DTU

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Mathematics in our research work

PROSYS

- Process Systems Engineering (PSE)
- Process Intensification and Integration (PII)
- Process design and control
- Industrial fermentation technology
- Biocatalysis
- Microfluidics

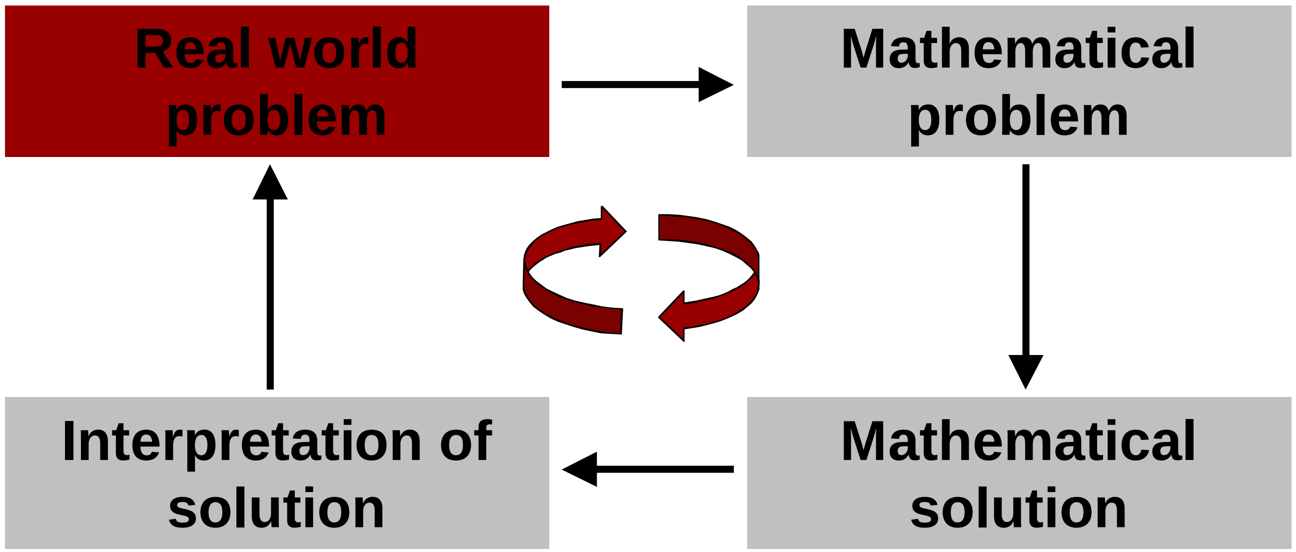
Very practically, we work with …

- Computational Fluid Dynamics
- Novel sensor equipment
- Digital twins and process simulation
- Scale-up / scale-down
- Novel processes
- Artificial intelligence / machine learning
- Process design / process optimisation

Introduction

Putting things in perspective …

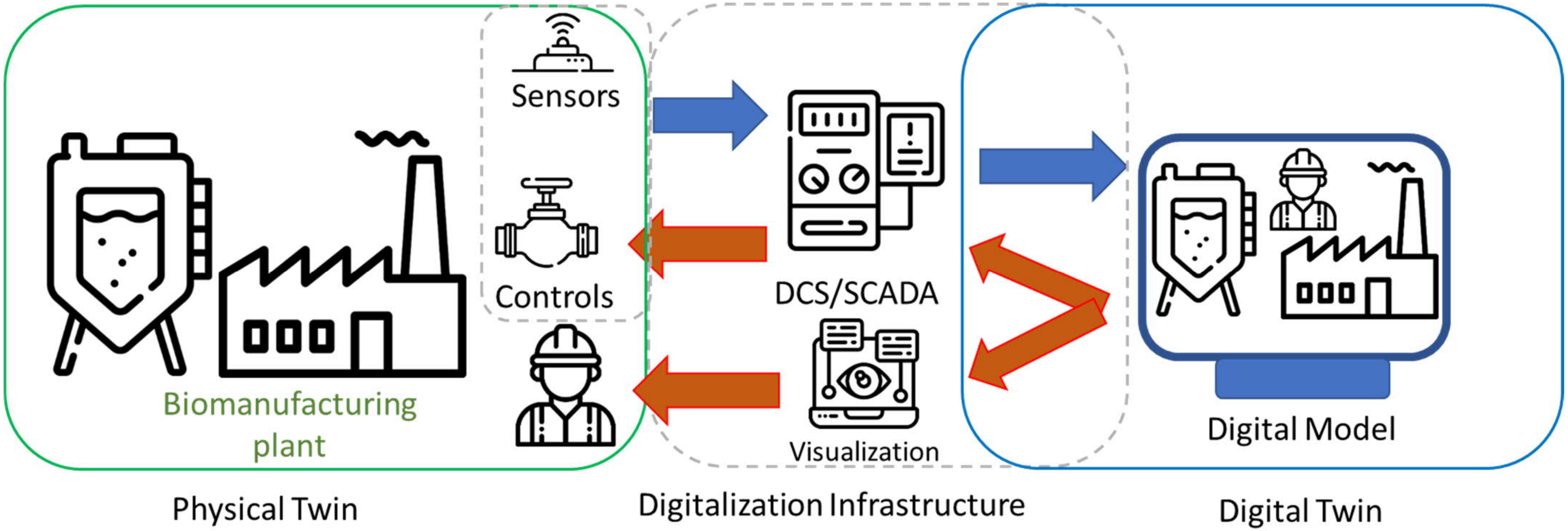
The use of a model



Applied mathematics!

Digital twin

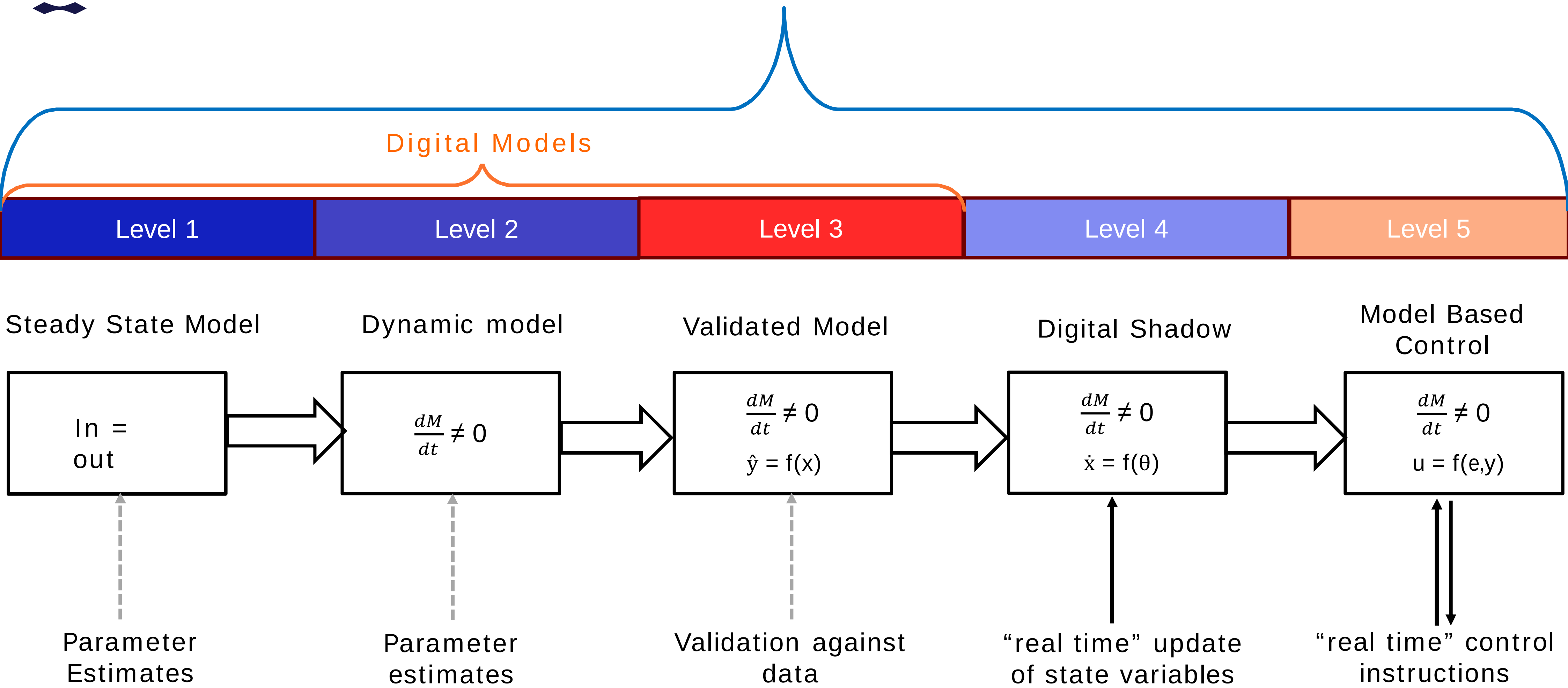
The buzzwords:
- **Big data?**
- AI – Machine learning
- **Industry 4.0**



What could this digital model be?

The ability to collect and process sufficient data is essential!!

Levels of Digital Twins



Udugama et al. (2020) Industrial & Engineering Chemistry Research, 59, 15283-15297.

I&EC research
Industrial & Engineering Chemistry Research

pubs.acs.org/IECR Article

The Role of Big Data in Industrial (Bio)chemical Process Operations

Isuru A. Udugama, Carina L. Gargalo, Yoshiyuki Yamashita, Michael A. Taube, Ahmet Palazoglu, Brent R. Young, Krist V. Gernaey, Murat Kulahci, and Christoph Bayer*

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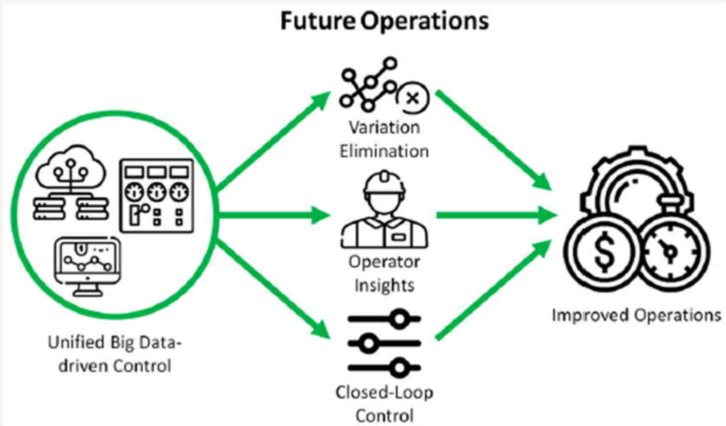
ABSTRACT: With the emergence of Industry 4.0 and Big Data initiatives, there is a renewed interest in leveraging the vast amounts of data collected in (bio)chemical processes to improve their operations. The objective of this article is to provide a perspective of the current status of Big-Data-based process control methodologies and the most effective path to further embed these methodologies in the control of (bio)chemical processes. Therefore, this article provides an overview of operational requirements, the availability and the nature of data, and the role of the control structure hierarchy in (bio)chemical processes and how they constrain this endeavor. The current state of the seemingly competing methodologies of statistical process monitoring and (engineering) process control is examined together with hybrid methodologies that are attempting to combine tools and techniques



Systems of coupled differential equations

Essential in an environment driven by first principles models …

Kinetic equations

- Growth (Monod equation)

$$r_X = \mu C_X = \left(\frac{\mu_{max} C_S}{K_S + C_S}\right) C_X [kg\ m^{-3}\ h^{-1}]$$

Biomass formation rate

- Substrate uptake (Herbert-Pirt equation)

$$r_S = q_S C_X = \left(\frac{\mu}{Y_{XS}} + m_S\right) C_X\ [kg\ m^{-3}\ h^{-1}]$$

Substrate uptake rate

- Product formation (Luedeking-Piret equation)

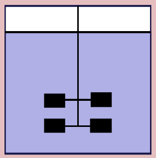
$$r_P = q_P C_X = \left(\underbrace{\frac{\mu}{Y_{XP}}}_{\alpha} + \beta\right) C_X\ [kg\ m^{-3}\ h^{-1}]$$

Product formation rate

C_X = biomass concentration; C_S = substrate concentration; K_S = half-saturation constant; μ = specific growth rate; μ_{max} = maximum specific growth rate; Y_{XS} = Yield coefficient, mass of biomass formed per mass of substrate consumed Y_{XP} = Yield coefficient, mass or biomass formed per mass of product produced; q_S = specific substrate uptake rate; q_P = specific product formation rate; m_S = maintenance coefficient; α, β = coefficients;

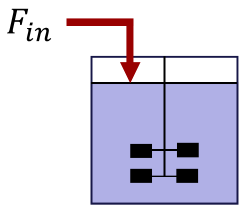
Types of bioreactor operation

Batch



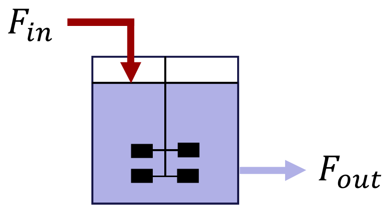
- **Substrate** addition only at the **beginning**
- **Constant volume** over time
- **Maximum rates**
- **Accumulation** of products

Fed-batch



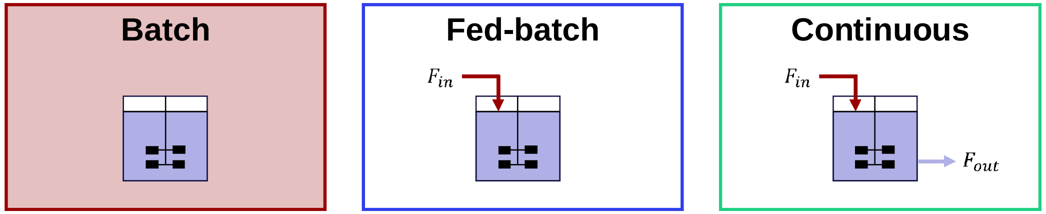
- **Substrate addition** (F_{in}) over time
- **Variable volume** over time
- **Rates** determined by **feed**
- **Accumulation** of products

Continuous



- **Substrate addition** (F_{in}) and **broth removal** (F_{out})
- **Constant volume** over time
- **Rates** determined by **dilution rate**
- **Continuous outflow** of biomass and products

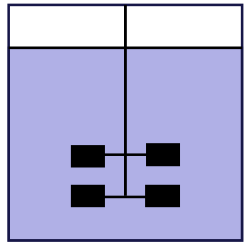
Batch operation



Volume balance (V)

$$\cancelto{0}{Input} + \cancelto{0}{Generation/Consumption} = \cancelto{0}{Output} + \cancelto{0}{Accumulation}$$

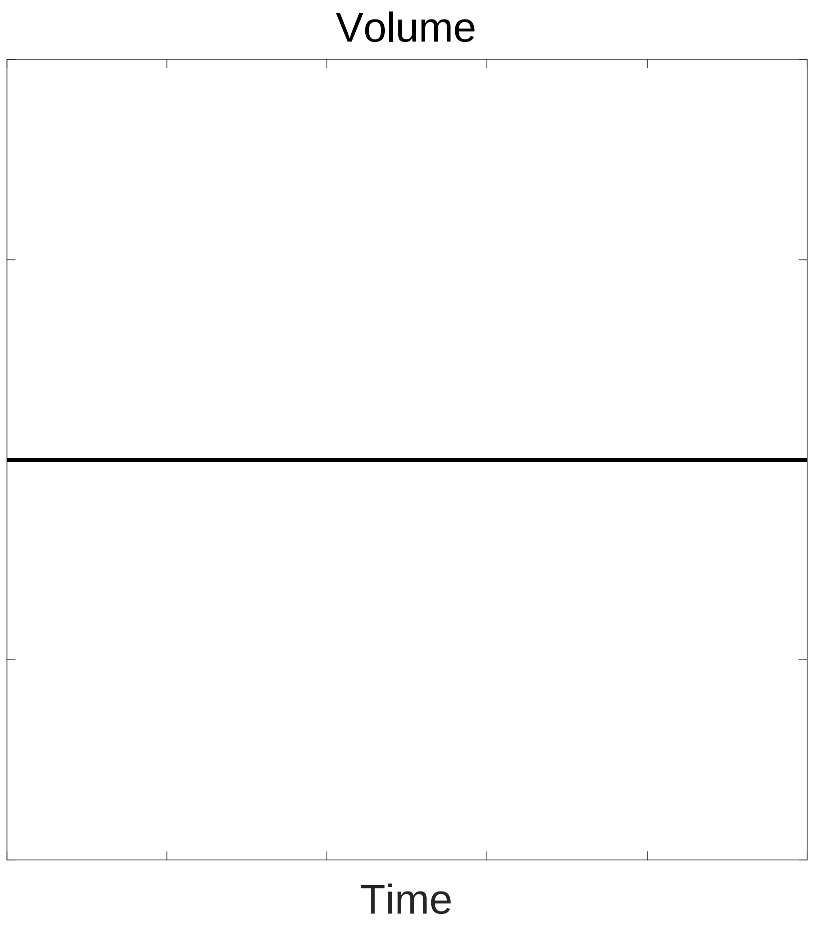
$$0 = \frac{dV}{dt}$$

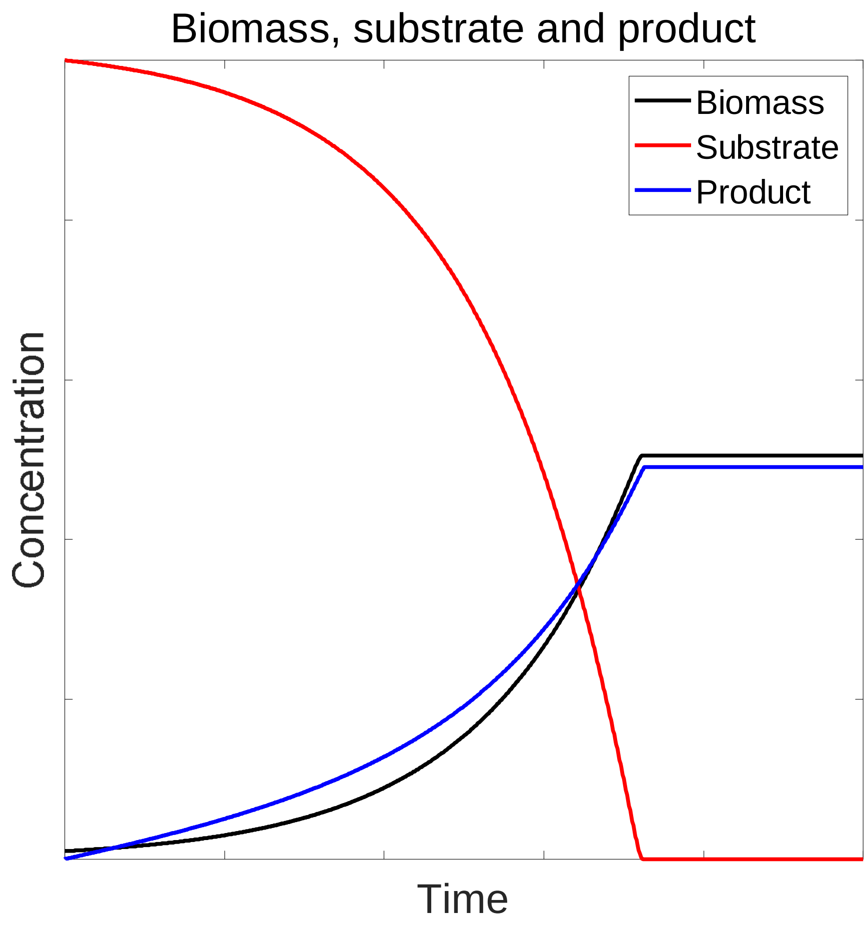


Biomass, substrate and product mass balances (M_i)

$$\cancelto{0}{Input} + Generation/Consumption = \cancelto{0}{Output} + Accumulation$$

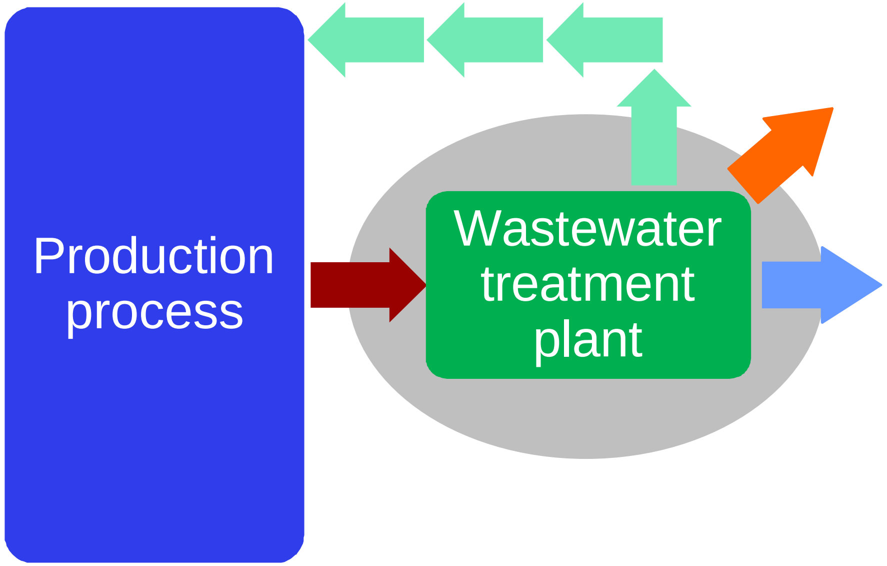
$$r_i V = \frac{dM_i}{dt}$$


Volume
Time


Biomass, substrate and product
Biomass
Substrate
Product
Concentration
Time

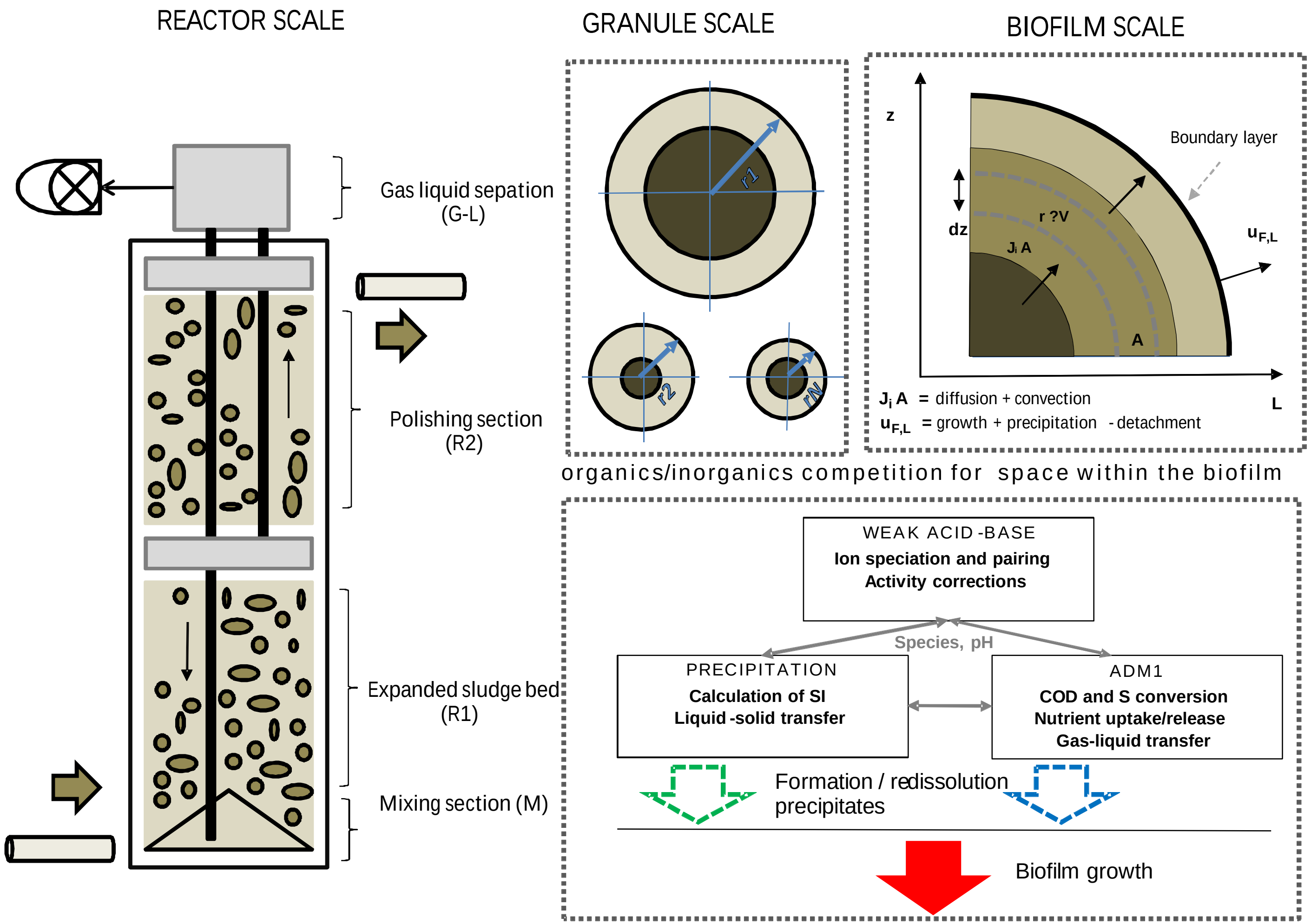
Application example: Modelling of a full-scale industrial granular anaerobic digester

Xavier Flores-Alsina, Hannah Feldman, Pedram Ramin, Krist V. Gernaey: PROSYS, DTU, Denmark
Kasper Kjellberg: Novozymes, Denmark
Damien Batstone: AWMC, University of Queensland, Australia
Ulf Jeppsson: IEA, Lund University, Sweden



- **Industrial wastewater**
- Q = 150 $m^3.h^{-1}$
- COD = 1600 kg $COD.h^{-1}$
- N = 70 $kg.h^{-1}$
- P = 40 $kg.h^{-1}$
- S:COD = 0.025 kg/kg

Multi-scale modelling representation



Feldman et al. (2018) Biotechnology & Bioengineering, 115, 2726-2739.

Model testing: Data set #1

HYDROLYSIS

ACIDOGENESIS

ACETOGENESIS

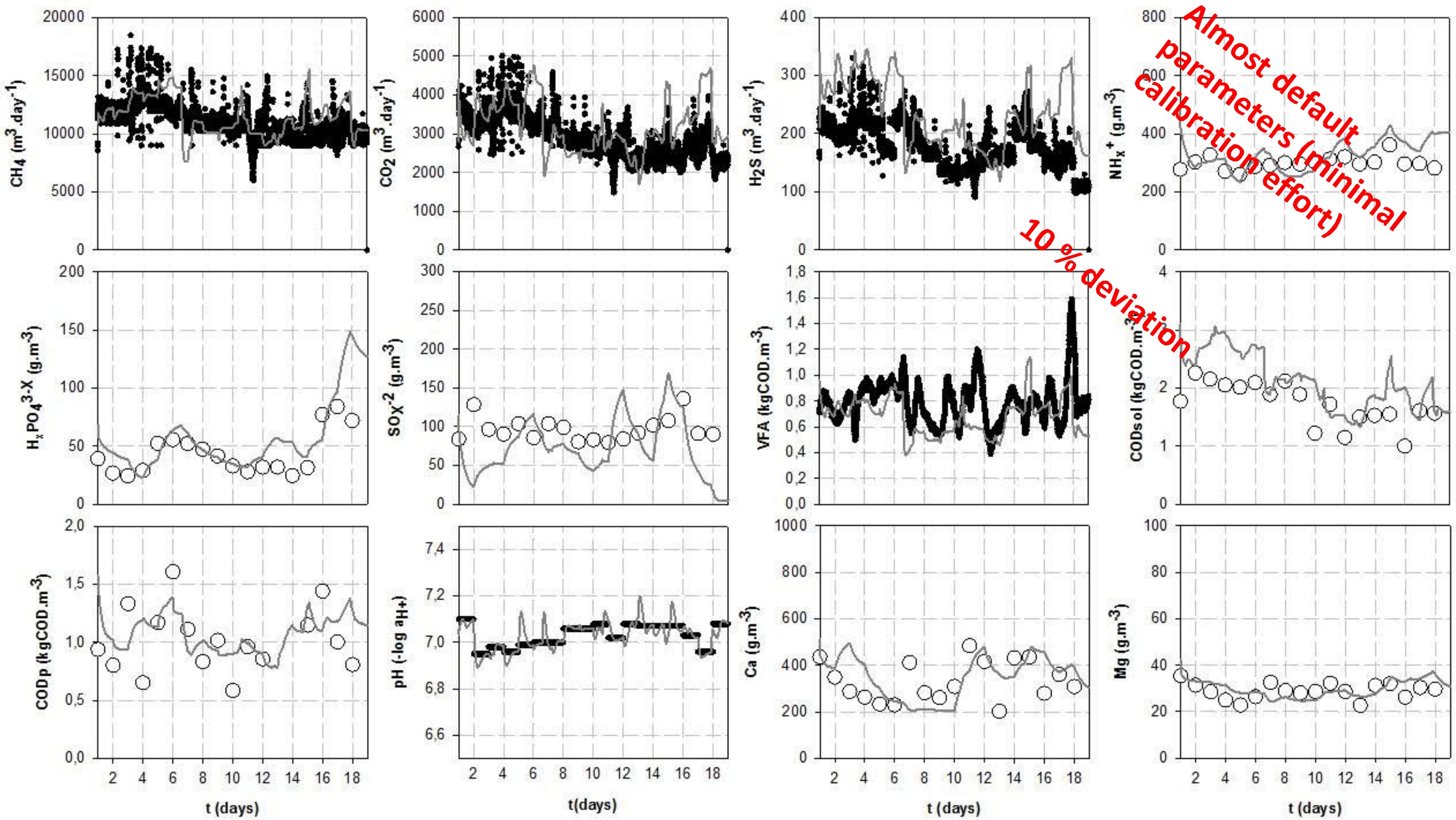
METHANOGENESIS

SULFIDOGENESIS

N AND P RELEASE

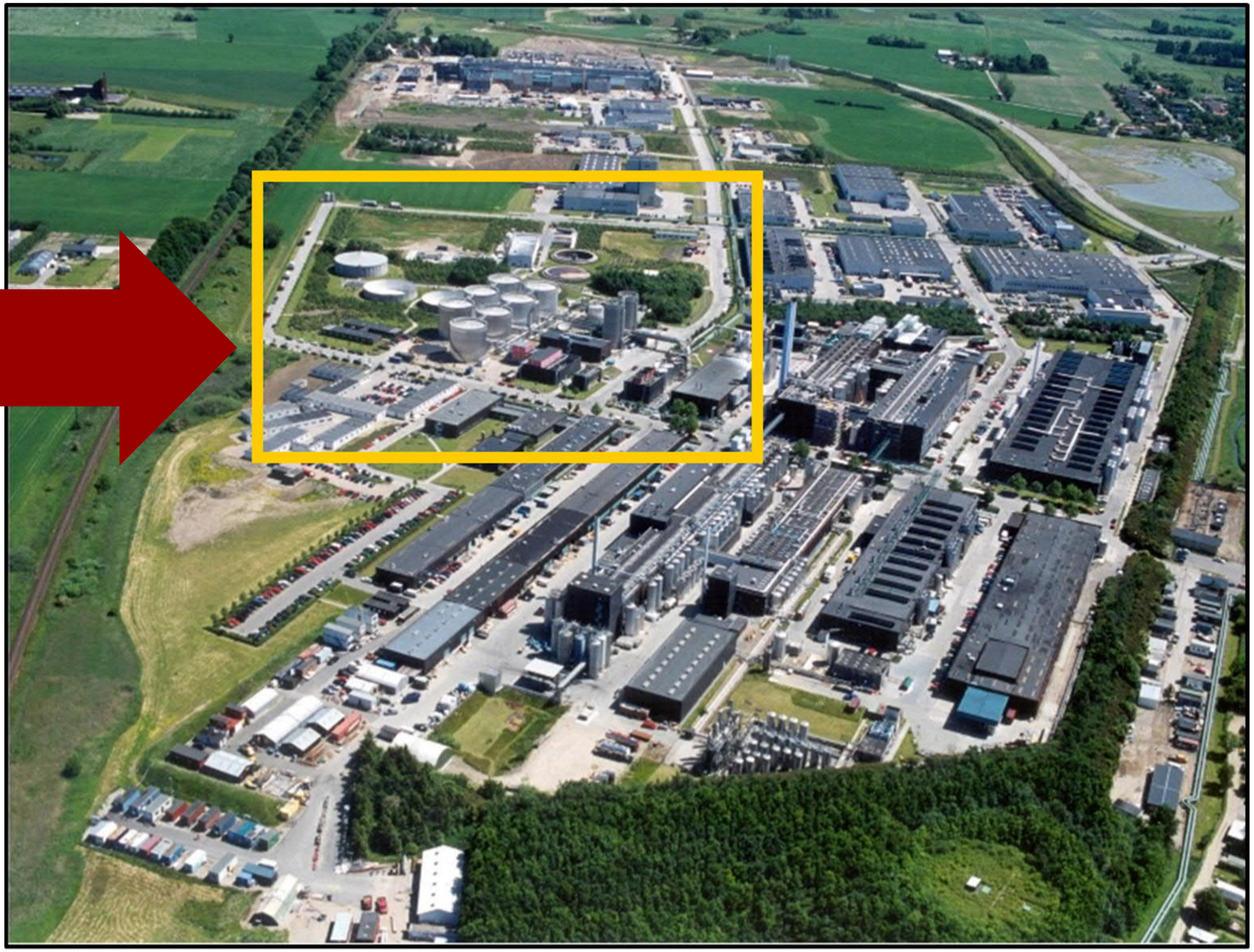
WEAK ACID BASE CHEMISTRY

ION BEHAVIOUR



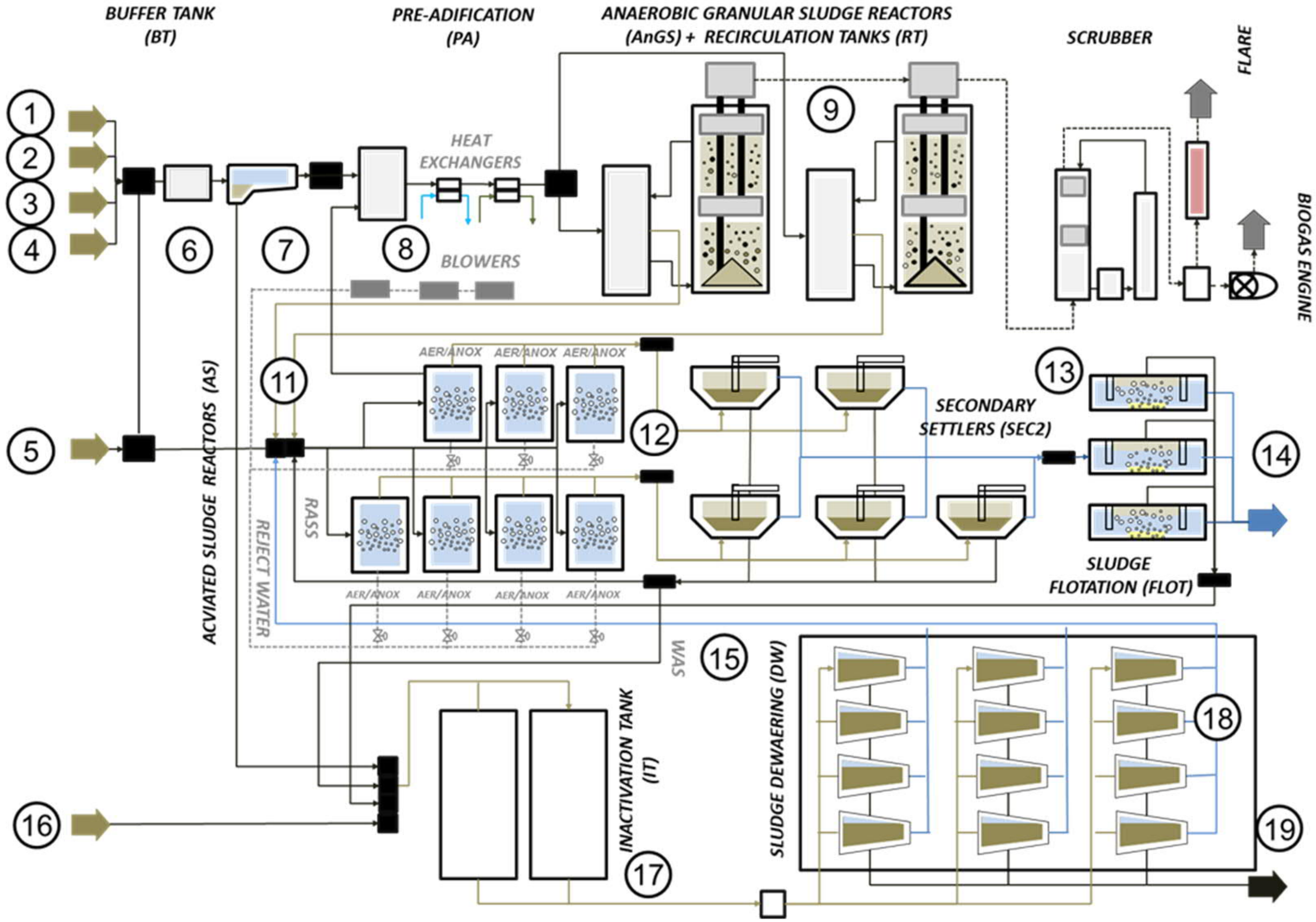
Feldman et al. (2017) Water Research, 126, 488-500.

Ongoing work



Novozymes and Novo Nordisk production site
Kalundborg, Denmark

Ongoing work – increased complexity!



Monje et al. (2021) Journal of Environmental Management, 293, 112806.

Optimization

When the best process is the only thing that is good enough …

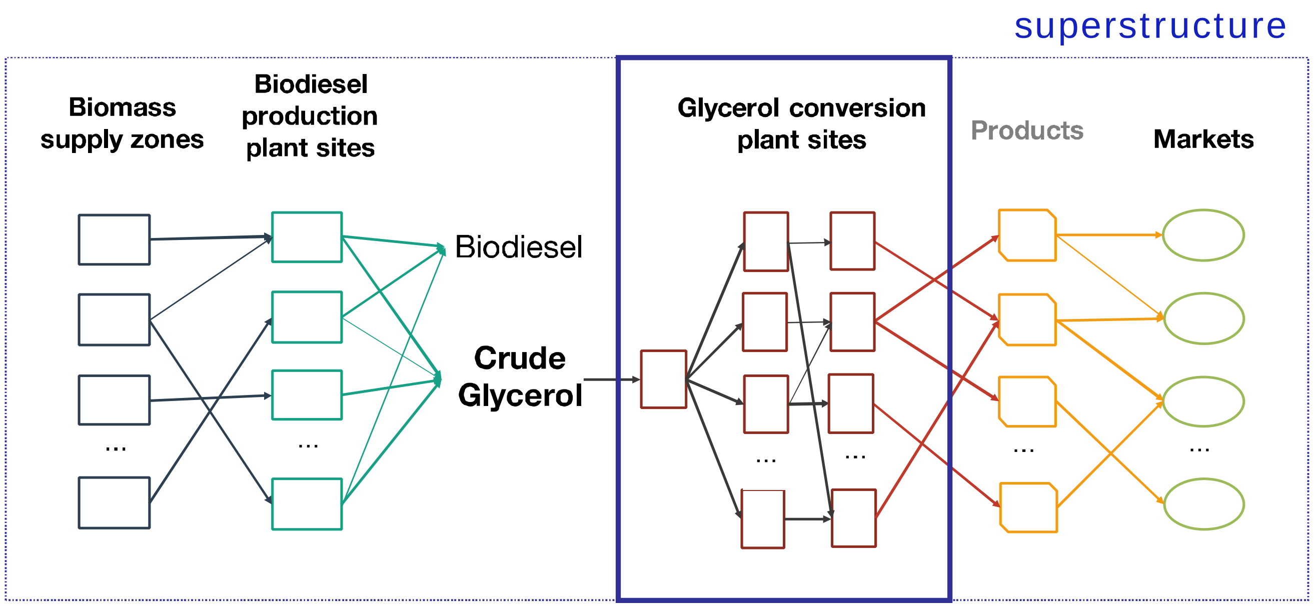
Glycerol Biorefinery – superstructure optimization

Glycerol surplus:

1 kg of glycerol per 10 kg of biodiesel produced!

Glycerol prices have been drastically decreasing along the years!

Valorization of glycerol to **high value-added chemicals** and **2nd generation biofuels** is **very promising**



Mathematical optimization (e.g. superstructure optimization) is used to identify the best candidates, under process, business and environmental constraints – on the path to sustainable designs

Bio-chemicals from glycerol fermentation

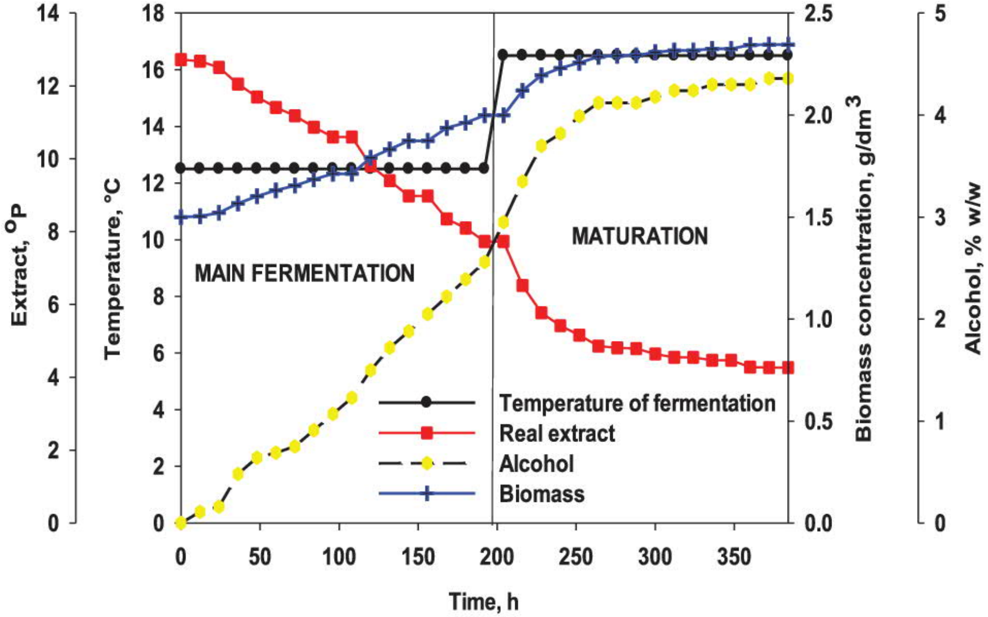
High value → Low value

Bio-chemicals	Uses
Succinic acid	bioplastics building block
Lactic acid	bioplastics building block, food items, cosmetics, etc.
1,3-PDO	composites, adhesive, polyesters, etc.
Polyhydroxybutyrate (PHB)	bioplastics building block
N-Butanol	biofuel
Bio-ethanol	biofuel

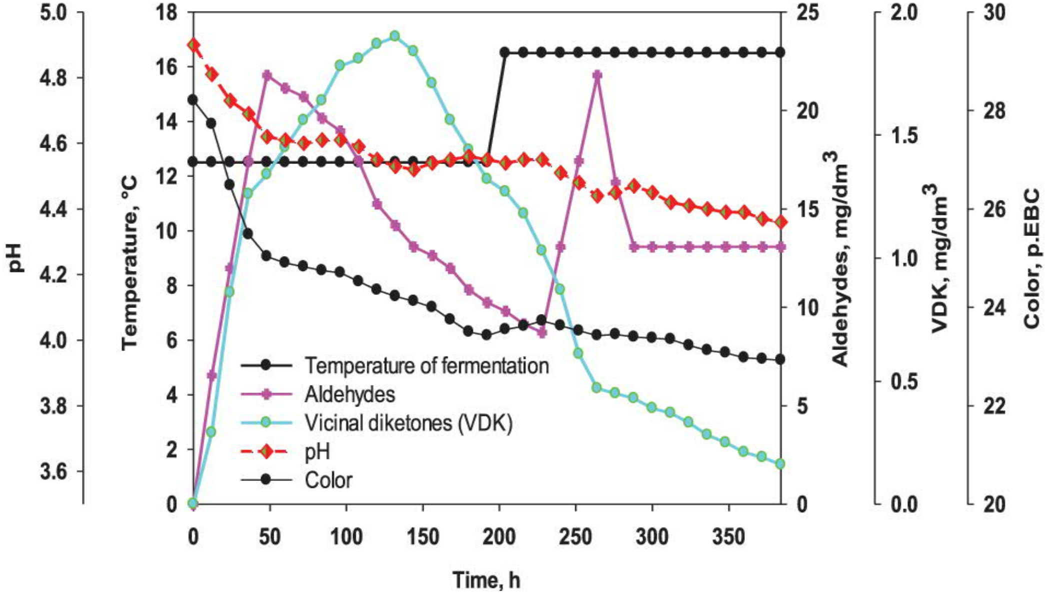
Another example - Beer fermentation model

<u>included in the model (system of differential equations):</u>

- ✓ sugar and amino acids uptake
- ✓ yeast growth
- ✓ ethanol production
- ✓ formation of four fusel alcohols (isobutanol, isoamyl alcohol, 2-methyl-1-butanol and n-propanol)
- ✓ formation of three esters (ethyl acetate, ethyl hexanoate and isoamyl acetate)
- ✓ VDKs and
- ✓ acetaldehyde.



The goal is to model and optimize the process dynamics!



[6]

Optimization strategy

- The goal is to obtain an optimal temperature and flavor profile
- Sequential Quadratic Programming (SQP), Sequential Annealing (SA) and Genetic Algorithm (GA) were considered as optimization strategies
- Genetic algorithm was selected as the optimization strategy → avoids local minima and it provides a better exploration of the search space

To minimize

Concentrations of off-flavors: fusel alcohols, VDKs and acetaldehyde

Fermentation time

To maximize

Concentrations of on- flavors: ethanol and esters

Thresholds of detection + max/min **concentrations are respected** → acting as model **constraints**

To penalize

- large fermentation times
- low concentrations of on-flavors
- high concentrations of off-flavors

Optimization scenarios

FF(O4)

FF(O2)

$$FF(O_1) = Q_{IB} + Q_{IA} + Q_{MB} + Q_P + Q_{EA} + Q_{EC} + Q_{IAc} + Q_{VDK} + Q_{AAI} + Q_{EtOH} + Q_t$$

FF(O3)

O1 ('master') = All the variables are included

O2 = Time and ethanol

O3 = Time and maximization variables

O4 = Time and minimization variables

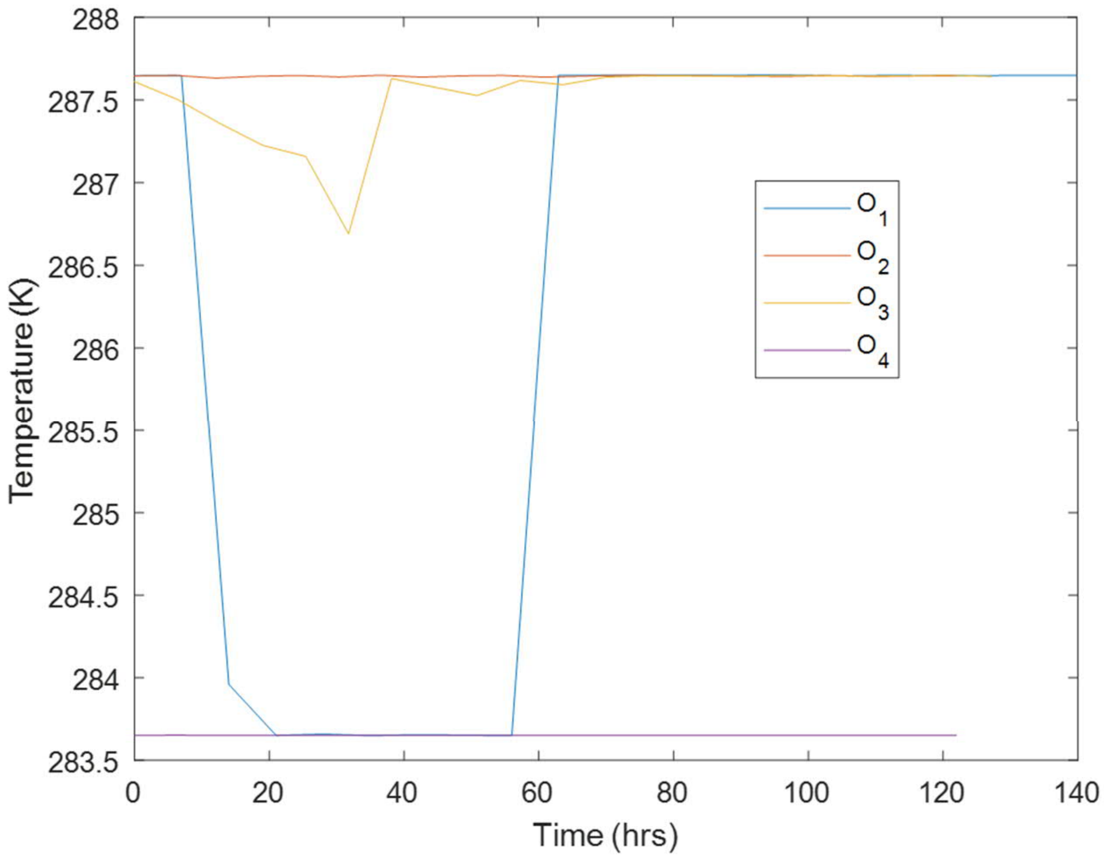
Fitness function definition (500 individuals population)

$$Q_i = \frac{([i]_f - [i]_{min})^2}{i_{desv}^2} \qquad FF = \sum Q_i$$

i = variables to optimize → [species] and time

Results

	O_1	O_2	O_3	O_4
FF	2.3970	0.0260	0.4640	1.5563
$Q_{alcohols}$	0.7855	7.6201	5.8161	0.0000
Q_{esters}	0.4803	1.5946	0.3369	30.3103
Q_{AAI}	0.1349	0.1947	0.1768	0.0000
Q_{VDK}	0.0087	0.0000	0.0000	1.5538
Q_{EtOH}	0.0855	0.0235	0.0045	4.0986
Q_t	0.9025	0.0025	0.1225	0.0025
t_F	140.0	121.7	127.3	122.0

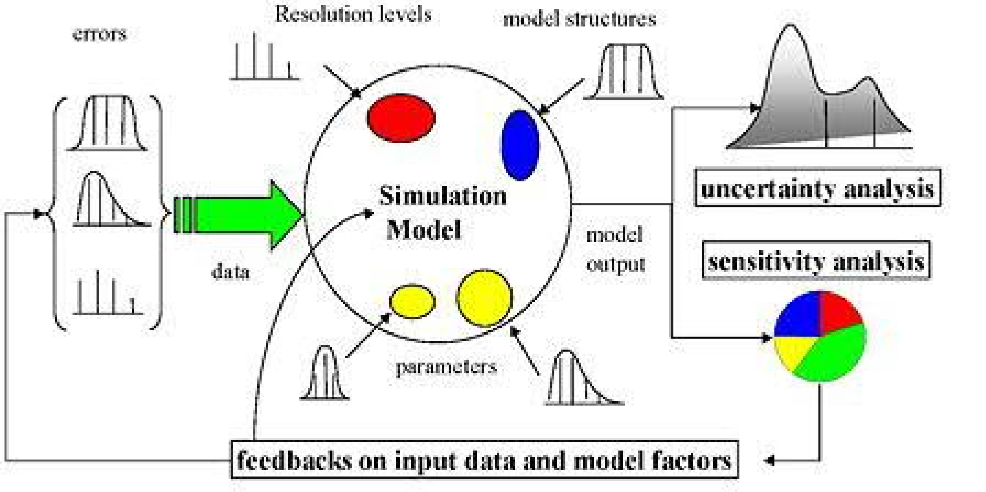


Applied statistics

Random phenomena are inherently present in any process we study …

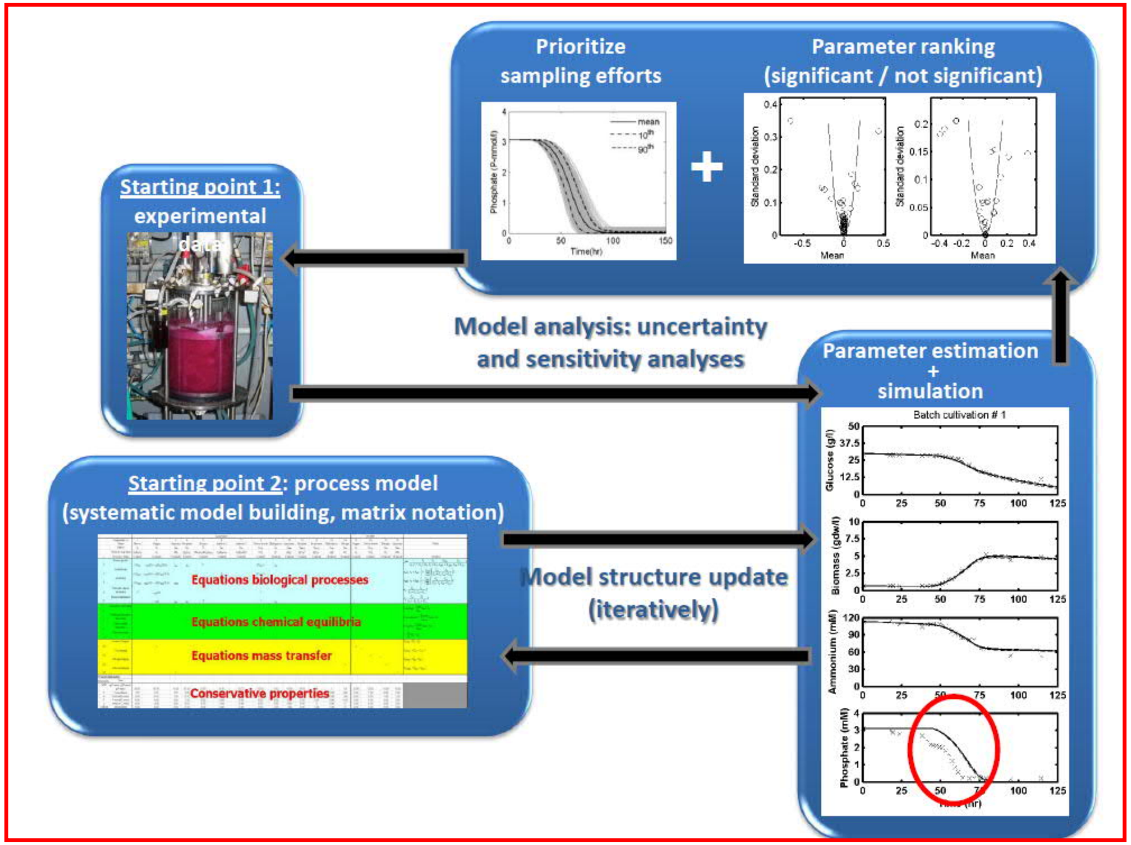
Uncertainty and sensitivity analysis

- Sensitivity analysis "studies how variation (uncertainty) in the outputs of a model can be apportioned to different sources in the input of a model"
- SA complimentary to uncertainty analysis: "quantifying uncertainty in the outputs of a model from uncertainty in its inputs"



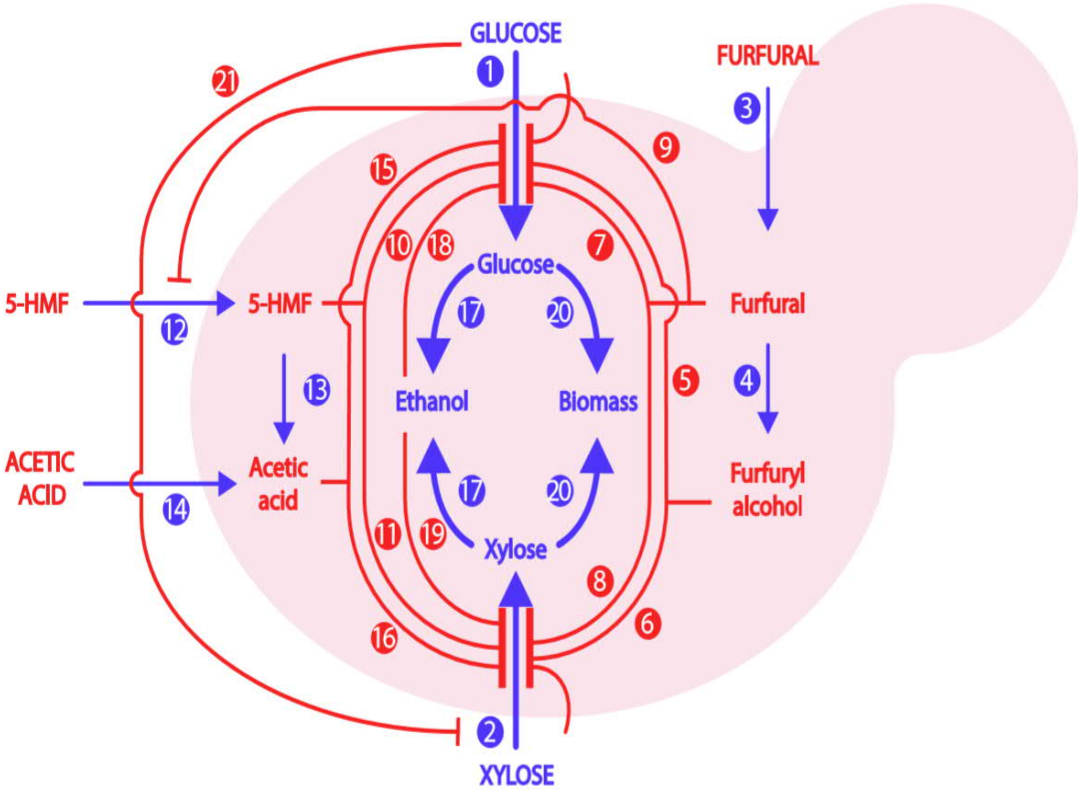
Saltelli et al., 2008

Uncertainty and sensitivity analysis



Gernaey et al. (2010) Trends Biotechnol., 28:346-354.

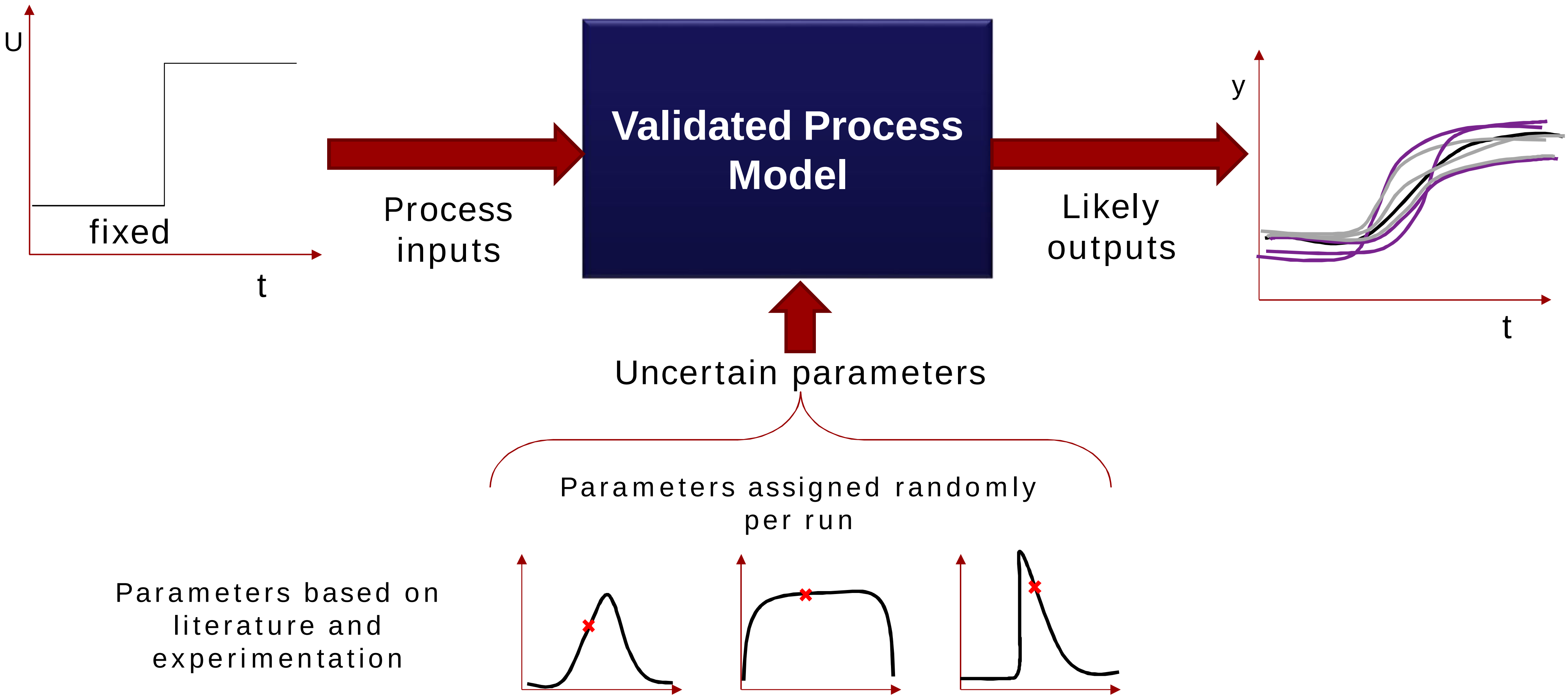
Example: Ethanol Fermentation Model – data generator



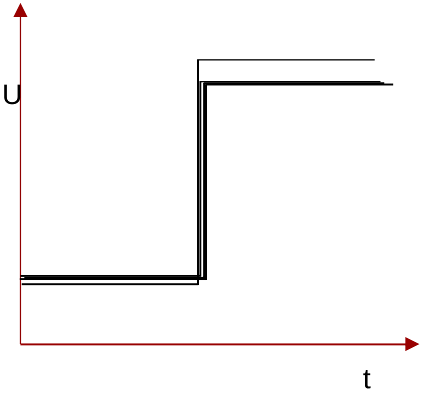
Comp. → Process ↓	X_{bio}	Glu	Xyl	Eth	Fur	Ac	HMF	FA	TIC
Glu uptake	$Y_{X/Glu}$	-1	0	$Y_{Eth/Glu}$	0	0	0	0	$Y_{CO2/Glu}$
Xyl uptake	$Y_{X/Xyl}$	0	-1	$Y_{Eth/Xyl}$	0	0	0	0	$Y_{CO2/Xyl}$
Fur uptake	~ 0	0	0	0	-1	0	0	$Y_{FA/Fur}$	0
Ac uptake	~ 0	0	0	0	0	-1	0	0	$Y_{CO2/Ac}$
HMF uptake	~ 0	0	0	0	0	$Y_{Ac/HMF}$	-1	0	0

	Equation expressed as substrate consumption
Glu uptake	$v_{Max} X_{bio} \frac{Glu}{K_{SGlu}+Glu+\frac{Glu^2}{K_{IGlu}}} \frac{1}{1+\frac{Fur}{J_{Fur}}} \frac{1}{1+\frac{HMF}{J_{HMF}}} \frac{1}{1+\frac{HAc}{J_{HAc}}} I(Xyl, Eth, pH)$
Xyl uptake	$v_{Max} X_{bio} \frac{Xyl}{K_{SXyl}+Xyl+\frac{Xyl^2}{K_{IXyl}}} \frac{1}{1+\frac{Fur}{J_{Fur}}} \frac{1}{1+\frac{HMF}{J_{HMF}}} \frac{1}{1+\frac{HAc}{J_{HAc}}} I(Glu, Eth, pH)$
Fur uptake	$v_{Max} X_{bio} \frac{Fur}{K_{SFur}+Fur}$
Ac uptake	$v_{Max} X_{bio} \frac{Ac}{K_{SAc}+Ac}$
HMF uptake	$v_{Max} X_{bio} \frac{Fur}{K_{SFur}+Fur}$

Software architecture



Ethanol Big Data Generator → Teaching



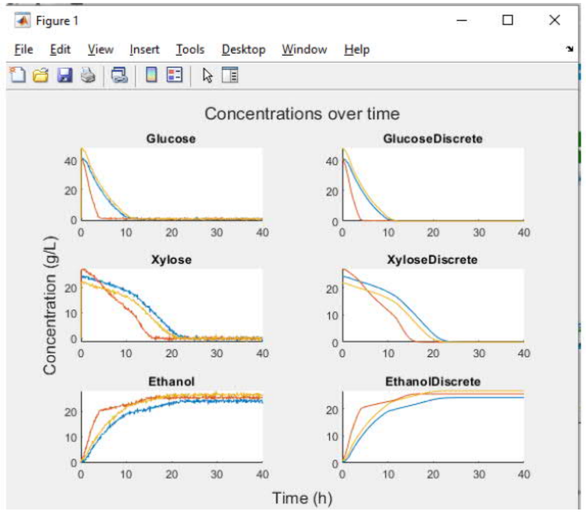
Data Generation Model

Validated Process Model

Actuator model

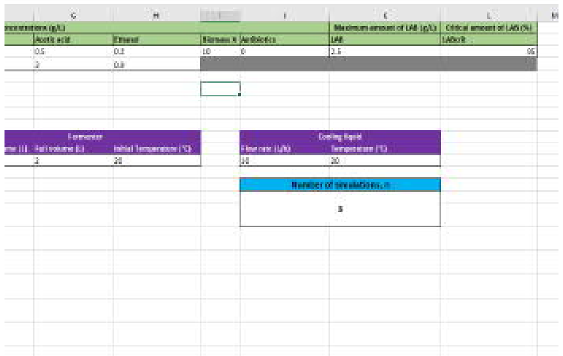
Process Variation

Sensor Model



MatLab

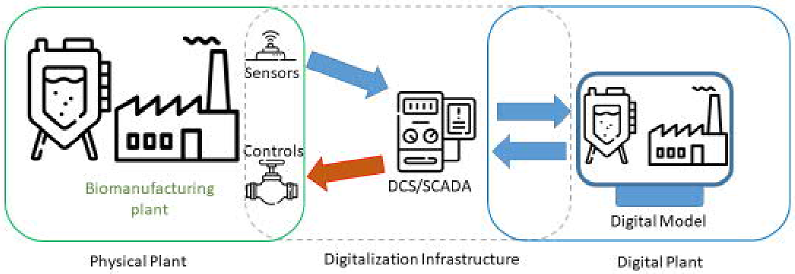
Excel



.CSV files

Conclusions / future perspectives

- Mathematical modelling as a versatile tool to support our daily work – focus on applications!
- Increased computing power leads to larger systems to be solved – basic methods the same
- Matlab, Python, ANSYS CFX as most frequently used software tools
- In recent years: increasing focus on combination of first principles and data-driven approaches – hybrid models
- Dare to share!!!



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