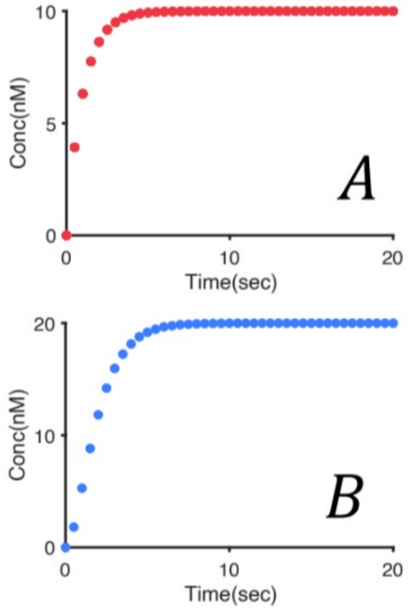
Approximating higher order reactions with lower order reactions by CRNN

20190978 / Seokhwan Moon / Dept. of Mathematics

Review of second presentation

$$0 \rightarrow A$$
$$A + B \rightarrow C$$
$$D \rightarrow 0$$
$$C \rightarrow E$$

Biochemical reactions



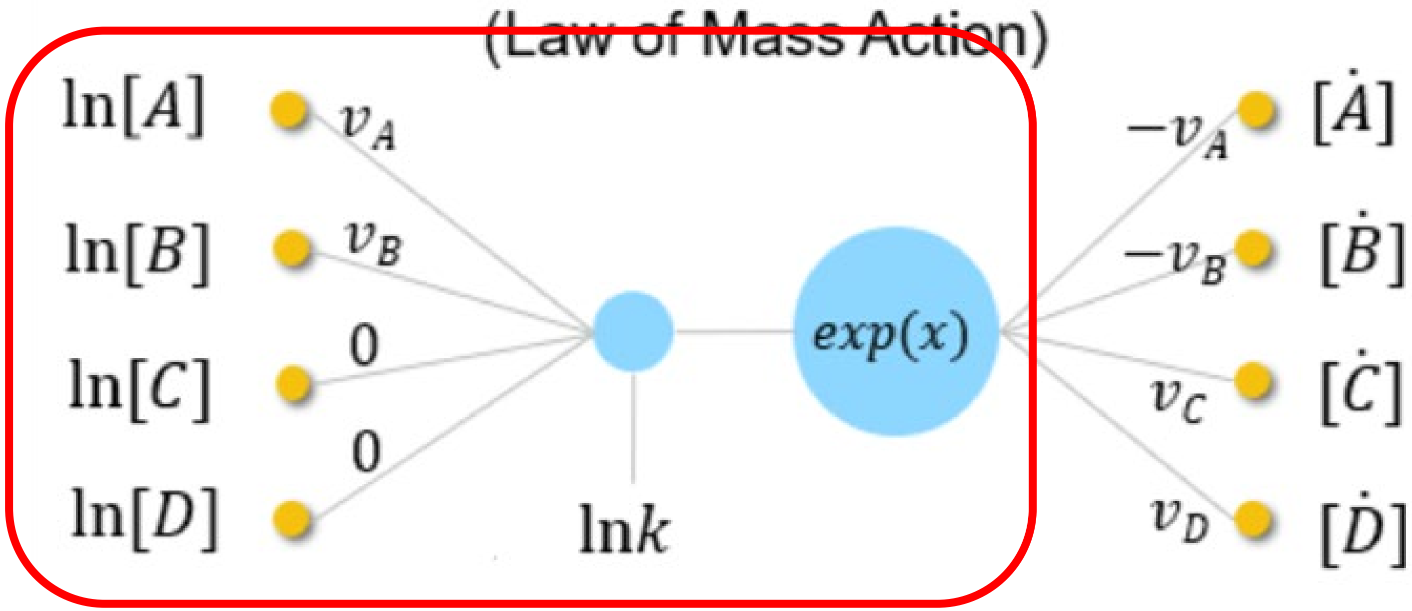
Concentration of chemical species

How to derive the chemical reaction from the measured data?

Ji, W., & Deng, S. Journal of Physical Chemistry A (2021).

Review of second presentation

$$v_A A + v_B B \xrightarrow{k} v_C C + v_D D$$

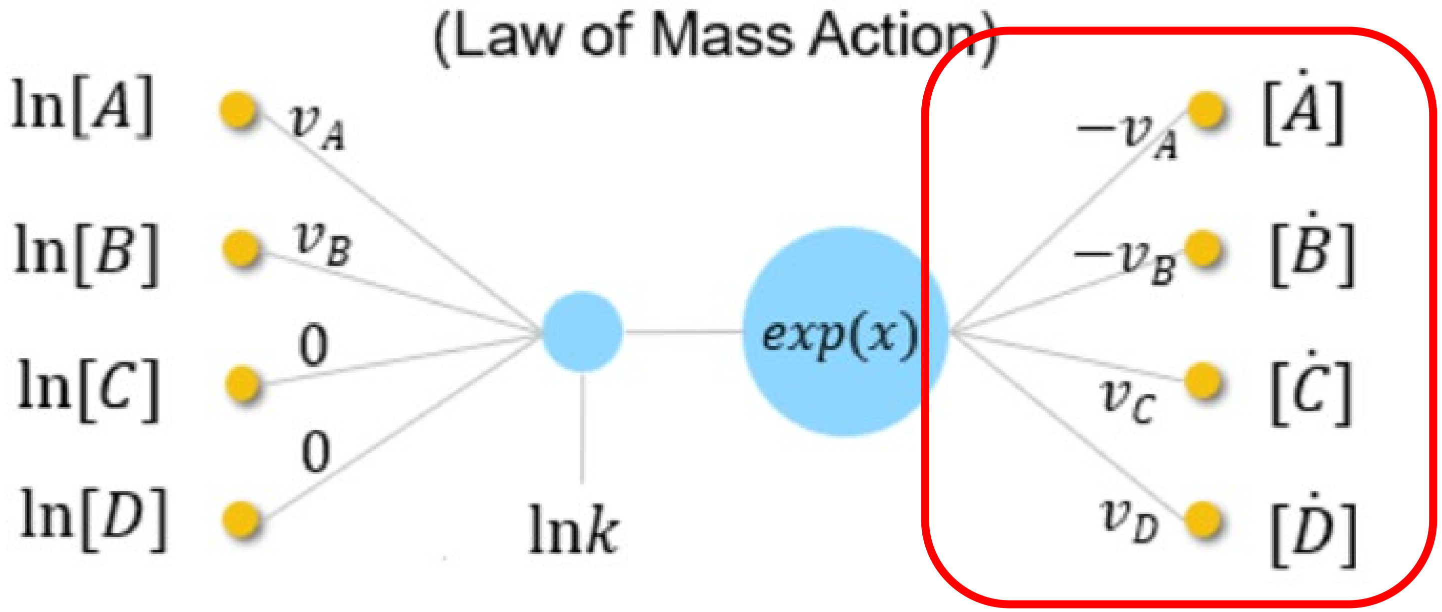


$$r = k[A]^{v_A}[B]^{v_B}[C]^0[D]^0$$
$$= \exp(\ln k + v_A \ln[A] + v_B \ln[B] + 0\ln[C] + 0\ln[D])$$

Ji, W., & Deng, S. Journal of Physical Chemistry A (2021).

Review of second presentation

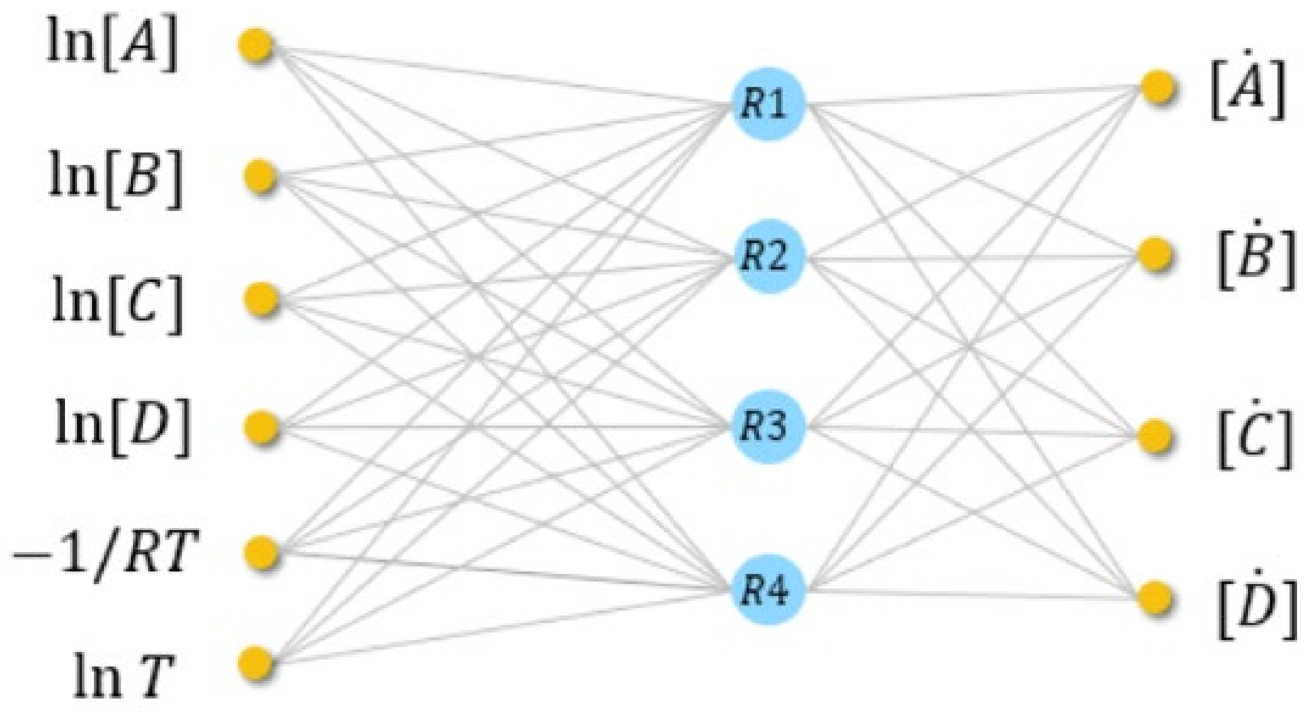
$$v_A A + v_B B \xrightarrow{k} v_C C + v_D D$$



$$\frac{d[A]}{dt} = -v_A r, \frac{d[B]}{dt} = -v_B r, \frac{d[C]}{dt} = v_C r, \frac{d[D]}{dt} = v_D r$$

Ji, W., & Deng, S. Journal of Physical Chemistry A (2021).

Review of second presentation



# of reaction is hyperparameter!

Ji, W., & Deng, S. Journal of Physical Chemistry A (2021).

Approximating higher-order reactions with second-order reactions

$$\mathrm{A} + 2\mathrm{X} \xrightarrow{k} 3\mathrm{X} \quad \Rightarrow \quad \mathrm{A} + \mathrm{X} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{Z}, \qquad \mathrm{X} + \mathrm{Z} \xrightarrow{k_2} 3\mathrm{X}$$

($k_{-1} \to \infty$)

Wilhelm, T. Journal of Mathematical Chemistry (2000).

Approximating higher-order reactions with second-order reactions

$$\nu_1^+ X_1 + \nu_2^+ X_2 + \nu_3^+ X_3 \xrightarrow{k} \nu_1^- X_1 + \nu_2^- X_2 + \nu_3^- X_3 + \sum_r \nu_r^- X_r$$

$$\sum_i \nu_i^+ = 3$$

$$X_i + X_j \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Z, \qquad (k_{-1} \to \infty)$$

$$X_k + Z \xrightarrow{k_2} \nu_i X_i + \nu_j X_j + \nu_k X_k + \sum_r \nu_r X_r + \nu_z Z$$

$$\nu_1^+ X_1 + \nu_2^+ X_2 + \nu_3^+ X_3 + \nu_4^+ X_4 \xrightarrow{k} \nu_1^- X_1 + \nu_2^- X_2 + \nu_3^- X_3 + \nu_4^- X_4 + \sum_r \nu_r^- X_r$$

$$\sum_i \nu_i^+ = 4$$

$$X_i + X_j \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Z_1,$$

$$X_k + Z_1 \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} Z_2,$$

$$X_l + Z_2 \xrightarrow{k_3} \nu_i X_i + \nu_j X_j + \nu_k X_k + \nu_l X_l + \sum_r \nu_r X_r + \nu_{z_1} Z_1 + \nu_{z_2} Z_2$$

$$k_{-1} = \mathcal{O}(k_{-2}) \to \infty$$

Wilhelm, T. Journal of Mathematical Chemistry (2000).

Approximating higher-order reactions with second-order reactions

$$\nu_1^+ X_1 + \nu_2^+ X_2 + \nu_3^+ X_3 \xrightarrow{k} \nu_1^- X_1 + \nu_2^- X_2 + \nu_3^- X_3 + \sum_r \nu_r^- X_r$$

$$\textstyle\sum_i \nu_i^+ = 3$$

$$X_i + X_j \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Z, \quad (k_{-1} \to \infty)$$

$$X_k + Z \xrightarrow{k_2} \nu_i X_i + \nu_j X_j + \nu_k X_k + \sum_r \nu_r X_r + \nu_z Z$$

Can CRNN capture this kind of approximations?

$$\nu_1^+ X_1 + \nu_2^+ X_2 + \nu_3^+ X_3 + \nu_4^+ X_4 \rightarrow \nu_1^- X_1 + \nu_2^- X_2 + \nu_3^- X_3 + \nu_4^- X_4 + \sum_r \nu_r^- X_r$$

$$\textstyle\sum_i \nu_i^+ = 4$$

$$X_i + X_j \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Z_1,$$

$$X_k + Z_1 \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} Z_2,$$

$$X_l + Z_2 \xrightarrow{k_3} \nu_i X_i + \nu_j X_j + \nu_k X_k + \nu_l X_l + \sum_r \nu_r X_r + \nu_{z_1} Z_1 + \nu_{z_2} Z_2$$

$$k_{-1} = \mathcal{O}(k_{-2}) \to \infty$$

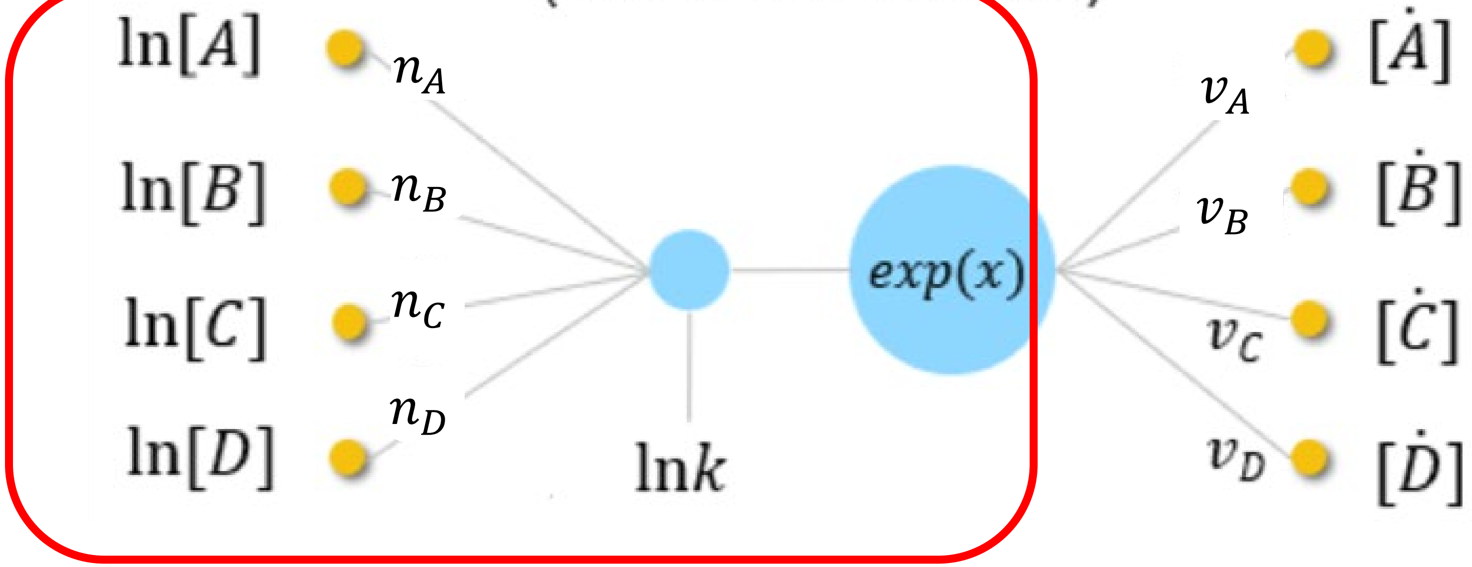
Wilhelm, T. Journal of Mathematical Chemistry (2000).

Loss function of chemical reaction neural network

Loss function : $MAE\left(Y^{CRNN}(t), Y^{data}(t)\right) = \sum_i (\frac{1}{T} \sum_t \left| Y_i^{CRNN}(t) - Y_i^{data}(t) \right|)/\sigma_i$

$+ \sum_{reactions} Relu((n_A + n_B + n_C + n_D) - 2)$

(Law of Mass Action)



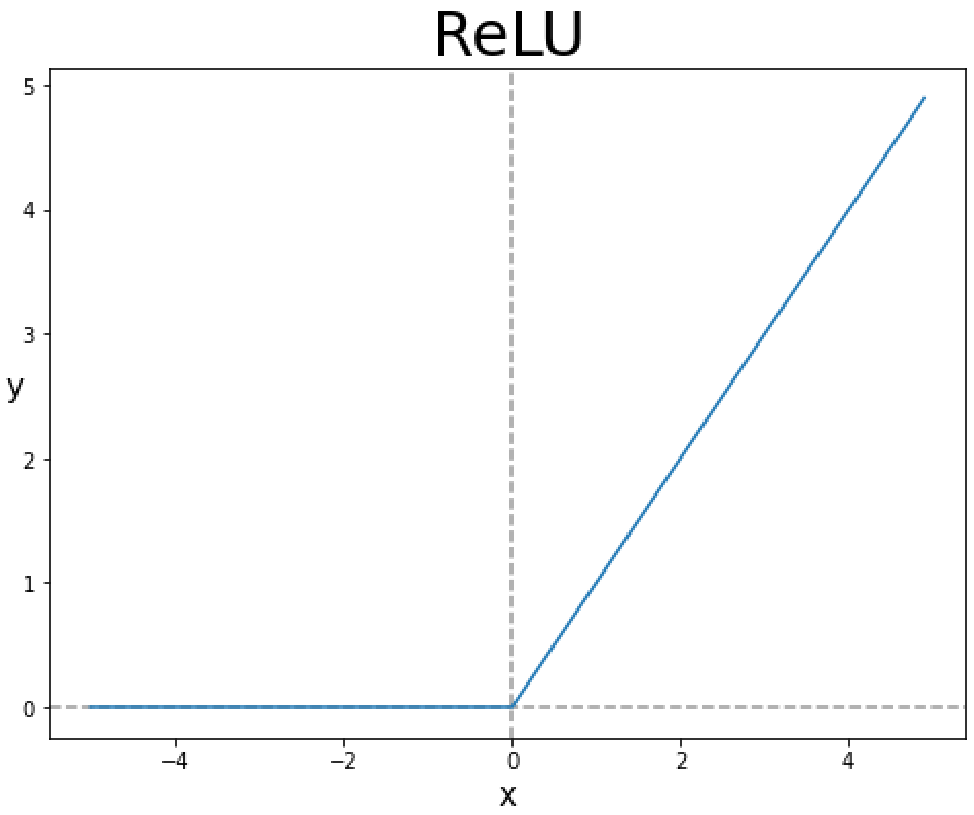
$$r = k[A]^{n_A}[B]^{n_B}[C]^{n_C}[D]^{n_D}$$

$$= \exp(\ln k + n_A \ln[A] + n_B \ln[B] + n_C \ln[C] + n_D \ln[D])$$

Loss function of chemical reaction neural network

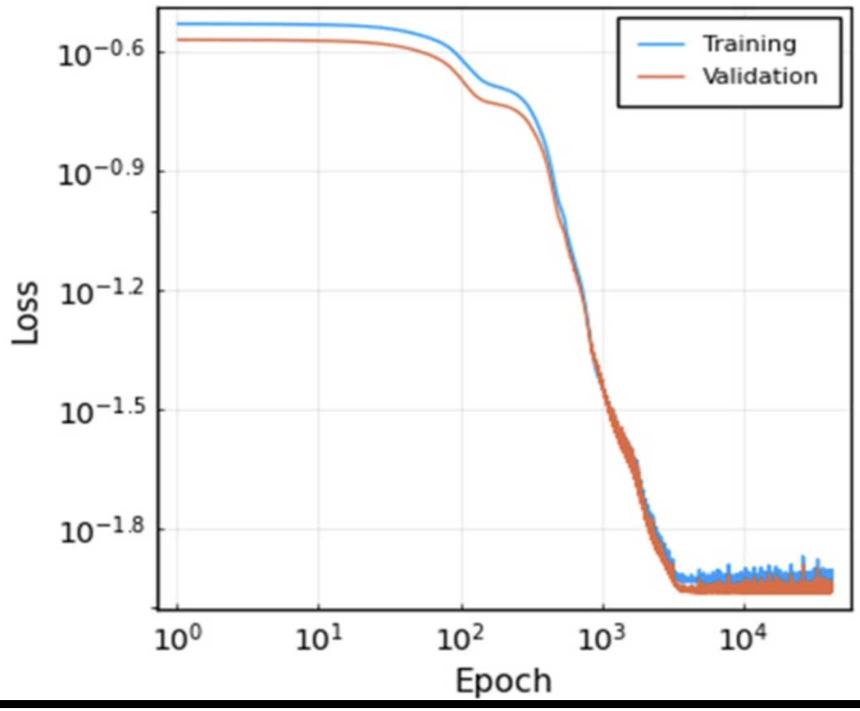
Loss function : $MAE\left(Y^{CRNN}(t), Y^{data}(t)\right) = \sum_i (\frac{1}{T} \sum_t \left| Y_i^{CRNN}(t) - Y_i^{data}(t) \right|)/\sigma_i$

$+ \sum_{reactions} Relu((n_A + n_B + n_C + n_D) - 2)$



Training result with modified loss function

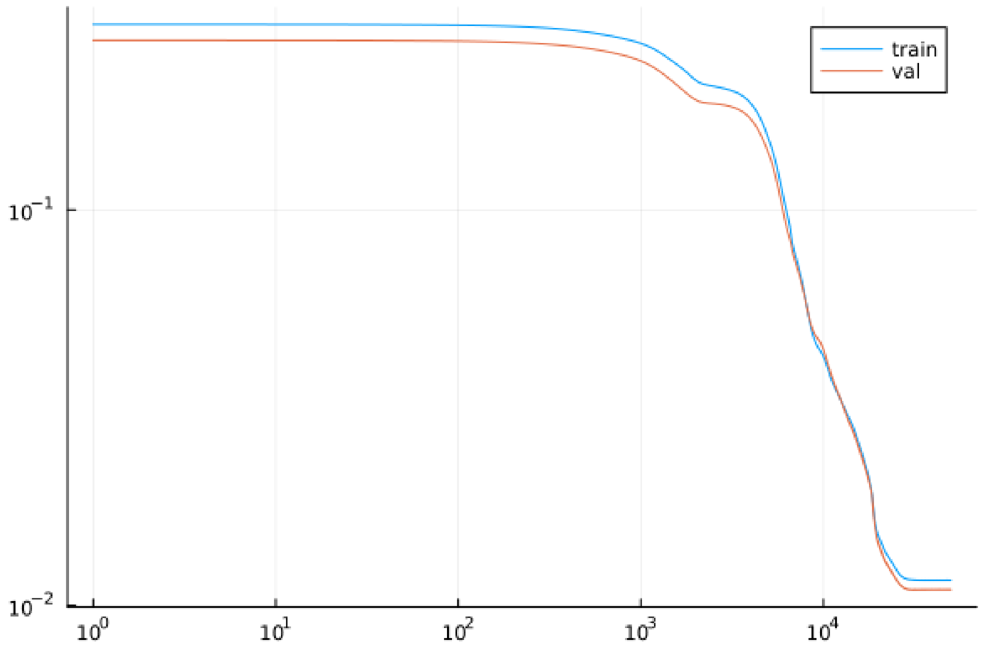
ground truth		learned CRNN	
equation	rate	equation	rate
$B + D \rightarrow E$	0.3	$B + 1.006D \rightarrow 1.006E$	0.307
$2A \rightarrow B$	0.1	$2.093A \rightarrow 1.107B$	0.101
$A \rightarrow C$	0.2	$1.004A \rightarrow 0.965C$	0.206
$C \rightarrow D$	0.13	$0.999C \rightarrow 1.011D$	0.13



Original loss function

Modified loss function

$$1.003B + 1.008D \rightarrow 1.007E, \quad 0.307$$
$$2.084A + 0.011E \rightarrow 1.115B + 0.006D \quad 0.102$$
$$1.004A \rightarrow 0.001B + 0.969C + 0.001D + 0.004E \quad 0.206$$
$$0.998C + 0.004E \rightarrow 0.002A + 0.002B + 1.01D, \quad 0.130$$



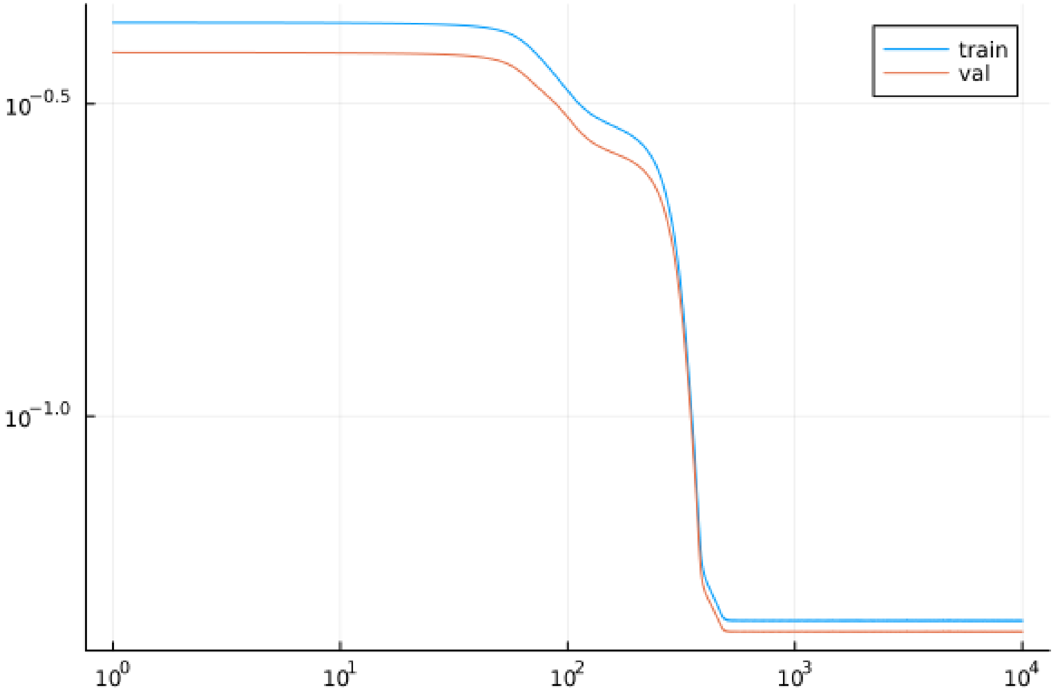
Case 1 : Without additional species

# of reaction : 2
# of species : 2

$$3A \rightarrow B, \qquad k_1 = 1.2$$

$$2.196A \rightarrow 0.719B, \qquad k_1 = 0.335$$
$$2.195A \rightarrow 0.796B, \qquad k_2 = 0.067$$

```
w_in
2x2 Matrix{Float64}:
 2.196  0.0
 2.195  0.0
w_b
1x2 Matrix{Float64}:
 0.334832  0.0672393
w_out
2x2 Matrix{Float32}:
 -2.196  0.719
 -2.195  0.796
```



Case 1 : Without additional species

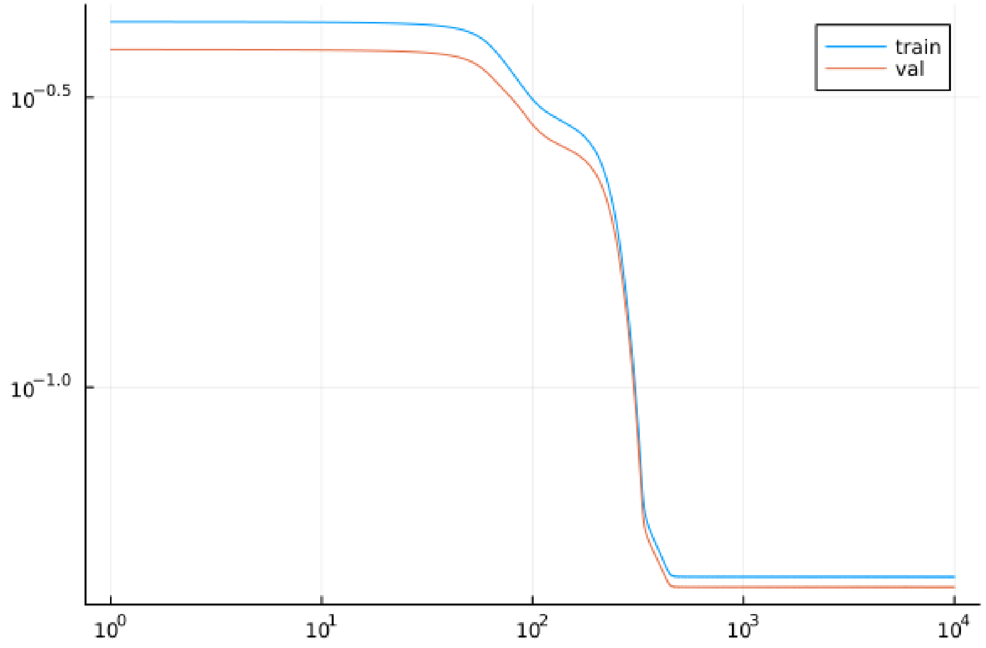
$$3A \rightarrow B, \qquad k_1 = 1.2$$

\# of reaction : 3
\# of species : 2

→

$$2.196A \rightarrow 0.669B, \qquad k_1 = 0.282$$
$$2.172A \rightarrow 0.59B, \qquad k_2 = 0.0012$$
$$2.198A \rightarrow 0.882B, \qquad k_3 = 0.1117$$

```
3×2 Matrix{Float64}:
 2.196  0.0
 2.172  0.0
 2.198  0.0
w_b
1×3 Matrix{Float64}:
 0.282409  0.00122938  0.117926
w_out
3×2 Matrix{Float32}:
 -2.196  0.669
 -2.172  0.59
 -2.198  0.882
```



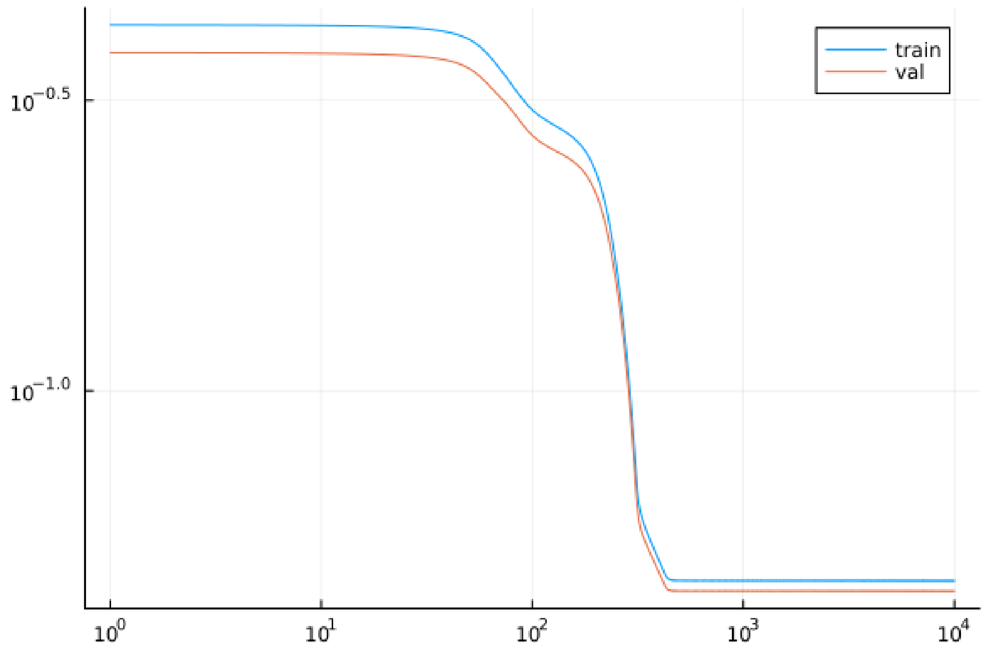
Case 1 : Without additional species

$$3A \rightarrow B, \qquad k_1 = 1.2$$

\# of reaction : 4
\# of species : 2

$$2.192A \rightarrow 0.7B, \qquad k_1 = 0.004$$
$$2.195A \rightarrow 0.699B, \qquad k_2 = 0.234$$
$$2.198A \rightarrow 0.779B, \qquad k_3 = 0.160$$
$$2.169A \rightarrow 0.631B, \qquad k_4 = 0.003$$

```
w_in
4×2 Matrix{Float64}:
 2.192  0.0
 2.195  0.0
 2.198  0.0
 2.169  0.0
w_b
1×4 Matrix{Float64}:
 0.00416153  0.234039  0.16037  0.00276923
w_out
4×2 Matrix{Float32}:
 -2.192  0.7
 -2.195  0.699
 -2.198  0.779
 -2.169  0.631
```



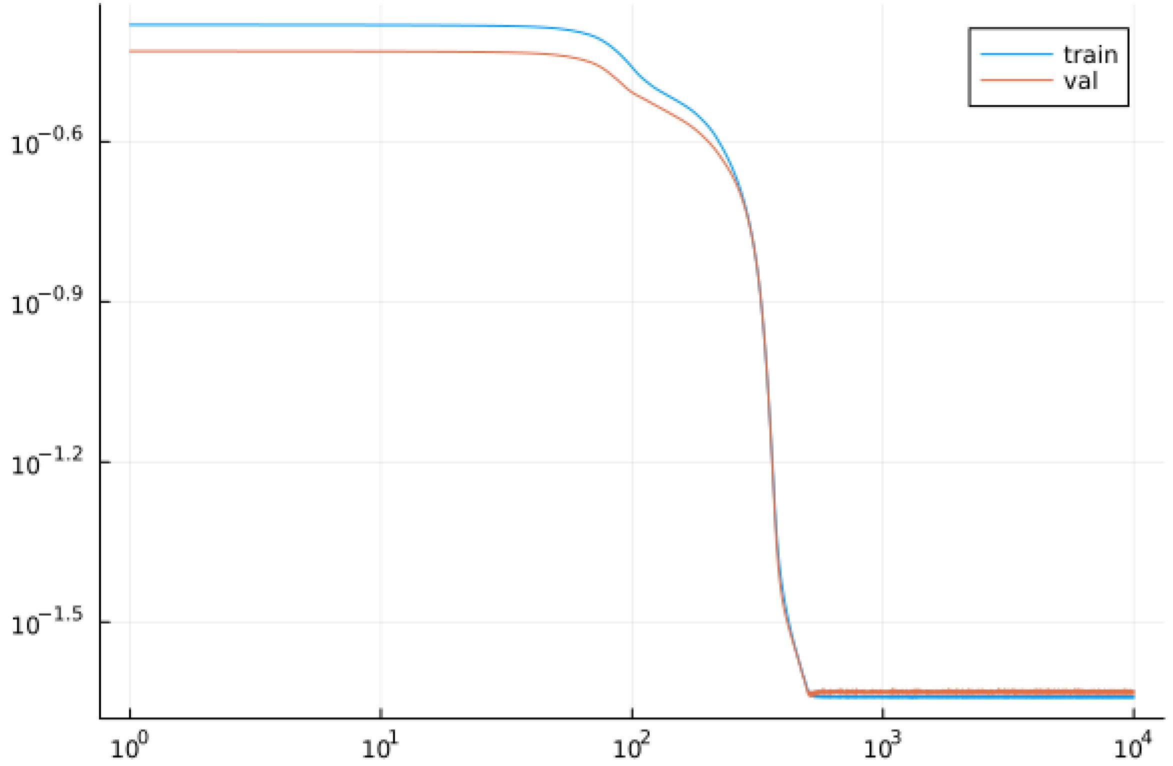
Case 1 : Without additional species

$$2A + B \rightarrow C, \qquad k_1 = 1.2$$

# of reaction : 2
# of species : 3

$$1.47A + 0.722B \rightarrow 0.669C, \quad k_1 = 0.550$$
$$1.47A + 0.689B \rightarrow 1.086C, \quad k_2 = 0.024$$

```
2x3 Matrix{Float64}:
 1.47   0.722  0.0
 1.468  0.689  0.0
w_b
1x2 Matrix{Float64}:
 0.549771  0.0237182
w_out
2x3 Matrix{Float32}:
 -1.47   -0.722  0.699
 -1.468  -0.689  1.086
```



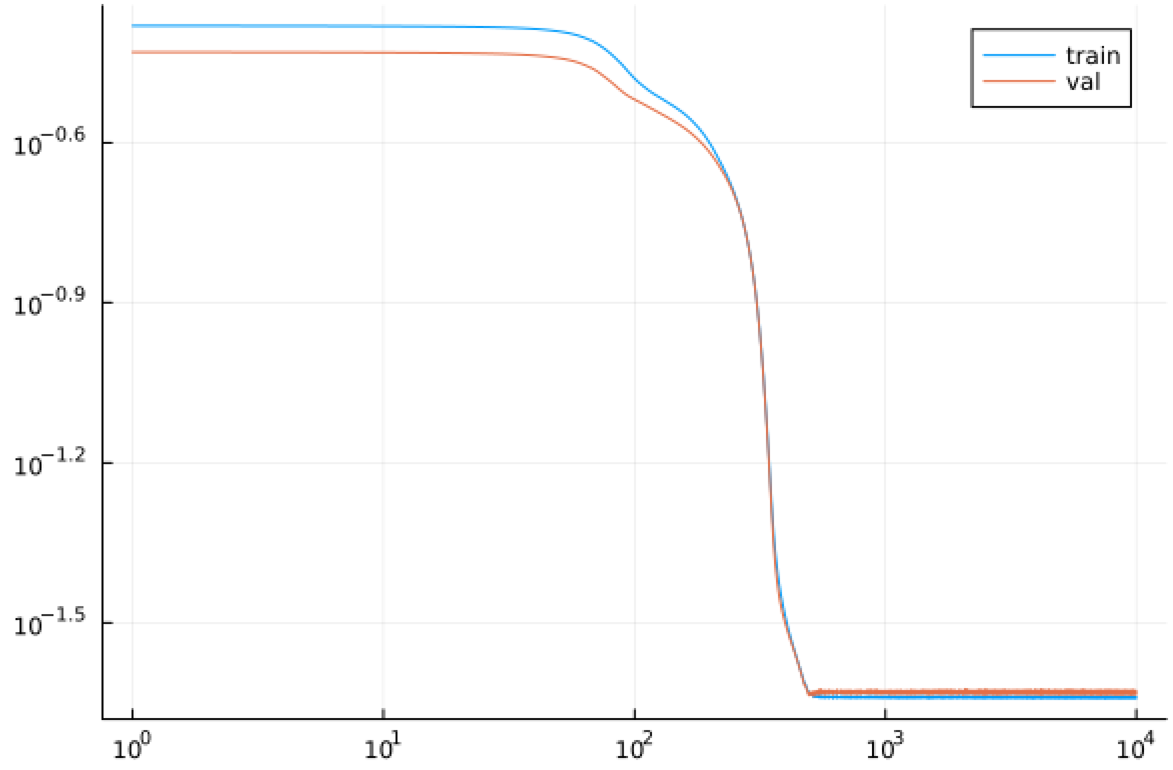
Case 1 : Without additional species

$$2A + B \rightarrow C, \qquad k_1 = 1.2$$

# of reaction : 3
# of species : 3

$$1.472A + 0.727B \rightarrow 0.646C, \qquad k_1 = 0.486$$
$$1.476A + 0.709B \rightarrow 1.027C, \qquad k_2 = 0.014$$
$$1.476A + 0.708B \rightarrow 1.129C, \qquad k_3 = 0.074$$

```
w_in
3x3 Matrix{Float64}:
 1.472  0.727  0.0
 1.476  0.709  0.0
 1.476  0.708  0.0
w_b
1x3 Matrix{Float64}:
 0.485644  0.0136641  0.07351
w_out
3x3 Matrix{Float32}:
 -1.472  -0.727  0.646
 -1.476  -0.709  1.027
 -1.476  -0.708  1.129
```



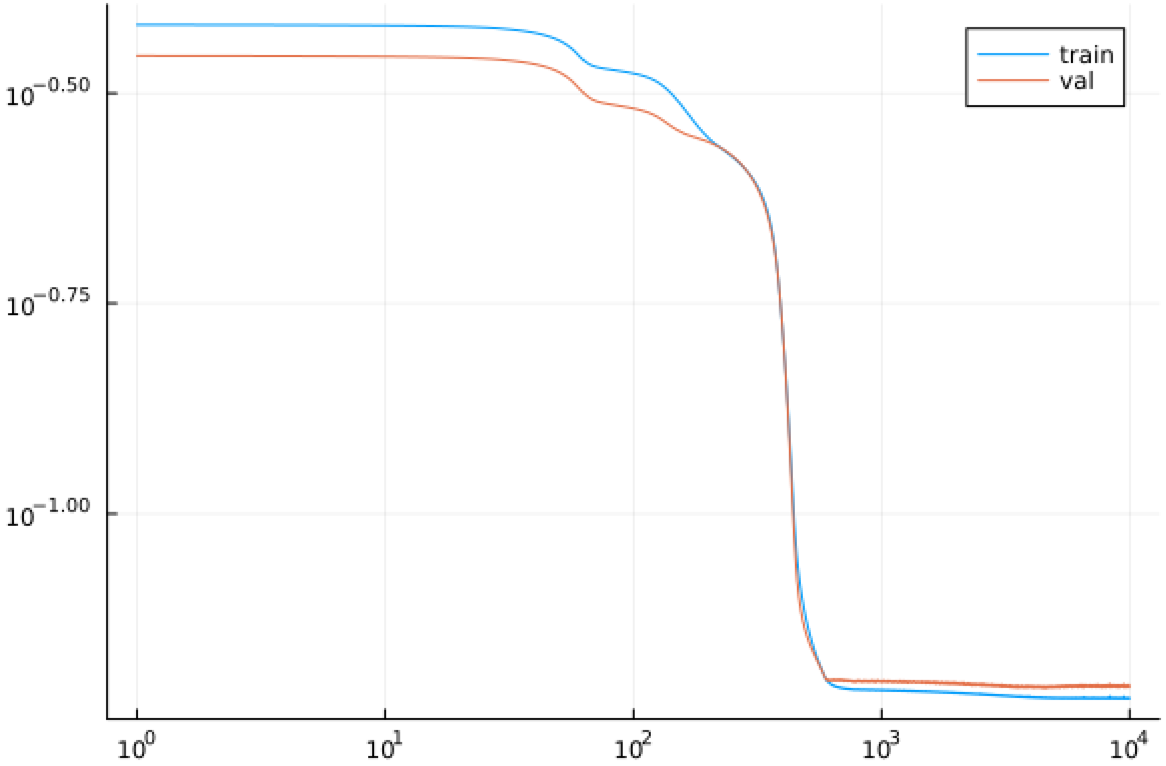
Case 1 : Without additional species

$$2A + B \rightarrow C, \qquad k_1 = 1.2$$
$$3C \rightarrow A + B, \qquad k_1 = 2.3$$

\# of reaction : 3
\# of species : 3

$$1.546A + 0.641B \rightarrow 0, \qquad k_1 = 0.538$$
$$1.151A + 0.468B \rightarrow 5.19C, \qquad k_2 = 0.011$$
$$1.515A + 0.624B \rightarrow 0, \qquad k_3 = 0.004$$

```
3x3 Matrix{Float64}:
 1.546  0.641  0.003
 1.151  0.468  0.0
 1.515  0.624  0.031
w_b
1x3 Matrix{Float64}:
 0.537748  0.0110621  0.00390487
w_out
3x3 Matrix{Float32}:
 -1.546  -0.641  -0.003
 -1.151  -0.468   5.19
 -1.515  -0.624  -0.031
```



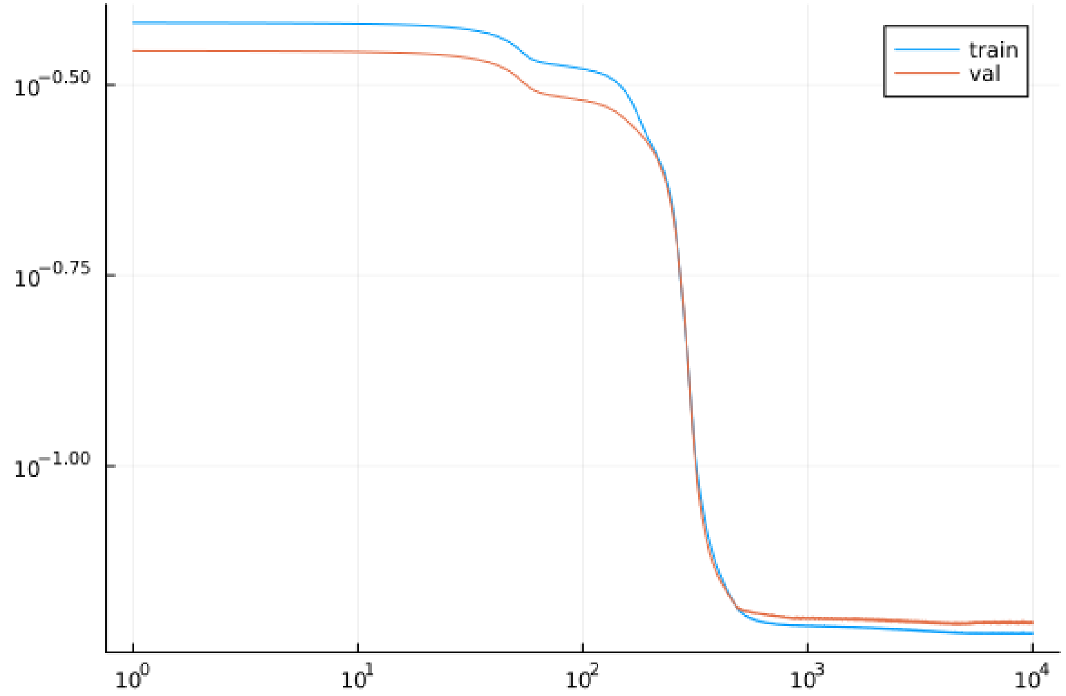
Case 1 : Without additional species

$$2A + B \rightarrow C, \qquad k_1 = 1.2$$
$$3C \rightarrow A + B, \qquad k_1 = 2.3$$

# of reaction : 4
# of species : 3

$$1.546A + 0.641B \rightarrow 0, \qquad k_1 = 0.518$$
$$1.15A + 0.467B \rightarrow 5.537C, \qquad k_2 = 0.010$$
$$1.47A + 0.603B + 0.031C \rightarrow 0, \qquad k_3 = 9.55 \times 10^{-7}$$
$$1.526A + 0.626B \rightarrow 0, \qquad k_4 = 0.024$$

```
w_in
4x3 Matrix{Float64}:
 1.546  0.641  0.0
 1.15   0.467  0.0
 1.47   0.603  0.031
 1.526  0.626  0.0
w_b
1x4 Matrix{Float64}:
 0.51797  0.0102556  9.55262e-7  0.0235929
w_out
4x3 Matrix{Float32}:
 -1.546  -0.641   0.001
 -1.15   -0.467   5.537
 -1.47   -0.603  -0.031
 -1.526  -0.626   0.01
```



Case 1 : Without additional species

Approximating higher order reaction with multiple reactions without additional species

Every reactions are similar

Case 2 : With additional species

$$A + 2X \rightarrow 3X$$

Original system

# of reaction : 3
# of species : 3

$$\mathrm{A} + \mathrm{X} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{Z}, \qquad \mathrm{X} + \mathrm{Z} \xrightarrow{k_2} 3\mathrm{X},$$

$$\mathrm{X} + \mathrm{X} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{Z}, \qquad \mathrm{A} + \mathrm{Z} \xrightarrow{k_2} 3\mathrm{X},$$

$$\mathrm{X} + \mathrm{X} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{Z}, \qquad \mathrm{A} + \mathrm{Z} \xrightarrow{k_2} \mathrm{X} + \mathrm{Z}.$$

Expected result

Case 2 : With additional species

# of reaction : 3
# of species : 3

$$A + 2X \xrightarrow{1.2} 3X$$
$$0 \xrightarrow[0.1]{} Z \xrightarrow[1000]{} 0$$

Original system

$$\mathrm{A} + \mathrm{X} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{Z}, \qquad \mathrm{X} + \mathrm{Z} \xrightarrow{k_2} 3\mathrm{X},$$
$$\mathrm{X} + \mathrm{X} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{Z}, \qquad \mathrm{A} + \mathrm{Z} \xrightarrow{k_2} 3\mathrm{X},$$
$$\mathrm{X} + \mathrm{X} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{Z}, \qquad \mathrm{A} + \mathrm{Z} \xrightarrow{k_2} \mathrm{X} + \mathrm{Z}.$$

Expected result

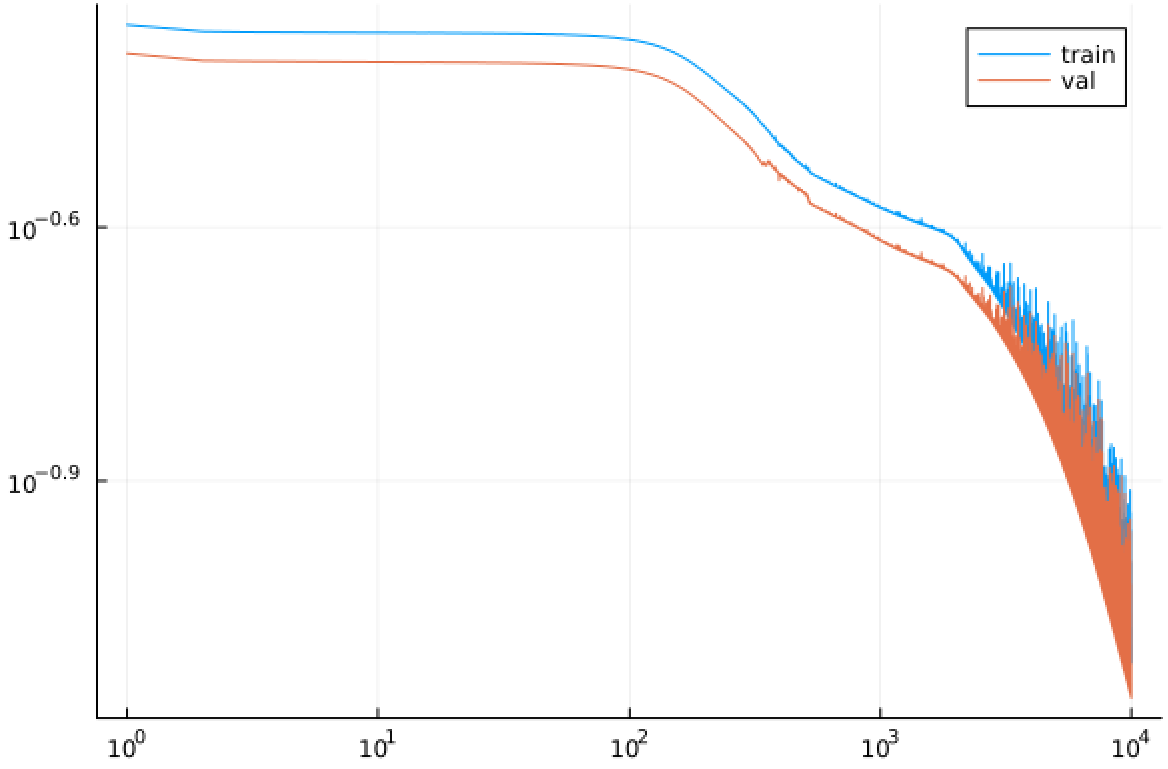
Case 2 : With additional species

$$A + 2X \xrightarrow{1.2} 3X$$
$$0 \xrightarrow{0.1} Z \xrightarrow{1000} 0$$

\# of reaction : 3
\# of species : 3

$$1.036A + 0.036Z \rightarrow 1.082X, \quad k_1 = 0.164$$
$$0.996A \rightarrow 2.404Z, \quad k_2 = 0.0006$$
$$1.062A \rightarrow 8.67X + 2.485Z, \quad k_3 = 0.001$$

```
w_in
3x3 Matrix{Float64}:
 1.036  0.0  0.036
 0.996  0.0  0.0
 1.062  0.0  0.0
w_b
1x3 Matrix{Float64}:
 0.164461  0.000640615  0.00109849
w_out
3x3 Matrix{Float32}:
 -1.036  1.082  -0.036
 -0.996  0.004   2.404
 -1.062  8.67    2.485
```



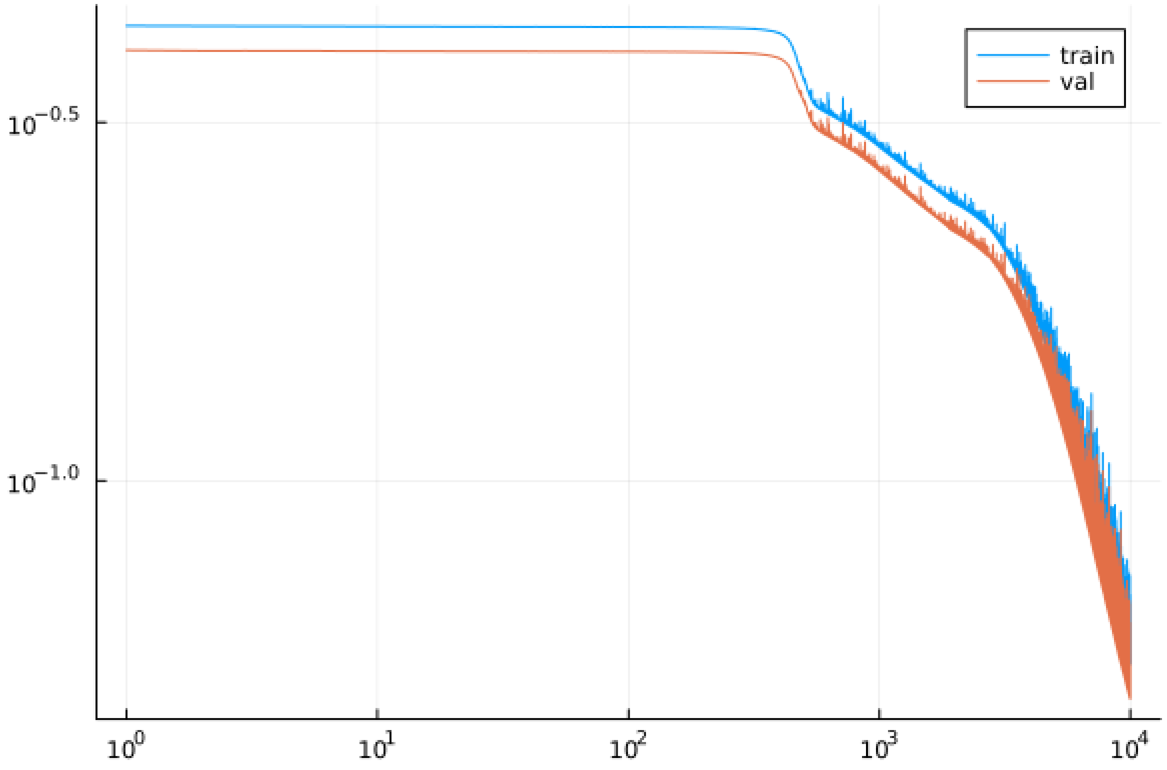
Case 2 : With additional species

# of reaction : 2
# of species : 3

$$A + 2X \xrightarrow{1.2} 3X$$
$$0 \xrightarrow[0.1]{} Z \xrightarrow[1000]{} 0$$

$$1.041A + 0.043Z \rightarrow 0.327X, \quad k_1 = 0.24$$
$$1.042A \rightarrow 7.746X + 0.369Z, \quad k_2 = 0.0188$$

```
w_in
2x3 Matrix{Float64}:
 1.041  0.0  0.043
 1.042  0.0  0.0
w_b
1x2 Matrix{Float64}:
 0.240092  0.0187862
w_out
2x3 Matrix{Float32}:
 -1.041  0.327  -0.043
 -1.042  7.746   0.369
```



Case 2 : With additional species

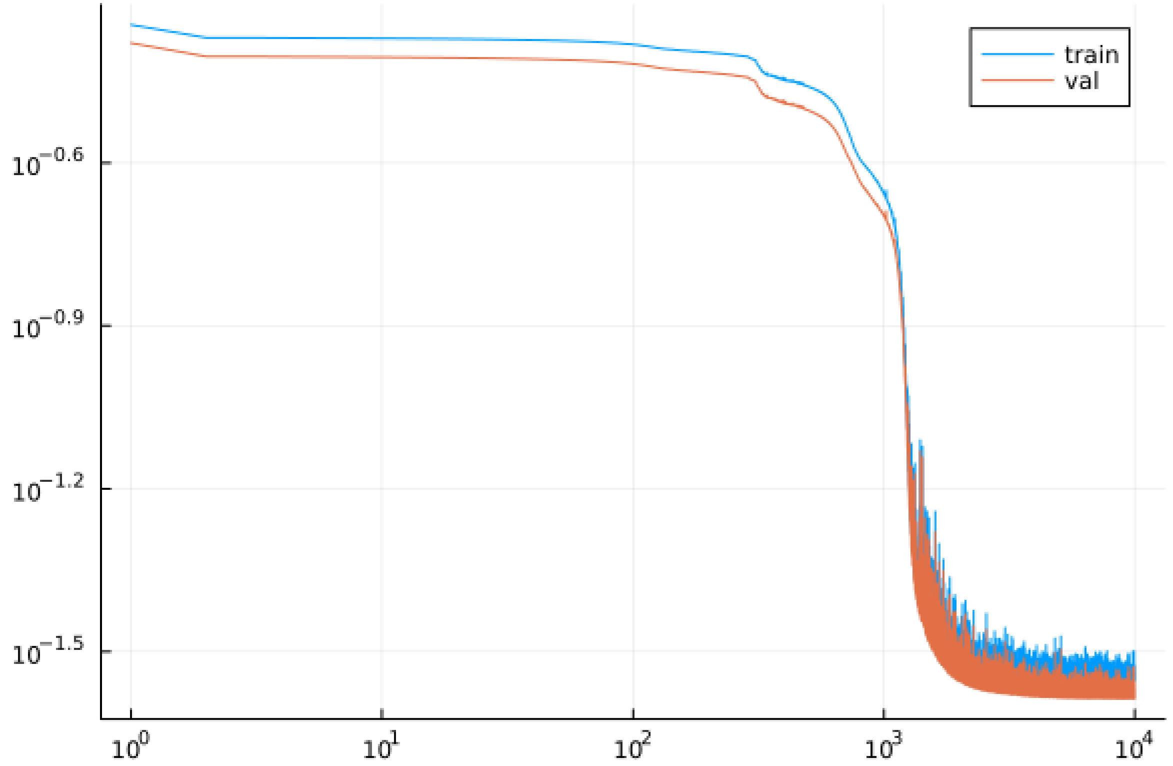
$$A + 2X \xrightarrow{1.2} 3X$$

$$0 \xrightarrow[0.1]{} Z \xrightarrow[1000]{} 0$$

\# of reaction : 4
\# of species : 3

$$1.175A \rightarrow 1.161X, \qquad k_1 = 1.215$$
$$0.463A \rightarrow 3.045X + 1.58Z, \qquad k_2 = 0.002$$
$$0.449A + 0.473Z \rightarrow 0.319X, \qquad k_3 = 0.202$$
$$0.473A + 0.457Z \rightarrow 0.307X, \qquad k_4 = 0.288$$

```
w_in
4x3 Matrix{Float64}:
 1.175  0.0  0.0
 0.463  0.0  0.0
 0.449  0.0  0.473
 0.473  0.0  0.457
w_b
1x4 Matrix{Float64}:
 1.21536  0.00201388  0.202343  0.287947
w_out
4x3 Matrix{Float32}:
 -1.175  1.161   0.0
 -0.463  3.045   1.58
 -0.449  0.319  -0.473
 -0.473  0.307  -0.457
```



Case 2 : With additional species

# of reaction : 4
# of species : 4

Original system

$$A + 2X \rightarrow 3X$$

$$2Y \rightarrow A$$

Expected result

$$A + X \rightleftarrows Z$$

$$X + Z \rightarrow 3X$$

$$2Y \rightarrow A$$

Case 2 : With additional species

Original system

1.2 $A + 2X \rightarrow 3X$

2.3 $2Y \rightarrow A$

$0 \rightarrow Z \rightarrow 0$ (0.1, 1000)

\# of reaction : 4

\# of species : 4

Expected result

$A + X \rightleftarrows Z$

$X + Z \rightarrow 3X$

$2Y \rightarrow A$

Case 2 : With additional species

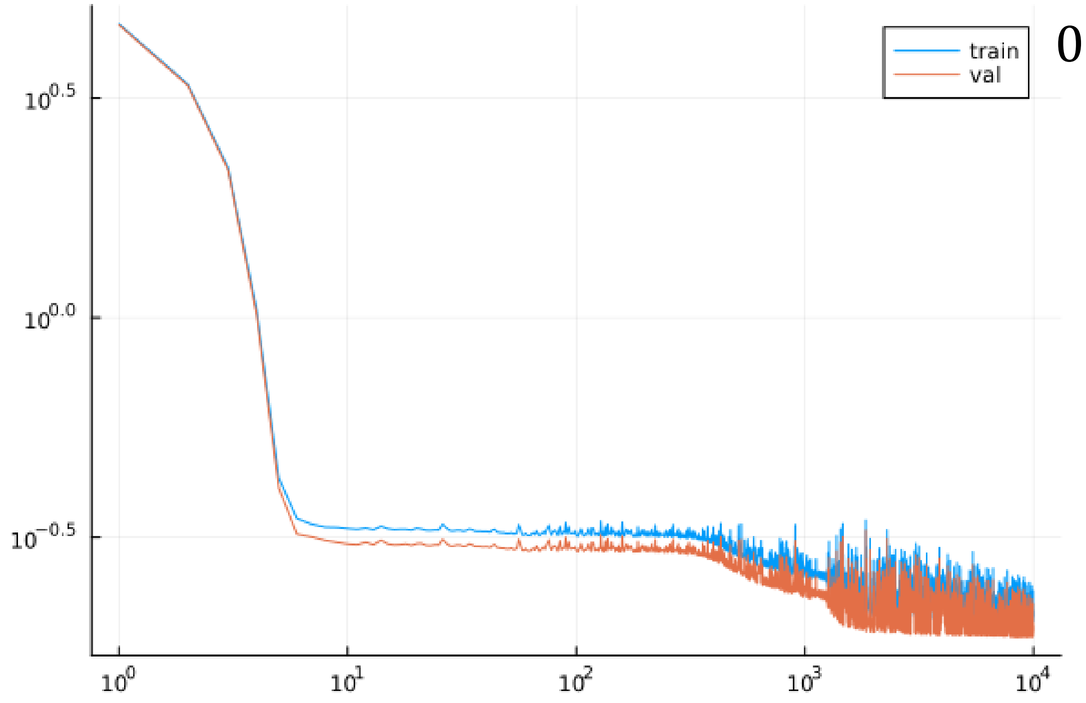
# of reaction : 4
# of species : 4

1.2 $A + 2X \rightarrow 3X$

2.3 $2Y \rightarrow A$

$0 \xrightarrow{0.1} Z \xrightarrow{1000} 0$

$$
\begin{aligned}
&0.085Y \rightarrow 0.017A + 72.085X + 2.092Z, && k_1 = 4.57 \times 10^{-5} \\
&0.085Y \rightarrow 0.017A + 72.334X + 2.024Z, && k_2 = 5.896 \times 10^{-5} \\
&0.736Z \rightarrow 0.004A + 77.284X, && k_3 = 0.141 \\
&0 \rightarrow 86.402X + 0.059Y + 0.67Z, && k_4 = 5.63 \times 10^{-5}
\end{aligned}
$$



Case 2 : With additional species

\# of reaction : 5
\# of species : 4

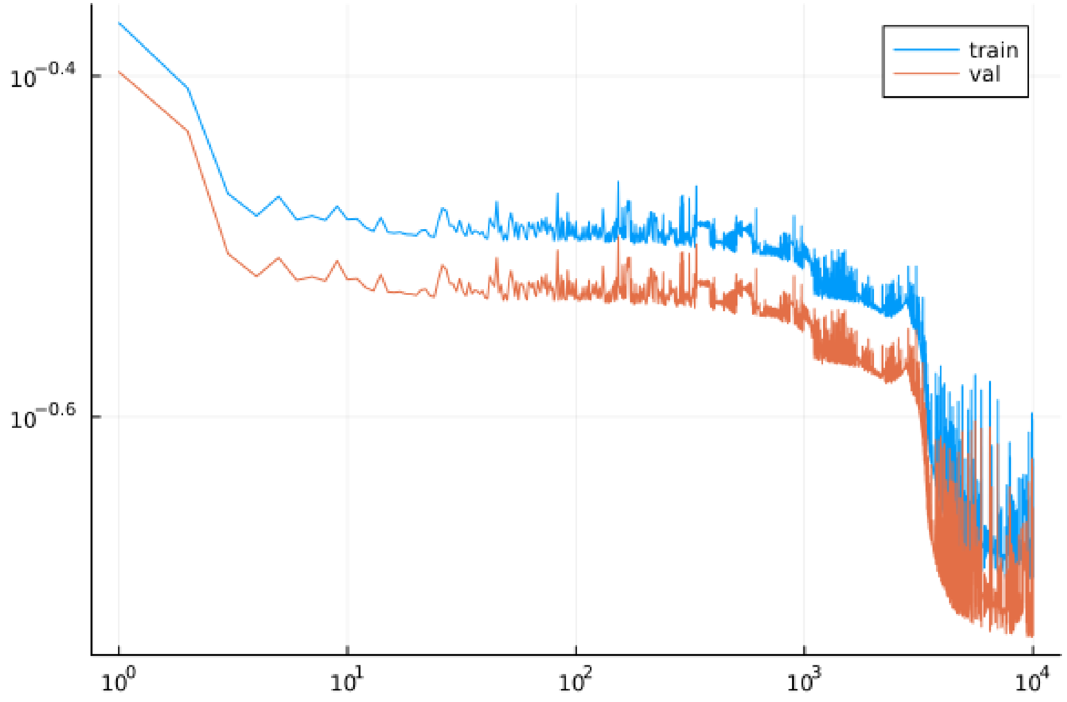
1.2 $A + 2X \rightarrow 3X$

2.3 $2Y \rightarrow A$

$0 \rightarrow Z \rightarrow 0$

0.1 1000

$$
\begin{aligned}
&0.988Z \rightarrow 91.88X + 2.092Z, && k_1 = 1.3 \\
&1.197Y + 0.339Z \rightarrow 0.017A + 42.55X, && k_2 = 5.01 \times 10^{-5} \\
&0.086Y \rightarrow 77.625X + 1.282Z, && k_3 = 2.79 \times 10^{-5} \\
&0 \rightarrow 94.124X + 0.018Y + 1.557Z, && k_4 = 8.09 \times 10^{-5} \\
&0.728Y \rightarrow 0.024A + 91.31X + 5.535Z, && k_5 = 0.003
\end{aligned}
$$



Case 2 : With additional species

Approximating higher order reaction with multiple reactions
with additional species

↓

Each reaction has different structure, but the loss is too high

Why does it not work well?

$$\nu_1^+ X_1 + \nu_2^+ X_2 + \nu_3^+ X_3 \xrightarrow{k} \nu_1^- X_1 + \nu_2^- X_2 + \nu_3^- X_3 + \sum_r \nu_r^- X_r$$

$$\sum_i \nu_i^+ = 3$$

$$X_i + X_j \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Z, \quad (k_{-1} \to \infty)$$

$$X_k + Z \xrightarrow{k_2} \nu_i X_i + \nu_j X_j + \nu_k X_k + \sum_r \nu_r X_r + \nu_z Z$$

$$\nu_1^+ X_1 + \nu_2^+ X_2 + \nu_3^+ X_3 + \nu_4^+ X_4 \xrightarrow{k} \nu_1^- X_1 + \nu_2^- X_2 + \nu_3^- X_3 + \nu_4^- X_4 + \sum_r \nu_r^- X_r$$

$$\sum_i \nu_i^+ = 4$$

$$X_i + X_j \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Z_1,$$

$$X_k + Z_1 \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} Z_2,$$

$$k_{-1} = \mathcal{O}(k_{-2}) \to \infty$$

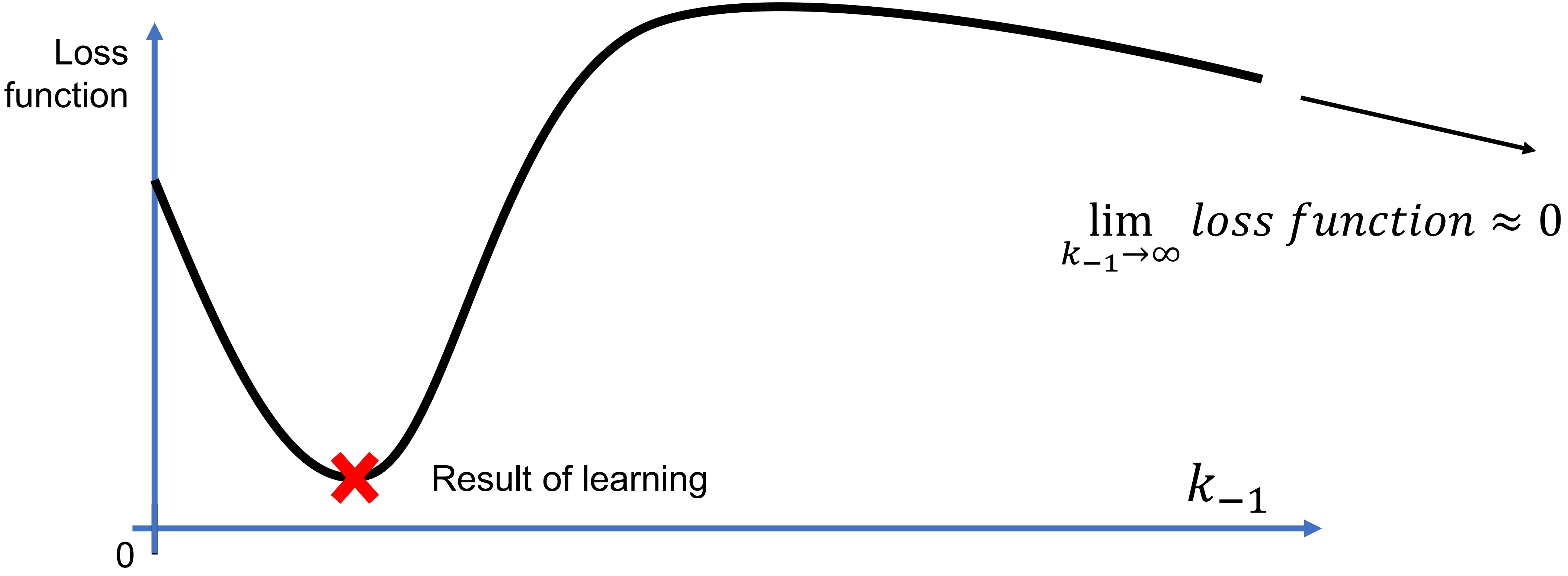
$$X_l + Z_2 \xrightarrow{k_3} \nu_i X_i + \nu_j X_j + \nu_k X_k + \nu_l X_l + \sum_r \nu_r X_r + \nu_{z_1} Z_1 + \nu_{z_2} Z_2$$

Wilhelm, T. Journal of Mathematical Chemistry (2000).

Why does it not work well?

$$X_i + X_j \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Z, \quad (k_{-1} \to \infty)$$

$$X_k + Z \xrightarrow{k_2} \nu_i X_i + \nu_j X_j + \nu_k X_k + \sum_r \nu_r X_r + \nu_z Z$$



One of the parameters should be infinity to find the global minimum, but hard to detect