Electronic Supplementary Material (ESI) for Molecular BioSystems.

Supplementary Data

Table S1. The Ordinary Differential Equations of the Mitotic Regulatory Network

$$\frac{d[\text{CDK1:CycB}]}{dt} = -\frac{k_0[\text{Wee1}][\text{CDK1:CycB}]}{k_1+[\text{CDK1:CycB}]} + \frac{k_2[\text{p-CDC25}][\text{p-CDK1:CycB}]}{k_3+[\text{p-CDK1:CycB}]} - \frac{k_{42}[\text{APC/C:CDC20}][\text{CDK1:CycB}]}{k_{43}+[\text{CDK1:CycB}]} \quad (1)$$

$$\frac{d[\text{p-CDK1:CycB}]}{dt} = \frac{k_0[\text{Wee1}][\text{CDK1:CycB}]}{k_1+[\text{CDK1:CycB}]} - \frac{k_2[\text{p-CDC25}][\text{p-CDK1:CycB}]}{k_3+[\text{p-CDK1:CycB}]} - \frac{k_{42}[\text{APC/C:CDC20}][\text{p-CDK1:CycB}]}{k_{43}+[\text{p-CDK1:CycB}]} \quad (2)$$

$$\frac{d[\text{CDK1}]}{dt} = -\frac{k_0[\text{Wee1}][\text{CDK1}]}{k_1+[\text{CDK1}]} + \frac{k_2[\text{p-CDC25}][\text{p-CDK1}]}{k_3+[\text{p-CDK1}]} + \frac{k_{42}[\text{APC/C:CDC20}][\text{CDK1:CycB}]}{k_{43}+[\text{CDK1:CycB}]} \quad (3)$$

$$\frac{d[\text{p-CDK1}]}{dt} = \frac{k_0[\text{Wee1}][\text{CDK1}]}{k_1+[\text{CDK1}]} - \frac{k_2[\text{p-CDC25}][\text{p-CDK1}]}{k_3+[\text{p-CDK1}]} + \frac{k_{42}[\text{APC/C:CDC20}][\text{p-CDK1:CycB}]}{k_{43}+[\text{p-CDK1:CycB}]} \quad (4)$$

$$\frac{d[\text{Wee1}]}{dt} = -\frac{k_4[\text{CDK1:CycB}][\text{Wee1}]}{k_5+[\text{Wee1}]} \quad (5)$$

$$\frac{d[\text{p-Wee1}]}{dt} = \frac{k_4[\text{CDK1:CycB}][\text{Wee1}]}{k_5+[\text{Wee1}]} - \frac{k_6[\text{p-PLK1}][\text{p-Wee1}]}{k_7+[\text{p-Wee1}]} \quad (6)$$

$$\frac{d[\text{p-CDC25}]}{dt} = \frac{k_8[\text{CDK1:CycB}][\text{CDC25}]}{k_9 + [\text{CDC25}]} + \frac{k_{10}[\text{p-PLK1}][\text{CDC25}]}{k_{11} + [\text{CDC25}]}$$

$$+\frac{k_{12}[\text{p-AurkA-cp}][\text{CDC25}]}{k_{13} + [\text{CDC25}]} \tag{7}$$

$$\frac{d[\text{CDC25}]}{dt} = -\frac{k_8[\text{CDK1:CycB}][\text{CDC25}]}{k_9 + [\text{CDC25}]} - \frac{k_{10}[\text{p-PLK1}][\text{CDC25}]}{k_{11} + [\text{CDC25}]}$$

$$-\frac{k_{12}[\text{p-AurkA-cp}][\text{CDC25}]}{k_{13} + [\text{CDC25}]} \tag{8}$$

$$\frac{d[\text{p-PLK1}]}{dt} = \frac{k_{14}[\text{p-AurkA-cp}][\text{Bora}][\text{PLK1}]}{k_{15} + [\text{PLK1}]} - \frac{k_{16}[\text{p-MYPT1-PP1C}][\text{p-PLK1}]}{k_{17} + [\text{p-PLK1}]} \tag{9}$$

$$\frac{d[\text{PLK1}]}{dt} = -\frac{k_{14}[\text{p-AurkA-cp}][\text{Bora}][\text{PLK1}]}{k_{15} + [\text{PLK1}]} + \frac{k_{16}[\text{p-MYPT1-PP1C}][\text{p-PLK1}]}{k_{17} + [\text{p-PLK1}]} \tag{10}$$

$$\frac{d[\text{p-AurkA-cs}]}{dt} = \frac{k_{18}[\text{p-AurkA-cp}]}{1 + \frac{[\text{Bora}]}{k_{19}}} \tag{11}$$

$$\frac{d[\text{p-AurkA-cp}]}{dt} = \frac{k_{20}[\text{p-AurkA-cp}][\text{AurkA}]}{k_{21} + [\text{AurkA}]} - \frac{k_{18}[\text{p-AurkA-cp}]}{1 + \frac{[\text{Bora}]}{k_{19}}} \tag{12}$$

$$\frac{d[\text{AurkA}]}{dt} = -\frac{k_{20}[\text{p-AurkA-cp}][\text{AurkA}]}{k_{21} + [\text{AurkA}]} \tag{13}$$

$$\frac{d[\text{Bora}]}{dt} = -\frac{k_{22}[\text{p-PLK1}][\text{Bora}]}{k_{23} + [\text{Bora}]} \tag{14}$$

$$\frac{d[\text{p-MYPT1-PP1C}]}{dt} = \frac{k_{24}[\text{CDK1:CycB}][\text{MYPT1-PP1C}]}{k_{25} + [\text{MYPT1-PP1C}]} \tag{15}$$

$$\frac{d[\text{MYPT1-PP1C}]}{dt} = -\frac{k_{24}[\text{CDK1:CycB}][\text{MYPT1-PP1C}]}{k_{25} + [\text{MYPT1-PP1C}]} \tag{16}$$

$$\frac{d[\text{p-AurkB}]}{dt} = \frac{k_{26}[\text{p-AurkB}][\text{AurkB}]}{k_{27} + [\text{AurkB}]} - \frac{k_{28}[\text{p-BUBR1}][\text{p-AurkB}]}{k_{29} + [\text{p-AurkB}]} \tag{17}$$

$$\frac{d[\text{AurkB}]}{dt} = -\frac{k_{26}[\text{p-AurkB}][\text{AurkB}]}{k_{27} + [\text{AurkB}]} + \frac{k_{28}[\text{p-BUBR1}][\text{p-AurkB}]}{k_{29} + [\text{p-AurkB}]} \tag{18}$$

$$\frac{d[\text{p-BUBR1}]}{dt} = \frac{k_{30}[\text{p-PLK1}][\text{BUBR1}]}{k_{31} + [\text{BUBR1}]} \tag{19}$$

$$\begin{aligned} \frac{d[\text{BUBR1}]}{dt} &= -\frac{k_{30}[\text{p-PLK1}][\text{BUBR1}]}{k_{31} + [\text{BUBR1}])} \\ &\quad + k_{32}[\text{p-AurkB}]\{1.2 \times 10^4 - ([\text{p-BUBR1}] + [\text{BUBR1}]\} \end{aligned} \tag{20}$$

$$\frac{d[\text{Attached}]}{dt} = k_{33}[\text{p-AurkA-cs}][\text{UnAttached}] - \frac{k_{34}[\text{p-AurkB}][\text{Attached}]}{1 + \frac{[\text{Attached}]}{k_{35}}} \tag{21}$$

$$\frac{d[\text{UnAttached}]}{dt} = -k_{33}[\text{p-AurkA-cs}][\text{UnAttached}] + \frac{k_{34}[\text{p-AurkB}][\text{Attached}]}{1 + \frac{[\text{Attached}]}{k_{35}}} \tag{22}$$

$$\begin{aligned} \frac{d[\text{CDC20}]}{dt} &= k_{36} - k_{37}[\text{UnAttached}][\text{CDC20}] - k_{38}[\text{CDC20}][\text{APC/C}] \\ &\quad - \frac{k_{39}[\text{CDC20}]}{k_{40} + [\text{CDC20}] + [\text{APC/C:CDC20}] + [\text{APC/C:MCC}]} \end{aligned} \tag{23}$$

$$\frac{d[\text{MCC}]}{dt} = k_{37}[\text{UnAttached}][\text{CDC20}] - k_{41}[\text{MCC}][\text{APC/C}] \tag{24}$$

$$\frac{d[\mathrm{APC/C}]}{dt} = -(k_{38}[\mathrm{CDC20}] + k_{41}[\mathrm{MCC}])[\mathrm{APC/C}]$$

$$+\frac{k_{39}([\mathrm{APC/C{:}CDC20}] + [\mathrm{APC/C{:}MCC}])}{k_{40} + [\mathrm{CDC20}] + [\mathrm{APC/C{:}CDC20}] + [\mathrm{APC/C{:}MCC}]} \tag{25}$$

$$\frac{d[\mathrm{APC/C{:}CDC20}]}{dt} = k_{38}[\mathrm{CDC20}][\mathrm{APC/C}]$$

$$-\frac{k_{39}[\mathrm{APC/C{:}CDC20}]}{k_{40} + [\mathrm{CDC20}] + [\mathrm{APC/C{:}CDC20}] + [\mathrm{APC/C{:}MCC}]} \tag{26}$$

$$\frac{d[\mathrm{APC/C{:}MCC}]}{dt} = k_{41}[\mathrm{MCC}][\mathrm{APC/C}]$$

$$-\frac{k_{39}[\mathrm{APC/C{:}MCC}]}{k_{40} + [\mathrm{CDC20}] + [\mathrm{APC/C{:}CDC20}] + [\mathrm{APC/C{:}MCC}]} \tag{27}$$

Table S2 Initial concentrations of the species

Species	Initial concentration molecules/cell	Reference
CDK1:CycB	$4.0 \times 10^3 \times a_0$ [b]	1
p-CDK1:CycB	$4.0 \times 10^3 \times (1 - a_0)$	1
CDK1	0	-
p-CDK1	0	-
Wee1	$2.5 \times 10^4 \times (1 - a_1)$	1
p-Wee1	$2.5 \times 10^4 \times a_1$	1
p-CDC25	$1.0 \times 10^4 \times a_2$	1
CDC25	$1.0 \times 10^4 \times (1 - a_2)$	1
p-PLK1	$9.6 \times 10^3 \times a_3$	1
PLK1	$9.6 \times 10^3 \times (1 - a_3)$	1
p-AurkA-cs [a]	0	-
p-AurkA-cp [a]	$7.2 \times 10^3 \times a_4$	1
AurkA	$7.2 \times 10^3 \times (1 - a_4)$	1
Bora	4.5×10^3	1
p-MYPT1-PP1C	$6.0 \times 10^3 \times a_5$	2
MYPT1-PP1C	$6.0 \times 10^3 \times (1 - a_5)$	2
p-AurkB	$3.6 \times 10^3 \times a_6$	3
AurkB	$3.6 \times 10^3 \times (1 - a_6)$	3
p-BUBR1	$1.2 \times 10^4 \times a_7$	4
BUBR1	$1.2 \times 10^4 \times (1 - a_7)$	4
Attached	0	-
UnAttached	1	-
CDC20	$2.8 \times 10^5 \times a_8$	5
MCC	$2.8 \times 10^5 \times (1 - a_8)$	5
APC/C	$8 \times 10^4 \times (1 - a_9 - a_{10})$	5
APC/C:CDC20	$8 \times 10^4 \times a_9$	5
APC/C:MCC	$8 \times 10^4 \times a_{10}$	5

[a] Different localization of Aurora A: cs = centrosome; cp = cytoplasm.

[b] a_i: initial concentration proportion parameter, possible value 0 to 1.

Table S3 Penalty Functions in the Objective Function

$$P_1 = max\left(0, 100\frac{sum\left([Attached]\,|_{k_{30}=0}\right)}{sum([Attached])} - 0.7\right)$$

$$P_2 = max\left(0, 100\left(a_9 + a_{10} - 1\right)\right)$$

$$P_3 = max\left(0, 100\left(0.8 - \left|\left([\mathrm{AurkA}]\,|_{t=120} - [\mathrm{AurkA}]\,|_{t=5}\right)\right|\right)\right)$$

$$P_4 = max\left(0, 100\left(0.9 - [Attached]\,|_{t=120}\right)\right)$$

$$P_5 = max\left(0, 100\left(0.2 - [\text{p-MYPT1-PP1C}]\,|_{t=120}\right)\right)$$

$$P_6 = max\left(0, 100\left(0.8 - \frac{min\left([\text{p-PLK1}]\right)}{[\text{p-PLK1}]|_{t=0}}\right)\right)$$

$$P_7 = max\left(0, 100\left(max\left([\text{p-AurkB}]\right) - 1.1\right)\right)$$

Figure S1 (Part 1) Distribution Range of Parameters

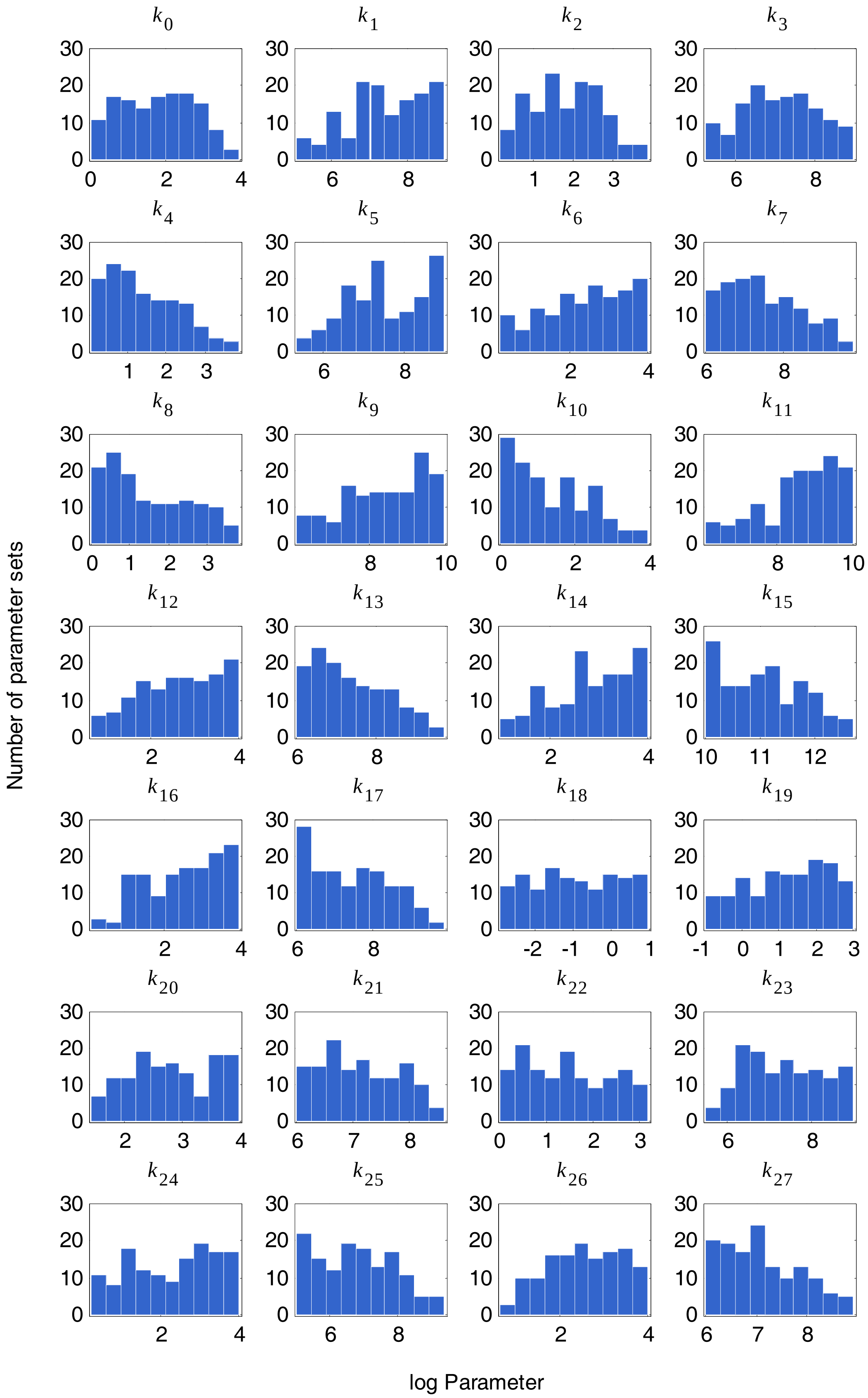


Figure S1 (Part 2) Distribution Range of Parameters

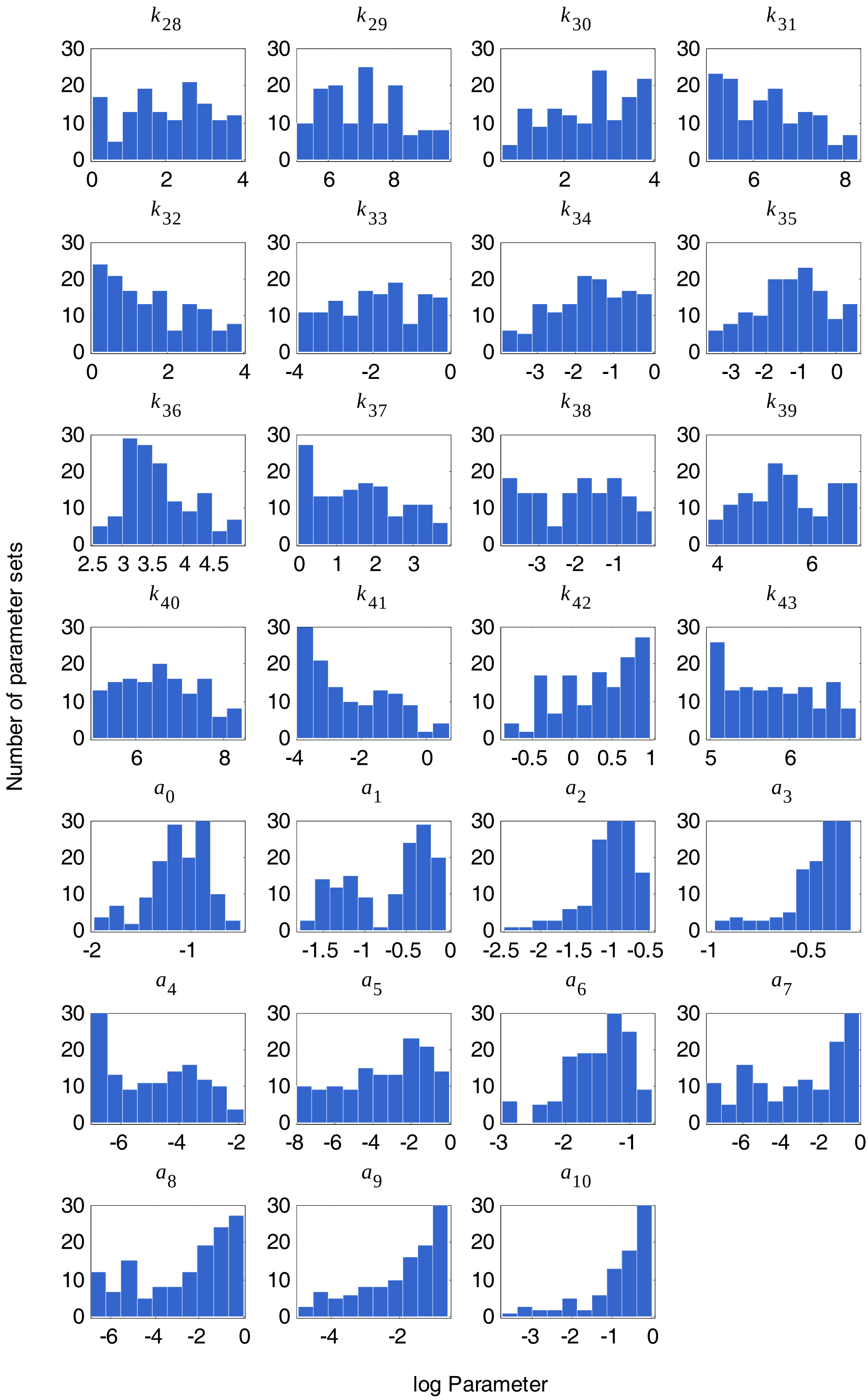


Figure S2 Simulated curves of species not used in fitting

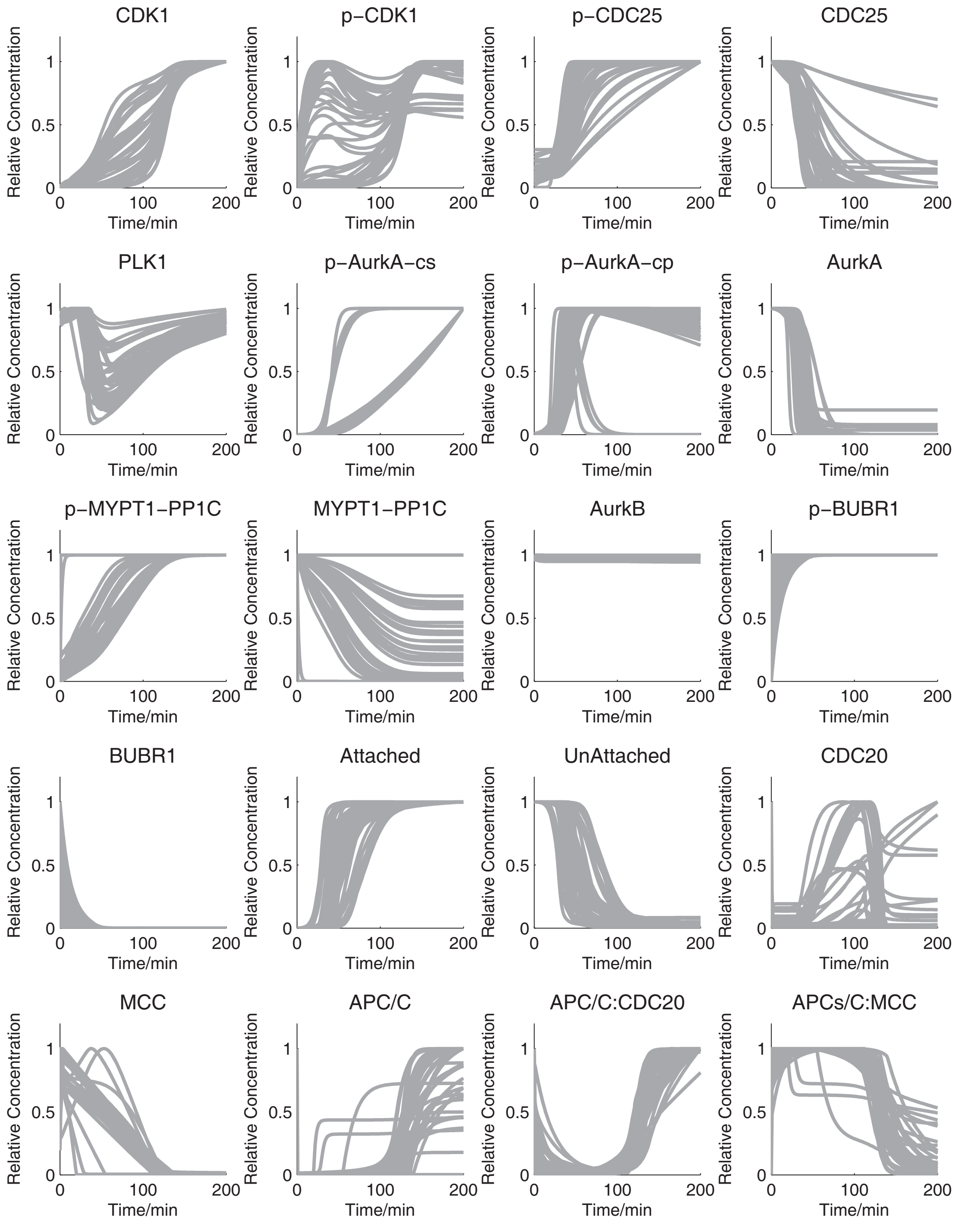
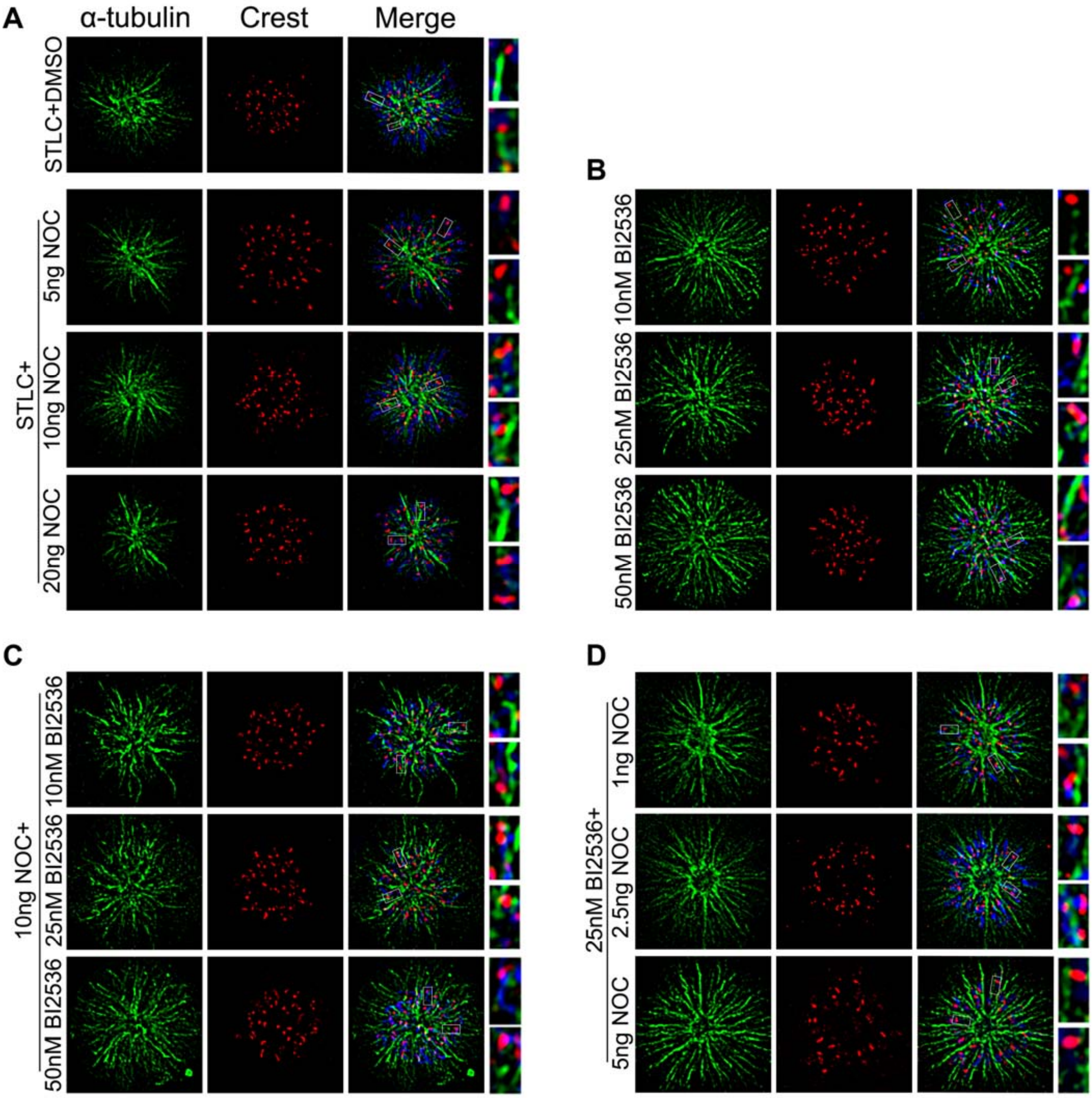


Figure S3 Kinetochore-microtubule attachment of HeLa cells interfered by nocodazole (NOC) and/or BI 2536. **A**. Singly nocodazole (*S*-trityl-L-cysteine, STLC, is used to generate mono-astral spindles as control of BI 2536); **B**. Singly BI 2536; **C**. Combination of nocodazole 10 ng with BI 2536 at different concentrations; **D**. Combination of BI 2536 10 nM with nocodazole at different concentrations



Reference

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