110f Genetic Network Driven Control of Phbv Copolymer Composition

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Polyhydroxyalkanoates (PHAs) have attracted a lot of interest as potential substitute to the petrochemically-based polymers. PHAs are produced from renewable resources, biodegradable in different environments, biocompatible to human tissues and blood and characterized by material properties comparable to those of the synthetic plastics. Despite these advantages, PHA production is tremendously smaller than that of the conventional polymers due to an unfavorable economics. A great effort has been undertaken toward improving design of the bacterial strands and developing better fermentation processes. Only a few attempts, however, have been carried out to control the structure of the PHA chains and design environmentally friendly biomaterials with desirable material properties.

Motivated by these challenges, in this work we have developed a strategy to control the mass fraction of poly(3-hydroxybutyrate-co-3-hydroxyvalerate) (PHBV) copolymers. The rationale behind the strategy was guided by a mathematical model that we derived to describe the coupling between the dynamics of molecular weight distribution of PHBV copolymers and those of formation of hydroxybutyrate (HB) and hydroxyvalerate (HV) monomer units. Sensitivity analysis of the model revealed that both the monomer composition and the molecular weight distribution of the copolymer chains are strongly affected by the ratio between the rates at which the two monomer units are incorporated into the chains. This ratio depends on the relative HB and HV availability, which in turn is a function of the expression levels of genes encoding enzymes that catalyze monomer formation. Regulation of gene expression was accomplished through the aid of an artificial genetic network, the patterns of expression of which can be controlled by appropriately tuning the concentration of an extracellular inducer.

Extensive simulations were used to study the effects of operating conditions and parameter uncertainties on the range of achievable copolymer compositions. Moreover, the ability of two different artificial genetic networks to effectively regulate gene expression was comparatively evaluated through simulations. The predicted conditions fell in the range of feasibility of bioprocessing manipulations. Thus, it is expected that such strategy could be successfully employed. As a result, this modeling framework constitutes a useful tool for designing processes that will yield PHBV copolymer structures with desirable characteristics.