1 Model

1.1 Transcriptional regulation

For the cases in which transcription factors are regulating other pieces or there is indirect miRNA regulation (e.g., μ_{34} regulating ROS) then the regulation is modeled as a shifted Hill function

$$H(X, X_0, n_{XY}, \lambda_{XY}) = \lambda_{XY} + \frac{1. - \lambda_{XY}}{1. + (X/X_0)^{n_{XY}}} \tag{1}$$

Where the transcription factor X is regulating Y. X_0 is the threshold of X when the regulation becomes stronger. The cooperativity, n, represents the sensitvity to X. The foldchange (λ_{XY}) represents the amount of regulation and can be $\lambda_{XY} < 1$, $\lambda_{XY} = 1$, or $\lambda_{XY} > 1$ representing inhibition, no regulation, or activation. Therefore maximum inhibition occurs when $\lambda_{XY} = 0$ but there is no upper bound on activation.

1.2 miRNA regulation

We utilize the framework for miRNA regulation developed by Lu and collaborators described in detail in Ref.[**?**]. This framework was developed to model the binding of miRNA and mRNA to form an miRNA-mRNA complex and the subsequent translation of a protein. The miRNA concentration is μ, the treshold of miRNA regulation is μ_0, the mRNA concentration is m, the number of mRNA binding sites for miRNA is n, and the protein concentration is B. The reaction is assumed to occur at steady state and the binding/unbinding of miRNA and mRNA is assumed to be much faster than production/degredation of the protein.

Any number of binding sites may be occupied resulting in C_i^n possible combinations when i binding sites are occupied, where

$$C_i^n = \frac{n!}{i!(n-i)!} \tag{2}$$

When i binding sites are occupied, then

$$[m_i] = mM_n^i(\mu) \tag{3}$$

where

$$M(i, n, \mu, \mu_0) = \frac{\frac{\mu}{\mu_0}^i}{1 + \frac{\mu}{\mu_0}^n} \tag{4}$$

leading to the total translation rate

$$mL(\mu) = \sum_{i=0}^{n} l_i C_i^n M_i^n(\mu, \mu_0) \tag{5}$$

the active mRNA degredation rate

$$mY_m(\mu) = \sum_{i=0}^{n} y_{mi} C_i^n M_i^n(\mu, \mu_0) \tag{6}$$

and the active miRNA degredation rate

$$mY_\mu(\mu) = \sum_{i=0}^{n} i y_{\mu i} C_i^n M_i^n(\mu, \mu_0) \tag{7}$$

Therefore, the deterministic rate equations for the miRNA-mRNA binding complex and trascribed protein B are,

$$\frac{d\mu}{dt} = g_\mu - mY_\mu(\mu) - k_\mu\mu \tag{8}$$

$$\frac{dm}{dt} = g_m - mY_m(\mu) - k_m m \tag{9}$$

$$\frac{dB}{dt} = g_B mL(\mu) - k_B B \tag{10}$$

1.3 Competition in metabolism model

In the metabolic circuit, AMPK and Hif1 competitively regulate the level of mtROS

$$C^{comp}_{Rmt}(\gamma, g_n, h, h^0_{hr_{mt}}, n_{hr_{mt}}, A, A^0_{ar_{mt}}, n_{ar_{mt}} = \frac{\gamma(g_n + (\frac{A}{A^0_{ar_{mt}}})^{n_{ar_{mt}}})}{1 + (\frac{h}{h^0_{hr_{mt}}})^{n_{hr_{mt}}} + (\frac{A}{A^0_{ar_{mt}}})^{n_{ar_{mt}}}} \tag{11}$$

and noxROS

$$C^{comp}_{Rnox}(g_0, h, h^0_{hr_{nox}}, n_{hr_{nox}}, g_1, A, A_0, g_2, n_{ar_{nox}}) = \frac{g_0 + g^h_{r_{nox}}(\frac{h}{h^0_{hr_{nox}}})^{n_{hr_{nox}}} + g^a_{r_{nox}}(\frac{A}{A^0_{ar_{nox}}})^{n_{ar_{nox}}}}{1 + (\frac{h}{h^0_{hr_{nox}}})^{n_{hr_{nox}}} + (\frac{A}{A^0_{ar_{nox}}})^{n_{ar_{nox}}}} \tag{12}$$

1.4 The coupled EMT-metabolism network

$$\frac{dZ}{dt} = g_Z m_z L(\mu_{200}, \mu_{200_0}, n_{\mu_{200}}) - k_Z Z \tag{13}$$

$$\frac{m_Z}{dt} = g_{m_Z} H(Z, Z_{0,m}, n_{Z,m}, \lambda_{Z,m}) H(S, S_{0,m}, n_{s,m}, \lambda_{S,m}) H(A, A_{0,m}, n_{A,m}, \lambda_{A,m}) - m_Z Y_m(\mu, \mu_0, n_\mu) - k_{m_Z} m_Z \tag{14}$$

$$\frac{S}{dt} = g_S m_S L(\mu_{34}, \mu_{34_0}, n_{\mu_{34}}) - k_S S \tag{15}$$

$$\frac{m_S}{dt} = g_{m_S} * H(S, S_{0,ms}, n_{sms}, \lambda_{Sms}) H(I, I_{0m}, n_{Im}, \lambda_{Im}) H(h, h_{0ms}, n_{hms}, \lambda_{hms}) H(A, A_{0ms}, n_{Ams}, \lambda_{Ams}) - m_s Ym(u3, u3_0, n_{u3}) - k_{ms} m_S \tag{16}$$

$$\frac{\mu_{200}}{dt} = gu * H(Z, Z_{0u}, n_{zu}, \lambda_{zu}) H(S, S_{0u}, n_{su}, \lambda_{Su}) H(h, h_{0u}, n_{hu}, \lambda_{hu}) H(A, A_{0u}, n_{Au}, \lambda_{Au}) - m_Z * Yu(u, u_0, n_u) - m_H * Yu(u, u_0, n_{uh}) - k_u * u \tag{17}$$

$$\frac{\mu_{34}}{dt} = g_{u3} * H(Z, Z_{0u3}, n_{zu3}, \lambda_{zu3}) * H(S, S_{0u3}, n_{su3}, \lambda_{Su3}) - m_S * Yu(u3, u3_0, n_{u3}) - k_{u3} * u3 \tag{18}$$

$$\frac{mh}{dt} = g_{mh} * H(A, A_{0ah}, n_{ah}, \lambda_{ah}) - k_{mh} * m_h * H(h, h_{0hh}, n_{hh}, \lambda_{hh}) H(R, R_{0rh}, n_{rh}, \lambda_{rh}) - m_h * Y_m(\mu, \mu_0, n_{\mu,h}, y_{mih}) \tag{19}$$

parameter	value	units
g_z	100	
g_{mz}	11	
g_S	100	
g_{ms}	90	
g_u	2100	
g_{u3}	1350	
k_z	0.1	
k_{mz}	0.5	
k_S	0.125	
k_{ms}	0.5	
k_u	0.05	
k_{u3}	0.05	
I	50000	
u0	10000	
nu	6	
u30	10000	
nu3	2	

Table 1: EMT parameters

$$\frac{h}{dt} = g_h m_h L(\mu, \mu_0, n_{\mu,h}, l_{ih}) - k_h h \tag{20}$$

$$\frac{A}{dt} = g_a H(R, R_{0ra}, n_{ra}, \lambda_{ra}) H(h, h_{0ha}, n_{ha}, \lambda_{ha}) H(A, A_{0aa}, n_{aa}, \lambda_{aa}) - k_a * A \tag{21}$$

$$R = R_{mt} + R_{nox} \tag{22}$$

$$\frac{R_{nox}}{dt} = g_{rn} * C^{comp}_{R_{nox}}(g_n, h, h_{0hrn}, n_{hrn}, g_1, A, A_{0rn}, g_2, n_{arn}) - k_{rn} * R_{nox} H(\mu_{34}, n_{u30rn}, n_{3n}, \lambda_{3n}) \tag{23}$$

$$\frac{R_{mt}}{dt} = g_{rm} H(A, A_{0aR}, n_{ar}, \lambda_{ar}) * C^{comp}_{R_{mt}}(\gamma, g_n, h, h_{0hrm}, n_{hrm}, A, A_{0rm}, n_{arm}) - k_{rm} * R_{mt} H(\mu_3, n_{u30rm}, n_{3m}, \lambda_{3m}) \tag{24}$$

1.5 Parameter determination for coupled EMT-metabolic network

Any parameter in Table 1.5 with a citation is an experimentally derived value that we are using. Any parameter without a reference is estimated based on what is known of the system and other parameters. The values for the L, Ym, and Yu functions are estimated and set in ranges to ensure the behavior mimics biological systems.

Since Hif1 is regulated by miRNA μ_{200}, it was required to also include Hif1 messenger RNA which was not inlcuded in the original circuit studied by Yu et al [**?**]. This ensured new parameters for Hif1, and Hif1 mRNA, were required therefore we went through a range of parameters and found the parameters that gave the most similar result with or without μ_{200} regulating Hif1. (SI ??)

parameter	value	units
g_A	30	
g_h	1.5	
g_{mh}	10	
g_{rn}	40	
g_{rm}	150	
k_A	0.2	
k_h	1.75	
k_{mh}	0.143	
k_{rn}	5	
k_{rm}	5	

Table 2: MR parameters

Reg	foldchange		cooperativity		Threshold	
	parameter	value	parameter	value	parameter	value
ZU	λ_{zu}	0.1	nzu	3	Z0u	220000
SU	λ_{Su}	0.1	nsu	2	S0u	180000
Input	λ_{Im}	10	nIm	2	I0m	50000
SS	λ_{SS}	0.1	nss	1	S0S	200000
Zu3	λ_{Zu3}	0.2	nzu3	2	Z0u3	600000
Su3	λ_{Su3}	0.1	nsu3	1	S0u3	300000
ZZ	λ_{ZZ}	7.5	nzz	2	Z0Z	25000
SZ	λ_{SZ}	10.	nsz	2	S0Z	180000

Table 3: EMT transcriptional regulation

Reg	foldchange		cooperativity		Threshold	
	parameter	value	parameter	value	parameter	value
RH	λ_{rh}	0.2	nrh	4	R0H	300
HH	λ_{hh}	0.1	nhh	4	H0H	80
AH	λ_{ah}	0.1	nah	1	A0H	250
AR	λ_{ar}	0.25	nar	2	A0R	350
RA	λ_{ra}	8.	nra	4	R0A	100
HA	λ_{HA}	0.1	nha	1	H0A	250
AA	λ_{AA}	0.2	naa	2	A0A	350

Table 4: MR transcriptional regulation

parameter	value
gn	0.2
g1	5
g2	0.2
γ	8
h0hrm	200
h0hrn	250
A0rn	150
A0rm	150
narm	4
nhrm	2
nhrn	2
narn	2

Table 5: MR competition function parameters

Reg	foldchange		cooperativity		Threshold	
	parameter	value	parameter	value	parameter	value
AS	λ_{AS}[?]	0.	nAS	2	A0S	300
AZ	λ_{AS}		nAZ[?]	2	A0Z	300
Au	λ_{Au}[?]	0.6	nAu[?]	1	A0u	300
HS	λ_{HS} [?]	7	nHS[?]	2	H0S	200
Hu	λ_{Hu}[?]	1.5	nHu	1	H0u	200
u3m	λ_{u3m}[?]	2	n3m	3	u30m	10000
u3n	λ_{AS}		n3n	2	u30n	10000
uh			nuh	2		

Table 6: Crosstalk transcriptional regulation

parameter	i=0	i=1	i=2	i=3	i=4	i=5	i=6
l_i	1	0.6	0.3	0.1	0.05	0.05	0.05
y_{mi}	0	0.04	0.2	1.0	1.0	1.0	1.0
$y_{\mu i}$	0	0.005	0.05	0.5	0.5	0.5	0.5

Table 7: Parameters for regulation by μ_{200}

parameter	i=0	i=1	i=2
l_i	1	0.6	0.3
y_{mi}	0	0.04	0.2
$y_{\mu i}$	0	0.005	0.05

Table 8: Parameters for regulation by μ_{34}

1.6 Coupled EMT-metabolism network without hybrid phenotypes

to generate a model that is missing the hybrid phenotype we adjusted the following parameters.

For the results labled noEM:
$\lambda_{Su} = 0.85$ and $\lambda_{SZ} = 17$

For the results labeled noWO:
kmh = 0.158, kh = 2.2, and $\gamma = 6$

For the results label noHH: We removed the initial ability to access the WO or EM states.
$\lambda_{Su} = 0.85$, $\lambda_{SZ} = 17$, kmh = 0.158, kh = 2.2, and $\gamma = 6$

The states were confirmed by calculating the nullclines of the EMT and metabolic circuit with the new parameters.

1.7 Coupled EMT-metabolism network with Phenotype stability factors

When introducing the PSFs OVOL and GRHL2 we add four equations to our model that represent the protein and mRNA levels of OVOL and GRHL2. We also must adjust the equations for μ_{200} to include inhibition by OVOl, Zeb mRNA to include inhibition by OVOL and GRHL2, and ROS to include upregulation by GRHL2.

$$\frac{m_Z}{dt} = g_{m_Z} H(Z, Z_{0,m}, n_{Z,m}, \lambda_{Z,m}) H(S, S_{0,m}, n_{s,m}, \lambda_{S,m}) H(A, A_{0,m}, n_{A,m}, \lambda_{A,m}) \\ H(O, O_{0,m}, n_{O,m}, \lambda_{O,m}) H(G, G_{0,m}, n_{G,m}, \lambda_{G,m}) - m_Z Y_m(\mu, \mu_0, n_\mu) - k_{m_Z} m_Z \quad (25)$$

$$\frac{\mu_{200}}{dt} = gu * H(Z, Z_{0u}, n_{zu}, \lambda_{zu}) H(S, S_{0u}, n_{su}, \lambda_{Su}) H(h, h_{0u}, n_{hu}, \lambda_{hu}) \\ H(A, A_{0u}, n_{Au}, \lambda_{Au}) H(O, O_{0,u}, n_{O,u}, \lambda_{O,u}) - m_Z * Yu(u, u_0, n_u) - m_H * Yu(u, u_0, n_{uh}) - k_u * u \quad (26)$$

$$\frac{G}{dt} = g_g m_g - k_{gg} G \quad (27)$$

$$\frac{m_g}{dt} = g_{m_g} H(Z, Z_{0,mg}, n_{z,mg}, \lambda_{z,mg}) - k_{m_g} m_g \quad (28)$$

$$\frac{O}{dt} = g_o m_o - k_o O \quad (29)$$

$$\frac{m_o}{dt} = g_{m_o} H(O, o_{0,mo}, n_{o,mo}, \lambda_{o,mo}) H(Z, Z_{0,mo}, n_{z,mo}, \lambda_{z,mo}) H(G, G_{0,mo}, n_{g,mo}, \lambda_{g,mo}) - k_{m_o} m_o \quad (30)$$

2 Methods

2.1 Solving the model

Starting from a set of 1000 distinct random conditions sampled from a unifrom distrubtion (ranges for each component in Table 10), we solve the model with the Euler method. For each initial condition we use a timestep of dt=0.1 with relaxation time of 1000 hr, and the values are assumed to have converged at the end of the simulation. The results presented here for each foldchange value, except for $\mu_{200} - |Hif1$, are the average of the results generated from these 1000 initial conditions. The regulation of Hif1 by μ_{200} has nine distinct parameter values that can be modified, so the results for each initial condition are individually analyzed and then combined. If the parameters for this crosstalk are changed the quantitative results may be misleading, therefore we focus on qualitative results for this crosstalk.

parameter	value
$\lambda_{I,S}$	16
$\lambda_{O,\mu}$	0.1
$\lambda_{O,Z}$	0.1
$\lambda_{O,O}$	0.1
$\lambda_{Z,O}$	0.5
$\lambda_{Z,G}$	0.5
$\lambda_{G,Z}$	0.1
$\lambda_{G,O}$	0.7
$\lambda_{G,R_{mt}}$	0.26
$\lambda_{G,R_{nox}}$	0.25
$n_{O,\mu}$	1
$n_{O,Z}$	1
$n_{O,O}$	2
$n_{Z,O}$	1
$n_{Z,G}$	3
$n_{G,Z}$	1
$n_{G,O}$	2
$n_{G,R_{mt}}$	1
$n_{G,R_{nox}}$	1
$O_{0,\mu}$	250000
$O_{0,Z}$	25000
$O_{0,O}$	25000
$Z_{0,O}$	10000
$Z_{0,G}$	10000
$G_{0,Z}$	25000
$G_{0,O}$	25000
$G_{0,R_{mt}}$	25000
$G_{0,R_{nox}}$	25000
g_g	200
g_{mg}	22
g_O	200
g_{mO}	22
k_O	0.1
k_{mO}	0.5
k_G	0.1
k_{mG}	0.5

Table 9: Coupled EMT-metabolic circuit with PSF function parameters

parameter	range
z	[0,700000]
mz	[0,2000]
S	[0,250000]
ms	[0,1000]
μ_{200}	[0,25000]
μ_{34}	[0,20000]
A	[0,1000]
h	[0,1000]
mh	[0,1000]
Rmt	[0,1000]
Rnox	[0,1000]

Table 10: Ranges for initial conditions

Table 11: Gene expression profiles used for state classification

2.2 Coupled state classification

To determine the states we compare to the coupled circuits with inactive crosstalks and original snail input (I=50000). The coupled network excluding the hybrid states were also compared to the inactive crosstalks. Because the coupled network with the PSFs generates the hybrid state with a different expression profile than the inactive circuit, we generated a new set of gene profiles corresponding to the E/M, E, and M states (comparison values for classification of all networks are in Table S11.

The state is then calculated by determining which of the 9 possible coupled states of the inactive system is closest to the coupled result

$$(d_i^C)^2 = min(\{\sum_j (log_{10}(\frac{x_{i,j}^C}{x_{k,j}^{IA}}))^2 : j \in \{H, A, Z, ...\}, k \in \{E\text{-}W, E\text{-}O, E\text{-}W/O, E/M\text{-}O...\}\}) \quad (31)$$

Whichever state (k) corresponds to the minimum distance for the ith generated expression profile (d_i^C) is then the assumed state. By taking the square of the log before summing we ensure that deviations from the gene expression profile in opposite directions do not cancel out.

2.3 Silencing Hif-1 mRNA

As the miRNA regulation has three sets of possible parameters changing (l,y_m, and y_μ), we utilize the silencing function to incorporate all changing parameters into a single variable.

The silencing function is defined as

$$P_H(\mu_{200}) = \frac{L(\mu_{200})}{1 + Y_m(\mu_{200})/k_{mh}} \quad (32)$$

We use the degradation rate of the Hif-1 mRNA($k_{mh} = 0.143$).

We calculate the silencing value of each initial condition for a distinct set of parameter.

2.4 Phase planes and calculating up/downregulations

To generate the how the possible coupled states change as the regulation changes we determine this by looking at a phase plane of the results. For all regulatory crosstalks that are modeled by a shifted Hill function (all crosstalks except miRNA regulation of Hif-1 by μ_{200}), all 1000 initial conditions at a specific value of the foldchange for that crosstalk $\lambda_{A->|B}$ are classified as one of the nine possible coupled states. For μ_{200}-— Hif1, the silencing value takes the place of the foldchange value. Thus, we have transformed potentially 1000 different results to between 1 and 9 different results (coupled states). So for each regulatory value ($\lambda_{A->|B}$ or $P_H(\mu_{200})$ we have a set of possible coupled states. Each set is identified by a unique color (with each set of possible coupled states noted either directly on the plot or in a nearby legend). As our focus is on the presence and stability of the E/M-W/O state, we can overlay all plots with black or red dots. The black dots overlaying a plot reference the regulatory parameters for which the E/M-W/O coupled state is possible, while the red dots overlaying a plot are in the regions of regulatory parameters where only the E/M-W/O coupled state exists (i.e., all other coupled states are suppressed).

To determine if a state is up/downregulated relative to the inactive circuit we simply calculate the fraction of initial conditions leading to the E/M-W/O state for the coupled circuit compared to the inactive system. For the coupled network and the coupled network excluding the hybrid states, the inactive network is the tristable network with all crosstalks inactive. For the coupled network including the PSFs, the inactive network is only able to access the E/M-W/O and E/M-O states.

2.5 Nullclines

To confirm the stability of these states we calculated the continuity and nullclines of the systems using PyDSTool[**?**].

((I'll put more details here for replication))

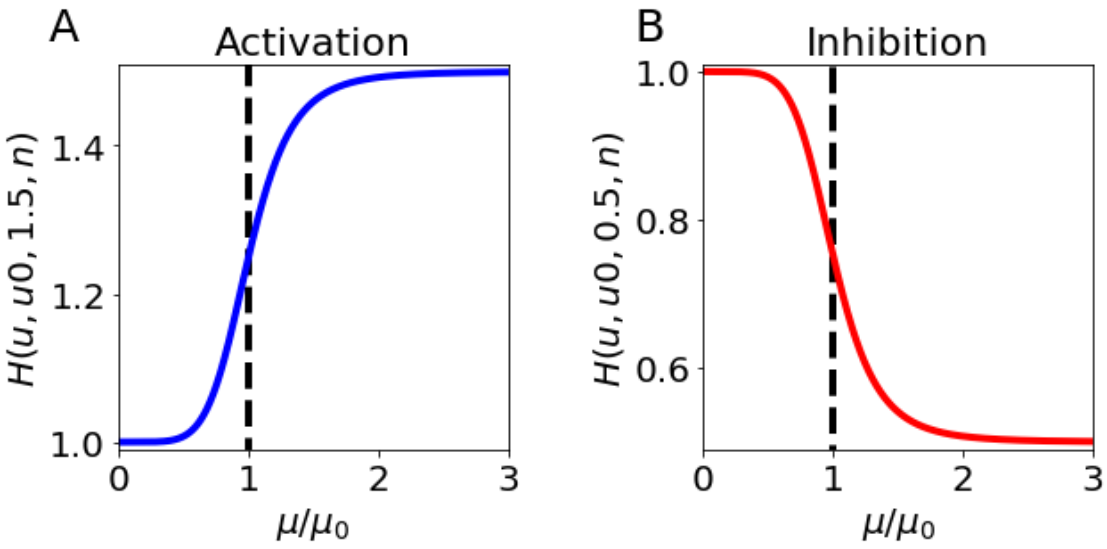


Figure 1:

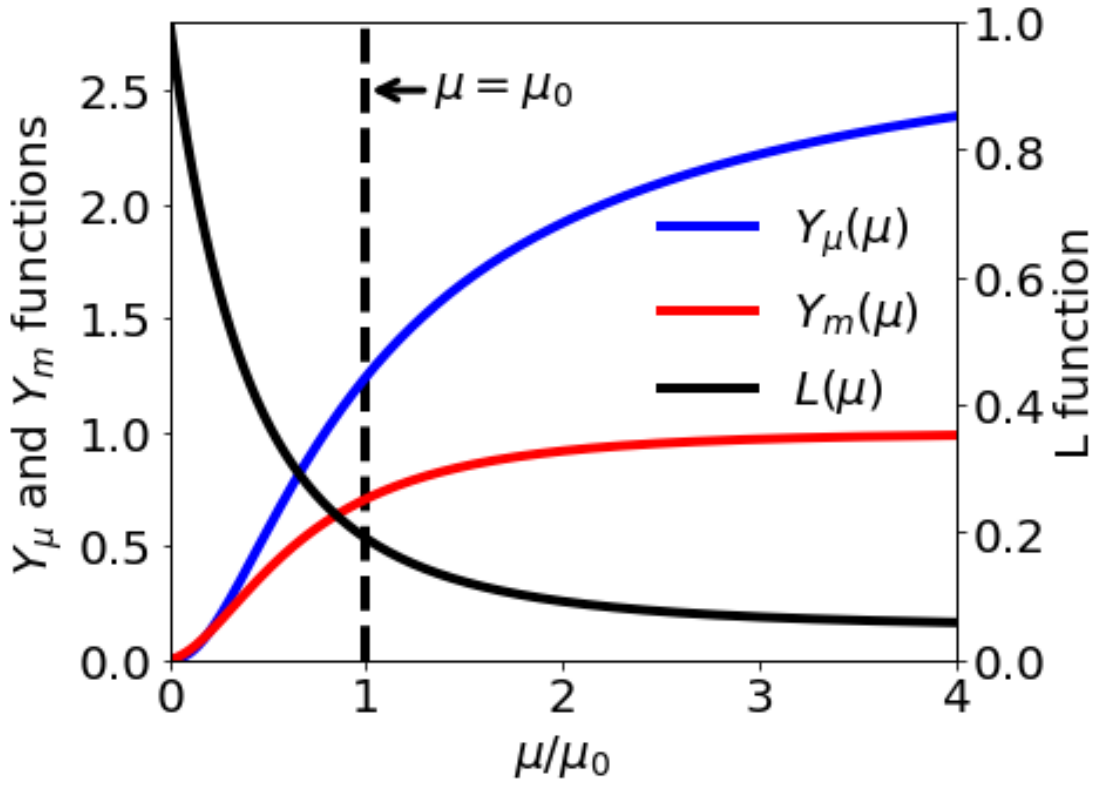


Figure 2:

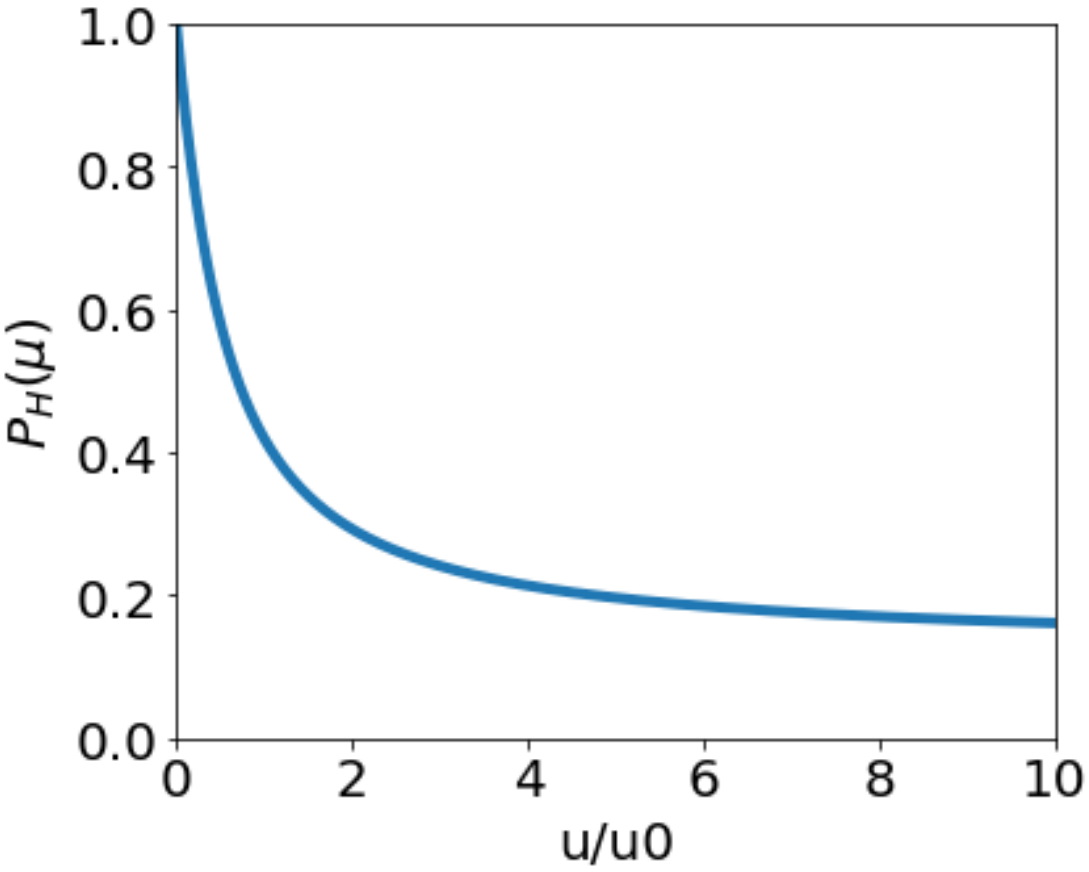
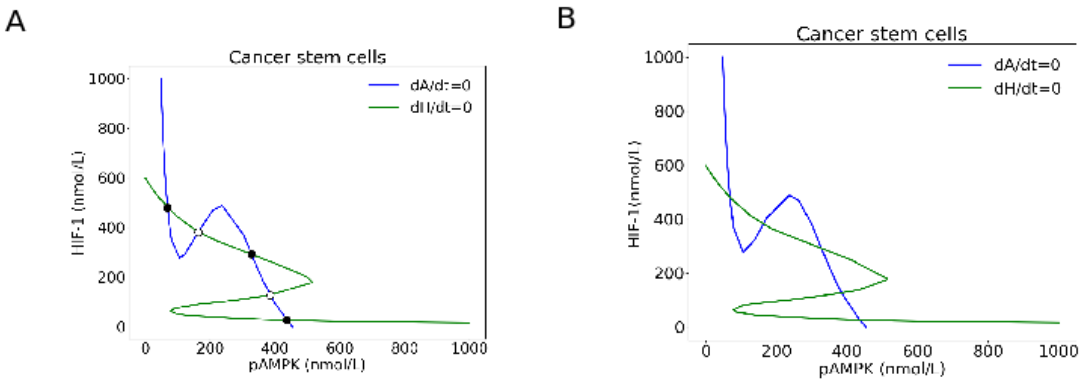


Figure 3:



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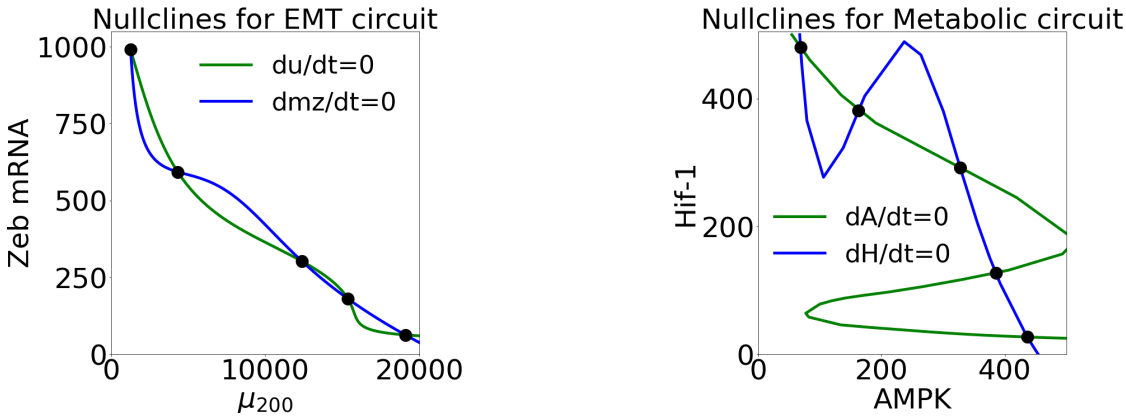
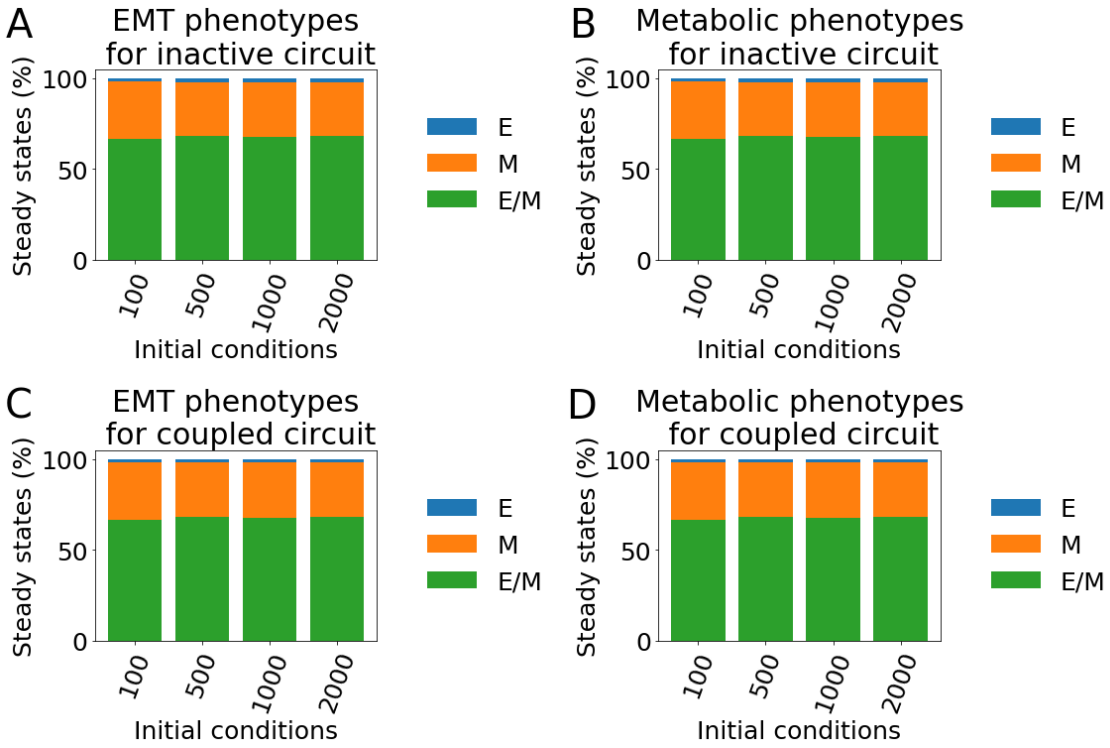


Figure 5: Should probably split this up



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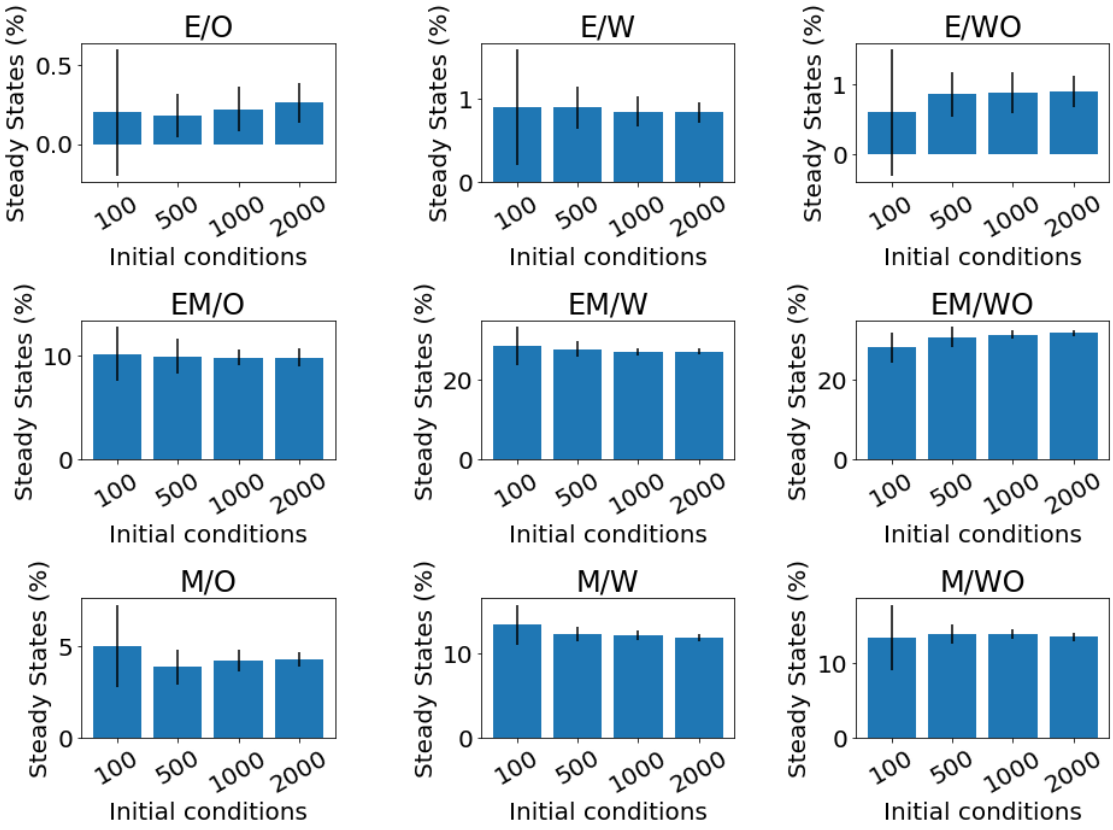
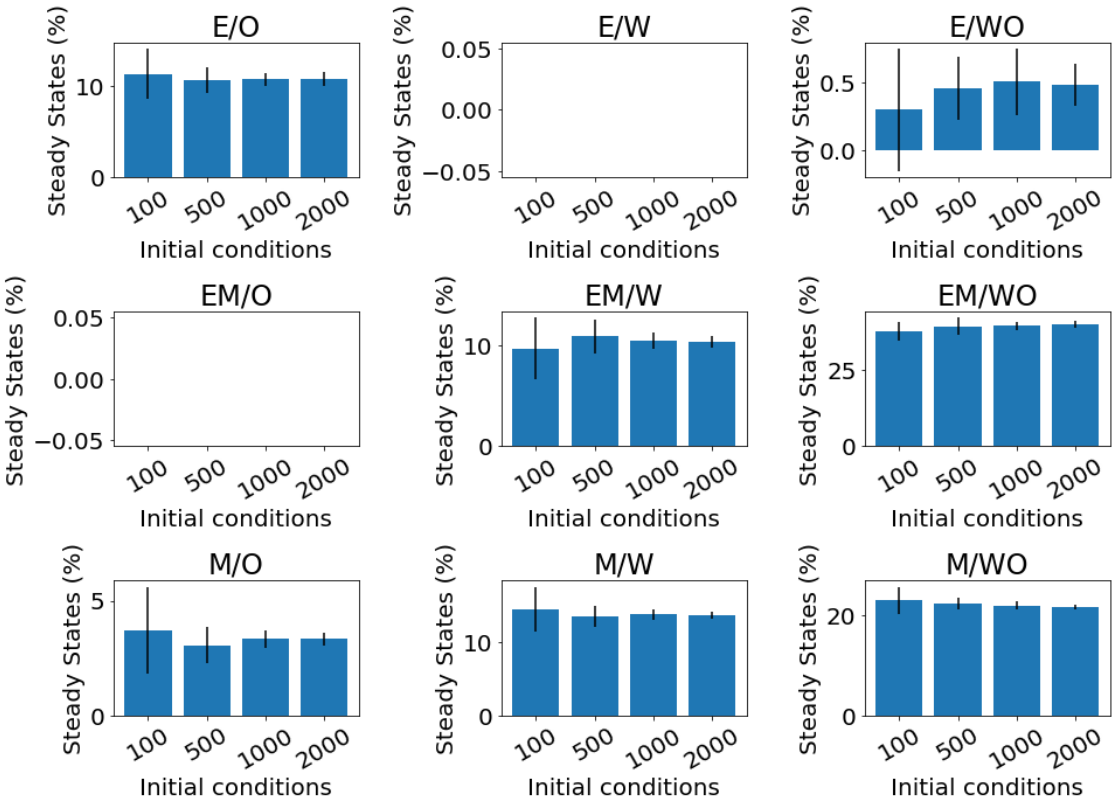

E/O
E/W
E/WO
EM/O
EM/W
EM/WO
M/O
M/W
M/WO
Steady States (%)
Initial conditions
100
500
1000
2000

Figure 7:



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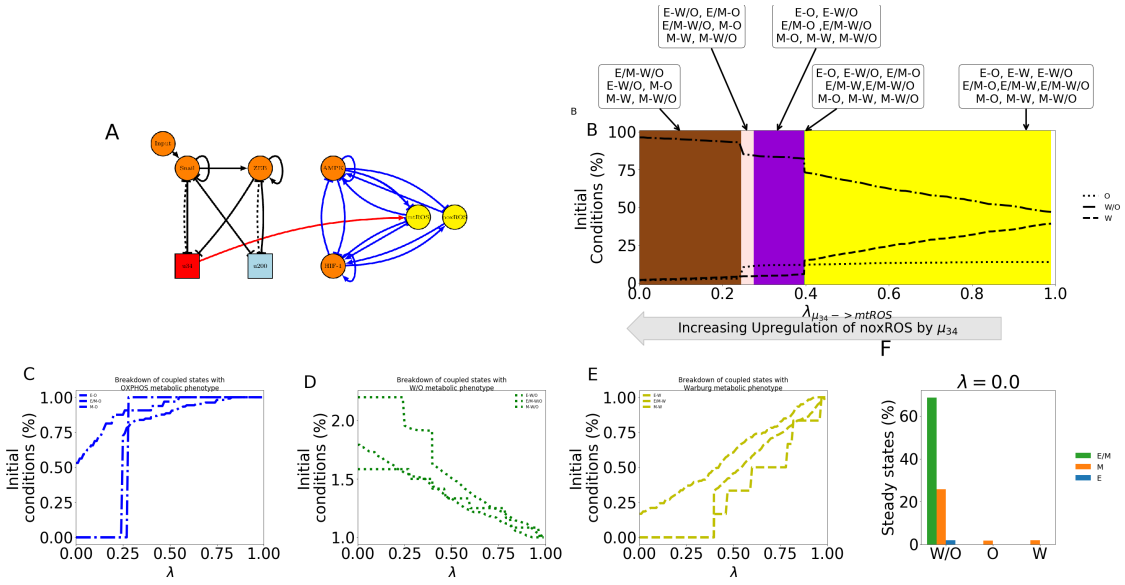
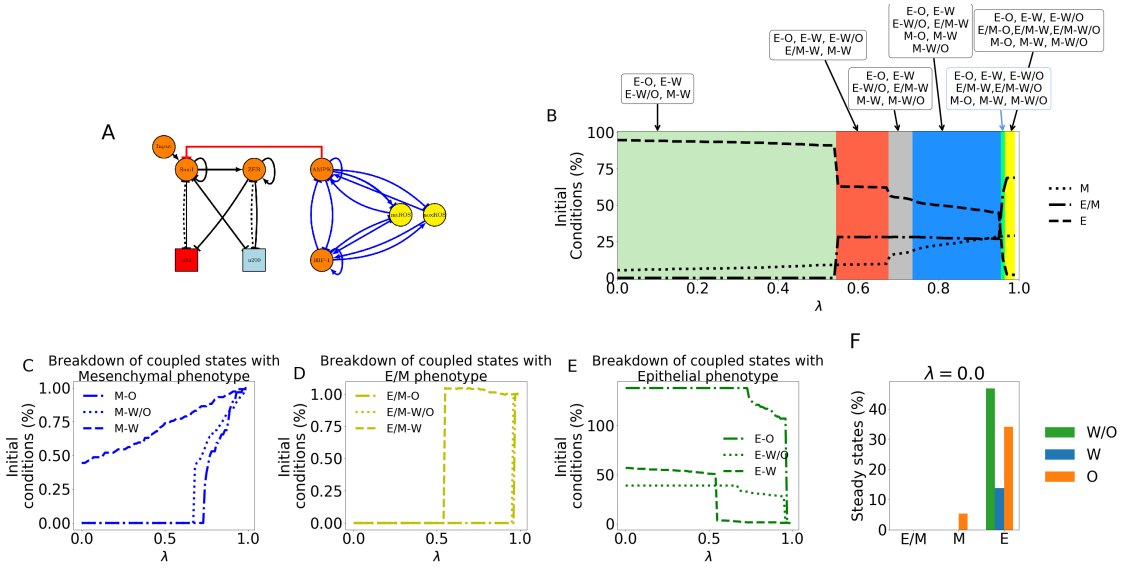


Figure 9:

Figure 10:



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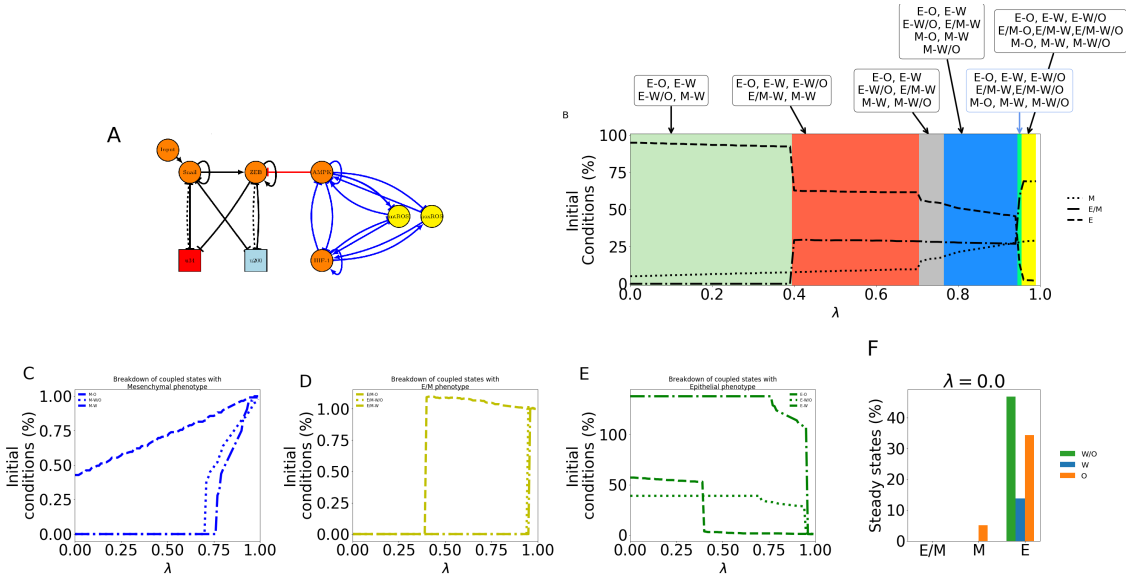

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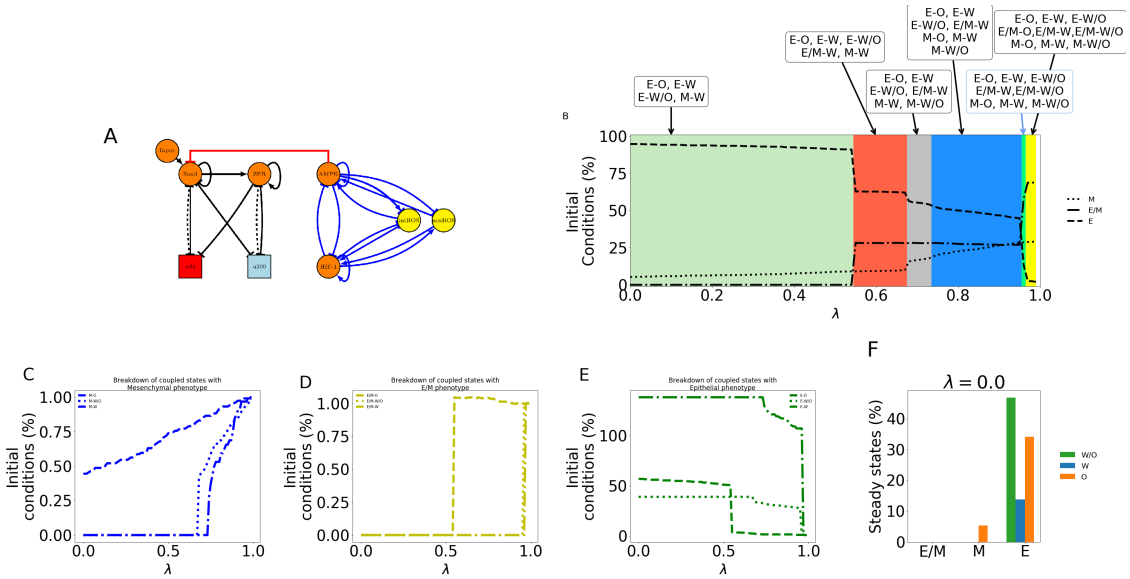

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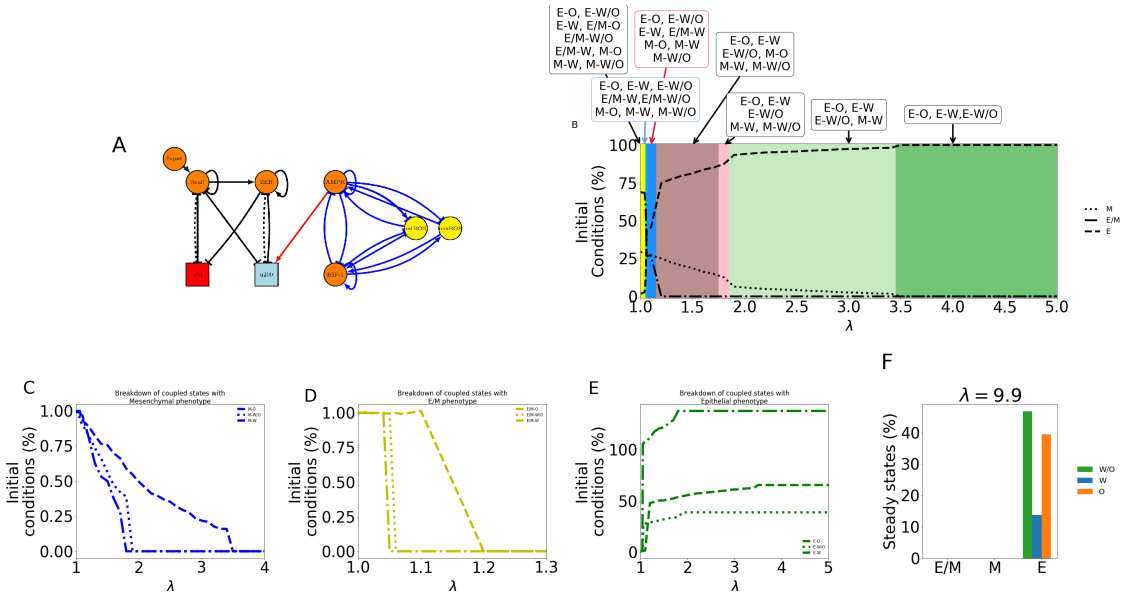

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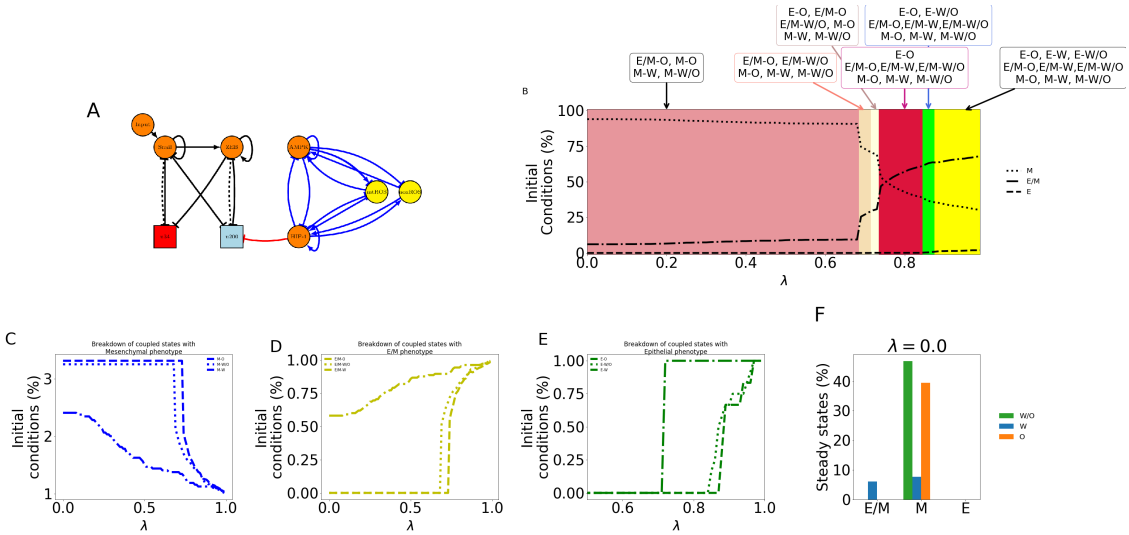


Figure 15:

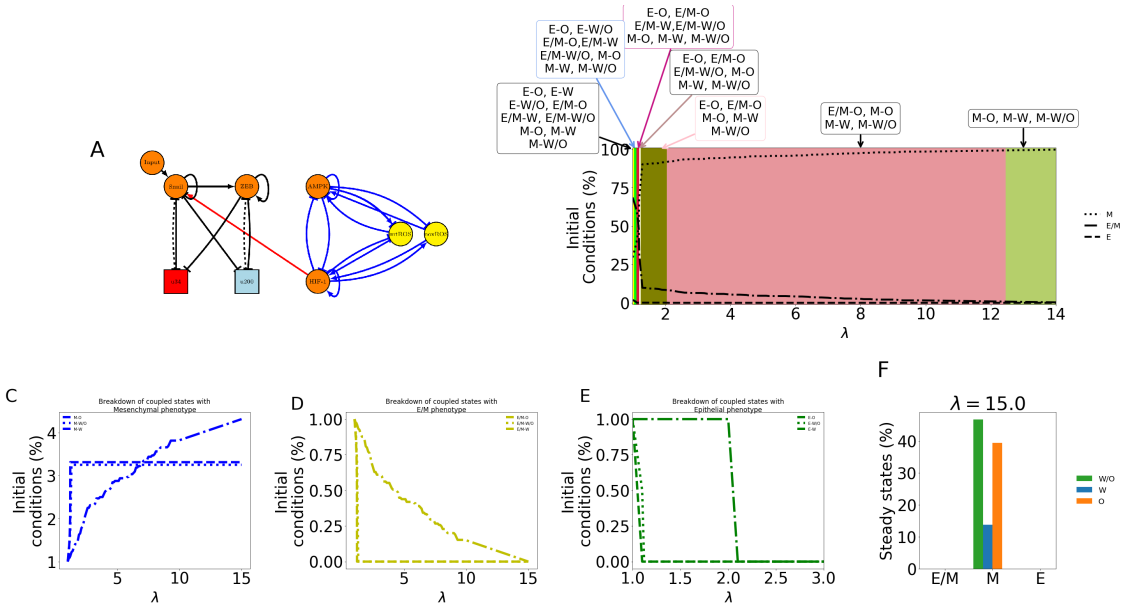


Figure 16:

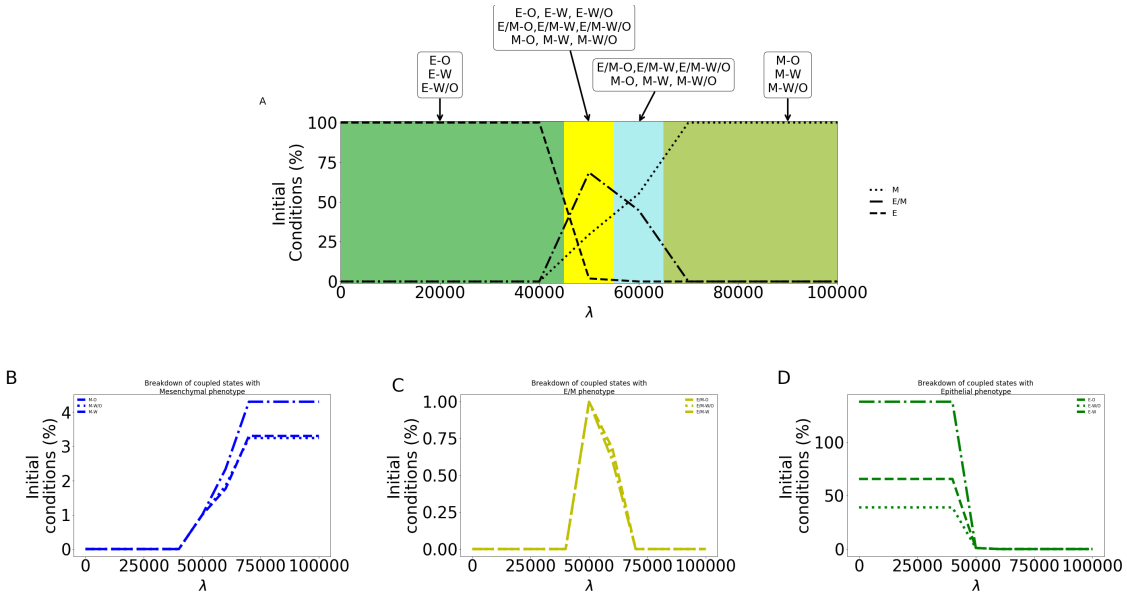
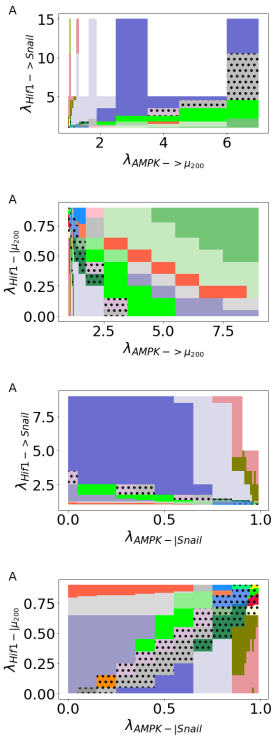

A
E-O, E-W, E-W/O
E/M-O,E/M-W,E/M-W/O
M-O, M-W, M-W/O
E-O
E-W
E-W/O
E/M-O,E/M-W,E/M-W/O
M-O, M-W, M-W/O
M-O
M-W
M-W/O
Initial Conditions (%)
100
75
50
25
0
0
20000
40000
60000
80000
100000
λ
M
E/M
E
B
Breakdown of coupled states with Mesenchymal phenotype
Initial conditions (%)
4
3
2
1
0
0
25000
50000
75000
100000
λ
C
Breakdown of coupled states with E/M phenotype
Initial conditions (%)
1.00
0.75
0.50
0.25
0.00
0
25000
50000
75000
100000
λ
D
Breakdown of coupled states with Epithelial phenotype
Initial conditions (%)
100
50
0
0
25000
50000
75000
100000
λ

Figure 17:


A
$\lambda_{Hif1 - > Snail}$
$\lambda_{AMPK - > \mu_{200}}$
$\lambda_{Hif1 - \mu_{200}}$
$\lambda_{AMPK - |Snail}$


['E/O', 'E/W', 'E/WO', 'M/W']
['E/O', 'E/WO', 'M/W', 'M/WO']
['E/O', 'E/W', 'E/WO']
['M/O', 'M/W', 'M/WO']
['E/O', 'E/WO', 'EM/WO', 'M/W', 'M/WO']
['E/O', 'E/W', 'E/WO', 'EM/W', 'M/W']
['E/O', 'EM/O', 'EM/W', 'EM/WO', 'M/O', 'M/W', 'M/WO']
['E/O', 'M/O', 'M/W', 'M/WO']
['E/O', 'E/W', 'E/WO', 'EM/W', 'M/O', 'M/W', 'M/WO']
['E/O', 'E/W', 'E/WO', 'M/W', 'M/WO']
['E/O', 'E/WO', 'M/W', 'M/WO']
['E/O', 'E/W', 'E/WO']
['E/O', 'E/WO', 'EM/WO', 'M/W', 'M/WO']
['E/O', 'EM/WO', 'M/W', 'M/WO']
['E/O', 'E/WO', 'M/W']
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['E/O', 'M/O', 'M/W', 'M/WO']
['E/O', 'EM/O', 'M/O', 'M/W', 'M/WO']
['E/O', 'E/WO', 'M/W']
['E/O', 'E/WO', 'M/W', 'M/WO']
['E/O', 'E/W', 'E/WO', 'M/W']
['E/O', 'M/O', 'M/W', 'M/WO']
['E/O', 'E/WO', 'EM/WO', 'M/W', 'M/WO']
['E/O', 'E/W', 'E/WO', 'EM/W', 'M/W']
['E/O', 'E/WO', 'EM/O', 'EM/W', 'EM/WO', 'M/O', 'M/W', 'M/WO']
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['E/O', 'EM/W', 'EM/WO', 'M/O', 'M/W', 'M/WO']
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['E/O', 'E/WO', 'M/W']
['E/O', 'EM/WO', 'M/W', 'M/WO']
['E/O', 'E/WO', 'EM/W', 'M/W', 'M/WO']
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['E/O', 'M/O', 'M/W', 'M/WO']
['E/O', 'E/WO', 'EM/W', 'M/O', 'M/W', 'M/WO']
['E/O', 'E/W', 'E/WO', 'EM/W', 'M/W', 'M/WO']
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['E/O', 'E/WO', 'M/W', 'M/WO']
['E/O', 'E/WO', 'EM/WO', 'M/W']
['EM/O', 'M/O', 'M/W', 'M/WO']
['E/O', 'EM/O', 'EM/W', 'EM/WO', 'M/O', 'M/W', 'M/WO']
['E/O', 'E/W', 'E/WO', 'EM/W', 'EM/WO', 'M/O', 'M/W', 'M/WO']
['E/O', 'E/WO', 'EM/O', 'EM/W', 'EM/WO', 'M/O', 'M/W', 'M/WO']
['E/O', 'E/WO', 'EM/W', 'EM/WO', 'M/O', 'M/W', 'M/WO']
['E/O', 'EM/W', 'EM/WO', 'M/O', 'M/W', 'M/WO']
['E/O', 'EM/WO', 'M/O', 'M/W', 'M/WO']
['E/O', 'E/W', 'E/WO', 'EM/W', 'M/O', 'M/W', 'M/WO']
['E/O', 'EM/WO', 'M/W']
['E/O', 'EM/O', 'EM/WO', 'M/O', 'M/W', 'M/WO']
['E/O', 'EM/O', 'M/O', 'M/W', 'M/WO']
['E/O', 'E/WO', 'EM/WO', 'M/O', 'M/W', 'M/WO']
['E/O', 'E/W', 'E/WO', 'EM/O', 'EM/W', 'EM/WO', 'M/O', 'M/W', 'M/WO']

Figure 18:

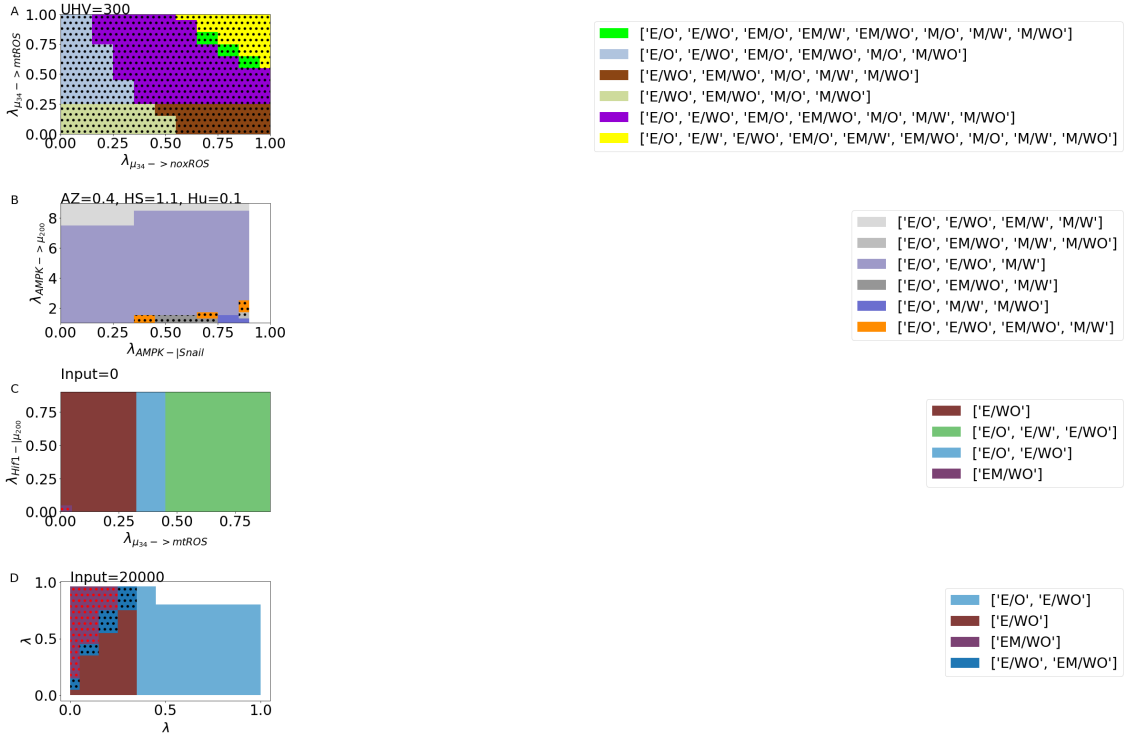

Figure 19:

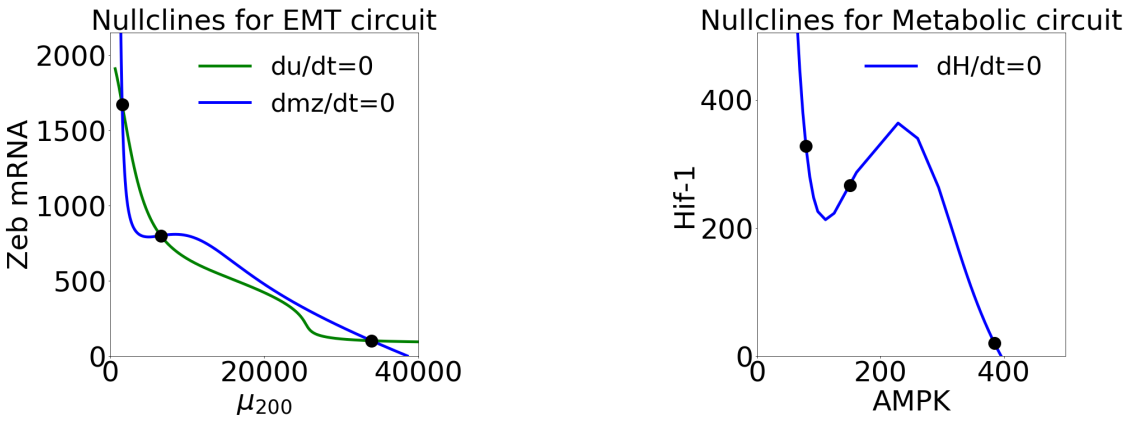

Figure 20:

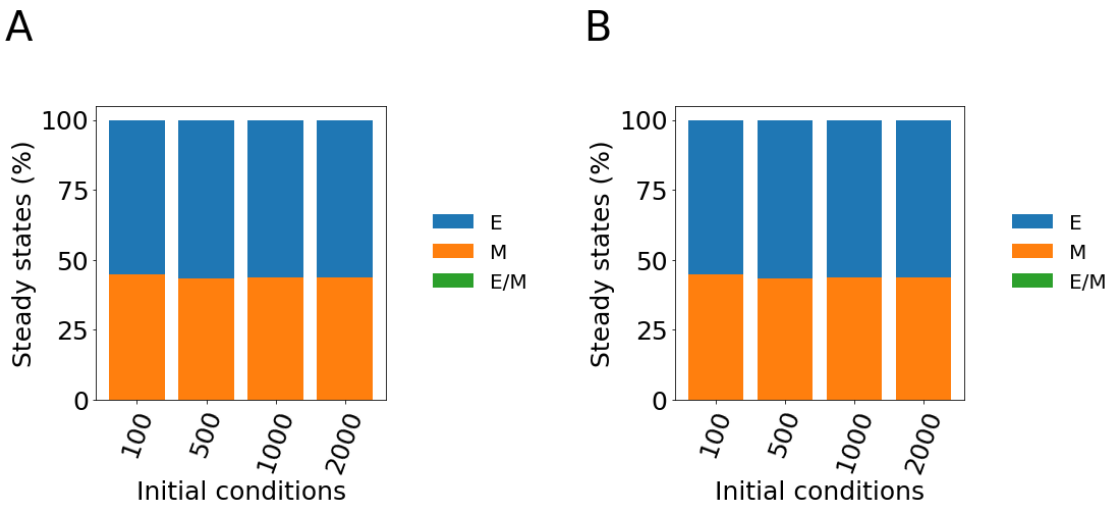

Figure 21:

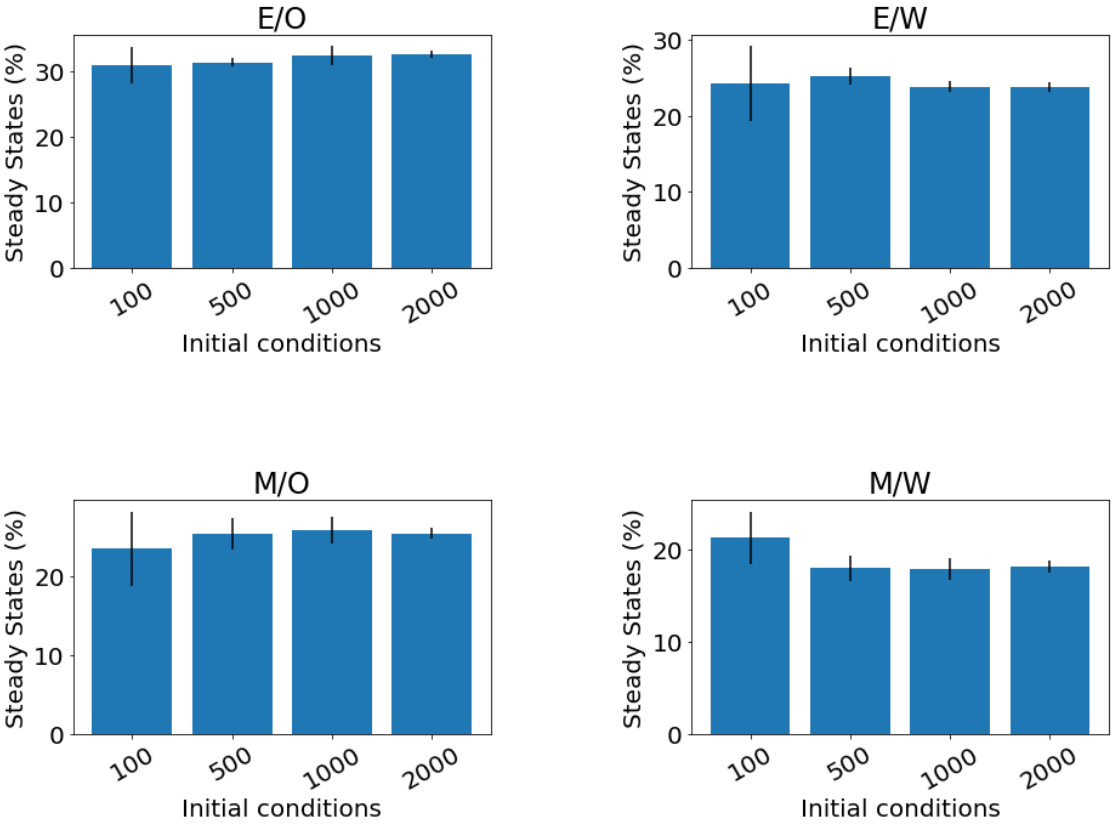

Figure 22:

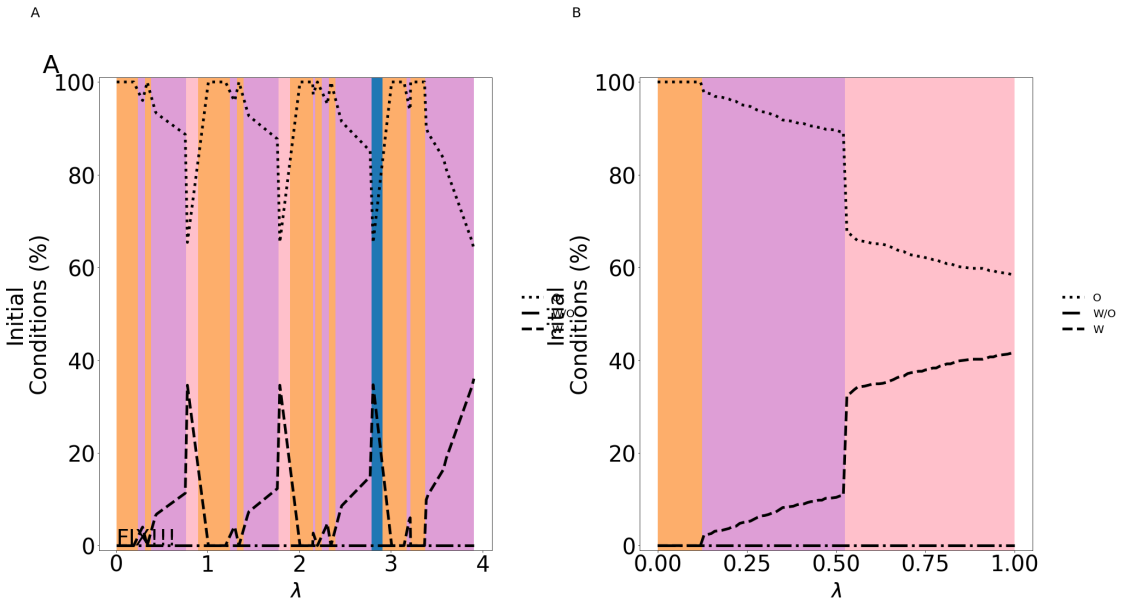

Figure 23:

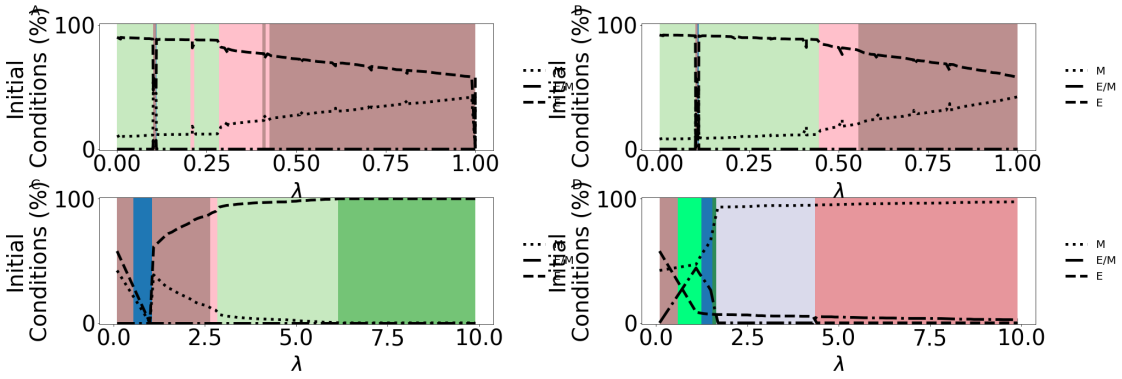

Figure 24:

Figure 25:

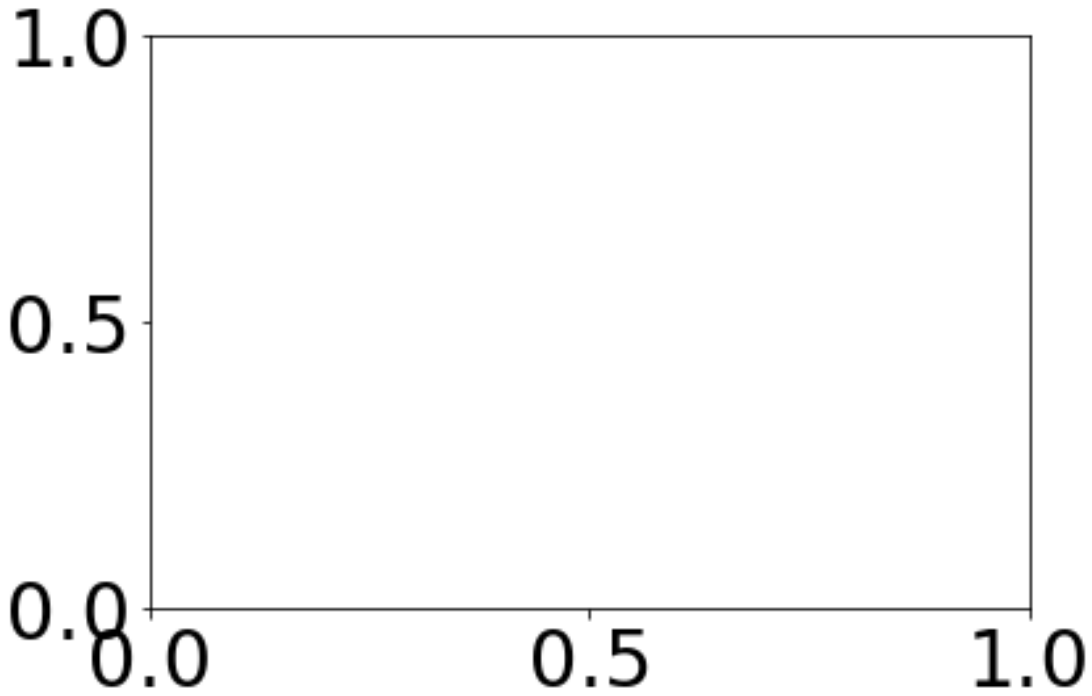

Figure 26:

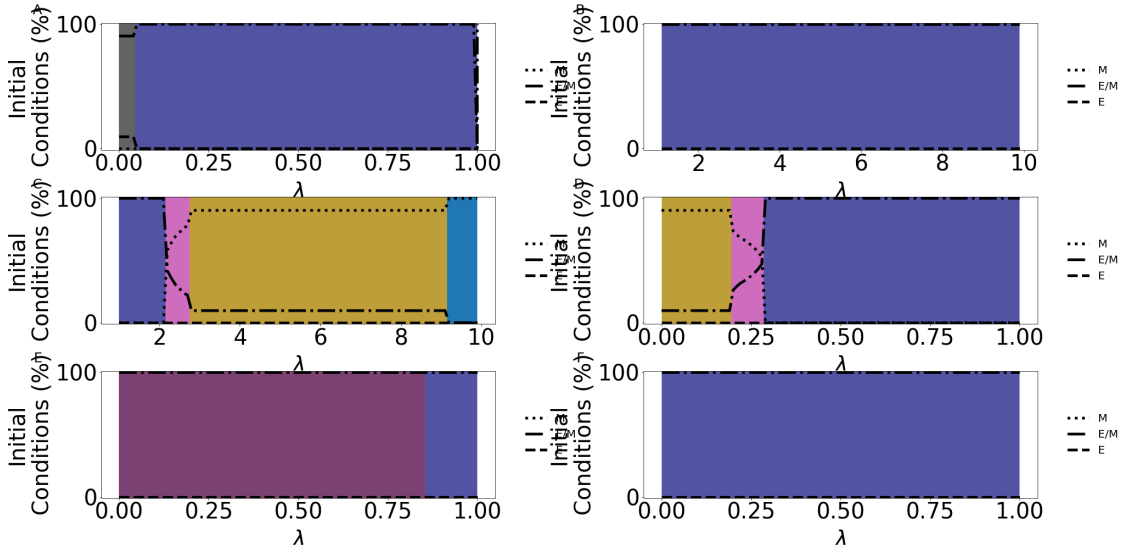

Figure 27:

A

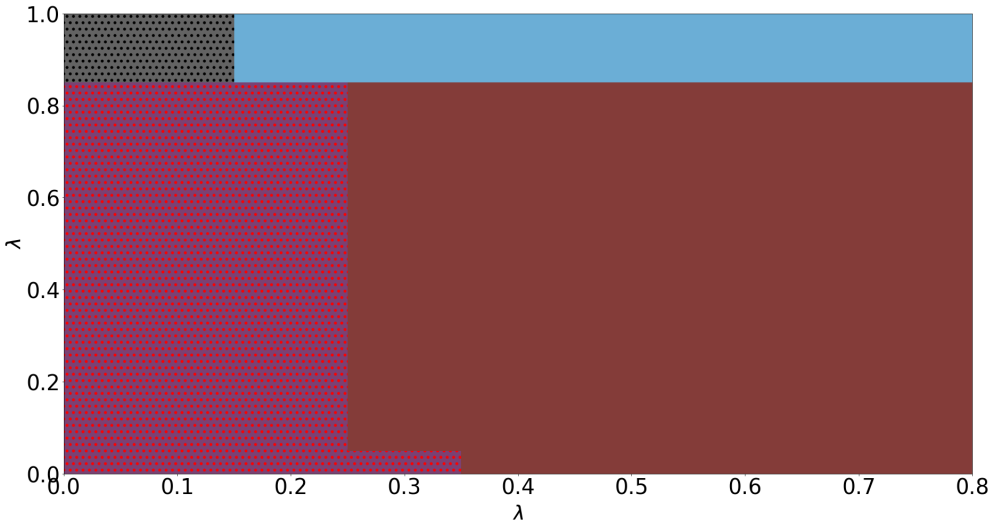

Figure 28: