SECTION II: KINETICS AND BIOREACTOR DESIGN:

LESSON 15. - Services, instrumentation and control

JAVIER CALZADA FUNES

Biotechnology Department, Biosciences School

UNIVERSIDAD FRANCISCO DE VITORIA

AIMS FOR TODAY'S LESSON

1.- SERVICES, INSTRUMENTATION AND CONTROL

2.- AUXILIARY SERVICES.

3.- CONTROL SYSTEMS

4.- TYPES OF CONTROL

REFERENCES:

- Atkinson, B. (2002), *Reactores Bioquímicos*, Reverté (Barcelona).
- Najafpour, G.D (2007), *Biochemical Engineering and Biotechnology*, Elsevier, Amsterdam.
- Rehm, H.J. y Reed, G, (1993) *Biotechnology. Volumen 3*, VCH Publishers, (Nueva York).
- Shuler, M.L. y Kargi, F. (2002), *Bioprocess engineering*, Prentice Hall, (Upper Saddle River, NJ, EE.UU).

1.- SERVICES, INSTRUMENTATION AND CONTROL

2.- AUXILIARY SERVICES

3.- CONTROL SYSTEMS

4.- TYPES OF CONTROL

1.- SERVICES, INSTRUMENTATION AND CONTROL

Universidad Francisco de Vitoria
UFV Madrid

1. SERVICES, INSTRUMENTATION AND CONTROL

Objectives of instrumentation and control of bioprocesses:

- Development of methods for monitoring and controlling the variables of a commercial bioprocess for:

- Obtaining **information** about the process for its understanding and use.
- Monitoring systems development **in real time** ➔ realistic models.
- **Record of changes in variables**.
- **Maintenance of optimal conditions** for the generation of the product.

1. SERVICES, INSTRUMENTATION AND CONTROL

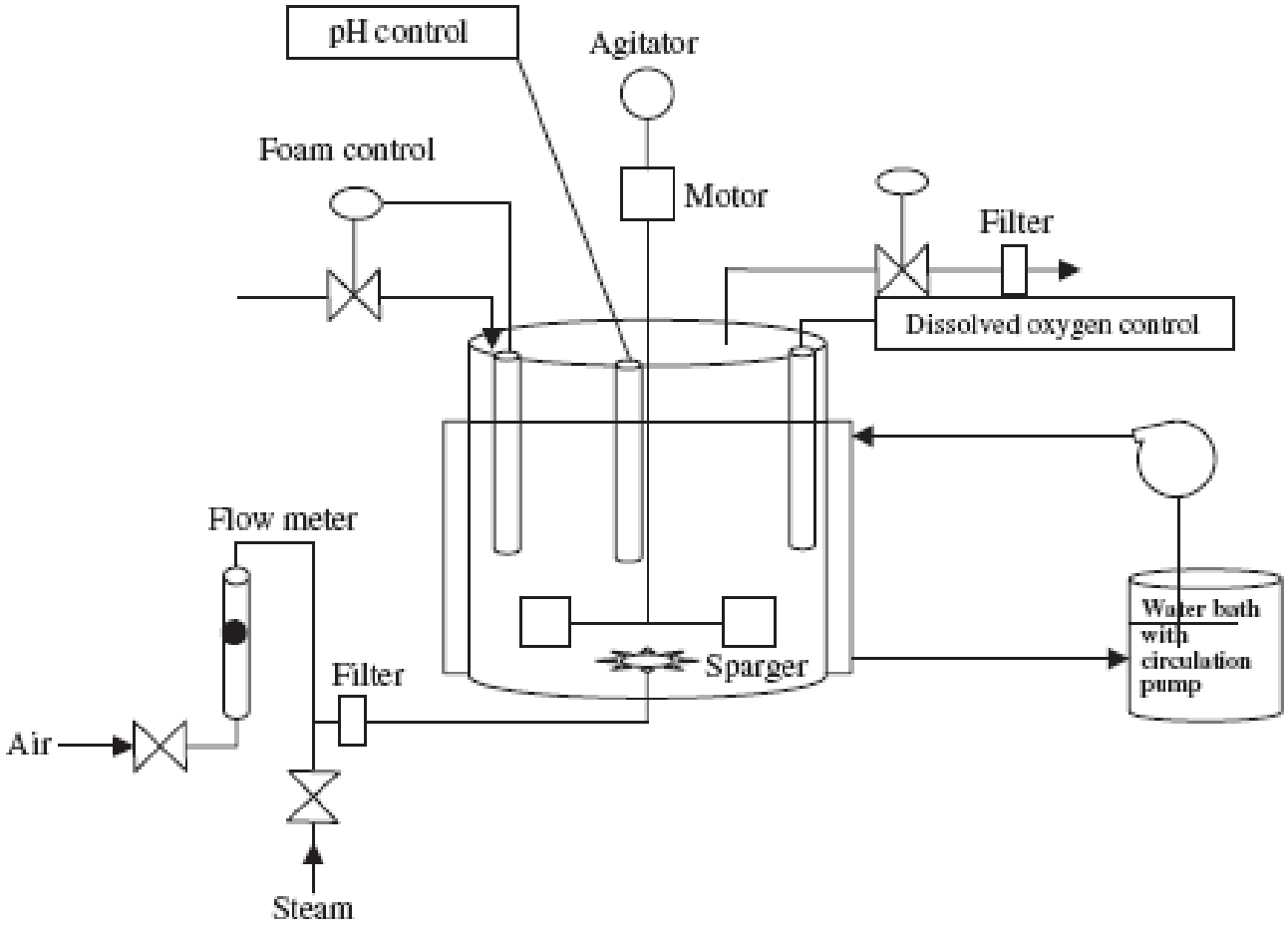


FIG. 4.1. Instrumentation control for continuous stirred tank (CSTR) bioreactor.

1. SERVICES, INSTRUMENTATION AND CONTROL

TABLE 4.1. *Bioreactor operating parameters*

Physical	Chemical	Biological and cell properties
Time	pH	Respiratory quotient
Temperature	Redox potential	O_2 uptake rate
Pressure	Dissolved oxygen	CO_2 production rate
Agitation speed	Dissolved carbon dioxide	Optical density
Total mass	O_2 in gas phase	Cell concentration
Total volume	CO_2 in gas phase	Viability of cells
Volume feed rate	Lipid	Cell morphology
Viscosity of culture	Carbohydrates	Cellular composition
Power input	Enzyme activities	Protein, DNA, RNA
Foam	Nitrogen	ATP/ADP/AMP
Shear	Ammonia if present	NAD^+/NADH
Mixing time	Mineral ions	Activities of whole cells
Circulation time	Precursors	Specific growth rate
Gas holdup	Inducers	Specific oxygen uptake rate
Bubble size distribution	Growth stimulants	Specific substrate uptake rate
Impeller flooding	Effective mineral as catalysts	Metabolites
Broth Rheology	Products	Growth factors
Gas mixing patterns	Volatile products	Growth inhibitors
Liquid level	Conductivity	Biomass composition
Reactor weight	Off gas composition	Biomass concentration
Foam level		

1. SERVICES, INSTRUMENTATION AND CONTROL

Parameters of bioprocesses instrumentation and control:

- **Physical parameters:** stirring power, stirring speed, culture volume, density color, foam, gas flow, inlet gas humidity, heat transfer rate, liquid flow, mass, osmotic pressure, temperature, ...
- **Chemical parameters:** measurement of concentration of oxygen and CO_2 in the gas, pH, redox potential, dissolved oxygen, dissolved CO_2, ...
- **Biochemical parameters:** those that show metabolic state.
- **Biological parameters:** those that describe the fermentor from the cellular point of view ➔ Distribution of cell ages, aggregation, contamination, generation time, genetic stability, morphology, total count, viable count, ...

1. SERVICES, INSTRUMENTATION AND CONTROL

Difficulty in bioprocesses instrumentation and control:

Complexity of biological systems:

Its control is complicated, especially in discontinuous or semi-continuous processes ← **high degree of non-linearity** (description by means of non-linear differential equations).

1. SERVICES, INSTRUMENTATION AND CONTROL

Requirements for analysis techniques

- Simplicity
- Rapid determination of the magnitude
- Process automation
- Equipment economy
- That does not alter the process

Characteristics of equipments

- Resistance to sterilization processes
- Use in media with turbidity
- Insensitivity to cell growth
- Resistance to mechanical forces and erosions
- Stability and specificity to the extent
- Sensitivity to low concentrations of metabolites
- Reproducibility or repeatability of the analysis
- Short response times
- Ease to transmit and communicate the signal to the equipment

1. SERVICES, INSTRUMENTATION AND CONTROL

Techniques and instruments for monitoring variables:

- How to perform the measurement: in situ / ex situ, offline / online

in-situ / ex-situ

in-situ: sensor **inside** bioreactor

ex-situ: sample **transferred to an external device** for analysis

on-line / off-line

on-line: measurement **can be registrated directly**. e.g. pH

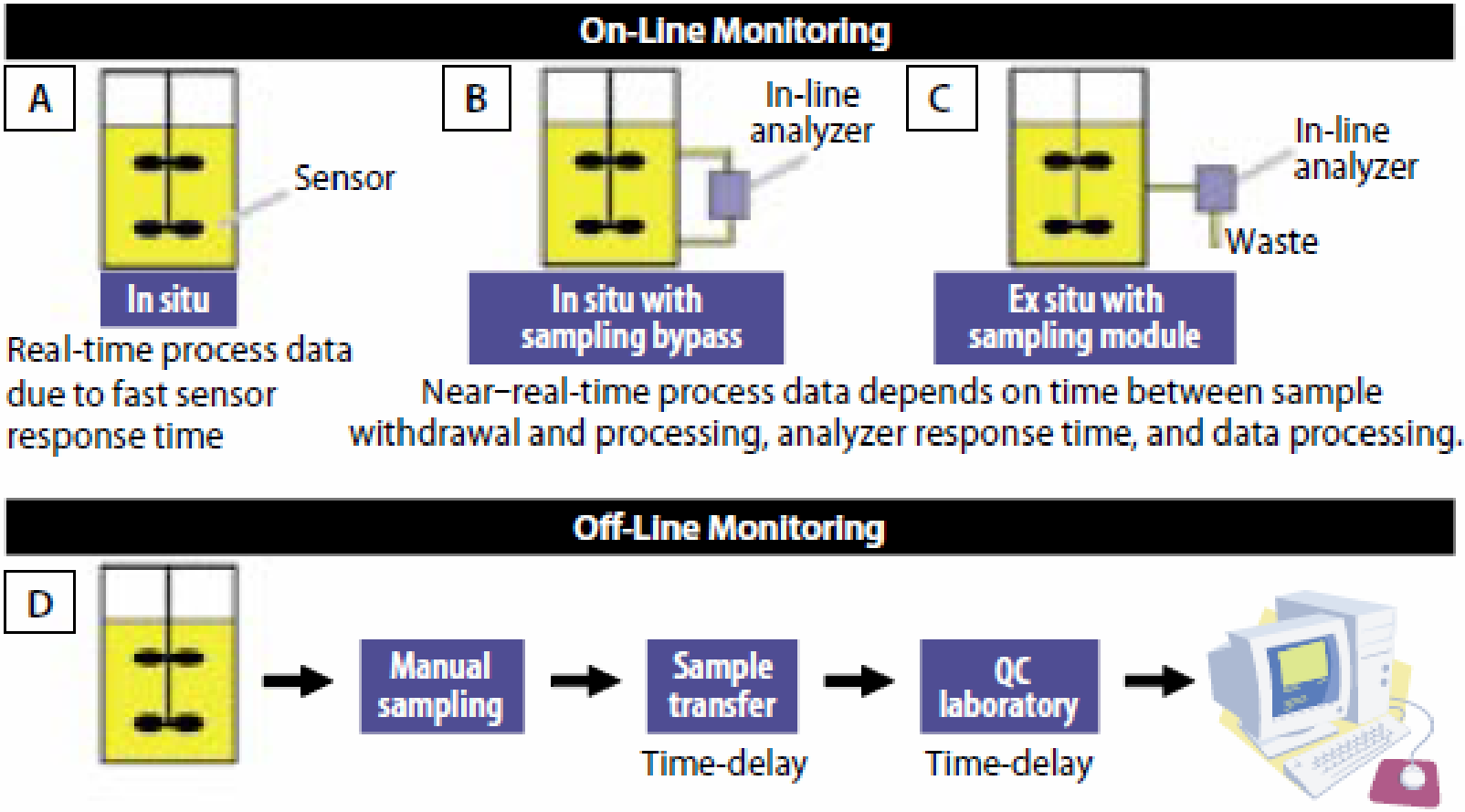
off-line: **sample taken and analysed extern / preparation of samples**

➔ delay

Ideal situation*: on-line, in-situ*

1. SERVICES, INSTRUMENTATION AND CONTROL

Figure 11: Classification of bioprocess monitoring, sensors, and analysis configurations, with respect to their degree of invasiveness

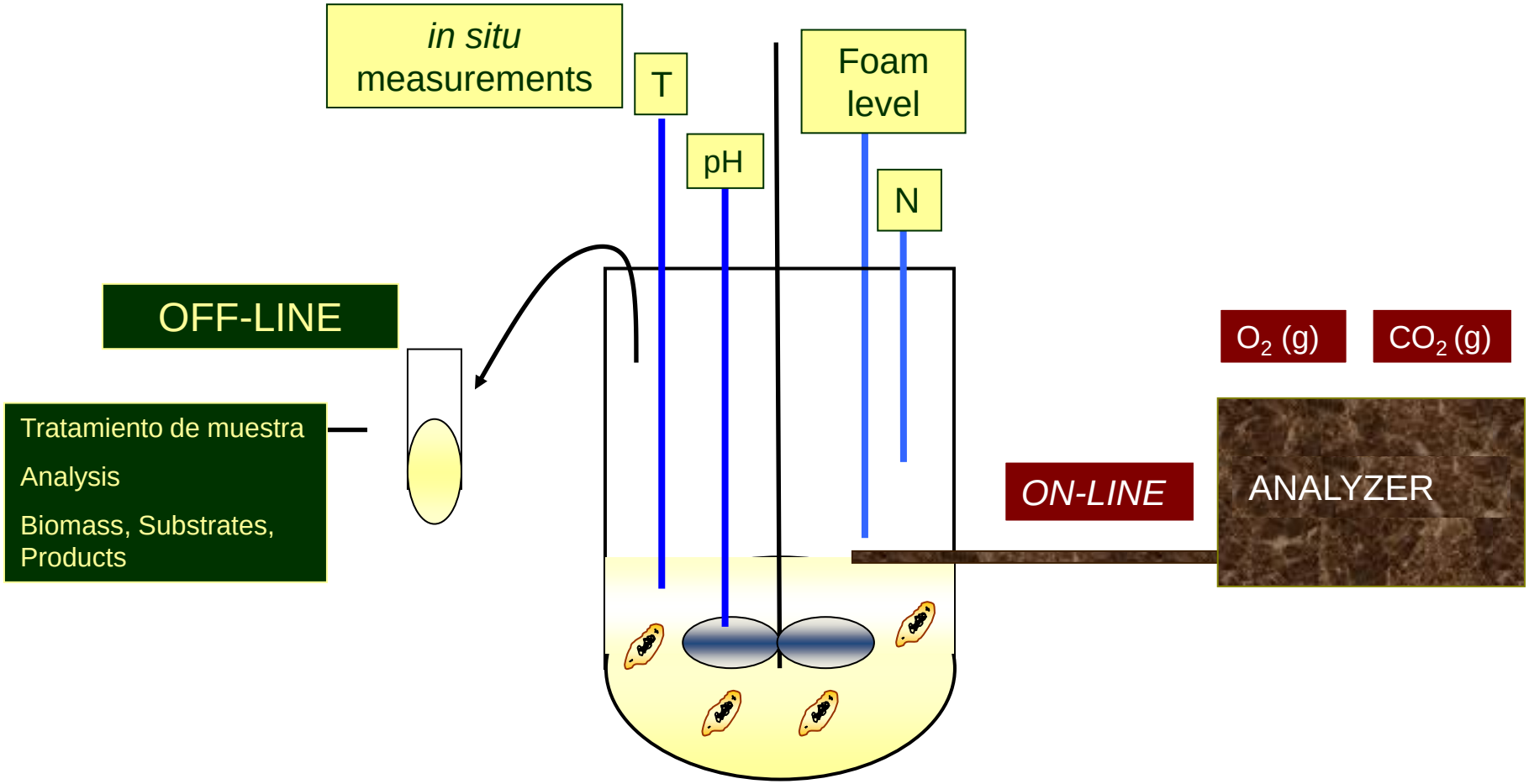


1. SERVICES, INSTRUMENTATION AND CONTROL

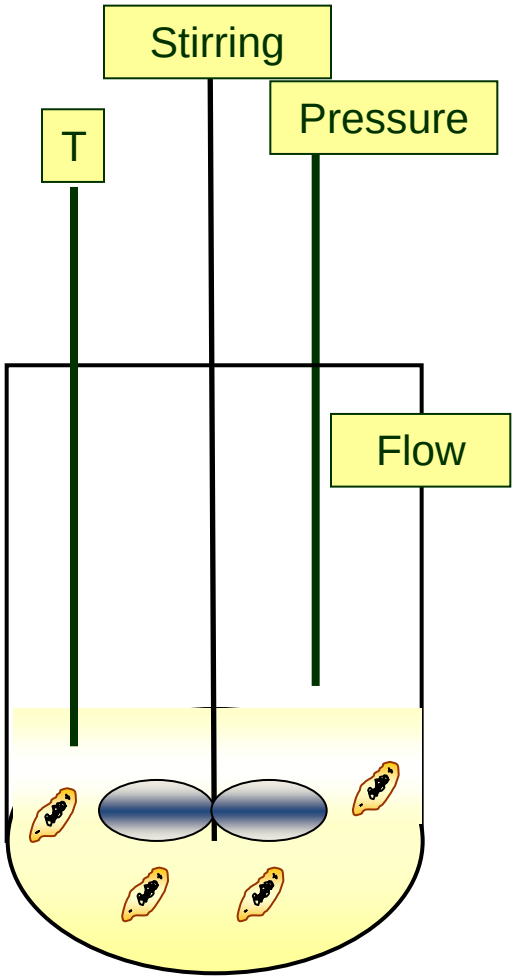
Techniques and instruments for monitoring variables:

-How to perform the measurement: in situ / ex situ, offline / online

-Type of property or variable analyzed: physicochemistry, hydrodynamics, biological



1. SERVICES, INSTRUMENTATION AND CONTROL

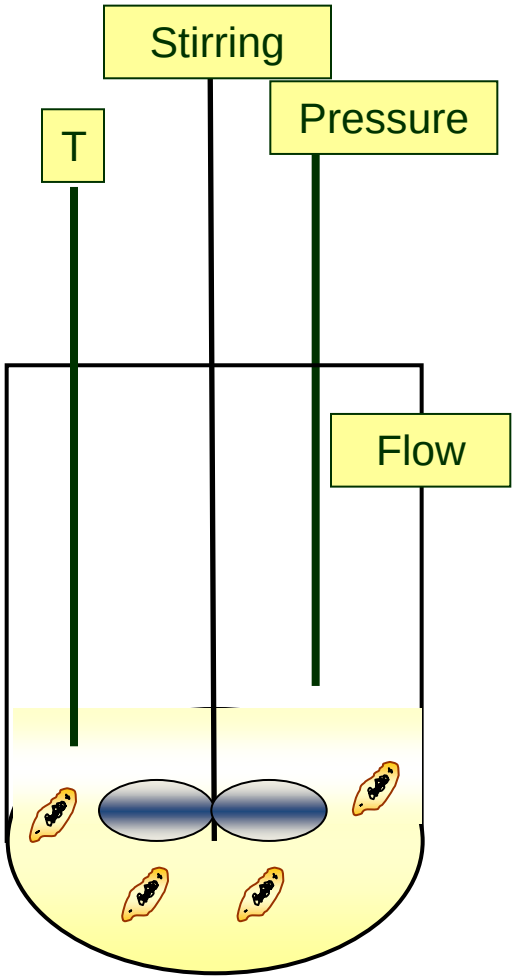


Analysis of physical parameters

• **Temperature.** Optimal growth and sterilization. Sensors: thermocouples, platinum resistors and thermistors.

• **Pressure.** It affects solubility of CO_2 , 0_2 and volatile substances (ethanol). little overpressure must be inside the bioreactor. However, if it's too high it may indicate saturation of output filters. Sensors: pressure transducers.

1. SERVICES, INSTRUMENTATION AND CONTROL



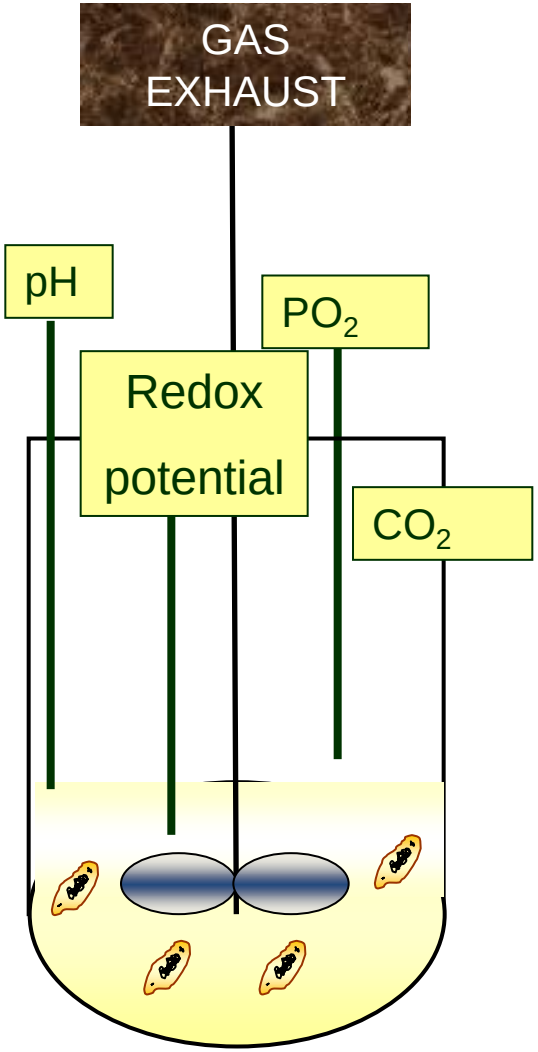
Analysis of physical parameters

- **Agitation.** Optical or magnetic sensors (small equipment) tachometers (large equipment).

- **Foam detectors** Probe whose conductivity varies when coming into contact with the foam**.**

- **Flow meters.** Gas flows. Rotameter, thermal flow meters (mass).

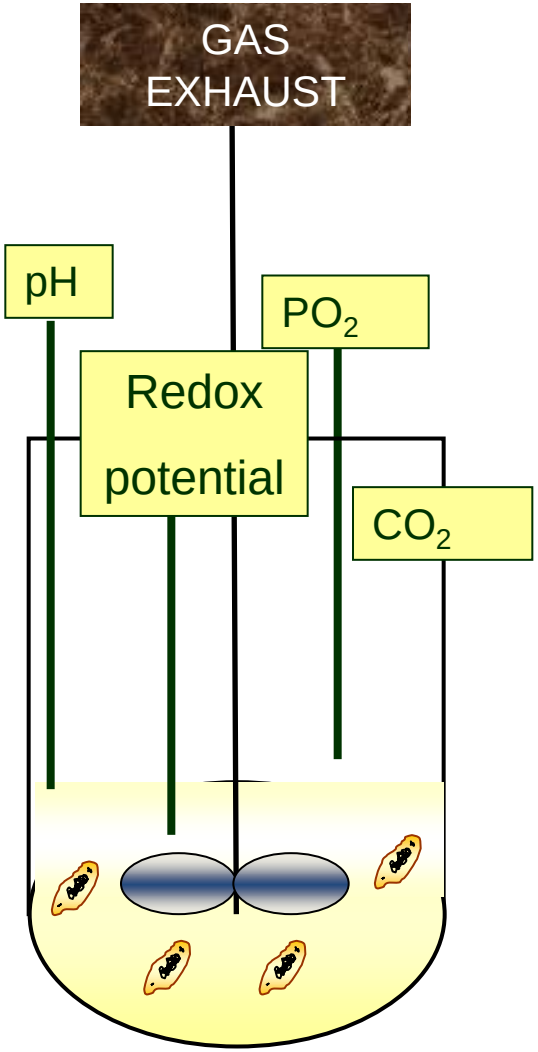
1. SERVICES, INSTRUMENTATION AND CONTROL



Analysis of chemical parameters

- **pH**. Measurement of electric potential. Calibration prior to sterilization. (deposits on the membrane), limited life time depending on {no. sterilizations, fermentation medium.
- **pO_2**. Dissolved oxygen probes: two electrodes and electrolyte separated from the medium by a membrane.

1. SERVICES, INSTRUMENTATION AND CONTROL



Analysis of chemical parameters

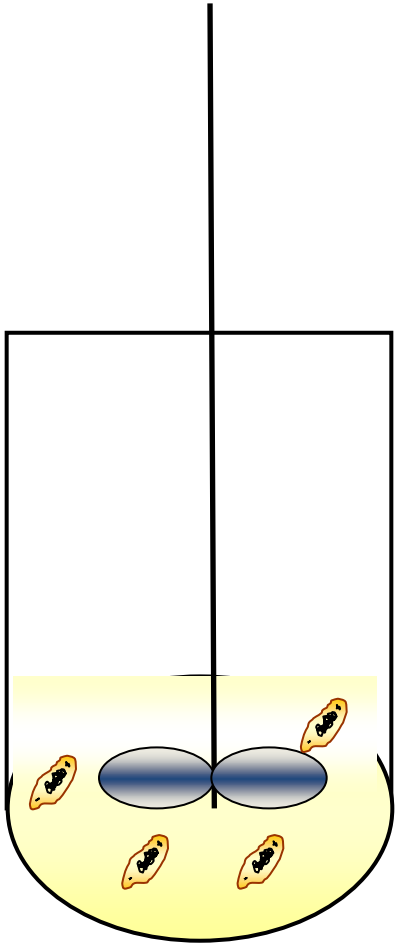
- **Dissolved CO_2** Technique based on pH measurement. [CO_2] proportional to [H^+]
- **Redox potential.** Redox potential probes. Difficulties in the analysis.
- **Output gases.** In the industry:

  Paramagnetic analyzer (0_2)

  Infrared detector (CO_2).

  Mass spectrometry ➔ volatile components of medium, operates for long periods of time and is fully automated.

1. SERVICES, INSTRUMENTATION AND CONTROL

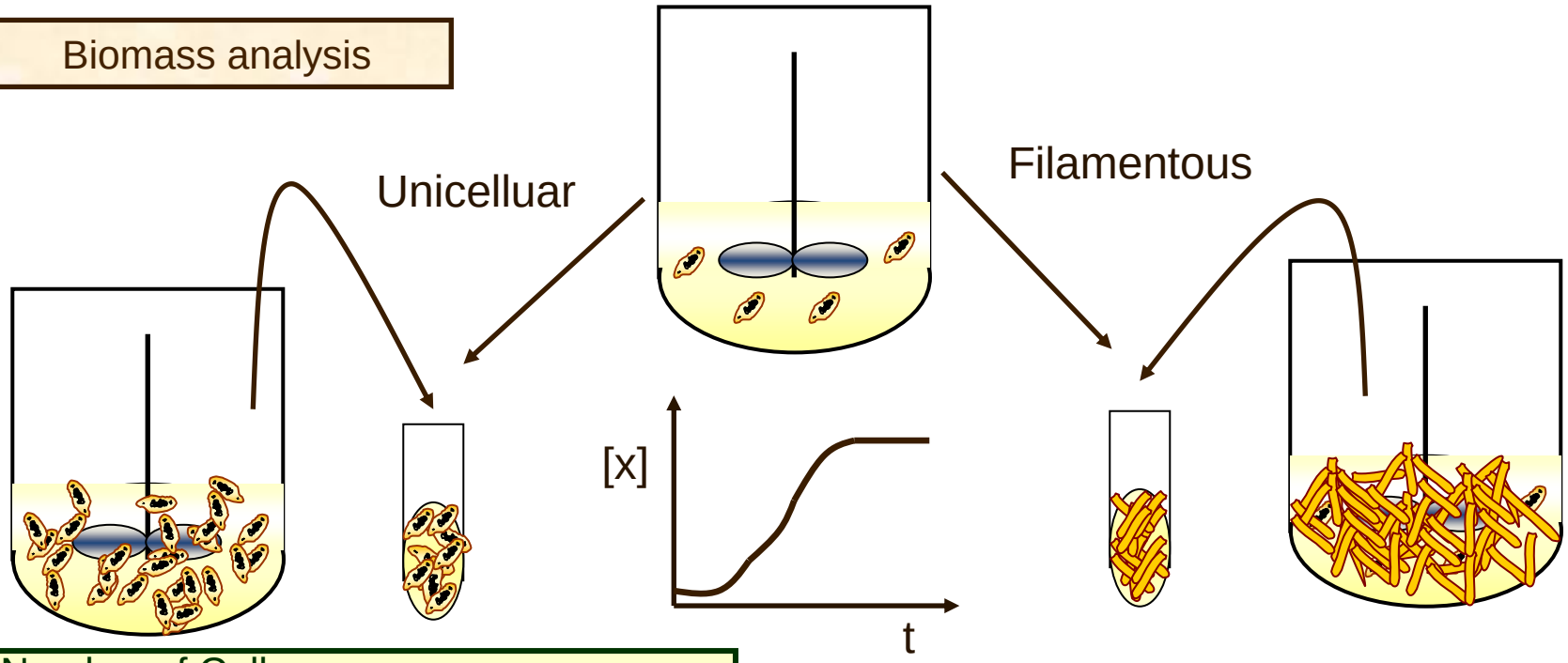


Analysis of hydrodynamic parameters

- Average speed
- Turbulence in the continuous phase
- Bubble size distribution
- Speed of the dispersed phase
- Relationship between gas volume and total volume (liquid + gas)
- Mixture of phases and transfers of matter between them.
- MEASUREMENTS: Anemometers based on Doppler effect (Doppler laser).

1. SERVICES, INSTRUMENTATION AND CONTROL

Biomass analysis



Number of Cells:

- Microscope counting
- Electronic counting

Concentration (g / L):

- Dry weight
- Turbidimetry (in situ)

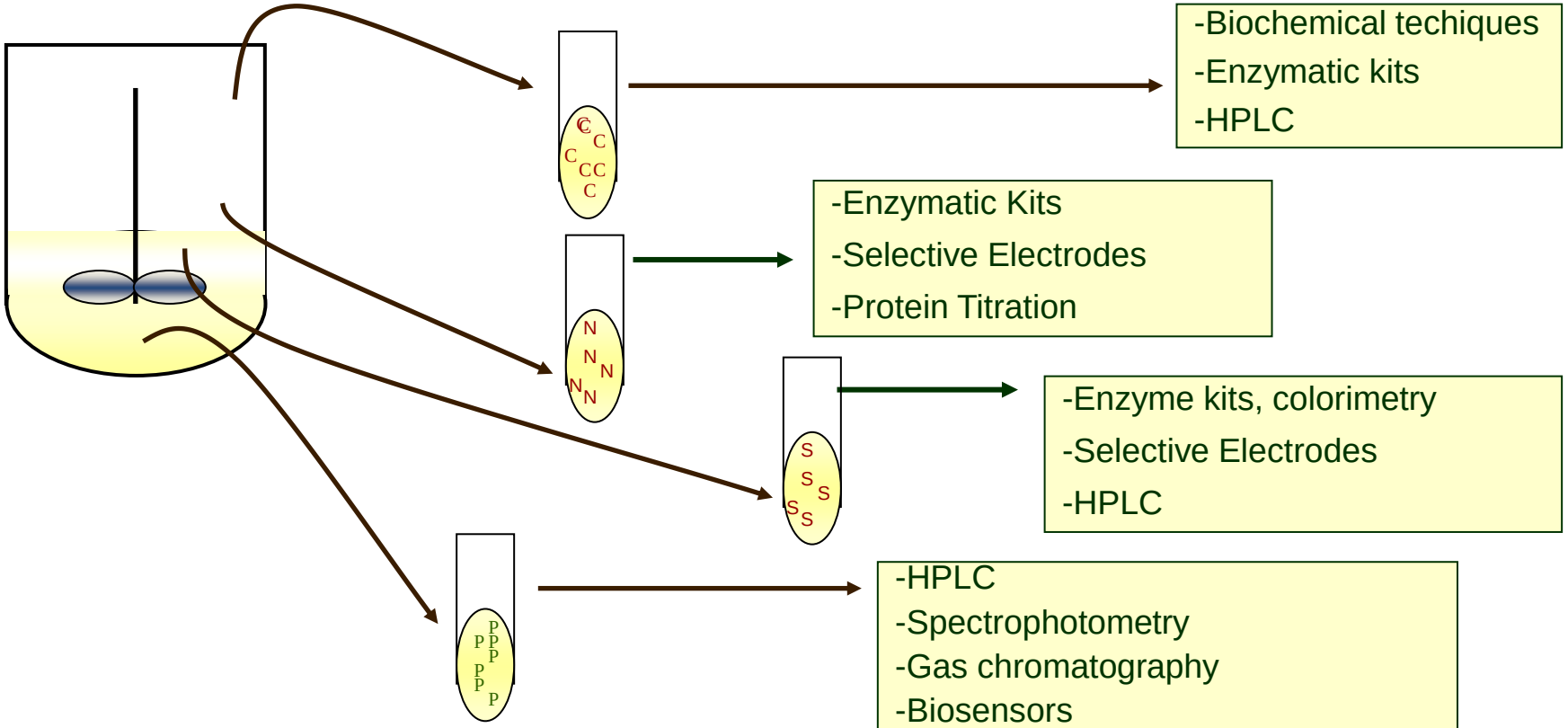
Only concentration (g / L):

- Dry weight
- Indirect measures:
- NADH
- Proteins
- ATP

1. SERVICES, INSTRUMENTATION AND CONTROL

SUBSTRATES:
- Carbon source
- Nitrogen source
- Sulphur source

PRODUCTS:
- Different chemical nature



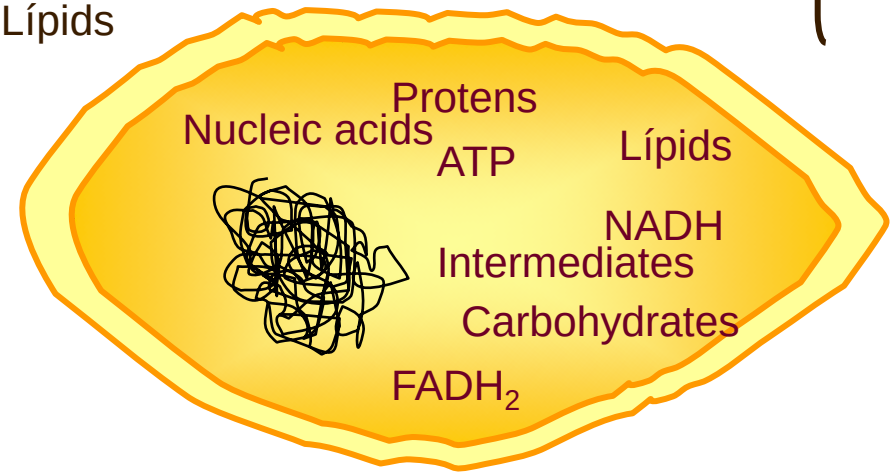
1. SERVICES, INSTRUMENTATION AND CONTROL

Analysis of cellular constituents

- Knowledge of microorganism metabolism.
- Development of Complex Kinetic Models

STRUCTURAL
- Proteins
- Nucleic acids
- Carbohydrates
- Lípids

FUNCTIONAL
- ATP
- Metabolic intermediates
- Cofactors: NADH, $FMNH_2$



1.- SERVICES, INSTRUMENTATION AND CONTROL

2.- AUXILIARY SERVICES

3.- CONTROL SYSTEMS

4.- TYPES OF CONTROL

2.- AUXILIARY SERVICES

Universidad Francisco de Vitoria
UFV Madrid

2. AUXILIARY SERVICES

Every service not strictly belonging to the bioprocess, but being necessary for its proper functioning:

- Electricity (KWh, Voltage, Frequency, Phases)
- Fuels (Type, quantities)
- Steam (Pressure, Temperature, Flow)
- Air (Pressure, Temperature, Quantity, Humidity)
- Security
- Dining rooms for staff
- Medical services
- …

1.- SERVICES, INSTRUMENTATION AND CONTROL

2.- AUXILIARY SERVICES

3.- CONTROL SYSTEMS

4.- TYPES OF CONTROL

3.- CONTROL SYSTEMS

SERVICES, INSTRUMENTATION AND CONTROL

Universidad Francisco de Vitoria UFV Madrid

3. CONTROL SYSTEMS

Set of components that can regulate **their own behavior or the way another system behaves** in order to achieve **the right operation**, so that the **probabilities of failures are reduced** and the **desired results are obtained**.

Set of elements that interact to **get the output of a process behaved as desired**, through a control action.

O**BJECTIVE: maintenance of a variable, within a certain value.**

3. CONTROL SYSTEMS

It is the **action or the effect** of being able to **decide on the development** of a process or system.

It is the way to **manipulate certain variables** to get them or other variables **to act in the desired way**.

3. CONTROL SYSTEMS

Aims:

- Reduction of the variability of a process.
- Improvement of productivity
- Quality improvement.
- Waste reduction.
- Avoid risks to operators.
- Improvement of the security of personnel, facilities and neighbors.

3. CONTROL SYSTEMS

Controlled Variables:

Are those variables whose value need to be known over time, and are usually used as indicator of quality of the product, or the level of production.

Manipulated Variables:

Are those that can be modified during the operation of the process, so that the controlled variables follow a certain way.

3. CONTROL SYSTEMS

Set Point:

Desired value of the controlled variable.

This variable may be constant or may vary over time

Disturbance:

Physical agent, alien to the process and random, which affects the controlled variable.

1.- SERVICES, INSTRUMENTATION AND CONTROL

2.- AUXILIARY SERVICES

3.- CONTROL SYSTEMS

4.- TYPES OF CONTROL

4.- TYPES OF CONTROL

Universidad Francisco de Vitoria
UFV Madrid

4.- TYPES OF CONTROL

Depending on the treatment that the control system performs using the output signal, two general control topologies can be distinguished:

- **open loop systems**
- **closed loop systems**

Open loop

The controlled parameter **is not measured** by the control system.

Closed loop

The controlled parameter **is measured** and fed back to the control system.

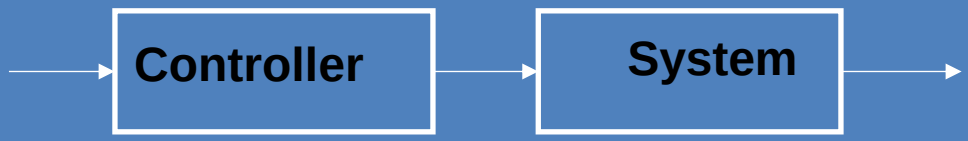
4.- TYPES OF CONTROL

Open-loop control

The **output has no effect on the control action**.

The output is not compared with any reference, therefore each input will correspond to a preset operation on the output signal.

Open-loop



The output has no effect on the control action.

4.- TYPES OF CONTROL

Open-loop control

ADVANTAGES

- Easy to implement
- Simple
- Economic

DISADVANTAGES

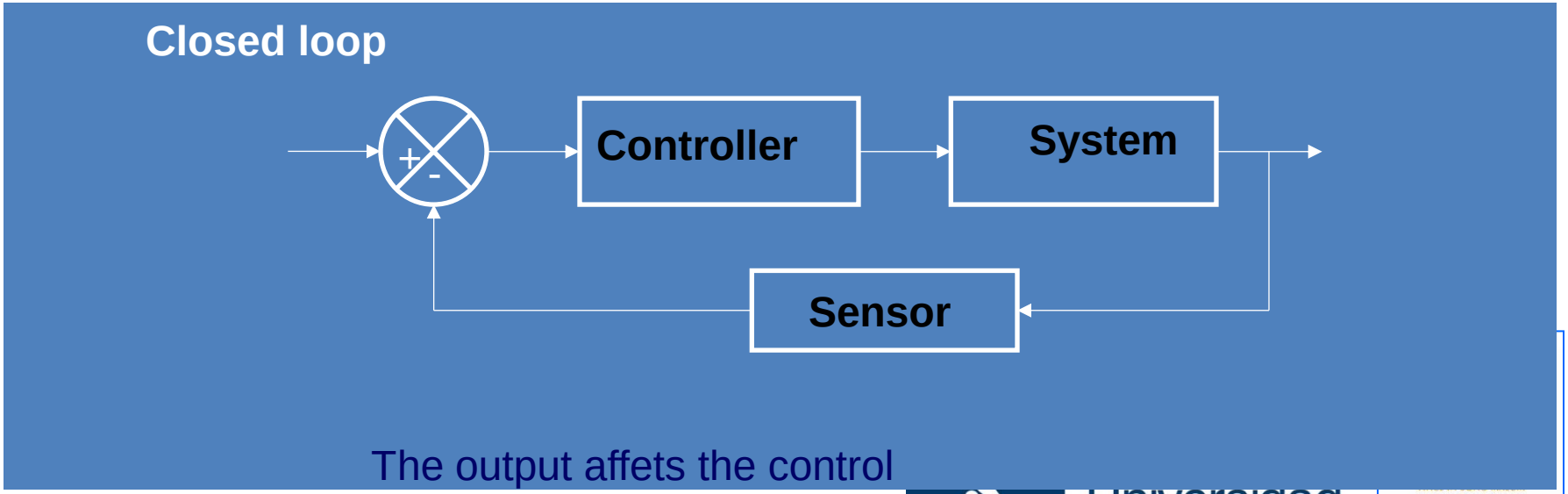
- If there is an error in the output, the control does not compensate it.
- If there are disturbances, the control does not compensate them.
- The effectiveness depends on the calibration.
- You need Accurate components.

4.- TYPES OF CONTROL

Closed-loop control:

The **output affect the control action**, whicht is called **feedback**.

The controlled signal must be **fed back and compared with the set point**, in order to correct the error or deviation that may exist.



4.- TYPES OF CONTROL

Closed-loop control

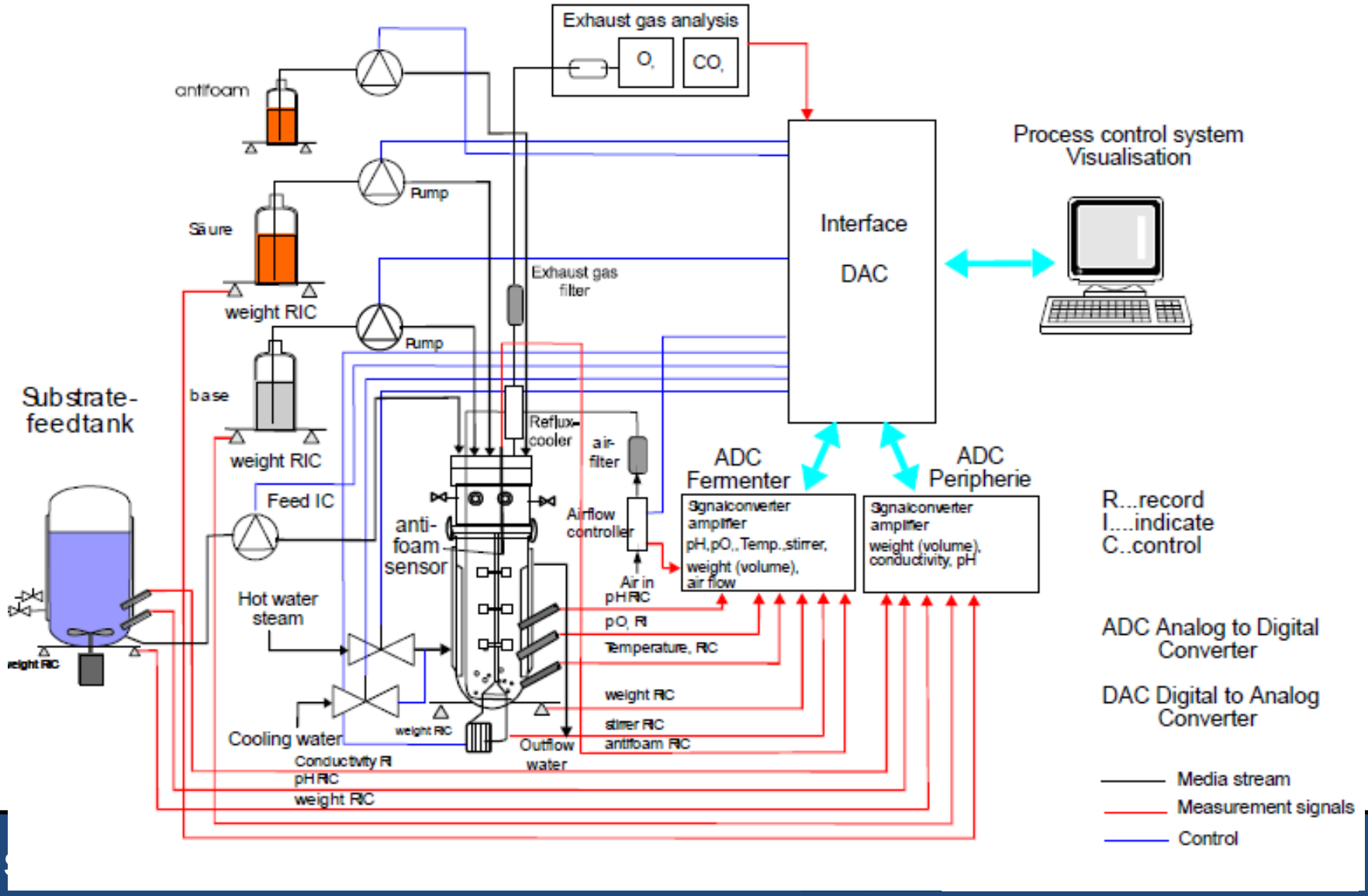
ADVANTAGES

- If there is an error in the output, the control makes up for it.
- If there are disturbances, the control compensates them.
- You can use inaccurate and cheap components.

DISADVANTAGES

- Sometimes complicated to implement.
- It needs more components than an open-loop control.
- Higher use of power
- Sensors may not be cheap.

Fermentation process monitoring and control



SECTION II: KINETICS AND BIOREACTOR DESIGN:

LESSON 15. - Services, instrumentation and control

JAVIER CALZADA FUNES

Biotechnology Department, Biosciences School

UNIVERSIDAD FRANCISCO DE VITORIA