Dynamic flux balance analysis of a genetic engineered cyanobacterium for ethanol production

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We present a Dynamic Flux Balance Analysis approach to study the production of ethanol by a mutant strain of the cyanobacterium *Synechocystis* sp. PCC 6803 obtained by Vidal [1]. This modified strain harbors the genes *pdc* and *adhB* from *Zymomonas mobilis* under the control of the gene *PetE* promoter. The model includes two major components: (a) a dynamic model with mass balances for biomass, ethanol, nitrate, phosphate, internal nitrogen and phosphorus [2] , and (b) a steady state genome-scale metabolic Lineal Programming (LP) model of 466 metabolites and 495 metabolic reactions. The biomass equation includes limiting functions for light, temperature and nutrients, kinetics of growth inhibition by ethanol toxicity and the decrease in the available light by biomass concentration increase. For the intracellular representation, we have modified the metabolic model developed by Yoshikawa *et al*. [3] in order to include the reactions catalyzed by 2-OGDC and SSADH, as it has been recently shown that they close the TCA cycle [4] .

We formulate a dynamic optimization problem for ethanol production maximization subject to mass balance equations and the intracellular LP model. The problem is solved in GAMS through a simultaneous optimization approach [5]. The model was validated with data obtained in experiments performed over 73 hours for mutant and wild type strains of *Synechocystis* in batch liquid cultures [2]. Numerical results provide useful insights on ethanol production by the genetic modified strain within the context of genomic-scale cyanobacterial metabolism.

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