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.

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1. KINETIC MODELS

MODELS	NON STRUCTURED	STRUCTURED
NON SEGREGATED	Cell population considered as a whole: **average individual** and **one single component**	Description of a **Average cell** whose **different components** vary along time
SEGREGATED	**Cell population** (distribution of any characteristic), **one single component**	**Multicomponent description** within a **una cell population**, heterogeneity from one cell to another cell

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

MODELS	NON STRUCTURED	STRUCTURED
NON SEGREGATED	Cell population conside[illegible]ed as a whole: **average [illegible]dividua[illegible]** **one s[illegible] [illegible]mponent**	Description of a [illegible]**verage cell** whose [illegible]**ferent c[illegible]ponents** vary a[illegible]ne
SEGREGATED	**Cel[illegible]lation** (dist[illegible]n of a[illegible] characteristic), **one single component**	**Multico[illegible]ent** [illegible]**criptio**[illegible]n a **una cell po[illegible]on**, heterogeneity from one cell to another cell

Balanced Growth

Average cell

Balanced Growth

Average cell

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.

1. KINETIC MODELS

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SEGREGATED	**Cell population** (distribution of any characteristic), **one single component**	**Multicomponent** de...on within a **una** ce...ation, heterogeneity ... cell to another ...

+ SIMPLICITY and – REALiTY

+ COMPLEXITY and REALITY

1. KINETIC MODELS

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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2. Structured but Non Segregated

- Cell Models
- Metabolic Models
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3. Non structured but Segregated

- Filamentous microorganisms
- Mixed culture

1. KINETIC MODELS

1. Non structured Nor Segregated models

- Growth Models.
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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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MAIN EXAMPLES:

- Malthus Law.
- Logistic Equation
- Monod equation

1.- MALTHUS MODEL

2.- LOGISTIC EQUATION

3.- MONOD EQUATION

4.- OTHER MODELS

1.- MALTHUS MODEL

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2. MALTHUS MODEL

1. Non structured Nor Segregated models

➢Growth Models.

$$Substrate \xrightarrow{Cells} Cells$$

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

- 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.

$$t = 0 \Leftrightarrow [X] = [X]_0$$

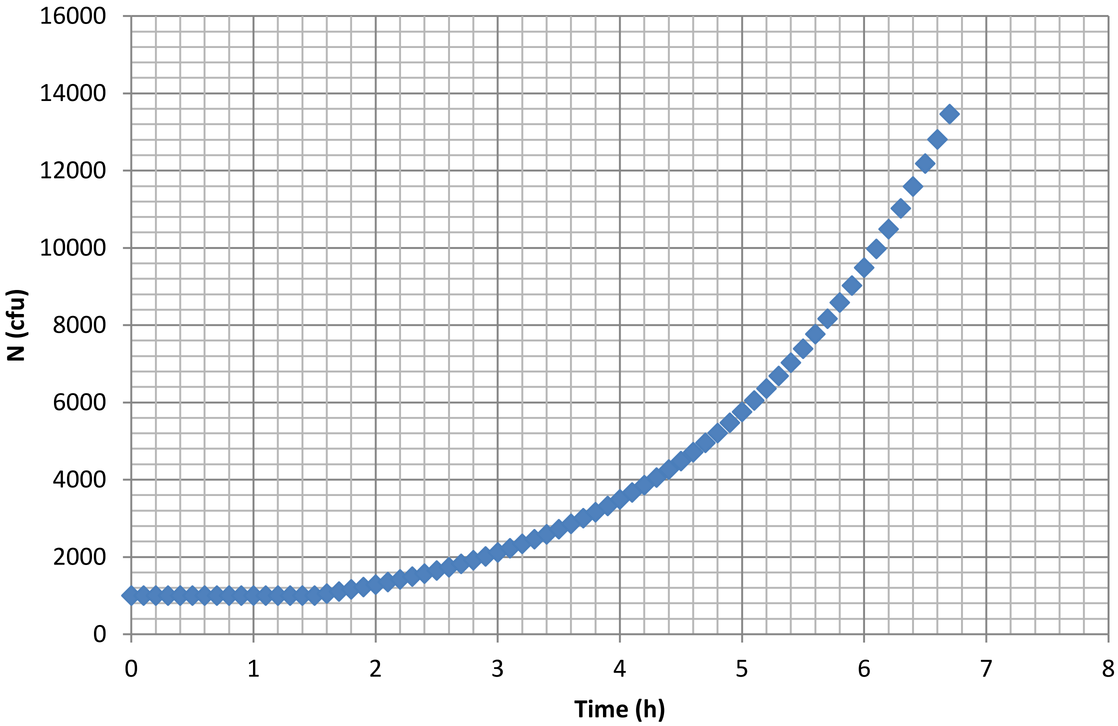
$$t = t_{lat} \Leftrightarrow [X] = [X]_0$$

$$\begin{cases} 0 \le t < t_{lat} \therefore \dfrac{d[X]}{dt} = 0 \Rightarrow X = X_0 \\ t \ge t_{lat} \therefore \dfrac{d[X]}{dt} = \mu \cdot [X] \Rightarrow X = X_0 \cdot \exp[\mu \cdot (t - t_{lat})] \end{cases}$$

2. MALTHUS MODEL

1. Non structured Nor Segregated models

- Growth Models.



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.

$$Substrate \xrightarrow{Cells} Cells$$

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

- Describing one single process
- Simple equations 🡸 only considering [X]

3. LOGISTIC EQUATION

1. Non structured Nor Segregated models

- Growth Models.

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

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

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

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3. LOGISTIC EQUATION

1. Non structured Nor Segregated models

- Growth Models.

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

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.

$$t = 0 \Leftrightarrow [X] = [X]_0$$

$$t = t_{lat} \Leftrightarrow [X] = [X]_0$$

$$\begin{cases} 0 \leq t < t_{lat} \therefore \dfrac{d[X]}{dt} = 0 \Rightarrow X = X_0 \\ t \geq t_{lat} \therefore \dfrac{d[X]}{dt} = \mu \cdot X \cdot \left[1 - \dfrac{X}{X_{\max}}\right]; \Rightarrow X = \dfrac{X_0 \cdot \exp(\mu \cdot [t - t_{lat}])}{1 - \dfrac{X_0}{X_{\max}} \cdot \left[1 - \exp(\mu \cdot [t - t_{lat}])\right]} \end{cases}$$

3. LOGISTIC EQUATION

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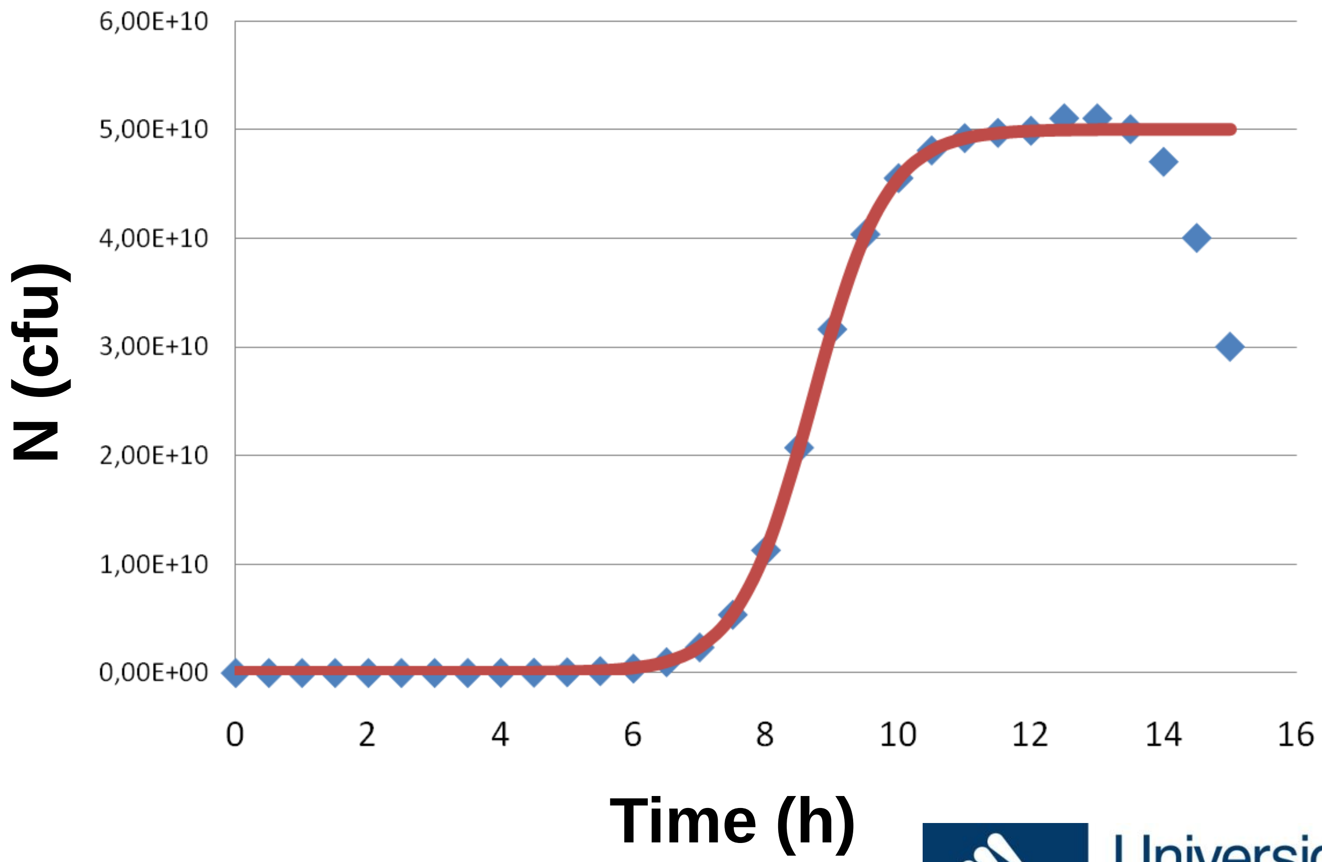
- Growth Models.



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1.- MALTHUS MODEL

2.- LOGISTIC EQUATION

3.- MONOD EQUATION

4.- OTHER MODELS

3.- MONOD EQUATION

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4. MONOD DEQUATION

1. Non structured Nor Segregated models

- Growth Models.

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

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

Predicts specific growth rate **according to substrate concentration**

Under limiting substrate conditions.

Hyperbolic kinetics ≈ Michaelis-Menten kinetics for an enzymatic process

4. MONOD DEQUATION

1. Non structured Nor Segregated models

- Growth Models.

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

μ = specific growth rate for a particular substrate concentration

μ_m = maximum = specific growth rate for a particular substrate concentration

S = substrate concentration

K_s = saturation constant ([S] for μ = 1/2 de μ_m)

4. MONOD DEQUATION

1. Non structured Nor Segregated models

- Growth Models.

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

$$K_S << [S] \Rightarrow \frac{d[X]}{dt} = \mu_m \cdot [X]$$

Malthus

$$K_S >> [S] \Rightarrow \frac{d[X]}{dt} = \frac{\mu_m}{K_S}\cdot[S]\cdot[X]$$

M'Kendrick y Pai

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4.- OTHER MODELS

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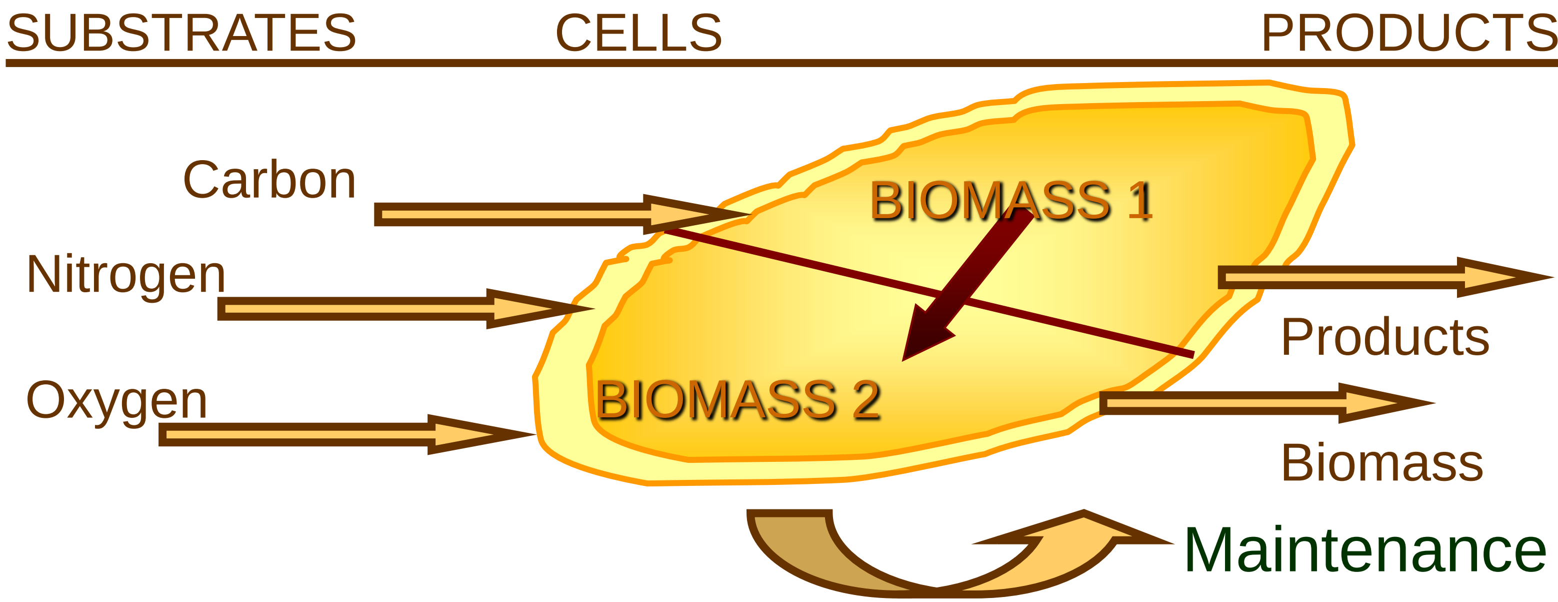
5. OTHER MODELS

2. Structured but Non Segregated

- Cell Models



5. OTHER MODELS

2. Structured but Non Segregated

- Cell Models

<u>Model of Wiliams (1967)</u>

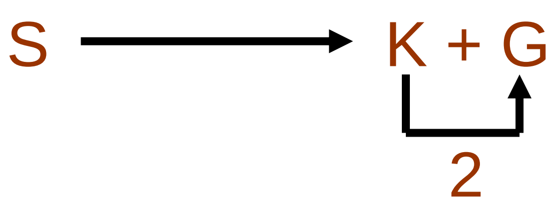
Two compartment:

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

Hypothesis

Cell Division ←→ G section doubling its size

Reaction Scheme



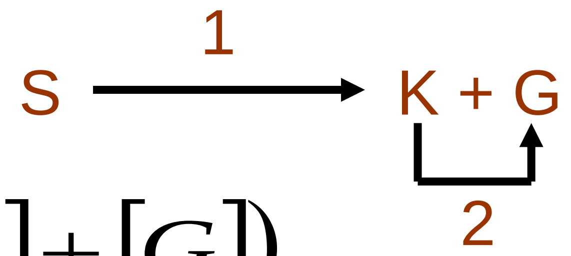
5. OTHER MODELS

2. Structured but Non Segregated

- Cell Models

Model of Wiliams (1967)

Reaction Scheme



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

Substrate   Catalytic agent

$$r_2 = k_2 \cdot [K] \cdot [G]$$

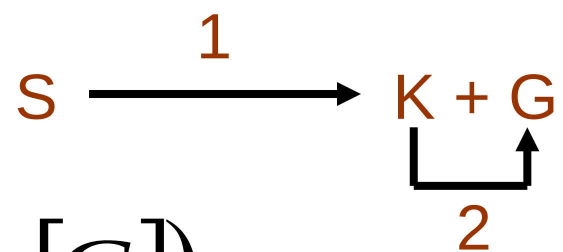
5. OTHER MODELS

2. Structured but Non Segregated

- Cell Models

Model of Wiliams (1967)

Reaction Scheme



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

$$r_2 = k_2 \cdot [K] \cdot [G]$$

$$\frac{d[S]}{dt} = -r_1; \frac{d[K]}{dt} = r_1 - r_2; \frac{d[G]}{dt} = r_1 + r_2$$

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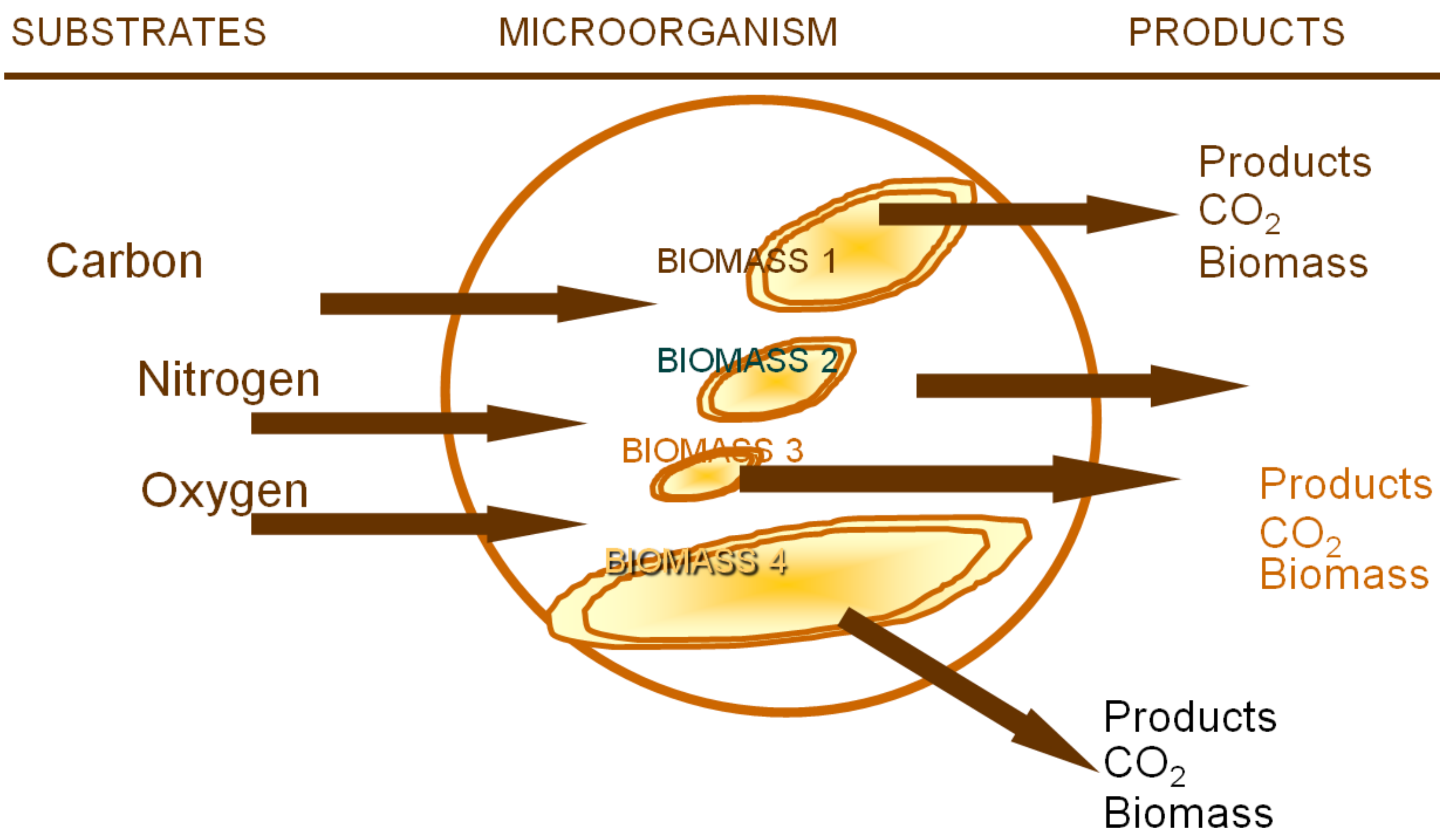


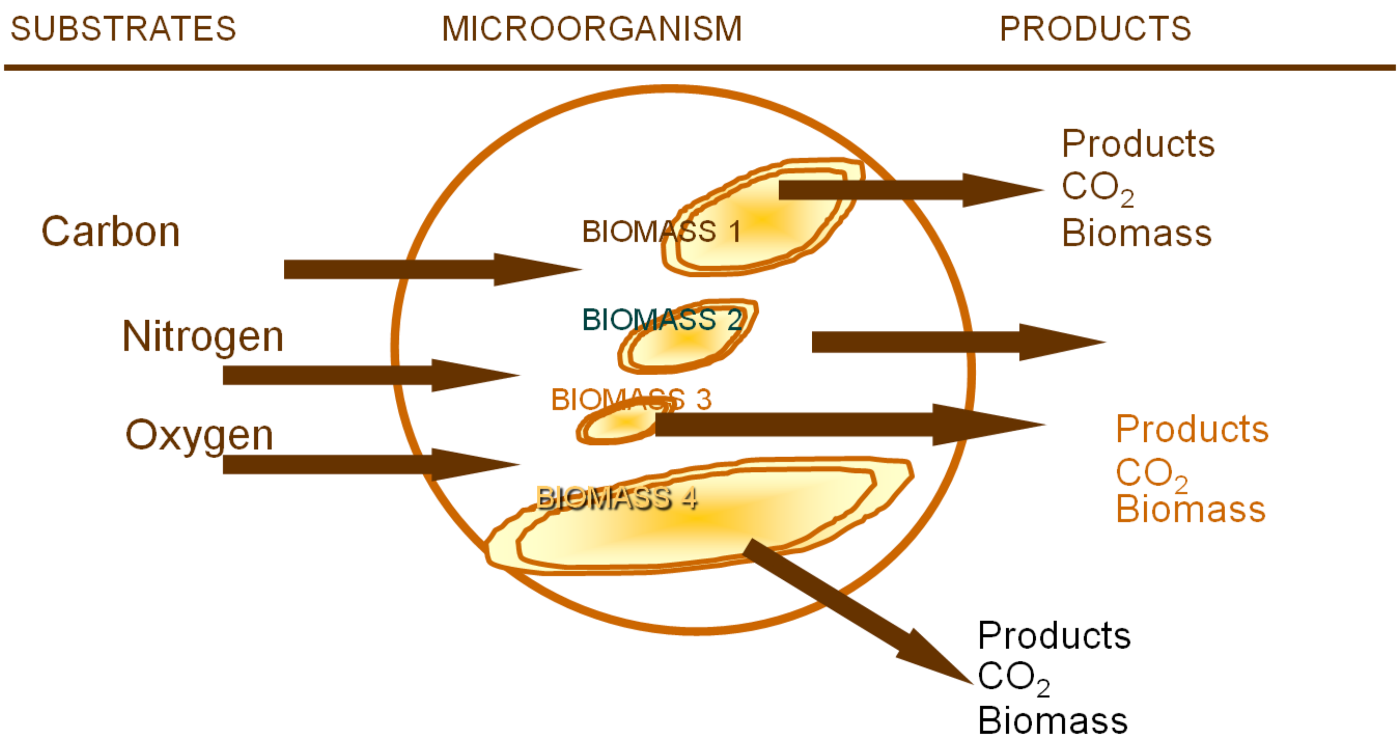
5. OTHER MODELS

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.

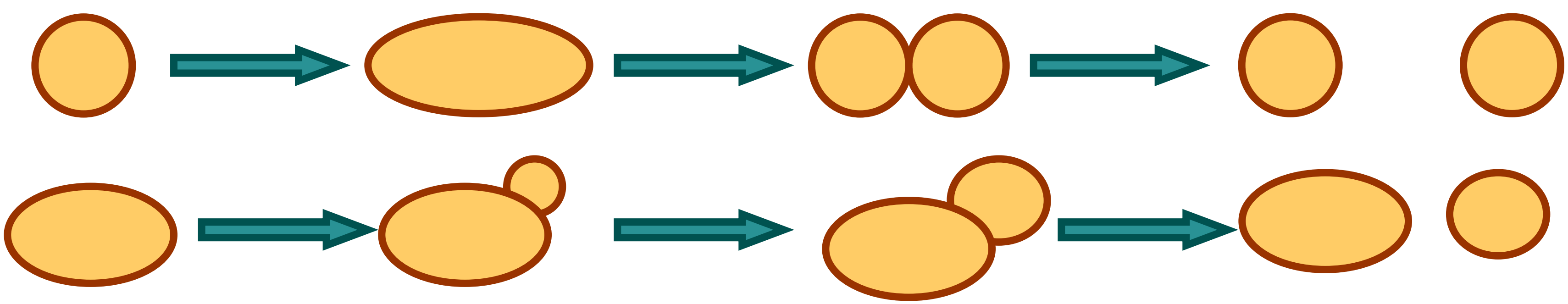


5. OTHER MODELS

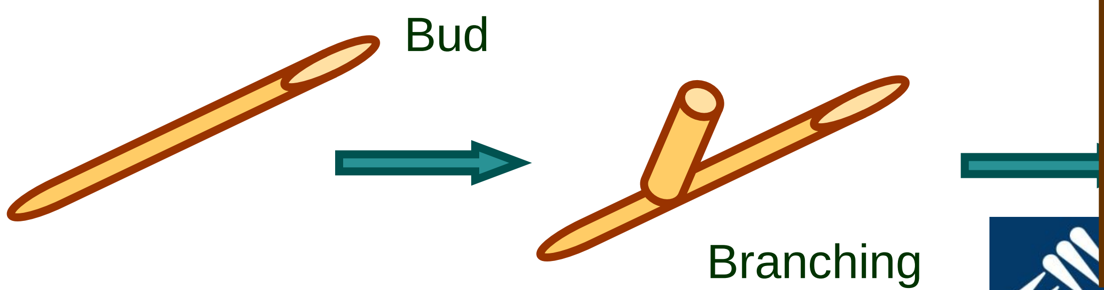
3. Non structured but Segregated

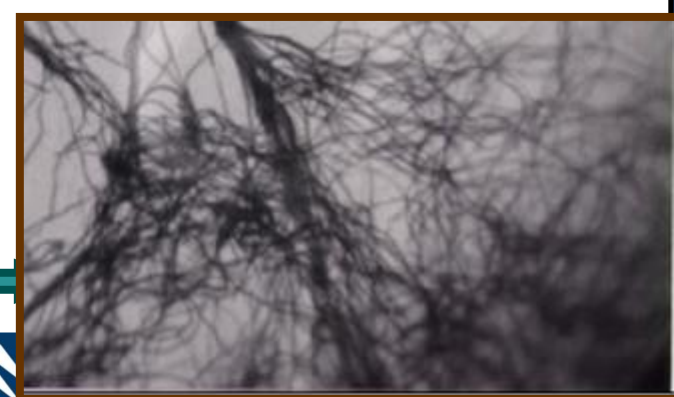
- **Filamentous microorganisms**

Unicellular | Fission and Budding



Filamentous | Mycelium



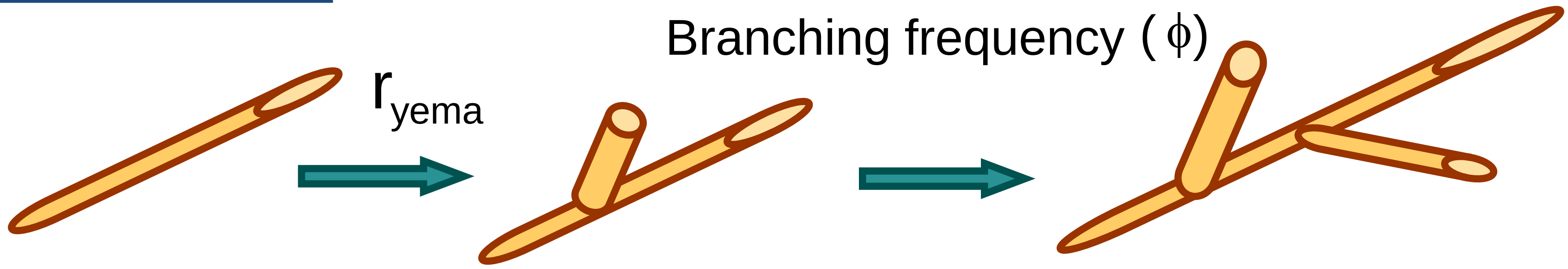


5. OTHER MODELS

3. Non structured but Segregated

- **Filamentous microorganisms**

Growth



ANY QUESTION?

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