Designing Reaction Pathways to Novel Chemicals and Materials Using Kinetic Modeling

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Reaction pathway analysis is a powerful tool to design routes to chemicals and materials that are novel and lead to materials with unique and tailored properties. We have developed methods for the assembly of kinetic models of substantive detail to be built that enable the atomic scale to be linked with the process scale. We have applied our methodology to a wide range of different problems, including production of silicon nanoparticles, biochemical transformations, polymerization and depolymerization, and tropospheric ozone formation. While the chemistries we have studied are seemingly very disparate, applying a common methodology to study them reveals that there are many features of complex reaction networks that are ubiquitous. This presentation will focus on two of the systems we have examined: biochemical production of fuels and chemicals and design of gradient copolymers. It will be shown how reaction pathway analysis can be used to discover novel routes to small molecules and also guide the transformation of small molecules to macromolecules with tailored backbone sequences.

The first portion of the talk will focus on designing novel pathways for the sustainable microbial production of high-value organic compounds as an attractive alternative to organic syntheses that utilize petrochemical feedstocks. For example, the high cost of and the numerous applications for 3-hydroxypropanoate (3HP) make it a valuable target for biosynthesis. We applied the Biochemical Network Integrated Computational Explorer (BNICE) framework for the automated construction and evaluation of metabolic pathways to explore novel biosynthetic routes for the production of 3HP from pyruvate. Among the pathways to 3HP generated by the BNICE framework were all of the known pathways for the production of 3HP and numerous promising novel pathways. The pathways generated for the biosynthesis of 3HP were ranked based on four criteria: pathway length, thermodynamic feasibility, maximum achievable yield to 3HP from glucose during anaerobic growth, and maximum achievable intracellular activity at which 3HP can be produced. Thermodynamic feasibility was assessed using a group contribution method in combination with Thermodynamics-based Metabolic Flux Analysis (TMFA). TMFA was also utilized in all yield and maximum achievable activity calculations. Four pathways emerged from this ranking as the most promising pathways for the biosynthesis of 3HP, and three of these pathways, including the two shortest pathways discovered, were novel. We also discovered novel routes for the biosynthesis of 28 commercially available compounds that are currently produced exclusively through organic synthesis.

The second part of the presentation will focus on the synthesis of gradient copolymers. A gradient copolymer has a gradient in the repeat units comprising the backbone of the polymer arranged from predominantly monomer A to predominantly monomer B along the copolymer chain. Because of the gradual change of the composition along the copolymer chains, gradient copolymers exhibit distinct physical properties compared to those of random or block copolymers of the same composition. Furthermore, the different sequence distribution along gradient copolymer chains may lead to quite different physical properties. Kinetic Monte Carlo (KMC) models, which track molecules instead of concentration, were developed in order to track the explicit sequence distribution for each copolymer chain. Nitroxide-mediated controlled radical polymerization (NM-CRP) was used in synthesizing S/AS and MMA/S gradient copolymers because of its' pseudo-living property. The effects of different synthesis factors on the formation of the compositional gradient along copolymer chains will be described, and the ability to tailor the monomer-by-monomer sequence will be demonstrated.