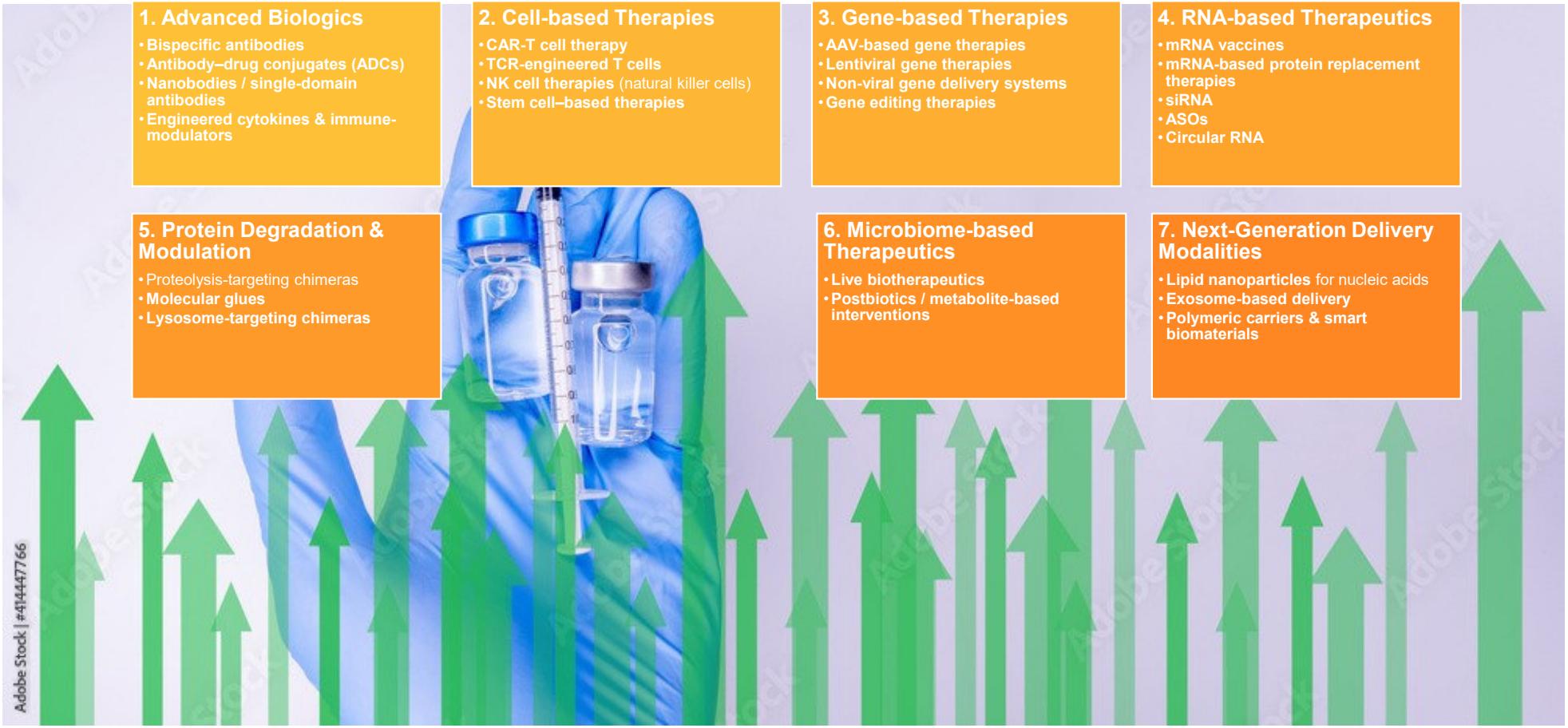
The Potential of Digital Tools to Bridge Research Innovations to Viable Bioprocesses

AFT 2026, Lille

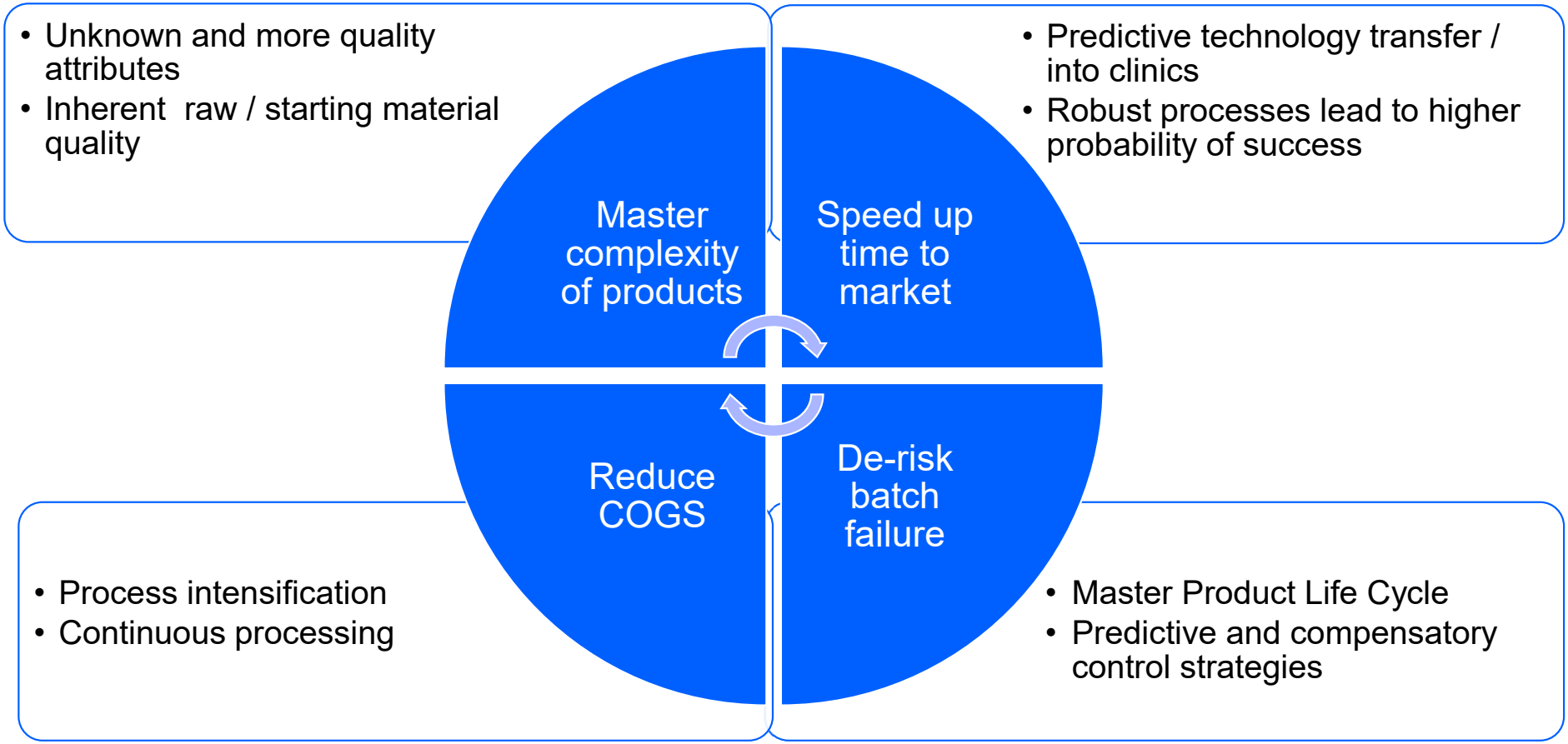
June 30th, 2026

Christoph Herwig

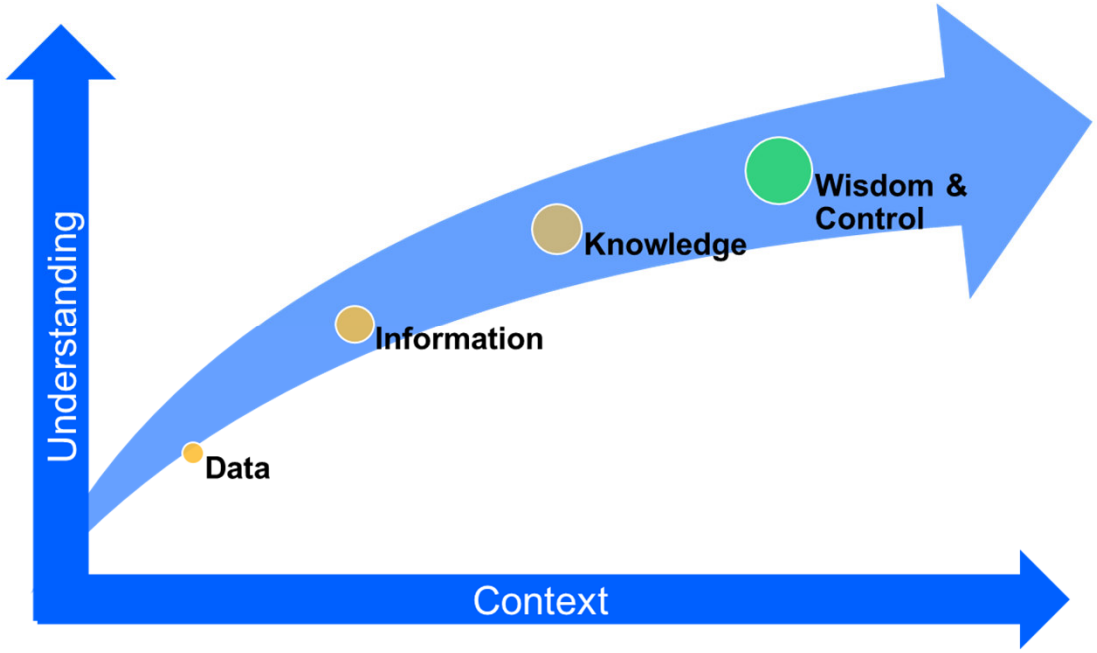
The Future of Biopharmaceuticals is more complex than Mabs



Business challenges and needs to succeed in the race – or just to survive…



Knowledge & Wisdom is the new oil



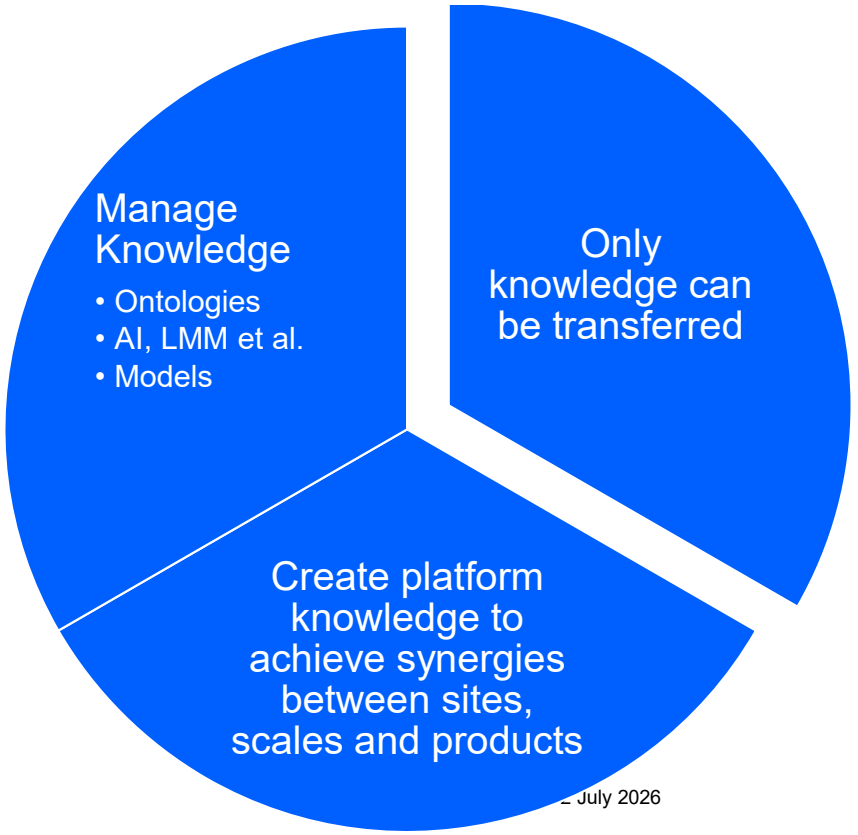
TIBTEC-1267; No. of Pages 7 ARTICLE IN PRESS

Opinion

CellPress

Knowledge management in the QbD paradigm: manufacturing of biotech therapeutics

Christoph Herwig[1,2], Oscar F. Garcia-Aponte[1,3], Aydin Golabgir[1], and Anurag S. Rathore[4]



Data – Information - Knowledge

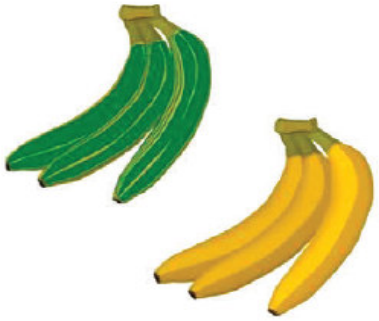
Data

to tell the color

Information

from color
(physical attribute)

establish sugar content
(chemical attribute)

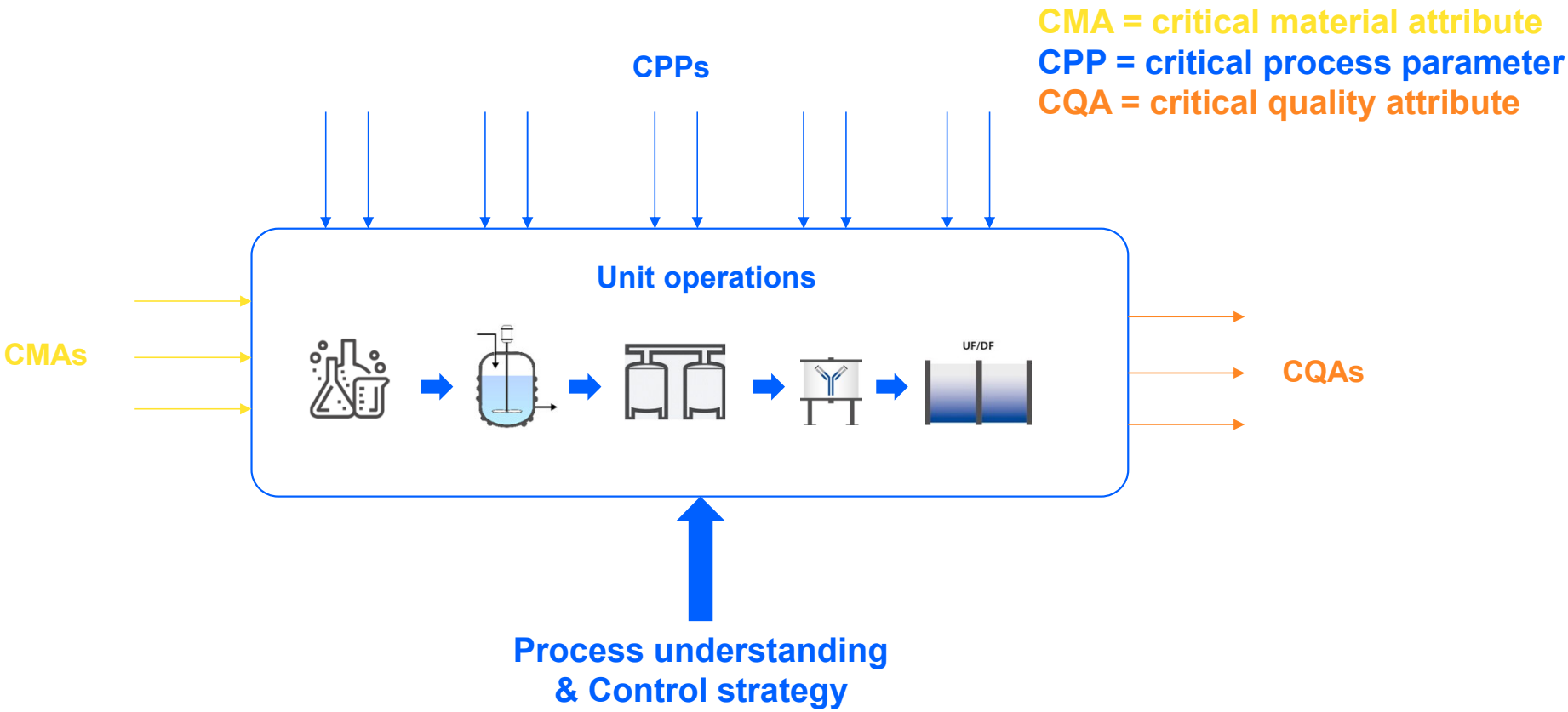


Knowledge

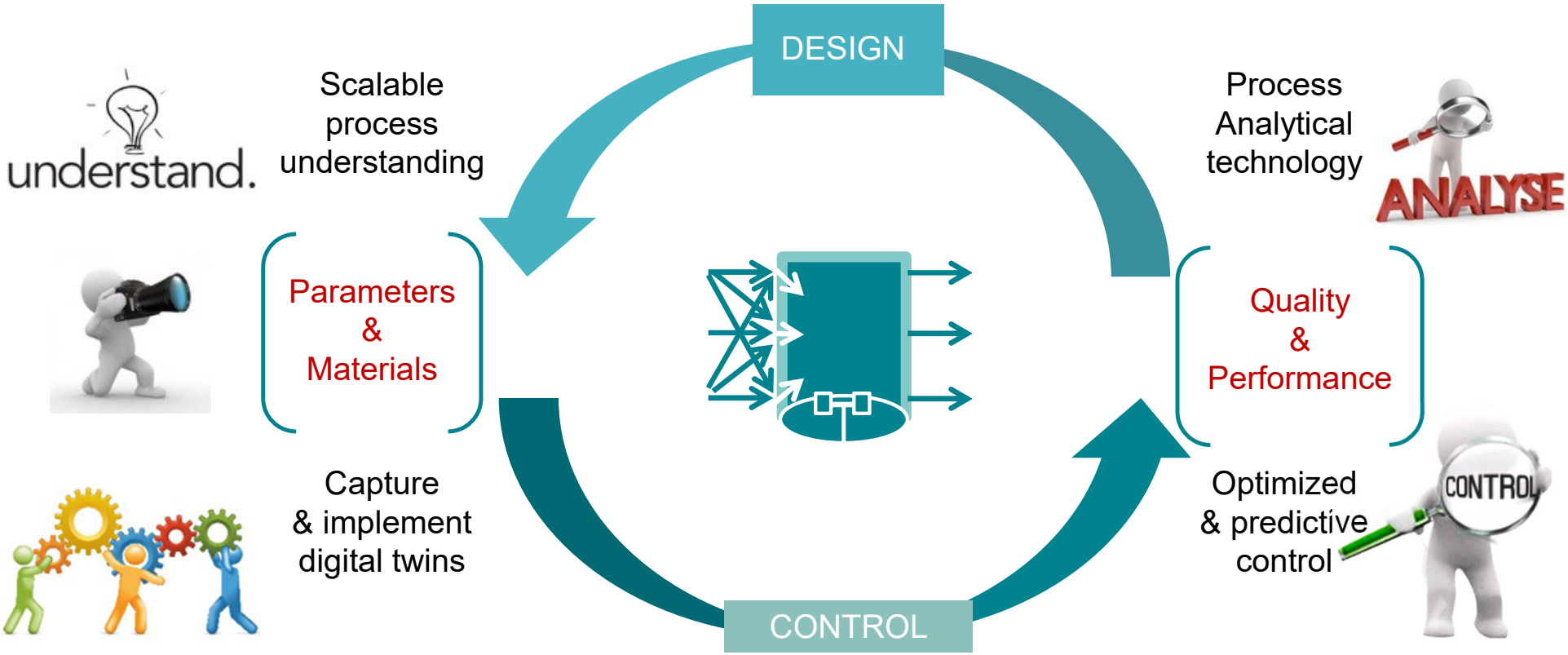
decide which ones to buy
(make decision by linking information to the objective)

Knowledge management: a "systematic approach to acquiring, storing, and disseminating information related to products, manufacturing processes, and components." (ICH Q10)

Quality by Design - Process understanding & Control strategy



Current Quality by Design Approach – From data to information to knowledge and control

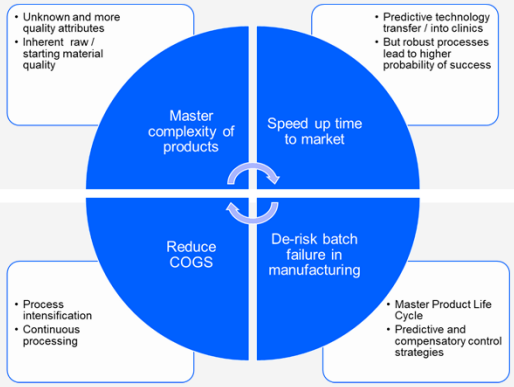


Why Modelling?

The trajectory matters!

Data

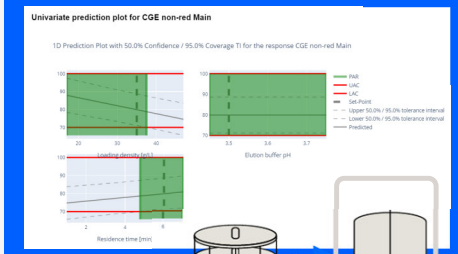
Tabular



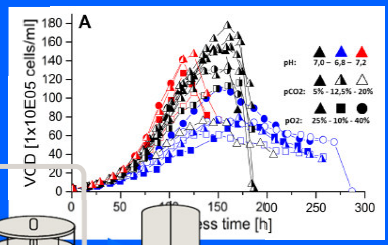
Time Series

Information

Static/DoE Modelling



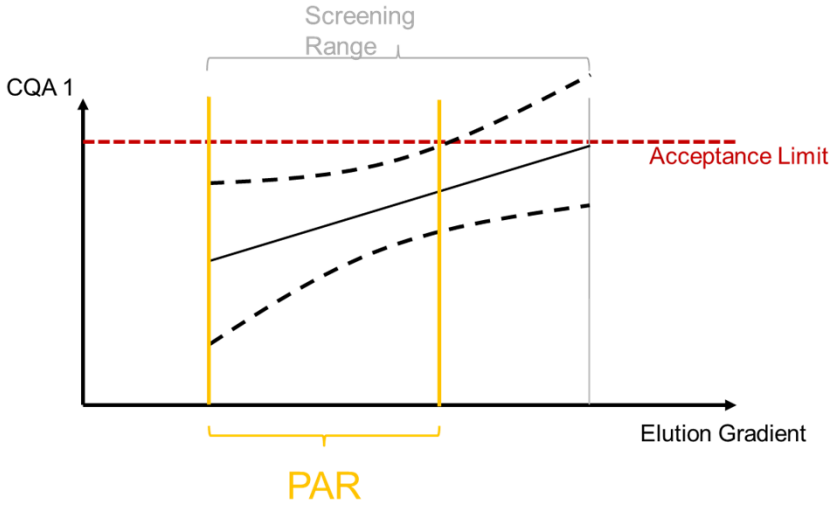
Dynamic Modelling



Use Case

- Simulation — What if?
- Optimization — What is optimal?
- Prediction — What will happen?
- Control — What should I do?

Model Credibility




TRUST

Verification, Validation and Uncertainty Quantification

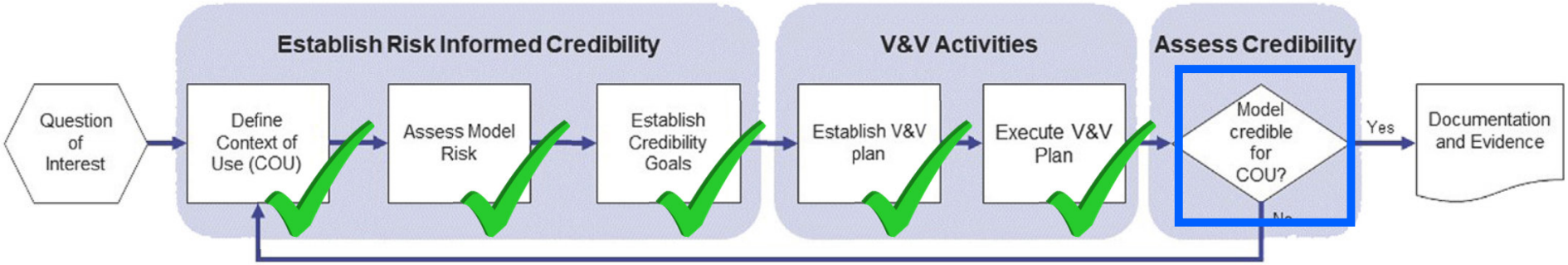
ASME V&V 40 risk-informed credibility assessment framework

GUIDANCE DOCUMENT

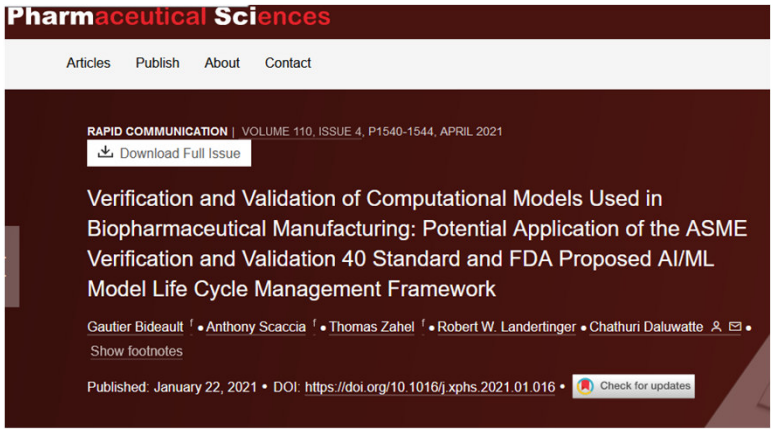
Considerations for the Use of Artificial Intelligence To Support Regulatory Decision-Making for Drug and Biological Products

Draft Guidance for Industry and Other Interested Parties

JANUARY 2025



Validation: the process of determining the degree to which a model or a simulation is an **accurate representation of the real world**



Is the model uncertainty smaller then the required acceptance for the context of use?

The Protein Alternative

Commercial Production

643 unhappy cows

205,760 L Methane

322 to 429 hectares land [1]

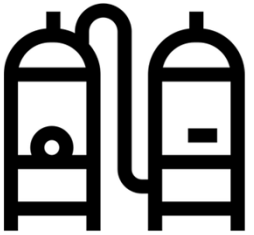
32M L water [2]

Highly dependent on external factors like inflations, climate, etc.

Output

133 tons
β-Casein
per Annum

fermify Technology



0 cows

85% less CO_2

98% less land, 4,000 L Tank

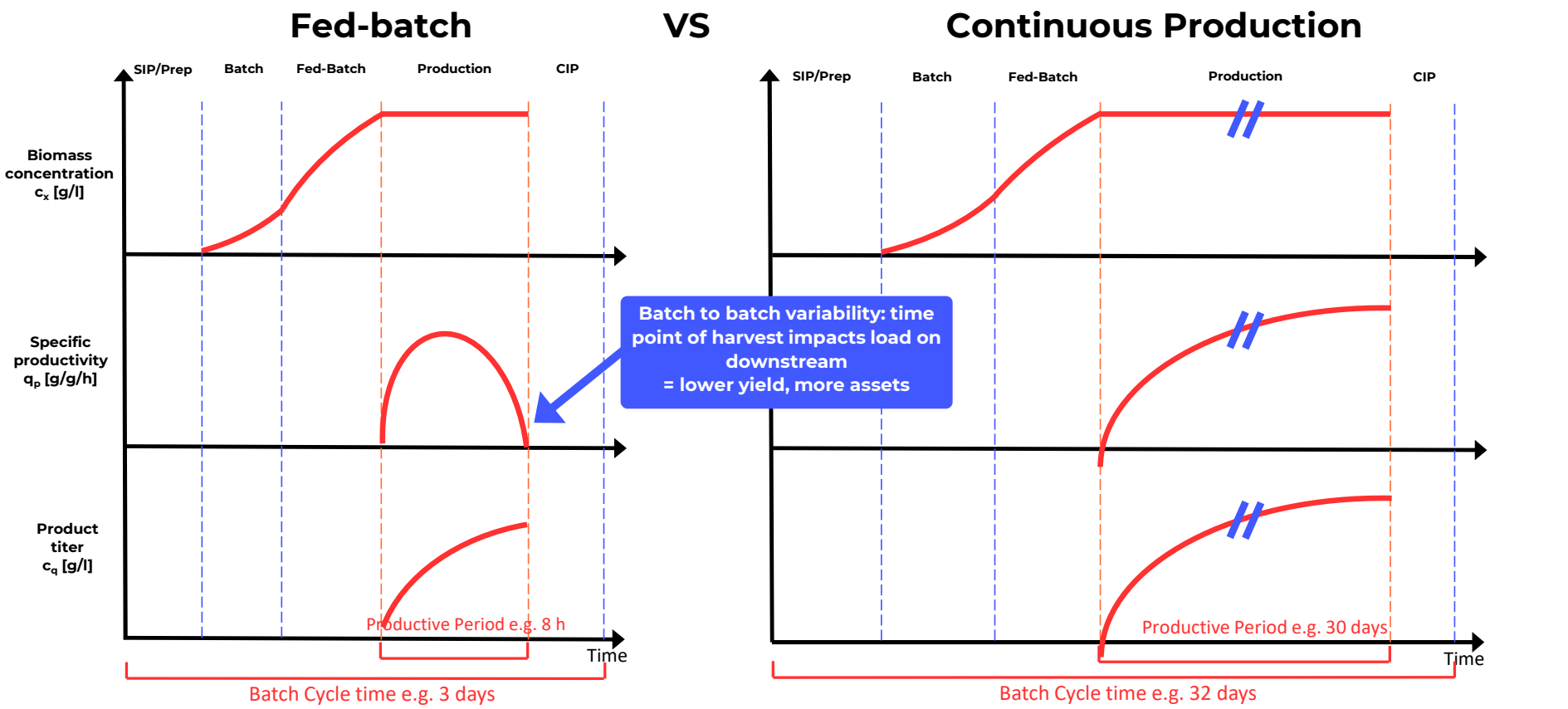
75% less water

Independent from milk price and supply fluctuations.

fermify

1. Hogan, J., Shaw, I., Berry, P., & Australian Bureau of Agricultural and Resource Economics. (2004). A review of the Australian dairy industry. In ABARE eReport 04.24. Australian Bureau of Agricultural and Resource Economics. https://www.accc.gov.au/system/files/public-registers/documents/D05%2B17526.pdf
2. Craig Thomas, Michigan State University Extension. (2011b, April 5). Drinking water for dairy cattle: Part 1. MSU Extension. https://www.canr.msu.edu/news/drinking_water_for_dairy_cattle_part_1

The unbeatable advantage of continuous processing



11%

OEE (Overall Equipment Effectiveness)

94%

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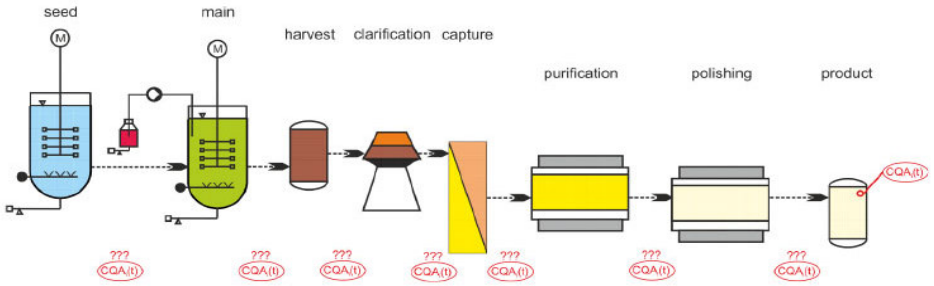
Intensified & Continuous Integrated Processing

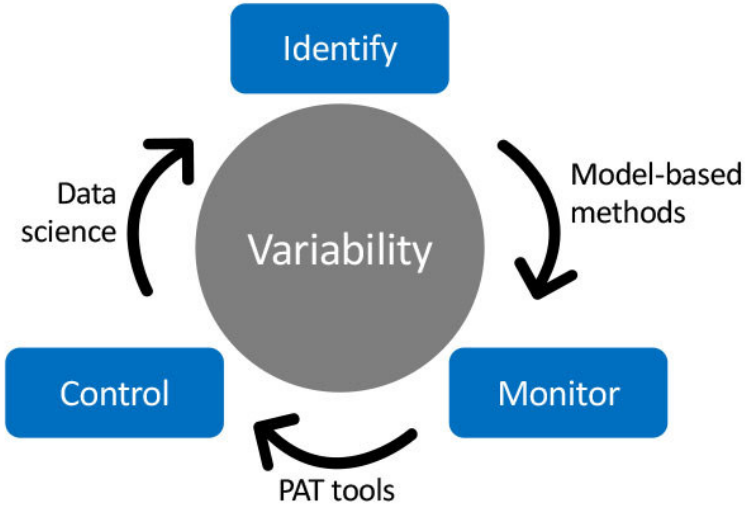


CM IN BIOTECH PROCESSES

Challenges for Implementation

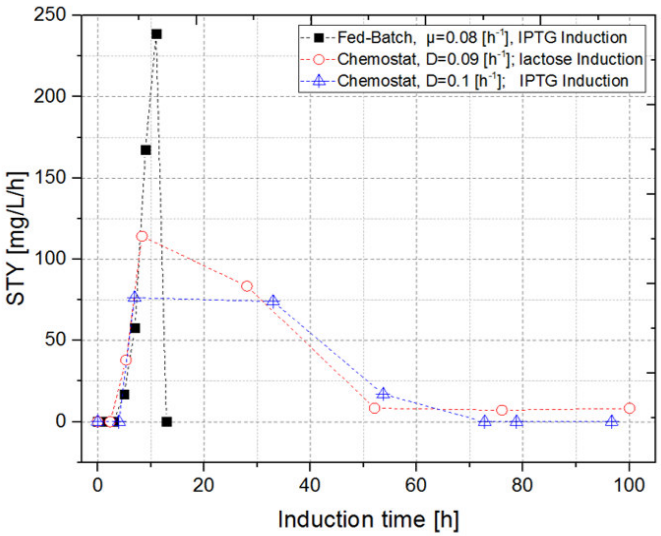
Robert Dream, CPIP, PE; Christoph Herwig, PhD; and Emilie Pelletier

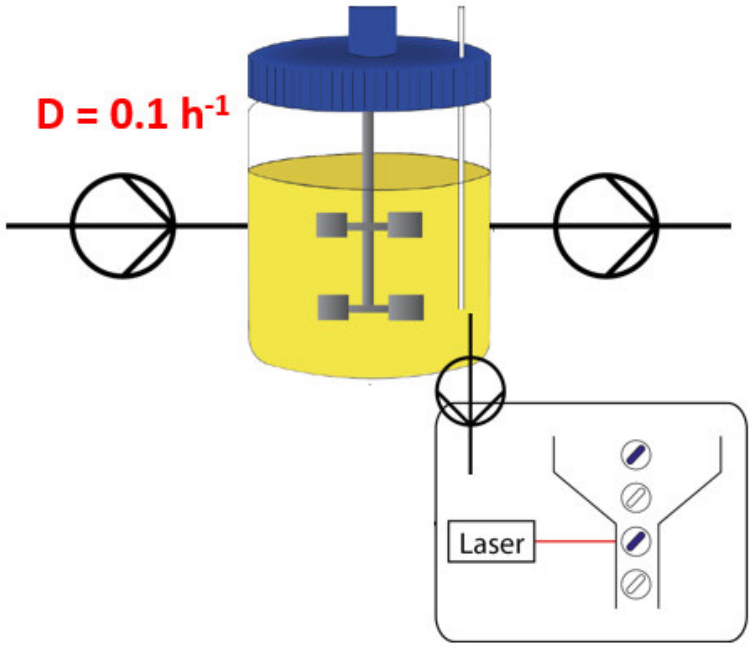
Roger F. Sherwood Article of the Year, ISPE



Population Analysis by Online Flow Cytometry

Does an online FCM enable to monitor the drop in productivity?
Can we gain more knowledge about populations with specific staining??





Population Analysis by Online Flow Cytometry

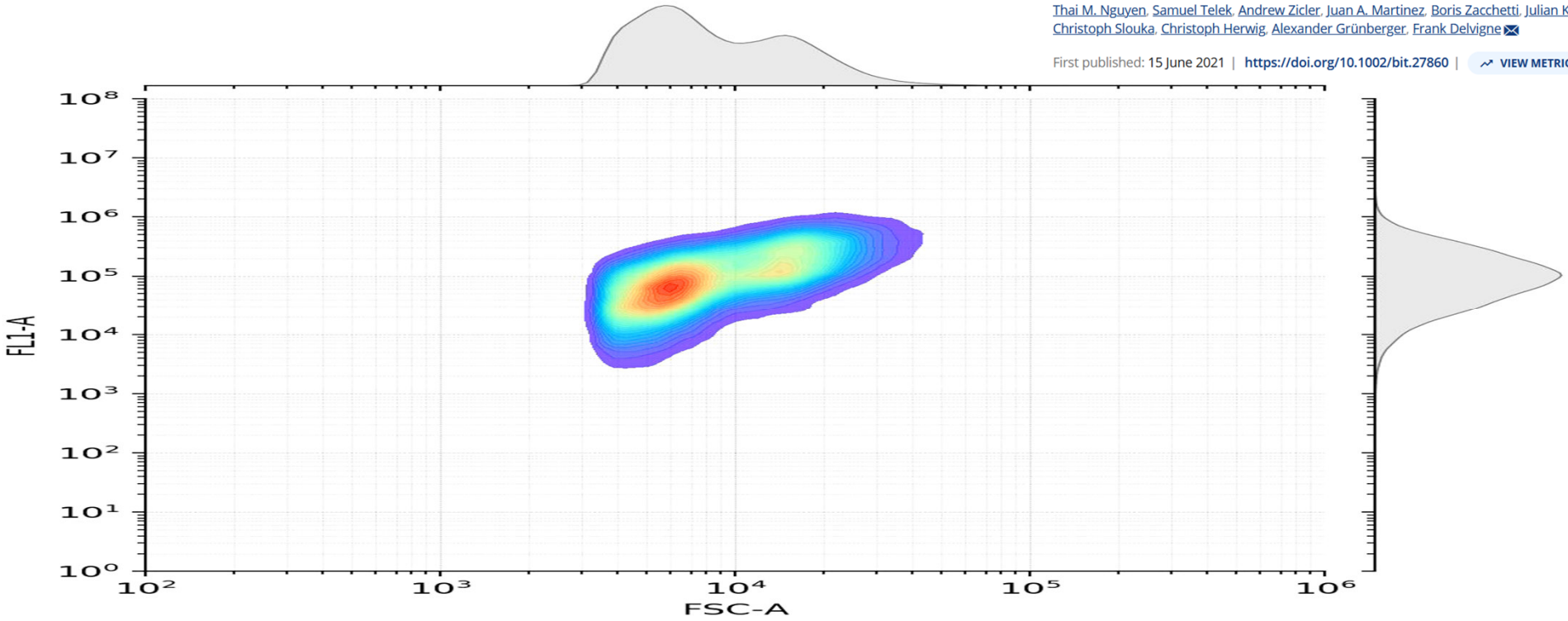
BIOTECHNOLOGY and BIOENGINEERING

ARTICLE

Reducing phenotypic instabilities of a microbial population during continuous cultivation based on cell switching dynamics

Thai M. Nguyen, Samuel Telek, Andrew Zicler, Juan A. Martinez, Boris Zacchetti, Julian Kopp, Christoph Slouka, Christoph Herwig, Alexander Grünberger, Frank Delvigne

First published: 15 June 2021 | https://doi.org/10.1002/bit.27860 | VIEW METRICS



High dynamics in subpopulations lead to decrease in productivity…

Main rationales for establishing a competitive & scalable technology

Keep reactors small

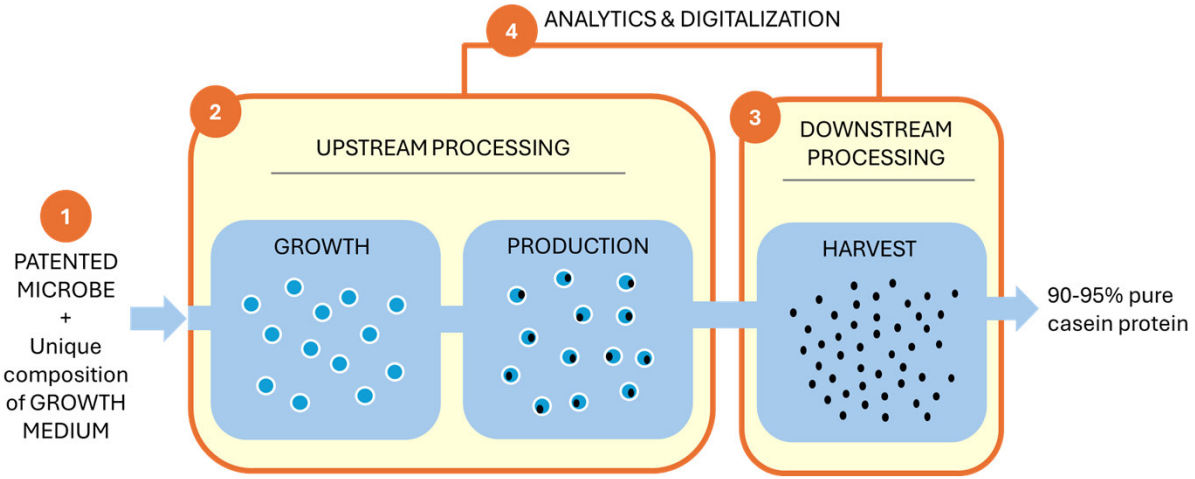
- Avoid mixing inhomogeneity, which may occur at more than 20 m3 scale

Yet achieve high productivity and allow full scalability

- Switch to continuous processing, which achieves >15 x higher productivities than fed-batch processes

Keep product quality constant and efficiency high

- Steady-state conditions along the complete process chain
- Avoid complete unit operations, achieve optimum economy



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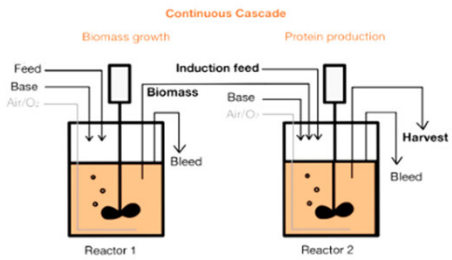
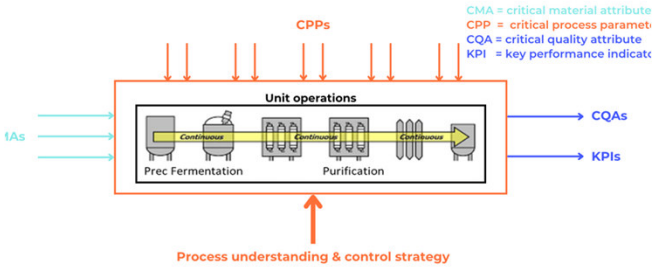
Key Elements...

...for economical and scalable production of heterologous proteins



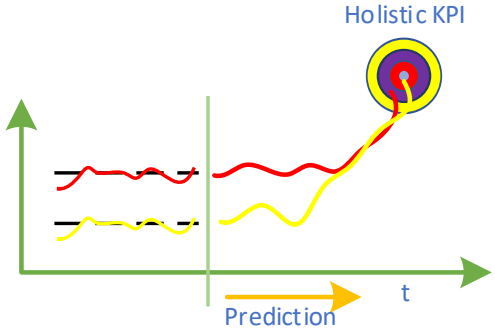
Continuous Production

Integrated Continuous Bio-manufacturing as the core basis for economic and ecological competitive advantages



Digitalization

Holistic understanding and control strategies of single unit operations and complete process chain



Control

Robust and optimum productivity with listening to the happiness of the cells

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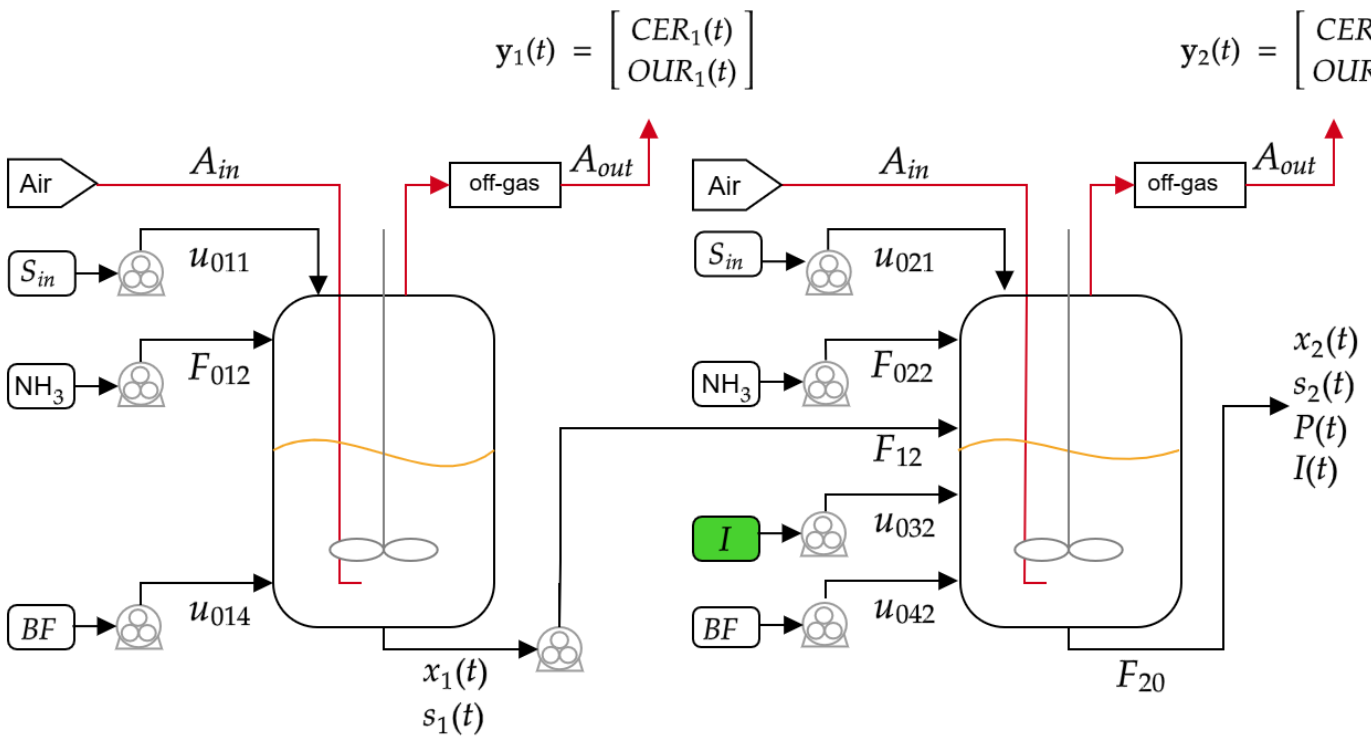
MIMO System: Multiple Input, Multiple Output Optimization Problem



Highly correlated system: Infinite combination of experimental setups can yield the **same result**

fermify

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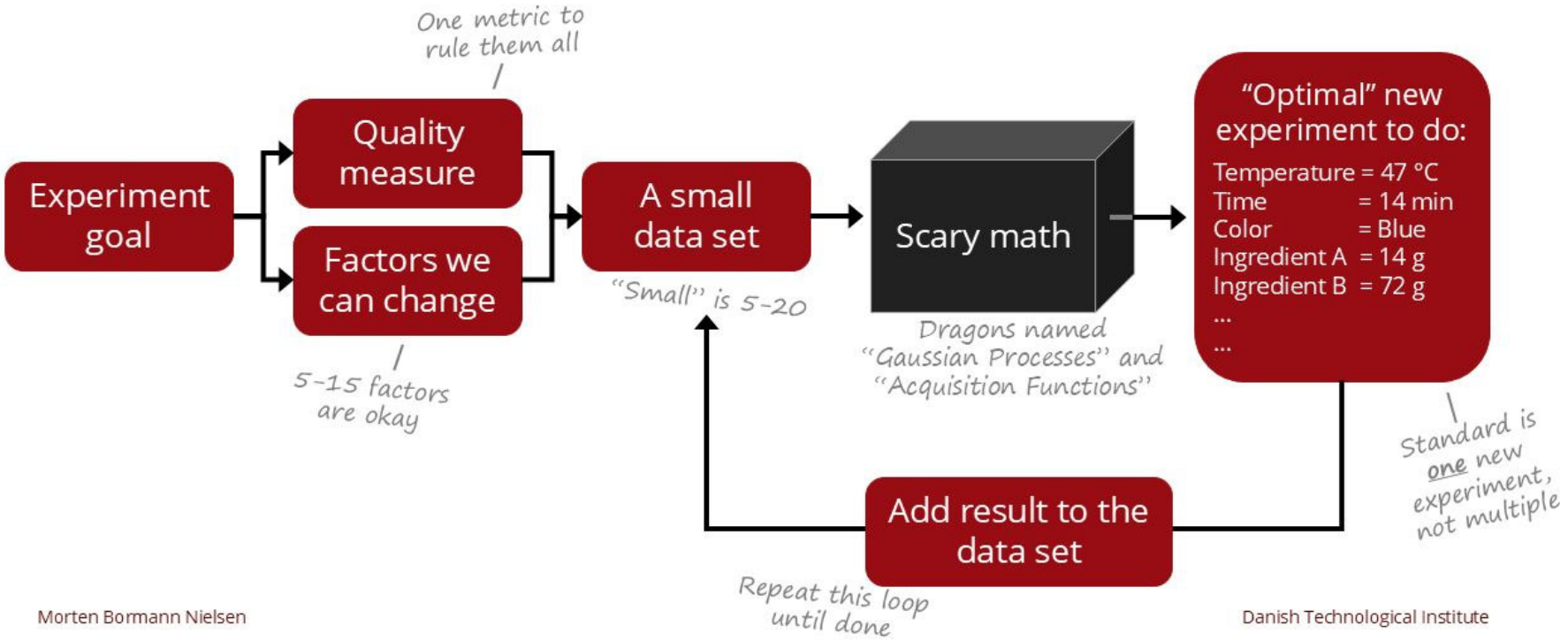
Bayesian optimization suggests an *optimal* next experiment to do, given your present data



For optimization, multiple inputs are required to change at the same time: NON OBVIOUS Adjustments

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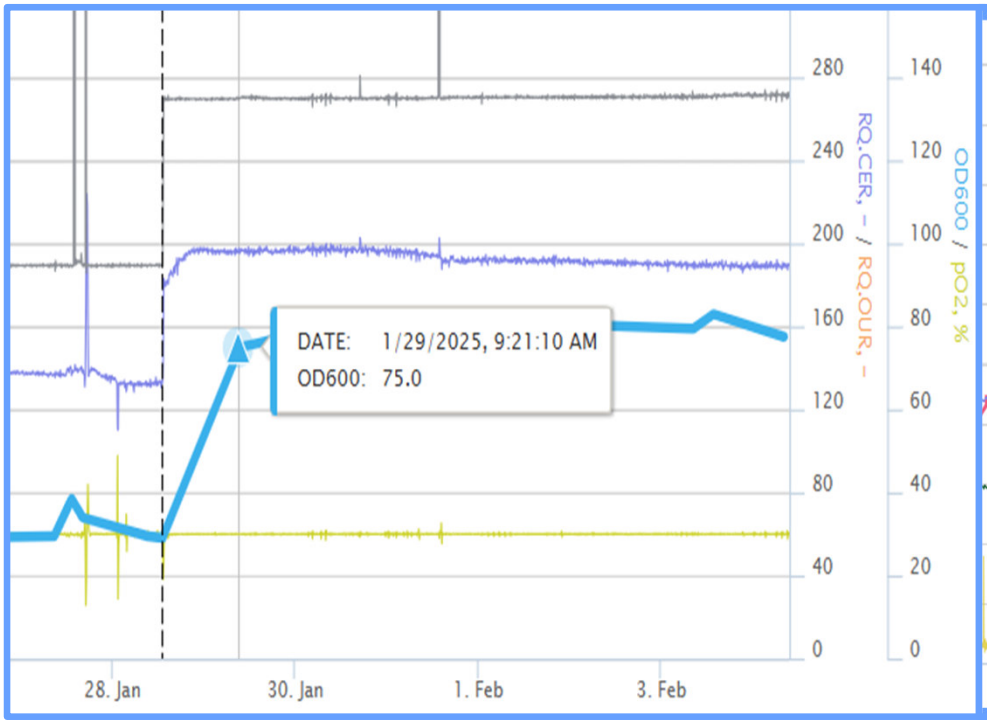
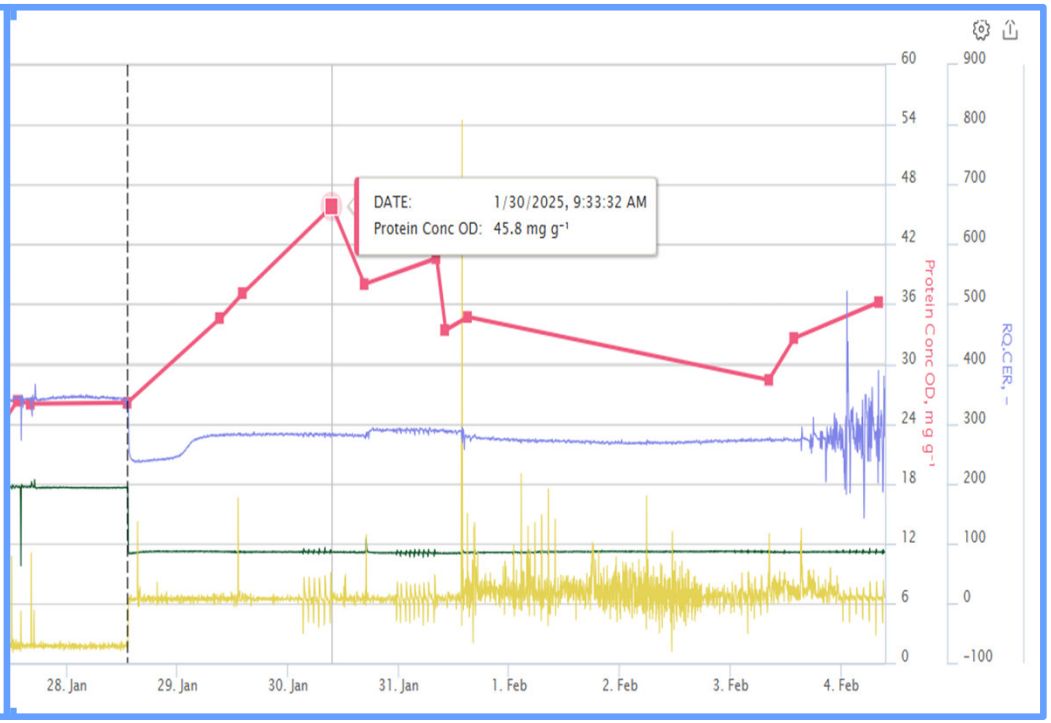
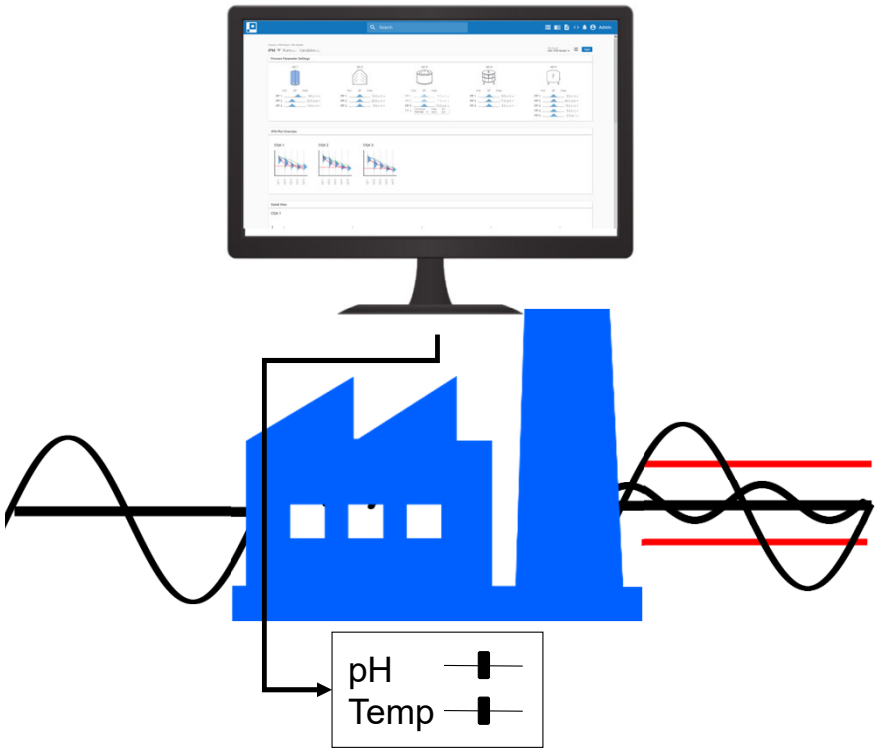
INPUTS



OUTPUTS

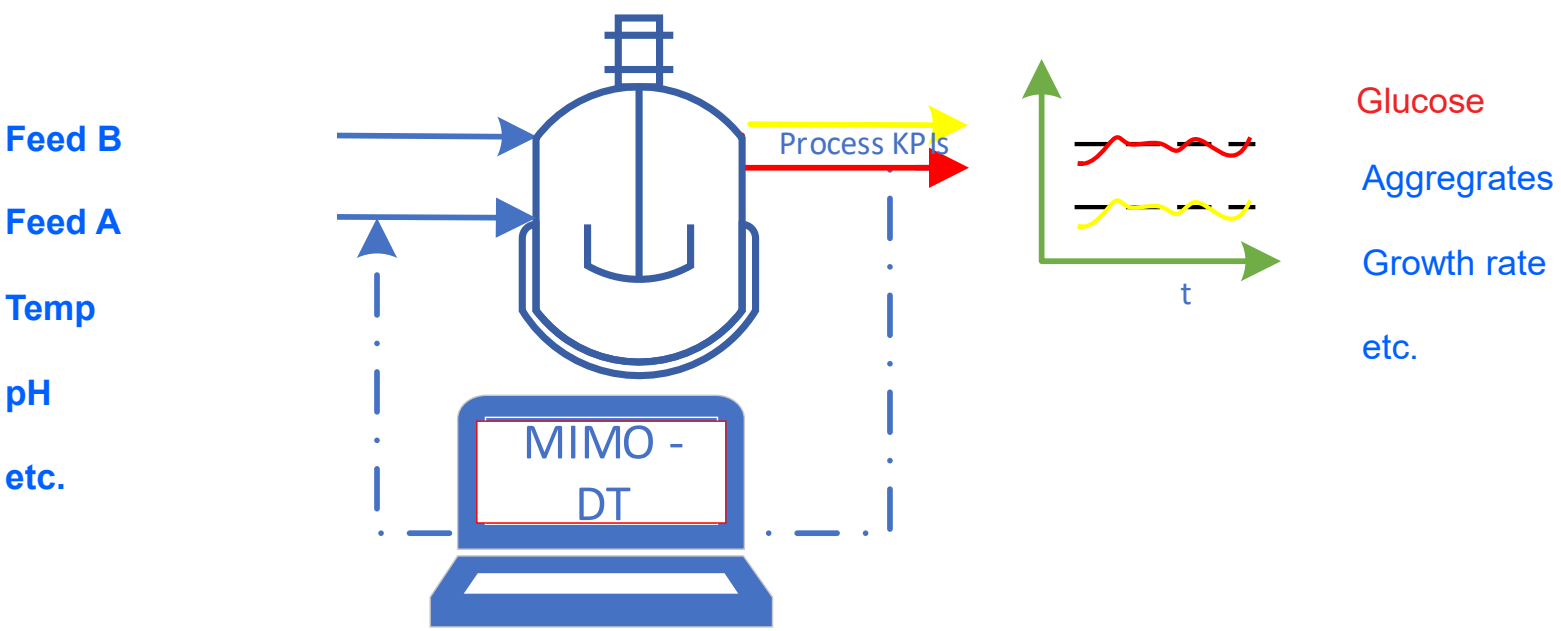


How to achieve process robustness

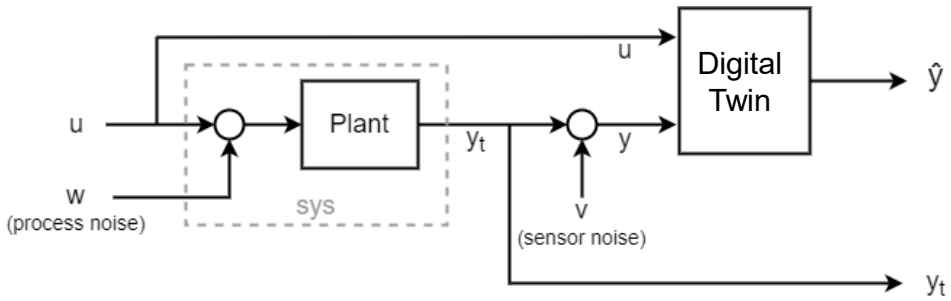


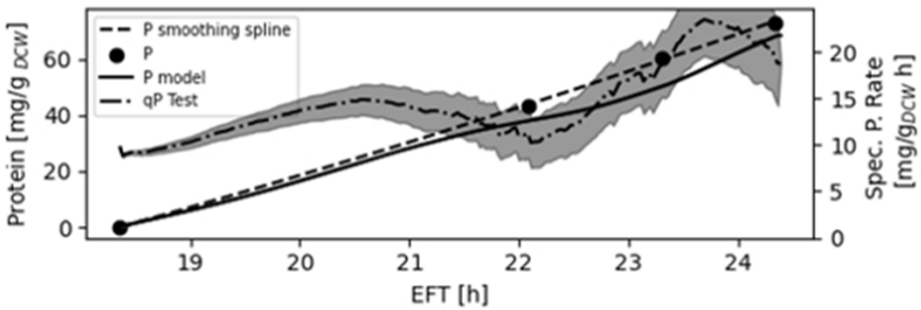
Reduction of OOS results
Increased space-time yield
Increased reproducability
Sustainability
Decrease cost of goods

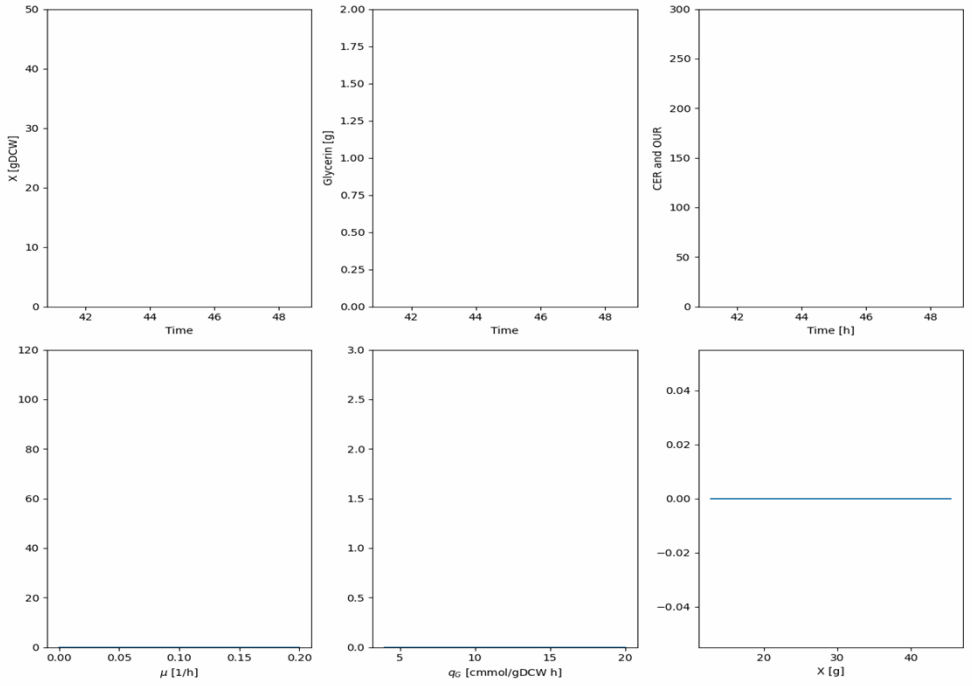
What needs to be optimized?
All outputs (responses) at the same time



Real-time estimation using Digital Twin Observers

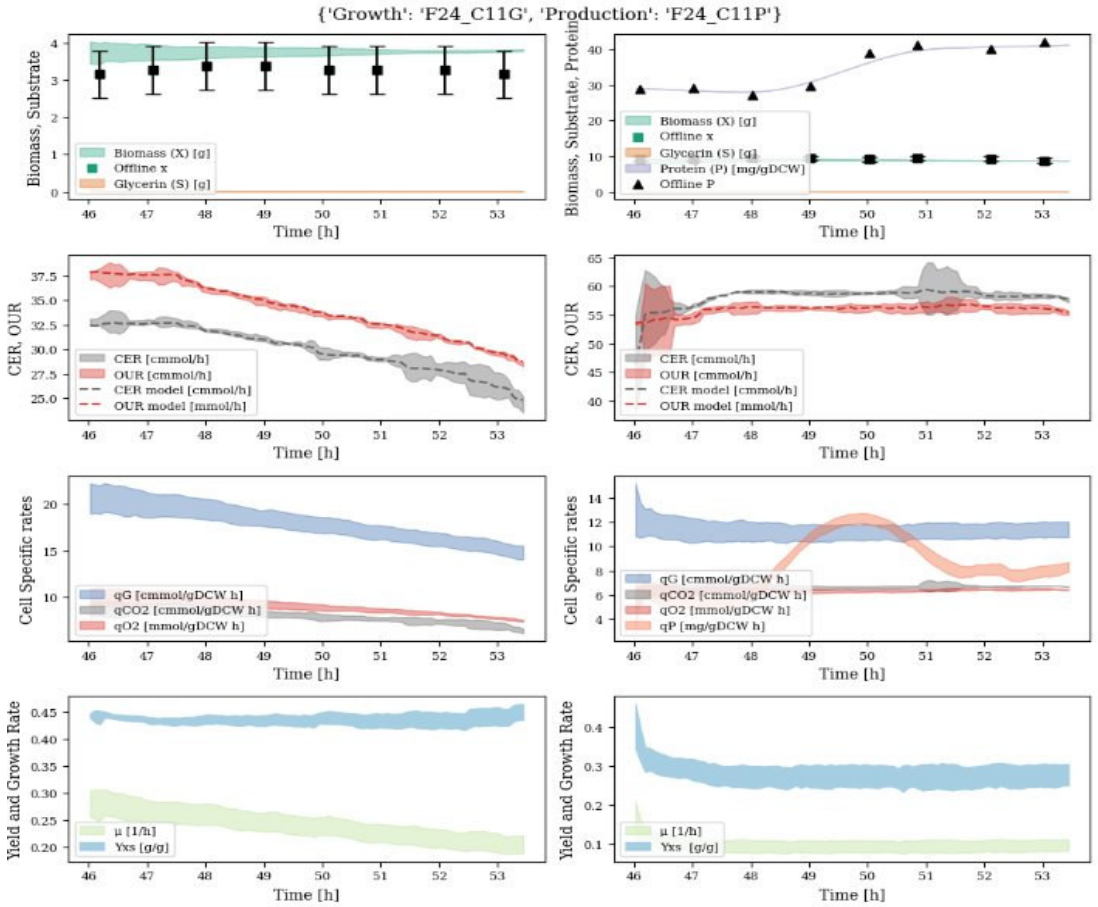






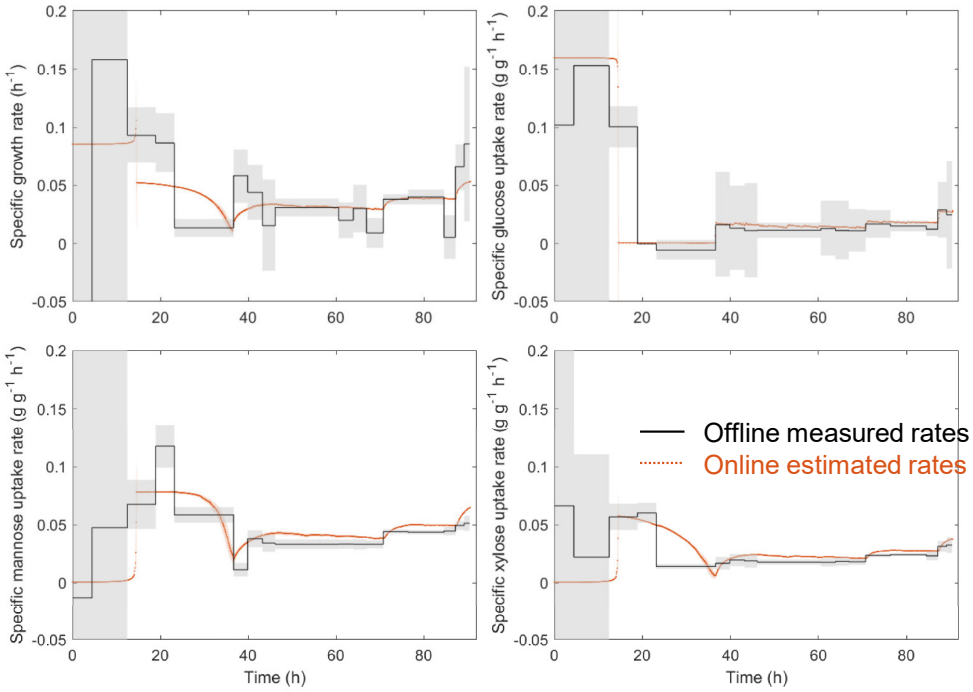
Real-Time Estimation capabilities of difficult to measure KPIs

fermify



Real time model-guided methodology to estimate initial conditions / raw material uncertainty

Real time fed-batch process monitoring of biomass specific rates



State estimation using particle filtering enables real process robustness despite raw material uncertainty

Bioresource Technology 321 (2021) 124395

Contents lists available at ScienceDirect

Bioresource Technology

journal homepage: www.elsevier.com/locate/biortech

Noninvasive online monitoring of *Corynebacterium glutamicum* fed-batch bioprocesses subject to spent sulfite liquor raw material uncertainty

Peter Sinner[a], Marlene Stiegler[a], Christoph Herwig[a], Julian Kager[a,*]

MIMO (Multiple Input Multiple Output) System

Contents lists available at ScienceDirect
Bioresource Technology
journal homepage: www.elsevier.com/locate/biortech

Addressing raw material variability: *In-line* FTIR sugar composition analysis of lignocellulosic process streams

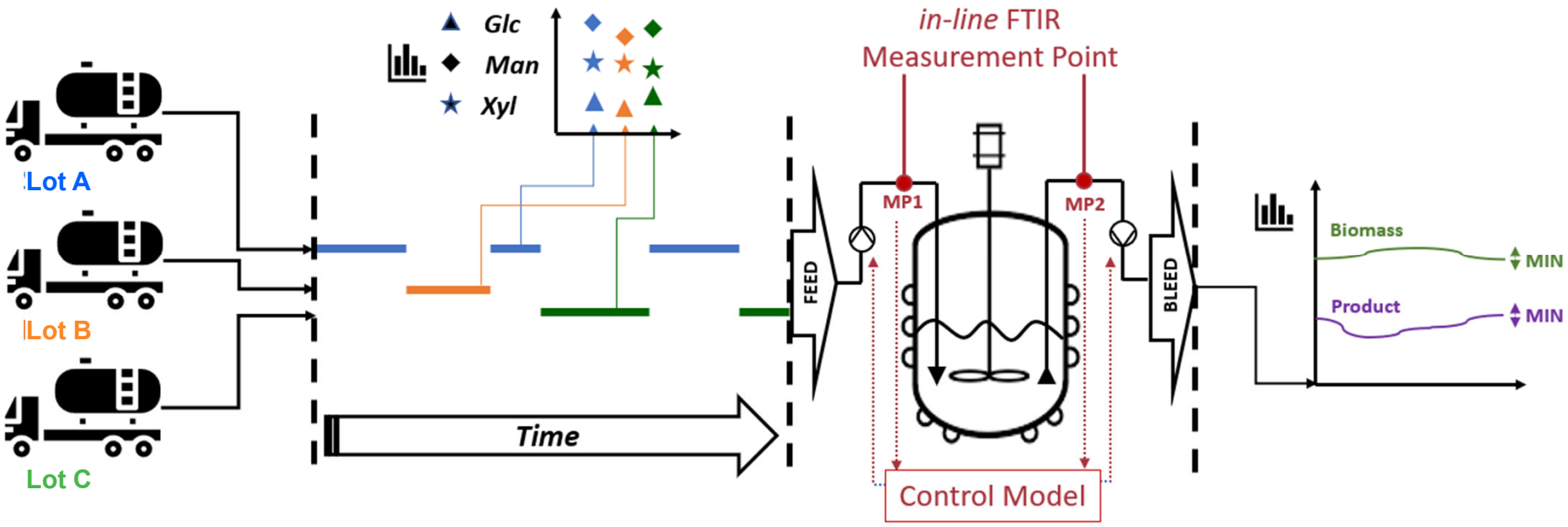
Raw Material
Batch wise changeup of sugar composition

Analysis
Time-Resolved measuring of spectra

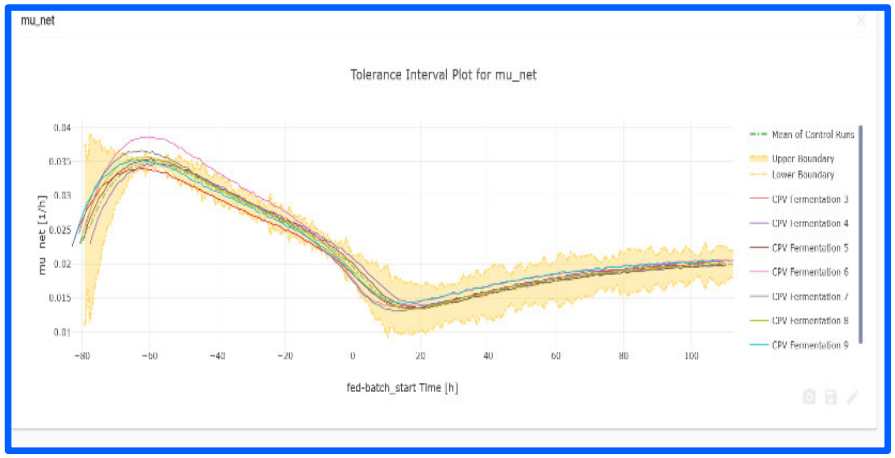
Computation
PLS model for sugar concentration

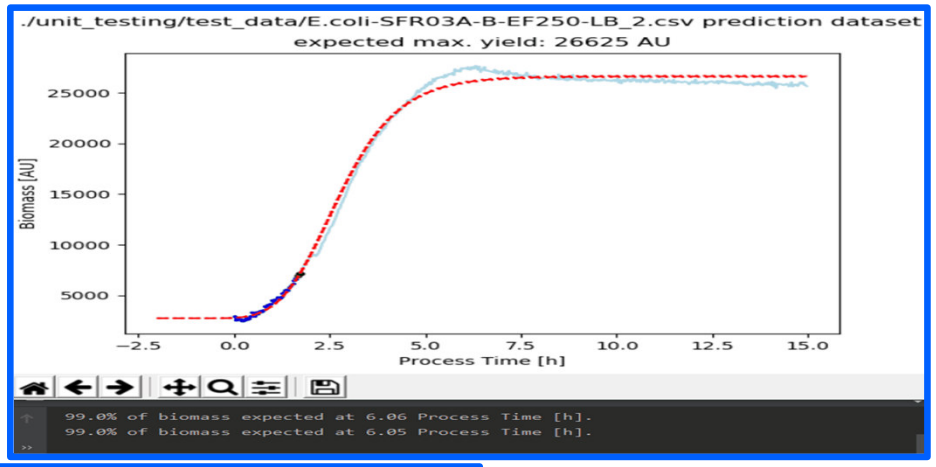
Control
Processmodel to keep culture in steady state

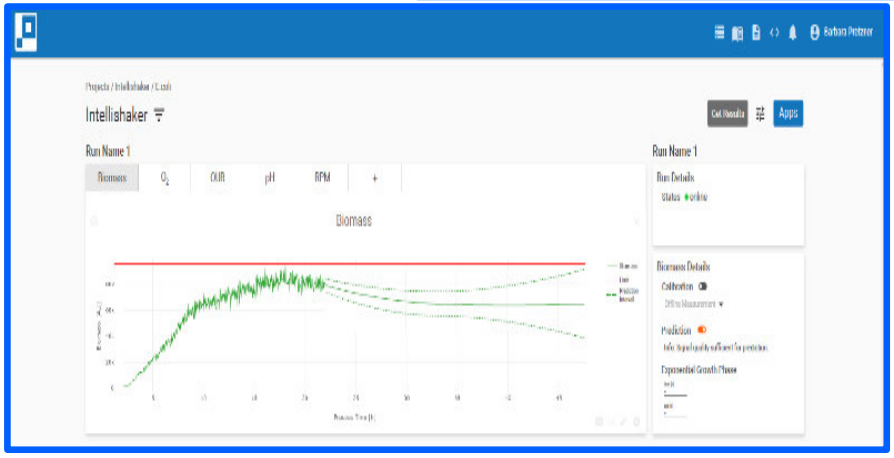
Reference
Measurements for validation of setpoints



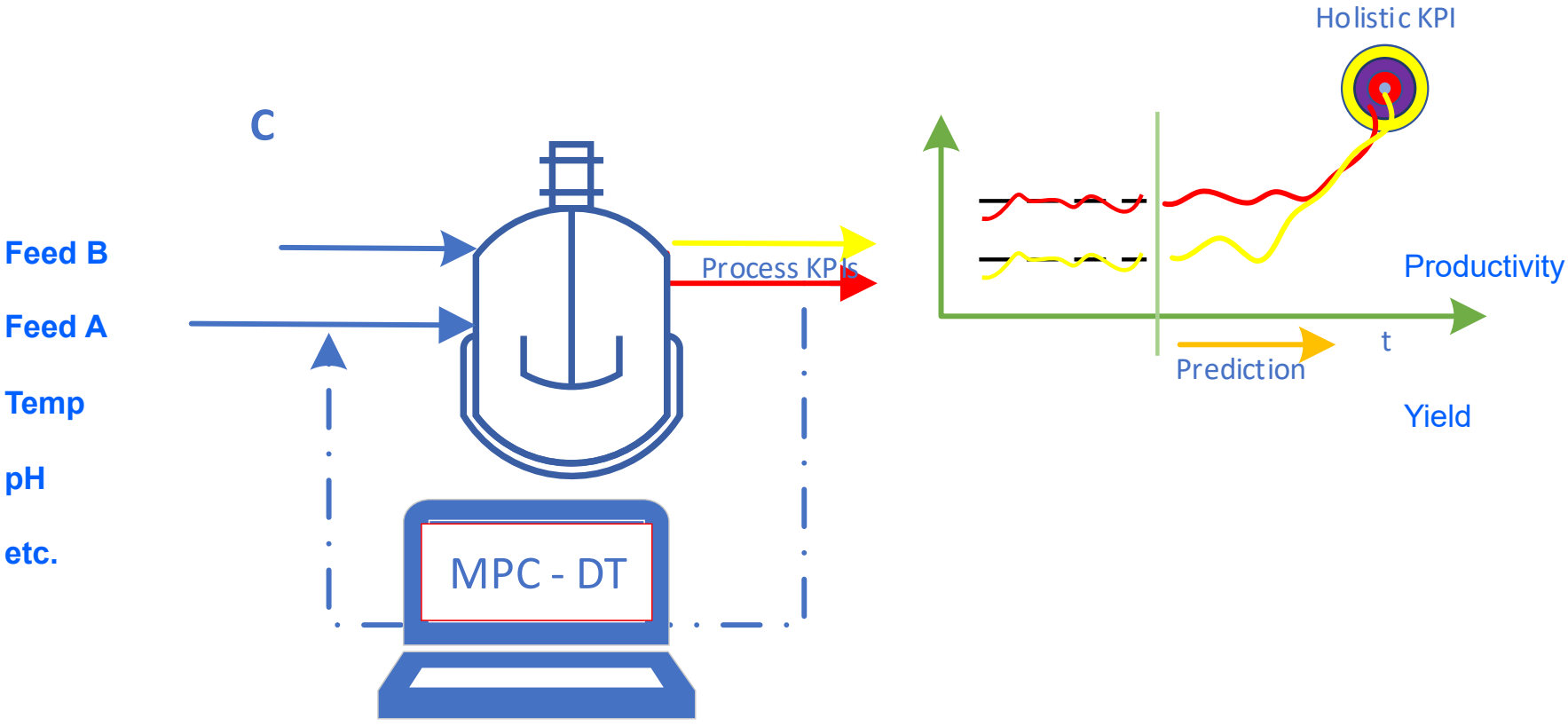
Prediction Capabilities



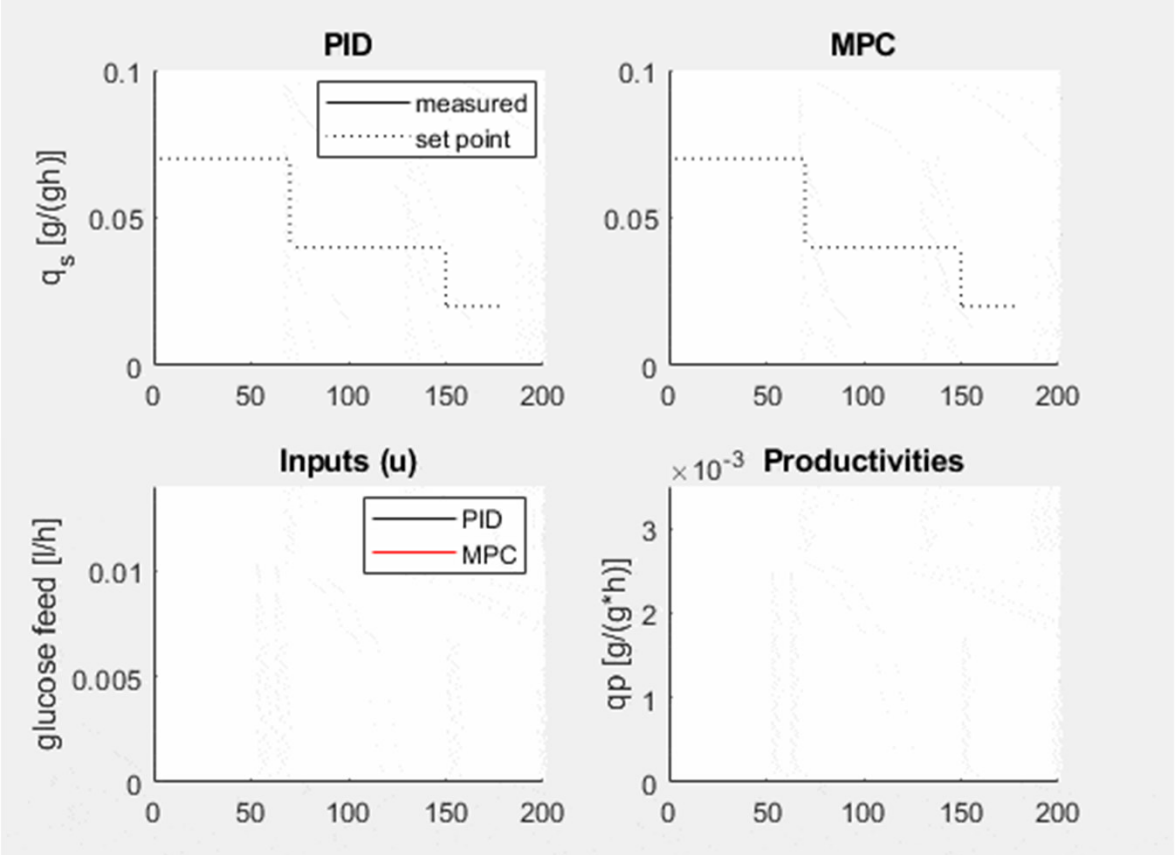




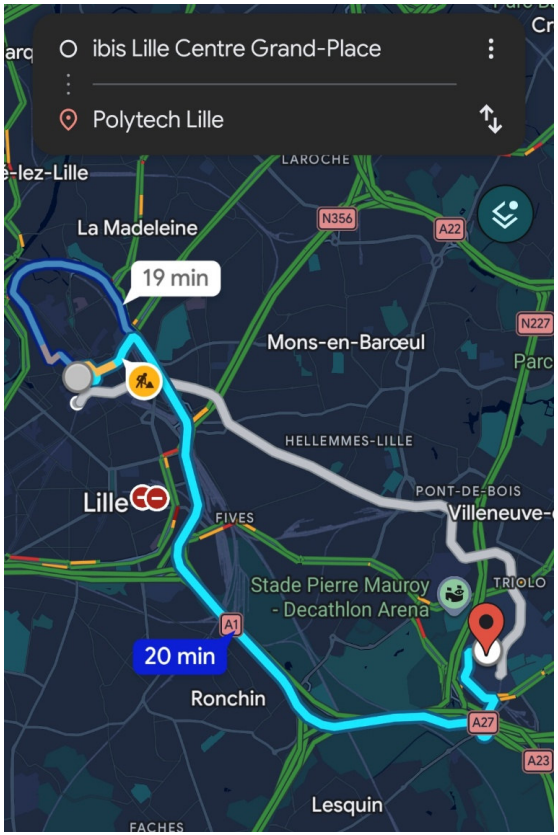
What needs to be optimized?
All outputs (responses) at the end of the process (DS)



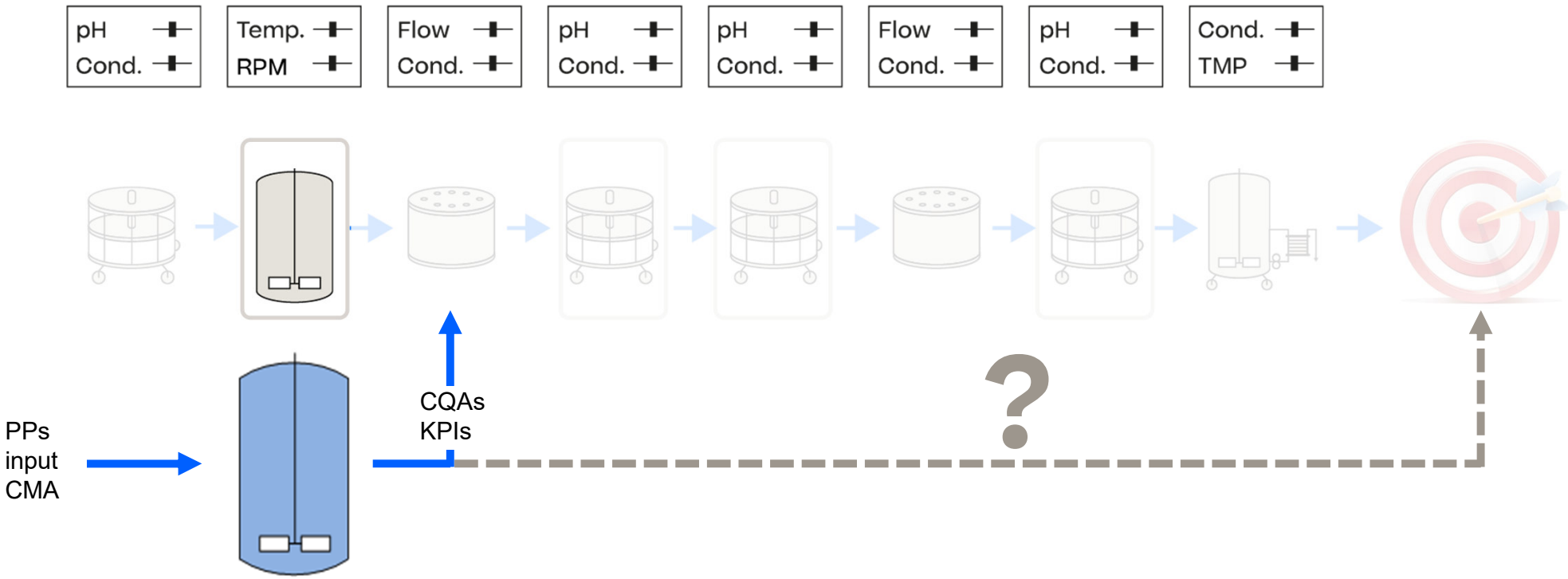
Digital Twin Based
Advanced Control using Model Predictive Control



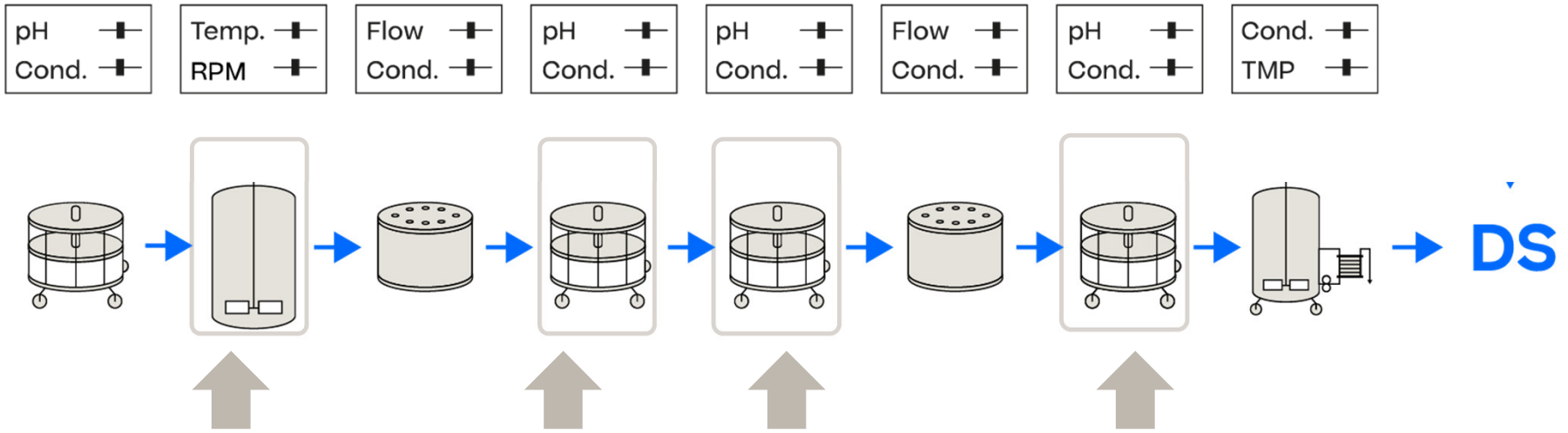
Kager, J., et al. (2019) , Ulonska, S, et al. (2018). Ulonska, S., et al. (2018).



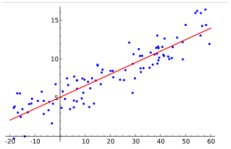
End-to-End Digital Twin as a Framework



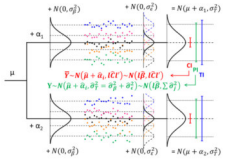
End-to-End Digital Twin as a Framework



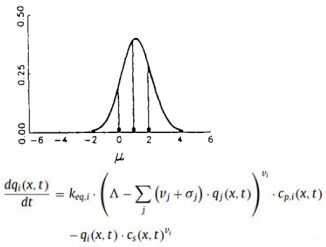
Ordinary Least-Squares (e.g. via DoE)



Linear Mixed Model

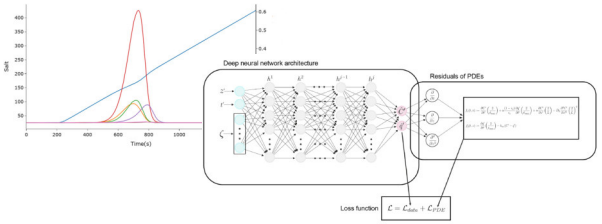


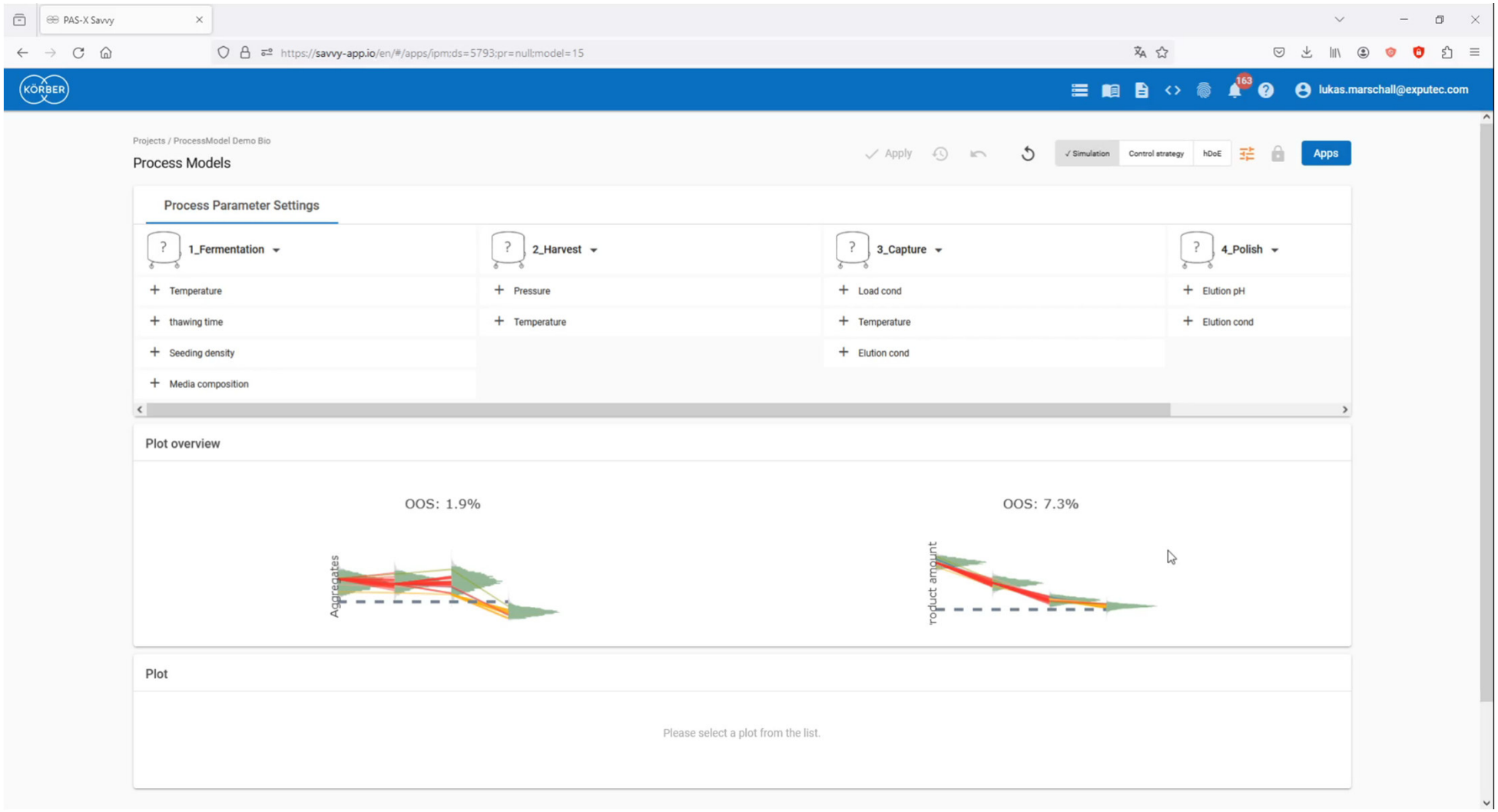
Mechanistic Models



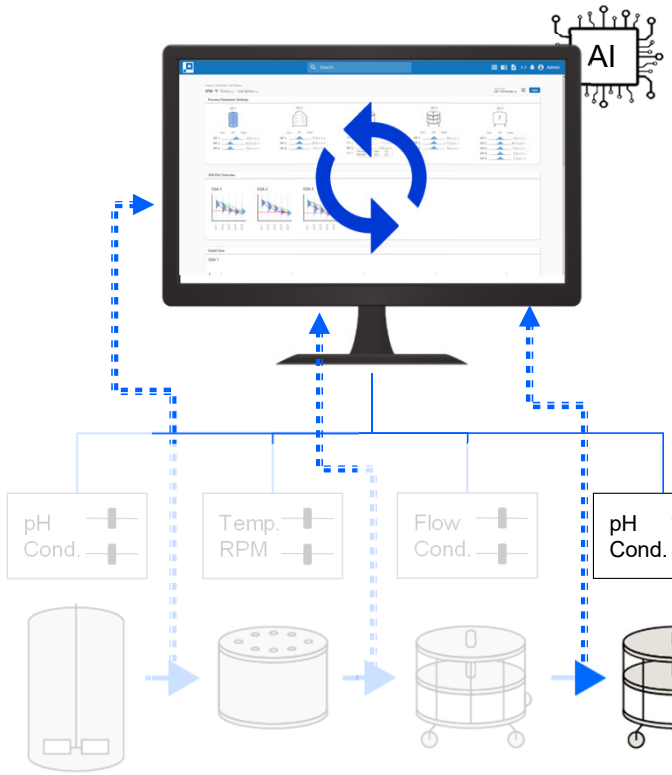
$$k_{kin,i} \cdot \frac{dq_i(x,t)}{dt} = k_{eq,i} \cdot \left(\Lambda - \sum_j (\nu_j + \sigma_j) \cdot q_j(x,t)\right)^{\nu_i} \cdot c_{p,i}(x,t) - q_i(x,t) \cdot c_s(x,t)^{\nu_i}$$

Hybrid and AI Models




PAS-X Savvy
https://savvy-app.io/en/#/apps/ipm;ds=5793;pr=null;model=15
lukas.marschall@exputec.com
Projects / ProcessModel Demo Bio
Process Models
Apply
Simulation
Control strategy
hDoE
Apps
Process Parameter Settings
1_Fermentation
Temperature
thawing time
Seeding density
Media composition
2_Harvest
Pressure
Temperature
3_Capture
Load cond
Temperature
Elution cond
4_Polish
Elution pH
Elution cond
Plot overview
OOS: 1.9%
Aggregates
OOS: 7.3%
roduct amount
Plot
Please select a plot from the list.

Real Time Application of End to End Digital Twins in Manufacturing

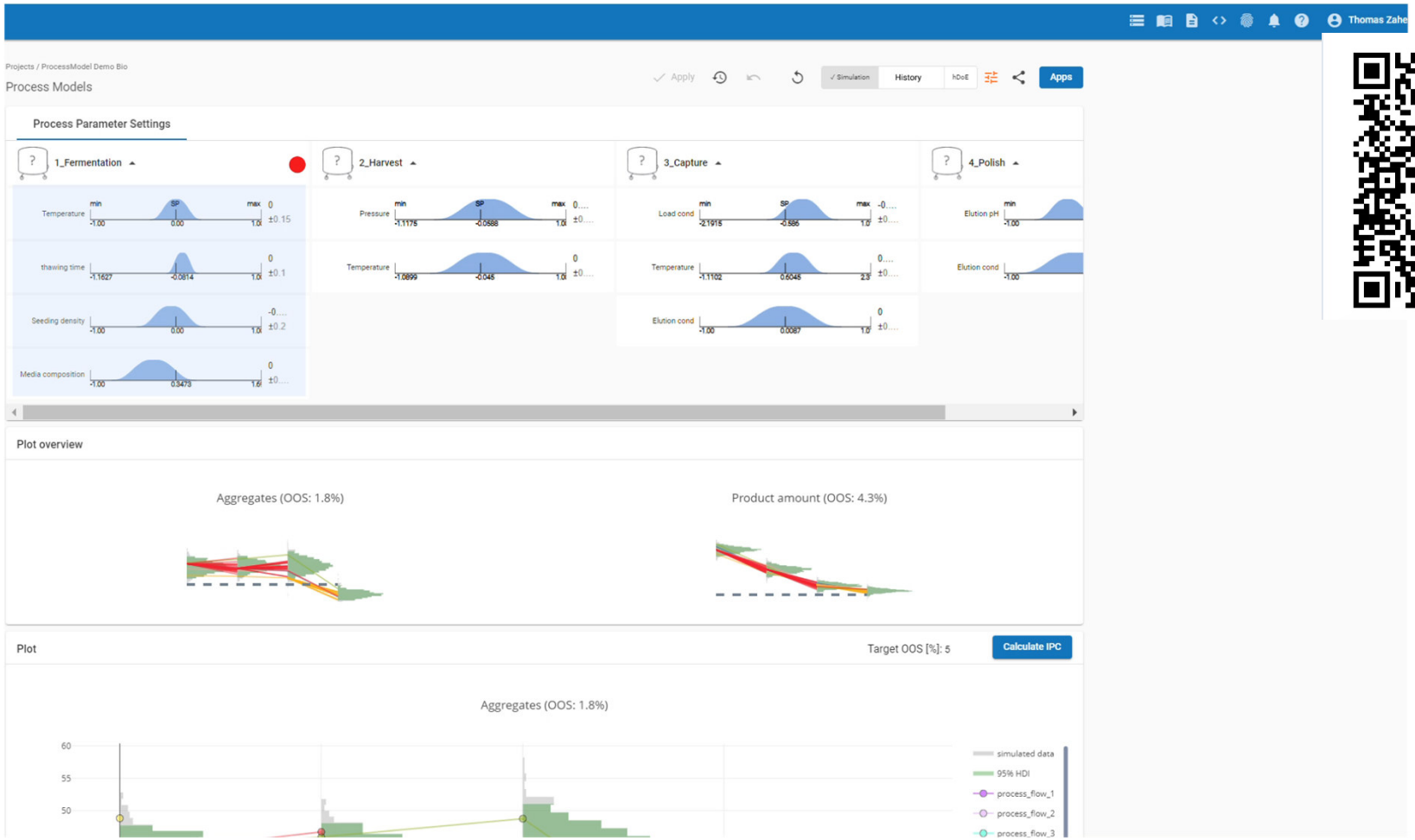


Final Yield 80%

Final Quality 99%

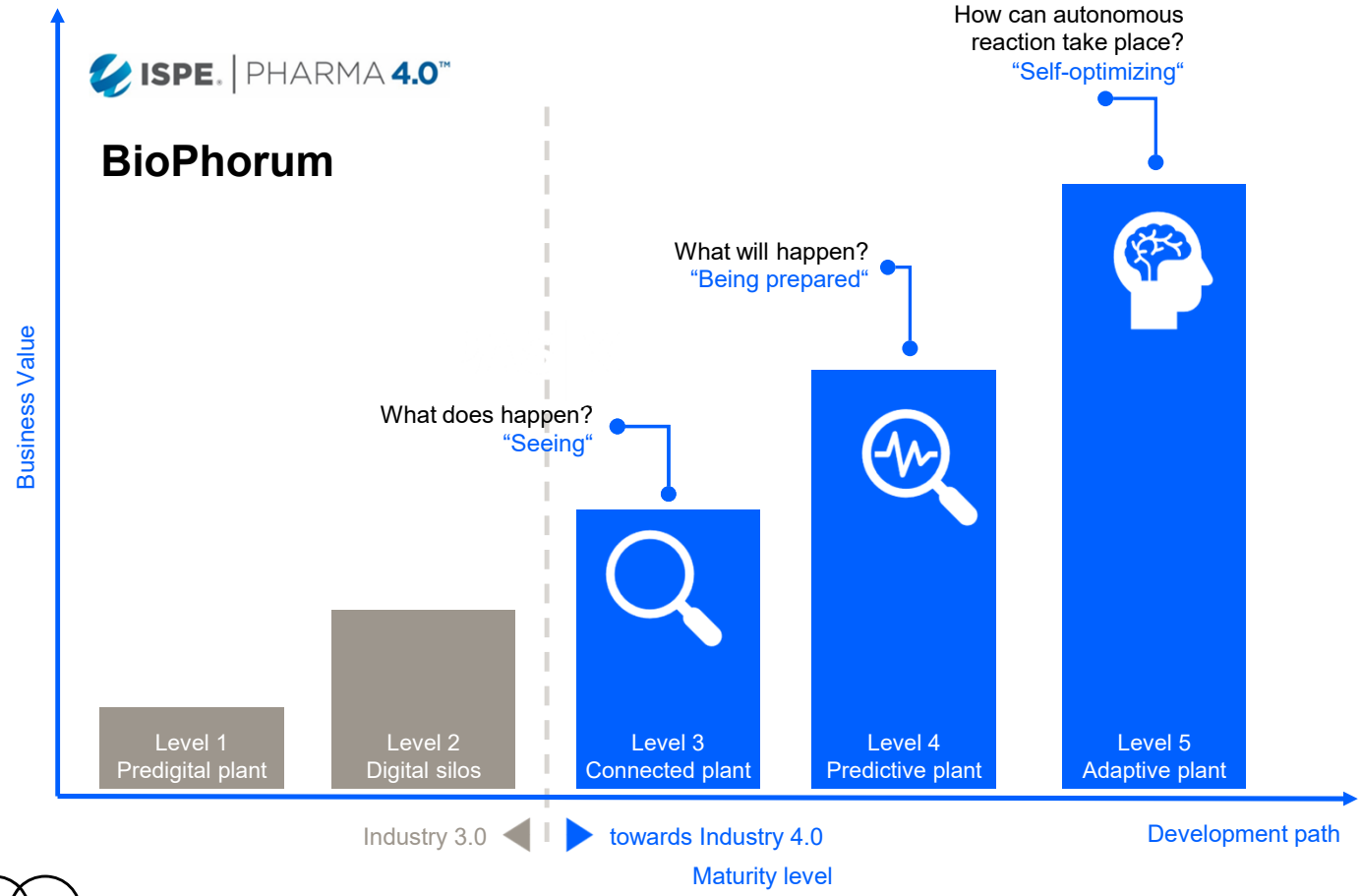
End-to-End Digital Twins as Recommender Systems in Manufacturing

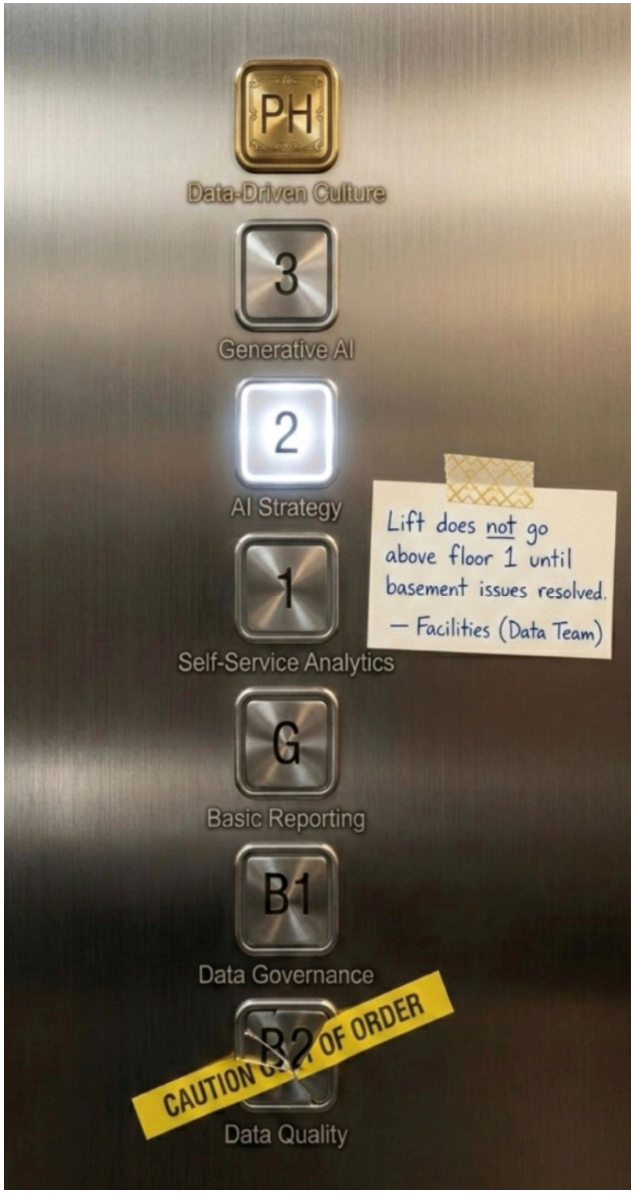
Multi-Input, Multi-Output & Multi UO Optimization Problem



Data Maturity Model

Maturity Models





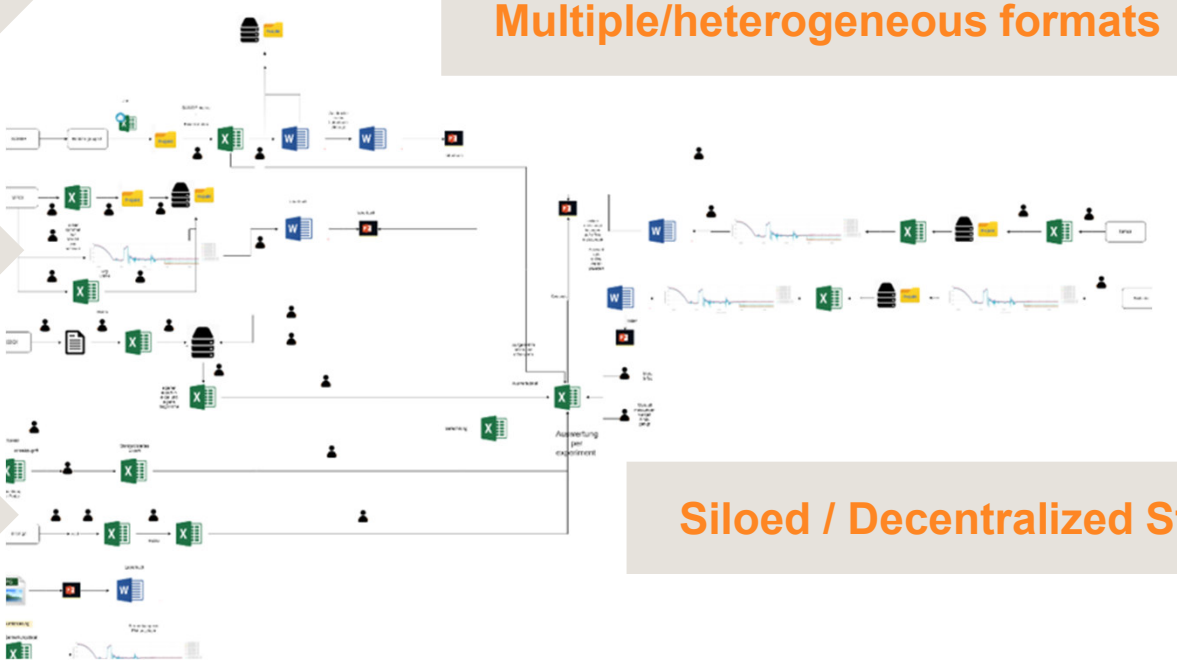

AI Strategy
GenAI Use Cases
Dashboards & Insights
Ownership
Lineage
Metadata
Data Quality
Definitions

Holistic Data Management: Challenges with data analysis

Lots of data source

Multiple/heterogeneous formats

Manual process

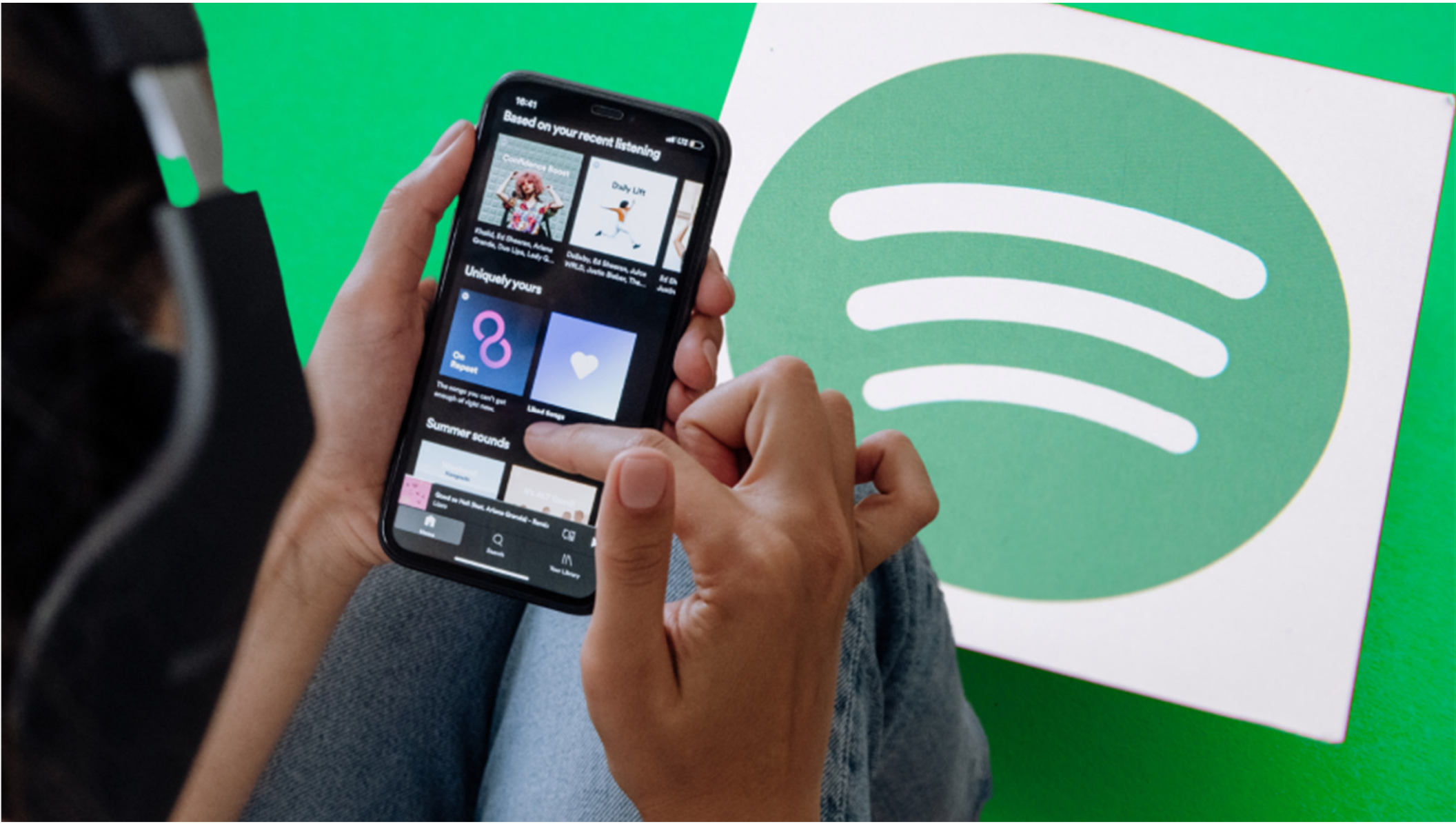


Transfer

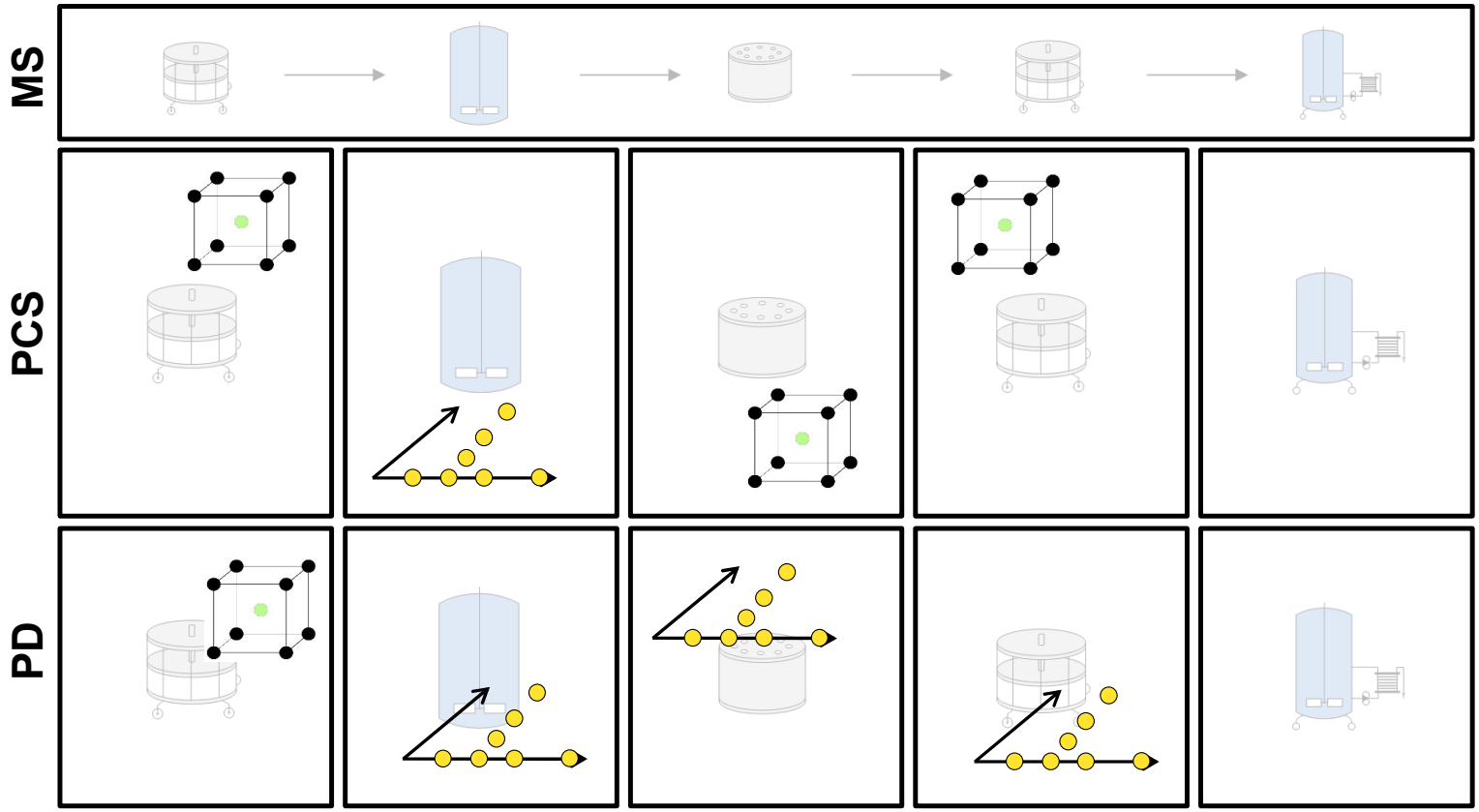
Siloed / Decentralized Storage

KÖRBER

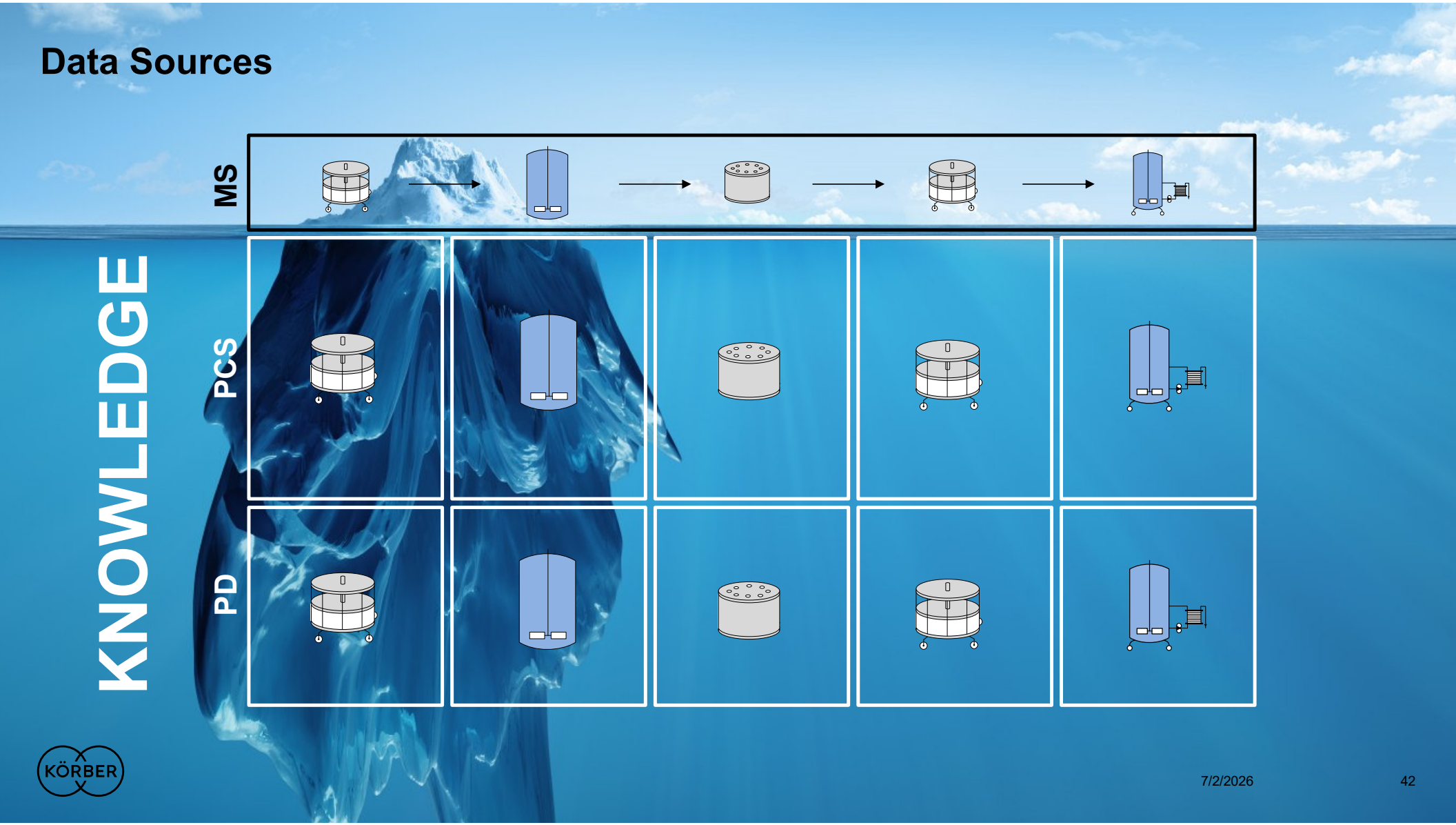

CFD-S28L
OPERATE
FUNCTION
SLEEP
STANDBY
PLAY MODE
MONO/ST.
ISS
OPR/BATT
TIMER
CLOCK
DISPLAY/ENT
MEMORY
CD
RADIO BAND
PRESET
VOLUME
MEGA BASS
SOUND
LOOP
FLASH
AUTO PRESET
TIME SET
TUNE
TDK
D90
PARTY 19/8
THE PIXIES / DOOLITTLE / BOSSANOVA
ECHO AND THE BUNNYMEN
HEAVEN UP HERE / OCEAN RAIN
THE MIGHTY LEMON DROPS
"HAPPY HEAD"
MARC BOLAN AND T REX
BEST OF THE 20TH CENTURY
R.E.M.
EPONYMOUS / DOCUMENT


Based on your recent listening
Daily Lift
Uniquely yours
On Repeat
Summer sounds

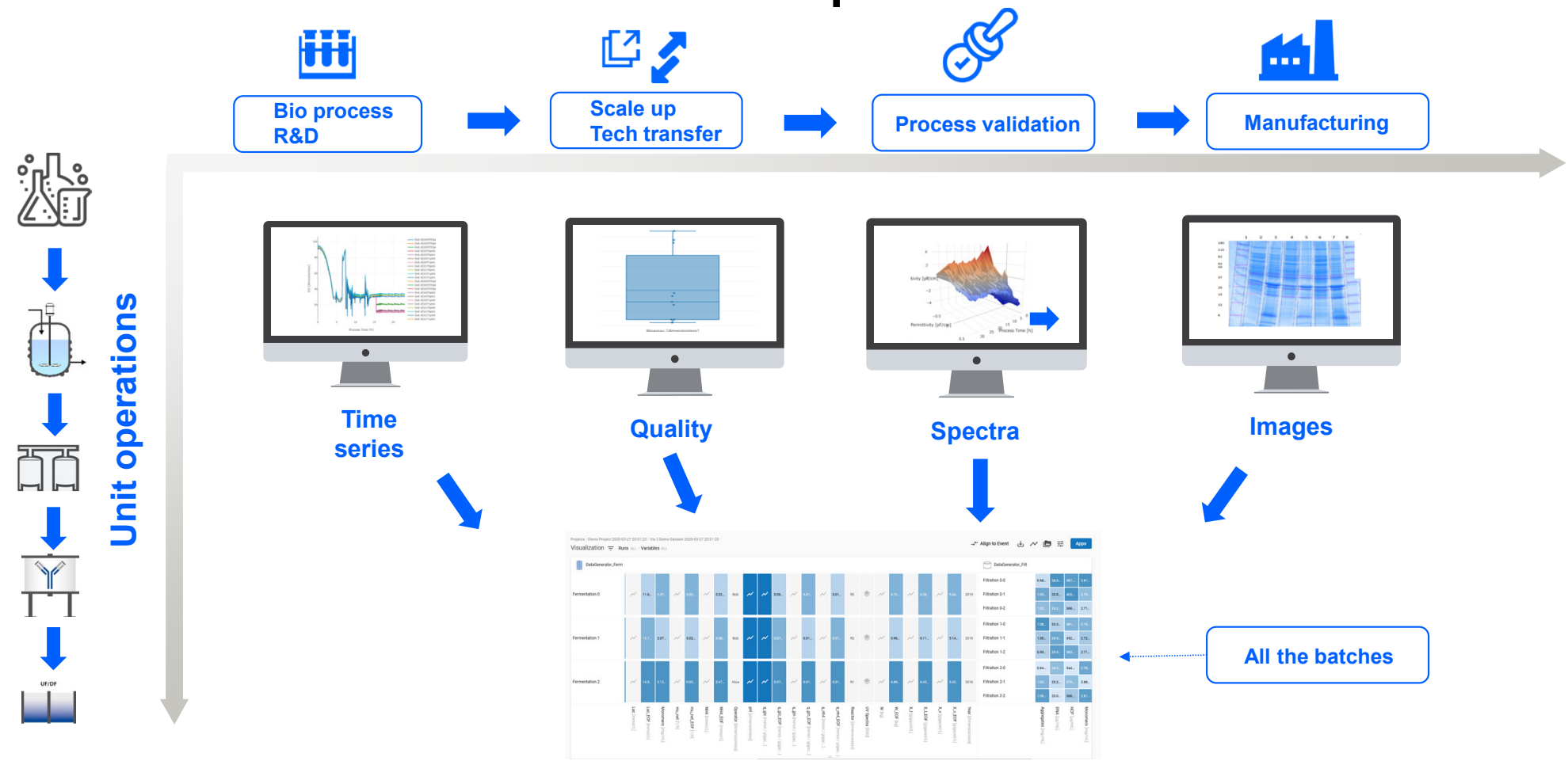
Data Sources



Data Sources

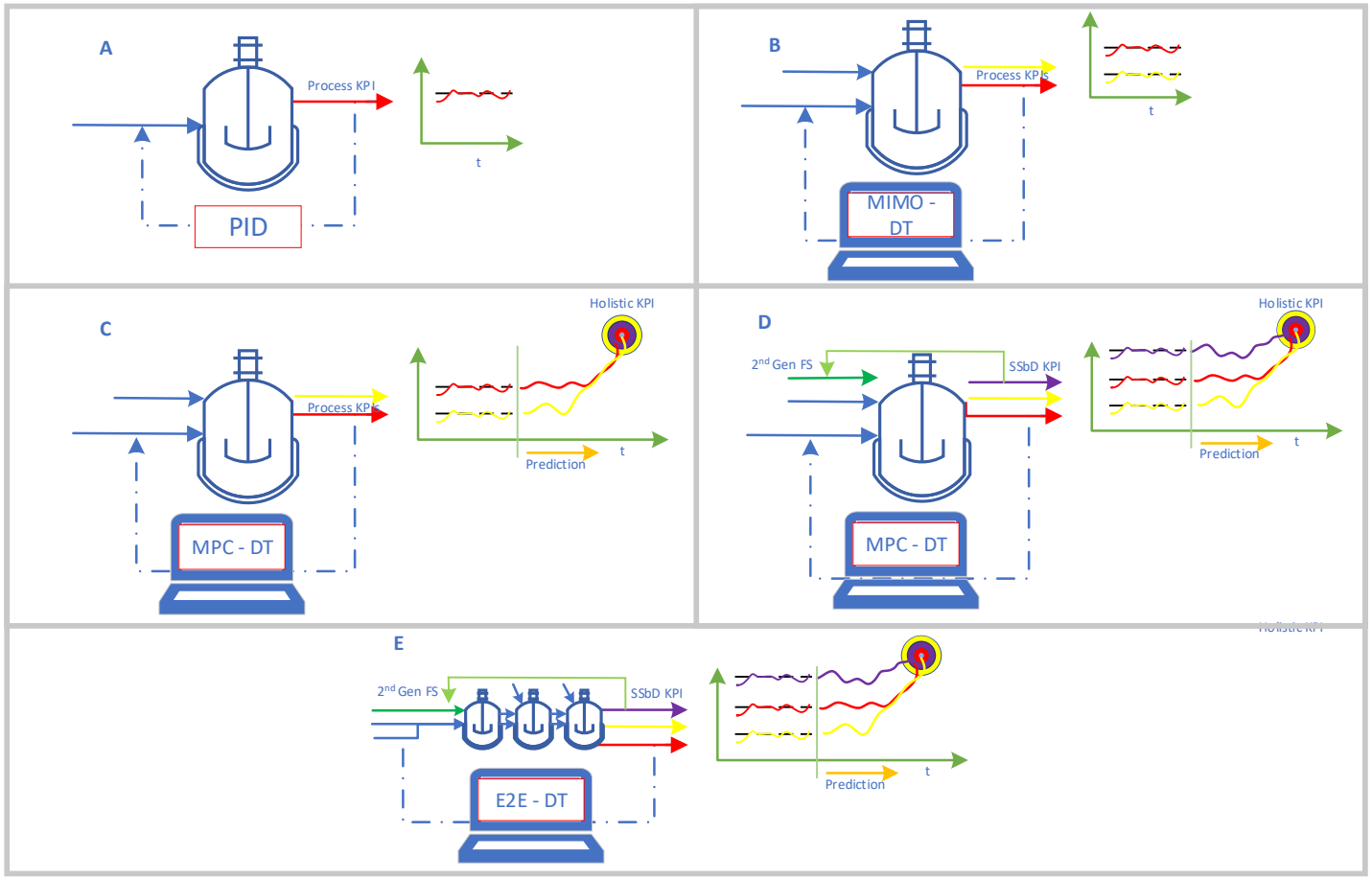


Data should be available from multiple dimensions



Conclusions

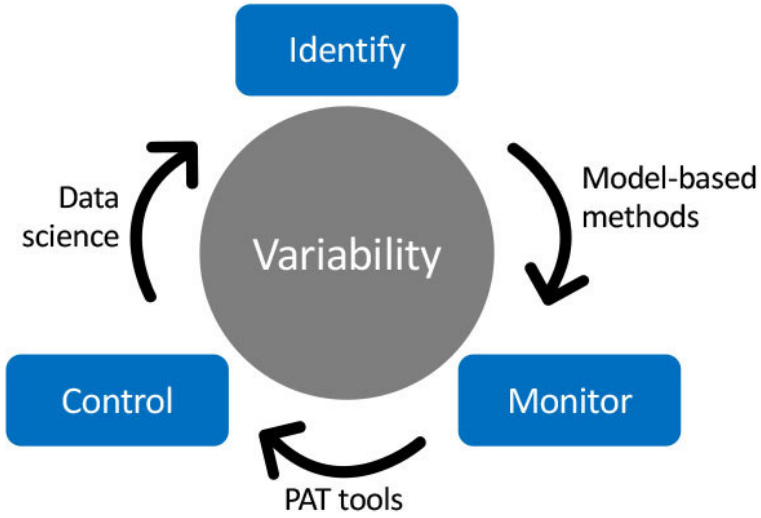
Control Options:
End-to-End Digital Twin: Predictive control along the process chain



Methodological success factors

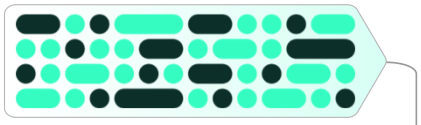
Intelligent & digitalized holistic continuous process control by

- Holistic data management
- Holistic design of experiments to gather holistic process understanding
- Formulation of process understanding and its capture in digital twins
- Control inside of the process understanding to achieve the right product quality and optimum KPIs
- Establish life cycle capability

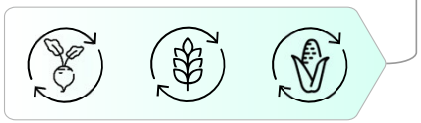


Revolutionizing protein biomanufacturing as a first vertical

FLEXIBLE INPUT



Bacterial strains

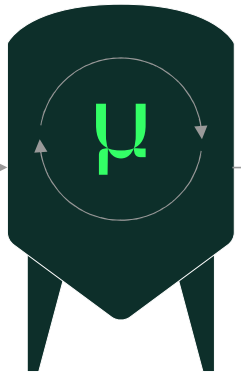


Agrifood side-streams

Fast growing, safe and natural bacterial strains

Flexibility to use regional agrifood side-streams

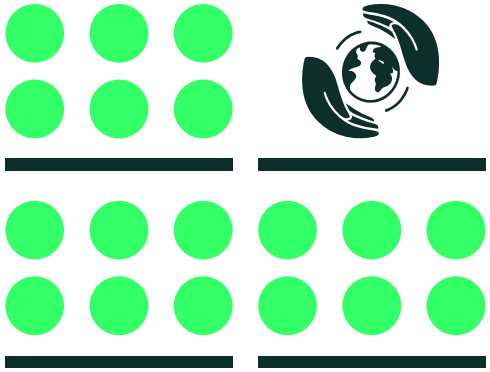
PROPRIETARY FERMENTATION



10x more productivity (grams / litre / hour) vs. gas fermentation or mycoprotein.

Industrial-scale continuous fermentation with lower CAPEX and COGS.

PREMIUM FOOD & FEED



Nutritious protein
full amino acid profile, proven palatability and digestibility.

~95% lower footprint
than conventional products and a lower water footprint

Thank you!

Christoph Herwig

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Mobile: +43 676 4737217

Location: Vienna, Austria

Christoph.Herwig@lisalis.at