Predicting chemical environments from receptor signaling

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***Short Abstract* — Outside the laboratory, bacteria live in complex microenvironments, characterized by nutrient supply and competition. Although often inaccessible by experiments their understanding is biomedically important. Assuming that bacteria evolved to sense best the gradients they typically encounter, we use prior knowledge from data, the signaling pathway, and cell behavior to reverse engineer *Escherichia coli's* habitat. Our identified gradients most likely stem from local nutrient sources and degradation by competing species, maximizing the drift velocity of swimming bacteria.**

***Keywords* — Bacterial chemotaxis | Weber's law | fold-change detection | information transmission | FRET | noise**

I. Introduction

BACTERIA live in complex chemical micro-environments with the spatio-temporal chemical concentration shaped by nutrient supply and depletion by surrounding bacteria. Although of physiological importance, we currently do not have a good understanding of what chemical gradients commensal microorganisms, as well as potential pathogens typically encounter in their habitat. One way forward is to exploit our accumulated knowledge about their sensory systems, which have evolved to detect typical stimuli relevant for the organism, e.g. the concentration of a particular nutrient in the environment. Hence, it is expected that sensory systems are optimized to encode these stimuli. Therefore, knowing the underlying principles in the design of sensory systems we ought to be able to predict typical stimuli such as concentration gradients by reverse engineering.

The best-characterized bacterium is *Escherichia coli,* which is a member of the highly stable commensal microbiota inhabiting the gastrointestinal tract of humans and animals. The chemotaxis sensory system enables these bacteria to detect and migrate in chemical gradients of nutrients and toxins. Unlike many sensory systems, it is relatively simple and its molecular components understood [1]. This and other sensory systems share common design principles including Weber's law, the Weber-Fechner law and fold-change detection (FCD) [2,3]. While these laws predict exponential gradients as sensed best [4,5], they do not quantify the complexity of the chemical environment in terms of distributions of concentrations and gradients, or provide functional importance of these in terms of cell-swimming behavior.

To fully characterize the chemical environments of chemotactic bacteria, we expect a matching between the statistical properties of typical stimuli and the corresponding cellular responses assuming certain optimization criteria. A reasonable assumption is that cells translate a stimulus (input) into a cellular response (output) in order to maximize the transmission of information [6,7], quantitatively described by Shannon's mutual information, which describe the correlations between the inputs and outputs with a fundamental link to thermodynamics [8].

II. Conclusion

Here, we go significantly beyond Weber's law and fold-change detection, which only predict average chemical gradients. We demonstrate the ability to predict distribution of typical gradients which *E. coli* likely encounters in its physiological microenvironment. For this purpose we use quantitative dose-response curves from *in vivo* fluorescence resonance energy transfer (FRET), information theory and simulations of swimming bacteria. Using our multidisciplinary approach, we show that maximizing mutual information implies maximizing the chemotactic index, and hence the drift velocity up the gradient. Our approach is a first step towards the prediction of typical environments of bacteria, shaped by cellular communities and dynamic turnover of nutrients.

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