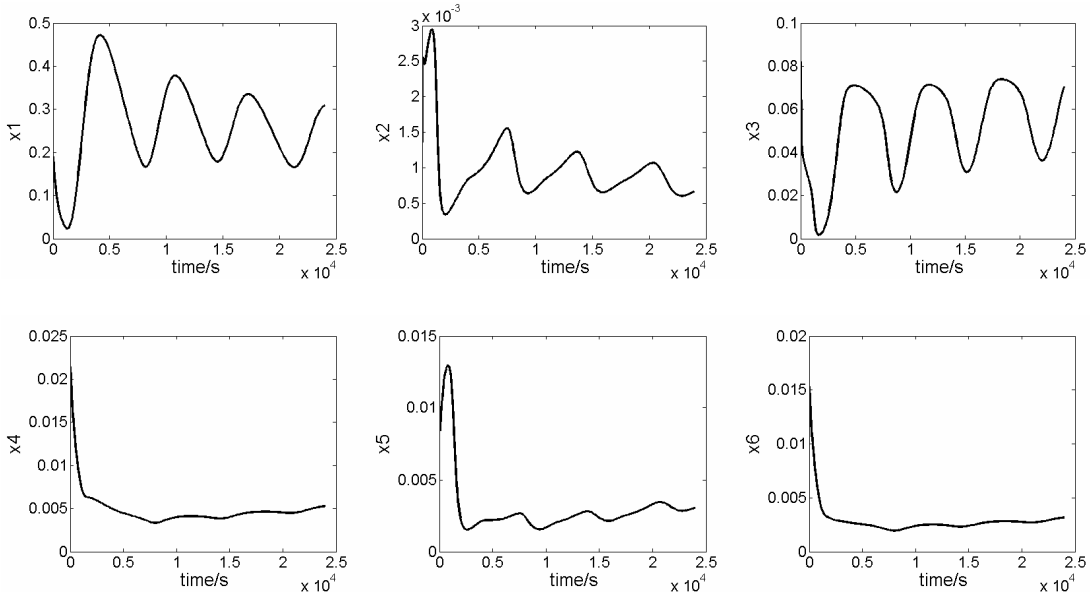
Index	Reactions	Description	Values	Units
1	IκBα + NF-κB → IκBα- NF-κB	IκBα- NF-κB association	0.5_10^{0}	$\mu M^{-1}\ s^{-1}$
2	IκBα- NF-κB→ NF-κB + IκBα	IκBα- NF-κB dissociation	0.5×10^{-3}	s^{-1}
3	IκBβ + NF-κB → IκBβ- NF-κB	IκBβ- NF-κB association	0.5_10^{0}	$\mu M^{-1}\ s^{-1}$
4	IκBβ- NF-κB → NF-κB + IκBβ	IκBβ- NF-κB dissociation	0.5×10^{-3}	s^{-1}
5	IκBε + NF-κB → IκBε- NF-κB	IκBε- NF-κB association	0.5_10^{0}	$\mu M^{-1}\ s^{-1}$
6	IκBε-NF-κB → NF-κB+ IκBε	IκBε- NF-κB dissociation	0.5×10^{-3}	s^{-1}
7	IKKIκBα + NF-κB → IKKIκBα–NF-κB	IKKIκBα–NF-κB association	0.5_10^{0}	$\mu M^{-1}\ s^{-1}$
8	IKKIκBα–NF-κB → NF-κB+ IKKIκBα	IKKIκBα–NF-κB dissociation	0.5×10^{-3}	s^{-1}
9	IKKIκBα-NF-κB→IKK + NF-κB	IKKIκBα–NF-κB catalysis	2.04×10^{-2}	s^{-1}
10	IKKIκBβ + NF-κB → IKKIκBβ–NF-κB	IKKIκBβ–NF-κB association	0.5_10^{0}	$\mu M^{-1}\ s^{-1}$
11	IKKIκBβ–NF-κB → NF-κB+ IKKIκBβ	IKKIκBβ–NF-κB dissociation	0.5×10^{-3}	s^{-1}
12	IKKIκBβ-NF-κB→IKK + NF-κB	IKKIκBβ–NF-κB catalysis	7.5×10^{-3}	s^{-1}
13	IKKIκBε + NF-κB → IKKIκBε–NF-κB	IKKIκBε–NF-κB association	0.5_10^{0}	$\mu M^{-1}\ s^{-1}$
14	IKKIκBε–NF-κB → NF-κB+ IKKIκBε	IKKIκBε–NF-κB dissociation	0.5×10^{-3}	s^{-1}
15	IKKIκBε-NF-κB→IKK + NF-κB	IKKIκBε–NF-κB catalysis	1.1×10^{-2}	s^{-1}
16	IκBα- NF-κB → NF-κB	constitutive IκBα degradation (complexed to NF-κB)	2.25×10^{-5}	s^{-1}
17	IκBβ- NF-κB → NF-κB	constitutive IκBβ degradation (complexed to NF-κB)	2.25×10^{-5}	s^{-1}
18	IκBε- NF-κB → NF-κB	constitutive IκBε degradation (complexed to NF-κB)	2.25×10^{-5}	s^{-1}
19	NF-κB → $NF\text{-}κB_n$	NF-κB nuclear import	0.9×10^{-1}	s^{-1}
20	$NF\text{-}κB_n$ → NF-κB	NF-κB nuclear export	0.8×10^{-4}	s^{-1}
21	$IκBα_n$+ $NF\text{-}κB_n$ → $IκBα_n$- $NF\text{-}κB_n$	IκBα- NF-κB nuclear association	0.5_10^{0}	$\mu M^{-1}\ s^{-1}$
22	$IκBα_n$- $NF\text{-}κB_n$ → $NF\text{-}κB_n$+ $IκBα_n$	IκBα- NF-κB nuclear dissociation	0.5×10^{-3}	s^{-1}
23	$IκBβ_n$+ $NF\text{-}κB_n$ → $IκBβ_n$- $NF\text{-}κB_n$	IκBβ- NF-κB nuclear association	0.5_10^{0}	$\mu M^{-1}\ s^{-1}$
24	$IκBβ_n$- $NF\text{-}κB_n$ → $NF\text{-}κB_n$+ $IκBβ_n$	IκBβ- NF-κB nuclear dissociation	0.5×10^{-3}	s^{-1}
25	$IκBε_n$+ $NF\text{-}κB_n$ → $IκBε_n$- $NF\text{-}κB_n$	IκBε- NF-κB nuclear association	0.5_10^{0}	$\mu M^{-1}\ s^{-1}$
26	$IκBε_n$- $NF\text{-}κB_n$ → $NF\text{-}κB_n$+ $IκBε_n$	IκBε- NF-κB nuclear dissociation	0.5×10^{-3}	s^{-1}
27	source → $IκBα_{-t}$	IκBα constitutive mRNA synthesis	1.54×10^{-6}	$\mu M^{-1}\ s^{-1}$
28	$NF\text{-}κB_n$ + $NF\text{-}κB_n$ → $IκBα_{-t}$ + $NF\text{-}κB_n$ + $NF\text{-}κB_n$	IκBα inducible mRNA synthesis	1.65×10^{-2}	$\mu M^{-1}\ s^{-1}$
29	$IκBα_{-t}$ → sink	IκBα mRNA degradation	2.8×10^{-4}	s^{-1}
30	source → $IκBβ_{-t}$	IκBβ constitutive mRNA synthesis	1.78×10^{-7}	$\mu M^{-1}\ s^{-1}$
31	$IκBβ_{-t}$ → sink	IκBβ mRNA degradation	2.8×10^{-4}	s^{-1}
32	source → $IκBε_{-t}$	IκBε constitutive mRNA synthesis	1.27×10^{-7}	$\mu M^{-1}\ s^{-1}$
33	$IκBε_{-t}$ → sink	IκBε mRNA degradation	2.8×10^{-4}	s^{-1}
34	IKK+ IκBα → IKKIκBα	IKK-IκBα association	22.5×10^{-3}	$\mu M^{-1}\ s^{-1}$
35	IKKIκBα → IKK + IκBα	IKK-IκBα dissociation	1.25×10^{-3}	s^{-1}
36	$IκBα_{-t}$ → IκBα + $IκBα_{-t}$	constitutive IκBα translation rate	4.08×10^{-3}	s^{-1}
37	IκBα → sink	constitutive IκBα degradation (free)	1.13×10^{-4}	s^{-1}
38	IκBα → $IκBα_n$ (Import)	IκBα nuclear import	3×10^{-4}	s^{-1}
39	$IκBα_n$ → IκBα (Export)	IκBα nuclear export	2×10^{-4}	s^{-1}
40	IKK+ IκBβ → IKKIκBβ	IKK-IκBβ association	6.0×10^{-3}	$\mu M^{-1}\ s^{-1}$
41	IKKIκBβ → IKK+ IκBβ	IKK-IκBβ dissociation	1.75×10^{-3}	s^{-1}
42	$IκBβ_{-t}$ → IκBβ + $IκBβ_{-t}$	constitutive IκBβ translation rate	4.08×10^{-3}	s^{-1}
43	IκBβ → sink	constitutive IκBβ degradation (free)	1.13×10^{-4}	s^{-1}

Index	Reactions	Description	Values	Units
44	IκBβ → IκBβ$_n$ (Import)	IκBβ nuclear import	1.5×10^{-4}	s^{-1}
45	IκBβ$_n$ → IκBβ (Export)	IκBβ nuclear export	1×10^{-4}	s^{-1}
46	IKK+ IκBε → IKKIκBε	IKK-IκBε association	9.0×10^{-3}	$\mu M^{-1}\ s^{-1}$
47	IKKIκBε → IKK+ IκBε	IKK-IκBε dissociation	1.75×10^{-3}	s^{-1}
48	IκBε$_{-t}$ → IκBε + IκBε$_{-t}$	constitutive IκBε translation rate	4.08×10^{-3}	s^{-1}
49	IκBε → sink	constitutive IκBε degradation (free)	1.13×10^{-4}	s^{-1}
50	IκBε → IκBε$_n$ (Import)	IκBε nuclear import	1.5×10^{-4}	s^{-1}
51	IκBε$_n$ → IκBε (Export)	IκBε nuclear export	1×10^{-4}	s^{-1}
52	IKK+ IκBα- NF-κB→ IKKIκBα- NF-κB	IKK-IκBαNF-κB association	1.85×10^{-1}	$\mu M^{-1}\ s^{-1}$
53	IKKIκBα- NF-κB → IKK+ IκBα- NF-κB	IKK-IκBαNF-κB dissociation	1.25×10^{-3}	s^{-1}
54	IκBα$_n$- NF-κB$_n$→ IκBα- NF-κB (Export)	IκBα- NF-κB nuclear export	1.38×10^{-2}	s^{-1}
55	IKK+ IκBβ- NF-κB→ IKKIκBβ- NF-κB	IKK-IκBβNF-κB association	4.8×10^{-2}	$\mu M^{-1}\ s^{-1}$
56	IKKIκBβ- NF-κB → IKK+ IκBβ- NF-κB	IKK-IκBβNF-κB dissociation	1.75×10^{-3}	s^{-1}
57	IκBβ$_n$- NF-κB$_n$→ IκBβ- NF-κB (Export)	IκBβ- NF-κB nuclear export	5.2×10^{-3}	s^{-1}
58	IKK+ IκBε- NF-κB→ IKKIκBε- NF-κB	IKK-IκBεNF-κB association	7.0×10^{-2}	$\mu M^{-1}\ s^{-1}$
59	IKKIκBε- NF-κB → IKK+ IκBε- NF-κB	IKK-IκBεNF-κB dissociation	1.75×10^{-3}	s^{-1}
60	IκBε$_n$- NF-κB$_n$→ IκBε- NF-κB (Export)	IκBε- NF-κB nuclear export	5.2×10^{-3}	s^{-1}
61	IKK → sink	Slow adaptation	1.2×10^{-4}	s^{-1}
62	IKKIκBα → IKK	IKK-IκBα catalysis	4.07×10^{-3}	s^{-1}
63	IKKIκBβ → IKK	IKK-IκBβ catalysis	1.5×10^{-3}	s^{-1}
64	IKKIκBε → IKK	IKK-IκBε catalysis	2.2×10^{-3}	s^{-1}

Concentration profiles of the 24 species in the NF-κB signalling pathway



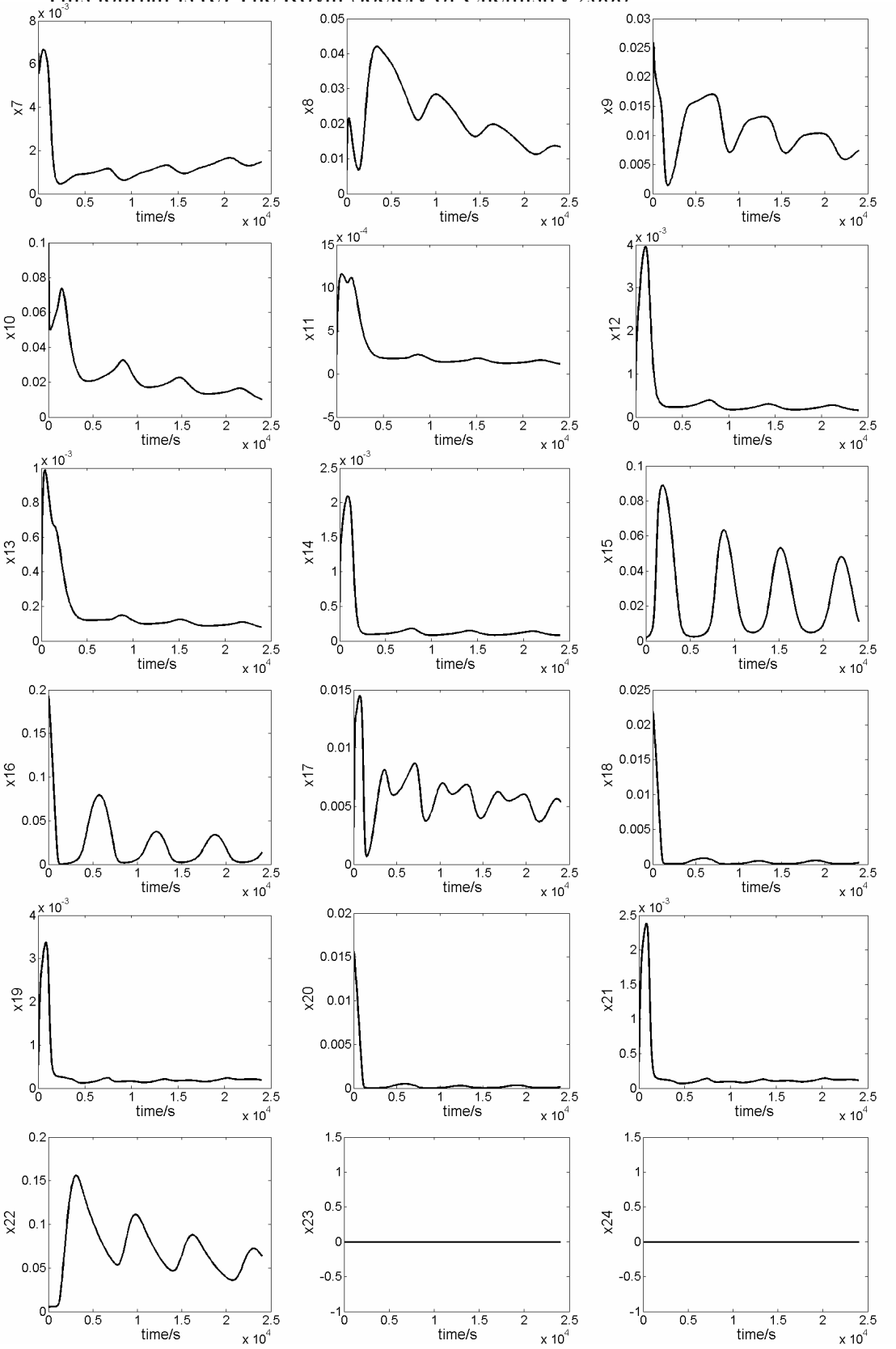


Fig.A1 Concentration profiles of the reaction species in the NF-κB model

Orthogonal procedure for identifiability analysis

1. Calculate the magnitude of each column of $\bar{S}$ by the Euclidean norm **Error! Reference source not found.**. The parameter corresponding to the column with maximum magnitude is the first identifiable parameter. This column is marked as X_L (L=1).

2. Formulate the residual matrix:

$$R_L = \left(I - X_L (X_L^T X_L)^{-1} X_L^T\right) \bar{S} \quad (1)$$

This removes the information contained in the selected columns and also the portion of information contained in the remaining columns that is linearly correlated with the selected columns.

3. Calculate the magnitude of the each column of R_L. The column with the largest magnitude corresponds to the next identifiable parameter because it has the largest effect on the response variables of all the remaining parameters, which is not correlated with the effects of the selected set of parameters.

4. Augment X_L with the column of $\bar{S}$ corresponding to this parameter. The augmented matrix is denoted as X_{L+1}.

5. Increase the iteration counter by 1 and repeat steps 2-4 for all parameters or until the maximum magnitude of the columns of R_L is less than a pre-specified threshold.