

Regulation of glycolytic oscillations by the dynamics of intracellular water

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We have explored the coupling of dynamics of intracellular water with metabolism in yeast cells. Using the polarity sensitive probe 6-acetyl-2-dimethylaminonaphthalene (ACDAN) we could show that glycolytic oscillations in the yeast *S. cerevisiae* BY4743 wild type strain are coupled to the Generalized Polarization function of ACDAN, which measures the ability of intracellular water to reorient in response to the excited state dipole of the probe. We analyzed the oscillatory dynamics in the wild type and 24 mutant strains with mutations in glycolytic, mitochondrial and vacuolar enzymes/ATPases, as well as proteins involved in actin polymerization and microtubule formation. Using fluorescence spectroscopy, we measured the amplitude and frequency of the metabolic oscillations and linked them to the ACDAN GP in the resting state of all 25 strains. The results show that there exist a lower and an upper threshold of ACDAN GP beyond which oscillations do not occur. The link between glycolytic oscillations and the ACDAN GP value also holds when ATP synthesis or the integrity of the cell cytoskeleton is perturbed. Our results represent the first demonstration that the dynamic behavior of a metabolic process can be, directly or indirectly regulated by a cell-wide physical property: the dynamic state of intracellular water. Our experimental data can be backed up by a mathematical model.