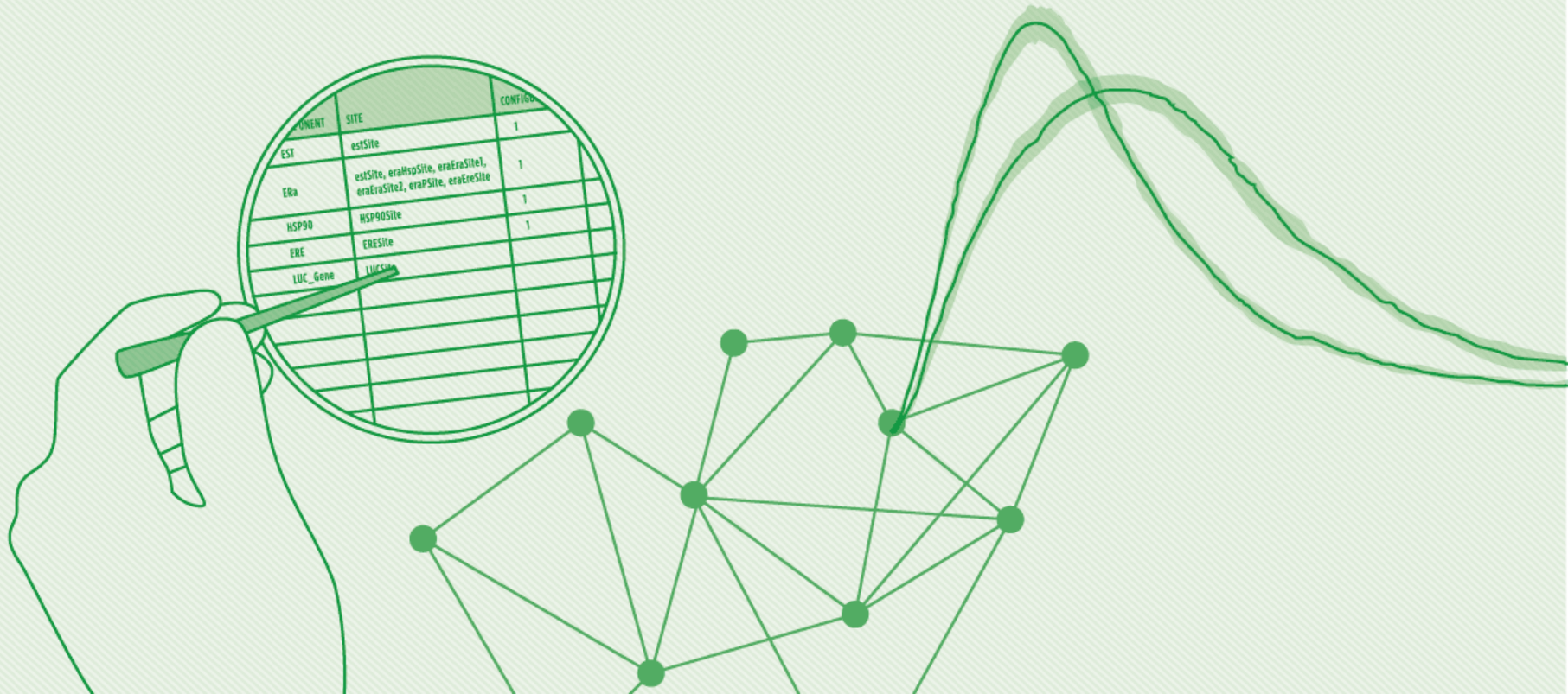


COSBI LAB

Modeling Philosophy



Intelligible Models

Intelligible Models

- Understandable to non-expert modelers

Intelligible Models

- Understandable to non-expert modelers
- Easy to write, modify and reuse

Intelligible Models

- Understandable to non-expert modelers
- Easy to write, modify and reuse
- Manage combinatorial complexity of dynamics



Intelligibility



< Obscure syntax



< Obscure syntax

< No bio keywords



< Obscure syntax

< No bio keywords



< Large size

< Obscure syntax

< No bio keywords



< Large size

< Complex mathematics

- < Obscure syntax
- < No bio keywords



Narrative Language



- < Large size
- < Complex mathematics

- < Obscure syntax
- < No bio keywords



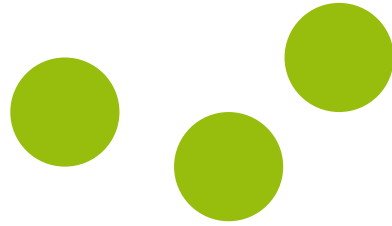
Narrative Language



- < Large size
- < Complex mathematics



Minimize required modeling information



Epidermal Growth Factor
(EGF)



Epidermal Growth Factor Receptor
(EGFR)

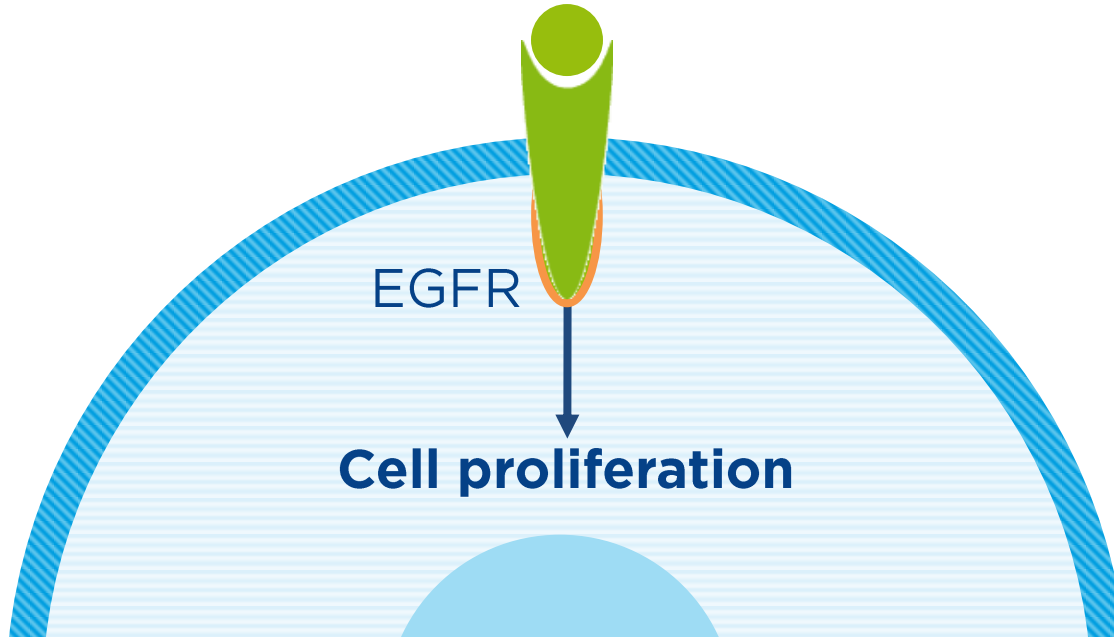


Epidermal Growth Factor
(EGF)



Epidermal Growth Factor Receptor
(EGFR)

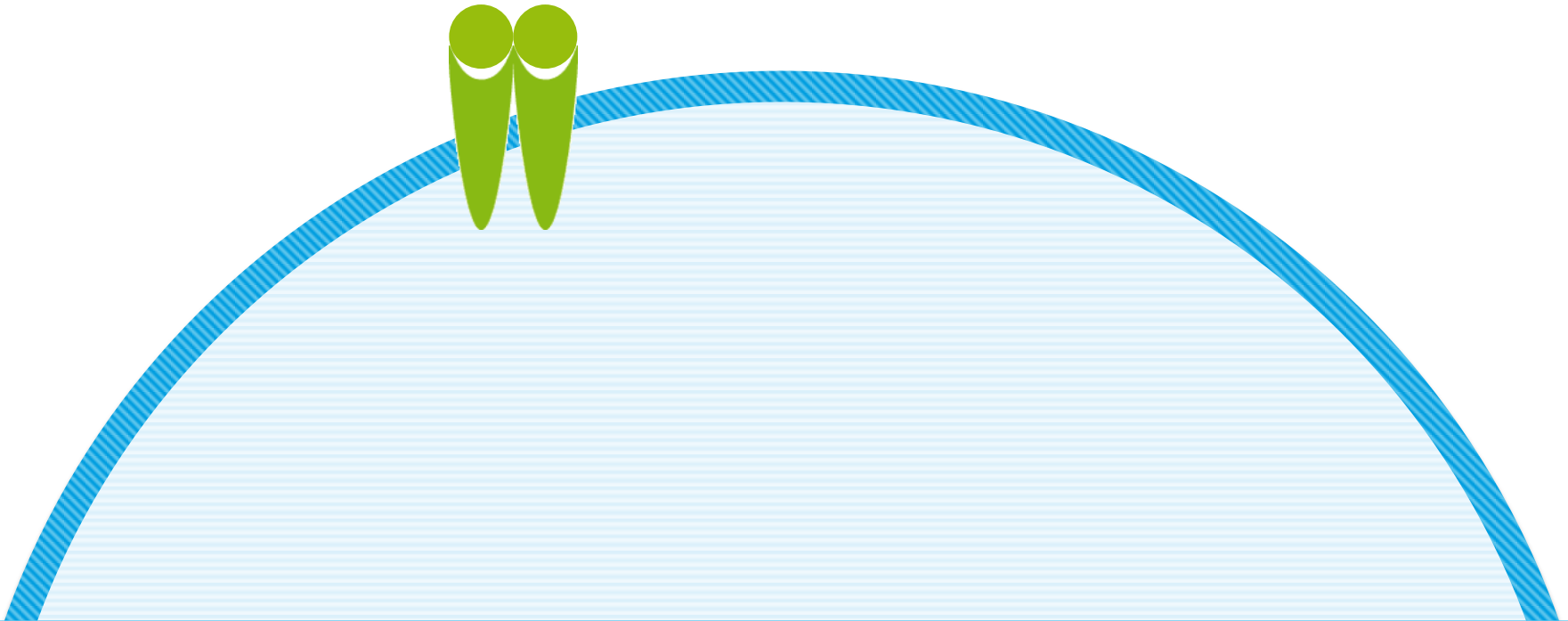
EGFR Receptor



EGFR

Cell proliferation

EGFR Receptor



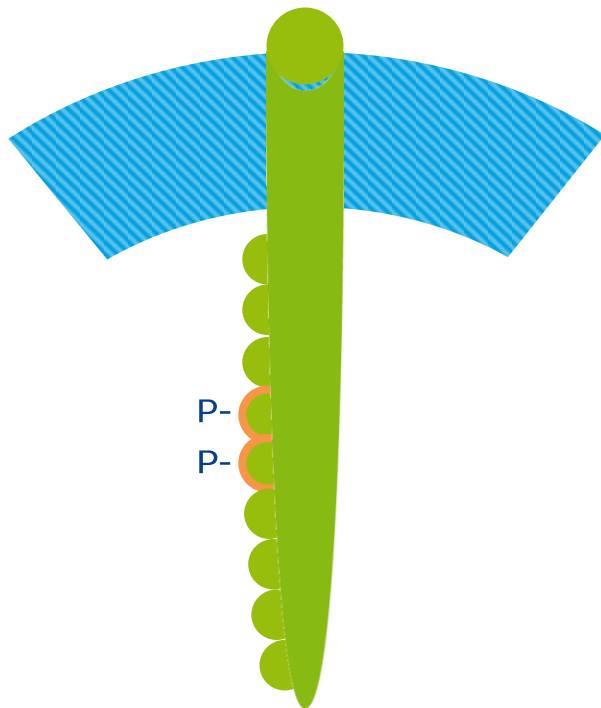
EGFR Receptor

transphosphorylation

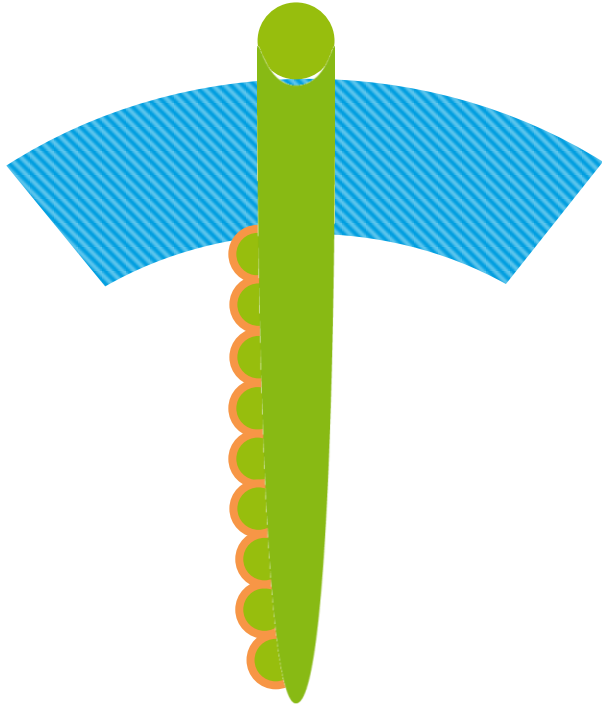


Cell proliferation

Monomer

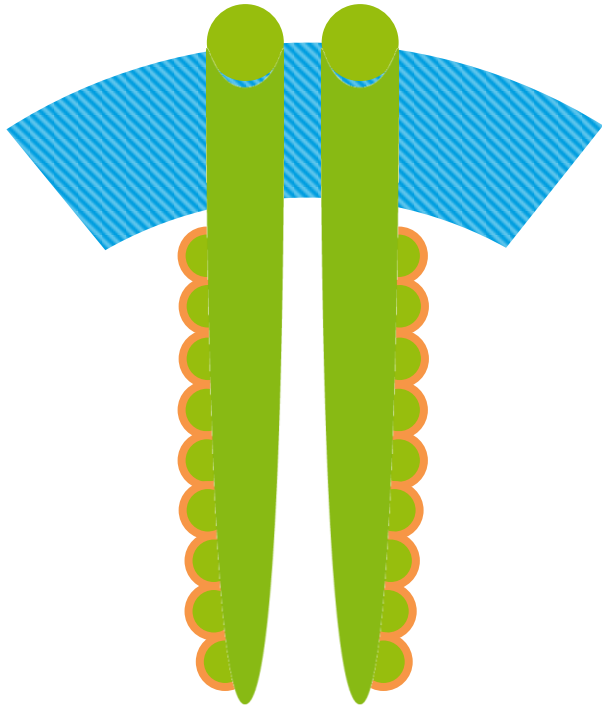


EGFR Molecule Configurations



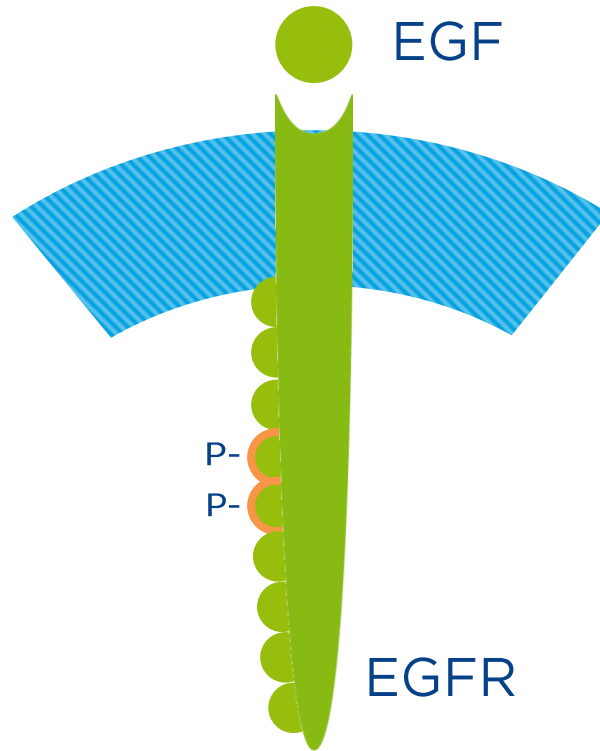
2⁹ configuration of EGFR Monomers
(**512** different states)

EGFR Molecule Configurations

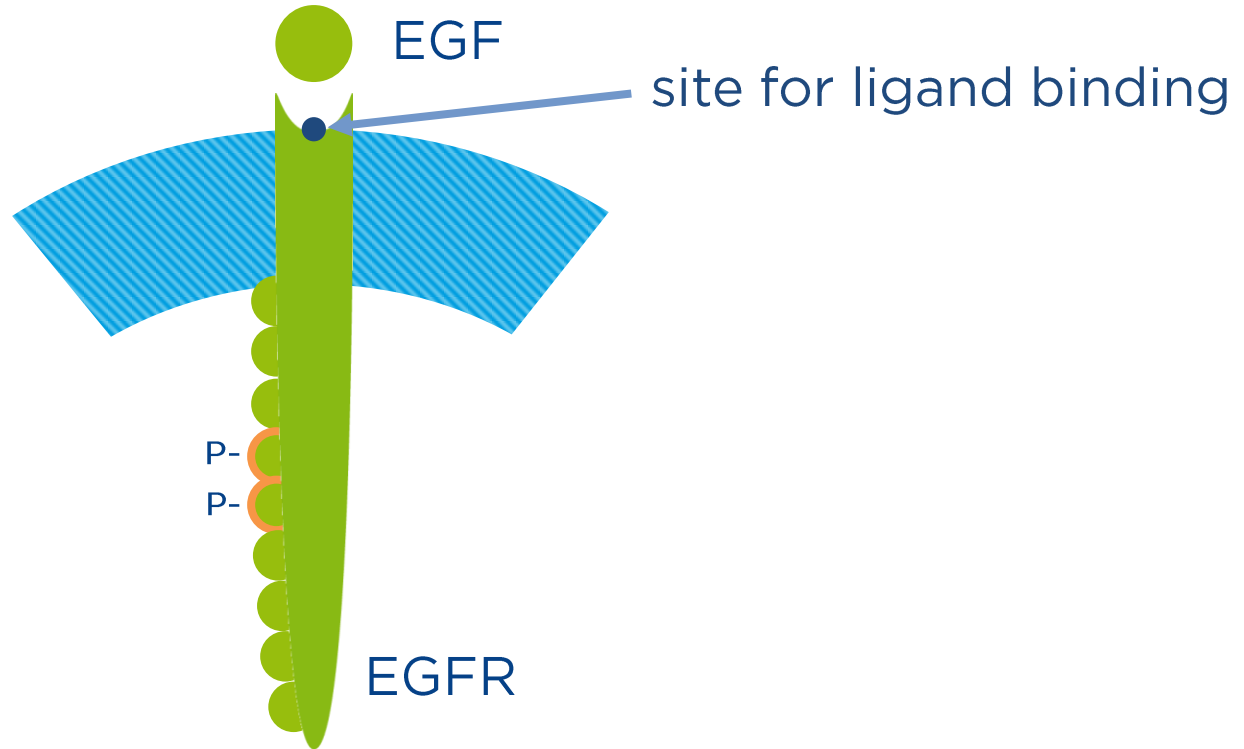


2^{18} configuration of EGFR Homodimers
(**250,000+** different states)

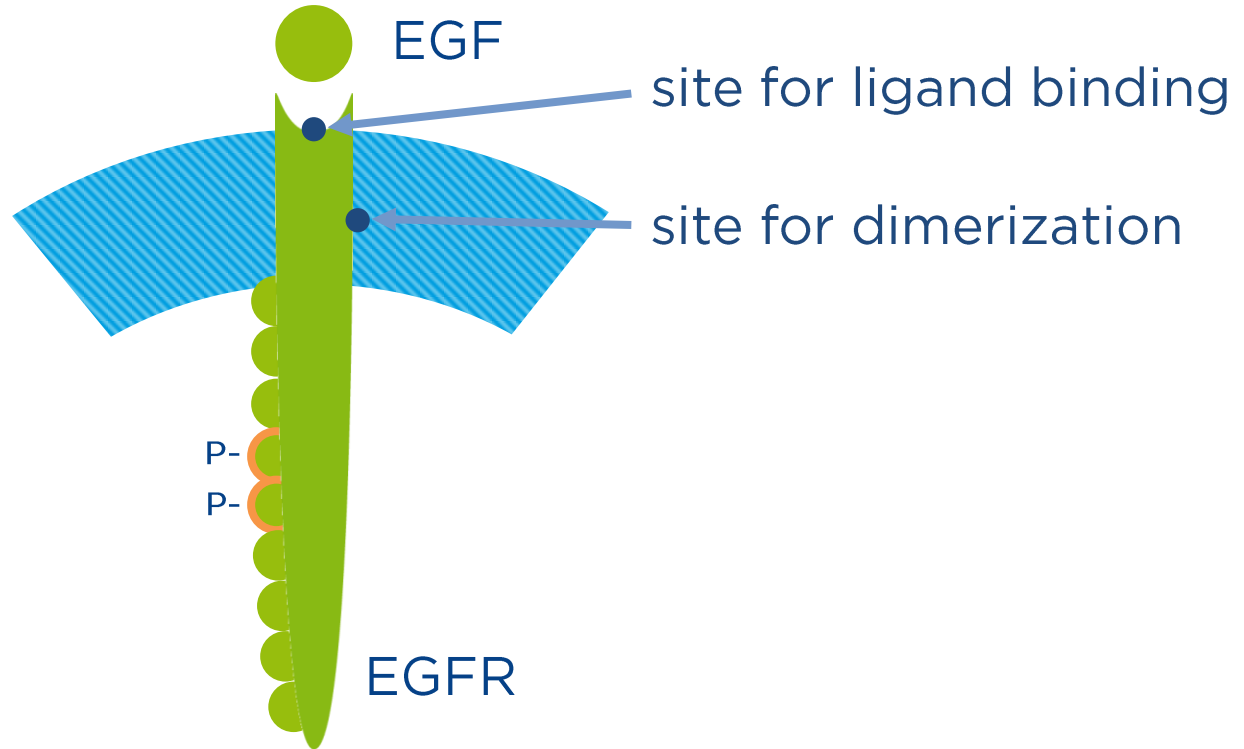
EGFR Molecule in COSBI LAB



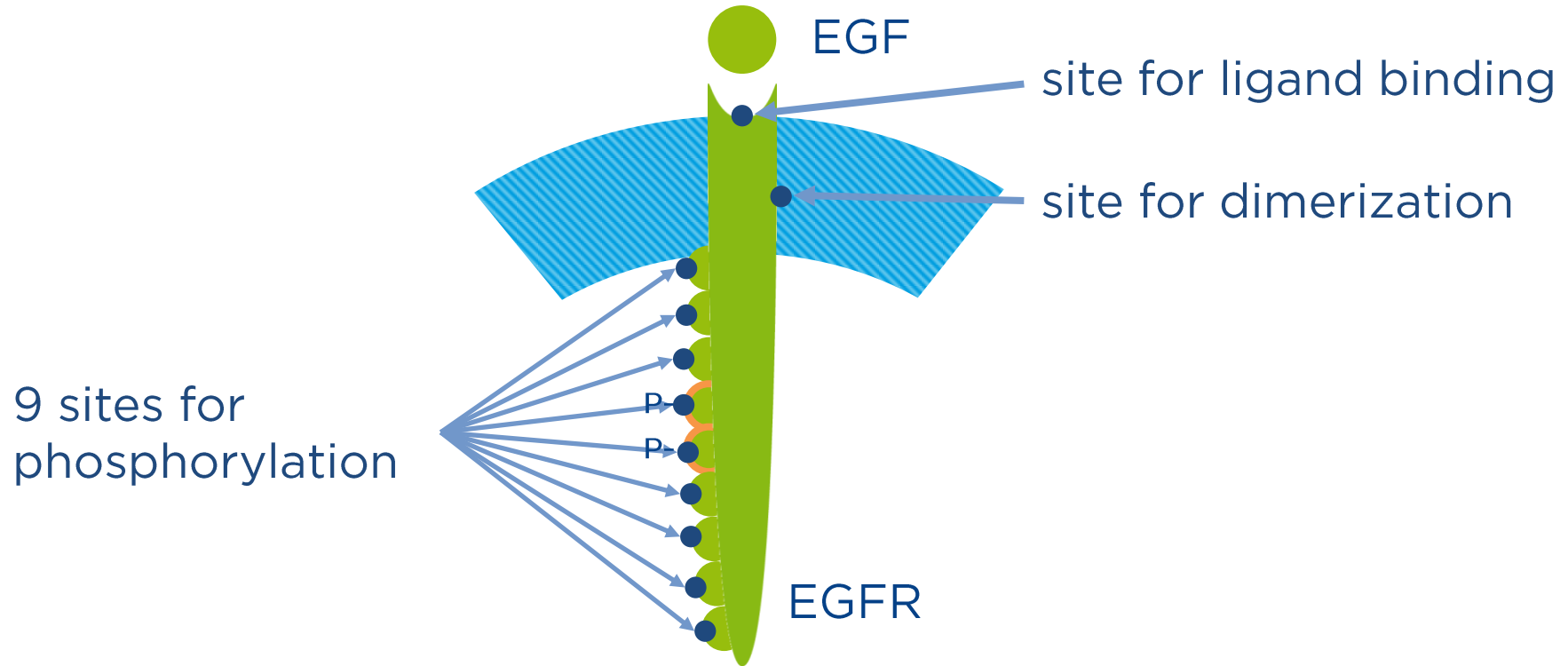
EGFR Molecule in COSBI LAB



EGFR Molecule in COSBI LAB

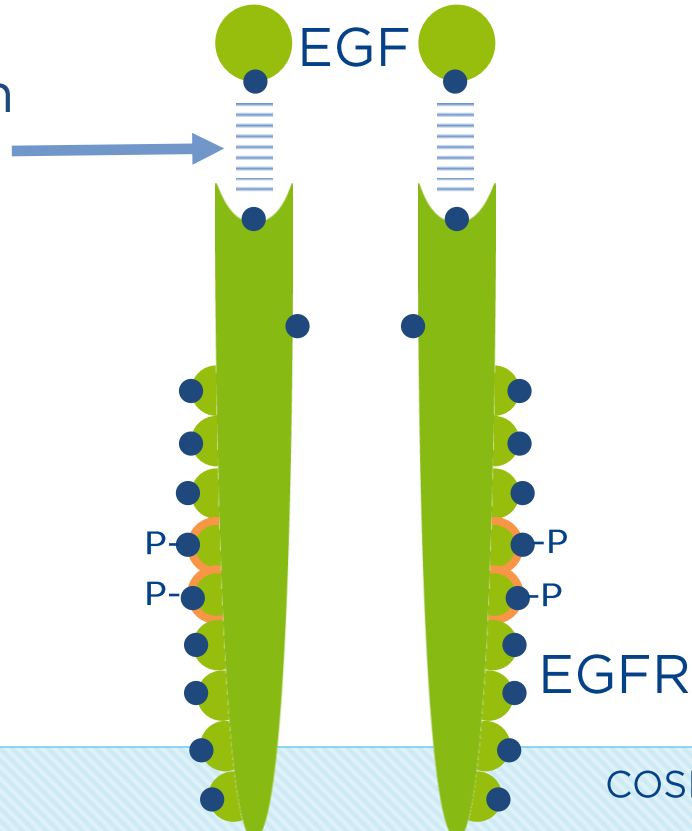


EGFR Molecule in COSBI LAB



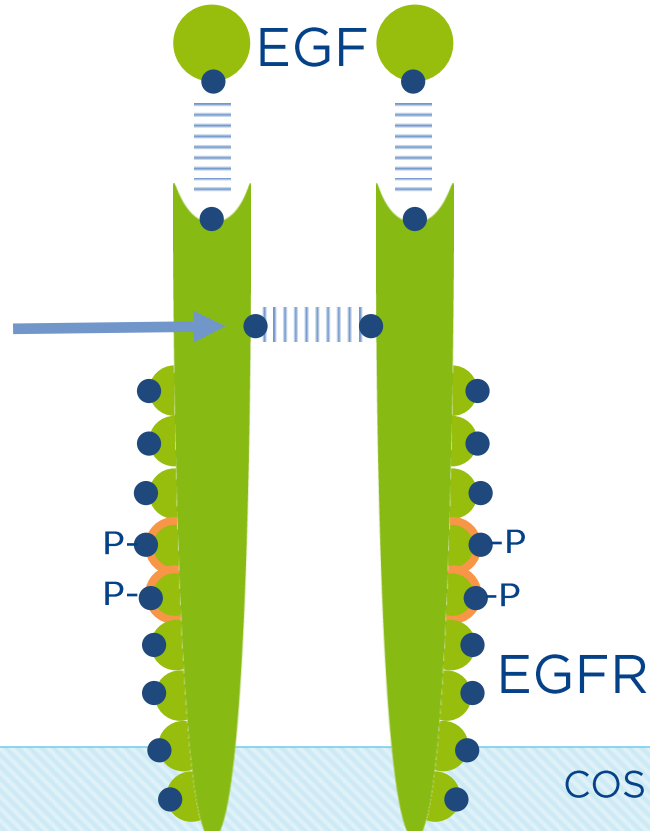
EGFR Molecule in COSBI LAB

Interaction between
EGFR and EGF



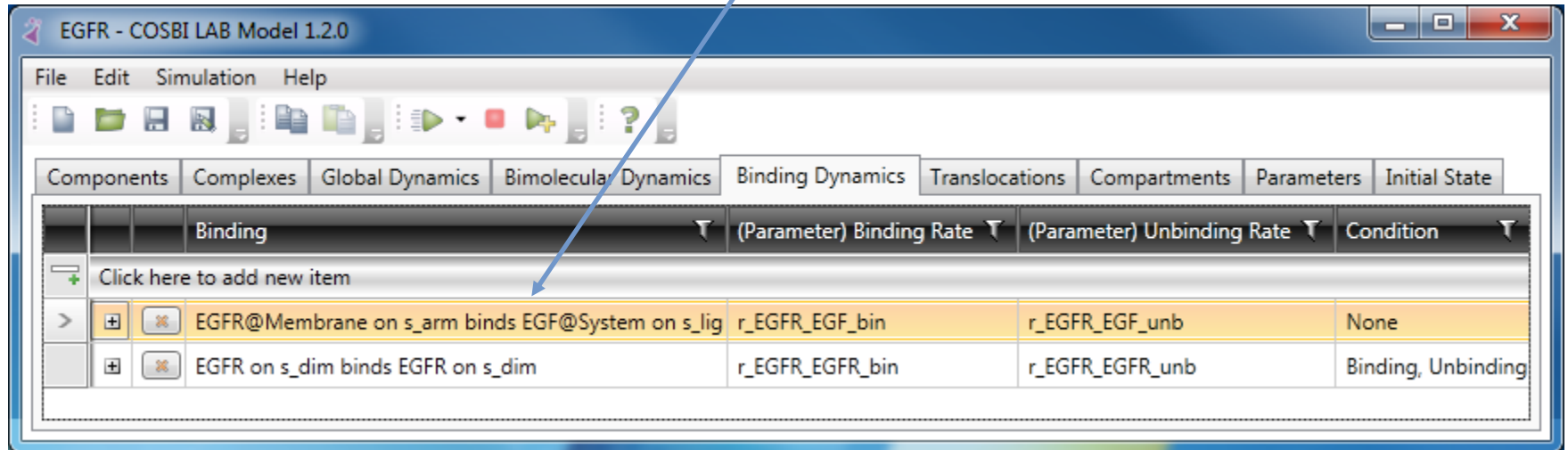
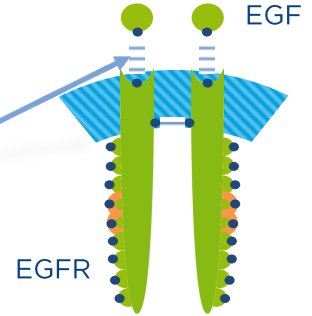
EGFR Molecule in COSBI LAB

Homodimerization
EGFR



EGFR Molecule in COSBI LAB

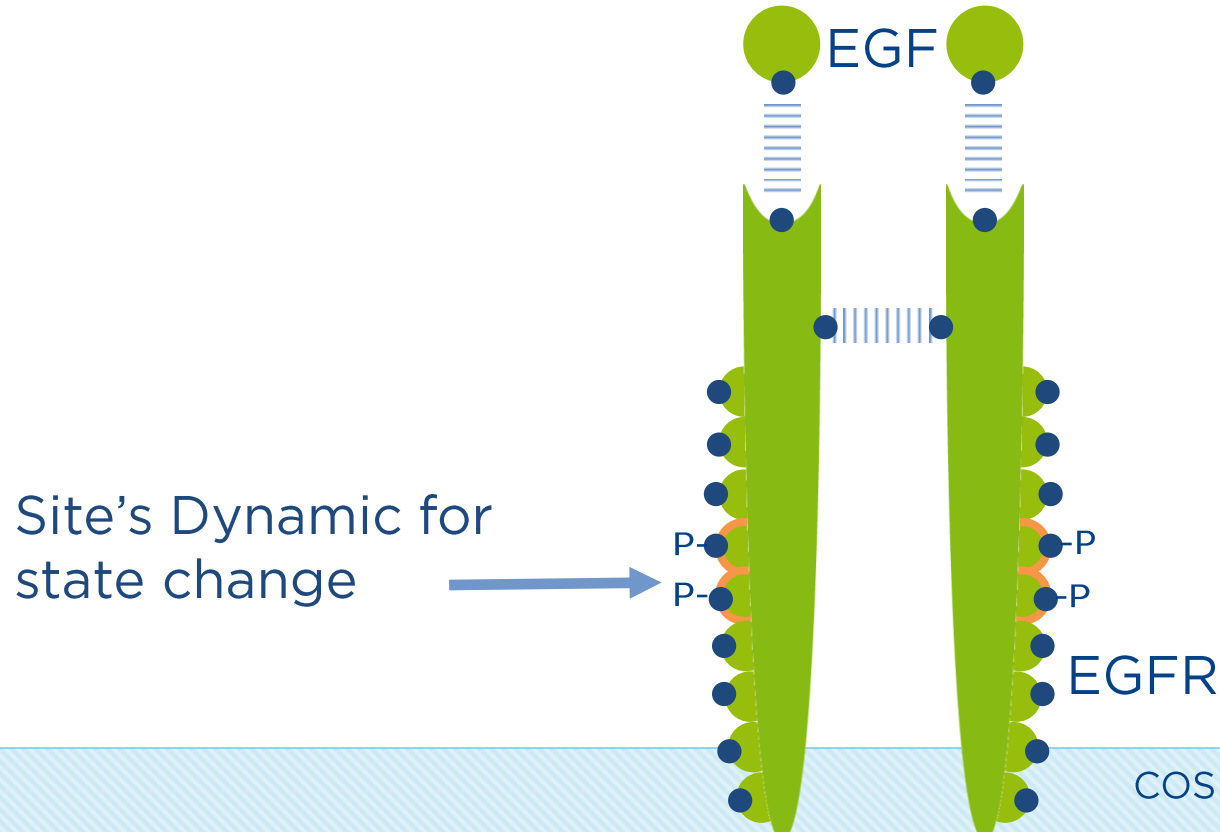
Interaction between EGFR and EGF
and Homodimerization



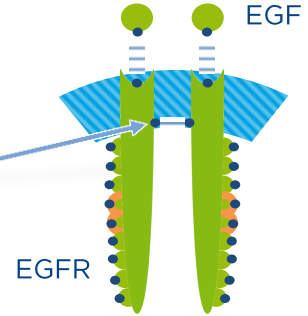
The screenshot shows the EGFR - COSBI LAB Model 1.2.0 software interface. The 'Binding Dynamics' tab is selected, and the 'Binding' table is displayed. The table has columns for 'Binding', '(Parameter) Binding Rate', '(Parameter) Unbinding Rate', and 'Condition'. The first row is highlighted in yellow and shows the binding of EGF to EGFR. The second row shows the homodimerization of EGFR.

Binding	(Parameter) Binding Rate	(Parameter) Unbinding Rate	Condition
Click here to add new item			
EGFR@Membrane on s_arm binds EGF@System on s_lig	r_EGFR_EGF_bin	r_EGFR_EGF_unb	None
EGFR on s_dim binds EGFR on s_dim	r_EGFR_EGFR_bin	r_EGFR_EGFR_unb	Binding, Unbinding

EGFR Molecule in COSBI LAB



EGFR Molecule in COSBI LAB



Interaction between
EGFR

EGFR - COSBI LAB Model 1.2.0

File Edit Simulation Help

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

	Binding	(Parameter) Binding Rate	(Parameter) Unbinding Rate	Condition
+ Click here to add new item				
> +	EGFR@Membrane on s_arm binds EGF@System on s_lig	r_EGFR_EGF_bin	r_EGFR_EGF_unb	None
+	EGFR on s_dim binds EGFR on s_dim	r_EGFR_EGFR_bin	r_EGFR_EGFR_unb	Binding, Unbinding

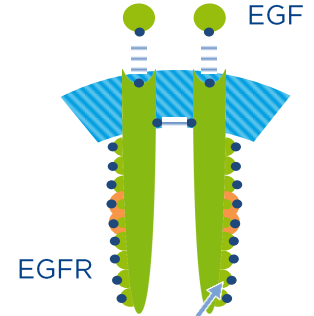
EGFR Molecule in COSBI LAB

The screenshot displays the COSBI LAB Model 1.0.0.59 interface. The main window shows the 'Component Site Definition' tab for the EGFR molecule. The table below lists the site definitions for the EGFR molecule, including the action, rate parameter, condition, and compartment.

Action	(Parameter) Rate	Condition	Compartment	Description
Phosphorylated on s_ph1	s_EGFR_ph1	s_dim is Bound	Membrane	
Phosphorylated on s_ph2	s_EGFR_ph2	s_dim is Bound	Membrane	
Phosphorylated on s_ph3	s_EGFR_ph3	s_dim is Bound	Membrane	
Phosphorylated on s_ph4	s_EGFR_ph4	s_dim is Bound	Membrane	
Phosphorylated on s_ph5	s_EGFR_ph5	s_dim is Bound	Membrane	
Phosphorylated on s_ph6	s_EGFR_ph6	s_dim is Bound	Membrane	
Phosphorylated on s_ph7	s_EGFR_ph7	s_dim is Bound	Membrane	
Phosphorylated on s_ph8	s_EGFR_ph8	s_dim is Bound	Membrane	
Phosphorylated on s_ph9	s_EGFR_ph9	s_dim is Bound	Membrane	

Below the table, the 'Component Configurations' tab shows the following configurations:

Component Name	Site	Configurations	Description
EGFR	s_arm, s_ph1, s_ph2, s_ph3, s_ph4, s_ph5, s_ph6, s_ph7, s_ph8, s_dim, s_ph9	1	

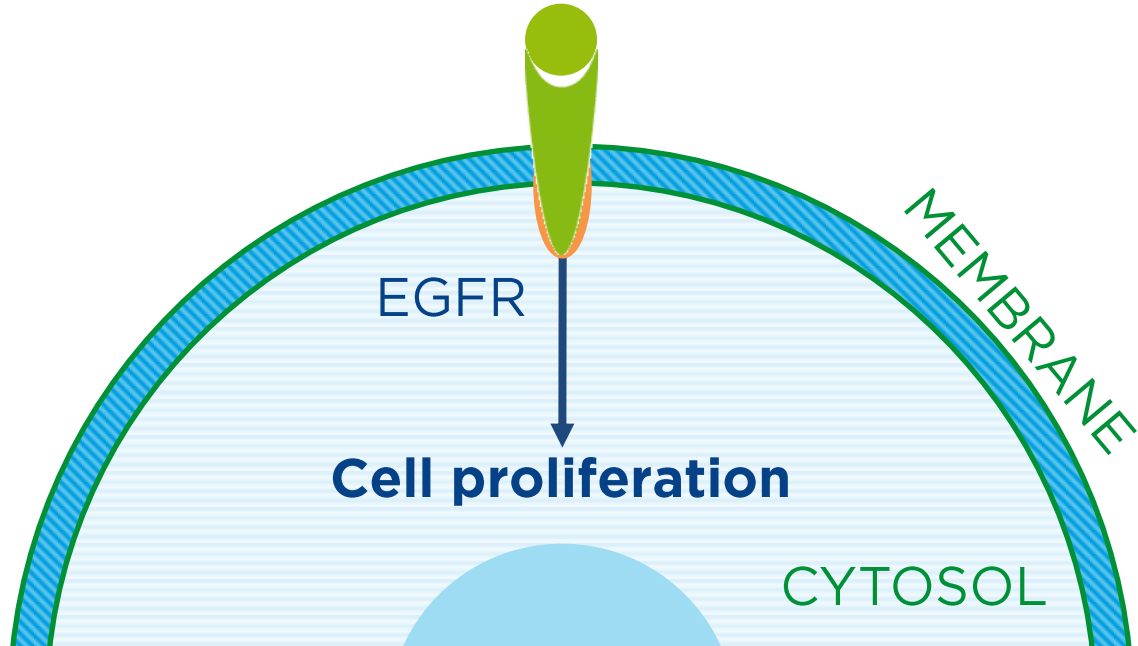


Site's Dynamic for state change

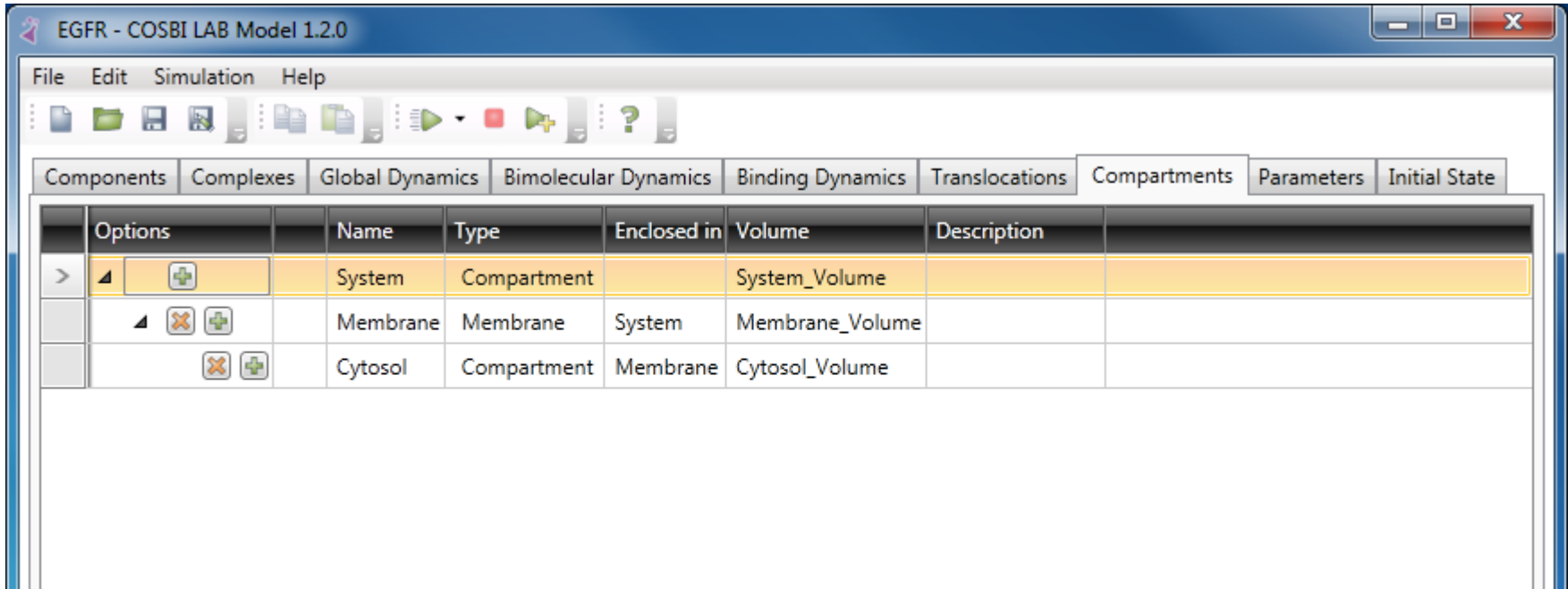
Space in COSBI LAB

EGF

SYSTEM



Space in COSBI LAB



The screenshot displays the 'EGFR - COSBI LAB Model 1.2.0' software window. The 'Compartments' tab is active, showing a table of compartments. The table has columns for Options, Name, Type, Enclosed in, Volume, and Description. The 'System' compartment is highlighted in yellow.

Options	Name	Type	Enclosed in	Volume	Description
> ▲ +	System	Compartment		System_Volume	
▲ ✕ +	Membrane	Membrane	System	Membrane_Volume	
✕ +	Cytosol	Compartment	Membrane	Cytosol_Volume	

EGFR Molecule in COSBI LAB

EGFR - COSBI LAB Model 1.2.0

File Edit Simulation Help

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

Component Name	Site	Configurations	Description
EGFR	s_arm, s_dim, s_ph1, s_ph2, s_ph3, s_ph4, s_ph5, s_ph6, s_ph7, s_ph8, s_ph9	1	

Component Site Definition Component Configurations Monomolecular Dynamics

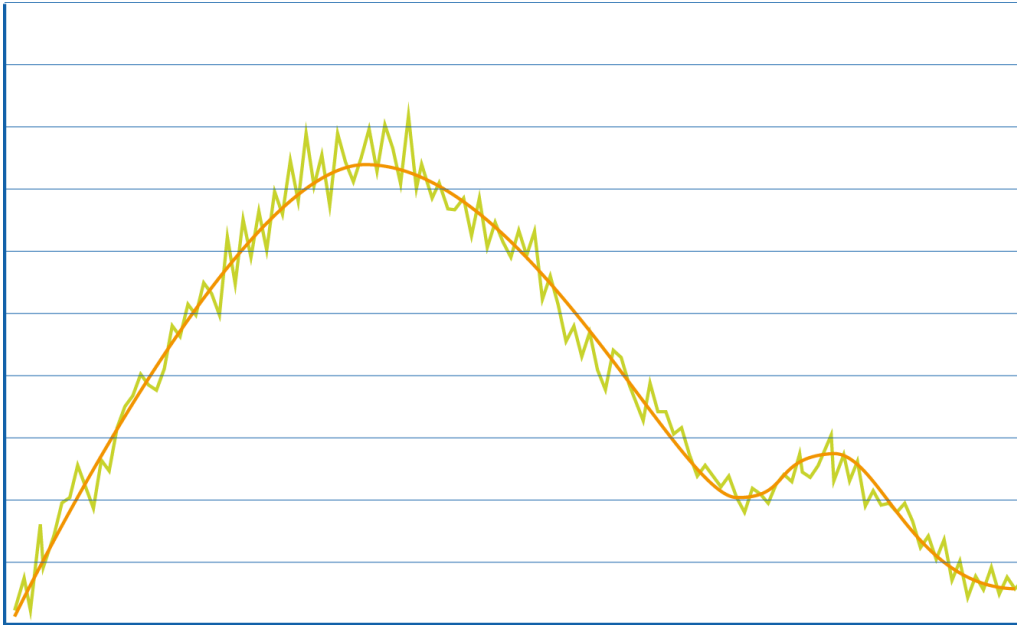
Action	(Parameter) Rate	Condition	Compartment	Description
Phosphorylated on s_ph1	r_EGFR_ph1	s_dim is Bound	Membrane	
Phosphorylated on s_ph2	r_EGFR_ph2	s_dim is Bound	Membrane	
Phosphorylated on s_ph3	r_EGFR_ph3	s_dim is Bound	Membrane	
Phosphorylated on s_ph4	r_EGFR_ph4	s_dim is Bound	Membrane	
Phosphorylated on s_ph5	r_EGFR_ph5	s_dim is Bound	Membrane	
Phosphorylated on s_ph6	r_EGFR_ph6	s_dim is Bound	Membrane	
Phosphorylated on s_ph7	r_EGFR_ph7	s_dim is Bound	Membrane	
Phosphorylated on s_ph8	r_EGFR_ph8	s_dim is Bound	Membrane	
Phosphorylated on s_ph9	r_EGFR_ph9	s_dim is Bound	Membrane	

EGF s_lig 1

SHC s_ph 1

Site's Dynamic
applies in
Membrane

Discrete Stochastic Approach



Discrete Stochastic Approach

- Receive more detailed information
- Able to produce more accurate predictions

COSBI LAB

- Offers intelligible models for non expert users
- Supports managing model's complexity
- Produces more accurate prediction due to stochastic simulation

