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Distances between RNA trajectories are distributed according to Planck's radiation law or the Gaussian distribution law depending on their metabolic functions

Abstract

The genome-wide RNA levels of budding yeast are measured with microarrays at 6 time points (0, 5, 120, 360 and 850 minutes after switching the nutrient from glucose to galactose) [Garcia-Martinez, Aaranda and Perez-Ortin , Mol Cell 15, 303-313 (2004)] and plotted in the 6-dimensional 'concentration-time' or 'trajectory' space, a cluster of about 6000 points is obtained, each point representing the trajectory of an RNA molecule, and the whole cluster can be organized into a group of 30-50 subclusters based on the similarities among the wave shapes of individual RNA trajectories. One challenging problem facing such analyses has been the difficulty of identifying the biological functions of the subclusters. In order to overcome this difficulty, we focused on characterizing the patterns (i.e., wave shapes) of the RNA trajectories (or the RNA concentration waves) unique to specific metabolic pathways of which there are about 200 in budding yeast. To this end, we calculated the n(n-1)/2 Euclidean distances between all possible RNA pairs belonging to a given pathway encoded by n RNA molecules, "binned" them into classes labeled '0-10', '11-20', '21-30', etc, and counted the number of the RNA molecules belonging to each bin. The resulting data can be visualized as a histogram or a 'distribution curve' unique to each metabolic pathway. We previously reported [S. Ji and K. So, Short Talk Abstract B1, The 102nd Statistical Mechanics Conference, 2009] that such distribution curves fitted an equation similar in form to Planck's (or blackbody) radiation law, i.e., $y = a(Ax+B)-5/(e^{(}-b/(Ax+B))-1)$, where a, b, A and B are constants. The purpose of this presentation is to report the following results:

(i) PROCESS-DEPENDENT NUMERICAL VALUES FOR THE PLANCK'S RADIATION LAW-LIKE EQUATION (PRLLE). We now have determined the numerical values of the four parameters of PRLLE as functions of the processes involved. For blackbody radiation, $a = 5.0x10 - 15, b = 4.8x10 - 13, A = 1, B = 0, y =$ spectral intensity, and $x =$ wavelength; for single-molecule cholesterol oxidase enzymic activity [Lu, Xun and Xie, Science 282, 1877-1882 (1998)], $a = 3.5x105, b = 2.0x102, A = 1, B = 0, y =$ frequency of occurrence

of a waiting time, and x = waiting time, i.e., the time an enzyme waits before it is thermally activated to perform simple catalysis; and for the distances in the 'RNA trajectory space' between functionally related RNA pairs, $a = 8.8x108, b = 50, A = 2.23, B = 3.21, y$ = frequency of occurrences of RNA distances, and x = the distance classes between all possible RNA trajectory pairs belonging to a metabolic pathway. It is interesting to note that the ratio, a/b, increases progressively from blackbody radiation (1.04x10-2) to single-molecule enzyme activity (1.75x103) to RNA trajectory pair distances (1.70x107). The cause underlying this regularity is unknown but may be related to the complexity of the systems being measured.

(ii) GAUSSIAN DISTRIBTUIONS. When the RNA pairs are chosen from two different metabolic pathways rather than from within an pathway (e.g., one of the pair from glycolysis and the other from respiration), the distances between the trajectories of such inter-pathway RNA pairs no longer satisfied the Planck's radiation law-like equation but rather were found to fit the Gaussian distribution law. The means and standard deviations of the Gaussian curves for the three pairs of the pathways examined so far, i.e., (a) respiration vs. oxidative phosphorylation, (b) respiration vs. glycolysis, and (c) glycolysis vs. oxidative phosphorylation, are found to be (a) 15 and 4, (b) 17 and 7, and (c) 22 and 5, respectively.

(iii) THE POSIBLE ROLE OF THERMAL FLUCTUATIONS IN CO-ACTIVATING TRANSCRIPTOSOMES AND DEGRADASOMES. The fact that blackbody radiation, single-molecule cholesterol oxidase enzymic activity, and the distances among the whole-cell RNA trajectories (whose shapes are determined by the balance between the rates of two opposing processes, namely transcription catalyzed by transcriptosomes and RNA degradation catalyzed by degradasomes) all obey the same mathematical equation formally similar to Planc's radiation law strongly indicates that thermal motions (also called thermal fluctuations or Brownian motions) are implicated in these processes. It was postulated elsewhere [S. Ji, Energy and Negentropy in Enzymic Catalysis, Ann. N. Y. Acad. Sci. 227, 419-437 (1974); Molecular Theory of the Living Cell: Concepts, Molecular Mechanisms, and Biomedical Applications, Springer, New York, 2011, to appear] that the Generalized Franck-Condon Principle entails an enzyme to undergo thermal fluctuations as a prelude to its electronic rearrange-

ment (also called 'quantum jump') leading to catalysis. Thus it seems necessary only to assume that this two-step mechanism, i.e., "thermal fluctuations –¿ quantum jump", is also implicated in the blackbody radiation, single-molecule enzymology, and the regulation of RNA levels inside the living cell, in order to account for the universality of the Planck radiation law-like equation described above. Just as thermal fluctuations are thought to bring a set of catalytic amino acid residues to transient proximity in the active site of an enzyme so that a quantum jump (i.e., a chemical reaction) can ensue [S. Ji, vide infra], so it is here postulated that thermal fluctuations synchronously activate the enzymic activities of transcriptosomes and their associated degradasomes in such a way as to co-regulate the levels of RNA molecules to meet the metabolic demands of the cell. The precise mechanisms underlying the coupling between a transcriptosome and its associated degradasome have yet to be worked out, but one attractive possibility appears to be that fluctuating transcriptosomes and degradasomes interact with one another through various types of phase-sensitive waves including the electromagnetic, chemical concentration, and non-local quantum waves that are generated ultimately by the covalent bond vibrations within the coupled enzyme complexes [S. Ji, 1974, vide infra].