Team work in (bio)chemical process modeling and control: two case studies

Ilse Smets

K.U.Leuven - BioTeC
Katholieke Universiteit Leuven

DYSCO Study Day, Mons, May 28, 2009

Outline

- Case study 1:
  Dynamic optimization of
  reverse flow chemical reactors

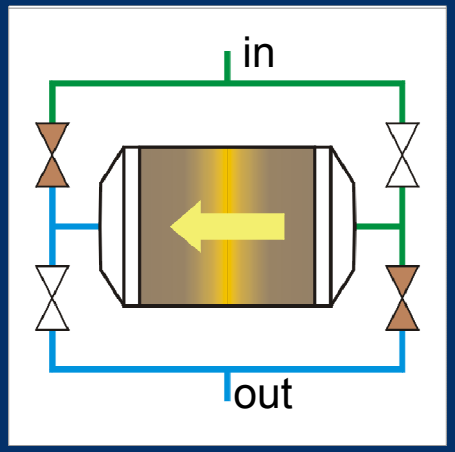
- Case study 2:
  Metabolic flux analysis of an underdetermined metabolic network

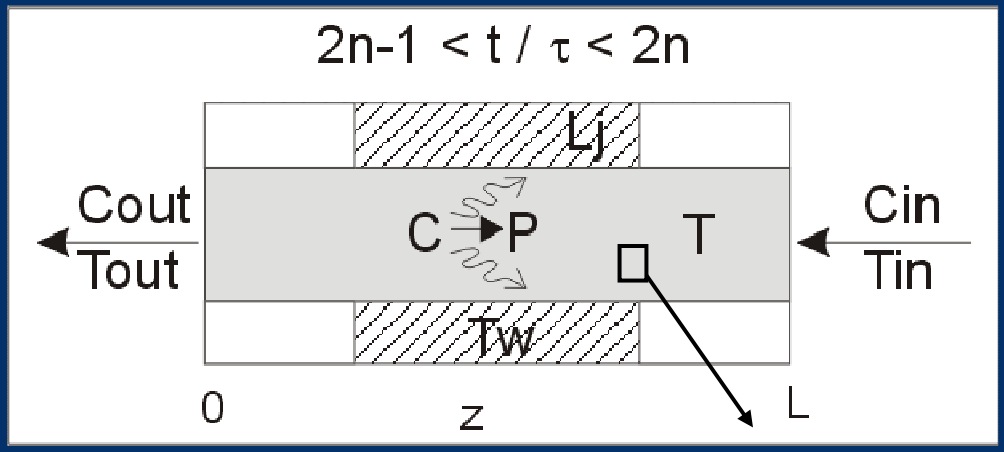
Case study 1
Dynamic optimization of reverse flow chemical reactors

Filip Logist and Jan Van Impe
K.U.Leuven - BioTeC
Katholieke Universiteit Leuven

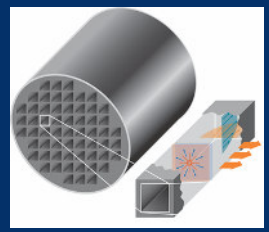
Alain Vande Wouwer
Faculté Polytechnique de Mons

Reverse flow reactor (RFR)



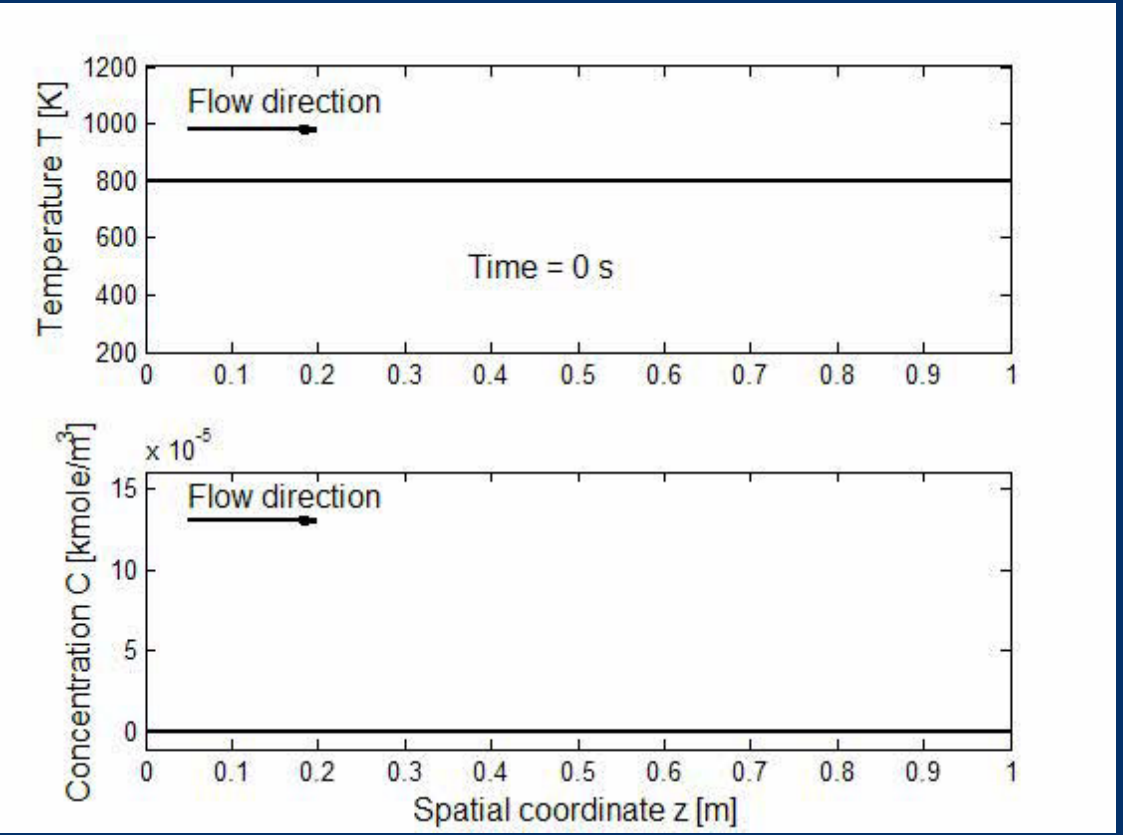


- Used for gas-solid reaction processes, e.g., combustion of Volatile Organic Compounds (VOCs)
- Periodic flow reversals cause the fixed bed to act as regenerative heat exchanger



Reverse flow reactor (RFR)

– In cyclic stationary state RFR exhibits trapezoidal temperature profiles moving back and forth



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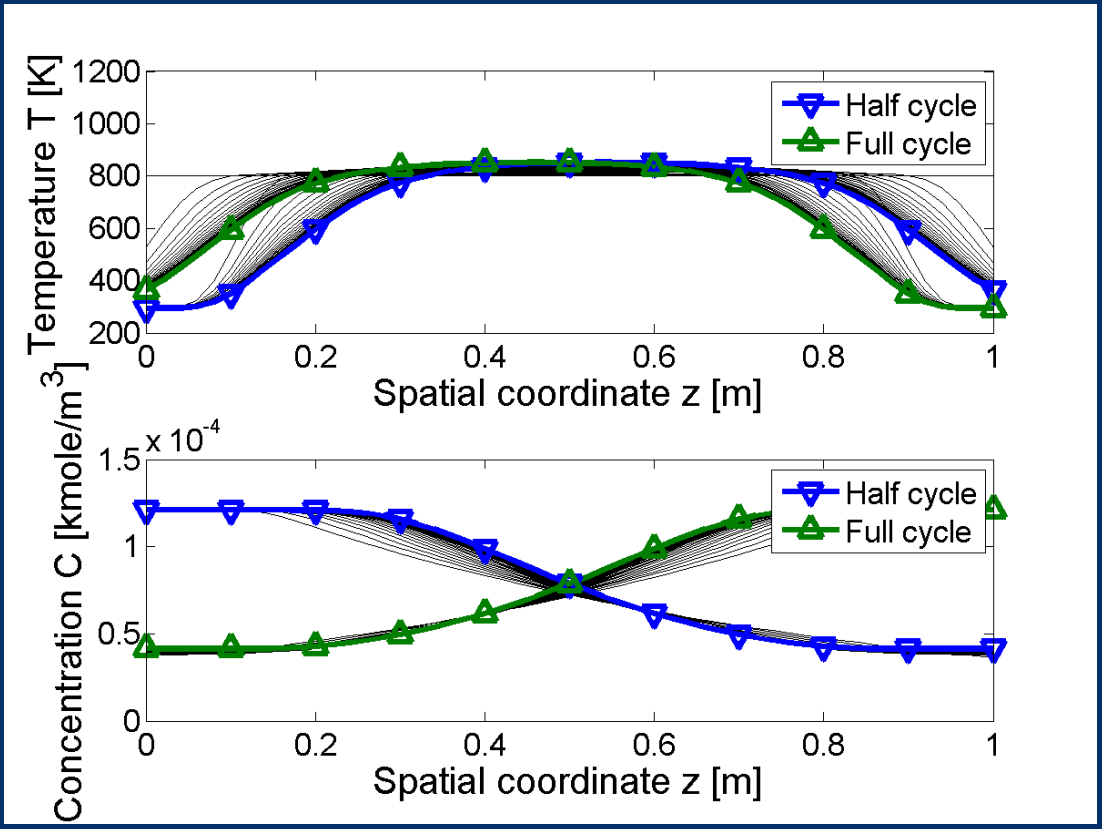


Optimization problem formulation

- Objectives:
  - 1 time averaged conversion cost
  - 3 time averaged energy costs
- Model:
  - Reverse Flow Reactor (RFR) *(Eigenberger & Nieken, 1988)*
  - jacket added for enhanced temperature control
- Constraints:
  - reactor temperature
  - jacket fluid temperature

Optimization problem formulation

- Example: RFR

$$J'_{\mathrm{TIC2}} = \boxed{(1-A)\frac{\int_0^{2\tau} C_{\mathrm{out}}(t)dt}{2\tau} +} \quad \text{conversion}$$

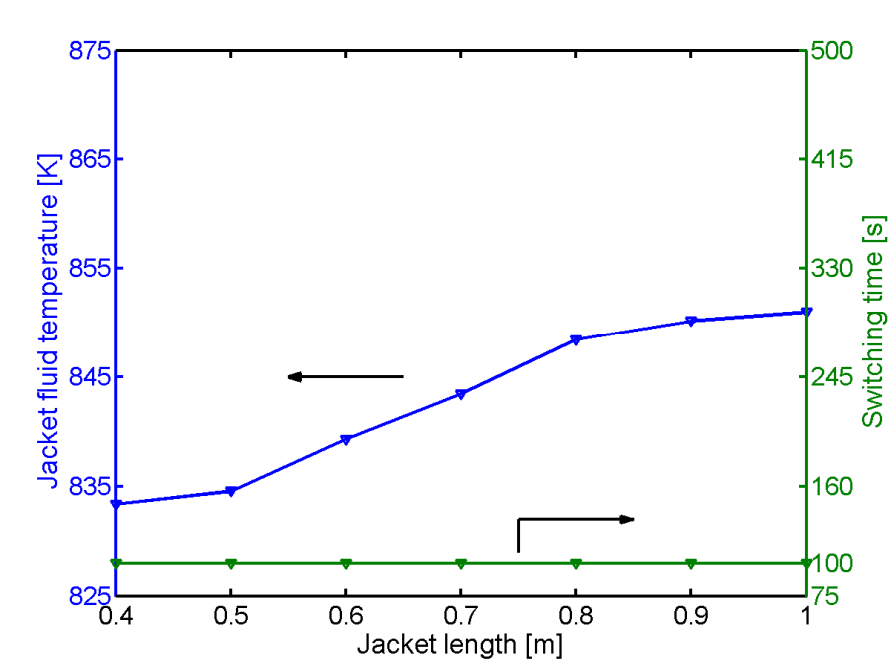
$$\boxed{\frac{A}{K_4}\frac{\int_0^{2\tau}\int_0^{L}\frac{4h}{\rho_g c_{pg} T_{\mathrm{in}} L d}(T_w - T(z,t))dz\ dt}{2\tau}} \quad \text{net heat exchange}$$

- Sensitivity analysis:
  - most important parameters: switching time τ, jacket fluid temperature T_w & jacket length L_j

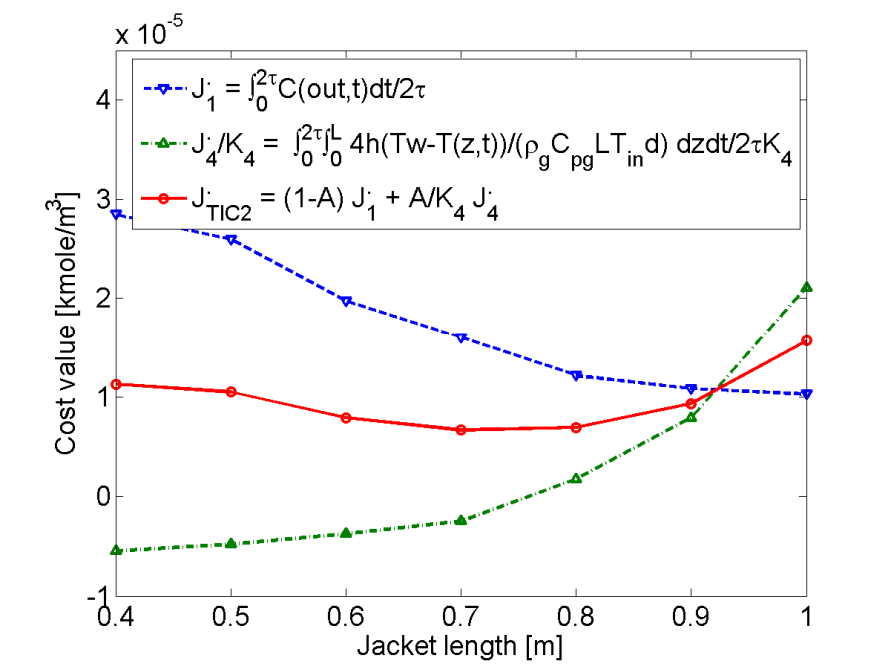
Results

- Optimization

Optimal jacket temperatures and switching times



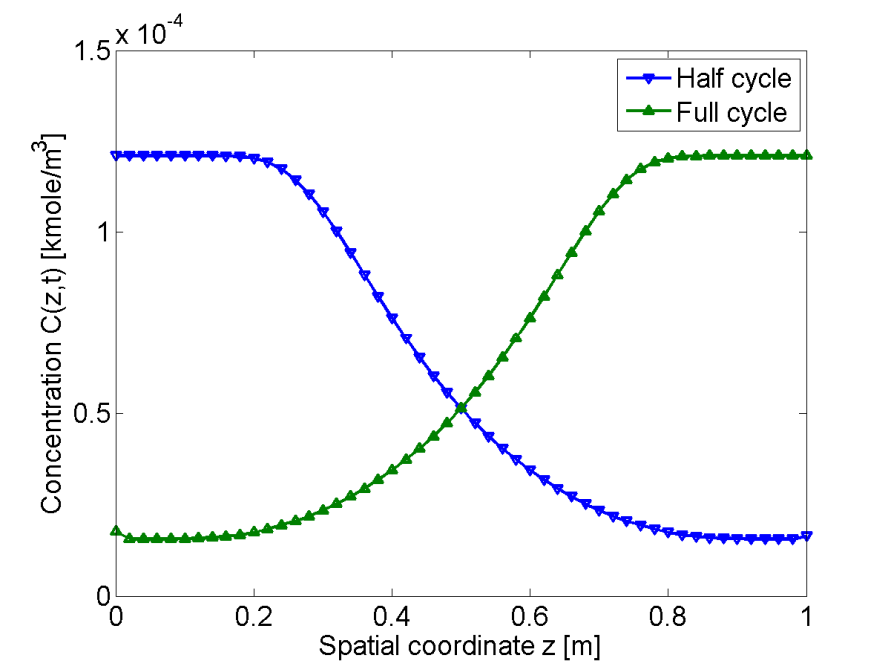
Optimal cost values



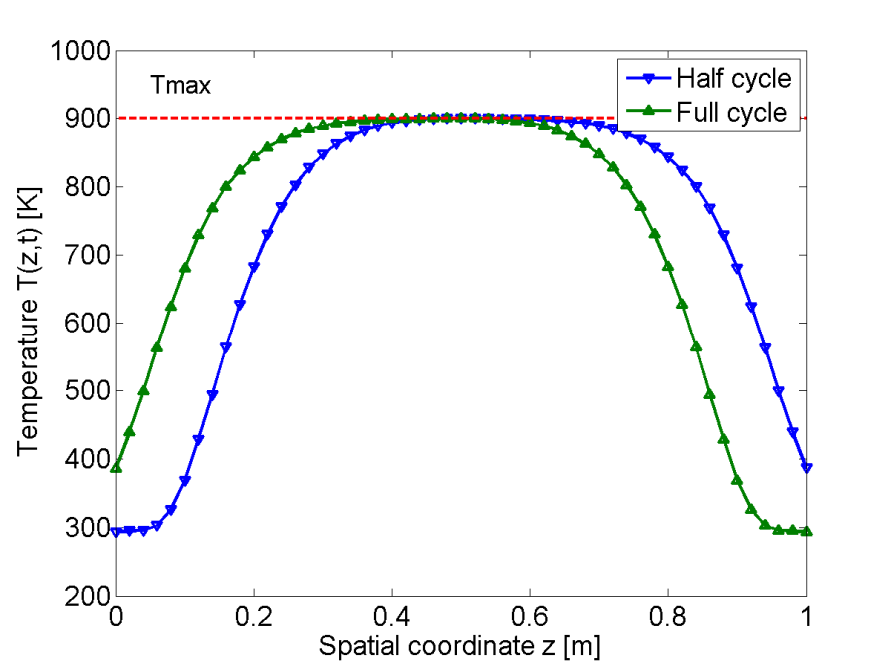
Results

- Optimized cyclic stationary state

Concentration profiles

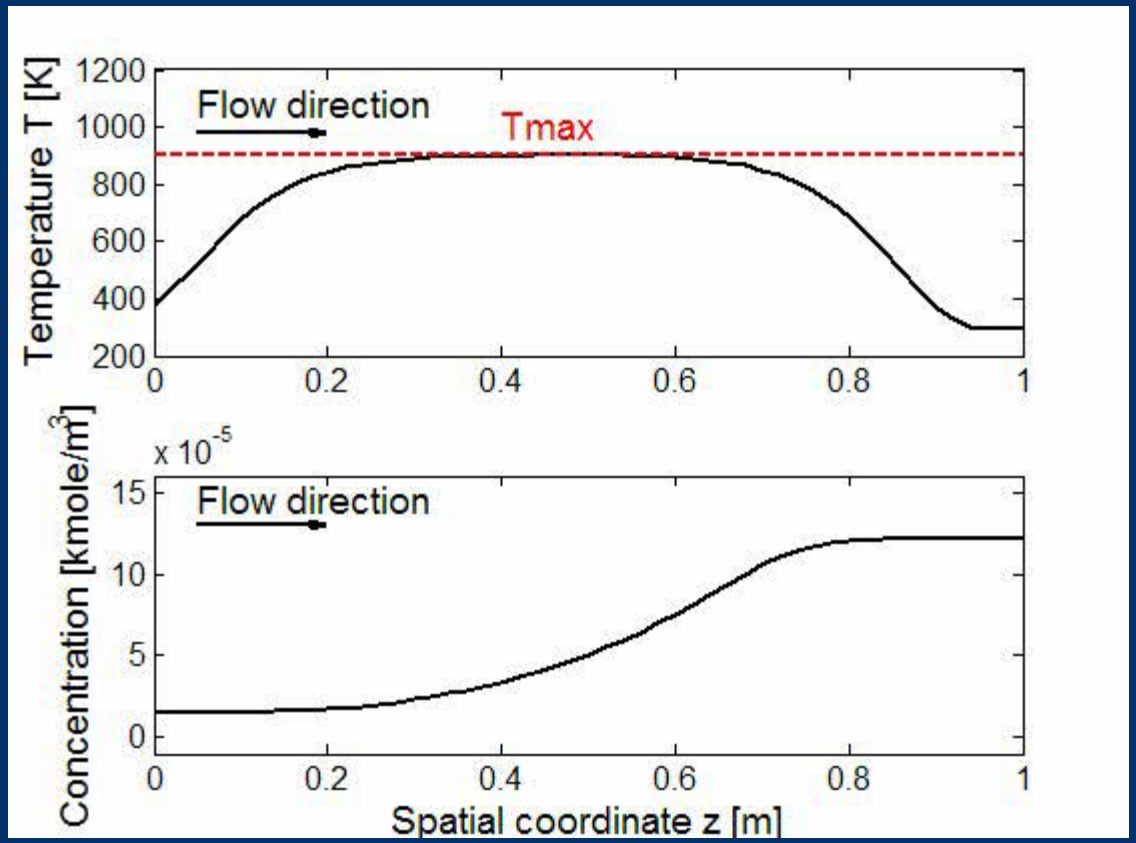


Temperature profiles



Results

- Optimized cyclic stationary state



Further improvements

- Multiple objective optimization through Normal Boundary Intersection (NBI) instead of weighted sum approach
- Optimization through *multiple shooting* instead of direct simulation

Outline

- Case study 1:
  Dynamic optimization of
  reverse flow chemical reactors

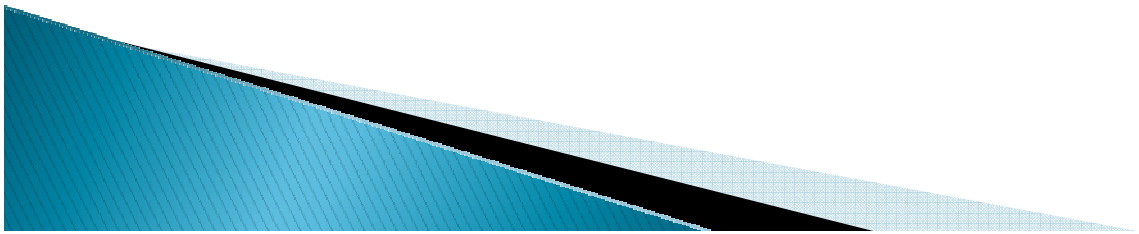
- Case study 2:
  Metabolic flux analysis of an underdetermined
  metabolic network

Case study 2

Metabolic Flux Analysis of an underdetermined metabolic network

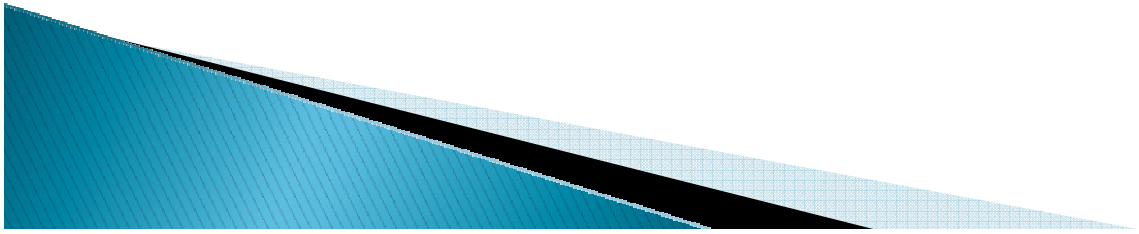
Francisca Zamorano,
A. Vande Wouwer,
Faculté Polytechnique de Mons,
Belgium

Georges Bastin,
Université Catholique
de Louvain, Belgium



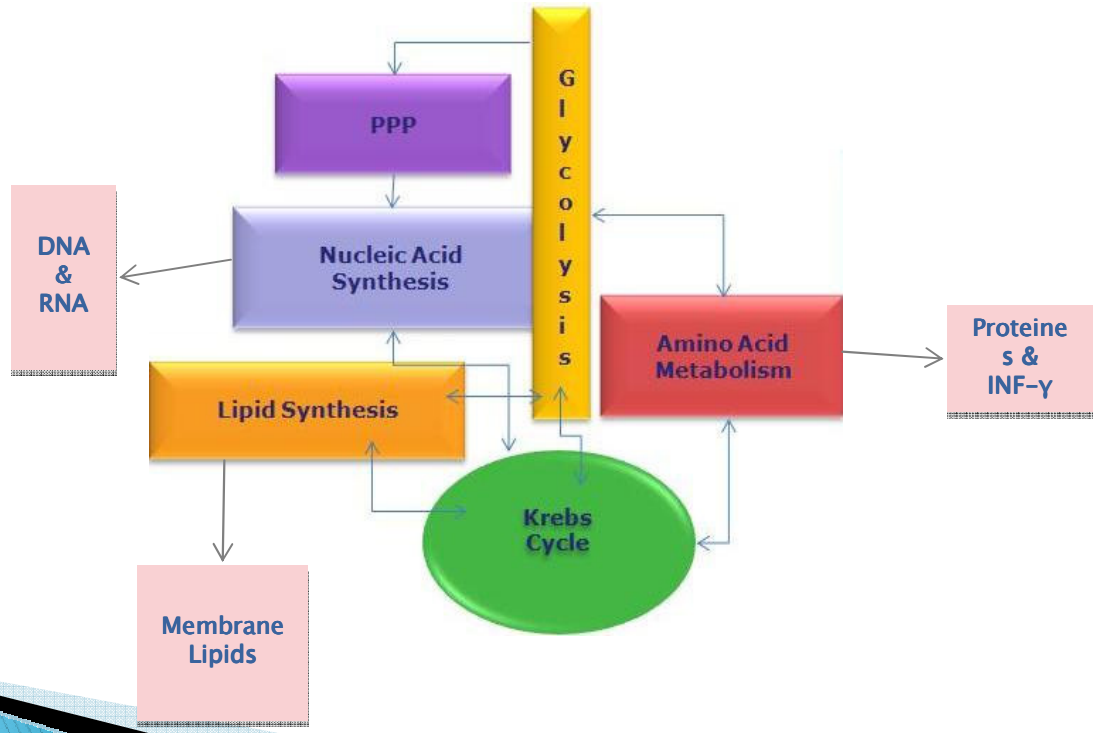
Objectives

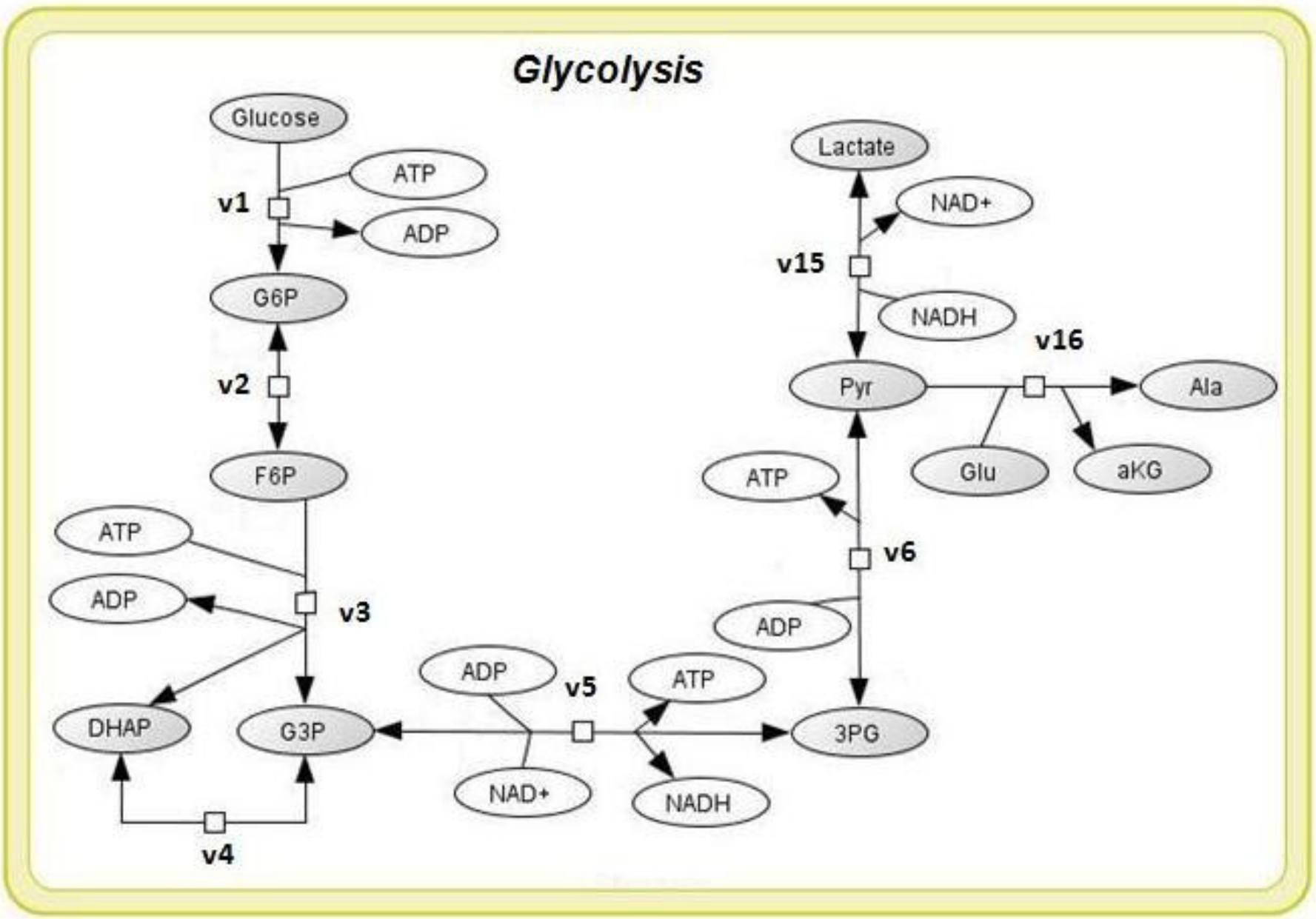
- Study a detailed metabolic network describing the metabolism of CHO-320 cells
- Estimate the metabolic fluxes of an underdetermined mass-balance system using tools of positive linear algebra
- Check the validity of the underlying network analyzing the results with respect to the hypothesis made.
- Identify which are the most informative measurements



Metabolic Network

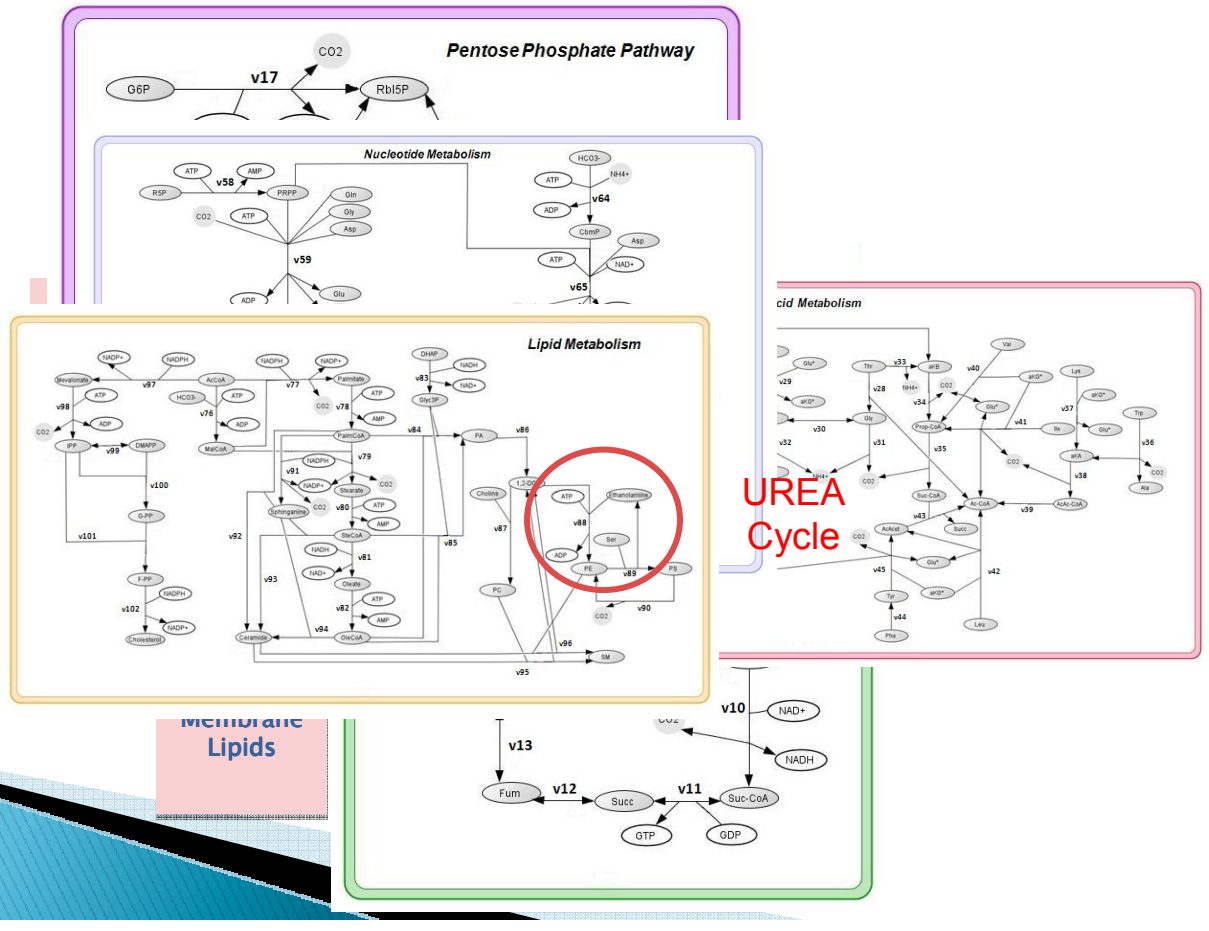
- Graphical representation of the metabolism of CHO-320 cells




Glycolysis
Glucose
ATP
v1
ADP
G6P
v2
F6P
ATP
ADP
v3
DHAP
G3P
v4
ADP
v5
ATP
NAD+
NADH
3PG
Lactate
NAD+
v15
NADH
v16
Pyr
Ala
Glu
aKG
ATP
v6
ADP

Metabolic Network

- Graphical representation of the metabolism of CHO-320 cells



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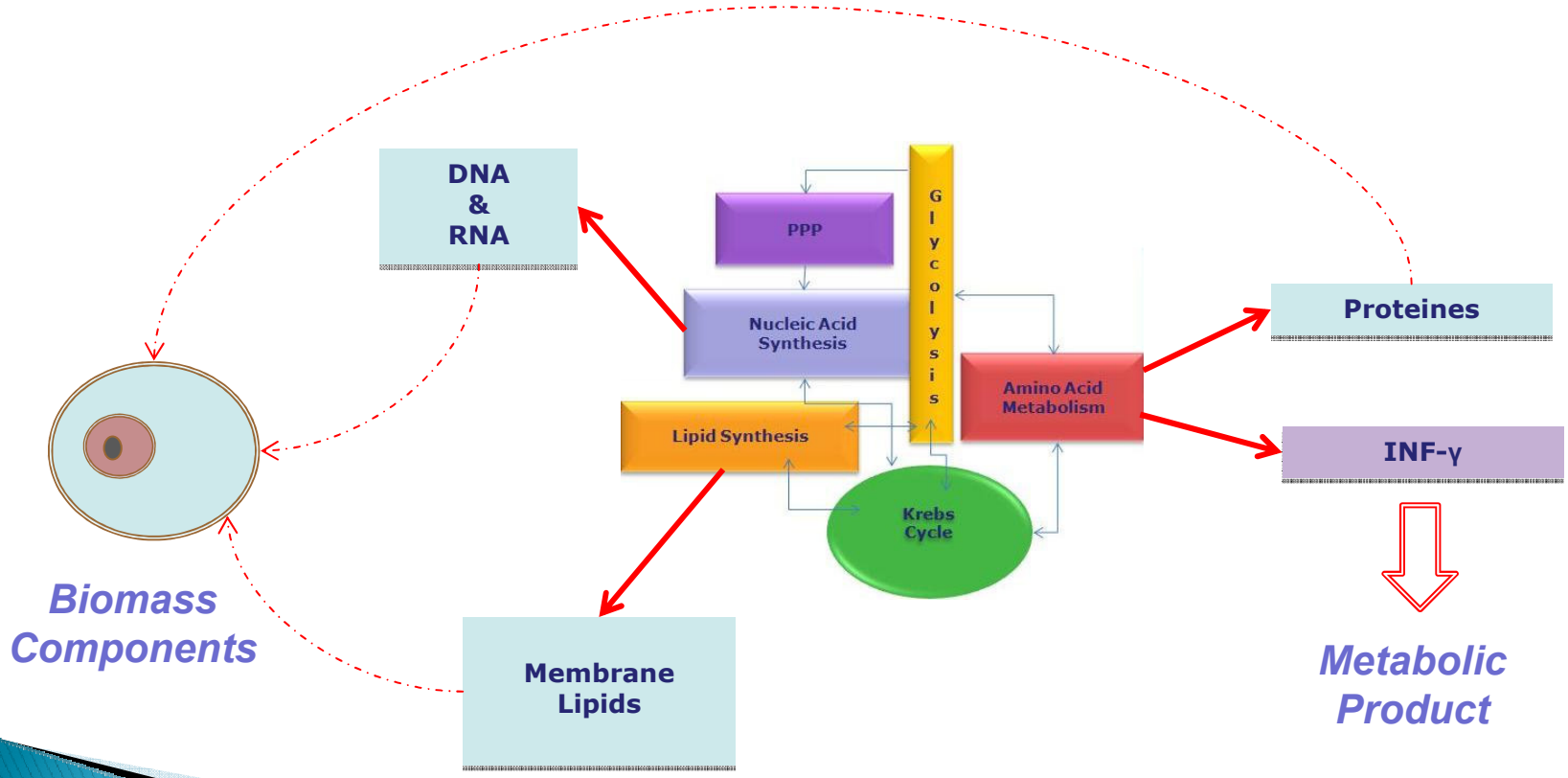
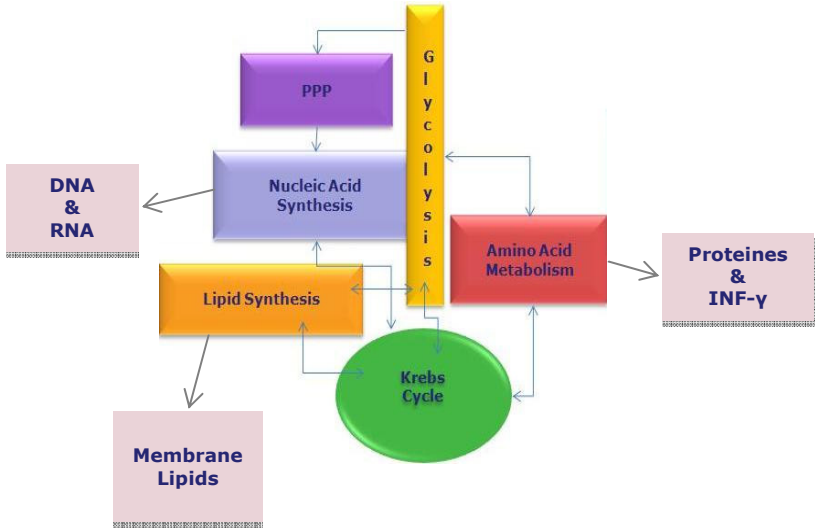


The metabolic network involves 118 reactions (unknown fluxes)

Metabolic Flux Analysis through flux intervals estimation



- A proper stoichiometric matrix represents the metabolic network

$$\mathrm{N}(80 \times 118)$$

- Pseudo steady-state assumption

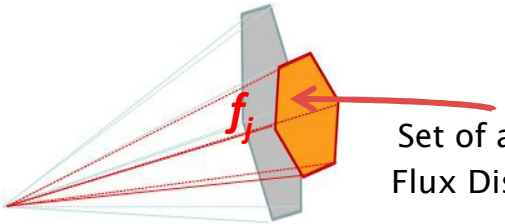
$$\mathrm{N} \cdot \nu = 0$$

- Additional constraints coming from the extracellular measurements

$$\mathrm{N}_m \cdot \nu = v_m$$

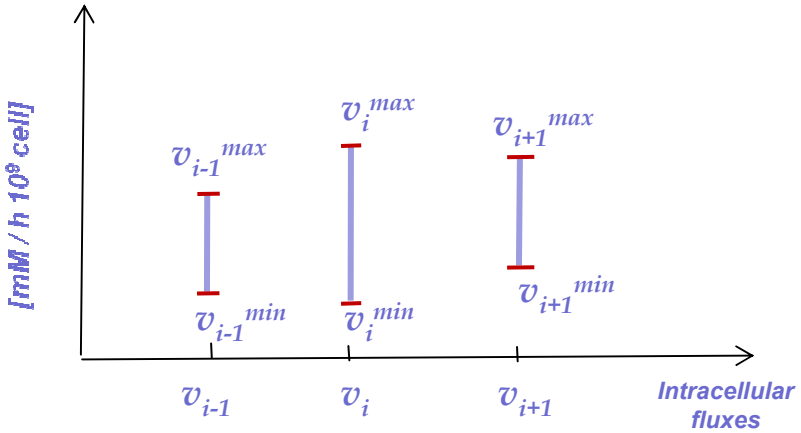
- Underdetermined System of Equations (Larger number of reactions than intracellular metabolites)

Metabolic Flux Analysis through flux intervals estimation



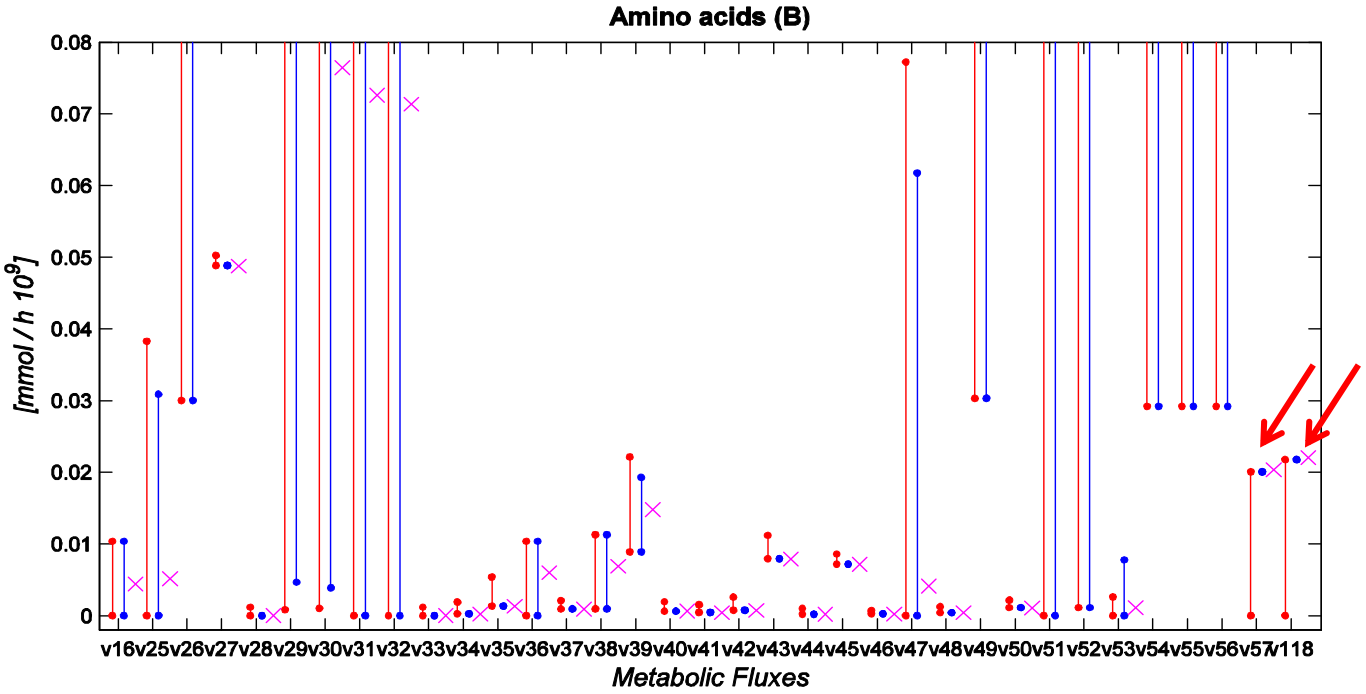
$$\begin{pmatrix} \mathrm{N} \\ \mathrm{N}_m \end{pmatrix} \cdot v = \begin{pmatrix} 0 \\ v_m \end{pmatrix}$$

- Determination of the intervals through the calculation of the set of admissible solutions.
- The limiting values (min/max) for each metabolic flux are found so as to establish a range of possible values for each metabolic flux.



Some Results

- Determination of the flux intervals
  - Only with the experimental data (RED)
  - Assuming that Threonine is exclusively used for protein synthesis (BLUE)
- Determination of a solution that maximizes the biomass production (lilac)



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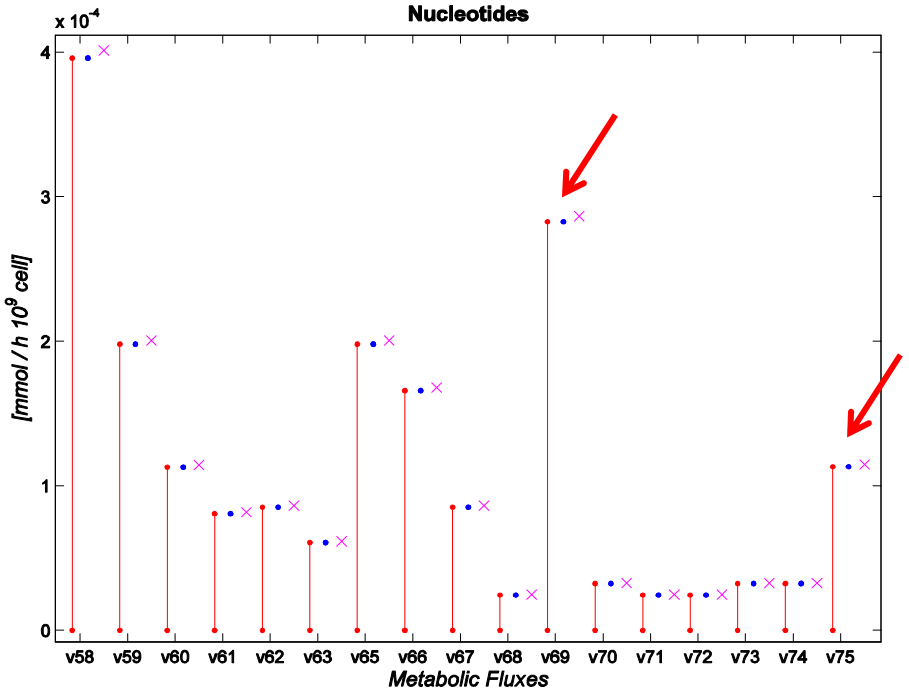

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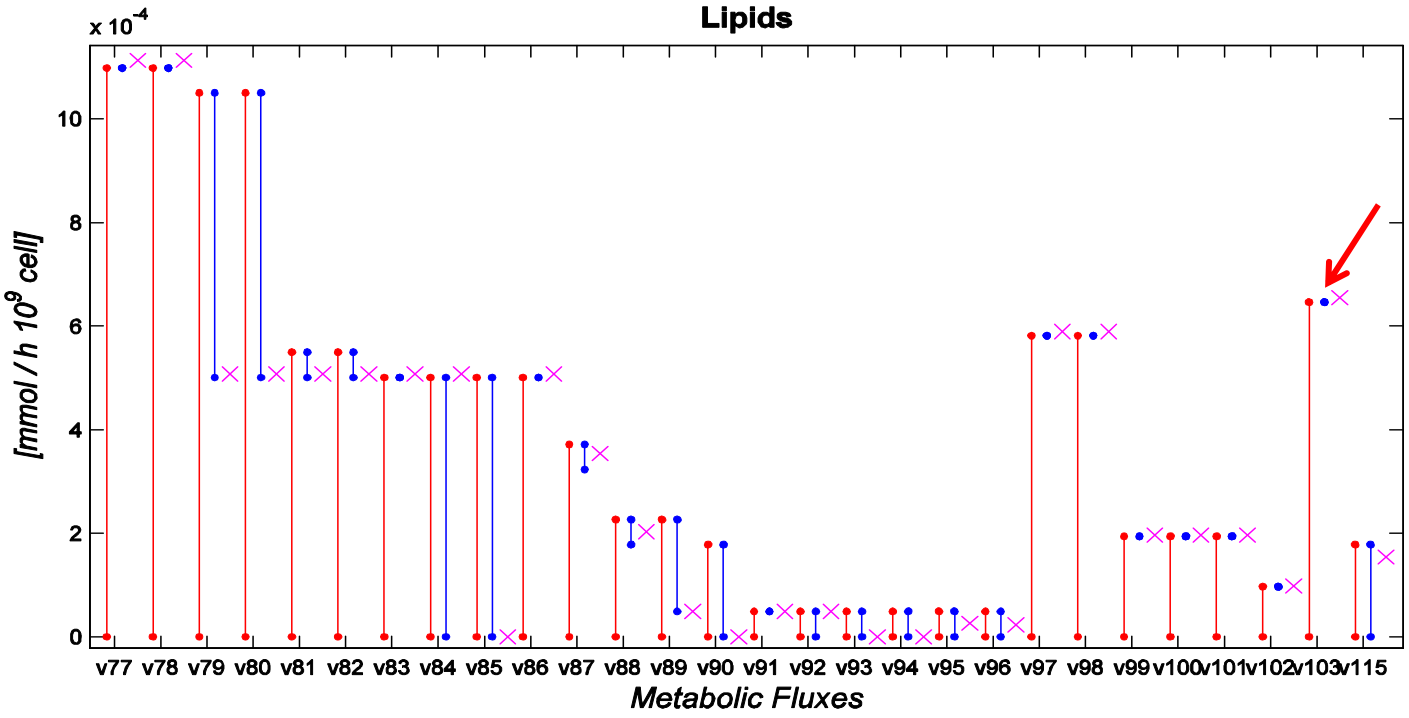
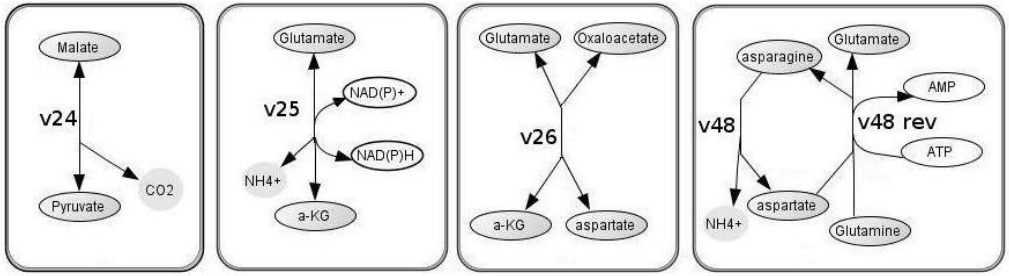


Some Results

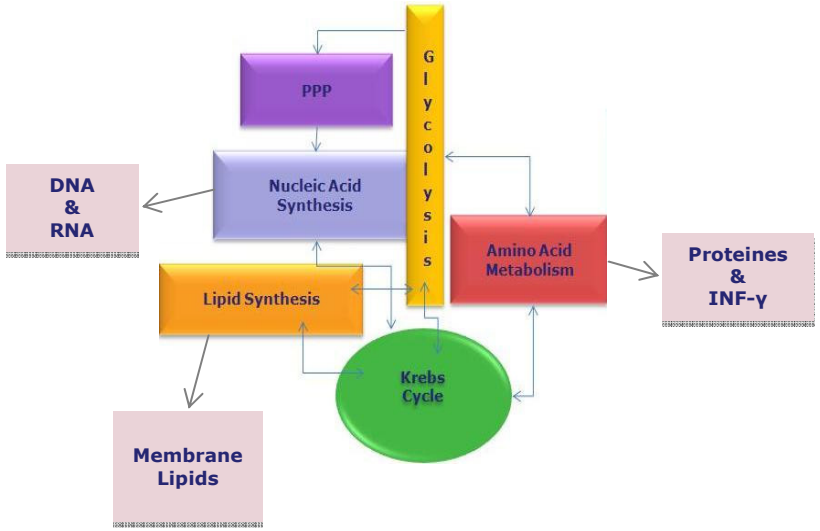
- Network Structure Analysis

The net direction of some reversible reactions cannot be decided only based on the metabolic state of the cells.



The configurations that might provide other sets of solutions are tested and only for 2 out of 16 structures a solution set is found.

Partial conclusions



- An underdetermined mass balance system can be analyzed in terms of flux intervals providing a useful insight in the cell metabolism.
- The information provided by certain measurements might be critical for the determination of the flux intervals.
- The solution set indicates whether the reaction flux directions, and in turn, the Network Structure have been well defined.

Future Work

- Model Reduction: minimal set of EFMs can be computed allowing to obtain a dynamical model describing the system.

- Validation: A perfused bioreactor for the culture of Hybridoma cells will be equipped with several online sensors including HPLC and NIR that will target the species that have been identified as more informative.