**Introduction.** Traditionally, scale-up is tackled using a step-wise experimental approach: from lab-scale to pilot-scale and ultimately to production-scale by following certain empirical criteria based on dimensionless numbers or ratios critical to performance. This approach is costly in terms of time and resources and has some limitations such as only one empirical criteria is kept constant during the scale-up. The new approach developed uses a rigorous model of bioreactor system including microbiology, mixing, rheology and mass transfer dynamics of the system and a multiobjective optimisation framework that can handle operational constraints as well as multi-criteria for scale-up. Here we illustrate with a case-study of monoclonal antibody production.

**To scale-up a 3 L stirred tank to 2.5 m³ for monoclonal antibody production**

**Definition of objectives and constraints**

- **Available information?**
- **Model development**
  - Fluid properties: 
    \[ \rho = f(C_i, T) \]
    \[ \mu = f(C_i, T) \]
- **Model corrections**
- **Design scale-up**
- **Invalid model**
- **Model validation at large scale**
- **Objectives not fulfilled**
- **Evaluation**
- **Scaled-up reactor**
- **Implementation**

**Design variables**

- **Stirring rate (N)**
- **Aeration flow (U_b)**

\[ \min J(N, U_b) = \min \left( \text{Operating cost} + \text{Capital cost} \right) \]

\[ \lambda_k = \left( \frac{\nu_k}{\mu} \right)^{0.25} \]

**Microbial kinetics**

**Mass transfer**

\[ k_i a = f(\mu, P, \lambda_k) \]

**Shear and mixing**

**Constraints and cost contour plots**

**Regime analysis**

**Sensitivity analysis of the optimum**

**Production cost**

\[ \text{Production cost} = 2243 \text{ euros kg}^{-1} \]

**Distance to constraints**

**References:**


ván’t Riet, K et al. 1991, Basic Bioreactor Design, 1st ed.- Marcel Dekker.


**Contact**

CAPEC DTU Chemical Engineering. Dr. Miguel Mauricio-Iglesias (mmi@kt.dtu.dk) and Assoc. Prof. Gürkan Sin (gs@kt.dtu.dk)