An algebraic-numeric algorithm for the model selection in kinetic networks

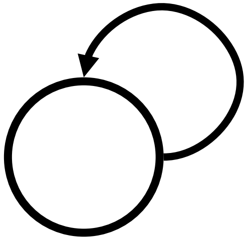
CASC2007, Bonn

Hiroshi Yoshida （Faculty of Math., Kyushu Univ.）
Koji Nakagawa (CBRC, AIST)
Hirokazu Anai (Fujitsu Lab. LTD./CREST JST.)
Katsuhisa Horimoto (CBRC, AIST)

Contents

Background

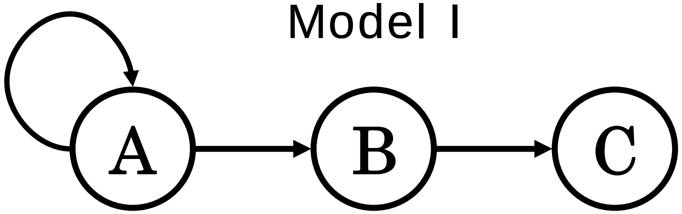
- Metacore: database of networks describing interactions between genes or proteins
- D-sep test: can deal with only directed **acyclic** graph (DAG)



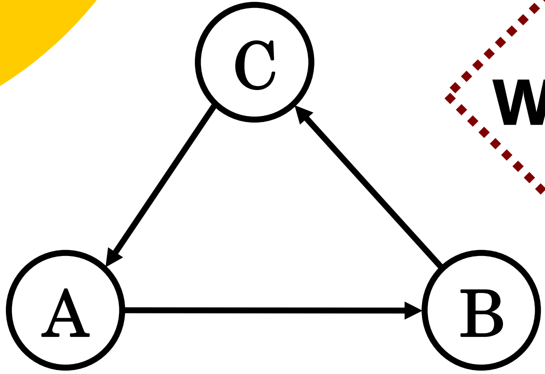
Cannot be dealt with

Aim：selection for the most/more consistent model with the observed data

Model I

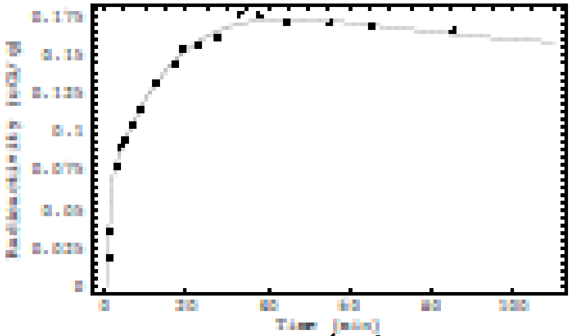


Model II

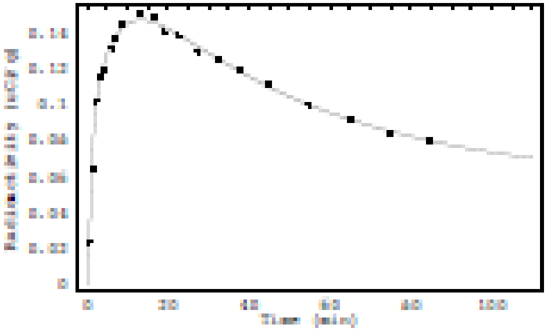


Which is Consistent?

(A)

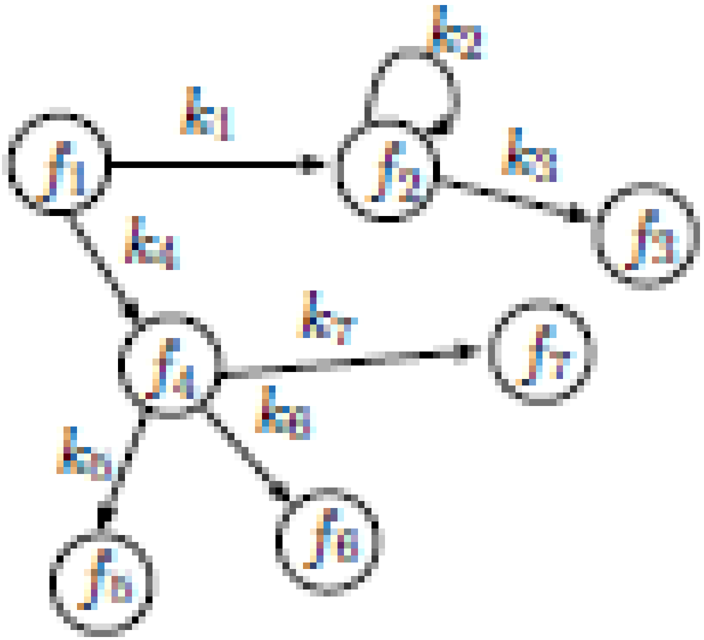


(B)



More…

- To select the model most/more consistent with the given sampling data
- We have performed model selection over Laplace domain using algebraic equations



Model (Example)

$$\frac{d}{dt}SLA(t) = -kSN\ SLA(t)$$

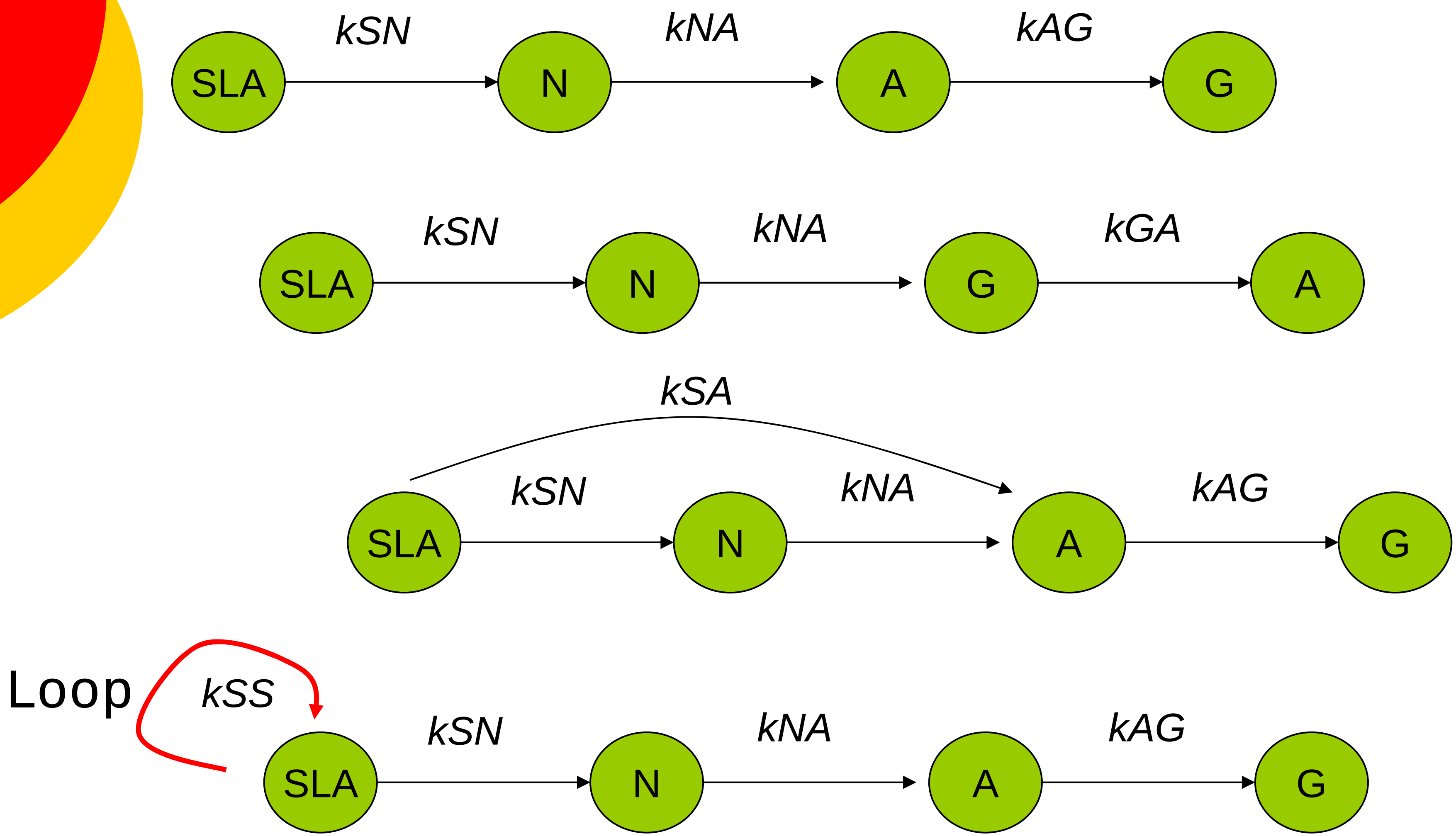
$$\frac{d}{dt}N(t) = kSN\ SLA(t) - kNA\ N(t)$$

$$\frac{d}{dt}A(t) = kNA\ N(t) - kAG\ A(t)$$

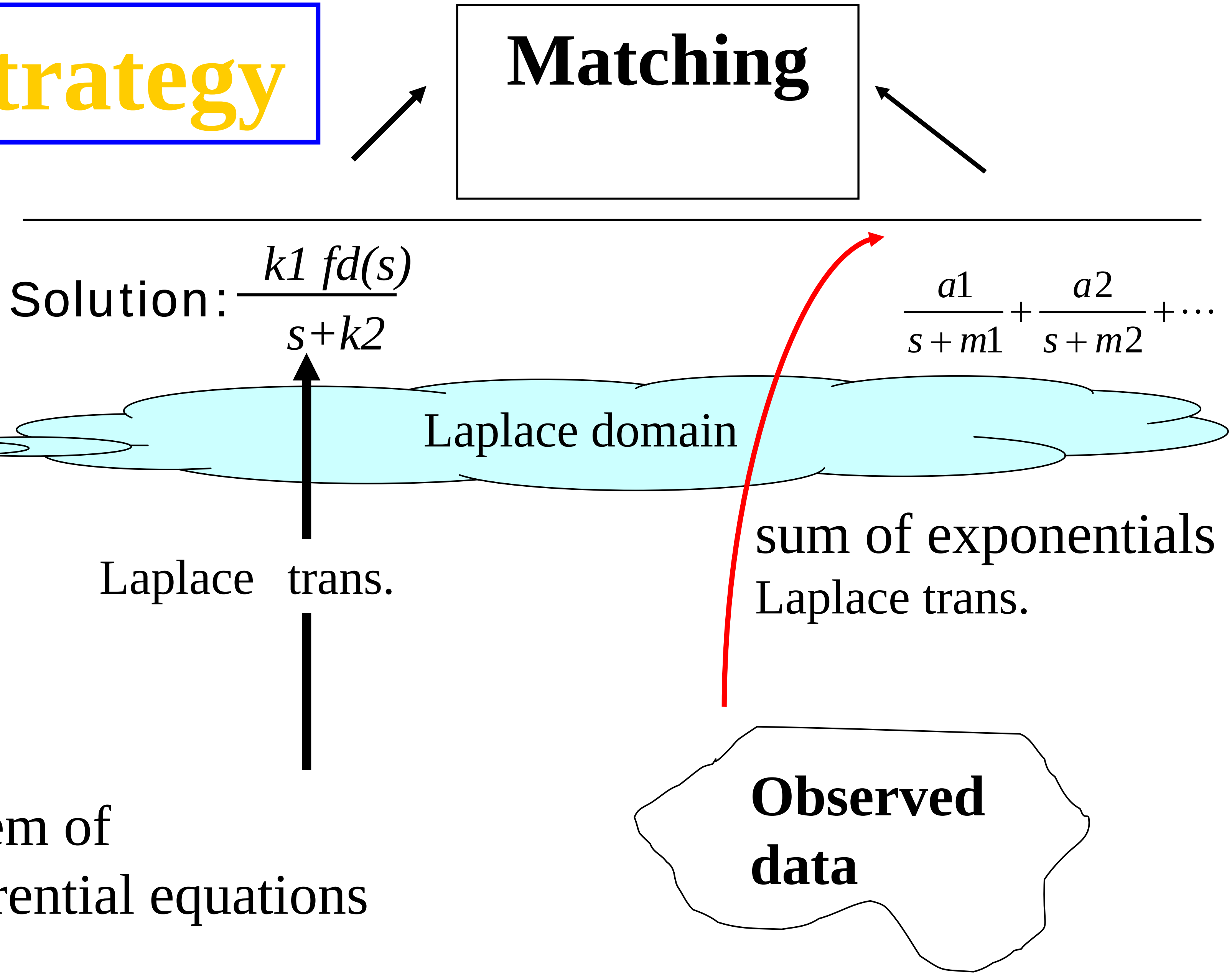
$$\frac{d}{dt}G(t) = kAG\ A(t)$$

Assuming a linear relation between the variables, the kinetics of the above network can be described as the system of deferential equations on the left.

More …


kSN
kNA
kAG
SLA
N
A
G
kSN
kNA
kGA
SLA
N
G
A
kSA
kSN
kNA
kAG
SLA
N
A
G
Loop
kSS
kSN
kNA
kAG
SLA
N
A
G

Strategy



Matching

Solution: $\frac{k1\ fd(s)}{s+k2}$

$$\frac{a1}{s+m1}+\frac{a2}{s+m2}+\cdots$$

Laplace domain

Laplace trans.

sum of exponentials
Laplace trans.

System of
differential equations

**Observed
data**

Method

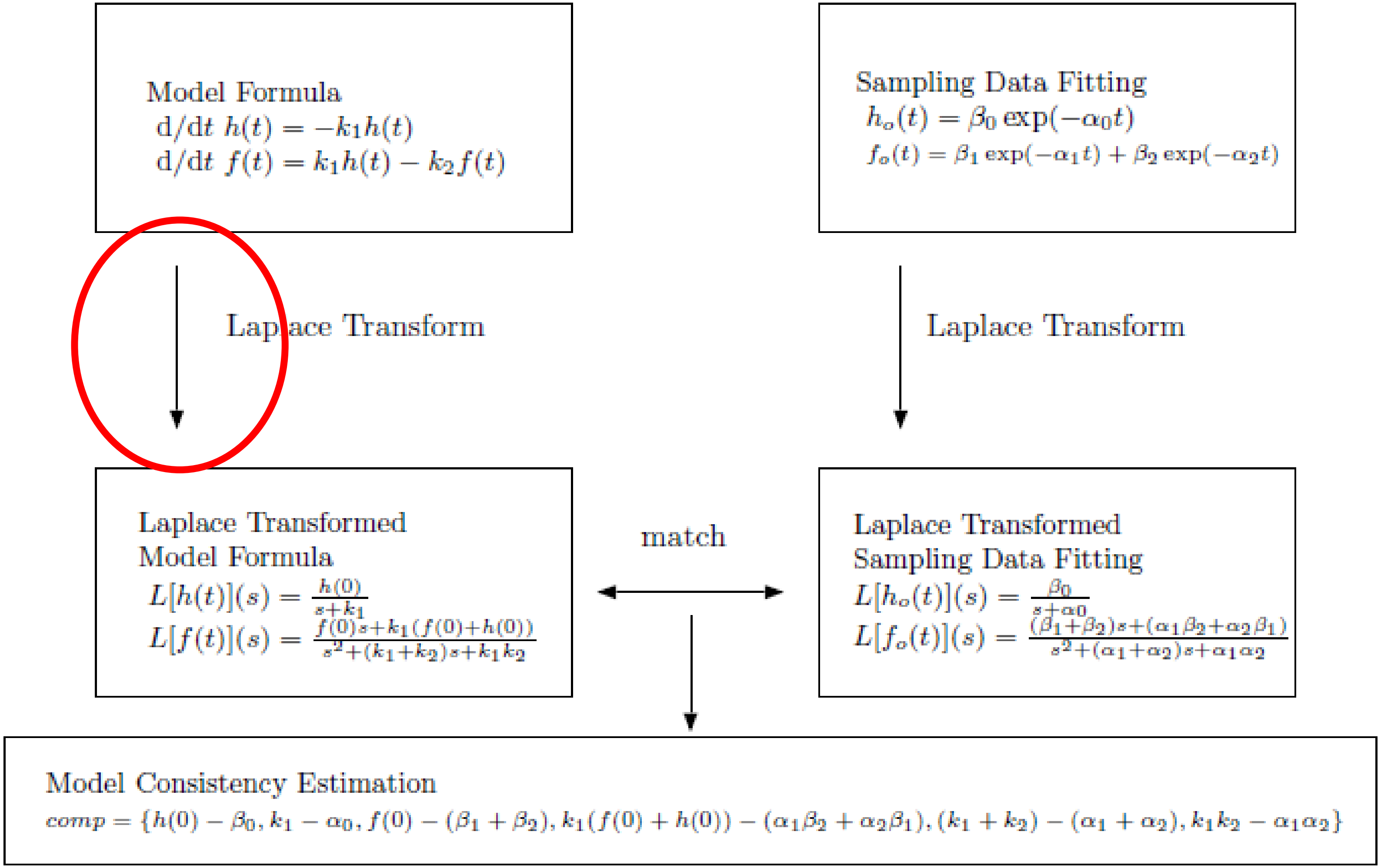
① The kinetics for describing biological phenomena are expressed by a system of differential equations

② The observed data are numerically fitted as a sum of exponentials

③ Both the system of differential equations and the sum of exponentials are transformed into the corresponding system of algebraic equations by Laplace transformation

④ The two systems of algebraic equations are compared according to ***measure***

Consistency estimation (1)



Model Formula

$\mathrm{d/dt}\ h(t) = -k_1 h(t)$

$\mathrm{d/dt}\ f(t) = k_1 h(t) - k_2 f(t)$

Sampling Data Fitting

$h_o(t) = \beta_0 \exp(-\alpha_0 t)$

$f_o(t) = \beta_1 \exp(-\alpha_1 t) + \beta_2 \exp(-\alpha_2 t)$

Laplace Transform

Laplace Transform

Laplace Transformed Model Formula

$L[h(t)](s) = \frac{h(0)}{s+k_1}$

$L[f(t)](s) = \frac{f(0)s+k_1(f(0)+h(0))}{s^2+(k_1+k_2)s+k_1k_2}$

match

Laplace Transformed Sampling Data Fitting

$L[h_o(t)](s) = \frac{\beta_0}{s+\alpha 0}$

$L[f_o(t)](s) = \frac{(\beta_1+\beta_2)s+(\alpha_1\beta_2+\alpha_2\beta_1)}{s^2+(\alpha_1+\alpha_2)s+\alpha_1\alpha_2}$

Model Consistency Estimation

$comp = \{h(0) - \beta_0, k_1 - \alpha_0, f(0) - (\beta_1 + \beta_2), k_1(f(0) + h(0)) - (\alpha_1\beta_2 + \alpha_2\beta_1), (k_1 + k_2) - (\alpha_1 + \alpha_2), k_1k_2 - \alpha_1\alpha_2\}$

Change the system of differential equations into algebraic equations by Laplace transformation

---

- Ex.) The system of algebraic equations

$$\frac{d}{dt}SLA(t) = -kSN\ SLA(t)$$
$$\frac{d}{dt}N(t) = kSN\ SLA(t) - kNA\ N(t)$$
$$\frac{d}{dt}A(t) = kNA\ N(t) - kAG\ A(t)$$
$$\frac{d}{dt}G(t) = kAG\ A(t)$$

- Into polynomials over Laplace domain

$$s\ L[SLA(t)] - SLA(0) = -kSN\ L[SLA(t)]$$
$$s\ L[N(t)] - N(0) = kSN\ L[SLA(t)] - kNA\ L[N(t)]$$
$$s\ L[A(t)] - A(0) = kNA\ L[N(t)] - kAG\ L[A(t)]$$
$$s\ L[G(t)] - G(0) = kAG\ L[A(t)]$$

The solution over Laplace domain is:

$$\mathrm{laplace}(\mathrm{SLA}(t), t, s) = \frac{\mathrm{SLA}(0)}{s + kSN}$$

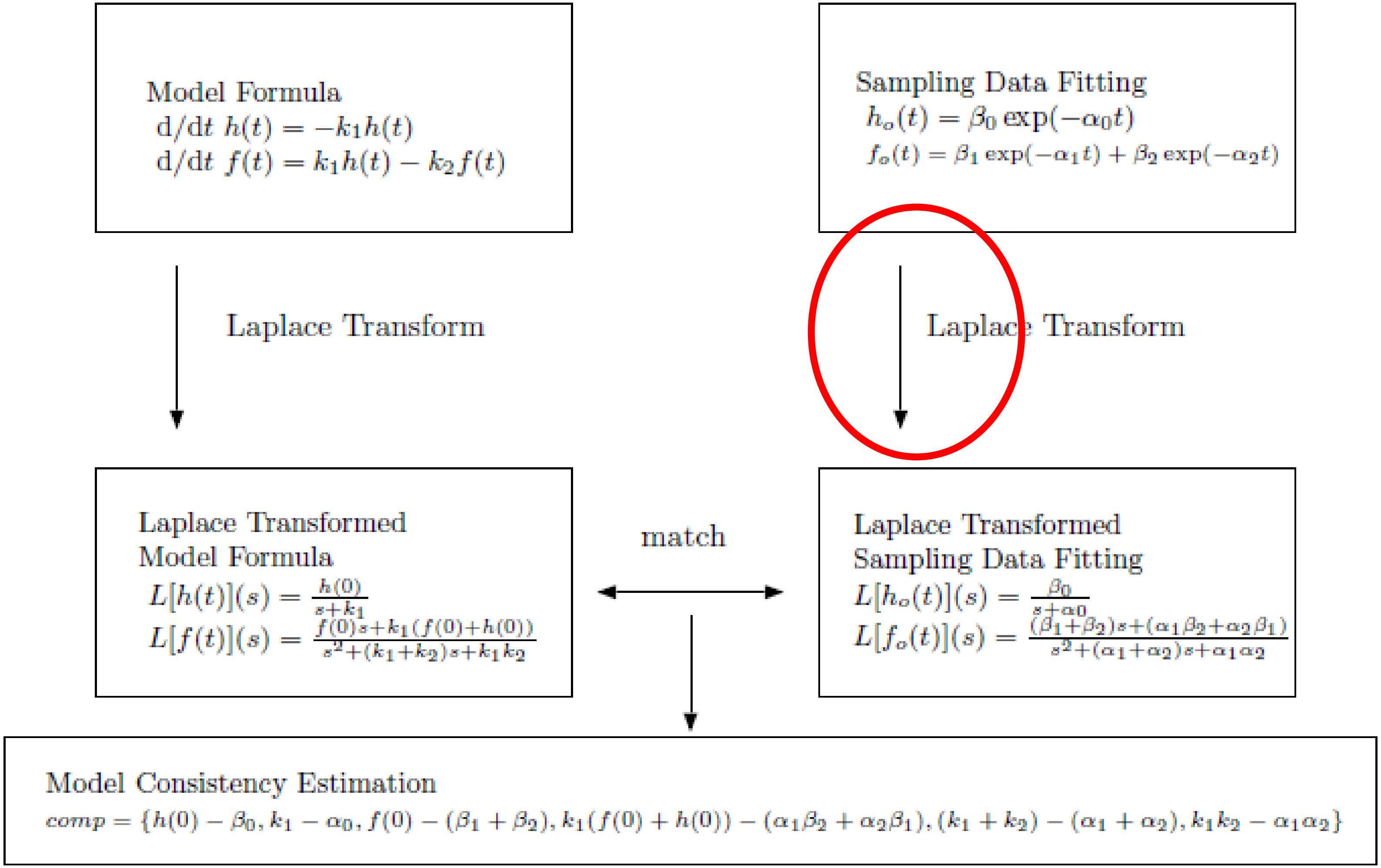
$$\mathrm{laplace}(\mathrm{A}(t), t, s) =$$

$$\frac{\mathrm{A}(0)\ s^2 + (kNA\ \mathrm{N}(0) + \mathrm{A}(0)\ kSN + \mathrm{A}(0)\ kNA)\ s + kNA\ \mathrm{N}(0)\ kSN + kNA\ kSN\ \mathrm{SLA}(0) + \mathrm{A}(0)\ kNA\ kSN}{s^3 + (kAG + kSN + kNA)\ s^2 + (kAG\ kSN + kAG\ kNA + kNA\ kSN)\ s + kAG\ kNA\ kSN}$$

$$\mathrm{laplace}(\mathrm{N}(t), t, s) = \frac{\mathrm{N}(0)\ s + \mathrm{N}(0)\ kSN + kSN\ \mathrm{SLA}(0)}{s^2 + (kSN + kNA)\ s + kNA\ kSN}$$

$$\begin{aligned}\mathrm{laplace}(\mathrm{G}(t), t, s) = {} & (\mathrm{G}(0)\ s^3 + (\mathrm{G}(0)\ kAG + \mathrm{G}(0)\ kNA + kAG\ \mathrm{A}(0) + \mathrm{G}(0)\ kSN)\ s^2 \\ & + (\mathrm{G}(0)\ kAG\ kNA + kAG\ kNA\ \mathrm{N}(0) + \mathrm{G}(0)\ kAG\ kSN + kAG\ \mathrm{A}(0)\ kNA + kAG\ \mathrm{A}(0)\ kSN + \mathrm{G}(0)\ kNA\ kSN)\ s \\ & + kAG\ kNA\ \mathrm{N}(0)\ kSN + kAG\ kNA\ kSN\ \mathrm{SLA}(0) + \mathrm{G}(0)\ kAG\ kNA\ kSN + kAG\ \mathrm{A}(0)\ kNA\ kSN) \Big/ (\\ & s^4 + (kAG + kSN + kNA)\ s^3 + (kAG\ kSN + kAG\ kNA + kNA\ kSN)\ s^2 + s\ kAG\ kNA\ kSN)\end{aligned}$$

Consistency estimation (2)



Model Formula
$\mathrm{d/dt}\ h(t) = -k_1 h(t)$
$\mathrm{d/dt}\ f(t) = k_1 h(t) - k_2 f(t)$

Sampling Data Fitting
$h_o(t) = \beta_0 \exp(-\alpha_0 t)$
$f_o(t) = \beta_1 \exp(-\alpha_1 t) + \beta_2 \exp(-\alpha_2 t)$

Laplace Transform

Laplace Transform

Laplace Transformed
Model Formula
$L[h(t)](s) = \frac{h(0)}{s+k_1}$
$L[f(t)](s) = \frac{f(0)s+k_1(f(0)+h(0))}{s^2+(k_1+k_2)s+k_1k_2}$

match

Laplace Transformed
Sampling Data Fitting
$L[h_o(t)](s) = \frac{\beta_0}{s+\alpha_0}$
$L[f_o(t)](s) = \frac{(\beta_1+\beta_2)s+(\alpha_1\beta_2+\alpha_2\beta_1)}{s^2+(\alpha_1+\alpha_2)s+\alpha_1\alpha_2}$

Model Consistency Estimation
$comp = \{h(0) - \beta_0, k_1 - \alpha_0, f(0) - (\beta_1 + \beta_2), k_1(f(0) + h(0)) - (\alpha_1\beta_2 + \alpha_2\beta_1), (k_1 + k_2) - (\alpha_1 + \alpha_2), k_1k_2 - \alpha_1\alpha_2\}$

Change the observed data into algebraic equations by Laplace transformation

- The observed data are fitted as a sum of exponentials:

$$\sum_{i=1}^{k} \beta_i \exp(-\alpha_i\, t)$$

  - *k* is the number of exponentials which can theoretically be determined
  - Into functions in s over Laplace domain:

$$\sum_{i=1}^{k} \frac{\beta_i}{s+\alpha_i}$$

Previous study: Identifiability problem

- **Cobelli, C**., Foster, D. and Toolo, G.: *Tracer Kinetics in Biomedical research: From data to model*, Kluwer Academic/Plenum Publishers, 2000.

$$\frac{dy}{dt} = -k2 \cdot y$$

$$\frac{dy}{dt} = -(k2 + k3)y$$

Both data are fitted as: *a exp(-m t)*

***k2* =m, uniquely determined**

globally identifiable

***k2+k3=m* …. unidentifiable**

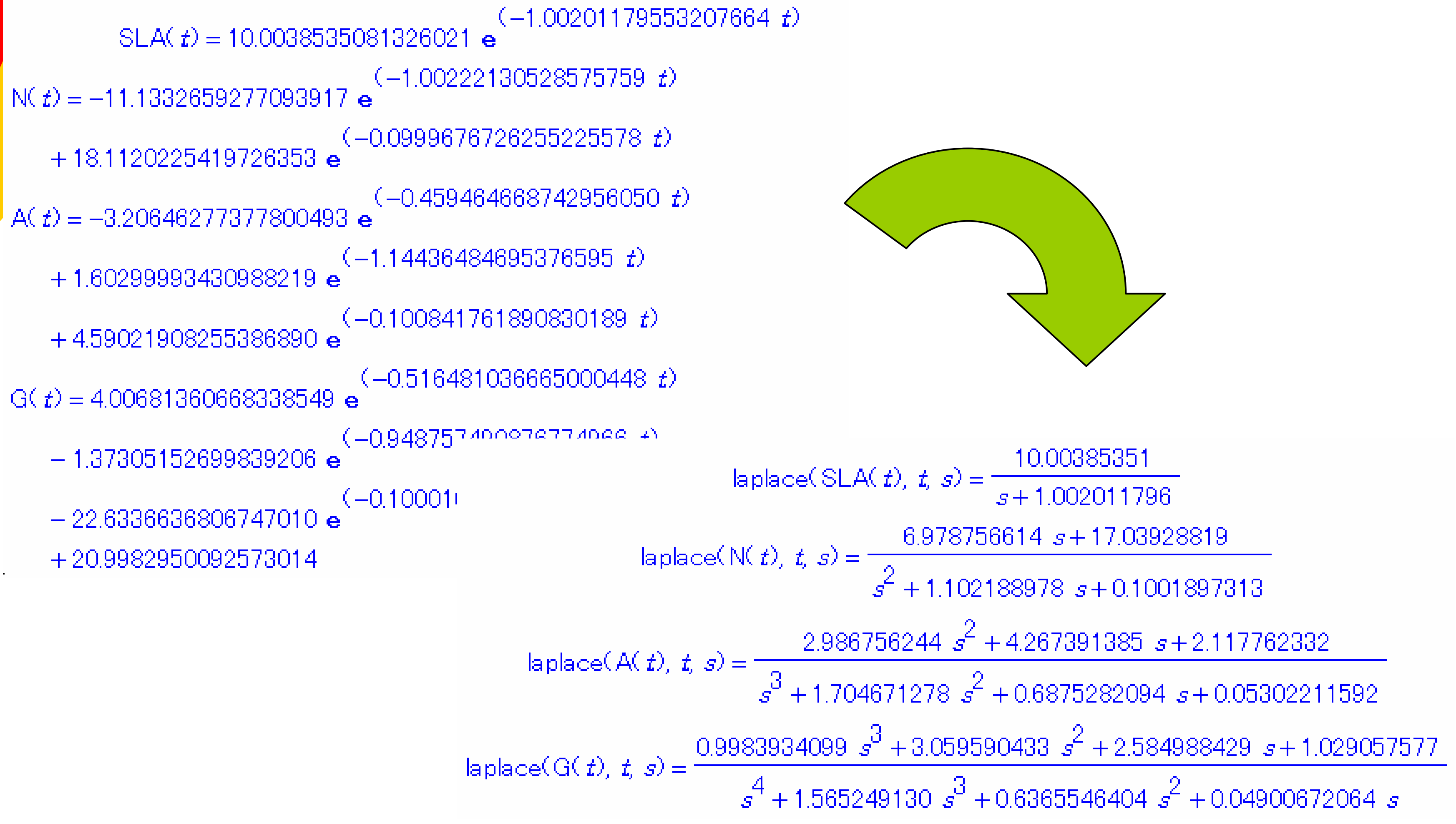
On the assumption of error-free data, … unrealistic situation

Our model: we handle noisy data

- We take the position that it is sufficient to fit a noisy observed data as a sum of exponentials:

$$a1e^{-m1t} + a2e^{-m2t} + a3e^{-m3t} + \cdots$$

Example: the observed data into Laplace domain



$$SLA(t) = 10.0038535081326021\, e^{(-1.00201179553207664\ t)}$$

$$N(t) = -11.1332659277093917\, e^{(-1.00222130528575759\ t)} + 18.1120225419726353\, e^{(-0.0999676726255225578\ t)}$$

$$A(t) = -3.20646277377800493\, e^{(-0.459464668742956050\ t)} + 1.60299993430988219\, e^{(-1.14436484695376595\ t)} + 4.59021908255386890\, e^{(-0.100841761890830189\ t)}$$

$$G(t) = 4.00681360668338549\, e^{(-0.516481036665000448\ t)} - 1.37305152699839206\, e^{(-0.94875} - 22.6336636806747010\, e^{(-0.10001} + 20.9982950092573014$$

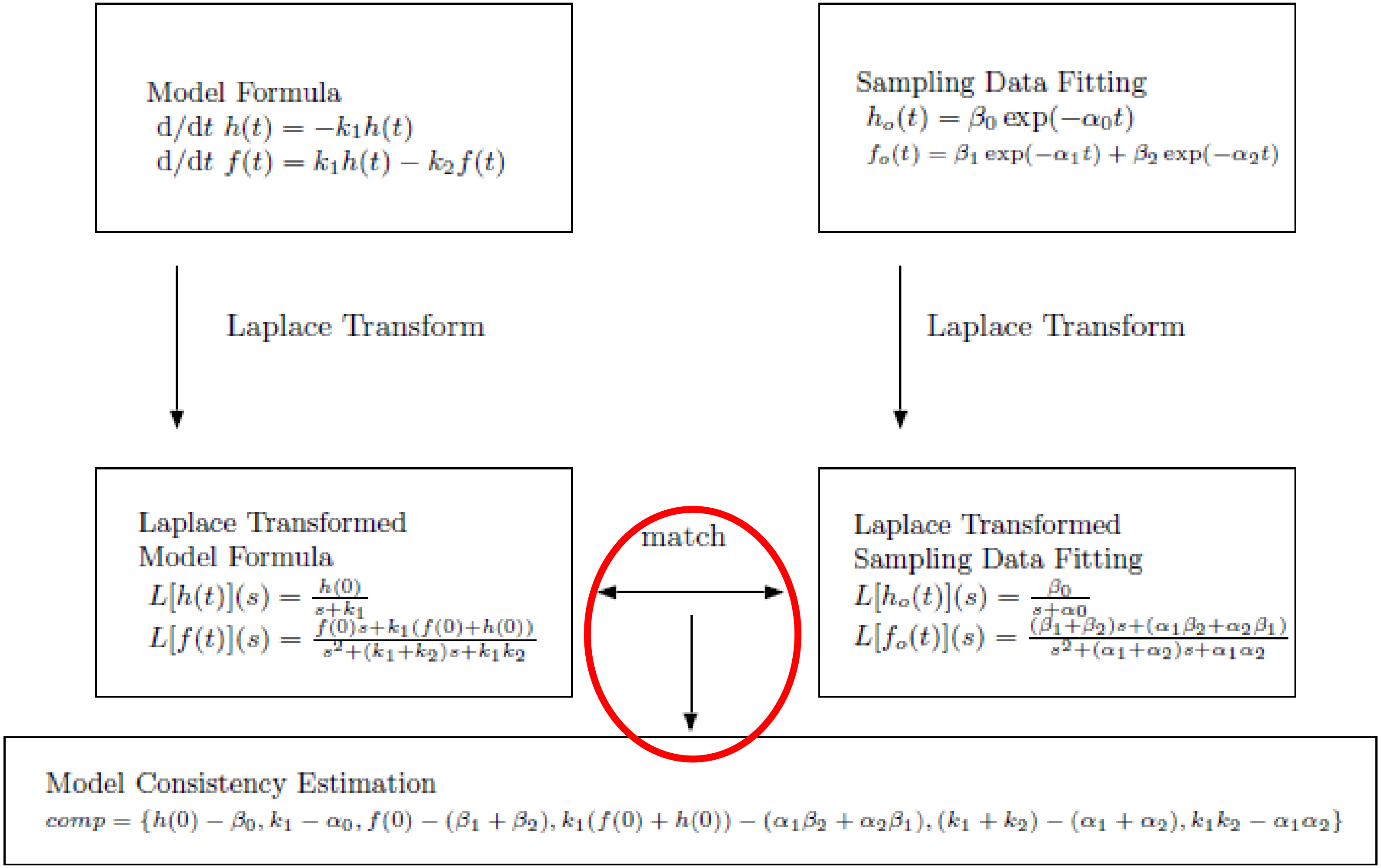
$$\mathrm{laplace}(SLA(t), t, s) = \frac{10.00385351}{s + 1.002011796}$$

$$\mathrm{laplace}(N(t), t, s) = \frac{6.978756614\ s + 17.03928819}{s^2 + 1.102188978\ s + 0.1001897313}$$

$$\mathrm{laplace}(A(t), t, s) = \frac{2.986756244\ s^2 + 4.267391385\ s + 2.117762332}{s^3 + 1.704671278\ s^2 + 0.6875282094\ s + 0.05302211592}$$

$$\mathrm{laplace}(G(t), t, s) = \frac{0.99839340999\ s^3 + 3.059590433\ s^2 + 2.584988429\ s + 1.029057577}{s^4 + 1.565249130\ s^3 + 0.6365546404\ s^2 + 0.04900672064\ s}$$

Consistency estimation procedure (3)



Model Formula

$\mathrm{d/dt}\ h(t) = -k_1 h(t)$

$\mathrm{d/dt}\ f(t) = k_1 h(t) - k_2 f(t)$

Sampling Data Fitting

$h_o(t) = \beta_0 \exp(-\alpha_0 t)$

$f_o(t) = \beta_1 \exp(-\alpha_1 t) + \beta_2 \exp(-\alpha_2 t)$

Laplace Transform

Laplace Transform

Laplace Transformed
Model Formula

$L[h(t)](s) = \frac{h(0)}{s+k_1}$

$L[f(t)](s) = \frac{f(0)s+k_1(f(0)+h(0))}{s^2+(k_1+k_2)s+k_1k_2}$

match

Laplace Transformed
Sampling Data Fitting

$L[h_o(t)](s) = \frac{\beta_0}{s+\alpha 0}$

$L[f_o(t)](s) = \frac{(\beta_1+\beta_2)s+(\alpha_1\beta_2+\alpha_2\beta_1)}{s^2+(\alpha_1+\alpha_2)s+\alpha_1\alpha_2}$

Model Consistency Estimation

$comp = \{h(0) - \beta_0, k_1 - \alpha_0, f(0) - (\beta_1 + \beta_2), k_1(f(0) + h(0)) - (\alpha_1\beta_2 + \alpha_2\beta_1), (k_1 + k_2) - (\alpha_1 + \alpha_2), k_1k_2 - \alpha_1\alpha_2\}$

Comparison of coefficient List in s

- Derive the coefficient List by comparing the algebraic equations of the model and the observed data over Laplace domain:

$$\mathrm{laplace}(\mathrm{SLA}(t), t, s) = \frac{\mathrm{SLA}(0)}{s + kSN}$$

$$\mathrm{laplace}(\mathrm{A}(t), t, s) =$$

$$\frac{\mathrm{A}(0)\, s^2 + (kNA\, \mathrm{N}(0) + \mathrm{A}(0)\, kSN + \mathrm{A}(0)\, kNA)\, s + kNA\, \mathrm{N}(0)\, kSN + kNA\, kSN\, \mathrm{SLA}(0) + \mathrm{A}(0)\, kNA\, kSN}{s^3 + (kAG + kSN + kNA)\, s^2 + (kAG\, kSN + kAG\, kNA + kNA\, kSN)\, s + kAG\, kNA\, kSN}$$

$$\mathrm{laplace}(\mathrm{N}(t), t, s) = \frac{\mathrm{N}(0)\, s + \mathrm{N}(0)\, kSN + kSN\, \mathrm{SLA}(0)}{s^2 + (kSN + kNA)\, s + kNA\, kSN}$$

$$\begin{aligned}\mathrm{laplace}(\mathrm{G}(t), t, s) = {} & (\mathrm{G}(0)\, s^3 + (\mathrm{G}(0)\, kAG + \mathrm{G}(0)\, kNA + kAG\, \mathrm{A}(0) + \mathrm{G}(0)\, kSN)\, s^2 \\ & + (\mathrm{G}(0)\, kAG\, kNA + kAG\, kNA\, \mathrm{N}(0) + \mathrm{G}(0)\, kAG\, kSN + kAG\, \mathrm{A}(0)\, kNA + kAG\, \mathrm{A}(0)\, kSN + \mathrm{G}(0)\, kNA\, kSN) \\ & + kAG\, kNA\, \mathrm{N}(0)\, kSN + kAG\, kNA\, kSN\, \mathrm{SLA}(0) + \mathrm{G}(0)\, kAG\, kNA\, kSN + kAG\, \mathrm{A}(0)\, kNA\, kSN) \Big/ (\\ & s^4 + (kAG + kSN + kNA)\, s^3 + (kAG\, kSN + kAG\, kNA + kNA\, kSN)\, s^2 + s\, kAG\, kNA\, kSN)\end{aligned}$$

$$\mathrm{laplace}(\mathrm{SLA}(t), t, s) = \frac{10.00385351}{s + 1.002011796}$$

$$\mathrm{laplace}(\mathrm{N}(t), t, s) = \frac{6.978756614\, s + 17.03928819}{s^2 + 1.102188978\, s + 0.1001897313}$$

$$\mathrm{laplace}(\mathrm{A}(t), t, s) = \frac{2.986756244\, s^2 + 4.267391385\, s + 2.117762332}{s^3 + 1.704671278\, s^2 + 0.6875282094\, s + 0.05302211592}$$

$$\mathrm{laplace}(\mathrm{G}(t), t, s) = \frac{0.9983934099\, s^3 + 3.059590433\, s^2 + 2.584988429\, s + 1.029057577}{s^4 + 1.565249130\, s^3 + 0.6365546404\, s^2 + 0.04900672064\, s}$$

Ex.) Coefficient List

- Without any error, these polynomials would be zero, but in the case of real noisy observed data, unfortunately not zero… => Least squares method (LSM)

$$kAG\ kNA\ kSN = 0.04900672064$$

$$kSN = 1.002011795532076640$$

$$16.98261012\ kSN = 17.03928819$$

$$20.96775977\ kAG\ kNA\ kSN = 1.029057577$$

$$10.96390626\ kAG\ kNA + 3.985149653\ kAG\ kSN + 0.99839341\ kNA\ kSN = 2.58498843$$

$$kAG\ kSN + kAG\ kNA + kNA\ kSN = 0.6875282094$$

$$kAG + kSN + kNA = 1.704671278$$

$$kAG\ kSN + kAG\ kNA + kNA\ kSN = 0.6365546405$$

$$kAG + kSN + kNA = 1.565249130$$

$$3.985149653\ kAG + 0.99839341\ kNA + 0.99839341\ kSN = 3.059590448$$

$$kNA\ kSN = 0.1001897313$$

$$kSN + kNA = 1.102188978$$

$$kAG\ kNA\ kSN = 0.05302211591$$

$$9.965512853\ kNA + 2.986756243\ kSN = 4.267391383$$

$$19.96936636\ kNA\ kSN = 2.117762332$$

Consistency measure:

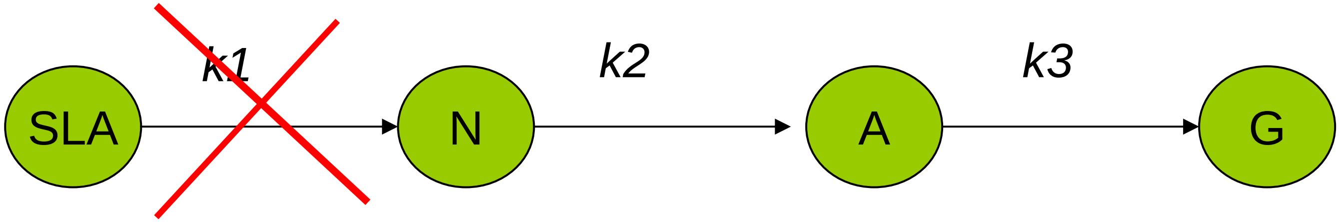
- The ***smallest*** sum-square value of the elements in Coefficient List under

$$k1 > 0,\ k2 > 0,\ .....,\ kn > 0 \quad (1)$$

Or

$$k1 >= 0,\ k2 >= 0,\ .....,\ kn >= 0 \quad (2)$$

If e.g. $k1 = 0$ ... *subnetwork*



Concrete procedure

- Coefficient List:

$$l_1(\vec{k}) = r_1, \cdots, l_n(\vec{k}) = r_n$$

- The consistency measure can be calculated as the smallest values of ***f(k)*** among various ***ks*** : => Least squares method:

$$f(\vec{k}) = \sum_{i=1}^{n} (l_i(\vec{k}) - r_i)^2$$

Measures (1) and (2)

- Under ***ki* > *0*** … Measure (1)

$$\frac{\partial f}{\partial k_1} = 0 \wedge \cdots \wedge \frac{\partial f}{\partial k_n} = 0$$

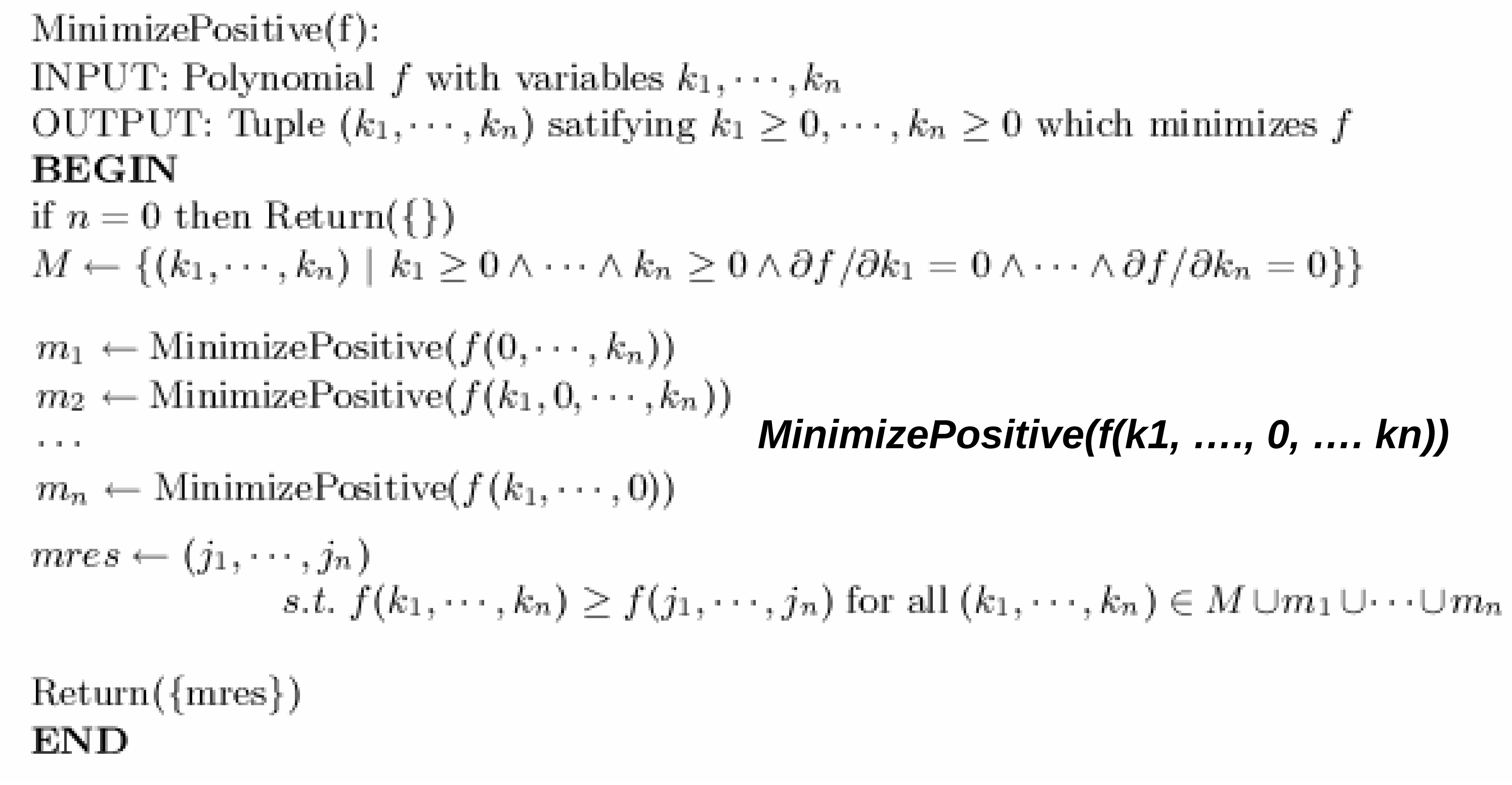
- Under ***ki* >= *0*** … Measure (2)

$$\frac{\partial f}{\partial k_1} = 0 \wedge \cdots \wedge \frac{\partial f}{\partial k_n} = 0$$

Including subnetworks

Algorithm to compute the measure (2) (Recursive procedure)

MinimizePositive.. Compute the measure (1)



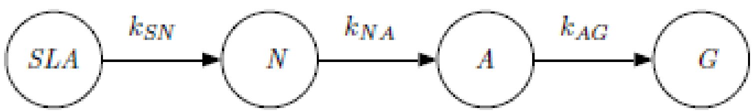
```
MinimizePositive(f):
INPUT: Polynomial $f$ with variables $k_1, \cdots, k_n$
OUTPUT: Tuple $(k_1, \cdots, k_n)$ satifying $k_1 \geq 0, \cdots, k_n \geq 0$ which minimizes $f$
BEGIN
if $n = 0$ then Return({})
$M \leftarrow \{(k_1, \cdots, k_n) \mid k_1 \geq 0 \wedge \cdots \wedge k_n \geq 0 \wedge \partial f / \partial k_1 = 0 \wedge \cdots \wedge \partial f / \partial k_n = 0\}$

$m_1 \leftarrow$ MinimizePositive($f(0, \cdots, k_n)$)
$m_2 \leftarrow$ MinimizePositive($f(k_1, 0, \cdots, k_n)$)
$\cdots$
$m_n \leftarrow$ MinimizePositive($f(k_1, \cdots, 0)$)

$mres \leftarrow (j_1, \cdots, j_n)$
            $s.t.\ f(k_1, \cdots, k_n) \geq f(j_1, \cdots, j_n)$ for all $(k_1, \cdots, k_n) \in M \cup m_1 \cup \cdots \cup m_n$

Return({mres})
END
```

MinimizePositive(f(k1, …., 0, …. kn))

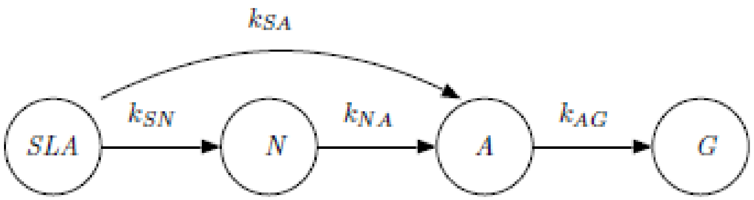
Result

We used the following five models

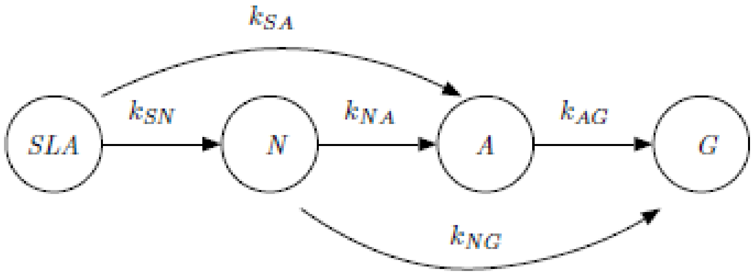
Model A:



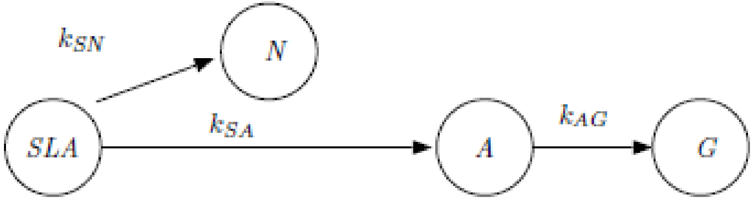
Model B:



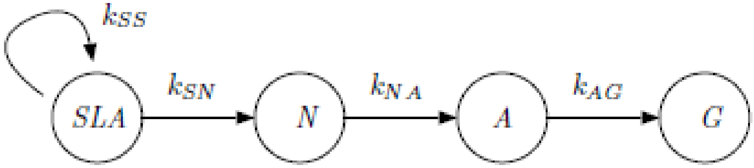
Model C:



Model D:

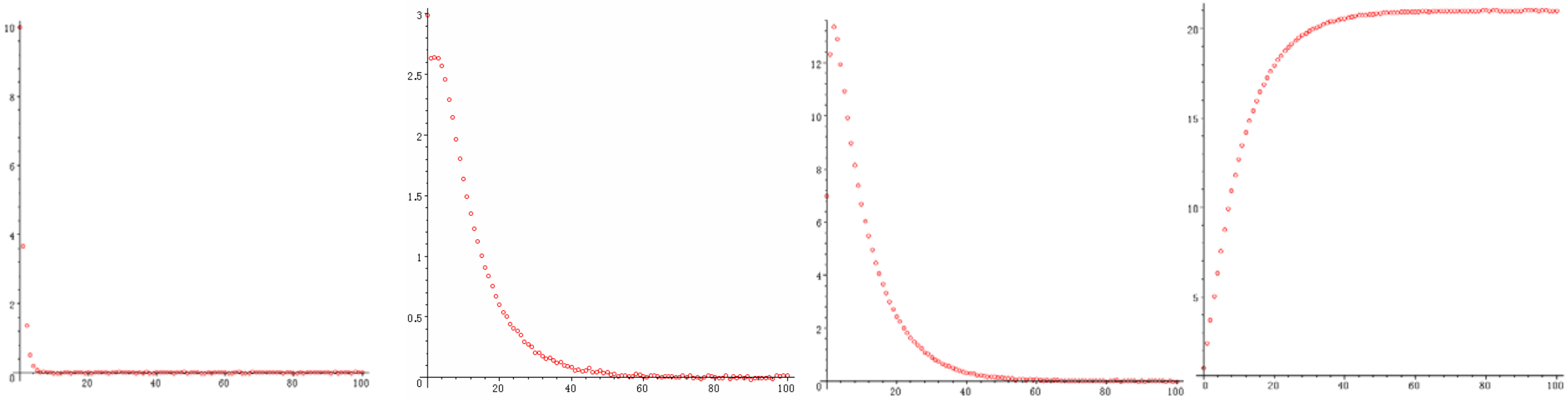


Model E:



Data generation for simulation

We have generated the time series of data for the consistent molecules for the simulation study, before the model consistency estimation.

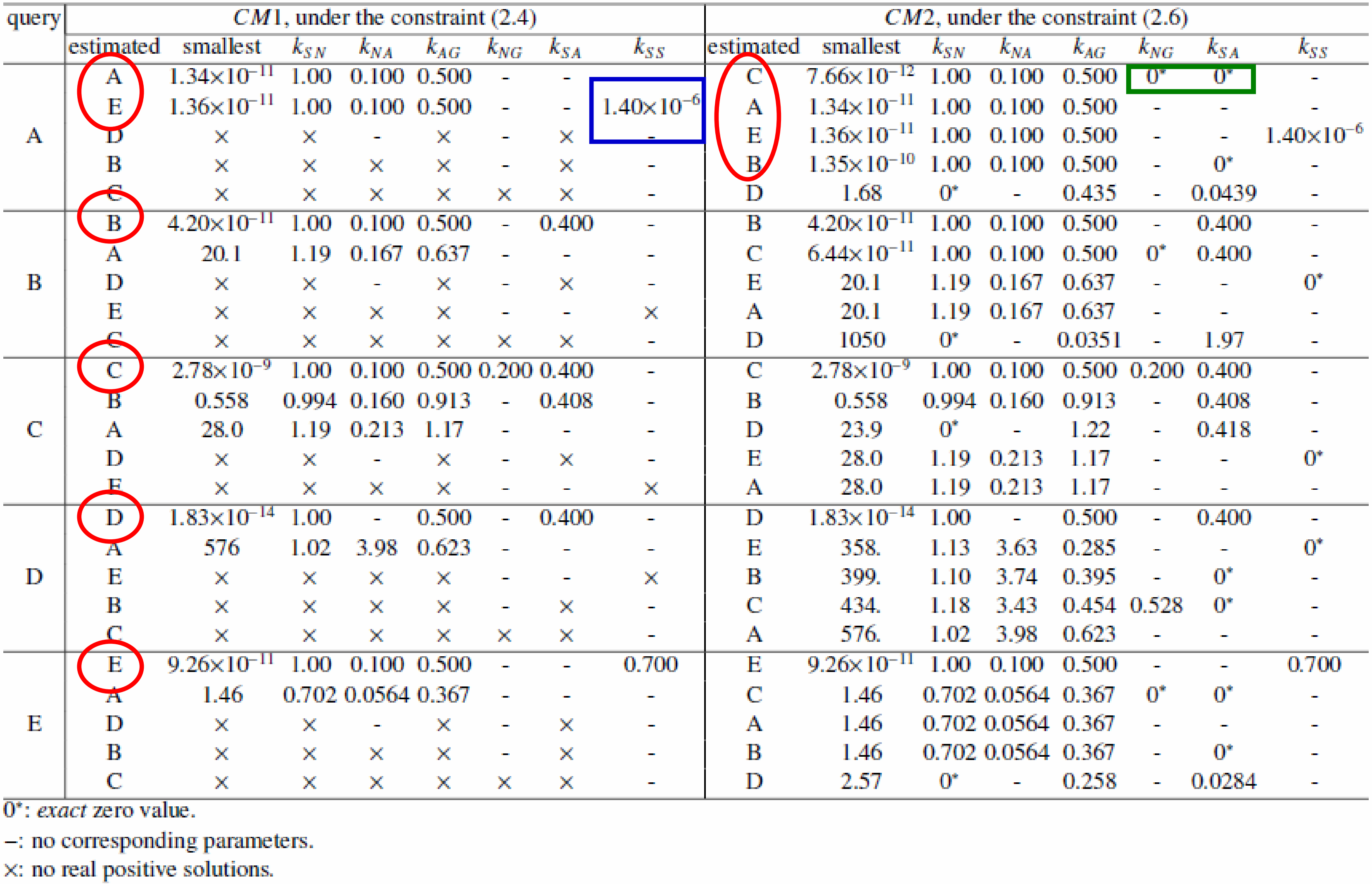


The given and estimated parameters
are as follows: *S LA*;1, 1 (given) and 1.00 (estimated); *S LA*;1, 10 and 10.0; *N*;1, 1/10 and 0.100; *N*;2, 1 and 1.00; *N*;1, 163/9 and 18.1; *N*;2, 100/9 and 11.1; *A*;1, 1/10 and 0.100; *A*;2, 1/2 and 0.500; *A*;3, 1 and 1.00; *A*;1, 163/36 and 4.53; *A*;2, □15=4 and □3:75; *A*;3, 20/9 and 2.22; *G*;1, 1/10 and 0.100; *G*;2, 1/2 and 0.500; *G*;3, 1 and 1.00; *G*;1, □815=36 and □22:6; *G*;2, 15/4 and 3.75; *G*;3, □10=9 and □1:11; *G*;4, 21 and 21.0. Each figure corresponds to the four variables (molecules) in the model: (a) *S LA*, (b) *N*, (c) *A*, (d) *G*.

Table of Consistency measure

Measure (1)

Measure (2).. Including subnetworks



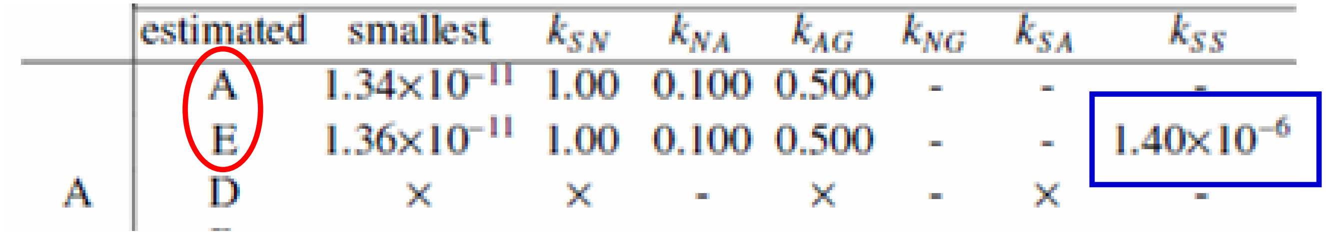
query	*CM*1, under the constraint (2.4)								*CM*2, under the constraint (2.6)							
	estimated	smallest	k_{SN}	k_{NA}	k_{AG}	k_{NG}	k_{SA}	k_{SS}	estimated	smallest	k_{SN}	k_{NA}	k_{AG}	k_{NG}	k_{SA}	k_{SS}
A	A	1.34×10^{-11}	1.00	0.100	0.500	-	-		C	7.66×10^{-12}	1.00	0.100	0.500	0^*	0^*	-
	E	1.36×10^{-11}	1.00	0.100	0.500	-	-	1.40×10^{-6}	A	1.34×10^{-11}	1.00	0.100	0.500	-	-	-
	D	×	×	-	×	-	×	-	E	1.36×10^{-11}	1.00	0.100	0.500	-	-	1.40×10^{-6}
	B	×	×	×	×	-	×	-	B	1.35×10^{-10}	1.00	0.100	0.500	-	0^*	-
	C	×	×	×	×	×	×	-	D	1.68	0^*	-	0.435	-	0.0439	-
B	B	4.20×10^{-11}	1.00	0.100	0.500	-	0.400	-	B	4.20×10^{-11}	1.00	0.100	0.500	-	0.400	-
	A	20.1	1.19	0.167	0.637	-	-	-	C	6.44×10^{-11}	1.00	0.100	0.500	0^*	0.400	-
	D	×	×	-	×	-	×	-	E	20.1	1.19	0.167	0.637	-	-	0^*
	E	×	×	×	×	-	-	×	A	20.1	1.19	0.167	0.637	-	-	-
	C	×	×	×	×	×	×	-	D	1050	0^*	-	0.0351	-	1.97	-
C	C	2.78×10^{-9}	1.00	0.100	0.500	0.200	0.400	-	C	2.78×10^{-9}	1.00	0.100	0.500	0.200	0.400	-
	B	0.558	0.994	0.160	0.913	-	0.408	-	B	0.558	0.994	0.160	0.913	-	0.408	-
	A	28.0	1.19	0.213	1.17	-	-	-	D	23.9	0^*	-	1.22	-	0.418	-
	D	×	×	-	×	-	×	-	E	28.0	1.19	0.213	1.17	-	-	0^*
	E	×	×	×	×	-	-	×	A	28.0	1.19	0.213	1.17	-	-	-
D	D	1.83×10^{-14}	1.00	-	0.500	-	0.400	-	D	1.83×10^{-14}	1.00	-	0.500	-	0.400	-
	A	576	1.02	3.98	0.623	-	-	-	E	358.	1.13	3.63	0.285	-	-	0^*
	E	×	×	×	×	-	-	×	B	399.	1.10	3.74	0.395	-	0^*	-
	B	×	×	×	×	-	×	-	C	434.	1.18	3.43	0.454	0.528	0^*	-
	C	×	×	×	×	×	×	-	A	576.	1.02	3.98	0.623	-	-	-
E	E	9.26×10^{-11}	1.00	0.100	0.500	-	-	0.700	E	9.26×10^{-11}	1.00	0.100	0.500	-	-	0.700
	A	1.46	0.702	0.0564	0.367	-	-	-	C	1.46	0.702	0.0564	0.367	0^*	0^*	-
	D	×	×	-	×	-	×	-	A	1.46	0.702	0.0564	0.367	-	-	-
	B	×	×	×	×	-	×	-	B	1.46	0.702	0.0564	0.367	-	0^*	-
	C	×	×	×	×	×	×	-	D	2.57	0^*	-	0.258	-	0.0284	-

0^*: *exact* zero value.

−: no corresponding parameters.

×: no real positive solutions.

The verification of our method , Measure 1

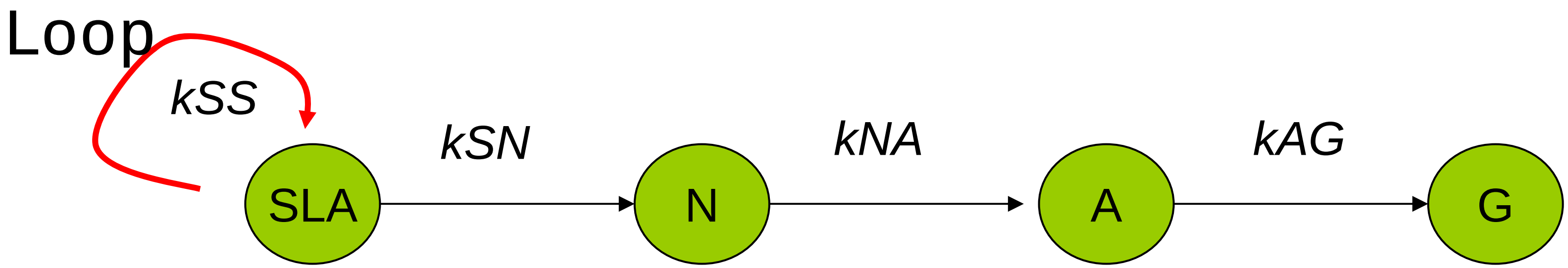


	estimated	smallest	k_{SN}	k_{NA}	k_{AG}	k_{NG}	k_{SA}	k_{SS}
	A	1.34×10^{-11}	1.00	0.100	0.500	-	-	-
	E	1.36×10^{-11}	1.00	0.100	0.500	-	-	1.40×10^{-6}
A	D	×	×	-	×	-	×	-

Model A

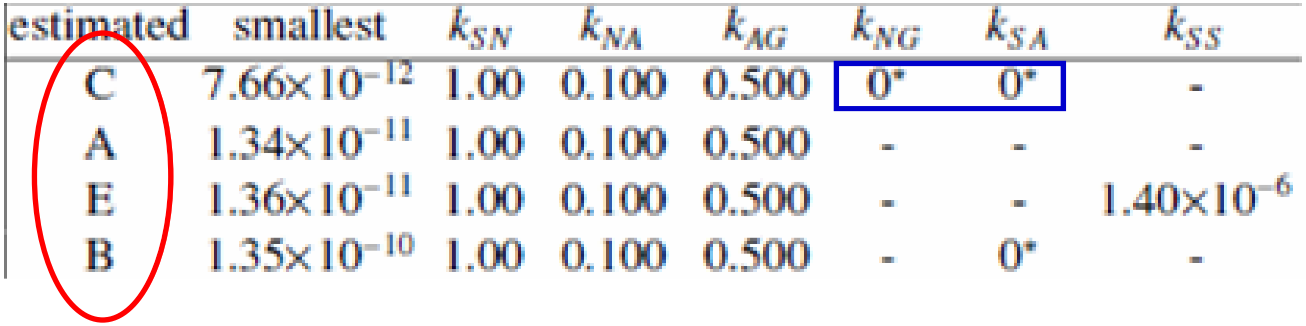
When *kSS* is small, Model E is almost equal to model A

Model E



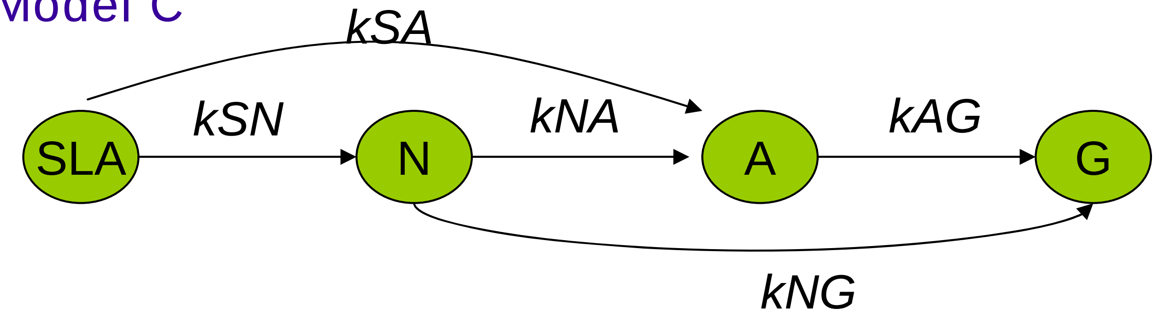
The verification of our method， Measure 2

Query A



estimated	smallest	k_{SN}	k_{NA}	k_{AG}	k_{NG}	k_{SA}	k_{SS}
C	7.66×10^{-12}	1.00	0.100	0.500	0^*	0^*	-
A	1.34×10^{-11}	1.00	0.100	0.500	-	-	-
E	1.36×10^{-11}	1.00	0.100	0.500	-	-	1.40×10^{-6}
B	1.35×10^{-10}	1.00	0.100	0.500	-	0^*	-

Model C



When *kSA* and *kNG* are exactly zero, Model C is equivalent to model A

Model A

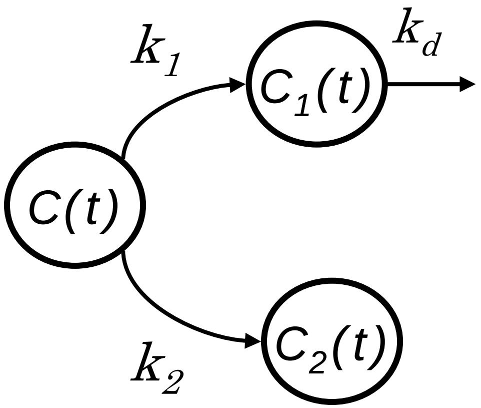
Summary

- We have proposed a method to select a model which is more/most consistent with the time series of observed data.
- We have verified our method, using generated data, handling a cyclic relationship hitherto unavailable in previous methods.

Future works … scalability

- Focusing on a local network within a large-scale network.
- Easy elimination of the unnecessary variables in virtue of algebraic equations

Eliminating *C(t)*,



$$k_2 C_1(t) = k_1 C_2(t) - k_1 k_d \int_0^t e^{-k_d(\tau - t)} C_2(\tau) d\tau$$

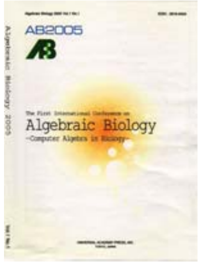
$$-(s k_2 + k_2 k_d) L[C_1(t)](s) + s k_1 L[C_2(t)](s) = 0$$

International Conference on Algebraic Biology

2005 (1st)

November 28-30
FUJITSU SOLUTION SQURE
Tokyo, Japan

organized by H. Anai, H. Hong, K. Horimoto



AB2005

The First International Conference on
Algebraic Biology
-Computer Algebra in Biology-

Algebraic Biology 2005

from *Universal Academy Press*

2007 (2nd)

July 2-4
RISC, Johannes Kepler University
Linz, Austria

organized by B. Buchberger, H. Hong, K. Horimoto

Hirokazu Anai
Katsuhisa Horimoto
Temur Kutsia (Eds.)

LNCS 4545

Algebraic Biology

Second International Conference, AB 2007
Castle of Hagenberg, Austria, July 2007
Proceedings

Springer

Lecture Notes in Computer Science

Anai · Horimoto
Kutsia (Eds.)

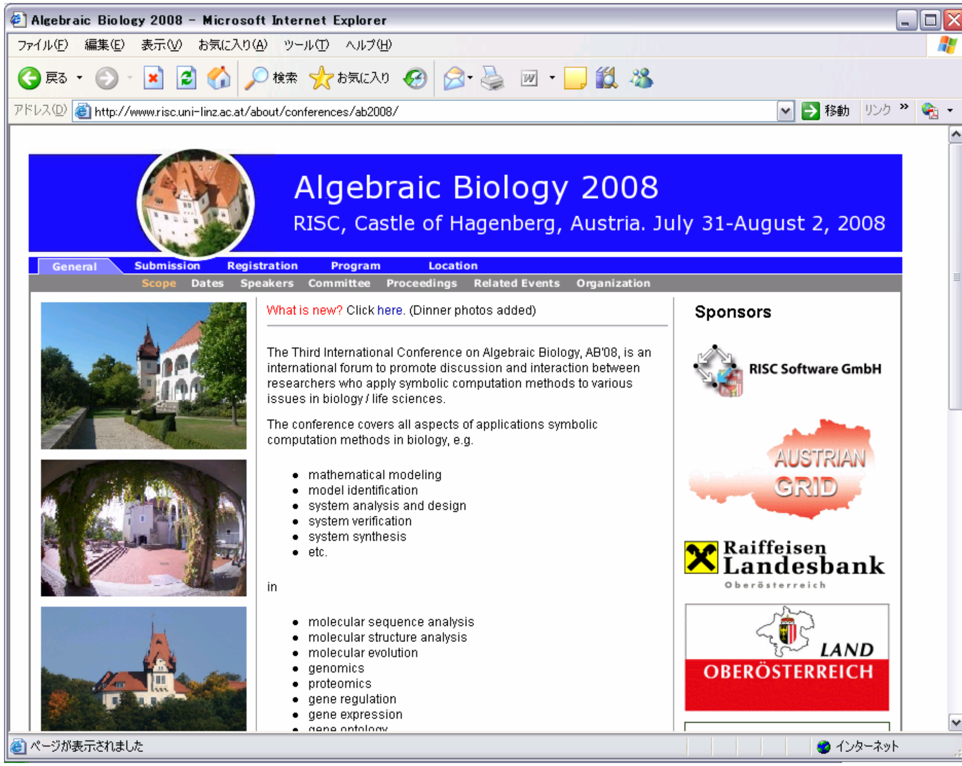
Algebraic Biology

LNCS 4545 from *Springer*

July 31-August 2
RISC, Johannes Kepler University
Linz, Austria

2008 (3rd)

organized by B. Buchberger, K. Horimoto, R. Laubenbacher, B. Mishra



Algebraic Biology 2008

RISC, Castle of Hagenberg, Austria. July 31-August 2, 2008

What is new? Click here. (Dinner photos added)

The Third International Conference on Algebraic Biology, AB'08, is an international forum to promote discussion and interaction between researchers who apply symbolic computation methods to various issues in biology / life sciences.

The conference covers all aspects of applications symbolic computation methods in biology, e.g.

- mathematical modeling
- model identification
- system analysis and design
- system verification
- system synthesis
- etc.

in

- molecular sequence analysis
- molecular structure analysis
- molecular evolution
- genomics
- proteomics
- gene regulation
- gene expression
- gene ontology

Paper deadline is Jan.-14, 2008

http://www.risc.uni-linz.ac.at/about/conferences/ab2008/

2009 (4th)

SAMSI, NC, USA
organized by R. Laubenbacher