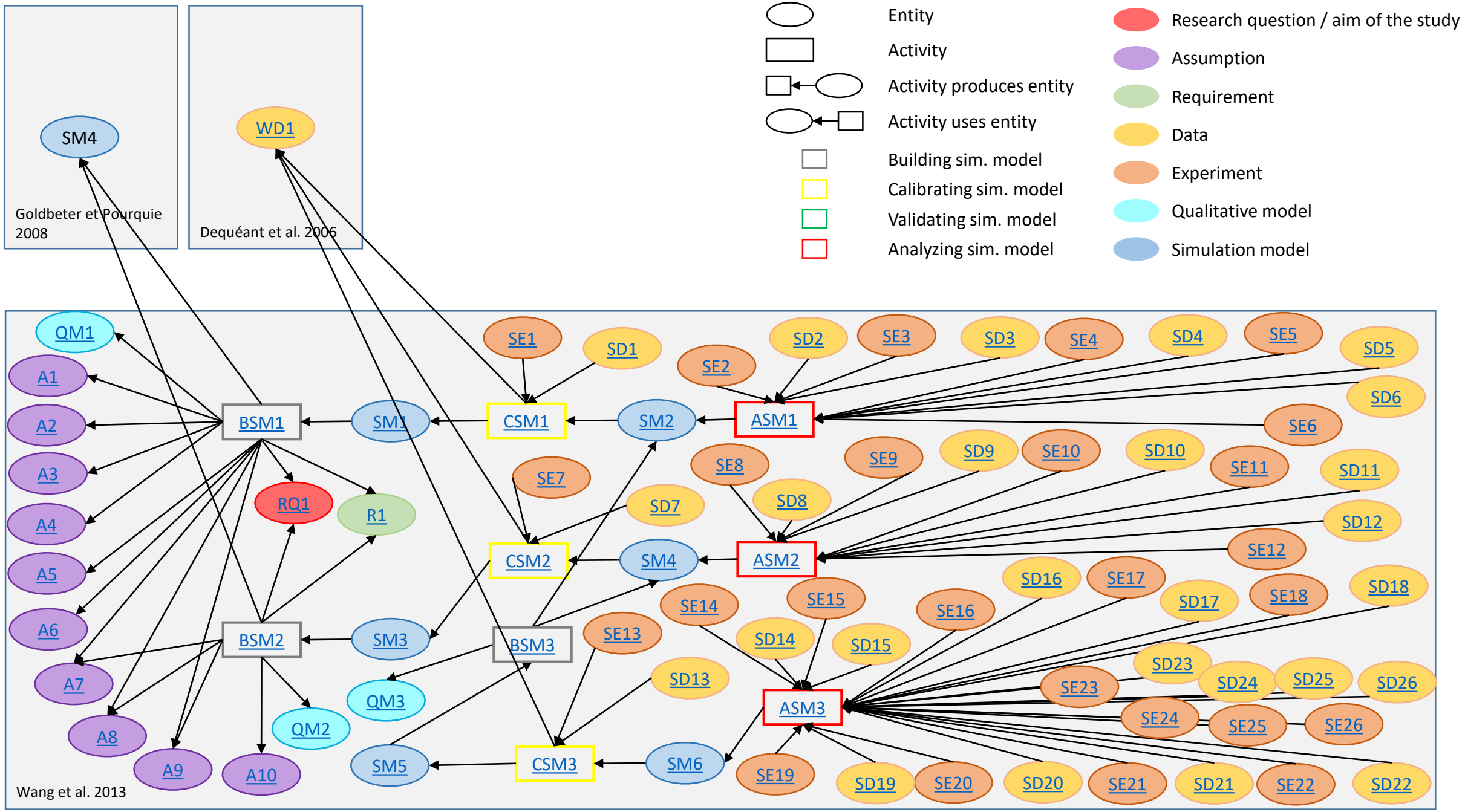
Entity
Activity
Activity produces entity
Activity uses entity
Building sim. model
Calibrating sim. model
Validating sim. model
Analyzing sim. model
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Requirement
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Experiment
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Simulation model
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Goldbeter et Pourquie 2008
Dequéant et al. 2006
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Wang et al. 2013

WD1 Wet-lab Data

Type	Label
Description	“Mutually exclusive activation of the notch-FGF and Wnt clusters during one segmentation clock oscillation. Expression profiles of cyclic genes of (A) notch, (B) FGF, and (C) Wnt pathways along the microarray time series.”
Reference	Figure 3
Type of experiment	in vitro
Organism	Mouse (embryo)
Tissue	presomitic mesoderm (PSM)
Study	Dequeant et al. 2006

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RQ1 Research question

Type	Label
Description	“simulate the dynamics of the Notch and Wnt pathways in somitogenesis, and are capable of reproducing the observations derived from wet experiments”
Study	Wang et al. 2013

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R1 Requirement

Type	Label
Description	“the oscillating period of target genes is taken as 120 minutes”
Related to	WD1 (Dequéant et al. 2006)
Main species	Notch target genes (Hes7 mRNA, Lfng mRNA)
Type	Quantitative
Study	Wang et al. 2013

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QM1 Qualitative model

Type	Label
Description	Notch: “Schematic diagram of the Notch signaling pathway”
Reference	Figure 1
Species	Notch, DLL1, NICD, RBP-j, Lfng, Lfng mRNA, Hes7, Hes7c mRNA
Compartments	Cytosol, nucleus
Study	Wang et al. 2013

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QM2 Qualitative model

Type	Label
Description	“Schematic diagram of the Wnt signaling pathway”
Reference	Figure 3
Species	Wnt (as Wnt+Fzd), Dsh, Axin2, Axin2 mRNA, GSK3, β-catenin, Lef1, DLL1, DLL1 mRNA
Compartments	Cytosol, nucleus
Study	Wang et al. 2013

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QM3 Qualitative model

Type	Label
Description	“schematic diagram of the combined model”
Reference	Figure 5
Species	Wnt (as Wnt+Fzd), Dsh, Axin2, Axin2 mRNA, GSK3, β-catenin, Lef1, DLL1, DLL1 mRNA, Notch, NICD, RBP-j, Lfng, Lfng mRNA, Hes7, Hes7 mRNA, Nkd1, Nkd1 mRNA
Compartments	Cytosol, nucleus
Study	Wang et al. 2013

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A1 Assumption

Type	Label
Description	“Transcription factors such as NICD and Hes7 can shuttle between the nucleus and cytoplasm and degrade in both compartment”
Category	Degradation (179)
Study	Wang et al. 2013

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A2 Assumption

Type	Label
Description	“Transcription factors such as NICD and Hes7 can shuttle between the nucleus and cytoplasm and degrade in both compartment”
Category	Transport (655)
Study	Wang et al. 2013

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A3 Assumption

Type	Label
Description	“the DLL1 ligand and the Notch receptor are synthesized at a constant rate and the degradation of these molecules obeys Michaelis-Menten kinetics”
Category	Henri-Michaelis-Menten rate law (29)
Study	Wang et al. 2013

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A4 Assumption

Type	Label
Description	“the DLL1 ligand and the Notch receptor are synthesized at a constant rate and the degradation of these molecules obeys Michaelis-Menten kinetics”
Category	Zeroth order rate constant (46)
Study	Wang et al. 2013

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A5 Assumption

Type	Label
Description	“the DLL1 ligand and the Notch receptor are synthesized at a constant rate and the degradation of these molecules obeys Michaelis-Menten kinetics”
Category	Degradation (179)
Study	Wang et al. 2013

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A6 Assumption

Type	Label
Description	“RBP-j is not degraded because we assume the total concentration of RBP-j remains constant”
Category	Concentration conservation law (362)
Study	Wang et al. 2013

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A7 Assumption

Type	Label
Description	“A cell is divided into two compartments, the nucleus where target genes are transcribed and the cytoplasm where proteins are translated”
Category	Physical Compartment (290)
Study	Wang et al. 2013

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A8 Assumption

Type	Label
Description	“mRNA molecules only can be transported from the nucleus to the cytoplasm and degrade there”
Category	Degradation (179)
Study	Wang et al. 2013

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A9 Assumption

Type	Label
Description	“mRNA molecules only can be transported from the nucleus to the cytoplasm and degrade there”
Category	Transport (655)
Study	Wang et al. 2013

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A10 Assumption

Type	Label
Description	“assumed the activation of Dsh is reversible and obeys Michaelis-Menten kinetics”
Category	Henri-Michaelis-Menten rate law (29)
Study	Wang et al. 2013

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BSM1 Building simulation model

Type	Label
Description	Creation of Notch model
Study	Wang et al. 2013

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SM1 Simulation model

Type	Label
Description	“A total of 12 ordinary differential equations (ODEs) for the Notch signaling model”
Reference	Not available
Study	Wang et al. 2013

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CSM1 Calibrating simulation model

Type	Label
Description	Parameter estimation with parameter learning algorithm
Study	Wang et al. 2013

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SE1 Experiment

Type	Label
Description	“parameter learning algorithm to adapt the model to” an oscillation period of 120 minutes
Reference	Not available
Category	Optimization
Study	Wang et al. 2013

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SD1 Data

Type	Label
Description	Simulation results of SE1
Reference	parameter values in Tables S1 and S2
Related to	SE1
Study	Wang et al. 2013

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SM2 Simulation model

Type	Label
Description	A trained model of “a total of 12 ordinary differential equations (ODEs) for the Notch signaling model”
Reference	Not available
Study	Wang et al. 2013

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ASM1 Analyzing simulation model

Type	Label
Description	Model simulation for the Notch pathway in isolation
Study	Wang et al. 2013

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SE2 Experiment

Type	Label
Description	“The simulated expression patterns of the Notch target genes under conditions of a constant extracellular signal” & “phase relationships of the Notch target genes, Hes7 and NICD.”
Reference	Not available
Category	Time course analysis
Study	Wang et al. 2013

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SD2 Data

Type	Label
Description	Simulation results of SE2
Reference	Figure 2A & 2F
Related to	SE2
Study	Wang et al. 2013

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SE3 Experiment

Type	Label
Description	“investigated the influence of the upstream Notch signals on the expressions of the target genes. When knocking out the Dll1 gene, the ligand of the Notch pathway, at time point 120 minutes”, observations: “The expression patterns of Notch target genes” & “The changes of concentration of NICD in the cytoplasm and nucleus and the transcriptional activator”
Reference	Not available
Category	Perturbation
Study	Wang et al. 2013

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SD3 Data

Type	Label
Description	Simulation results of SE3
Reference	Figure 2B & 2C
Related to	SE3
Study	Wang et al. 2013

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SE4 Experiment

Type	Label
Description	“investigated the influence of the feedback loops on the oscillating expressions of the Notch pathway target genes. After knocking out the Lfng gene at time point 120 minutes”, observations: “expression patterns of the Hes7 gene” & “changes of concentration of NICD”
Reference	Not available
Category	Perturbation
Study	Wang et al. 2013

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SD4 Data

Type	Label
Description	Simulation results of SE4
Reference	Figure 2D & 2G
Related to	SE4
Study	Wang et al. 2013

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SE5 Experiment

Type	Label
Description	Knocking out the Hes7 gene at time point 120 minutes, observations: “expression patterns of the Lfng gene” & “changes of concentrations of NICD and the complex of NICD and RBP-j”
Reference	Not available
Category	Perturbation
Study	Wang et al. 2013

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SD5 Data

Type	Label
Description	Simulation results of SE5
Reference	Figure 2E & 2H
Related to	SE5
Study	Wang et al. 2013

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SE6 Experiment

Type	Label
Description	Sensitivity analysis
Reference	Not available
Category	Sensitivity analysis
Study	Wang et al. 2013

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SD6 Data

Type	Label
Description	Simulation results of SE6
Reference	Figure S1-S3
Related to	SE6
Study	Wang et al. 2013

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BSM2 Building simulation model

Type	Label
Description	Creation of Wnt model
Study	Wang et al. 2013

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SM3 Simulation model

Type	Label
Description	“A total of 13 ODEs for the Wnt signaling model”
Reference	Not available
Study	Wang et al. 2013

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CSM2 Calibrating simulation model

Type	Label
Description	Parameter estimation with parameter learning algorithm
Study	Wang et al. 2013

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SE7 Experiment

Type	Label
Description	“parameter learning algorithm to adapt the model to” an oscillation period of 120 minutes
Reference	Not available
Category	Optimization
Study	Wang et al. 2013

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SD7 Data

Type	Label
Description	Simulation results of SE7
Reference	parameter values in Tables S3 and S4
Related to	SE7
Study	Wang et al. 2013

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SM4 Simulation model

Type	Label
Description	A trained model of “A total of 13 ODEs for the Wnt signaling model”
Reference	Not available
Study	Wang et al. 2013

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ASM2 Analyzing simulation model

Type	Label
Description	Model simulation for the Wnt pathway in isolation
Study	Wang et al. 2013

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SE8 Experiment

Type	Label
Description	“simulated expression patterns of Wnt target genes when there is a constant extracellular signal” & expression of downstream and upstream Wnt signals (β-catenin-Lef1 / Dsh) & “phase relationships between active Dsh, the GSK3-Axin2 complex, the β-catenin-Lef1 complex and Axin2.”
Reference	Not available
Category	Time course analysis
Study	Wang et al. 2013

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SD8 Data

Type	Label
Description	Simulation results of SE8
Reference	Figure 4A & 4D & 4G
Related to	SE8
Study	Wang et al. 2013

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SE9 Experiment

Type	Label
Description	“extracellular Wnt signals were removed at time point 120 minutes”, observations: “expressions of the Wnt pathway target genes” & “changes of concentration of active Dsh and the β-catenin- Lef1 complex and the expression patterns of the Wnt target genes”
Reference	Not available
Category	Perturbation
Study	Wang et al. 2013

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SD9 Data

Type	Label
Description	Simulation results of SE9
Reference	Figure 4B & 4E
Related to	SE9
Study	Wang et al. 2013

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SE10 Experiment

Type	Label
Description	“extracellular Wnt signals was doubled”, observations: “expression levels and oscillating period of the target genes”
Reference	Not available
Category	Time course analysis
Study	Wang et al. 2013

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SD10 Data

Type	Label
Description	Simulation results of SE10
Reference	Figure 4C
Related to	SE10
Study	Wang et al. 2013

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SE11 Experiment

Type	Label
Description	“knocking out the Axin2 gene at time point 120 minutes”, observations: “expression patterns of the DLL1 gene” & “changes of concentration of Axin2, active Dsh, the GSK3-Axin2 complex and the β-catenin-Lef1 complex”
Reference	Not available
Category	Perturbation
Study	Wang et al. 2013

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SD11 Data

Type	Label
Description	Simulation results of SE11
Reference	Figure 4F & 4H
Related to	SE11
Study	Wang et al. 2013

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SE12 Experiment

Type	Label
Description	Sensitivity analysis
Reference	Not available
Category	Sensitivity analysis
Study	Wang et al. 2013

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SD12 Data

Type	Label
Description	Simulation results of SE12
Reference	Figure S4-S6
Related to	SE12
Study	Wang et al. 2013

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BSM3 Building simulation model

Type	Label
Description	Establish a combined model of the two pathways by introducing three levels of crosstalk
Study	Wang et al. 2013

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SM5 Simulation model

Type	Label
Description	A total of 32 ODEs for the combined signaling model
Reference	Not available
Study	Wang et al. 2013

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CSM3 Calibrating simulation model

Type	Label
Description	Parameter estimation with parameter learning algorithm
Study	Wang et al. 2013

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SE13 Experiment

Type	Label
Description	“parameter learning algorithm to adapt the model to” an oscillation period of 120 minutes
Reference	Not available
Category	Optimization
Study	Wang et al. 2013

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SD13 Data

Type	Label
Description	Simulation results of SE13
Reference	parameter values in Tables S5 and S6
Related to	SE13
Study	Wang et al. 2013

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SM6 Simulation model

Type	Label
Description	A trained model of a total of 32 ODEs for the combined signaling model
Reference	Not available
Study	Wang et al. 2013

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ASM3 Analyzing simulation model

Type	Label
Description	Model simulation for the combined pathways
Study	Wang et al. 2013

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SE14 Experiment

Type	Label
Description	“condition of a constant Wnt ligand concentration”
Reference	Not available
Category	Time course analysis
Study	Wang et al. 2013

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SD14 Data

Type	Label
Description	Simulation results of SE14
Reference	Figure 6A
Related to	SE14
Study	Wang et al. 2013

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SE15 Experiment

Type	Label
Description	“knocking out the Dll1 gene at time point 120 minutes”, observations: “expression patterns of the Notch and Wnt target genes”
Reference	Not available
Category	Perturbation
Study	Wang et al. 2013

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SD15 Data

Type	Label
Description	Simulation results of SE15
Reference	Figure 6B
Related to	SE15
Study	Wang et al. 2013

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SE16 Experiment

Type	Label
Description	“knocking out the Lfng gene at time point 120 minutes”, observations: “expression patterns of the Hes7 gene and the Wnt target genes”
Reference	Not available
Category	Perturbation
Study	Wang et al. 2013

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SD16 Data

Type	Label
Description	Simulation results of SE16
Reference	Figure 6C
Related to	SE16
Study	Wang et al. 2013

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SE17 Experiment

Type	Label
Description	Knocking out the Hes7 gene at time point 240 minutes, observations: “expression patterns of the Lfng gene and the Wnt target genes”
Reference	Not available
Category	Perturbation
Study	Wang et al. 2013

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SD17 Data

Type	Label
Description	Simulation results of SE17
Reference	Figure 6D
Related to	SE17
Study	Wang et al. 2013

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SE18 Experiment

Type	Label
Description	“Wnt signals were halved”, observations: “changes in gene-expression oscillation periods of the Wnt and Notch pathways”
Reference	Not available
Category	Time course analysis
Study	Wang et al. 2013

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SD18 Data

Type	Label
Description	Simulation results of SE18
Reference	Figure 7A
Related to	SE18
Study	Wang et al. 2013

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SE19 Experiment

Type	Label
Description	“upregulated the Wnt signals 10-fold”, observations: “changes in gene expression oscillation periods of the Wnt and Notch pathways”
Reference	Not available
Category	Time course analysis
Study	Wang et al. 2013

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SD19 Data

Type	Label
Description	Simulation results of SE19
Reference	Figure 7B
Related to	SE19
Study	Wang et al. 2013

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SE20 Experiment

Type	Label
Description	“knocked out the Wnt signals at time point 200 minutes”, observations: “changes in gene-expression oscillation periods of the Wnt and Notch pathways”
Reference	Not available
Category	Perturbation
Study	Wang et al. 2013

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SD20 Data

Type	Label
Description	Simulation results of SE20
Reference	Figure 7C
Related to	SE20
Study	Wang et al. 2013

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SE21 Experiment

Type	Label
Description	“knocked out the Axin2 gene”, observations: “changes in gene expression oscillation periods of the Wnt and Notch pathways”
Reference	Not available
Category	Perturbation
Study	Wang et al. 2013

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SD21 Data

Type	Label
Description	Simulation results of SE21
Reference	Figure 7D
Related to	SE21
Study	Wang et al. 2013

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SE22 Experiment

Type	Label
Description	“knocked out the Wnt signals at time point 240 minutes”, observations: “expression patterns of the NkSD1”
Reference	Not available
Category	Perturbation
Study	Wang et al. 2013

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SD22 Data

Type	Label
Description	Simulation results of SE22
Reference	Figure 7E
Related to	SE22
Study	Wang et al. 2013

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SE23 Experiment

Type	Label
Description	“knocked out the Dll1 gene at time point 240 minutes”, observations: “expression patterns of the NkSD1”
Reference	Not available
Category	Perturbation
Study	Wang et al. 2013

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SD23 Data

Type	Label
Description	Simulation results of SE23
Reference	Figure 7F
Related to	SE23
Study	Wang et al. 2013

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SE24 Experiment

Type	Label
Description	“knocked out the Hes7 gene at time point 120 minutes”, observations: “expression patterns of the NkSD1”
Reference	Not available
Category	Perturbation
Study	Wang et al. 2013

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SD24 Data

Type	Label
Description	Simulation results of SE24
Reference	Figure 7G
Related to	SE24
Study	Wang et al. 2013

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SE25 Experiment

Type	Label
Description	“knocked out the NkSD1 gene at time point 120 minutes”, observations: “expression patterns of the target genes of the Wnt and Notch pathways”
Reference	Not available
Category	Perturbation
Study	Wang et al. 2013

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SD25 Data

Type	Label
Description	Simulation results of SE25
Reference	Figure 7H
Related to	SE25
Study	Wang et al. 2013

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SE26 Experiment

Type	Label
Description	Sensitivity analysis
Reference	Not available
Category	Sensitivity analysis
Study	Wang et al. 2013

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SD26 Data

Type	Label
Description	Simulation results of SE26
Reference	Figure S7-S12
Related to	SE26
Study	Wang et al. 2013

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