

Effects of stochastic fluctuations on the coordination of flagella in bacterial chemotaxis

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Short Abstract — Chemotaxis allows bacteria to respond and adapt to the environment, by tuning tumbling and running motions due to the rotation of their flagella. We defined a model of chemotaxis and performed stochastic simulations of the dynamics of a pivotal protein, CheYp. These results allowed to compare the mean time of running, tumbling and adaptation with respect to different numbers of flagella. Our results suggest that the interplay between stochastic fluctuations of CheYp and the synchronization of flagella might represent a relevant component for the proper functionality of chemotaxis.

Keywords — Bacterial chemotaxis, mechanistic modeling stochastic simulation.

I. INTRODUCTION

In bacterial chemotaxis, the presence of a gradient of external ligands triggers a cascade of intracellular events, tightly regulated by feedback mechanisms, that affect the cytoplasmic amount of the phosphorylated form of CheY [1]. By interacting with the proteins of the flagellar motors, CheYp induces the clockwise (CW) and counterclockwise (CCW) rotation of each flagellum. When *all* flagella are turning CCW, they form a synchronized bundle and the cell performs a running motion; otherwise, the cell will tumble. An adaptation mechanism assures that, in presence of homogeneous environments, the switch frequency between running and tumbling is reset to the prestimulus level.

The aim of our work is to analyse the effects that the intrinsic randomness of the chemotactic pathway can have on the coordination of flagella. This is done by measuring the mean time intervals of running and tumbling – and the adaptation times after ligand binding – with respect to a varying number of flagella.

II. METHODS AND RESULTS

A. Modeling, simulation and synchronization

Our model consists of 62 reactions and 32 molecular species, describing the chemotactic response to attractants in *E. coli* [2]. Stochastic simulations [3,4] are performed to analyze the dynamics of CheYp under various conditions.

To distinguish between CW and CCW rotations, we assume that each flagellum is sensitive to a threshold level of CheYp (evaluated as the mean value of CheYp at steady

state) and that, when the amount of CheYp is below this threshold, the flagellum is rotating CCW [5]. To identify the running motion, we use an automatic procedure to measure the time intervals during which all flagella are rotating CCW. Similar considerations hold for the analysis of tumbling motions and adaptation times. This analysis has been carried out for a number $n=1,\dots,10$ of cellular flagella.

B. Results

According to biological expectations, our analysis on the effect of stochastic fluctuations shows that: (a) the running-to-tumbling ratio decreases as n increases – this highlights the role of the number of flagella in the individual cell, and the necessity of their synchronization for a proper chemotactic behavior; (b) the adaptation time does not depend strongly on the value of n in individual cells – this guarantees an appropriate adaptation mechanism, independently from phenotypic variations in a population of cells (see [2] for more details).

III. CONCLUSION

The original contribution of our work consists in linking, with a quantitative modeling approach, the synchronization of a number of flagella to the stochastic fluctuations of CheYp. As a further extension, other aspects of chemotaxis are currently under investigation by our group. The first concerns the presence of the cytoplasmic gradient of CheYp, which diffuses from the area where it is phosphorylated (close to receptors) to the area of its activity (close to flagella) [6]. Its spatial localization, together with the localization of protein CheZ (that dephosphorylates CheYp) and of flagella, might have a significant role in chemotaxis. The second concerns the interaction between CheYp and the proteins of the flagellar motor [7]. In this case, we are interested in determining if and how stochastic fluctuations can affect the probability of throwing the reversal switch between CW and CCW rotations.

REFERENCES

- [1] Wadhams GH, Armitage JP (2004) *Nat. Rev. Mol. Cell. Biol.* **5**, 1024-1037.
- [2] Besozzi D, Cazzaniga P, Dugo M, Pescini D, Mauri G (2009) *EPTCS* **6**, 47-62.
- [3] Cao Y, Gillespie DT, Petzold LR (2006) *J. Chem. Phys.* **124**, 044109.
- [4] Cazzaniga P, Pescini D, Besozzi D, Mauri G (2006) *LNCS* **4361**, 298-313.
- [5] Morton-Firth CJ, Bray D (1998) *J. Theor. Biol.* **192**, 117-128.
- [6] Lipkow K, Andrews AA, Bray D (2005) *J. Bacteriol.* **187**, 45-53.
- [7] Bren A, Eisenbach M (2001) *J. Mol. Biol.* **312**, 913-917.

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