Response rescaling in bacterial chemotaxis

Milena D. Lazova[1], Tanvir Ahmed[2], Domenico Bellomo[3], Roman Stocker[2], <u>Thomas S. Shimizu</u>[1*]

Short Abstract** — **We study response rescaling in *Escherichia coli* chemotaxis, where adaptation dynamically tunes the cells' motile response during searches for nutrients. Using *in vivo* FRET measurements on immobilized cells, complemented by microfluidics-based behavioral assays on free swimming cells (see abstract by Ahmed et al.), we find that the design of this prokaryotic signaling network follows the fold-change-detection (FCD) strategy – responding faithfully to the shape of the input profile irrespective of its absolute magnitude – hitherto reported only in eukaryotic cell-sensory systems. These observations in a highly optimized bacterial system support the notion that FCD represents a robust sensing strategy for spatial searches.

*   **Keywords** — **fold-change detection (FCD), MWC model, *in vivo* FRET***

I. Purpose

MAXIMIZING the information content of perceived signals is a non-trivial problem for biological sensory systems, as it requires knowledge of the statistical distribution of input signals [1]. Remarkably, strategies for inferring this distribution through incomplete sampling appear to be 'hard coded' in many adaptive sensory systems, leading to well-defined relationships between recently experienced background inputs and response sensitivity [2]. The most prevalent of such relationships is Weber's law [3], which prescribes that the response, Δr, immediately following a small step change in input, Δs, will be invariant upon proportional scaling of Δs with the background input level, s_0, by a constant factor, γ, *i.e.*, $\Delta r(\Delta s, s_0) = \Delta r(\gamma \Delta s, \gamma s_0)$.

Recently, a response-rescaling strategy that applies to a broader class of input stimuli, called fold-change detection (FCD), has been described in some eukaryotic cell sensory systems [4,5]. FCD is conceptually similar to Weber's law – it yields invariant responses under scaling of the stimulus with background – but it applies to the entire time series of the response, *i.e.*, $\Delta r(\Delta s(t), s_0; t) = \Delta r(\gamma \Delta s(t), \gamma s_0; t)$. It has been suggested that FCD is important for adaptive sensory systems involved in spatial searches by motile organisms [6].

We tested whether FCD-type response rescaling occurs in the signaling network of *E. coli* chemotaxis, which guides this bacterium's searches for nutrients, and is arguably the simplest sensory network known to exhibit adaptation over a broad dynamic range.

II. Results

To study how *E. coli* rescales its chemotactic response to smoothly varying inputs, we carried out *in vivo* FRET measurements on immobilized cells while temporally modulating chemoeffector concentrations using a computer-controlled fluid mixing apparatus. The response time series of the chemotaxis pathway, $\Delta a(t)$, was found to be invariant under proportionate scaling of a time-varying stimulus, $\Delta[L](t)$, with the background, $[L]_0$, over a broad dynamic range. Thus, the *E. coli* chemotaxis system demonstrates FCD, as recently predicted on theoretical grounds [6]. The FRET experiments identified two adjacent but distinct FCD regimes of background concentrations in which this invariance holds, together spanning a ~500-fold range. Parallel experiments with free-swimming cells using a microfluidic device confirmed that the FCD property extends to the behavioral level (see abstract by Ahmed et al.). We identified a set of sufficient conditions for FCD within a coarse-grained model of chemotaxis signaling [7], and confirmed with additional FRET experiments that these constraints are met in the design of this signaling pathway.

III. Conclusion

We have demonstrated experimentally that *E. coli* chemotaxis exhibits not only Weber's law [8], but also FCD-type response rescaling. We further identified sufficient conditions for Weber's law and FCD within a minimal model of this signaling pathway.

References

[1] Laughlin S (1981) A simple coding procedure enhances a neuron's information capacity. *Z Naturforsch C* 36(:910-912.
[2] Stevens SS (1970) Neural events and the psychophysical law. *Science* 170, 1043.
[3] Fechner GT (1966) *Elements of Psychophysics.* (Holt, Rinehart and Winston, New York).
[4] Goentoro L, Kirschner MW (2009) Evidence that fold-change, and not absolute level, of beta-catenin dictates Wnt signaling. *Mol Cell* 36:872-884.
[5] Cohen-Saidon C, et al. (2009) Dynamics and variability of ERK2 response to EGF in individual living cells. *Mol Cell* 36:885-893.
[6] Shoval O, et al. (2010) Fold-change detection and scalar symmetry of sensory input fields. *PNAS* 107:15995-16000.
[7] Tu Y, Shimizu TS, Berg HC (2008) Modeling the chemotactic response of *Escherichia coli* to time-varying stimuli. *PNAS* 105:14855-14860.
[8] Mesibov R, Ordal GW, Adler J (1973) The range of attractant concentrations for bacterial chemotaxis and the threshold and size of response over this range. Weber law and related phenomena. *J Gen Physiol* 62:203-22.