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Lactate reduction in CHO cell cultures through metabolic analysis

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1. Lactate generation in CHO cell cultures

CHO cells display Warburg metabolism characterized by high lactate production, which ultimately inhibits cell growth in culture. The current study explored through metabolic flux analysis both process and cell engineering approaches to avoid lactate accumulation, with potential implications in the industry of bioproducts.

2. Background and Experimental Data

The metabolic profile of CHO cells was investigated in batch bioreactor cultures performed under three conditions.

3. Experimental Overview and Results

- Conventional metabolism
- Lactate generation
- Bioprocess Engineering
- Cell engineering
- Transcription
- Protein synthesis
- Metabolism
- Core Metabolism
- Model Reduction
- CHO Bioprocess
- CHO WT
- CHO-ZeLa
- CHO-S
- CHO-ZeLa Phase 1
- CHO-ZeLa Phase 2
- CHO-S Phase 1
- CHO-S Phase 2
- Constrained-Based Modelling
- Flux Balance Analysis
- Dynamic Flux Balance Analysis
- Oxygen Uptake Rate
- Lactate generation suppression
- Glucose/Lactate (mM)
- pH
- Lactic acid
- Glucose

- Lactate is produced in Phase 1 to fulfill the NADH regeneration requirements in the cytoplasm.
- In both Phase 2 (concomitant consumption) and CHO-ZeLa (no lactate generation), glucose uptake was significantly reduced and a balance between glycolysis/lactate consumption and TCA cycle fluxes was reached.
- 13C and oxygen consumption showed a slight increase in TCA cycle flux in CHO-ZeLa to counter the drop in ATP generation from glycolysis.

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References: