

# STATE OF THE ART MEDIA DEVELOPMENT AND IMPLEMENTATION IN BIOPHARMACEUTICAL PROCESSES



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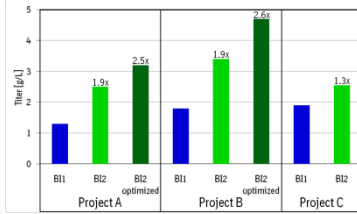
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## Abstract

Cell Culture media play a major role in developing high performance mammalian cell culture processes. Rational media design was used to develop a novel animal component free and chemically defined medium. The BI2 medium was implemented in the BI-HEX platform for superior cell culture performance and improved final product titer.

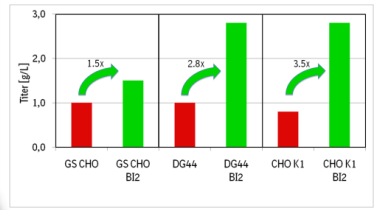
## Titer improvement

- Media implemented in current BI-HEX platform
- Demonstrated titer improvement in several projects

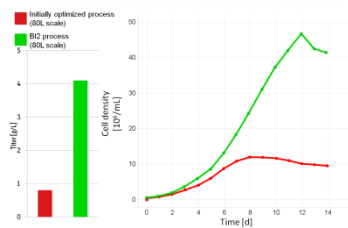


## Suitability for different cell types

- Comparison to initially optimized processes
- Up to 3.5x higher titer achieved with different medium & feed

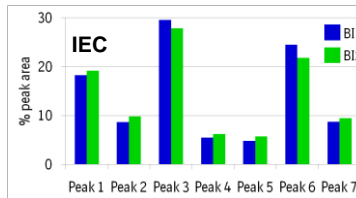


## High cell density process



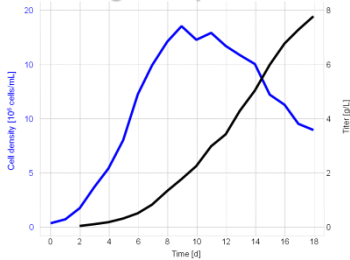
- Cell densities up to  $45 \times 10^6$  c/mL
- >4-fold titer improvement
- Platform harvest procedure suitable

## Comparability of product quality



- Various analytical methods applied: IEC, HIC, SEC, Glyco, Biacore, Bioassay, ...
- Comparable product quality

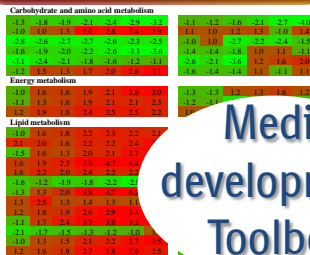
## High titer process



- Process at 8 L scale
- Titer up to 8 g/L

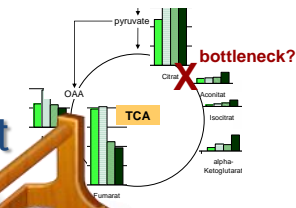
## System-level data analysis

- Identification of deregulated metabolic pathways
- Information on global cellular behaviour



## Metabolomics

- Spent media analysis
- Focus on central carbon metabolism
- Rational media optimization



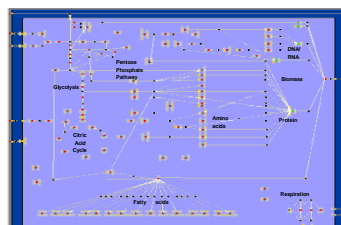
Media development Toolbox

## Conclusions

- Medium & Feed implemented in BI-HEX platform
  - Scale-up to 2kL (GMP, stainless steel)
  - Scale-up to 500 L (GMP, disposable)
  - Scale-up to 12kL planned in Q4 2013
- Chemically defined & animal component-free
  - Low process variability
- Tested with various cell lines
  - BI-HEX cells, CHO K1, GS CHO, DG44
  - Final titer up to 8 g/L
  - Viable cell densities up to  $45 \times 10^6$  c/mL

## Metabolic Flux Analysis

- Calculation of intracellular metabolic fluxes
- Focus on central carbon metabolism
- Medium suits metabolism



## Screening, DOE

- Redesign of formulation
- Experimental verification
- Integration of concepts

