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Modeling Energy Production Across the Microbial Tree of Life

New high-throughput pipeline enables study of central metabolism in more than 8,000 bacterial species

The Science

The biochemical mechanisms an organism uses to produce energy from nutrients in the environment under various conditions are critically important in defining and predicting its behavior and growth. To simulate and understand plant and microbial energy metabolism, researchers generate metabolic models based on annotated genome sequences. Although powerful, these models—whether automatically reconstructed or manually curated—can produce inaccurate predictions of energy yield because of the challenges in representing complex, interlinking processes and pathways involved in energy biosynthesis. Moreover, draft metabolic models typically contain "gaps," or key missing reactions arising from incorrect or incomplete genome annotations. Gapfilling algorithms provide a solution but also can lead to the inclusion of energy pathways not actually present in the species being modeled. To overcome these prediction challenges, researchers with the DOE Systems Biology Knowledgebase (KBase) have developed a set of high-throughput tools and analyses for understanding microbial energy synthesis using "core metabolic models." Compared to genome-scale models, core metabolic models have a reduced scope

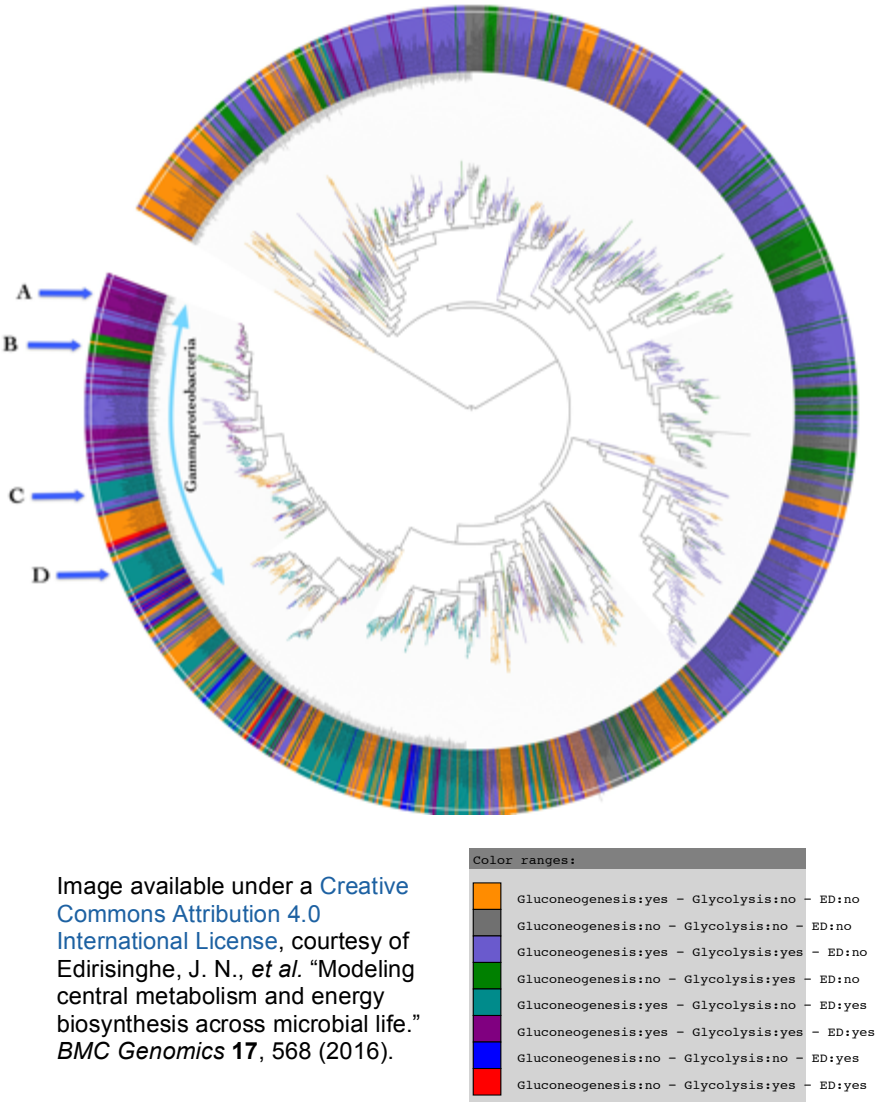

Figure 1: This microbial phylogenetic tree depicts the presence and absence of two sugar degradation pathways (glycolysis and Entner-Doudoroff) and the anabolic pathway of gluconeogenesis. Solid blocks of color indicate which clades gained or lost certain metabolic pathways, while variation in color shows rapid adaptation or evolution (i.e., sparse phylogeny). The curved arrow indicates the range of the Gammaproteobacteria group, and the straight arrows depict regions where members of this group—(A) *Escherichia* and *Salmonella* (purple), (B) *Buchnera* (green), (C) *Shewanella* (light blue), and (D) *Pseudomonas* (light blue)—display different phenotypes.

consisting of well-annotated pathways involved in central metabolism, fermentation, and electron transport chains. The researchers constructed and analyzed more than 8,000 of these models for a well-studied, phylogenetically diverse set of microbes.

The Impact

Using their new modeling and analysis pipeline, researchers were able to examine the variability of core metabolic pathways across the microbial tree of life and accurately predict energy yields for these microbes based on a highly curated model template. This large-scale study also presents a methodology for systematically identifying and correcting inconsistent genome annotations using a combination of core metabolic modeling and phylogenetic analysis. Furthermore, the research demonstrates the value of core metabolic models in identifying the respiratory capabilities of any sequenced microbe, generating hypotheses about the environmental conditions favoring its growth, and evaluating its ability to produce useful fermentation products such as biofuels.

Summary

Core metabolic models representing 48 major phylogenetic microbial groups were constructed based on a core model template consisting of a highly curated set of biochemical reactions derived from a diverse set of model organisms. Researchers selected nearly 200 unique reactions comprising 12 key energy biosynthesis pathways linked to central metabolism and variations of bacterial electron transport chains. The models produced by the new pipeline had minimal need for gapfilling, demonstrating their value as functional models that align as closely as possible with raw annotation output, minimizing the number of model-driven conjectures. This study demonstrates that core metabolic models can be used to quickly and accurately (1) determine and predict microbial respiration types and energy (ATP) yields; (2) identify electron acceptors that can be reduced during anaerobic respiration; (3) determine the presence or absence of functional pathways in central metabolism and the phylogenetic distribution of these key pathways; (4) evaluate a microbe's fermentation capabilities; and (5) assess its ability to produce key pathway intermediates in central metabolism that are precursors of essential biomass compounds.

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Publication

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Related Links

The authors' core metabolic model construction pipeline and supporting commentary can be accessed through KBase's Narrative Interface at narrative.kbase.us/narrative/ws.15253.obj.1.