ALS Scheme using Extent-based Constraints for the Analysis of Chemical Reaction Systems

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Outline

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- Use of extents in ALS
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Introduction and Motivation

Introduction

ALS algorithm leads to a solution ($\mathbf{C}$, $\mathbf{E}$) for the factorization of L-dim. spectroscopic data $\mathbf{A}$ of S species at K times, so that $\mathbf{A} = \mathbf{C}\,\mathbf{E}$.

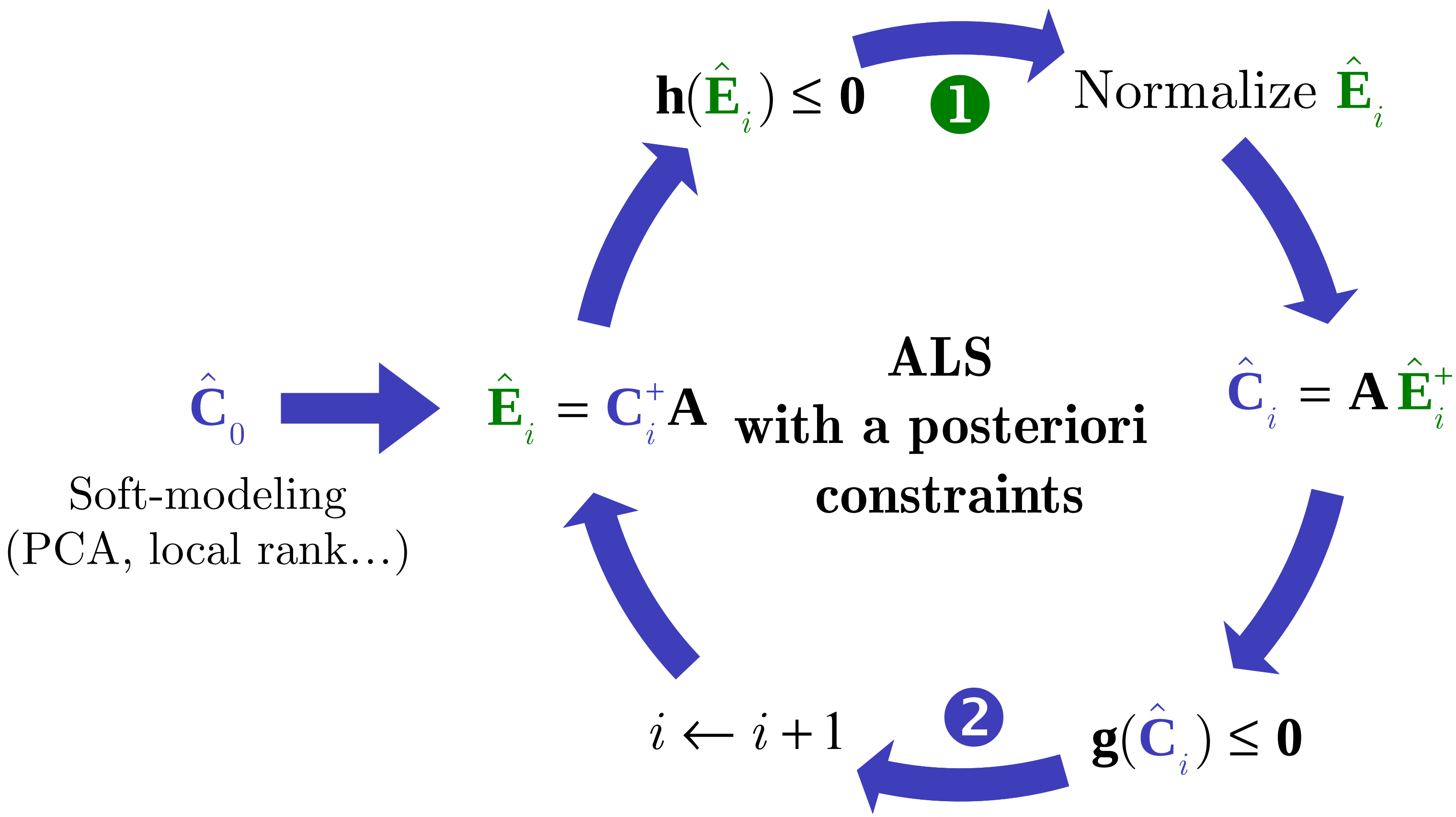
Motivation

- Working in a d-dim. space with $d \leq S$ ($\mathbf{C} \rightarrow$ extents $\mathbf{X}$)
- Constraints in $\mathbf{X}$ are numerous and stronger than in $\mathbf{C}$
- More constraints in the *time* direction (on $\mathbf{X}$) means fewer constraints in the *wavelength* direction (on $\mathbf{E}$).

Scope of this work

Absorbance data measured under batch and fed-batch conditions

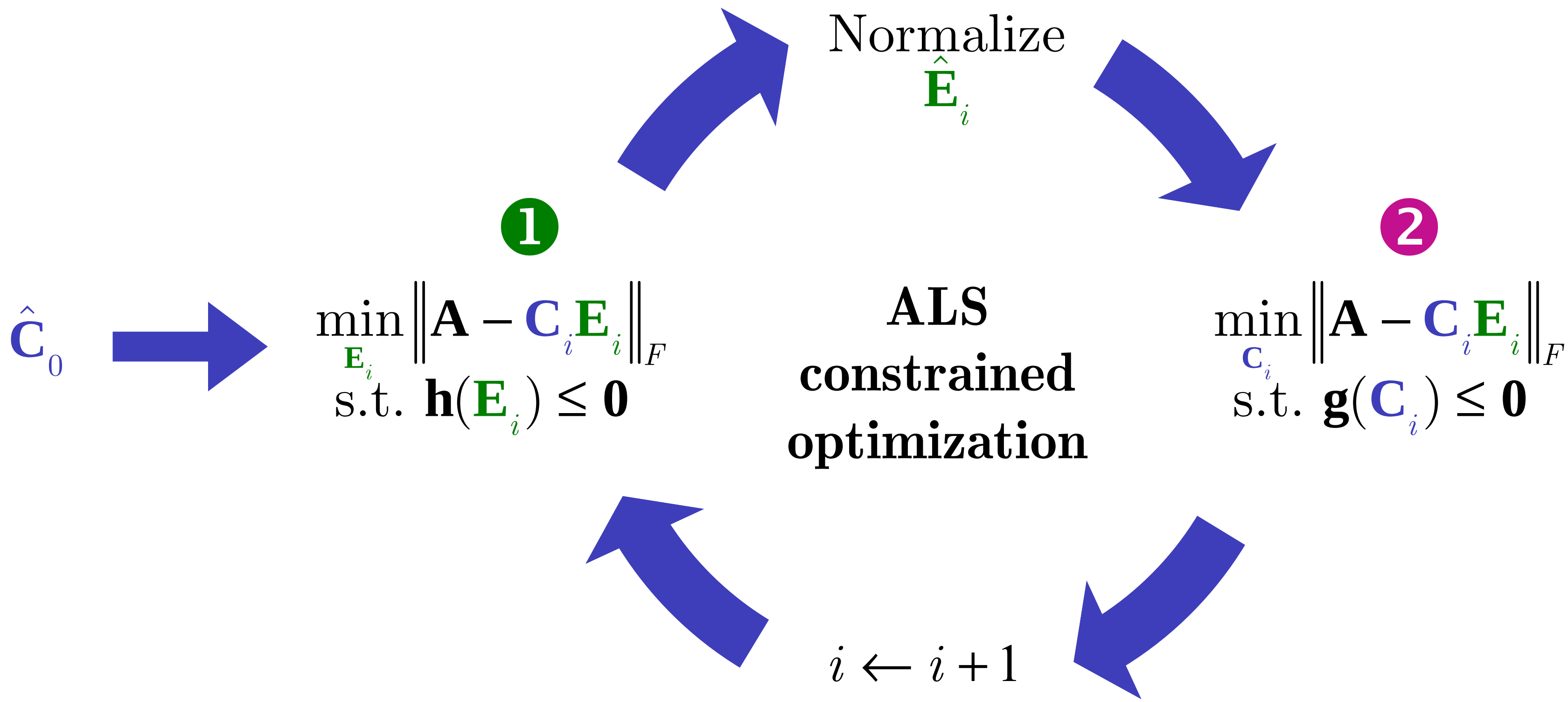
ALS algorithm with a posteriori constraints



☹ Estimates at points ❶ and ❷ are not least-squares estimates!

💣 Problems of convergence

ALS algorithm with constrained optimization



☺ Estimates at points ❶ and ❷ are least-squares estimates!

ALS algorithm with implicit calibration

- Solve the problem of finding $\mathbf{C}$ and $\mathbf{E}$ as a **combined constrained optimization problem** where only $\mathbf{C}$ is adjusted and $\mathbf{E}$ is estimated by **implicit calibration** ($\mathbf{E} = \mathbf{C}^{+}\mathbf{A}$)

$$\min_{\mathbf{C}} \left\| \mathbf{A} - \mathbf{C}\,\mathbf{E} \right\|_F$$

$$\begin{aligned} \text{s.t. } & \mathbf{E} = \mathbf{C}^{+}\mathbf{A} \\ & \mathbf{g}(\mathbf{C}) \le \mathbf{0}, \\ & \mathbf{h}(\mathbf{E}) \le \mathbf{0} \\ & \text{Normalize } \mathbf{E} \end{aligned}$$

- Typical constraints
  - $\mathbf{g}(\mathbf{C})$: nonnegativity, monotonicity, unimodality, closure
  - $\mathbf{h}(\mathbf{E})$: nonnegativity
- **Constraints and normalization of $\mathbf{E}$ are required, as well as** rank $\mathbf{C}$ = rank $\mathbf{E}$ = S **!**

Concept of Extents
Homogeneous reaction systems with inlets

- Material balance in terms of numbers of moles $\mathcal{N}$ $(K \times S)$

$$\dot{\mathbf{n}}(t) = \mathbf{N}^{\mathrm{T}}\mathbf{r}(t) + \mathbf{C}_{in}\mathbf{q}_{in}(t), \quad \mathbf{n}(0) = \mathbf{n}_0$$

- S numbers of moles $\mathcal{N}$ $\rightarrow$ $\boxed{d = R + p \leq S}$ extents $\mathbf{X}$

$$\mathbf{X} = \left[\mathbf{X}_r, \ \mathbf{X}_{in}\right] = \left(\mathcal{N} - \mathbf{1}_{nt}\mathbf{n}_0^{\mathrm{T}}\right)\mathbf{T} \quad \text{with} \quad \mathbf{T} = [\mathbf{N}; \ \mathbf{C}_{in}^{\mathrm{T}}]^{+}$$

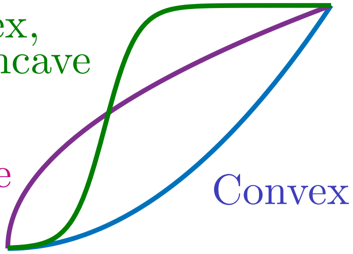
$$\dot{\mathbf{x}}_r(t) = \mathbf{r}(t), \qquad \mathbf{x}_r(0) = \mathbf{0}_R$$

$$\dot{\mathbf{x}}_{in}(t) = \mathbf{q}_{in}(t), \quad \mathbf{x}_{in}(0) = \mathbf{0}_p$$

- Reconstruction equation

$$\mathcal{N} = \mathbf{X}_r\mathbf{N} + \mathbf{X}_{in}\mathbf{C}_{in}^{\mathrm{T}} + \mathbf{1}_{nt}\mathbf{n}_0^{\mathrm{T}}$$

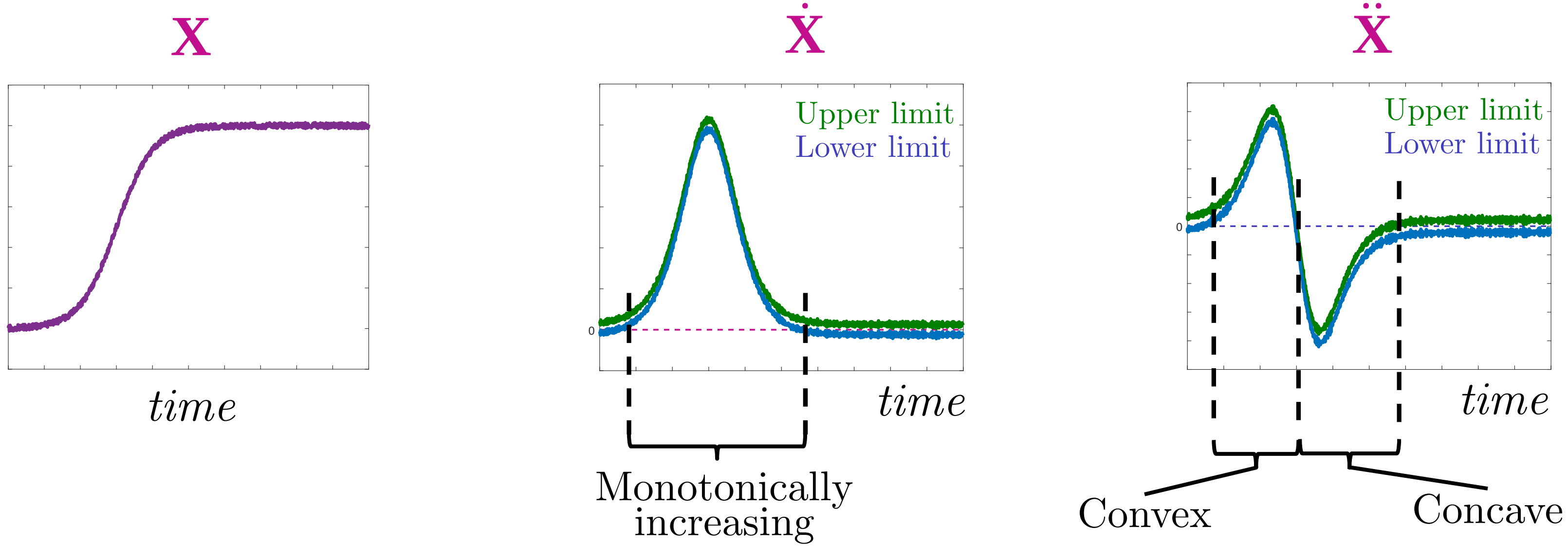
Constraints on Extents based on prior knowledge



- $\mathbf{x}(0) = \mathbf{0}_d$ (initial conditions of $\mathbf{X}$)
- $\mathbf{X} \geq \mathbf{0}_{K \times d}$ and $\mathcal{N}(\mathbf{X}) \geq \mathbf{0}_{K \times S}$ (nonnegative)
- $\mathbf{X}_{in}$ **monotonically increasing**,
  $x_{in,j}(t)$ **concave** (convex) if $q_{in,j}$ monotonically **decreasing** (increasing)
- $\mathbf{X}_r$ **monotonically increasing** (for *irreversible reactions*)
  $x_{r,i}(t)$ **concave** (convex) if $r_i(t)$ monotonically **decreasing** (increasing)
- **Initial** and **Terminal equality constraints** on $\mathcal{N}(\mathbf{X})$ are enforced
  $\mathbf{n}_0 = \mathbf{n}_k(0)$ and $\mathbf{n}(\mathbf{x}(t_{end})) = \mathbf{n}_k(\mathbf{x}_k(t_{end}))$, sub k indicates a known value
- **Path equality constraints** on $\mathbf{X}$ can be enforced
  $\mathbf{x}_i(t) = \mathbf{x}_{i,k}(t)$ (e.g. an extent is known a priori to be zero)

Constraints on Extents based on measurements

1. Estimate numerically the 1st and 2nd time derivatives of $\mathbf{X}$, i.e. $\dot{\mathbf{X}}$ and $\ddot{\mathbf{X}}$
2. Design **convex/concave constraints** based on the sign of $\ddot{\mathbf{X}}$
3. If step 2 failed, design **monotonicity constraints** based on the sign of $\dot{\mathbf{X}}$



Remark: this approach could also be applied to concentration profiles to detect regions where monotonicity and/or unimodality constraints apply.

Initialization with Concentration submatrices and local rank information

⓪ **Assumption**: The **initial** and **final concentrations** of $S_a \geq d$ species are known for any experiment

① The $(S - S_a)$ remaining conc. are reconstructed via the extents

② $\mathbf{E}$ is estimated via $N = ½(S + S \bmod 2)$ experiments

③ $\mathcal{N}_0$ and $\mathbf{X}_0$ are computed from the estimate of $\mathbf{E}$,

$$\underset{(2N \times S_a)}{\mathcal{N}_{c,a}} = \begin{bmatrix} [\mathbf{n}_{0,a}^{(1)};\ \mathbf{n}_{f,a}^{(1)}]^{\mathrm{T}} \\ \vdots \\ [\mathbf{n}_{0,a}^{(j)};\ \mathbf{n}_{f,a}^{(j)}]^{\mathrm{T}} \\ \vdots \\ [\mathbf{n}_{0,a}^{(N)};\ \mathbf{n}_{f,a}^{(N)}]^{\mathrm{T}} \end{bmatrix} \xrightarrow{\mathbf{T}_a} \underset{(2N \times d)}{\mathbf{X}_c} \xrightarrow{\mathbf{T}^+} \underset{(2N \times S)}{\mathcal{N}_c} \xrightarrow{\mathbf{A}_{v,c}(2N \times L)} \hat{\mathbf{E}} = \mathcal{N}_c^+ \mathbf{A}_{v,c} \rightarrow \underset{(K \times S)}{\hat{\mathcal{N}}_0} = \mathbf{A}_v \hat{\mathbf{E}}^+ \xrightarrow{\mathbf{T}} \underset{(K \times d)}{\hat{\mathbf{X}}_0}$$

⓪ ① ② ③

c: calibration, a: available species, f: final conditions

ALS algorithm with Extents and implicit calibration

- $\mathbf{A} = \mathbf{C}\mathbf{E} \rightarrow \mathbf{A}_v := \mathbf{V}\mathbf{A} = \mathcal{N}\mathbf{E}$, with $\mathbf{V}$ the volume
- Solve the **constrained optimization** where $\mathbf{X}$ is adjusted and $\mathbf{E}$ is estimated by **implicit calibration** ($\mathbf{E} = \mathcal{N}(\mathbf{X})^+\mathbf{A}_v$).

$$\min_{\mathbf{X}} \left\| \mathbf{A}_v - \mathcal{N}(\mathbf{X})\,\mathbf{E} \right\|_F$$

$$\text{s.t. } \mathbf{E} = \mathcal{N}(\mathbf{X})^+ \mathbf{A}_v$$

$$\mathbf{f}(\mathbf{X}) \leq \mathbf{0},$$

$$\mathbf{g}(\mathcal{N}(\mathbf{X})) \leq \mathbf{0}$$

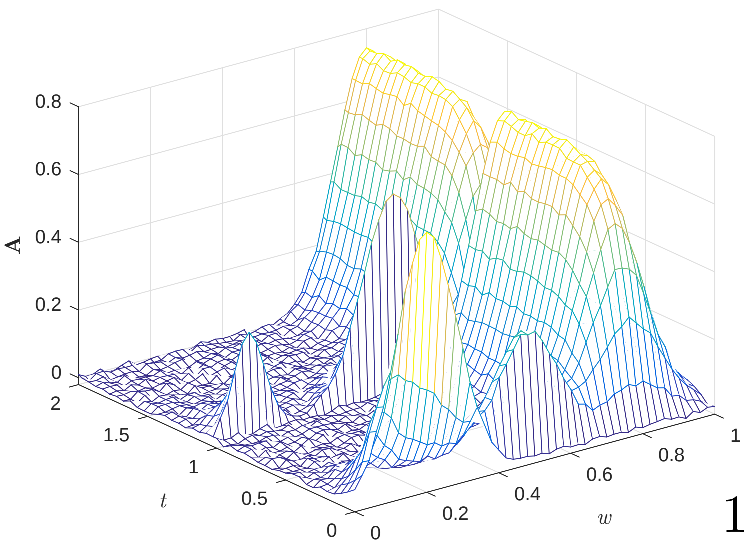
- Typical constraints
  - $\mathbf{f}(\mathbf{X})$: nonnegativity, monotonicity, convexity/concavity, path constraints
  - $\mathbf{g}(\mathcal{N}(\mathbf{X}))$: nonnegativity, initial and final equality constraints
- **No constraints on $\mathbf{E}$ are required!**

Simulated case study
Difference absorbance spectra

$$A \rightarrow B \rightarrow C$$

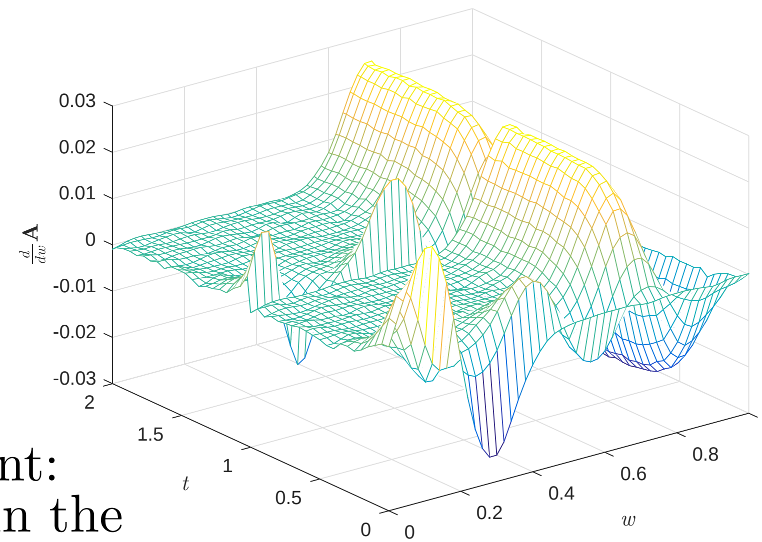
2 combined experiments:

- Experiment 1 (only A initially present)
- Experiment 2 (only B initially present)



Noise:
1% uniformly distributed

Pretreatment:
1^{st} derivative in the *wavelength* direction



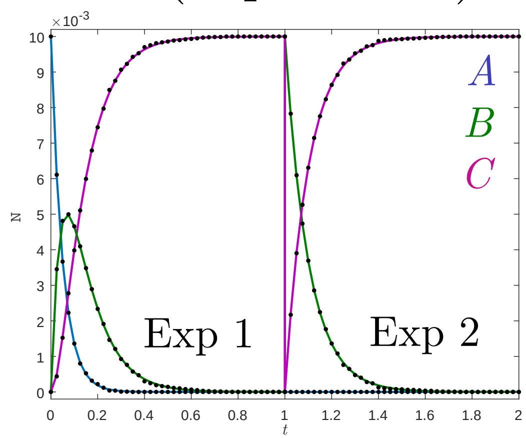
Simulated case study
Constraints applied

- Regular ALS does not work as $\mathbf{E}$ cannot be constrained positively
- ALS based on $\mathbf{X}$ with **implicit calibration** resolves both the rotational and intensity ambiguities with the following constraints:
  - Initialization $\mathbf{X}_0$ from **conc. submatrices** and **local rank information**
  - **Constraints on Experiment 1**
    - Initial and terminal $\mathbf{n}$'s imposed
    - $\mathbf{x}_1$ and $\mathbf{x}_2$ monotonically increasing
    - $\mathbf{x}_1$ concave, $\mathbf{x}_2$ convex then concave
  - **Constraints on Experiment 2**
    - Initial and terminal $\mathbf{n}$'s imposed
    - $x_1(t) = 0, \quad \forall t$ (path constraint)
    - $\mathbf{x}_2$ concave

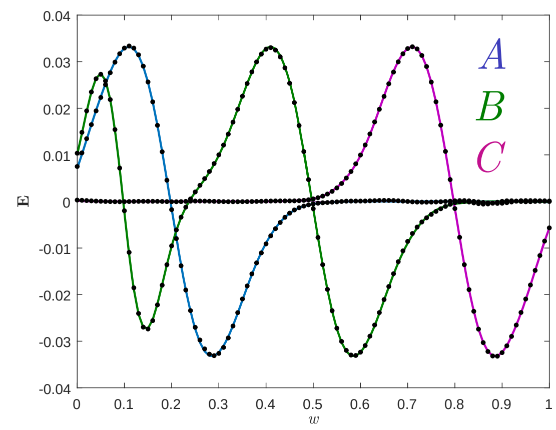
Remarks: No constraint or normalization on $\mathbf{E}$ is required!
Constraints $\mathbf{X}_0 \geq \mathbf{0}$, $\mathcal{N}(\mathbf{X}) \geq \mathbf{0}$ are not even necessary!

Simulated case study
ALS based on X with implicit calibration

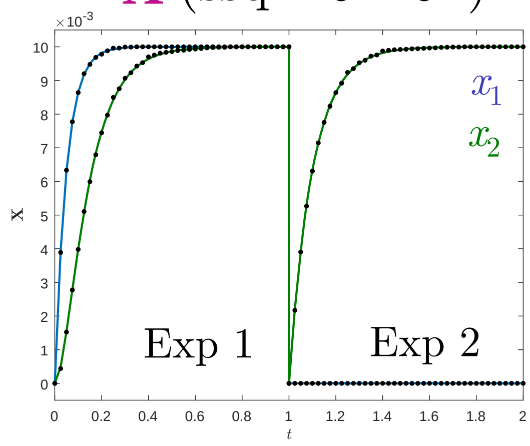
$\mathcal{N}$ (ssq 7.5×10^{-8})



E (ssq 1.4×10^{-5})

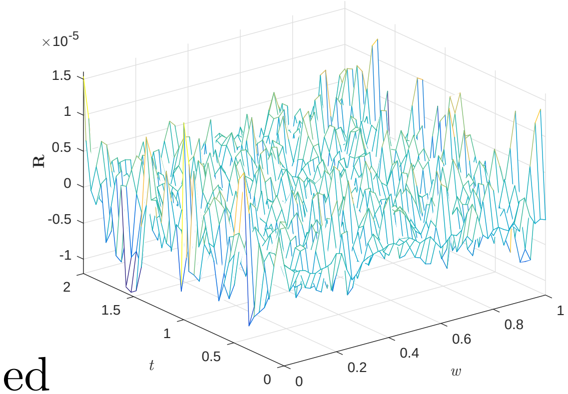


X (ssq 4.6×10^{-4})



— true
• ALS-estimated

Residuals (ssq 1.6×10^{-7})



Conclusion
ALS with extents and implicit calibration

- **Optimization in a reduced space**
  - $S \cdot K$ decision variables in **C** versus $d \cdot K$ in **X**, with $d \leq S$
- **Better handling of the constraints**
  - Simpler constraints formulation
  - Large number of constraints based on prior knowledge
  - Stronger constraints (concavity/convexity vs unimodality)
- **No constraints on E**
  - Use of data pre-treatment along *wavelength* direction (e.g. 1^{st} derivative correction…)

Perspectives
ALS with extents and implicit calibration

- **Analysis of rank-deficient data**
  - Subtraction of the initial and inlet contributions
    $\mathbf{A} \rightarrow \mathbf{H} = \mathbf{X}_r\,(\mathbf{N}\mathbf{E}) \rightarrow$ ALS on $\mathbf{X}_r$ and $(\mathbf{N}\mathbf{E})$ with rank $R < S$
- **Use of hard constraints in terms of extents**
  - Each extent of reaction represents the effect of a single reaction independently of all the others. The use of hard constraints in terms of extents should allow a constant diagnosis of each postulated kinetic step.

Final word

Thank you for your attention

References

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