Successful Scale-up of Industrial Fermentations: Process Development, Engineering and Economics

by

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Principal

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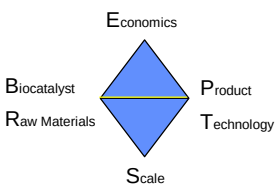
Key Factors for Bioprocess Technology Selection, Scale-up and Engineering of New Facilities

- **B**iocatalyst
- **R**aw Materials
- Process **T**echnologies
- **P**roducts
- **S**cale
- **E**conomics



Success is through

Early Integration of

Process Development, Engineering & Economics

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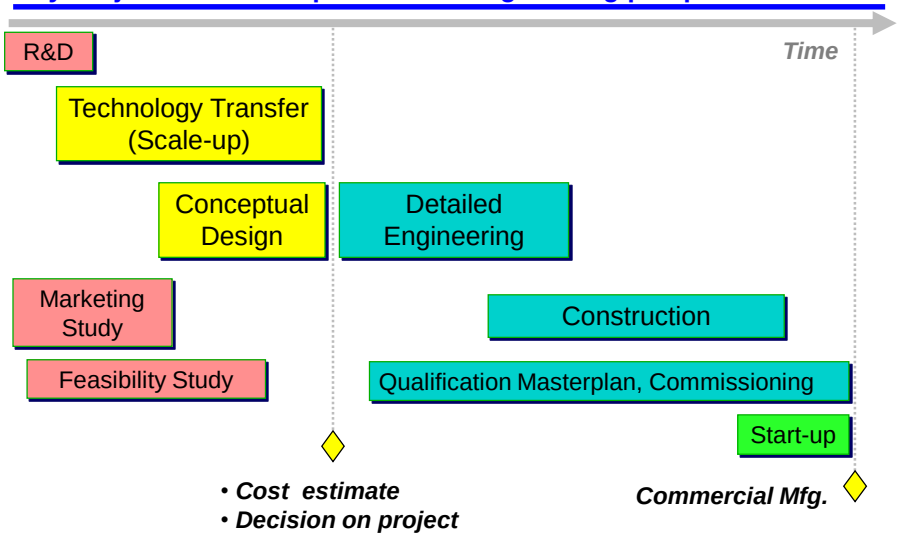
From R&D to Commercial Manufacturing Facility

Key Project Phases – Operations & Engineering perspectives



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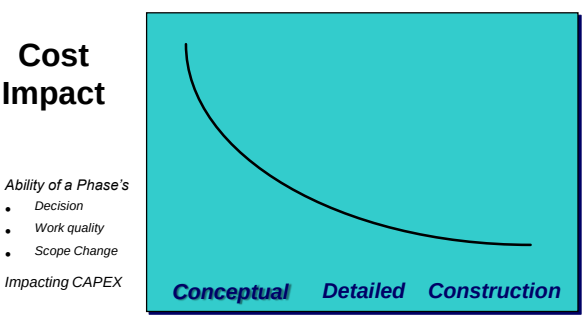
Cost Impact of Key Engineering Project Phases



Key Success Factor:

- *Early Integration* of Process Development and Engineering *Concepts* for Successful Commercial Bioprocesses and Facilities.

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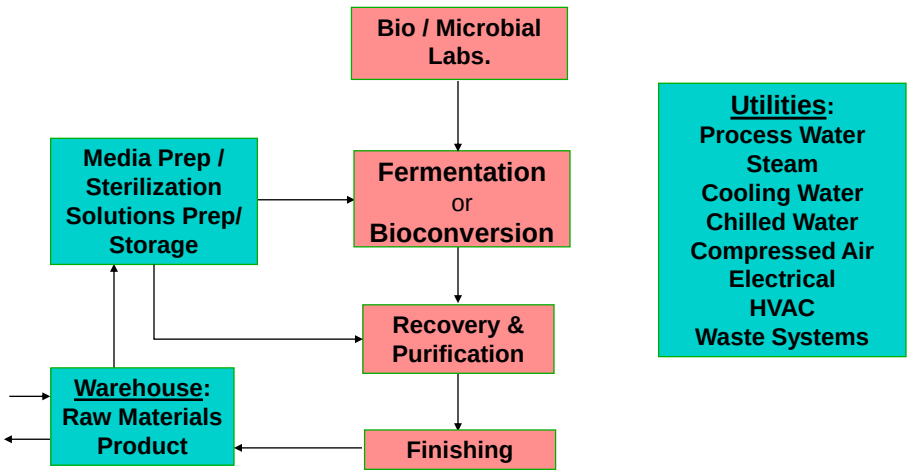
Typical BioProcess Block Flow Diagram

Basis for Facility Concept Design



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BioProcess Design Basis & Scale-up - Upstream

Fermentation & Bioreactor Critical Design Parameters

Biological & Chemical

- Culture type
- Containment
- Operating and Optimal ranges for:
  - pH , Temperature
  - Foam type & control
  - Shear, Viscosity
  - DO_2 , CO_2 , Pressure

Process Engineering

- Process type (batch, continuous, fed-batch)
- Oxygen Transfer Rate (OTR)
- Heat Transfer
- Bioreactor type & Scale-up
- Instrumentation & Controls
- Sterile/ rDNA Design, MOC
- Media Prep./ Sterilization
- CIP & Waste systems

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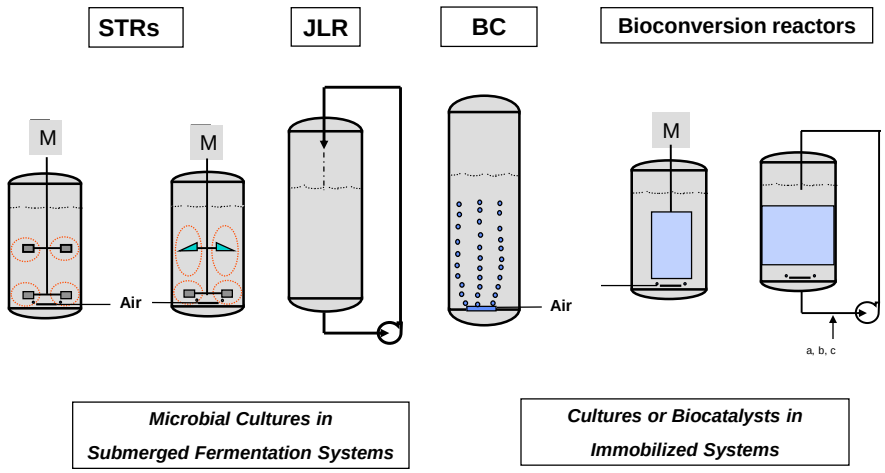
Typical Bioreactor Designs



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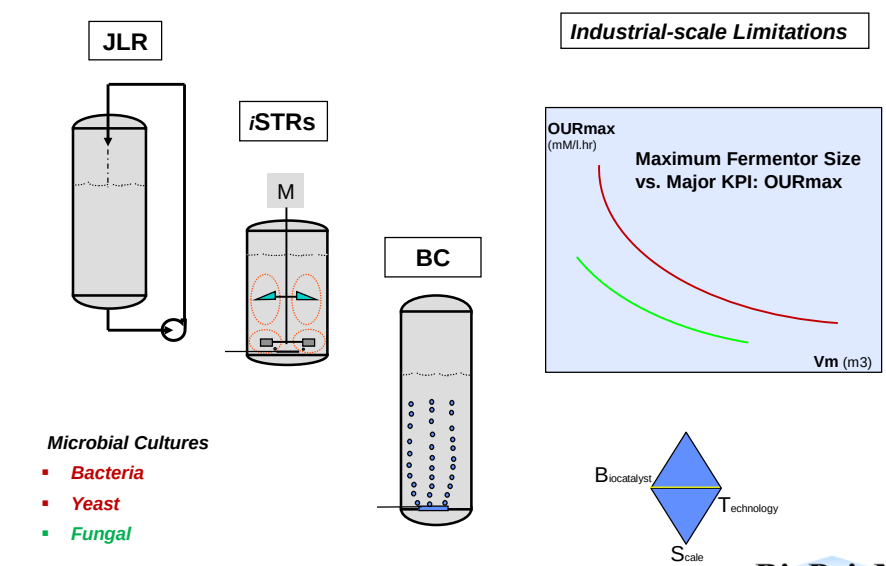
Bioreactor Design Selection – Industrial Realities
Biocatalyst, Process KPI & Scale: *All Inter-related*



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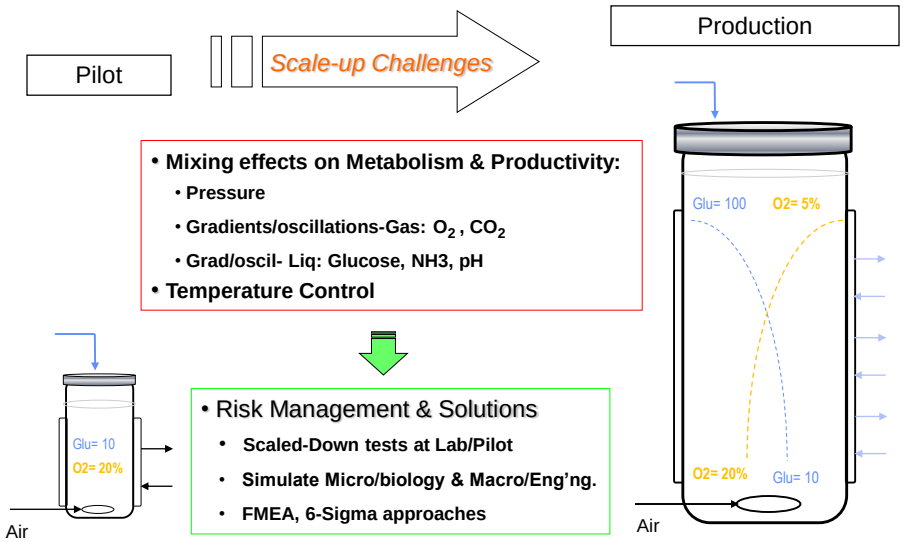
Commercial Fermentation Scale-up Challenges & Options
Case study of BC



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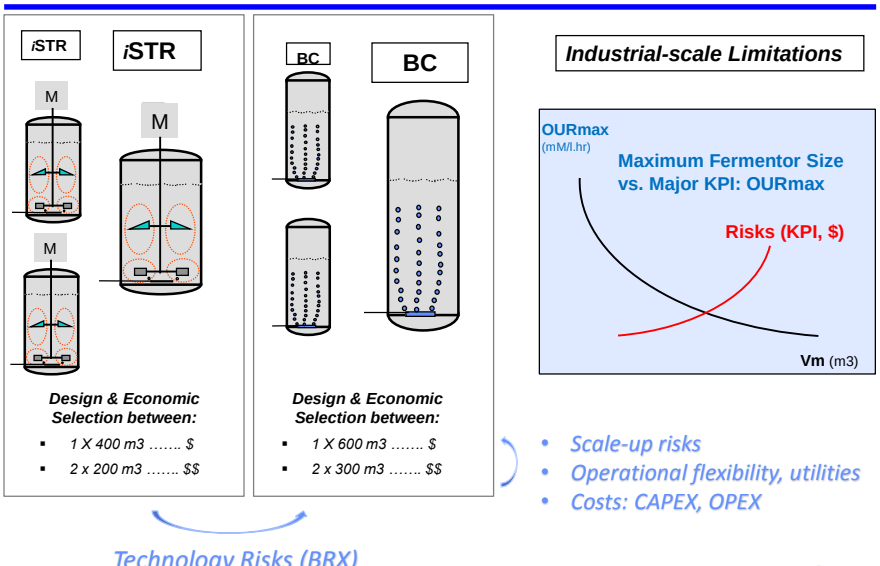
Fermentation Facility Definition: Risks & Economics
Selection of Bioreactor Design, Size & Quantities



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Optimum Industrial Process Selection – KPI's

Which Key Performance Indicators (KPI's) to select ?

- **High Cell Density, Maximum Fermentation Titer ?**
  …. Not Always ! Don't disregard industrial limitations !
- **Yield of Feedstock Bioconversion can be *a* major KPI for Cost of Goods Sold (COGs), but impact can change with Product, Technology & Scale**

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Typical Microbial Fermentation Process Kinetics

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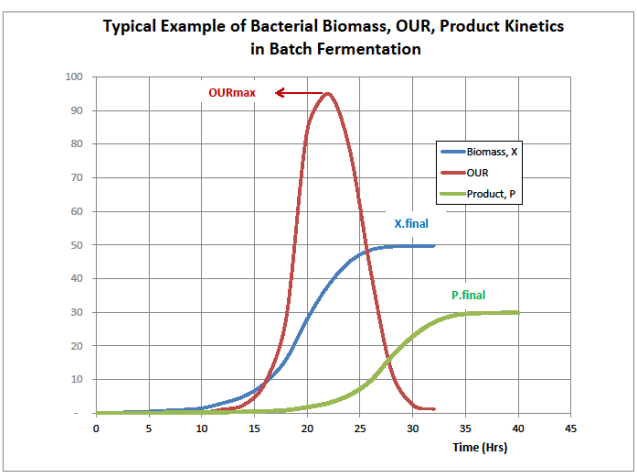

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Process & Project Engineering , Economics and Strategy

Selecting Industrial Fermentation Process – *Design Space*

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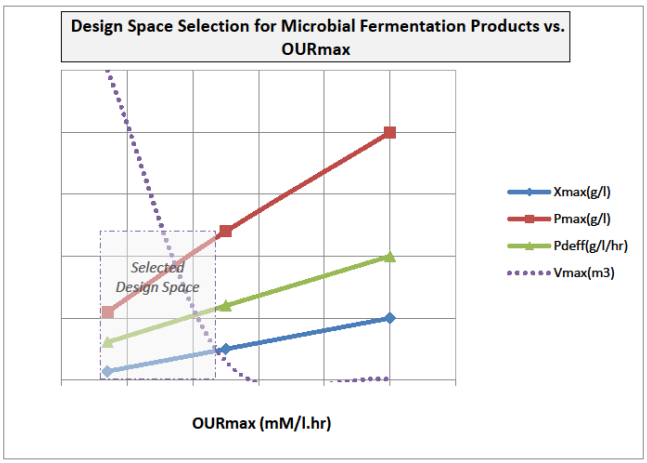

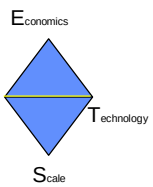

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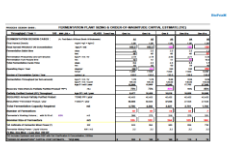
BioProcess Modeling is Key for Economic Optimizations

- **Modeling and Cost Sensitivity Analysis:**
  Need Simulation by Professionals Experienced in Real Commercial Scenarios for Reliable Estimation of Facility CAPEX & OPEX



CAPEX reduced by 60%
from $203 to $78 MM

❖ ***Industrial Process Modeling is a major Guide for R&D and Project Objectives… i.e. What to Focus on ?***

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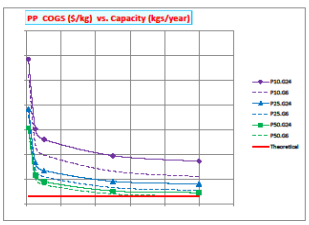
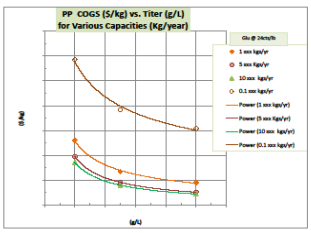
COGS vs. Capacity, Media Costs, Titer

COGS vs. Capacity at Various Titers & Media Costs



COGS vs. Titers at Various Capacities



❖ ***Economic analysis defines "Critical" or Minimum Capacity or Titer for Optimum COGS***

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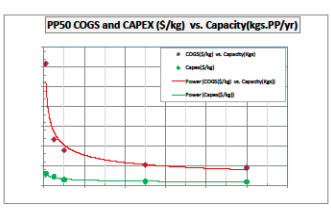
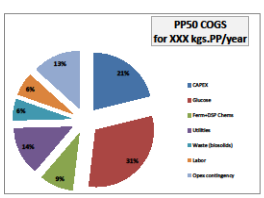
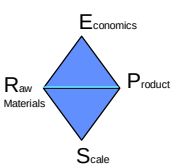
Costs vs. Scale. Product impact on COGS Distribution

- **COGS decreases with increased Capacity or Scale.**
- **CAPEX % of COGS changes with Scale, Technology & Product**







Product-type impact

- **Raw Materials cost % of COGS in *Industrial Biotech* is More than for *BioPharma***
- **CAPEX % of COGS in *Industrial Biotech* is Less than *BioPharma*.**

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Conclusions
BioProcess Commercialization: Success factors

- ***Integrate***, ***early on***, **R&D, Engineering and Manufacturing** ***Teams***
- **Assess each Bioprocess option from an** ***Integrated industrial*** **view**
- **Select optimal option based on** ***Scale-up*** **reliability & economics**
- **Use** ***Modeling*** **to evaluate each Bioprocess impact on** ***Facility*** **Design, Utilities & Costs**
- **Perform a** ***Conceptual Design*** **with preliminary CAPEX and OPEX**

From Concept to Commercial: DuPont BioPDO

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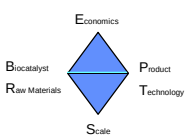
THANK YOU !



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