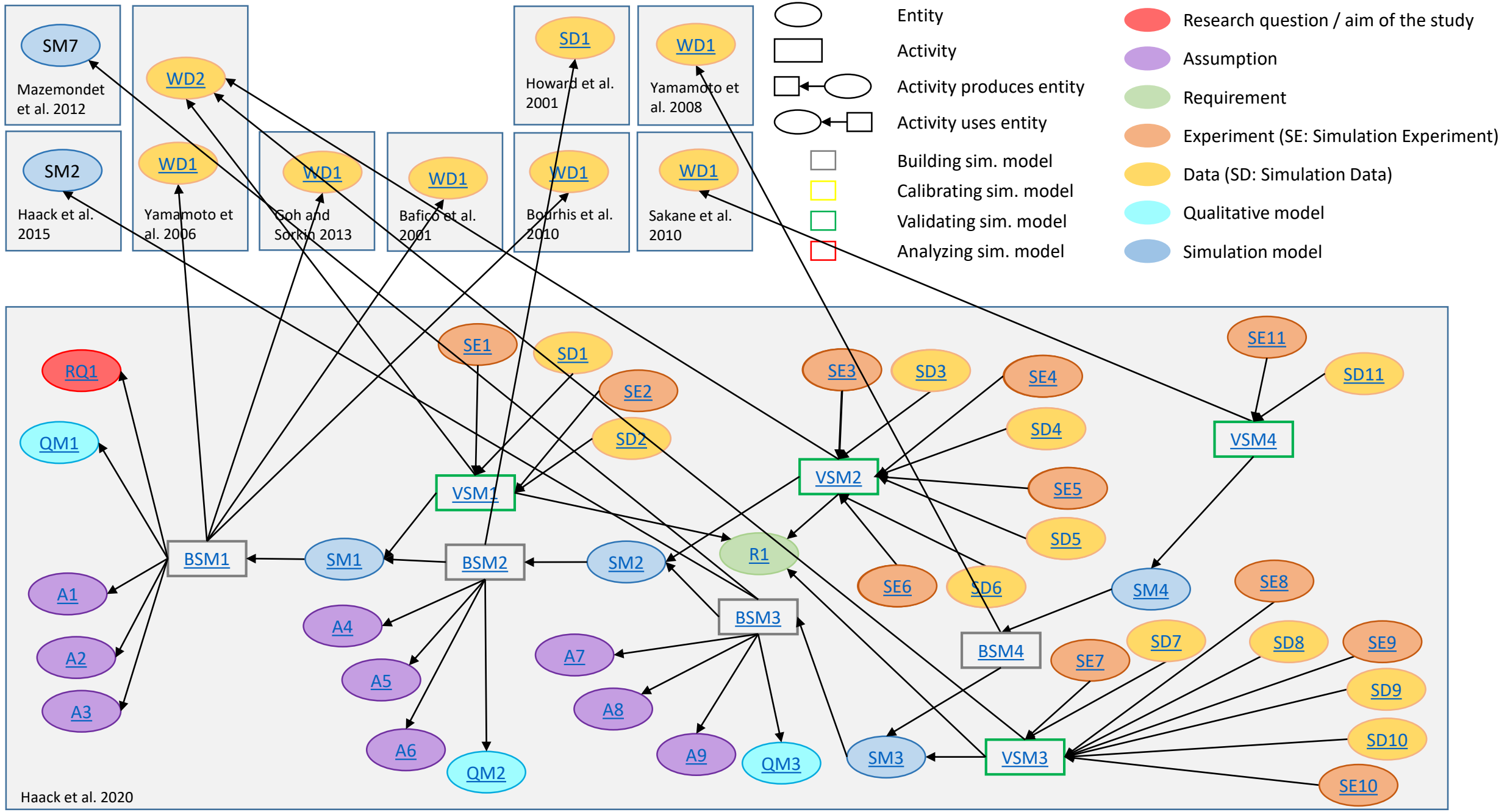
SM7
Mazemondet et al. 2012
WD2
SD1
Howard et al. 2001
WD1
Yamamoto et al. 2008
SM2
Haack et al. 2015
WD1
Yamamoto et al. 2006
WD1
Soh and Sorkin 2013
WD1
Bafico et al. 2001
WD1
Bourhis et al. 2010
WD1
Sakane et al. 2010
Entity
Activity
Activity produces entity
Activity uses entity
Building sim. model
Calibrating sim. model
Validating sim. model
Analyzing sim. model
Research question / aim of the study
Assumption
Requirement
Experiment (SE: Simulation Experiment)
Data (SD: Simulation Data)
Qualitative model
Simulation model
RQ1
QM1
SE1
SD1
SE2
SD2
SE3
SD3
SE4
SD4
SE5
SD5
SE6
SD6
SE11
SD11
VSM1
VSM2
VSM4
BSM1
SM1
BSM2
SM2
R1
BSM3
BSM4
SM4
SE8
SD7
SD8
SE9
SD9
SD10
SE10
SE7
A1
A2
A3
A4
A5
A6
QM2
A7
A8
A9
QM3
SM3
VSM3
Haack et al. 2020

WD1 Data

Type	Label
Description	Fz5 and LRP6 are both activated through WNT3a and internalized in a similar way and dynamics
Reference	Figure 1A and 3A
Type of experiment	In vitro
Organism	Human
Cell line	HeLa S3 cells
Study	Yamamoto et al. 2006

Back to the provenance graph

WD2 Data

Type	Label
Description	“Wnt-3a Induces LRP6 Internalization”
Reference	Figure 1C
Type of experiment	In vitro
Organism	Human
Cell line	HeLa S3 cells
Study	Yamamoto et al. 2006

Back to the provenance graph

WD1 Data

Type	Label
Description	Pathways of receptor tyrosine kinases (RTKs) endocytosis. -> endocytosis rate constants (Review)
Reference	Figure 1
Type of experiment	In vitro
Organism	Not applicable
Cell line	Not applicable
Study	Goh and Sorkin 2013

Back to the provenance graph

WD1 Data

Type	Label
Description	A Scatchard plot of the data for [^{125}I] Dkk-1 binding to NIH3T3 cells
Reference	Figure 2f
Type of experiment	In vitro
Organism	Mouse
Cell line	Fibroblasts NIH/3T3
Study	Bafico et al. 2001

Back to the provenance graph

WD1 Data

Type	Label
Description	“Binding affinities and kinetic constants for various Wnts and Dkk1”
Reference	Table 1
Type of experiment	In vitro
Organism	Mouse
Cell line	Fibroblast L-cells
Study	Bourhis et al. 2010

Back to the provenance graph

WD1 Data

Type	Label
Description	“Dkk1 induces clathrin-dependent internalization of endogenous LRP6.”
Reference	Figure 3
Type of experiment	In vitro
Organism	Human
Cell line	HeLa S3 cells
Study	Sakane et al. 2010

Back to the provenance graph

WD1 Data

Type	Label
Description	Number of Dkk
Reference	Figure ?
Type of experiment	In vitro
Organism	Human
Cell line	HEK293 or HeLaS3 cells
Study	Yamamoto et al. 2008

Back to the provenance graph

SD1 Simulation Data

Type	Label
Description	“Shuttling rate constant between lo and ld domains”
Reference	Figure ?
Related to	Not applicable
Study	Howard et al. 2001

Back to the provenance graph

RQ1 Research question

Type	Label
Description	“elucidate the mechanisms involved in the internalization of LRP6 and reevaluate existing theories on the regulation of LRP6 receptor internalization”
Study	Haack et al. 2020

Back to the provenance graph

QM1 Qualitative model

Type	Label
Description	“Basic internalization model”
Reference	Figure 1a (abstract model) & 2a
Species	WNT3a (ligand), LRP6 (receptor)
Compartments	Cytosol, endosome
Study	Haack et al. 2020

Back to the provenance graph

A1 Assumption

Type	Label
Description	“the interaction between LRP6 and frizzled (FZ) is modeled implicitly (i.e. we assume that LRP6 and FZ receptors are already in close proximity upon WNT binding and immediately form the WNT/FZ/LRP6 trimeric complex)”
Category	Omitted process (397)
Study	Haack et al. 2020

Back to the provenance graph

A2 Assumption

Type	Label
Description	“the corresponding ligand/receptor complex (LR) is a simplified abstract representation of the WNT/FZ/LRP6 complex that can be internalized without regard for its phosphorylation state or association of additional binding partners such as axin or dishevelled (Dvl)”
Category	Omitted process (397)
Study	Haack et al. 2020

Back to the provenance graph

A3 Assumption

Type	Label
Description	“assume that FZ is either implicitly part of the WNT/LRP6 complex or that WNT– LRP6 interaction alone is sufficient for inducing LRP6 internalization”
Category	Transport (655)
Study	Haack et al. 2020

Back to the provenance graph

BSM1 Building simulation model

Type	Label
Description	Constructing first internalization model
Study	Haack et al. 2020

Back to the provenance graph

SM1 Simulation model

Type	Label
Description	“Basic internalization model of WNT/LRP6”
Reference	https://github.com/SFB-ELAINE/SI_LRP6_Endocytosis_Model/blob/master/models/M1_General.mlrj
Study	Haack et al. 2020

Back to the provenance graph

R1 Requirement

Type	Label
Description	“considered a parameter configuration of the model as valid if the fraction of internalized LRP6 receptors corresponded to experimental values at all time points”
Related to	WD2 (Yamamoto et al. 2006)
Main species	LRP6
Type	Quantitative
Study	Haack et al. 2020

Back to the provenance graph

VSM1 Validating simulation model

Type	Label
Description	Model validation
Study	Haack et al. 2020

Back to the provenance graph

SE1 Simulation Experiment

Type	Label
Description	“basic internalization model of WNT/LRP6 (…) for CME”
Reference	https://github.com/SFB-ELAINE/SI_LRP6_Endocytosis_Model/tree/master/experiments/M1_General_S01_A
Category	Parameter scan
Study	Haack et al. 2020

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SD1 Simulation Data

Type	Label
Description	Simulation results of SE1 (validation unsuccessful)
Reference	Figure 3a
Related to	SE1
Study	Haack et al. 2020

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SE2 Simulation Experiment

Type	Label
Description	“basic internalization model of WNT/LRP6 (…) for CIE”
Reference	https://github.com/SFB-ELAINE/SI_LRP6_Endocytosis_Model/tree/master/experiments/M1_General_S01_B
Category	Parameter scan
Study	Haack et al. 2020

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SD2 Simulation Data

Type	Label
Description	Simulation results of SE2 (validation unsuccessful)
Reference	Figure 3b
Related to	SE2
Study	Haack et al. 2020

Back to the provenance graph

A4 Assumption

Type	Label
Description	“approximately 30 % of the membrane is occupied by lo membrane domains (lipid rafts)”
Category	Concentration of reactant (509)
Study	Haack et al. 2020

Back to the provenance graph

A5 Assumption

Type	Label
Description	“because LRP6 is homogeneously distributed in the membrane, on average 30 % of total LPR6 receptors are located in lipid rafts”
Category	Concentration of reactant (509)
Study	Haack et al. 2020

Back to the provenance graph

A6 Assumption

Type	Label
Description	“as in the abstract model A1, the internalization route depends on the localization of the WNT/LRP6 receptor complex”
Category	Transport (655)
Study	Haack et al. 2020

Back to the provenance graph

QM2 Qualitative model

Type	Label
Description	“Compartment-based model of endocytosis”
Reference	Figure 1b (abstract model) & 2b
Species	WNT3a (ligand), LRP6 (receptor)
Compartments	Cytosol, membrane, lipid raft, endosome
Study	Haack et al. 2020

Back to the provenance graph

BSM2 Building simulation model

Type	Label
Description	Including lipid rafts to internalization model
Study	Haack et al. 2020

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SM2 Simulation model

Type	Label
Description	“Compartment-based model of LRP6 endocytosis”
Reference (DOI)	https://github.com/SFB-ELAINE/SI_LRP6_Endocytosis_Model/blob/master/models/M2_Microdomains.mlrj
Study	Haack et al. 2020

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VSM2 Validating simulation model

Type	Label
Description	Model validation
Study	Haack et al. 2020

Back to the provenance graph

SE3 Simulation Experiment

Type	Label
Description	Compartment-based WNT/LRP6 model for CME
Reference	https://github.com/SFB-ELAINE/SI_LRP6_Endocytosis_Model/tree/master/experiments/M2_Microdomains_S02_A
Category	Parameter scan
Study	Haack et al. 2020

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SD3 Simulation Data

Type	Label
Description	Simulation results of SE3 (validation unsuccessful)
Reference	Figure 4a
Related to	SE3
Study	Haack et al. 2020

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SE4 Simulation Experiment

Type	Label
Description	Compartment-based WNT/LRP6 model for CIE inside lipid rafts
Reference	https://github.com/SFB-ELAINE/SI_LRP6_Endocytosis_Model/tree/master/experiments/M2_Microdomains_S02_C
Category	Parameter scan
Study	Haack et al. 2020

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SD4 Simulation Data

Type	Label
Description	Simulation results of SE4 (validation unsuccessful)
Reference	Figure 4b
Related to	SE4
Study	Haack et al. 2020

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SE5 Simulation Experiment

Type	Label
Description	Compartment-based WNT/LRP6 model for CIE outside of lipid rafts
Reference	https://github.com/SFB-ELAINE/SI_LRP6_Endocytosis_Model/tree/master/experiments/M2_Microdomains_S03_A
Category	Parameter scan
Study	Haack et al. 2020

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SD5 Simulation Data

Type	Label
Description	Simulation results of SE5 (validation unsuccessful)
Reference	Figure 4c
Related to	SE5
Study	Haack et al. 2020

Back to the provenance graph

SE6 Simulation Experiment

Type	Label
Description	Compartment-based WNT/LRP6 model for CIE inside and outside of lipid rafts
Reference	https://github.com/SFB-ELAINE/SI_LRP6_Endocytosis_Model/tree/master/experiments/M2_Microdomains_S03_B
Category	Parameter scan
Study	Haack et al. 2020

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SD6 Simulation Data

Type	Label
Description	Simulation results of SE6 (validation unsuccessful)
Reference	Figure 4d
Study	Haack et al. 2020

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A7 Assumption

Type	Label
Description	“Axin, a representative member of the destruction complex, is recruited to the membrane and binds to the phosphorylated LRP6/receptor complex. Thus, the LRP6 signalosome is represented by a simplified form comprising phosphorylated LRP6, WNT and axin.”
Category	Equivalence (392)
Study	Haack et al. 2020

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A8 Assumption

Type	Label
Description	“Although the WNT/LRP6 complex can shuttle between raft and non-raft domains, the LRP6 signalosome cannot shuttle between membrane domains.”
Category	Transport (655)
Study	Haack et al. 2020

Back to the provenance graph

A9 Assumption

Type	Label
Description	“Similar to the previous internalization model, the internalization route is determined by the domain association of LRP6.”
Category	Transport (655)
Study	Haack et al. 2020

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QM3 Qualitative model

Type	Label
Description	“Coupling signalosome formation, endocytosis, and intracellular signaling in a compartment-based model”
Reference	Figure 1c (abstract model) & 2c
Species	WNT3a, LRP6, CK1γ, Axin, β-catenin
Compartments	Cytosol, membrane, lipid raft, endosome, nucleus
Study	Haack et al. 2020

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BSM3 Building simulation model

Type	Label
Description	Including downstream signaling
Study	Haack et al. 2020

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SM3 Simulation model

Type	Label
Description	“Coupling compartment-based internalization model with intracellular WNT model”
Reference (DOI)	https://github.com/SFB-ELAINE/SI_LRP6_Endocytosis_Model/blob/master/models/M3_Wnt.mlrj
Study	Haack et al. 2020

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VSM3 Validating simulation model

Type	Label
Description	Model validation
Study	Haack et al. 2020

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SE7 Simulation Experiment

Type	Label
Description	“canonical WNT pathway-specific implementation” with CME outside of lipid rafts
Reference	https://github.com/SFB-ELAINE/SI_LRP6_Endocytosis_Model/tree/master/experiments/M3_Wnt_S04_A
Category	Parameter scan
Study	Haack et al. 2020

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SD7 Simulation Data

Type	Label
Description	Simulation results of SE7 (validation unsuccessful)
Reference	Figure 5a
Related to	SE7
Study	Haack et al. 2020

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SE8 Simulation Experiment

Type	Label
Description	“canonical WNT pathway-specific implementation” with CIE outside of lipid rafts
Reference	https://github.com/SFB-ELAINE/SI_LRP6_Endocytosis_Model/tree/master/experiments/M3_Wnt_S05_A
Category	Parameter scan
Study	Haack et al. 2020

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SD8 Simulation Data

Type	Label
Description	Simulation results of SE8 (validation unsuccessful)
Reference	Figure 5b
Related to	SE8
Study	Haack et al. 2020

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SE9 Simulation Experiment

Type	Label
Description	“canonical WNT pathway-specific implementation” with CIE inside lipid rafts
Reference	https://github.com/SFB-ELAINE/SI_LRP6_Endocytosis_Model/tree/master/experiments/M3_Wnt_S04_C
Category	Parameter scan
Study	Haack et al. 2020

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SD9 Simulation Data

Type	Label
Description	Simulation results of SE9 (validation unsuccessful)
Reference	Figure S1b
Related to	SE9
Study	Haack et al. 2020

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SE10 Simulation Experiment

Type	Label
Description	“canonical WNT pathway-specific implementation” with CIE inside and outside of lipid rafts
Reference	https://github.com/SFB-ELAINE/SI_LRP6_Endocytosis_Model/tree/master/experiments/M3_Wnt_S05_B
Category	Parameter scan
Study	Haack et al. 2020

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SD10 Simulation Data

Type	Label
Description	Simulation results of SE10 (validation successful)
Reference	Figure 5c
Related to	SE10
Study	Haack et al. 2020

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BSM4 Building simulation model

Type	Label
Description	Exchanging WNT for DKK
Study	Haack et al. 2020

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SM4 Simulation model

Type	Label
Description	“Combined model with Dkk1-mediated shift of the internalization pathway”
Reference	https://github.com/SFB-ELAINE/SI_LRP6_Endocytosis_Model/blob/master/models/M4_Dkk.mlrj
Study	Haack et al. 2020

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VSM4 Validating simulation model

Type	Label
Description	Model validation
Study	Haack et al. 2020

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SE11 Simulation Experiment

Type	Label
Description	“internalization dynamics for the coupled compartmental model in which WNT is replaced by Dkk1 (including its specific disassociation and association rates)”
Reference	https://github.com/SFB-ELAINE/SI_LRP6_Endocytosis_Model/tree/master/experiments/M4_Dkk_S06_A
Category	Parameter scan
Study	Haack et al. 2020

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SD11 Simulation Data

Type	Label
Description	Simulation results of SE11 (validation successful)
Reference	Figure 5d
Related to	SE11
Study	Haack et al. 2020

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