Kinetic and Stoichiometric Calculations in Clonalyzer

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Introduction

This document explains the core kinetic and stoichiometric calculations implemented in the `Clonalyzer` toolkit. These formulas are commonly used to analyze mammalian cell cultures, particularly CHO cells in fed-batch processes, but they are generalizable to other systems and process modes.

All calculations are performed per biological replicate (Clone $\times$ Rep), using volume-normalized data to maintain mass balance integrity.

1 Specific Growth Rate (μ)

The specific growth rate is defined as the slope of the natural logarithm of viable cell density (X) with respect to time:

$$\mu = \frac{\ln X_2 - \ln X_1}{t_2 - t_1} \tag{1}$$

Where:

- X_1, X_2 are viable cell densities at times t_1 and t_2
- Units: X in cells/mL, t in hours
- Result: μ in h^{-1}

This formula assumes exponential growth in the interval $[t_1, t_2]$.

2 Integral of Viable Cell Density (IVCD)

The IVCD is a measure of biomass exposure over time and is calculated as the area under the VCD curve:

$$\mathrm{IVCD}_{\mathrm{mL}} = \int_{t_1}^{t_2} X(t)\,dt \approx \frac{X_1 + X_2}{2} \cdot \Delta t \tag{2}$$

To compute total biomass exposure in the culture volume:

$$\text{IVCD}_{\text{tot}} = \text{IVCD}_{\text{mL}} \cdot \frac{V_1 + V_2}{2} \tag{3}$$

Where V_1, V_2 are the culture volumes at t_1 and t_2 in mL.
Units: cells·h

3 Metabolite or Biomass Balance (ΔS, ΔX)

The net change of a species (cells, glucose, lactate) is calculated as the difference in total quantity (concentration × volume):

$$\Delta X = X_2 \cdot V_2 - X_1 \cdot V_1 \tag{4}$$

$$\Delta S = S_1 \cdot V_1 - S_2 \cdot V_2 \tag{5}$$

Where:

- X in cells/mL
- S (substrate) in mol/mL
- V in mL

ΔS is positive if the substrate was consumed, and negative if it was produced (e.g., lactate).

4 Yield on Substrate ($Y_{X/S}$)

Yield is defined as the ratio of biomass produced per mole of substrate consumed:

$$Y_{X/S} = \frac{\Delta X}{\Delta S} \tag{6}$$

Units: cells/mol

5 Specific Rate (q_S)

The specific rate is the substrate consumption or production rate per cell per hour. It is normalized to IVCD:

$$q_S = \frac{\Delta S \cdot 10^{12}}{\text{IVCD}_{\text{tot}}} \tag{7}$$

Where:

- ΔS is in mol
- IVCD_{tot} is in cell·h
- q_S is in pmol/(cell·h)

The conversion factor 10^{12} changes mol to pmol.

References

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