Bioprocess examples : from yeast to ... yeast

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Content

- Food engineering
- Plant growth
- Waste & water treatment
- Biopolymers
- Enzymes
- Pharmacy

Food Engineering

4 classes of processes :

1. Bioconversion
2. Separation and purification :
   (micro-)filtration, evaporation, drying, extraction, distillation,...
3. Preservation processes :
   thermal treatment, smoking, salting, freeze-drying,...
4. Structuring processes :
   extrusion, emulsification, crystallisation,...

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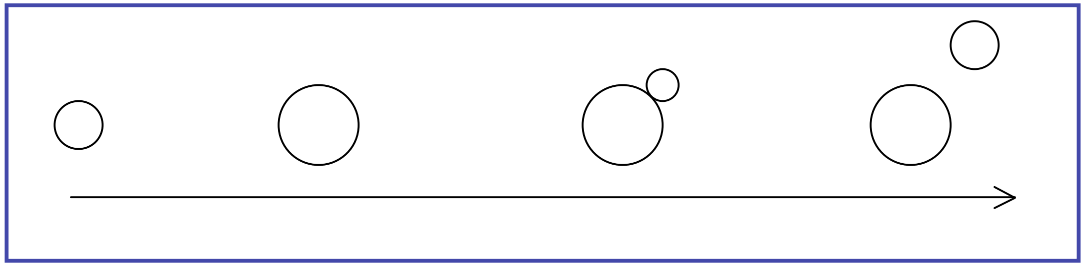
Example #1 : yeast growth



Budding (mother - daughter)

Example : Yeast growth

1. Respirative growth on glucose

$$S + C \rightarrow X + P$$

2. Fermentative growth on glucose

$$S \rightarrow X + E + P$$

3. Respirative growth on ethanol

$$C + E \rightarrow X + P$$

4. Maintenance

$$S + C \rightarrow P$$

S : glucose, C : oxygen, X : yeast, P :CO_2, E : ethanol

Example : Yeast growth

Two partial models

1. Oxygen reductive regime (RF)

$$\frac{d\xi}{dt} = K_{RF}\rho_{RF} - D\xi + F - Q$$

$$\xi = \begin{pmatrix} S \\ C \\ X \\ P \\ E \end{pmatrix} \qquad K_{RF} \begin{pmatrix} -k_1 & -k_2 & -k_{10} \\ -k_3 & 0 & -1 \\ 1 & 1 & 0 \\ k_5 & k_6 & k-11 \\ 0 & k_8 & 0 \end{pmatrix} \qquad \rho_{RF} = \begin{pmatrix} \mu_0 X \\ \mu_r X \\ q_m X \end{pmatrix}$$

2. Respirative regime (RF)

$$\frac{d\xi}{dt} = K_R\rho_R - D\xi + F - Q$$

$$K_R \begin{pmatrix} -k_1 & -k_2 & -k_{10} \\ -k_3 & -k_4 & -1 \\ 1 & 1 & 0 \\ k_5 & k_7 & k-11 \\ 0 & k_9 & 0 \end{pmatrix} \quad \rho_R = \begin{pmatrix} \mu_0 X \\ \mu_e X \\ q_m X \end{pmatrix}$$

- Measured components : ethanol, dissolved oxygen, CO_2
  But not independent

  $$\rightarrow \text{ dissolved oxygen and} CO_2$$

- Estimation of 2 kinetic parameters :
  1) Oxydo reductive regime : μ_0 and μ_r
  2) Respirative regime :μ_0 and μ_e

- q_m known (experimentally determined)

Dynamical equations of the measured components (RF regime) :

$$\begin{aligned}\frac{dC}{dt} &= -DC - k_3\mu_0 X - q_m X - Q_1\\ \frac{dP}{dt} &= -DP = k_6\mu_r X + k_{11} q_m X - Q_1\end{aligned}$$

Transformation : $\psi = K_U^{-1}\xi$

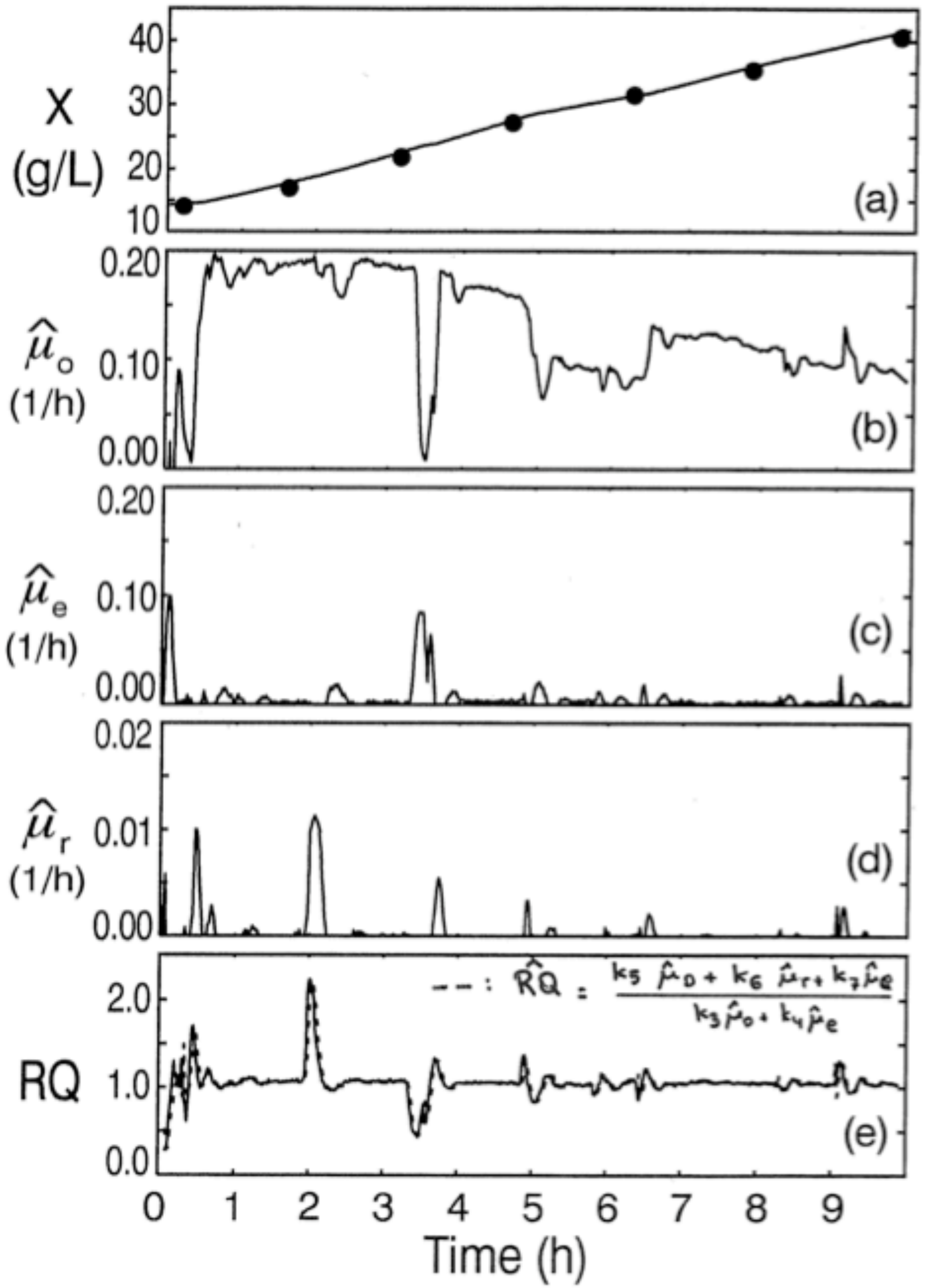
$$K_U = \begin{pmatrix} -k_3 & 0 \\ k_5 & k_6 \end{pmatrix} \rightarrow \begin{cases} \psi_1 = -\frac{1}{k_3} C \\ \psi_2 = -\frac{k_5}{k_3 k_6} C + \frac{1}{k_6} P \end{cases}$$

Observer-based estimator :

$$\left\{\begin{array}{lcl}\dfrac{d\hat{\psi}_1}{dt} & = & +\hat{\mu}_0 X - D\psi_1 + \dfrac{1}{k_3} q_m X - \dfrac{1}{k_3} Q_{in} + \omega_1(\psi_1 - \hat{\psi}_1) \\ \dfrac{d\hat{\mu}_0}{dt} & = & \dfrac{\bar{\gamma}_1}{X}(\psi_1 - \hat{\psi}_1)\end{array}\right.$$

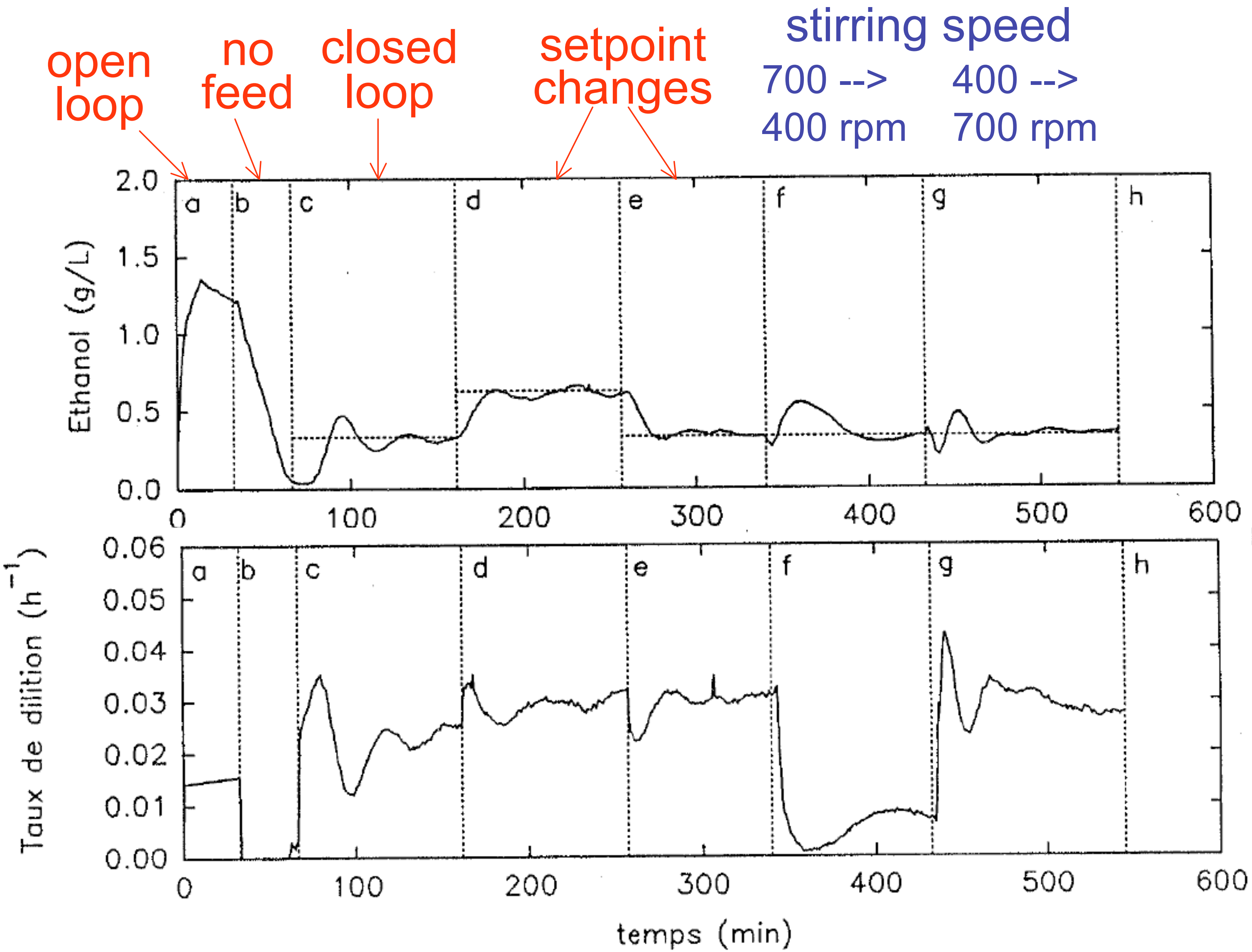
$$\left\{\begin{array}{lcl}\dfrac{d\hat{\psi}_2}{dt} & = & +\hat{\mu}_r X - D\psi_2 + \dfrac{1}{k_6} q_m X - \dfrac{1}{k_6} Q_1 + -\dfrac{k_5}{k_3 k_6} Q_{in} \omega_2(\psi_2 - \hat{\psi}_2) \\ \dfrac{d\hat{\mu}_r}{dt} & = & \dfrac{\bar{\gamma}_2}{X}(\psi_2 - \hat{\psi}_2)\end{array}\right.$$

Remark : X **given by an asymptotic observer**



X (g/L)
(a)
$\hat{\mu}_o$ (1/h)
(b)
$\hat{\mu}_e$ (1/h)
(c)
$\hat{\mu}_r$ (1/h)
(d)
RQ
(e)
$- - : \hat{RQ} = \frac{k_5 \hat{\mu}_o + k_6 \hat{\mu}_r + k_7 \hat{\mu}_e}{k_3 \hat{\mu}_o + k_4 \hat{\mu}_e}$
Time (h)

Example : yeast growth --> adaptive linearizing control



But yeast is also used in other food processes, like brewery and wine making

Example #2 : lactic fermentation

→Yoghurt production

- 2 bacteria :
  Lactobacillus bulgaricus and *Streptoccus thermophilus*

- Symbiosis between both micro-organisms when cultivated together :
  - *Streptococcus thermophilus* produces pyruvic and formic acid and CO_2 --> stimulates the growth of *Lactobacillus bulgaricus*
  - *Lactobacillus bulgaricus* produces peptides and aminoacids --> stimulates the growth of *Streptococcus thermophilus* (lower proteolytic activity)

- Stable association between *L. bulgaricus* and *S. thermophilus* : difficult and often unsuccessful process

On-line estimation of reaction rates

- Production of lactic acid (S) from lactose (P_3)
- Biomass (L. Bulgaricus) growth : negligible
- Reaction scheme :

galactose

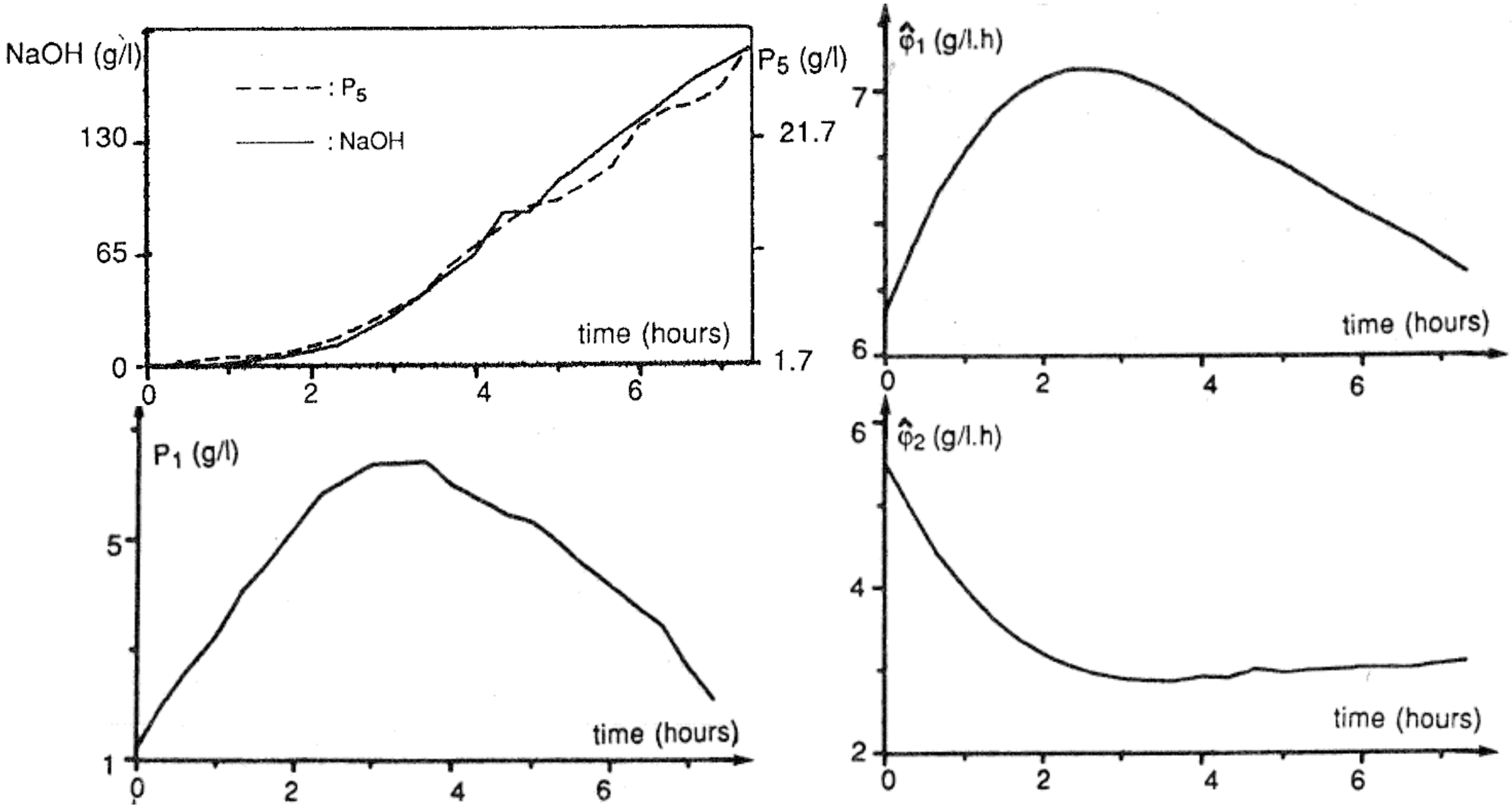
$$S \dashrightarrow k_1 P_1 + k_2 P_2$$
$$k_3 P_1 + X \dashrightarrow X + P_3$$

glucose

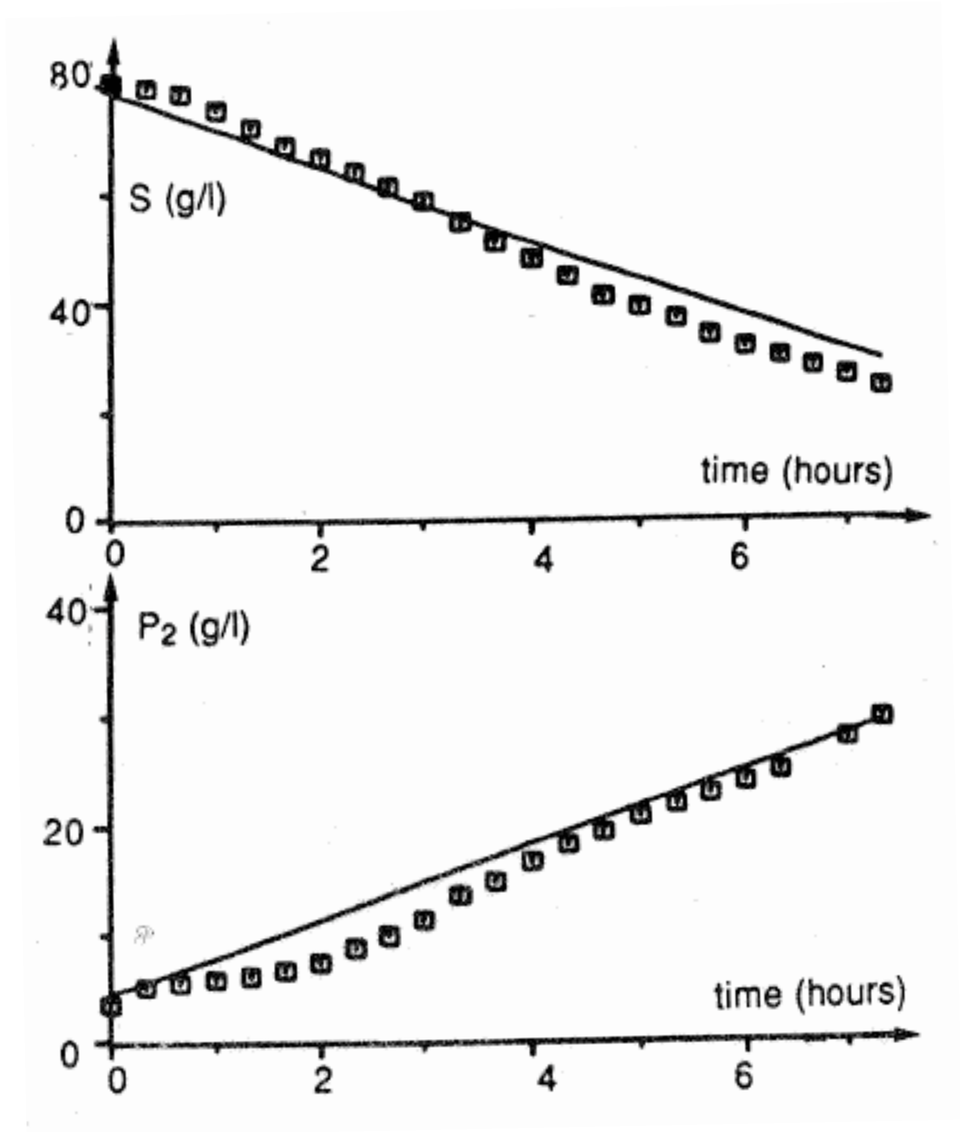
- Measurements : glucose (P_1) and lactic acid (P_2) (via NaOH)
- Remark : k_1, k_2, k_3 known (stoichiometry)

0.5 0.5 1

On-line estimation results



Validation on other variables (lactose (S) and galactose (P_2)



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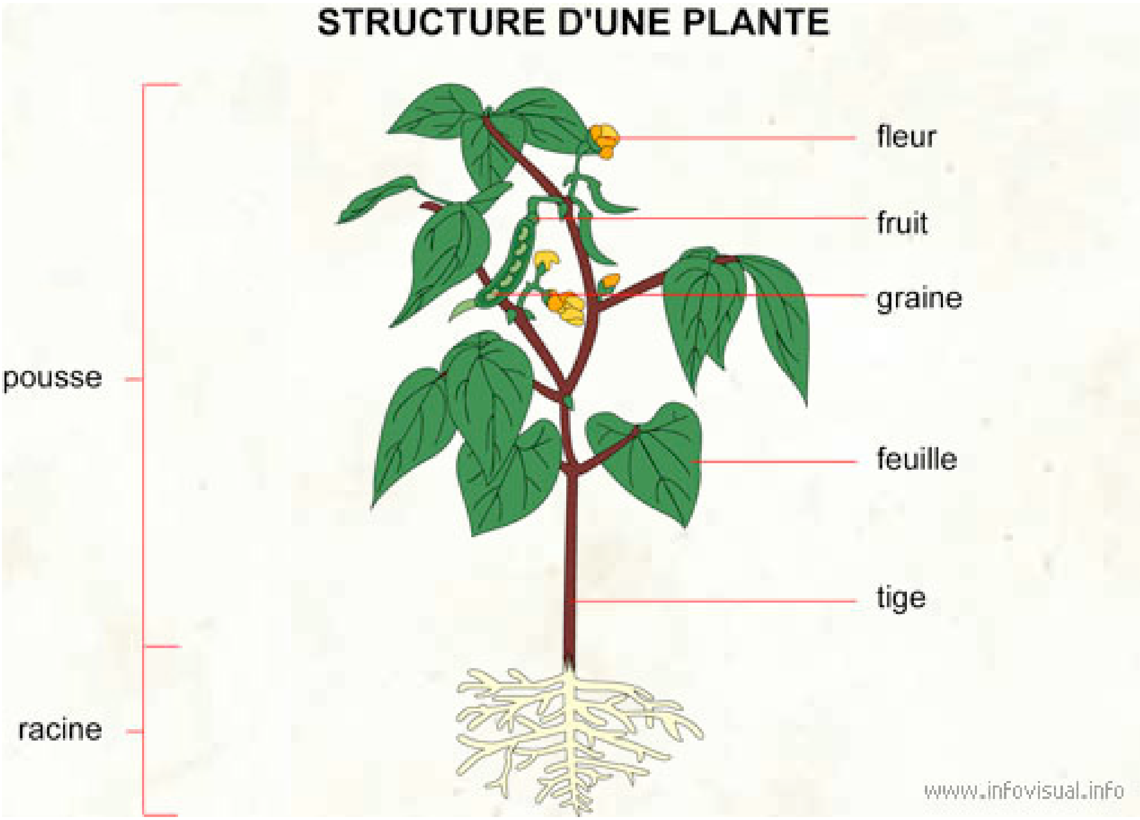
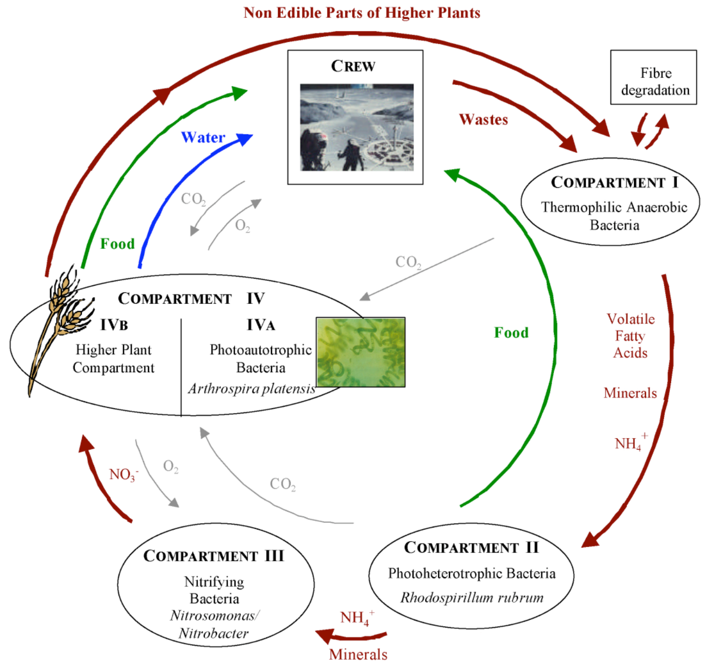
Example : plant growth

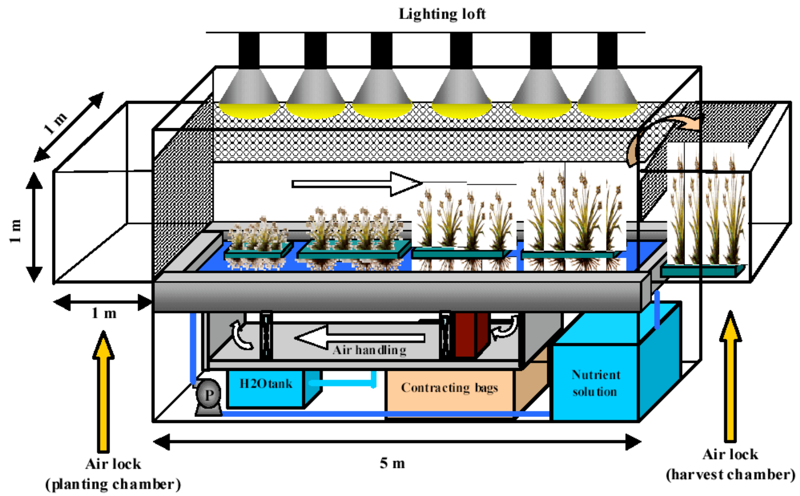


Main reactions : photosynthesis, (photo)respiration

- Context : MELISSA project (ESA)
  Objective : to have autonomous space stations, also in terms of food production



- Objective of the plant growth :
  to guarantee a sufficient constant production by using at best the available resources (nitrogen, carbon) while minimizing the energy consumption and the waste production

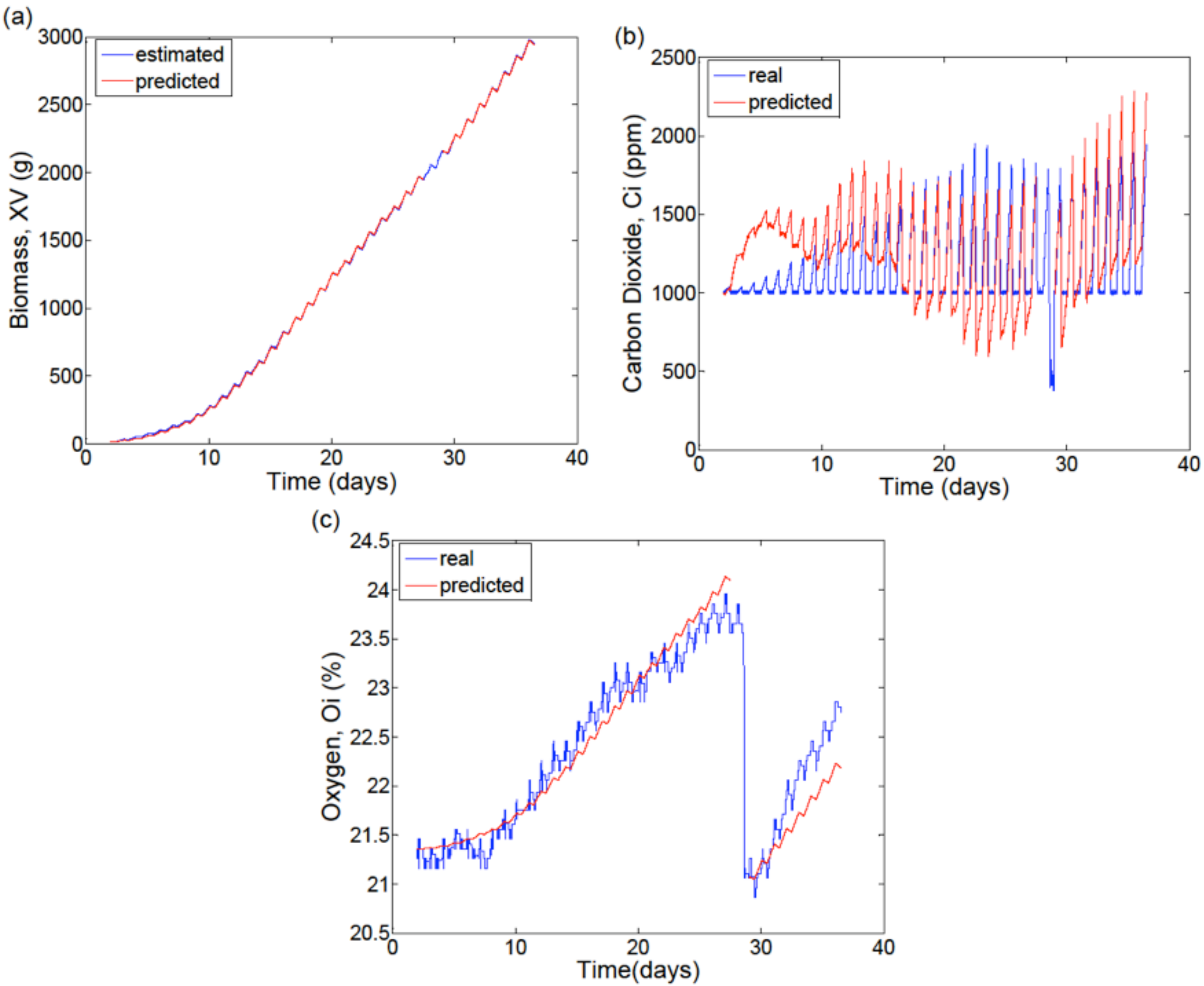


Modelling may not be a long quiet river...

- Constraints :
  - duration of the experiments
  - variability of the growth
  - diversity of elements (roots, shoot, leaves, flowers, fruits)
  - measurements (e.g., how to measure the biomass?)

- Choice of the model : simple or complex?

Experimental results (lettuce)



Waste and Water Treatment

- 2 major classes of waste :
  1) industrial waste
     - well known composition
     - potentially high toxicity
  2) municipal/domestic waste
     - diversified and varying composition
     - often low toxicity

- Waste treatment has a cost, rarely a benefit
  - the spreading of sewage sludge : more and more regulated
  - the exception : composting (domestic waste)

- Diverse Eurpean directives on waste treatment

Some examples

- Wastewater treatment
  - Activated sludge
  - Anaerobic digestion
  - Lagoons (Ponds)
- Solid waste treatment : composting
- Contaminated soil treatment
- Drinkable water treatment

Some examples

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Wastewater treatment : activated sludge

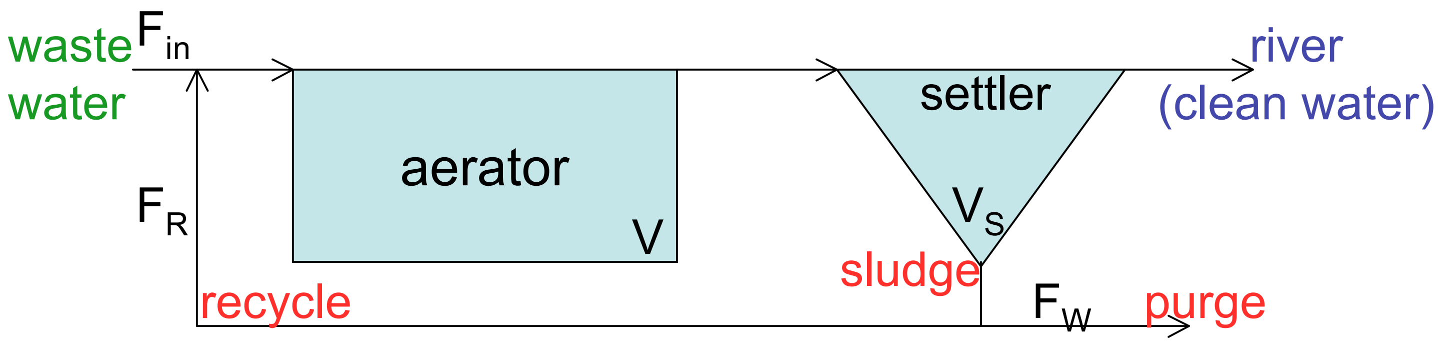
Wastewater treatment plant of Strasbourg

Montréal

Sart-Messire-Guillaume

Monstreux

Basic scheme



On-line estimation of biomass and substrate concentrations from the measurements of oxygen

Assumption : one biodegradation reaction : S + C --> X

- aerator : substrate S : $$\frac{dS}{dt} = \frac{F_{in}}{V} S_{in} - \frac{F_{in} + F_R}{V} S - k_1 \mu X$$

  oxygen C : $$\frac{dC}{dt} = k_L a \, (C_S - C) - k_2 \mu X - \frac{F_{in} + F_R}{V} C$$

  biomass X : $$\frac{dX}{dt} = \mu X - \frac{F_{in} + F_R}{V} X$$

- settler (biomass X_R) : $$\frac{dX_R}{dt} = \frac{F_{in} + F_R}{V_S} X - \frac{F_W + F_R}{V_S} X_R$$

Asymptotic observer

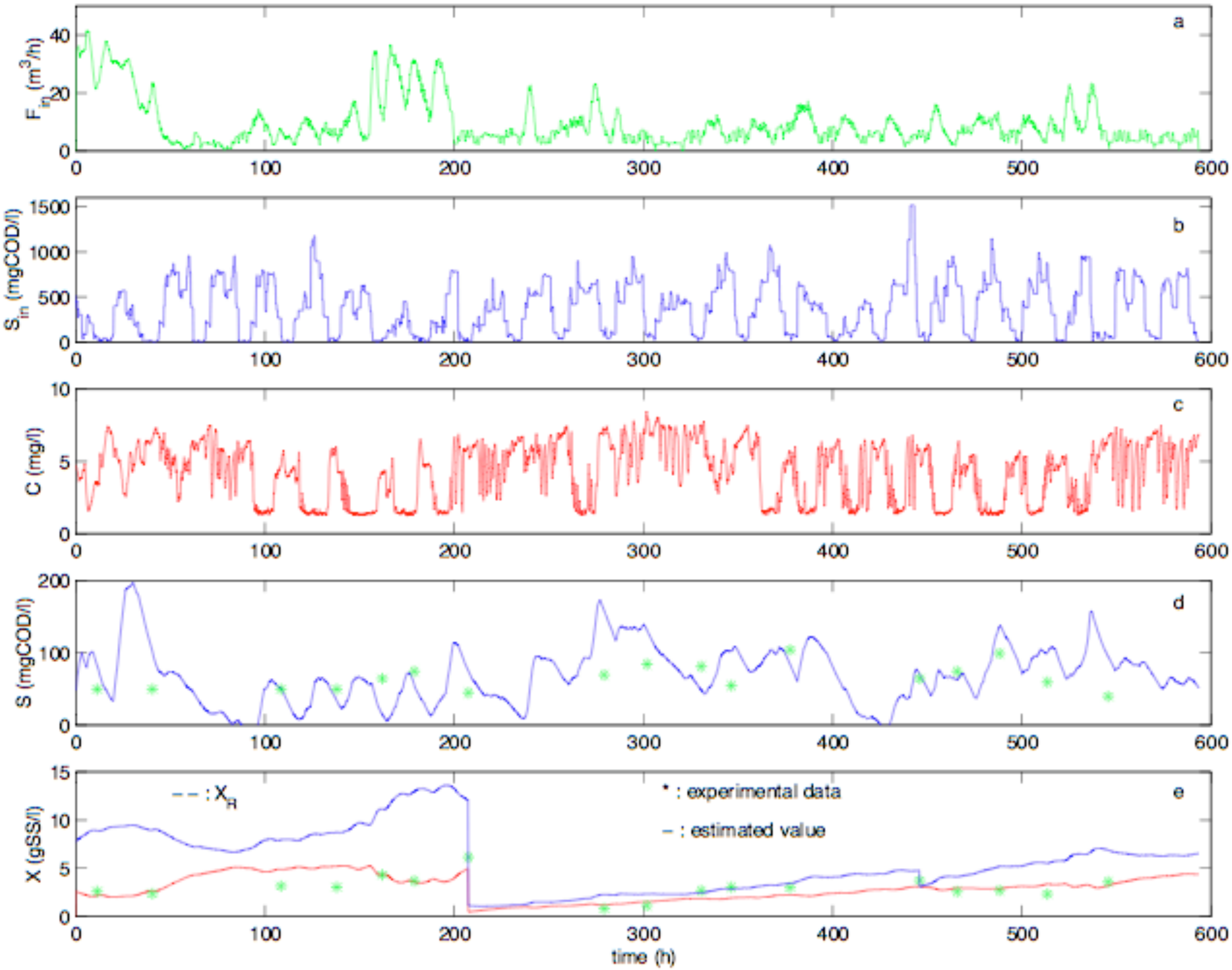
$$\frac{dZ_1}{dt} = \frac{F_{in}}{V} S_{in} - k_L a\,(C_S - C) - \frac{F_{in} + F_R}{V} Z_1$$

$$\frac{dZ_2}{dt} = k_L a\,(C_S - C) - \frac{F_{in} + F_R}{V} Z_2$$

$$S_e = Z_1 + \frac{k_1}{k_2} C$$

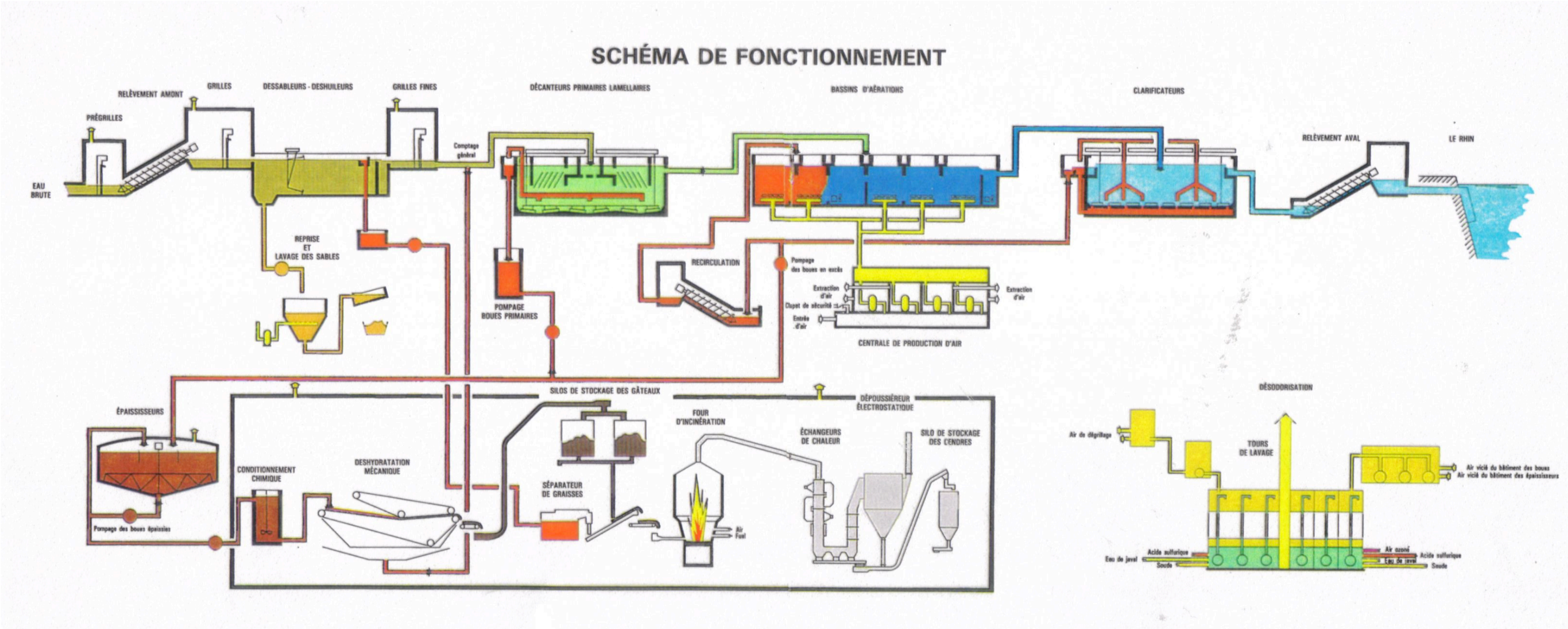
$$X_e = \frac{Z_2 - C}{k_2}$$

$$\frac{dX_{Re}}{dt} = \frac{F_{in} + F_R}{V_S} X_e - \frac{F_W + F_R}{V_S} X_{Re}$$



a
F_{in} (m^3/h)
b
S_{in} (mgCOD/l)
c
C (mg/l)
d
S (mgCOD/l)
e
X (gSS/l)
-- : X_R
* : experimental data
– : estimated value
time (h)

A wastewater treatment plant is a complex entity



Some challenges in the activated sludge process :

- appropriate use of methanol
- limitation of the sludge production
- stability of the micro-organisms in the settler and limitation of the formation of filamentous micro-organisms
- what about CO_2?

Appropriate use of methanol

- Context : denitrification
  --> addition of carbon

$$\text{dénitratation} \quad : \quad NO_3 + C \longrightarrow NO_2$$
$$\text{dénitritation} \quad : \quad NO_2 + C \longrightarrow N_2$$

- Important operating cost in a wastewater treatment plant

Sludge production

- Traditionally : spreading on fields (50 to 60%)
  (20-25% waste disposal et 15-20% incinerated)
- More and more restrictive legislation --> to avoid the concentration of toxic substances (heavy métals, organic compounds,...) in the soil and in food
  --> European directive 86/278
- Directive : defines the quality norms for having a sludge that can be spread --> determines the limit values for the concentrations in trace-elements (Cd, Cr, Cu, Hg, Ni, Pb, Zn) and organic trace-components (PCB, (benzo(b))fluoranthene, benzo(a)pyrene,...).
- Development of new technologies that allow to reduce the sludge production (including separation via membranes)

Stability of the micro-organisms in the settler and limitation of the formation of filamentous organisms

- 2 types of micro-organisms :
  1) flocs : high density --> settle
  2) filaments : low density --> poorly settle --> may be found at the outlet of the wastewater treatment plant

- Need to monitor (and possibly to control) the growth of filamentous micro-organisms

Some examples

- Wastewater treatment
  - Activated sludge
  - **Anaerobic digestion**
  - Lagoons (Ponds)
- Solid waste treatment : composting
- Contaminated soil treatment
- Drinkable water treatment

Anaerobic digestion

- Wastewater biological process + production of methane (CH_4)
- Complex process
  → simplified reaction scheme

1) acidogenesis : $S_1 \rightarrow X_1 + S_2 + P_2$

organic matter (S_1), acidogenic bacteria (X_1), CO_2 (P_2)

2) méthanisation : $S_2 \rightarrow X_2 + P_1 + P_2$

volatile fatty acids (S_2), methanogenic bacteria (X_2), CH_4 (P_1)

- Very old process (since more than 2000 years in China)
  (cfr also the cut grass pile)

- At the heart of the first oil crisis...
  ...but enormous problems of implementation (negative effect of the H_2S, for instance) and of process operation (instability due to organic overloads)
  + low yields

- Applications mainly to small installations (e.g. farms with energy supply for the lighting of the barn)

- Today : more and more in wastewater treatment plants
  --> allows to treat the hardly biodegradable organic matters

Application of modelling, monitoring and control

- Model identification (including experiment design and long term validation)
- On-line estimation of the process reaction rates
- Adaptive linearizing control of the organic matter concentration

Model identification
Case study : the AMOCO model

- Context : EC project AMOCO (Advanced MOnitoring and COntrol of the operation of wastewater treatment processes of the wood industry in order to improve the process efficiency)

- Process : anaerobic digestion in a fixed bed reactor

- Control objective : to maintain the process in stable conditions via the control of the alkalinity Z.

Dynamical model

Assumptions

- 35°C ≤ T ≤ 38°C, 6 ≤ pH ≤ 8
- $C = CO_2 + B$

inorganic carbon

bicarbonate

- Volatile fatty acids (acetate) S_2 and alkalinity Z

$$Z = B + S_2 = f_B(pH)C + S_2$$

with : $$f_B(pH) = \frac{K_b}{K_b + 10^{-pH}}$$

dissociation constant of CO_2

$$K_b = \frac{[H^+]B}{CO_2}$$

detachment rate

acidogenic bacteria
$$\frac{dX_1}{dt} = \mu_1 X_1 - \alpha D X_1$$

methanogenic bacteria
$$\frac{dX_2}{dt} = \mu_2 X_2 - \alpha D X_2$$

organic matter
$$\frac{dS_1}{dt} = D(S_{1in} - S_1) - k_1 \mu_1 X_1$$

volatile fatty acids
$$\frac{dS_2}{dt} = D(S_{2in} - S_2) + k_2 \mu_1 X_1 - k_3 \mu_2 X_2$$

alkalinity
$$\frac{dZ}{dt} = D(Z_{in} - Z)$$

inorganic carbon
$$\frac{dC}{dt} = D(C_{in} - C) - q_C + k_4 \mu_1 X_1 + k_5 \mu_2 X_2$$

CO_2 flow rate $$q_C = k_L a(C + S_2 - Z - K_H P_C)$$

CO_2 partial pressure $$P_C = \frac{\phi - \sqrt{\phi^2 - 4K_H P_T(C + S_2 - Z)}}{2K_H}$$

$$\phi = C + S_2 - Z + K_H P_T + \frac{k_6}{k_L a}\mu_2 X_2$$

CH_4 flow rate $$q_M = k_6 \mu_2 X_2$$

$$pH = -log_{10}\left(K_b \frac{C - Z + S_2}{Z - S_2}\right)$$

Specific growth rates

Monod $$\mu_1 = \frac{\mu_{max1} S_1}{K_{S1} + S_1}$$

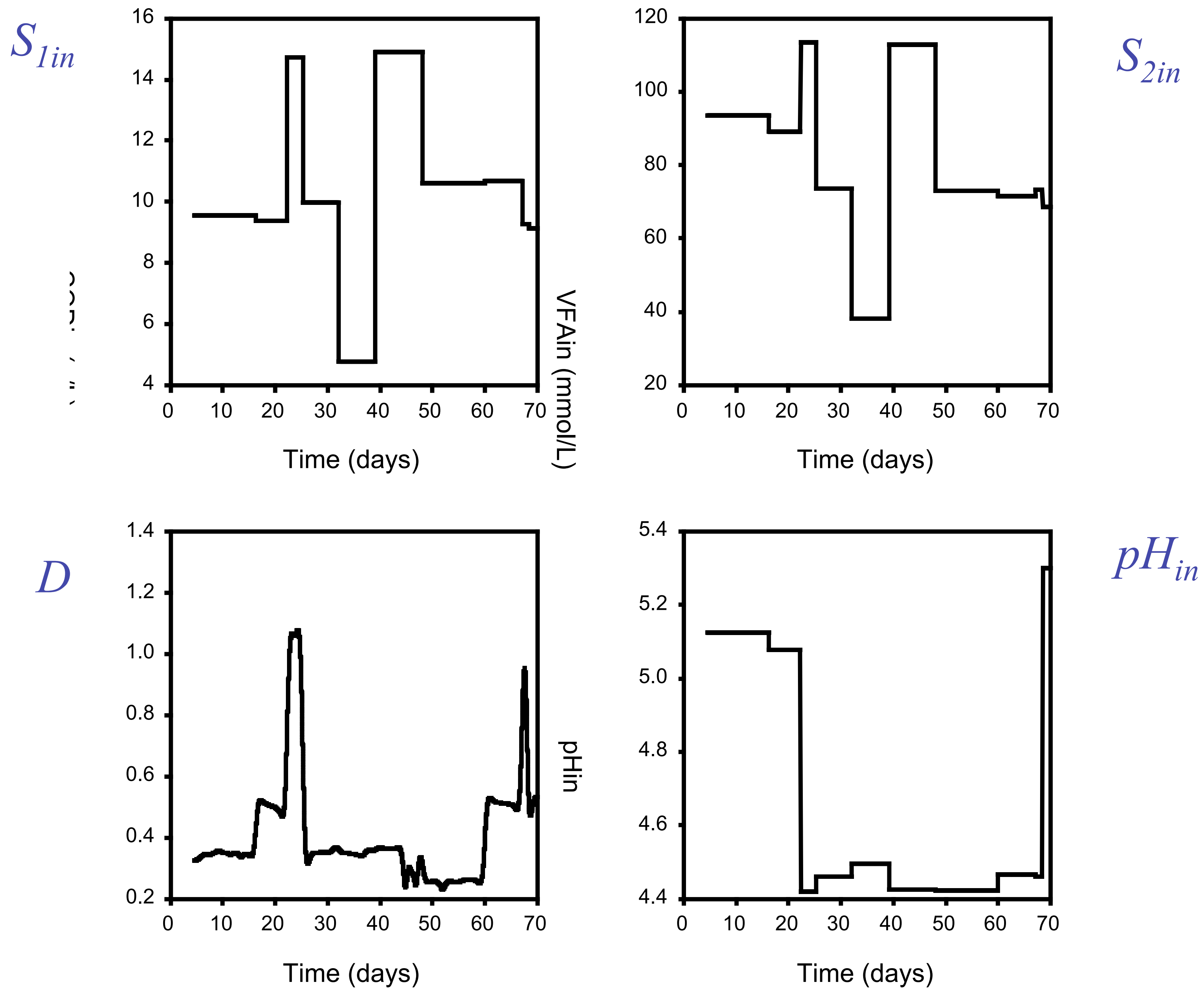
Haldane $$\mu_2 = \frac{\mu_0 S_2}{K_{S2} + S_2 + S_2^2/K_{I2}}$$

Experiment design

- Based on the practical constraints of the process and the time limitation of the process
- Unstable operation...

→admissible wide range of operation + expected unstable mode (large D and S_{in}) at the end

D (day^{-1})	S_{1in} (g COD/l)	S_{2in} (mmol/l)	pH_{in}
0.34	2.82	93.6	5.12
0.50	2.98	89.09	5.08
0.35	4.68	73.68	4.46
0.35	2.05	38.06	4.49
0.36	6.77	112.7	4.42
0.26	5.35	72.98	4.42
0.51	5.53	71.6	4.47
0.53	4.20	68.78	5.30



S1in
16
14
12
10
8
6
4
0 10 20 30 40 50 60 70
Time (days)
VFAin (mmol/L)
120
100
80
60
40
20
0 10 20 30 40 50 60 70
Time (days)
S2in
D
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0 10 20 30 40 50 60 70
Time (days)
pHin
5.4
5.2
5.0
4.8
4.6
4.4
0 10 20 30 40 50 60 70
Time (days)
pHin

Parameter Identification

- Available measurements : S_1 (COD), S_2, Z, C, $X_1 + X_2$ (VSS)
- Separation of the parameters (yield coefficients, kinetic parameters, transfer parameters)
- Calibration on the steady-state data (to improve steady-state performance of the model), validation on the transients

- Kinetic parameters

  Steady state biomass balance equations :

$$
\begin{aligned}
\frac{1}{D} &= \frac{\alpha}{\mu_{1\max}} + K_{S1}\frac{\alpha}{\mu_{1\max}}\frac{1}{\bar{S}_1} \\
\frac{1}{D} &= \frac{\alpha}{\mu_0} + K_{S2}\frac{\alpha}{\mu_0}\frac{1}{\bar{S}_2} + \frac{1}{K_{I2}}\frac{\alpha}{\mu_0}\bar{S}_2
\end{aligned}
$$

linear in the parameters $\frac{\alpha}{\mu_{1\max}},\ K_{S1}\frac{\alpha}{\mu_{1\max}},\ \frac{\alpha}{\mu_0},\ K_{S2}\frac{\alpha}{\mu_0},\ \frac{1}{K_{I2}}\frac{\alpha}{\mu_0}$

→least squares estimation

Only the ratio α/μ_{1max} is identifiable --> μ_{1max} from the literature

- Transfer coefficient $k_L a$

$$
\begin{aligned}
q_C &= k_L a(CO_2 - K_H P_C) \\
CO_2 &= \frac{C}{1 + K_b 10^{pH}}
\end{aligned}
$$

Parameter	**Units**	**Value**	**Standard deviation**
$\mu_{1\,\max}$	day^{-1}	1.2	
K_{S1}	g/l	7.1	5.0
μ_0	day^{-1}	0.74	0.9
K_{S2}	mmol	9.28	13.7
K_{I2}	mmol	16	17.9
α	/	0.5	0.4
k_La	day^{-1}	19.8	3.5

Yield coefficients

- In absence of measurements for X_1 and X_2, only ratios of yield coefficients (simple argument : rescaling of X_i ($X_i' = \lambda_i X_i$) compensated by rescaling of the yield coefficients : $k_i' = \lambda_1 k_i$ $(i = 1, 2, 4)$, $k_i' = \lambda_2 k_i$ $(i = 3, 5, 6)$

- Two steps
  1) calibration of the ratios $k_2/k_1,\ k_6/k_3,\ k_5/k_3,\ k_4/k_1$

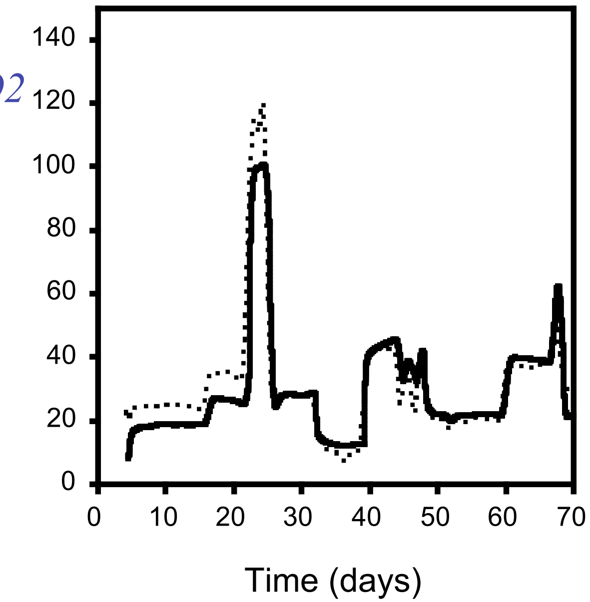
$$
\begin{aligned}
q_C &= D(C_{in} - C) + \left(\frac{k_4}{k_1} + \frac{k_2 k_5}{k_1 k_3}\right) D(S_{1in} - S_1) + \frac{k_5}{k_3} D(S_{2in} - S_2) \\
q_M &= \frac{k_2 k_6}{k_1 k_3} D(S_{1in} - S_1) + \frac{k_6}{k_3} D(S_{2in} - S_2)
\end{aligned}
$$

  2) VSS measurements (= X_1 + X_2) and assumption of the ratio of X_1 over X_1 + X_2 (0.2 from the literature)

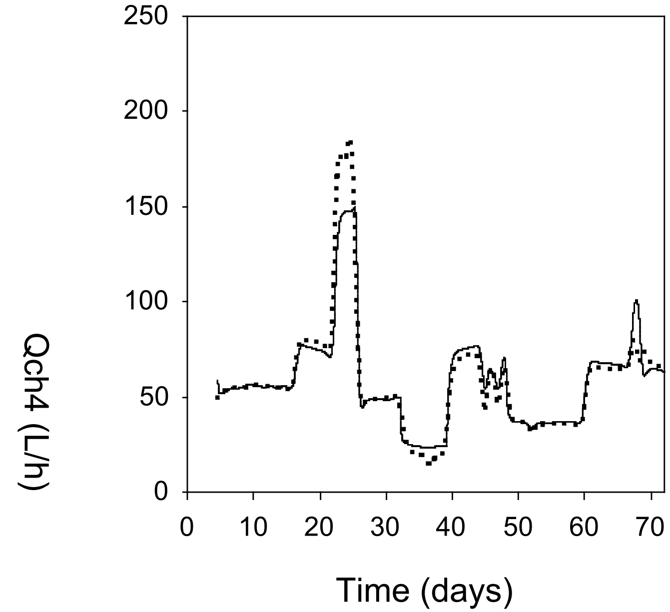
Ratio	**Units**	**Value**	**Standard deviation**
k_2/k_1	mmol/g	2.72	2.16
k_6/k_3	/	1.62	0.12
k_5/k_3	/	1.28	0.13
k_4/k_1	mmol/g	1.18	3.02

Parameter	**Units**	**Value**	**Standard deviation**
k_1	g S_1 /g X_1	42.14	18.94
k_2	mmol S_2 /g X_1	116.5	113.6
k_3	mmol S_2 /g X_2	268	52.31
k_4	mmol CO_2 /g X_1	50.6	143.6
k_5	mmol CO_2 /g X_2	343.6	75.8
k_6	mmol CH_4 /g X_2	453.0	90.9

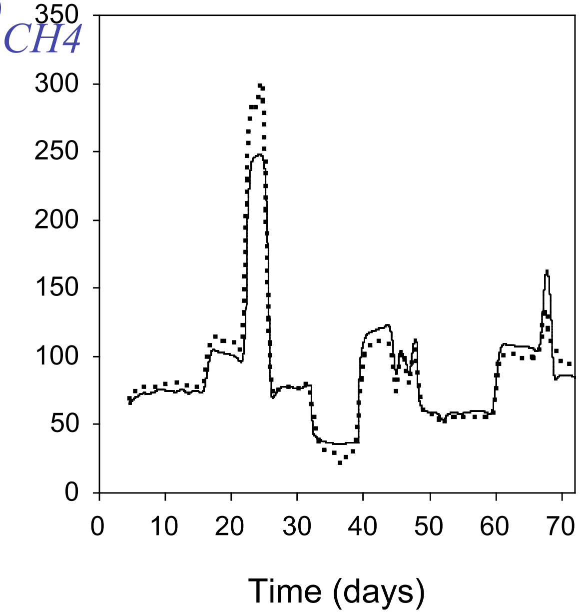
Q_{CO2}



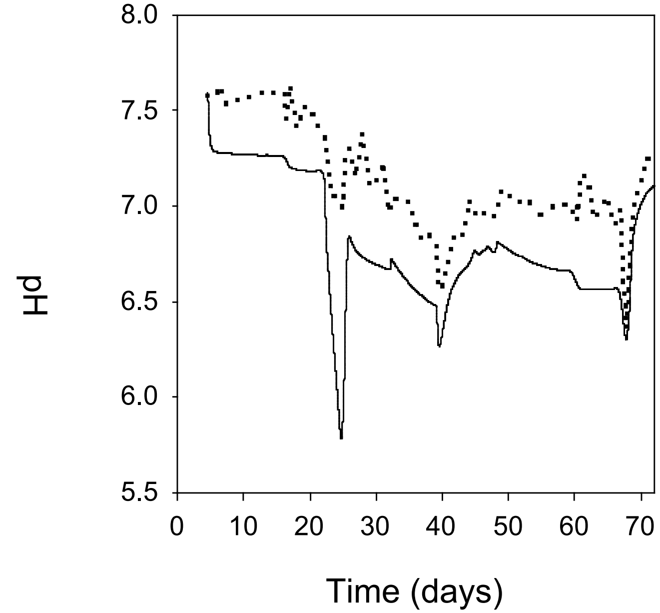
Q_{CH4}

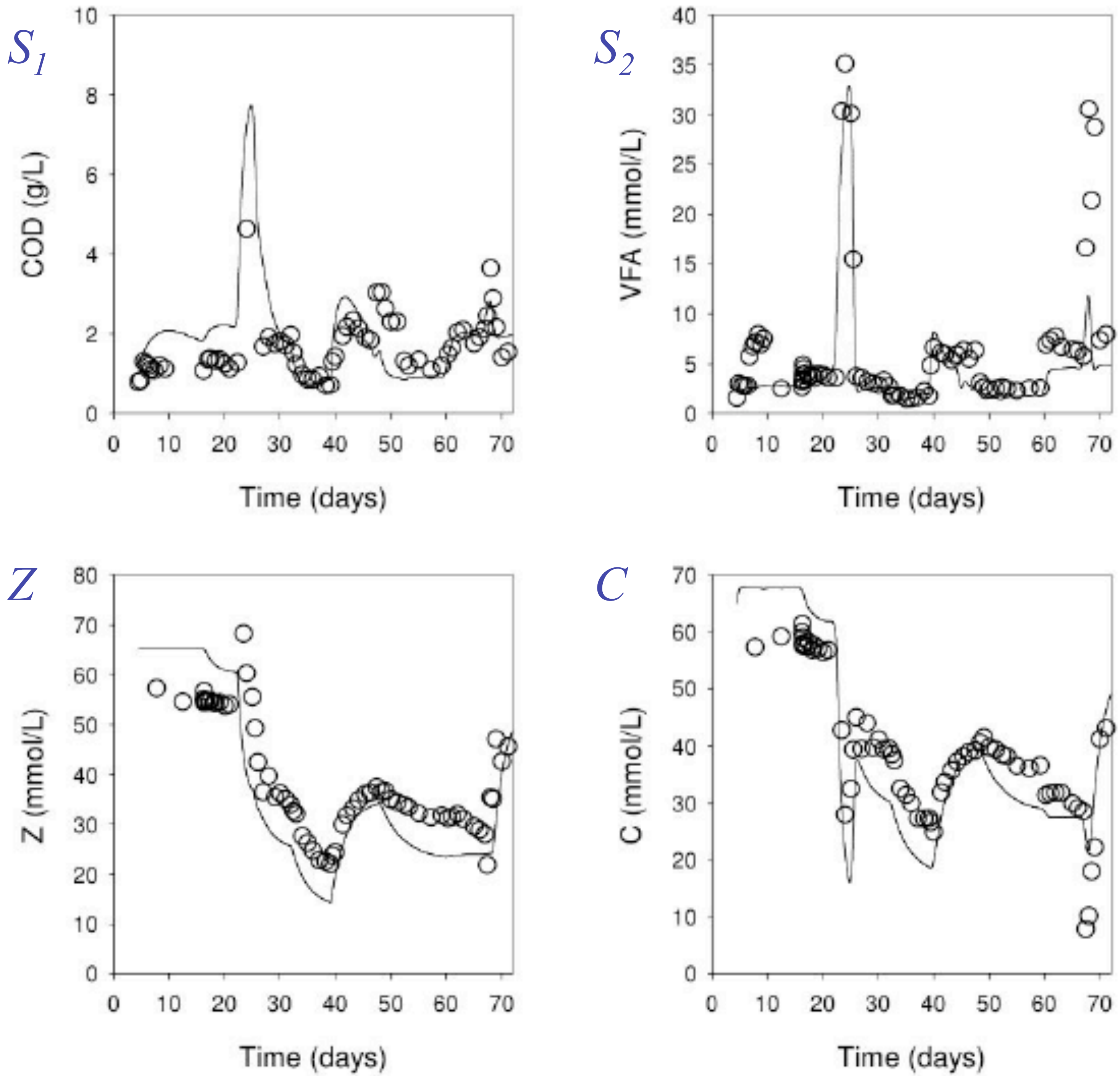


$Q_{CO2} + Q_{CH4}$

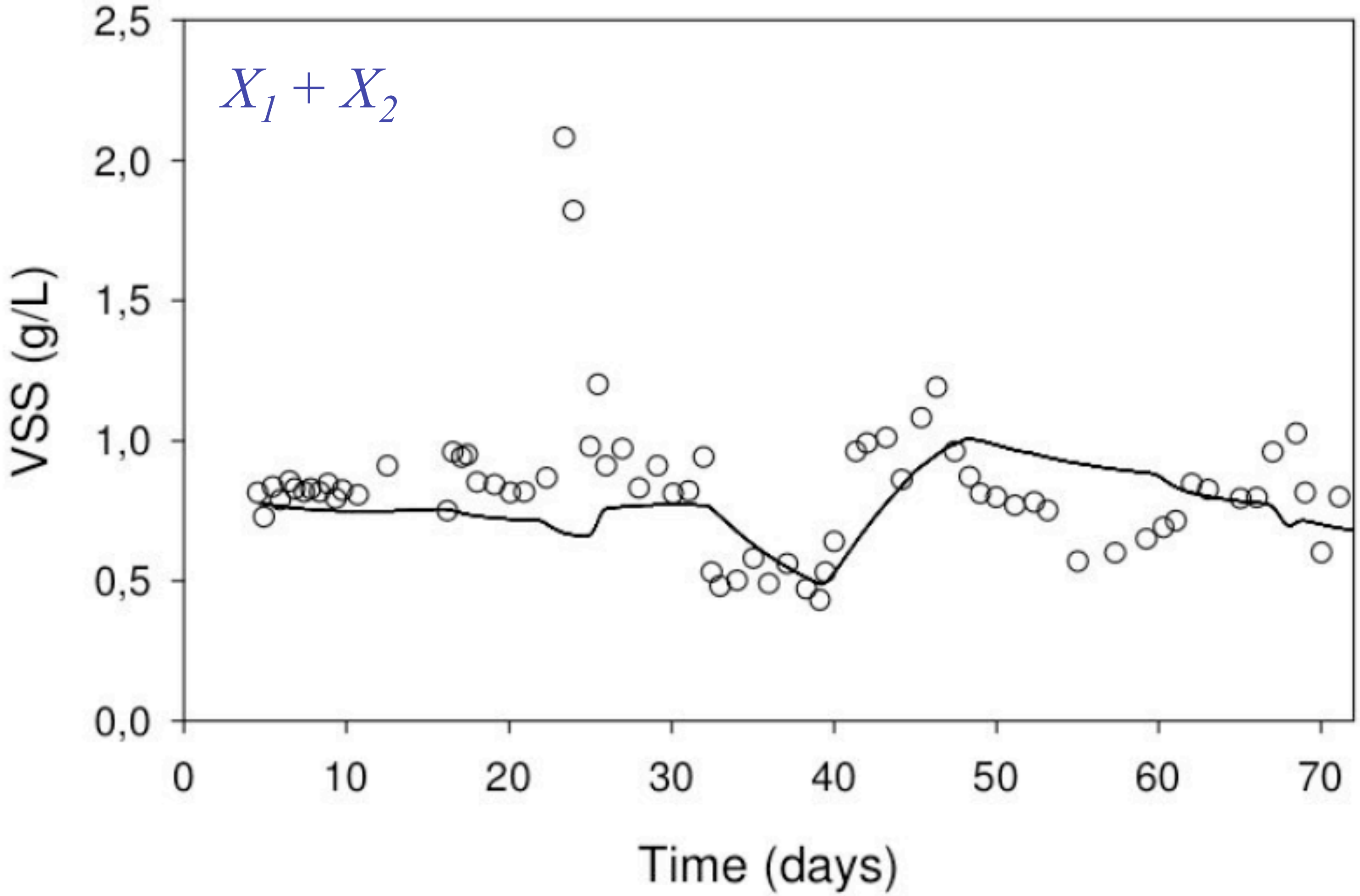


pH





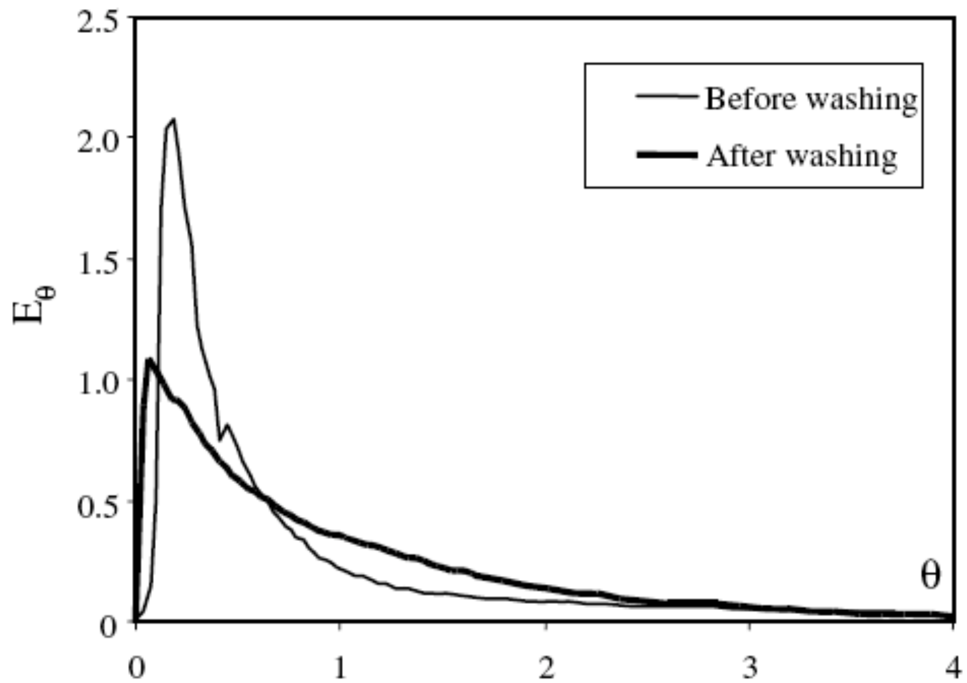
S1
COD (g/L)
Time (days)
S2
VFA (mmol/L)
Time (days)
Z
Z (mmol/L)
Time (days)
C
C (mmol/L)
Time (days)

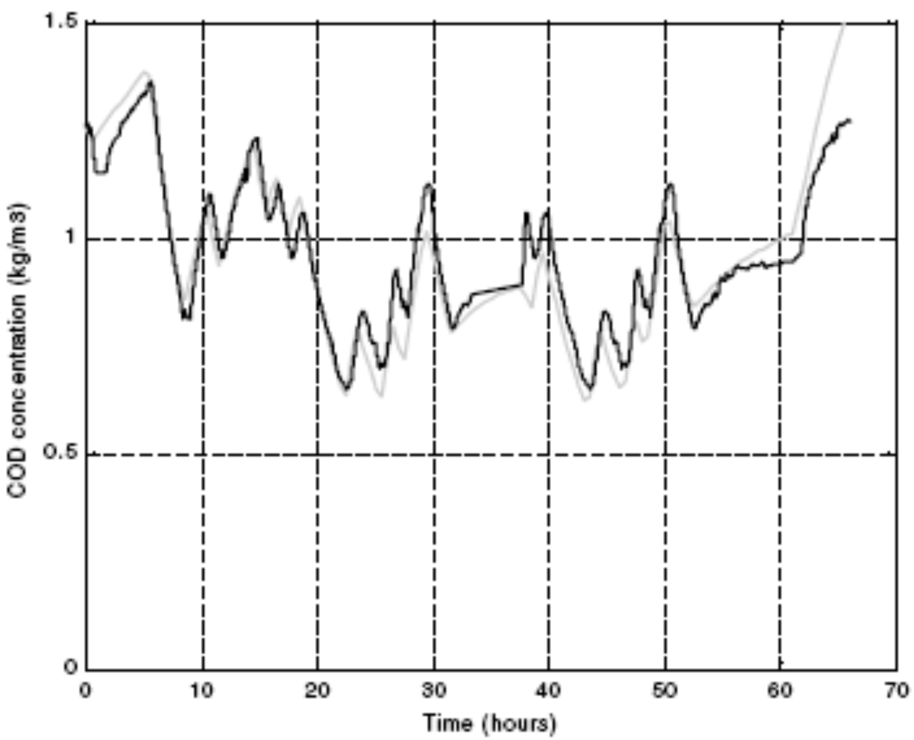


$X_1 + X_2$
VSS (g/L)
Time (days)
2,5
2,0
1,5
1,0
0,5
0,0
0
10
20
30
40
50
60
70

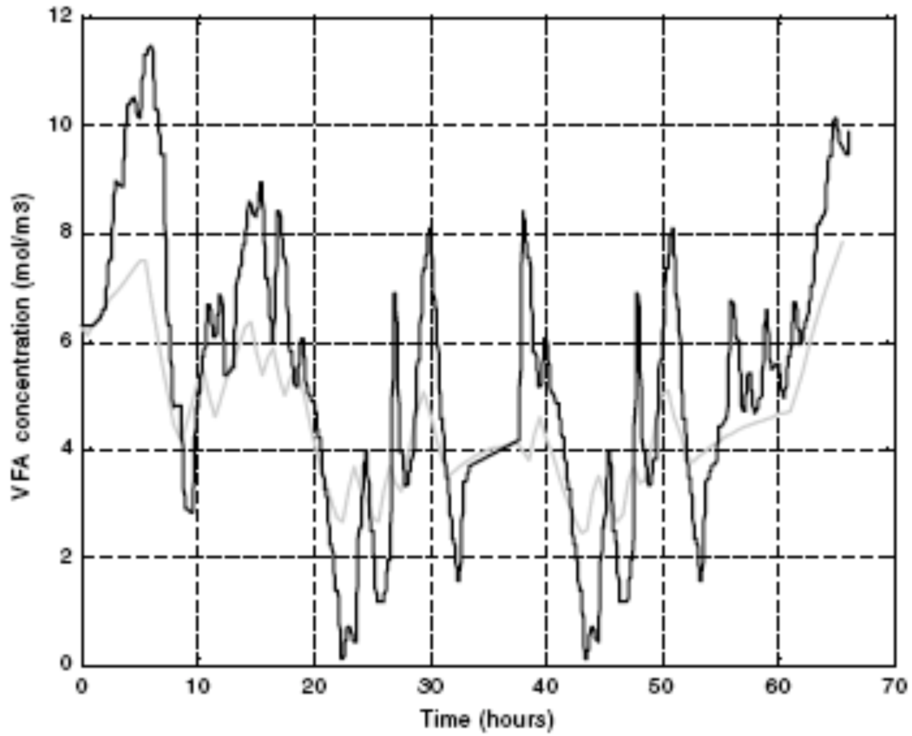
Long term validation

- Model still valid after a few years even if reactor clogging
- The only change : active volume V
- Confirmed by a tracer experiment and RTD (residence time distribution) analysis

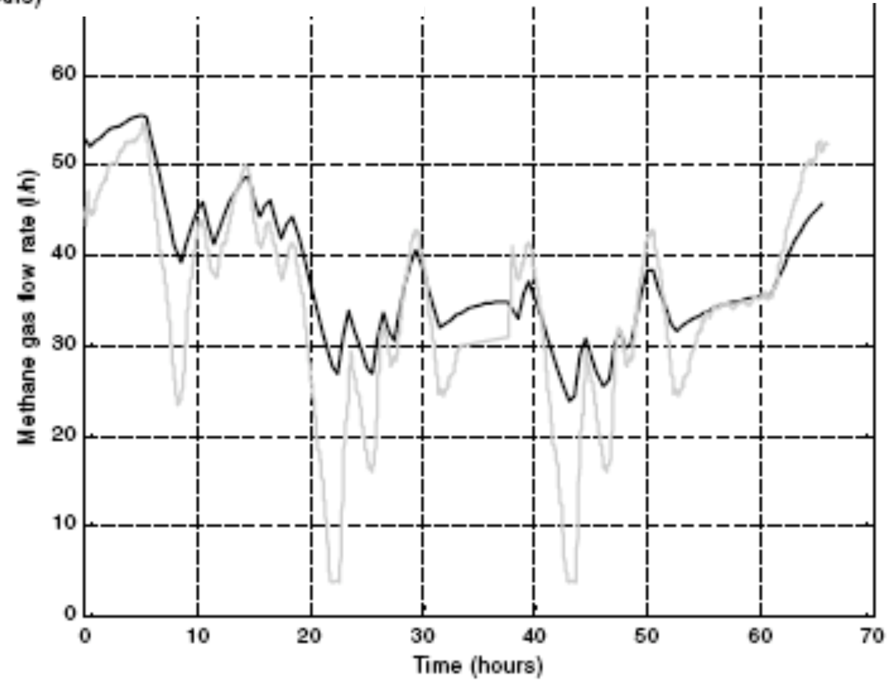




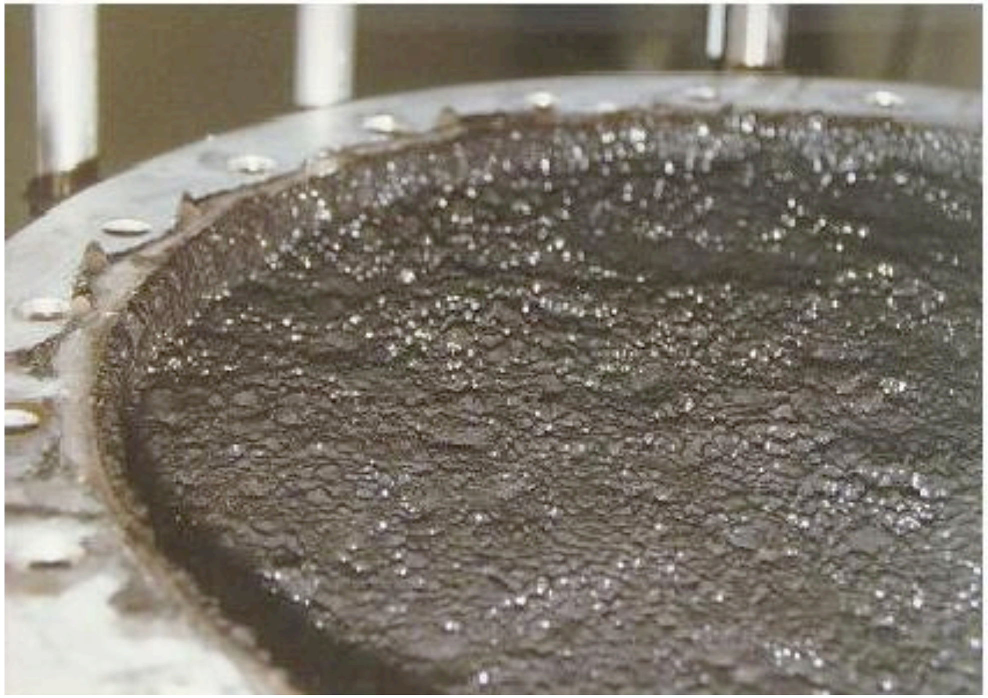
COD concentration (kg/m3)
1.5
1
0.5
0
0
10
20
30
40
50
60
70
Time (hours)

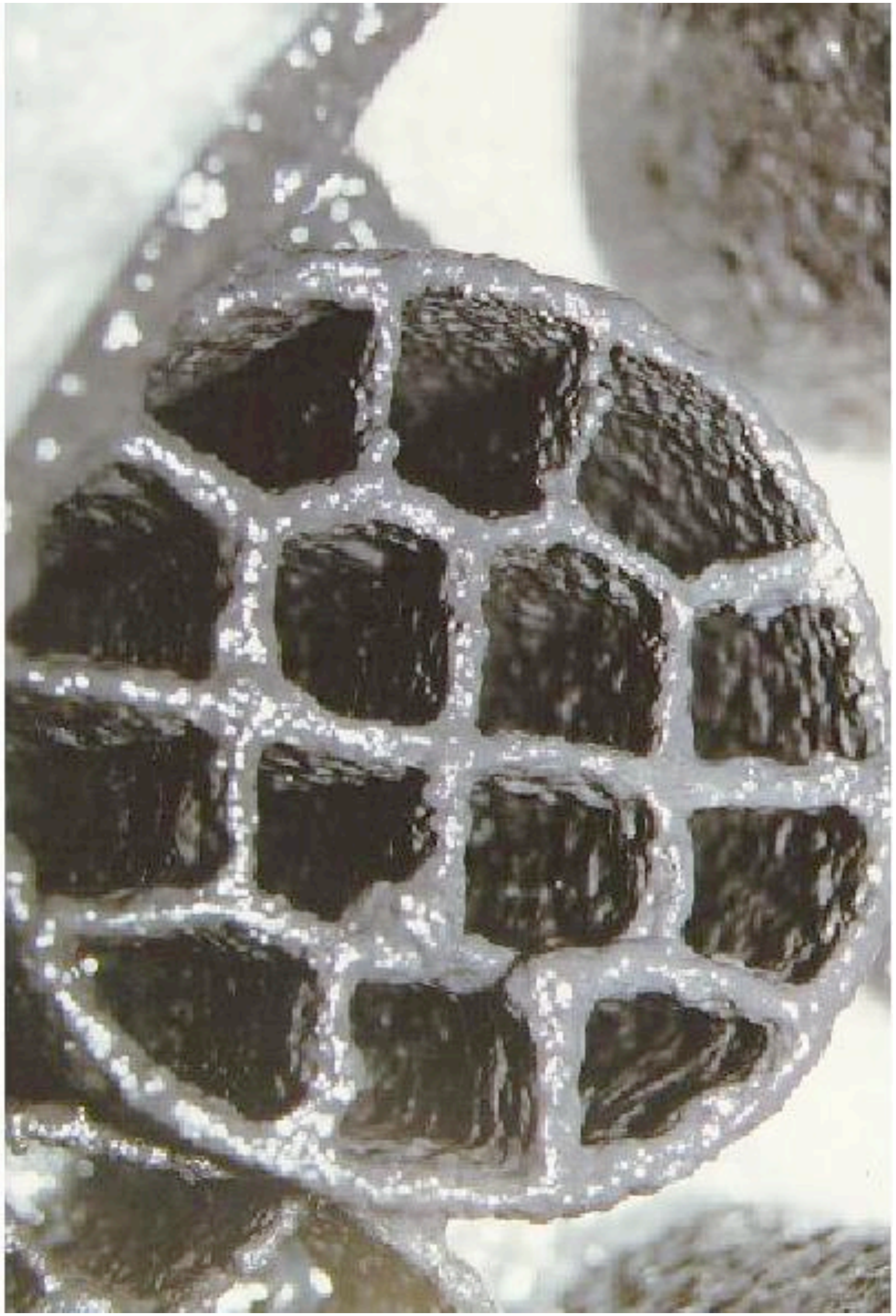


VFA concentration (mol/m3)
12
10
8
6
4
2
0
0
10
20
30
40
50
60
70
Time (hours)

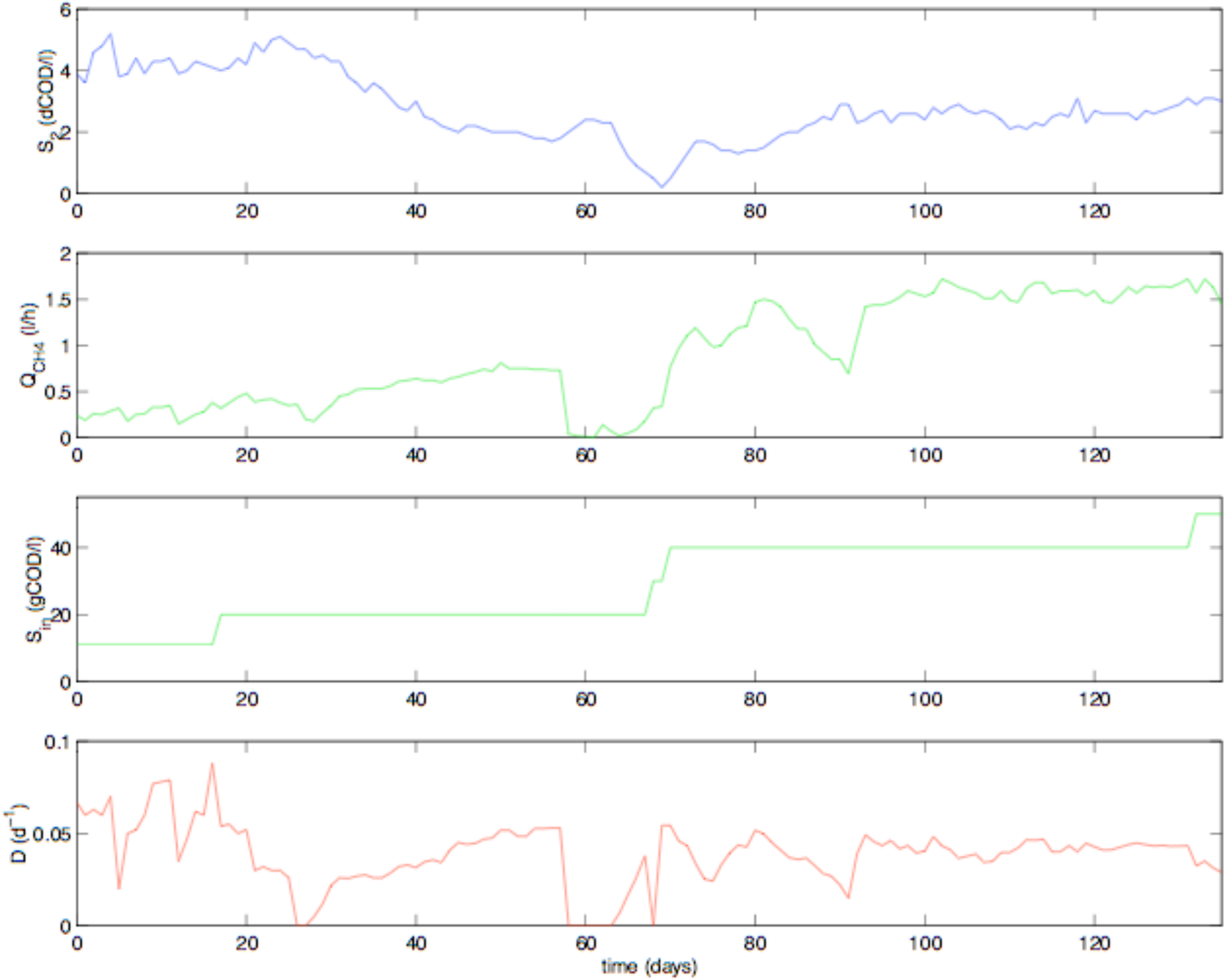


Methane gas flow rate (l/h)
60
50
40
30
20
10
0
0
10
20
30
40
50
60
70
Time (hours)

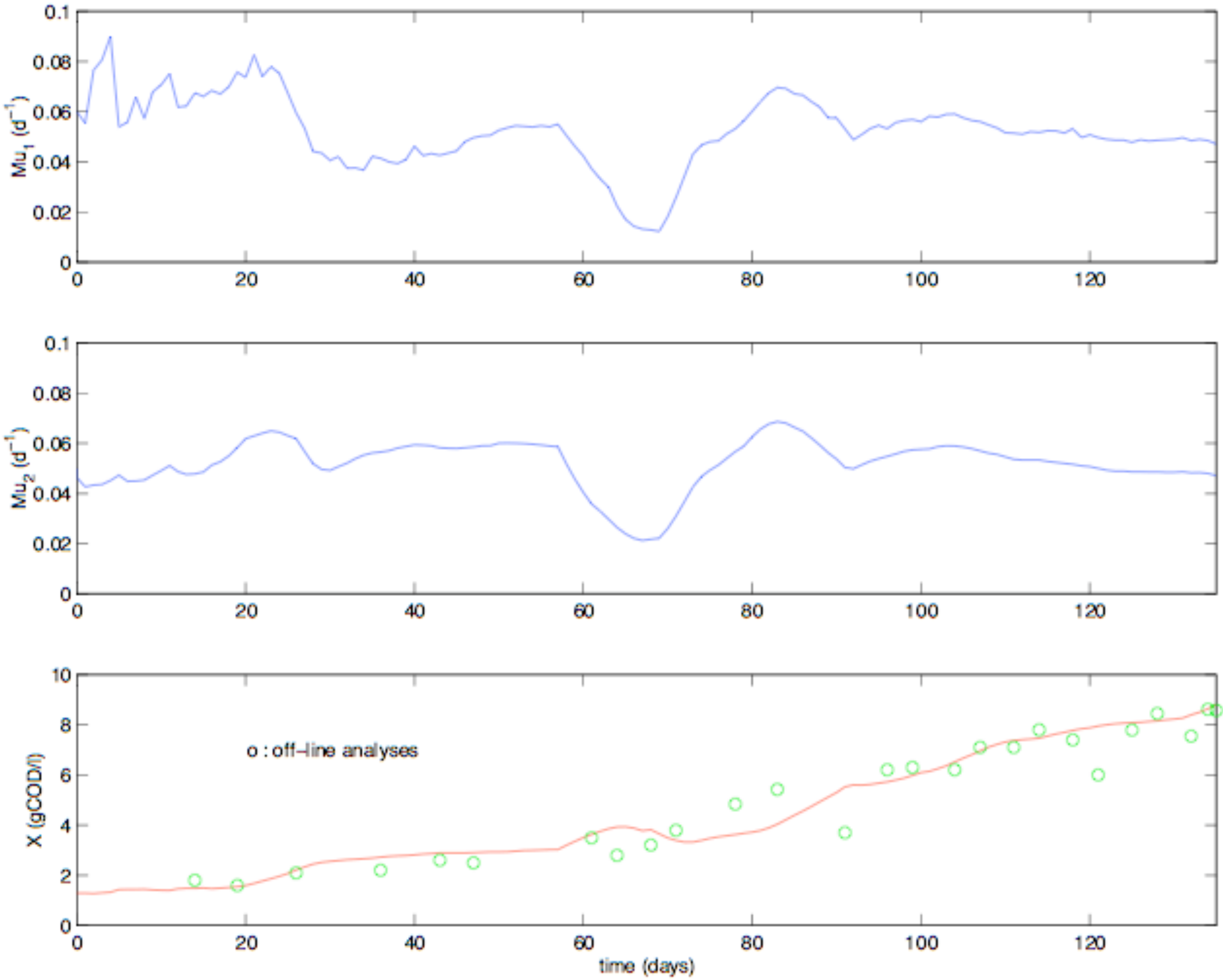




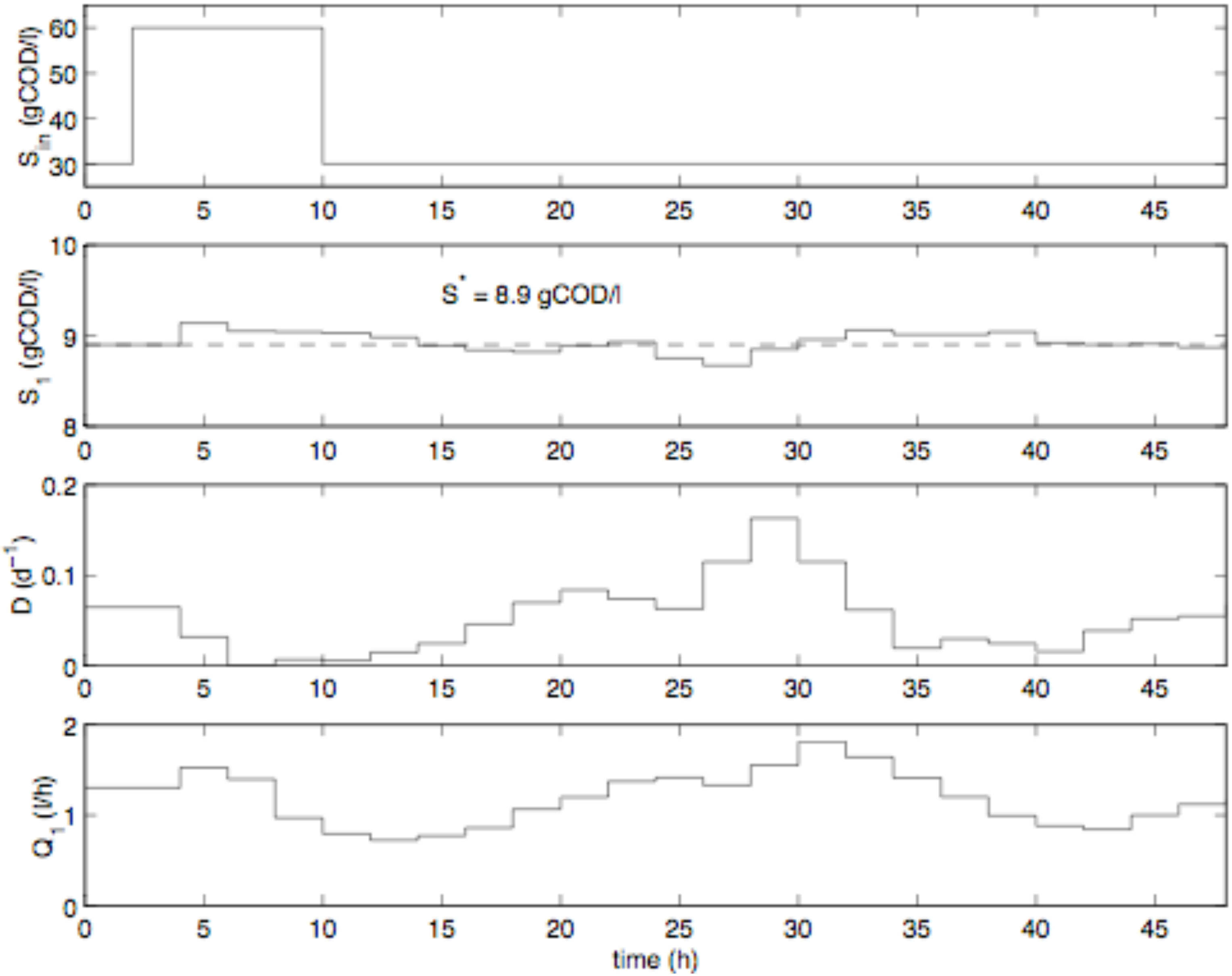
On-line estimation of the reaction rates : measured data



On-line estimation of the reaction rates : results



Adaptive linearizing control of the organic matter concentration



Some examples

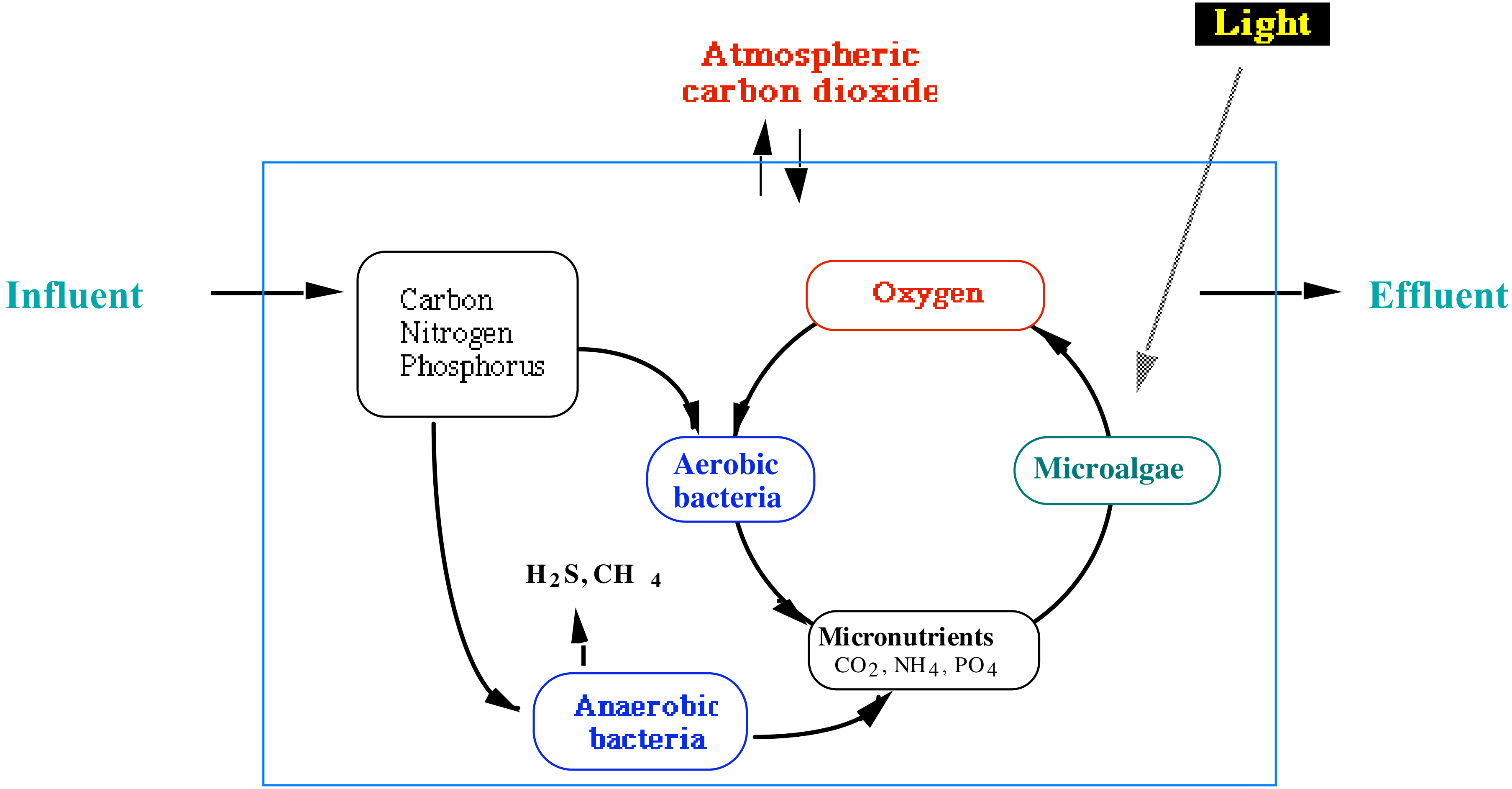
- Wastewater treatment
  - Activated sludge
  - Anaerobic digestion
  - **Lagoons (Ponds)**
- Solid waste treatment : composting
- Contaminated soil treatment
- Drinkable water treatment

Lagoons (ponds)

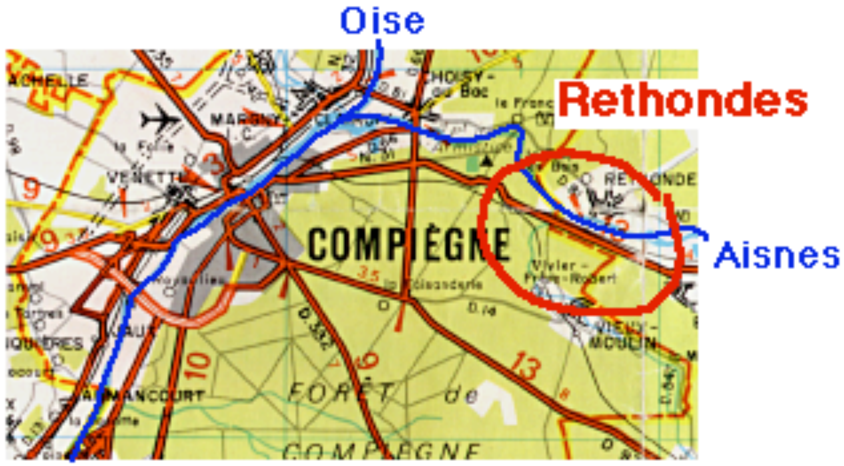
- About 2500 lagoons in France (the first on in 1964)
- Usually 3 basins («ponds») (50%, 25% and 25 % of the total area)
- Usually 100 to 1000 inhabitant-equivalents

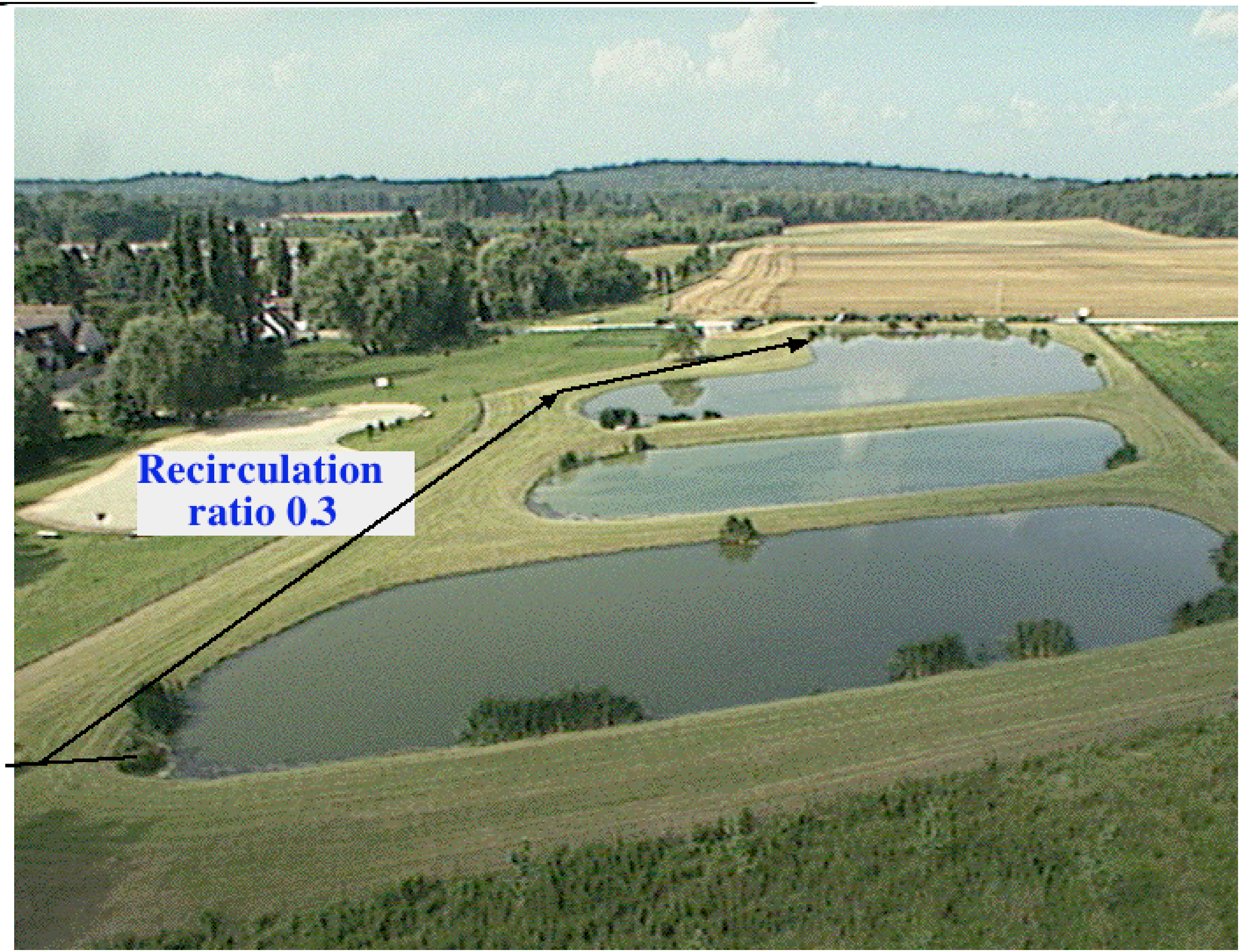
- Uncertainty on the performances in « cold » regions (e.g. North of France)
- Possible odour production

Basic elements of a lagoon




Oise
department
Paris

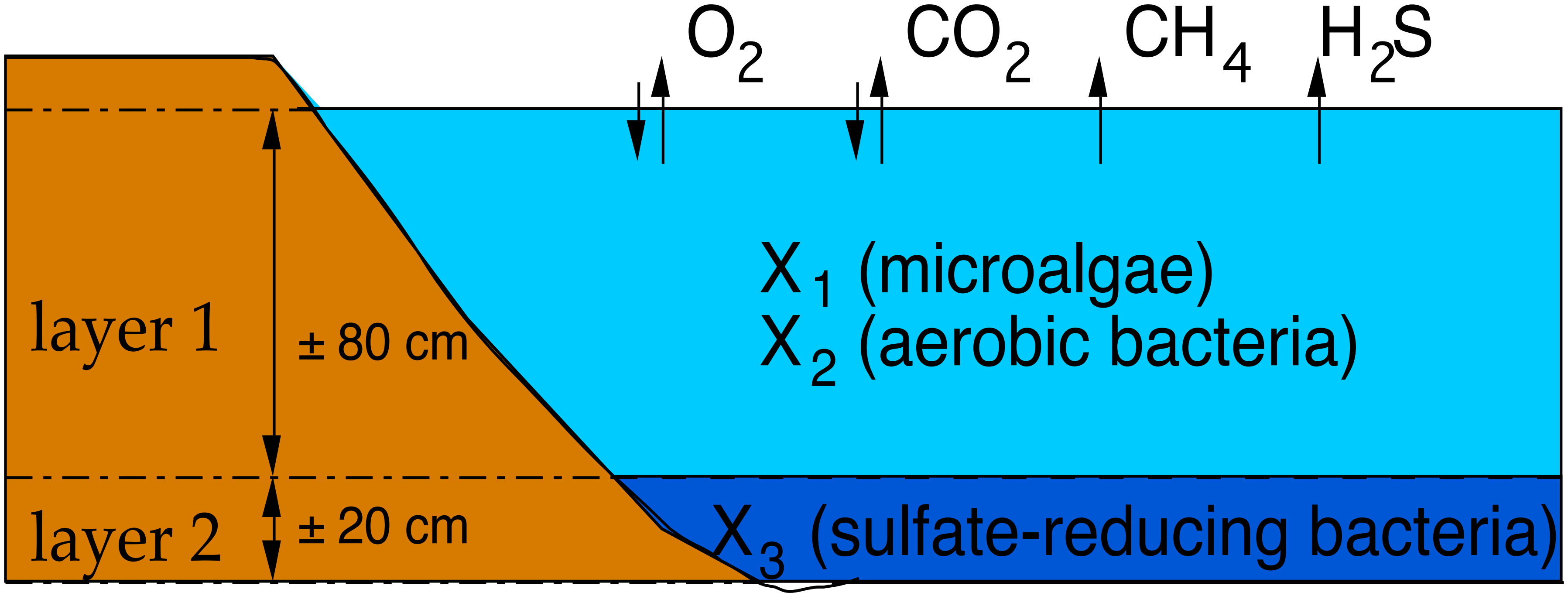

Oise
Rethondes
Aisnes
COMPIÈGNE


Recirculation
ratio 0.3

Odour production

- Non correlated to wastewater treatment performance
- Regularly appears at thaw and in the summer :
    - Often in the morning
    - Sometimes during short periods
    - Always in the first basin
- Depends on the meteorological variables that control the oxygenation level via the photosynthesis of the algae (light intensity and temperature)

Mathematical model : lagoon stratification

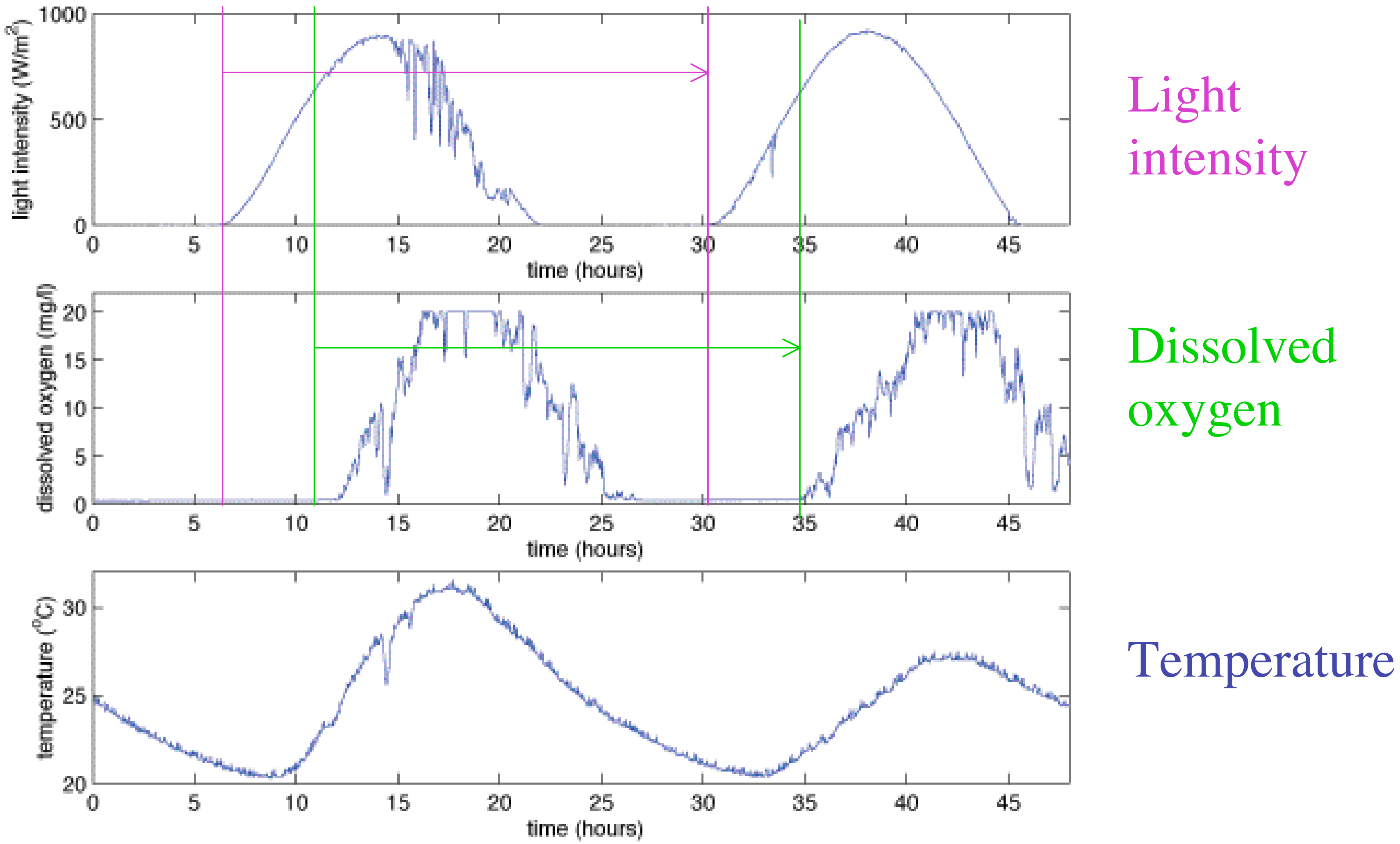


Reaction scheme :

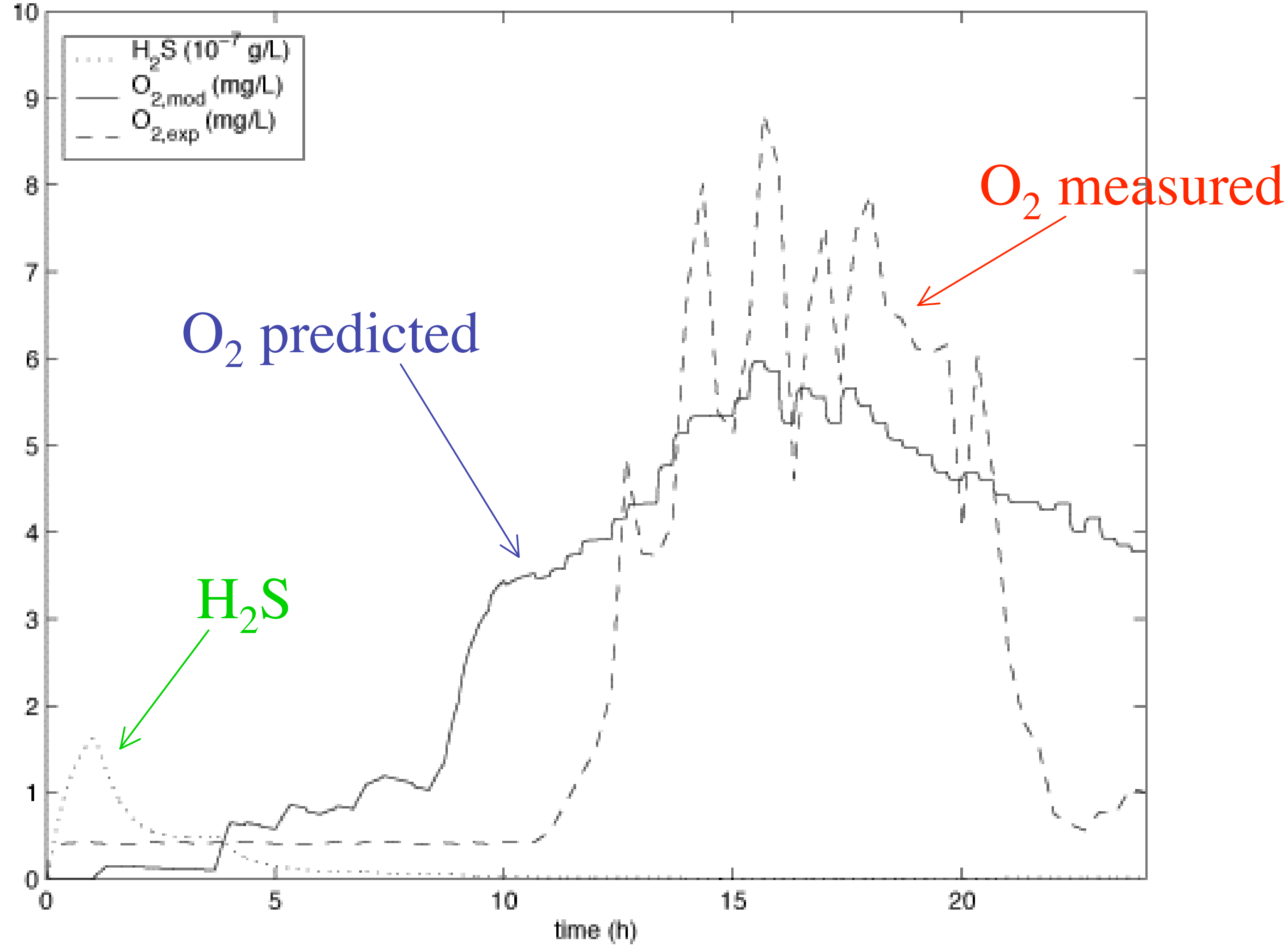
- Microalgae X_1
  - Growth : $CO_2 + S_1$ -- Light --> $X_1 + O_2$
  - Respiration : $O_2 + X_1 \text{ ---> } X_1 + CO_2$
  - Mortality : $X_1 \text{ ---> } S_2$
- Aerobic bacteria X_2
  - Growth : $S_1 + O_2 \text{ ----> } X_2 + CO_2$
  - Mortality : $X_2 \text{ ---> } S_2$
- Sulfato-reducing bacteria X_3
  - Growth : $S_2 \text{ ----> } X_3 + CO_2 + H_2S$
  - Mortality : $X_3 \text{ ---> } S_2$
- (bio)chemical oxidation of H_2S

$$2\,H_2S + O_2 \text{ ----> } 2\,H_2O + 2\,S$$

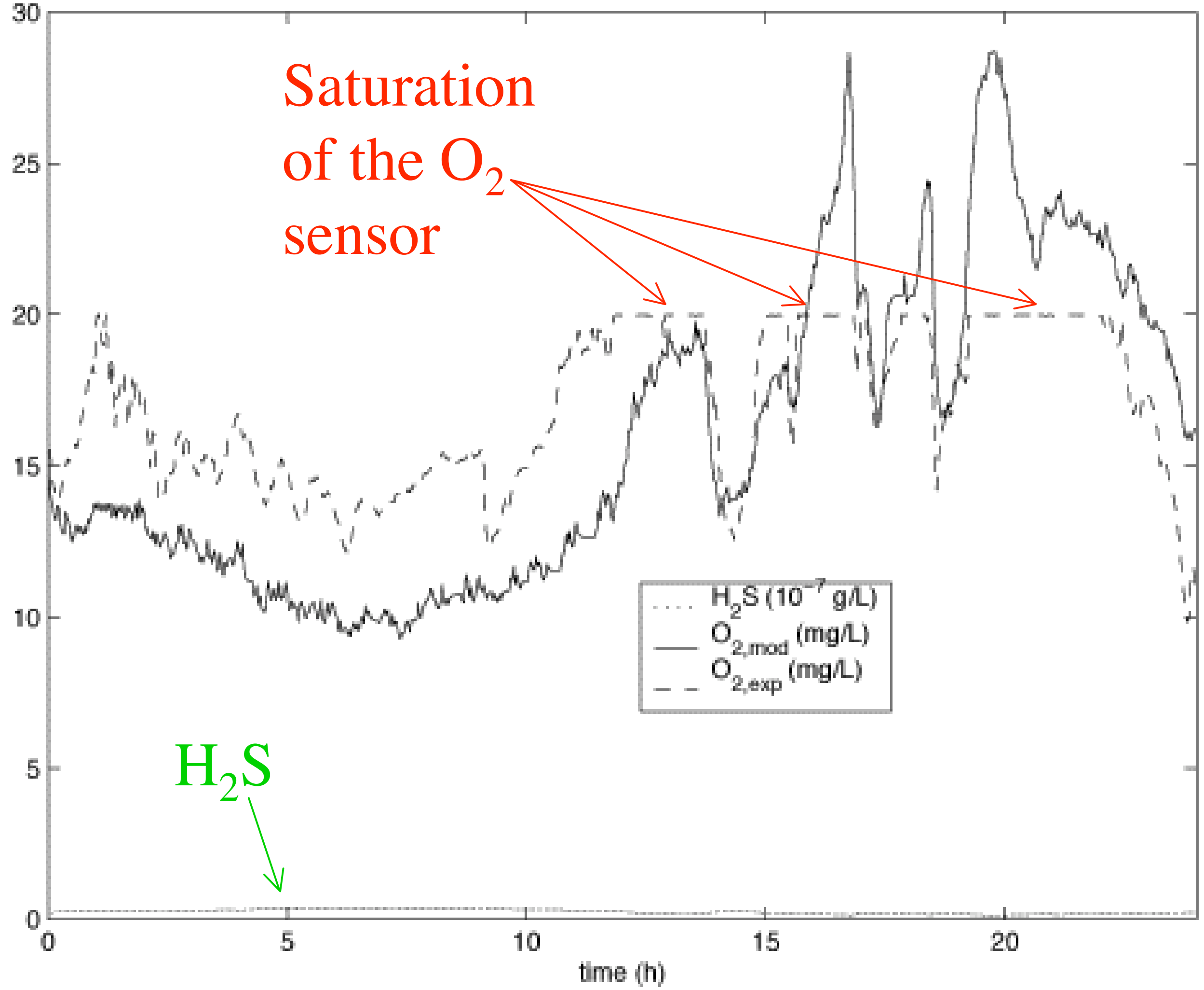
Typical set of experimental data



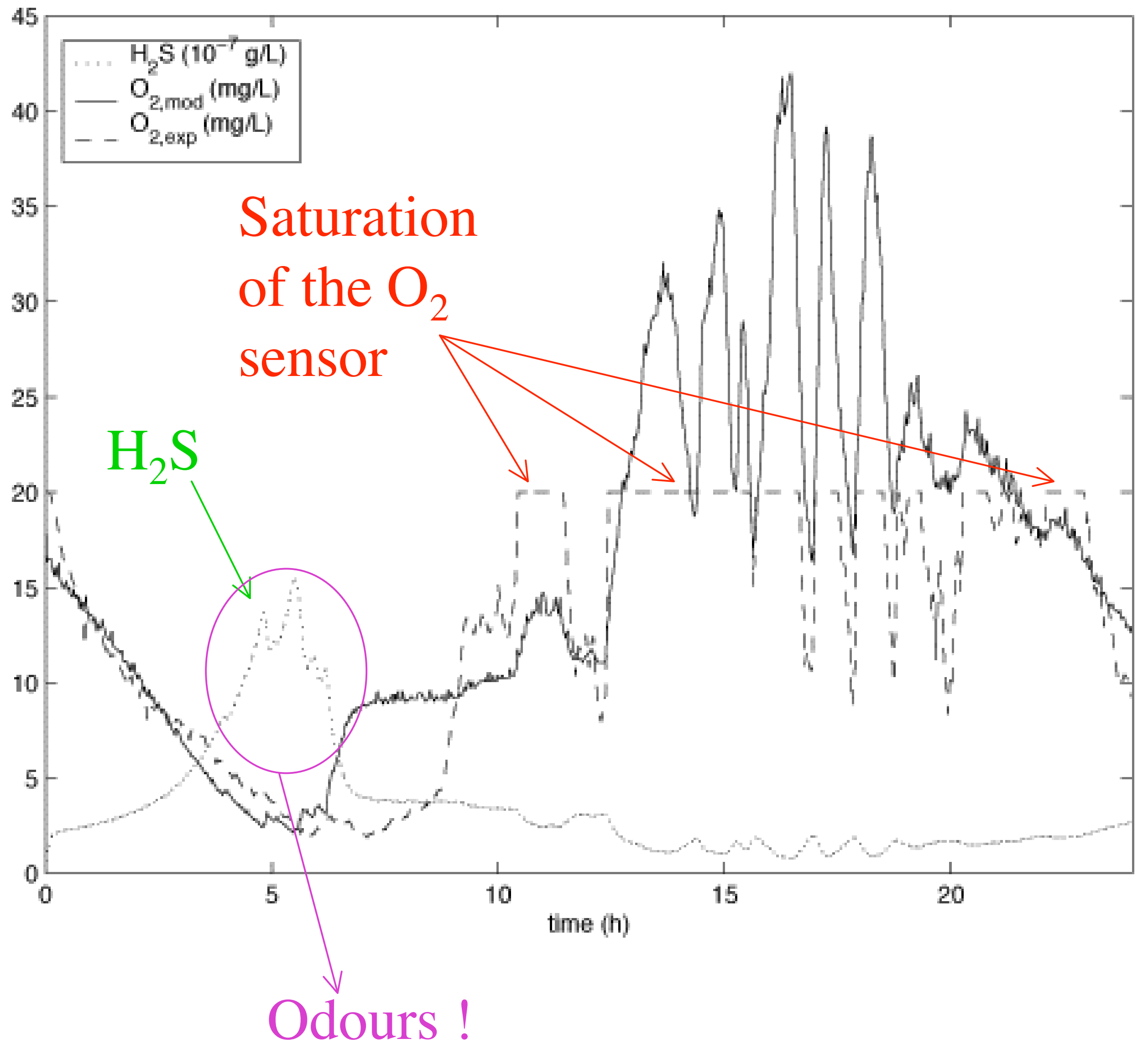
Typical validation data for the autumn



Typical validation data for the spring



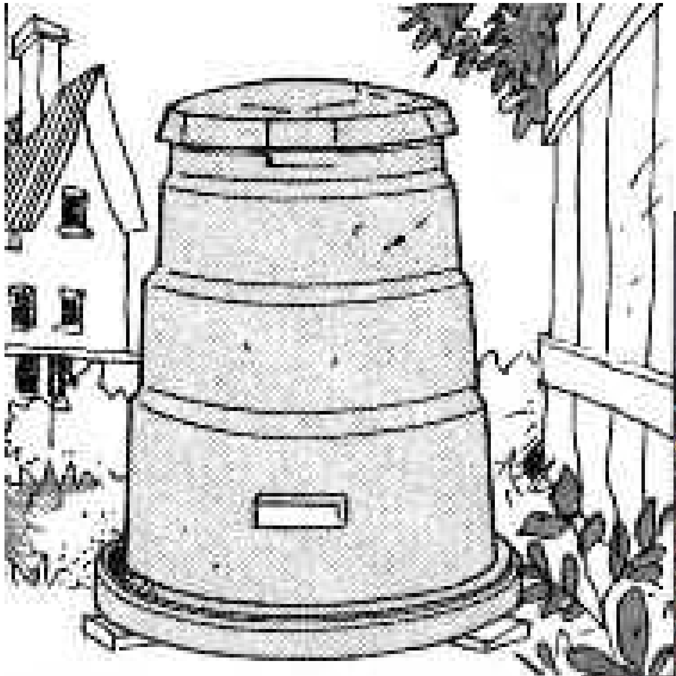
Typical validation data for the summer

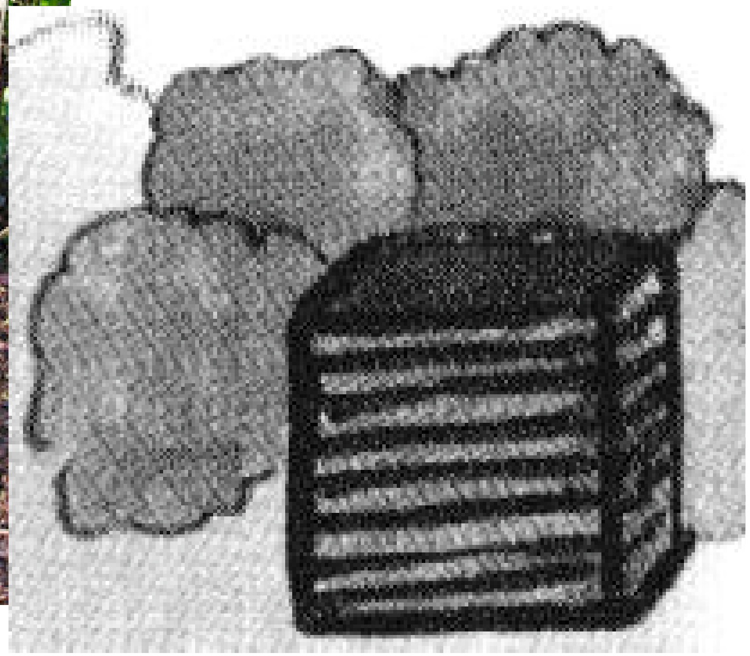


Some examples

- Wastewater treatment
  - Activated sludge
  - Anaerobic digestion
  - Lagoons (Ponds)
- **Solid waste treatment : composting**
- Contaminated soil treatment
- Drinkable water treatment

Composting





- Biological degradation and stabilisation of organic substrates

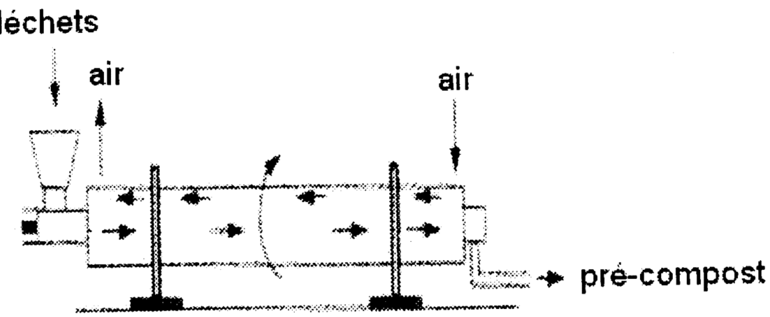
  in thermophilic conditions

  → stable final product

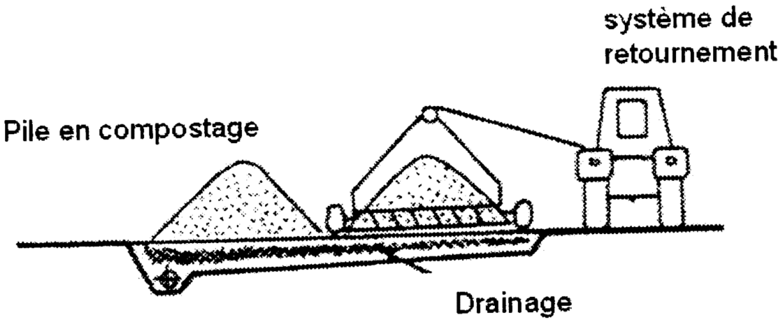
  - without pathogenic elements
  - ready to be spread on soils

- Matter to be composted : disposed on piles (*andains* in French)

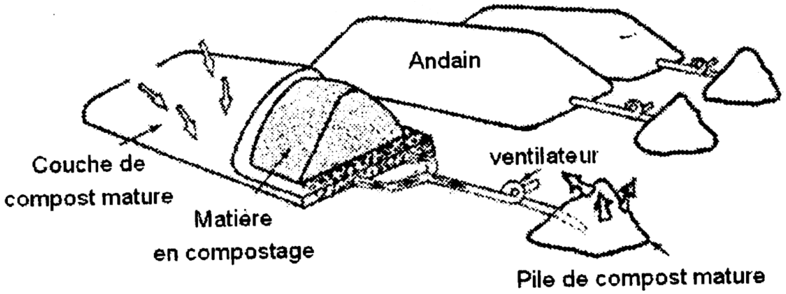
  (2m high, 2 to 4m large, length > 10m)



(a) Tambour tournant



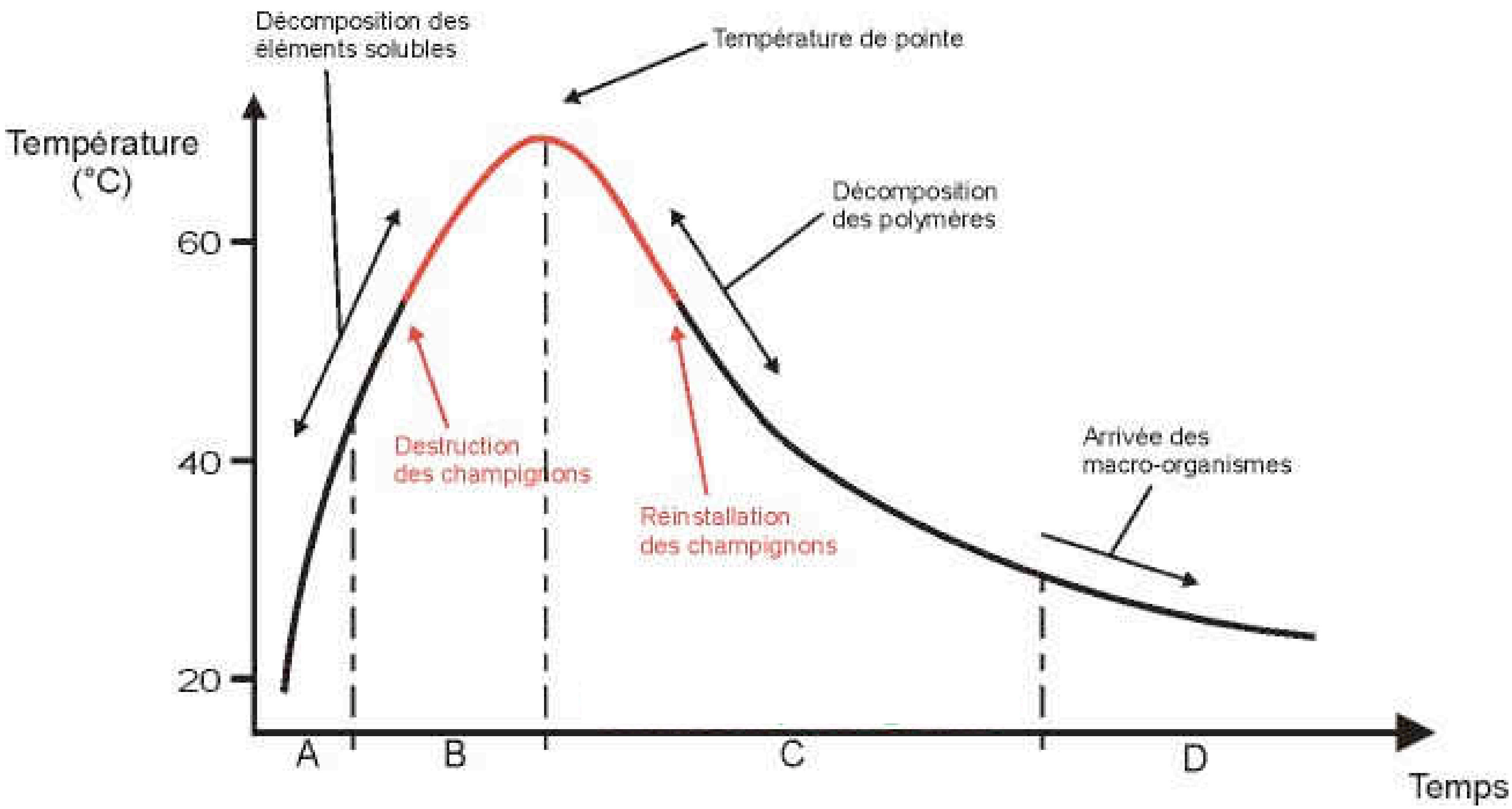
(b) Pile retournée



(c) Pile statique

Biology of the composting

- Bio-oxidation of the organic matter
- Microorganisms : bacteria, fungi and actinomycetes (95% of the microbial activity)
- Bacteria :
  - 80 to 90% of the microorganisms
  - high humidity élevée and low C/N ratio
  - large pH spectrum values
  - mesophilic at the beginning, then thermophilic
  - end of the activity : humidity level < 20%
- Fungi (high C/N ratio, low humidity level, 2 < pH < 9) --> hardly biodegradable substrates
- Actinomyces (filamentous) : in hard conditions + maturation



Décomposition des
éléments solubles
Température de pointe
Température
(°C)
60
40
20
Décomposition
des polymères
Destruction
des champignons
Reinstallation
des champignons
Arrivée des
macro-organismes
A
B
C
D
Temps

Dynamical model : energy and mass balances

$$
\begin{aligned}
\frac{dT}{dt} &= \frac{q_{air}}{mc}(h_{in} - h_{out}) + \frac{q_{H_2O_{in}} c_{p,H_20} + UA}{mc}(T_a - T) \\
&\quad - \frac{\Delta H}{mc} Y_{S/X} \mu X \\
\frac{dS}{dt} &= -Y_{S/X} \mu(S,T,C,M) X \\
\frac{dX}{dX} &= \mu(S,T,C,M) X - \delta X \\
\frac{dC}{dt} &= -\frac{Y_{O_2/X}}{\rho_{As}\epsilon} \mu(S,T,C,M) X + \frac{q_{air}}{\rho_{As}\epsilon V}(C_{in} - C) \\
\frac{dM}{dt} &= \frac{Y_{H_2O/X}}{m_{bh}} \mu(S,T,C,M) X + \frac{q_{air}}{m_{bh}}(f_{in} - f_{sat}) \\
&\quad + \frac{q_{H_2O_{in}} - q_{H_2O_{out}}}{m_{bh}}
\end{aligned}
$$

Some examples

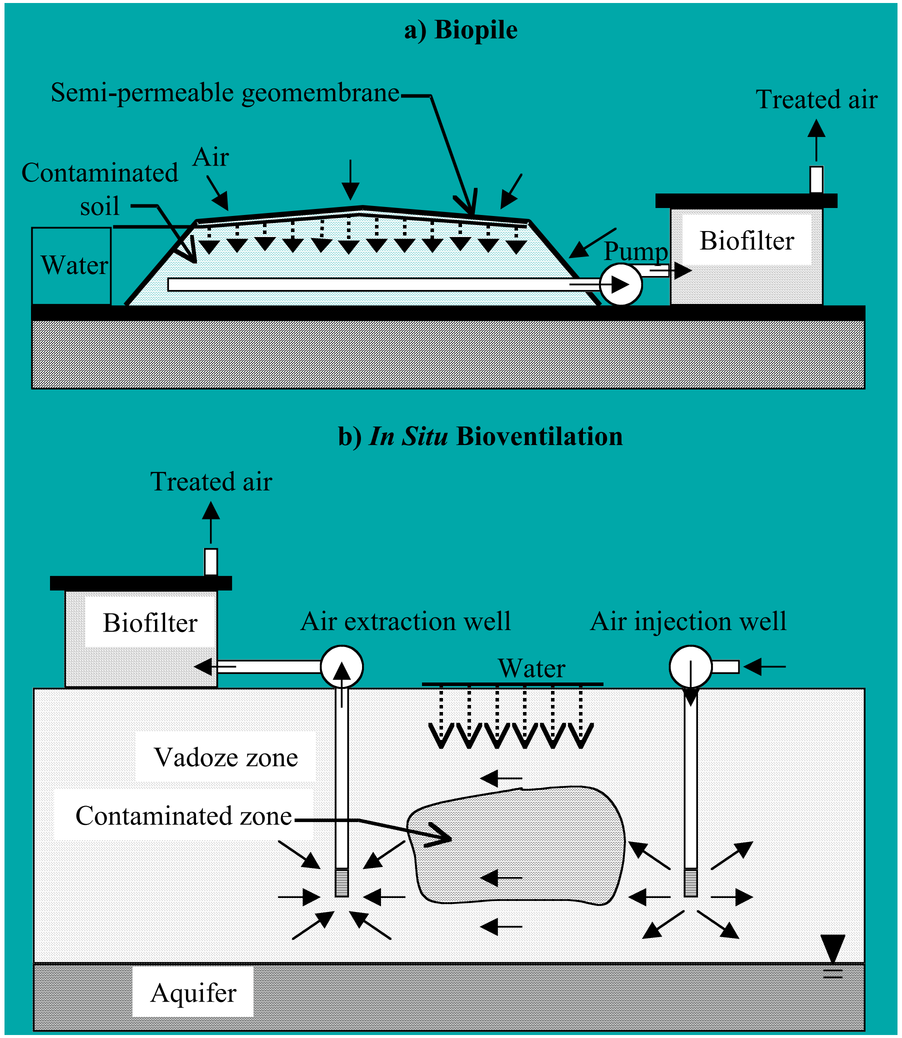
- Wastewater treatment
  - Activated sludge
  - Anaerobic digestion
  - Lagoons (Ponds)
- Solid waste treatment : composting
- **Contaminated soil treatment**
- Drinkable water treatment

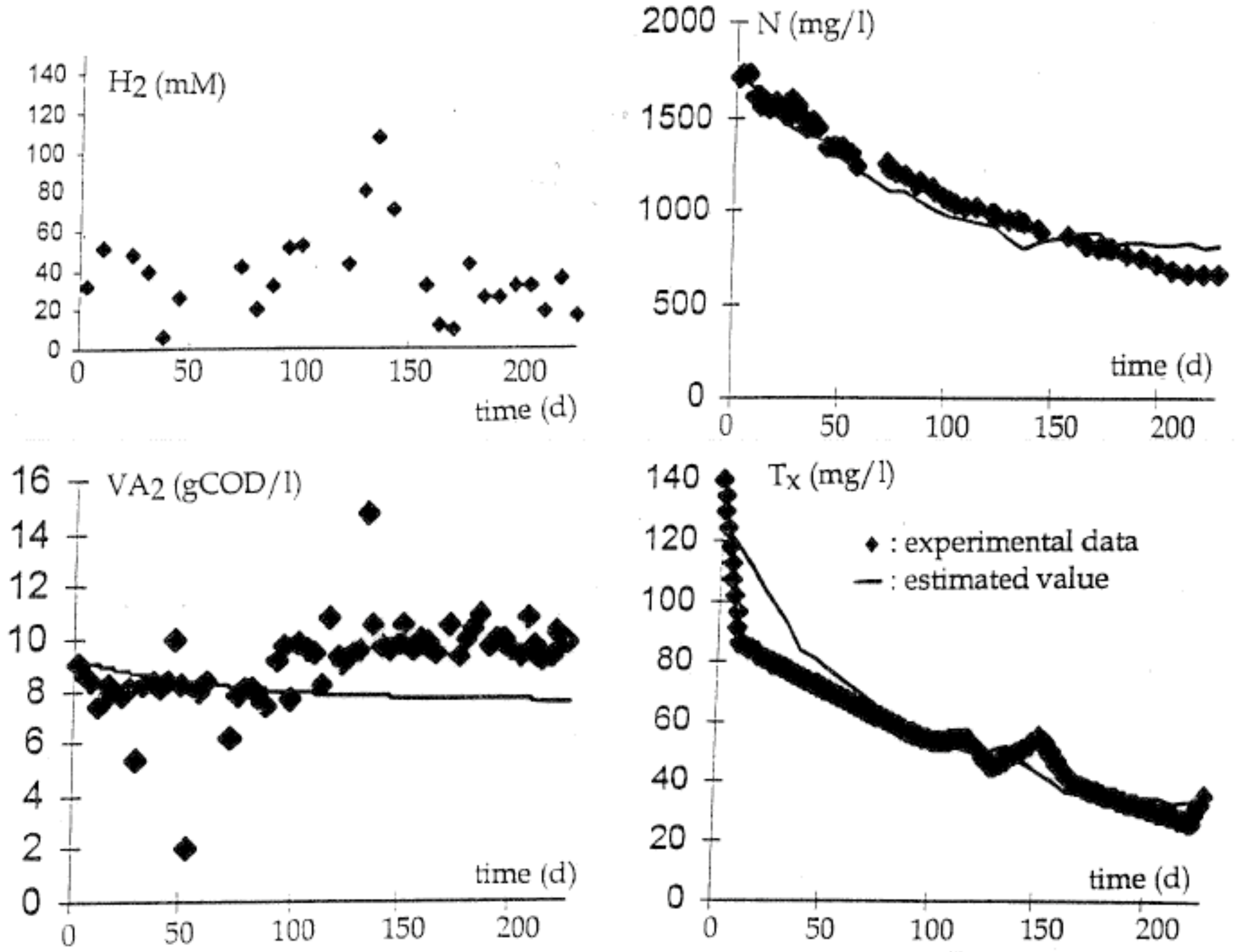
Bioremediation

- Rehabilitation of contaminated soils
  (often industrial sites)

- Example : Tertre (Carcoke)

- 2 main techniques
  - in-situ
  - biopile





H2 (mM)
time (d)
N (mg/l)
time (d)
VA2 (gCOD/l)
time (d)
Tx (mg/l)
♦ : experimental data
— : estimated value
time (d)

Some examples

- Wastewater treatment
  - Activated sludge
  - Anaerobic digestion
  - Lagoons (Ponds)
- Solid waste treatment : composting
- Contaminated soil treatment
- **Drinkable water treatment**

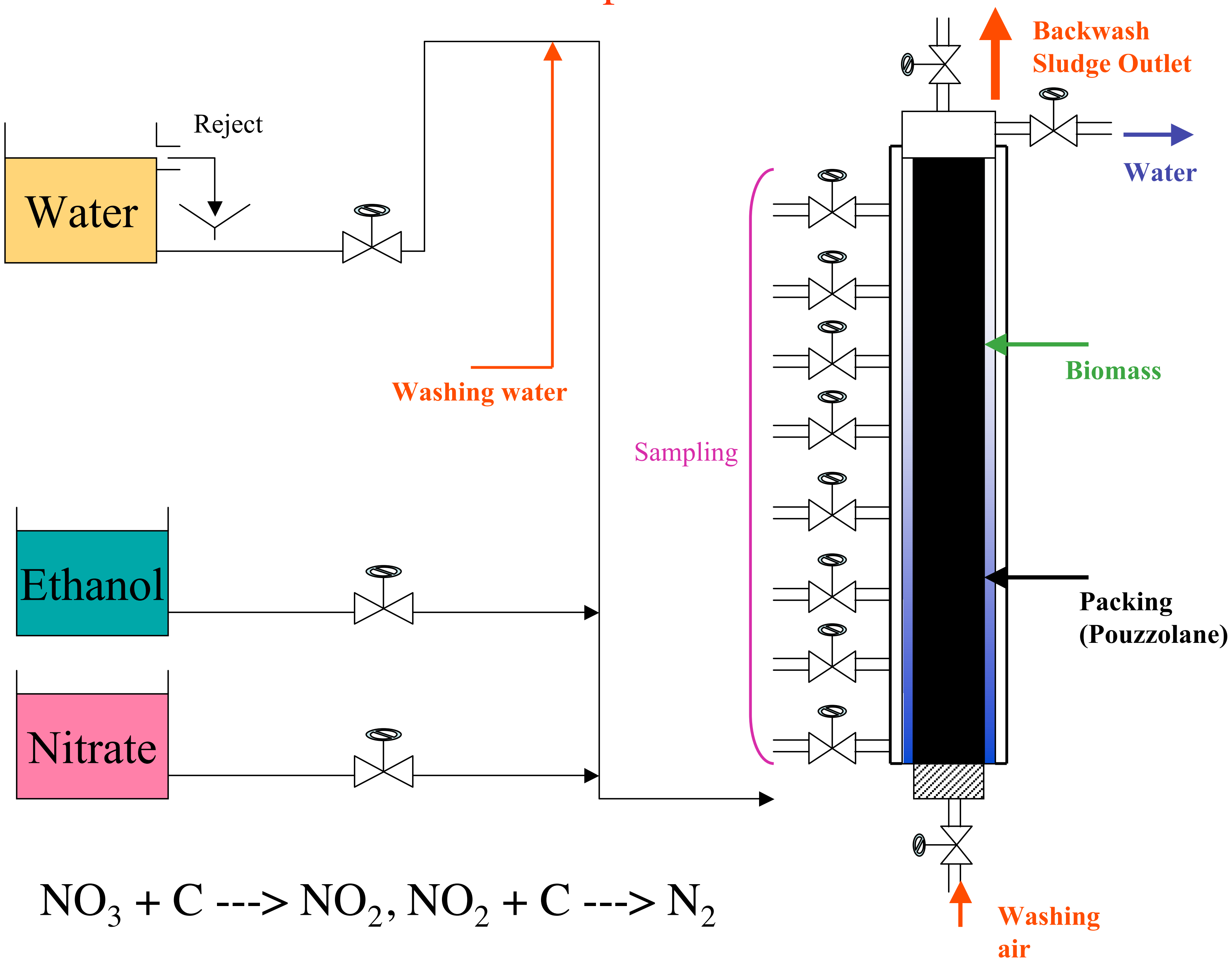
Denitrification of drinkable water

- Human health issue
  In presence of too high nitrogen level, risk for babies (mainly) and for elderly persons to fix the nitrogen instead of the oxygen

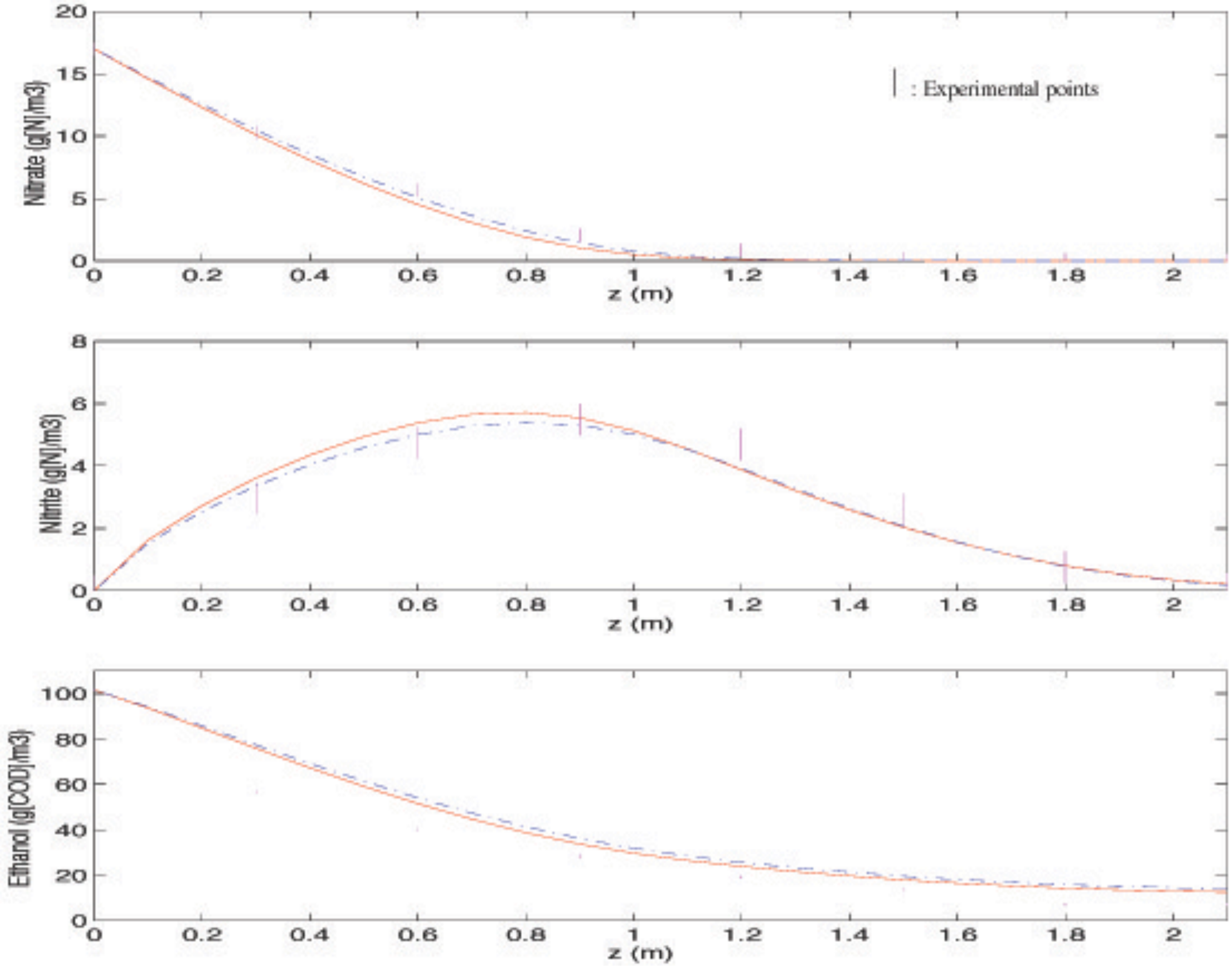
- In particular, consequence of the massive spread of manure on fields (e.g. Brittany)

- Denitrification (with carbon addition, for instance)

Drinkable water denitrification process



$$NO_3 + C \dashrightarrow NO_2,\ NO_2 + C \dashrightarrow N_2$$



: Experimental points
Nitrate (g[N]/m3)
Nitrite (g[N]/m3)
Ethanol (g[COD]/m3)
z (m)
z (m)
z (m)

Content

- Food engineering
- Plant growth
- Waste & water treatment
- **Biopolymers**
- Enzymes
- Pharmacy

Biopolymers

= polymers that are « easily » biodegradable

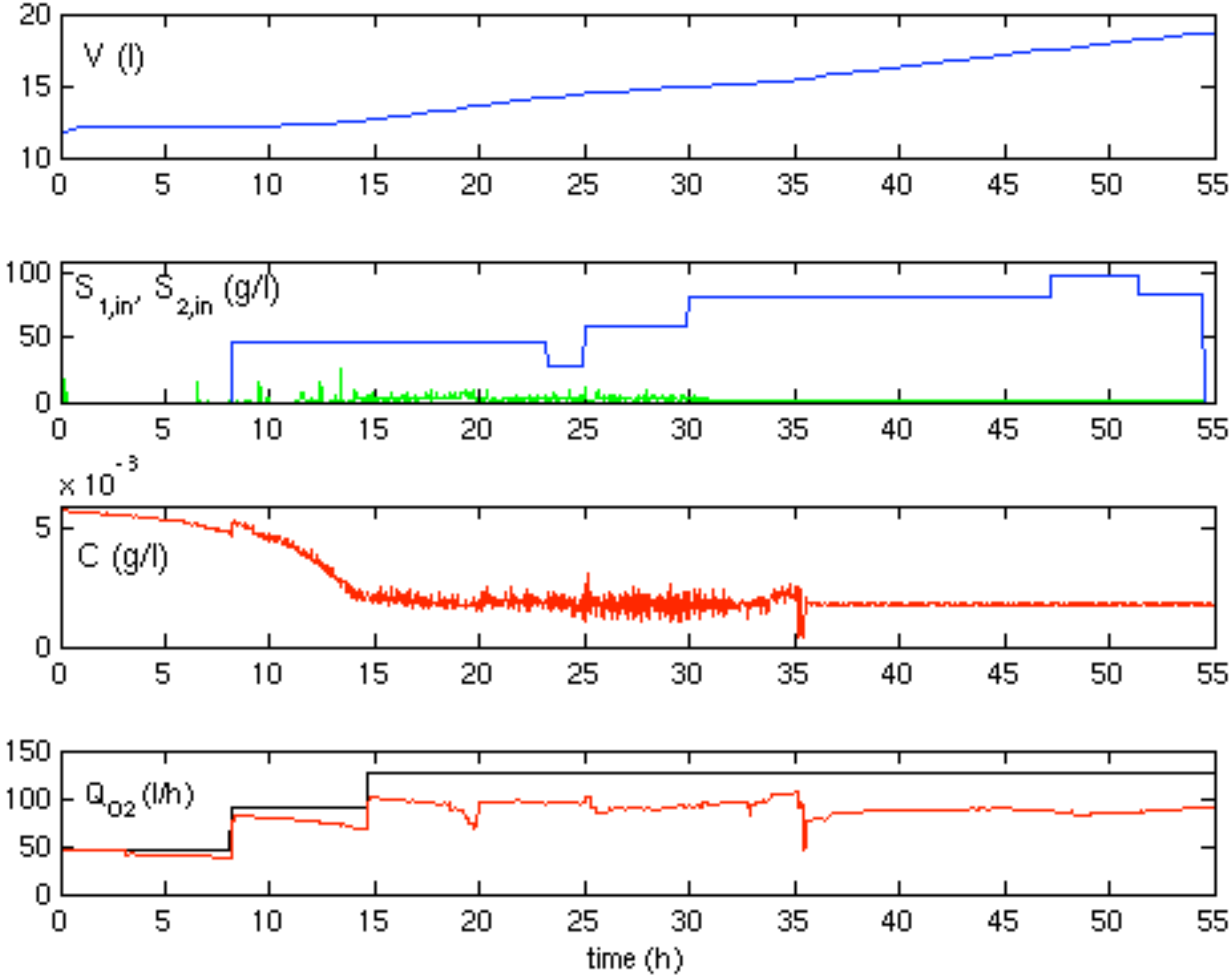
- Mainly PHB (Poly-β-hydroxybutyric acid)

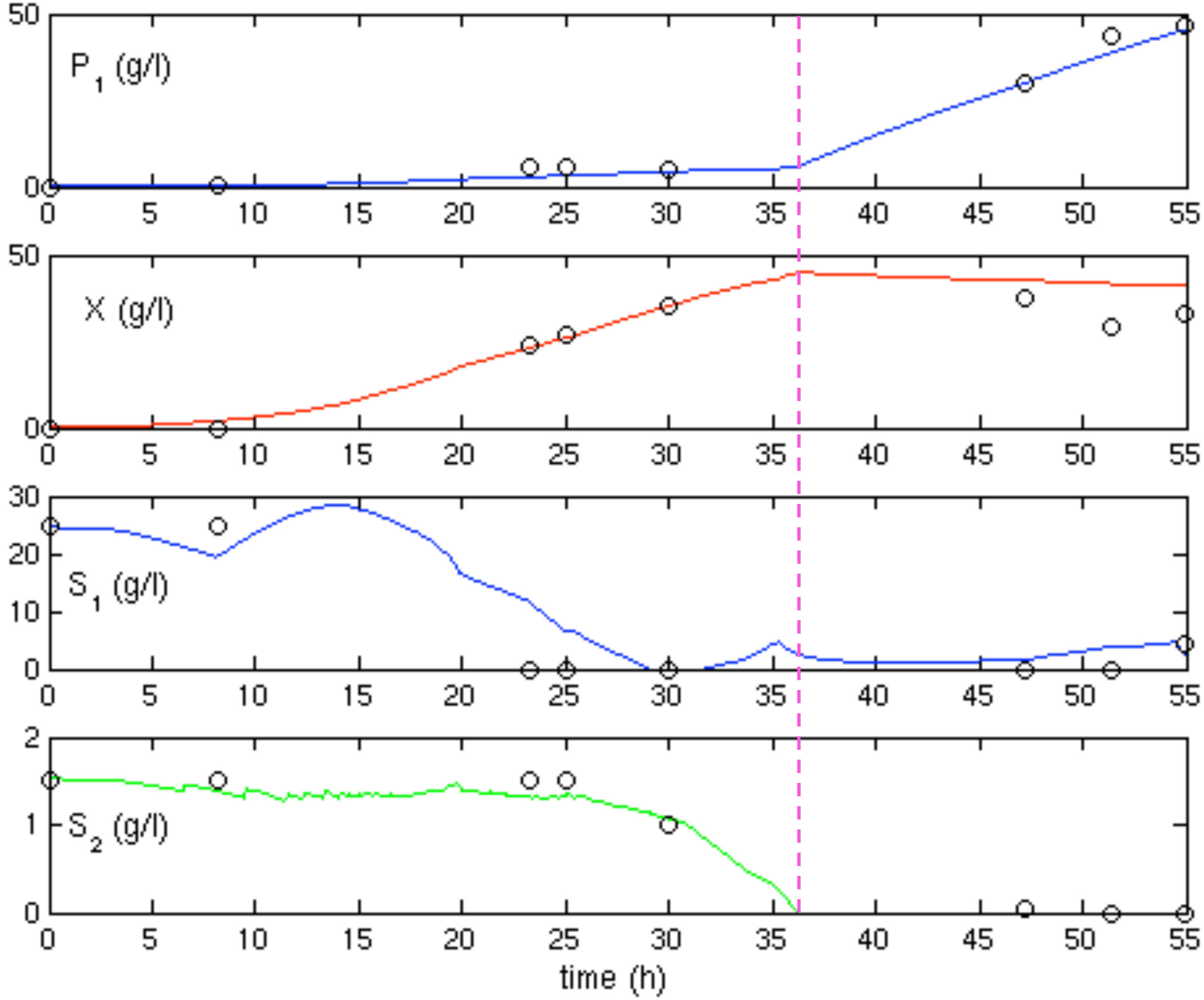
→intracellular synthesis by *Alcaligenes eutrophus*

- Application : motor oil bottles

On-line estimation of PHB, biomass and substrates

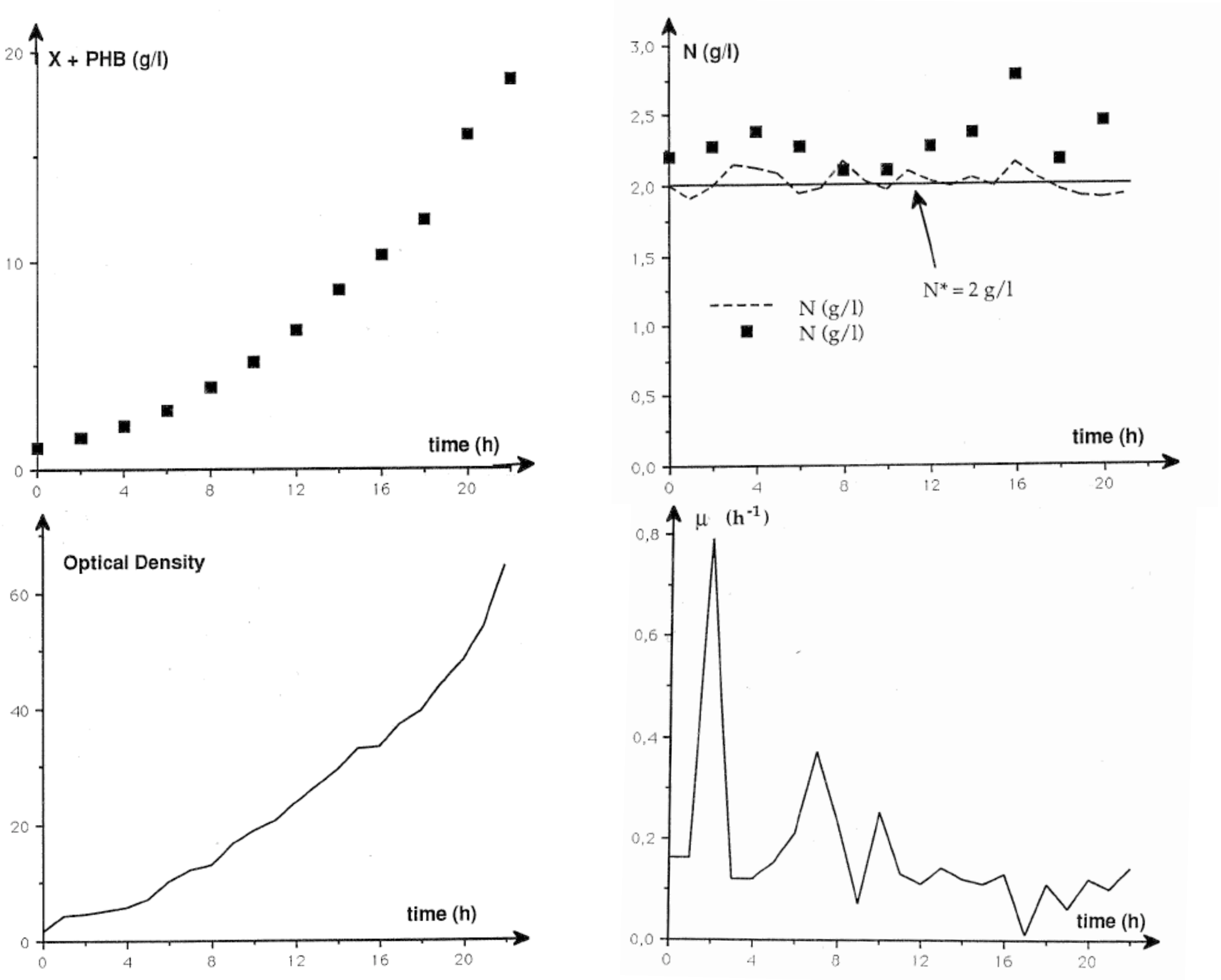
Data





o : off-line analyses

Inferential control of the ammonia N



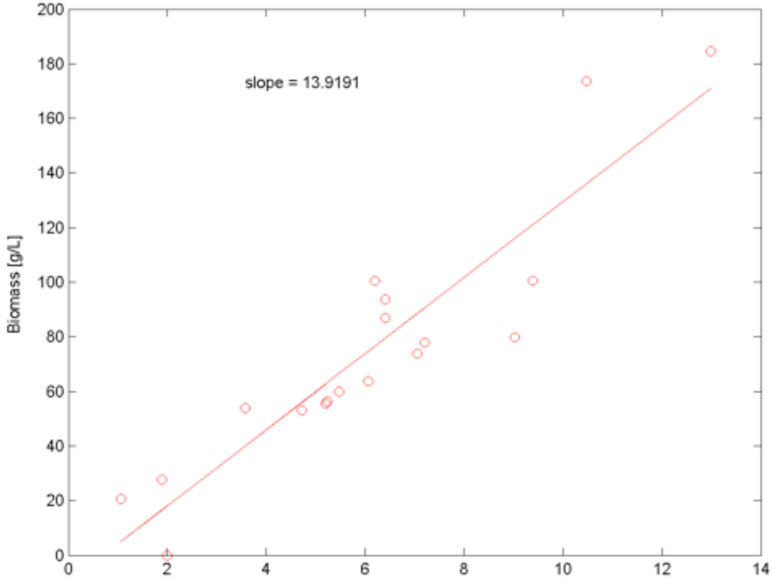
Content

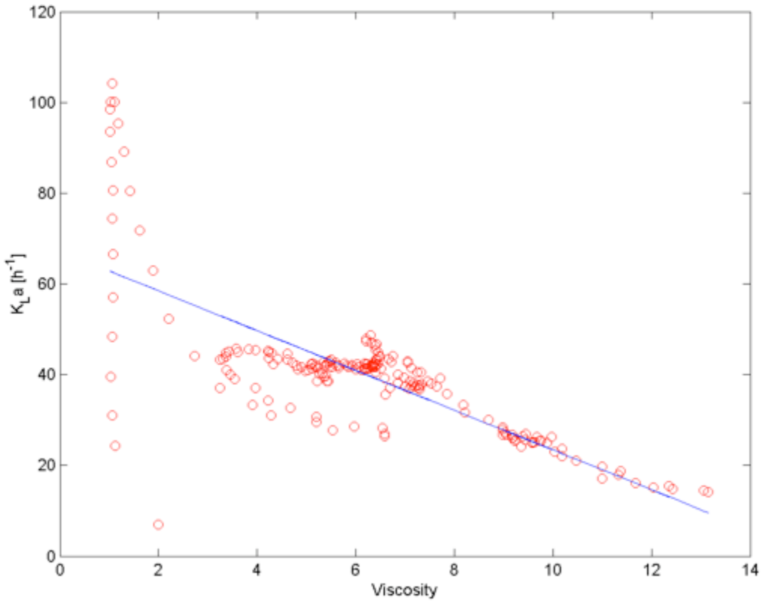
- Food engineering
- Plant growth
- Waste & water treatment
- Biopolymers
- **Enzymes**
- Pharmacy

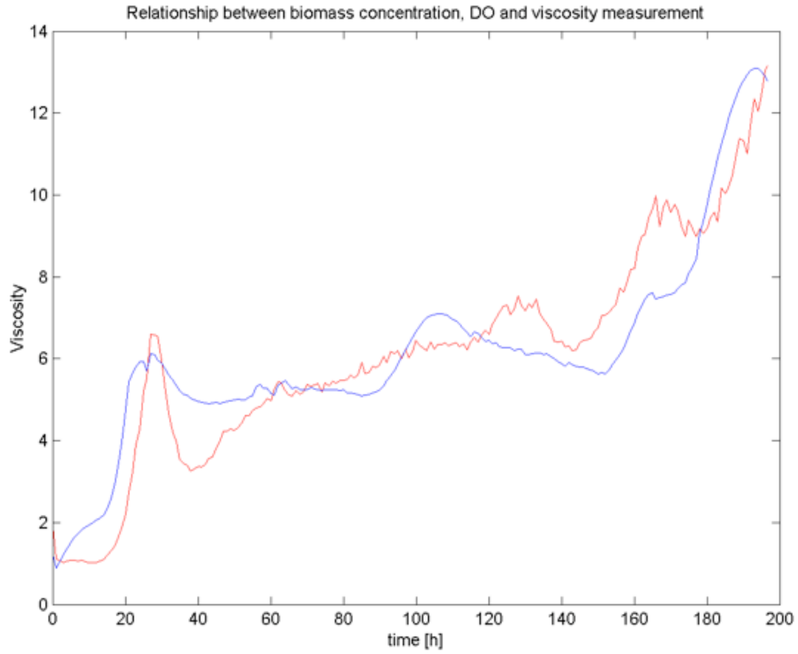
Enzymes

- Enzymes by micro-organisms (e.g. filamentous fungi)
- Applications : food industry (bread), detergent,...

Modelling issue : link between viscosity vs biomass concentration + transfer coefficient







Content

- Food engineering
- Plant growth
- Waste & water treatment
- Biopolymers
- Enzymes
- **Pharmacy**

Pharmaceutical processes and medical applications

- Antibiotics (penicillin, nikkomycines)
- Diagnosis (antibiotics tests)
- Animal cell culture
- Vaccines

Penicillin

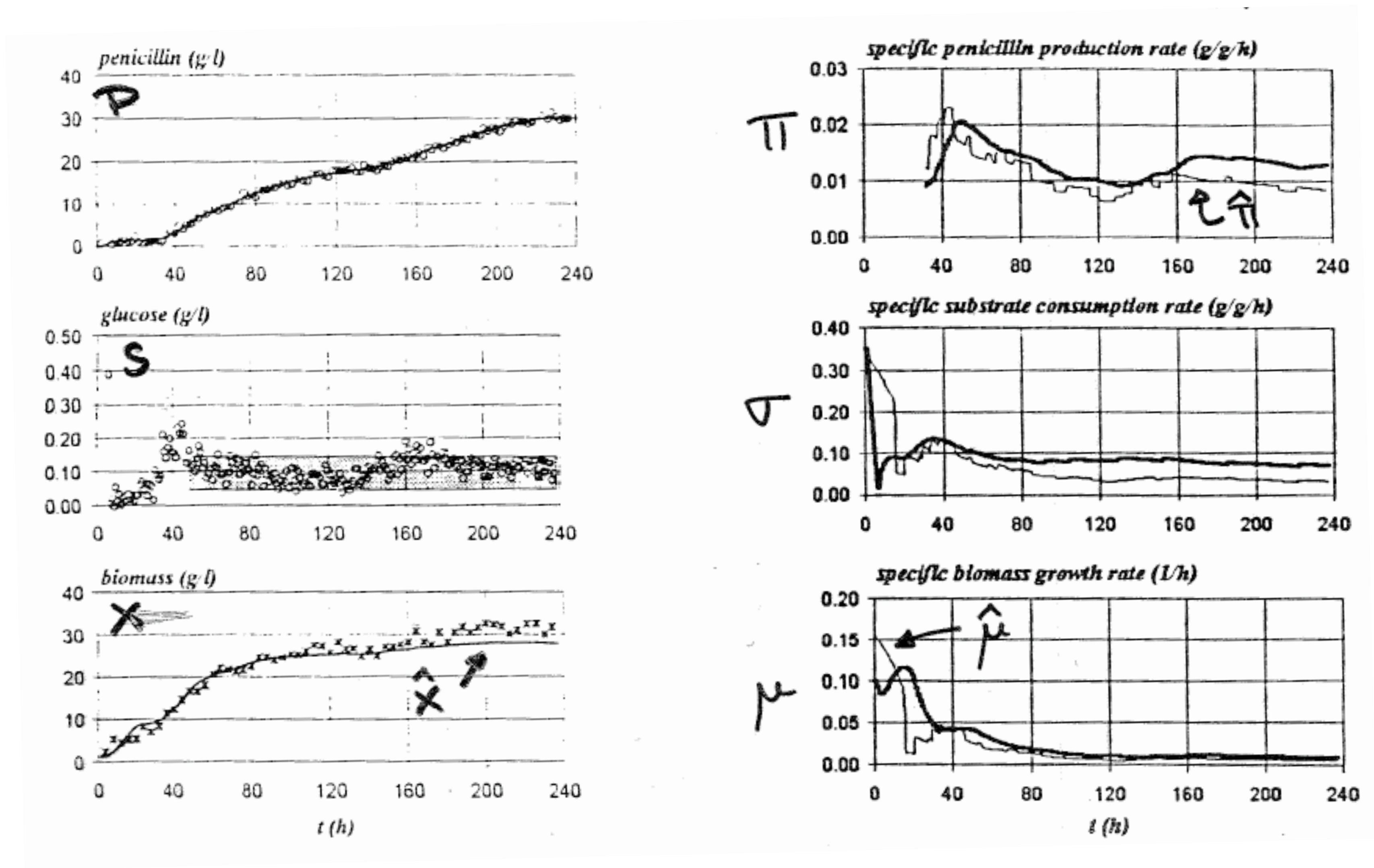
- The most traditionally used antibiotics

- Two reaction process :

  biomass growth : S ---> X

  non-growth associated production : S + X ---> X + P

Adaptive linearizing control of the substrate S



Nikkomycines

- Another antibiotics
- Application : biological insecticide, medecine
- Growth of Streptomyces tendae

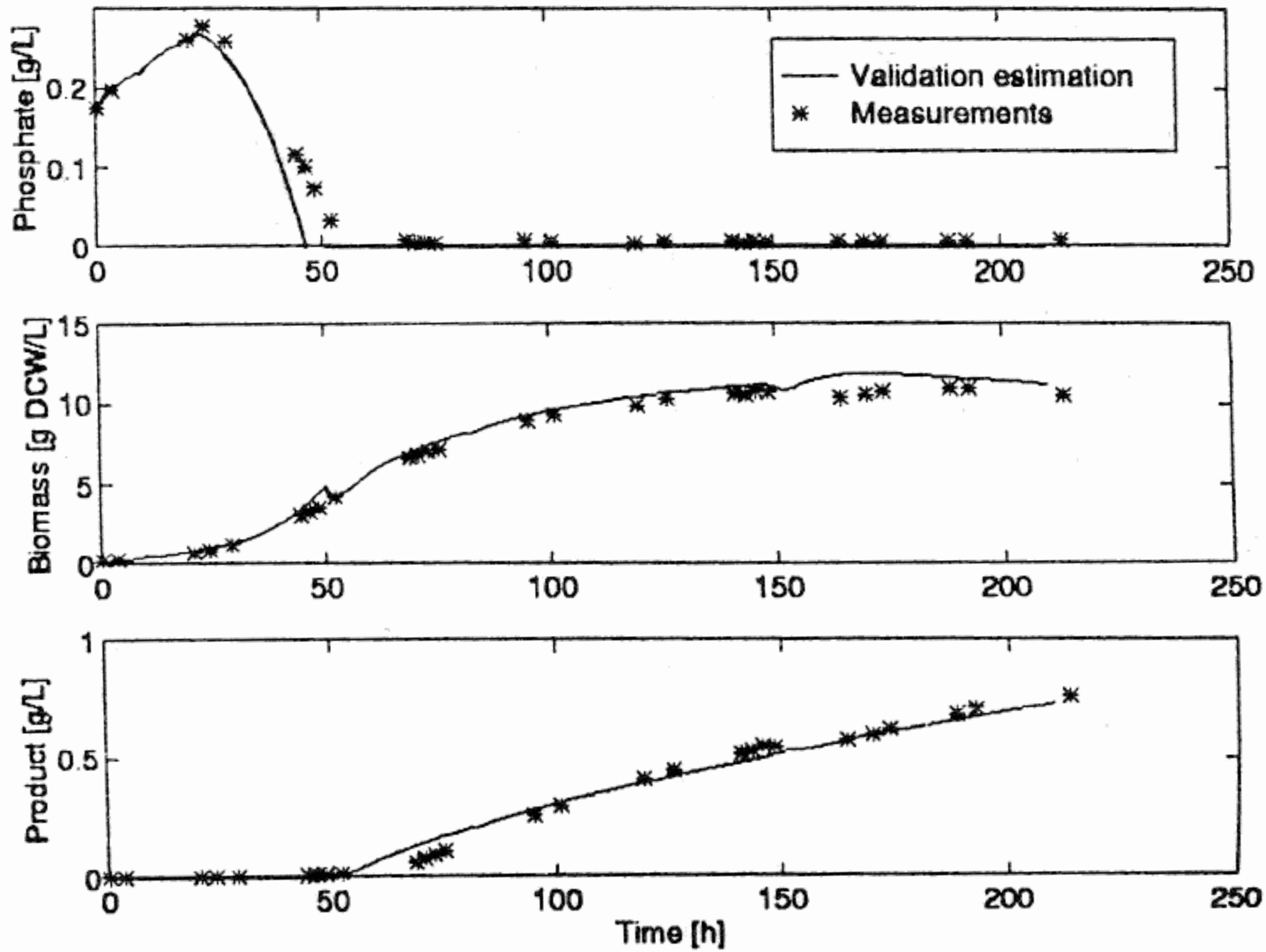
- Reaction scheme : 2 phases

1) $Am + Gl + Ph + O_2 \text{ ---> } X + CO_2$ growth
$Gl + O_2 + X \text{ ---> } X + CO_2$ maintenance

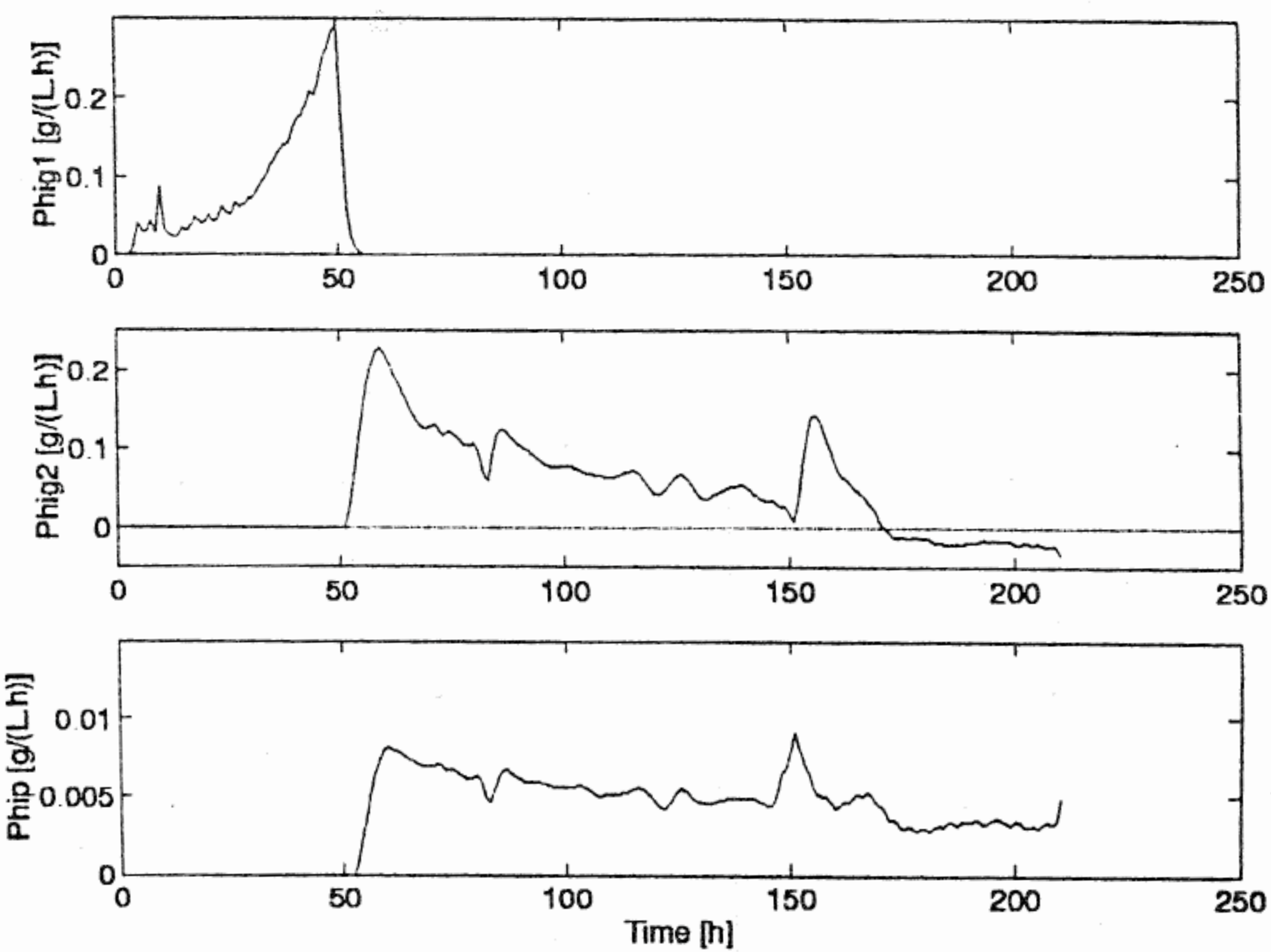
2) $Am + Gl + O_2 \text{ ---> } X + CO_2$ growth
$Am + Gl + O_2 + X \text{ ---> } X + P + CO_2$ production
$Gl + O_2 + X \text{ ---> } X + CO_2$ maintenance

Am : ammonia; Gl : glucose; Ph : phosphate

Asymptotic observer

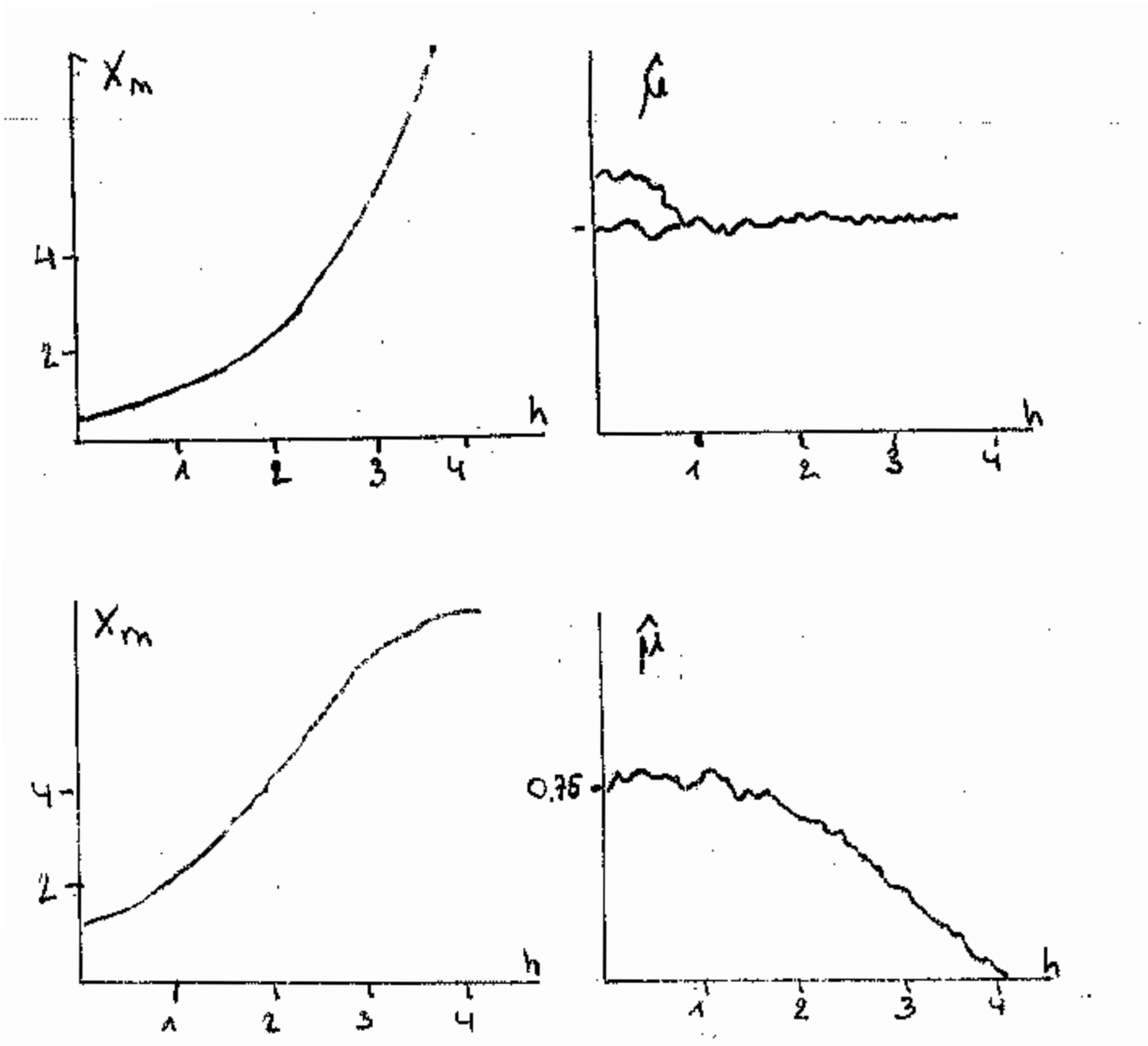


On-line estimation of the reaction rates



Antibiotics tests

On-line estimation of the specfic growth rates



Animal cell cultures

- Applications : production of vaccines, monoclonal antibodies, molecules with therapeutic property (e.g. tissue-type plasmigen activators)

- Reaction scheme

  A --> X

  A + G --> X + P

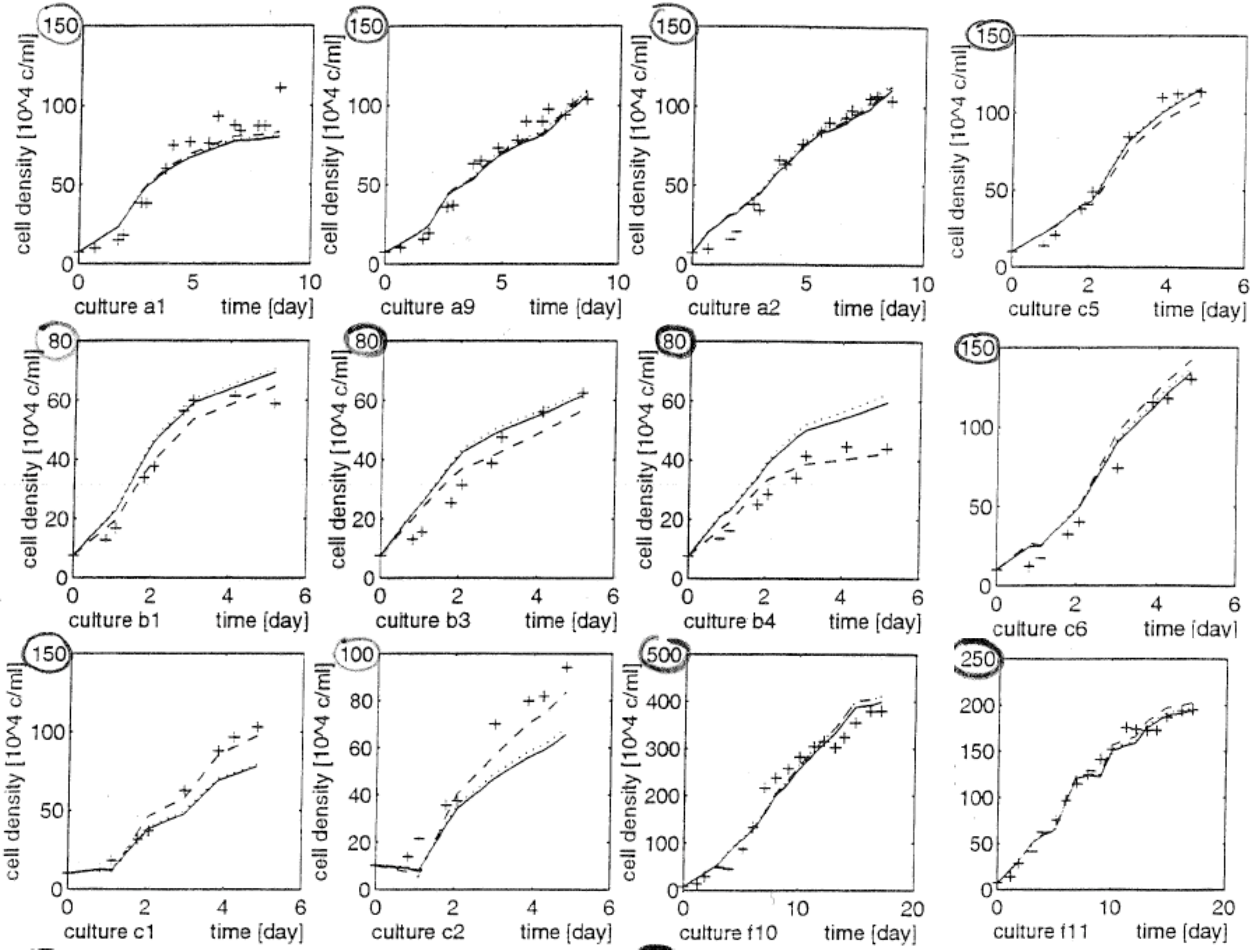
  A --> N

  P + $3O_2$ --> 3 CO_2 + 3 H_2O

  P --> L

A : amino-acids, X : cells, G : glucose, P :pyruvate,
N : ammonia, L : lactate

Validation of the reaction scheme

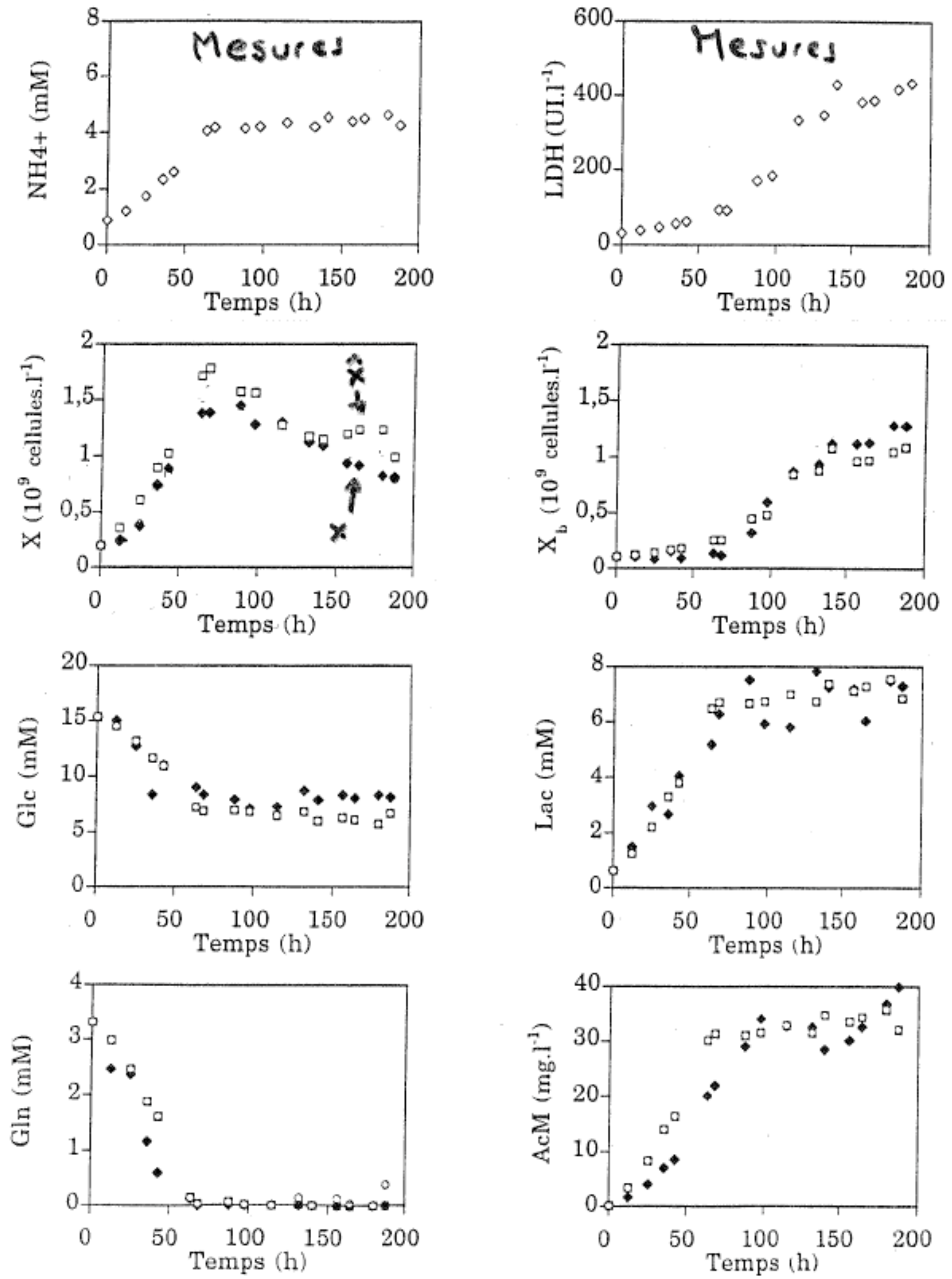


Asymptotic observer

Reaction scheme :

Gl + G --> X + L + MA
X --> Xd + LDH

Gl : glutamine
MA : monoclonal antibodies
Xd : dead cells
LDH : deshydrogenase lactate



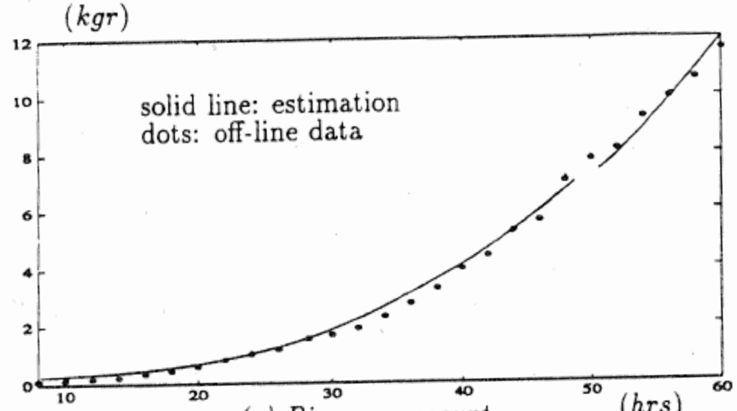
Vaccine production

Example : Vaccine against the Hepatitis B

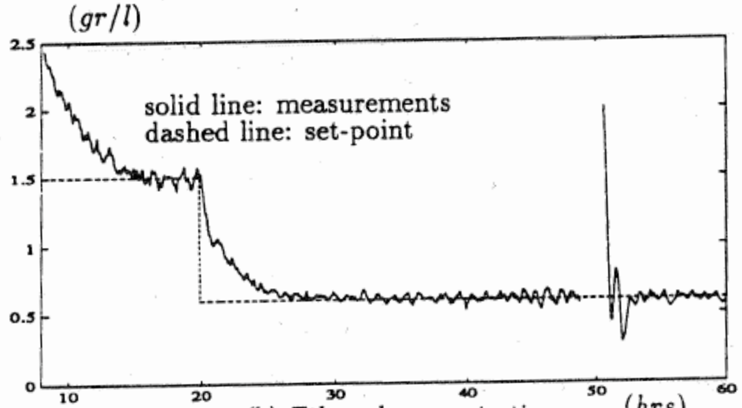
- Genetically modified yeast --> intracellular production of the vaccie “ingredients”

- Fed-batch fermentation of yeast

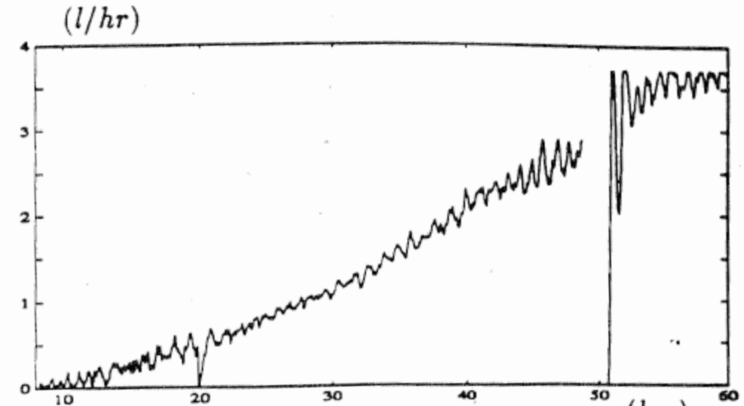
- Adaptive linearizing control of ethanol



(a) Biomass amount



(b) Ethanol concentration



(c) Feed rate


ZZZZZZ
CHTOK
?
LOI DE LA GRAVITATION.


QUANT À ISAAC NEWTON, IL AURAIT SÛREMENT ÉTÉ BIEN INCAPABLE DE FORMULER SA THÉORIE SUR LA GRAVITATION UNIVERSELLE.
CE QUI AURAIT ÉTÉ DOMMAGE POUR LE MONDE SCIENTIFIQUE EN GÉNÉRAL...
NOTEZ BIEN: LE CHOC VA LE FAIRE TOMBER DANS LES CITROUILLES
...ET POUR LES LECTEURS DE LA R.A.B. EN PARTICULIER.
KALINKA KALINKA MAYA
HEY!


EH BEN ET LUI ALORS? IL REÇOIT UNE POMME SUR LA TÊTE...
...CRAC, IL SE MET À DÉLIRER!
(REMARQUEZ QUE LÀ, IL EST PLUS EX-CUSABLE. LE CHOC, COMPRENEZ-VOUS...)
ET SI LES CORPS S'ATTI-RAIENT EN RAISON INVERSE DU CARRÉ DE LEUR DISTANCE?


ET ALORS, UN JOUR, ISAAC NEWTON FAI-SAIT UNE PROMENADE DIGESTIVE.
SOUDAIN, IL REÇUT UN BOUTON SUR LA TÊTE, CE QUI EST DÉJÀ UNE ANEC-DOTE AMUSANTE EN SOI.
PLINK
CE FAIT EUT POUR CONSÉ-QUENCE DE L'AMENER À NE FORMULER AUCUNE LOI NI AUCUNE THÉORIE SUR QUOI QUE CE SOIT.
?