Quantitative Analysis of the Effective Functional Structure in Yeast Glycolysis

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Appendix S2: Metabolic oscillatory behavior in cellular conditions

During the last four decades, extensive studies of dynamical biochemical behaviors in cellular conditions both in prokaryotic and eukaryotic cells have shown the spontaneous emergence of molecular oscillations in most of the fundamental metabolic processes. For instance, there are oscillatory biochemical processes involved in: NAD(P)H concentration [1], biosynthesis of phospholipids [2], cyclic AMP concentration [3], ATP [4] and other adenine nucleotide levels [5], intracellular glutathione concentration [6], actin polymerization [7], ERK/MAPK metabolism [8], mRNA levels [5], intracellular free amino acid pools [9], cytokinins [10], cyclins [11], transcription of cyclins [12], gene expression [13-16], microtubule polymerization [17], membrane receptor activities [18], membrane potential [19], intracellular pH [20], respiratory metabolism [21], glycolysis [22], intracellular calcium concentration [23], metabolism of carbohydrates [24], beta-oxidation of fatty acids [25], metabolism of mRNA [26], tRNA [27], proteolysis [28], urea cycle [29], Krebs cycle [30], mitochondrial metabolic processes [31], nuclear translocation of the transcription factor [32], amino acid transports [33], peroxidase-oxidase reactions [34], protein kinase activities [35] and photosynthetic reactions [36].

The transition from simple periodic behavior to complex oscillatory phenomena, including bursting (oscillations with one large spike and series of secondary oscillations) [37] and chaos (irregular oscillations)[38] is often observed in metabolic behaviors.

In the conditions prevailing inside the cell, the oscillations seem to represent one of the most striking manifestations of dynamic behavior, of not only qualitative but also quantitative importance in cell metabolic systems; e.g., considering only the transcription processes, it has been reported that at least 60% of all gene expression in Saccharomyces cerevisae oscillate with an approximate period of 300 min [39] and at least 10% of the rest of cellular transcripts oscillate in a circadian manner [40].

This new type of supra-molecular self-organization that operates in far from equilibrium conditions was called dissipative structures by Prigogine [41,42] and the enzymatic functional structures that provide the temporal self-organization of metabolism find their roots in the many regulatory processes that control the dynamics of the enzymes that belong to them [42,43].

The dissipative structure constitutes a fundamental element to understand the emergence of the spatial-functional architecture in cells and provide a conceptual framework that allows us to unify the dynamic, self-organized metabolic processes that occur in all biological organisms [44]. On the other hand, it was also suggested using dissipative metabolic networks that a dynamic global metabolic structure could be present in all living cells [45-49].

Quantitative studies by means of non-linear tools and computational approaches are particularly valuable for exploring dynamic phenomena associated with dissipative metabolic structures, and these methods will be crucial in making sense of the functional metabolic architecture of the cell [44].

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