found that signaling noise in bacterial chemotaxis can significantly extend the space explored by foraging bacteria. Furthermore, we show that for the range of noise observed in wild-type bacteria, the chemotactic response to gradients of attractants is not compromised.

To facilitate the construction of our models, we have developed a new simulation platform named the Network Free Stochastic Simulator (NFsim) [6]. NFsim uses a novel agent and rule-based approach that allows simulation and coarse-graining of complex biological systems, such as chemotaxis signaling, where the numbers of possible molecular interactions are overwhelming. We demonstrate the versatility and performance of NFsim with a wide range of practical examples drawn from signaling in the immune system and actin polymerization. NFsim is available online at: http://emonet.biology.yale.edu/nfsim.

III. CONCLUSION

Our work highlights that under certain conditions, biological systems may actually take advantage of noise to enhance behavioral responses or strategies.

REFERENCES

[1] Korobkova, E., Emonet, et al. From molecular noise to behavioural variability in a single bacterium. *Nature* **428**, 574-578 (2004).

[2] Tu, Y. & Grinstein, G. How White Noise Generates Power-Law Switching in Bacterial Flagellar Motors. *Phys. Rev. Lett.* **94**, 208101 (2005).

[3] Darnton, N.C., et al. On Torque and Tumbling in Swimming Escherichia coli. *J Bacteriol* **189**, 1756-1764 (2007).

[4] Ishihara, A., Segall, J.E., Block, S.M. & Berg, H.C. Coordination of flagella on filamentous cells of Escherichia coli. *J. Bacteriol* **155**, 228-237 (1983).

[5] Berg, H.C. & Brown, D.A. Chemotaxis in Escherichia coli analysed by three-dimensional tracking. *Nature* **239**, 500-504 (1972).

[6] Sneddon MW, Faeder JR, and Emonet T. Efficient modeling, simulation and coarse-graining with NFsim. (*in preparation*).