SECTION II: KINETICS AND BIOREACTOR DESIGN:

LESSON 9.3. - Enzymatic kinetics, microbial kinetics and metabolic stoichiometry – Models and Metabolic Stoichiometry

JAVIER CALZADA FUNES

Biotechnology Department, Biosciences School

UNIVERSIDAD FRANCISCO DE VITORIA
AIMS FOR TODAY’S LESSON

1.- KINDS OF MODELS
   Using concepts as “segregation” and “structure”.

2.- MALTHUS MODEL and its prediction capability.

3.- LOGISTIC EQUATION and its prediction capability.

4.- MONOD EQUATION and its prediction capability.

5.- OTHER MODELS
1. KINETIC MODELS

A model is a simplified representation of a biological phenomenon, designed to facilitate predictions and calculations that can be expressed in mathematical form.

A model is an approximation to a real phenomenon.

"All models are wrong but useful“

Modeling involves an agreement between the reliability, degree of complexity and the effort required to produce the model.
## 1. KINETIC MODELS

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1. KINETIC MODELS

**Structured Model** ➔ considering a large network of enzymatic reactions within the cell.

**Totally Segregated Model** ➔ considering that every cell in the culture is different in both size and metabolic state.
1. KINETIC MODELS

**Balanced Growth** ➔ cell growth is defined as a function of a limiting **component**, which controls its rate of limiting substrate, while the other components are in adequate concentrations and not limiting growth.

**Average Cell** ➔ cells within a population are equal and behave in the same way.
## 1. KINETIC MODELS

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**Balanced Growth**
1. KINETIC MODELS

Real case ➔ Growth of cells in the system is segregated and structured ➔ very complex to describe.

Simplest case ➔ cell population is considered as a non-segregated and unstructured system.
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1. Non structured Nor Segregated models
2. **Structured** but Non Segregated
3. Non structured but **Segregated**.
1. KINETIC MODELS

1. Non structured Nor Segregated models
   - Growth Models.
   - Models describing both growth and substrate uptake.
   - Models describing growth, substrate uptake and product generation.

2. Structured but Non Segregated

3. Non structured but Segregated.
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2. Structured but Non Segregated
   - Cell Models
   - Metabolic Models
   - Chemically Structured Models

3. Non structured but Segregated
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3. **Non structured but Segregated**
   - Filamentous microorganisms
   - Mixed culture
1. KINETIC MODELS

1. Non structured Nor Segregated models

➢ Growth Models.
➢ Models describing both growth and substrate uptake.
➢ Models describing growth, substrate uptake and product generation.

MAIN CHARACTERISTICS:

• Black box: what happens inside the cells?
• Non structured
• Homogeneously distributed population ➔ Non segregated.
• Great simplification of the reality.
• Useful for technological purposes.
• Can be applied under different situations.
1. KINETIC MODELS

1. Non structured Nor Segregated models
   - Growth Models.
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   - Models describing growth, substrate uptake and product generation.

**MAIN EXAMPLES:**

- Malthus Law.
- Logistic Equation
- Monod equation
1. - MALTHUS MODEL

2. - LOGISTIC EQUATION

3. - MONOD EQUATION

4. - OTHER MODELS
1. - MALTHUS MODEL
2. MALTHUS MODEL

1. **Non structured Nor Segregated models**
   - Growth Models.

   \[
   \frac{d[X]}{dt} = r = \mu \cdot f([X])
   \]

   - Describing one single process
   - Simple equations only considering [X]
2. MALTHUS MODEL

1. Non structured Nor Segregated models
   ➢ Growth Models.

\[
\frac{d[X]}{dt} = \mu \cdot f ([X]) \\
\frac{d[X]}{dt} = \mu \cdot [X] \Rightarrow [X] = [X]_0 \cdot \exp(\mu \cdot t)
\]

Valid only to describe the exponential growth stage.

**Unable to describe the stationary phase.**
2. MALTHUS MODEL

1. Non structured Nor Segregated models

- Growth Models.

\[ t = 0 \iff [X] = [X]_0 \]
\[ t = t_{lat} \iff [X] = [X]_0 \]
\[
\begin{cases}
0 \leq t < t_{lat} \therefore \frac{d[X]}{dt} = 0 \Rightarrow X = X_0 \\
t \geq t_{lat} \therefore \frac{d[X]}{dt} = \mu[X] \Rightarrow X = X_0 \cdot \exp[\mu(t - t_{lat})]
\end{cases}
\]
2. MALTHUS MODEL

1. Non structured Nor Segregated models

➢ Growth Models.

![Graph showing growth over time](image_url)
1. - MALTHUS MODEL

2. - LOGISTIC EQUATION

3. - MONOD EQUATION

4. - OTHER MODELS
2.- LOGISTIC EQUATION
3. LOGISTIC EQUATION

1. Non structured Nor Segregated models

➢ Growth Models.

\[
\text{Substrate} \xrightarrow{\text{Cells}} \text{Cells} \\
\frac{d[X]}{dt} = r = \mu \cdot f ([X])
\]

- Describing one single process
- Simple equations \( \leftarrow \) only considering \([X]\)
3. LOGISTIC EQUATION

1. Non structured Nor Segregated models

- Growth Models.

\[
\frac{d[X]}{dt} = \mu \cdot f([X])
\]

\[
\frac{d[X]}{dt} = \mu \cdot \left( [X] \left( 1 - \frac{[X]}{[X]_{\text{max}}} \right) \right)
\]

\[
X = \frac{X_0 \cdot \exp(\mu \cdot t)}{1 - \frac{X_0}{X_{\text{max}}} \left[ 1 - \exp(\mu \cdot t) \right]}
\]
3. LOGISTIC EQUATION

1. Non structured Nor Segregated models

- Growth Models.

\[
X = \frac{X_0 \cdot \exp(\mu \cdot t)}{1 - \frac{X_0}{X_{\text{max}}} \cdot [1 - \exp(\mu \cdot t)]}
\]

It predicts exponential and stationary phase,

but it does not consider the influence of the substrate (limiting nutrient).
3. LOGISTIC EQUATION

1. Non structured Nor Segregated models

➢ Growth Models.

\[ t = 0 \iff [X] = [X]_0 \]

\[ t = t_{lat} \iff [X] = [X]_0 \]

\[
\begin{cases}
0 \leq t < t_{lat} \therefore \frac{d[X]}{dt} = 0 \implies X = X_0 \\
t \geq t_{lat} \therefore \frac{d[X]}{dt} = \mu \cdot X \left(1 - \frac{X}{X_{max}}\right); \implies X = \frac{X_0 \cdot \exp(\mu \cdot [t - t_{lat}])}{1 - \frac{X_0}{X_{max}} \cdot [1 - \exp(\mu \cdot [t - t_{lat}])]} 
\end{cases}
\]
3. LOGISTIC EQUATION

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3. - MONOD EQUATION
4. - OTHER MODELS
3.- MONOD EQUATION
4. MONOD DEQUATION

1. Non structured Nor Segregated models

➢ Growth Models.

\[ \frac{d[X]}{dt} = \mu \cdot f ([X], [S]) \]

\[ \frac{d[X]}{dt} = \mu([S])[X] = \frac{\mu_m[S]}{K_s + [S]}[X] \]

Predicts specific growth rate according to substrate concentration

Under limiting substrate conditions.

Hyperbolic kinetics \( \approx \) Michaelis-Menten kinetics for an enzymatic process.
4. MONOD EQUATION

1. **Non structured Nor Segregated models**

   - Growth Models.

   \[
   \frac{d[X]}{dt} = \frac{\mu_m \cdot [S]}{K_S + [S]} \cdot [X]
   \]

   - \( \mu = \) specific growth rate for a particular substrate concentration
   - \( \mu_m = \) maximum = specific growth rate for a particular substrate concentration
   - \( S = \) substrate concentration
   - \( K_S = \) saturation constant ([S] for \( \mu = 1/2 \) de \( \mu_m \))
4. MONOD DÉQUATION

1. **Non structured Nor Segregated models**

   ➢ Growth Models.

\[
\frac{d[X]}{dt} = \mu([S])[X] = \frac{\mu_m[S]}{K_S + [S]}[X]
\]

\[
K_S \ll [S] \Rightarrow \frac{d[X]}{dt} = \mu_m[X] \quad \text{Malthus}
\]

\[
K_S \gg [S] \Rightarrow \frac{d[X]}{dt} = \frac{\mu_m[S][X]}{K_S} \quad \text{M'Kendrick y Pai}
\]
1. MALTHUS MODEL

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2. Structured but Non Segregated

- Cell Models

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<tr>
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<th>CELLS</th>
<th>PRODUCTS</th>
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<tr>
<td>Carbon</td>
<td>BIOMASS 1</td>
<td>Products</td>
</tr>
<tr>
<td>Nitrogen</td>
<td>BIOMASS 2</td>
<td>Biomass</td>
</tr>
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<td></td>
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2. Structured but Non Segregated

- Cell Models

**Model of Williams (1967)**

Two compartment:

- **Synthetic section (K):** RNA + small biomolecules.
- **Genetic-Structural section (G):** DNA + proteins

**Hypothesis**

Cell Division $\leftrightarrow$ G section doubling its size

**Reaction Scheme**

$$ S \rightarrow K + G $$

Universidad Francisco de Vitoria
UFV Madrid
5. OTHER MODELS

2. Structured but Non Segregated

- Cell Models
  
  Model of Williams (1967)

**Reaction Scheme**

\[
\begin{align*}
  r_1 &= k_1 \cdot [S] \cdot ([K] + [G]) \\
  r_2 &= k_2 \cdot [K] \cdot [G]
\end{align*}
\]
2. Structured but Non Segregated

- Cell Models

*Model of Williams (1967)*

Reaction Scheme

\[ r_1 = k_1 \cdot [S] \cdot ([K] + [G]) \]
\[ r_2 = k_2 \cdot [K] \cdot [G] \]

\[ \frac{d[S]}{dt} = -r_1; \quad \frac{d[K]}{dt} = r_1 - r_2; \quad \frac{d[G]}{dt} = r_1 + r_2 \]
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5. OTHER MODELS

3. Non structured but Segregated

SEGREGATION based on a property distribution function

Cellular age: difficult to measure and to relate to composition

Biomass: filamentous fungi.
5. OTHER MODELS

3. Non structured but Segregated

- Filamentous microorganisms

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<th>Unicellular</th>
<th>Fission and Budding</th>
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- Filamentous Mycelium

- Bud

- Branching
5. OTHER MODELS

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Growth: $r_{yema}$ → Branching frequency ($\phi$)
ANY QUESTION?
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