Fold change detection and scalar symmetry of sensory input fields

Oren Shoval[1], Lea Goentoro[2], Yuval Hart[1], Avi Mayo[1], Eduardo Sontag[3] and Uri Alon[1]

Recent studies suggest that certain cellular sensory systems display fold-change detection (FCD): a response whose entire shape, including amplitude and duration, depends only on fold-changes in input, and not on absolute changes. We discuss benefits of FCD in fields with scalar symmetry, which occurs in a wide range of sensory inputs. Furthermore, we present a wide class of mechanisms that have FCD. This study thus suggests a connection between properties of biological sensory systems and scalar symmetry stemming from physical properties of their input-fields.

Keywords — sensory response, adaptation

Organisms and cells sense their environment using sensory systems. Certain sensory systems have been extensively studied, and their input-output relations are well-characterized, including human senses such as vision, touch and hearing [1-2], and unicellular senses such as bacterial chemotaxis [3-5].

Recent studies of the input-output properties of certain cellular signaling systems [6-7] suggest that these systems show a feature called fold-change detection (FCD): a response whose entire shape, including its amplitude and duration, depend only on fold changes in input, and not on absolute changes [8]. For example, a step change in input from, say, level 1 to 2, gives precisely the same output as a step from level 2 to 4, since the two steps have the same fold change. FCD is more general than Weber's law and exact adaptation: Weber's law concerns only the maximal initial response, and exact adaptation concerns only the steady-state of the response, whereas FCD concerns the entire shape of the response (fig. 1).

Here, we ask what might be the biological function of FCD, and analyze sensory searches in which an organism moves through a spatial sensory field with varying amplitudes. For example, source strength that multiplies the diffusing/convecting chemical fields sensed in chemotaxis, ambient light that multiplies the contrast field in vision, and stochastically varying protein concentrations that multiply the output in many cellular signaling systems.

Furthermore, we ask what molecular mechanisms might give rise to FCD. FCD places strong constraints on potential mechanisms. A recent study showed theoretically that most known models for biological regulation do not show FCD [8]. That study identified one mechanism that can provide FCD, based on the incoherent feedforward loop (IFFL). The IFFL is one of the most common network motifs (recurring circuits in transcription networks), in which an activator activates both an output gene, and a repressor of that gene [9]. Here, we ask whether one can define a larger class of mechanism for FCD, and present a large class of mechanisms that show FCD. These include specific kinds of non-linear integral-feedback loops. We demonstrate that one such loop is found in the bacterial chemotaxis sensory circuit.

Finally, we demonstrate that FCD entails both exact adaptation and Weber's law, but that these two features are not sufficient for FCD. This study suggests a relationship between symmetries of the physical world and the response and design of evolved sensors.

[1]Department of Molecular Cell Biology, Weizmann Institute of Science, Rehovot, Israel.
[2]Department of Systems Biology, Harvard Medical School, Boston, MA, USA.
[3]Department of Mathematics, Rutgers University, Piscataway, NJ, USA.

References

[1] Kandel ER, Schwartz JH and Jessell TM, Principles of Neural Science, 4th Ed., McGraw-Hill (2000).
[2] Keener J and Sneyd J, Mathematical Physiology, 2nd ed., Springer (2009).
[3] Tu Y, Shimizu TS and Berg HC, Modeling the chemotactic response of Escherichia coli to time-varying stimuli, Proc. Nat. Acad. Sci. USA, 105 (2008), pp. 14855-14860.
[4] Levchenko A and Iglesias PA, Models of eukaryotic gradient sensing: application to chemotaxis of amoebae and neutrophils, Biophys J, 82 (2002), pp. 50-63.
[5] Tyson JJ, Chen KC and Novak B, Sniffers, buzzers, toggles and blinkers: dynamics of regulatory and signaling pathways in the cell, Curr Opin Cell Biol, 15 (2003), pp. 221-231.
[6] Goentoro L and Kirschner MW, Evidence that fold-change, and not absolute level, of β-catenin dictates Wnt signaling, Mol. Cell 36 (2009), pp. 872-884.
[7] Cohen-Saidon C, Cohen AA, Sigal A, Liron Y and Alon U, Dynamics and variability of ERK2 response to EGF in individual living cells, Mol. Cell 36 (2009), pp. 885-893.
[8] Goentoro L, Shoval O, Kirschner MW and Alon U, The incoherent feedforward loop can provide fold-change detection in gene regulation, Mol. Cell 36 (2009), pp. 894-899.
[9] Alon U, Network motifs: theory and experimental approaches, Nat. Rev. Genet 8 (2007), pp. 450.