

Supplementary Information

A Hybrid Stochastic Model of the Budding Yeast Cell Cycle

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Cell cycle model

The main regulator of the cell cycle in budding yeast is a cyclin-dependent protein kinase (Cdc28) that is constitutively expressed but periodically activated and inhibited during progression through the cell cycle. Cdc28 forms an active kinase by binding to two families of cyclin partners, Cln1-3 and Clb1-6, each of which is synthesized and degraded in different phases of the cell cycle. In early G1 phase, Cln3 is the only available partner of Cdc28. As a newborn cell grows, the heterodimer of Cln3:Cdc28 accumulates until the cell reaches a critical size, when there is sufficient Cln3:Cdc28 (and a back-up protein, Bck2) to activate the transcription factors SBF and MBF. These transcription factors are responsible for the production of Cln2 and Clb5, respectively. Cln2 accumulation induces emergence of the bud and Clb5 initiates DNA synthesis.

In G1 phase the cyclin-dependent kinase inhibitors (CKI), Sic1 and Cdc6, are in high abundance, and they inhibit the activity of Clb5:Cdc28. However, as the activity of Cln2:Cdc28 increases, these inhibitors get phosphorylated and degraded by the SCF-proteasome pathway. As a result Clb5 accumulates to initiate DNA synthesis (S phase). Clb2 is the cyclin responsible for driving the

cell into mitosis (M phase). As CKIs are removed, Clb2 level rises because Clb2 activates its own transcription factor Mcm1 in an autocatalytic reaction. Rising Clb2:Cdc28 activity phosphorylates and inactivates the transcription factors SBF and MBF. In telophase, Clb2 must be degraded below a threshold so that the cell can exit mitosis and return to G1 phase. Clb2 degradation is initiated by two proteins, Cdc20 and Cdh1. Cdc20 has been kept inactive in the early stages of mitosis by the 'mitotic checkpoint complex'. When all chromosomes are properly aligned on the mitotic spindle, Cdc20 becomes active and facilitates the degradation of Clb2.

Moreover, as a yeast cell exits mitosis, Cdh1 is activated by a phosphatase, Cdc14, which has been sequestered in the nucleolus by binding to Net1. After full chromosome alignment on the metaphase plate, first Tem1 and then Cdc15 become active. Cdc15 phosphorylates Net1, which leads to the release of Cdc14. Next, Cdc14 activates Cdh1 (which takes over for Cdc20 as the primary initiator of Clb1-6 degradation in G1), and Cdc14 also activates the transcription factor, Swi5, for production of CKIs in G1 phase. In this way the scene is set for the cell to return to G1 phase, when the CKIs are abundant and all cyclins (except for Cln3) are out of the picture.

Variables, equations, reactions and parameter values

Table S1. Variables and initial values. Except for mass which is a normalized (dimensionless) variable, all other variables are based on number of molecules per cell. Initial values are given for all variables that are governed by differential equations. Some other variables are expressed in algebraic functions of the time-dependent variables, so their initial values are not listed here.

Variable	Description	Initial value
mass	Indicator of cell size (dimensionless)	1.04
Cln2	Total cyclins Cln1 and Cln2 (represented as Cln2 in the model)	21
Clb5	Active forms of cyclins Clb5 and Clb6 (represented as Clb5 in the model)	48
Clb2	Active forms of Clb1 and Clb2 (represented as Clb2 in the model)	233
Sic1	A stoichiometric inhibitor of Cdc28/Clb2 and Cdc28/Clb5	8
Sic1P	Phosphorylated form of Sic1	6
C2	A complex formed by Clb2 and Sic1	149
C5	A complex formed by Clb5 and Sic1	32
C2P	Phosphorylated form of C2	31
C5P	Phosphorylated form of C5	6
Cdc6	A stoichiometric inhibitor of Cdc28/Clb2	22
Cdc6P	Phosphorylated form of Cdc6	11
F2	A complex formed by Clb2 and Cdc6	66
F5	A complex formed by Clb5 and Cdc6	0
F2P	Phosphorylated form of F2	26
F5P	Phosphorylated form of F5	0

Swi5	Transcription factor for Sic1 and Cdc6	613
Swi5 _T	Total Swi5	634
APC	Anaphase Promoting Complex	285
APCP	Active (phosphorylated) form of APC	16
Cdc20 _T	Total Cdc20	4059
Cdc20A	Active form of Cdc20 (an APC partner)	752
Cdh1 _T	Total Cdh1	1273
Cdh1	Active Cdh1 (an APC partner)	895
Tem1	A GTP-binding protein	1140
Tem1 _T	Total Tem1	1166
Cdc15	A kinase required for nuclear division	342
Cdc15 _T	Total Cdc15	518
Cdc14	A phosphatase required for mitosis exit	121
Cdc14 _T	Total of Cdc14	607
Net1	A stoichiometric inhibitor of Cdc14	7
Net1 _T	Total Net1	838
Net1P	Phosphorylated form of Net1	-
RENT	A protein complex of Net1 and Cdc14 that regulates nuclear silencing and telophase	324
RENTP	Phosphorylated form of RENT	-
Cdc55	Active form of CDC55 phosphatase	1161
Esp1	A protein required for sister chromatid separation	9
Esp1 _T	Total Esp1	42
Pds1	A stoichiometric inhibitor of Esp1	2

ORI	An auxiliary variable representing proteins that signal the onset of DNA synthesis	2374
BUD	An auxiliary variable representing proteins that initiate a new bud	0
SPN	An auxiliary variable representing proteins that signal the alignment of all chromosomes	0
SBF	Transcription factor for Cln2	-
SBF _T	Total SBF	527
MBF	Transcription factor for Clb5	-
MBF _T	Total MBF	442
Mcm1	Transcription factor for Clb2, Cdc20 and Swi5	-
Mcm1 _T	Total Mcm1	10363
Cln3	A G1-cyclin initiating START events	50
Bck2	A back-up protein initiating START events	25
Clb5 _T	Total Clb5	-
Clb2 _T	Total Clb2	-
Sic1 _T	Total Sic1	-
Cdc6 _T	Total Cdc6	-
CKI _T	Total cyclin inhibitors Sic1 and Cdc6	-
<i>mCdh1</i>	Cdh1 messenger RNA	4
<i>mTem1</i>	Tem1 messenger RNA	2
<i>mCdc15</i>	Cdc15 messenger RNA	2
<i>mCdc14</i>	Cdc14 messenger RNA	6
<i>mNet1</i>	Net1 messenger RNA	3

<i>mCdc55</i>	Cdc55 messenger RNA	4
<i>mEsp1</i>	Esp1 messenger RNA	2
<i>mSBF</i>	SBF messenger RNA	4
<i>mMBF</i>	MBF messenger RNA	4
<i>mMcm1</i>	Mcm1 messenger RNA	3
<i>mAPC</i>	APC messenger RNA	4
<i>mCln2</i>	Cln2 messenger RNA	1
<i>mClb5</i>	Clb5 messenger RNA	1
<i>mClb2</i>	Clb2 messenger RNA	4
<i>mSic1</i>	Sic1 messenger RNA	3
<i>mCdc6</i>	Cdc6 messenger RNA	4
<i>mSwi5</i>	Swi5 messenger RNA	9
<i>mCdc20</i>	Cdc20 messenger RNA	5
<i>mPds1</i>	Pds1 messenger RNA	4

Table S2. Equations.

$\frac{dmass}{dt} = k_g \cdot mass$
$\frac{dCln2}{dt} = (k'_{s,n2} \cdot c_{cln2} \cdot mass + k''_{s,n2} \cdot \frac{c_{cln2}}{c_{sbf}} \cdot SBF) \cdot mass \cdot mCln2 - k_{d,n2} \cdot Cln2 + k_g \cdot Cln2$
$\frac{dClb5}{dt} = (k'_{s,b5} \cdot c_{clb5} \cdot mass + k''_{s,b5} \cdot \frac{c_{clb5}}{c_{mbf}} \cdot MBF) \cdot mass \cdot mClb5 + (k_{d3,c1} \cdot C5P + k_{di,b5} \cdot C5) + (k_{d3,f6} \cdot F5P + k_{di,f5} \cdot F5) - (V_{d,b5} + \frac{k_{as,b5}}{c_{sic1} \cdot mass} \cdot Sic1 + \frac{k_{as,f5}}{c_{cdc6} \cdot mass} \cdot Cdc6) \cdot Clb5 + k_g \cdot Clb5$
$\frac{dClb2}{dt} = (k'_{s,b2} \cdot c_{clb2} \cdot mass + k''_{s,b2} \cdot \frac{c_{clb2}}{c_{mcm1}} \cdot Mcm1) \cdot mass \cdot mClb2 + (k_{d3,c1} \cdot C2P + k_{di,b2} \cdot C2) + (k_{d3,f6} \cdot F2P + k_{di,f2} \cdot F2) - (V_{d,b2} + \frac{k_{as,b2}}{c_{sic1} \cdot mass} \cdot Sic1 + \frac{k_{as,f2}}{c_{cdc6} \cdot mass} \cdot Cdc6) \cdot Clb2 + k_g \cdot Clb2$
$\frac{dSic1}{dt} = (k'_{s,c1} \cdot c_{sic1} \cdot mass + k''_{s,c1} \cdot \frac{c_{sic1}}{c_{swi5}} \cdot Swi5) \cdot mSic1 + (V_{d,b2} + k_{di,b2}) \cdot C2P + (V_{d,b5} + k_{di,b5}) \cdot C5P + \frac{k_{pp,c1}}{c_{cdc14} \cdot mass} \cdot Cdc14 \cdot Sic1P - (\frac{k_{as,b2}}{c_{clb2} \cdot mass} \cdot Clb2 + \frac{k_{as,b5}}{c_{clb5} \cdot mass} \cdot Clb5 + V_{kp,c1}) \cdot Sic1 + k_g \cdot Sic1$
$\frac{dSic1P}{dt} = V_{kp,c1} \cdot Sic1 - (\frac{k_{pp,c1}}{c_{cdc14} \cdot mass} \cdot Cdc14 + k_{d3,c1}) \cdot Sic1P + V_{d,b2} \cdot C2P + V_{d,b5} \cdot C5P + k_g \cdot Sic1P$
$\frac{dC2}{dt} = \frac{k_{as,b2}}{c_{clb2} \cdot mass} \cdot Clb2 \cdot Sic1 + \frac{k_{pp,c1}}{c_{cdc14} \cdot mass} \cdot Cdc14 \cdot C2P - (k_{di,b2} + V_{d,b2} + V_{kp,c1}) \cdot C2 + k_g \cdot C2$
$\frac{dC5}{dt} = \frac{k_{as,b5}}{c_{clb5} \cdot mass} \cdot Clb5 \cdot Sic1 + \frac{k_{pp,c1}}{c_{cdc14} \cdot mass} \cdot Cdc14 \cdot C5P - (k_{di,b5} + V_{d,b5} + V_{kp,c1}) \cdot C5 + k_g \cdot C5$
$\frac{dC2P}{dt} = V_{kp,c1} \cdot C2 - (\frac{k_{pp,c1}}{c_{cdc14} \cdot mass} \cdot Cdc14 + k_{d3,c1} + V_{d,b2}) \cdot C2P + k_g \cdot C2P$
$\frac{dC5P}{dt} = V_{kp,c1} \cdot C5 - (\frac{k_{pp,c1}}{c_{cdc14} \cdot mass} \cdot Cdc14 + k_{d3,c1} + V_{d,b5}) \cdot C5P + k_g \cdot C5P$
$\frac{dCdc6}{dt} = (k'_{s,f6} \cdot c_{cdc6} \cdot mass + k''_{s,f6} \cdot \frac{c_{cdc6}}{c_{swi5}} \cdot Swi5 + k'''_{s,f6} \cdot \frac{c_{cdc6}}{c_{sbf}} \cdot SBF) \cdot mCdc6 + (V_{d,b2} + k_{di,f2}) \cdot F2 + (V_{d,b5} + k_{di,f5}) \cdot F5 + \frac{k_{pp,f6}}{c_{cdc14} \cdot mass} \cdot Cdc14 \cdot Cdc6P - (\frac{k_{as,f2}}{c_{clb2} \cdot mass} \cdot Clb2 + \frac{k_{as,f5}}{c_{clb5} \cdot mass} \cdot Clb5 + V_{kp,f6}) \cdot Cdc6 + k_g \cdot Cdc6$
$\frac{dCdc6P}{dt} = V_{kp,f6} \cdot Cdc6 - (\frac{k_{pp,f6}}{c_{cdc14} \cdot mass} \cdot Cdc14 + k_{d3,f6}) \cdot Cdc6P + V_{d,b2} \cdot F2P + V_{d,b5} \cdot F5P + k_g \cdot Cdc6P$
$\frac{dF2}{dt} = \frac{k_{as,f2}}{c_{clb2} \cdot mass} \cdot Clb2 \cdot Cdc6 + \frac{k_{pp,f6}}{c_{cdc14} \cdot mass} \cdot Cdc14 \cdot F2P - (k_{di,f2} + V_{d,b2} + V_{kp,f6}) \cdot F2 + k_g \cdot F2$
$\frac{dF5}{dt} = \frac{k_{as,f5}}{c_{clb5} \cdot mass} \cdot Clb5 \cdot Cdc6 + \frac{k_{pp,f6}}{c_{cdc14} \cdot mass} \cdot Cdc14 \cdot F5P - (k_{di,f5} + V_{d,b5} + V_{kp,f6}) \cdot F5 + k_g \cdot F5$
$\frac{dF2P}{dt} = V_{kp,f6} \cdot F2 - (\frac{k_{pp,f6}}{c_{cdc14} \cdot mass} \cdot Cdc14 + k_{d3,f6} + V_{d,b2}) \cdot F2P + k_g \cdot F2P$
$\frac{dF5P}{dt} = V_{kp,f6} \cdot F5 - (\frac{k_{pp,f6}}{c_{cdc14} \cdot mass} \cdot Cdc14 + k_{d3,f6} + V_{d,b5}) \cdot F5P + k_g \cdot F5P$
$\frac{dSwi5T}{dt} = (k'_{s,swi} \cdot c_{swi5} \cdot mass + k''_{s,swi} \cdot \frac{c_{swi5}}{c_{mcm1}} \cdot Mcm1) \cdot mSwi5 - k_{d,swi} \cdot Swi5T + k_g \cdot Swi5T$
$\frac{dSwi5}{dt} = (k'_{s,swi} \cdot c_{swi5} \cdot mass + k''_{s,swi} \cdot \frac{c_{swi5}}{c_{mcm1}} \cdot Mcm1) \cdot mSwi5 + \frac{k_{a,swi}}{c_{cdc14} \cdot mass} \cdot Cdc14 \cdot (Swi5T - Swi5) - (k_{d,swi} + \frac{k_{i,swi}}{c_{clb2} \cdot mass} \cdot Clb2) \cdot Swi5 + k_g \cdot Swi5$

(continued)

Table S2. (continued)

$\frac{dAPCP}{dt} = \frac{k_{a,apc} \cdot c_{apc} \cdot Clb2 \cdot (APC - APCP)}{J_{a,apc} \cdot c_{apc} \cdot mass + APC - APCP} - \frac{k_{i,apc} \cdot c_{apc} \cdot mass \cdot APCP}{J_{i,apc} \cdot c_{apc} \cdot mass + APCP} + k_g \cdot APCP$
$\frac{dCdc20T}{dt} = (k'_{s,20} \cdot c_{cdc20} \cdot mass + k''_{s,20} \cdot \frac{c_{cdc20}}{c_{mcm1}} \cdot Mcm1) \cdot mCdc20 - k_{d,20} \cdot Cdc20T + k_g \cdot Cdc20T$
$\frac{dCdc20A}{dt} = (k'_{a,20} + \frac{k''_{a,20}}{c_{cdc20} \cdot mass} \cdot APCP) \cdot (Cdc20T - Cdc20A) - (k_{mad2} + k_{d,20}) \cdot Cdc20A + k_g \cdot Cdc20A$
$\frac{dCdh1T}{dt} = k_{s,cdh} \cdot c_{cdh1} \cdot mass \cdot mCdh1 - k_{d,cdh} \cdot Cdh1T + k_g \cdot Cdh1T$
$\frac{dCdh1}{dt} = k_{s,cdh} \cdot c_{cdh1} \cdot mass \cdot mCdh1 - k_{d,cdh} \cdot Cdh1 + \frac{V_{a,cdh} \cdot c_{cdh1} \cdot mass \cdot (Cdh1T - Cdh1)}{J_{a,cdh} \cdot c_{cdh1} \cdot mass + Cdh1T - Cdh1} - \frac{V_{i,cdh} \cdot c_{cdh1} \cdot mass \cdot Cdh1}{J_{i,cdh} \cdot c_{cdh1} \cdot mass + Cdh1} + k_g \cdot Cdh1$
$\frac{dTem1}{dt} = \frac{k_{lte1} \cdot c_{tem1} \cdot mass \cdot (Tem1T - Tem1)}{J_{a,tem} \cdot c_{tem1} \cdot mass + Tem1T - Tem1} - \frac{k_{bub2} \cdot c_{tem1} \cdot mass \cdot Tem1}{J_{i,tem} \cdot c_{tem1} \cdot mass + Tem1} + k_g \cdot Tem1$
$\frac{dCdc15}{dt} = (\frac{k'_{a,15}}{c_{tem1} \cdot mass} \cdot (Tem1T - Tem1) + \frac{k''_{a,15}}{c_{tem1} \cdot mass} \cdot Tem1 + \frac{k'''_{a,15}}{c_{cdc14} \cdot mass} \cdot Cdc14) \cdot (Cdc15T - Cdc15) - k_{i,15} \cdot Cdc15 + k_g \cdot Cdc15$
$\frac{dCdc14T}{dt} = k_{s,14} \cdot c_{cdc14} \cdot mass \cdot mCdc14 - k_{d,14} \cdot Cdc14T + k_g \cdot Cdc14T$
$\frac{dCdc14}{dt} = k_{s,14} \cdot c_{cdc14} \cdot mass \cdot mCdc14 - k_{d,14} \cdot Cdc14 + k_{d,net} \cdot (RENT + RENTP) + k_{di,rent} \cdot RENT + k_{di,rentp} \cdot RENTP + k_g \cdot Cdc14 - (\frac{k_{as,rent}}{c_{net1} \cdot mass} \cdot Net1 + \frac{k_{as,rentp}}{c_{net1} \cdot mass} \cdot Net1P) \cdot Cdc14$
$\frac{dNet1T}{dt} = k_{s,net} \cdot c_{net1} \cdot mass \cdot mNet1 - k_{d,net} \cdot Net1T + k_g \cdot Net1T$
$\frac{dNet1}{dt} = k_{s,net} \cdot c_{cdc14} \cdot mass \cdot mNet1 - k_{d,net} \cdot Net1 + k_{d,14} \cdot RENT + k_{di,rent} \cdot RENT - \frac{k_{as,rent}}{c_{cdc14} \cdot mass} \cdot Cdc14 \cdot Net1 + V_{pp,net} \cdot Net1P - V_{kp,net} \cdot Net1 + k_g \cdot Net1$
$\frac{dRENT}{dt} = -(k_{d,14} + k_{d,net}) \cdot RENT - k_{di,rent} \cdot RENT + \frac{k_{as,rent}}{c_{cdc14} \cdot mass} \cdot Cdc14 \cdot Net1 + V_{pp,net} \cdot RENTP - V_{kp,net} \cdot RENT + k_g \cdot RENT$
$\frac{dCdc55}{dt} = k_{s,55} \cdot c_{cdc55} \cdot mass \cdot mCdc55 - V_{d,55} \cdot Cdc55 + k_g \cdot Cdc55$
$\frac{dPds1}{dt} = (k'_{s,pds} \cdot c_{pds1} \cdot mass + k''_{s1,pds} \cdot \frac{c_{pds1}}{c_{sbf}} \cdot SBF + k''_{s2,pds} \cdot \frac{c_{pds1}}{c_{mcm1}} \cdot Mcm1) \cdot mPds1 + k_{di,esp} \cdot PE - (V_{d,pds} + \frac{k_{as,esp}}{c_{esp1} \cdot mass} \cdot Esp1) \cdot Pds1 + k_g \cdot Pds1$
$\frac{dEsp1}{dt} = -\frac{k_{as,esp}}{c_{pds1} \cdot mass} \cdot Pds1 \cdot Esp1 + (k_{di,esp} + V_{d,pds}) \cdot PE + k_g \cdot Esp1$
$\frac{dORI}{dt} = k_{s,ori} \cdot (e_{ori,b5} \cdot \frac{c_{ori}}{c_{clb5}} \cdot Clb5 + e_{ori,b2} \cdot \frac{c_{ori}}{c_{clb2}} \cdot Clb2) - k_{d,ori} \cdot ORI + k_g \cdot ORI$

(continued)

Table S2. (continued)

$\frac{dBUD}{dt} = k_{s,bud} \cdot (e_{bud,n2} \cdot \frac{c_{bud}}{c_{cln2}} \cdot Cln2 + e_{bud,n3} \cdot \frac{c_{bud}}{c_{cln3}} \cdot Cln3 + e_{bud,b5} \cdot \frac{c_{bud}}{c_{clb5}} \cdot Clb5) - k_{d,bud} \cdot BUD + k_g \cdot BUD$
$\frac{dSPN}{dt} = \frac{k_{s,spn} \cdot c_{spn} \cdot mass \cdot Clb2}{J_{spn} \cdot c_{clb2} \cdot mass + Clb2} - k_{d,spn} \cdot SPN + k_g \cdot SPN$
$\frac{dTem1_T}{dt} = k_{s,tem1t} \cdot c_{tem1} \cdot mass \cdot mTem1 - k_{d,tem1t} \cdot Tem1_T + k_g \cdot Tem1_T$
$\frac{dCdc15_T}{dt} = k_{s,cdc15t} \cdot c_{cdc15} \cdot mass \cdot mCdc15 - k_{d,cdc15t} \cdot Cdc15_T + k_g \cdot Cdc15_T$
$\frac{dEsp1_T}{dt} = k_{s,esp1t} \cdot c_{esp1} \cdot mass \cdot mEsp1 - k_{d,esp1t} \cdot Esp1_T + k_g \cdot Esp1_T$
$\frac{dSBF_T}{dt} = k_{s,SBFt} \cdot c_{SBF} \cdot mass \cdot mSBF - k_{d,SBFt} \cdot SBF_T + k_g \cdot SBF_T$
$\frac{dMBF_T}{dt} = k_{s,MBFt} \cdot c_{MBF} \cdot mass \cdot mMBF - k_{d,MBFt} \cdot MBF_T + k_g \cdot MBF_T$
$\frac{dMcm1_T}{dt} = k_{s,mcm1t} \cdot c_{mcm1} \cdot mass \cdot mMcm1 - k_{d,mcm1t} \cdot Mcm1_T + k_g \cdot Mcm1_T$
$\frac{dAPC}{dt} = k_{s,apct} \cdot c_{apc} \cdot mass \cdot mAPC - k_{d,apct} \cdot APC + k_g \cdot APC$
$\frac{dCln3}{dt} = k_{s,n3} \cdot c_{cln3} \cdot mass^2 - k_{d,n3} \cdot Cln3 + k_g \cdot Cln3$
$\frac{dBck2}{dt} = k_{s,k2} \cdot c_{bck2} \cdot mass^2 - k_{d,k2} \cdot Bck2 + k_g \cdot Bck2$
$G(V_a, V_i, J_a, J_i) = \frac{2J_i V_a}{V_i - V_a + J_a V_i + J_i V_a + \sqrt{(V_i - V_a + J_a V_i + J_i V_a)^2 - 4(V_i - V_a) J_i V_a}}$
$SBF = G(V_{a,SBF}, V_{i,SBF}, J_{a,SBF}, J_{i,SBF}) \cdot SBF_T$
$MBF = G(V_{a,SBF}, V_{i,SBF}, J_{a,SBF}, J_{i,SBF}) \cdot MBF_T$
$Mcm1 = G(\frac{k_{a,mcm}}{c_{clb2} \cdot mass} \cdot Clb2, k_{i,mcm}, J_{a,mcm}, J_{i,mcm}) \cdot Mcm1_T$
$Clb5_T = Clb5 + C5 + C5P + F5 + F5P$
$Clb2_T = Clb2 + C2 + C2P + F2 + F2P$
$Sic1_T = Sic1 + Sic1P + C2 + C2P + C5 + C5P$
$Cdc6_T = Cdc6 + Cdc6P + F2 + F2P + F5 + F5P$
$CKI_T = Sic1_T + Cdc6_T$
$RENTP = Cdc14_T - RENT - Cdc14$
$Net1P = Net1_T - Net1 - Cdc14_T + Cdc14$

(continued)

Table S2. (continued)

$PE = Esp1_T - Esp1$
$V_{d,b5} = k'_{d,b5} + k''_{d,b5} \cdot Cdc20A$
$V_{d,b2} = k'_{d,b2} + k''_{d,b2} \cdot Cdh1 + k_{d,b2p} \cdot Cdc20A$
$V_{a,sbf} = k_{a,sbf} \cdot (e_{sbf,n2} \cdot Cln2 + e_{sbf,n3} \cdot (Cln3 + Bck2)) + e_{sbf,b5} \cdot Clb5$
$V_{i,sbf} = k'_{i,sbf} + k''_{i,sbf} \cdot Clb2$
$V_{kp,c1} = k_{d1,c1} + \frac{k_{d2,c1}}{J_{d2,c1} + Sic1_T} \cdot (e_{c1,n3} \cdot Cln3 + e_{c1,k2} \cdot Bck2 + e_{c1,n2} \cdot Cln2 + e_{c1,b5} \cdot Clb5 + e_{c1,b2} \cdot Clb2)$
$V_{kp,f6} = k_{d1,f6} + \frac{k_{d2,f6}}{J_{d2,f6} + Cdc6} \cdot (e_{f6,n3} \cdot Cln3 + e_{f6,k2} \cdot Bck2 + e_{f6,n2} \cdot Cln2 + e_{f6,b5} \cdot Clb5 + e_{f6,b2} \cdot Clb2)$
$V_{a,cdh} = k'_{a,cdh} + k''_{a,cdh} \cdot Cdc14$
$V_{i,cdh} = k'_{i,cdh} + k''_{i,cdh} \cdot (e_{cdh,n3} \cdot Cln3 + e_{cdh,n2} \cdot Cln2 + e_{cdh,b2} \cdot Clb2 + e_{cdh,b5} \cdot Clb5)$
$V_{pp,net} = k'_{pp,net} + k''_{pp,net} \cdot Cdc55$
$V_{kp,net} = (k'_{kp,net} + k''_{kp,net} \cdot Cdc55) \cdot mass$
$V_{d,55} = k'_{d,55} + k''_{d,55} (J_{20,55} + Cdc20A) \cdot \frac{J_{pds}}{J_{pds} + Pds1}$
$V_{d,pds} = k'_{d1,pds} + k''_{d2,pds} \cdot Cdc20A + k''_{d3,pds} \cdot Cdh1$

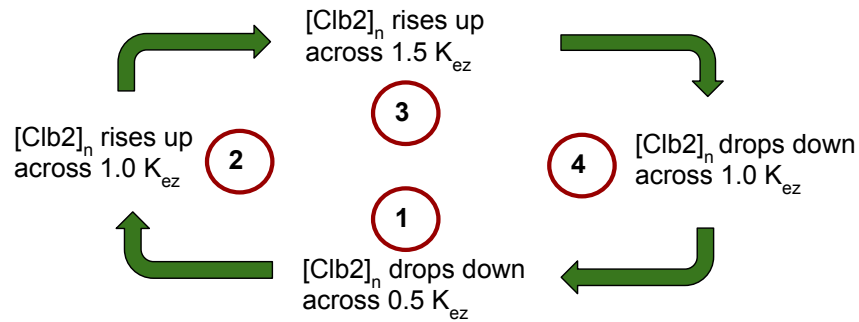
Reset rules: When the normalized concentration of Clb2 (denoted as $[Clb2]_n$) drops below K_{ez} , we reset the auxiliary proteins $[BUD]_n$ and $[SPN]_n$ to zero, and divide all species in the cell, except for Cln3 and Bck2, between daughter and mother cells with a 40:60 ratio, according to observations by Di Talia *et al.* [1]. This ratio for Cln3 and Bck2 is set to 20:80 to match with the experimental observations in [2, 3]. When $[Clb2] + [Clb5]$ drops below K_{ez2} , $[ORI]_n$ is reset to zero. These auxiliary proteins are used as flags to specify particular events (check points in the budding yeast cell cycle). That is $[BUD]_n = 1$ indicates bud emergence, $[ORI]_n = 1$ specifies initiation of DNA synthesis and $[SPN]_n = 1$ signals that the chromosome alignment on spindle is completed.

The reset rules in our hybrid model are similar to the deterministic model by Chen *et al.* [4]. However, to prevent events from misfiring multiple times due to stochastic fluctuations in the hybrid model, we follow specific tactics [5]. In our model, there are two types of events: *First*, events that are associated with the states of certain species that change across predefined thresholds in only one direction (increasing or

decreasing), taking BUD as an example. *Second*, events that are associated with the states of certain species that change across predefined thresholds in both directions (increasing and decreasing), taking Clb2 as an instance.

For the first type of events, the thresholds are set to the original predefined values at the beginning of the cell cycle. Once an event is triggered, the corresponding threshold is increased by multiplying it with a large number (e.g., 1000) to prevent misfiring.

For the second type of events, we add two dummy events to prevent misfiring. Supplementary figure S1 illustrates an example which describes the procedure we use to monitor type-two events for Clb2. The goal is to monitor the occurrence of events 2 and 4. We add events 1 and 3 to prevent misfiring of events 2 and 4 in our hybrid stochastic model. At the beginning of cell cycle, all thresholds are set to very high values except for the first event which is set to $0.5K_{ez}$. Once event i occurs, the threshold for i is set to a very large value and the threshold for event $i + 1$ is reset to its original predefined value. Using this procedure, we guarantee that events 2 and 4 take place in a correct manner in the presence of stochastic fluctuations.



Supplementary Figure S 1: **Type-two event monitoring procedure [6]**. Events 2 and 4 are the original events from the deterministic model [4]. Events 1 and 3 are the dummy events added to avoid misfiring of the original events in the presence of stochastic fluctuations. K_{ez} is a dimensionless concentration.

Table S3. Reaction channels and corresponding propensity functions for the slow subset in the hybrid model.

Reaction	Propensity Function	Reaction	Propensity Function
$\phi \rightarrow mCdh1$	$k_{s,mc dh1}$	$mCdh1 \rightarrow \phi$	$k_{d,mc dh1} \cdot mCdh1$
$\phi \rightarrow mTem1$	$k_{s,mtem1}$	$mTem1 \rightarrow \phi$	$k_{d,mtem1} \cdot mTem1$
$\phi \rightarrow mCdc15$	$k_{s,mc dc15}$	$mCdc15 \rightarrow \phi$	$k_{d,mc dc15} \cdot mCdc15$
$\phi \rightarrow mCdc14$	$k_{s,mc dc14}$	$mCdc14 \rightarrow \phi$	$k_{d,mc dc14} \cdot mCdc14$
$\phi \rightarrow mNet1$	$k_{s,mnet1}$	$mNet1 \rightarrow \phi$	$k_{d,mnet1} \cdot mNet1$
$\phi \rightarrow mCdc55$	$k_{s,mc dc55}$	$mCdc55 \rightarrow \phi$	$k_{d,mc dc55} \cdot mCdc55$
$\phi \rightarrow mEsp1$	$k_{s,mesp1}$	$mEsp1 \rightarrow \phi$	$k_{d,mesp1} \cdot mEsp1$
$\phi \rightarrow mSBF$	$k_{s,msbf}$	$mSBF \rightarrow \phi$	$k_{d,msbf} \cdot mSBF$
$\phi \rightarrow mMBF$	$k_{s,mmbf}$	$mMBF \rightarrow \phi$	$k_{d,mmbf} \cdot mMBF$
$\phi \rightarrow mMcm1$	$k_{s,mmcm1}$	$mMcm1 \rightarrow \phi$	$k_{d,mmcm1} \cdot mMcm1$
$\phi \rightarrow mAPC$	$k_{s,mapc}$	$mAPC \rightarrow \phi$	$k_{d,mapc} \cdot mAPC$
$\phi \rightarrow mCln2$	$k_{s,mcln2} \cdot (k'_{s,n2} \cdot c_{cln2} \cdot mass + k''_{s,n2} \cdot \frac{c_{cln2}}{c_{sbf}} \cdot SBF)$	$mCln2 \rightarrow \phi$	$k_{d,mcln2} \cdot mCln2$
$\phi \rightarrow mClb5$	$k_{s,mclb5} \cdot (k'_{s,b5} \cdot c_{clb5} \cdot mass + k''_{s,b5} \cdot \frac{c_{clb5}}{c_{mbf}} \cdot MBF)$	$mClb5 \rightarrow \phi$	$k_{d,mclb5} \cdot mClb5$
$\phi \rightarrow mClb2$	$k_{s,mclb2} \cdot (k'_{s,b2} \cdot c_{clb2} \cdot mass + k''_{s,b2} \cdot \frac{c_{clb2}}{c_{mcm1}} \cdot Mcm1)$	$mClb2 \rightarrow \phi$	$k_{d,mclb2} \cdot mClb2$
$\phi \rightarrow mSic1$	$k_{s,msic1} \cdot (k'_{s,c1} \cdot c_{sic1} \cdot mass + k''_{s,c1} \cdot \frac{c_{sic1}}{c_{swi5}} \cdot Swi5)$	$mSic1 \rightarrow \phi$	$k_{d,msic1} \cdot mSic1$
$\phi \rightarrow mCdc6$	$k_{s,mc dc6} \cdot (k'_{s,f6} \cdot c_{cdc6} \cdot mass + k''_{s,f6} \cdot \frac{c_{cdc6}}{c_{swi5}} \cdot Swi5 + k'''_{s,f6} \cdot \frac{c_{cdc6}}{c_{sbf}} \cdot SBF)$	$mCdc6 \rightarrow \phi$	$k_{d,mc dc6} \cdot mCdc6$

$\phi \rightarrow mS_{wi5}$	$k_{s,mswi5} \cdot (k'_{s,swi5} \cdot c_{swi5} \cdot mass + k''_{s,swi5} \cdot \frac{c_{swi5}}{c_{mcm1}} \cdot M_{cm1})$	$mS_{wi5} \rightarrow \phi$	$k_{d,mswi5} \cdot mS_{wi5}$
$\phi \rightarrow mC_{dc20}$	$k_{s,mc20} \cdot (k'_{s,20} \cdot c_{cdc20} \cdot mass + k''_{s,20} \cdot \frac{c_{cdc20}}{c_{mcm1}} \cdot M_{cm1})$	$mC_{dc20} \rightarrow \phi$	$k_{d,mc20} \cdot mC_{dc20}$
$\phi \rightarrow mP_{ds1}$	$k_{s,mpds1} \cdot (k'_{s,pds} \cdot c_{pds1} \cdot mass + k''_{s1,pds} \cdot \frac{c_{pds1}}{c_{sbf}} \cdot SBF + k''_{s2,pds} \cdot \frac{c_{pds1}}{c_{mcm1}} \cdot M_{cm1})$	$mP_{ds1} \rightarrow \phi$	$k_{d,mpds1} \cdot mP_{ds1}$

Table S4. Basal parameter values for the wild-type cell cycle. Parameters that start with lower case k are rate constants (min^{-1}). All other parameter are dimensionless.

$k_g = 0.0072$	$k'_{s,n2} = 0$	$k''_{s,n2} = 0.03$	$k_{d,n2} = 0.12$
$k'_{s,b5} = 0.0001$	$k''_{s,b5} = 0.0007$	$k'_{d3,c1} = 1$	$k_{di,b5} = 0.06$
$k_{as,f5} = 0.01$	$k_{d3,f6} = 1$	$k_{di,f5} = 0.01$	$k_{as,b5} = 50$
$k'_{s,b2} = 0.0003$	$k''_{s,b2} = 0.0114$	$k_{di,b2} = 0.05$	$k_{di,f2} = 0.5$
$k_{as,b2} = 50$	$k_{as,f2} = 15$	$k'_{s,c1} = 0.0036$	$k''_{s,c1} = 0.0359$
$k_{pp,c1} = 4$	$k'_{s,f6} = 0.0059$	$k''_{s,f6} = 0.0295$	$k'''_{s,f6} = 0.0001$
$k_{pp,f6} = 4$	$k'_{s,swi} = 0.0007$	$k''_{s,swi} = 0.0114$	$k_{d,swi} = 0.08$
$k_{a,swi} = 2$	$k_{i,swi} = 0.05$	$k_{a,apc} = 0.1$	$k_{i,apc} = 0.15$
$k'_{s,20} = 0.0014$	$k''_{s,20} = 0.1364$	$k'_{a,20} = 0.05$	$k''_{a,20} = 0.2$
$k_{d,20} = 0.3$	$k_{s,cdh} = 0.0014$	$k_{d,cdh} = 0.01$	$k'_{a,15} = 0.002$
$k''_{a,15} = 1$	$k'''_{a,15} = 0.001$	$k_{i,15} = 0.5$	$k_{s,14} = 0.02$
$k_{d,14} = 0.1$	$k_{d,net} = 0.03$	$k_{di,rent} = 1$	$k_{di,rentp} = 2$
$k_{as,rent} = 200$	$k_{as,rentp} = 1$	$k_{s,net} = 0.0134$	$k_{s,55} = 0.0143$
$k'_{s,pds} = 0$	$k''_{s1,pds} = 0.0043$	$k''_{s2,pds} = 0.0079$	$k_{di,esp} = 0.5$
$k_{as,esp} = 50$	$k_{s,ori} = 2$	$k_{d,ori} = 0.06$	$k_{s,bud} = 0.2$
$k_{d,bud} = 0.06$	$k_{s,spn} = 0.1$	$k_{d,spn} = 0.06$	$k_{s,tem1t} = 0.0150$
$k_{d,tem1t} = 0.046$	$k_{s,cdc15t} = 0.0142$	$k_{d,cdc15t} = 0.046$	$k_{s,esp1t} = 0.0139$
$k_{d,esp1t} = 0.046$	$k_{s,sbft} = 0.007$	$k_{d,sbft} = 0.0462$	$k_{a,mcm} = 5$
$k_{s,mbft} = 0.0066$	$k_{d,mbft} = 0.046$	$k_{s,apct} = 0.0065$	$k_{d,apct} = 0.0462$
$k_{s,mcm1t} = 0.0078$	$k_{d,mcm1t} = 0.046$	$k_{i,mcm} = 0.15$	$k''_{d3,pds} = 0.04$
$k_{a,ssf} = 0.38$	$k'_{i,ssf} = 0.6$	$k''_{i,ssf} = 8$	$k'_{d,b5} = 0.01$
$k'_{d,b2} = 0.003$	$k''_{d,b2} = 0.4$	$k_{d,b2p} = 0.15$	$k_{d1,c1} = 0.01$
$k_{d2,c1} = 1$	$k''_{d,b5} = 0.16$	$k_{d1,f6} = 0.01$	$k_{d2,f6} = 1$
$k'_{a,cdh} = 0.01$	$k''_{a,cdh} = 0.8$	$k'_{i,cdh} = 0.001$	$k''_{i,cdh} = 0.08$
$k'_{pp,net} = 0.05$	$k''_{pp,net} = 3$	$k'_{kp,net} = 0.01$	$k''_{kp,net} = 0.6$
$k'_{d,55} = 0.17$	$k''_{d,55} = 2$	$k'_{d1,pds} = 0.01$	$k''_{d2,pds} = 0.2$

Table S4.(continued)

$k_{s,n3} = 0.0080$	$k_{d,n3} = 0.12$	$k_{s,k2} = 0.0048$	$k_{d,k2} = 0.12$
$k_{\text{mad}2} = 8$ for $[\text{ORI}]_n > 1$ and $[\text{SPN}]_n < 1$; otherwise 0.01			
$k_{\text{bud}2} = 1$ for $[\text{ORI}]_n > 1$ and $[\text{SPN}]_n < 1$; otherwise 0.2			
$k_{\text{lte}1} = 1$ for $[\text{SPN}]_n > 1$ and $[\text{Clb}2]_n > 1$; otherwise 0.1			
$K_{ez} = 0.3$	$K_{ez2} = 0.2$	$J_{i,\text{cdh}} = 0.03$	$J_{a,\text{apc}} = 0.1$
$J_{i,\text{apc}} = 0.1$	$J_{a,\text{cdh}} = 0.03$	$J_{\text{pds}} = 0.04$	$J_{a,\text{sbf}} = 0.01$
$J_{n3} = 6$	$J_{a,\text{tem}} = 0.1$	$J_{i,\text{tem}} = 0.1$	$J_{\text{spn}} = 0.14$
$J_{d2,\text{f6}} = 0.05$	$J_{a,\text{mcm}} = 0.1$	$J_{i,\text{mcm}} = 0.1$	$J_{d2,\text{c}1} = 0.05$
$J_{i,\text{sbf}} = 0.01$	$J_{20,55} = 0.15$	$e_{\text{cdh},\text{b}2} = 1.2$	$e_{\text{cdh},\text{b}5} = 8$
$e_{\text{bud},\text{n}3} = 0.05$	$e_{\text{ori},\text{b}5} = 0.9$	$e_{\text{ori},\text{b}2} = 0.45$	$e_{\text{bud},\text{n}2} = 0.12$
$e_{\text{sbf},\text{b}5} = 2$	$e_{\text{bud},\text{b}5} = 0.25$	$e_{\text{sbf},\text{n}2} = 2$	$e_{\text{sbf},\text{n}3} = 10$
$e_{\text{c}1,\text{b}5} = 0.1$	$e_{\text{c}1,\text{n}3} = 0.3$	$e_{\text{c}1,\text{k}2} = 0.03$	$e_{\text{c}1,\text{n}2} = 0.06$
$e_{\text{f}6,\text{n}2} = 0.06$	$e_{\text{c}1,\text{b}2} = 0.45$	$e_{\text{f}6,\text{n}3} = 0.3$	$e_{\text{f}6,\text{k}2} = 0.03$
$e_{\text{cdh},\text{n}2} = 0.4$	$e_{\text{f}6,\text{b}5} = 0.1$	$e_{\text{f}6,\text{b}2} = 0.55$	$e_{\text{cdh},\text{n}3} = 0.25$
$c_{\text{clb}2} = 479.2$	$c_{\text{cln}2} = 239.6$	$c_{\text{cln}3} = 599$	$c_{\text{bck}2} = 599$
$c_{\text{cdh}1} = 1198$	$c_{\text{ori}} = 119.8$	$c_{\text{bud}} = 119.8$	$c_{\text{spn}} = 119.8$
$c_{\text{tem}1} = 178.2$	$c_{\text{clb}5} = 479.2$	$c_{\text{cdc}20} = 1797$	$c_{\text{sic}1} = 479.2$
$c_{\text{cdc}6} = 479.2$	$c_{\text{cdc}14} = 275.54$	$c_{\text{net}1} = 275.54$	$c_{\text{cdc}15} = 479.2$
$c_{\text{pds}1} = 39.5$	$c_{\text{esp}1} = 39.5$	$c_{\text{sbf}} = 479.2$	$c_{\text{mbf}} = 479.2$
$c_{\text{apc}} = 263.56$	$c_{\text{cdc}55} = 4193$	$c_{\text{rent}} = 4193$	$c_{\text{mcm}1} = 4193$
$k_{s,\text{mCdc}15} = 0.45$	$k_{d,\text{mCdc}15} = 0.14$	$k_{s,\text{mTem}1} = 0.43$	$k_{d,\text{mTem}1} = 0.14$
$k_{s,\text{mNet}1} = 0.5$	$k_{d,\text{mNet}1} = 0.1$	$k_{s,\text{mCdc}14} = 1.5$	$k_{d,\text{mCdc}14} = 0.14$
$k_{s,\text{mEsp}1} = 0.3$	$k_{d,\text{mEsp}1} = 0.08$	$k_{s,\text{mCdc}55} = 0.97$	$k_{d,\text{mCdc}55} = 0.14$
$k_{s,\text{mMBF}} = 0.97$	$k_{d,\text{mMBF}} = 0.14$	$k_{s,\text{mSBF}} = 0.94$	$k_{d,\text{mSBF}} = 0.14$
$k_{s,\text{mPds}1} = 0.24$	$k_{d,\text{mPds}1} = 0.14$	$k_{s,\text{mMcm}1} = 0.8$	$k_{d,\text{mMcm}1} = 0.14$
$k_{s,\text{mAPC}} = 0.97$	$k_{d,\text{mAPC}} = 0.14$	$k_{s,\text{mCln}2} = 0.0117$	$k_{d,\text{mCln}2} = 0.23$
$k_{s,\text{mClb}5} = 0.3916$	$k_{d,\text{mClb}5} = 0.14$	$k_{s,\text{mClb}2} = 0.0034$	$k_{d,\text{mClb}2} = 0.35$

Table S4.(continued)

$k_{s,mSic1} = 0.0067$	$k_{d,mSic1} = 0.14$	$k_{s,mCdc6} = 0.0083$	$k_{d,mCdc6} = 0.14$
$k_{s,mSwi5} = 0.0016$	$k_{d,mSwi5} = 0.14$	$k_{s,mCdc20} = 0.0001$	$k_{d,mCdc20} = 0.14$
$k_{s,mCdh1} = 0.97$	$k_{d,mCdh1} = 0.14$		

The FORTRAN code that implements the model described in Tables S1-S4 is provided in Supplementary Code. We notice that the parameters listed in Table S4 are the values that are computed after converting the concentration of species into population. In the code, however, to provide more flexibility in tuning the parameters, the original parameters from Chen's model are listed and then converted. See the README file that further elaborates on the Supplementary Code.

Supplementary Table S5: List of mutant strains. Simulation results of our hybrid stochastic model (in column 6) are compared with experimental data (in column 4) and simulation results of the deterministic model by Chen *et al.* [4] (in column 5). The parameter modification column reports the changes made to the parameter values in order to simulate each strain. ‘V’ means ‘viable’, ‘In’ means inviable, and ‘pV’ partially viable. We generate a sufficiently large population of mother and daughter cells, expanding over time, to compute probability of division. In column 6, we report the probability of division as well as the number of simulations used to calculate this probability. Orange typeface in column 5 indicates disagreement between the Chen deterministic model and the experimental observations. Red typeface in column 6 indicates disagreement between the hybrid model and the experimental observations.

No	Mutant strain	Parameter modification	Experiment	Chen model	Hybrid model
1	Wild-type (WT) on glucose (Glc)	-	V	V	V : 0.97 (11,000)
2.1	WT on galactose (Gal)	$k_g=0.004621$ (MDT=150)	V	V	V : 0.93 (22,762)
2.2	WT on raffinose (Raff)	$k_g=0.00433$ (MDT=160)	V	V	V : 0.93 (14,198)
3	<i>cln1</i> Δ <i>cln2</i> Δ	$k''_{s,n2}=0$	V	V	V : 0.92 (13,710)
4	<i>GAL-CLN2 cln1</i> Δ <i>cln2</i> Δ	$k'_{s,n2}=0.12$, $k''_{s,n2}=0$, $k_g=0.004621$	V	V	V : 0.90 (24,500)
5	<i>cln1</i> Δ <i>cln2</i> Δ <i>sic1</i> Δ	$k''_{s,n2}=0$, $k'_{s,c1} = k''_{s,c1}=0$	V	V	V : 0.75 (14,010)
6	<i>cln1</i> Δ <i>cln2</i> Δ <i>cdh1</i> Δ	$k''_{s,n2}=0$, $k_{s,cdh}=0$, init CDH1T=CDH1=0	V	V	In : 0.30 (9,373)
7	<i>GAL-CLN2 cln1</i> Δ <i>cln2</i> Δ <i>cdh1</i> Δ	$k'_{s,n2}=0.12$, $k''_{s,n2}=0$, $k_{s,cdh}=0$, $k_g=0.004621$, init CDH1T=CDH1=0	V	V	V : 0.76 (11,594)

8	<i>cln3Δ</i>	$k_{s,n3}=0$	V	V	V : 0.98 (9,990)
9	<i>GAL-CLN3</i>	$k_{s,n3}=5 \times k_{s,n3},$ $k_g=0.004621$	V	V	V : 0.94 (9,610)
10	<i>bck2Δ</i>	$k_{s,k2}=0$	V	V	V : 0.97 (11,326)
11	multi-copy <i>BCK2</i>	$k_{s,k2}=5 \times k_{s,k2}$	V	V	V : 0.96 (10,032)
12	<i>cln1Δ cln2Δ bck2Δ</i>	$k''_{s,n2}=0, k_{s,k2}=0$	V	V	V : 0.84 (11,294)
13	<i>cln3Δ bck2Δ</i>	$k_{s,n3}=0, k_{s,k2}=0$	In	In	In : 0.10 (9,310)
14	<i>cln3Δ bck2Δ GAL-CLN2 cln1Δ cln2Δ</i>	$k_{s,n3}=0, k_{s,k2}=0,$ $k'_{s,n2}=0.12, k''_{s,n2}=0,$ $k_g=0.004621$	V	V	V : 0.95 (17,452)
15	<i>cln3Δ bck2Δ multi-copy CLN2</i>	$k_{s,n3}=0, k_{s,k2}=0$ $k''_{s,n2}=5 \times k''_{s,n2}$	In	In	In : 0.40 (16,523)
16	<i>cln3Δ bck2Δ sic1Δ</i>	$k_{s,n3}=0, k_{s,k2}=0,$ $k'_{s,c1} = k''_{s,c1}=0$	In	In	In : 0.44 (9,614)
17	<i>cln1Δ cln2Δ cln3Δ</i>	$k'_{s,n2}=k''_{s,n2}=0,$ $k_{s,n3}=0$	In	In	In : 0.04 (9,700)
18	<i>cln1Δ cln2Δ cln3Δ GAL-CLN2</i>	$k''_{s,n2}=0, k_{s,n3}=0,$ $k'_{s,n2}=0.12,$ $k_g=0.004621$	V	V	V : 0.95 (17,640)
19	<i>cln1Δ cln2Δ cln3Δ GAL-CLN3</i>	$k'_{s,n2}=k''_{s,n2}=0,$ $k_{s,n3}=5 \times k_{s,n3},$ $k_g=0.004621$	V	V	V : 0.84 (12,598)

20	<i>cln1Δ cln2Δ cln3Δ sic1Δ</i>	$k'_{s,n2}=0, k''_{s,n2}=0,$ $k_{s,n3}=0,$ $k'_{s,c1} = k''_{s,c1} = 0$	V	V	V : 0.76 (12,904)
21	<i>cln1Δ cln2Δ cln3Δ cdh1Δ</i>	$k'_{s,n2}=k''_{s,n2}=0,$ $k_{s,n3}=0, k_{s,cdh}=0,$ init CDH1=CDH1T=0	In	In	In : 0.03 (9,800)
22	<i>cln1Δ cln2Δ cln3Δ</i> multi-copy <i>CLB5</i>	$k'_{s,n2}=k''_{s,n2}=0,$ $k_{s,n3}=0,$ $k'_{s,b5}=4 \times k'_{s,b5},$ $k''_{s,b5}=4 \times k''_{s,b5}$	V	V	V : 0.86 (20,376)
23	<i>cln1Δ cln2Δ cln3Δ</i> <i>GAL-CLB5</i>	$k'_{s,n2}=0, k''_{s,n2}=0,$ $k_{s,n3}=0,$ $k'_{s,b5}=15 \times k'_{s,b5},$ $k_g=0.004621$	V	V	V : 0.99 (17,856)
24	<i>cln1Δ cln2Δ cln3Δ</i> multi-copy <i>BCK2</i>	$k'_{s,n2}=k''_{s,n2}=0,$ $k_{s,n3}=0,$ $k_{s,k2}=10 \times k_{s,k2}$	V	V	V : 0.89 (11,486)
25	<i>cln1Δ cln2Δ cln3Δ</i> <i>GAL-CLB2</i>	$k'_{s,n2}=k''_{s,n2}=0,$ $k_{s,n3}=0,$ $k'_{s,b2}=2 \times k'_{s,b2},$ $k_g=0.004621$	In	In	In : 0.01 (10,030)
26	<i>cln1Δ cln2Δ cln3Δ apc-ts</i>	$k'_{s,n2}=k''_{s,n2}=0,$ $k_{s,n3}=0, k_{s,cdh}=0,$ $k'_{s,20}=k''_{s,20}=0,$ init CDH1=CDH1T=0	In	In	In : 0 (10,000)
27	<i>sic1Δ</i>	$k'_{s,c1} = k''_{s,c1} = 0$	V	V	V : 0.87 (16,198)

28	<i>GAL-SIC1</i>	$k'_{s,c1}=10\times k'_{s,c1},$ $k_g=0.004621$	V	V	V : 0.90 (9,848)
29	<i>GAL-SIC1dbΔ</i>	$k'_{s,c1}=10\times k'_{s,c1},$ $k_{d3,c1}=0,$ $k_g=0.004621$	In	In	In : 0 (10,000)
30	<i>GAL-SIC1 cln1Δ cln2Δ</i>	$k'_{s,c1}=10\times k'_{s,c1},$ $k''_{s,n2}=0,$ $k_g=0.004621$	In	In	In : 0 (1,000)
31	<i>GAL-SIC1 GAL-CLN2</i> <i>cln1Δ cln2Δ</i>	$k'_{s,c1}=10\times k'_{s,c1},$ $k'_{s,n2}=0.12, k''_{s,n2}=0,$ $k_g=0.004621$	V	V	V : 0.90 (11,180)
32	<i>GAL-SIC1 cln1Δ cln2Δ</i> <i>cdh1Δ</i>	$k'_{s,c1}=k''_{s,c1}=0.12,$ $k''_{s,n2}=k_{s,cdh}=0,$ $k_g=0.004621,$ init CDH1T=CDH1=0	In	In	In : 0 (1,000)
33	<i>GAL-SIC1 GAL-CLN2</i> <i>cln1Δ cln2Δ cdh1Δ</i>	$k'_{s,c1}=0.12,$ $k'_{s,n2}=0.12, k''_{s,n2}=0,$ $k_{s,cdh}=0,$ $k_g=0.004621,$ init CDH1T=CDH1=0	V	V	V : 0.80 (14,376)
34	<i>cdh1Δ</i>	$k_{s,cdh}=0,$ init CDH1T=CDH1=0	V	V	In : 0.49 (15,078)
35	<i>Cdh1</i> constitutively active	$k''_{i,cdh}=0,$ $k_g=0.004621,$ $k_{s,cdh}=3\times k_{s,cdh}$	In	In	In : 0.32 (9,238)

36	<i>sic1Δ cdh1Δ</i>	$k'_{s,c1}=k''_{s,c1}=0,$ $k_{s,cdh}=0,$ init CDH1T=CDH1=0	In	In	In : 0 (10,000)
37	<i>sic1Δ cdh1Δ GAL- CDC20</i>	$k'_{s,c1}=k''_{s,c1}=0,$ $k_{s,cdh}=0, k'_{s,20}=10,$ $k_g=0.004621$	V	V	Gal : In : 0.28 (9,640) Glc : pV : 0.71 (10,708)
38	<i>cdc6Δ2-49</i>	$k'_{s,f6}=k''_{s,f6}=k'''_{s,f6}=0$	V	V	V : 0.97 (11,482)
39	<i>sic1Δ cdc6Δ2-49</i>	$k'_{s,c1}=k''_{s,c1}=0,$ $k'_{s,f6}=k''_{s,f6}=k'''_{s,f6}=0$	V	V	In : 0.01 (9,016)
40	<i>cdh1Δ cdc6Δ2-49</i>	$k'_{s,f6}=k''_{s,f6}=k'''_{s,f6}=0,$ $k_{s,cdh}=0,$ init CDH1T=CDH1=0	V	V	In : 0.16 (10,331)
41 ¹	<i>sic1Δ cdc6Δ2-49 cdh1Δ</i>	$k'_{s,c1}=k''_{s,c1}=0,$ $k_{s,cdh}=0, k'_{s,f6}=$ $k''_{s,f6}=k'''_{s,f6}=0,$ init CDH1T=CDH1=0	In	In	In
42	<i>sic1Δ cdc6Δ2- 49 cdh1Δ GAL-CDC20</i>	$k'_{s,c1}=k''_{s,c1}=0,$ $k'_{s,f6}=k''_{s,f6}=k'''_{s,f6}=0,$ $k_{s,cdh}=0, k'_{s,20}=4,$ $k_g=0.004621,$ init CDH1T=CDH1=0	V	V	In : 0.02 (10,088)
43	<i>swi5Δ</i>	$k'_{s,swi}=k''_{s,swi}=0$	V	V	In : 0.53 (23,878)

¹Experimental observations show that *sic1Δ cdc6Δ2-49 cdh1Δ* (mutant # 41) and *swi5Δ cdh1Δ* (mutant # 45) strains are not able to undergo the cell division and thus are inviable [7]; both strains have similar phenotype and become arrested as binucleate cells with 4C DNA content. Our simulation (similar to Chen's deterministic simulation [4]) shows that the cells are inviable; however, they become arrested in telophase with 2C DNA content. We consider this simulation result as an inconsistency with experimental observations.

44	<i>swi5Δ GAL-CLB2</i>	$k'_{s,swi}=k''_{s,swi}=0,$ $k_{s,b2}=0.12,$ $k_g=0.004621$	In	In	In : 0.34 (9,790)
45 ¹	<i>swi5Δ cdh1Δ</i>	$k'_{s,swi}=k''_{s,swi}=0,$ $k_{s,cdh}=0,$ init CDH1T=CDH1=0	In	In	In
46	<i>swi5Δ cdh1Δ GAL-SIC1</i>	$k'_{s,swi}=k''_{s,swi}=0,$ $k_{s,cdh}=0,$ $k'_{s,c1}=10\times k'_{s,c1},$ $k_g=0.004621,$ init CDH1T=CDH1=0	V	V	V : 0.83 (10,636)
47	<i>clb1Δ clb2Δ</i>	$k'_{s,b2}=k''_{s,b2}=0$	In	In	In : 0 (10,000)
48	<i>CLB1 clb2Δ</i>	$k'_{s,b2}=0.0003,$ $k''_{s,b2}=0.013$ (33% WT)	V	In	V : 0.82 (26,466)
49	<i>GAL-CLB2</i>	$k'_{s,b2}=0.12,$ $k_g=0.004621$	V	V	V : 0.86 (17,714)
50	multi-copy <i>GAL-CLB2</i>	$k'_{s,b2}=0.96$ (8 copies of <i>GAL-CLB2</i>), $k_g=0.004621$	In	In	In : 0 (10,000)
51 ²	<i>CLB1 clb2Δ cdh1Δ</i>	$k'_{s,b2}=0.0003,$ $k''_{s,b2}=0.013$ (33% WT), $k_{s,cdh}=0,$ init CDH1T=CDH1=0	Gal : V Glc : pV	Gal : V Glc : V	Gal : V : 0.79 (17,608), Glc : In : 0.62 (14,719)

²Experimental observations (see supplementary figure 1, panel A in [8]) show that *CLB1 clb2Δ cdh1Δ* cells grow well on galactose; however, they exhibit poor viability on glucose. That is why in column 4 we report this mutant strain as partially viable (pV). 'Glc' refers to growth in glucose medium; 'Gal' to galactose.

52 ³	<i>CLB1 clb2Δ pds1Δ</i>	$k'_{s,b2}=0.0003,$ $k''_{s,b2}=0.013$ (33% WT), $k''_{s1,pds}=k''_{s2,pds}=0$	In	V	In
53	<i>GAL-CLB2 sic1Δ</i>	$k'_{s,b2}=0.12,$ $k'_{s,c1}=k''_{s,c1}=0,$ $k_g=0.004621$	In	In	In : 0.20 (10,090)
54	<i>GAL-CLB2 cdh1Δ</i>	$k'_{s,b2}=0.12, k_{s,cdh}=0,$ $k_g=0.004621,$ init CDH1T=CDH1=0	In	In	In : 0 (10,000)
55	<i>CLB2-dbΔ</i>	$k_{d,b2p}=0, k''_{d,b2}=0.03$ (8.5% activity left due to KEN box).	In	In	In : 0.27 (9,892)
56	<i>CLB2-dbΔ</i> on galactose	$k_{d,b2p}=0,$ $k''_{d,b2}=0.03,$ $k_g=0.004621$	In	In	In : 0.59 (13,848)
57	<i>CLB2-dbΔ</i> multi-copy <i>SIC1</i>	$k_{d,b2p}=0,$ $k''_{d,b2}=0.03,$ $k'_{s,c1}=10 \times k'_{s,c1},$ $k''_{s,c1}=10 \times k''_{s,c1}$	V	V	V : 0.79 (11,900)
58	<i>CLB2-dbΔ GAL-SIC1</i>	$k_{d,b2p}=0,$ $k''_{d,b2}=0.03,$ $k'_{s,c1}=10 \times k'_{s,c1},$ $k_g=0.004621$	V	V	V : 0.79 (9,044)

³Simulation results show that *CLB1 clb2Δ pds1Δ* (mutant # 52), and *pds1Δ* (mutant # 80) strains are able to exit mitosis; however, Esp1 is active throughout the cell cycle (even before spindle alignment). Thus, according to our viability rules, these mutants are inviable.

59	<i>CLB2-dbΔ</i> multi-copy <i>CDC6</i>	$k_{d,b2p}=0,$ $k''_{d,b2}=0.03,$ $k'_{s,f6}=5 \times k'_{s,f6},$ $k''_{s,f6}=5 \times k''_{s,f6},$ $k'''_{s,f6}=5 \times k'''_{s,f6}$	V	V	In : 0.57 (13,484)
60	<i>CLB2-dbΔ clb5Δ</i>	$k_{d,b2p}=0,$ $k''_{d,b2}=0.03,$ $k'_{s,b5}=k''_{s,b5}=0$	In	In	In : 0.24 (9,672)
61	<i>CLB2-dbΔ clb5Δ</i> on galactose and raffinose	$k_{d,b2p}=0,$ $k''_{d,b2}=0.03,$ $k'_{s,b5}=k''_{s,b5}=0,$ $k_g=0.004621$ (Gal), $k_g=0.00433$ (Raff)	pV	V	Gal : In : 0.62 (17,338) Raff : pV : 0.68 (13,364)
62	<i>GAL-CLB2-dbΔ</i>	$k_{d,b2p}=0,$ $k''_{d,b2}=0.03,$ $k''_{s,b2}=0.12,$ $k_g=0.004621$	In	In	In : 0.03 (10,118)
63	<i>clb5Δ clb6Δ</i>	$k'_{s,b5}=k''_{s,b5}=0$	V	V	V : 0.98 (16,653)
64	<i>cln1Δ cln2Δ clb5Δ clb6Δ</i>	$k'_{s,n2}=k''_{s,n2}=0,$ $k'_{s,b5}=k''_{s,b5}=0$	In	In	In : 0 (10,000)
65	<i>GAL-CLB5</i>	$k'_{s,b5}=15 \times k'_{s,b5},$ $k_g=0.004621$	V	V	V : 0.94 (9,612)
66 ⁴	<i>GAL-CLB5 sic1Δ</i>	$k'_{s,b5}=15 \times k'_{s,b5},$ $k'_{s,c1}=k''_{s,c1}=0,$ $k_g=0.004621$	In	In	In

⁴Simulation results show that mutant strains *GAL-CLB5 sic1Δ* (mutant # 66), *CLB5-dbΔ sic1Δ* (mutant # 69), and *GAL-CLB5-dbΔ* (mutant # 72) are able to exit mitosis; however, [ORI] is not relicensed (due to high activity of Clb5 in G1 phase). Thus, according to our viability rules, these mutants are inviable.

67	<i>GAL-CLB5 cdh1Δ</i>	$k'_{s,b5}=10 \times k'_{s,b5},$ $k_{s,cdh}=0,$ $k_g=0.004621,$ init CDH1T=CDH1=0	In	V	In : 0.60 (20,782)
68	<i>CLB5-dbΔ</i>	$k''_{d,b5}=0$	V	V	V : 0.95 (11,656)
69 ⁴	<i>CLB5-dbΔ sic1Δ</i>	$k''_{d,b5}=0,$ $k'_{s,c1}=k''_{s,c1}=0$	In	In	In
70	<i>CLB5-dbΔ pds1Δ</i>	$k''_{d,b5}=0,$ $k''_{s1,pds}=k''_{s2,pds}=0$	V	V	V : 0.97 (12,539)
71	<i>CLB5-dbΔ pds1Δ</i> <i>cdc20Δ</i>	$k''_{d,b5}=0,$ $k''_{s1,pds}=k''_{s2,pds}=0,$ $k'_{s,20}=k''_{s,20}=0$	In	In	pV : 0.65, (12,846)
72 ⁴	<i>GAL-CLB5-dbΔ</i>	$k'_{s,b5}=15 \times k'_{s,b5},$ $k''_{d,b5}=0,$ $k_g=0.004621$	In	In	In
73	<i>cdc20-ts</i>	$k'_{s,20}=k''_{s,20}=0$	In	In	In : 0.31 (9,710)
74	<i>cdc20Δ clb5Δ</i>	$k'_{s,20}=k''_{s,20}=0,$ $k'_{s,b5}=k''_{d,b5}=0$	In	In	In : 0.58 (9,944)
75	<i>cdc20Δ pds1Δ</i>	$k'_{s,20}=k''_{s,20}=0,$ $k''_{s1,pds}=k''_{s2,pds}=0$	In	In	pV : 0.66 (16,274)
76	<i>cdc20Δ pds1Δ clb5Δ</i>	$k'_{s,20}=k''_{s,20}=0,$ $k'_{s,b5}=k''_{d,b5}=0,$ $k''_{s1,pds}=k''_{s2,pds}=0$	V	V	V : 0.95 (10,920)
77	<i>GAL-CDC20</i>	$k'_{s,20}=6,$ $k_g=0.004621$	In	In	V : 0.99 (11,355)

78	<i>cdc20-ts mad2Δ</i>	$k'_{s,20}=k''_{s,20}=0,$ $k_{mad2}=0.01$	In	In	In : 0.31 (9,720)
79	<i>cdc20-ts bub2Δ</i>	$k'_{s,20}=k''_{s,20}=0,$ $k_{bub2}=0,$ init BUB2=0	In	In	In : 0.25 (9,586)
80 ³	<i>pds1Δ</i>	$k''_{s1,pds}=k''_{s2,pds}=0$	V	In	In
81 ⁵	<i>esp1-ts</i>	$k_{as,esp} = 0.1, k_{di,esp} =$ 0.002, (1/500 × WT)	In	In	In
82 ⁶	<i>PDS1-dbΔ</i>	$k''_{d2,pds}=k''_{d3,pds}=0$	In	In	In
83 ⁶	<i>GAL-PDS1-dbΔ</i>	$k'_{s,pds} = 0.1,$ $k_g=0.004621$ $k''_{d2,pds}=k''_{d3,pds}=0$	In	In	In
84 ⁶	<i>GAL-PDS1-dbΔ esp1-ts</i>	$k'_{s,pds} = 0.1,$ $k''_{d2,pds} = k''_{d3,pds}=0,$ $k_{as,esp}=0.1,$ $k_{di,esp}=0.002,$ (1/500 × WT), $k_g=0.004621$	In	In	In
85	<i>GAL-ESP1 cdc20-ts</i>	$k'_{s,20}=k''_{s,20}=0,$ $k'_{s,esp1t}=3 \times k'_{s,esp1t},$ $k_g=0.004621$	In	In	In : 0.47 (10,057)
86	<i>tem1Δ</i>	$k''_{a,15}=0.002 (=$ $k'_{a,15}), k_{s,mTem1}=0$	In	In	pV : 0.73 (14,096)

⁵Simulation results show that *esp1-ts* strains are able to exit mitosis while the sister chromatids are not yet separated. Therefore, according to our viability rule this mutant is inviable.

⁶Simulation results show that *PDS1-dbΔ* (mutant # 82), *GAL-PDS1-dbΔ* (mutant # 83), and *GAL-PDS1-dbΔ esp1-ts* (mutant # 84) strains are able to exit mitosis; however, Esp1 is inactive throughout the cell cycle which means sister chromatids are still attached. Thus, according to our viability rules, these mutants are inviable.

87	<i>GAL-TEM1</i>	$k_{s,tem1t}=5 \times k_{s,tem1t},$ $k_g=0.004621$	V	V	V : 0.93 (15,072)
88	<i>tem1-ts</i> multi-copy <i>CDC15</i>	$k''_{a,15}=0.002,$ $k_{s,mTem1}=0,$ $k_{s,tem1t}=0,$ $k_{s,cdc15t}=5 \times k_{s,cdc15t}$	V	V	V : 0.77 (17,050)
89	<i>tem1-ts GAL-CDC15</i>	$k''_{a,15}=0.002,$ $k_{s,mTem1}=0,$ $k_{s,tem1t}=0,$ $k_{s,cdc15t}=15 \times k_{s,cdc15t},$ $k_g=0.004621$	V	V	V : 0.81 (15,616)
90	<i>tem1Δ net1-ts</i>	$k''_{a,15}=0.002,$ $k_{s,mTem1}=0,$ $k_{s,tem1t}=0,$ $k_{as,rent}=10,$ $k_{as,rentp}=0.05,$ (5% WT)	V	V	V : 0.99 (16,436)
91	<i>tem1-ts</i> multi-copy <i>CDC14</i>	$k''_{a,15}=0.002,$ $k_{s,14}=0.4$ (2 copies), $k_{s,mTem1}=k_{s,tem1t}=0$	V	V	V : 0.96 (10,470)
92	<i>cdc15Δ</i>	$k''_{kp,net}=0,$ $k_{s,cdc15t}=0$	In	In	pV : 0.73 (13,862)
93	multi-copy <i>CDC15</i>	$k_{s,cdc15t}=5 \times k_{s,cdc15t}$	V	V	V : 0.97 (15,020)
94	<i>cdc15-ts</i> multi-copy <i>TEM1</i>	$k''_{kp,net}=0,$ $k_{s,cdc15t}=0,$ $k_{s,tem1t}=5 \times k_{s,tem1t}$	In	In	pV : 0.73 (14,076)

95	<i>cdc15Δ net1-ts</i>	$k''_{kp,net}=0,$ $k_{as,rentp}=0.05,$ $k_{as,rent}=10,$ (5% WT)	V	V	V : 0.99 (27,612)
96	<i>cdc15-ts</i> multi-copy <i>CDC14</i>	$k''_{kp,net}=0, k_{s,14}=0.4$ (2 copies)	V	V	V : 0.96 (24,884)
97	<i>net1-ts</i>	$k_{as,rentp}=0.05,$ $k_{as,rent}=10,$ (5% WT)	V	V	V : 0.99 (30,3160)
98	<i>GAL-NET1</i>	$k_{s,net}=5 \times k_{s,net},$ $k_g=0.004621$	In	In	In : 0.50 (10,966)
99	<i>cdc14-ts</i>	$k_{s,14}=0$	In	In	In : 0.08 (9,600)
100	<i>GAL-CDC14</i>	$k_{s,14}=4 \times k_{s,14},$ $k_g=0.004621$	In	In	In : 0.04 (10,004)
101	<i>GAL-NET1 GAL-</i> <i>CDC14</i>	$k_{s,net}=3 \times k_{s,net},$ $k_{s,14}=3 \times k_{s,14},$ $k_g=0.004621$	V	V	V : 0.94 (10,651)
102	<i>net1Δ cdc20-ts</i>	$k_{as,rentp}=0.05,$ $k_{as,rent}=10,$ (5% WT) $k'_{s,20}=k''_{s,20}=0$	In	In	In : 0.55 (10,974)
103	<i>cdc14-ts GAL-SIC1</i>	$k_{s,14}=0,$ $k'_{s,c1}=10 \times k'_{s,c1},$ $k_g=0.004621$	In	In	In : 0.49 (10,482)

104	<i>cdc14-ts</i> then <i>GAL-SIC1</i>	$k_{s,14}=0$ for 180 min, then 3 copies of GAL-SIC1 ($k'_{s,c1}=3\times k'_{s,c1}$, $k_g=0.004621$)	able to exit mitosis	exits	not able to exit mitosis
105	<i>cdc14-ts sic1Δ</i>	$k'_{s,c1}=k''_{s,c1}=0$, (16% Cdc14 activity) $k_{pp,c1}=k_{pp,f6}=0.64$, $k_{a,swi}=0.32$, $k''_{a,cdh}=0.128$	In	In	In : 0.27 (9,725)
106	<i>cdc14-ts cdh1Δ</i>	$k_{s,cdh}=0$, init CDH1=CDH1T=0 (30% Cdc14 activity) $k_{pp,c1}=k_{pp,f6}=1.2$, $k_{a,swi}=0.6$, $k''_{a,cdh}=0.13$	In	In	In : 0.16 (9,200)
107	<i>cdc14-ts GAL-CLN2</i>	$k'_{s,n2}=0.12$, $k''_{s,n2}=0$, $k_g=0.004621$, (10% Cdc14 activity) $k_{pp,c1}=k_{pp,f6}=0.8$, $k_{a,swi}=0.4$, $k''_{a,cdh}=0.16$	In	In	In : 0.61 (11,612)
108	<i>TAB6-1</i>	$k_{as,rentp}=0.05$, $k_{as,rent}=10$, (5% WT)	V	V	V : 0.99 (13,010)
109	<i>TAB6-1 cdc15Δ</i>	$k_{as,rentp}=0.05$, $k_{as,rent}=10$ (5% WT), $k''_{kp,net}=0$	V	V	V : 0.99 (12,960)

110	<i>TAB6-1 clb5Δ clb6Δ</i>	$k_{as,rentp}=0.05,$ $k_{as,rent}=10$ (5% WT), $k'_{s,b5}=k''_{s,b5}=0$	In	In	V : 0.99 (11,638)
111	<i>TAB6-1 CLB1 clb2Δ</i>	$k_{as,rentp}= 0.05,$ $k_{as,rent}=10$ (5% WT), $k'_{s,b2}=0.0003,$ $k''_{s,b2}=0.013,$ (33% WT)	V	V	V : 0.98 (11,314)
112	<i>mad2Δ</i>	$k_{mad2}=0.01$	V	V	V : 0.98 (16,510)
113	<i>bub2Δ</i>	$k_{bub2}=0,$ init BUB2=0	V	V	V : 0.98 (12,488)
114	<i>mad2Δ bub2Δ</i>	$k_{bub2}=0,$ $k_{mad2}=0.01,$ init BUB2=0	V	V	V : 0.99 (11,659)
115	<i>APC-A</i>	$k''_{a,20}=0$	V	V	V : 0.97 (12,113)
116	<i>APC-A cdh1Δ</i>	$k''_{a,20}=0, k_{s,cdh}=0,$ init CDH1T=CDH1=0	In	In	In : 0.18 (9,911)
117	<i>APC-A cdh1Δ</i> on galactose	$k''_{a,20}=0, k_{s,cdh}=0,$ init CDH1T=CDH1=0. $k_g=0.004621$	In	In	In : 0.47 (10,796)
118	<i>APC-A cdh1Δ</i> multi-copy <i>SIC1</i>	$k''_{a,20}=0, k_{s,cdh}=0,$ $k'_{s,c1}=15 \times k'_{s,c1},$ $k''_{s,c1}=15 \times k''_{s,c1},$ init CDH1T=CDH1=0	V	V	V : 0.83 (16,949)

119	<i>APC-A cdh1Δ GAL-SIC1</i>	$k''_{a,20}=0, k_{s,cdh}=0,$ $k'_{s,c1}=20 \times k'_{s,c1},$ $k_g=0.004621,$ init CDH1T=CDH1=0	V	V	V : 0.75 (9,934)
120	<i>APC-A cdh1Δ multi-copy CDC6</i>	$k''_{a,20}=0, k_{s,cdh}=0,$ $k'_{s,f6}=10 \times k'_{s,f6},$ $k''_{s,f6}=10 \times k''_{s,f6},$ $k'''_{s,f6}=10 \times k'''_{s,f6},$ init CDH1T=CDH1=0	V	V	V : 0.78 (12,700)
121	<i>APC-A cdh1Δ GAL-CDC6</i>	$k''_{a,20}=0, k_{s,cdh}=0,$ $k'_{s,f6}=15 \times k'_{s,f6},$ $k_g=0.004621,$ init CDH1T=CDH1=0	V	V	V : 0.82 (11,321)
122	<i>APC-A cdh1Δ multi-copy CDC20</i>	$k''_{a,20}=0, k_{s,cdh}=0,$ $k'_{s,20}=25 \times k'_{s,20},$ $k''_{s,20}=25 \times k''_{s,20},$ init CDH1T=CDH1=0	V	V	V : 0.79 (26,557)
123	<i>APC-A sic1Δ</i>	$k''_{a,20}=0,$ $k'_{s,c1}=k''_{s,c1}=0$	V	V	V : 0.83 (14,922)
124	<i>APC-A GAL-CLB2</i>	$k''_{a,20}=0, k'_{s,b2}=0.48,$ $k_g=0.004621$	In	In	In : 0 (10,000)

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