



Fig. S1. Average effective degradation rate of Her7 protein in different genetic backgrounds. Error bars represent normalized standard errors.



Movie 1. Wild type. Simulations of *her1* mRNA levels in 4x4 cells located in the posterior PSM in wild-type embryos. Each hexagon represents a cell, with its color indicating its level of *her1* mRNA. Darker colors indicate lower levels, whereas lighter colors represent higher levels.



Movie 2. *her1*^{-/-} mutant. Simulations of *her1* mRNA levels in 4×4 cells located in the posterior PSM in *her1*^{-/-} mutant embryos. Each hexagon represents a cell, with its color indicating its level of *her1* mRNA. Darker colors indicate lower levels, whereas lighter colors represent higher levels.



Movie 3. *her7*^{-/-} mutant. Simulations of *her1* mRNA levels in 4×4 cells located in the posterior PSM in *her7*^{-/-} mutant embryos. Each hexagon represents a cell, with its color indicating its level of *her1* mRNA. Darker colors indicate lower levels, whereas lighter colors represent higher levels.



Movie 4. *hes6*^{-/-} mutant. Simulations of *her1* mRNA levels in 4×4 cells located in the posterior PSM in *hes6*^{-/-} mutant embryos. Each hexagon represents a cell, with its color indicating its level of *her1* mRNA. Darker colors indicate lower levels, whereas lighter colors represent higher levels.



Movie 5. *her^{-/-};hes6^{-/-}* mutant. Simulations of *her1* mRNA levels in 4×4 cells located in the posterior PSM in *her7^{-/-};hes6^{-/-}* mutant embryos. Each hexagon represents a cell, with its color indicating its level of *her1* mRNA. Darker colors indicate lower levels, whereas lighter colors represent higher levels.



Movie 6. *notch1a^{-/-}* mutant. Simulations of *her1* mRNA levels in 4×4 cells located in the posterior PSM in *notch1a^{-/-}* mutant embryos. Each hexagon represents a cell, with its color indicating its level of *her1* mRNA. Darker colors indicate lower levels, whereas lighter colors represent higher levels.

Table S1. Parameter ranges and values used in the study. The initial parameter ranges (second column) were broadly selected and centered around the literature information. These ranges have been narrowed down by comparing deterministic and stochastic simulations of our model to the wild-type and mutant period, amplitude and synchronization observations (third column). One of the parameter sets that has passed these comparisons is shown in the fourth column. This parameter set has been used to create the Figs 2-4.

Parameter	Initial range	Final range	Value in Figs 2-4
psh ₁	5-60	30-60	49.9139
psh ₆	5-60	27-57	34.3117
psh ₇	5-60	10-57	28.5626
psd	5-60	22-59	37.7828
pdh ₁	0.1-0.4 1/min	0.12-0.37 1/min	0.34951
pdh ₆	0.1-0.4 1/min	0.11-0.39 1/min	0.14824
pdh ₇	0.1-0.4 1/min	0.11-0.4 1/min	0.249715
pdd	0.1-0.4 1/min	0.15-0.38 1/min	0.324316
msh ₁	15-65	32-63	48.3084
msh ₆	15-65	31-62	36.4073
msh ₇	15-65	34-62	39.685
msd	15-65	31-65	60.5577
mdh ₁	0.1-0.4 1/min	0.2-0.38 1/min	0.322965
mdh ₆	0.1-0.4 1/min	0.13-0.39 1/min	0.146372
mdh ₇	0.1-0.4 1/min	0.28-0.4 1/min	0.381738
mdd	0.1-0.4 1/min	0.12-0.39 1/min	0.352056
pdh _{1,1}	0.1-0.4 1/min	0.25-0.4 1/min	0.390961
pdh _{1,6}	0.1-0.4 1/min	0.1-0.36 1/min	0.29774
pdh _{1,7}	0.1-0.4 1/min	0.16-0.34 1/min	0.320157
pdh _{6,6}	0.1-0.4 1/min	0.11-0.34 1/min	0.268042
pdh _{6,7}	0.1-0.4 1/min	0.26-0.4 1/min	0.352037
pdh _{7,7}	0.1-0.4 1/min	0.12-0.4 1/min	0.251601
nmh ₁	5-12 min	8.8-12 min	10.0213
nmh ₇	5-12 min	8.6-11.6 min	10.4515
nmd	5-12 min	6.1-12 min	7.74472
nph ₁	0.3-2 min	0.8-2 min	1.5398
nph ₆	0.3-2 min	0.6-1.8 min	0.886233
nph ₇	0.3-2 min	0.4-1.8 min	0.539972
npd	9-27 min	10-18 min	13.2661
dah _{1,1}	0.0003-0.03	0.005-0.03	0.0179429
ddh _{1,1}	0.003-0.3	0.06-0.3	0.220856
dah _{1,6}	0.0003-0.03	0.006-0.029	0.0270209
ddh _{1,6}	0.003-0.3	0.004-0.18	0.0917567
dah _{1,7}	0.0003-0.03	0.0006-0.009	0.00120525
ddh _{1,7}	0.003-0.3	0.03-0.28	0.258167
dah _{6,6}	0.0003-0.03	0.001-0.016	0.0148271
ddh _{6,6}	0.003-0.3	0.05-0.29	0.251173
dah _{6,7}	0.0003-0.03	0.007-0.03	0.0216093
ddh _{6,7}	0.003-0.3	0.03-0.3	0.188923
dah _{7,7}	0.0003-0.03	0.002-0.024	0.0202756
ddh _{7,7}	0.003-0.3	0.07-0.3	0.161018
critph _{1,1}	30-1500	160-720	587.298
critph _{6,7}	30-1500	200-920	769.628
critpd	30-1500	240-720	490.254

APPENDIX S1

DELAY DIFFERENTIAL EQUATION (DDE) MODEL

A. INTRODUCTION

A.1. Mass Action Kinetics

Mass action kinetics describe the behavior of reactants and products in chemical reactions. The behavior is described as an equation where the rate of the reaction is directly proportional to the concentration of reactants. We have used mass action kinetics to create our delay differential equation model.

Chemical reactions can be classified according to the dependency of the reaction rate on the number of reactants, which is called the order of a reaction. In a zero order reaction, the reaction rate does not depend on the concentration of reactants. In first and second order reactions, the reaction rates depend on the concentrations of one reactant or two reactants, respectively. The reaction rates for zero, first and second order reactions can be written as described in the table below. Here, r represents the unit rate for each reaction.

Zero Order Reaction	$\emptyset \xrightarrow{r} P$	Reaction Rate = r
First Order Reaction	$R_1 \xrightarrow{r} P$	Reaction Rate = $r \cdot R_1$
Second Order Reaction	$R_1 + R_2 \xrightarrow{r} P$	Reaction Rate = $r \cdot R_1 \cdot R_2$

In our model *hes6* mRNA synthesis is a zero order reaction. Translation of mRNA to protein, degradation of mRNA and protein, and dimer dissociation reactions are first order reactions. Dimer association reactions are second order reactions.

A.2. Model Variables

In the delay differential equation model, m_{h_i} where $i \in \{1, 7, 6\}$ and m_d represent the number of mRNA molecules of *her1*, *her7*, *hes6* and *deltaC*, respectively. p_{h_i} where $i \in \{1, 7, 6\}$ and p_d represent the number of protein monomers of Her1, Her7, Hes6 and DeltaC, respectively. $p_{h_i, j}$ where $i \leq j$ and $i, j \in \{1, 7, 6\}$ represent the number of molecules of Her1-Her1, Her1-Her7, Her1-Hes6, Her7-Her7, Her7-Hes6 and Hes6-Hes6 dimers. In the model equations, we represent the k^{th} cell as c_k and time as t .

B. MONOMER PROTEIN LEVELS

B.1. Her1 Monomer Protein Levels

[Rate of Change in Her1 Monomer Protein Levels] = [Her1 Protein Synthesis] – [Her1 Protein Degradation] + [Her1-Her1 Dimer Dissociation] + [Her1-Her7 Dimer Dissociation] + [Her1-Hes6 Dimer Dissociation] – [Her1-Her1 Dimer Association] – [Her1-Her7 Dimer Association] – [Her1-Hes6 Dimer Association]

(i) Rate of Change in Her1 Monomer Protein Levels = $\frac{\partial ph_1(c_k, t)}{\partial t}$.

(ii) Her1 Protein Synthesis ($mh_1 \rightarrow ph_1$): $psh_1 \cdot mh_1(c_k, t - nph_1)$ where psh_1 represents the Her1 protein synthesis rate and nph_1 represents the Her1 translation time delay.

(iii) Her1 Protein Degradation ($ph_1 \rightarrow \emptyset$): $pdh_1 \cdot ph_1(c_k, t)$ where pdh_1 represents the Her1 protein degradation rate.

(iv) Her1-Her1 Dimer Dissociation ($ph_{1,1} \rightarrow ph_1 + ph_1$): $2 \cdot ddh_{1,1} \cdot ph_{1,1}(c_k, t)$ where $ddh_{1,1}$ represents the Her1-Her1 dimer dissociation rate. We use 2 in the equation since a Her1-Her1 dimer is formed by two Her1 monomers.

(v) Her1-Her7 Dimer Dissociation ($ph_{1,7} \rightarrow ph_1 + ph_7$): $ddh_{1,7} \cdot ph_{1,7}(c_k, t)$ where $ddh_{1,7}$ represents the Her1-Her7 dimer dissociation rate.

(vi) Her1-Hes6 Dimer Dissociation ($ph_{1,6} \rightarrow ph_1 + ph_6$): $ddh_{1,6} \cdot ph_{1,6}(c_k, t)$ where $ddh_{1,6}$ represents the Her1-Hes6 dimer dissociation rate.

(vii) Her1-Her1 Dimer Association ($ph_1 + ph_1 \rightarrow ph_{1,1}$): $2 \cdot dah_{1,1} \cdot ph_1(c_k, t) \cdot ph_1(c_k, t)$ where $dah_{1,1}$ represents the Her1-Her1 dimer association rate. We use 2 in the equation since a Her1-Her1 dimer is formed by two Her1 monomers.

(viii) Her1-Her7 Dimer Association ($ph_1 + ph_7 \rightarrow ph_{1,7}$): $dah_{1,7} \cdot ph_1(c_k, t) \cdot ph_7(c_k, t)$ where $dah_{1,7}$ represents the Her1-Her7 dimer association rate.

(ix) Her1-Hes6 Dimer Association ($ph_1 + ph_6 \rightarrow ph_{1,6}$): $dah_{1,6} \cdot ph_1(c_k, t) \cdot ph_6(c_k, t)$ where $dah_{1,6}$ represents the Her1-Hes6 dimer association rate.

Combining (i)-(ix) we obtain the equation for the rate of change of Her1 monomer protein levels.

$$\begin{aligned} \frac{\partial \text{ph}_1(c_k, t)}{\partial t} = & \text{psh}_1 \cdot \text{mh}_1(c_k, t - \text{nph}_1) - \text{pdh}_1 \cdot \text{ph}_1(c_k, t) + 2 \cdot \text{ddh}_{1,1} \cdot \text{ph}_{1,1}(c_k, t) + \text{ddh}_{1,7} \cdot \text{ph}_{1,7}(c_k, t) \\ & + \text{ddh}_{1,6} \cdot \text{ph}_{1,6}(c_k, t) - 2 \cdot \text{dah}_{1,1} \cdot \text{ph}_1(c_k, t) \cdot \text{ph}_1(c_k, t) - \text{dah}_{1,7} \cdot \text{ph}_1(c_k, t) \cdot \text{ph}_7(c_k, t) - \text{dah}_{1,6} \cdot \text{ph}_1(c_k, t) \cdot \text{ph}_6(c_k, t) \end{aligned}$$

If we use the summation symbol (\sum) and define $C_{1,1} = 2$, $C_{1,7} = 1$ and $C_{1,6} = 1$ we can rewrite this equation as

$$\frac{\partial \text{ph}_1(c_k, t)}{\partial t} = \text{psh}_1 \cdot \text{mh}_1(c_k, t - \text{nph}_1) - \text{pdh}_1 \cdot \text{ph}_1(c_k, t) + \sum_{j \in \{1,7,6\}} C_{1,j} \cdot [\text{ddh}_{1,j} \cdot \text{ph}_{1,j}(c_k, t) - \text{dah}_{1,j} \cdot \text{ph}_1(c_k, t) \cdot \text{ph}_j(c_k, t)]$$

B.2. Her/Hes Monomer Protein Levels (General Formula)

Similar steps to the Her1 derivation can be used to derive the equations for Her7 and Hes6 monomer protein levels. We can combine the equations for Her1, Her7 and Hes6 monomer levels in one equation.

$$\begin{aligned} \frac{\partial \text{ph}_i(c_k, t)}{\partial t} = & \text{psh}_i \cdot \text{mh}_i(c_k, t - \text{nph}_i) - \text{pdh}_i \cdot \text{ph}_i(c_k, t) + \sum_{\substack{i \leq j \\ i, j \in \{1,7,6\}}} C_{i,j} \cdot [\text{ddh}_{i,j} \cdot \text{ph}_{i,j}(c_k, t) - \text{dah}_{i,j} \cdot \text{ph}_i(c_k, t) \cdot \text{ph}_j(c_k, t)] \\ & \text{where } C_{i,j} = 2, \text{ if } i=j \text{ and } C_{i,j} = 1, \text{ if } i \neq j \end{aligned}$$

In this equation psh_i and pdh_i where $i \in \{1, 7, 6\}$ represent the Her1, Her7 and Hes6 protein synthesis and degradation rates, respectively. $\text{dah}_{i,j}$ and $\text{ddh}_{i,j}$ where $i \leq j$ and $i, j \in \{1, 7, 6\}$ represent the Her1-Her1, Her1-Her7, Her1-Hes6, Her7-Her7, Her7-Hes6 and Hes6-Hes6 dimer association and dissociation rates, respectively.

B.3. DeltaC Protein Levels

[Rate of Change in DeltaC Protein Levels] = [DeltaC Protein Synthesis] – [DeltaC Protein Degradation]

(i) Rate of Change in DeltaC Protein Levels = $\frac{\partial \text{pd}(c_k, t)}{\partial t}$.

(ii) DeltaC Protein Synthesis ($\text{md} \rightarrow \text{pd}$) : $\text{psd} \cdot \text{md}(c_k, t - \text{npd})$ where psd represents the DeltaC protein synthesis rate and npd represents the DeltaC translation time delay.

(iii) DeltaC Protein Degradation ($\text{pd} \rightarrow \emptyset$) : $\text{pdd} \cdot \text{pd}(c_k, t)$ where pdd represents the DeltaC protein degradation rate.

Combining (i)-(iii) we obtain the equation for the rate of change of DeltaC protein levels.

$$\frac{\partial \text{pd}(c_k, t)}{\partial t} = \text{psd} \cdot \text{md}(c_k, t - \text{npd}) - \text{pdd} \cdot \text{pd}(c_k, t)$$

C. DIMER PROTEIN LEVELS

C.1. Her1-Her1 Dimer Levels

[Rate of Change in Her1-Her1 Dimer Levels] = [Her1-Her1 Dimer Association] – [Her1-Her1 Dimer Dissociation] – [Her1-Her1 Dimer Degradation]

(i) Rate of Change in Her1 Dimer Protein Levels = $\frac{\partial \text{ph}_{1,1}(\mathbf{c}_k, t)}{\partial t}$.

(ii) Her1-Her1 Dimer Association ($\text{ph}_1 + \text{ph}_1 \rightarrow \text{ph}_{1,1}$) : $\text{dah}_{1,1} \cdot \text{ph}_1(\mathbf{c}_k, t) \cdot \text{ph}_1(\mathbf{c}_k, t)$ where $\text{dah}_{1,1}$ represents the Her1-Her1 dimer association rate.

(iii) Her1-Her1 Dimer Dissociation ($\text{ph}_{1,1} \rightarrow \text{ph}_1 + \text{ph}_1$) : $\text{ddh}_{1,1} \cdot \text{ph}_{1,1}(\mathbf{c}_k, t)$ where $\text{ddh}_{1,1}$ represents the Her1-Her1 dimer dissociation rate.

(iv) Her1-Her1 Dimer Degradation ($\text{ph}_{1,1} \rightarrow \emptyset$) : $\text{pdh}_{1,1} \cdot \text{ph}_{1,1}(\mathbf{c}_k, t)$ where $\text{pdh}_{1,1}$ represents the Her1-Her1 dimer degradation rate.

Combining (i)-(iv) we obtain the equation for the rate of change of Her1-Her1 dimer levels.

$$\frac{\partial \text{ph}_{1,1}(\mathbf{c}_k, t)}{\partial t} = \text{dah}_{1,1} \cdot \text{ph}_1(\mathbf{c}_k, t) \cdot \text{ph}_1(\mathbf{c}_k, t) - \text{ddh}_{1,1} \cdot \text{ph}_{1,1}(\mathbf{c}_k, t) - \text{pdh}_{1,1} \cdot \text{ph}_{1,1}(\mathbf{c}_k, t)$$

C.2. Her/Hes Dimer Levels

Similar steps to the above derivation can be used to derive the equations for Her1-Her7, Her1-Hes6, Her7-Her7, Her7-Hes6 and Hes6-Hes6 dimer levels. We can combine the equations for Her1-Her1, Her1-Her7, Her1-Hes6, Her7-Her7, Her7-Hes6 and Hes6-Hes6 dimer levels in one equation.

$$\frac{\partial \text{ph}_{i,j}(\mathbf{c}_k, t)}{\partial t} = \text{dah}_{i,j} \cdot \text{ph}_i(\mathbf{c}_k, t) \cdot \text{ph}_j(\mathbf{c}_k, t) - \text{ddh}_{i,j} \cdot \text{ph}_{i,j}(\mathbf{c}_k, t) - \text{pdh}_{i,j} \cdot \text{ph}_{i,j}(\mathbf{c}_k, t)$$

where $i \leq j$ and $i, j \in \{1, 7, 6\}$

In this equation $\text{dah}_{i,j}$, $\text{ddh}_{i,j}$ and $\text{pdh}_{i,j}$ where $i \leq j$ and $i, j \in \{1, 7, 6\}$ represent the Her1-Her1, Her1-Her7, Her1-Hes6, Her7-Her7, Her7-Hes6 and Hes6-Hes6 dimer association, dissociation and degradation rates, respectively.

D. mRNA LEVELS

D.1. *hes6* mRNA Levels

[Rate of Change in *hes6* mRNA Levels] = [*hes6* mRNA Synthesis] – [*hes6* mRNA Degradation]

(i) Rate of Change in *hes6* mRNA Levels = $\frac{\partial mh_6(c_k, t)}{\partial t}$.

(ii) *hes6* mRNA Synthesis ($\emptyset \rightarrow mh_6$) : msh_6 where msh_6 represents the maximum *hes6* mRNA synthesis rate. Since transcription of *hes6* is not regulated by Notch signaling and Her/Hes transcription factors in the posterior presomitic mesoderm, transcription rate is assumed to be constant (msh_6) in our model.

(iii) *hes6* mRNA Degradation ($mh_6 \rightarrow \emptyset$) : $mdh_6 \cdot mh_6(c_k, t)$ where mdh_6 represents the *hes6* mRNA degradation rate.

Combining (i)-(iii) we obtain the equation for the rate of change of *hes6* mRNA levels.

$$\frac{\partial mh_6(c_k, t)}{\partial t} = msh_6 - mdh_6 \cdot mh_6(c_k, t)$$

D.2. *her1* mRNA Levels

[Rate of Change in *her1* mRNA Levels] = [*her1* mRNA Synthesis] – [*her1* mRNA Degradation]

(i) Rate of Change in *her1* mRNA Levels = $\frac{\partial mh_1(c_k, t)}{\partial t}$.

(ii) *her1* mRNA Synthesis ($\emptyset \rightarrow mh_1$) :

$$msh_1 \frac{1 + [\frac{1}{6} \sum_{c_n \in N} \frac{pd(c_n, t - nmh_1)}{critpd}]}{1 + [\frac{1}{6} \sum_{c_n \in N} \frac{pd(c_n, t - nmh_1)}{critpd}] + [\frac{ph_{1,1}(c_k, t - nmh_1)}{critph_{1,1}}]^2 + [\frac{ph_{6,7}(c_k, t - nmh_1)}{critph_{6,7}}]^2}$$

where msh_1 represents the

maximum *her1* mRNA synthesis rate, $critph_{1,1}$, $critph_{6,7}$ and $critpd$ are DNA-binding dissociation constants for Her1-Her1, Her7-Hes6 and NICD, respectively. Also N represents all the neighbors of the k^{th} cell and nmh_1 represents *her1* mRNA transcription time delay.

Form of Transcription Term:

Transcriptions of *her1* and *her7* are repressed by Her-Her1 and Her7-Hes6 dimer proteins but activated by Notch signaling. The activity of Notch signaling is proportional to the levels of DeltaC protein.

In our model, we assume that transcription rate of *her1* is proportional to the ratio:

$$\frac{\text{"DNA states free of repressors"}}{\text{"Total DNA state"}}$$

“DNA states free of repressor” = “Vacant DNA” + “Activator (NICD)-bound DNA”

“Total DNA states” = “Vacant DNA” + “NICD-bound DNA” + “Her1-Her1 homodimer bound DNA” + “Her7-Hes6 heterodimer bound DNA”

Please note that in our model it is assumed that two Her1-Her1, Her7-Hes6 dimers bind to DNA as a tetramer and NICD, which is activated by DeltaC protein from six neighboring cells, bind as a monomer. Because of that, we square the terms for Her1-Her1 and Her7-Hes6 dimers but not DeltaC term.

(iii) *her1* mRNA Degradation ($mh_1 \rightarrow \emptyset$) : $mdh_1 \cdot mh_1(c_k, t)$ where mdh_1 represents the *her1* mRNA degradation rate.

Combining (i)-(iii) we obtain the equation for the rate of change of *her1* mRNA levels.

$$\frac{\partial mh_1(c_k, t)}{\partial t} = msh_1 \frac{1 + \left[\frac{1}{6} \sum_{c_n \in N} \frac{pd(c_n, t-nmh_1)}{critpd} \right]}{1 + \left[\frac{1}{6} \sum_{c_n \in N} \frac{pd(c_n, t-nmh_1)}{critpd} \right] + \left[\frac{ph_{1,1}(c_k, t-nmh_1)}{critph_{1,1}} \right]^2 + \left[\frac{ph_{6,7}(c_k, t-nmh_1)}{critph_{6,7}} \right]^2} - mdh_1 \cdot mh_1(c_k, t)$$

D.3. *her1* and *her7* mRNA Levels

Similar steps to the *her1* derivation can be used to derive the equations for *her7* mRNA levels. We can combine the equations for *her1* and *her7* mRNA levels in one equation.

$$\frac{\partial mh_i(c_k, t)}{\partial t} = msh_i \frac{1 + \left[\frac{1}{6} \sum_{c_n \in N} \frac{pd(c_n, t-nmh_i)}{critpd} \right]}{1 + \left[\frac{1}{6} \sum_{c_n \in N} \frac{pd(c_n, t-nmh_i)}{critpd} \right] + \left[\frac{ph_{1,1}(c_k, t-nmh_i)}{critph_{1,1}} \right]^2 + \left[\frac{ph_{6,7}(c_k, t-nmh_i)}{critph_{6,7}} \right]^2} - mdh_i \cdot mh_i(c_k, t)$$

where $i \in \{1, 7\}$

In this equation msh_i and mdh_i where $i \in \{1, 7\}$ represent the *her1* and *her7* mRNA max synthesis rate and degradation rate, respectively. $critph_{1,1}$, $critph_{6,7}$ and $critpd$ are DNA-binding dissociation constants for Her1-Her1, Her7-Hes6 and NICD, respectively. N represents

all the neighbors of the k^{th} cell and nmh_i where $i \in \{1, 7\}$ represents *her1* and *her7* mRNA transcription time delay.

D.4. *deltaC* mRNA Levels

[Rate of Change in *deltaC* mRNA Levels] = [*deltaC* mRNA Synthesis] – [*deltaC* mRNA Degradation]

(i) Rate of Change in *deltaC* mRNA Levels = $\frac{\partial \text{md}(c_k, t)}{\partial t}$.

(ii) *deltaC* mRNA Synthesis ($\emptyset \rightarrow \text{md}$) : $\text{msd} \frac{1}{1 + \left[\frac{\text{ph}_{1,1}(c_k, t - \text{nmd})}{\text{critph}_{1,1}} \right]^2 + \left[\frac{\text{ph}_{6,7}(c_k, t - \text{nmd})}{\text{critph}_{6,7}} \right]^2}$ where

msd represents the maximum *deltaC* mRNA synthesis rate. *critph*_{1,1} and *critph*_{6,7} are DNA-binding dissociation constants for Her1-Her1 and Her7-Hes6. *nmd* represents *deltaC* mRNA transcription time delay.

Form of Transcription Term:

Transcription of *deltaC* is repressed by Her-Her1 and Her7-Hes6 dimer proteins. In our model, we assume that transcription rate of *deltaC* is proportional to the ratio:

$$\frac{\text{"DNA states free of repressors"}}{\text{"Total DNA state"}}$$

“DNA states free of repressor” = “Vacant DNA”

“Total DNA states” = “Vacant DNA” + “Her1-Her1 homodimer bound DNA” + “Her7-Hes6 heterodimer bound DNA”

Please note that in our model it is assumed that two Her1-Her1 and Her7-Hes6 dimers bind to DNA as a tetramer. Because of that we square the terms for Her1-Her1 and Her7-Hes6 dimers.

(iii) *deltaC* mRNA Degradation ($\text{md} \rightarrow \emptyset$) : $\text{mdd} \cdot \text{md}(c_k, t)$ where *mdd* represents the *deltaC* mRNA degradation rate.

Combining (i)-(iii) we obtain the equation for the rate of change of *hes6* mRNA levels.

$$\frac{\partial \text{md}(c_k, t)}{\partial t} = \text{msd} \frac{1}{1 + \left[\frac{\text{ph}_{1,1}(c_k, t - \text{nmd})}{\text{critph}_{1,1}} \right]^2 + \left[\frac{\text{ph}_{6,7}(c_k, t - \text{nmd})}{\text{critph}_{6,7}} \right]^2} - \text{mdd} \cdot \text{md}(c_k, t)$$

STOCHASTIC SIMULATIONS

Reactions and propensities used in stochastic simulations.

Reaction (for each cell)	Propensity (for each cell c_k)
Reaction 1: $mh_1 \rightarrow ph_1$ (Her1 protein synthesis)	$a_1(c_k) = psh_1 \cdot mh_1(c_k)$
Reaction 2: $ph_1 \rightarrow \emptyset$ (Her1 protein degradation)	$a_2(c_k) = pdh_1 \cdot ph_1(c_k)$
Reaction 3: $ph_1 + ph_1 \rightarrow ph_{1,1}$ (Her1-Her1 dimer association)	$a_3(c_k) = dah_{1,1} \cdot ph_1(c_k) \cdot (ph_1(c_k) - 1)/2$
Reaction 4: $ph_{1,1} \rightarrow ph_1 + ph_1$ (Her1-Her1 dimer dissociation)	$a_4(c_k) = ddh_{1,1} \cdot ph_{1,1}(c_k)$
Reaction 5: $ph_1 + ph_7 \rightarrow ph_{1,7}$ (Her1-Her7 dimer association)	$a_5(c_k) = dah_{1,7} \cdot ph_1(c_k) \cdot ph_7(c_k)$
Reaction 6: $ph_{1,7} \rightarrow ph_1 + ph_7$ (Her1-Her7 dimer dissociation)	$a_6(c_k) = ddh_{1,7} \cdot ph_{1,7}(c_k)$
Reaction 7: $ph_1 + ph_6 \rightarrow ph_{1,6}$ (Her1-Hes6 dimer association)	$a_7(c_k) = dah_{1,6} \cdot ph_1(c_k) \cdot ph_6(c_k)$
Reaction 8: $ph_{1,6} \rightarrow ph_1 + ph_6$ (Her1-Hes6 dimer dissociation)	$a_8(c_k) = ddh_{1,6} \cdot ph_{1,6}(c_k)$
Reaction 9: $mh_7 \rightarrow ph_7$ (Her7 protein synthesis)	$a_9(c_k) = psh_7 \cdot mh_7(c_k)$
Reaction 10: $ph_7 \rightarrow \emptyset$ (Her7 protein degradation)	$a_{10}(c_k) = pdh_7 \cdot ph_7(c_k)$
Reaction 11: $ph_7 + ph_7 \rightarrow ph_{7,7}$ (Her7-Her7 dimer association)	$a_{11}(c_k) = dah_{7,7} \cdot ph_7(c_k) \cdot (ph_7(c_k) - 1)/2$
Reaction 12: $ph_{7,7} \rightarrow ph_7 + ph_7$ (Her7-Her7 dimer dissociation)	$a_{12}(c_k) = ddh_{7,7} \cdot ph_{7,7}(c_k)$
Reaction 13: $ph_7 + ph_6 \rightarrow ph_{6,7}$ (Her7-Hes6 dimer association)	$a_{13}(c_k) = dah_{6,7} \cdot ph_7(c_k) \cdot ph_6(c_k)$
Reaction 14: $ph_{6,7} \rightarrow ph_7 + ph_6$ (Her7-Hes6 dimer dissociation)	$a_{14}(c_k) = ddh_{6,7} \cdot ph_{6,7}(c_k)$
Reaction 15: $mh_6 \rightarrow ph_6$ (Hes6 protein synthesis)	$a_{15}(c_k) = psh_6 \cdot mh_6(c_k)$
Reaction 16: $ph_6 \rightarrow \emptyset$ (Hes6 protein degradation)	$a_{16}(c_k) = pdh_6 \cdot ph_6(c_k)$
Reaction 17: $ph_6 + ph_6 \rightarrow ph_{6,6}$ (Hes6-Hes6 dimer association)	$a_{17}(c_k) = dah_{6,6} \cdot ph_6(c_k) \cdot (ph_6(c_k) - 1)/2$
Reaction 18: $ph_{6,6} \rightarrow ph_6 + ph_6$ (Hes6-Hes6 dimer dissociation)	$a_{18}(c_k) = ddh_{6,6} \cdot ph_{6,6}(c_k)$
Reaction 19: $ph_{1,1} \rightarrow \emptyset$ (Her1-Her1 dimer degradation)	$a_{19}(c_k) = pdh_{1,1} \cdot ph_{1,1}(c_k)$
Reaction 20: $ph_{1,7} \rightarrow \emptyset$ (Her1-Her7 dimer degradation)	$a_{20}(c_k) = pdh_{1,7} \cdot ph_{1,7}(c_k)$
Reaction 21: $ph_{1,6} \rightarrow \emptyset$ (Her1-Hes6 dimer degradation)	$a_{21}(c_k) = pdh_{1,6} \cdot ph_{1,6}(c_k)$
Reaction 22: $ph_{7,7} \rightarrow \emptyset$ (Her7-Her7 dimer degradation)	$a_{22}(c_k) = pdh_{7,7} \cdot ph_{7,7}(c_k)$
Reaction 23: $ph_{6,7} \rightarrow \emptyset$ (Her7-Hes6 dimer degradation)	$a_{23}(c_k) = pdh_{6,7} \cdot ph_{6,7}(c_k)$
Reaction 24: $ph_{6,6} \rightarrow \emptyset$ (Hes6-Hes6 dimer degradation)	$a_{24}(c_k) = pdh_{6,6} \cdot ph_{6,6}(c_k)$
Reaction 25: $md \rightarrow pd$ (Delta protein synthesis)	$a_{25}(c_k) = psd \cdot md(c_k)$
Reaction 26: $pd \rightarrow \emptyset$ (Delta protein degradation)	$a_{26}(c_k) = pdd \cdot pd(c_k)$
Reaction 27: $\emptyset \rightarrow mh_1$ (<i>her1</i> mRNA synthesis)	$a_{27}(c_k) = fh_1$
Reaction 28: $mh_1 \rightarrow \emptyset$ (<i>her1</i> mRNA degradation)	$a_{28}(c_k) = mdh_1 \cdot mh_1(c_k)$
Reaction 29: $\emptyset \rightarrow mh_7$ (<i>her7</i> mRNA synthesis)	$a_{29}(c_k) = fh_7$
Reaction 30: $mh_7 \rightarrow \emptyset$ (<i>her7</i> mRNA degradation)	$a_{30}(c_k) = mdh_7 \cdot mh_7(c_k)$
Reaction 31: $\emptyset \rightarrow mh_6$ (<i>hes6</i> mRNA synthesis)	$a_{31}(c_k) = psh_6$
Reaction 32: $mh_6 \rightarrow \emptyset$ (<i>hes6</i> mRNA degradation)	$a_{32}(c_k) = mdh_6 \cdot mh_6(c_k)$
Reaction 33: $\emptyset \rightarrow md$ (<i>deltaC</i> mRNA synthesis)	$a_{33}(c_k) = fd$
Reaction 34: $md \rightarrow \emptyset$ (<i>deltaC</i> mRNA degradation)	$a_{34}(c_k) = mdd \cdot md(c_k)$

Transcription of *her1*, *her7* and *deltaC* mRNAs have been approximated by the following functions in stochastic simulations.

Genes	Transcription Term
<i>her1</i>	$fh_1 = msh_1 \frac{1 + [\frac{1}{6} \sum_{c_n \in N} \frac{pd(c_n)}{critpd}]}{1 + [\frac{1}{6} \sum_{c_n \in N} \frac{pd(c_n)}{critpd}] + [\frac{ph_{1,1}(c_k)}{critph_{1,1}}]^2 + [\frac{ph_{6,7}(c_k)}{critph_{6,7}}]^2}$
<i>her7</i>	$fh_7 = msh_7 \frac{1 + [\frac{1}{6} \sum_{c_n \in N} \frac{pd(c_n)}{critpd}]}{1 + [\frac{1}{6} \sum_{c_n \in N} \frac{pd(c_n)}{critpd}] + [\frac{ph_{1,1}(c_k)}{critph_{1,1}}]^2 + [\frac{ph_{6,7}(c_k)}{critph_{6,7}}]^2}$
<i>deltaC</i>	$fd = msd \cdot \frac{1}{1 + [\frac{ph_{1,1}(c_k)}{critph_{1,1}}]^2 + [\frac{ph_{6,7}(c_k)}{critph_{6,7}}]^2}$
<p>where N represents all the neighbors of the k^{th} cell (c_k).</p>	