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BHK cells physiological response to spin-filter stress condition

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**Introduction**

- Perfusion cultivation strategy provides both high cell concentrations in a small volume bioreactor and low product’s residence time, allowing high productivity and almost instantaneous recovery of the product.
- BHK-21 cells were cultivated in batch and perfusion modes using an internal spin-filter as the cell-retaining device and the physiological parameters of cells cultivated in perfusion revealed a metabolic shift similar to that observed towards stressful conditions.
- Experiments were carried out in a Biostat B bioreactor (Sartorius, AG, Germany) stirred at 80 rpm with 1,5 L working volume, IMDM/DMEM/5% FBS medium, 50% air sat. dissolved oxygen, pH and temperature controlled at 7,2 and 37°C respectively.

**Batch and perfusion runs**

- The Batch run was used to collect preliminary physiological data.
- The Perfusion run lasted 48 days and can be divided in **batch**, **continuous** (withdrawal tube draining medium from **outside the spin-filter**), and **perfusion phases** (withdrawal tube draining medium from **inside the spin-filter**).
- The batch phase of the Perfusion run was used to calculate physiological parameters to compare with parameters obtained in the Batch run.

**Results**

- Specific rates of glucose $q_{GLC}$ and glutamine $q_{GLN}$ consumption, in the presence of the spin-filter, were 84% and 32% **higher**, respectively.
- Specific rates of lactate $q_{LAC}$ and ammonium $q_{NH_4}$ production, in the presence of the spin-filter, were 78% and 102% **higher**, respectively.

**Discussion**

- It is suggested that higher substrate consumption and metabolites production can be associated with stress factors.
- BHK21/C13, cultivated up to 24 h, under shear stress varying from **0.75 to 1.0 Pa**, had their **viability** and **morphology** affected$^1$.
- The wall shear stress caused by a rotating filter (100 rpm) vary from **1.57 to 1.67 Pa** depending on the recirculation rate$^2$. Nevertheless, that shear stress is not the only stress factor present in a bioreactor cultivation.
- Presented data suggest a correlation between cell stress and the presence of a spin-filter.

References