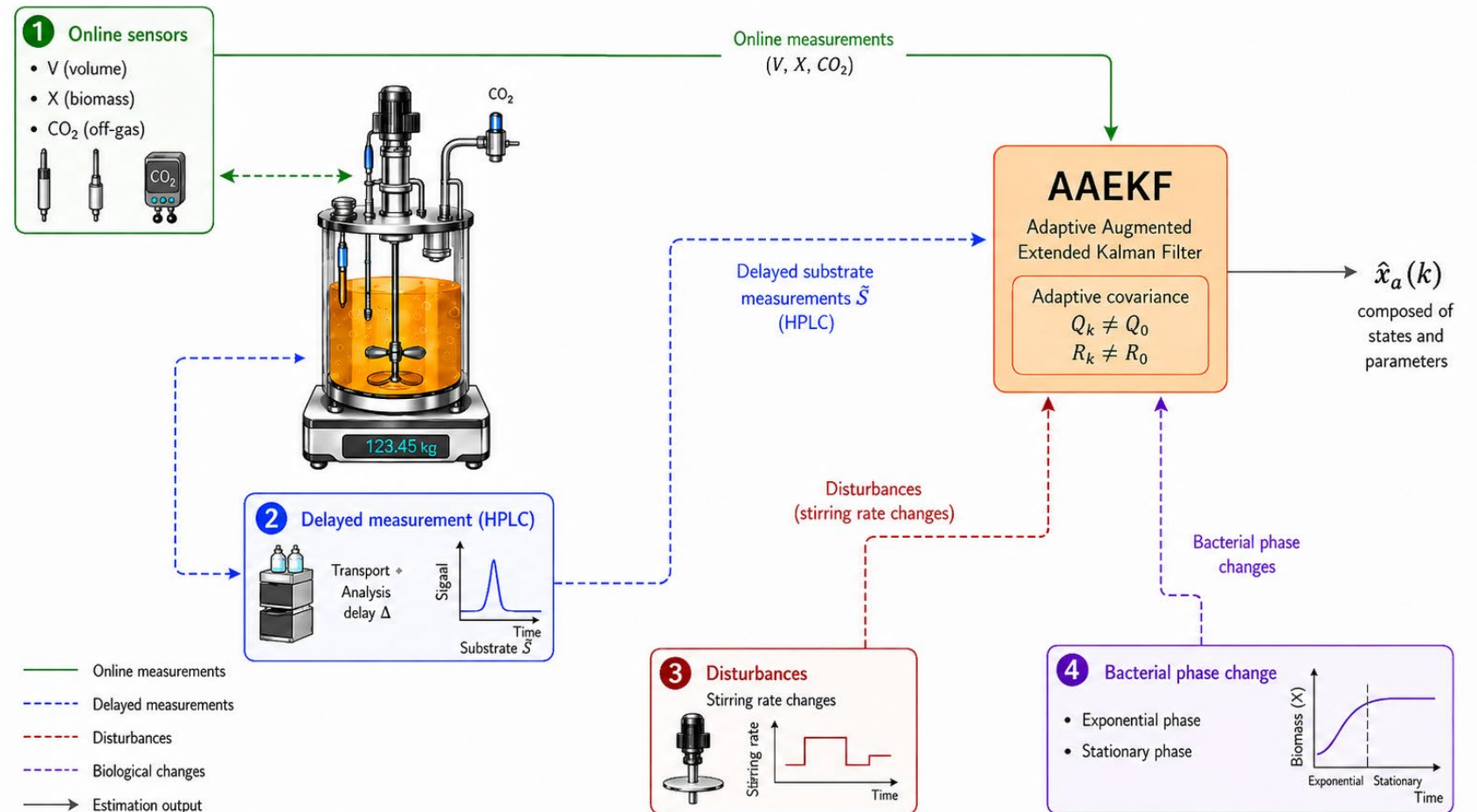


# DISTURBANCE ROBUST ADAPTIVE AEKF ESTIMATION FOR BIOPROCESSING

Giacomo Sartori, Nadav Bar  
(NTNU)

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NPC 2026



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# CASE STUDY – 2 EXPERIMENTAL DATASETS

- **2 Experimental Datasets:** Constant feeding after initial batch
  - **Problem 1 (Pb.1): Disturbance** in biomass measurements due to stirring changes
  - **Problem 2 (Pb.2): Phase-switch** in one of the two datasets
  - Augmented Extended Kalman Filter (AEKF) estimation
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State and parameter estimation with  
AEKF



**Adaptive AEKF (AAEKF)**, i.e  
 $(Q_k, R_k) \neq (Q_0, R_0)$  in general

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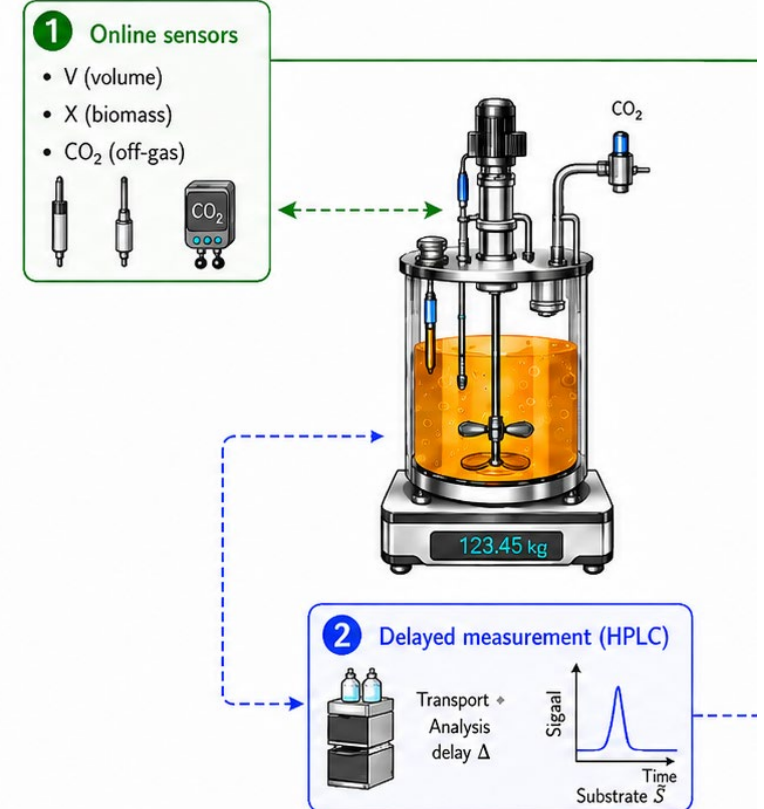
# MODEL

$$\frac{d\bar{x}(t)}{dt} = \begin{bmatrix} \dot{V} \\ \dot{X} \\ \dot{S} \\ C\dot{O}_2 \end{bmatrix} = \begin{pmatrix} F_{in} - F_{out} \\ -\left(\frac{F_{in}}{V}\right)X + \mu_{max} \frac{S}{K_s + S} X - k_d X \\ (S_{in} - S) \frac{F_{in}}{V} - \mu_{max} \frac{S}{K_s + S} \frac{X}{Y_{XS}} \\ -CO_2 Q + \mu_{max} \frac{S}{K_s + S} \frac{X}{Y_{XCO_2}} \end{pmatrix}$$

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# AUGMENTED MODEL

$$\frac{dx(t)}{dt} = \begin{pmatrix} \dot{V} \\ \dot{X} \\ \dot{S} \\ C\dot{O}_2 \\ \dot{\mu}_{max} \\ Y_{XCO_2} \\ Y_{XS} \end{pmatrix} = \begin{pmatrix} F_{in} - F_{out} \\ -\left(\frac{F_{in}}{V}\right)X + \mu_{max} \frac{S}{K_s + S}X - k_d X \\ (S_{in} - S) \frac{F_{in}}{V} - \mu_{max} \frac{S}{K_s + S} \frac{X}{Y_{XS}} \\ -CO_2 Q + \mu_{max} \frac{S}{K_s + S} \frac{X}{Y_{XCO_2}} \\ 0 \\ 0 \\ 0 \end{pmatrix}$$



# AEKF

Prediction step

$$\hat{x}_k^{(p)} = f(\hat{x}_{k-1}^{(f)}, u_{k-1})$$

$$P_k^{(p)} = F_{k-1} P_{k-1}^{(f)} F_{k-1}^T + Q_k$$

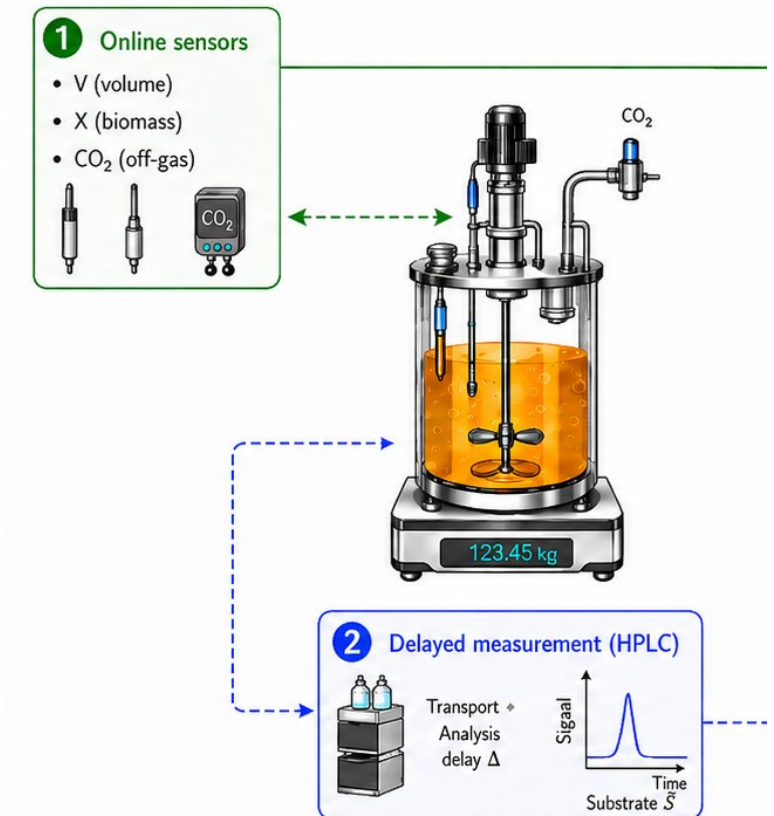
Update step

$$K_k = P_k^{(p)} H_k^T (H_k P_k^{(p)} H_k^T + R)^{-1}$$

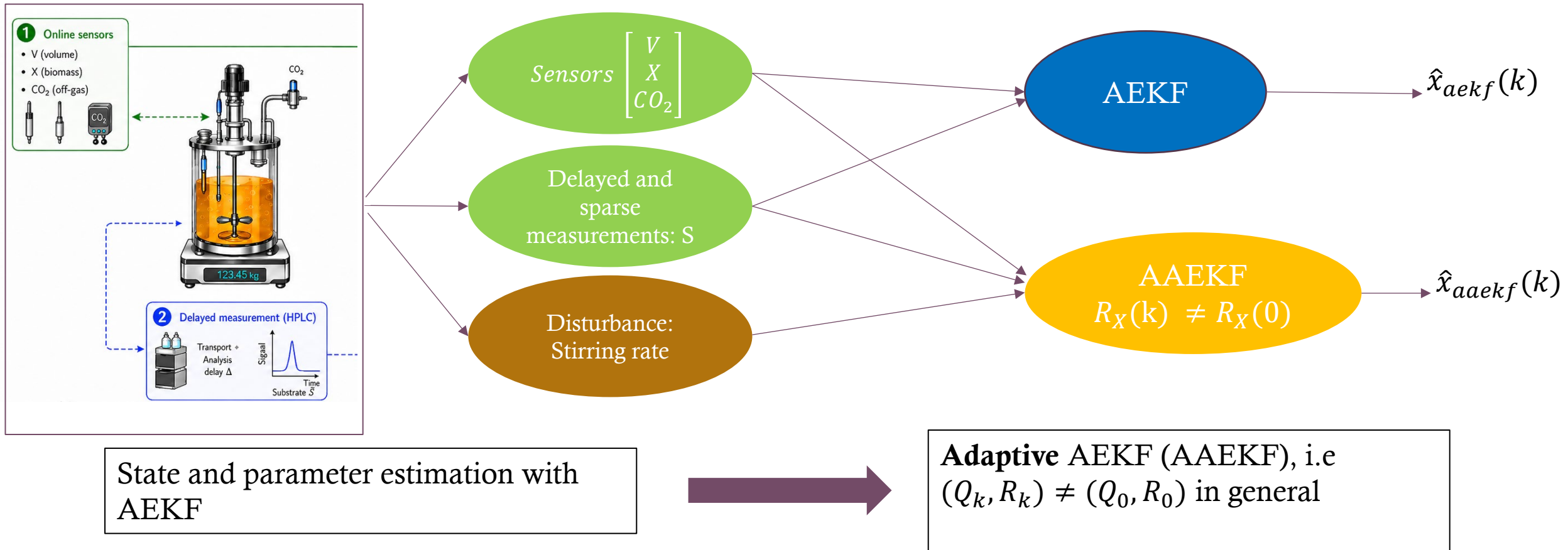
$$\hat{x}_k^{(f)} = \hat{x}_k^{(p)} + K_k (y_k - h(\hat{x}_k^{(p)}))$$

$$P_k^{(f)} = (I - K_k H_k) P_k^{(p)} (I - K_k H_k)^T + K_k R K_k^T$$

$$F_k = \frac{df(\hat{x}_k^{(f)}, u_k)}{dx} \quad \omega_k \sim \mathcal{N}(0, Q) \quad H_k = \frac{dh(\hat{x}_k^{(p)})}{dx}$$



# CASE STUDY – BLOCK SCHEME PB.1



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# EVENT-BASED MEASUREMENT NOISE INFLATION

- Keep model simple
- Inflate  $R_k^X$  with significant stirring actuation jumps,  $|\Delta N_k| > \theta_N$
- $R_k^X = R_0^X \left(1 + \gamma(\bar{k}, k)\right)$ , where the amplification function  $\gamma(\bar{k}, k)$  is defined as
- $$\gamma(\bar{k}, k + i) = \begin{cases} \gamma_{ss} \left( \frac{1 - e^{-\alpha(\bar{k} - i)}}{1 - e^{-\alpha\bar{k}}} \right), & \text{if } i \leq \bar{k} \\ 0, & \text{if } i > \bar{k} \end{cases},$$

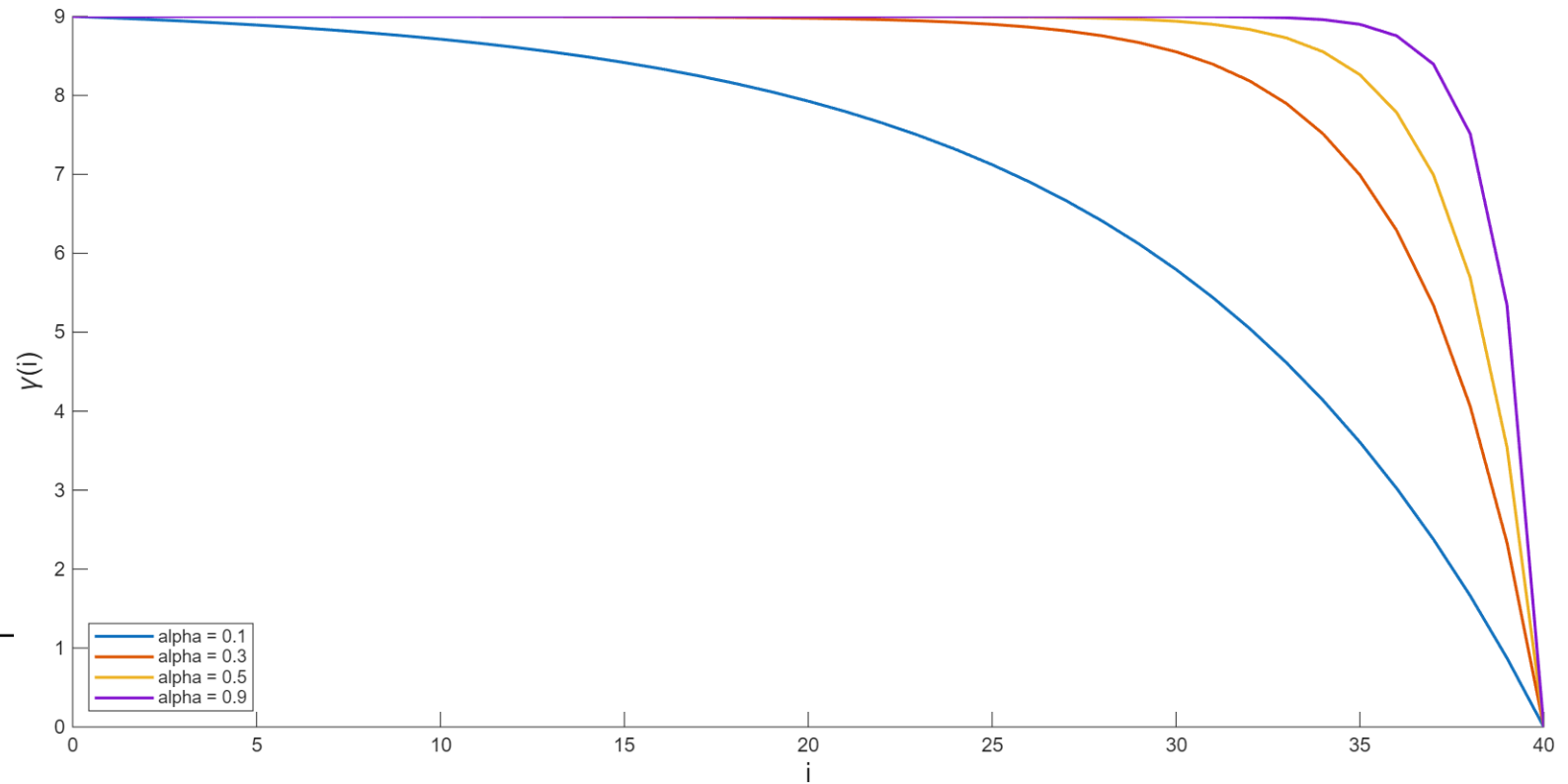
where  $\gamma_{ss}$  is the amplification gain (on at iteration  $k$ ),  $\alpha$  the decaying velocity and  $\bar{k}$  the number of iterations where the amplification is on (i.e.  $\bar{k} = \text{round}(|\Delta N_k| * \Psi)$ , where  $\Psi$  is a conversion factor from stirring increase to iterations where the function is on).

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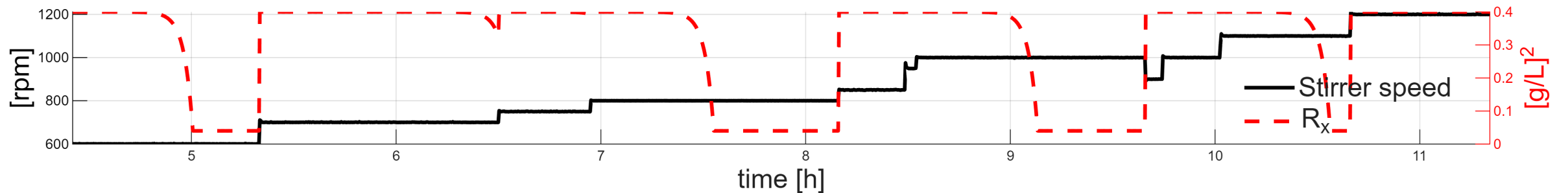
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# EVENT-BASED MEASUREMENT NOISE INFLATION

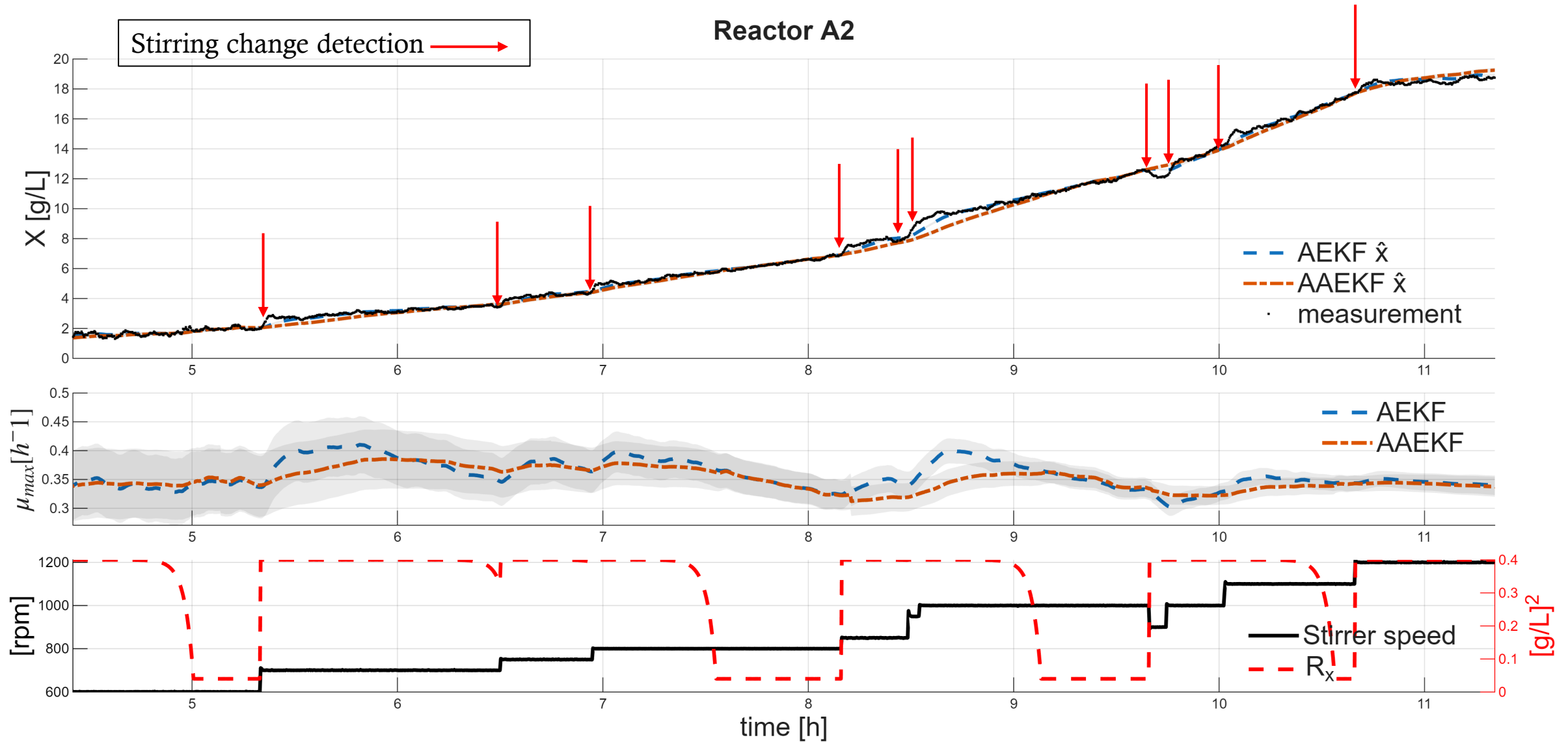
- $\gamma(\bar{k}, k + i) = \gamma_{ss} \left( \frac{1 - e^{-\alpha(\bar{k} - i)}}{1 - e^{-\alpha\bar{k}}} \right)$ ,  $\gamma_{ss} = 9$ ,  $\bar{k} = 40$ .
- Chosen  $\alpha = 0.1$ ,  $\gamma_{ss} = 9$ .



# SMOOTHED BIOMASS ESTIMATES – A2

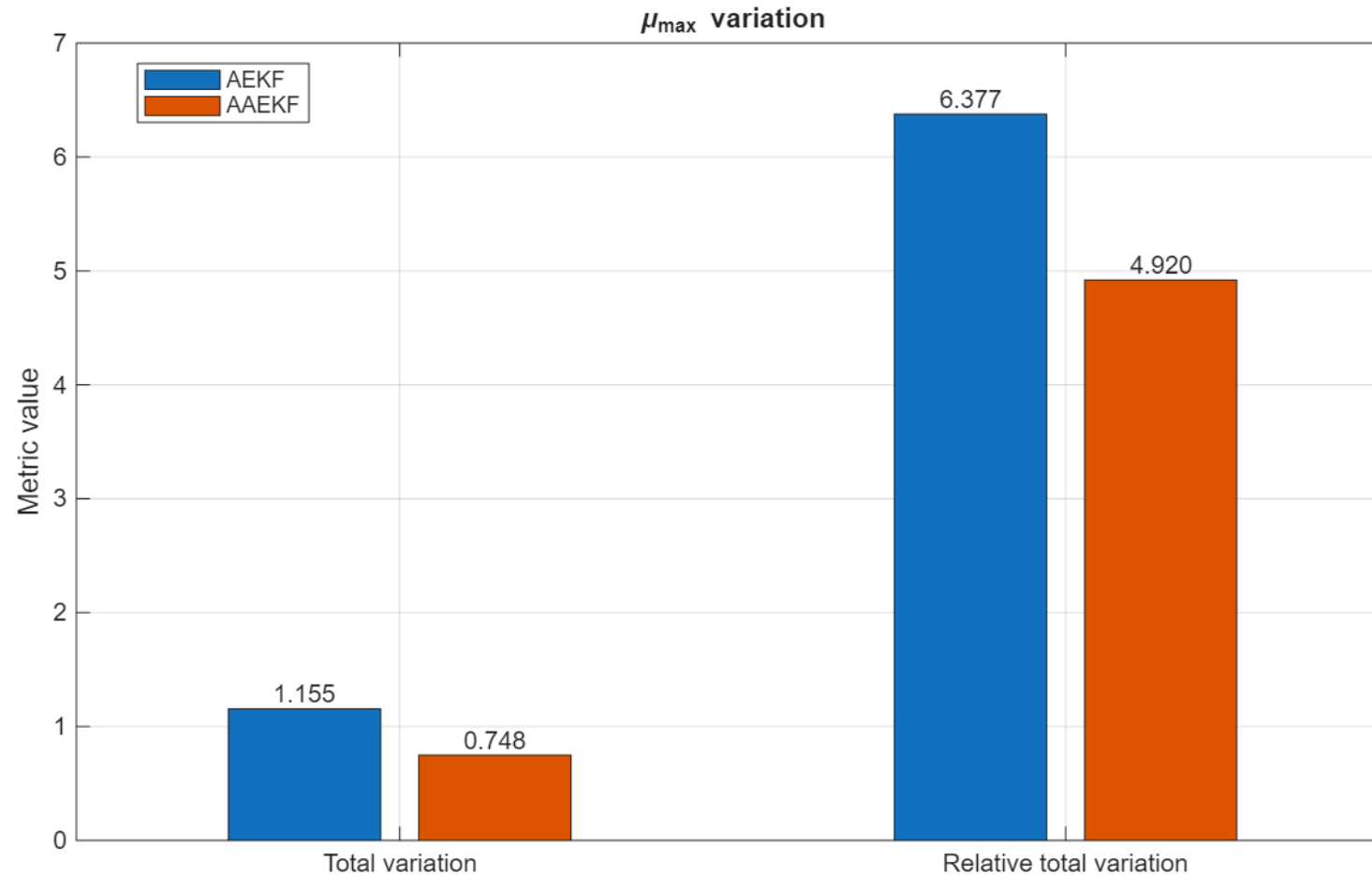


# SMOOTHED BIOMASS ESTIMATES – A2



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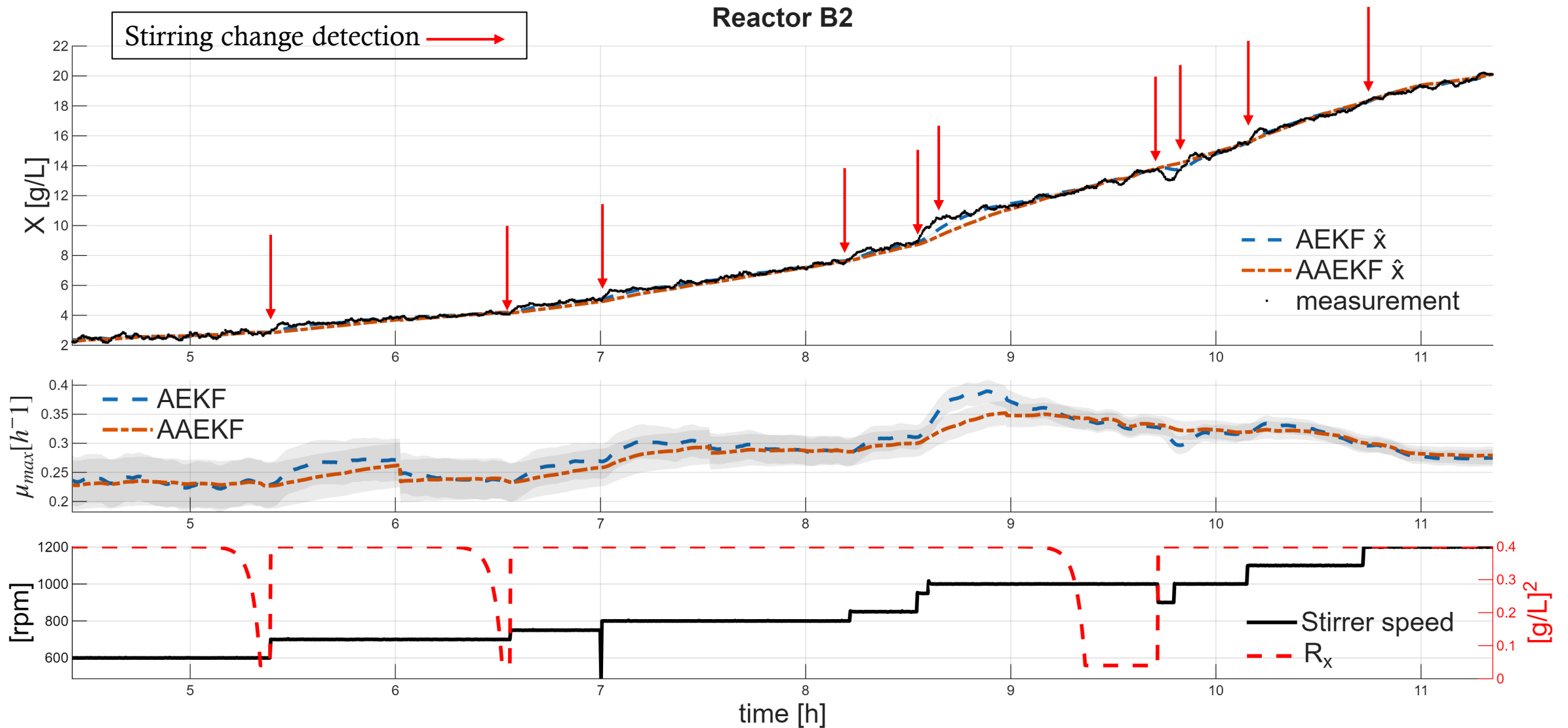
# SMOOTHED BIOMASS ESTIMATES – A2



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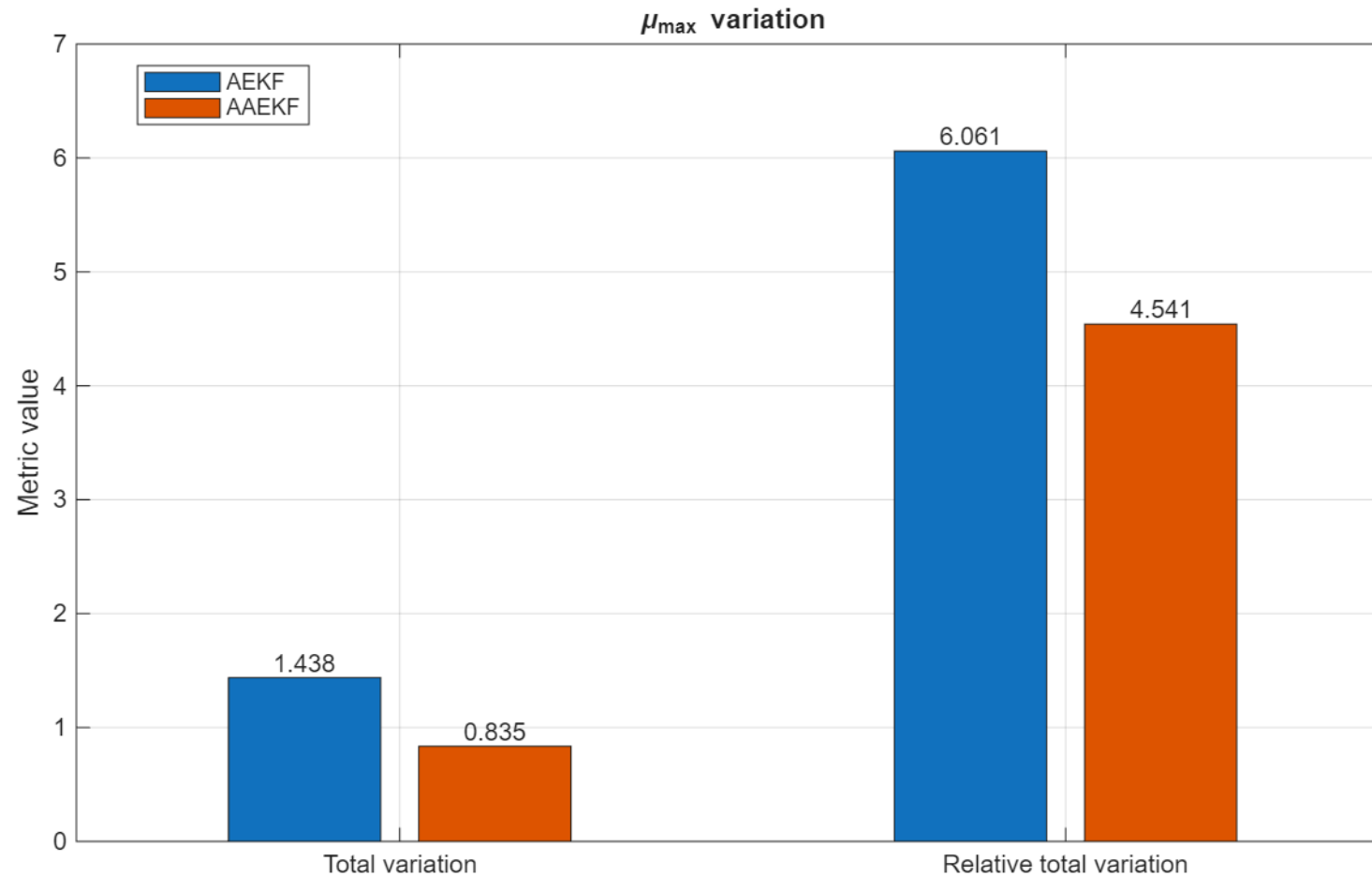
$$TV = \sum_k |\mu_{\max}(k) - \mu_{\max}(k-1)| \quad TV_{\text{rel}} = \frac{TV}{\max(\mu_{\max}) - \min(\mu_{\max})}$$

# SMOOTHED BIOMASS ESTIMATES – B2

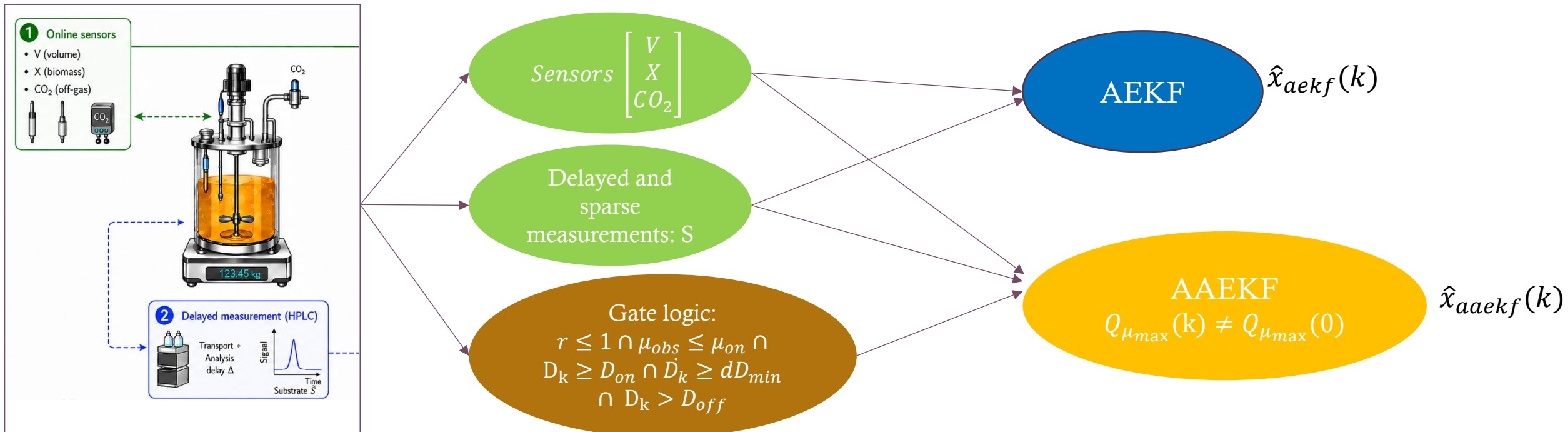


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# SMOOTHED BIOMASS ESTIMATES – B2



# CASE STUDY – BLOCK SCHEME PB.2



State and parameter estimation with augmented extended Kalman filter (AEKF)



**Adaptive AEKF (AA-EKF)**, i.e  $(Q_k, R_k) \neq (Q_0, R_0)$  in general

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# $Q_k^{\mu_{max}}$ TERM ADAPTATION

Combine available information to detect unmodelled stop growth

Infer quality of bacteria status by using:

- $\hat{\mu}_{max}$  as the cell life status quality detector, must have good estimate of it (AEKF)
  - $\mu_{obs} = \mu(S) = \mu_{max} \frac{S}{S+k_S}$  can be empirically observed from  $\mu_{obs} = \frac{\frac{dX}{dt}}{\hat{X}} + k_d + \frac{F_{in}}{V}$ ,
  - $CO_2$  as a growing detector sensor
-

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# $Q_k^{\mu_{max}}$ TERM ADAPTATION

- If  $\mu_{obs} \leq \mu_{on}$  (e.g.  $\mu_{on} = 0.05h^{-1}$ ), stopped growth might happen
  - Difference between  $\mu_{max}$  and  $\mu_{obs}$  when  $S \approx 0$ .  $\mu_{obs}$  is analytical but not always a good indicator of *growth/no growth* (when bacteria do not grow might be for unknown conditions, not because *sugar* is too little)
  - Need for another indicator (when  $S \approx 0$ ):  $r = \frac{demand}{supply}$
  - $demand = X \left( \frac{\mu_{obs}}{Y_{XS}} \right), \quad supply = \frac{F_{in}}{V} (S_{in} - S)$
  - If  $r \leq 1 \cap \mu_{obs} \leq \mu_{on}$ , bacteria should grow as they have enough sugar. If they don't, they have stopped growing for some other unmodelled reason.
-

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# $Q_k^{\mu_{max}}$ TERM ADAPTATION

- $CO_2$  as a growing detector sensor. Idea: compare  $\widehat{CO}_2$  with an healthy growth baseline  $CO_2^{ref}$
  - $CO_{2k}^{ref} = \lambda CO_{2k-1}^{ref} + (1 - \lambda) \widehat{CO}_{2k-1}$
  - Define a normalized drop as  $D_k = \frac{CO_{2k}^{ref} - \widehat{CO}_{2k}}{CO_{2k}^{ref}}$
  - Define derivative of the drop (to ignore short drifts) as  $\dot{D}_k \approx \frac{D_k - D_{k-1}}{T_S}$  (better calculated over a smoothed window)
  - Turn **on** when  $D_k \geq D_{on} \cap \dot{D}_k \geq dD_{min}$  ( $dD_{min}$  is a min threshold change)
  - Turn **off** when  $D_k \leq D_{off}$ , ( $D_{off} < D_{on}$ ).
-

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# $Q_k^{\mu_{max}}$ TERM ADAPTATION

- When all conditions for adapting the term  $Q_k^{\mu_{max}}$  are **on** ( $r \leq 1 \cap \mu_{obs} \leq \mu_{on} \cap D_k \geq D_{on} \cap \dot{D}_k \geq dD_{min} \cap D_k > D_{off}$ )
- Inflate  $Q_k^{\mu_{max}}$  using an increasing function
- $Q_k^{\mu_{max}} = Q_0^{\mu_{max}} \left( 1 + \varphi(\bar{k}, k) \right)$ , where the amplification function is defined as
- $$\varphi(\bar{k}, k + i) = \begin{cases} \varphi_{ss} \left( \frac{1 - e^{-\beta(i)}}{1 - e^{-\beta\bar{k}}} \right), & \text{if } i \leq \bar{k} \\ 0, & \text{if } i > \bar{k} \end{cases}$$

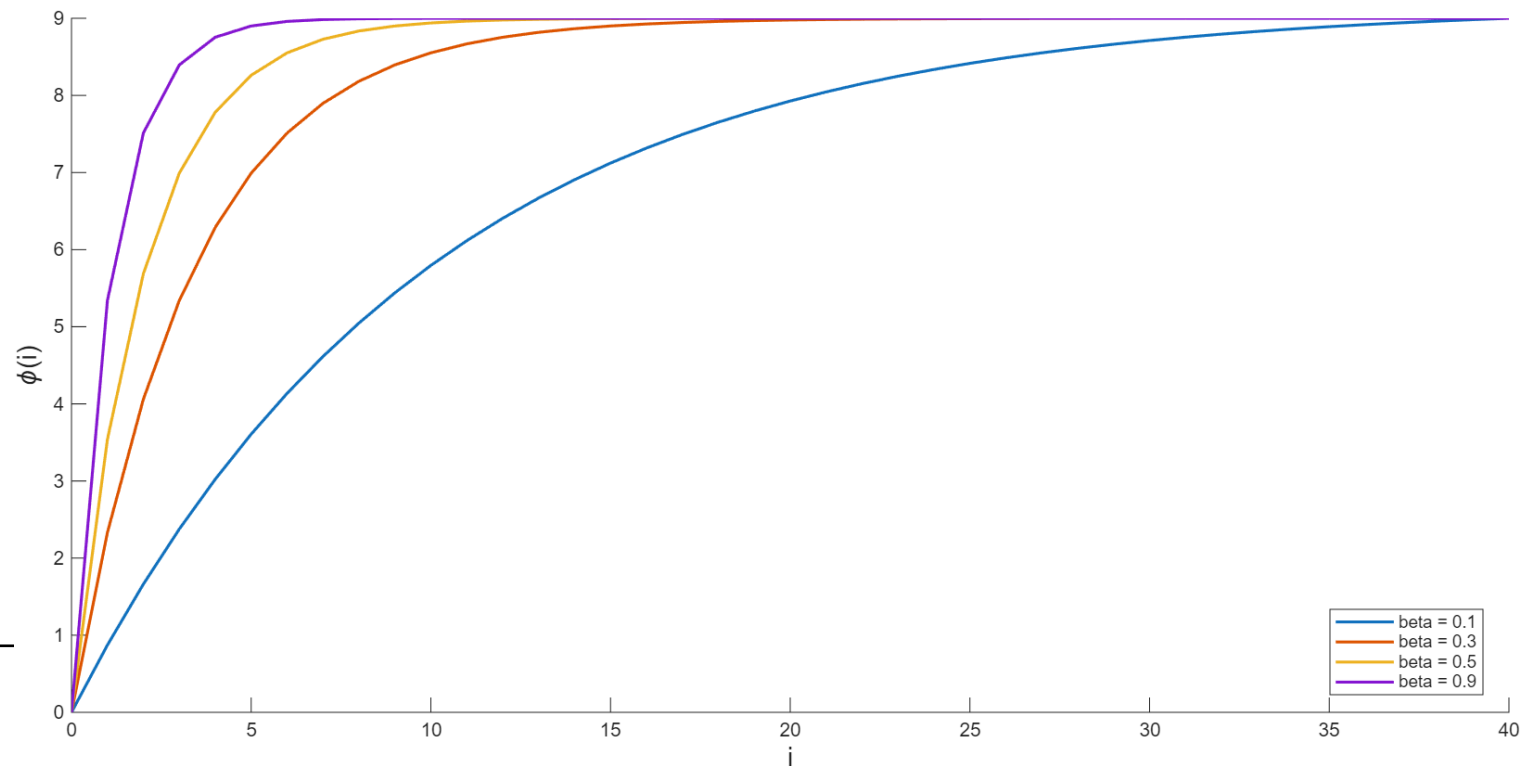
$\varphi_{ss}$  is the amplification gain (on at iteration  $k$ ),  $\beta$  the damping factor and  $\bar{k}$  the number of iterations to reach the maximum amplification.

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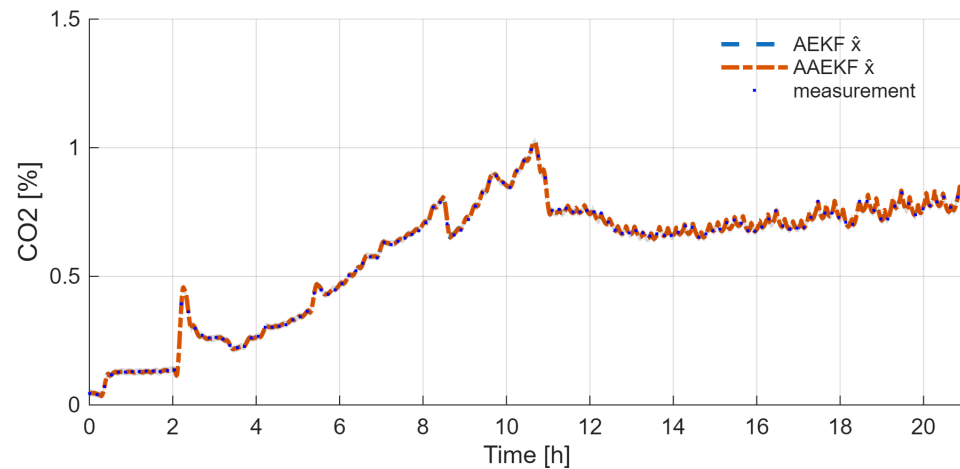
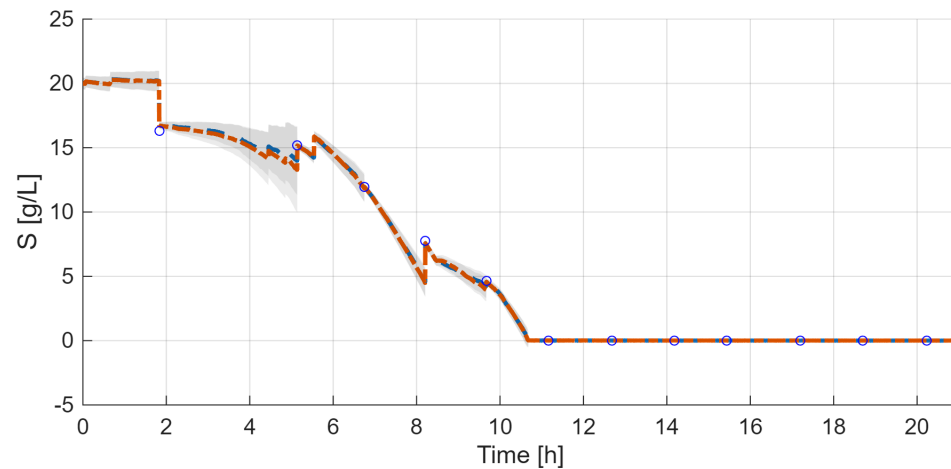
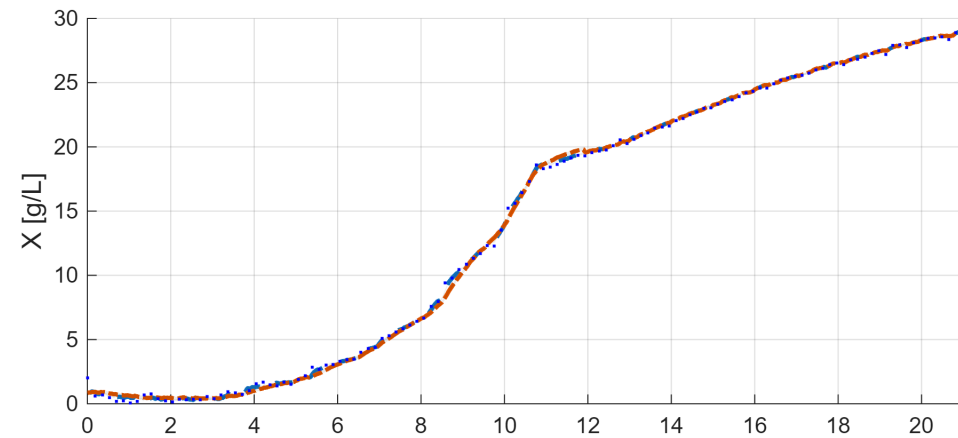
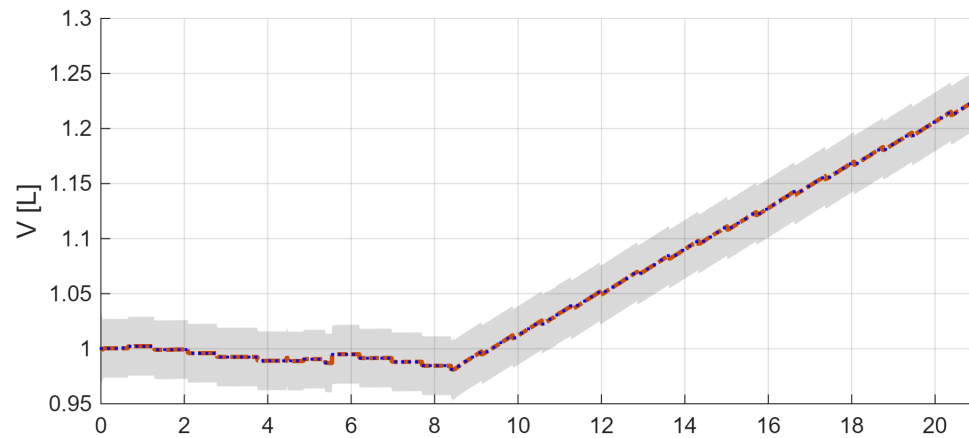
# $Q_k^{\mu_{max}}$ TERM ADAPTATION

- $\varphi(\bar{k}, k + i) = \varphi_{ss} \left( \frac{1 - e^{-\beta(i)}}{1 - e^{-\beta\bar{k}}} \right), \varphi_{ss} = 9, \bar{k} = 40.$
- Chosen  $\beta = 0.9, \varphi_{ss} = 1999.$



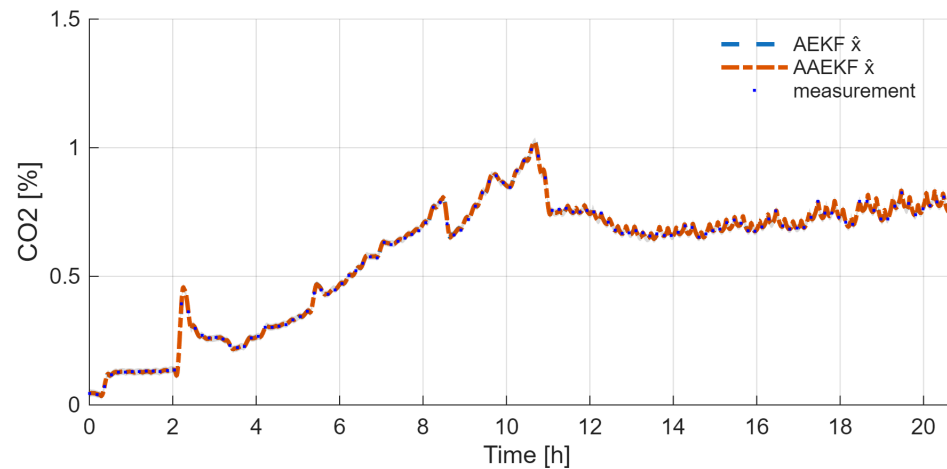
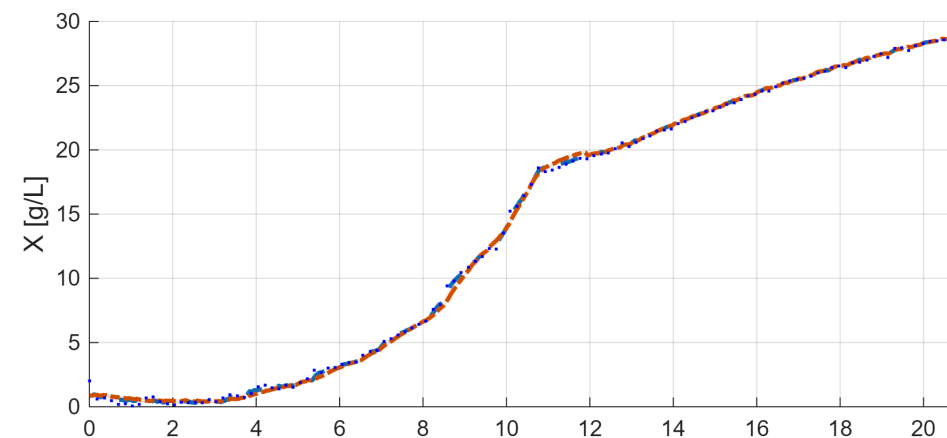
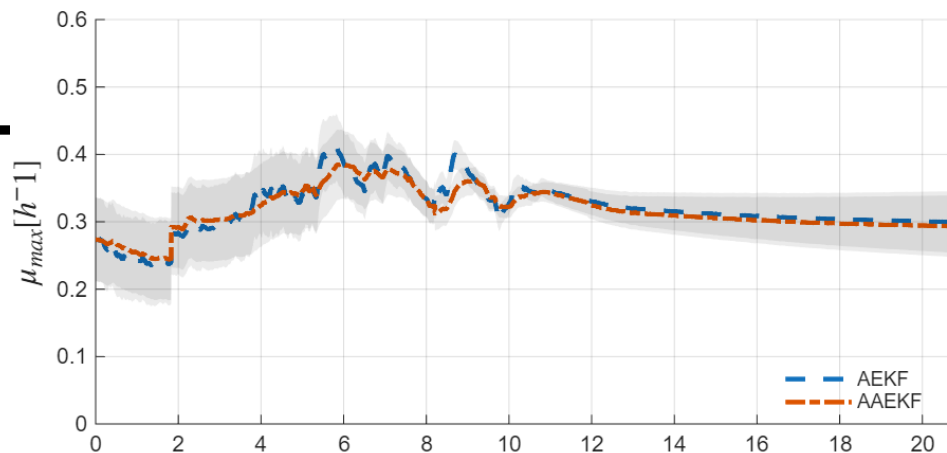
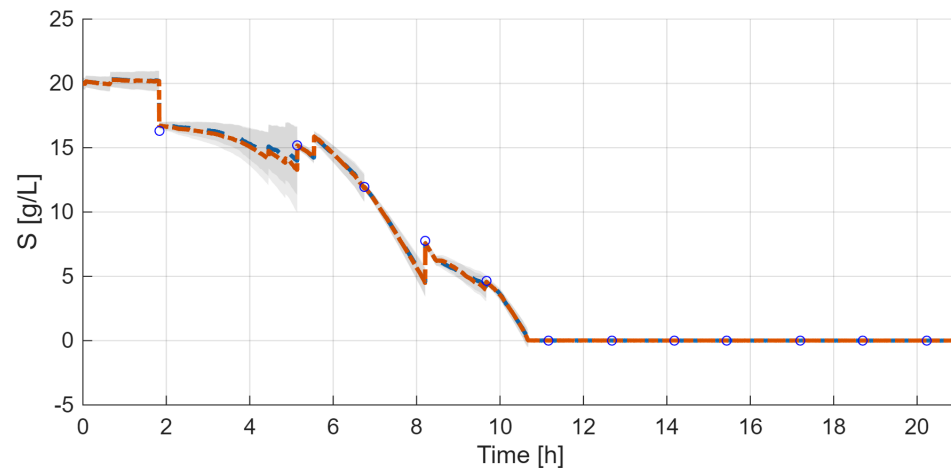
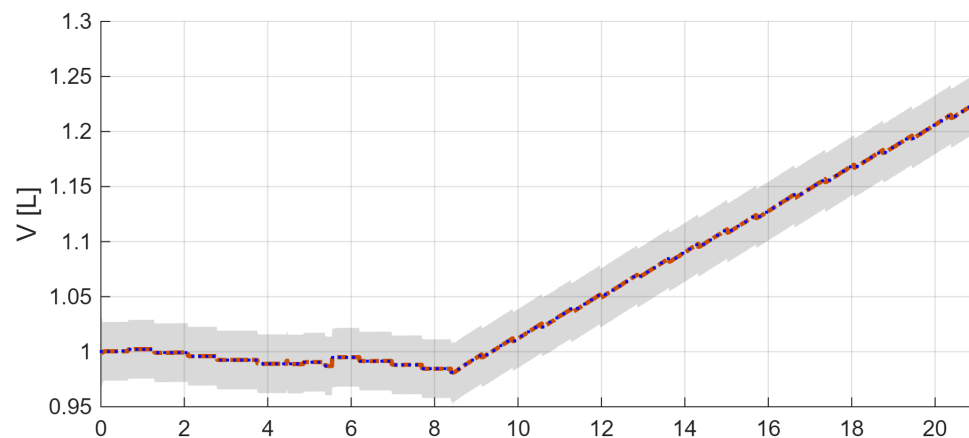
# CASE A2

Reactor A2

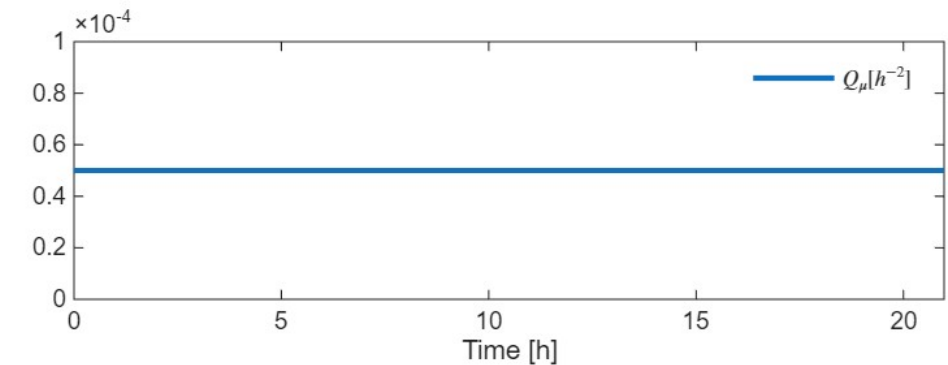
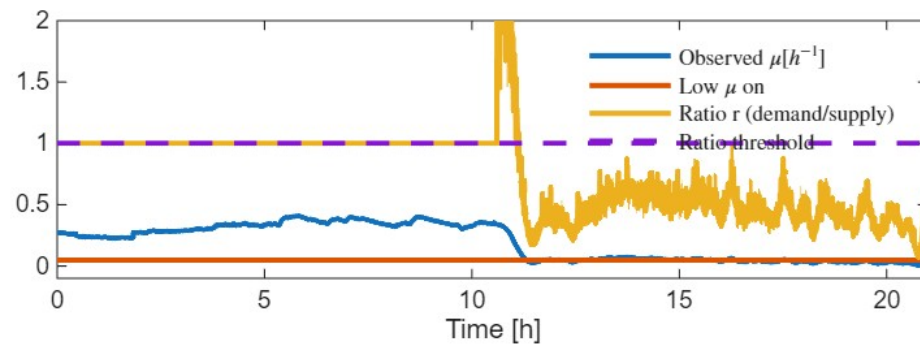
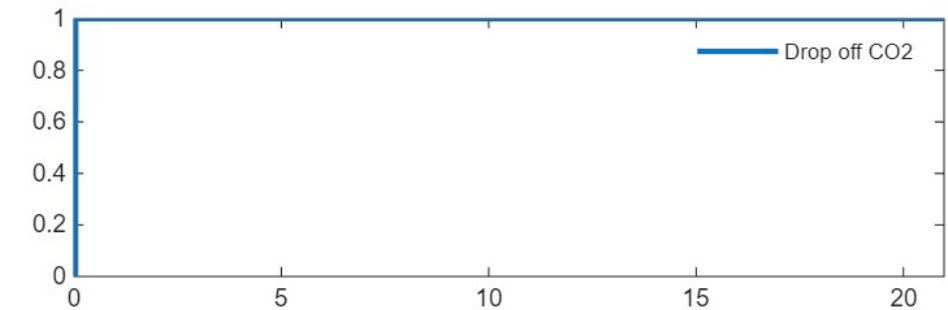
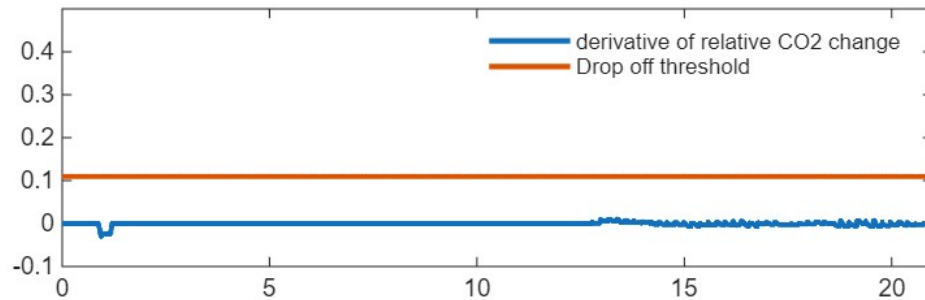
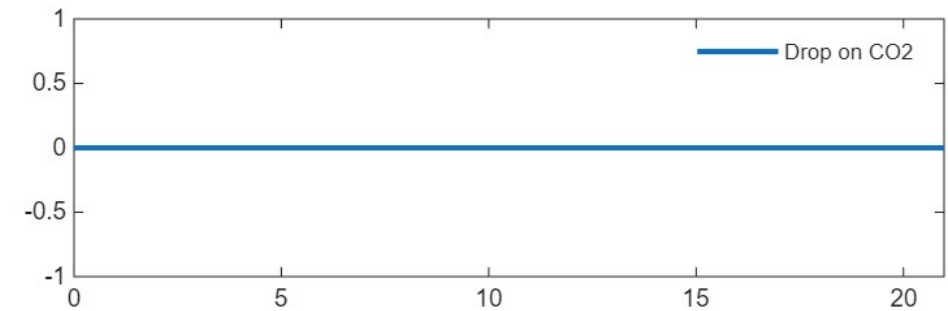
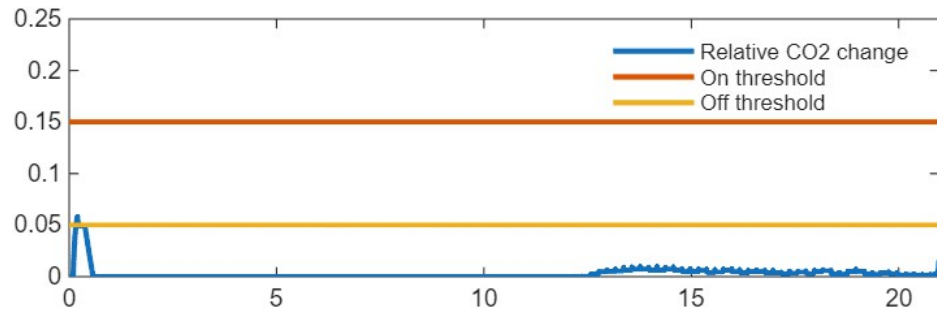


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Reactor A2

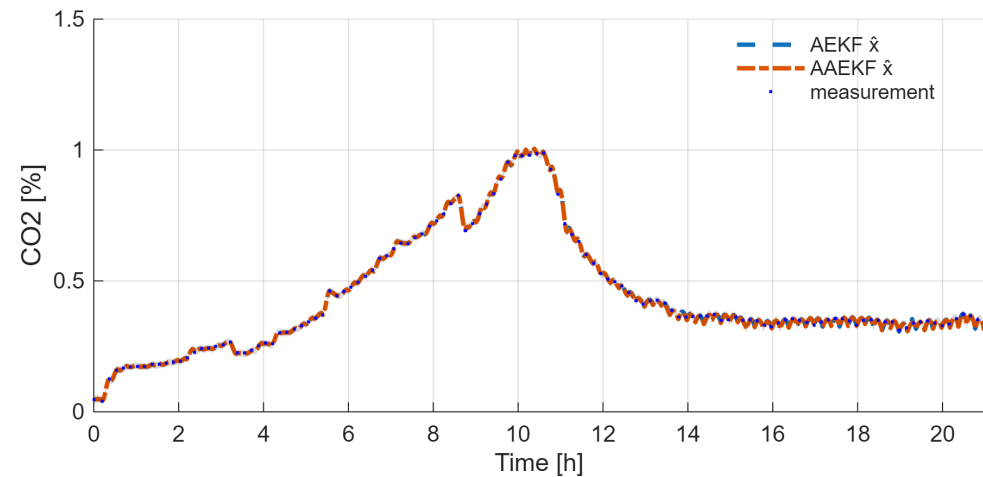
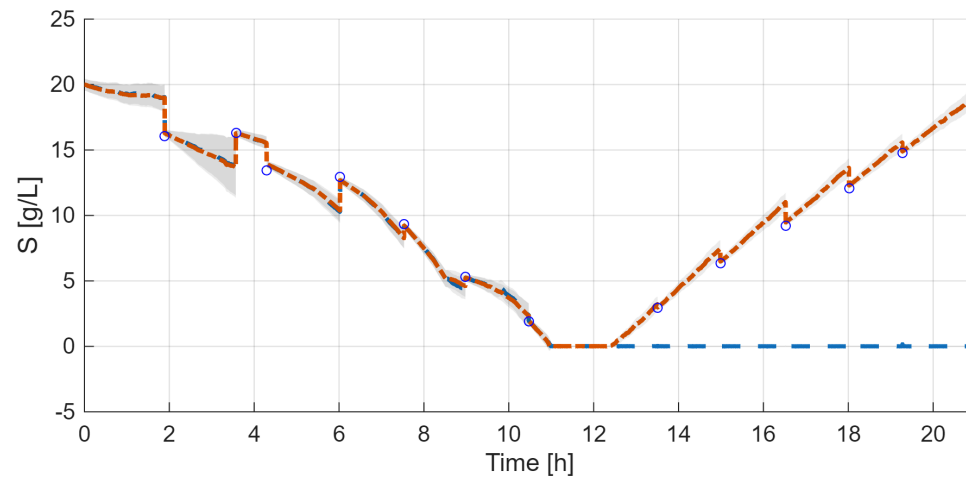
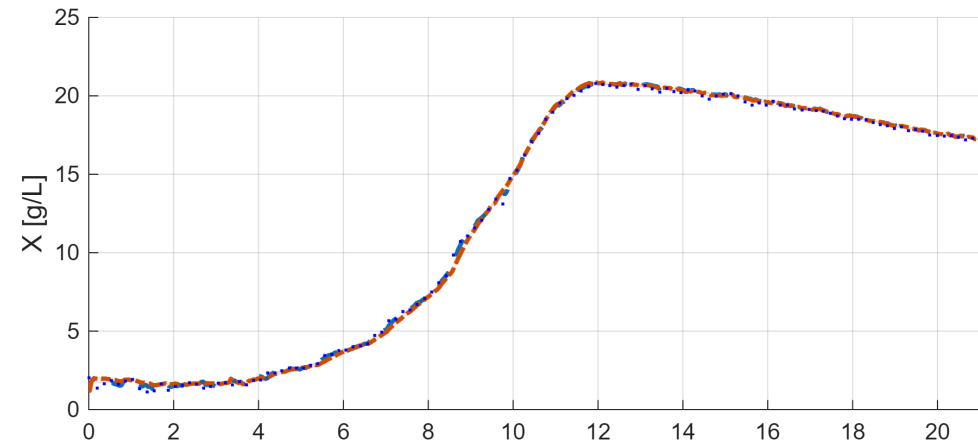
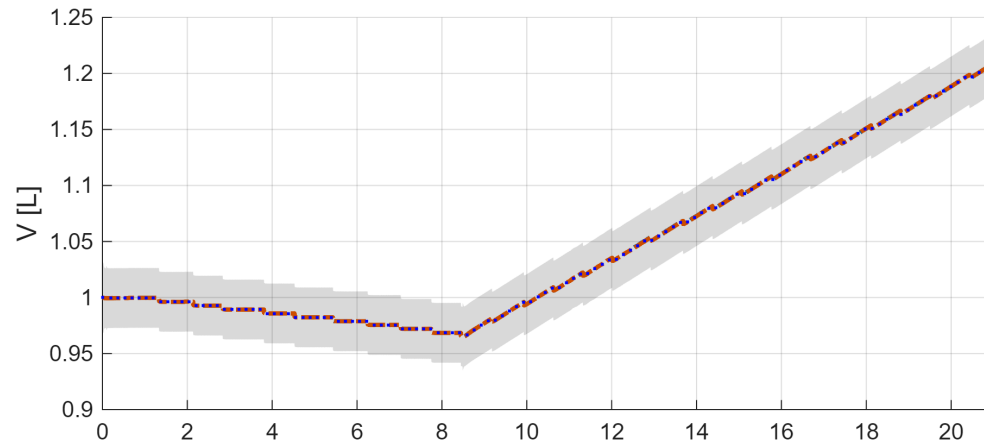


# CASE A2 – NO PHASE CHANGE

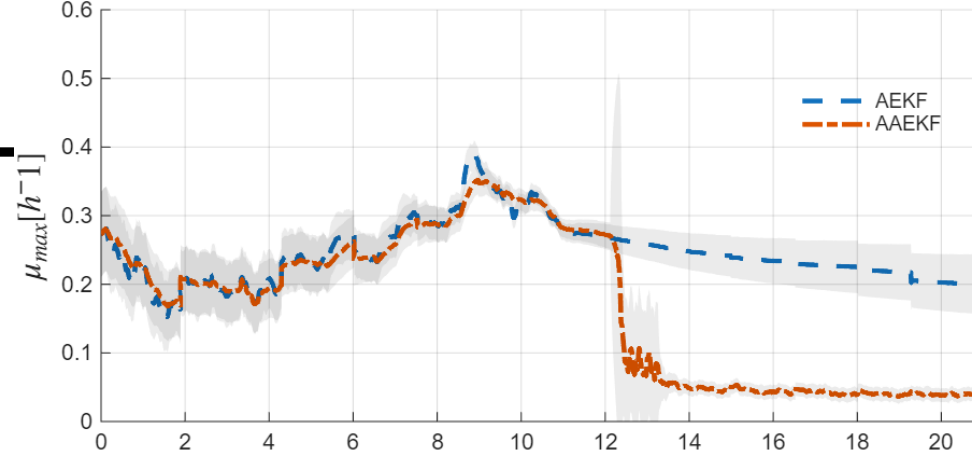


# CASE B2 – PHASE CHANGE

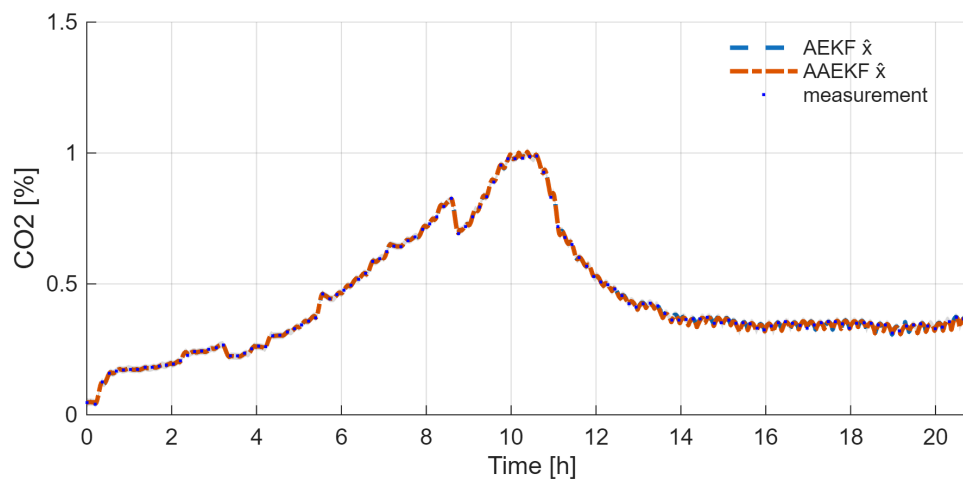
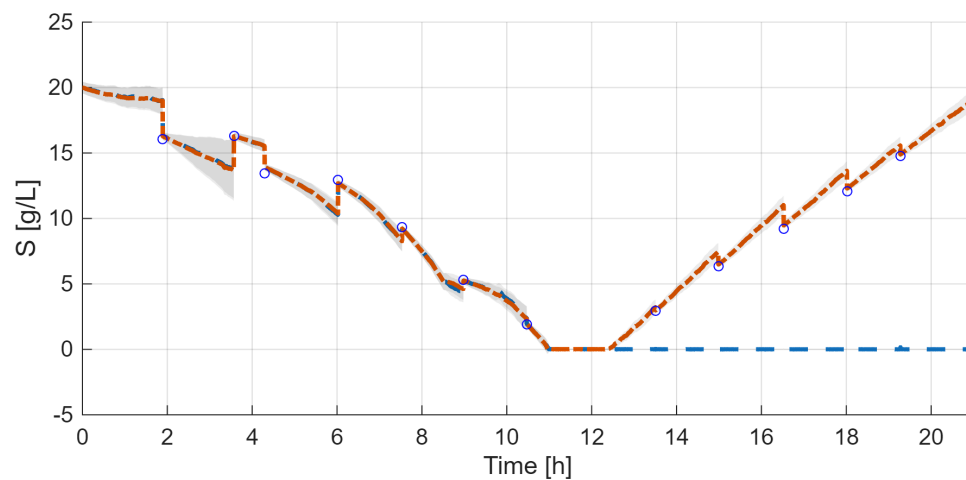
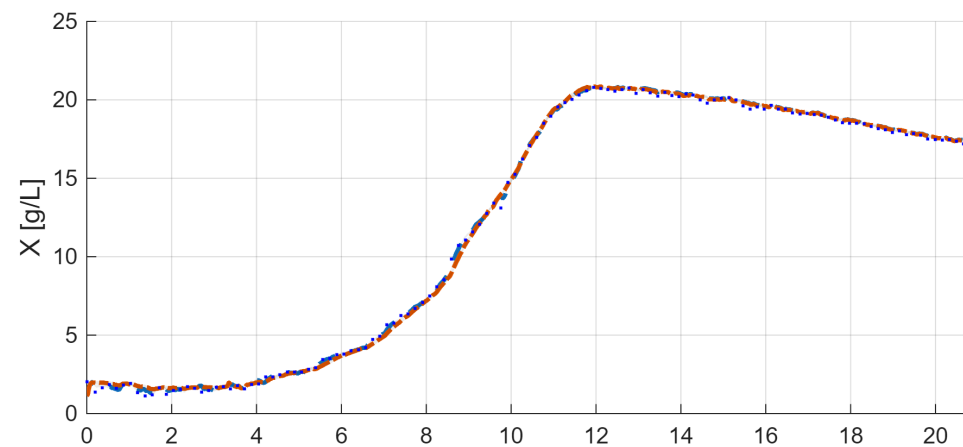
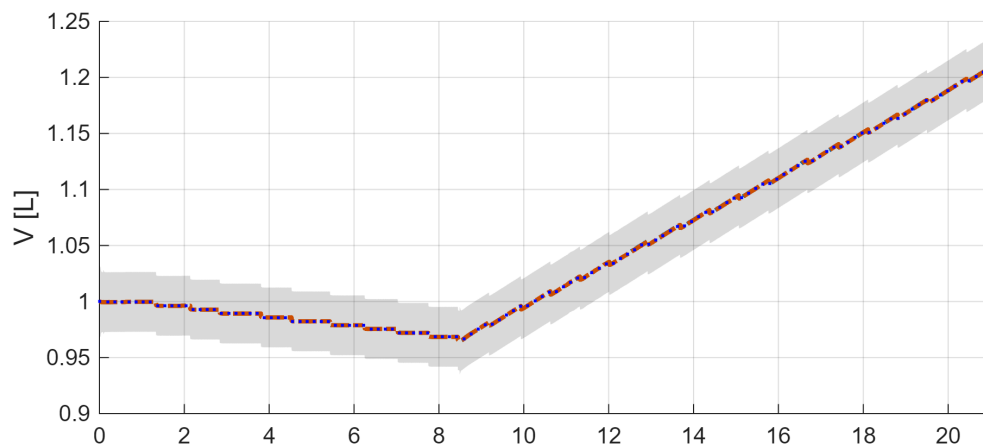
Reactor B2



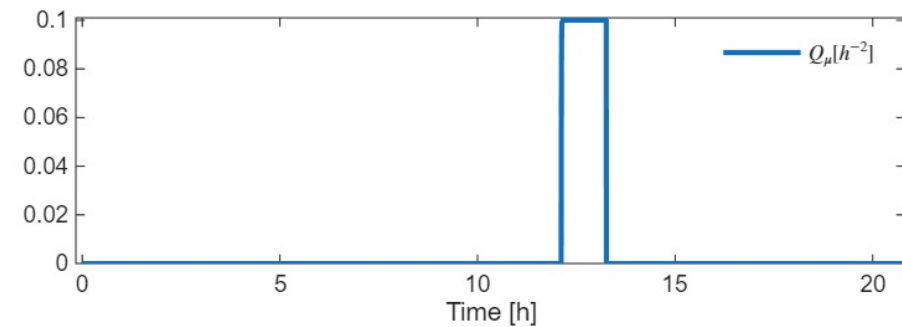
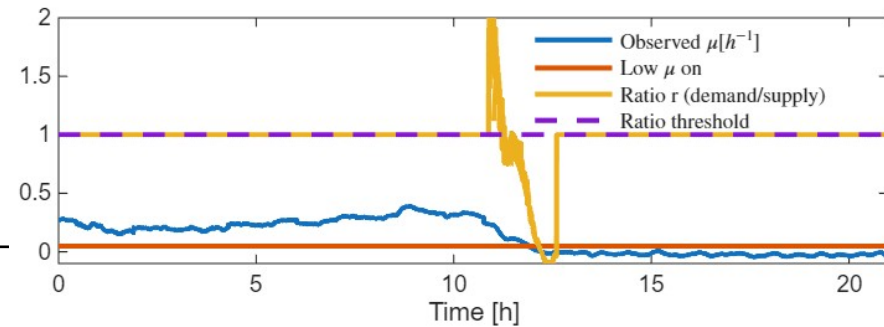
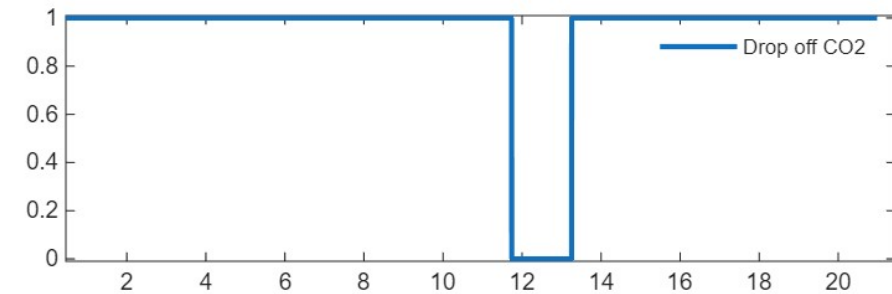
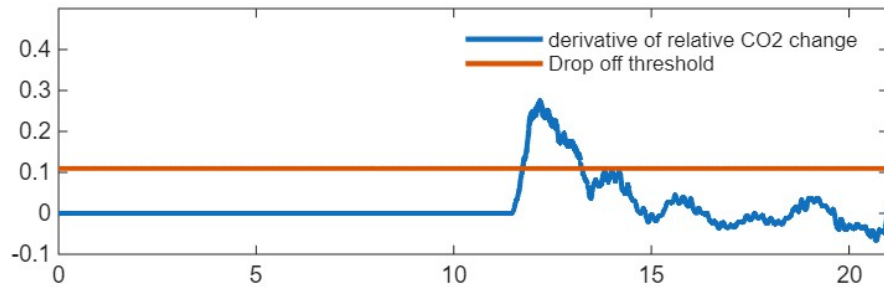
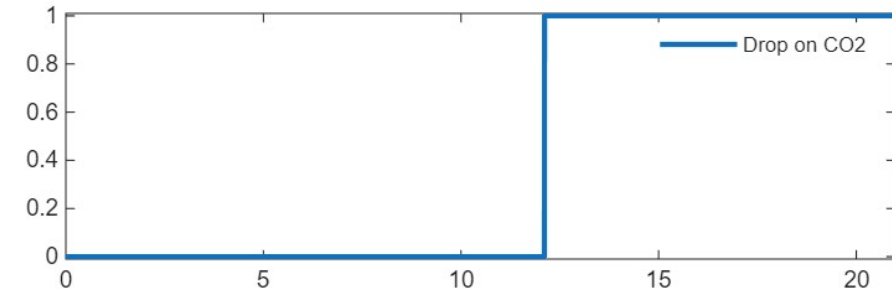
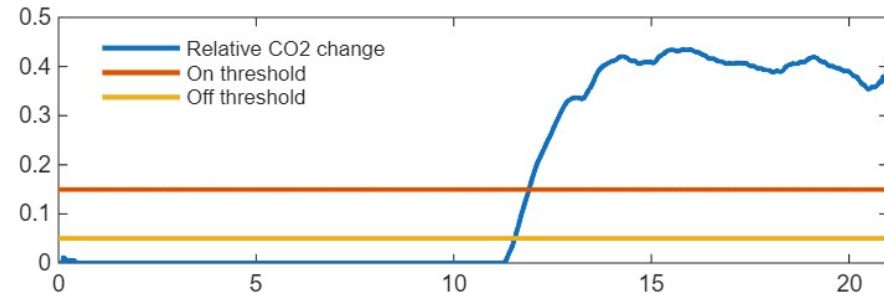
# CASE B2 – PHASE CHANGE



Reactor B2



# CASE B2 – PHASE CHANGE



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# NIS ANALYSIS

$$NIS_X(k) = \frac{v_X(k)^2}{S_{X,X}(k)} = \frac{(z_X(k) - H_X \hat{x}_X(k|k-1))^2}{(HP_{k|k-1}H^T + R_k)_{X,X}}$$

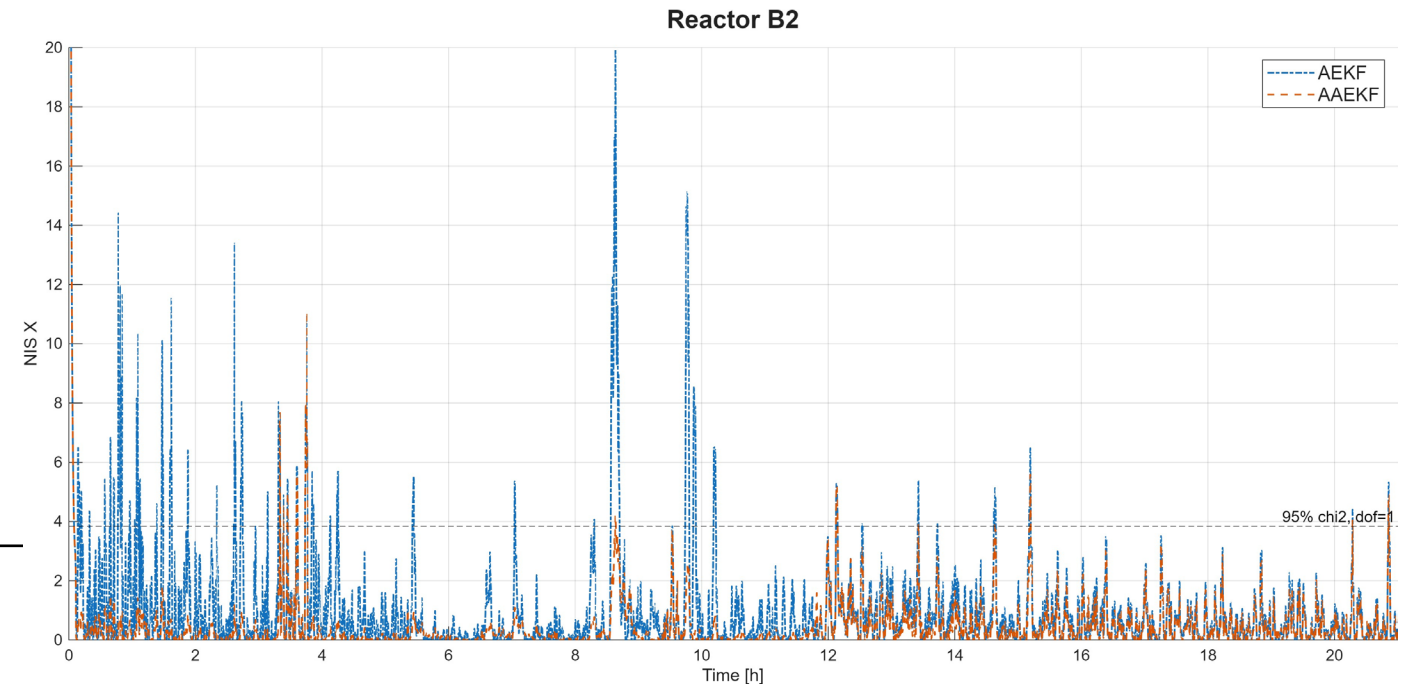
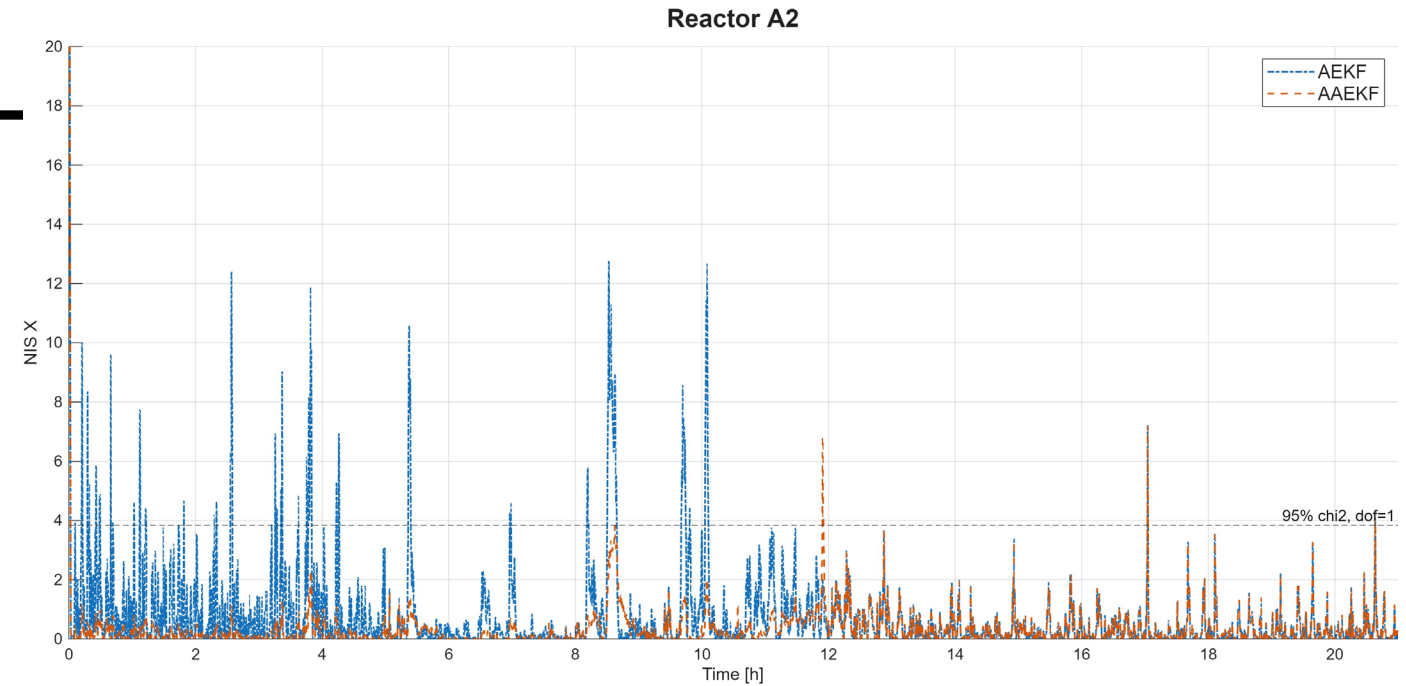
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$$NIS_X(k) = \frac{v_X(k)^2}{S_{X,X}(k)} = \frac{(z_X(k) - H_X \hat{x}_X(k|k-1))^2}{(HP_{k|k-1}H^T + R_k)_{X,X}}$$

In both A2 and B2, the  $NIS_X$  for AA-EKF has more consistency with the theoretical mean of 1 and upper bound of 3.8415 (i.e. 95<sup>th</sup> percentile of a chi-square distribution with one degree of freedom).

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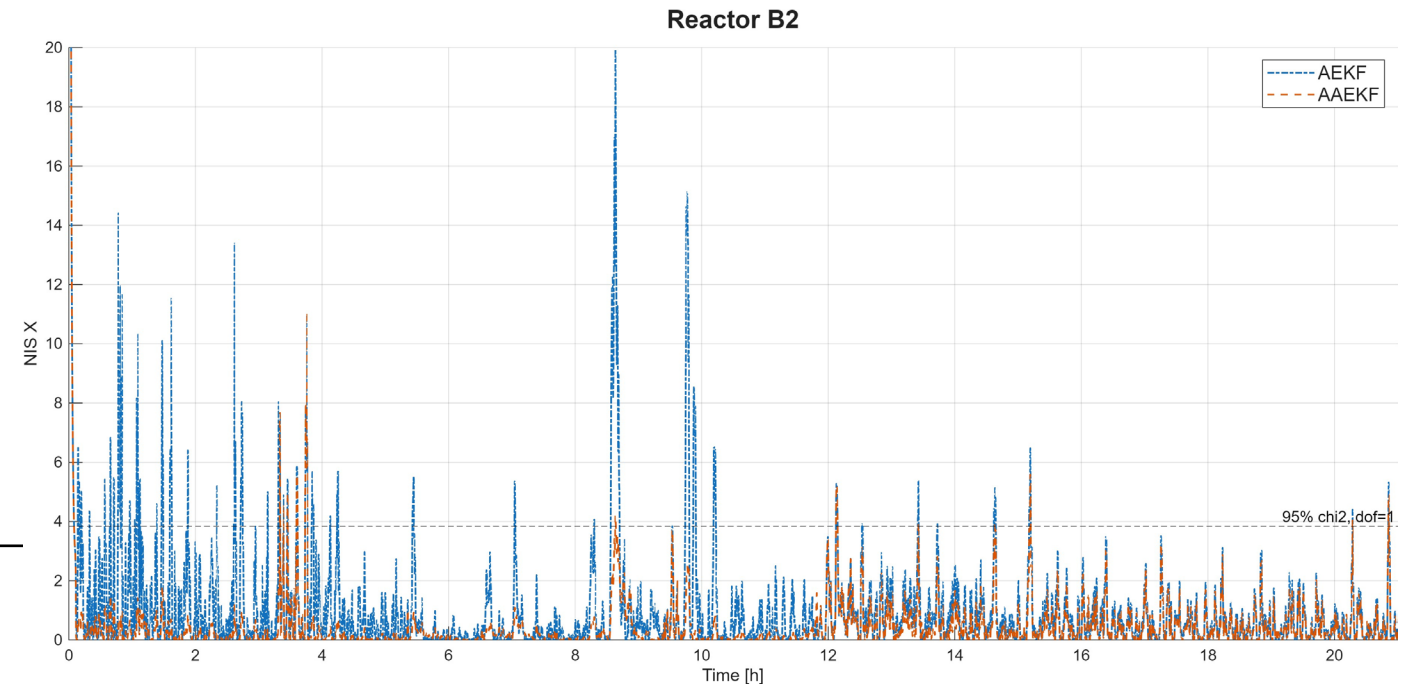
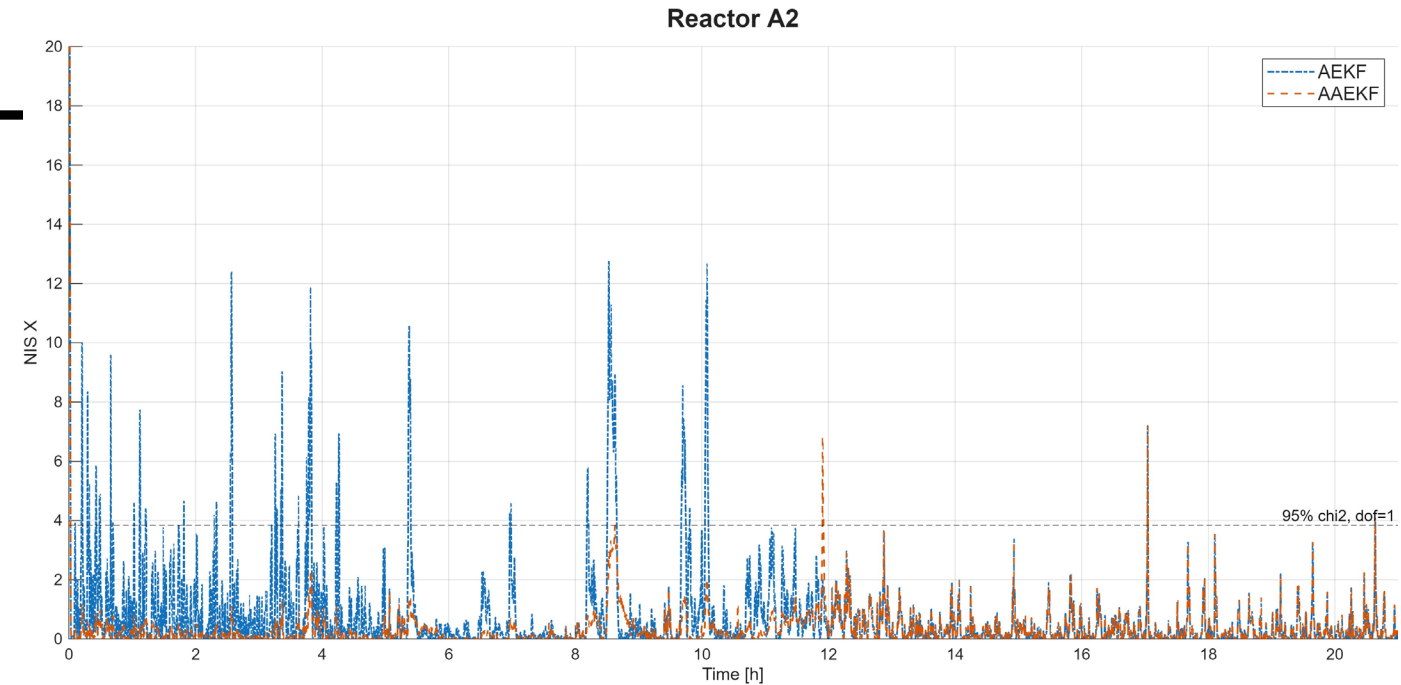
# NIS ANALYSIS

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**% of passed discrete points w.r.t.  $NIS_X$**

|       | Reactor A2 | Reactor B2 |
|-------|------------|------------|
| AEKF  | 96.82      | 95.28      |
| AAEKF | 99.82      | 99.04      |



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# FINAL REMARKS

- Selective adaptation of  $R_X$  and  $Q_{\mu_{\max}}$  improved estimator behavior under measurement disturbance and biological phase change
  - Advantages:
    - keep model simple
    - reduction of NIS spikes for X and TV for  $\mu_{\max}$ (Pb.1)
    - estimation tracking of substrate accumulation (Pb.2)
    - Multiple biological based gate activation robustness (one can choose how many gate components to use)
  - Disadvantages:
    - Some additional tuning parameters
    - Additional noise could destabilize the filter in presence of other unknown factors
  - Need for validation on more experiments
-