Kinetic hard-modelling and spectral validation of rank-deficient spectroscopic data

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Direct fitting by modelling concentrations

\[ Y = C A + R \]

Beer’s law
Direct fitting by modelling concentrations

Modelled concentrations
\[ C_{\text{modelled}} = \text{function (k)} \]

Y: Measured absorbance

Beer’s law
\[ Y = C A + R \]

A: Pure component spectra

Implicit calibration \[ A = C_{\text{modelled}}^+ Y \]
Explicit calibration \[ A = (C^+ Y)_{\text{calibration}} \]
Direct fitting by modelling concentrations

Modelled concentrations

\[ C_{\text{modelled}} = \text{function } (k) \]

Beer’s law

\[ Y = C A + R \]

Y: Measured absorbance

R: Residuals

A: Pure component spectra

Implicit calibration

\[ A = C_{\text{modelled}}^+ Y \]

Explicit calibration

\[ A = (C^+ Y)_{\text{calibration}} \]

Least squares fitting

\[ \min_k \| Y - C_{\text{modelled}} A \|^2 \]
Rank deficiency in spectroscopy

\[
\begin{align*}
Y \\
A + B & \xrightarrow{k_1} C \\
A + C & \xrightarrow{k_2} D
\end{align*}
\]
Rank deficiency in spectroscopy

Beer's law \( Y = C A \)

\( ns = 4 \) species

\[ A + B \xrightarrow{k_1} C \]
\[ A + C \xrightarrow{k_2} D \]
Rank deficiency in spectroscopy

Beer's law \((Y = CA)\)

\(ns = 4\) species

\(\begin{align*}
Y & = A + B \xrightarrow{k_1} C \\
& = A + C \xrightarrow{k_2} D
\end{align*}\)

PCA / TFA \((\tilde{Y} = \tilde{U} \tilde{S} \tilde{V})\)

\(nc = 3\) factors

Where \(T\) is a transformation matrix of dimensions \((nc \times nc)\)
Rank deficiency in spectroscopy

Beer's law \( \mathbf{Y} = \mathbf{C} \mathbf{A} \)

\( ns = 4 \) species

\[ \mathbf{Y} = \begin{cases} \mathbf{A} + \mathbf{B} & \mathbf{k}_1 \rightarrow \mathbf{C} \\ \mathbf{A} + \mathbf{C} & \mathbf{k}_2 \rightarrow \mathbf{D} \end{cases} \]

PCA / TFA \( \tilde{\mathbf{Y}} = \tilde{\mathbf{U}} \tilde{\mathbf{S}} \tilde{\mathbf{V}} \)

\( nc = 3 \) factors

\[ \mathbf{C} = \tilde{\mathbf{U}} \mathbf{T} \]

\[ \mathbf{A} = \mathbf{T}^{-1} \mathbf{S} \mathbf{V} \]

Where \( \mathbf{T} \) is a transformation matrix of dimensions \( nc \times nc \)

Spectroscopic data matrix \( \mathbf{Y} \) is rank deficient when:

**Significant factors \( (nc) \) in PCA < number of reactive species \( (ns) \) \iff \text{rank}(\mathbf{Y}) < ns**
Sources and problems of rank deficiency

\[ Y = CA \]
Sources and problems of rank deficiency

\[ Y = CA \]

Rank deficiency in \( Y \) is due to

- Linear dependencies in \( C \)
- Linear dependencies in \( A \)
- Mathematical ambiguity in case of implicit calibration
  \( A \) cannot be computed by \( C^+Y \) as \( A \) is not unique

Not discussed here

All spectra in \( A \) are assumed to be linearly independent

Example: two species that are consumed or generated at the same rate

\[
\text{rank}(Y) = \min\left[\text{rank}(C), \text{rank}(A)\right] = \text{rank}(C)
\]
Strategies to treat rank deficiency in concentrations

Strategies to treat rank deficiency in concentrations

Model reduction

Strategy 1
define \( nu \) uncoloured species

Strategy 2
include \( nks \) known spectra in the analysis (explicit calibration)

---

Strategies to treat rank deficiency in concentrations

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Strategy 1
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Rank augmentation

Strategy 3
dose one or more species in \( nf \) dosing steps

Strategy 4:
perform \( ne \) additional experiments by varying the initial concentrations (second order global analysis)

Without dosing With dosing

Partial spectral resolution

Full spectral resolution

Strategies to treat rank deficiency in concentrations

Model reduction

Strategy 1
define $nu$ uncoloured species

Strategy 2
include $nks$ known spectra in the analysis (explicit calibration)

Rank augmentation

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dose one or more species in $nf$ dosing steps

Strategy 4:
perform $ne$ additional experiments by varying the initial concentrations (second order global analysis)

How to identify the species to include in these four Strategies?

Rank and kernel of the concentration matrix

**Rank of C**
Number of linearly independent columns or rows in C
>> Defines the maximum number of columns (species) to keep in Strategy 1 \((ns – nu)\) and Strategy 2 \((ns – nks)\)

**kernel of C**
Vector space spanned by the vectors forming the null space \(\mathbf{0}\) when multiplied by C
>> \(\ker C\) defines a mass balance equation: \(C\) \((\ker C) = \mathbf{0}\)
>> \(\ker C\) defines which columns of \(C\) are linearly dependent or independent

\[\begin{bmatrix}
0.8 & 0.1 \\
-0.3 & -0.7 \\
0 & 0 \\
0.5 & -0.6
\end{bmatrix}\]

\(A\) \(B\) \(C\) \(D\)
Interpretation of the kernel of $C$

$$\begin{bmatrix} 0.8 & 0.1 \\ -0.3 & -0.7 \\ 0 & 0 \\ 0.5 & -0.6 \end{bmatrix}$$

Species without zero rows in $\ker C$ | Linearly dependent species
---|---
Species with zero rows in $\ker C$ | Linearly independent species

Consequences for Strategies 1 – 4?
Interpretation of the kernel of $C$

Species without zero rows in ker $C$  

<table>
<thead>
<tr>
<th>kernel of $C$</th>
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<tbody>
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<td></td>
<td>Linearly dependent species</td>
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</tbody>
</table>

Species with zero rows in ker $C$  

<p>| | | | | | | |</p>
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<td></td>
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</tr>
</tbody>
</table>

Consequences for Strategies 1 – 4

Strategy 1  
Define this species as uncoloured...

Strategy 2  
Include its pure spectrum...

Strategy 3  
Dose this species...

Strategy 4  
Vary its initial concentration...

... to break/avoid rank deficiency in $C$

$e.g. \ker C = \begin{bmatrix} 0.8 & 0.1 & A \\ -0.3 & -0.7 & B \\ 0 & 0 & C \\ 0.5 & -0.6 & D \end{bmatrix}$
Interpretation of the kernel of $C$

e.g. $\ker C = \begin{bmatrix} 0.8 & 0.1 \\ -0.3 & -0.7 \\ 0 & 0 \\ 0.5 & -0.6 \end{bmatrix}$

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**Consequences for Strategies 1 – 4**

<table>
<thead>
<tr>
<th>Strategy 1</th>
<th>Strategy 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Define this species as uncoloured...</td>
<td>Include its pure spectrum...</td>
</tr>
<tr>
<td>Do not define this species as uncoloured...</td>
<td>Do not provide its pure spectrum...</td>
</tr>
<tr>
<td>Do not dose this species...</td>
<td>Do not dose this species...</td>
</tr>
<tr>
<td>Do not vary its initial concentration...</td>
<td>Do not vary its initial concentration...</td>
</tr>
</tbody>
</table>

... to break/avoid rank deficiency in $C$

Can we obtain this information without numerical integration of the rate laws, i.e. using a time invariant approach?
Modelling kinetic concentration profiles

Kinetic rate law

\[ \dot{x}_t = \prod_{\text{along columns}} \left( c_t^T \cdot 1 \right)^{E^T} \text{DIAG}(k) \]

Reactant coefficients \( E \ (nr \times ns) \)

Rate constants \( k \ (1 \times nr) \)

Stoichiometric coefficients \( N \ (nr \times ns) \)

Concentration profiles

\[ \dot{c}_t = \dot{x}_t \cdot N + f_{in,t} v_t^{-1} (c_{in,t} - c_t) - f_{out,t} v_t^{-1} c_t \]

This system of ODE is numerically integrated with initial concentrations \( c_0 \ (1 \times ns) \) and results in the concentration matrix \( C \ (nt \times ns) \)
Modelling kinetic concentration profiles

\[ A + B \xrightarrow{k_1} C \]
\[ A + C \xrightarrow{k_2} D \]

Kinetic rate law

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This system of ODE is numerically integrated with initial concentrations \( c_0 \ (1 \times ns) \) and results in the concentration matrix \( C \ (nt \times ns) \).
A time invariant matrix $\Omega$ equivalent to $C$

$$\Omega = \begin{bmatrix} (\mu 1)^{E^T} \text{DIAG}(k) N \\ c_0 \\ C_{\text{in}} \\ C_0^{\text{ne}} \end{bmatrix} (ns + 1 + nf + ne \times ns - nu - nks) \quad \ker \Omega = (\ker C)^{T_{\text{lin}}}$$

- $\mu$ an arbitrary positive scalar different from 0 and 1
- $1$ $(ns \times nr)$ matrix comprised of ones
- $E$ $(nr \times ns)$ matrix of reactant coefficients
- $E^T$ element-wise raise to the power of $E^T$
- $\text{DIAG}$ operator generating a diagonal matrix from a vector argument

**Advantages of the time invariant approach:**
No numerical integration required
Analytical (symbolic) relationship between the experimental conditions $(c_0, C_{\text{in}}, C_0^{\text{ne}})$

**Mathematical description and proof:** Billeter et al, Chemom. Intell. Lab. Syst., 95 (2009), 170
Strategies to treat rank deficiency in concentrations

**Model reduction**

**Strategy 1**
define *nu* uncoloured species

**Strategy 2**
include *nks* known spectra in the analysis (explicit calibration)

**Rank augmentation**

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dose one or more species in *nf* dosing steps

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Billeter et al., Chemom. Intell. Lab. Syst., 95 (2009), 170 – 187
Spectral consequence of Strategy 1

Model reduction

**Strategy 1**
define *nu* uncoloured species

Time variant

<table>
<thead>
<tr>
<th>C</th>
<th>C&lt;sub&gt;c&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>nt</em></td>
<td><em>ns</em></td>
</tr>
</tbody>
</table>

Time invariant

<table>
<thead>
<tr>
<th>Ω&lt;sub&gt;c&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>ns</em></td>
</tr>
<tr>
<td><em>nt</em></td>
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Billeter et al., Chemom. Intell. Lab. Syst., 95 (2009), 170 – 187
Spectral consequence of Strategy 1

Model reduction

**Strategy 1**
define $nu$ uncoloured species

Spectral contributions of the $nu$ uncoloured species are linearly transferred into the fitted pure spectra of the coloured species.

The fitted component spectra $A_c$ of the $(ns-nu)$ coloured species are comprised of linear combinations of the $ns$ true pure component spectra $A$.
Spectral consequence of Strategy 1

Model reduction

Strategy 1
define \( nu \) uncoloured species

Spectral contributions of the \( nu \) uncoloured species are linearly transferred into the fitted pure spectra of the coloured species

The fitted component spectra \( A_c \) of the \((ns-nu)\) coloured species are comprised of linear combinations of the \( ns \) true pure component spectra \( A \)

\[
A_c = \Delta A
\]

(Spectral balance)
Spectral consequence of Strategy 1

Model reduction

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define \( nu \) uncoloured species

Spectral contributions of the \( nu \) uncoloured species are linearly transferred into the fitted pure spectra of the coloured species.

The fitted component spectra \( A_c \) of the \((ns-nu)\) coloured species are comprised of linear combinations of the \( ns \) true pure component spectra \( A \).

\[
A_c = \Delta A
\]

(Spectral balance)

\[
\Delta (ns - nu \times ns) = C_c^+ C = \left( \Omega \right| \text{comprised of coloured species} \right)^+ \left( \Omega \right| \text{comprised of all species}
\]

Example: Calculation of the kernel

\[ A + B \xrightarrow{k_1} C \]
\[ A + C \xrightarrow{k_2} D \]
Example: Calculation of the kernel

\[
\Omega = \left[ \mu \mathbf{1}^T \right] \mathbf{c}_0 \cdot \mathbf{N} = \begin{bmatrix}
A & B & C & D \\
-\mu k_1 - \mu k_2 & -\mu k_1 & \mu k_1 - \mu k_2 & \mu k_2 \\
-\mu k_1 - k_2 & -\mu k_1 & \mu k_1 - k_2 & k_2 \\
-k_1 - \mu k_2 & -k_1 & k_1 - \mu k_2 & k_2 \\
-k_1 - k_2 & -k_1 & k_1 - k_2 & k_2 \\
c_{0,A} & \alpha c_{0,A} & 0 & 0
\end{bmatrix}
\]

Matlab code (8 lines)

```matlab
>> syms c0A alpha mu k1 k2
>> N = [-1 -1 1 0; -1 0 -1 1];
>> E = [1 1 0 0; 1 0 1 0];
>> k = [k1, k2];
>> c0 = [c0A, alpha*c0A, 0, 0];
>> one = ones(size(E'));
>> omega = [(mu*one).^E'*diag(k)*N; c0];
>> null(omega)
ans =
-alpha
1
1-alpha
1-2*alpha
```

\[
\alpha = \frac{c_{0,B}}{c_{0,A}}
\]
Example: Calculation of the kernel

\[
\Omega = \begin{bmatrix}
(\mu 1)\cdot E^T & \text{DIAG}(k) \cdot N
\end{bmatrix}
\]

\[
\ker \Omega = \begin{bmatrix}
-\alpha & A \\
1 & B \\
1 - \alpha & C \\
1 - 2\alpha & D \\
\end{bmatrix}
\]

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>> k = [k1, k2];
>> c0 = [c0A, alpha*c0A, 0, 0];
>> one = ones(size(E'));
>> omega = [(mu*one).^E'*diag(k)*N; c0];
>> null(omega)
ans =
   -alpha
      1
   -alpha
   -1+2*alpha
>> alpha = c0/B
```

\[\alpha = \frac{C_{0,B}}{C_{0,A}}\]
Example: Calculation of the kernel

\[
\Omega = \frac{1}{c_0} (\mu \mathbf{1})^T \text{diag}(k) \mathbf{N}
\]

\[
\begin{bmatrix}
A & B & C & D \\
-\mu k_1 - \mu k_2 & -\mu k_1 & \mu k_1 - \mu k_2 & \mu k_2 \\
-\mu k_1 - k_2 & -\mu k_1 & \mu k_1 - k_2 & k_2 \\
-k_1 - \mu k_2 & -k_1 & k_1 - \mu k_2 & \mu k_2 \\
-k_1 - k_2 & -k_1 & k_1 - k_2 & k_2 \\
\end{bmatrix}
\]

\[
\begin{bmatrix}
-\alpha & 1 & 1 - \alpha & 1 - 2\alpha \\
\end{bmatrix}
\]

\[
\ker \Omega = \begin{bmatrix}
-\alpha & 1 & 1 - \alpha & 1 - 2\alpha \\
\end{bmatrix}
\]

Matlab code (8 lines)

```matlab
>> syms c0A alpha mu k1 k2
>> N = [-1 -1 1 0; -1 0 -1 1];
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>> one = ones(size(E'));
>> omega = [(mu*one).^T*diag(k)*N; c0];
>> null(omega)
ans =
   -alpha
    1
  1-alpha
1-2*alpha
```

Determination of the roots of the kernel

If \( \alpha = 1 \), species \( C \) is linearly independent from the others

If \( \alpha = 0.5 \), species \( D \) is linearly independent from the others

If \( \alpha \neq 1 \) or \( 0.5 \), all species are linearly dependent from the others
Example: Design of experiments

\[ \text{ker } \Omega \ (4 \times 1) = \begin{bmatrix} A & B & C & D \end{bmatrix}^T = \begin{bmatrix} -\alpha & 1 & 1 - \alpha & 1 - 2\alpha \end{bmatrix} \]

\[ \dim(\text{ker } \Omega) = 1, \text{ i.e. only one species has to be considered in Strategies (1) – (4)} \]
Example: Design of experiments

\[ \ker \Omega (4 \times 1) = \begin{bmatrix} A & B & C & D \\ -\alpha & 1 & 1-\alpha & 1-2\alpha \end{bmatrix}^T \]

\[ \dim(\ker \Omega) = 1, \text{ i.e. only one species has to be considered in Strategies (1)–(4)} \]

Species treated with current Strategy
- A
- B
- C
- D

Species not treated with current Strategy
- B, D, C
- A, D, C
- Not possible
- A, B, C

\[ A + B \xrightarrow{k_1} C \]
\[ A + C \xrightarrow{k_2} D \]
Example: Design of experiments

\[ \ker \Omega (4 \times 1) = \begin{bmatrix} A & B & C & D \\ -\alpha & 1 & 1 - \alpha & 1 - 2\alpha \end{bmatrix}^T \]

\( \dim(\ker \Omega) = 1 \), i.e. only one species has to be considered in Strategies (1) – (4)

**Species treated with current Strategy**

<table>
<thead>
<tr>
<th>Strategy (1) – (4)</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>D</td>
<td></td>
<td></td>
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</table>

**Species not treated with current Strategy**

<table>
<thead>
<tr>
<th></th>
<th>A, B, C</th>
<th>B, C, D</th>
<th>A, D, C</th>
<th>Not possible</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D</td>
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</tbody>
</table>

**Initial conditions**

- \( \alpha = 1 \)
- \( \alpha = 0.5 \)
Example: Design of experiments

$$\ker \, \mathbf{\Omega} \ (4 \times 1) = \begin{bmatrix} A & B & C & D \\ -\alpha & 1 & 1-\alpha & 1-2\alpha \end{bmatrix}^T$$

$$\dim(\ker \, \mathbf{\Omega}) = 1$$, i.e. only one species has to be considered in Strategies (1) – (4)

<table>
<thead>
<tr>
<th>Initial conditions</th>
<th>Strategy</th>
<th>Species treated with current Strategy</th>
<th>Species not treated with current Strategy</th>
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<tr>
<td>( \alpha = 1 )</td>
<td>Strategy (1) – (4)</td>
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<td>( B, D, [C] )</td>
</tr>
<tr>
<td>( \alpha = 0.5 )</td>
<td>Strategy (1) – (4)</td>
<td>( B )</td>
<td>( A, D, [C] )</td>
</tr>
<tr>
<td>( \alpha \neq 1 ) or 0.5</td>
<td>Strategy (1) – (4)</td>
<td>( C )</td>
<td>( Not possible )</td>
</tr>
<tr>
<td></td>
<td></td>
<td>( D )</td>
<td>( A, B, [C] )</td>
</tr>
</tbody>
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\[ A + B \xrightarrow{k_1} C \]
\[ A + C \xrightarrow{k_2} D \]
Example: Spectral consequence of Strategy 1

Model reduction

Strategy 1
define $nu$ uncoloured species

Time variant

Time invariant
Example: Spectral consequence of Strategy 1

Model reduction

**Strategy 1**
define \( nu \) uncoloured species

Species \( A \) uncoloured

Time variant

\[
\begin{align*}
A & \quad (4 \times nw) \\
A_c & \quad (3 \times nw)
\end{align*}
\]

Time invariant

\[
\begin{align*}
A & \quad (4 \times nw) \\
A_c & \quad (3 \times nw)
\end{align*}
\]
Example: Spectral consequence of Strategy 1

Model reduction

**Strategy 1**
define \( nu \) uncoloured species

Species A uncoloured

\[
\Omega_{\text{comprised of all species}} =
\begin{bmatrix}
-\mu_k - \mu_k & -\mu_k & \mu_k & \mu_k \\
-\mu_k & -\mu_k & \mu_k & \mu_k \\
-\mu_k & -\mu_k & -\mu_k & -\mu_k \\
-k_1 & k_2 & -k_1 & k_2 \\
\end{bmatrix}
\]

\[
\Omega_{\text{comprised of coloured species}} =
\begin{bmatrix}
-\mu_k & \mu_k & \mu_k & \mu_k \\
-\mu_k & -\mu_k & -\mu_k & -\mu_k \\
-k_1 & k_2 & k_1 & -k_2 \\
\end{bmatrix}
\]

\[\begin{bmatrix}
A_c \ 'B' \\
A_c \ 'C' \\
A_c \ 'D'
\end{bmatrix} = \Delta \begin{bmatrix}
\begin{bmatrix}
\Omega_{\text{comprised of coloured species}}
\end{bmatrix}^+ & \Omega_{\text{comprised of all species}}
\end{bmatrix} \begin{bmatrix}
A \\
A_c \\
A_d
\end{bmatrix} = \begin{bmatrix}
\alpha^{-1} & 1 & 0 & 0 \\
\alpha^{-1} & -1 & 0 & 1 \\
\alpha^{-1} & -2 & 0 & 1
\end{bmatrix} \begin{bmatrix}
A_A \\
A_B \\
A_c \\
A_d
\end{bmatrix}
\]
Example: Spectral consequence of Strategy 1

**Model reduction**

**Strategy 1**
Define $nu$ uncoloured species

Species $A$ uncoloured

$$\Omega_{\text{comprised of all species}} = \begin{bmatrix} \frac{A}{c_{0,A}} & B & C & D \\ -\mu k_1 - \mu k_2 & -\mu k_1 & \mu k_1 - \mu k_2 & \mu k_2 \\ -\mu k_1 - k_2 & -\mu k_1 & k_1 - \mu k_2 & k_2 \\ -k_1 - \mu k_2 & -k_1 & k_1 - k_2 & k_2 \\ -k_1 - k_2 & -k_1 & k_1 - k_2 & k_2 \end{bmatrix}$$

**Coloured species**

$$\Omega_{\text{comprised of coloured species}} = \begin{bmatrix} c_{0,A} & \alpha c_{0,A} & 0 & 0 \end{bmatrix}$$

**Time variant**

$$\begin{array}{c}
\text{Strategy 1} \\
\text{ns} & \rightarrow & \text{ns-nu} & \rightarrow & \text{nu} \\
\downarrow & & \downarrow & & \downarrow \\
C & \rightarrow & C_c & \rightarrow & C_c \\
\text{A (4 x nw)} & \rightarrow & \text{A} (3 x nw) & \rightarrow & \text{A} (3 x nw)
\end{array}$$

True: $A (4 x nw)$

Fitted: $A_c (3 x nw)$

**Time invariant**

$$\begin{array}{c}
\text{Strategy 1} \\
\text{ns} & \rightarrow & \text{ns-nu} & \rightarrow & \text{nu} \\
\downarrow & & \downarrow & & \downarrow \\
\Omega & \rightarrow & \Omega_c & \rightarrow & \Omega_c \\
\text{A (4 x nw)} & \rightarrow & \text{A} (3 x nw) & \rightarrow & \text{A} (3 x nw)
\end{array}$$

True: $A (4 x nw)$

Fitted: $A_c (3 x nw)$

When $\alpha = 2$

$$\begin{bmatrix} a_{A_c} \end{bmatrix} = \Delta A = (CC^+) A = \left( \Omega_{\text{comprised of coloured species}} \right)^+ \Omega_{\text{comprised of all species}} A = \begin{bmatrix} \alpha^{-1} & 1 & 0 & 0 & \alpha^{-1} & -1 & 0 & 0 & \alpha^{-1} & -2 & 0 & 0 \end{bmatrix} \begin{bmatrix} a_{A_c} \end{bmatrix} = \begin{bmatrix} 0.5 \end{bmatrix} a_{A_c} + \begin{bmatrix} 1 \end{bmatrix} a_{B_c} + \begin{bmatrix} 0 \end{bmatrix} a_{C_c} + \begin{bmatrix} 0 \end{bmatrix} a_{D_c}$$
An experimental case study

Overall reaction

\[
\text{Benzophenone (B)} + \text{Phenylhydrazine (P)} + \text{Acetic Acid (Aa)} \xrightarrow{\text{CH}_3\text{COOH in THF}} \text{Benzophenone-Phenylhydrazone (BP)} + \text{H}_2\text{O}
\]

Kinetic mechanism

\[ B + P + Aa \xrightarrow{k} BP + Aa \]

Experimental conditions

25°C, mid-IR (1200–1650 cm\(^{-1}\)), UV-vis (240–400 nm)

Batch conditions

Dosing Aa

Dosing B

Dosing B + Aa

Dosing P

Reactor: CRC.v4 with FT-IR and UV-vis

Billeter et al, Chemom. Intell. Lab. Syst., submitted
Spectral validation

Species $B$ and $Aa$ dosed

**Full spectral resolution**

- **Mid-IR**
  - $B$
  - $P$
  - $Aa$
  - $BP$

- **UV-vis**
  - $B$
  - $P$
  - $Aa$
  - $BP$

Fitted spectra: solid line

Measured spectra: dotted line

Predicted spectra: dashed line

$B + P + Aa \xrightarrow{k_1} BP + Aa$
Spectral validation

**Strategy (1): uncoloured species**

Species $P$ and $Aa$ set uncoloured

Partial spectral resolution

**Strategy (1)+(2): provided known spectrum**

Pure spectrum of $B$ provided

$Aa$ set uncoloured

Partial spectral resolution

**Strategy (3): dosing**

Species $B$ and $Aa$ dosed

Full spectral resolution

**Strategy (1)+(4): second order global analysis**

Initial concentration of $B$ varied, $Aa$ set uncoloured

Fitted spectra  Measured spectra  Predicted spectra

$B + P + Aa \xrightarrow{k_1} BP + Aa$
Conclusions

Ker $C$
Linear dependencies, leading to rank deficiency in concentration matrix, can be elucidated using the concept of kernel

$C(ker C) = 0$
This equation defines a mass balance equation with time-invariant coefficients

Model reduction / rank augmentation Strategies
Species to be included in Strategies 1 – 4 can be identified by selecting the species with non zero rows in the kernel

Matrix $\Omega$
The kernel of the time-variant concentrations can be calculated without numerical integration using a simple time-invariant approach

Matrix $\Delta$
Linear combinations, observed in the fitted pure spectra when Strategy 1 (defining uncoloured species) is used, can be explained by a spectral balance equation

Spectral validation of kinetic models
Spectral validation of kinetic models is now possible even in case of rank deficient spectroscopic data
Reaction Analysis at ETH Zürich

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**Reaction Analysis Group**
Leader: Dr. Bobby Neuhold

under supervision of **Prof. K. Hungerbühler**
Thank you for your attention

Publications

Systematic prediction of linear dependencies in the concentration profiles and implications on the kinetic hard-modelling of spectroscopic data

Kinetic hard-modelling and spectral validation of rank-deficient spectroscopic data: a case study
Billeter et al, Chemom. Intell. Lab. Syst., submitted