AN ADVANCED MODEL-BASED STRATEGY TO OPTIMIZE THE MICROBIAL PRODUCTION OF BIODEGRADABLE POLYMERS UNDER FED-BATCH CONDITIONS

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Polyhydroxyalkanoates (PHAs), a class of microbially produced and completely biodegradable polymers with excellent mechanical properties, have the potential of partially replacing currently used synthetic polymers (e.g., polypropylene, etc.) in several applications.[1,2] Despite the fact that their fermentative production is well known and demonstrated, their commercial development is still impeded by their high production cost, low productivity, high separation cost and the inability to efficiently control their molecular properties.[1] To overcome the above limitations, an integrated mathematical model, consisting of metabolic, polymerization and macroscopic sub-models, was developed in this work to simulate and optimize the fermentative production of polyhydroxybutyrate (PHB, i.e., the first that was discovered and most studied PHA).[2] This multi-scale mathematical model was validated against a series of statistically design experimental data, using a robust wild-type PHB producer, namely, *Azohydromonas lata* bacteria.

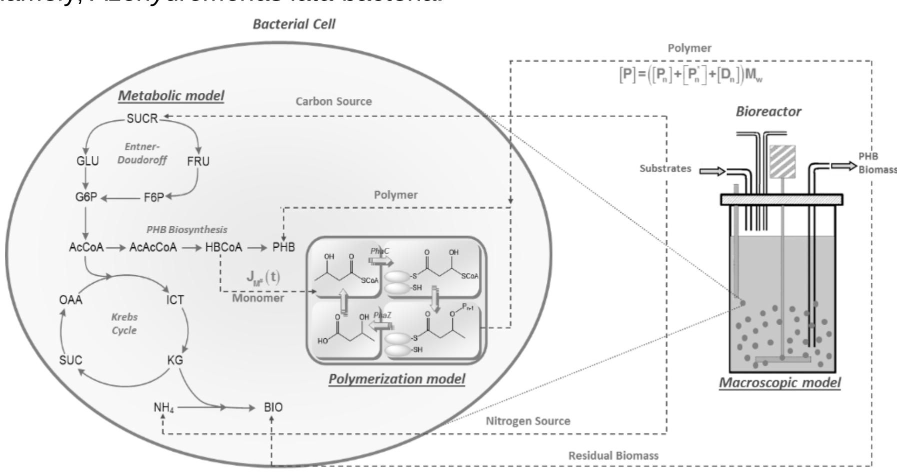

Figure 2 – Combined metabolic-macroscopic-polymerization kinetic model for the production of PHB in Azohydromonas lata.[1]

As can be seen in Figure 1, the model accounted for biomass growth, PHB accumulation, carbon and nitrogen sources consumption, oxygen transfer and uptake rates and average molecular weights (i.e., number and weight average) of the produced biopolymer, under batch and fed-batch cultivation strategies. It should be noted that the intracellular monomer concentration (i.e., precursor of PHB) was the connecting point between the polymerization and macroscopic sub-models. Upon its validation, the model was utilized to estimate several bioprocess operating conditions and feeding strategies, in order to maximize the production rate of PHB with controlled molecular properties. Among the different fed-batch strategies that were simulated, two optimal policies were selected for further experimental evaluation: (1) a nitrogen-limited fed-batch policy based on the single-step feeding of a limited growth medium, aiming at the maximization of the intracellular PHB content, and (2) a nitrogen-sufficient fed-batch policy based on the continuous feeding of a well-designed growth medium, aiming at the maximization of the biomass growth and PHB production rate. These two strategies resulted in a PHB content equal to 94% g/g in the dried biomass and a PHB productivity equal to of 4.2 g/(l·h), respectively. It should be noted that depending on the selection of the operating fed-batch strategies, different biopolymer grades were produced: weight average molecular weight values up to 1,513,000 g/mole.
The present multi-scale modelling approach was developed to clearly demonstrate its potential utilization as a more generic bioreactor simulation and intensification tool for bioprocess optimization.

References

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