

Towards Sharing Rule-based Models

<http://www.bionetgen.org>

<http://vcell.org/bionetgen>

<http://getbonnie.org>

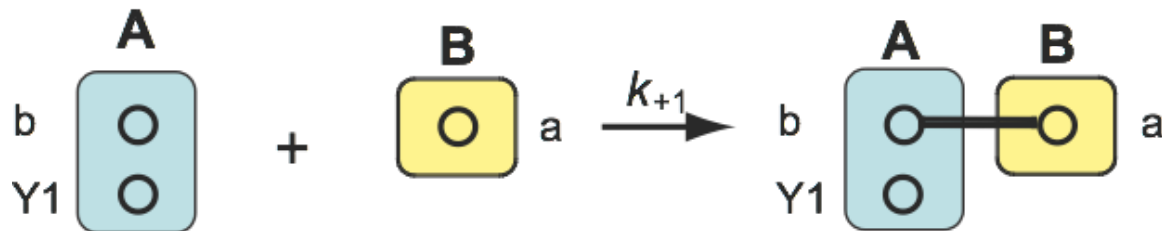
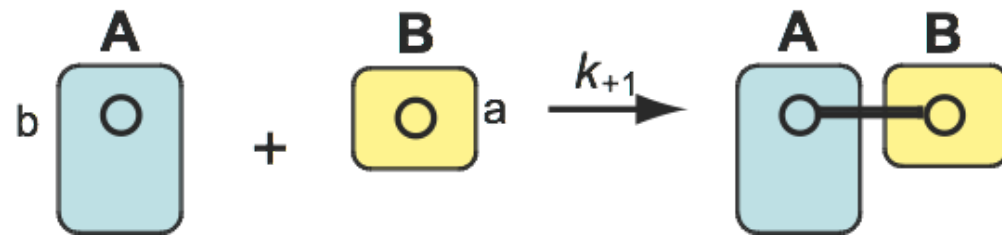
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BioNetGen

- Rule-based modeling
- Current development
- www.bionetgen.org
- www.getbonnie.org
- vcell.org/bionetgen

Rule-based Modeling



Rule-based Modeling



12 sites of tyrosine phosphorylation

⇒ $2^{12} = 4096$ phosphorylation states

Each site has ≥ 1 binding partner

⇒ 5,225,472 states



Schulze et al. (2005)

```
simpleEGFR.bngl
# This is a demo model of EGFR signaling.
# The parameters and rules have been modified to keep things
# as simple as possible.

#version("2.0.41");

begin parameters
# Concentrations in number per cell
EGF_tot      1.2e6
EGFR_tot     1.8e5
Grb2_tot     1.5e5
Sos_tot      6.2e4

# Biomolecular rate constants are in (# per cell)^-1 s^-1,
# obtained by dividing constants in M^-1 s^-1 by Na*V,
# where Na is Avogadro's number and V is the volume
# of the relevant compartment (the cytoplasm for all cases here).
# Unimolecular rate constants are in s^-1
kp1      1.667e-06 # ligand-monomer binding
km1      0.06 # ligand-monomer dissociation

kp2      5.556e-06 # aggregation of bound monomers
km2      0.1 # dissociation of bound monomers

kp3      0.5 # dimer transphosphorylation
km3      4.505 # dimer dephosphorylation

kp4      8.333e-07 # binding of Grb2 to receptor
km4      0.05 # dissociation of Grb2 from receptor

kp5      5.556e-06 # binding of Grb2 to Sos
km5      0.06 # dissociation of Grb2 from Sos
kdeg     0.01
end parameters

begin molecule types
EGF(r)
EGFR(l,r,Y1068~U~P,Y1148~U~P)
Grb2(SH2,SH3)
Shc(PTB,Y317~U~P)
Sos(PR)
NULL()
end molecule types

begin species
EGF(r)                EGF_tot
EGFR(l,r,Y1068~U,Y1148~U)  EGFR_tot
Grb2(SH2,SH3)         Grb2_tot
Sos(PR)                Sos_tot
end species

begin reaction rules
-:-- simpleEGFR.bngl Top of 2.7k (33,0) (Perl) 11:27PM 0.15
Beginning of buffer
```

BNGL

BNGL



Molecules

A(b)

B(a,Y~U~P,location~Cyt~Nuc)

Patterns

B_tot

B()

B_unbound

B(a)

B_bound

B(a!+)

B_phospho_all

B(Y~P!?)

B_phospho_unbound

B(Y~P)

B_phospho_bound

B(Y~P!+)

A_B_complex

A().B()

Reaction rules

A(b) + B(a) -> A(b!1).B(a!1) p

a bond between two components

B(Y~P) -> B(Y~U) d

Model Definitions

- Currently in use:
 - BNGL
 - BNGL XML
- To exchange models defined in BNGL:
 - **GetBonnie** www.getbonnie.org
 - Plan to support SBML multi-* package

GetBonNie

- Web-based platform for rule-based models
 - Model construction
 - Model visualization
 - Model simulation
 - Model sharing
- Free for academia users

<http://getbonnie.org>

- [-] Model
 - [+] Parameters
 - [-] Molecule Types
 - EGF
 - EGFR
 - Grb2
 - Sos1
 - Trash
 - [-] Seed Species
 - EGF(R)
 - EGFR(L,CR1,Y1068~U)
 - Grb2(SH2,SH3)
 - Sos1(PxxP)
 - [-] Observables
 - EGFR_tot
 - Lig_free
 - Dim
 - RP
 - Grb2Sos1
 - Sos1_act
 - [-] Rules
 - R1
 - R2
 - R3
 - R4
 - R5
 - R6
 - R7
 - [-] Actions
 - step1
 - step2

Input
BNGL
Build Help ✕

BNGL Textbox Editor

Enter BNGL code here:

EGFR(Y1068~P) + Grb2(SH2) <-> EGFR(Y1068~P!1).Grb2(SH2!1) kp4,km4

Annotation:

The adapter protein Grb2 reversibly binds phosphorylated Y1068 in the EGF receptor via its SH2 domain.

This BNGL code defines: Rule ▼

Update
Add
Delete
Clear

Action Assistant

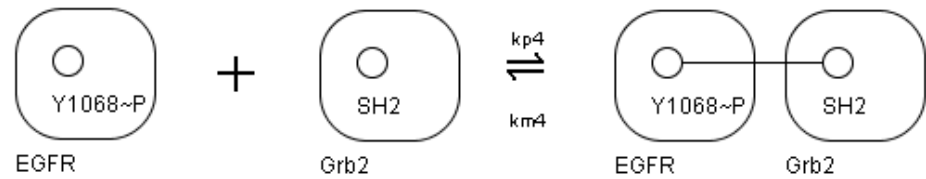
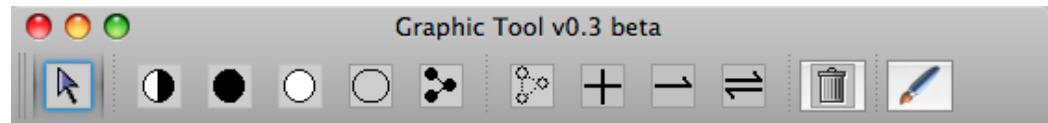
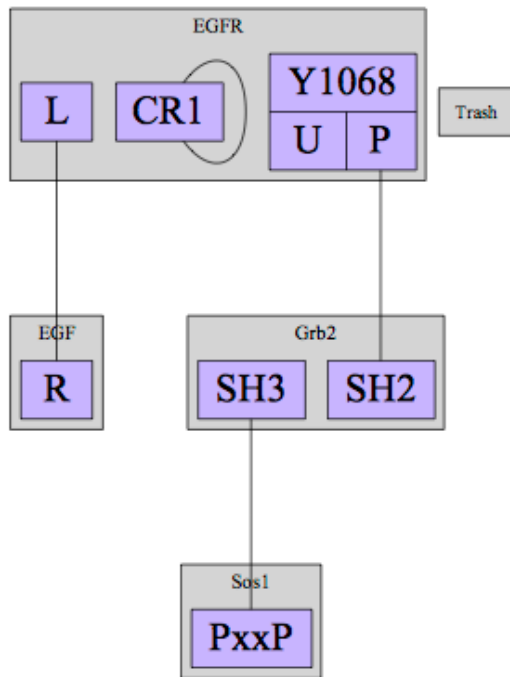
Supported actions

generate_network() ▼

Option

overwrite on off

Add to BNGL Textbox Editor



Object Manipulation Mode

BNGL String: `EGFR(Y1068~P) + Grb2(SH2) <-> EGFR(Y1068~P!0).Grb2(SH2!0) kp4,km4`

BNGL XML

- <http://getbonnie.cs.unm.edu/GetBonNie/document/xml>

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