Studies of glycolysis in yeast provide strong support for Gilbert Ling's Association-Induction hypothesis

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We have explored the coupling of dynamics of intracellular water with metabolism in cells of the yeast *Saccharomyces cerevisiae* exhibiting glycolytic oscillations. Our study demonstrates a tight coupling between the level of ATP and the dynamical state of intracellular water, revealing that the latter parameter is crucial for the emergence of the oscillation. We found that this coupling requires a functional cytoskeleton. We also found that cell volume, heat flux and temperature oscillate synchronously with intracellular ATP. These results are consistent with a recently proposed thermodynamic formalism in which isentropic thermodynamic systems can display coupled oscillations in all extensive and intensive variables. We propose that glycolytic oscillations may arise as a consequence of the requirement of living cells for a constant low-entropy state while remaining metabolically active. We think that these results agree with the Association-Induction hypothesis (AIH) developed by Gilbert Ling (Ling 1962, Ling 2001) proposing that the cell interior behaves as a highly structured near-equilibrium system, constraining the emergence and development of metabolism and coupled phenomena.

We also studied the behavior of intracellular potassium. It is well recognized that a high intracellular K^+ is essential for many processes in both prokaryotic and eukaryotic cells. According to the current view on intracellular ions, e.g. K^+, these are mostly in a free state and their intracellular concentrations are regulated through pumps. An alternative view is offered by the AIH, where a predominantly adsorbed state of intracellular K^+ is proposed. The AIH postulates that the extent of adsorbed intracellular K^+ is regulated by the concerted action of intracellular ATP levels and cytoskeleton proteins (e.g. actin). To test if intracellular K^+ is free or in a bound state we measured temporal oscillations of intracellular K^+ concentration in suspensions of non-dividing yeast cells under conditions that induce temporal glycolytic oscillations. Interestingly, these K^+ oscillations showed the same period as those of glycolytic metabolites (NADH, ATP) and other thermodynamic variables. We experimentally ruled out that oscillations originate in extra- or intracellular K^+ fluxes and conclude that these oscillations arise from fluctuations in free and adsorbed states of K^+ in the cell interior. These results are also consistent with the Association-Induction hypothesis.

Ling, G. N. (1962). A Physical Theory of the Living State: the Association-Induction Hypothesis. New York, Blaisdell Publishing Co, A Division of Random House, Inc.

Ling, G. N. (2001). Life at the cell and below cell level. The hidden history of a fundamental revolution in biology, Pacific Press.