

# Selection of chemically defined media for production of biopharmaceuticals

Sub title

01-June-2018, Dirk Martens



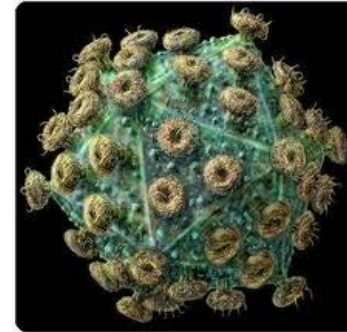
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# Content

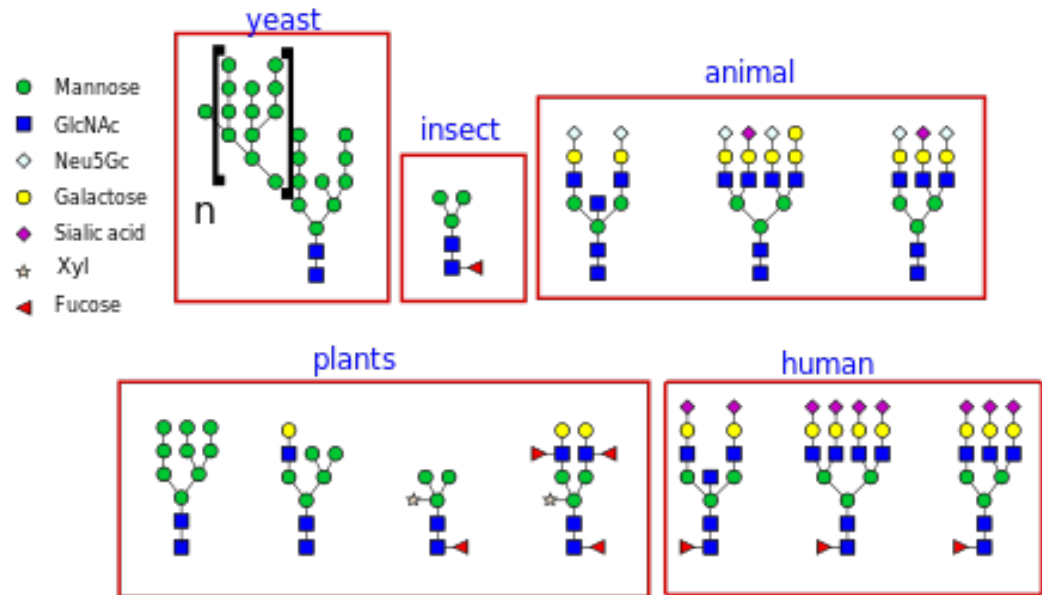
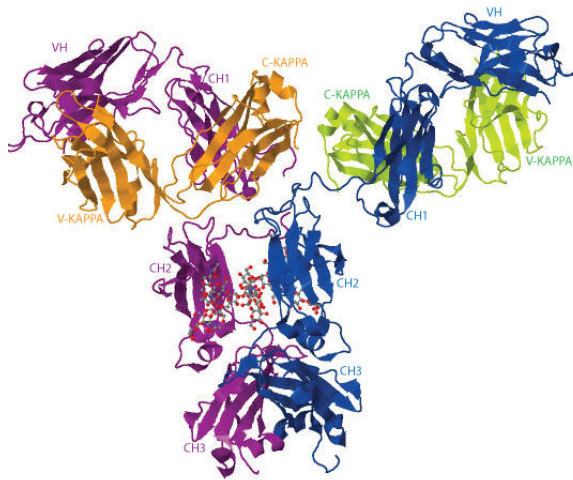
- Background industrial cell cultivation
- Serum (History)
- Chemically defined media
  - Relevance of cell volume

# Products

## Viral vaccines



## Pharmaceutical proteins



# Industrial scale

- Chinese Hamster Ovary Cell Line
- Fed-batch
- Stirred tank reactors
  - Disposable up to 2 m<sup>3</sup>
  - Stainless steel up to 20 m<sup>3</sup>

# Process development

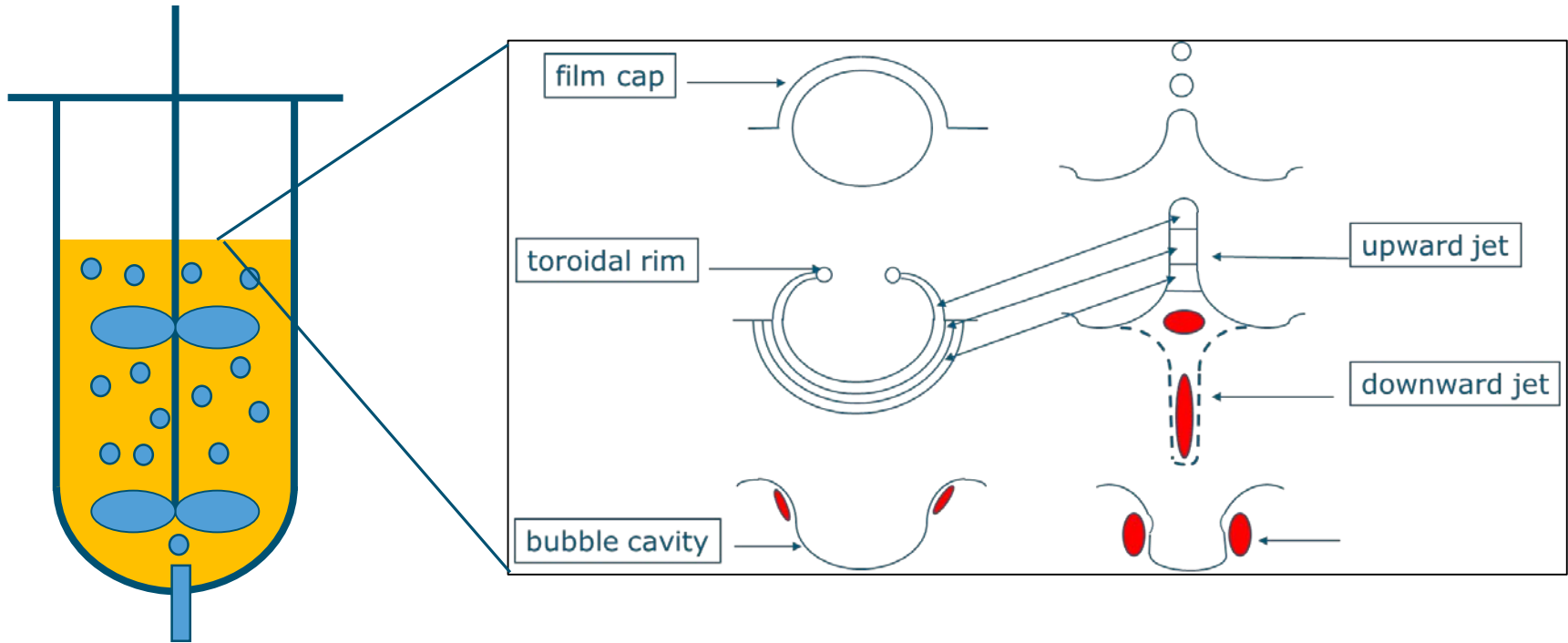
- Safety
  - No contaminants
  - Proper protein structure
- Speed
  - Predictable & robust process
  - Robust scale-up
- Volumetric productivity and product concentration

# Serum

- Infectious agents (viruses, prions)
- Variable undefined composition
- High protein content problems in DSP
- Serum replacement
  - Growth factors
  - Transferrin (Fe)
  - Lipids
  - Detoxification
  - **Shear protection**
  - .....

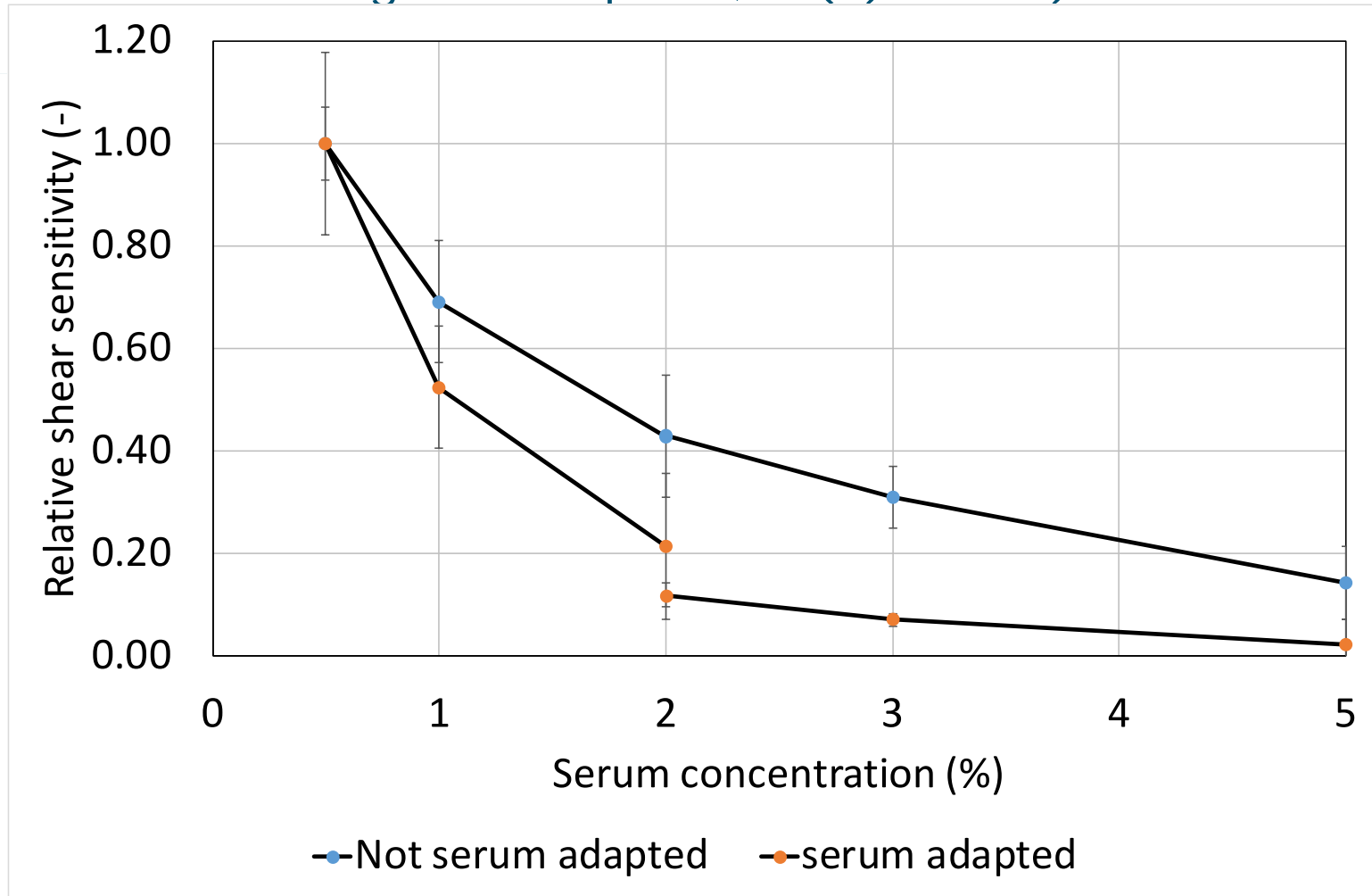
# Scale-up: Mixing & Gas transfer

## Stirred Tank Reactor



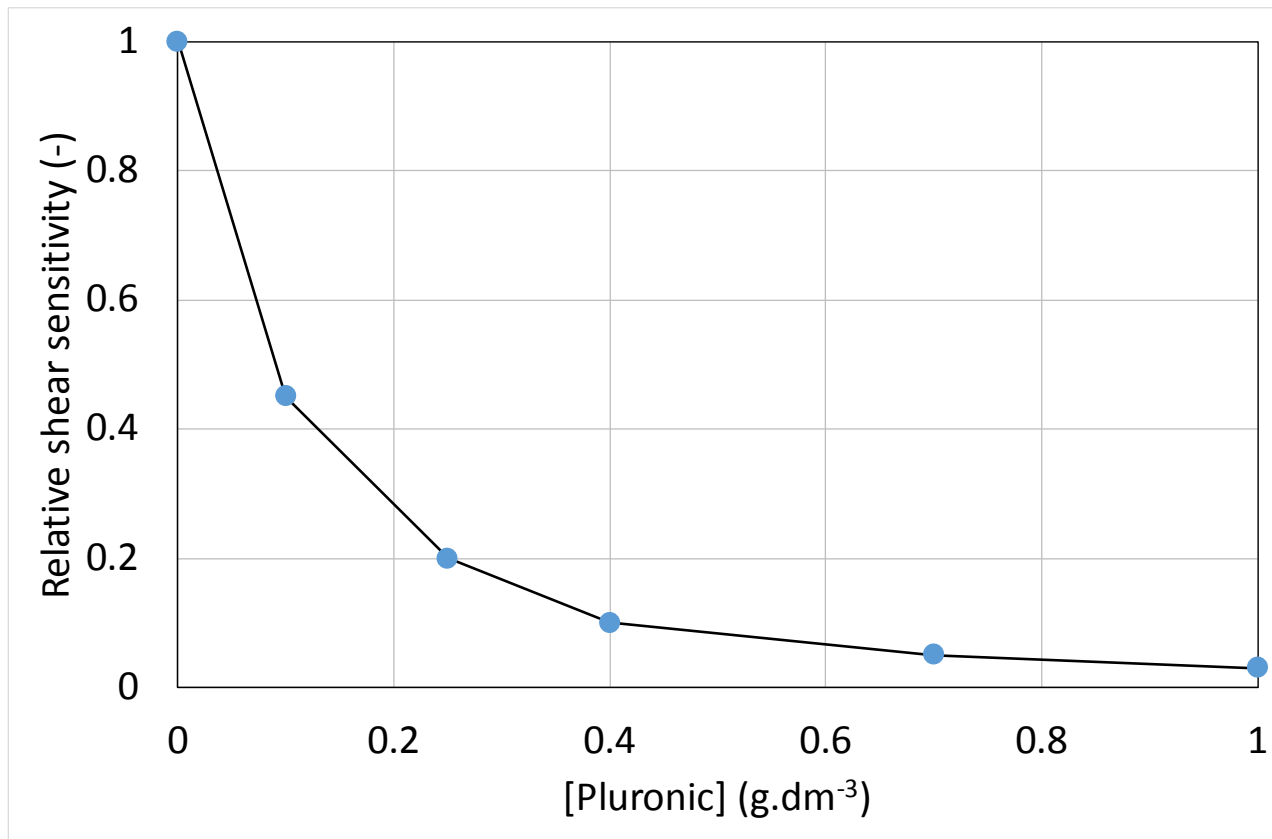
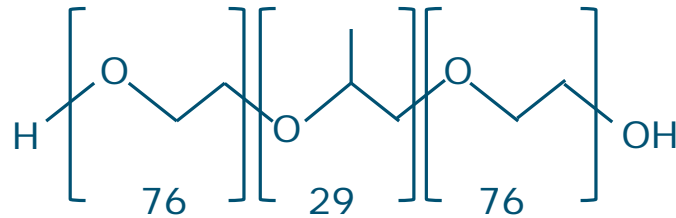
# Effect of serum

(Biotechnol Bioeng. 1992 Apr 15; 39(9):891-7)

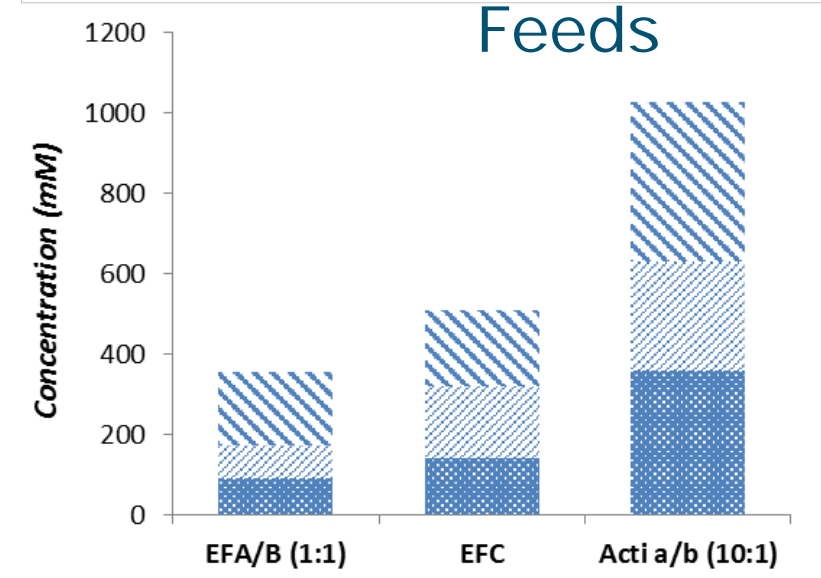
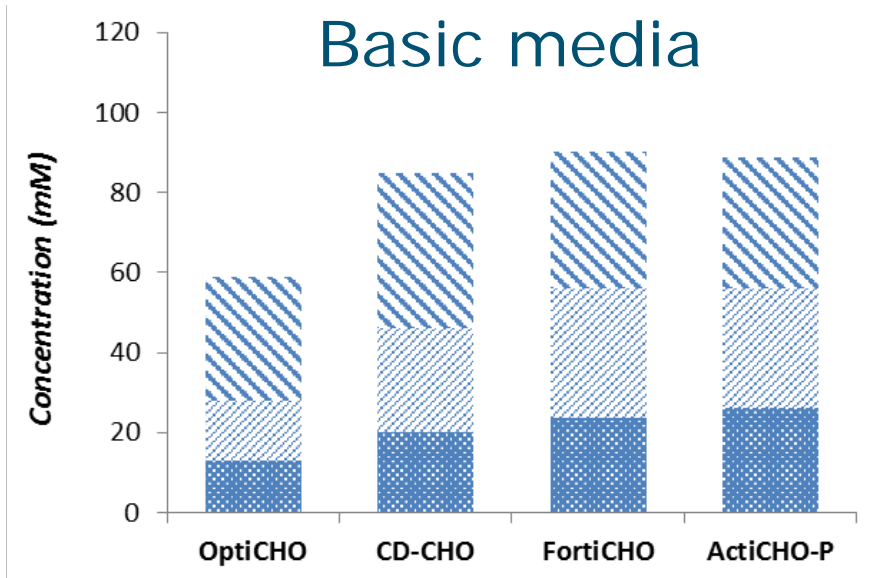




# Pluronic F68



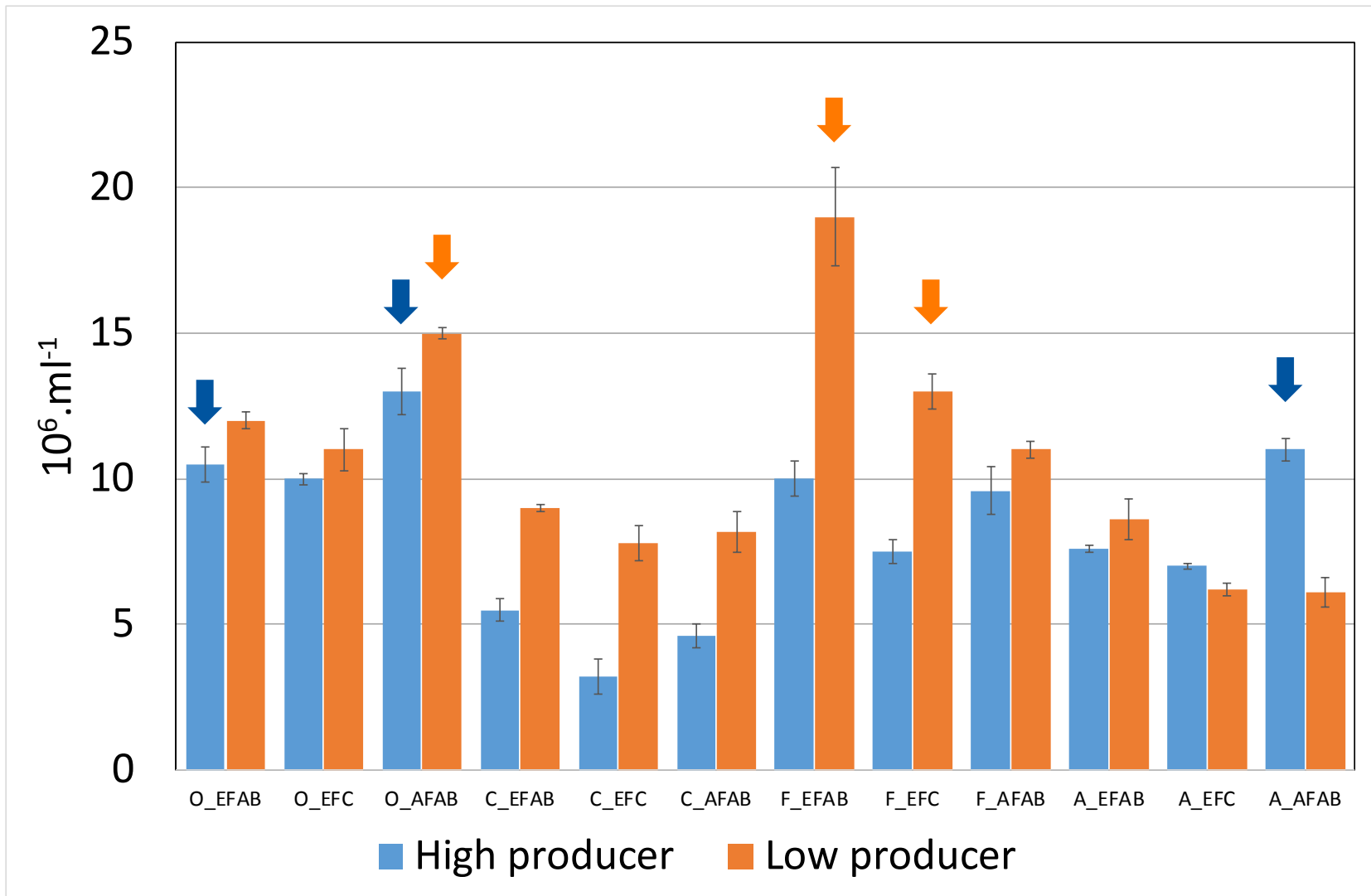
# Media selection



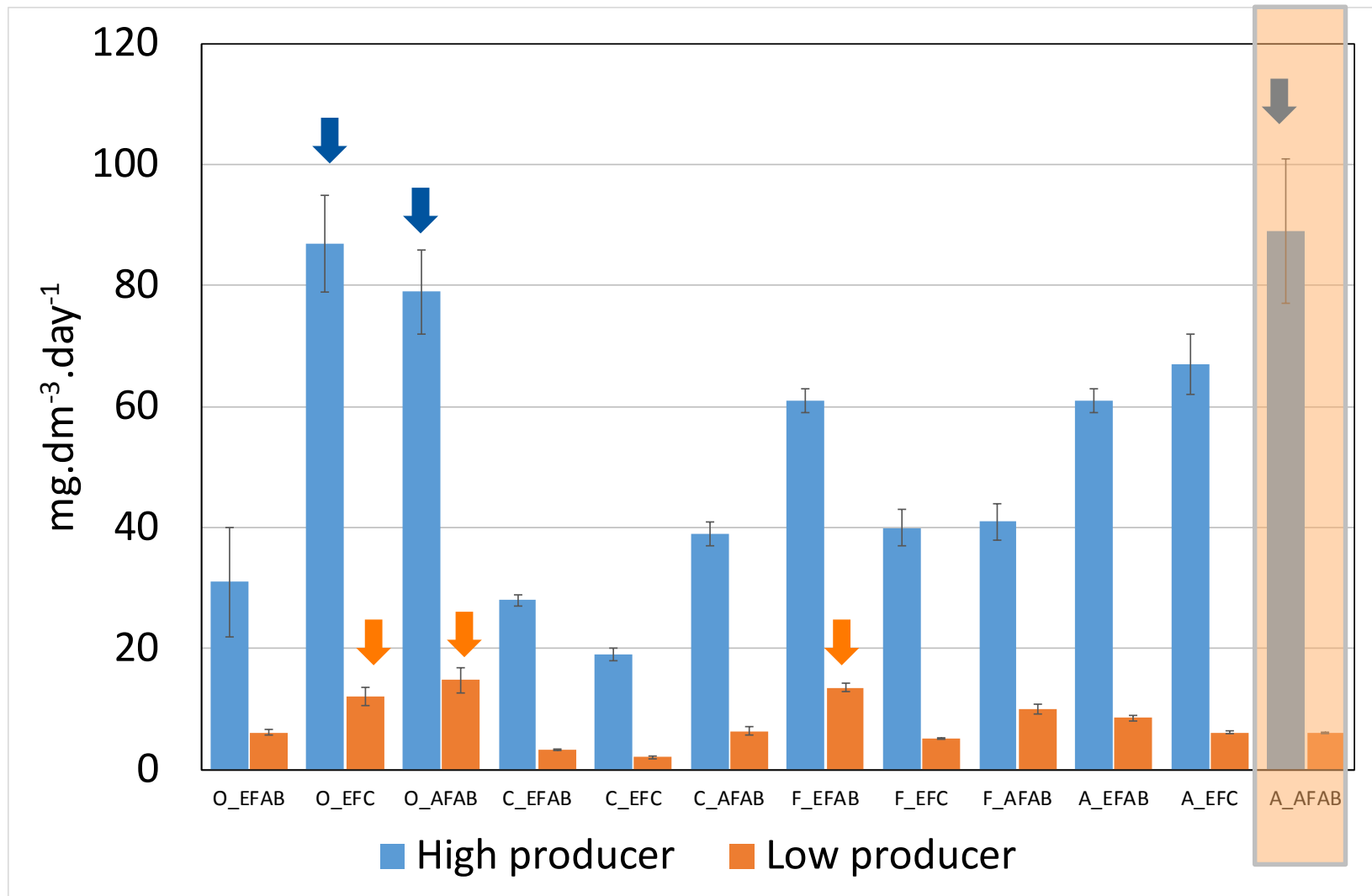
■ Glucose ■ Non-essential amino acids ■ Essential amino acids

- CHO cells: High producer and low producer
- Fed-batch (starting day 3)
- 12 Shake flasks (duplicate)

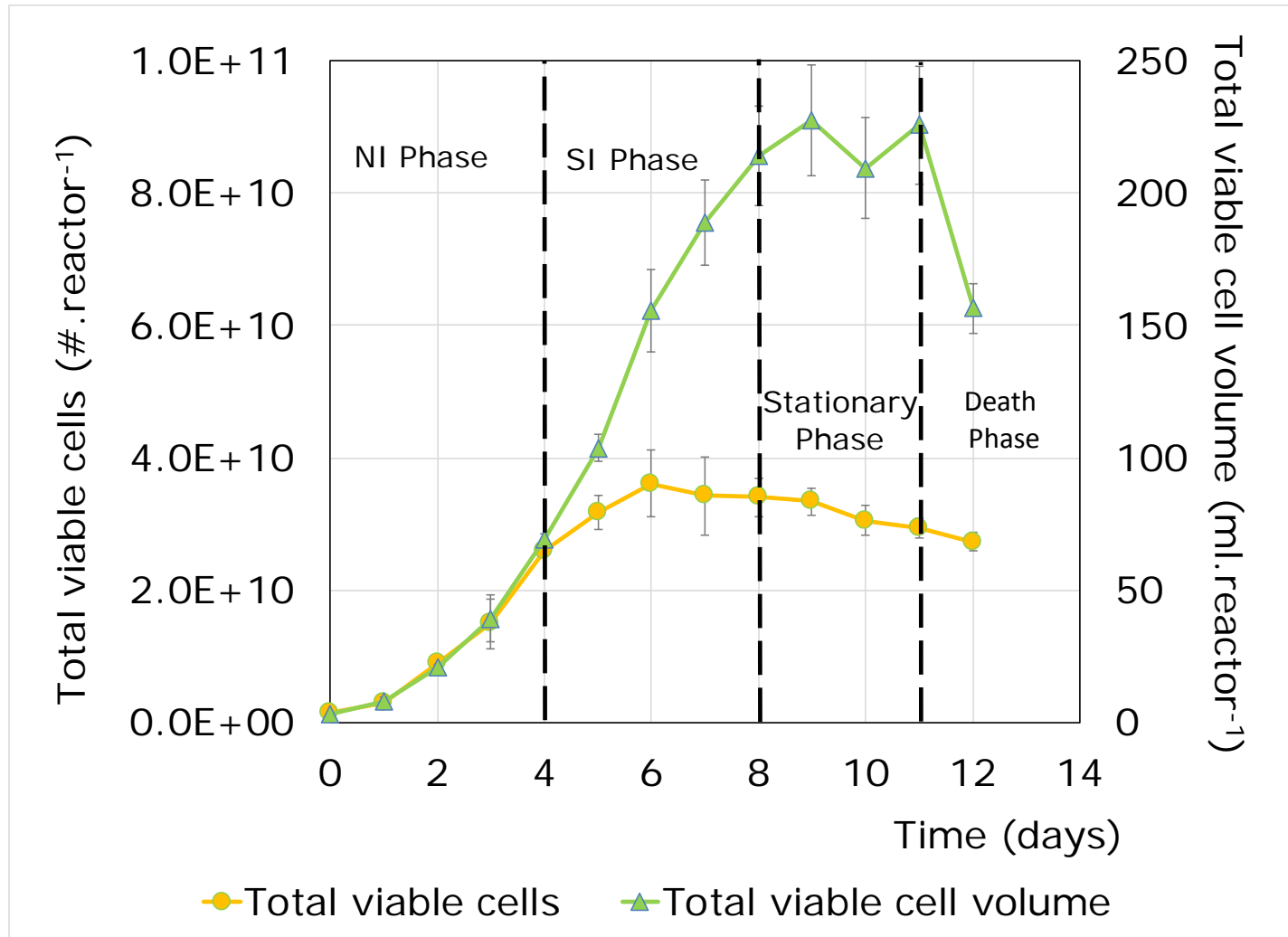
# Cell numbers



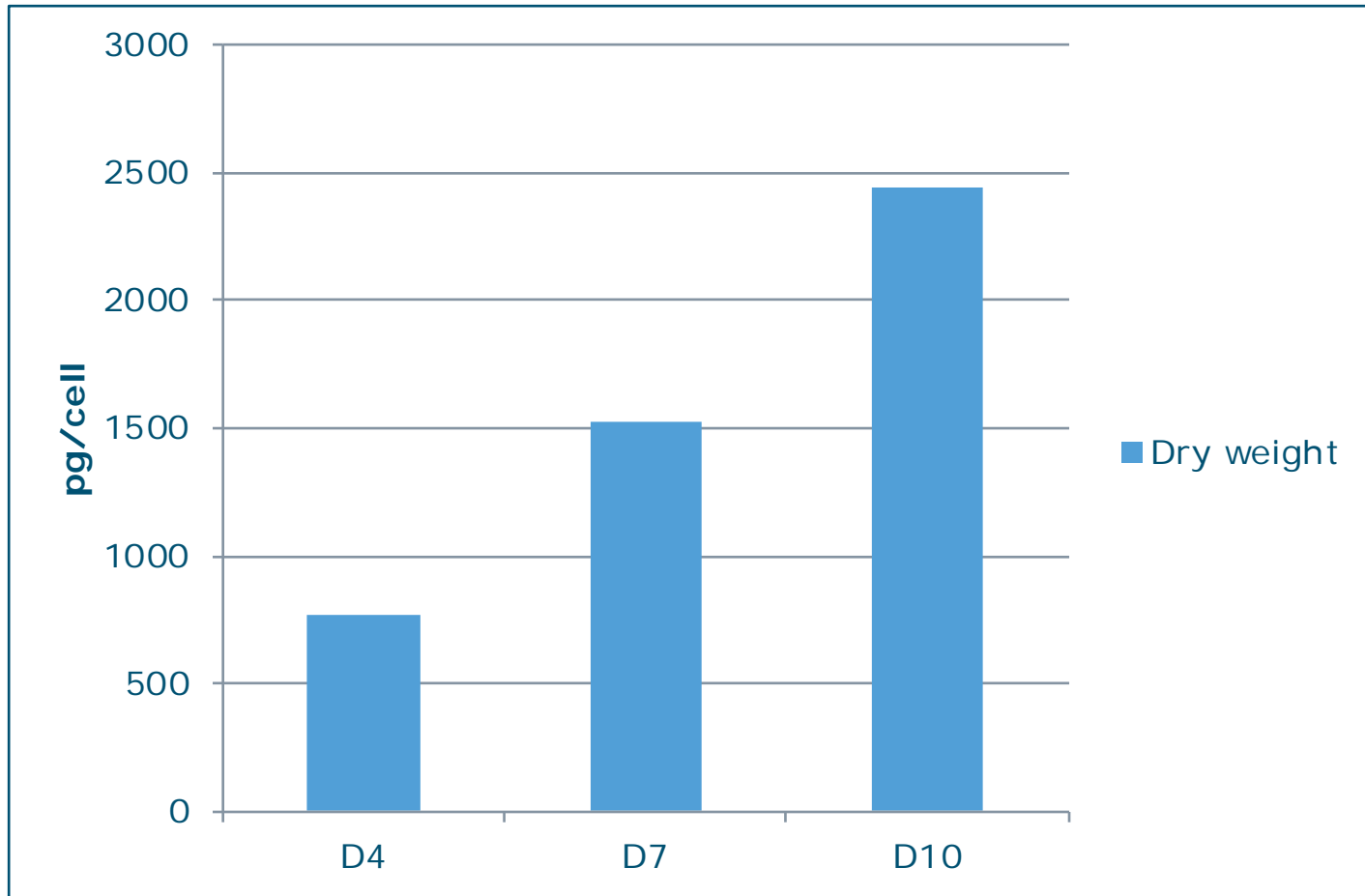
# Volumetric productivity



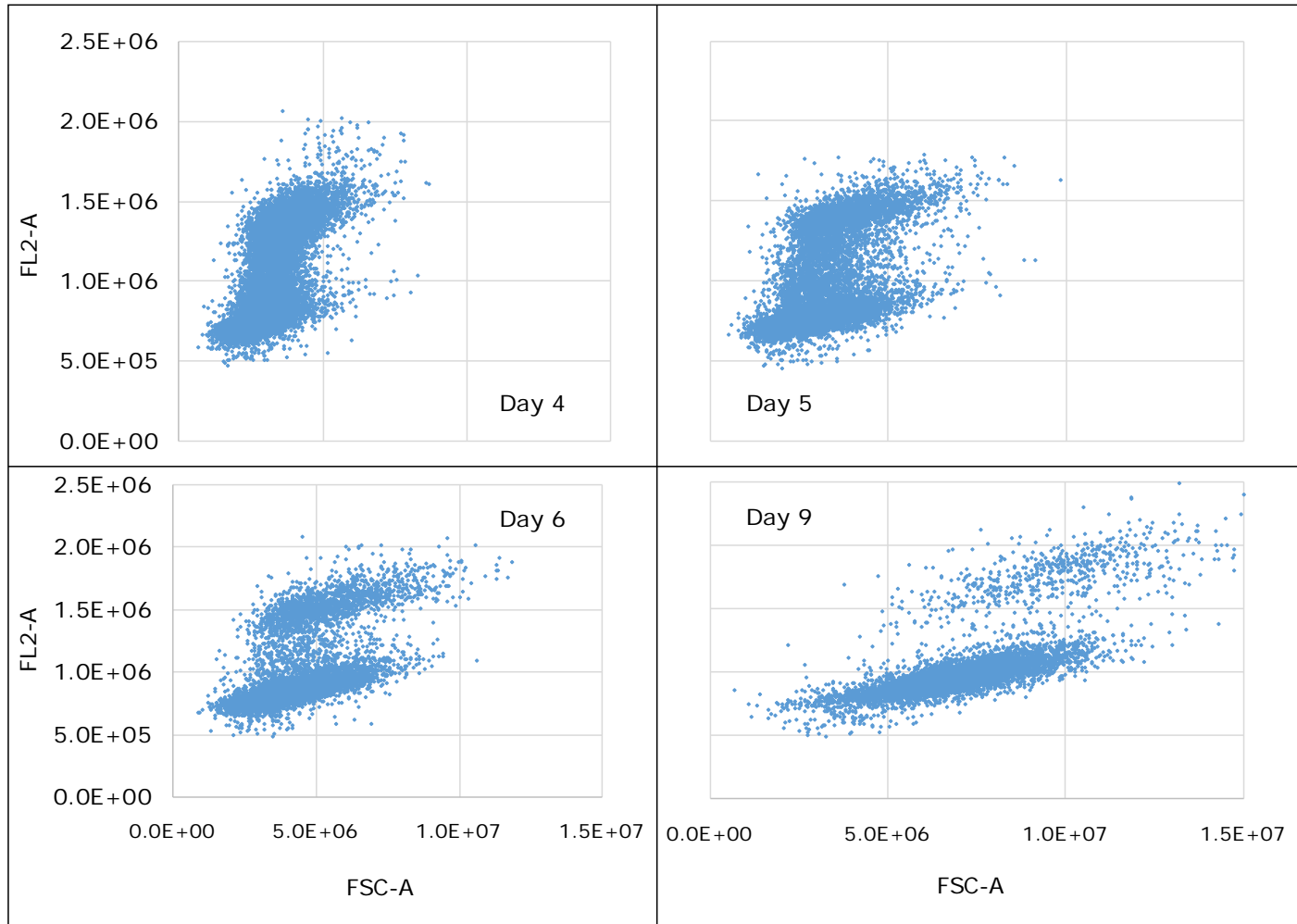
# Cell density and volume



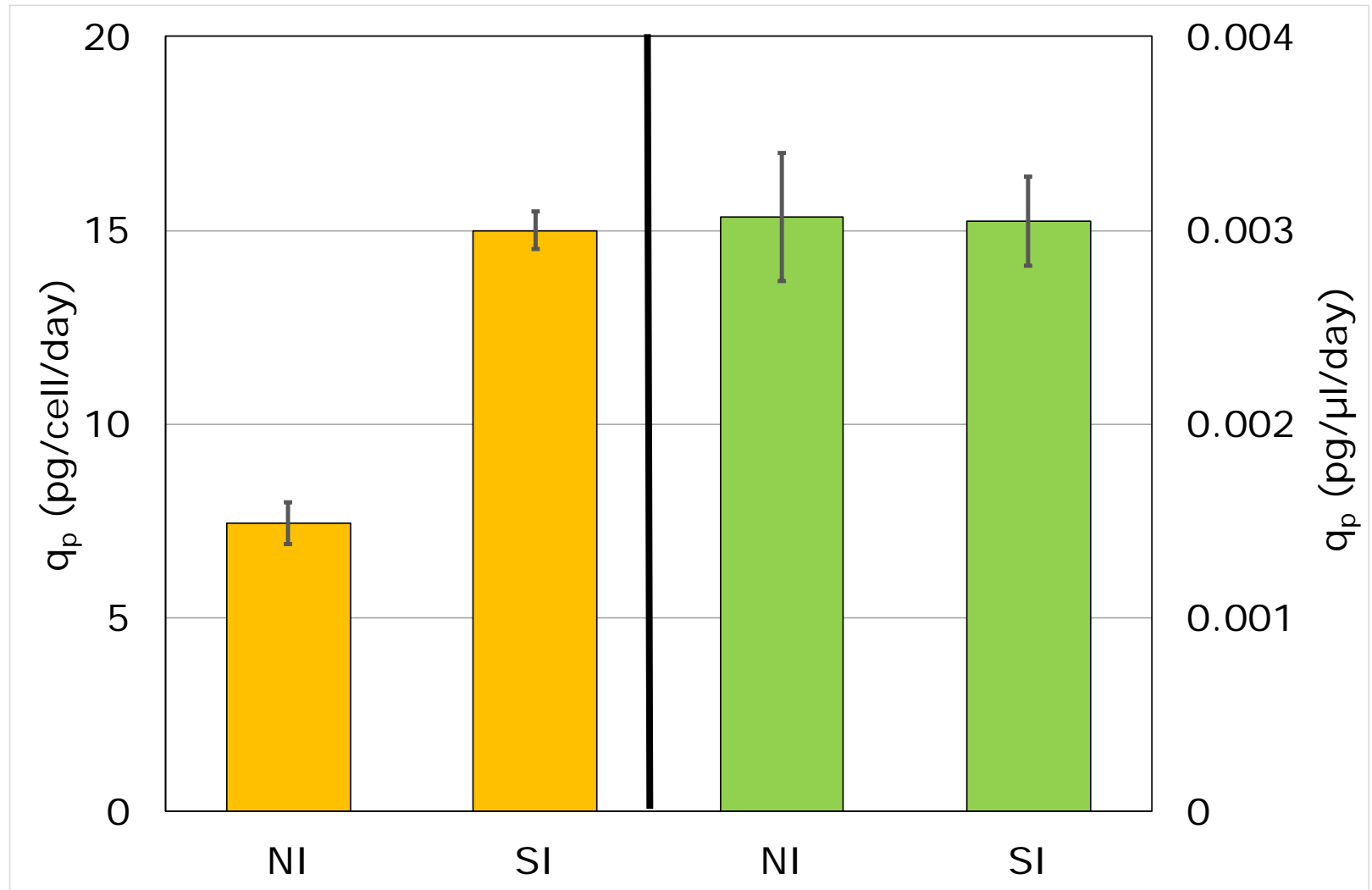
# Cell dry weight



# Cell cycle arrest

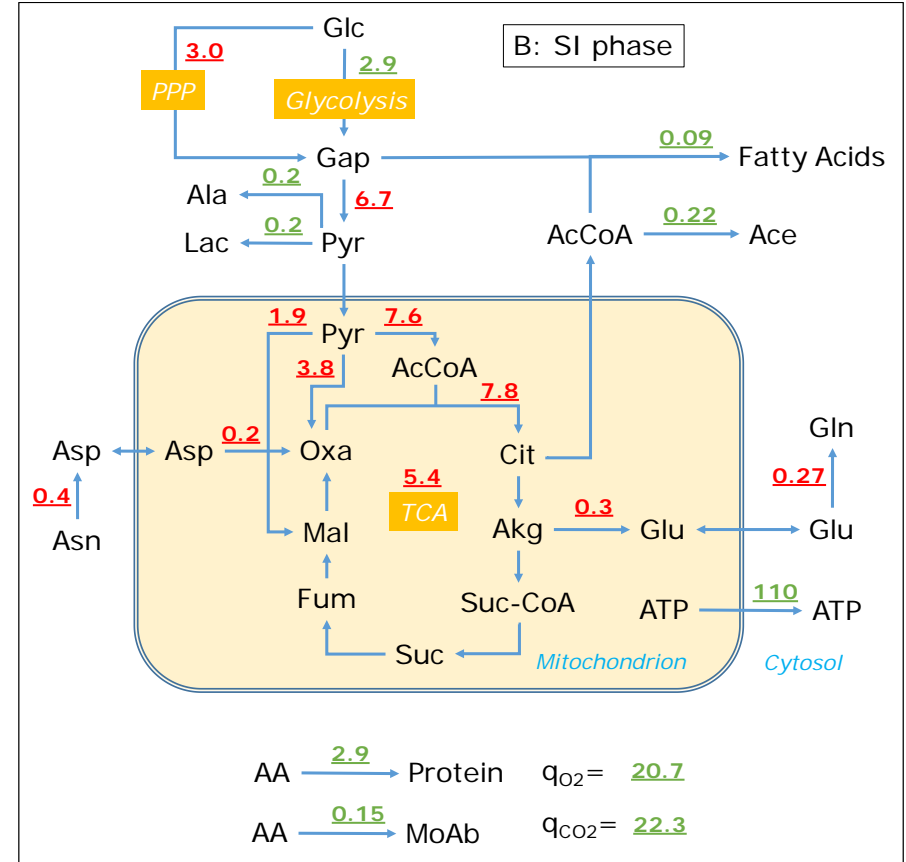
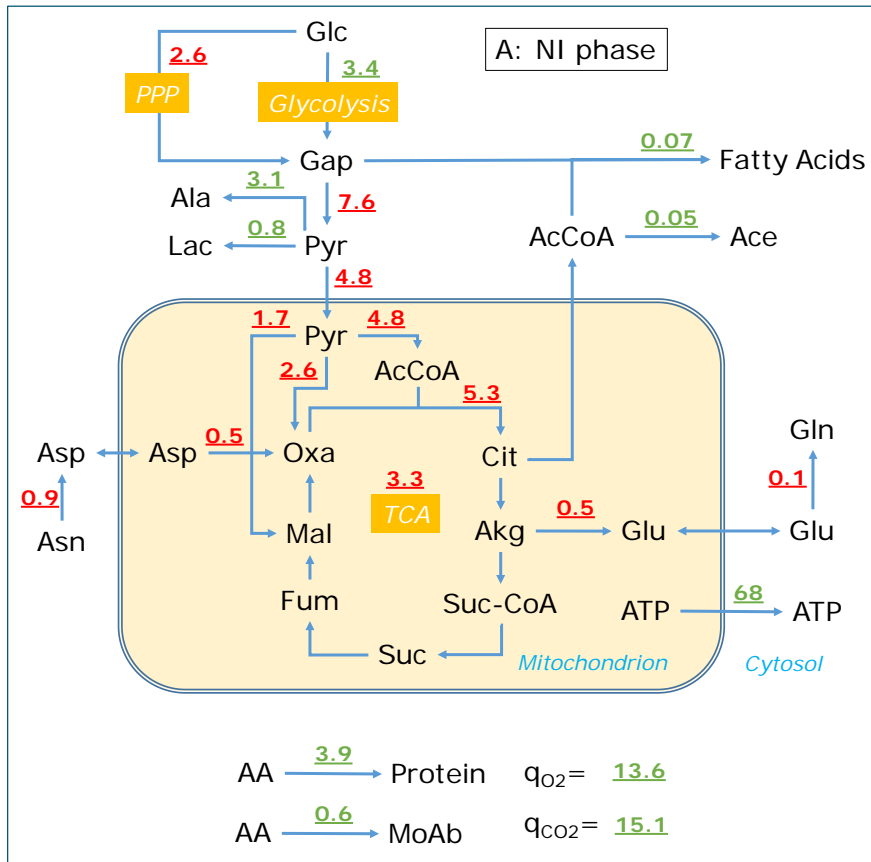


# Specific productivity

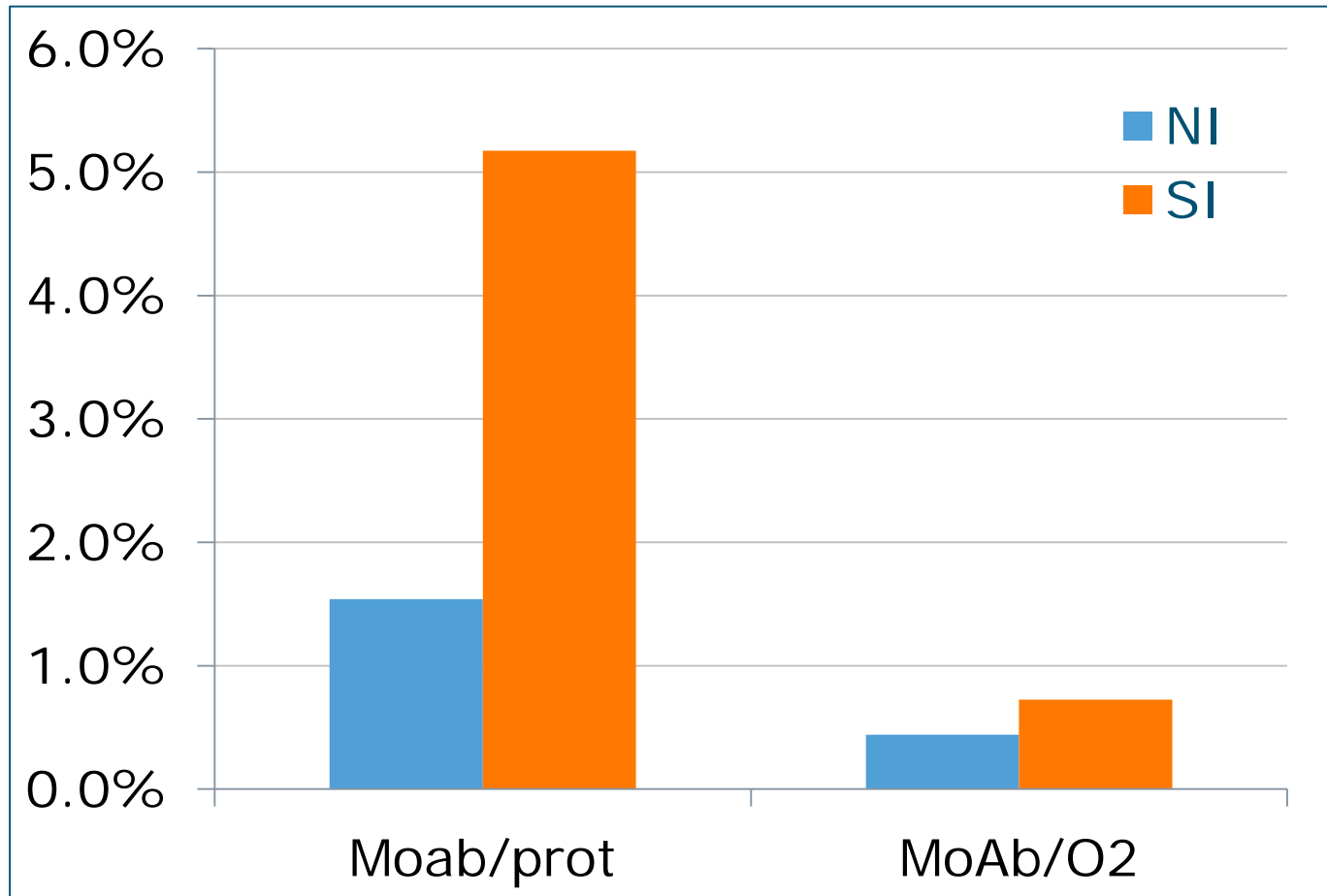




# Metabolic analysis



# Efficiency



# Concluding remarks

- Chemically defined media are available.
- Clone specific
  - Effect difficult to predict
- Very specific effects
  - Cell cycle arrest and volume increase
- Cell volume is an important parameter
  - Represents biomass
  - Better efficiency
- Composition not publically available

# Acknowledgements

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