A Framework for the Identification of Economically Promising Bio-Based Chemicals

Tony (Wenzhao) Wu[1]* (wwu67@wisc.edu), Matthew Long,[1] Xiaolin Zhang,[1] Jennifer Reed,[1] and **Christos Maravelias**[1]

[1]University of Wisconsin, Madison;

Project Goals

Recent progress in metabolic engineering enables the use of engineered microorganisms for the production of chemicals ("bio-based chemicals")[1,2,3,4]. However, it is still unclear which chemicals have the highest economic prospect. To this end, we develop a screening framework (see **Figure 1**) to identify economically promising ones. Specifically, we first develop a genome-scale constraint-based metabolic modeling approach (based on Flux Balance Analysis - FBA), which is used to identify a candidate pool of 209 chemicals (together with the estimated yield, productivity and residence time for each) from the intersection of the High-Production-Volume (HPV) chemicals[5] and the KEGG and MetaCyc databases. Second, we design 3 screening criteria based on a chemical's profit margin, market volume and market size. The total process cost, including the downstream separation cost, is systematically incorporated into the evaluation[6,7,8]. Third, given the 3 criteria assumed in this work, we identify 32 products which are economically promising if the maximum yields estimated based on the FBA (g product/g glucose) can be achieved, while 22 are promising if the maximum productivities (g product L^{-1} day^{-1}) can be achieved. Comparisons between producing the products extracellularly and intracellularly, as well as between using *E. coli* and *S. cerevisiae* are also discussed (see **Figure 2**). The proposed framework provides important guidance for future studies in the production of bio-based chemicals. It is also flexible in that the databases, yield estimations, and criteria can be modified to customize the screening.

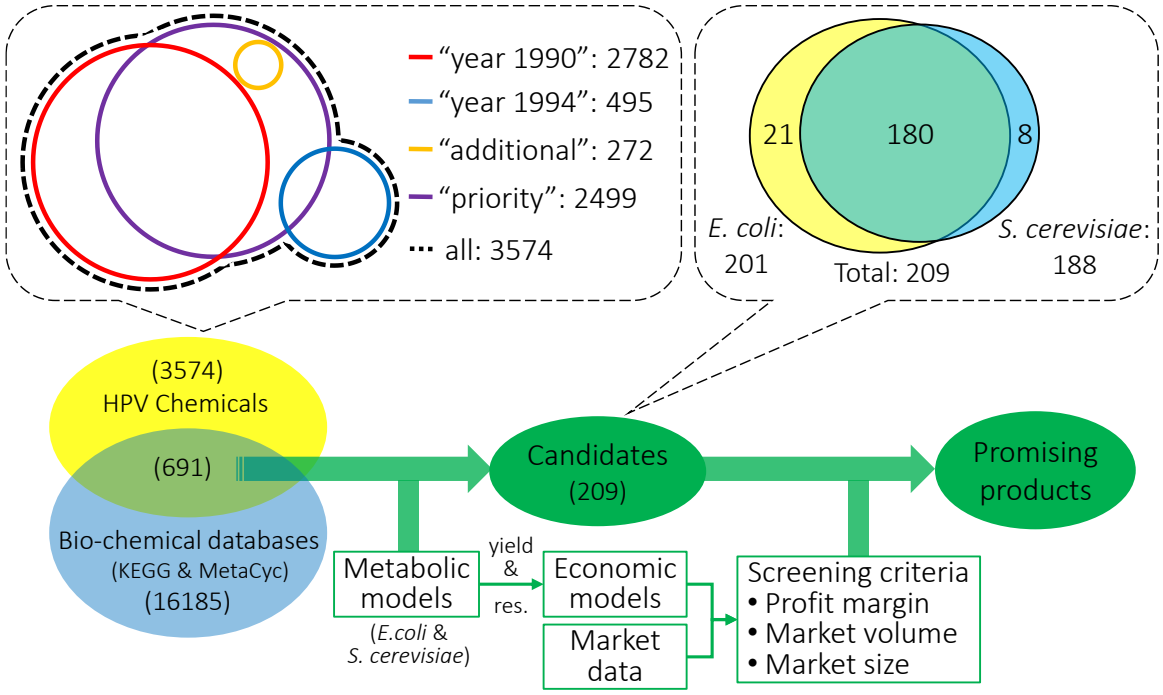

Figure 1. Promising products identification framework, including the compilation of HPV chemicals, identification of the candidate pool and development of the screening criteria. "Res." = residence time.

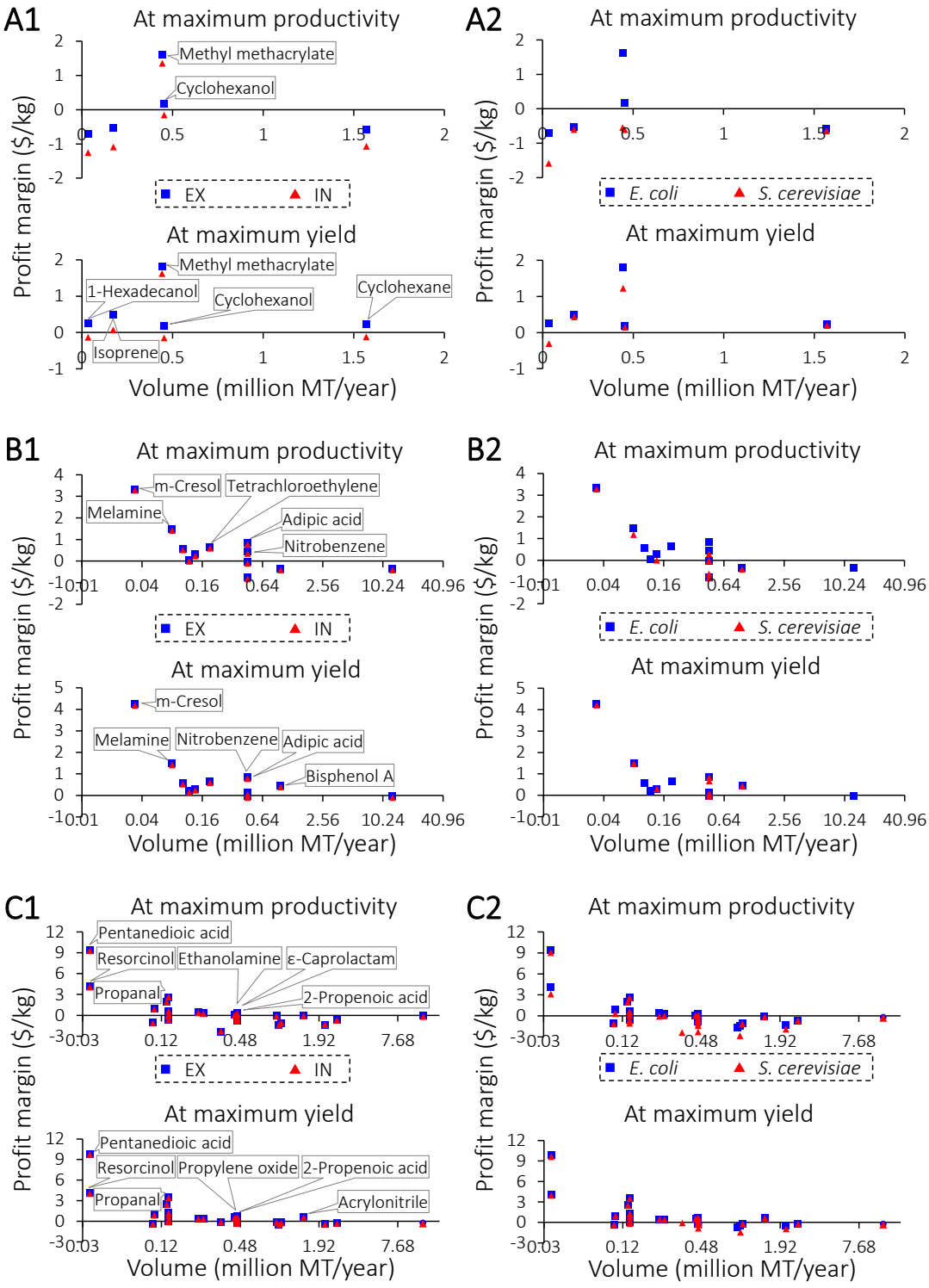

Figure 2. Graphical representation of the screening results at the maximum yield and maximum productivity. (A) Insoluble and light (in terms of density with respect to water) products; (B) insoluble and heavy products; (C) soluble products. A1, B1 and C1 compare EX (extracellular) and IN (intracellular) under the optimal microorganism condition; A2, B2 and C2 compare microorganisms under the optimal localization condition. B1-C2 are plotted on logarithmic scales. Promising products with top 3 profit margins and volumes are labeled in A1, B1 and C1.

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