MAR17-2016-009706

Abstract for an Invited Paper
for the MAR17 Meeting of
the American Physical Society

Temporal coding in gene regulation[1]

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Cells face the fundamental problem of having to respond to a nearly unlimited set of distinct input signals with a highly limited set of signaling pathways. Accordingly, many signaling networks exhibit a bow-tie topology: multiple distinct signal inputs (e.g. hormone or stress exposure) converge on a single master regulator, often a transcription factor (TF), which then controls the expression of different downstream target genes. This raises the question of how specificity is achieved. We will discuss recent evidence[2] that signal input specificity is *encoded* through regulation of TF activation dynamics. For example, in budding yeast the master TF Msn2 exhibits short pulses of activity with dose-dependent frequency in response to glucose starvation, but sustained activation with dose-dependent amplitude in response to oxidative stress[3]. Combining high-throughput microfluidics with quantitative time-lapse microscopy, we will show that gene promoters exhibit different activation timescales (slow vs. fast) and thresholds (low vs. high), such that four extreme promoter classes exist[4]. Further, we will show that each promoter class can be preferentially induced by a specific set of Msn2 dynamics such that four distinct gene expression programs can be encoded in the dynamics of a single TF[5] and that promoter class correlates with gene function. Together, our results reveal a temporal code where cells *encode* both signal *identity* and *intensity* information in the activation dynamics of TFs and then *decode* this information at the promoter level. This may allow cells to respond specifically to many signal inputs despite having few signaling pathways.

[1]This research was supported by HHMI.

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[3]Hao, N. and O'Shea, E.K., 2012. NSMB, 19(1), pp.31-39.
[4]Hansen, A.S. and O'Shea, E.K., 2013. MSB, 9(1), p.704.
[5]Hansen, A.S. and OShea, E.K., 2016. Current Biology, 26(7), pp.R269-R271.