THE UNIVERSITY OF TOKYO Chemical System Engineering

Soft Sensor : Chemoinformatic Model for Efficient Control and Operation in Chemical Plants

Kimito Funatsu

Department of Chemical System Engineering

The University of Tokyo

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Contents

Introduction

In operating chemical plants, operators have to monitor operating condition of the plants and control process variables.

temperature, pressure, concentration of products, etc.

Process variables need to be measured online.

But, all of them are not easy to measure online.

✓technical difficulties ✓large measurement delays

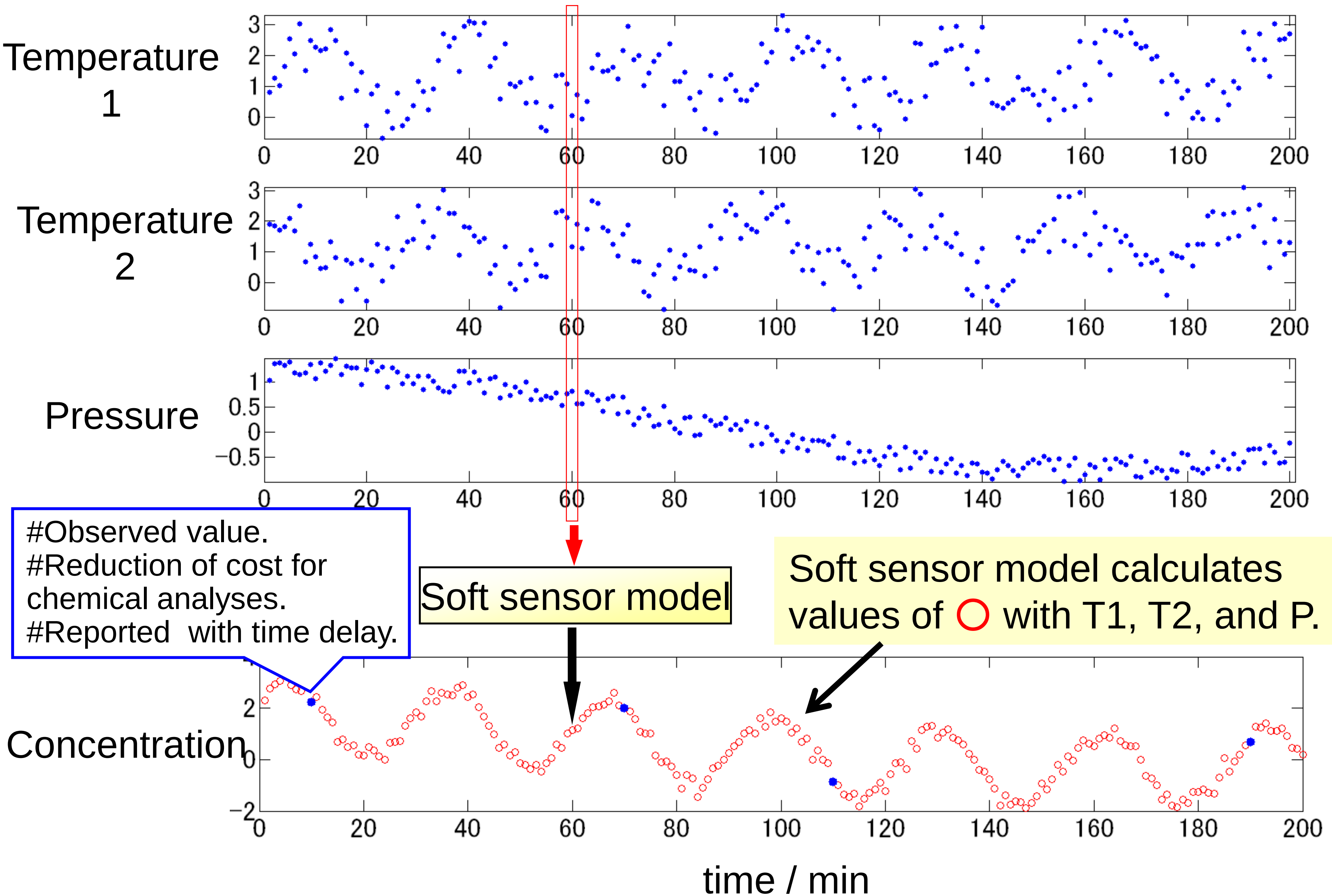
X: temperature, pressure, ... **y**: concentration, ... Database

input output

temperature, pressure, ... → Model : **y**=f(**X**) → concentration, ...

measure online Soft sensor estimate online

Soft Sensor


Temperature 1
Temperature 2
Pressure
Concentration
#Observed value.
#Reduction of cost for chemical analyses.
#Reported with time delay.
Soft sensor model
Soft sensor model calculates values of ○ with T1, T2, and P.
time / min

Process Analytical Technology (PAT)

To appropriately measure, monitor and control the quality of drug products and intermediates at each process in real time

To monitor the quality of all tablets non-destructively in real time ⇨ IR and NIR spectroscopy

e.g.Active Pharmaceutical Ingredient (API) content

Soft sensors can achieve Real Time Release Testing (RTRT), in which the quality is controlled in each process by monitoring the quality and doing appropriate actions in real time, and the final product test would not be required. In addition, control limits can be set and the quality of products can be controlled by using soft sensors, which is Quality by Design (QbD) . The use of soft sensors is expanding now in pharmaceutical processes.

Process Analytical Technology (PAT)

To appropriately measure, monitor and control the quality
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To monitor the quality of all tablets
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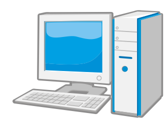
⇨ IR and NIR spectroscopy

Database



Easy to measure

Difficult to measure

IR and NIR spectra (**X**)

API, etc (**y**)

Soft sensor

$\mathbf{y} = f(\mathbf{X})$

IR and NIR spectra

Input

Output

API, etc

Measured in real time

Estimated online

Application of Soft Sensor

- Pharmaceutical process
- Chemical process
  - Polymer reactor
  - Distillation column

  etc
- Agricultural process
  - Rice field
  - Fruit sorting

  etc
- Biological process
  - Membrane bioreactor
  - Biomass ethanol process

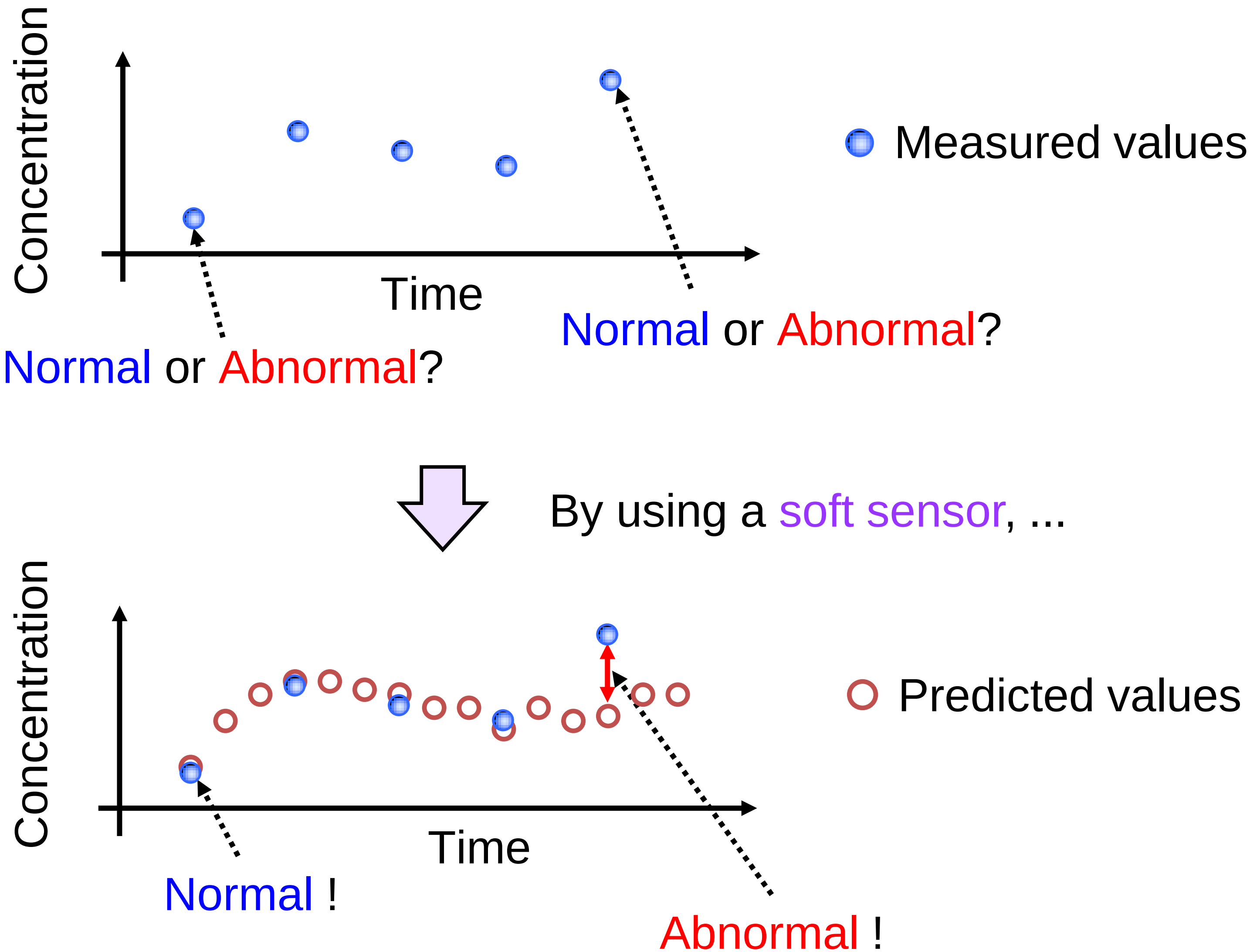
  etc

Role of Soft Sensors

- Analyzer alternative
  - Continuous prediction → Process control
  - Reduction of measurement frequency of analyzer

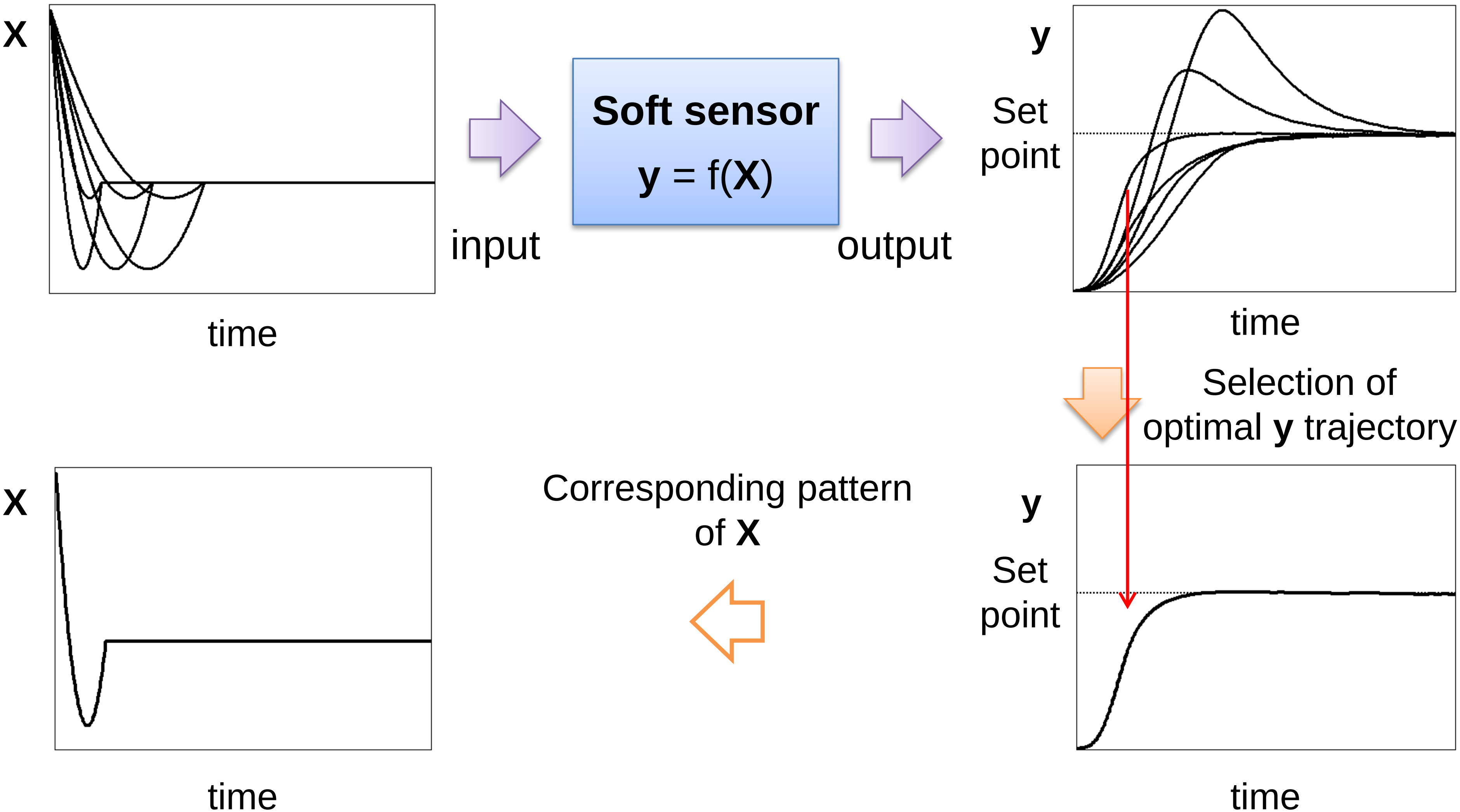
Role of Soft Sensors

- Abnormal detection of analyzer



Role of Soft Sensors

- Efficient process control



Kimura, I.; Kaneko, H.; Funatsu, K. Kagaku Kougaku Ronbunshu, 2015;41:29-37.

Flow of Soft Sensor analysis and Problems

Flow of soft sensor analysis

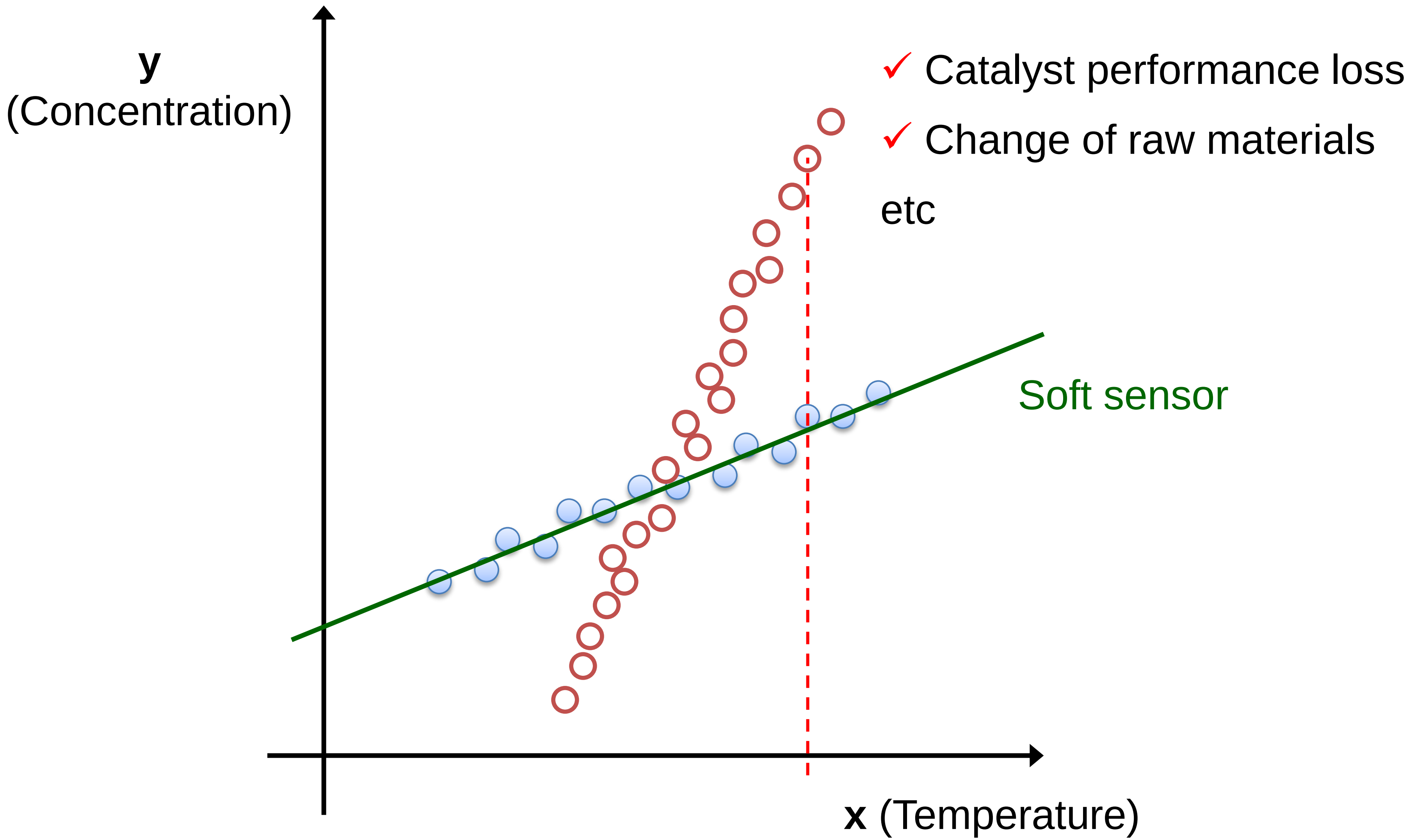
- Data collection
- Data preprocessing
- Modeling
- Model analysis
- Model operation

Problems

- Reliability of data, data selection
- Outlier detection, noise treatment
- Which is an appropriate regression method?
- Over-fitting
- Nonlinearity among process variables
- Variable selection
- Dynamics in process
- Model interpretation
- Model validation
- Applicability domain and predictive accuracy
- Degradation of a model
- Maintenance of a model
- Detection and diagnosis of abnormal data

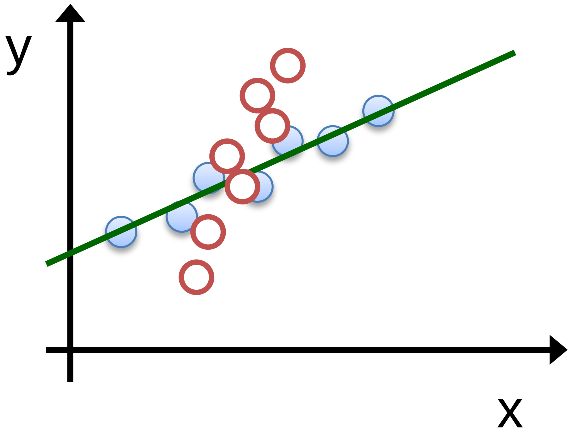
Contents

Model Degradation

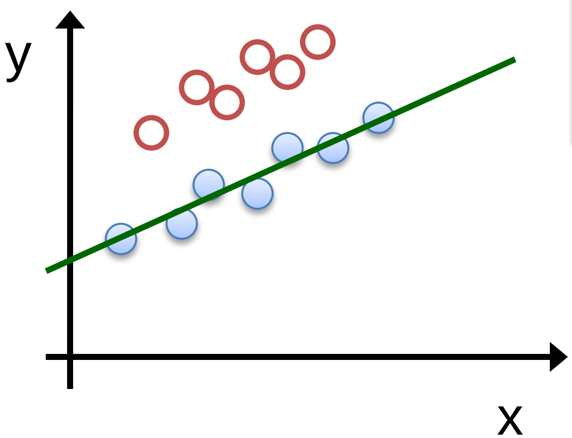


Model Degradation

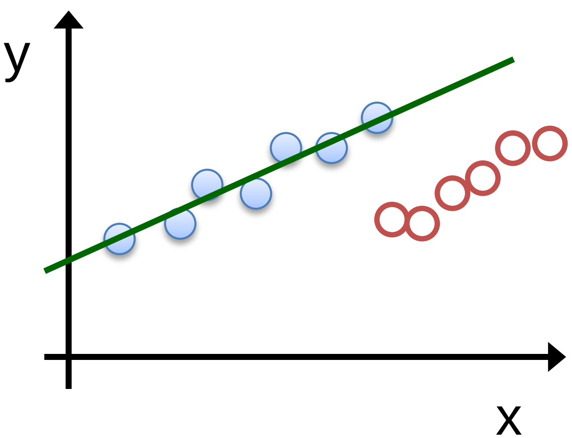
Slope change [1]



Shift of
y-values [1]



Shift of
x-values [1]



[1] Kaneko H, Funatsu K. *AIChE J.* 2013;59: 2339–2347.

Objective

To solve model degradation

and

To construct highly predictive soft sensor models

Adaptive Soft Sensor Models

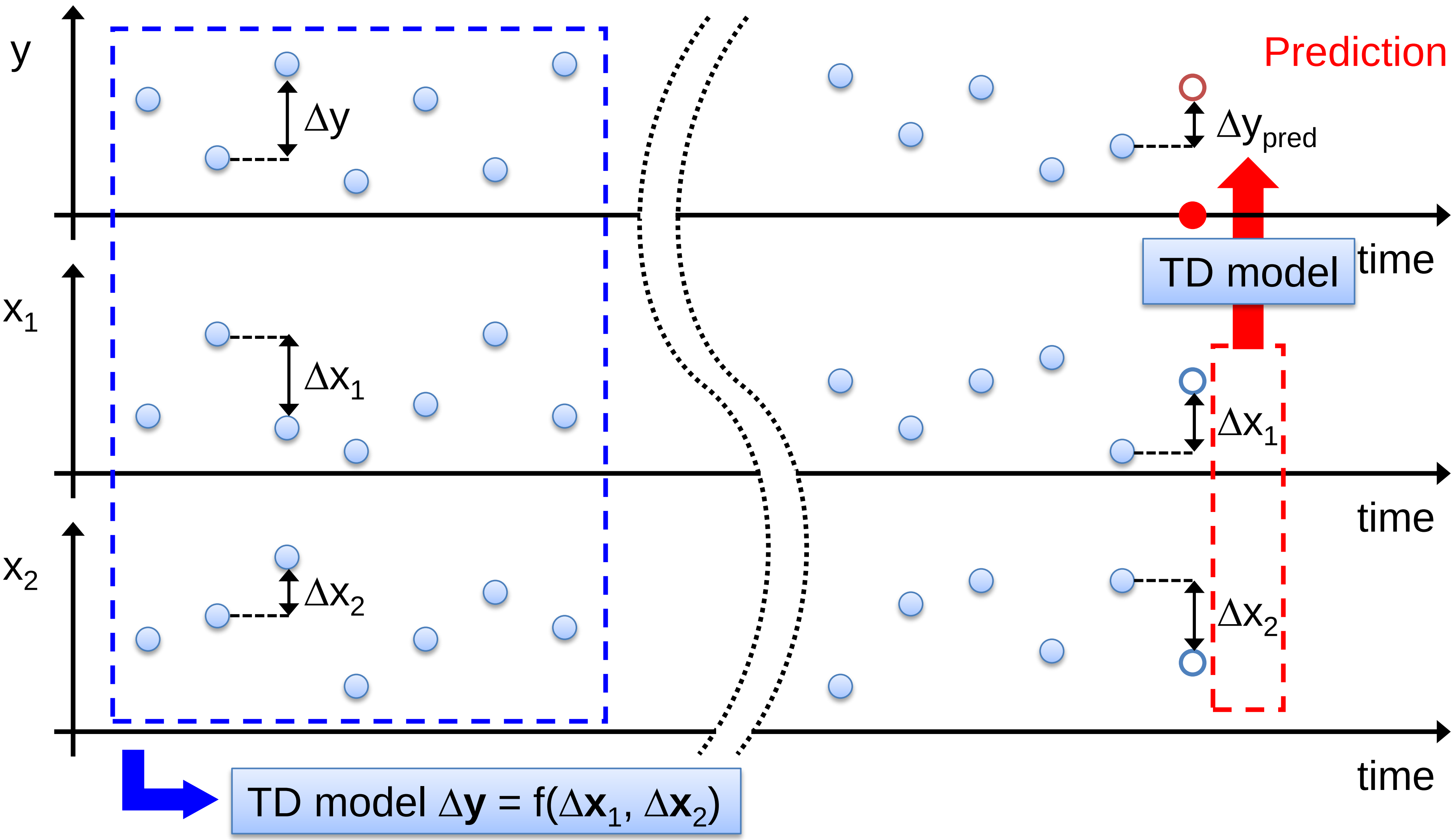
Soft sensor models adapting to changes in chemical plants.

- Moving Window (MW) model
  - PLS-based MW model [1]
  - Recursive model [2]
  - Ensemble MW model [3]
- Just-In-Time (JIT) model
  - Distance-based JIT model [4]
  - Correlation-based JIT model [5]
  - Locally-weighted PLS model [6]
- Time Difference (TD) model
  - Normal TD model [7]
  - Nonlinear TD model [8]
  - Ensemble TD model [9]

[1] Kaneko H, *et al*., *AIChE J.* 2009;55:87–98.
[2] Qin SJ., *Comput. Chem. Eng.* 1998;22:503–514.
[3] Kadlec P, Gabrys B. *AIChE J.* 2010;57:1288–1301.
[4] Cheng C, Chiu MS., *Chem. Eng. Sci.* 2004;59:2801–2810.
[5] Fujiwara K, *et al*., *AIChE J.* 2009;55:1754–1765.
[6] Kim, S., *et al*., *Int. J. Pharm*. 2011;421:269-274.
[7] Kaneko H, Funatsu K. *Chemom. Intell. Lab. Syst.* 2011;107:312–317.
[8] Kaneko H, Funatsu K. *Ind. Eng. Chem. Res. 2011;*50:10643–10651.
[9] Kaneko H, Funatsu K. *Chemom. Intell. Lab. Syst.* 2011;109:197–206.

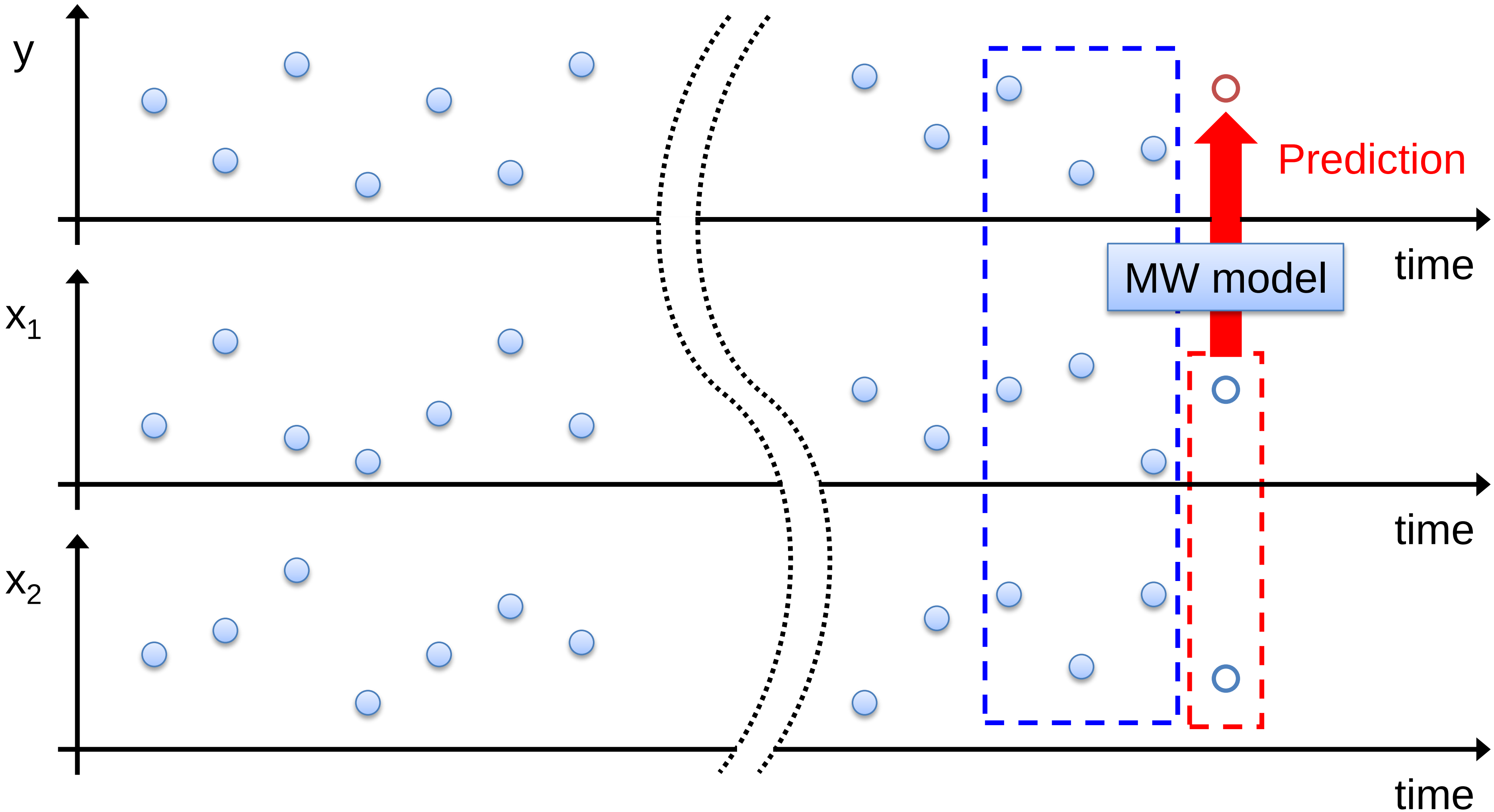
Time Difference (TD) Model

- Model constructed between TD of **X** and TD of **y**

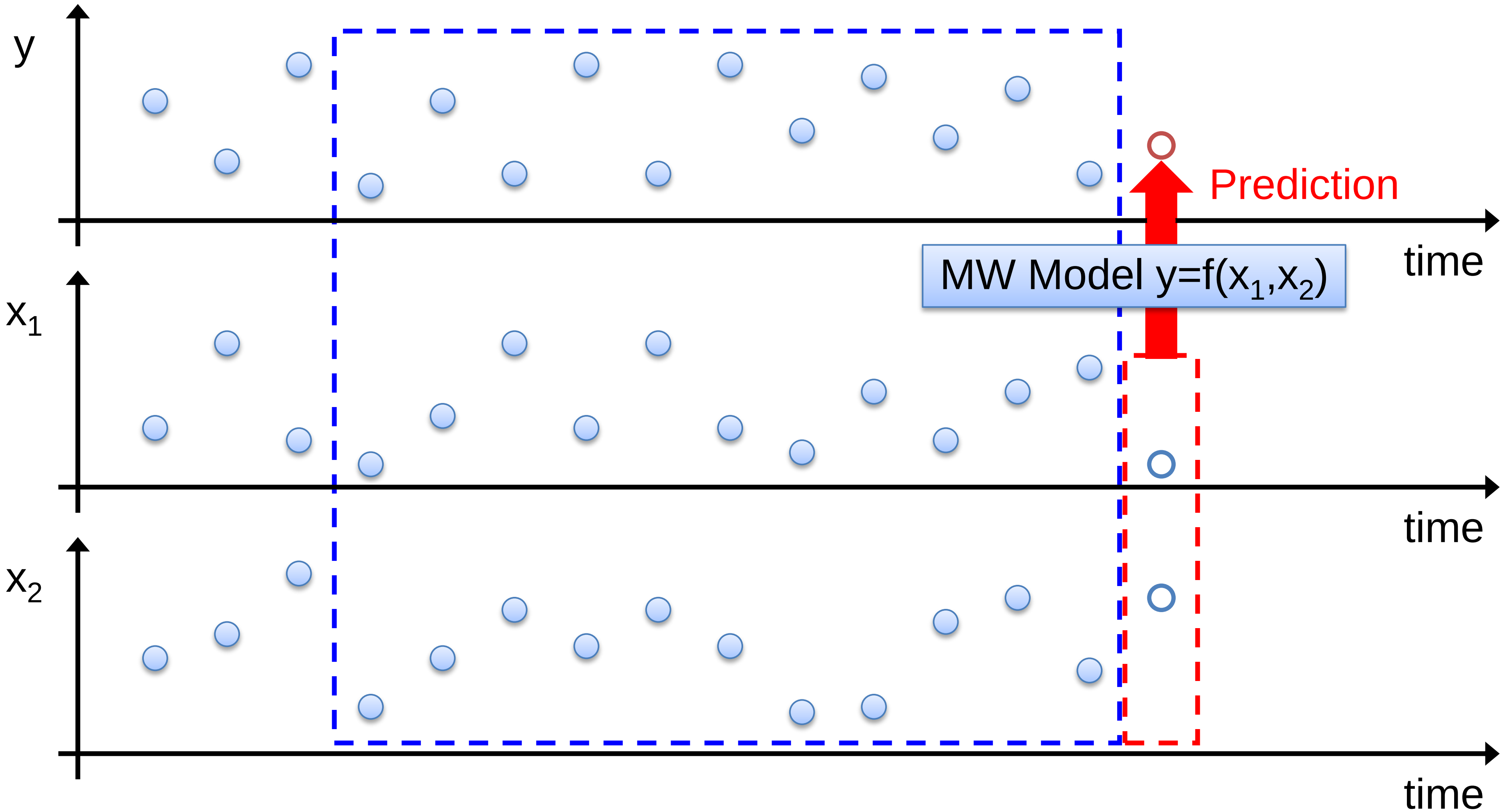


Moving Window (MW) Model

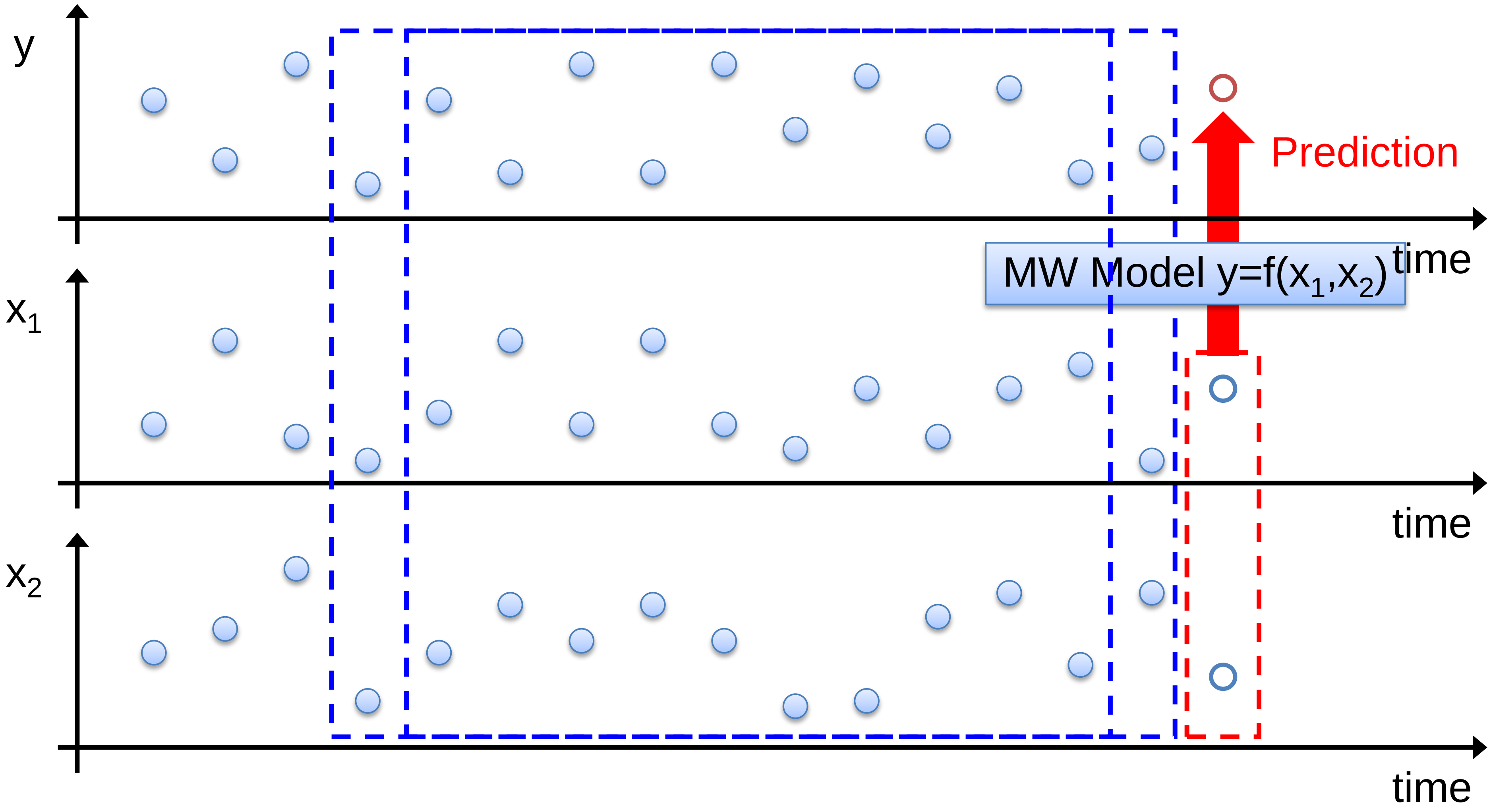
- Model constructed with data that are measured most recently



Moving Window (MW) Model

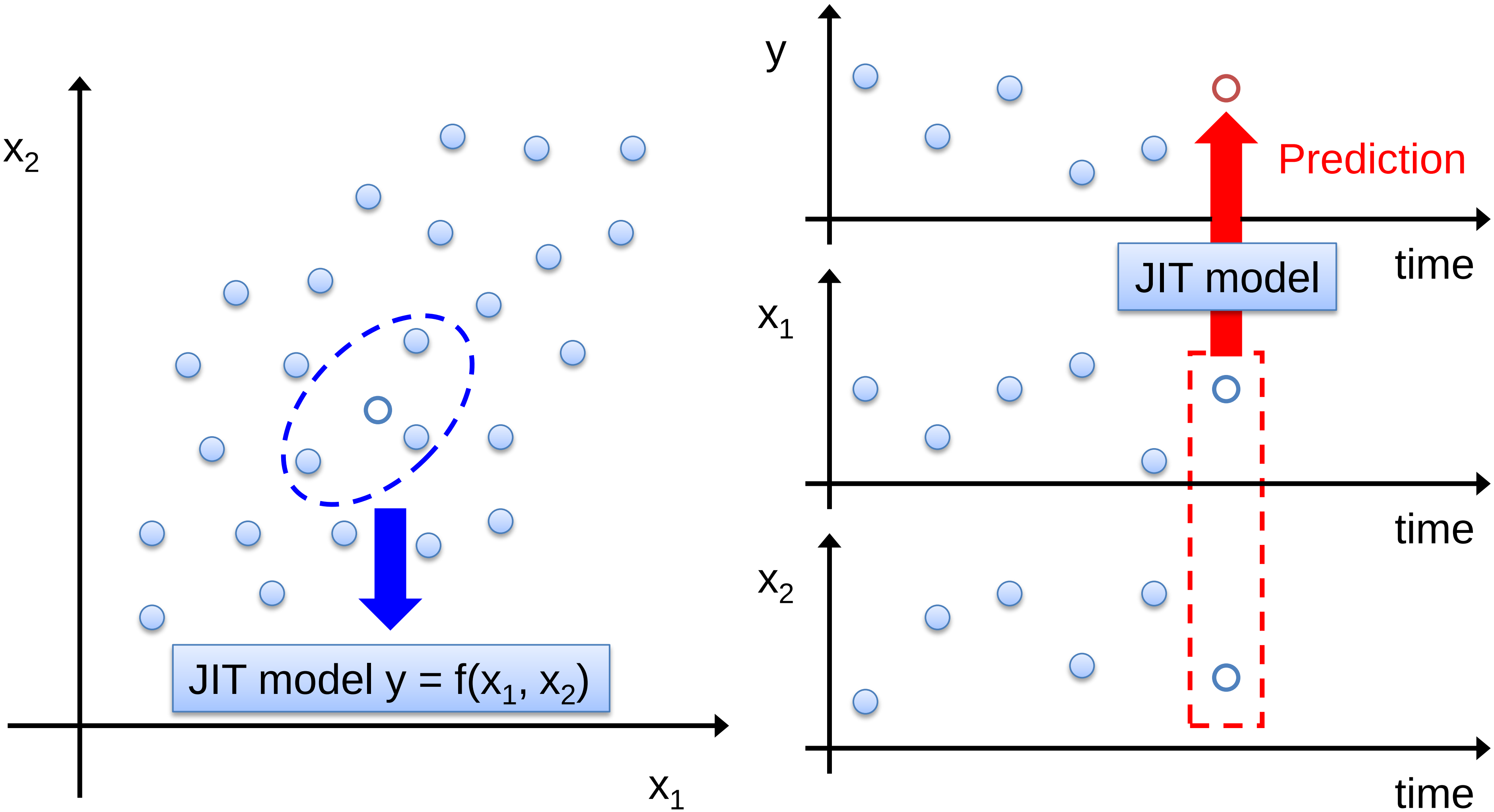


Moving Window (MW) Model



Just-In-Time (JIT) Model

- Model constructed with data similar to prediction data



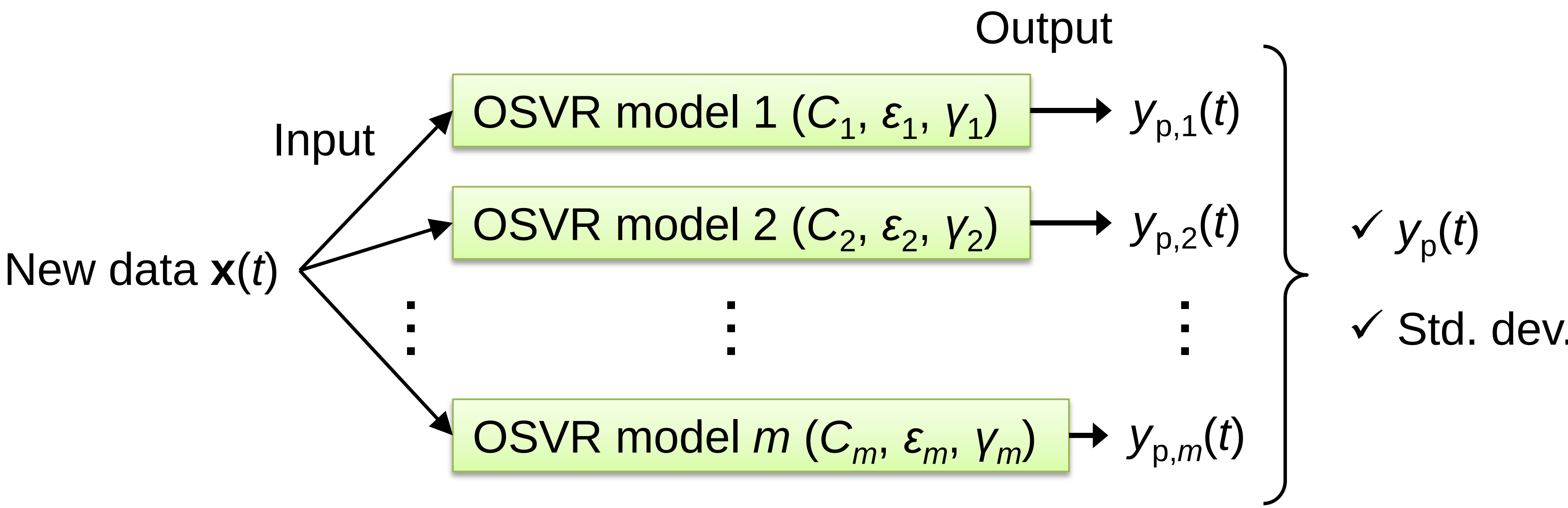
Characteristics of Adaptive Models [1]

Degradation of model: Type	Degradation of model: Speed	TD model	MW model	JIT model
Shift of **y**-values	Gradual	○	○	×
	Rapid	○	△	×
	Abrupt	○	×	×
Shift of **x**-values	Gradual	○	○	○
	Rapid	○	△	○
	Abrupt	○	×	○
Change of the slope	Gradual	×	○	△
	Rapid	×	△⇒○[3]	△
	Abrupt	×	×	△

No all-round adaptive models ! ⇨ Right models for a right type of degradation [2] !!

[1] H. Kaneko, K. Funatsu, *AIChE J.* 2013;59: 2339–2347.
[2] H. Kaneko, T. Okada, K. Funatsu, Ind. Eng. Chem. Res., 2014;53:15962-15968
[3] H. Kaneko, K. Funatsu, Chemom. Intell. Lab. Syst., 2014;137:56-66.

Proposed Method (Ensemble OSVR, EOSVR)



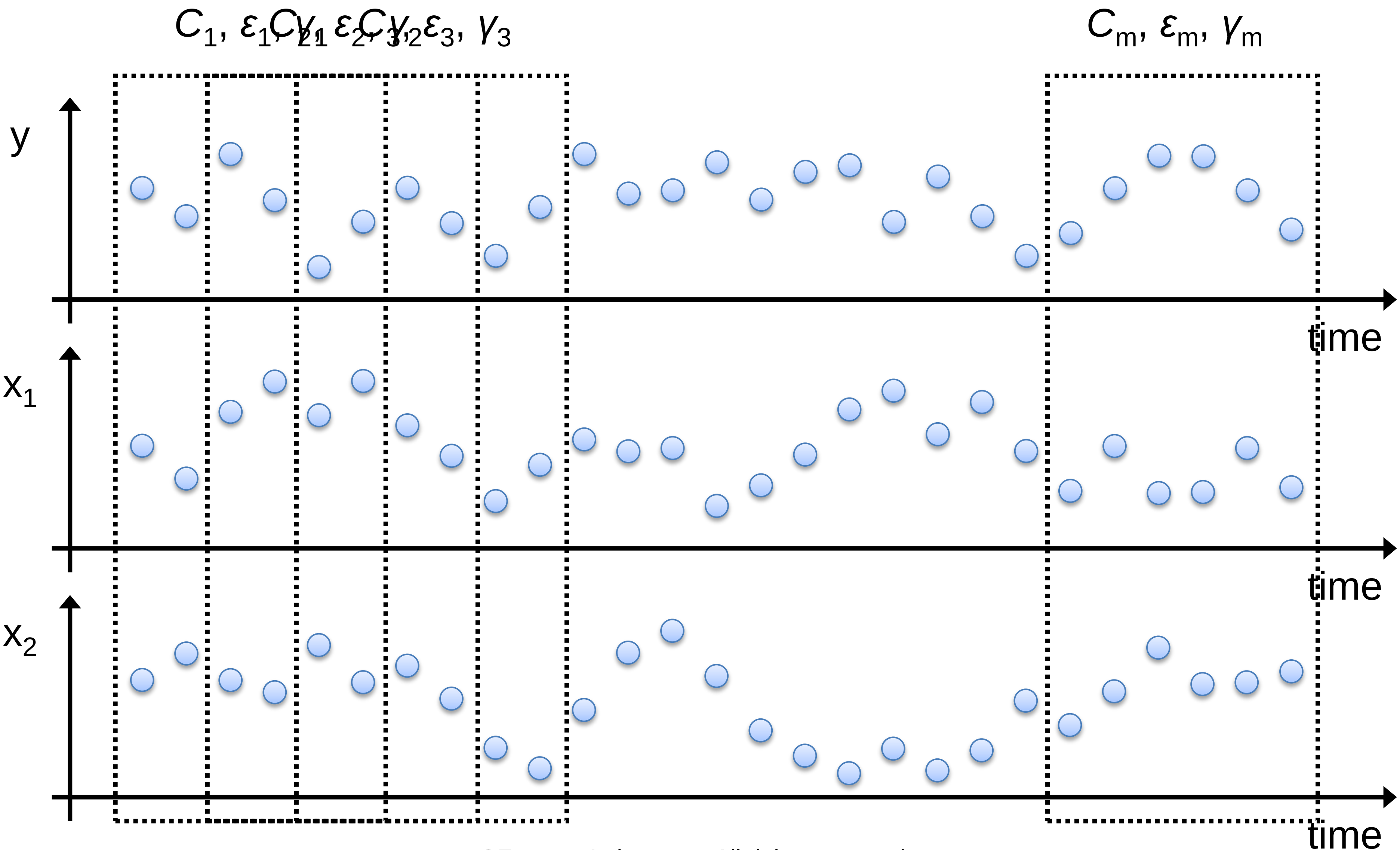
$$\frac{1}{\mathrm{RMSE}^2}$$

(Calculated using the recent data set)

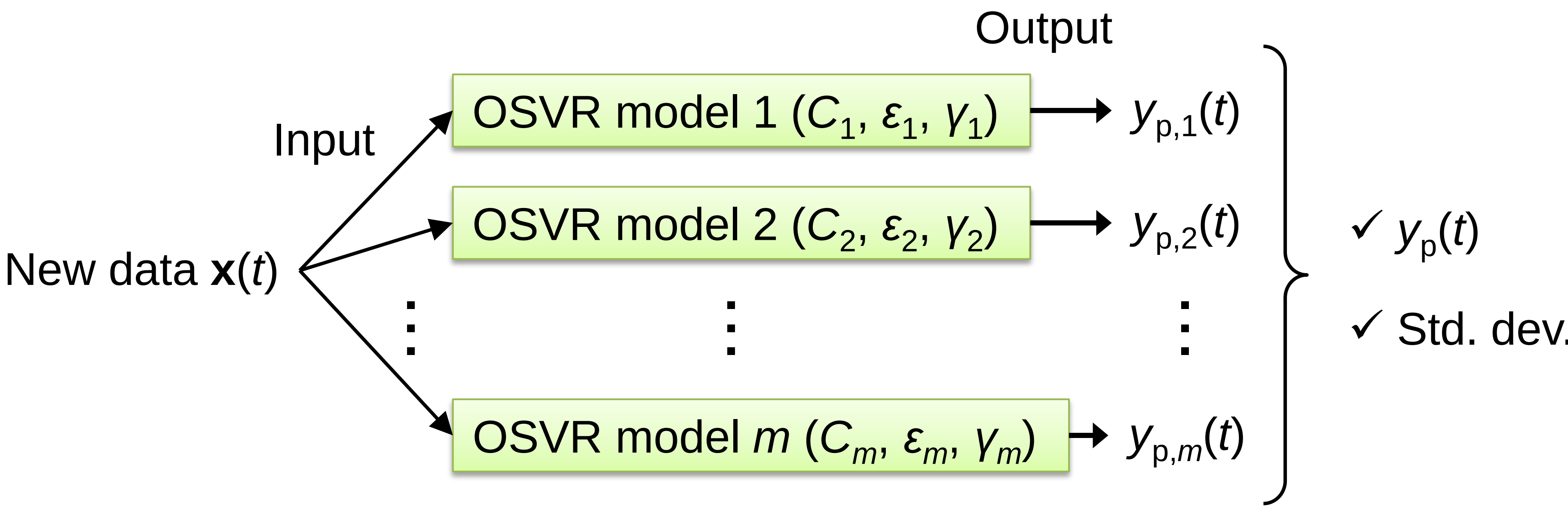
[1] H. Kaneko, K. Funatsu, Chemom. Intell. Lab. Syst., 137, 57–66 , 2014.

How to get parameter sets

Initial Database



Proposed Method (Ensemble OSVR, EOSVR)

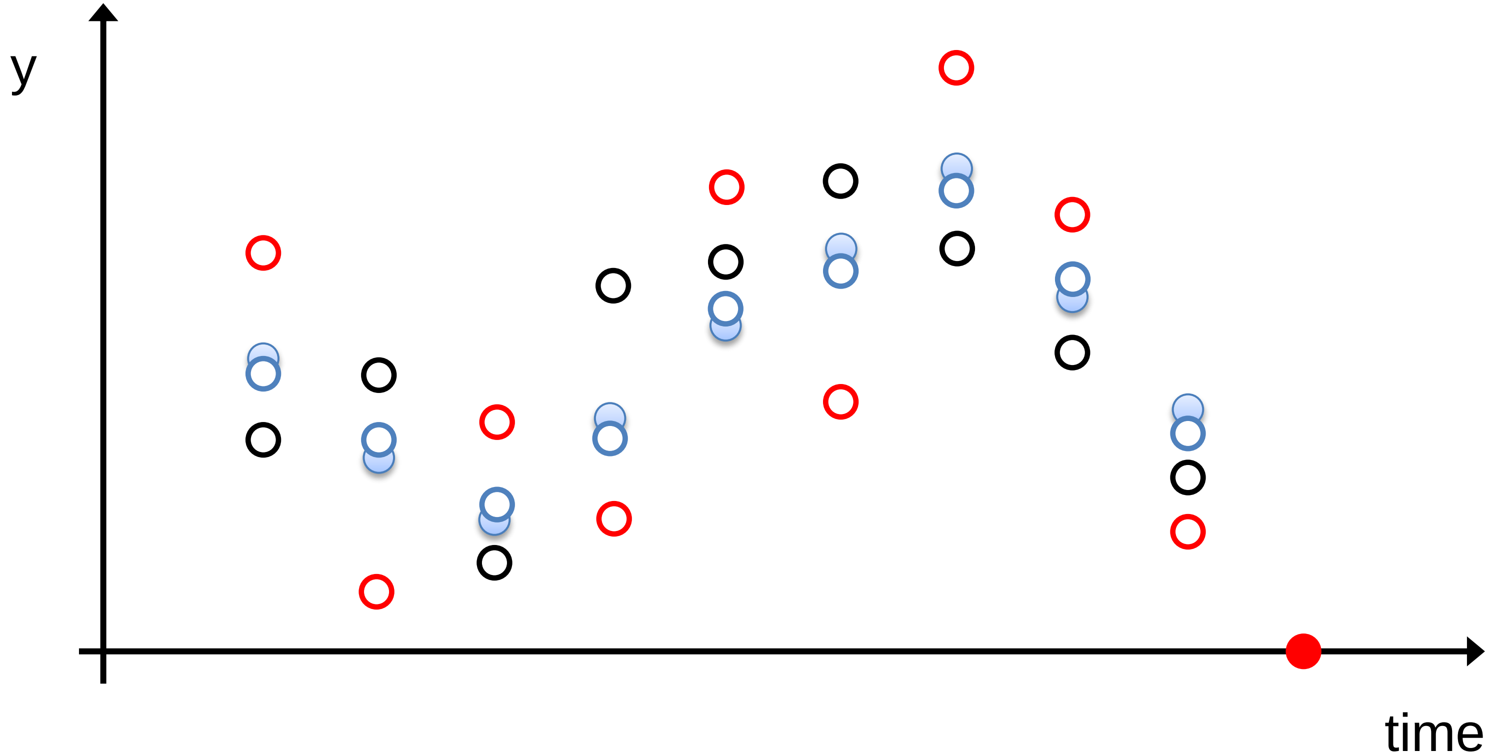


$$\frac{1}{\mathrm{RMSE}^2}$$

(Calculated using the recent data set)

[1] H. Kaneko, K. Funatsu, Chemom. Intell. Lab. Syst., 137, 57–66 , 2014.

Calculation of RMSE



	Model 1	Model 2	Model 3
RMSE	Large	Small	Large
Weight : $\frac{1}{RMSE^2}$	Small	Large	Small

- Exhaust gas denitration process at Mitsui Chemicals, Inc.

Catalyst

$$4NO + 4NH_3 + 2O_2 \rightarrow 4N_2 + 6H_2O$$

$$NO + NO_2 + 2NH_3 \rightarrow 2N_2 + 3H_2O$$

Variables

y ① NH_3 concentration at the outlet of the denitration reactor
② NO_X concentration at the outlet of the denitration reactor

X 23 variables: temperature, pressure, flow rate, and so on

[1] H. Kaneko, K. Funatsu, Chemom. Intell. Lab. Syst., 137, 57–66 , 2014.

Data Set

- 20,000 data in November 2012
  - First 10,000 data : training data
  - Remaining 10,000 data : test data

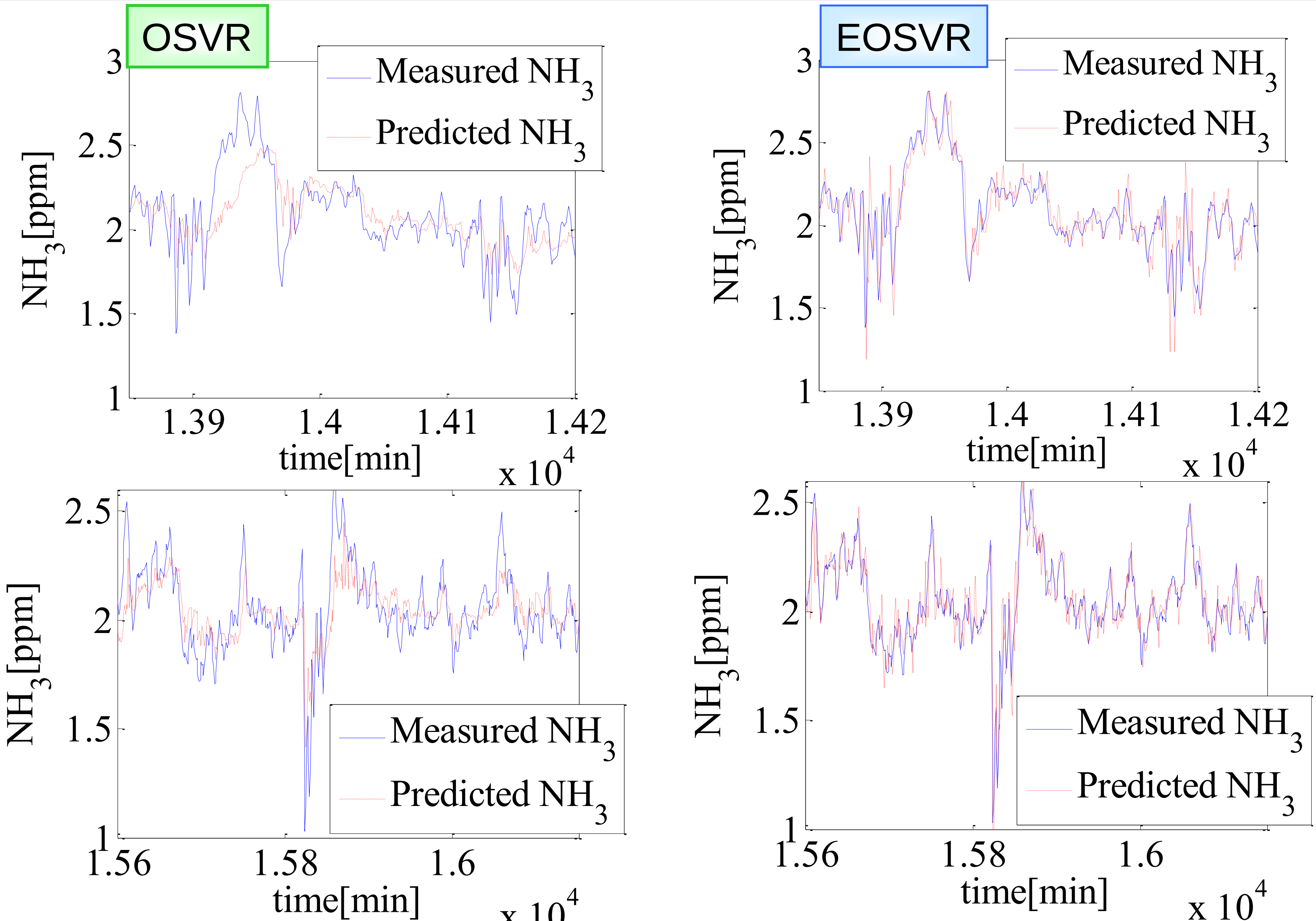
[1] H. Kaneko, K. Funatsu, Chemom. Intell. Lab. Syst., 137, 57–66 , 2014.

Prediction Results

	Denitration outlet NH_3		Denitration outlet NO_X	
Model	r_p^2	$RMSE_P$	r_p^2	$RMSE_P$
OSVR	0.742	0.119	0.960	1.51
EOSVR	**0.863**	**0.087**	**0.975**	**1.21**

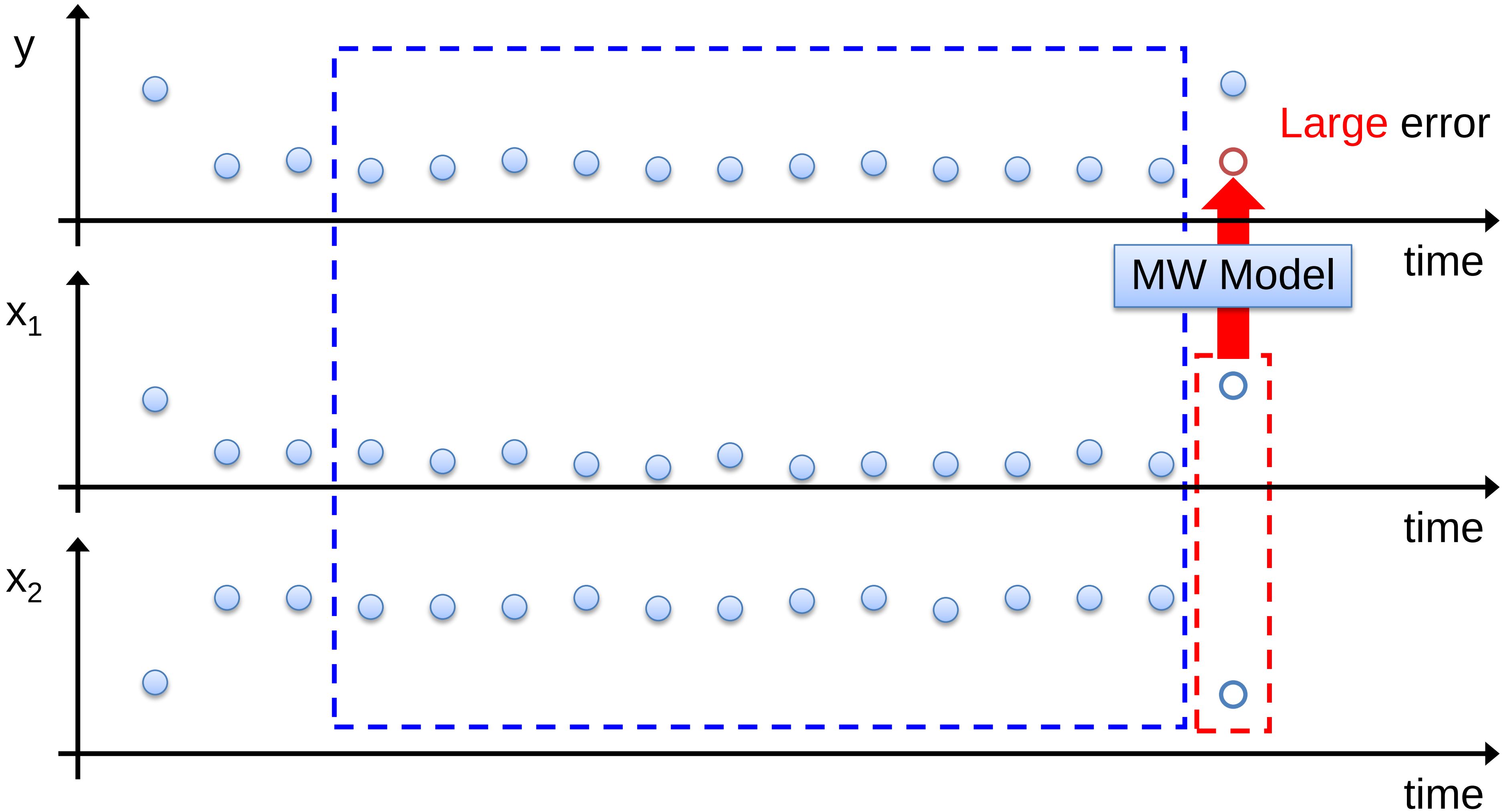
[1] H. Kaneko, K. Funatsu, Chemom. Intell. Lab. Syst., 137, 57–66 , 2014.

Time Plots of Denitration Outlet NH_3



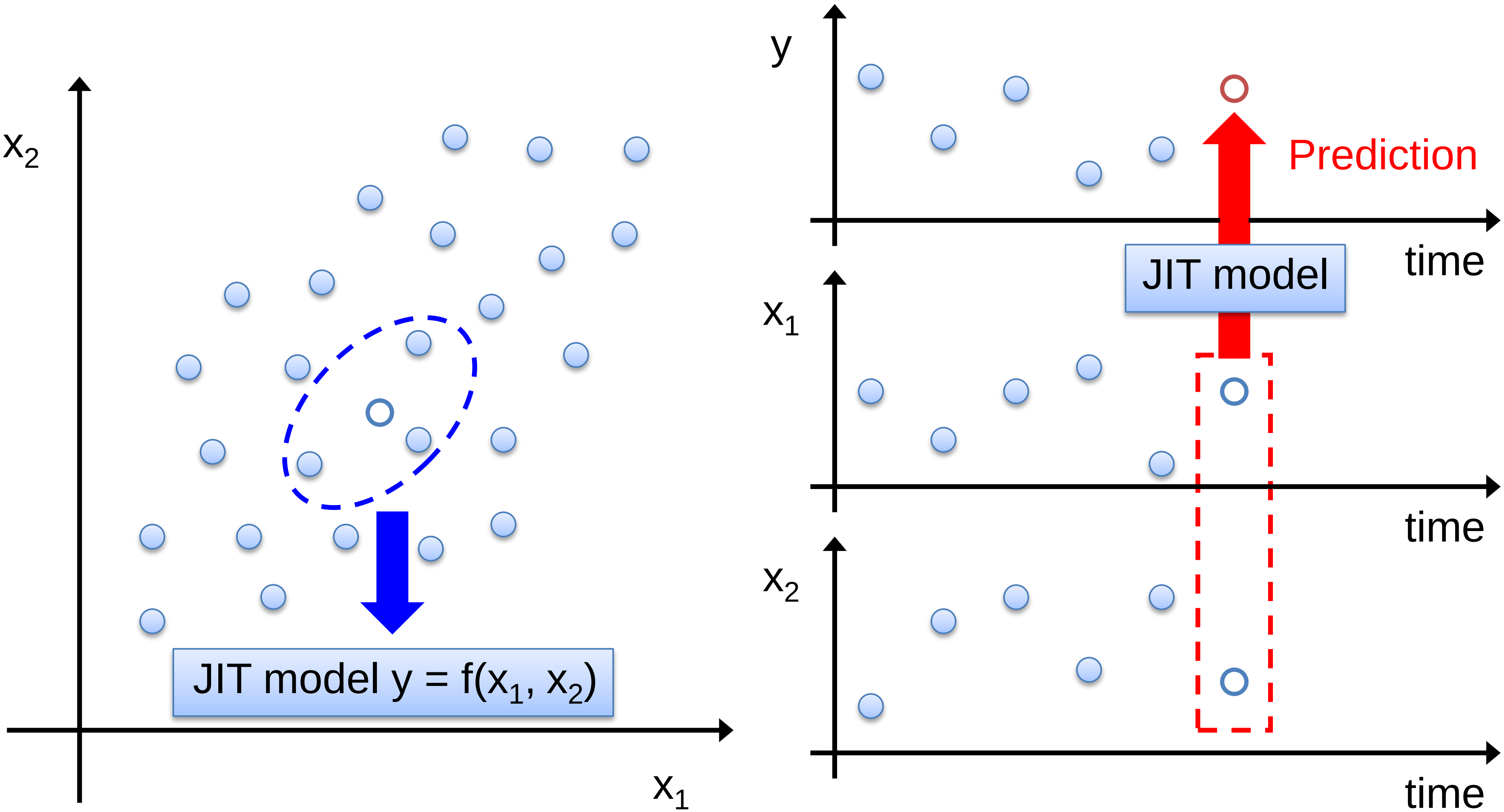
Contents

Problem of MW Model

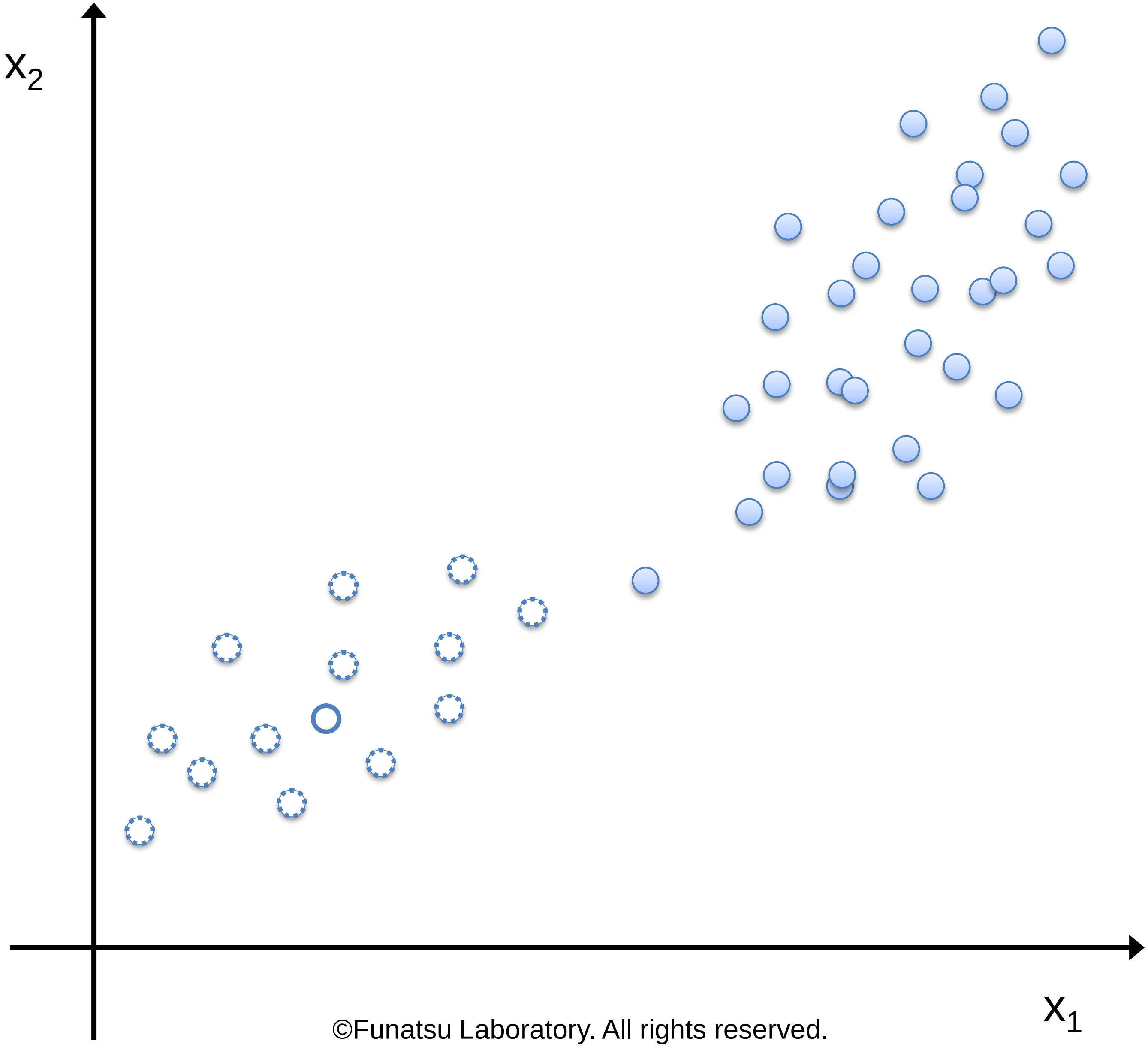


Just-In-Time (JIT) Model

- Model constructed with data similar to prediction data



Problem of JIT Model

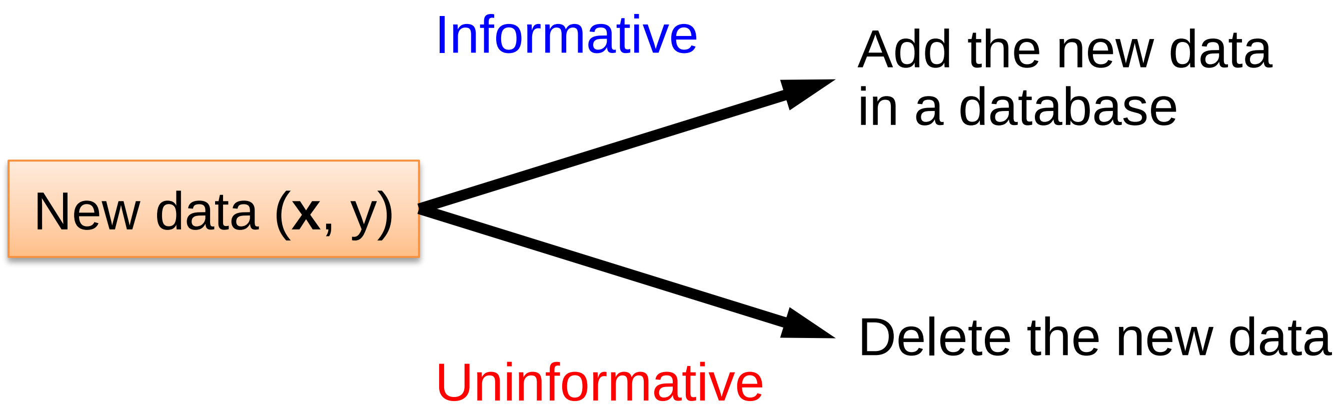


Database Monitoring

To construct adaptive models (MW and JIT models)

with high predictive accuracy for wide data range

Appropriate database monitoring [1]



[1] H. Kaneko, K. Funatsu, AIChE J., 60, 160-169, 2014.

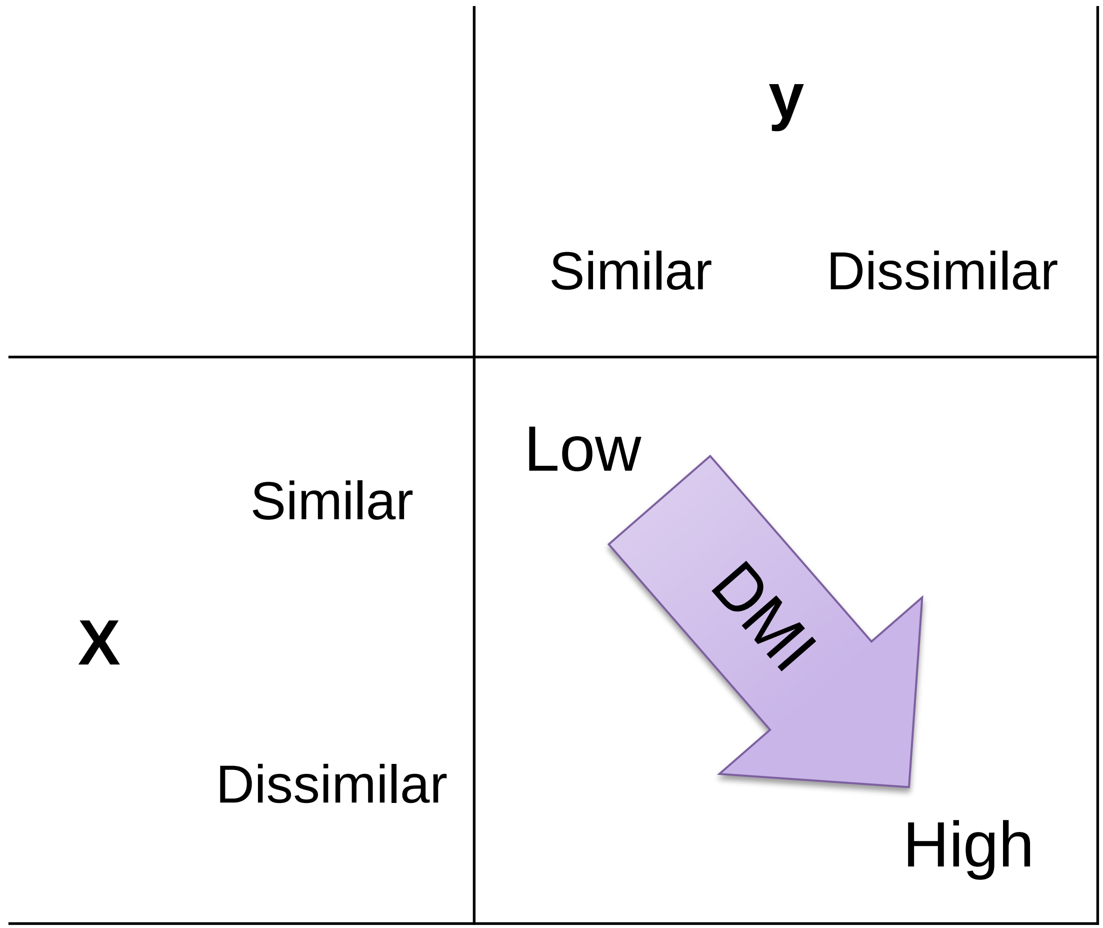
Database Monitoring Index (DMI) [1]

- The DMI is calculated between two data ($\mathbf{x}_i$, y_i) and ($\mathbf{x}_j$, y_j)

$$\mathrm{DMI} = \frac{\left| y_i - y_j \right|^a}{\mathrm{sim}\left(\mathbf{x}_i, \mathbf{x}_j \right)}$$

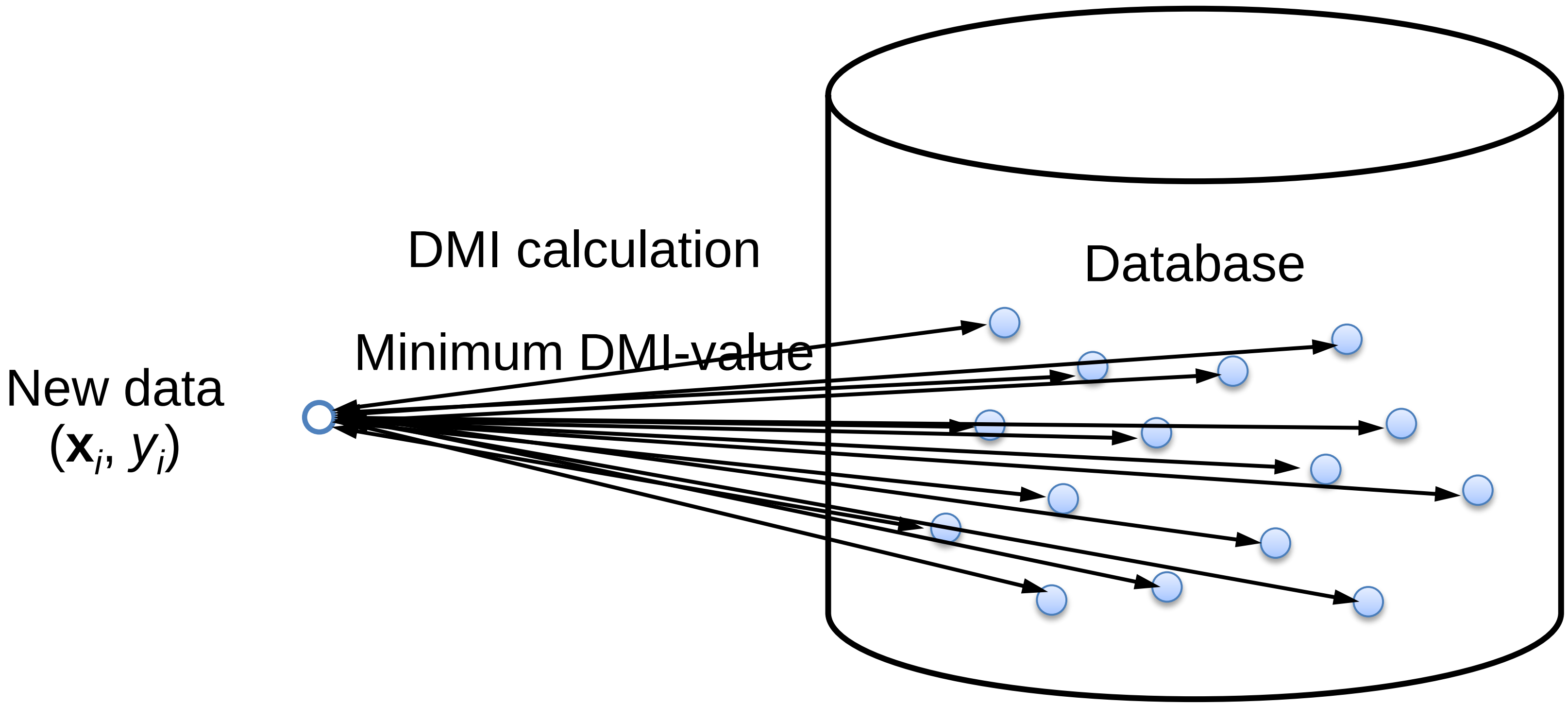
sim($\mathbf{x}_i$, $\mathbf{x}_j$) : Similarity between $\mathbf{x}_i$ and $\mathbf{x}_j$

a : Constant



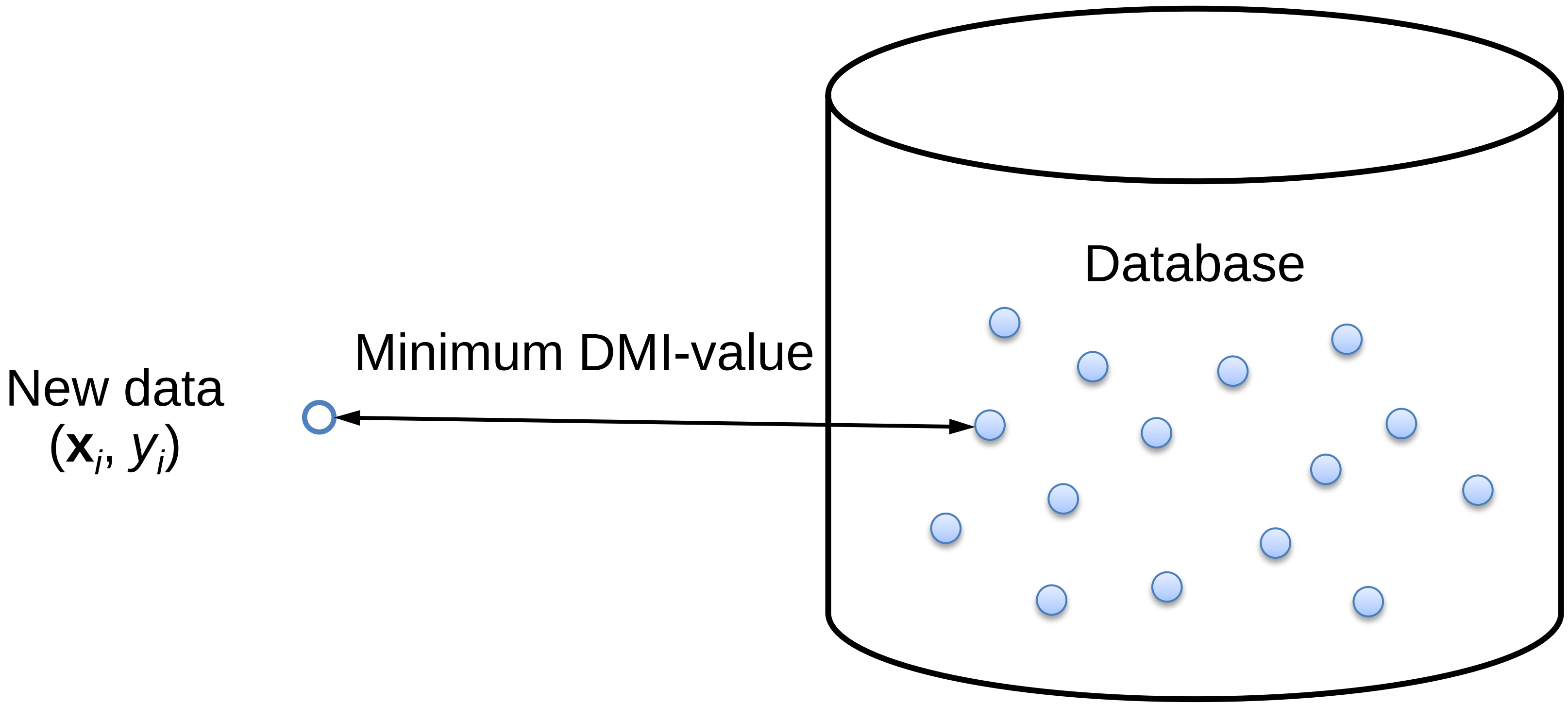
[1] H. Kaneko, K. Funatsu, AIChE J., 60, 160-169, 2014.

Flow of Monitoring Database with the DMI



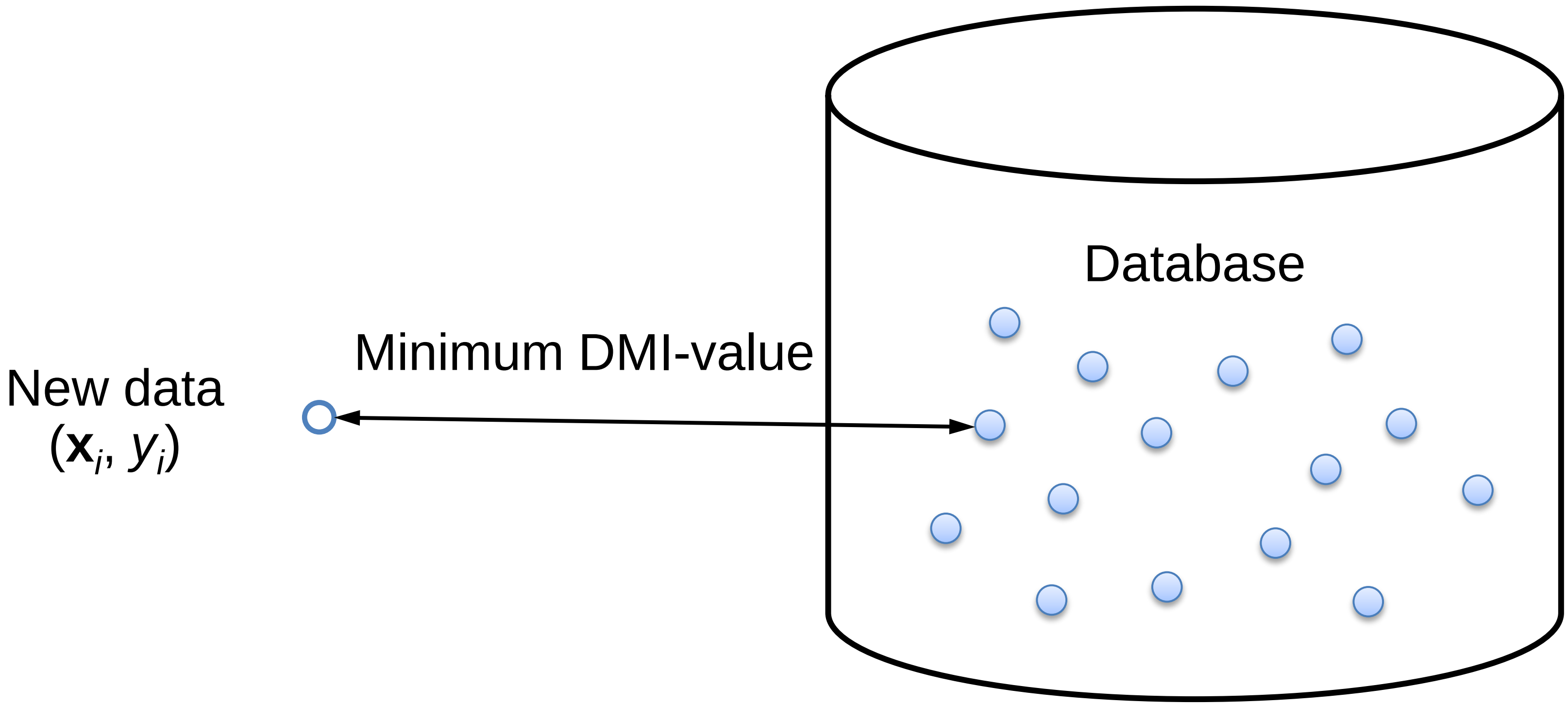
Threshold P_{DMI} **<** Minimum DMI-value ⇨ Informative

Flow of Monitoring Database with the DMI



Threshold P_{DMI} > Minimum DMI-value ⇨ Uninformative

Flow of Monitoring Database with the DMI



Threshold P_{DMI} > Minimum DMI-value ⇨ Uninformative

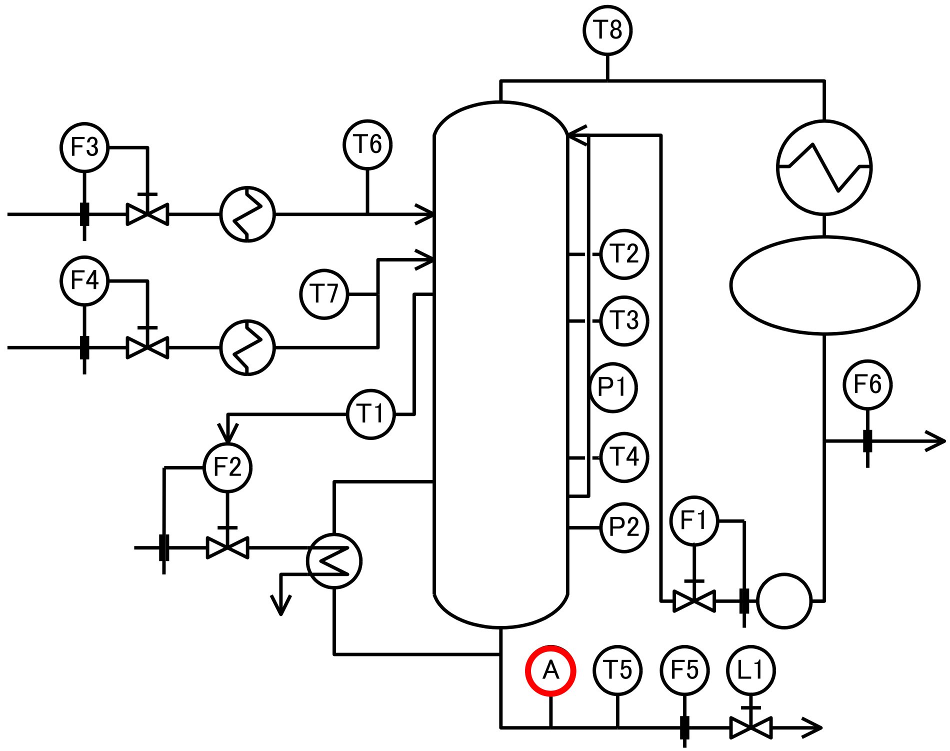
Case Study

- Numerical simulation data
  - The relationship between **X** and **y** is nonlinear.
  - The data whose variation comes from only noise exist.

- Industrial distillation column data

Case Study

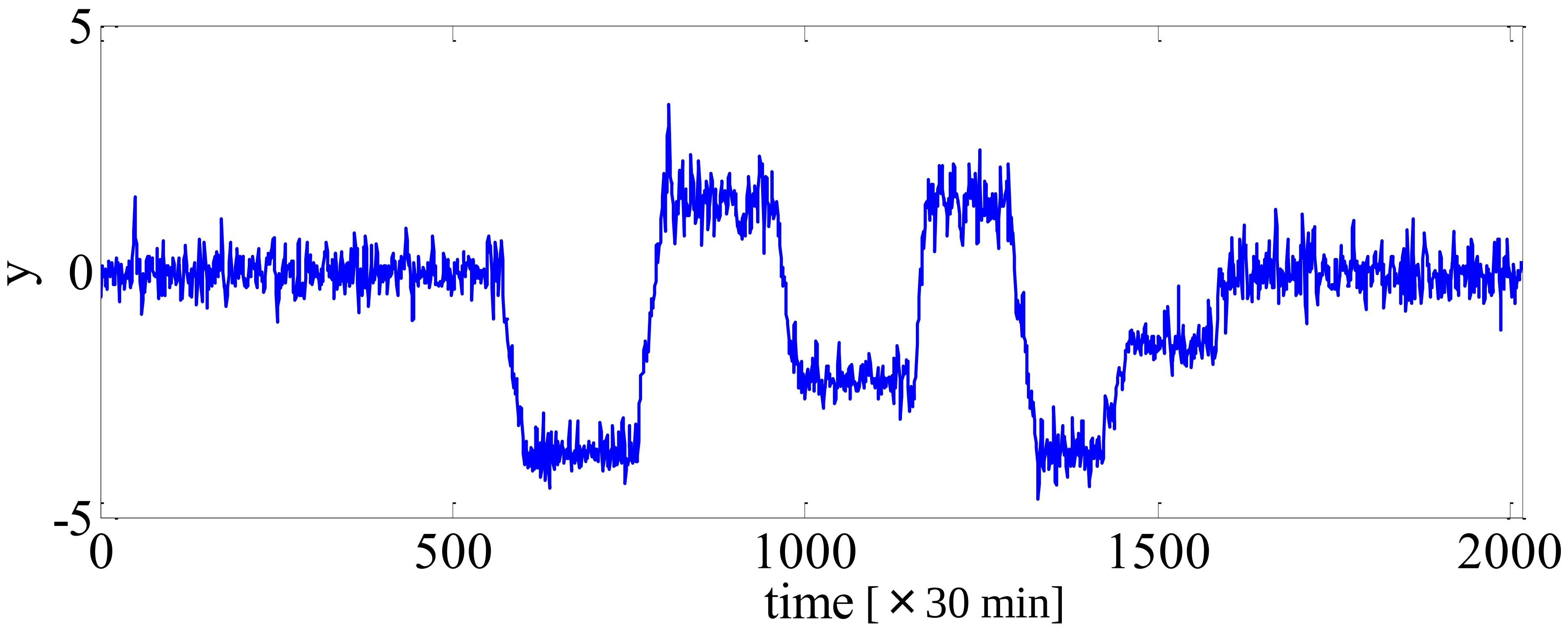
A distillation column at Mitsubishi Chemical Corporation



Variables

y Concentration of bottom product with lowest boiling point
The measurement interval is 30 minutes.

X 19 variables: temperatures, pressures, liquid level, reflux ratio, and so on


5
0
-5
y
0
500
1000
1500
2000
time [×30 min]

Adaptive Models and Setting of DMI

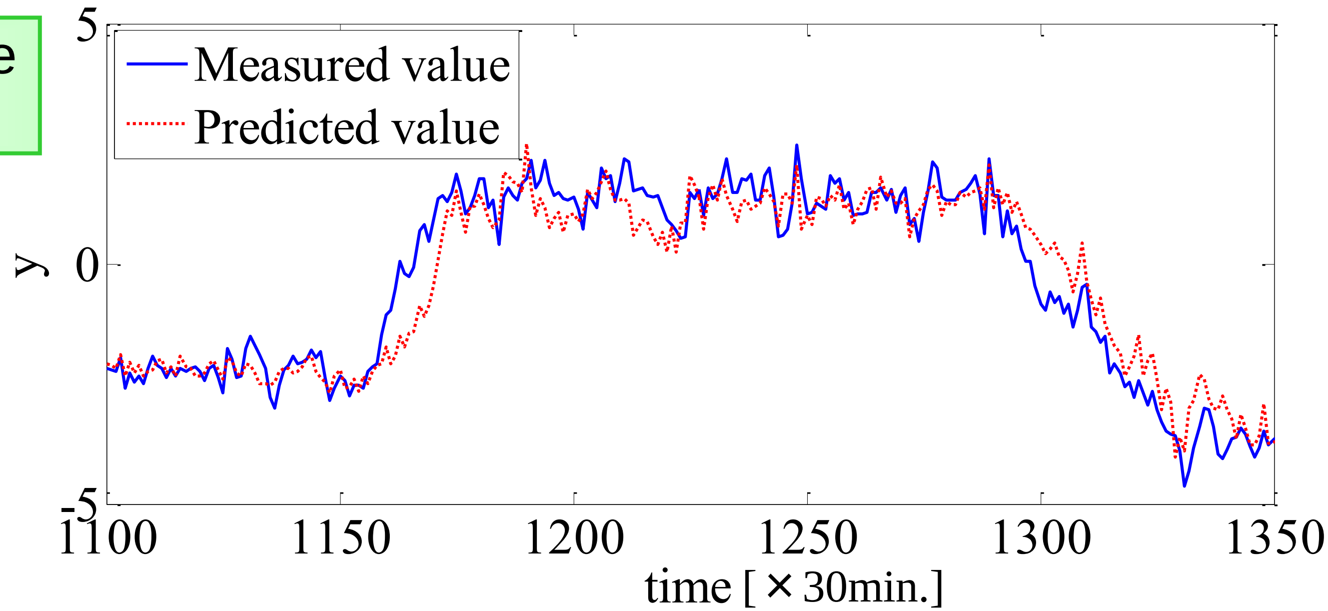
- MW model
  - Online support vector regression [1]
  - The upper limit of the number of data in the database : 50
- JIT model
  - Locally-weighted partial least squares [2]
  - The upper limit of the number of data in the database : 500
    - The old data was deleted automatically.
- DMI
  - Similarity: Gaussian kernel

$$\mathrm{DMI} = \frac{\left| y_i - y_j \right|^a}{\exp\left(-\gamma \left\| \mathbf{x}_i - \mathbf{x}_j \right\|^2 \right)}$$

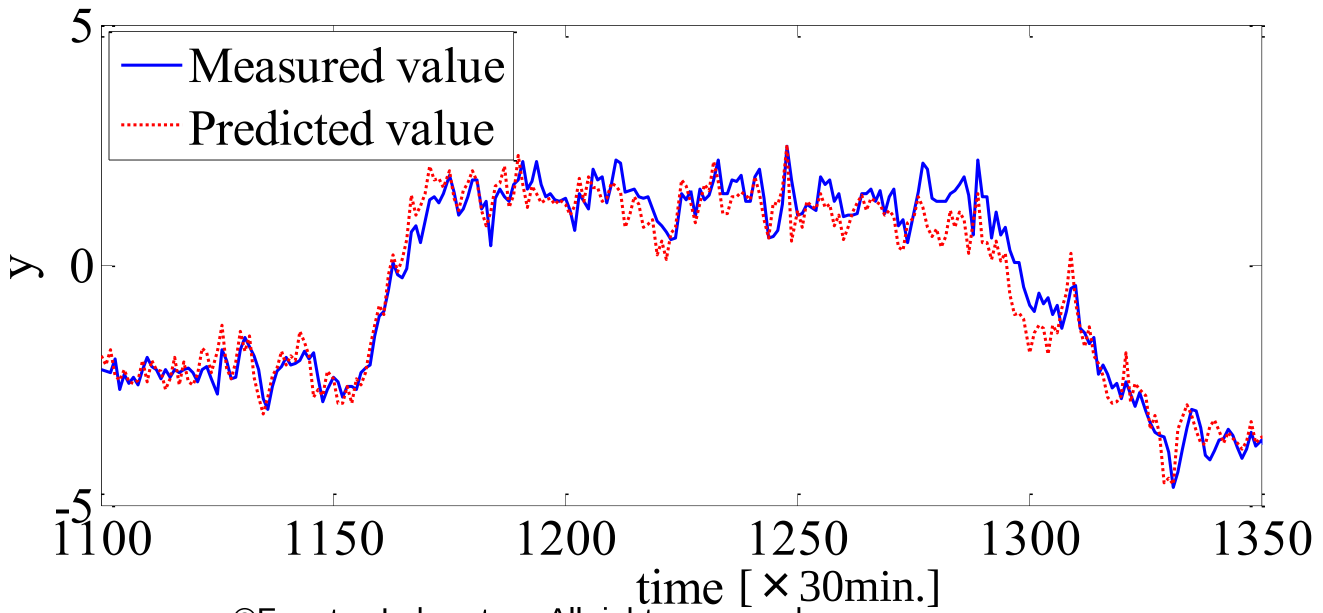
[1] H. Kaneko, K. Funatsu, *Comput. Chem. Eng*., 2013;58:288-297.
[2] S. Kim, M. Kano, H. Nakagawa, S. Hasebe, *Int. J. Pharm.,* 2011;421:269–274.

Time Plots of Measured and Predicted **y** (MW)

Without database management

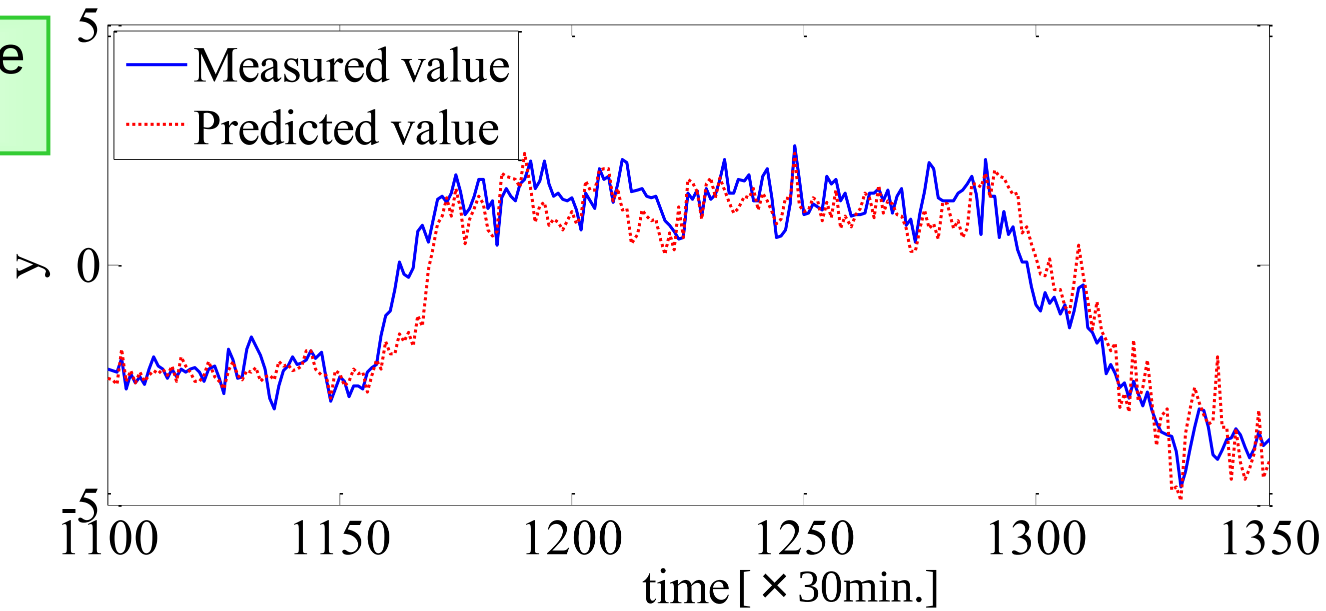


With database management

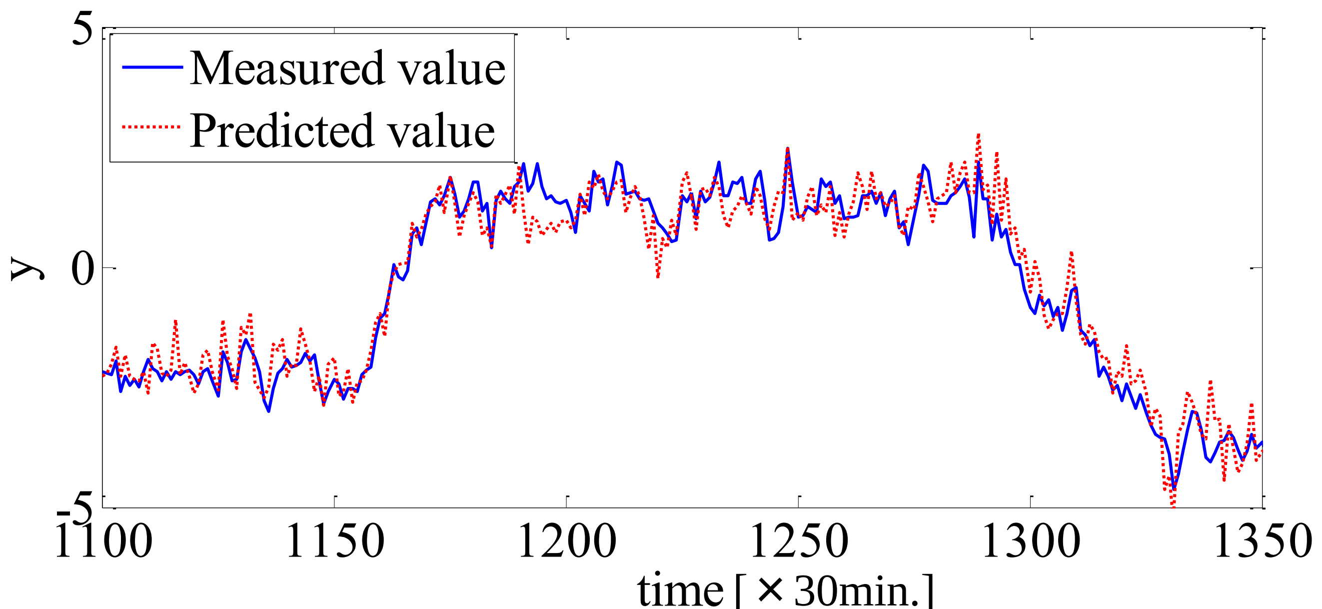


Time Plots of Measured and Predicted **y** (JIT)

Without database management

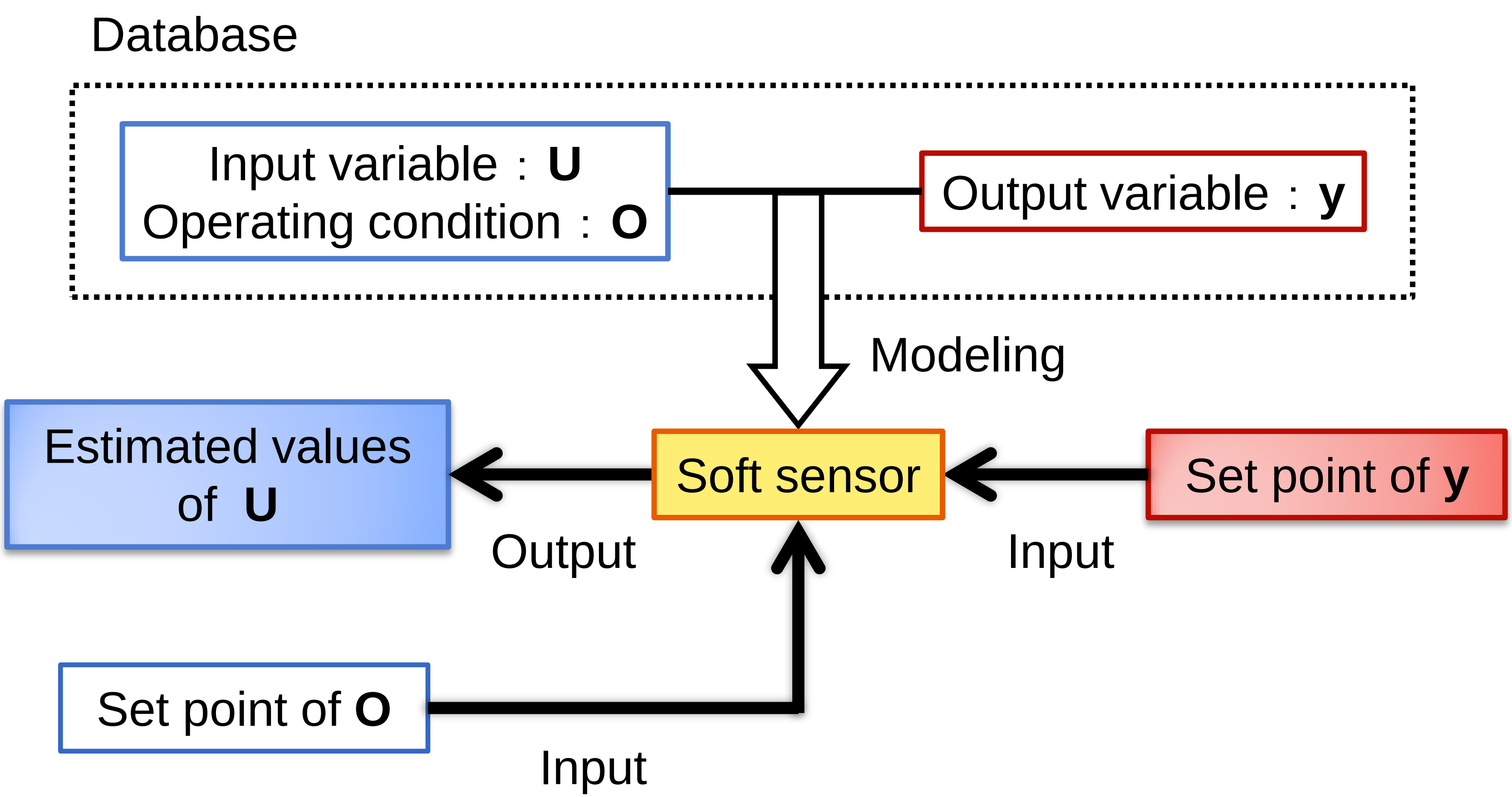


With database management

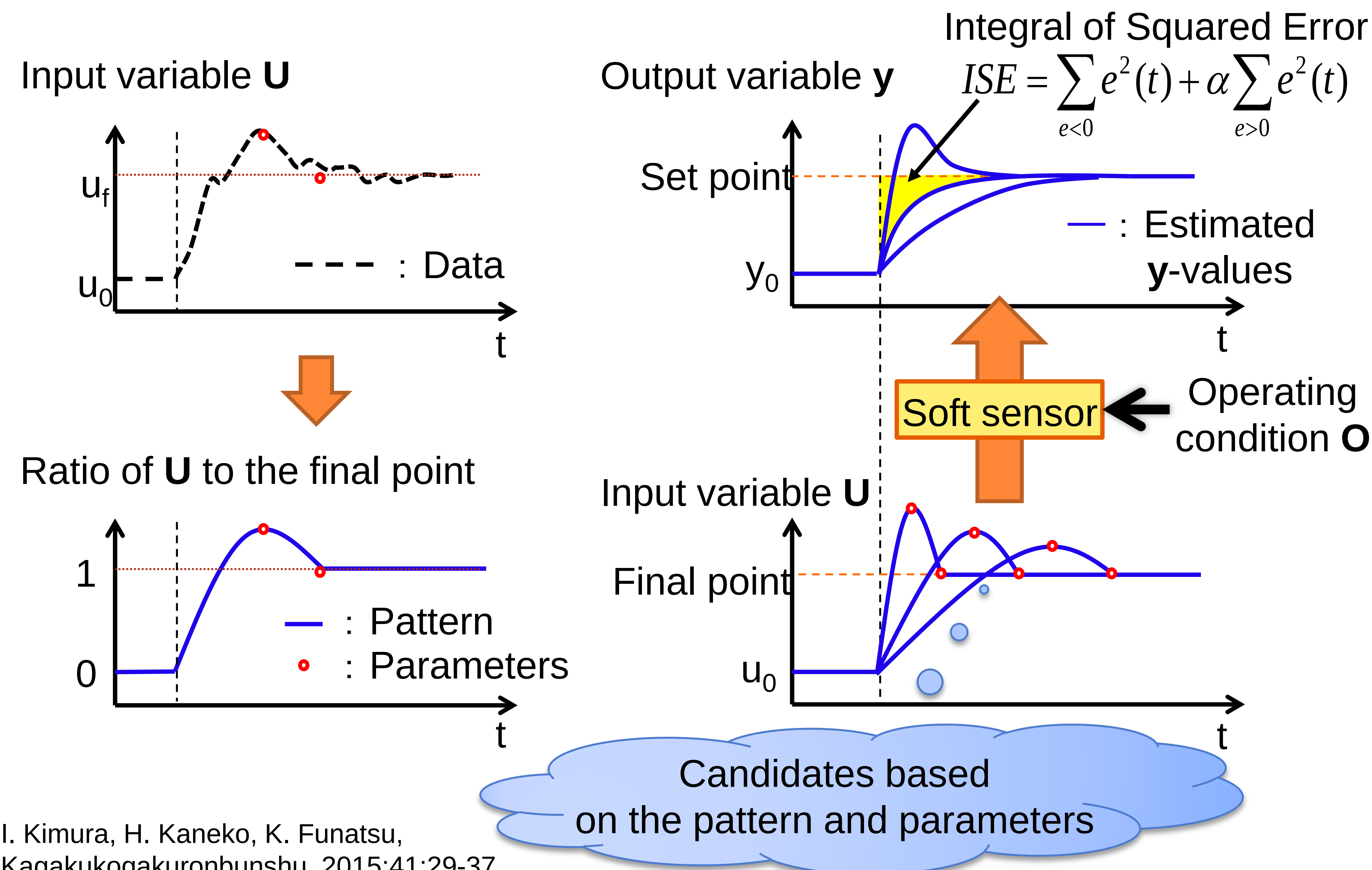


Contents

Process Control Using Soft Sensor



Inverse Soft sensor-based Feed Forward (ISFF) Control



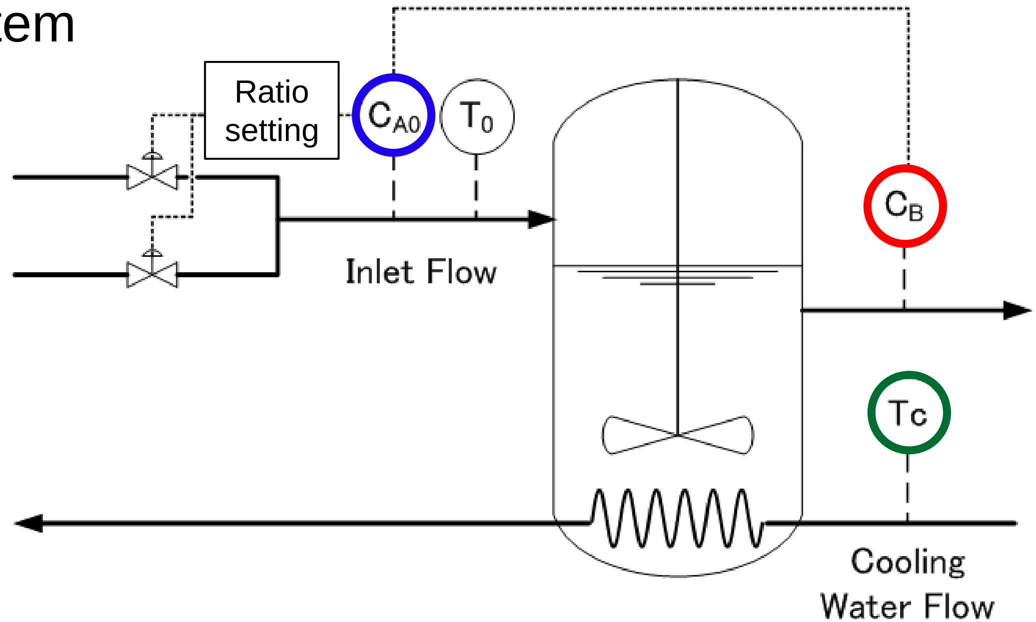
I. Kimura, H. Kaneko, K. Funatsu, Kagakukogakuronbunshu, 2015;41:29-37.

Case Study

continuous stirred-tank reactor system

(CSTR simulator [1])

- ✓Irreversible 1st-order exothermic reaction
- ✓A → B



Process variables

- ✓Output variable **y** : Outlet B-concentration C_B
- ✓Input variable **U** : Set point of inlet A-concentration C_{A0}
- ✓Operating condition **O** : Temperature of cooling water Tc

Measurement interval

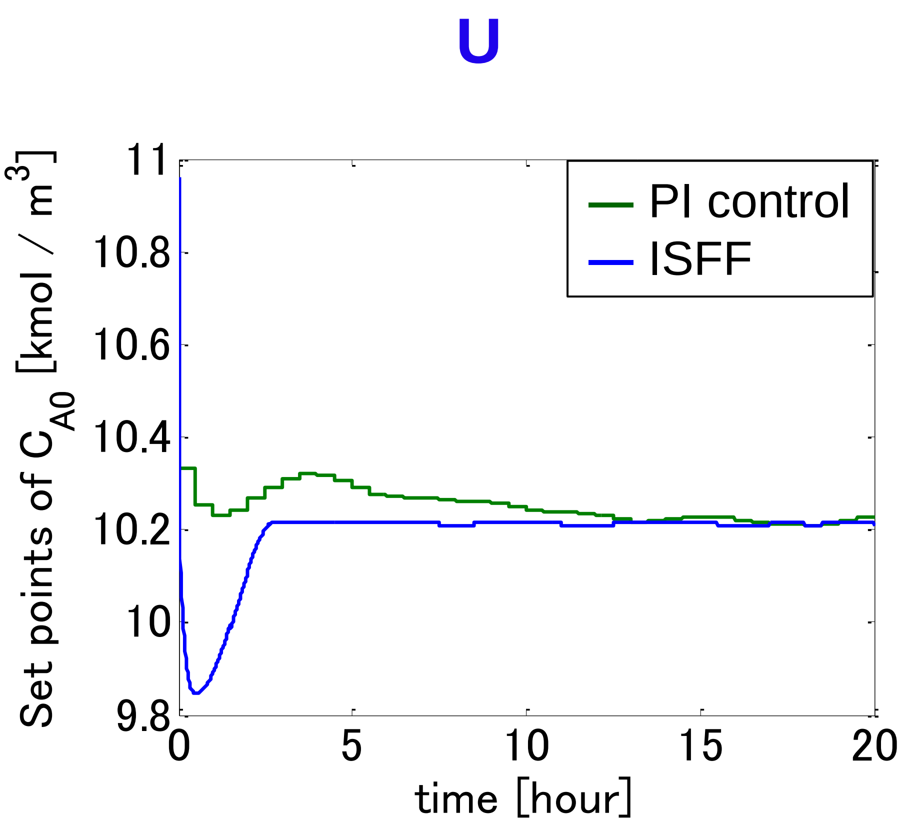
- ✓Concentration : 30 min. (30 min. delay)
- ✓Temperature : 1 min. (No delay)

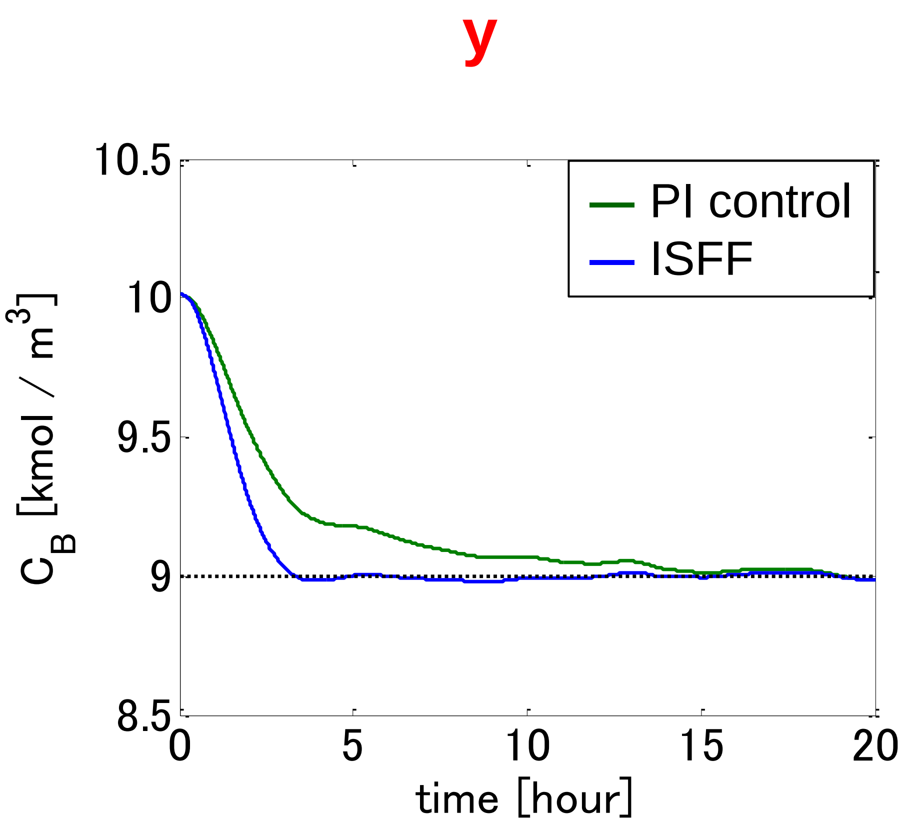
Soft sensor

- ✓Support vector regression (nonlinear)

[1] Seborg, D. E., T. F. Edgar, and D. A. Mellichamp, Process Dynamics and Control, 2nd Edition, Wiley, 2004, pp. 34–36 and 94–95.

Control Results





Control performance improved.

Summary

- Soft sensors are a key technique to predict the quality of products and to control the process.

- Ensemble Online Support Vector Regression (EOSVR) can predict y-values accurately when process states are time-varying and process changes are nonlinear.

- The prediction ability of adaptive soft sensors can improve by monitoring database appropriately.

- Efficient process control can be performed by using Inverse Soft sensor-based Feed Forward (ISFF) control

Papers

- Adaptive Soft Sensors

  H. Kaneko, K. Funatsu, Chemometr Intell. Lab. Syst., 137, 57-66, 2014.
  H. Kaneko, T. Okada, K. Funatsu, Ind. Eng. Chem. Res., 53, 15962-15968, 2014
  H. Kaneko, K. Funatsu, AIChE J., 62, 717-725, 2016

- Database Monitoring for Soft Sensors

  H. Kaneko, K. Funatsu, AIChE J., 60, 160-169, 2014
  H. Kaneko, K. Funatsu, Chemometr Intell. Lab. Syst., 146, 179-185, 2015

- Efficient Process Control Using Soft Sensors

  I. Kimura, H. Kaneko, K. Funatsu, Kagakukogakuronbunshu, 41, 29-37, 2015

- Application of soft sensors to pharmaceutical process

  H. Kaneko, K. Muteki, K. Funatsu, Chemometr Intell. Lab. Syst., 147, 176-184, 2015
  S. Shibayama, H. Kaneko, K. Funatsu, AAPS PharmSciTech, accepted.