Transient Phenomena in Microbial Dynamics: A Systems Biology Approach

Philippe Nimmegeers, Dries Telen, Filip Logist, Jan Van Impe

CPMF² - Flemish Cluster Predictive Microbiology in Foods (www.cpmf2.be)
BioTeC+ - Chemical and Biochemical Process Technology and Control, Department of Chemical Engineering, KU Leuven

Home institution

KU Leuven

- Founded in 1425
- Biggest university of Belgium
- 16 faculties
- Faculty of Engineering Science
- BioTeC+ research division

Research at BioTeC+

- Focus on modelling, model based optimisation, monitoring and control of microbial conversion processes.
- Interdisciplinary research:
  →mathematical modelling and systems and control,
  →detailed microbiological/biochemical knowledge.

PhD research

Microorganisms play an important role in industry, mainly food industry and industrial biotechnology, for instance in:

- food safety: avoid spoilage and counteract growth of pathogens,
- stimulating the production of high added value chemical compounds in bioprocesses.

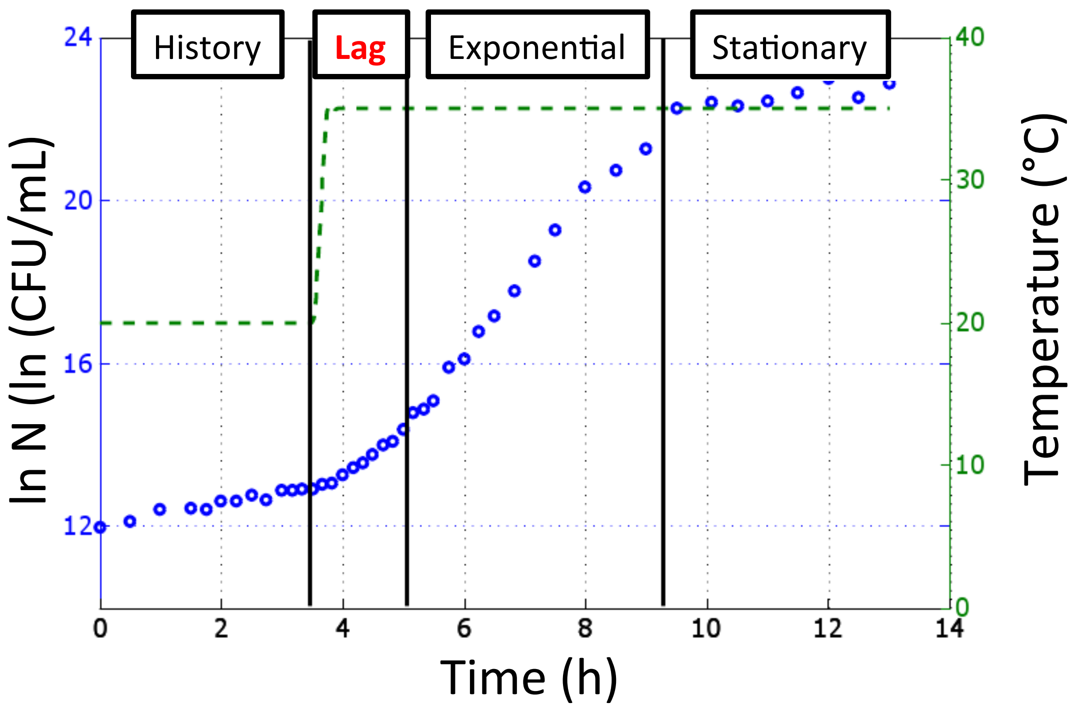
In microbial growth transient phenomena occur due to a change in environmental conditions. Macroscale models do not succeed in explaining and describing these phenomena appropriately such that microscale knowledge should be included.

Aims of this research:

- Develop mathematical strategies for the description and prediction of the dynamic fluxes in metabolic networks.
- Use of optimal control strategies for a better understanding of (in)activation mechanisms in biochemical pathways during transient phenomena.

Approach

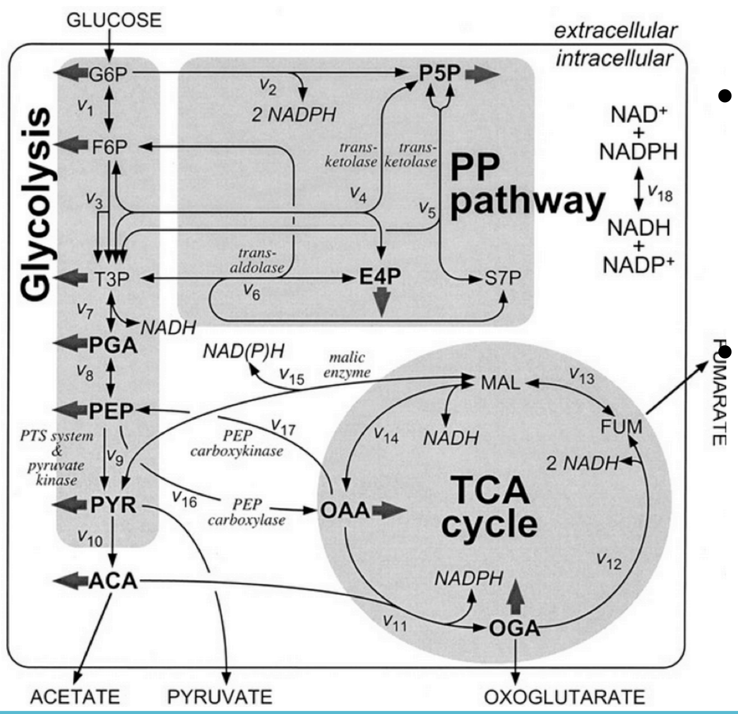
Microbial growth curve – lag phase due to temperature shift (macroscale)



To ensure food safety this lag phase should be well modelled:

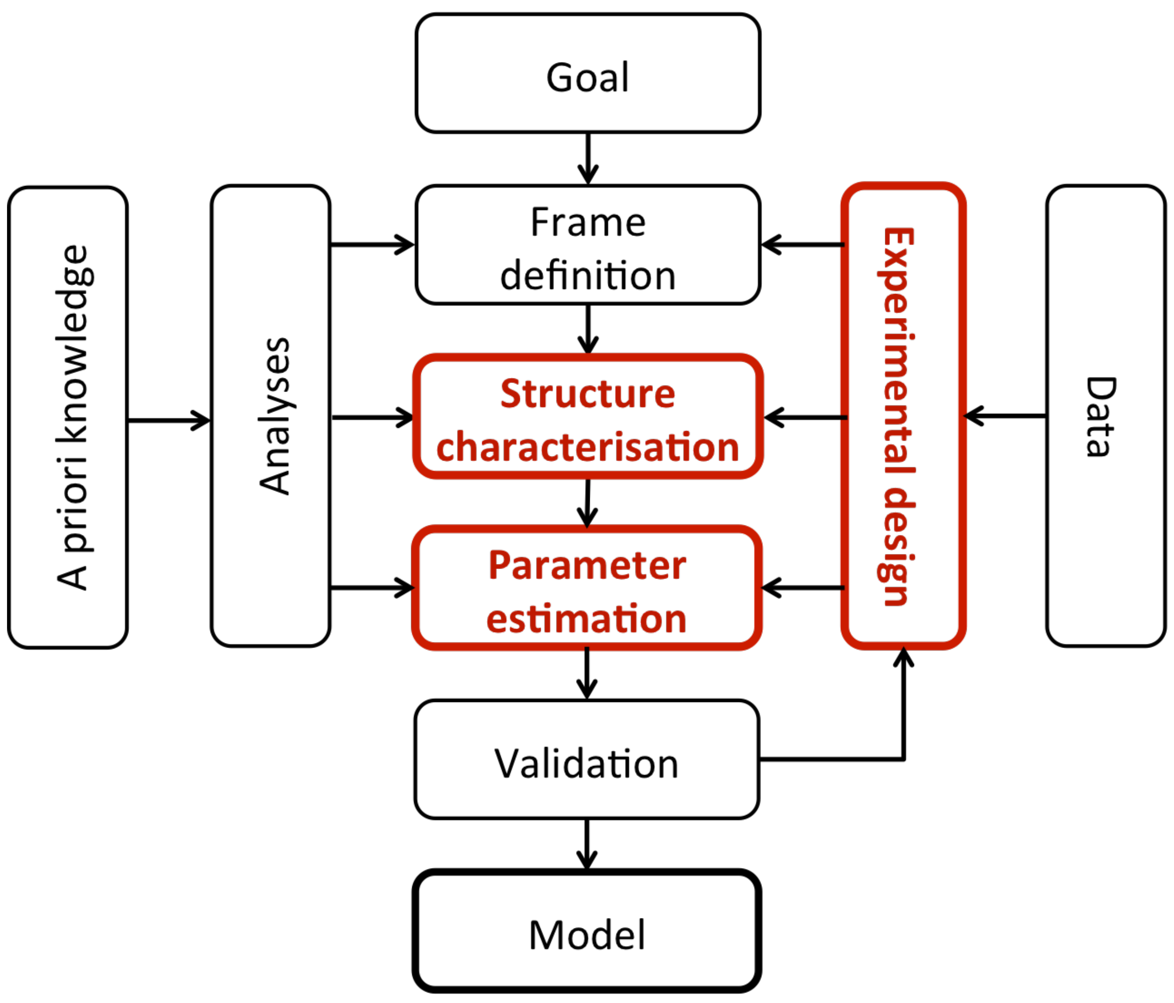
- predict accurately the shelf life of food products,
- increase duration of lag phase → increase shelf life.

Metabolic reaction networks (microscale)



- Knots
  → metabolites produced/ consumed within the cell
- Links
  → fluxes through the different reaction pathways within the cell

Process modelling cycle



Multiscale dynamic model – Fluxes with respect to time

$$\frac{d\mathbf{C}_{ext}}{dt} = \mathbf{S}_{ext}\cdot\mathbf{v}\cdot C_X$$
$$\frac{d\mathbf{C}_{int}}{dt} = \mathbf{S}_{int}\cdot\mathbf{v} - \mu\cdot\mathbf{C}_{int}$$

Assume:

$$\mu\cdot\mathbf{C}_{int} = 0$$
$$\frac{d\mathbf{C}_{int}}{dt} = 0$$

$$\frac{d\mathbf{C}_{ext}}{dt} = \mathbf{S}_{ext}\cdot\mathbf{v}\cdot C_X$$
$$0 = \mathbf{S}_{int}\cdot\mathbf{v}$$

DMFA

Dynamic Metabolic Flux Analysis

- Measure extracellular metabolite concentrations or fluxes
- Estimate intracellular fluxes

DFBA

Dynamic Flux Balance Analysis

- Cellular behaviour follows an intracellular objective
- Objective function synthesis
- Bi-level optimisation
  →Predict intracellular fluxes

Acknowledgements

Research supported in part by Project PFV/10/002 (OPTEC Optimization in Engineering Center) of the Research Council of the KU Leuven, KU Leuven Knowledge Platform SCORES4CHEM (www.scores4chem.be), FWO KAN2013 1.5.189.13, FWO-G.0930.13 and the Belgian Program on Interuniversity Poles of Attraction initiated by the Belgian Federal Science Policy Office.

With the support of the Erasmus+ programme of the European Union, Project No: 2014-1-MT01-KA200-000327