W. Szafran* and S. Ji, Rutgers University

Blackbody radiation law-based estimation of the coupling constant between transcriptosomes and degradosomes in budding yeast

Abstract

When DNA microarrays are used to measure RNA levels (also called transcript levels or TLs) in budding yeast at 0, 5, 120, 360, 450 and 850 minutes after switching glucose to galactose, most of the over 6000 different kinds of RNA molecules undergo a decrease in their concentrations during the first 2-3 hours (due to lack of ATP) followed by an increase toward the control levels after this time period when the enzymes needed to metabolize galactose to generate ATP are induced [1, 2]. We have investigated the time course of TLs (to be referred to as RNA trajectories or RNA waves) of about 300 RNA molecules belonging to 15 metabolic pathways. These trajectories can be mapped onto a cluster of 300 points in a 6-dimensional RNA concentration space. The similarity between any pair of RNA trajectories can be calculated as the Euclidean distance between two points in the concentration space. The following observations have been made:

(i) Most (70-90between the trajectories of all possible RNA pairs belonging to a given metabolic pathway obey the blackbody radiation-like equation (BRE), i.e., y = (a/(Ax + B)5)/(exp(b/(Ax + B), where x is distances between RNA trajectories, y is the frequency of observing different distance classes, and a, b, A and B are constants [3,4].

(ii) When RNA pairs are selected from two different metabolic pathways (rather than from within one pathway), the distances between the inter-pathway RNA pairs no longer satisfy BRE but obey instead the Gaussian distribution law [4], indicating that most of the intra-pathway RNA trajectories are mutually correlated (or mechanistically coupled) with one another but the inter-pathway trajectory pairs are not.

(iii) Not all the distances between intra-pathway RNA pairs obey BRE. The percentage of the intra-pathway RNA pairs that satisfy BRE (which is defined as the "coupling constant" between a transcriptosome and its 'conjugate' degradosome for the reason explained below) can be computed from the 'frequency vs. RNA pair distance plot' based on the formula, [1 - (Number of RNA pairs not obeying

BRE)]x100/(Total number of RNA pairs). The following 'coupling constants' have been obtained for the three metabolic pathways examines so far: Glycolysis = 85.7wall biogenesis = 79.3reasonably coherent explanation for the varied 'coupling constants' observed above, we find it necessary to postulate that: (a) Transcriptosomes catalyzing transcription in the interior of the nucleus [5] and degradosomes catalyzing transcript degradation in the cytosol [6] are co-regulated by the yeast cell through as-yet-unknown mechanisms. (b) Each metabolic pathway possesses its own transcriptosome and degradosome, the combination of which can be viewed as an example of the metabolon [7], the hyperstructure [8] and the SOWAWN (Self-Organizing-Whenever-And-Wherever-Needed) machine [9]. (c) Pathway-specific metabolons can exist in at least three internal states designated as the (+)-, (0)- and (-)-states which, respectively, catalyze the increase in, the steady state of, and the decrease in the levels of RNA molecules belonging to a given metabolic pathway. (d) The transcriptosome and degradosome constituting a pathway-specific metabolon are mechanistically coupled, and the degree of coupling is given by "the coupling constant" computed from the "frequency vs. RNA pair distance plot" (see above). The coupling between transcriptosomes and degradosomes is postulated to depend on thermal co-activation of these enzyme complexes in agreement with the fact that the distances between the intra-pathway RNA pairs obey BRE, which is considered to be the Universal Law of Thermal Transitions (or Activations) [3]. Postulate (a) is necessary to explain the fact that the kinetics of TLs (i.e., RNA trajectories or waves) is not random but exhibit regularities as evident in the correlations found among RNA trajectories (see Observations (i) and (ii)). Postulate (b) is required to account for the fact that average RNA trajectories belonging to two different metabolic pathways (e.g., glycolysis and oxidative phoshorylation) can exhibit opposite patterns (see Observation (ii) and [10]). Postulate (c) is mandated by the fact that the kinetics of TLs shows three distinct patterns increasing (+), decreasing (-) or remaining constant (0), which supp[orts the assumption that the metabolon catalyzing the coupled transcription and degradation of RNAs of a metabolic pathway exists in these three states. Since TLs can increase or decrease with n different rates (where n can range from a few to dozens), it would be necessary to further assume that each of the (+)- and (-)-states of a metabolon consists of n substates, just as each electronic energy level in an atom consists of multiple vibrational levels. Postulate (d) highlights the fundamental

role of thermal fluctuations (or Brownian motions) in the mechanism of co-regulating two or more enzymic complexes to effectuate functionally significant whole-cell metabolism. If this postulate is correct, we can conclude that thermal fluctuations are fundamental not only for blackbody radiation and single-molecule enzymology [3, 9] but also for co-regulating two or more enzymic complexes in whole-cell metabolism.

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