

# Linking Overflow Metabolism and Growth Cessation in *C. thermocellum*

## Background

- Most studies of *C. thermocellum* metabolism have focused on relatively low (< 10 g/L) substrate concentrations.
- However commercial viability requires substrate loadings of at least 100 g/L cellulosic materials.

## Approach

- Employed genome-scale metabolic model of *C. thermocellum*, thermodynamic analysis, and fermentations to analyze the cellular state during high substrate loading batch fermentations to answer specifically:
  - Why does *C. thermocellum* produce overflow metabolites when growth stops, instead of continuing to produce the major fermentation products at higher yields, and
  - Does growth cessation dictate the appearance of reduced overflow metabolites?

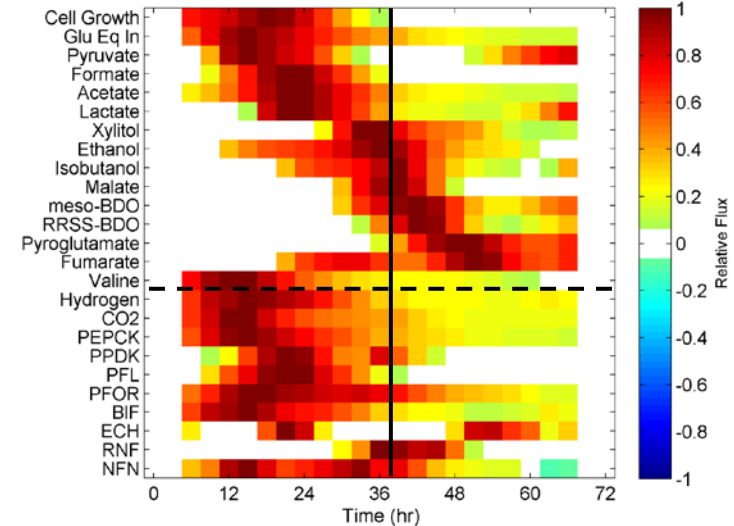
## Outcome

- Hydrogen and formate accumulation perturbed the complex redox metabolism and limited conversion of pyruvate to acetyl-CoA conversion, likely leading to overflow metabolism and growth cessation.
- Manipulation of fermentation conditions to alleviate hydrogen accumulation could dramatically alter the fate of pyruvate, providing valuable insight into process design for enhanced production of chemicals and biofuels.

## Significance

- Findings of growth cessation and overflow metabolism provide metabolic engineering and fermentation strategies for high substrate loading fermentations to achieve high product yields.

Dynamic flux distribution during 100g/L cellulose loading batch fermentation



Proposed mechanism of growth cessation and overflow metabolism

