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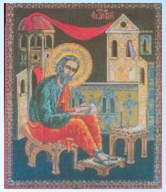
Почетен член на "Съвета на Европейската научна и културна общност”



Interactive System for Education in Modelling and Control of Bioprocesses

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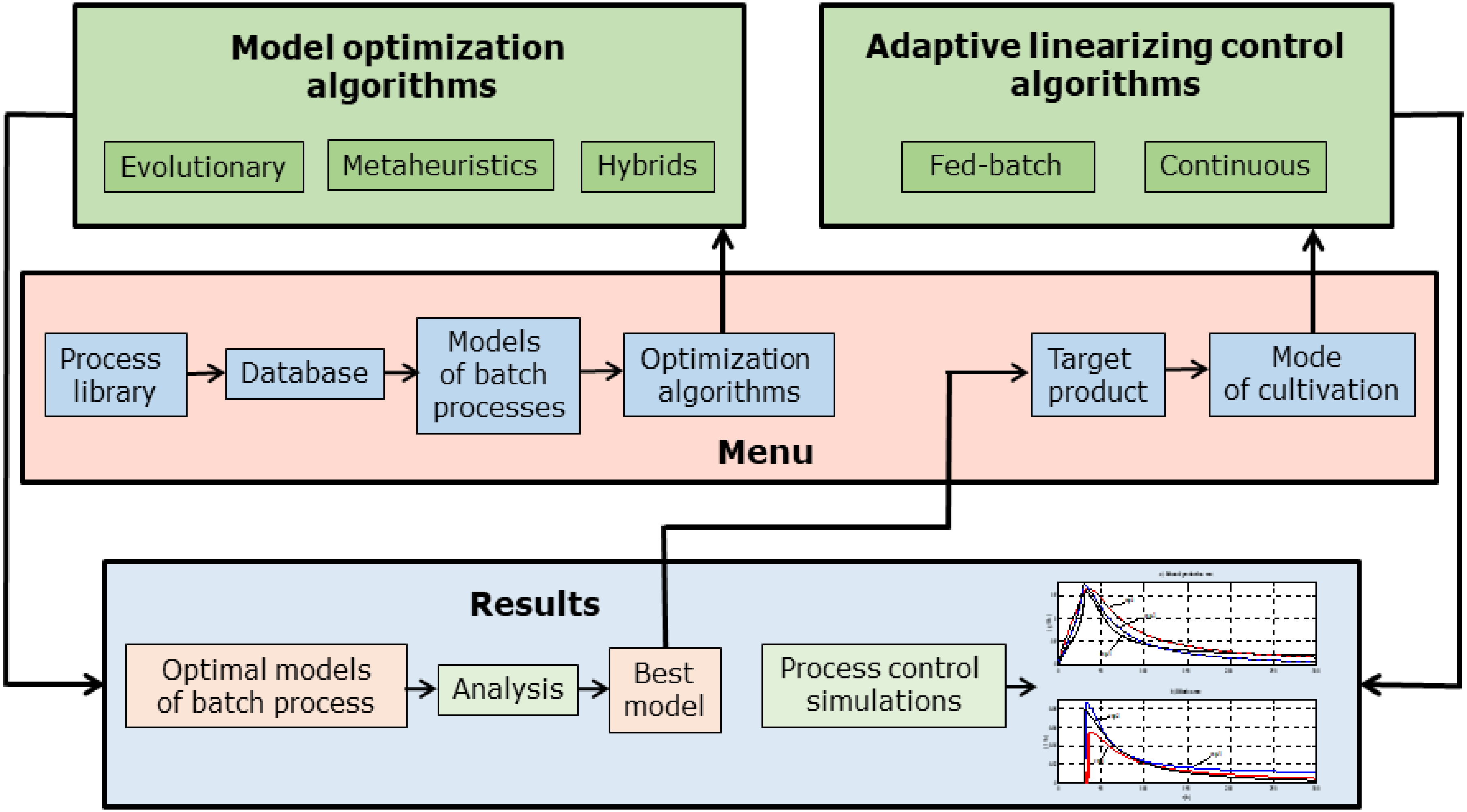
Craiova, Roumania

Interactive System for Education in Modelling and Control of Bioprocesses

InSEMCoBio



Model optimization algorithms

Evolutionary

Metaheuristics

Hybrids

Adaptive linearizing control algorithms

Fed-batch

Continuous

Process library → Database → Models of batch processes → Optimization algorithms

Target product → Mode of cultivation

Menu

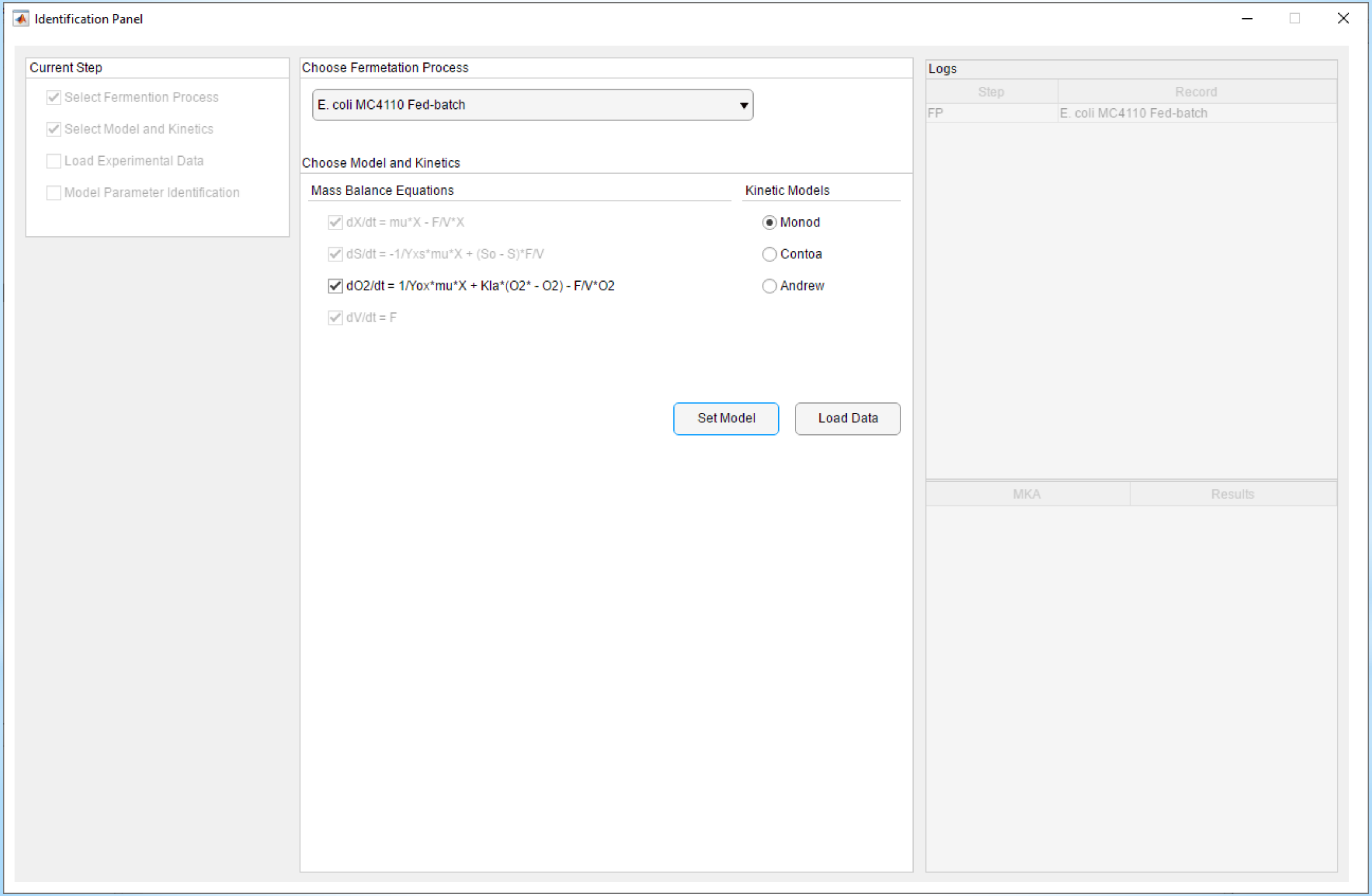
Results

Optimal models of batch process → Analysis → Best model

Process control simulations →

Fig. 1. Open source system InSEMCoBio

Setting up a fermentation process model and metaheuristic algorithm parameters in InSEMCoBio



Identification Panel

Current Step

☑ Select Fermention Process
☑ Select Model and Kinetics
☐ Load Experimental Data
☐ Model Parameter Identification

Choose Fermetation Process

E. coli MC4110 Fed-batch

Choose Model and Kinetics

Mass Balance Equations

☑ dX/dt = mu*X - F/V*X
☑ dS/dt = -1/Yxs*mu*X + (So - S)*F/V
☑ dO2/dt = 1/Yox*mu*X + Kla*(O2* - O2) - F/V*O2
☑ dV/dt = F

Kinetic Models

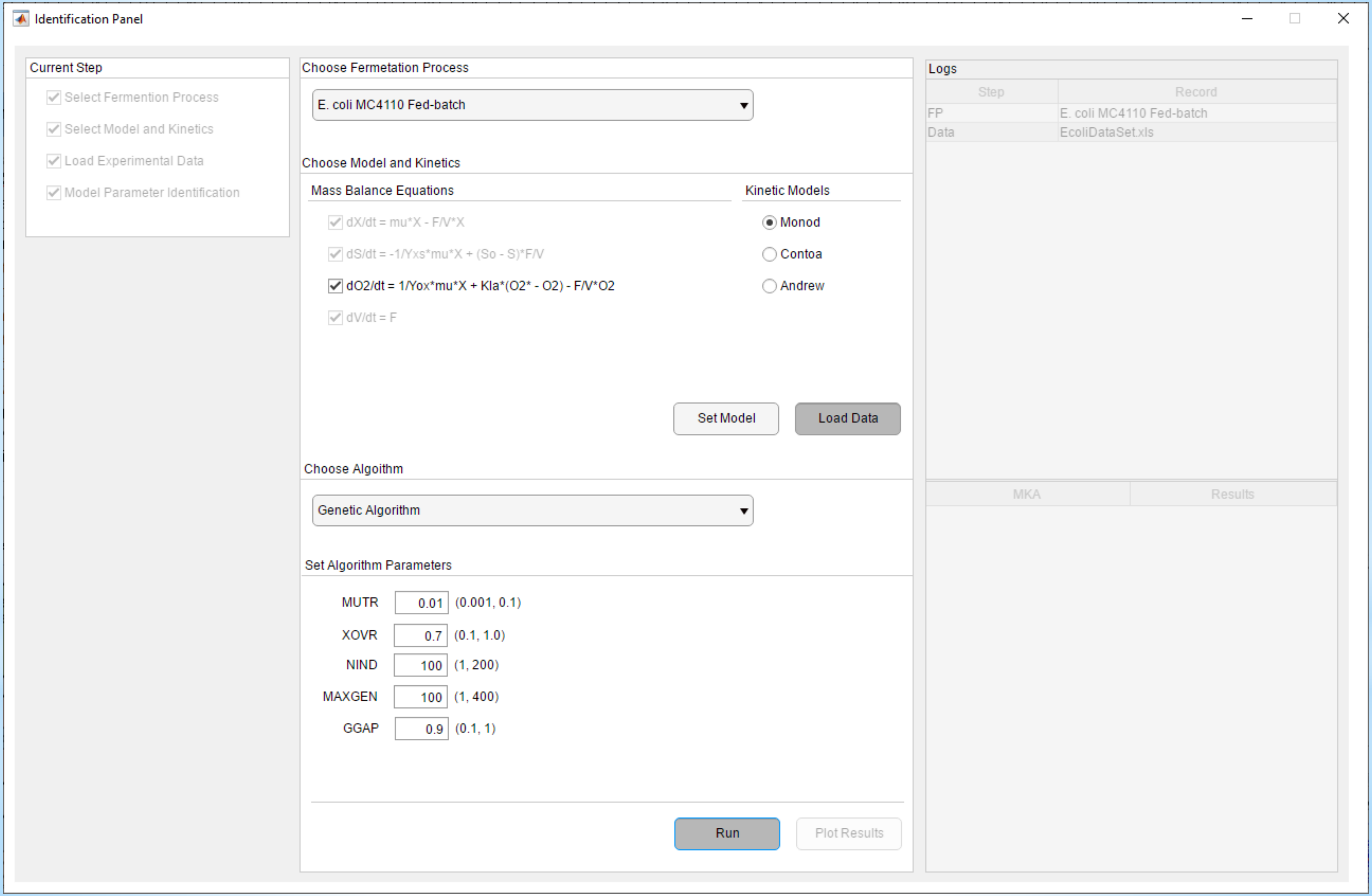
● Monod
○ Contoa
○ Andrew

Logs

Step	Record
FP	E. coli MC4110 Fed-batch

MKA	Results

Setting up a fermentation process model and metaheuristic algorithm parameters in InSEMCoBio



Current Step

- ☑ Select Fermention Process
- ☑ Select Model and Kinetics
- ☑ Load Experimental Data
- ☑ Model Parameter Identification

Choose Fermetation Process

E. coli MC4110 Fed-batch

Choose Model and Kinetics

Mass Balance Equations

- ☑ dX/dt = mu*X - F/V*X
- ☑ dS/dt = -1/Yxs*mu*X + (So - S)*F/V
- ☑ dO2/dt = 1/Yox*mu*X + Kla*(O2* - O2) - F/V*O2
- ☑ dV/dt = F

Kinetic Models

- ● Monod
- ○ Contoa
- ○ Andrew

Choose Algoithm

Genetic Algorithm

Set Algorithm Parameters

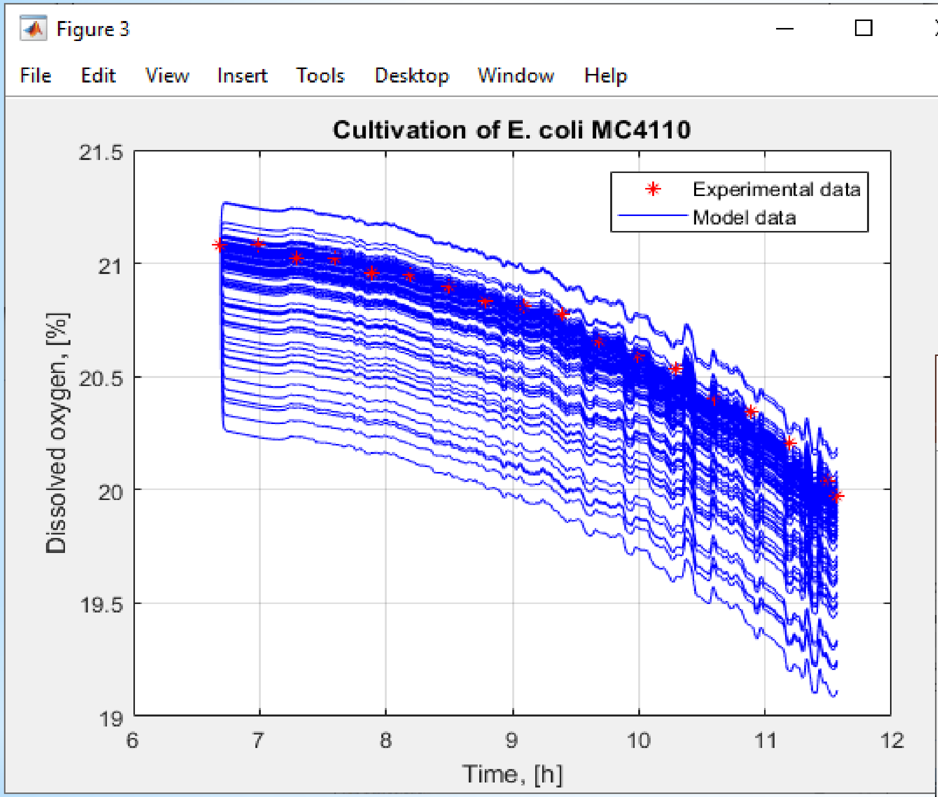
MUTR	0.01	(0.001, 0.1)
XOVR	0.7	(0.1, 1.0)
NIND	100	(1, 200)
MAXGEN	100	(1, 400)
GGAP	0.9	(0.1, 1)

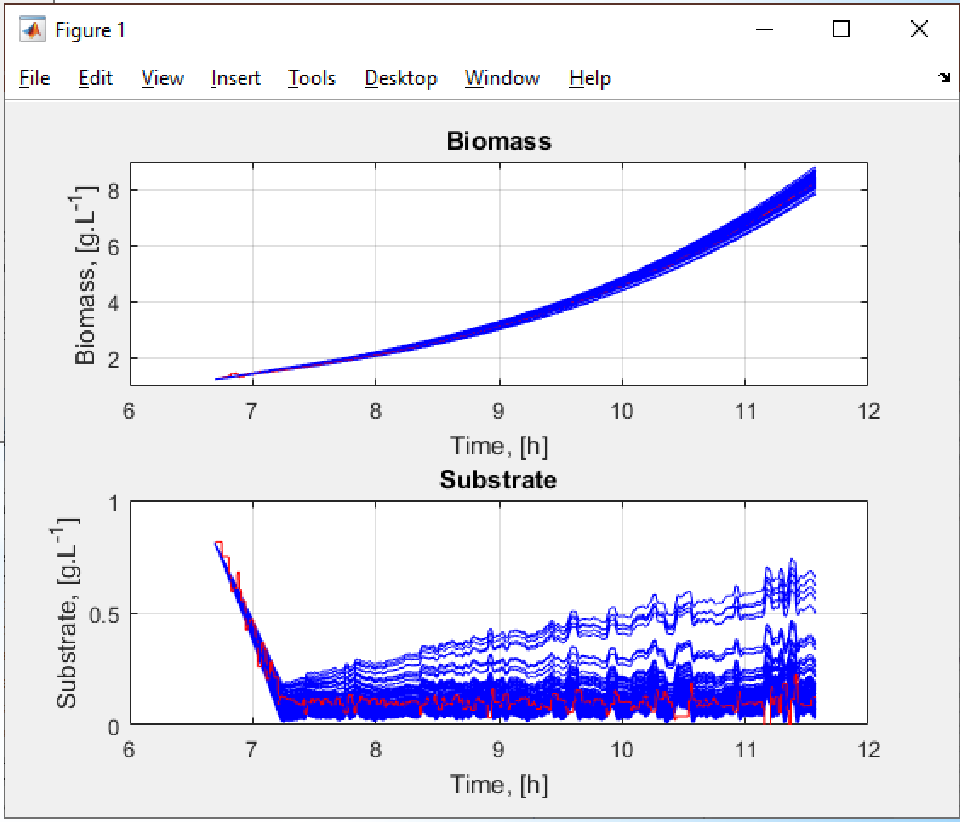
Logs

Step	Record
FP	E. coli MC4110 Fed-batch
Data	EcoliDataSet.xls

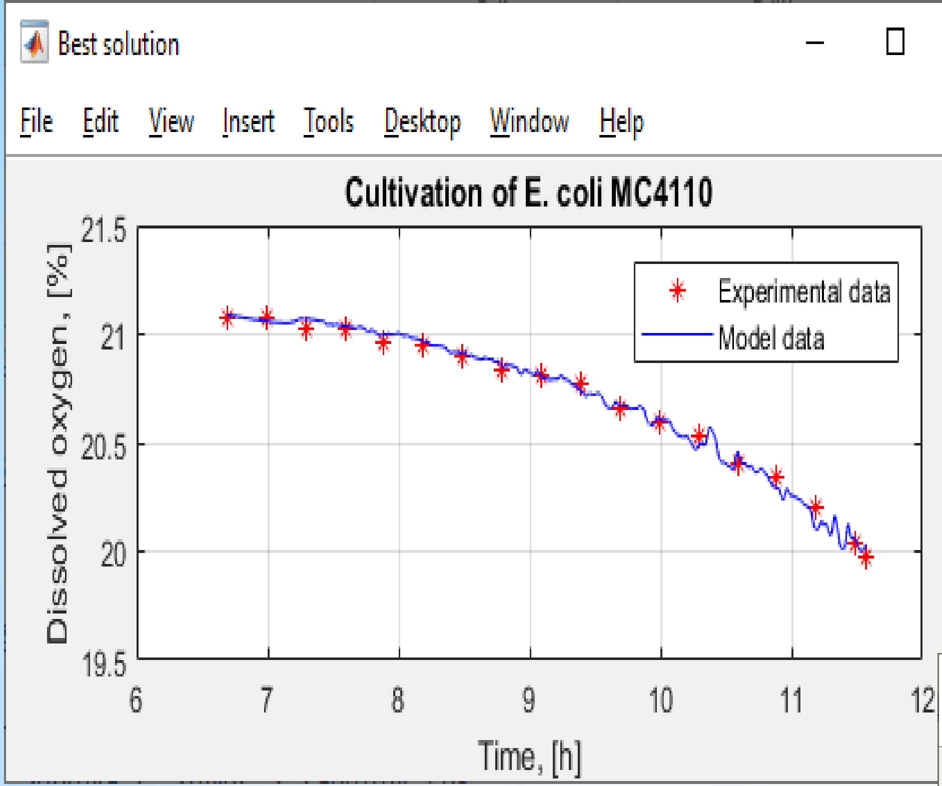
MKA	Results

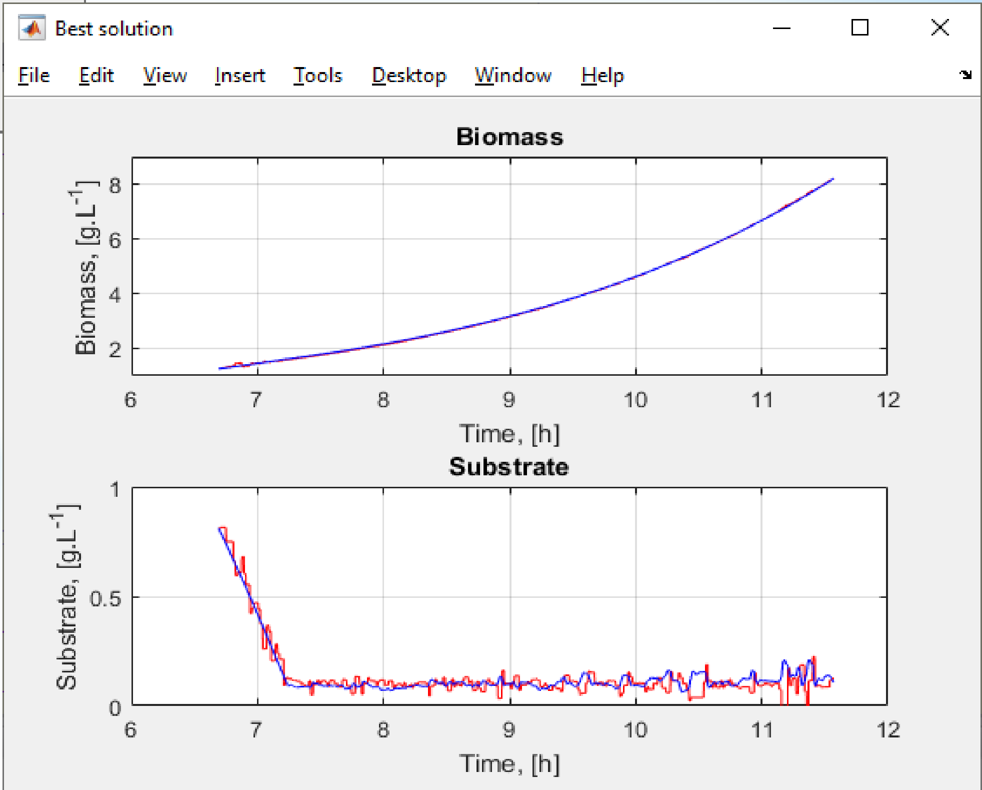
Visualizing the results of the identification procedure in InSEMCoBio





Visualizing the results of the identification procedure in InSEMCoBio





Algorithms for modelling, monitoring and control prepared for build into the system InSEMCoBio

Model Identification of E. coli MC4110 fed-batch cultivation for proteins production

- *already built-in*

Model Identification and Monitoring of E. Coli strain BL21(DE3)pPhyt109 fed-batch cultivation for extracellular production of bacterial phytase

Model Identification, *Monitoring and Continous Control of Aspergillus Niger* Fermentation for Gluconic Acid Production

Model Identification and Monitoring of E. Coli fed-batch cultivation for extracellular production of bacterial phytase

Oxidative-fermentative growth model on glucose

$$k_1 S + k_5 O \xrightarrow{\mu 1} X + k_8 C$$

Oxidative growth on glucose

Model

$$\frac{d}{dt}\begin{bmatrix} X \\ S \\ A \\ O \\ C_r \end{bmatrix} = \begin{bmatrix} 1 \\ -k_1 \\ 0 \\ -k_5 \\ k_8 \end{bmatrix} \mu_1 X - D \begin{bmatrix} X \\ S \\ A \\ O \\ C_r \end{bmatrix} + \frac{F_{in,S}}{W}\begin{bmatrix} 0 \\ S_{in} \\ 0 \\ 0 \\ 0 \end{bmatrix} + \begin{bmatrix} 0 \\ 0 \\ 0 \\ OTR \\ -CTR \end{bmatrix}$$

$$q_s = q_{s,\max} S/(K_S + S)$$

$$\mu_1 = q_s / k_1$$

$$R_{ac} = 0$$

Marker

$$R_{ac} = \frac{dA}{dt} + \frac{F_{in,s}}{W} A$$

$$k_1 S + k_5 O \xrightarrow{\mu 1} X + k_8 C$$

$$k_2 S + k_6 O \xrightarrow{\mu 2} X + k_3 C + k_9 A$$

Oxidative-fermentative growth on glucose

Model

$$R_{ac} > 0$$

$$\frac{d}{dt}\begin{bmatrix} X \\ S \\ A \\ O \\ C_r \end{bmatrix} = \begin{bmatrix} 1 & 1 \\ -k_1 & -k_2 \\ 0 & k_3 \\ -k_5 & -k_6 \\ k_8 & k_9 \end{bmatrix} \begin{bmatrix} \mu_1 \\ \mu_2 \end{bmatrix} X - D \begin{bmatrix} X \\ S \\ A \\ O \\ C_r \end{bmatrix} + \frac{F_{in,S}}{W}\begin{bmatrix} 0 \\ S_{in} \\ 0 \\ 0 \\ 0 \end{bmatrix} + \begin{bmatrix} 0 \\ 0 \\ 0 \\ OTR \\ -CTR \end{bmatrix}$$

$$\mu_1 = q_{s,crit} / k_1$$

$$\mu_2 = (q_s - q_{s,crit}) / k_2$$

$$q_{s,crit} = \frac{q_{o,\max}}{k_{os}} \frac{K_{i,o}}{K_{i,o} + A}$$

Oxidative-fermentative growth model on glucose and oxidative on acetate

$$k_1 S + k_5 O \xrightarrow{\mu 1} X + k_8 C$$
$$k_2 S + k_6 \mathrm{O} \xrightarrow{\mu 2} X + k_3 C + k_9 A$$

Oxidative-fermentative growth on glucose

Model

$$\frac{d}{dt}\begin{bmatrix} X \\ S \\ A \\ O \\ C_r \end{bmatrix} = \begin{bmatrix} 1 & 1 \\ -k_1 & -k_2 \\ 0 & k_3 \\ -k_5 & -k_6 \\ k_8 & k_9 \end{bmatrix} \begin{bmatrix} \mu_1 \\ \mu_2 \end{bmatrix} X - D \begin{bmatrix} X \\ S \\ A \\ O \\ C_r \end{bmatrix} + \frac{F_{in,S}}{W} \begin{bmatrix} 0 \\ S_{in} \\ 0 \\ 0 \\ 0 \end{bmatrix} + \begin{bmatrix} 0 \\ 0 \\ 0 \\ OTR \\ -CTR \end{bmatrix}$$

$$\mu_1 = \mathrm{q}_{\mathrm{s,crit}} / \mathrm{k}_1$$

$$\mu_2 = (\mathrm{q}_{\mathrm{s}} - \mathrm{q}_{\mathrm{s,crit}}) / \mathrm{k}_2$$

$$\mathrm{q}_{\mathrm{s,crit}} = \frac{\mathrm{q}_{\mathrm{o,max}}}{\mathrm{k}_{\mathrm{os}}} \frac{\mathrm{K}_{\mathrm{i,o}}}{\mathrm{K}_{\mathrm{i,o}} + A}$$

$$R_{ac} > 0$$

Marker

$$R_{ac} = \frac{dA}{dt} + \frac{F_{in,s}}{W} A$$

$$k_1 S + k_5 O \xrightarrow{\mu 1} X + k_8 C$$
$$k_4 \mathrm{A} + k_7 \mathrm{O} \xrightarrow{\mu_3} X + k_{10} \mathrm{C}$$

Oxidative growth on glucose and acetate

$$R_{ac} < 0$$

$$\frac{d}{dt}\begin{bmatrix} X \\ S \\ A \\ O \\ C_r \end{bmatrix} = \begin{bmatrix} 1 & 1 \\ -k_1 & 0 \\ 0 & -k_4 \\ -k_5 & -k_7 \\ k_8 & k_{10} \end{bmatrix} \begin{bmatrix} \mu_1 \\ \mu_3 \end{bmatrix} \mathrm{X} - \mathrm{D} \begin{bmatrix} X \\ S \\ A \\ O \\ C_r \end{bmatrix} + \frac{F_{in,S}}{W} \begin{bmatrix} 0 \\ S_{in} \\ 0 \\ 0 \\ 0 \end{bmatrix} + \begin{bmatrix} 0 \\ 0 \\ 0 \\ OTR \\ -CTR \end{bmatrix}$$

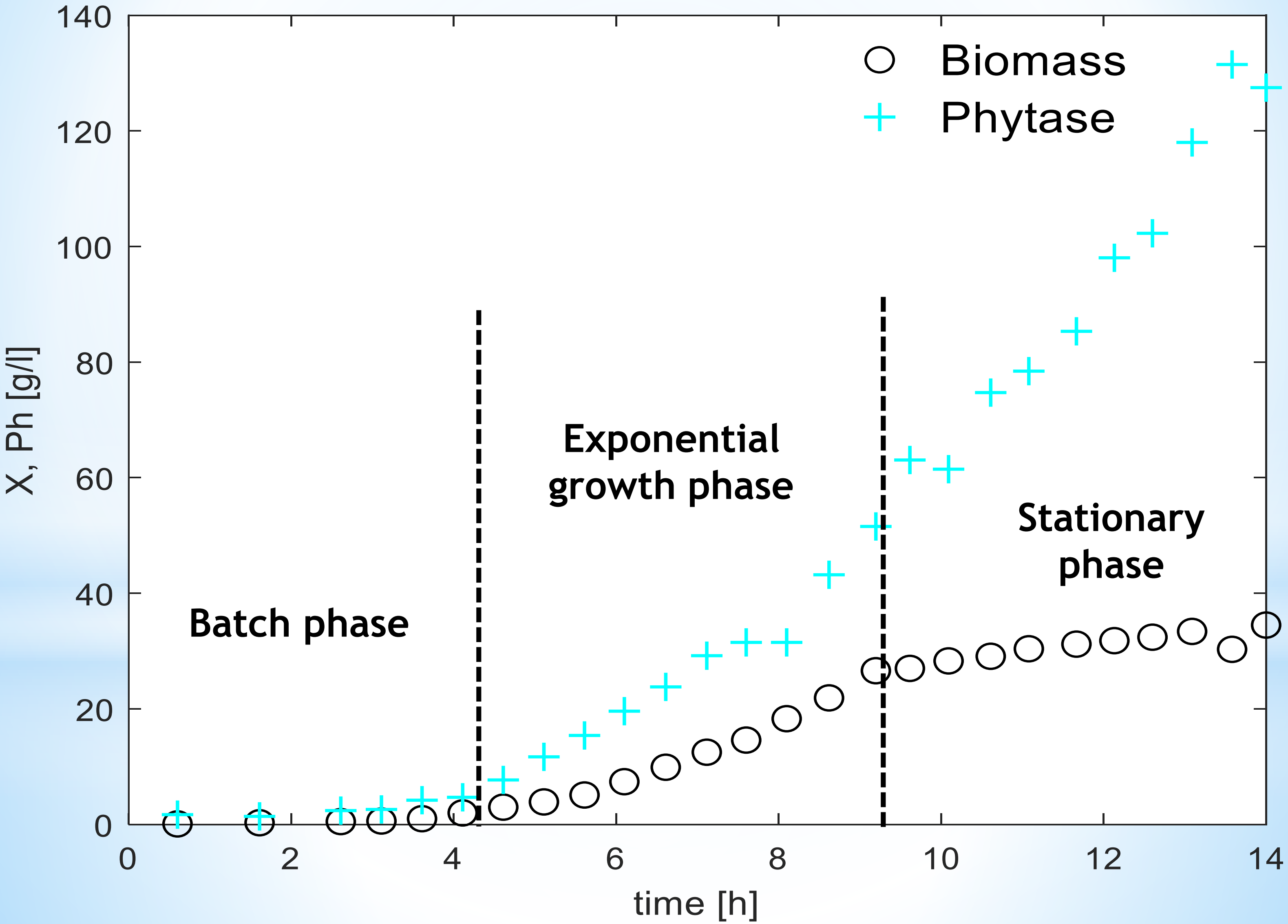
Model

$$\mu_1 = \mathrm{q}_{\mathrm{s,crit}} / \mathrm{k}_1 \qquad \mu_3 = q_{ac} / k_4$$

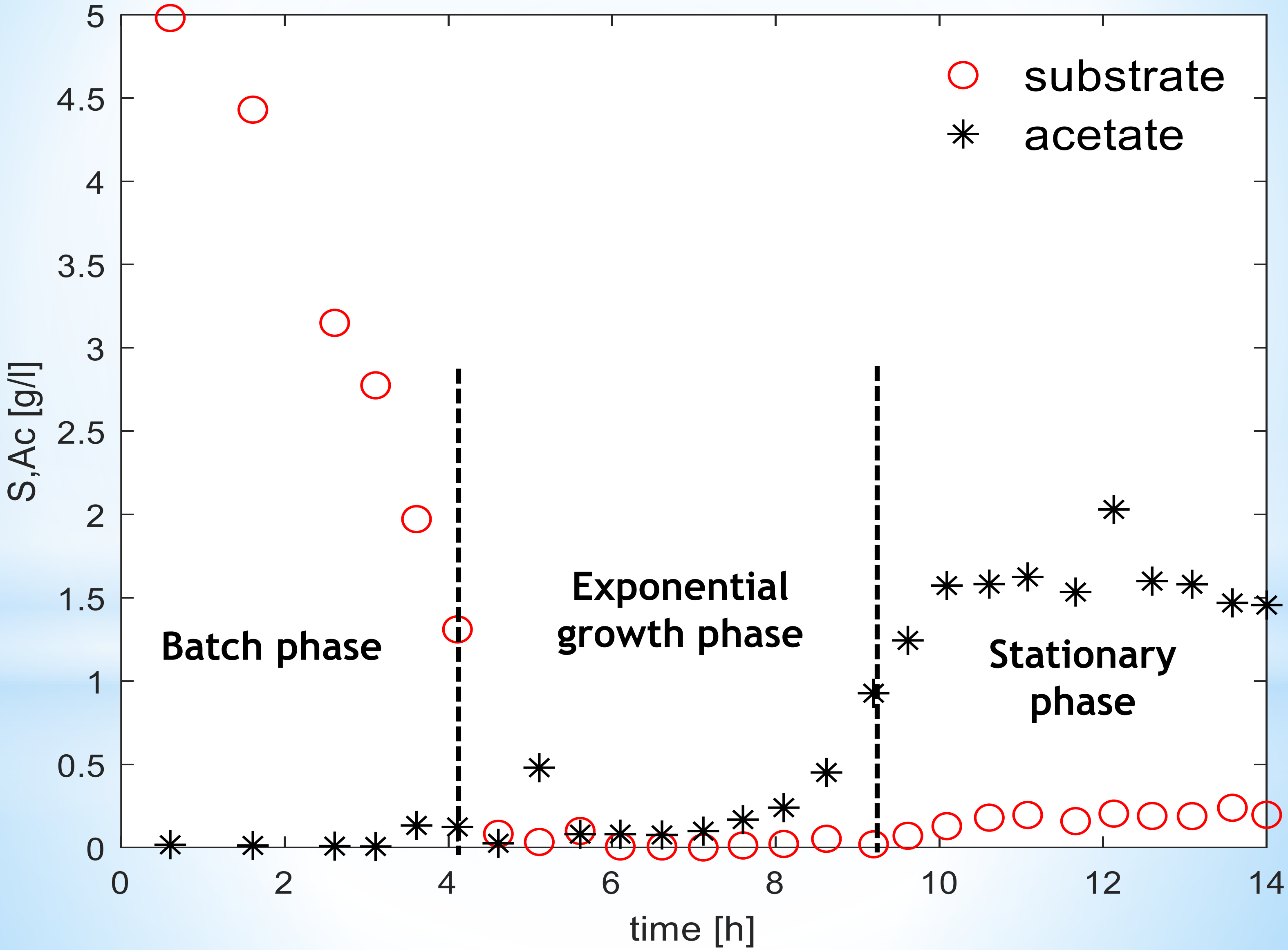
$$\mathrm{q}_{\mathrm{s,crit}} = \frac{\mathrm{q}_{\mathrm{o,max}}}{\mathrm{k}_{\mathrm{os}}} \frac{\mathrm{K}_{\mathrm{i,o}}}{\mathrm{K}_{\mathrm{i,o}} + A}$$

$$q_{ac} = q_{ac,max} \left(\frac{A}{K_A + A}\right) \left(\frac{K_{i,A}}{K_{i,A} + A}\right)$$

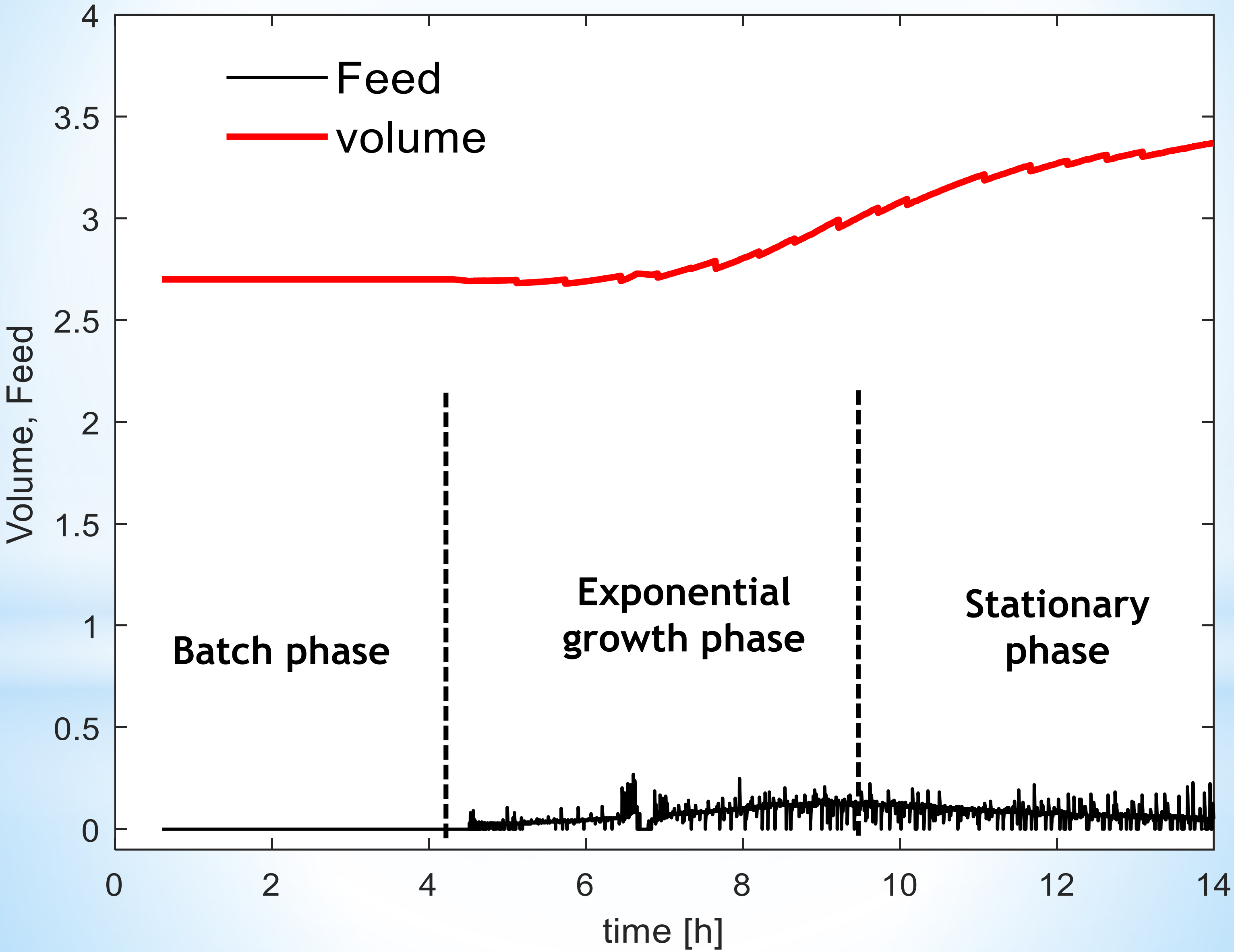
Experimental data on biomass and phytase concentrations



Experimental data on substrate and acetate concentrations



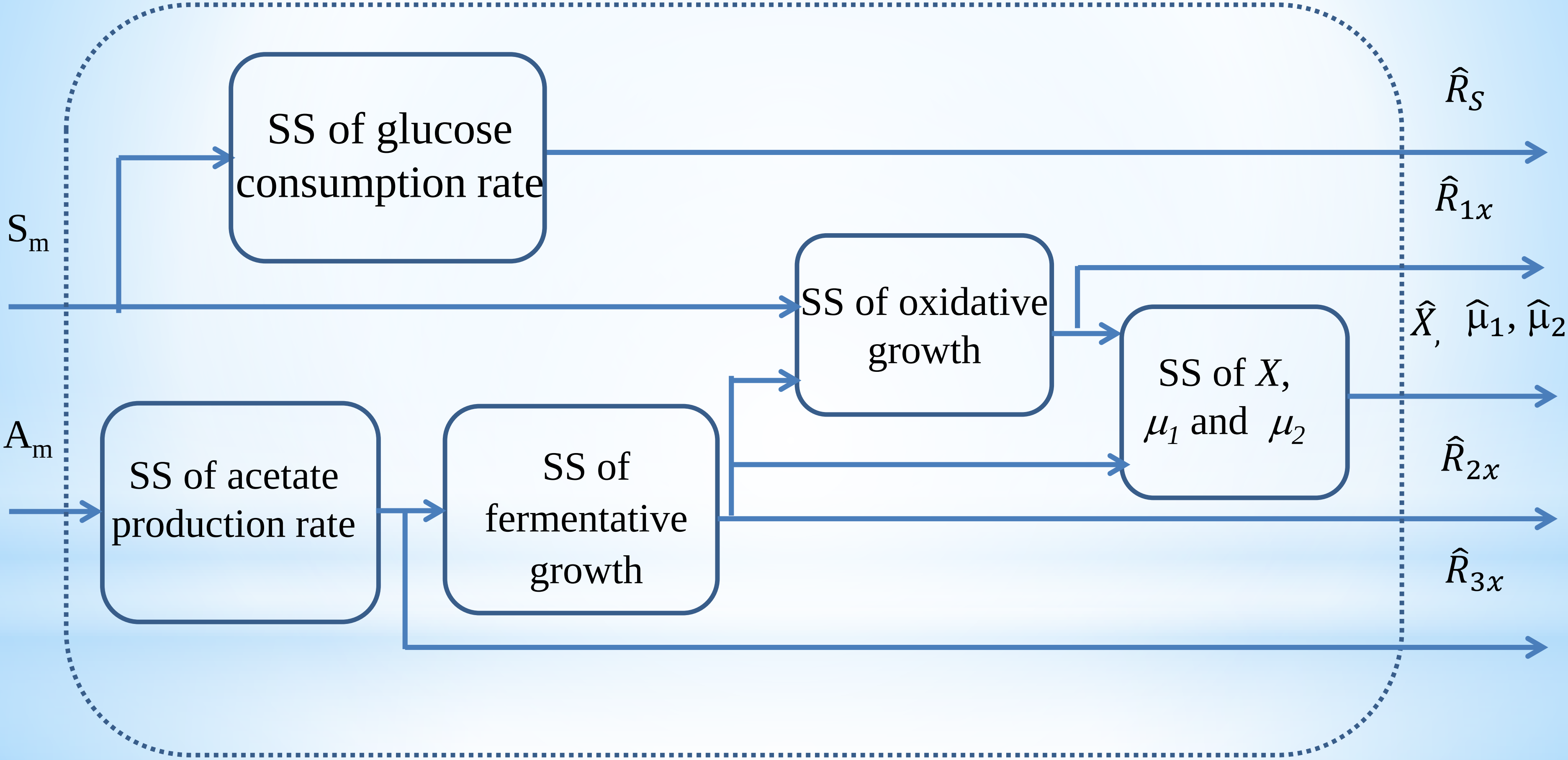
Experimental data on reactor volume and glucose feed



Comparison of the coefficients of the best models for the three phases

	q_{smax}	k_s	k_{is}	q_{omax}	k_{os}	k_{io}	q_{acmax}	k_a	k_{ia}	k_1	k_2	k_3	k_4	k_5	k_6	k_7
1 phase	4.19	0.19	5.54	1.1	2.15	0.088	0.082	1.17	-	3.69	0.557	0.187	4.6	1.41	2.66	0.45
2 phase	34.24	0.79	1.83	0.469	2.53	0.197	0.143	0.97	0.246	2.08	2.167	0.049	4.1	2.88	1.52	0.5
3 phase	77.11	0.47	12.3	2.1	3.29	0.134	0.0021	0.295	0.228	16.6	11.66	0.42	9.9	39.45	9.53	0.56

Scheme of the cascade software sensor of the process kinetics



On-line estimation of acetate production and consumption rates

Acetate production

$$\frac{d\hat{A}}{dt} = \hat{R}_{ap} - DA_m + w_1(A_m - \hat{A})$$

$$\frac{d\hat{R}_{ap}}{dt} = w_2(A_m - \hat{A})$$

Acetate consumption

$$\frac{d\hat{A}}{dt} = -\hat{R}_{ac} - DA_m + \lambda_1(A_m - \hat{A})$$

$$\frac{d\hat{R}_{ac}}{dt} = -\lambda_2(A_m - \hat{A})$$

On-line estimation of R_{1x} , $R_{2x,}$ R_{3x} and X

$$\frac{d\hat{S}}{dt} = -k_1\hat{R}_{1X} - k_2\hat{R}_{ap}/k_3 - \frac{F}{V}S_m + \frac{F_{in,S}}{V}S_{in} + \lambda_1(S_m - \hat{S})$$

$$\frac{d\hat{R}_{1x}}{dt} = \lambda_2(S_m - \hat{S})$$

$$\hat{\mu}_1 = \hat{R}_{1X}/\hat{X}$$

$$\hat{R}_{2X} = \hat{R}_{ap}/k_3$$

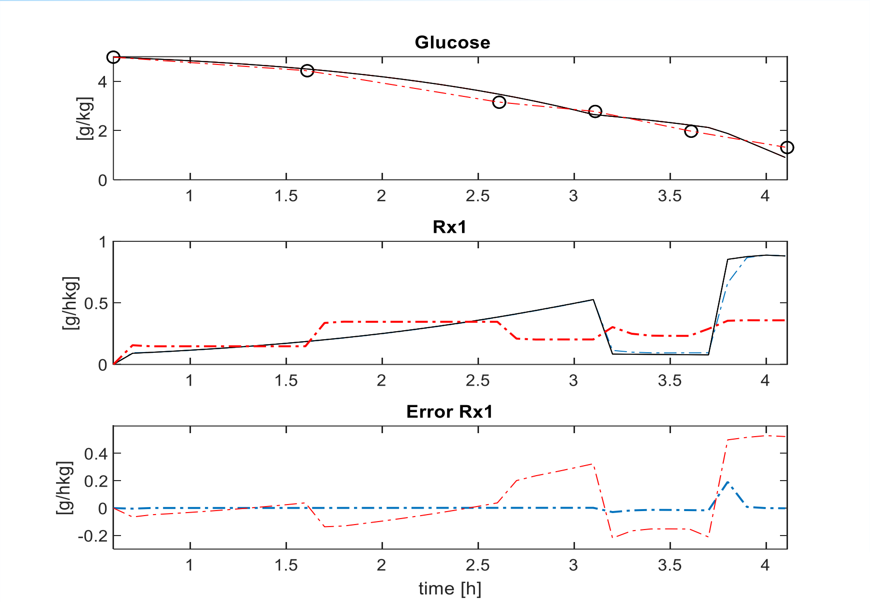
$$\hat{\mu}_2 = \hat{R}_{2X}/\hat{X}$$

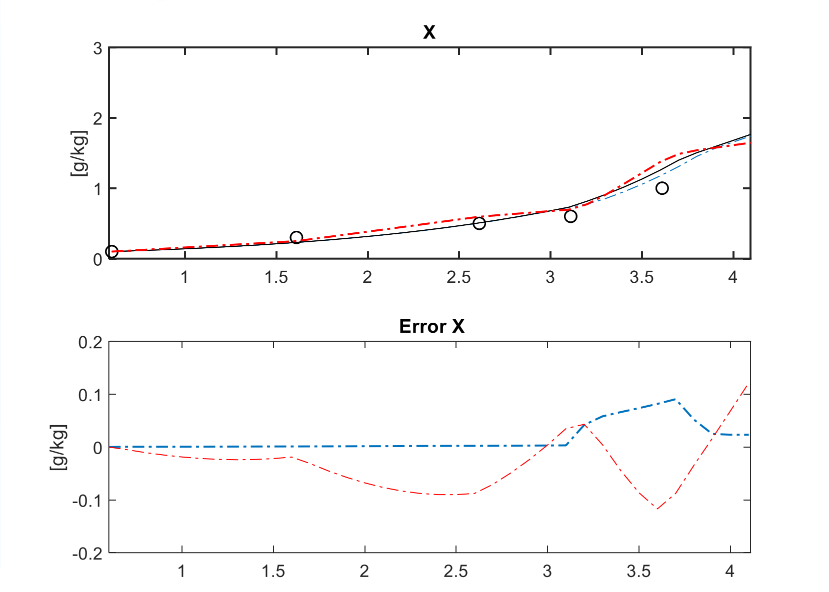
$$\hat{R}_{3X} = -\hat{R}_{ac}/k_4$$

$$\hat{\mu}_3 = \hat{R}_{3X}/\hat{X}$$

$$\frac{d\hat{X}}{dt} = \hat{R}_{1X} + \hat{R}_{2X} + \hat{R}_{3X} - D\hat{X}$$

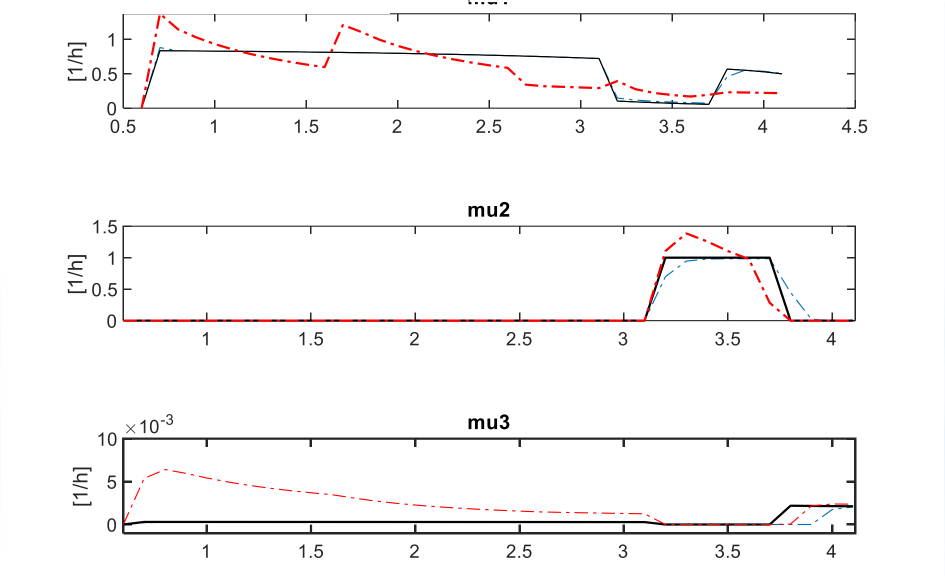
Monitoring results– I phase





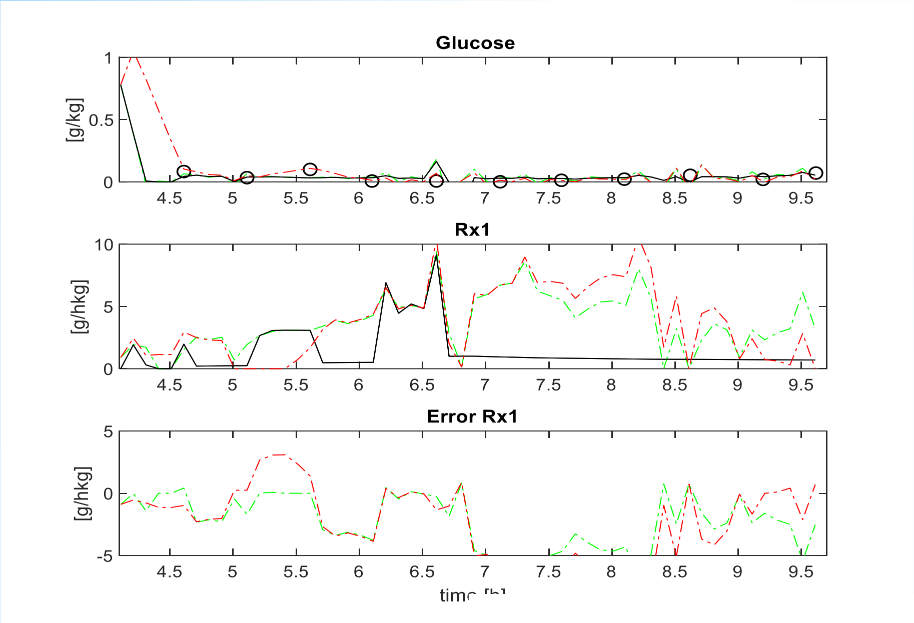
Tuning parameters
C1=50;
C2=50;

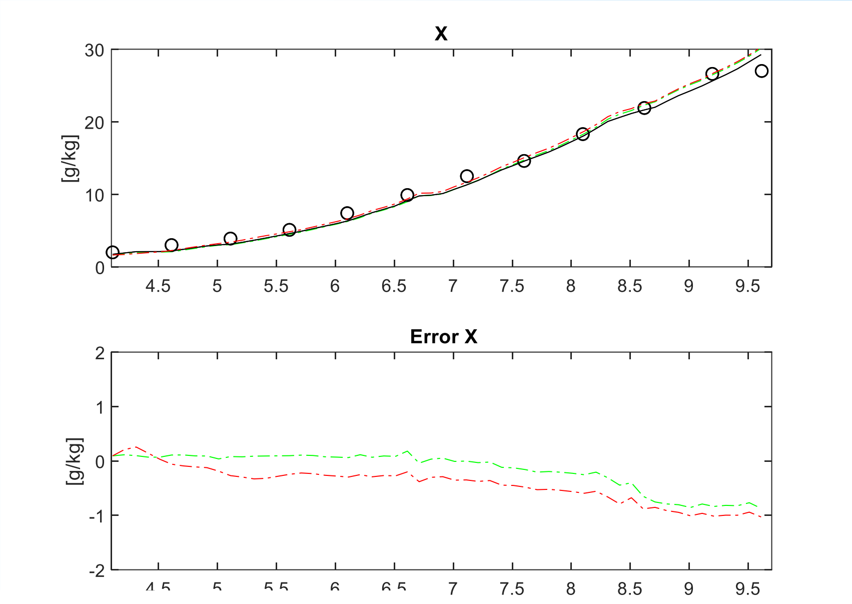
Black lines- model data



SS results: with red lines - inputs are experimental data, with blue lines – inputs are model data

Monitoring results– II phase



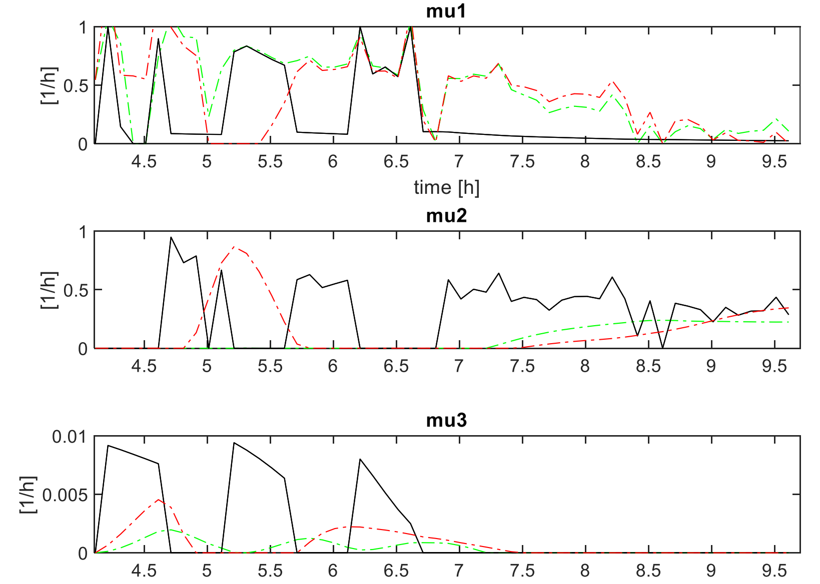


SS tuning parameters

C1= 54.7764;

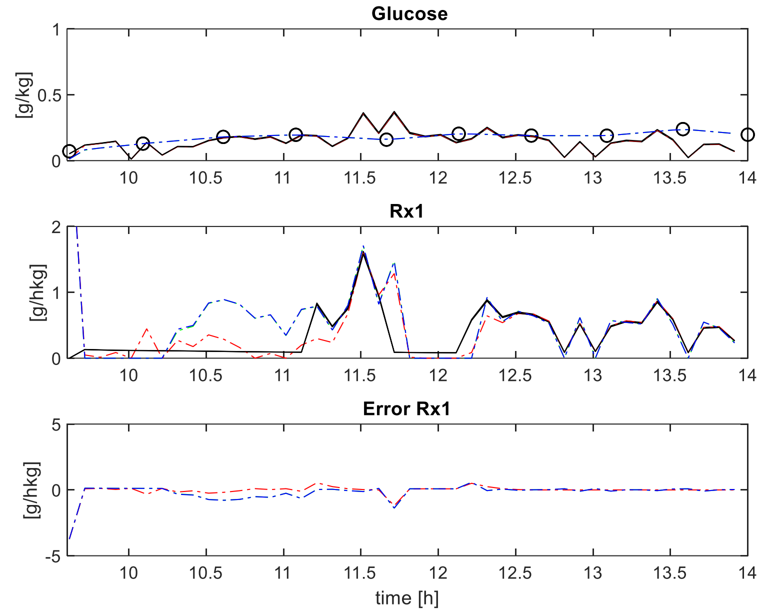
C2= 2.7926;

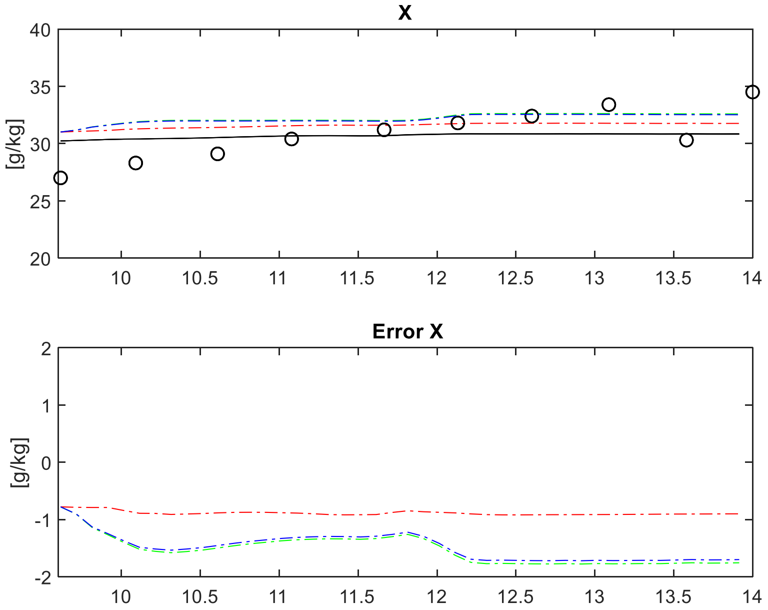
Black lines- model data



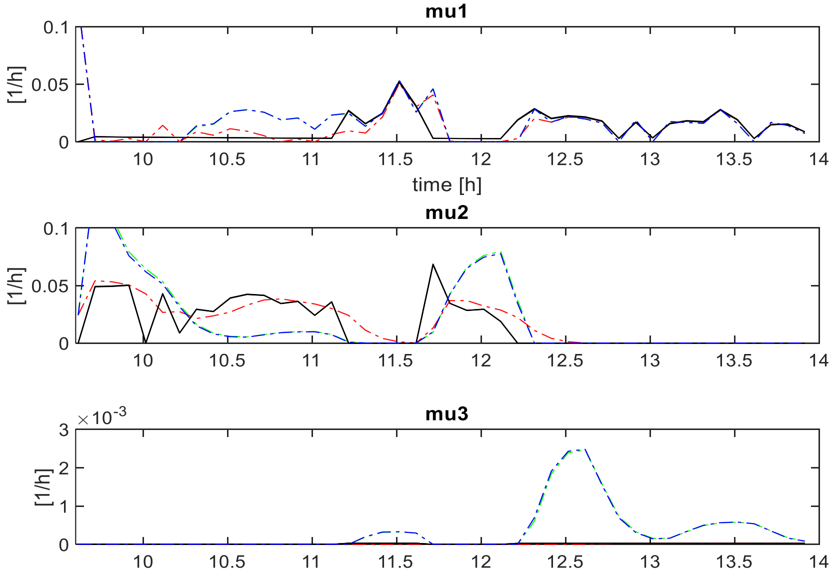
SS results: with red lines - inputs are experimental data, with green lines – inputs are model data

Monitoring results– III phase



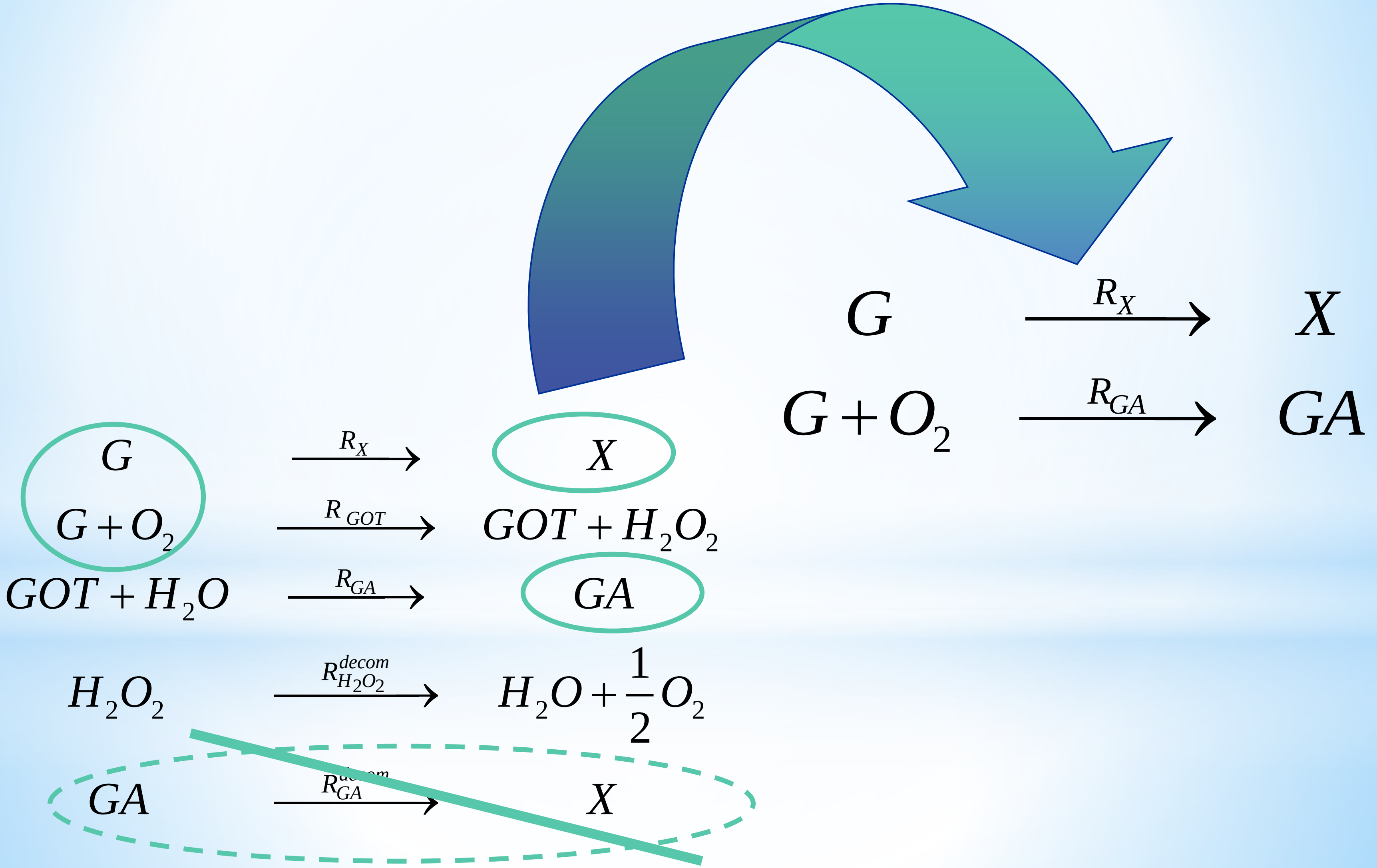


SS tuning parameters
C1=77.0215
C2=25
red lines – model data
green lines (C2=1.3) и blue lines (C2=25)
– experimental data



Model Identification, *Monitoring and Continous Control of Aspergillus Niger* Fermentation for Gluconic Acid Production

Biochemical model and reaction scheme reduction



$$\begin{aligned}
G &\xrightarrow{R_X} X\\
G+O_2 &\xrightarrow{R_{GOT}} GOT+H_2O_2\\
GOT+H_2O &\xrightarrow{R_{GA}} GA\\
H_2O_2 &\xrightarrow{R^{decom}_{H_2O_2}} H_2O+\frac{1}{2}O_2\\
\cancel{GA} &\cancel{\xrightarrow{R^{decom}_{GA}} X}
\end{aligned}$$

$$\begin{aligned}
G &\xrightarrow{R_X} X\\
G+O_2 &\xrightarrow{R_{GA}} GA
\end{aligned}$$

Reducted biochemical model

$$\frac{dX}{dt} = R_x;$$

$$\frac{dG}{dt} = -R_x - R_{GOT};$$

$$\frac{dGOT}{dt} = R_{GOT} - R_{GA};$$

$$\frac{dGA}{dt} = R_{GA};$$

$$\frac{dO}{dt} = -R_{GOT} + 0.5R_{H_2O_2} + K_L a(O_2^* - O_2);$$

$$\frac{dH_2O_2}{dt} = -R_{H_2O_2};$$

where

$$R_{H_2O_2} = R_{GOT} - R_{H_2O_2}^{decom};$$

$$R_x = \mu_{\max} X \frac{k - X}{k};$$

$$R_{GA} = \mu_{GA} GA \frac{(k_{GA} - GA)}{k_{GA}};$$

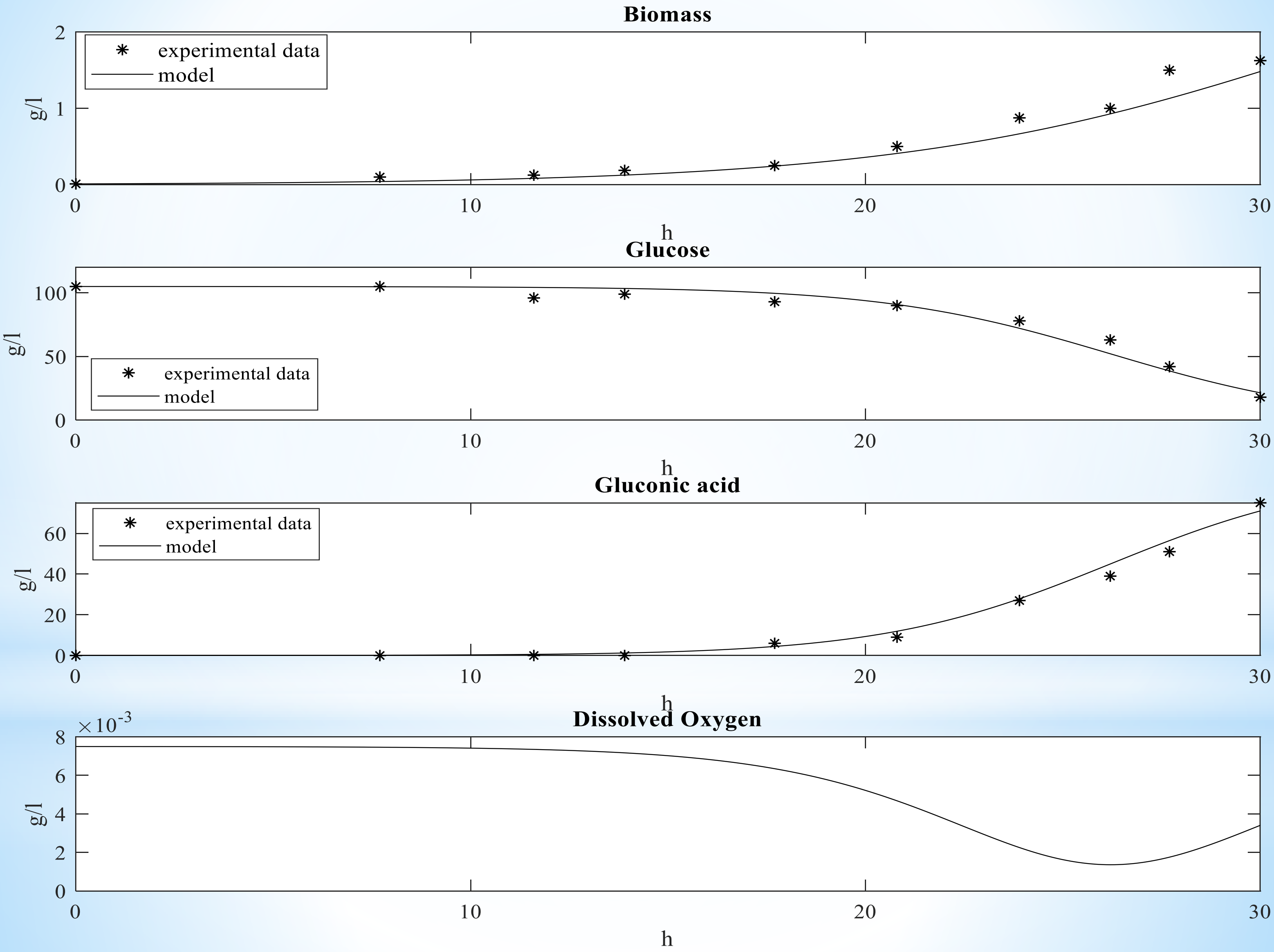
$$\frac{dX}{dt} = R_x;$$

$$\frac{dG}{dt} = -R_x - R_{GA};$$

$$\frac{dGA}{dt} = R_{GA};$$

$$\frac{dO}{dt} = -0.5R_{GA} + K_L a(O_2^* - O_2),$$

Reducted model simulation



Adaptive linearizing control design for continuous process

Reaction scheme

$$G \xrightarrow{\varphi_1} X$$

$$G + O_2 \xrightarrow{\varphi_2} GA$$

General model

$$\dot{X} = \varphi_1 - DX$$

$$\dot{G} = -k_1\varphi_1 - k_2\varphi_2 - D(G - G_{in})$$

$$\dot{O}_2 = -k_3\varphi_2 - DO_2 + K_La(O_2^* - O_2)$$

$$\dot{GA} = \varphi_1 - DGA$$

Reaction rates

$$\varphi_1 = GX\alpha_1$$

$$\varphi_2 = GO_2\alpha_2$$

General model in linear regression form

$$\dot{X}_e = X_eG\theta_1 - DX$$

$$\dot{G} = -X_eG\theta_2 - GO_2\theta_3 - D(G - G_{in})$$

$$\dot{O}_2 = -GO_2\theta_4 - DO_2 - K_La(O_2^* - O_2)$$

$$\dot{GA}_e = GO_2\theta_5 - DGA$$

Input (*D*)/output(*G*) model

Reference model for the regulation error

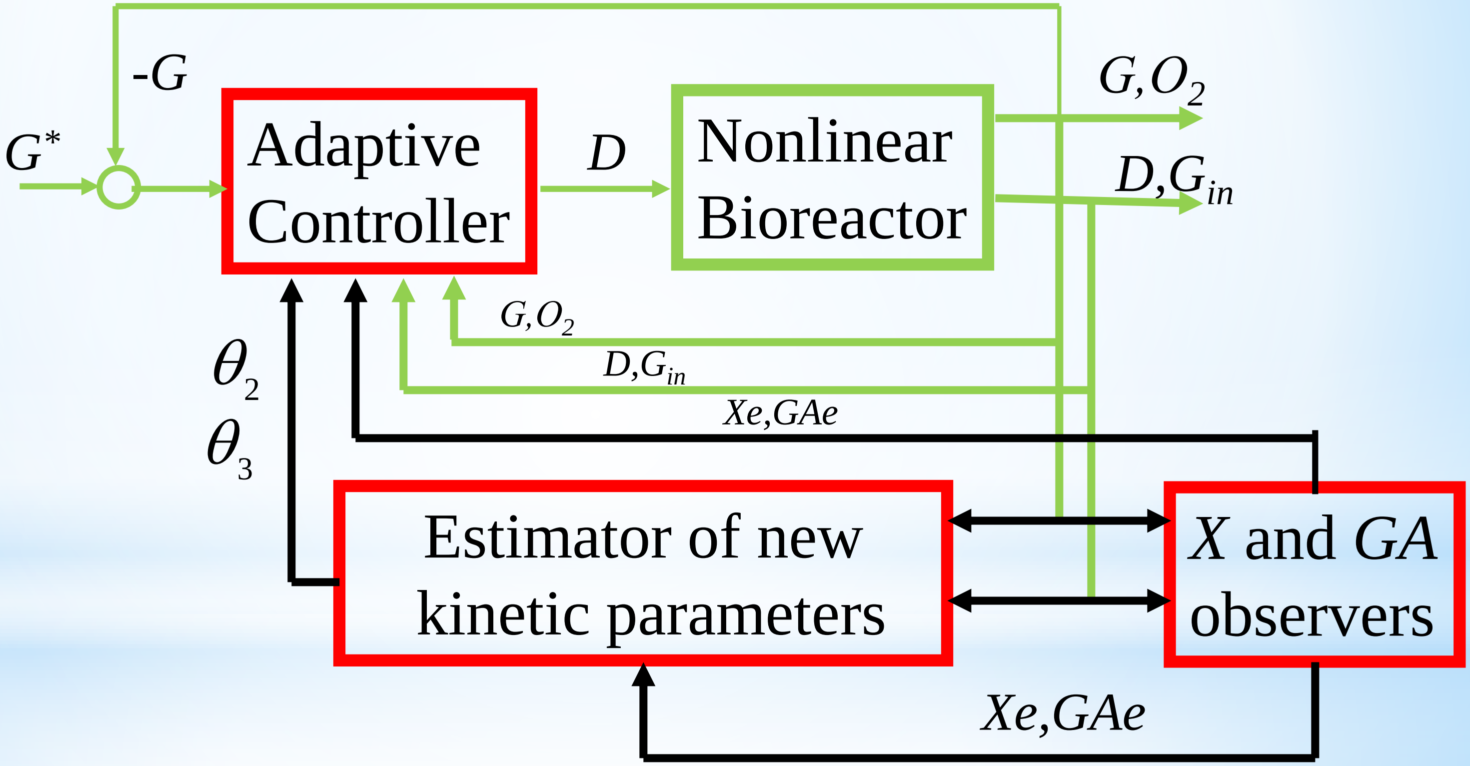
$$\frac{d(G^* - G)}{dt} + \lambda(G^* - G) = 0$$

$$\boxed{\frac{dG^*}{dt} = 0}$$

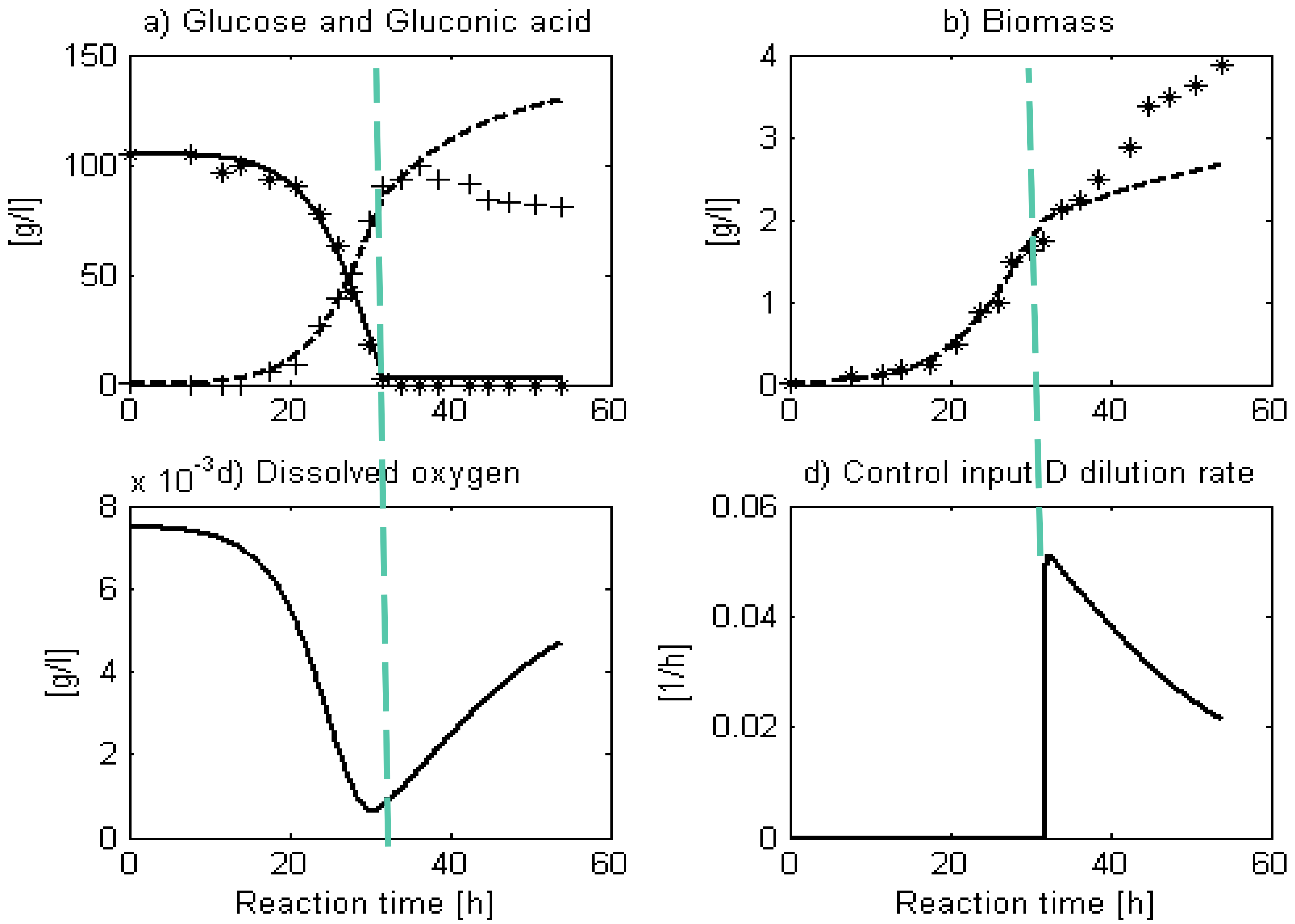
$$\lambda(G^* - G) = \frac{dG}{dt}$$

$$D = \frac{-\lambda(G^* - G) + X_eG\enclose{circle}{\theta_2} - GO_2\enclose{circle}{\theta_3}}{G - G_{in}}$$

Control scheme



Simulation of the control scheme



Adaptive linearizing control design for continuous process

Reaction scheme

$$G \xrightarrow{\varphi_1} X$$

$$G + O_2 \xrightarrow{\varphi_2} GA$$

General model

$$\dot{X} = \varphi_1 - DX$$

$$\dot{G} = -k_1\varphi_1 - k_2\varphi_2 - D(G - G_{in})$$

$$\dot{O}_2 = -k_3\varphi_2 - DO_2 + K_La(O_2^* - O_2)$$

$$\dot{GA} = \varphi_1 - DGA$$

Reaction rates

$$\varphi_1 = GX\alpha_1$$

$$\varphi_2 = GO_2\alpha_2$$

Reference model for the regulation error

$$\frac{d(GA^* - GA_e)}{dt} + \lambda(GA^* - GA_e) = 0$$

$$\frac{dG^*}{dt} = 0$$

General model in linear regression form

$$dX_e / dt = X_e G\theta_1 - DX_e$$

$$dG / dt = -X_e G\theta_2 - GO_2\theta_3 - D(G - G_{in})$$

$$dO_2 / dt = -GO_2\theta_4 - DO_2 - K_La(O_2^* - O_2)$$

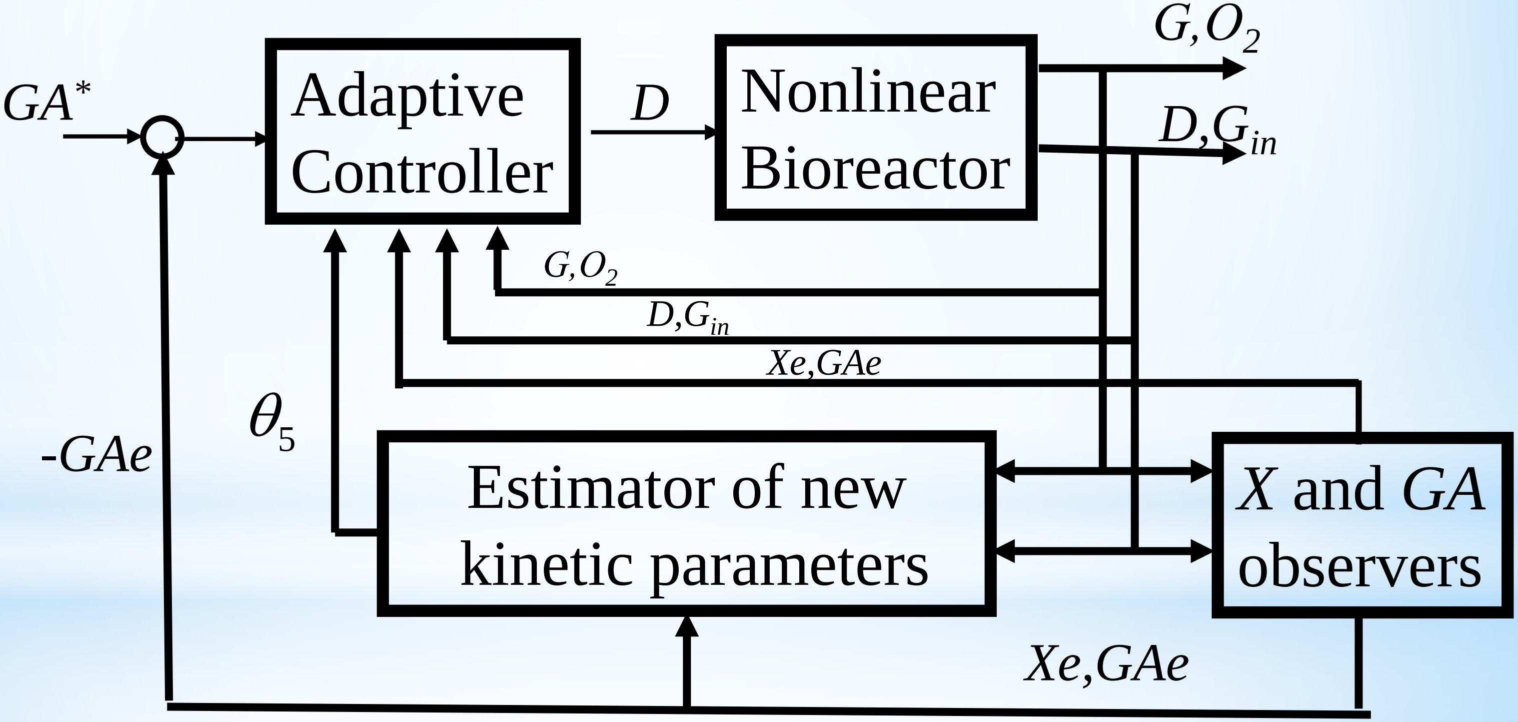
$$dGA_e / dt = GO_2\theta_5 - DGA_e$$

Input (***D***)/output(***GA***) model

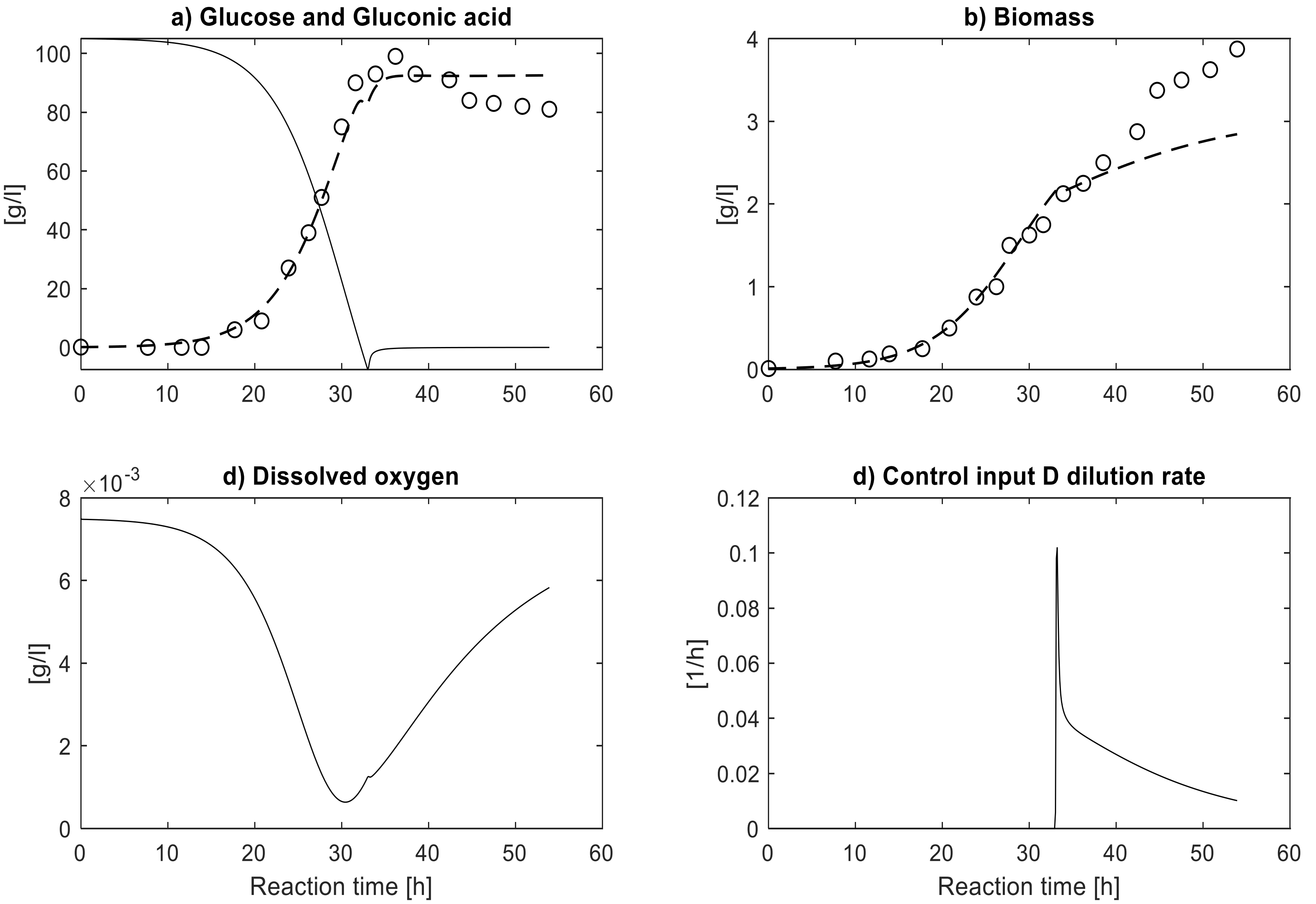
$$\lambda(GA^* - GA_e) = \frac{dGA_e}{dt}$$

$$D = \frac{-\lambda(GA^* - GA_e) + GO_2\theta_5}{GA_e}$$

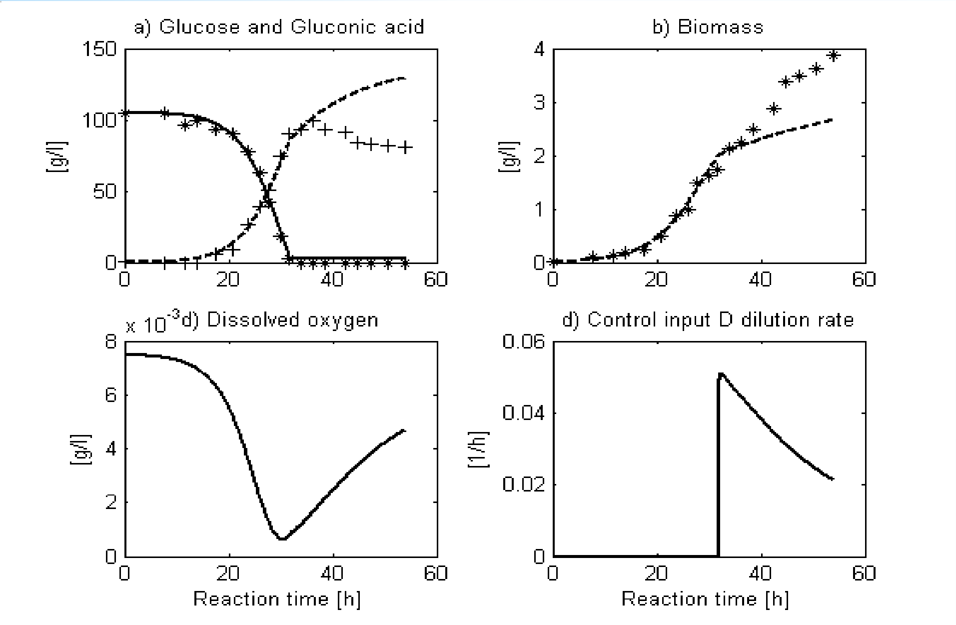
Control scheme

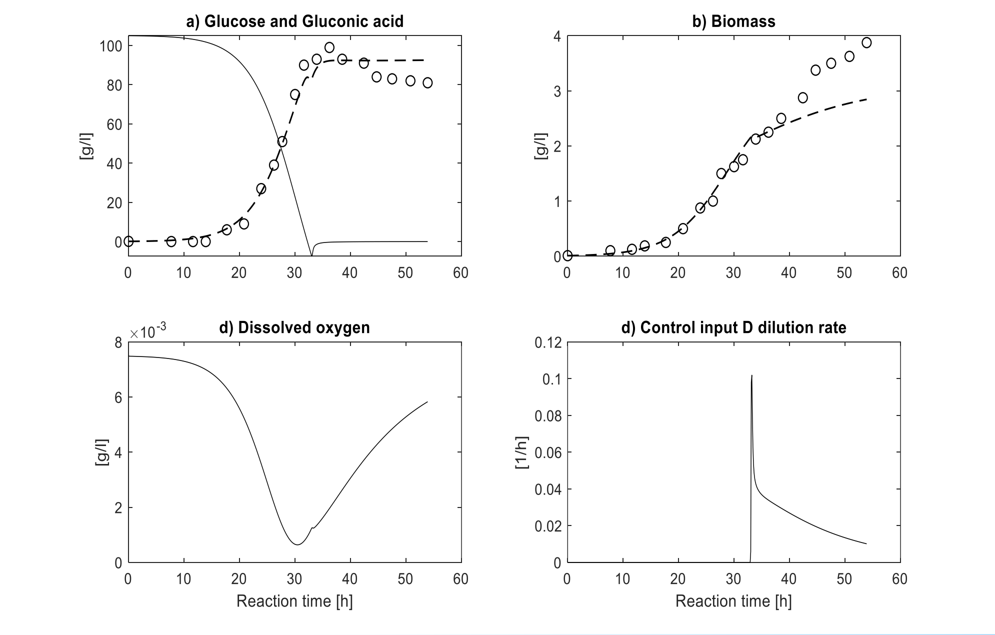


Simulation of the control scheme



Comparison of results for the two control schemes





Futher research

The module for a model parameter identification of the system InSemCoBio will be expanded with new hybrid metaheuristic algorithms. The following activities are planned for the purpose:

- ✓ Comparative analysis of the most commonly used metaheuristic algorithms in case of parameter identification of non-linear cultivation processes models;
- ✓ Selection of the most promising metaheuristic algorithms for hybridization; Development of new hybrid metaheuristic algorithms;
- ✓ Testing the proposed hybridizations on benchmark functions;
- ✓ Testing the proposed hybridizations on problems in the field of biotechnology;
- ✓ Comparative analysis of the proposed hybrid metaheuristic algorithms with existing metaheuristics or hybrid metaheuristic.
- ✓ Integrating the newly developed hybrid algorithms into the system.

The work on the system InSEMCoBio will continue further by developing a module for an adaptive control design

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