

BioPAX Support in CellDesigner

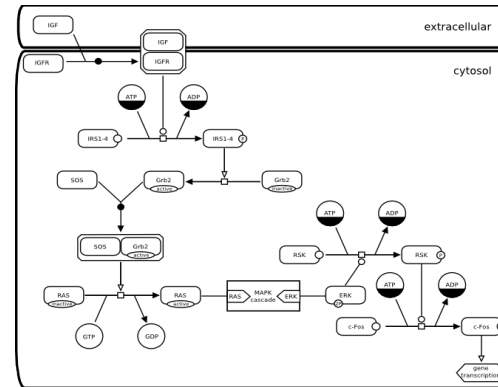
Huaiyu Mi
SRI International



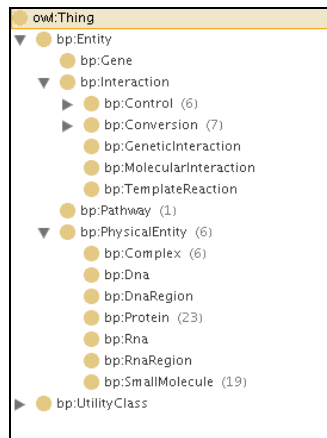
Oct. 7, 2010, COMBINE 2010, Edinburgh, UK



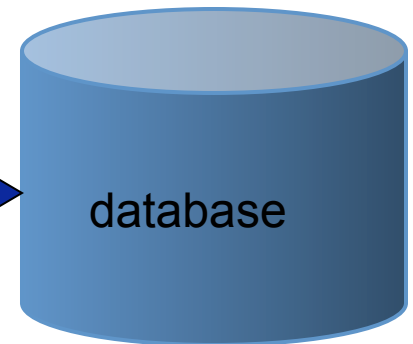
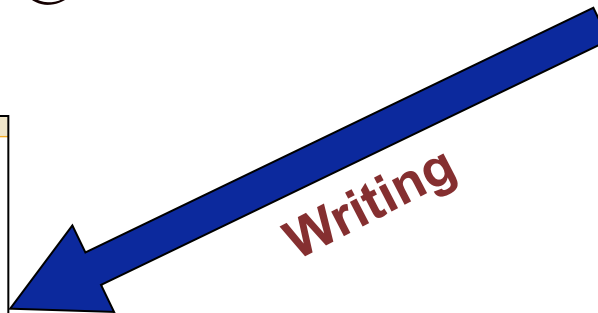
Goals



Model diagram



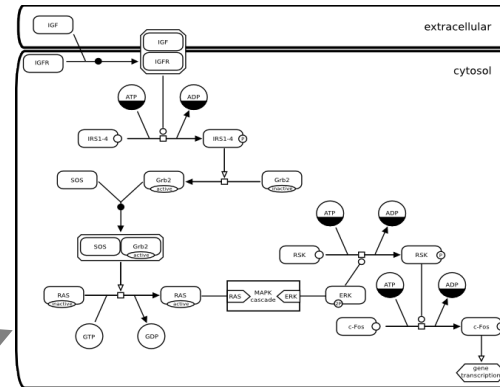
BioPAX file



database

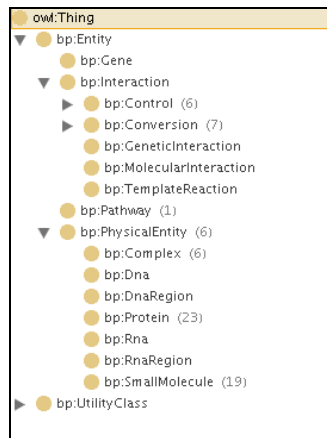
- Allow users to create an SBGN compliant diagram and save it in BioPAX format.

Goals



Reading

Model diagram



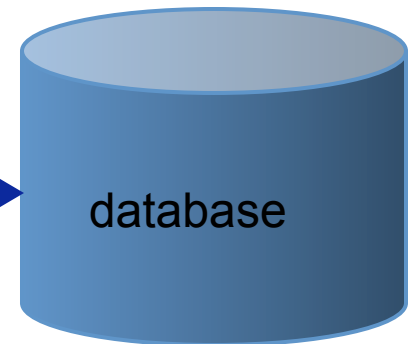
BioPAX file

Writing

Validation

Parsing

Loading

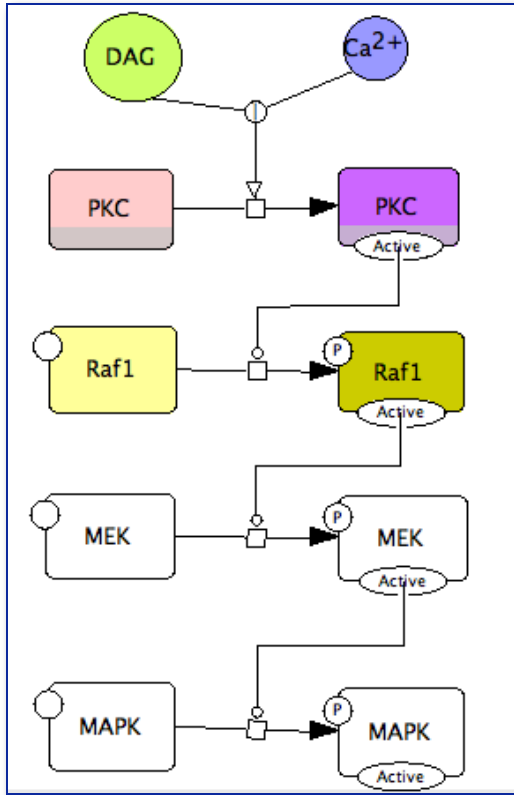


database

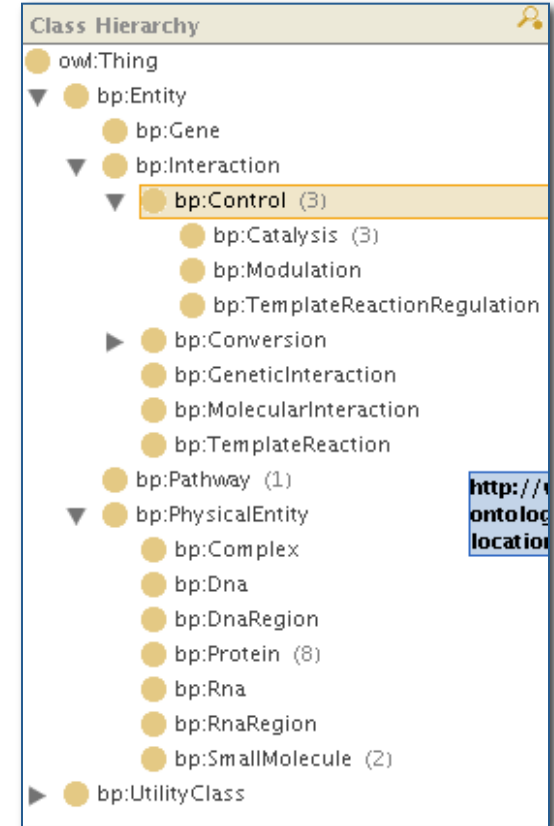
- Allow users to create an SBGN compliant diagram and save it in BioPAX format.
- Allow users to read an BioPAX file and create an SBGN compliant diagram.



Approach

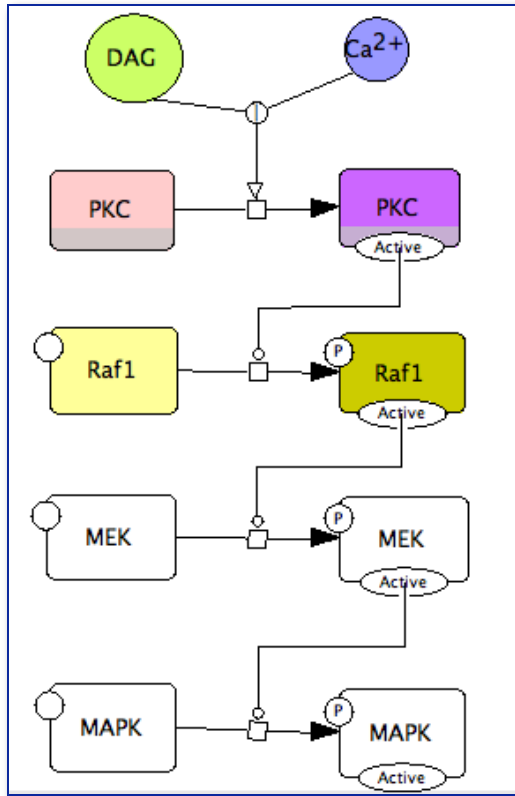


SBGN

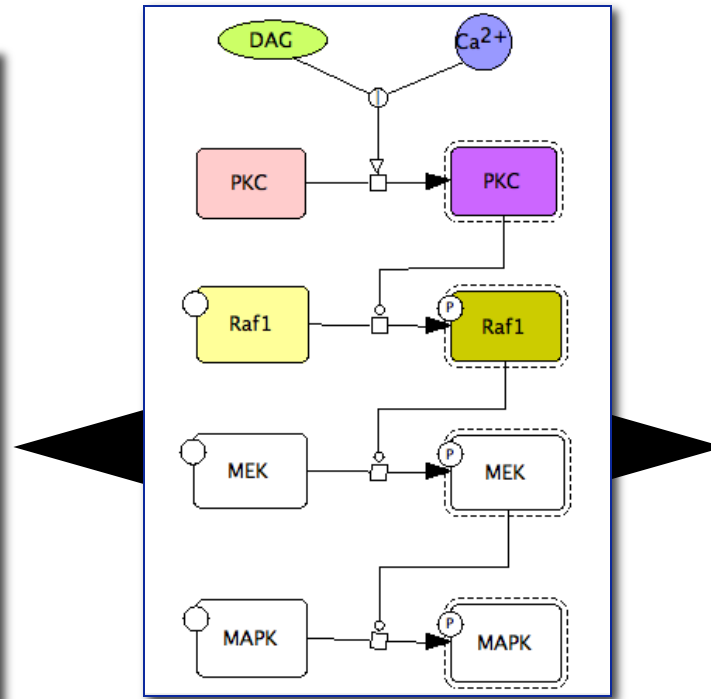


BioPAX

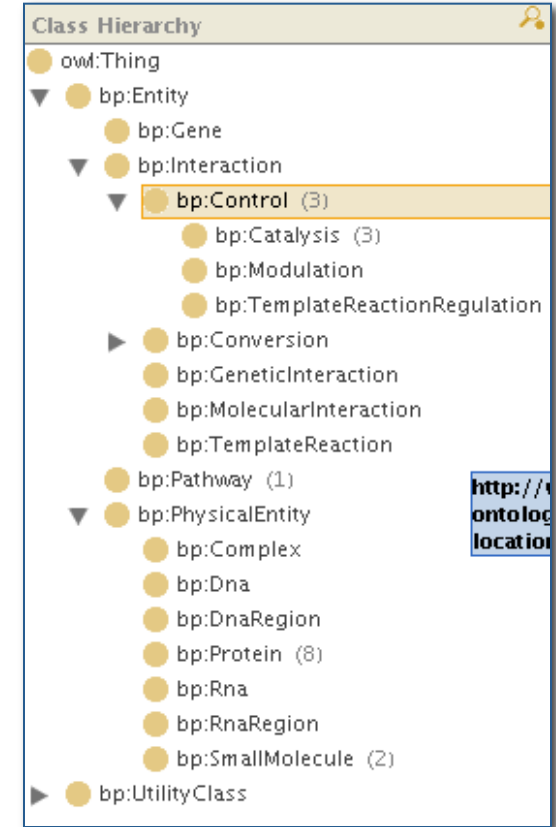
Approach



SBGN



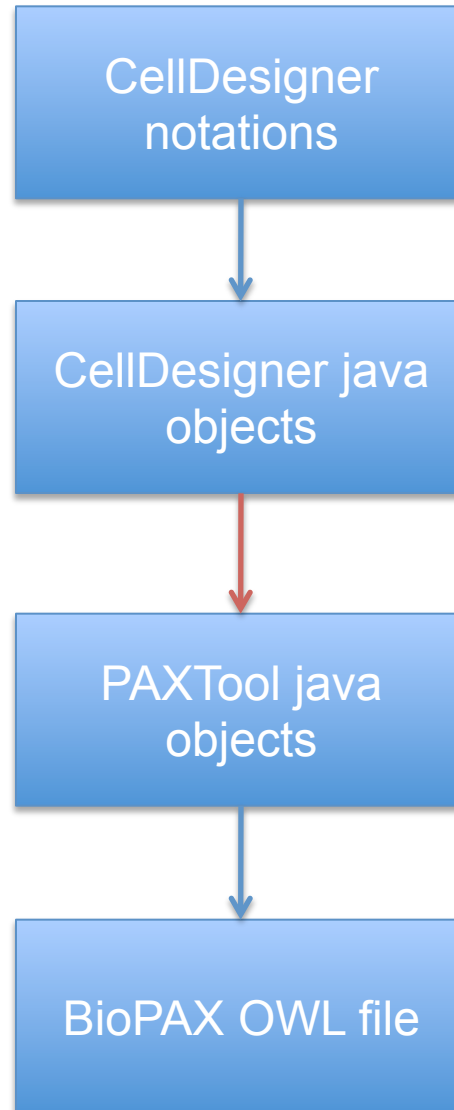
CellDesigner



<http://ontology.gn>

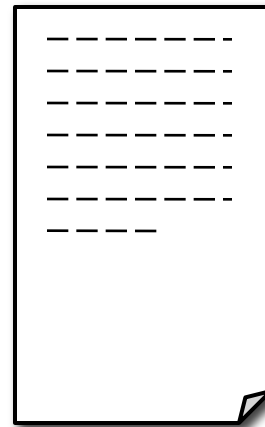
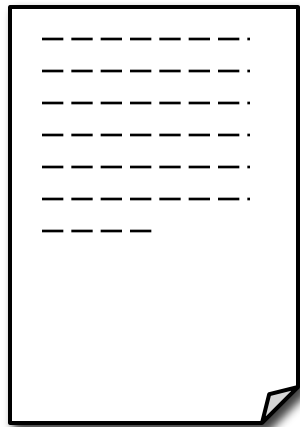
BioPAX

Diagram → BioPAX



CellDesigner BioPAX Converter

- Java application
- Uses CellDesigner library to create input data types.
- Map to PAXTool library data type.
- Writes the PAXTools library to output an OWL file.



PAXTool

Mapping CellDesigner to BioPAX

CellDesigner	BioPAX
Model	Pathway
Species	Physical entity
Reaction	Interaction
Compartment	CellularLocationVocabulary

Mapping CellDesigner to BioPAX (Species)

CellDesigner	BioPAX
Protein	Protein
RNA and AntiSenseRNA	RNA
Gene	DNA
Simple molecule	Small molecule
Ion	Small molecule
Unknown, Degraded, Drug	PhysicalEntity
Phenotype	Pathway
Heterodimer	Complex
Modification	modificationFeature
Binding region	bindingFeature

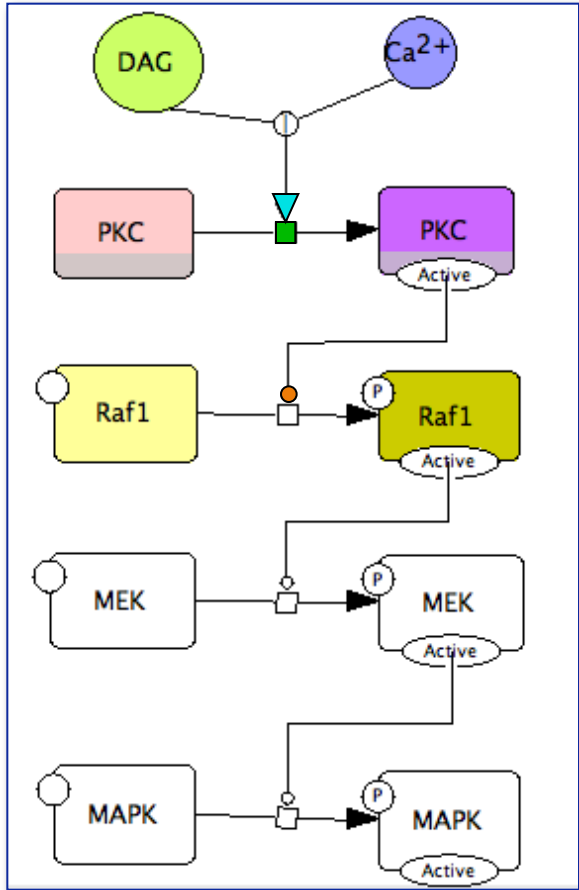
Mapping CellDesigner to BioPAX (Reactions)

CellDesigner	BioPAX
State transition, truncation, transcription, translation	BiochemicalReaction
Association or dissociation	ComplexAssembly
Transport	Transport with biochemical reaction
Degradation	Degradation
Catalysis	Catalysis
physical stimulation, modulation, trigger, inhibition, unknown inhibition	Control

BioPAAAAAXXXXXXzzzzzz...



Mapping Example



CellDesigner

Species ID: s61
Name: DAG
s61 is a Simple Chemical

Species ID: s65
Name: Ca²⁺
s65 is an Ion

Species ID: s71_a1
Name: PKC
s1_a1 is a protein

Species ID: s71_a2
Name: PKC
s1_a2 is a protein
s1_a2 is Active

Reaction ID: r1
r1 is a State_transition
reactant is s71_a1
product is s71_a2

modifier is s61
modifier is s65
modification type is Stimulation
logical_operator is Or

Species ID: s72
Name: Raf1
s72 is a protein

Species ID: S73
Name: Raf1
s73 is a protein
s73has Modification State as phospho
s73 is active

Reaction ID: r2
r2 is a State_Transition
reactant is s72
product is s73

modifier is s71_a2
modification type is Catalysis

BioPAX

DAG is a SmallMolecule

Ca²⁺ is a SmallMolecule

PKC.1 is a protein
has proteinReference PKC
has notEntityFeature Active

PKC.2 is a protein
has proteinReference PKC
has EntityFeature Active

reaction 1 is BiochemicalReaction
has left PKC.1
has right PKC.2
is left-to-right

control1 is a Control
has controller1 DAG
has controller2 Ca²⁺
has controlled Reaction1
has direction in left-to-right

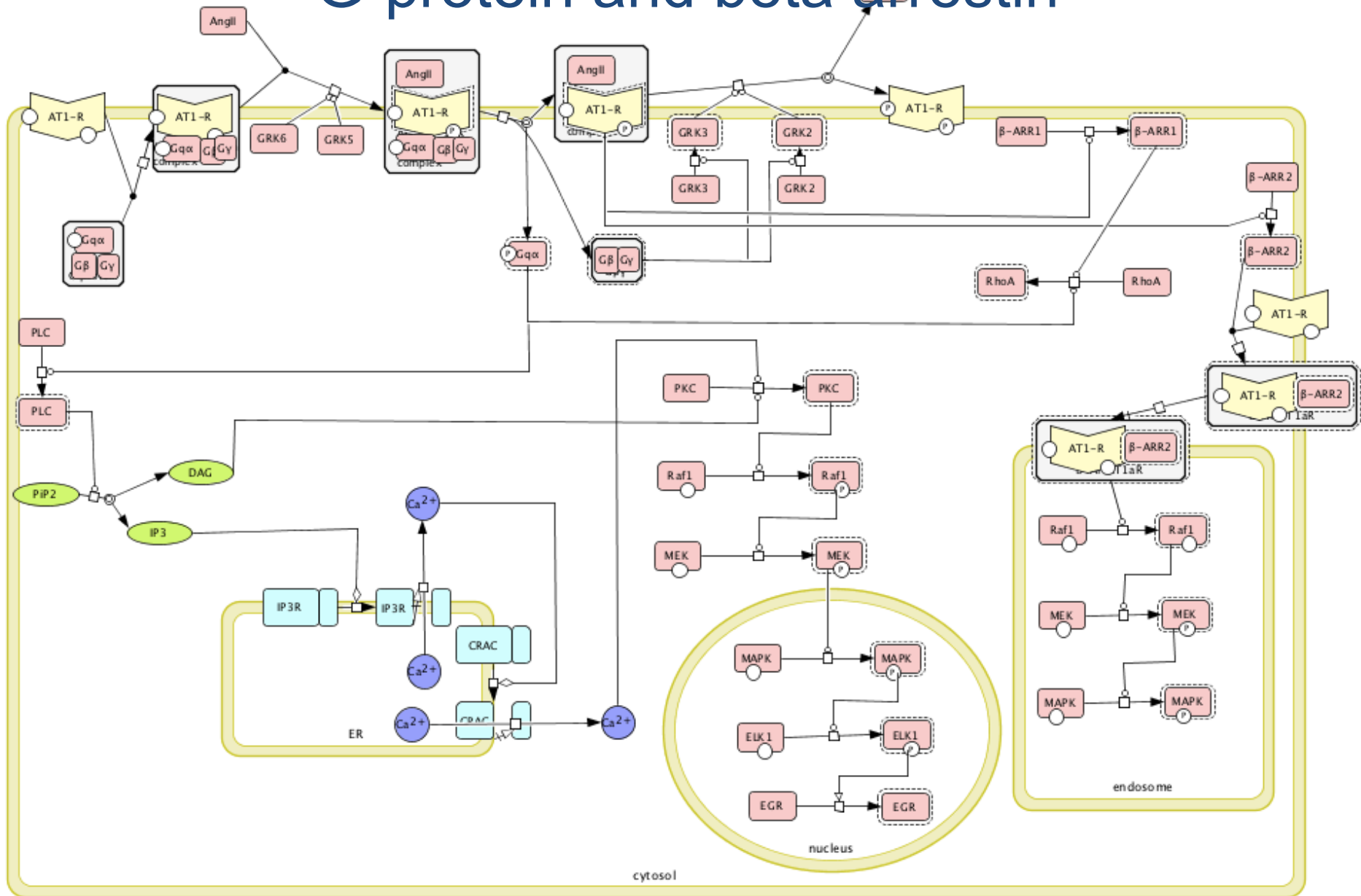
Raf1.1 is a protein
has proteinReference Raf1
has notEntityFeature Active
has notModificationFeature phospho

Raf1.2 is a protein
has proteinReference Raf1
has EntityFeature Active
has ModificationFeature phospho

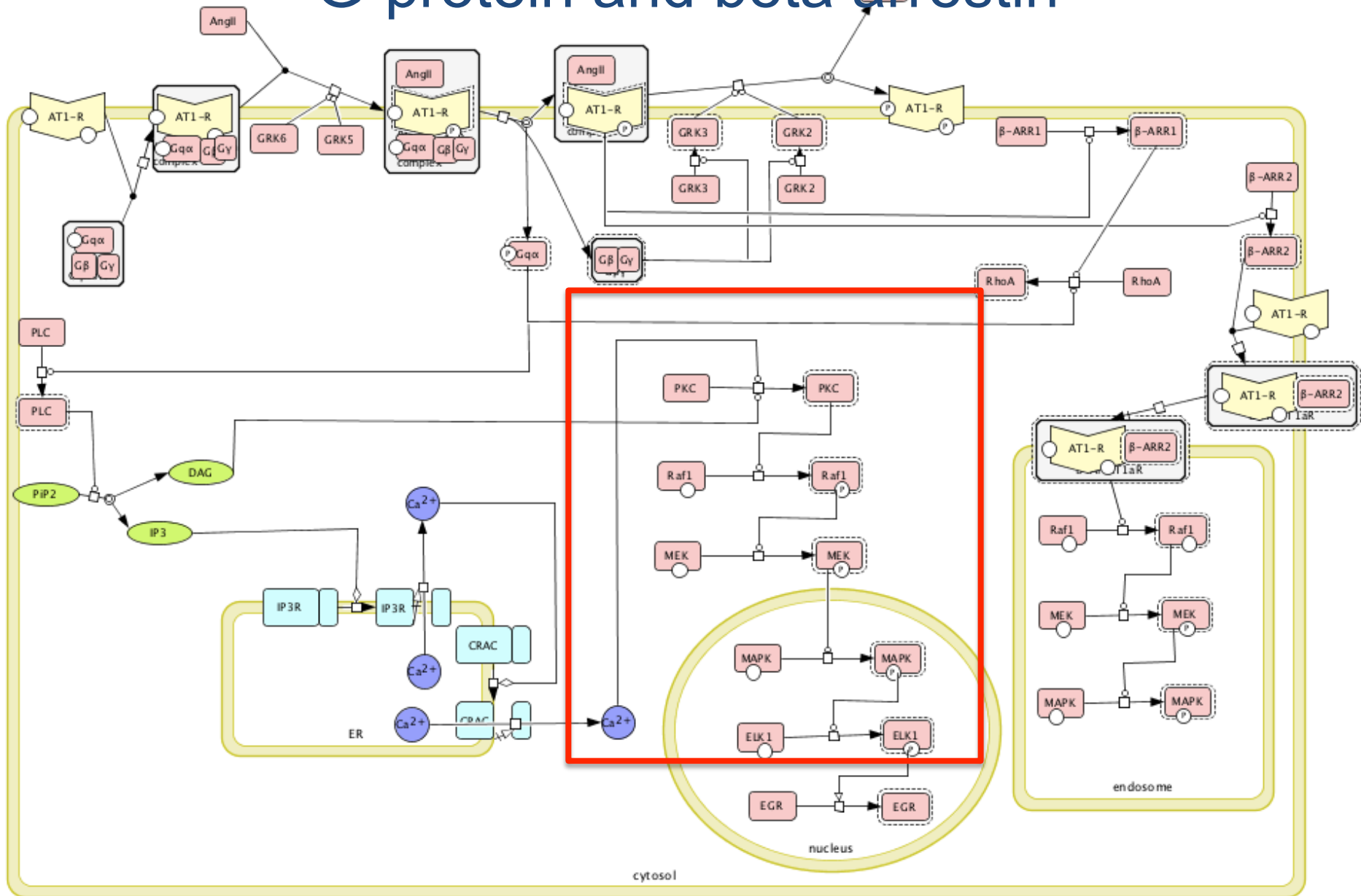
reaction 2 is BiochemicalReaction
has left Raf1.1
has right Raf2.2
is left-to-right

catalysis1 is a Catalysis
has controller1 Raf1.2
has controlled Reaction2
has direction in left-to-right

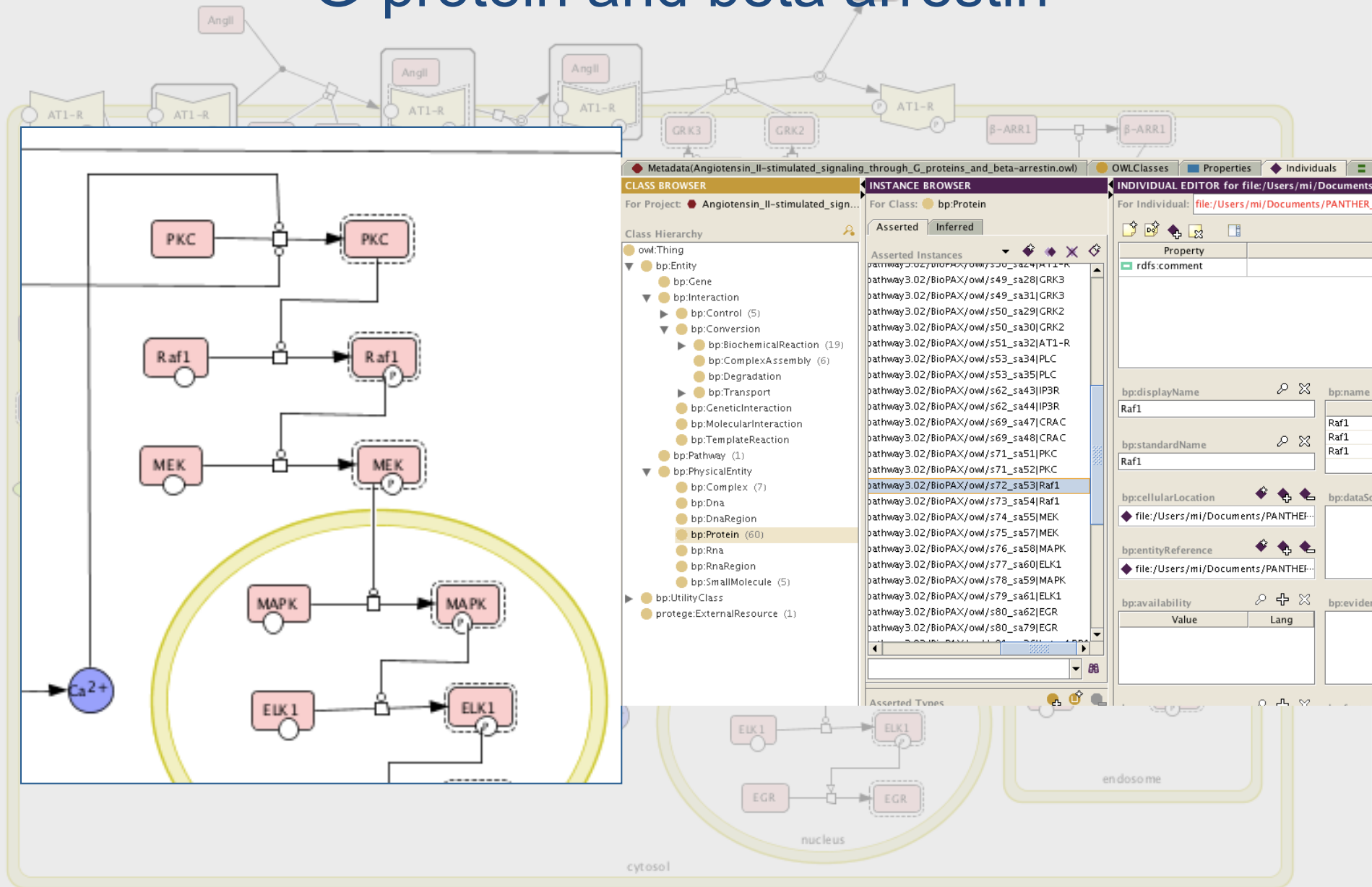
Angiotensin-II stimulating signaling through G-protein and beta arrestin



Angiotensin-II stimulating signaling through G-protein and beta arrestin



Angiotensin-II stimulating signaling through G-protein and beta arrestin



BioPAX support in CellDesigner

The screenshot displays the CellDesigner 4.1 software interface. The 'File' menu is open, and the option 'Export BioPAX Level 3...' is highlighted with a red arrow. The main workspace shows a signaling pathway diagram titled 'Angiotensin_II-stimulated_signaling_through_G_proteins_and_beta-arrestin.xml'. The diagram illustrates the following components and interactions:

- AngII** (Angiotensin II) binds to **AT1-R** (Angiotensin Type 1 Receptor).
- The **AT1-R** is associated with a **Gqα** protein, which is part of a **Gβ** **Gγ** complex.
- The **Gqα** protein is phosphorylated (**P Gqα**).
- The **Gβ** **Gγ** complex is phosphorylated (**P Gβ Gy**).
- The **Gqα** protein activates **GRK5** and **GRK6**.
- The **Gβ** **Gγ** complex activates **GRK3** and **GRK2**.
- GRK5** and **GRK6** phosphorylate the **AT1-R**.
- GRK3** and **GRK2** phosphorylate the **Gqα** protein and the **Gβ** **Gγ** complex.
- The phosphorylated **AT1-R** and **Gqα** protein interact with **PLC** (Phospholipase C).
- PLC** activates **PKC** (Protein Kinase C).
- The phosphorylated **Gqα** protein and **Gβ** **Gγ** complex also interact with **PKC**.
- The phosphorylated **Gqα** protein and **Gβ** **Gγ** complex interact with **AngII**.

BioPAX is supported by PANTHER Pathway



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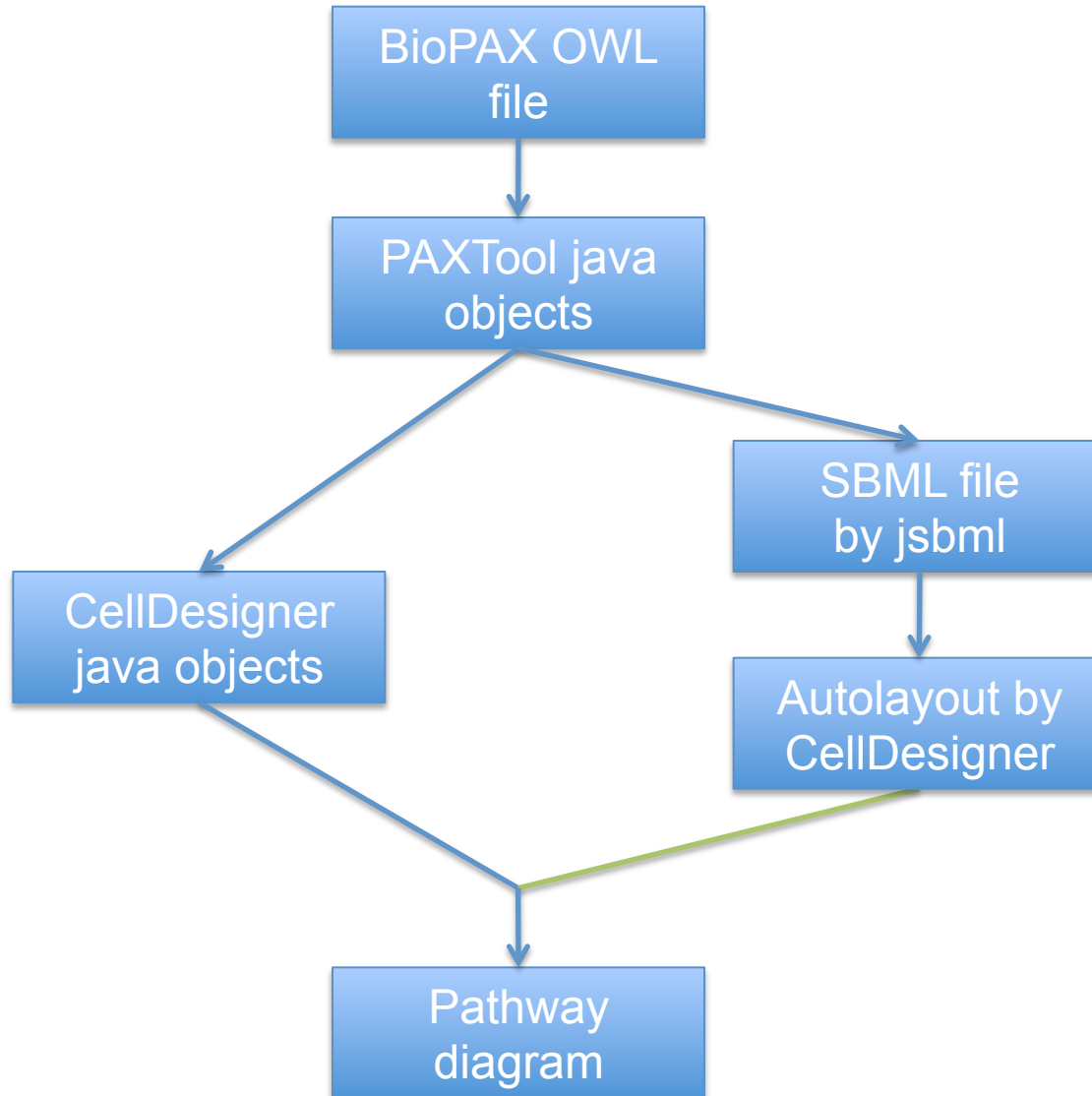
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PANTHER PATHWAYS

Pathway	BioPAX	SBML
2-arachidonoylglycerol biosynthesis	Download	View
5-Hydroxytryptamine biosynthesis	Download	View
5-Hydroxytryptamine degradation	Download	View
5HT1 type receptor mediated signaling pathway	Download	View
5HT2 type receptor mediated signaling pathway	Download	View
5HT3 type receptor mediated signaling pathway	Download	View
5HT4 type receptor mediated signaling pathway	Download	View
Acetate utilization	Download	View
Adenine and hypoxanthine salvage pathway	Download	View
Adrenaline and noradrenaline biosynthesis	Download	View
Alanine biosynthesis	Download	View
Allantoin degradation	Download	View
Alpha adrenergic receptor signaling pathway	Download	View
Alzheimer disease-amyloid secretase pathway	Download	View
Alzheimer disease-presenilin pathway	Download	View
Aminobutyrate degradation	Download	View
Anandamide biosynthesis	Download	View
Anandamide degradation	Download	View



BioPAX → diagram



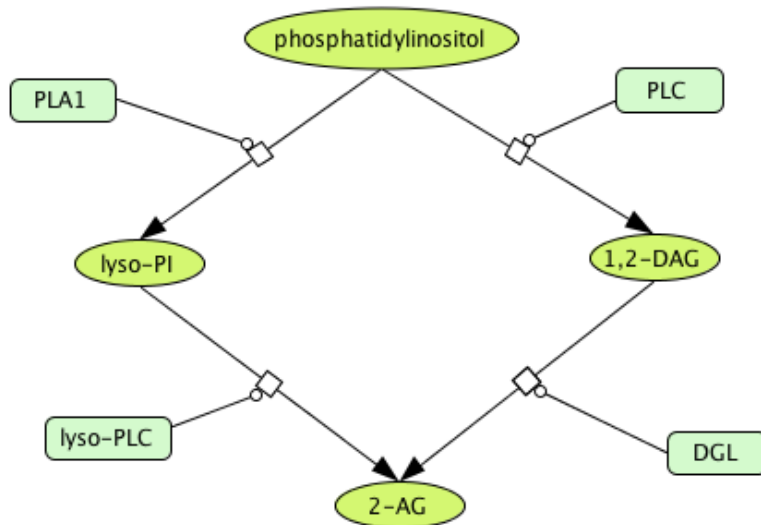
Tests

- PANTHER Pathway diagrams in CellDesigner → BioPAX → Back to CellDesigner.
- BioPAX file from other pathway databases (Reactome, BioCyc) → CellDesigner.

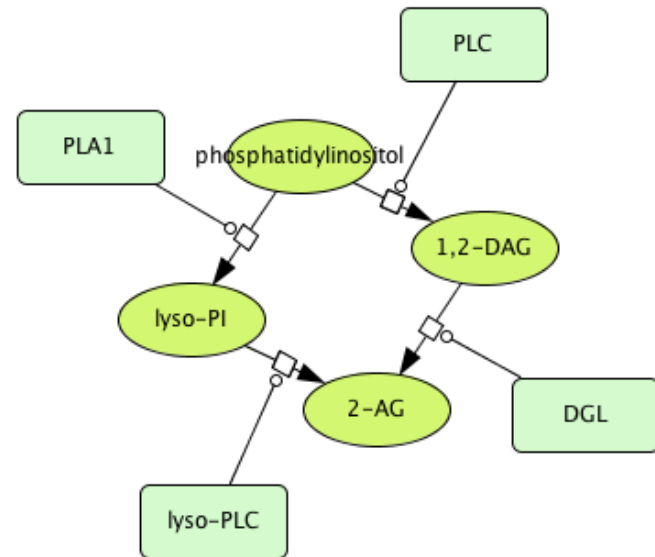
Example

-2-arachidonylglycerol biosynthesis

Curated

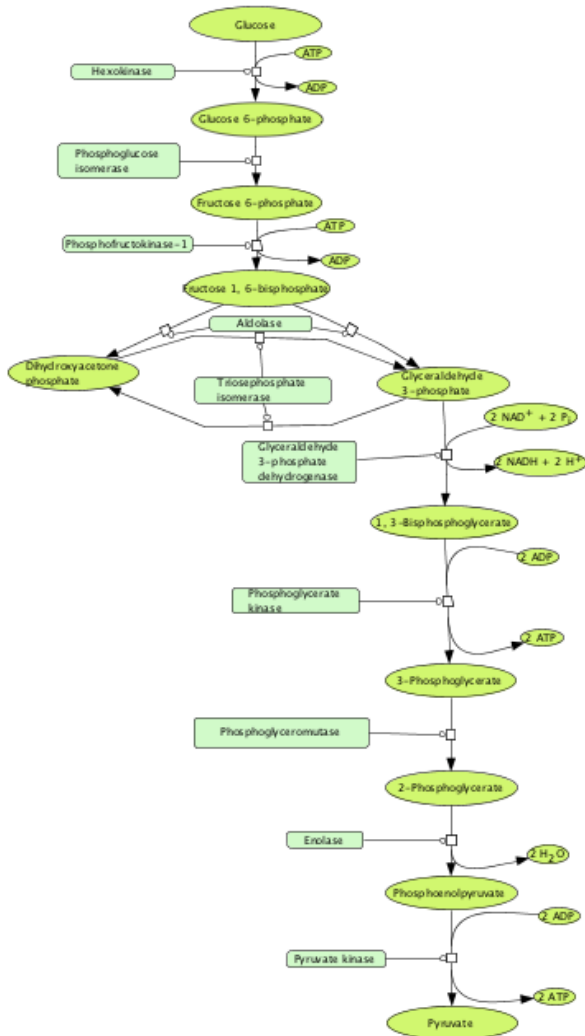


Autolayout

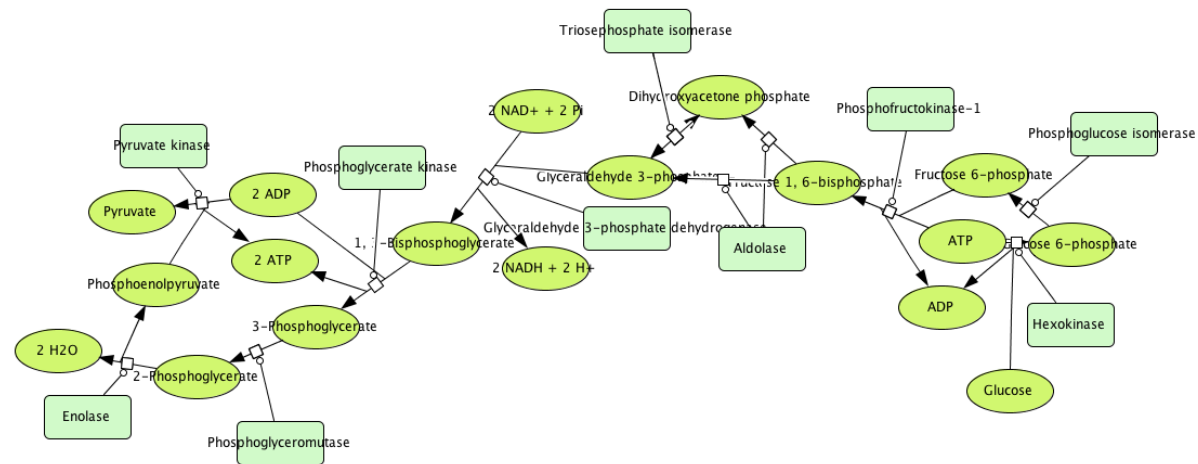


Example -glycolysis

Curated



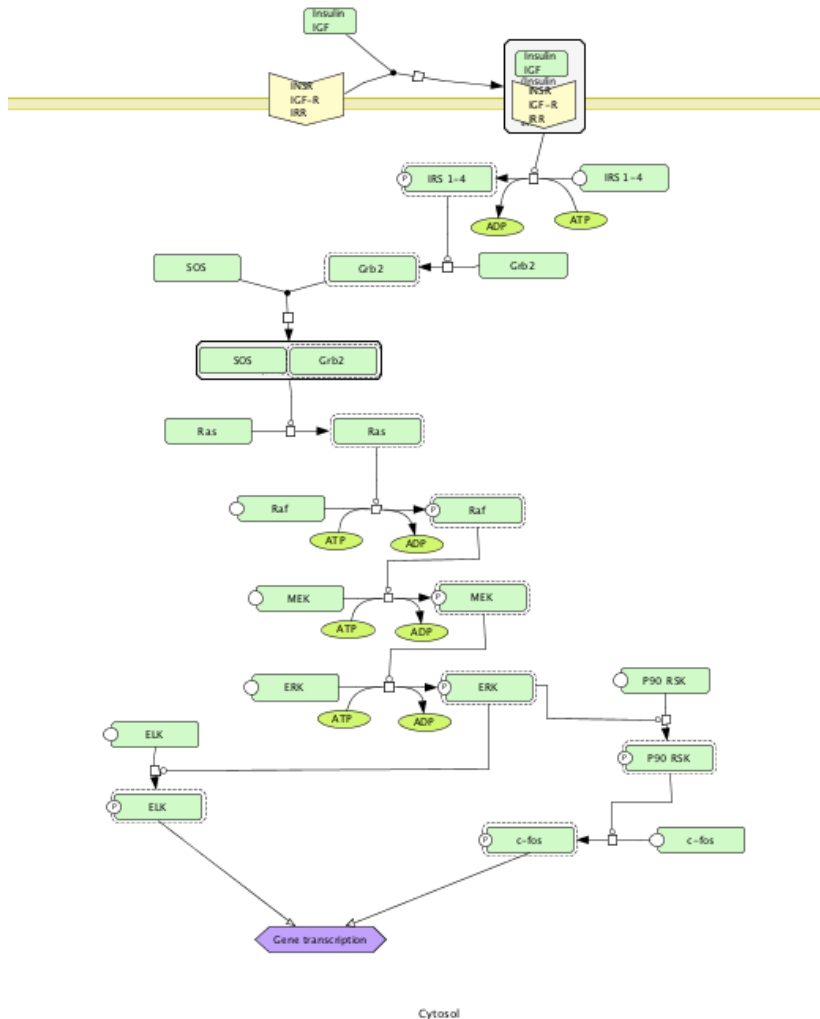
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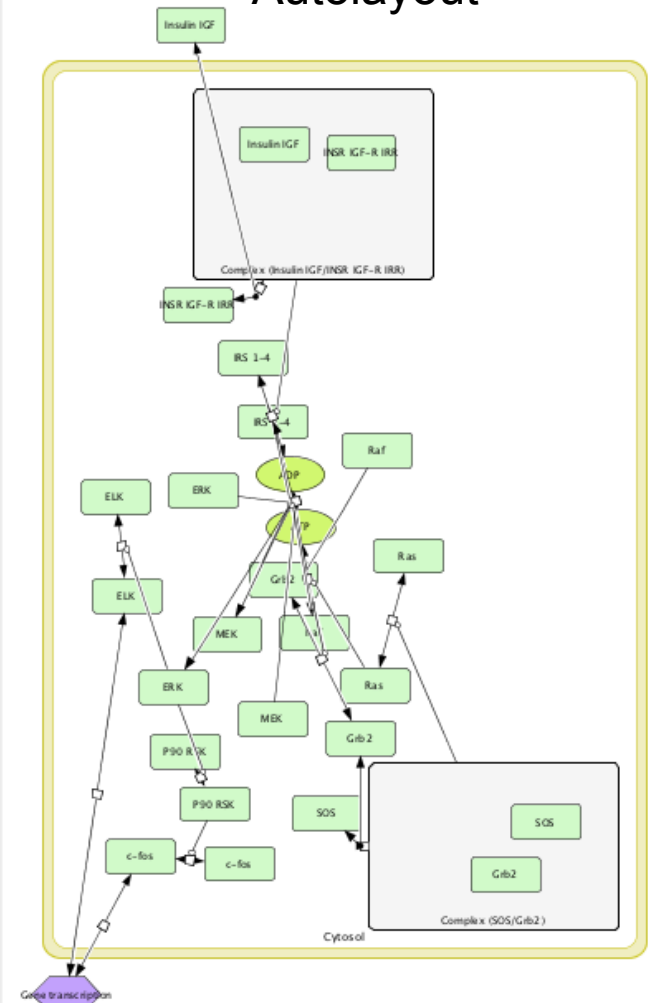
Example

- Insulin/IGF pathway MAP kinase cascade

Curated



Autolayout



Notch signaling pathway from Reactome



Future directions

- Store coordinates using SBGN-ML for BioPAX pathway layout.
- Refine mapping – complex, .
- Improve the layout – SBGN layout rules.

Acknowledgements

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 - Anushya Muruganujan
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