



Consortium *CELLPAT*

*Analyses physiques et biochimiques en ligne
et modélisation des bioprocédés industriels*

du 1 nov 2013 au 31 oct 2016

Une collaboration entre :



SANOFI PASTEUR 



CELLPAT

● LES ACTEURS

Industriels : Sanofi Pasteur (Leader projet) ;
Merial ; Transgene

PME : The CoSMo Company

Institut Public : CNRS LASIR Univ Lille



● SPÉCIALITES

Expertises des bioprocédés

SANOFI PASTEUR



Expertises de modélisation



Expertises en technologie Raman et chimiométrie



Expertises en métabolomique (Lyon)



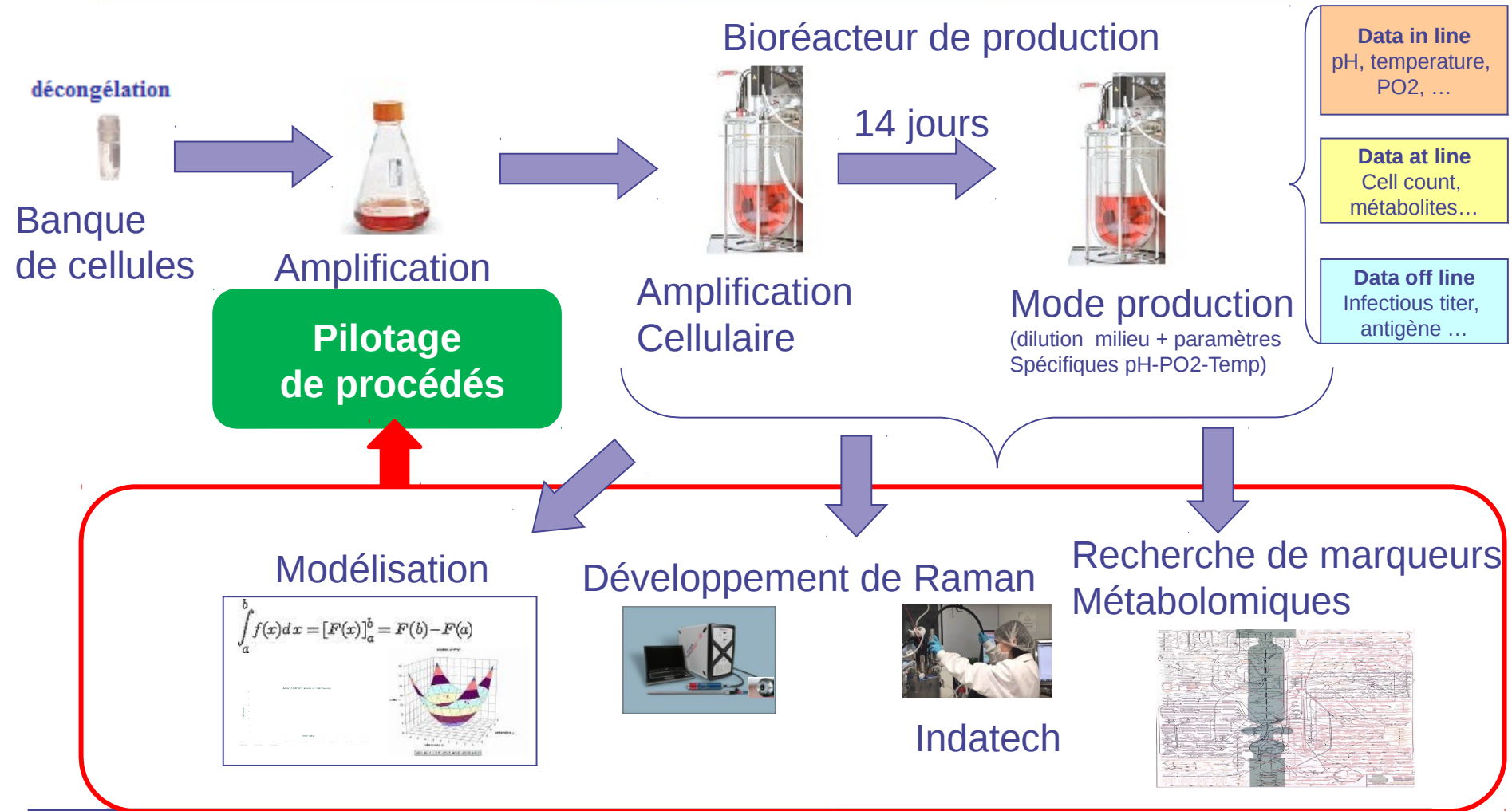
Expertises Raman : Indatech (Montpellier)



SANOFI PASTEUR



La stratégie de développement



Exemple de ce qui est fait



Cell counting



amino acid
Analysis



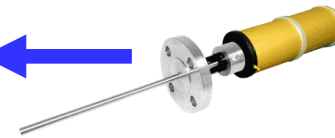
Analysis
AB-Virus



A la fin du projet



pH-PO₂-
temperature
measurment



Raman
analysis



Microscopic
observation



Ce que nous mesurons actuellement

	In-line	On-line	At-line	Off-line
pH, T°, PO2, (pCO2)				
Glucose				
Lactate				
Viabilité				
VCD				
Metabolites extra C				
Amino acids				
[Virus]				
[Antibodies]				
Glycosylation				
Metabolism intra C				

A la fin de Cellpat 2016

	In-line	On-line	At-line	Off-line
pH, T°, PO2, (pCO2)	In-line	On-line	At-line	Off-line
Glucose				
Lactate				
Viabilité				
VCD				
Metabolites extra C				
Amino acids				
[Virus]				
[Antibodies]				
Glycosylation				
Acid/base				
Metabolism intra C				




The CoSMo Company




Break the silos. Predict the unpredictable.

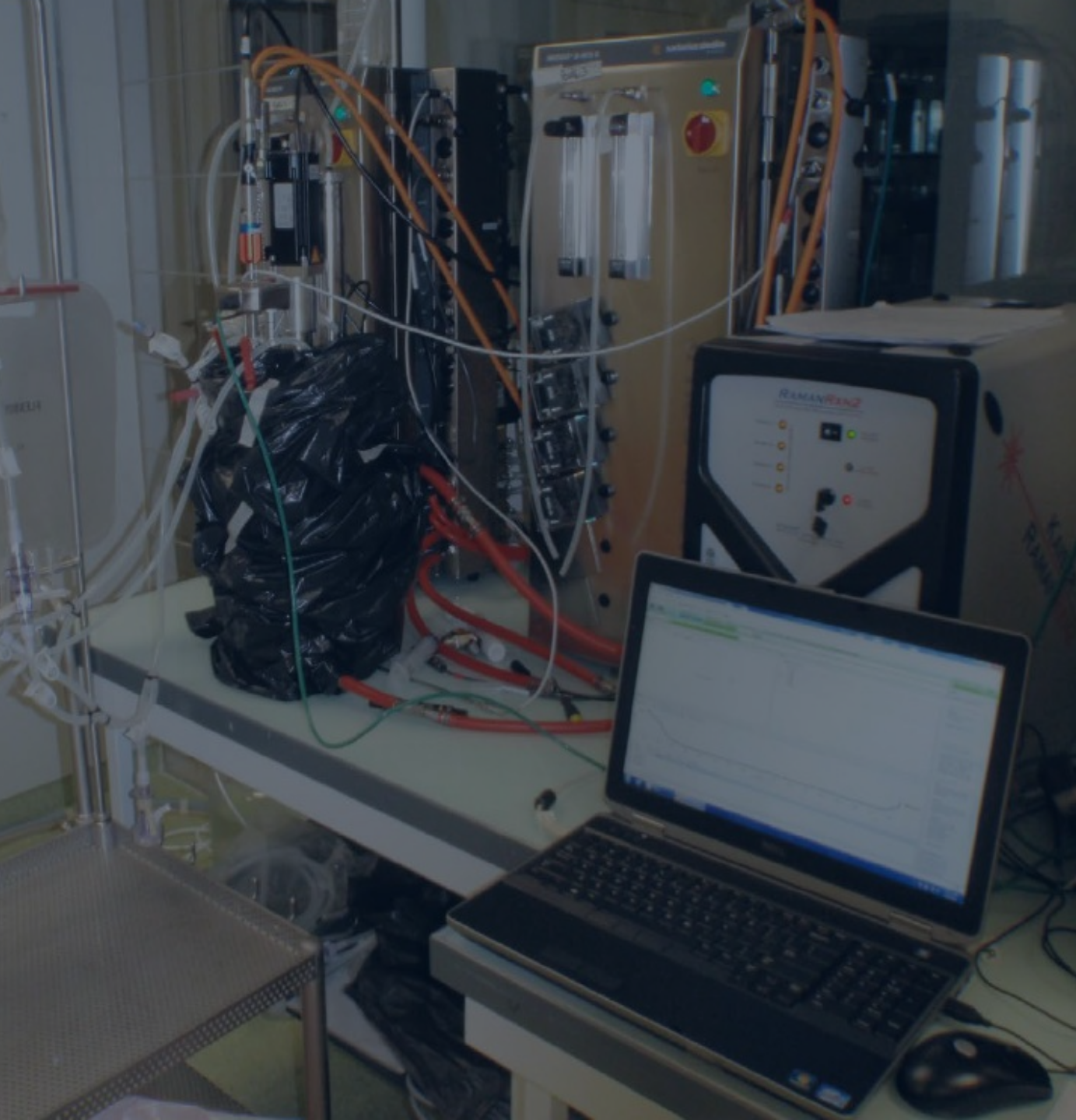
Consortium Cellpat : Analyses physiques et biochimiques en ligne et modélisation des bioprocédés industriels

Fanny Moïni

 www.thecosmocompany.com

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**Le logiciel
COMPAT**
-
**Démonstrati
on**

General view

10

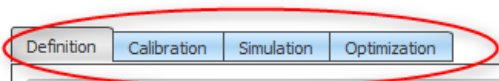
COMPAT

File Help About



Default model

Hide configuration tabs



Please select a model :

Product of interest :

Cells culture with a unique substrate (Glucose), and a unique setpoint that is continuous feeding in glucose. The product of interest is a replicative virus that infects healthy cells.

- Biomarker
- Setpoint
- Product of interest
- Bioreactor state variable

Variable	Short name	Type	Unit
Continuous feed	Feed	Feeding setpoint	L/h
Total Volume	Vol	Volume	L
Glucose	Glc	Substrate	mmol/L
Dead cells	DC	Dead cells	10e6 Cells/mL
Healthy cells	HCD	Healthy cells	10e6 Cells/mL

Variable information :

Name : Continuous feed
Unit : L/h
Type : Feeding setpoint
Subtype : Feeding setpoint
Description : Feeding rate into the bioreactor

Click on the Edit button to get more information.



Calibration / Validation

HeLa model

Hide configuration tabs

Definition
Calibration
Simulation
Optimization

Experimental data

Import...

Dataset	Calibration	Validation
ExampleDat...	<input type="checkbox"/>	<input checked="" type="checkbox"/>
ExampleDat...	<input checked="" type="checkbox"/>	<input type="checkbox"/>

Variables' weights

Glucose 1,00

Glutamine 1,00

Ammonium 1,00

Lactate 1,00

Poxvirus 1,00

Adjust constants

HCD yield per Glc consumed 0,2779

pH's optimality for HCD 0,4722

HCD's maximum death rate 0,0066

Initial guess for constants' values

Use current sliders' positions

Use previous constants' values:

Default

Con...

Glc

NH

Glc

NH

pH

HCD

Tox

Glc

Reset
Calibrate
Validate

Poxvirus

Glucose

Plots parameters

Confidence interval

Condition A

ExampleData_ExampleSheet1

SEM for Condition A

Condition B

ExampleData_ExampleSheet2

Calibration

Validation

Results

Product of interest concentration :

Simulated : 0.0

Calibration results

Total fitness score : -3.919 ↑

Best fitness score : -0.259

Validation results

Validity percentage : 62.778 %

Total fitness score : -2.161

Simulation

HeLa model

Hide configuration tabs

Definition Calibration **Simulation** Optimization

Settings

Duration (h)

Tot Volume (L)

Process setpoints

pH 0

Continuous feed (L/h)

Initial concentrations

Glucose (mmol/L)

Glutamine (mmol/L)

Ammonium (mmol/L)

Lactate (mmol/L)

Poxvirus (10e6 U/mL)

Punctual events

Time (h)	Type	Name
100.0	Punctual feed	

Automatic update

Plots parameters

- Confidence interval
- Simulation
- Condition A
 - ExampleData__ExampleSheet1
 - SEM for Condition A
- Condition B
 - ExampleData__ExampleSheet2
- Calibration
- Validation

Results

Product of interest concentration :
Simulated : 22.383

Time (h) Poxvirus

Time (h)	10e6 U/mL
0	0.0001
100	1
200	10
300	15
360	18

Time (h) Glucose

Time (h)	mmol/L
0	30
100	25
200	10
300	2
360	0

Time (h) Glutamine

Time (h)	mmol/L
0	10
100	5
200	1
300	0.2
360	0

Time (h) Ammonium

Time (h)	mmol/L
0	0
100	0
200	0
300	0
360	0

Optimization

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CHO model

Hide configuration tabs

Definition Calibration Simulation **Optimization**

Objective

Main purpose : **Final concentrations**

Maximize cells concentration : **Healthy CHO Ce**

Maximize product of interest

Other...

Optimization parameters

Bioreactor capacity (L) : **6,000**

Duration of action intervals (h) : **12**

Initial conditions : **Current simulation** **Display**

Biomarkers

Dead cells (10e6 Cells/mL)

Minimum : **0,00**

Maximum : **100,00**

Healthy CHO Cells (10e6 Cells/mL)

Minimum : **0,00**

Maximum : **100,00**

Setpoint variables

Temperature (Celsius degree)

Minimum : **33**

Maximum : **37**

Continuous feed (L/h)

Minimum : **0**

Maximum : **0,12**

Reset **Optimize**

Plots parameters

Optimization result

Results

Product of interest concentration :

Simulated : **0,00**

Experimental : **0,00**

Rate of increase (%) : **0,00**

Validation results

Validity percentage : **100,00**

Total fitness score : **0,00**

Optimization solution

Status : **Solve_Succeeded**

Optimal cost : **0,0**

Continuous feed

Time (h)	Continuous feed (L/h)
0 - 220	0
220 - 240	0,01
240 - 260	0,02
260 - 280	0,02
280 - 300	0,12

Temperature

Time (h)	Temperature (Celsius degree)
0 - 290	33
290 - 300	37

Dead cells

Time (h)	Dead cells (10e6 Cells/mL)
0 - 300	0
300	100,00
300 - 360	0

Tot Volume

Time (h)	Tot Volume (L)
0 - 300	6000
300 - 360	0

COMPAT - Conclusion

- ▶ **En R&D**, COMPAT peut vous aider à:
 - Diminuer le temps de manipulations
 - Trouver l'optimum de production ...
 - ... tout en respectant les contraintes logistiques
 - Evaluer la robustesse d'un procédé en simulant des incidents

- ▶ Et à terme, **en production**:
 - « Rejouer » un incident pour mesurer son ampleur



COMPAT peut être testé grâce à des données historiques.

Démonstration sur demande

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