



Metabolic Flux Analysis:

Software Tools for Modeling, Simulation and Experimental Design of ^{13}C Labeling Experiments

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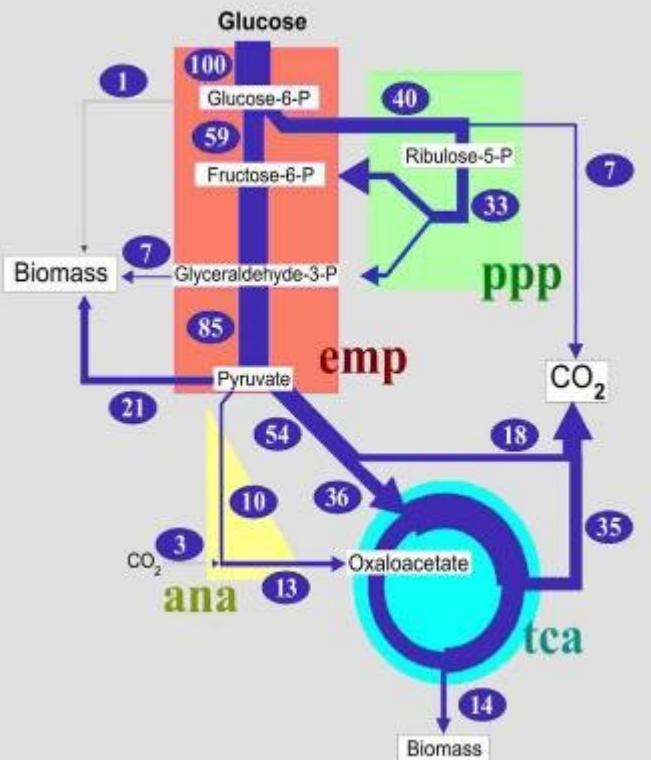
The Challenge

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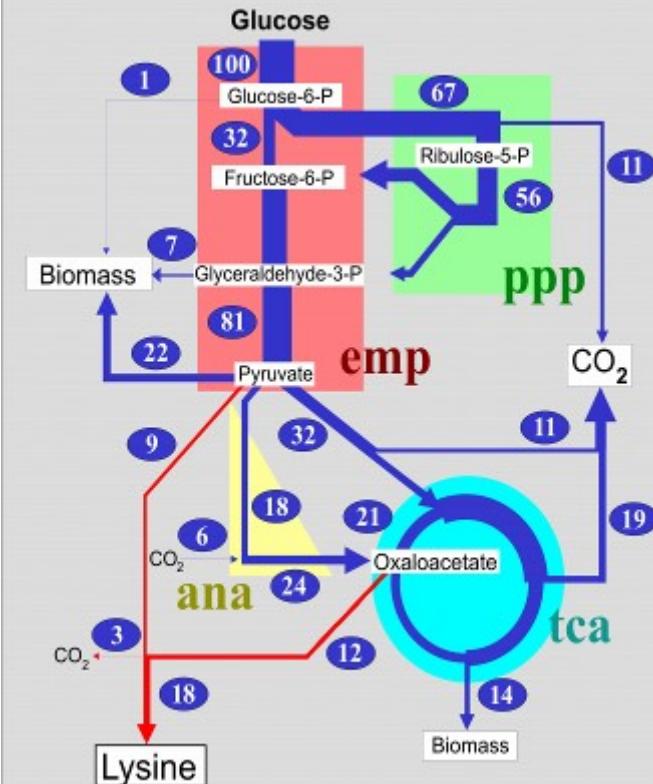


Flux Analysis Example: *Corynebacterium glutamicum*

Wild strain



Lysine producer



- Screening: strain comparison
- Design: detecting „bottlenecks“
- Diagnostics: genetic manipulations

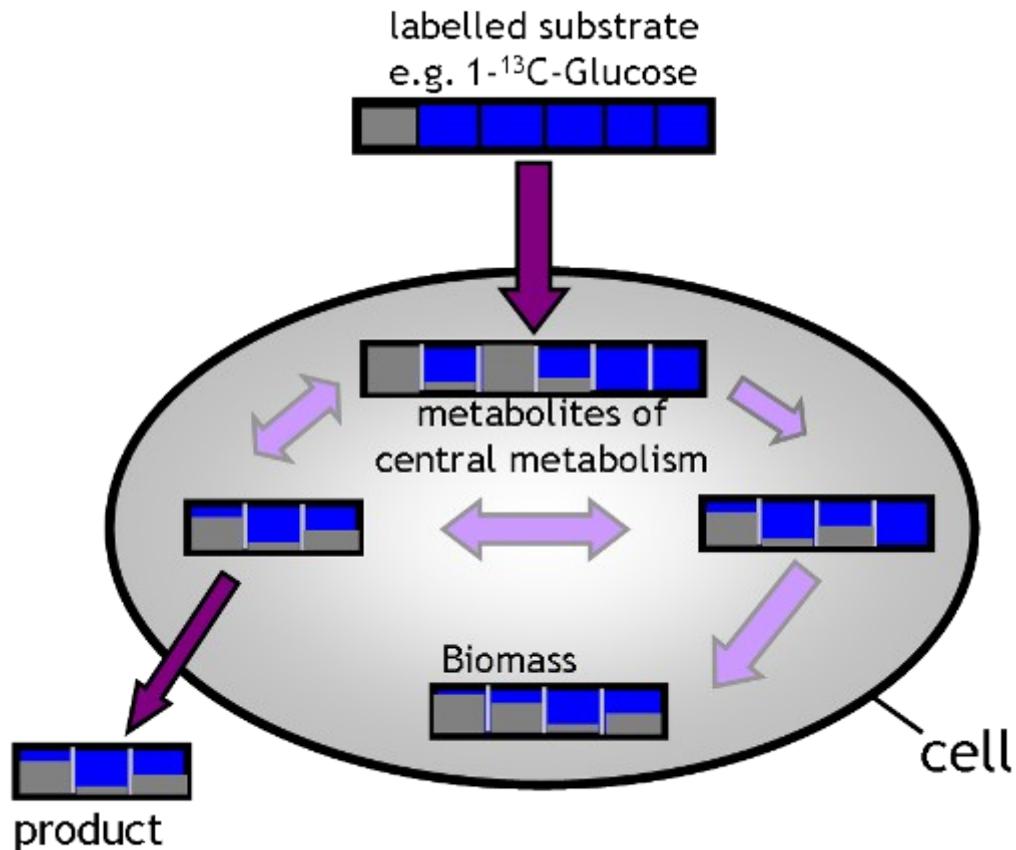


The Experiment

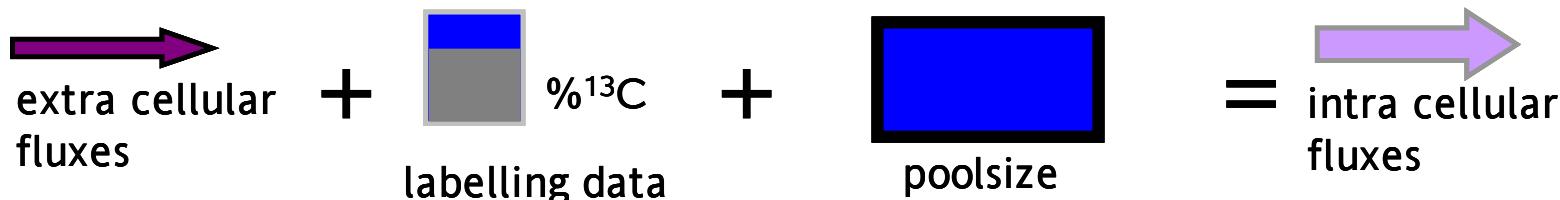
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The Principle of ^{13}C Metabolic Flux Analysis

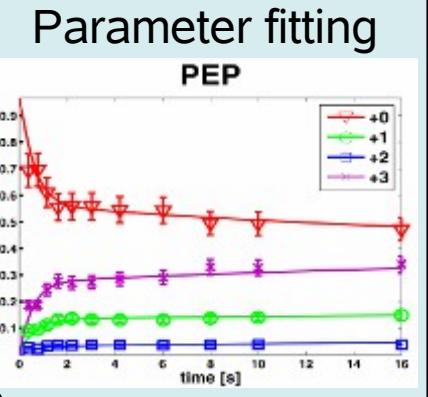
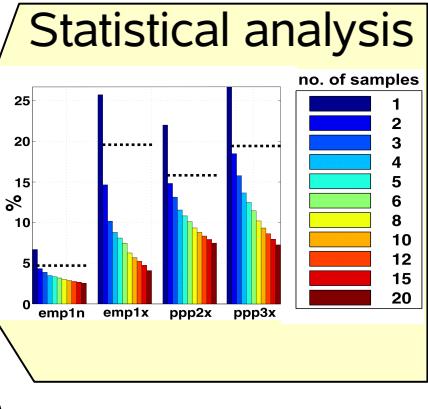
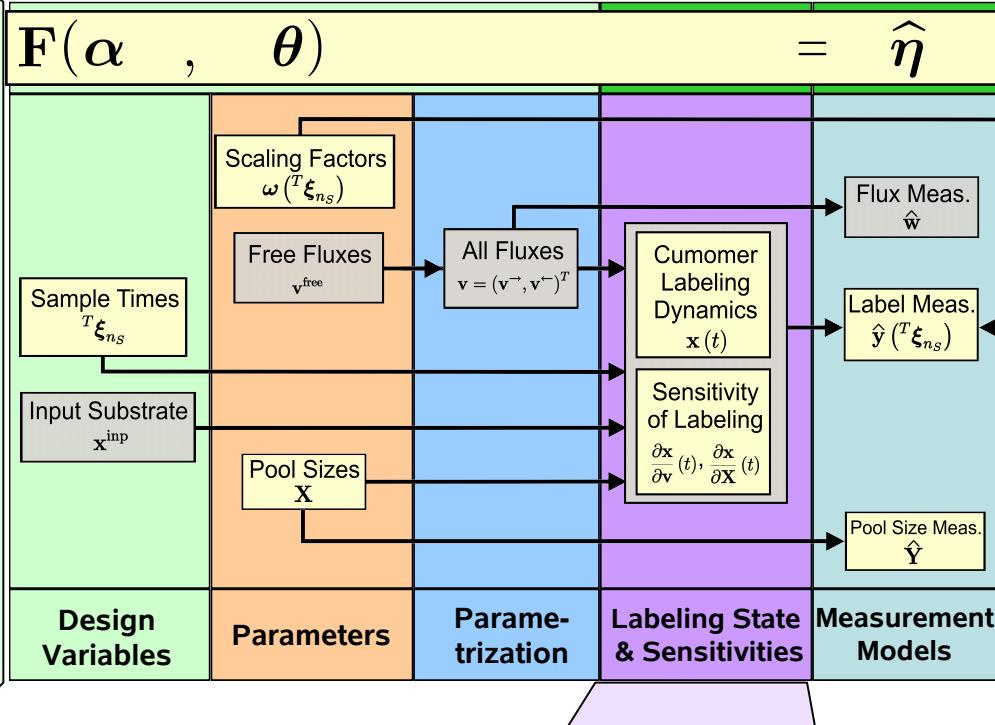
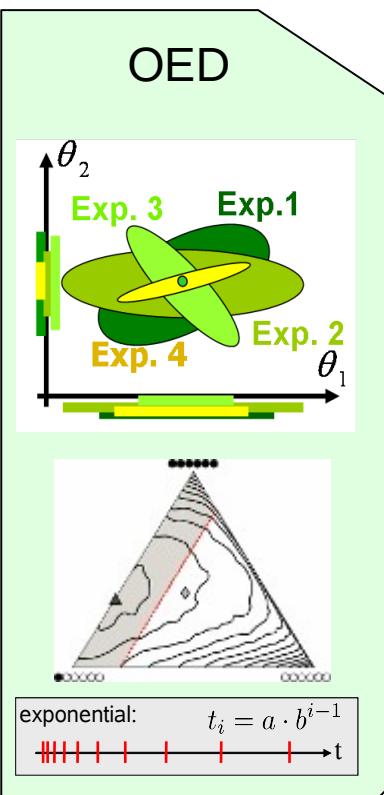


- Incorporation of ^{13}C -substrate
- Metabolic stationarity assumption
- Analysis of ^{13}C distribution in intermediate components
- Network stoichiometry & extracellular fluxes



The Computational Tools

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Model structure

$$\text{diag}({}^i\mathbf{X}) \cdot {}^i\dot{\mathbf{x}} = {}^i\mathbf{A}(\mathbf{v}) \cdot {}^i\mathbf{x} + {}^i\mathbf{b}(\mathbf{v}, \mathbf{x}^{\text{inp}}, {}^{<i}\mathbf{x}), i = 1(1)m$$

1000 labeling equations
>> 100.000 sensitivity equations