Noise in Bacterial Chemotaxis

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***Short Abstract* — Using a molecular level model of the underlying signaling pathway, we have identified the dominating internal and external noise sources that affect the single cell *E. coli* chemotactic behavior. We find that the system acts as a different filter for each source of noise, and we have evaluated the relative relevance of these noises under physiologically realistic conditions. From the molecular details of the pathway, we derive the classical Berg&Pucell result on noise averaging in receptor systems. The signal average time, the key but unknown parameter in the original Berg&Purcell picture, is now determined from the microscopic processes (e.g., receptor methylation and CheY dephosphorylation) of the system.**

***Keywords* — Noise, Chemotaxis, Adaptation**

I. Chemotaxis: a Noisy System

A Bacterial cell such as *Escherichia Coli* can swim to higher (lower) concentrations of chemical attractant (repellent) in a process known as chemotaxis [1]. The signal processing is that of an integral feedback, where adaptation is provided by receptor methylation and demethylation, facilitated by the enzymes CheR and CheB. Depending on the external signal (ligand) and its internal state (methylation level), receptors change the auto-phosporylation rate of the attached histidine kinase CheA, which promptly transfers its phosphate group to the response regulator protein CheY. CheY-P then binds to the flagella motor biasing the random swim of the bacteria towards higher nutrient concentrations. Another key element of the pathway is the enzyme CheZ, that removes the signal by removing the phosphate group of CheY-P.

It has recently been established [2] that on average the signal the bacteria read from the environment is the time derivative of the logarithmic ligand concentration. At the single cell level, this signaling process is noisy. Stochastic fluctuations from the ligand-receptor binding process has been considered before ([3,4]). However, we believe the noise in this system is dominated by two different mechanisms. First, the stochastic nature of the chemical reactions in the signaling pathway generates what we call the internal noise. The internal noise can be large because of the small number of molecules involved in the pathway, especially in the receptor adaptation process. The internal noise is also intrinsic to the signaling pathway itself as it exists even in the absence of chemical ligand. Second, the motion of a bacterial cell has a large random component, therefore even in a well defined chemical gradient the chemical concentration a swimming bacterium experiences can fluctuate greatly, leading to noise levels that can be much greater than that caused by the stochastic nature of the ligand-receptor binding process. In our study we use an exponential spatial ramp of nutrient concentration [2] to systematically studied these two sources of noise.

II. How to Treat the Noise

Previous studies [3,4] have explored the possibility that the chemotaxis pathway acts to reduce the noise in the signal. However, only ligand-receptor binding noise was considered, leaving out the main sources of noise untreated. In addition, No explanation of how the pathway averages signal noise is given and the signal average time, a key feature in previous studies, remains an unknown parameter of the previous treatments of the problem.

In our study, we introduce a complete model [5] of the chemotaxis pathway, where methylation/demethylation (by CheR/CheB interacting with the receptor) and signal removal (dephosphorylation of CheY-P by CheZ) play essential roles in averaging the noise of the output, the CheY-P level. Also, each source of noise is treated as having a certain correlation time, and is introduced consequently with its origin connected to specific biological mechanisms. The mathematical tools used are master equations and Langevin equations depending on the convenience, and the result the variance of the CheY-P concentration. In the final result one can see how the averaging time that was arbitrarily introduced in [3,4] comes naturally from the interplay of the different timescales relevant to the system. Furthermore, depending on whether the noise is internal or external a different timescale emerges as the dominating time scale for temporal signal averaging.

Other secondary effects such as the interplay of the different sources of noise, and the effect of the methylation feedback in the first passage time distribution [6] of the activity have also been considered and quantified.

III. Conclusions

We have identified the relevant sources of noise in the bacterial chemotaxis signaling process at the systems level. We have quantitatively evaluated the effects of different sources of noise on the output of the system by using a complete description of the signaling pathway involved.

References

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