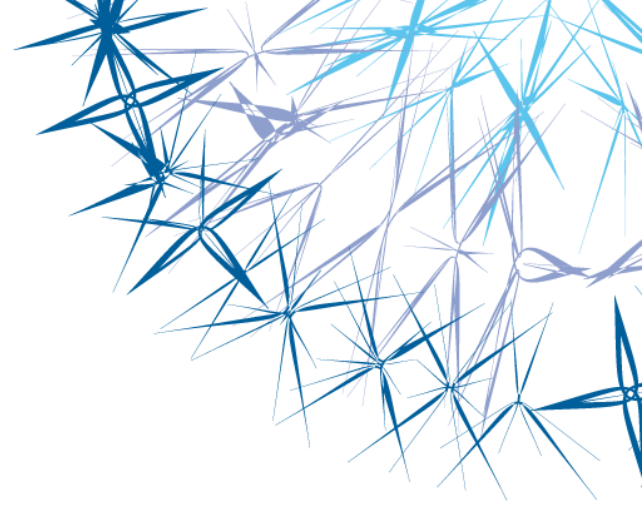
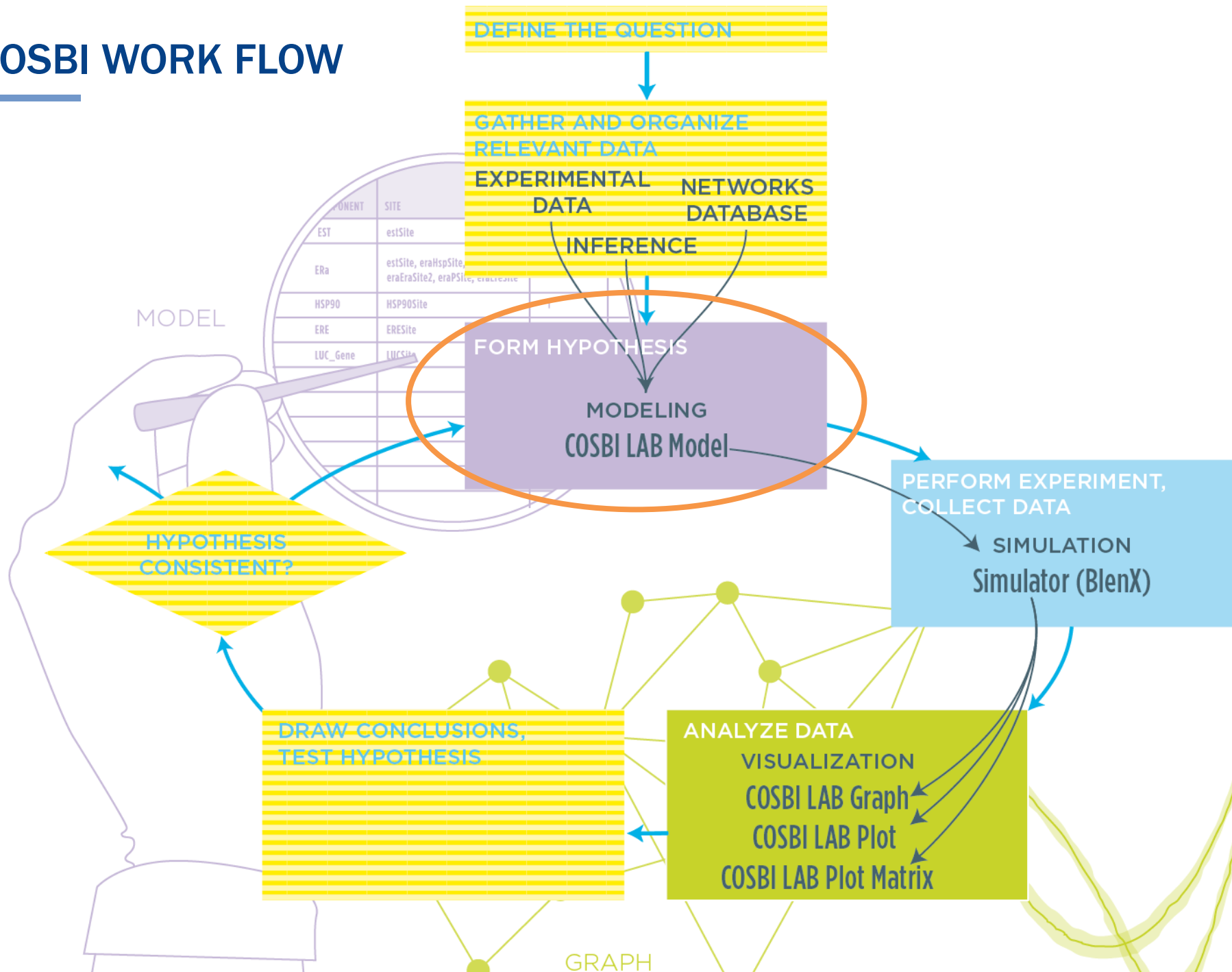


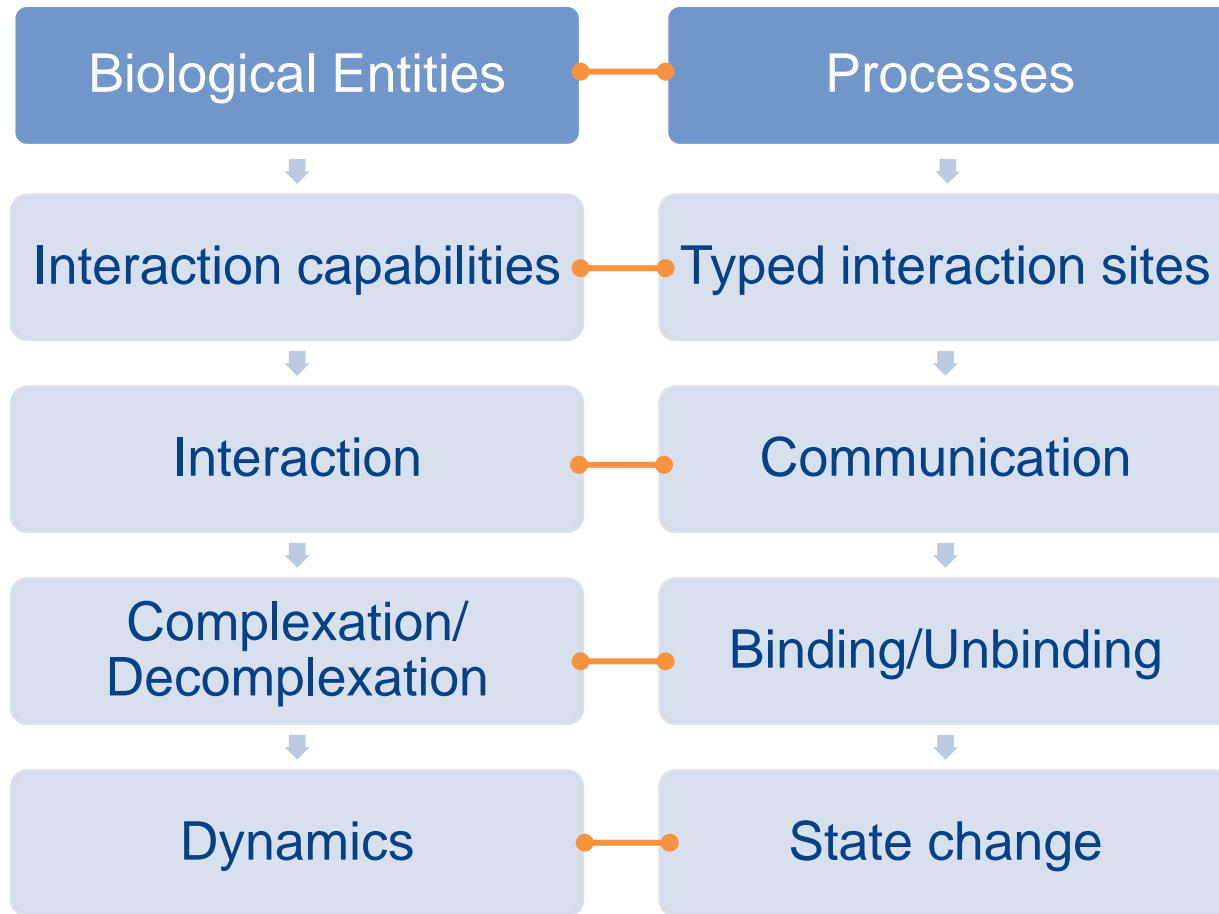
IN SILICO SCIENCE WITH COSBI LAB



COSBI WORK FLOW



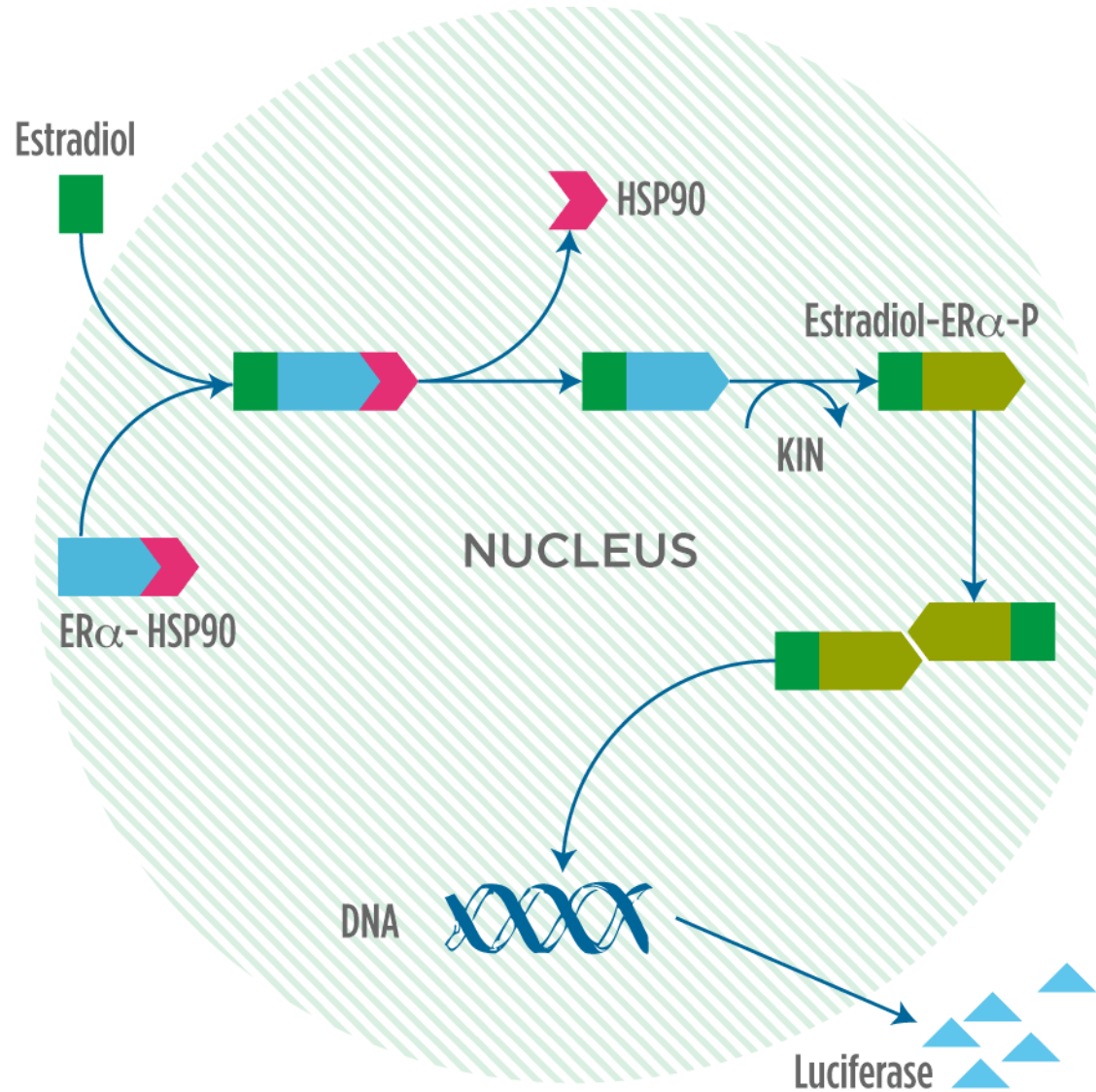
COSBI MODELING: REPRESENT BIOLOGY AS A PROCESS



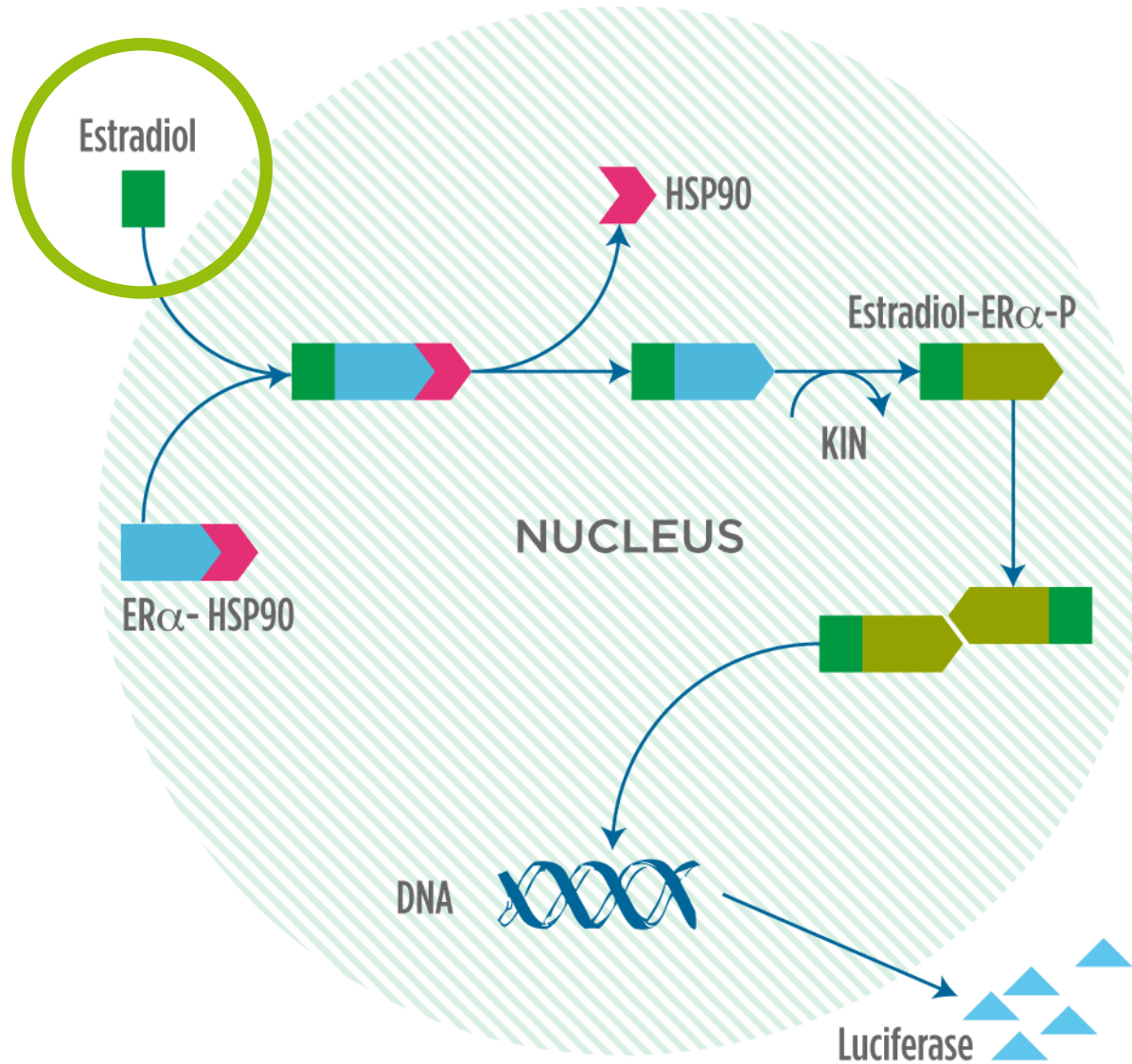
Operational description of dynamics , message passing, reactive systems.

Created to better represent the biological basic entities and their behaviors.

MODEL OF ESTROGEN RECEPTOR-ALPHA IN MOUSE LIVER



MODELING: COMPONENTS



MODELING: COMPONENTS

The image displays two overlapping windows of the 'Estrogen - COSBILAB MODEL' software. The top window shows the 'Components' tab with a table containing one entry:

Component Name	Site	Configurations	Description
EST		0	

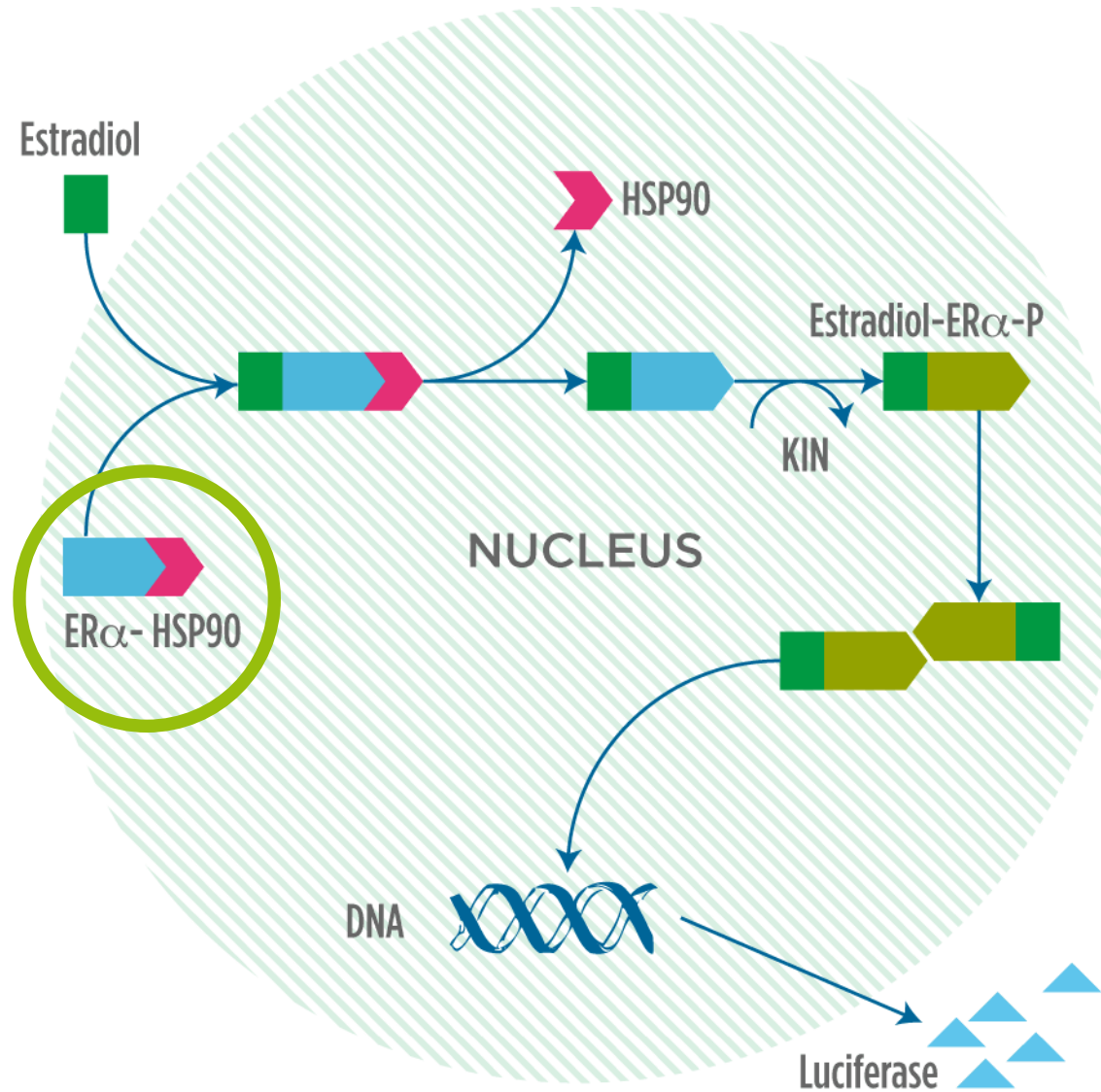
The bottom window shows the 'Component Site Definition' tab for the 'EST' component. It features a table for 'Component Configuration Name', 'Site State', and 'Description':

Component Configuration Name	Site State	Description
EST_init	estSite:Free	

To the right of the bottom window is a biological pathway diagram within a light green circular area labeled 'NUCLEUS'. The diagram shows the following components and interactions:

- Estradiol** (green square) binds to **ER α - HSP90** (blue and red shapes).
- ER α - HSP90** is converted to **ER α - HSP90** (green and red shape).
- ER α - HSP90** binds to **DNA** (blue double helix).
- ER α - HSP90** is converted to **Estradiol-ER α -P** (green and red shape).
- Estradiol-ER α -P** is converted to **ER α - HSP90** (green and red shape) via a **KIN** reaction.
- ER α - HSP90** binds to **DNA**.
- DNA** leads to the production of **Luciferase** (blue triangles).

MODELING: COMPONENTS AND COMPLEXES



MODELING: COMPONENTS AND COMPLEXES

Estrogen - COSBILAB MODEL

File Edit Simulation Help

Components Complexes Global Dynamics Bimolecular Dynamics Binding Dynamics Parameters Compartments Initial State

Component Name	Site
Click here to add new item	
EST	estSite
ERa	eraSite

Component Site Definition

Site Name	Description
eraEreSite	
eraSite	
eraHspSite	
eraEraSite1	
eraEraSite2	
eraPSite	

Estrogen - COSBILAB MODEL

File Edit Simulation Help

Components Complexes Global Dynamics Bimolecular Dynamics Binding Dynamics Parameters Compartments

Component Name	Site
Click here to add new item	
EST	estSite
ERa	eraSite
HSP90	HSP90Site

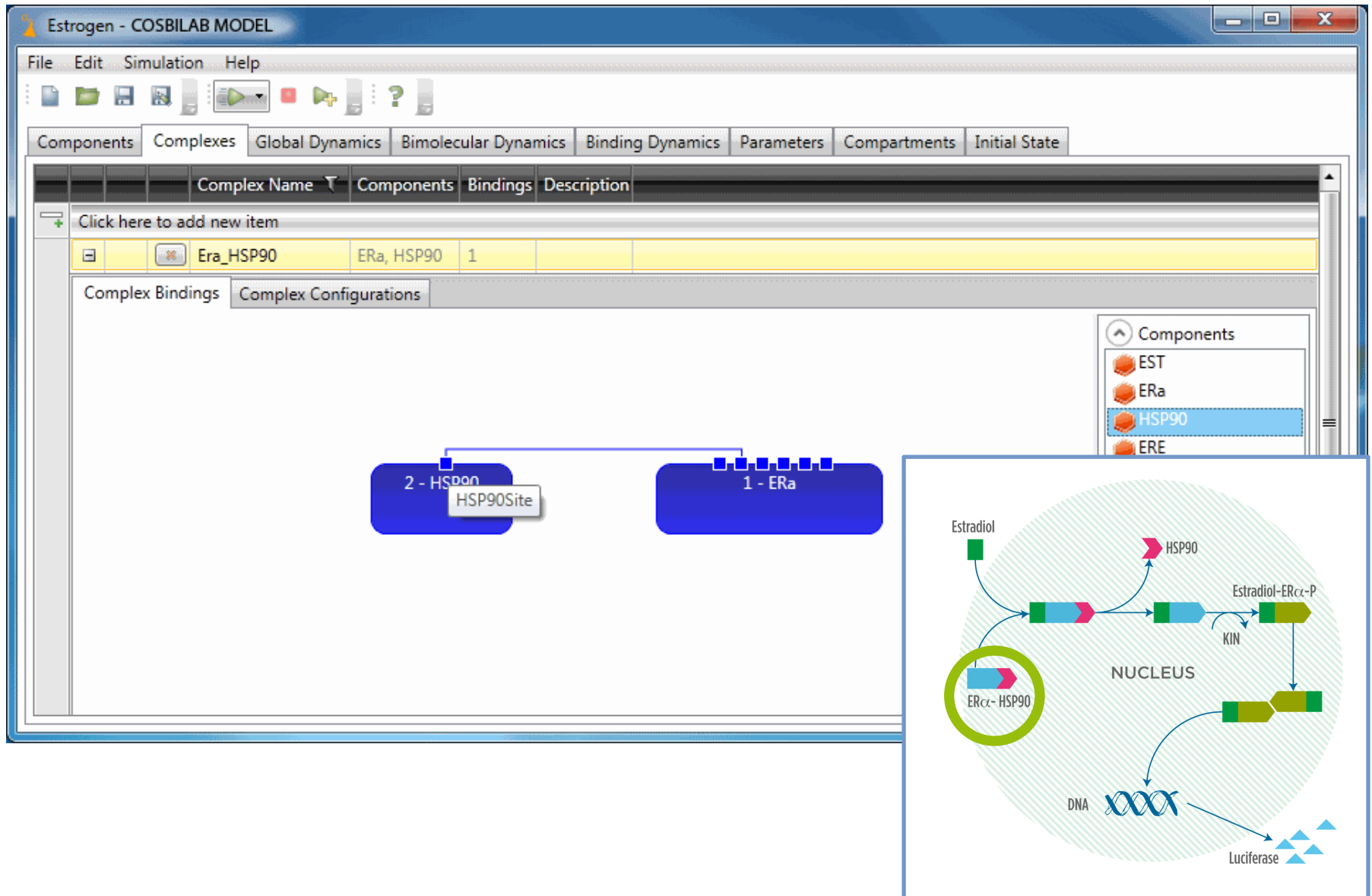
Component Site Definition

Site Name	Description
Click here to add new item	
HSP90Site	

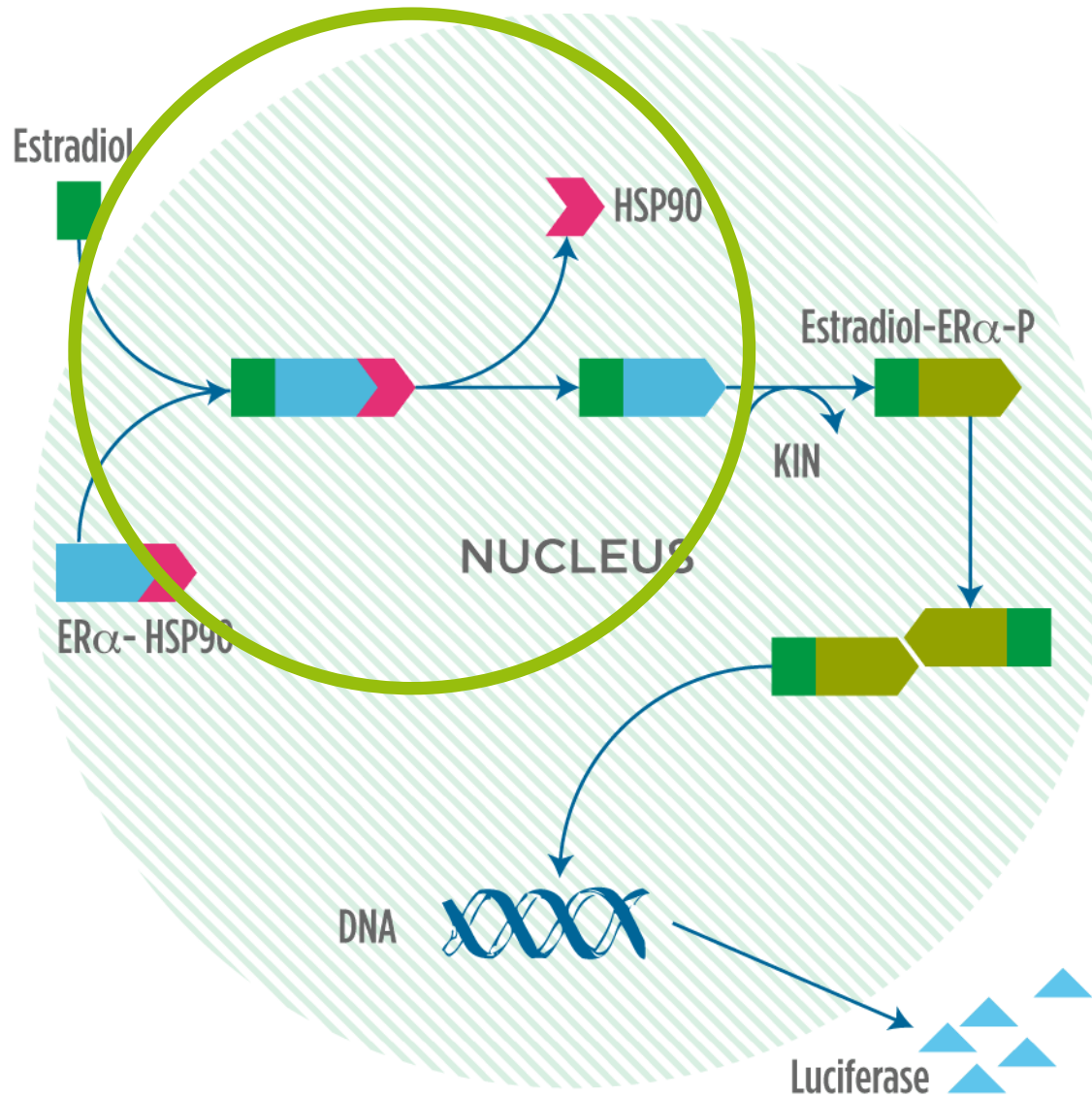
Diagram illustrating the Estrogen signaling pathway in the NUCLEUS:

- Estradiol binds to ERα.
- ERα binds to HSP90.
- The ERα-HSP90 complex binds to DNA.
- The complex activates Luciferase.
- The diagram shows the formation of Estradiol-ERα-P (KIN) and the subsequent binding to DNA.

MODELING: COMPONENTS AND COMPLEXES



MODELING: BINDING/UNBINDING



MODELING: BINDING/UNBINDING

Estrogen - COSBILAB MODEL

File Edit Simulation Help

Components Complexes Global Dynamics Bimolecular Dynamics Binding Dynamics Parameters Compartments Initial State

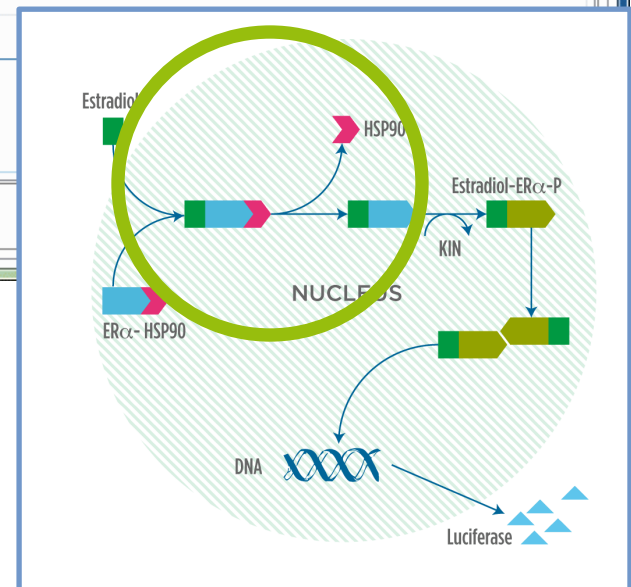
	Component 1	Site 1	Component 2	Site 2	(Parameter) Binding Rate	(Parameter) Unbinding Rate	Condition	Compartment	Description	
+	Click here to add new item									
>	EST	estSite	ERa	eraSite	e2Binding	e2Unbinding	None	System		
+	HSP90	HSP90Site	ERa	eraHspSite	NoBinding	RateParameter_2	None	System		

Component 1 Component 2

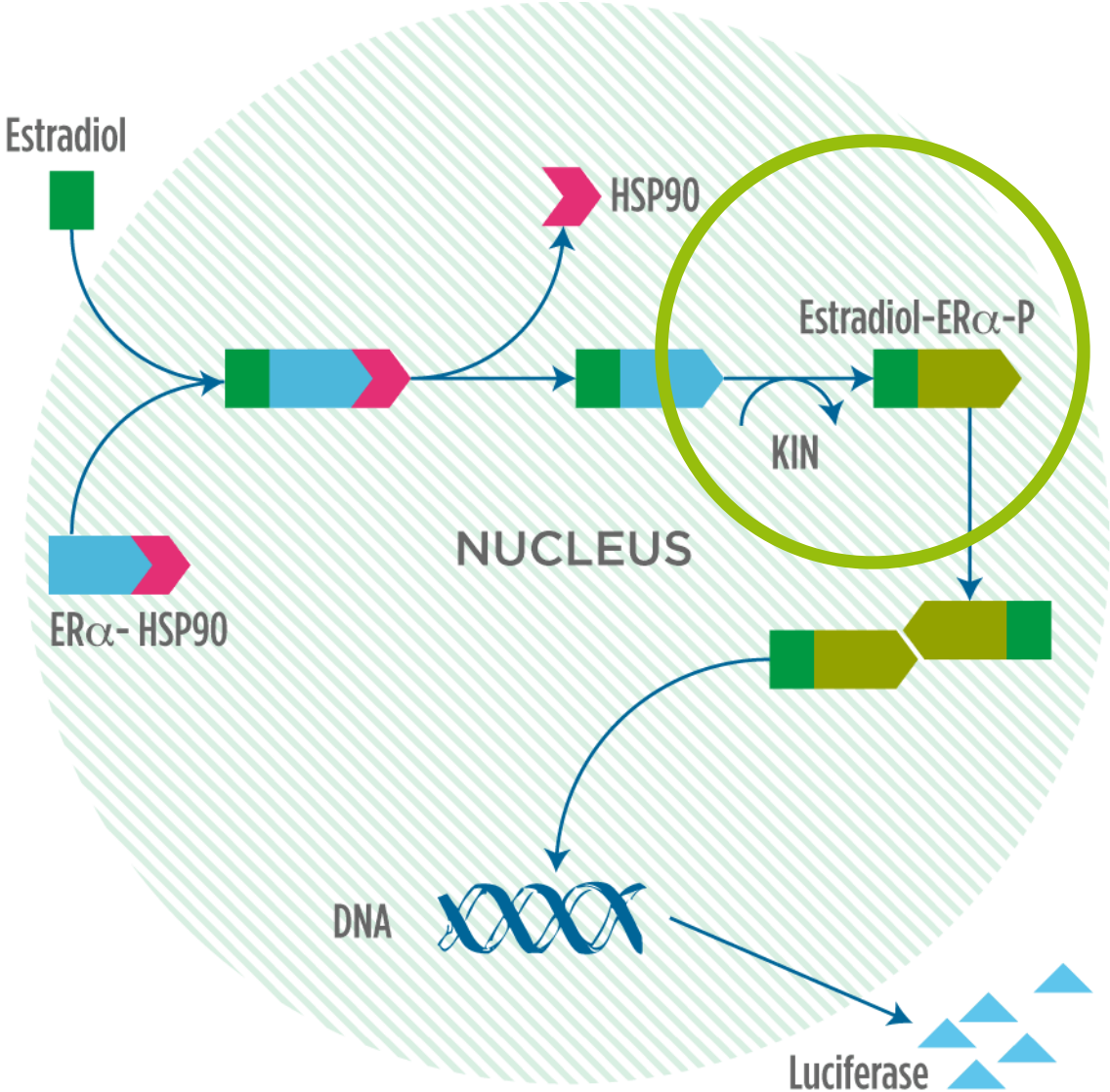
Binding condition for Component 2:

Unbinding condition for Component 2:
eraSite is Bound

Unbinding condition for Component 2:
eraSite is Bound



MODELING: REACTIONS



THE MODEL: REACTIONS

Estrogen - COSBILab BlenX4Bio

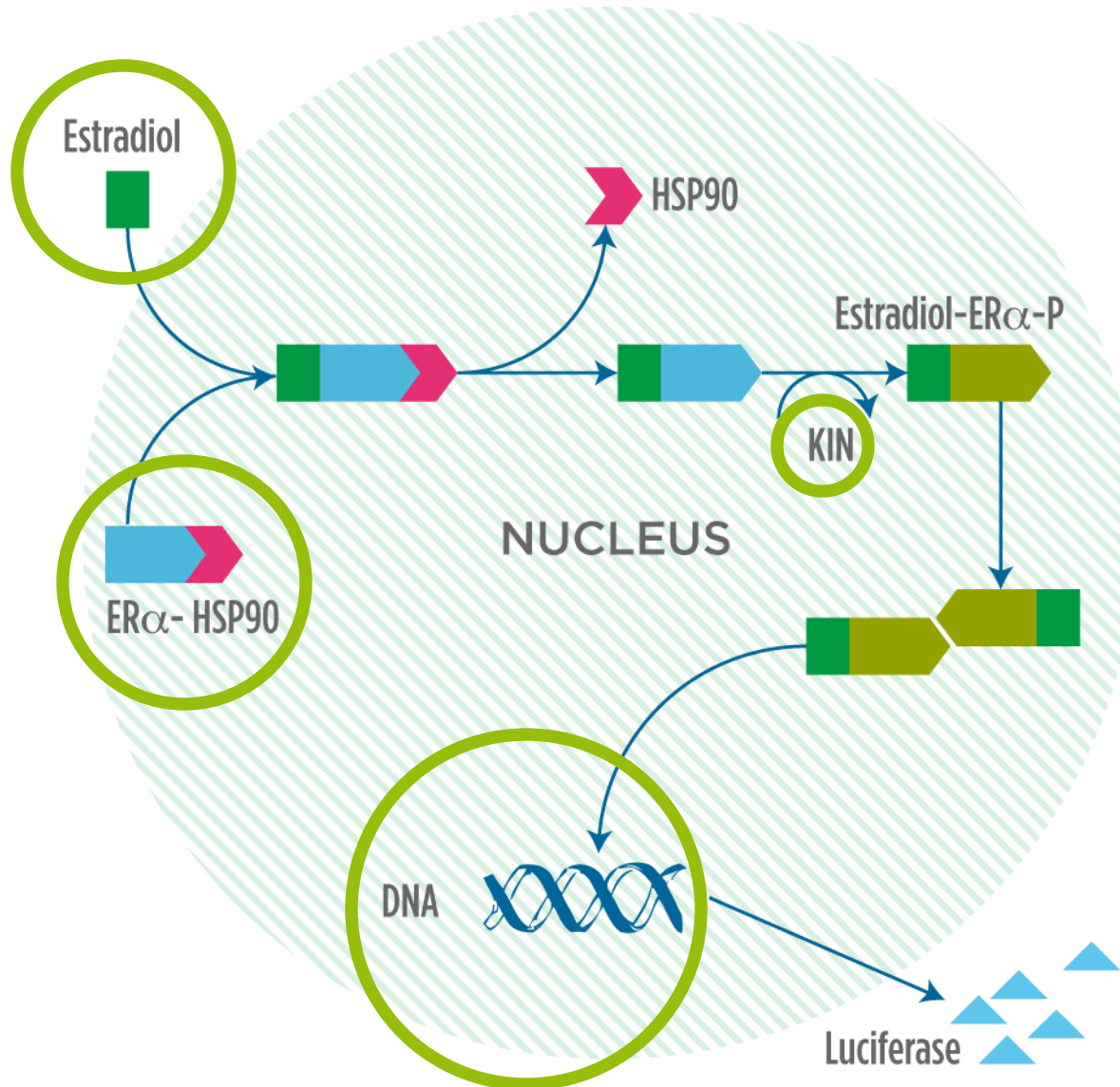
File Edit Simulation Help

Components Complexes Global Dynamics Bimolecular Dynamics Binding Dynamics Parameters Compartments Initial State

Action	(Parameter) Rate	Active Condition	Passive Condition	Des
Click here to add new item				
KIN makes ERα Phosphorylated on eraPSite	phospho		eraSite is Bound	?

The diagram illustrates the signaling pathway in the nucleus. Estradiol (green square) binds to ERα (blue and red shape), which is associated with HSP90 (pink shape). The complex then binds to DNA (blue double helix), leading to the production of Luciferase (blue triangles). The diagram shows the transition from ERα-HSP90 to Estradiol-ERα-P, which then binds to DNA. The phosphorylation step is catalyzed by KIN. The final product is Luciferase, represented by blue triangles.

THE MODEL: INITIAL STATE



MODELING: INITIAL STATE

The screenshot displays the 'Estrogen - COSBILAB MODEL' software interface. The top window shows the 'Initial State' tab with a table of component configurations. The bottom window shows the same interface with a different table of configurations and a biological pathway diagram.

Top Window: Initial State Configuration

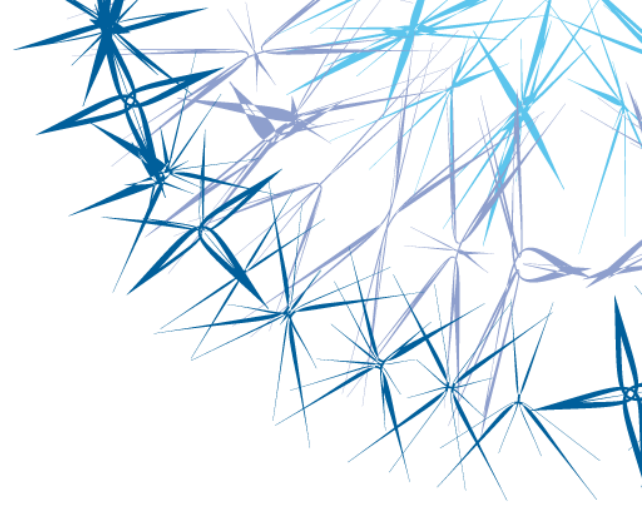
Component/Complex Configuration	Type	(Parameter) Quantity	Compartment	Replica	Description
Era_HSP90_30			System	1	

Bottom Window: Initial State Configuration

Component/Complex Configuration	Type	(Parameter) Quantity	Compartment	Replica	Description
Click here to add new item					
EST_init	Component	qEST			
ERE_init	Component	qERE			
LUC_Gene_Inactive	Component	qLUC_Gene			
LUC_init	Component	qLUC			
KIN_init	Component	qKIN			
Era_HSP90_30	Complex	qEraHSP90			

Biological Pathway Diagram:

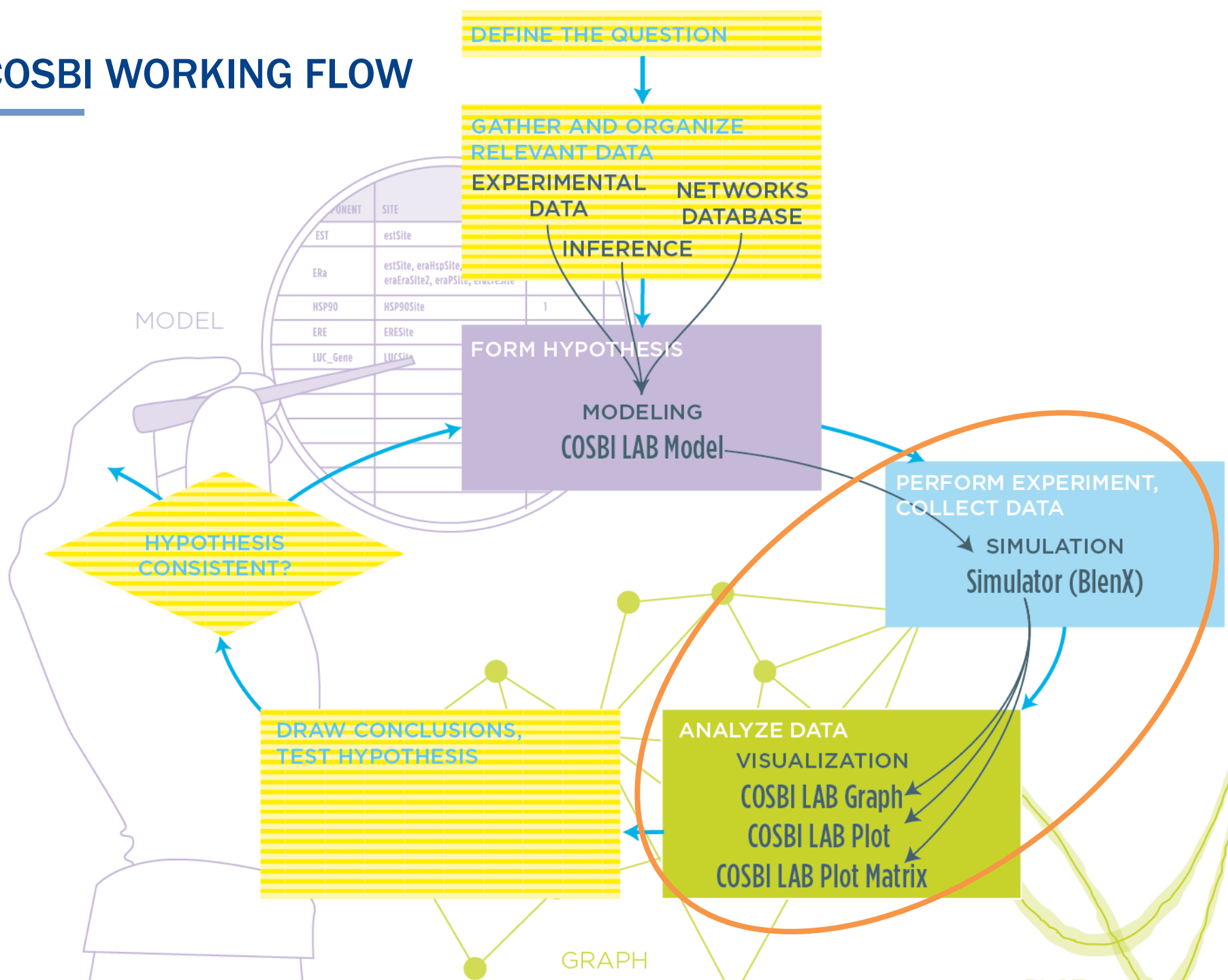
The diagram illustrates the signaling pathway within the NUCLEUS. Estradiol (green square) binds to the ERα-HSP90 complex (blue and red arrowheads). This complex then binds to DNA, leading to the production of Estradiol-ERα-P (green arrowhead). Kinase (KIN, green circle) is involved in the phosphorylation of ERα. The final product, Estradiol-ERα-P, leads to the production of Luciferase (blue triangles).



RUN SIMULATIONS AND VISUALIZE RESULTS



COSBI WORKING FLOW



MODELING: DEFINE EXPERIMENTS

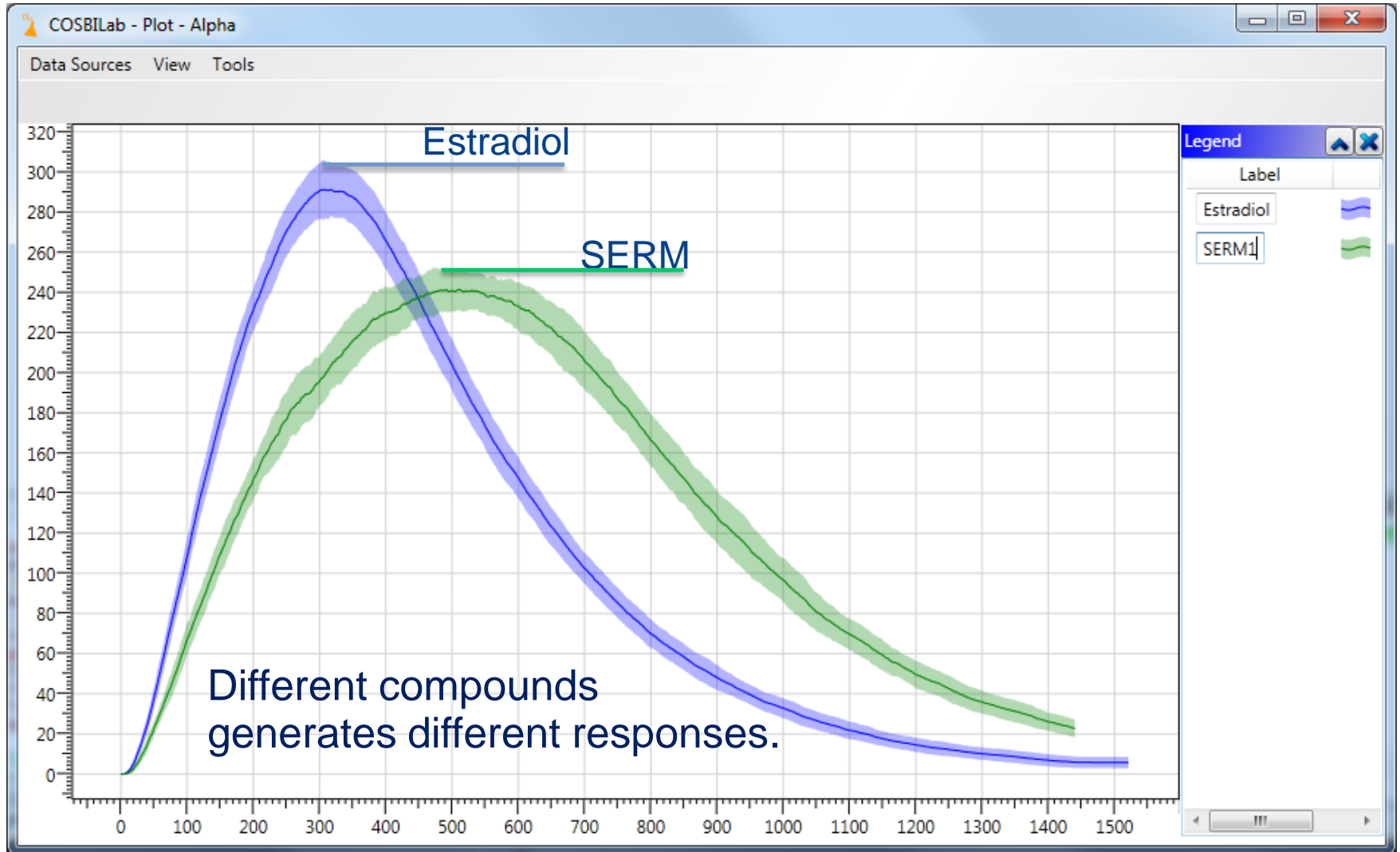
The screenshot displays the 'estradiol_expression - COSBI LAB Model' software interface. The main window shows a table of components and their associated sites. A 'COSBI LAB Simulation Wizard' dialog box is open, titled 'Select Parameter to Scan'. The dialog box contains a list of parameters to scan, with 'qER_HSP' and 'qKIN' selected. The 'qER_HSP' row shows a start value of 10000, an end value of 25000, and a step size of 500. The 'qKIN' row shows a start value of 1000, an end value of 10000, and a step size of 1000. The dialog box also includes a 'Back' button, a 'Next' button, and a 'Cancel' button.

Component Name	Site	Configurations	Description
ESTRADIOLnucleus		1	
ER	site_er_hsp, site_er_estradiolo, site_er_ph, site_er_dim, site_er_dna	2	
HSP	site_hsp_er	1	
DNA	site_dna_er, site_dna_met	2	
LUCIFERASE		1	
ESTRADIOLcyto	site_estradiolo_er	1	
KIN		1	

Scan	Parameter	Start	End	Step Size
<input type="checkbox"/>	b_er_hsp			
<input type="checkbox"/>	b_estradiolo_er			
<input type="checkbox"/>	u_estradiolo_er			
<input type="checkbox"/>	luciferase_synth			
<input type="checkbox"/>	luciferase_degr			
<input checked="" type="checkbox"/>	qER_HSP	10000	25000	500
<input checked="" type="checkbox"/>	qKIN	1000	10000	1000
<input type="checkbox"/>	dim_er			

Optimize your time and resources running multiple experiments with different conditions.

MODELING: VISUALIZE RESULTS



COSBI LAB MODEL: MODELING & SIMULATING COMPLEX SYSTEMS

Create models via tabular interface.
No expertise in programming or math needed.

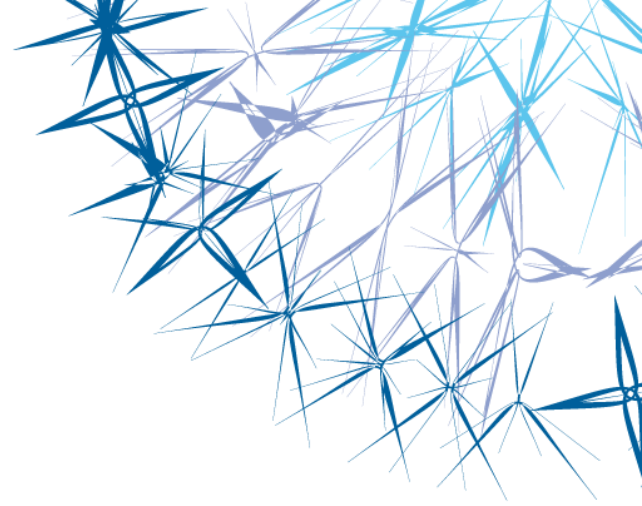
Easily manage experiments:
knock-down genes, change rates,
add a “virtual” drug.

Share models & results with
colleagues, wherever they are.

Allow life scientist creating and
analyzing models.

In silico science: adding knowledge,
saving time.

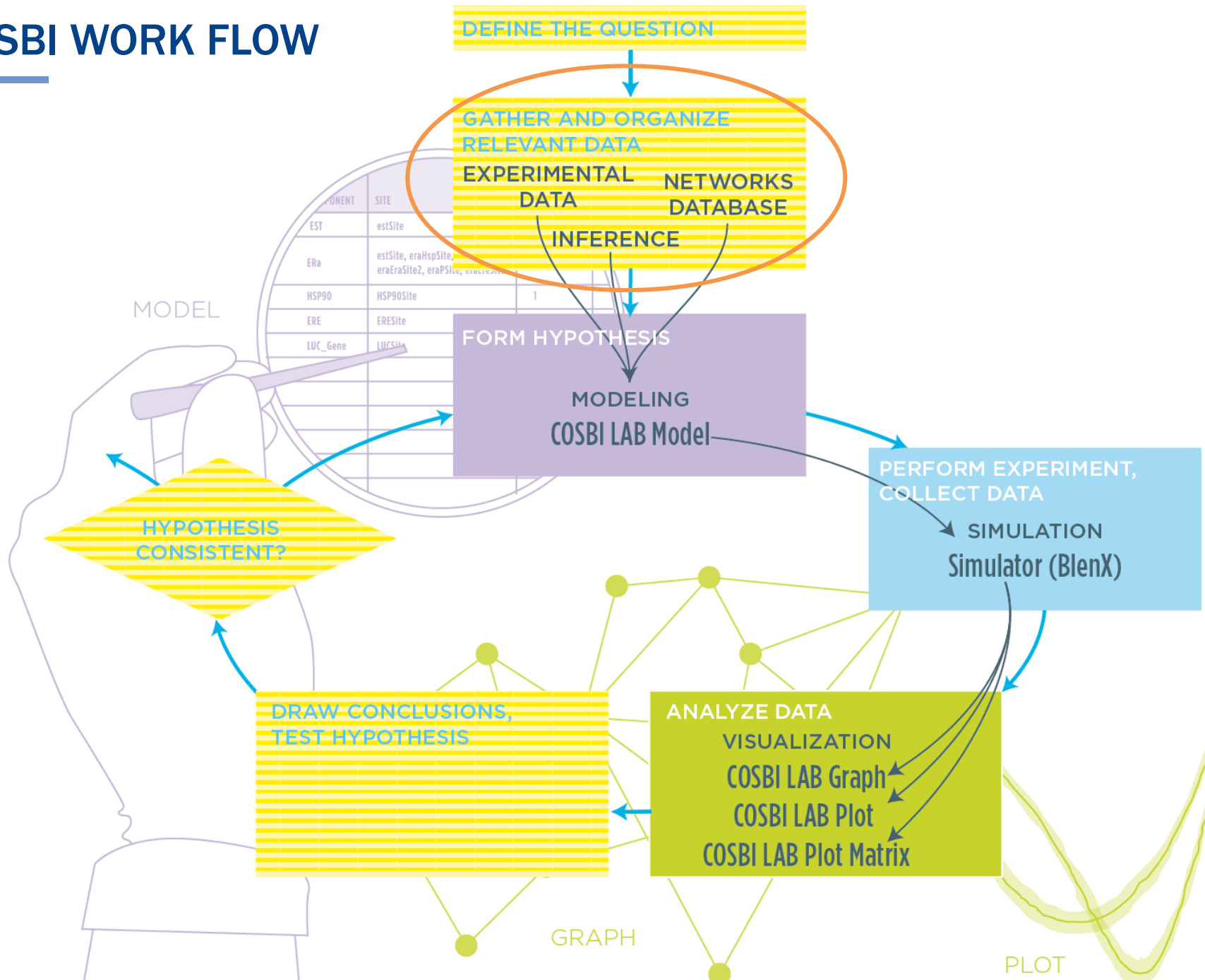
Accelerate discovery process, add
value to your work.



CREATE AND MANAGE NEW KNOWLEDGE

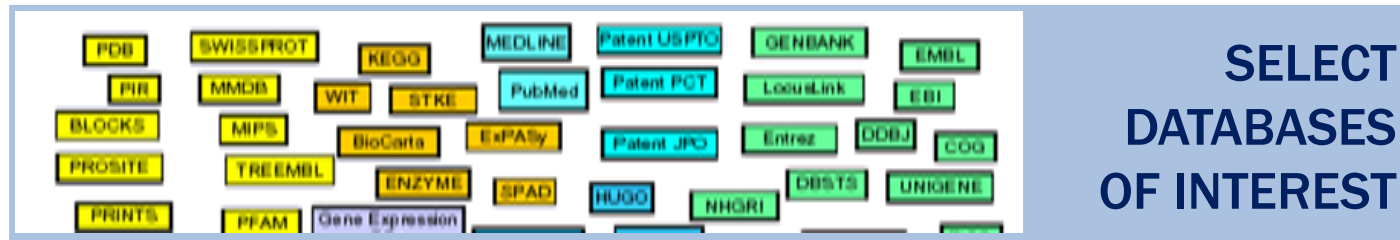


COSBI WORK FLOW



KNOWLEDGE EXTRACTION AND MODELING

Define the problem you want to address



Clinical

omics experiments

Ontological

DATA MINING

Organize, integrate and analyze data

KNOWLEDGE EXTRACTION

Model identification
Network inference

Model analysis
Network analysis

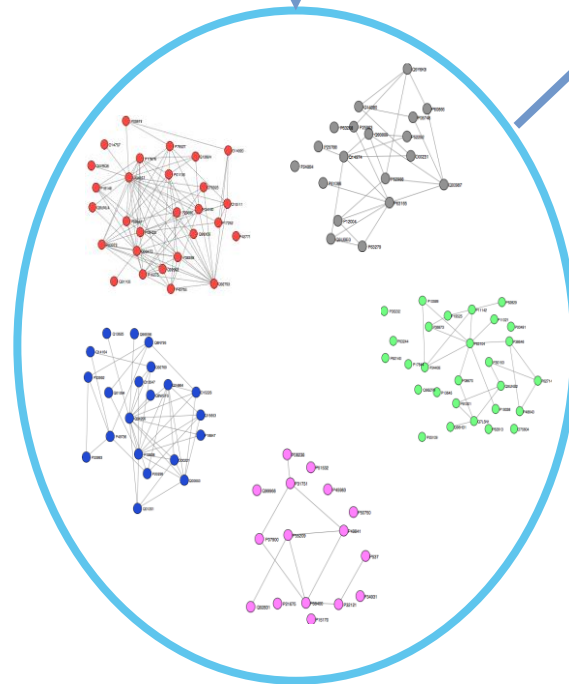
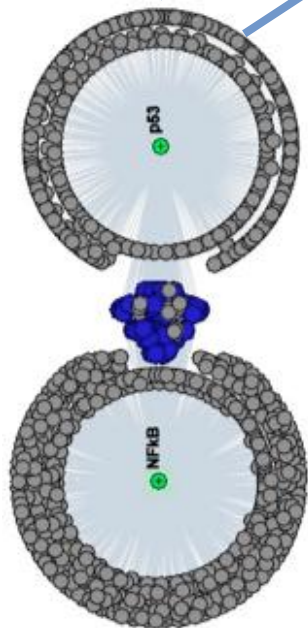
Model calibration
Parameter inference

KNOWLEDGE EXTRACTION AND MODELING

Model identification
Network inference

Model analysis
Network analysis

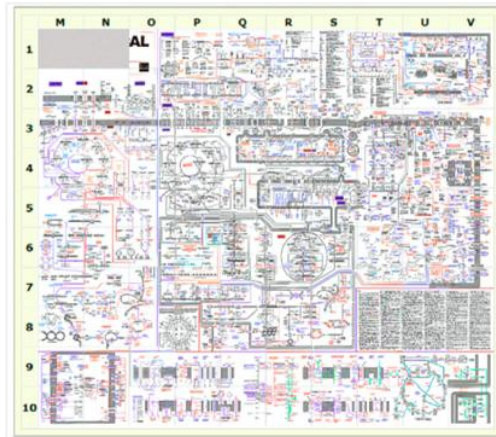
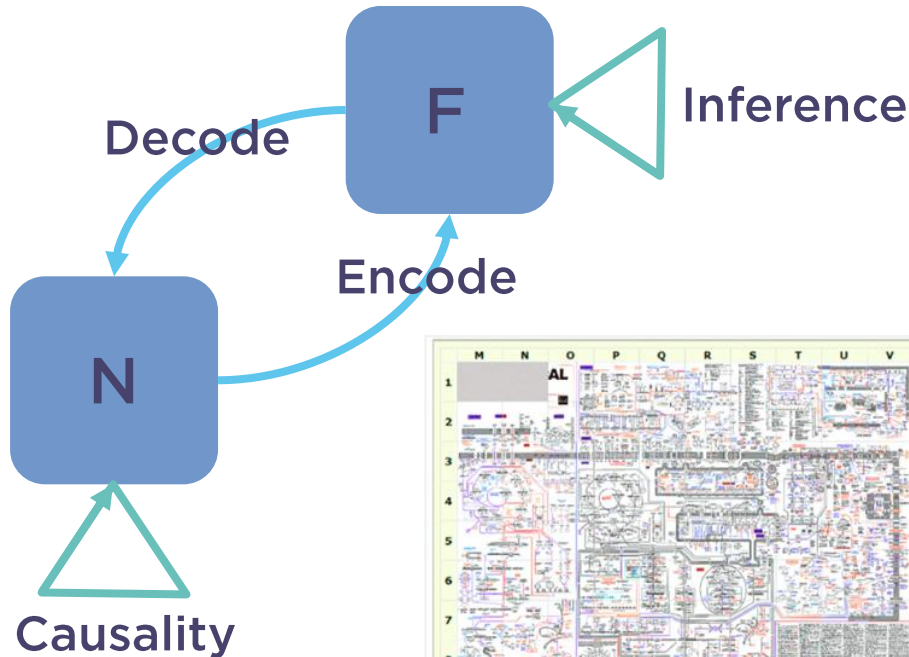
Model calibration
Parameter inference



Parameter	Value ($\sigma = 0.008$)	Value ($\sigma = 0.01$)	Value ($\sigma = 0.04$)	Value ($\sigma = 0.19$)	Value ($\sigma = 1.66$)
k_1	0.0945	0.0954	0.0955	1.104	0.012
k_{-1}	0.164	0.146	0.140	0.024	0.726
k_2	3.669	3.640	3.0556	1.176	1.0526
k_{-2}	0.499	0.439	0.442	0.129	1.281
k_3	0.498	0.497	0.498	0.549	0.194
k_{-3}	0.127	0.123	0.144	0.254	0.074
k_4	0.554	0.557	0.577	0.552	0.444
k_{-4}	0.00183	0.00186	0.00256	0.0287	0.00668

Algorithmic
modeling

A MODELING FORMALISM



Encode info manipulation by bio-systems

A formal framework to reason about bio-systems

Predict biological behavior and identify new hypotheses

Unambiguous description to share knowledge

FORMALISM FEATURES

Complementary to and **Interoperable** with mathematical modeling

Addressing **Complexity, Concurrency, and Mobility**

Algorithmic and **Quantitative**

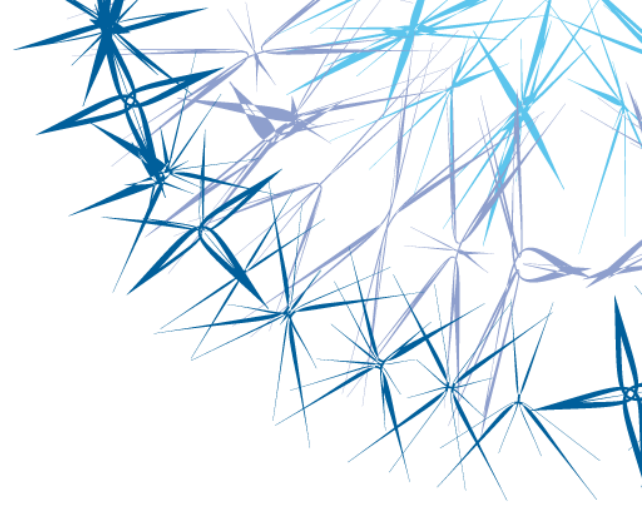
Expressing **Causality**

Interaction-driven, **synchronous**

Dynamically changing interaction capabilities

Compositional and **Modular**

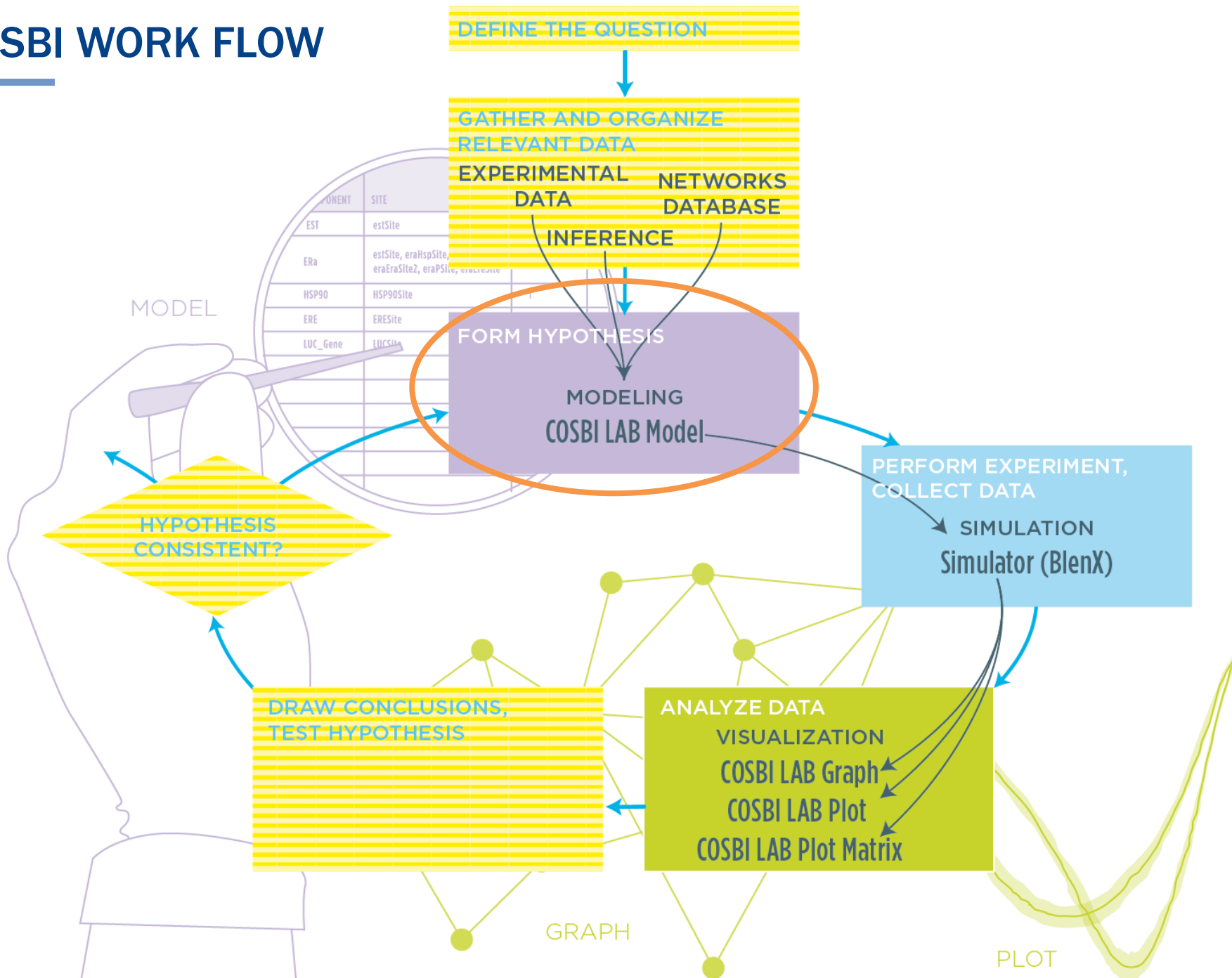
A FURTHER BRICK OF THE FOUNDATIONS OF SYSTEMS BIOLOGY



NEW KNOWLEDGE FEEDS MODELS CREATION

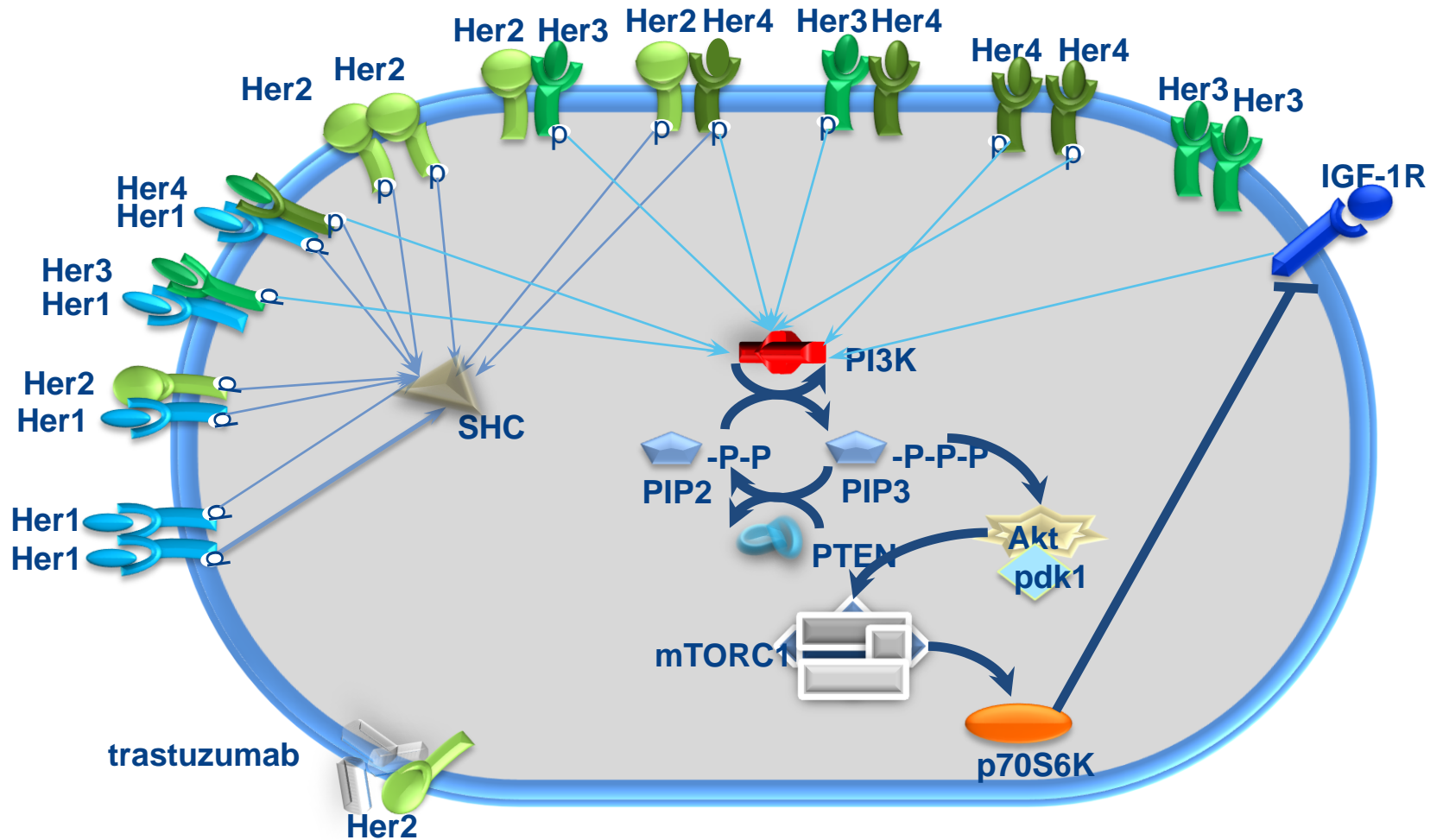


COSBI WORK FLOW



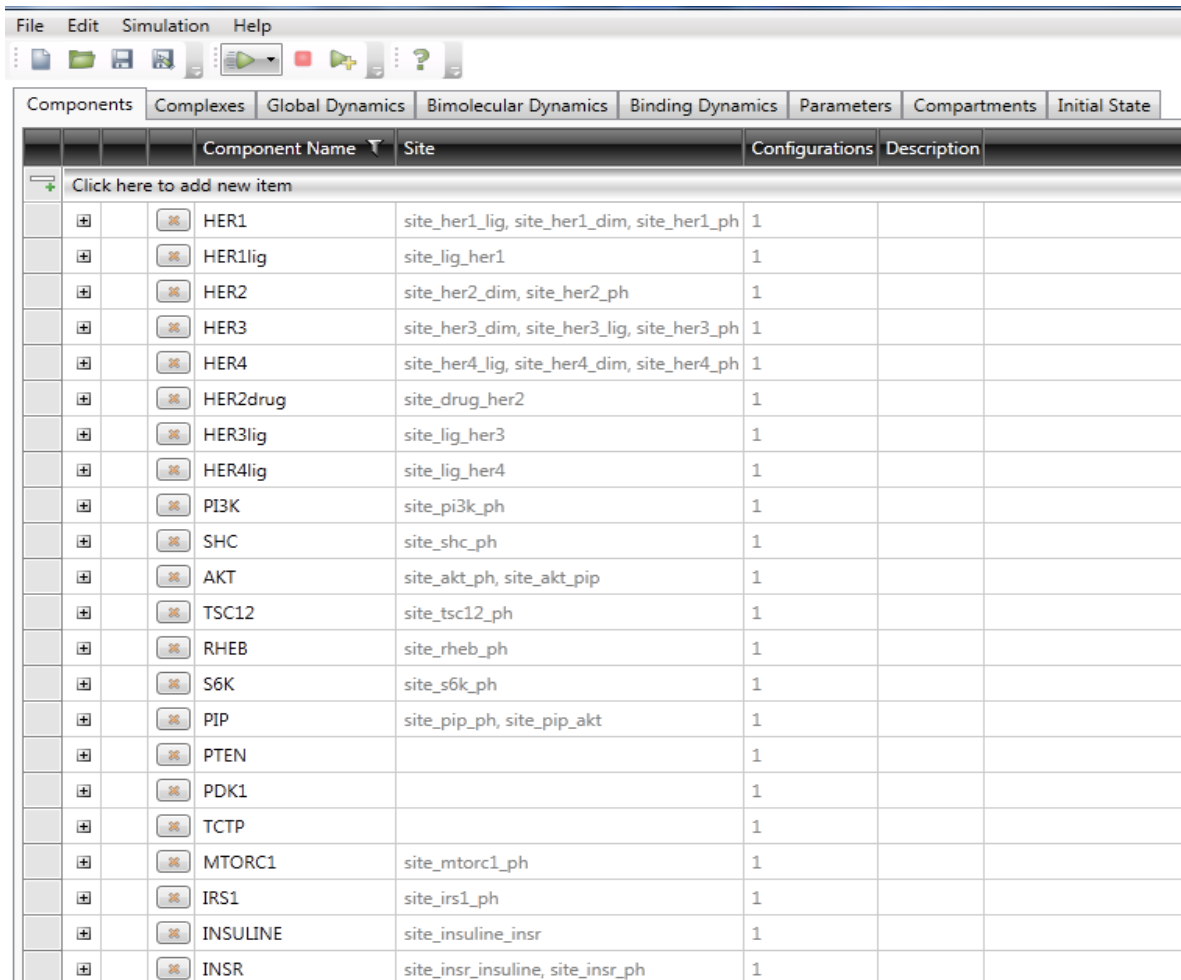
KNOWLEDGE INFERENCE SUPPORT MODELING BY GENERATING

NEW HYPOTHESIS



COSBI LAB MODELS: SIMULATE AND TESTS HYPOTHESIS

PREVIOUSLY INFERRED



The screenshot shows a software interface with a menu bar (File, Edit, Simulation, Help) and a toolbar. Below the toolbar are tabs for 'Components', 'Complexes', 'Global Dynamics', 'Bimolecular Dynamics', 'Binding Dynamics', 'Parameters', 'Compartments', and 'Initial State'. The 'Components' tab is active, displaying a table with columns for Component Name, Site, Configurations, and Description. The table lists various components and their associated sites, with a 'Configurations' column containing the value '1' for each row.

Component Name	Site	Configurations	Description
HER1	site_her1_lig, site_her1_dim, site_her1_ph	1	
HER1lig	site_lig_her1	1	
HER2	site_her2_dim, site_her2_ph	1	
HER3	site_her3_dim, site_her3_lig, site_her3_ph	1	
HER4	site_her4_lig, site_her4_dim, site_her4_ph	1	
HER2drug	site_drug_her2	1	
HER3lig	site_lig_her3	1	
HER4lig	site_lig_her4	1	
PI3K	site_pi3k_ph	1	
SHC	site_shc_ph	1	
AKT	site_akt_ph, site_akt_pip	1	
TSC12	site_tsc12_ph	1	
RHEB	site_rheb_ph	1	
S6K	site_s6k_ph	1	
PIP	site_pip_ph, site_pip_akt	1	
PTEN		1	
PDK1		1	
TCTP		1	
MTORC1	site_mtorc1_ph	1	
IRS1	site_irs1_ph	1	
INSULINE	site_insuline_insr	1	
INSR	site_insr_insuline, site_insr_ph	1	

COSBI LAB MODELS: SIMULATE AND TESTS HYPOTHESIS

PREVIOUSLY INFERRED

