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Towards the Integration of Genome Scale Models and Bioreactors for the Production of Commodity Chemical

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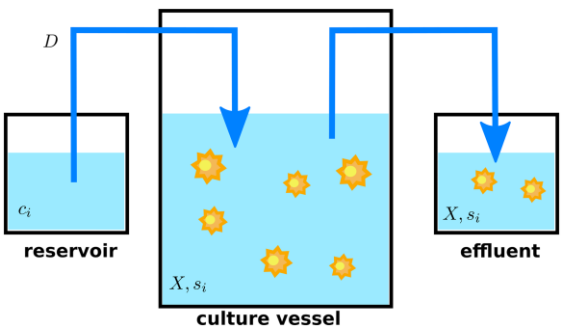
Abstract: Most processes for the production of commodity chemicals rely on fossil fuels, and hence, are highly pollutant. A promising alternative is to develop bioprocesses that make use of genetically engineered cells. A novel modeling framework is proposed to speed up the overall design of bioprocesses and optimize their productivity.

Bioreactor



Bioreactors are devices in which cell cultures can be grown. In continuous fermentation, fresh medium is supplied continuously to the tank while used medium with toxic metabolites, consumed nutrients and cells are removed simultaneously.

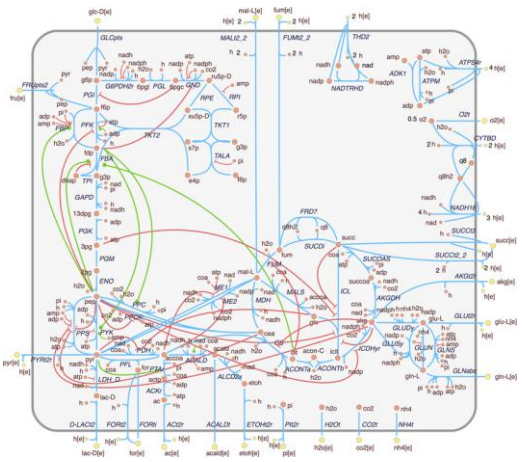
The state of the tank is represented by the following variables: nutrient concentration (glucose), biomass (cell density) and product concentration (citramalate). These variables are modeled by the *places* G, X and C, respectively. The dynamics of X is ruled by the Eq. (1) and G and C are ruled by the Eq. (2).

(1) $$\frac{\mathrm{d}X}{\mathrm{d}t} = (\mu - D)X$$

(2) $$\frac{\mathrm{d}s_i}{\mathrm{d}t} = (c_i - s_i)D - u_i X$$

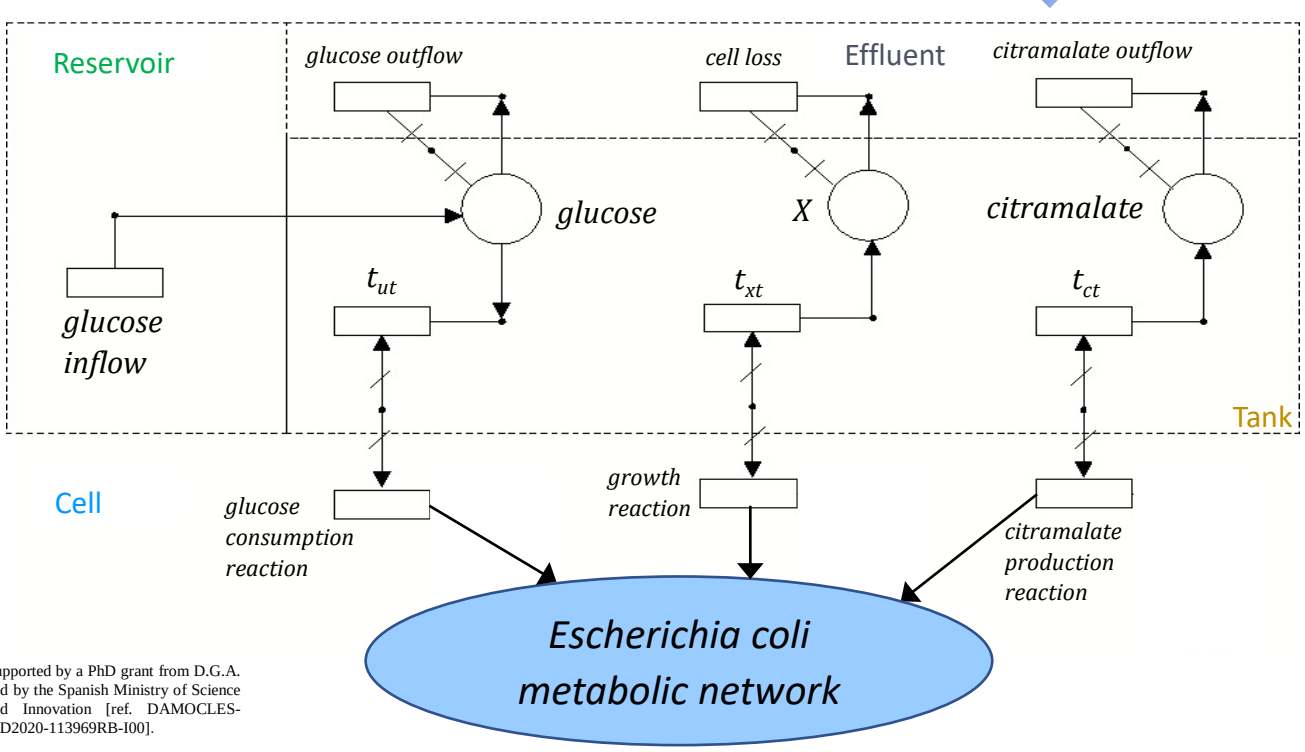
Fernandez-de-Cossio-Diaz J, Leon K, Mulet R. 2017

Genome-scale *E. coli* metabolic network



iJO1366 model:
1805 metabolites, 2583 reactions and 1367 genes
\+ *CimA* gene from *M. janaschii*

Combination and translation into a Flexible Net



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A suitable model for the *E. coli* metabolic network **including a bioreactor** to simulate the nutrient supply and the removal of the metabolites has been successfully designed **using Flexible Nets**. The predictions of the **simulations were consistent** with the values of **citramalate production** provided by collaborators in the University of Nottingham.