

BioPAX Support in CellDesigner

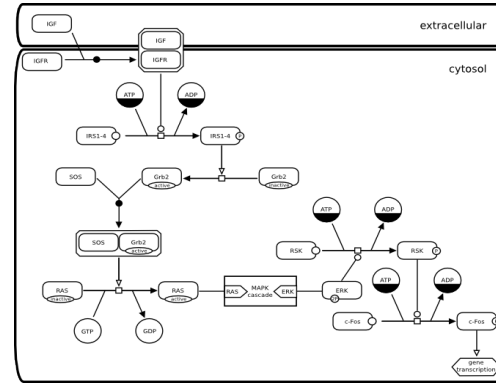
Huaiyu Mi
SRI International



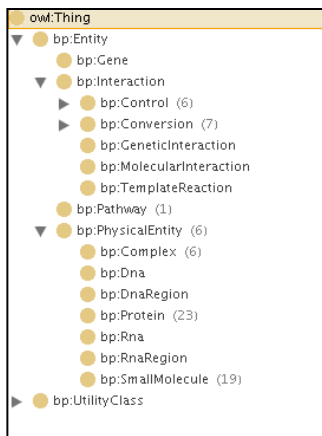
Oct. 7, 2010, COMBINE 2010, Edinburgh, UK



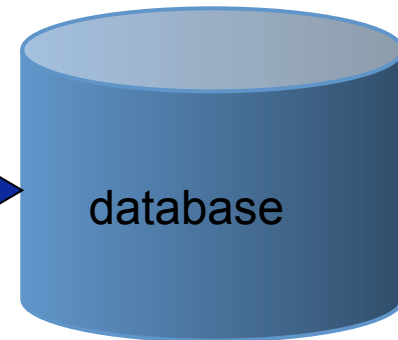
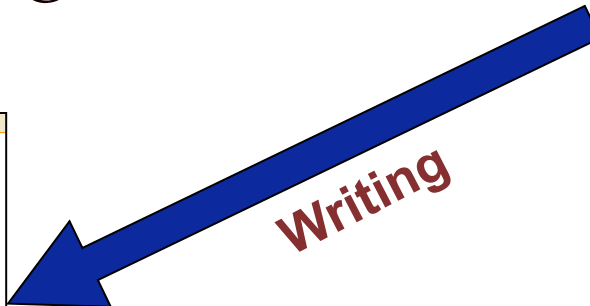
Goals



Model diagram



BioPAX file

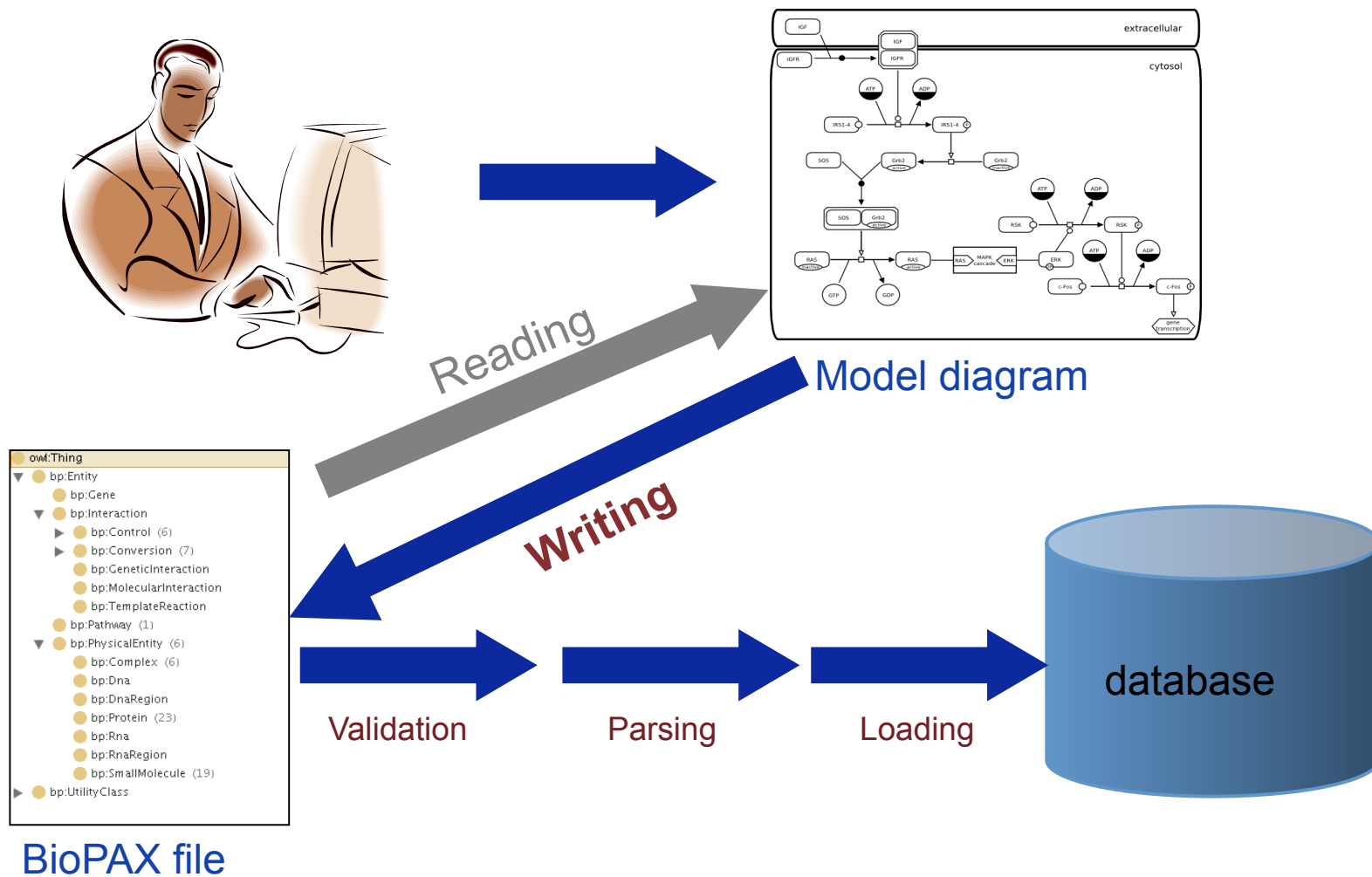


database

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



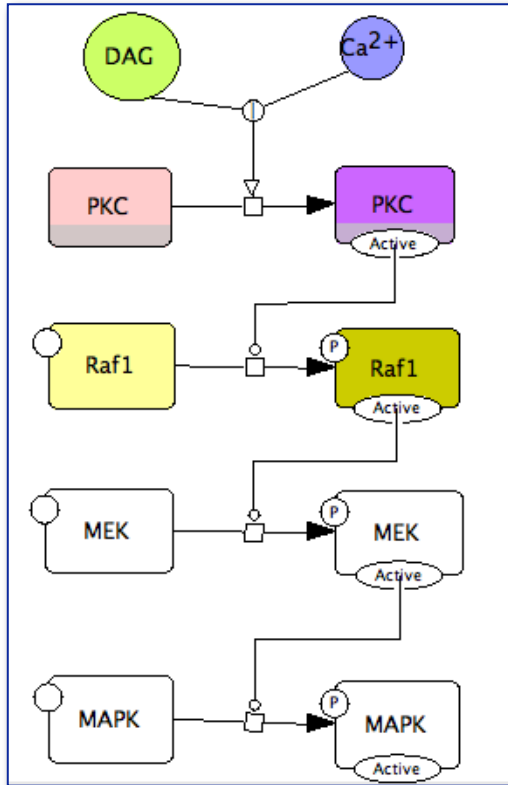
Goals



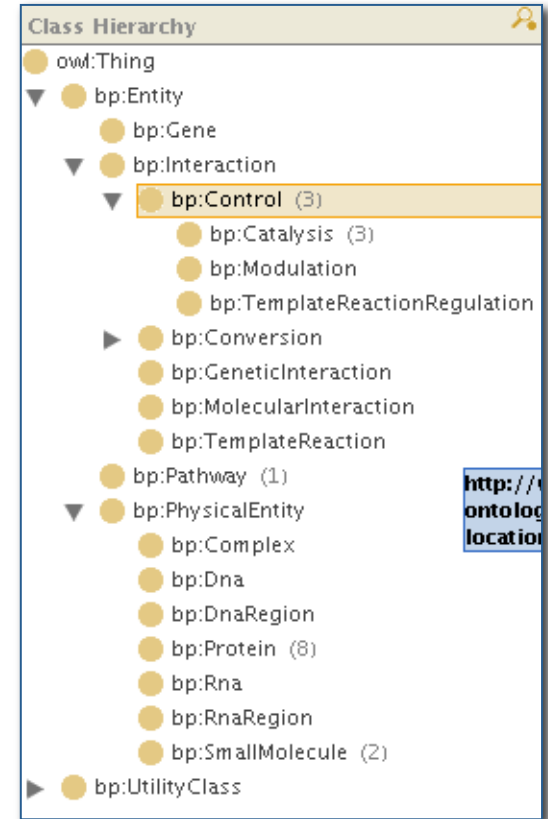
- Allow users to create an SBGN compliant diagram and save it in BioPAX format.
- Allow users to read an BioPAX file and create an SBGN compliant diagram.



Approach

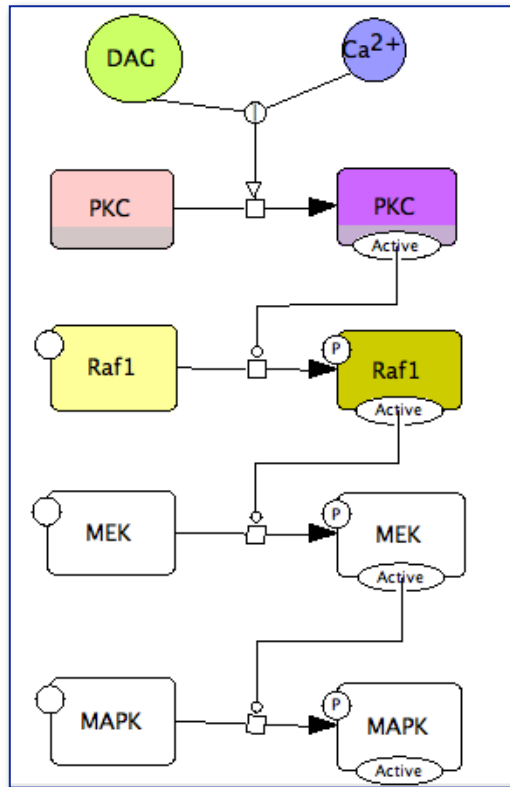


SBGN

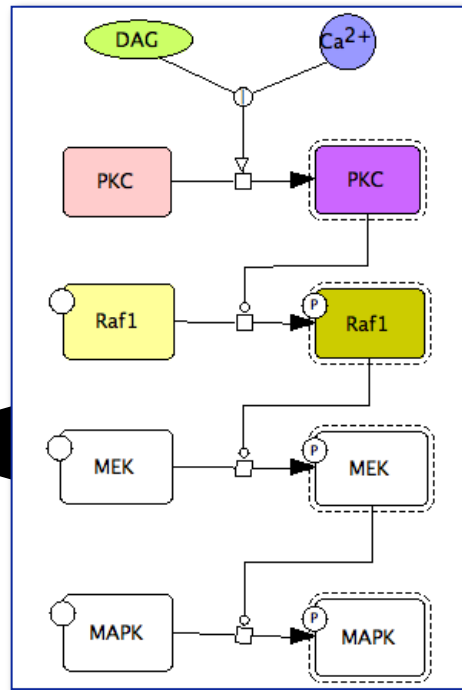


BioPAX

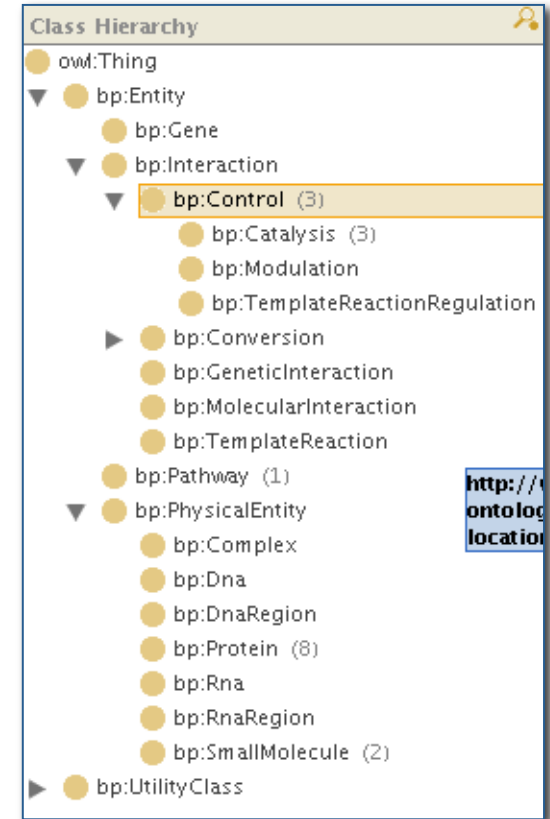
Approach



SBGN



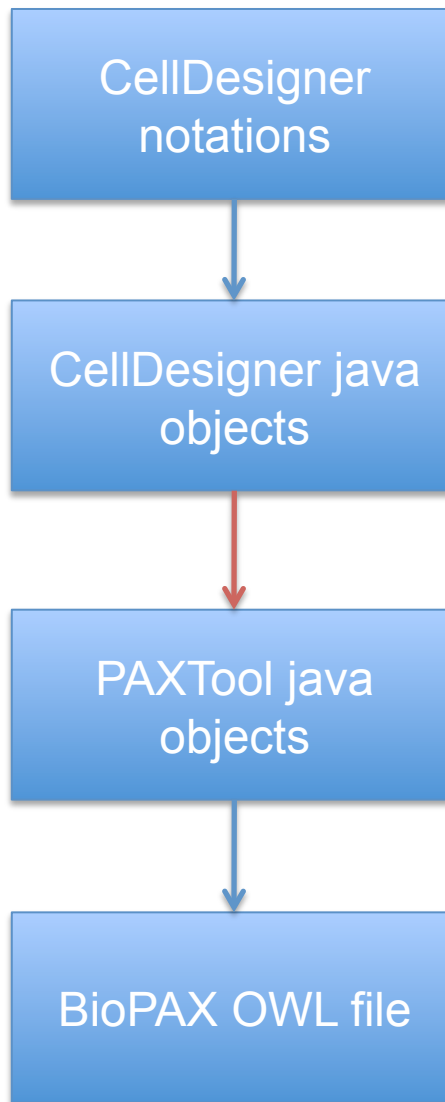
CellDesigner



<http://ontology.location>

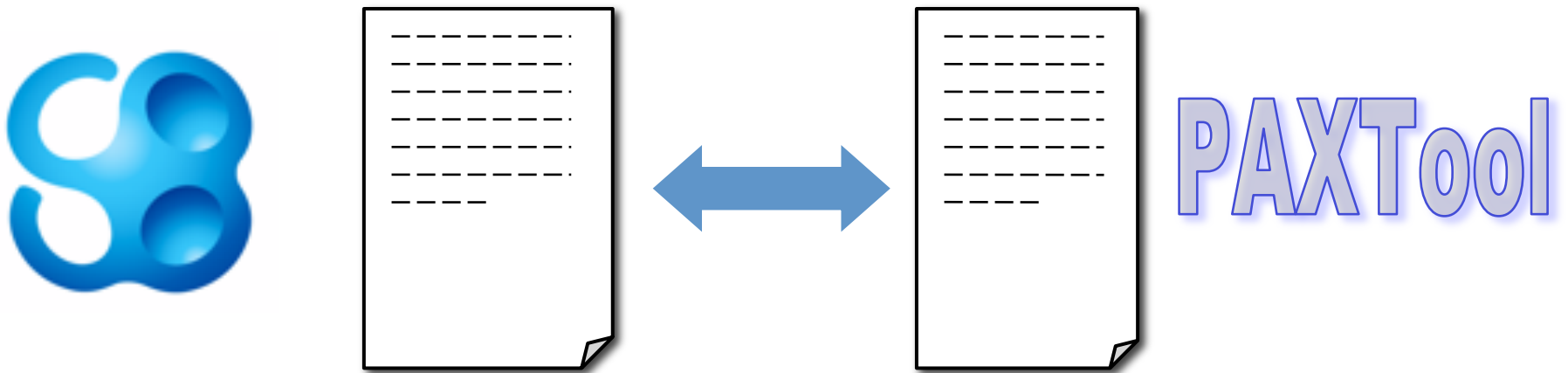
BioPAX

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.



Mapping CellDesigner to BioPAX

| CellDesigner | BioPAX |
|--------------|----------------------------|
| Model | Pathway |
| Species | Physical entity |
| Reaction | Interaction |
| Compartment | CellularLocationVocabulary |

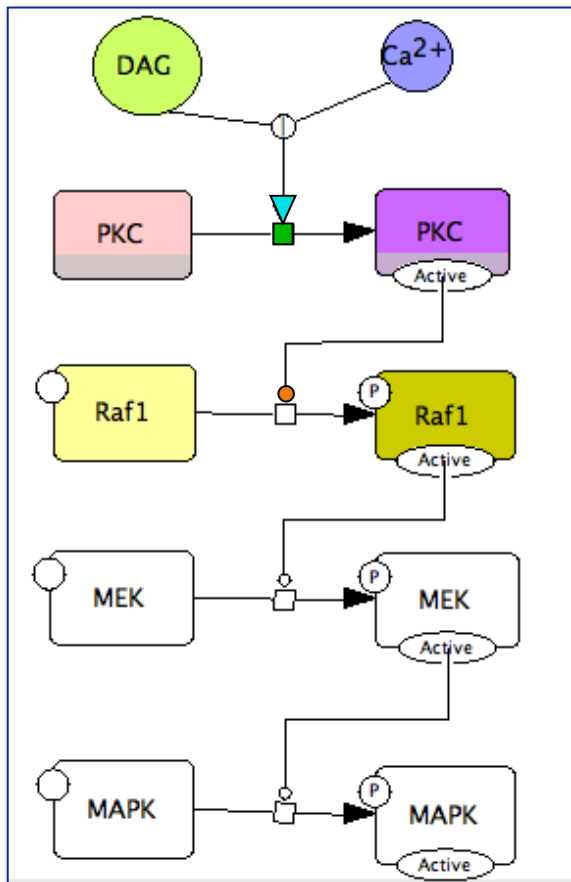
Mapping CellDesigner to BioPAX (Species)

| 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 |

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

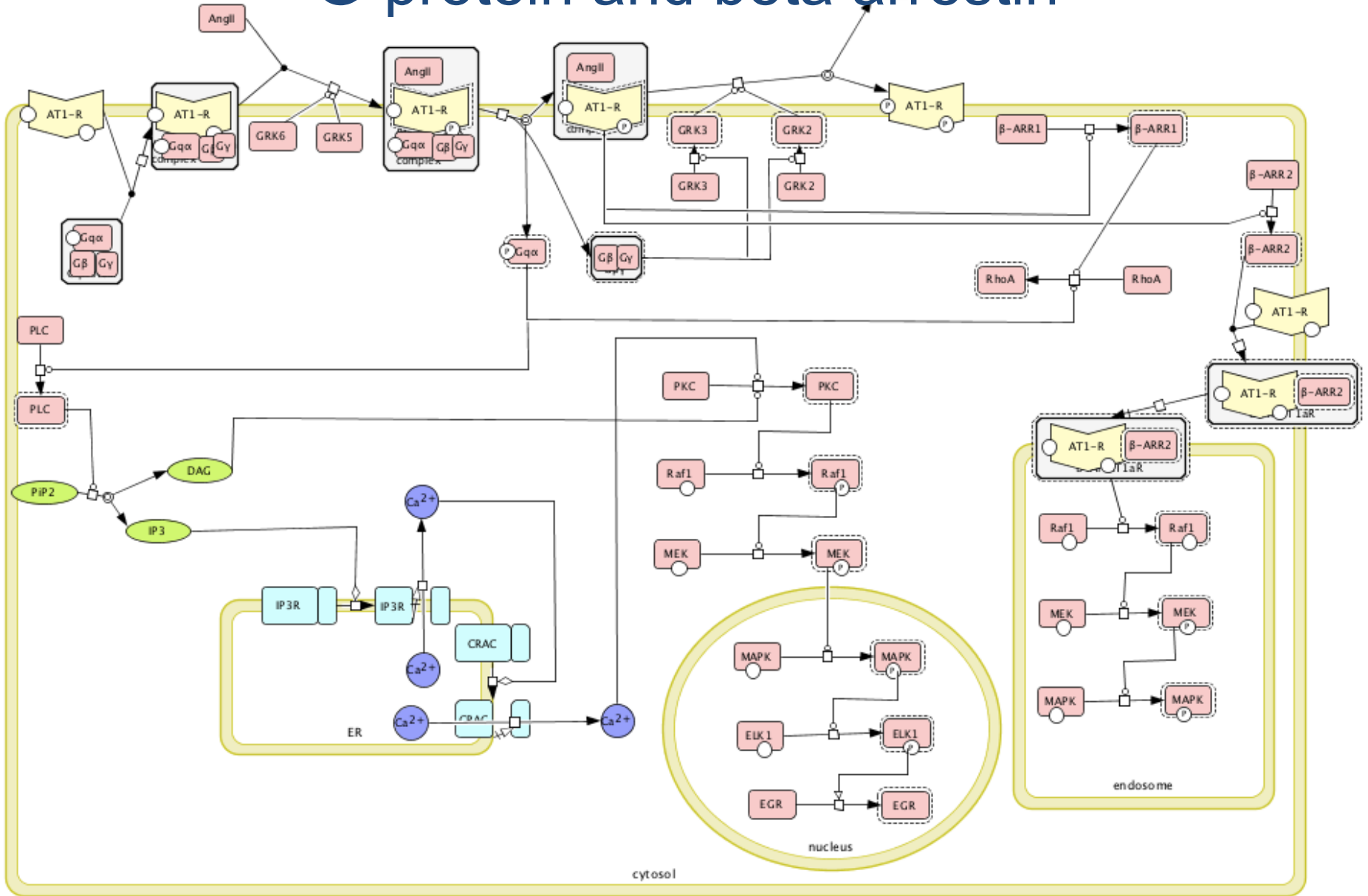
Raf1.1 is a protein
has proteinReference Raf1
has notEntityFeature Active
has notModificationFeature phospho

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

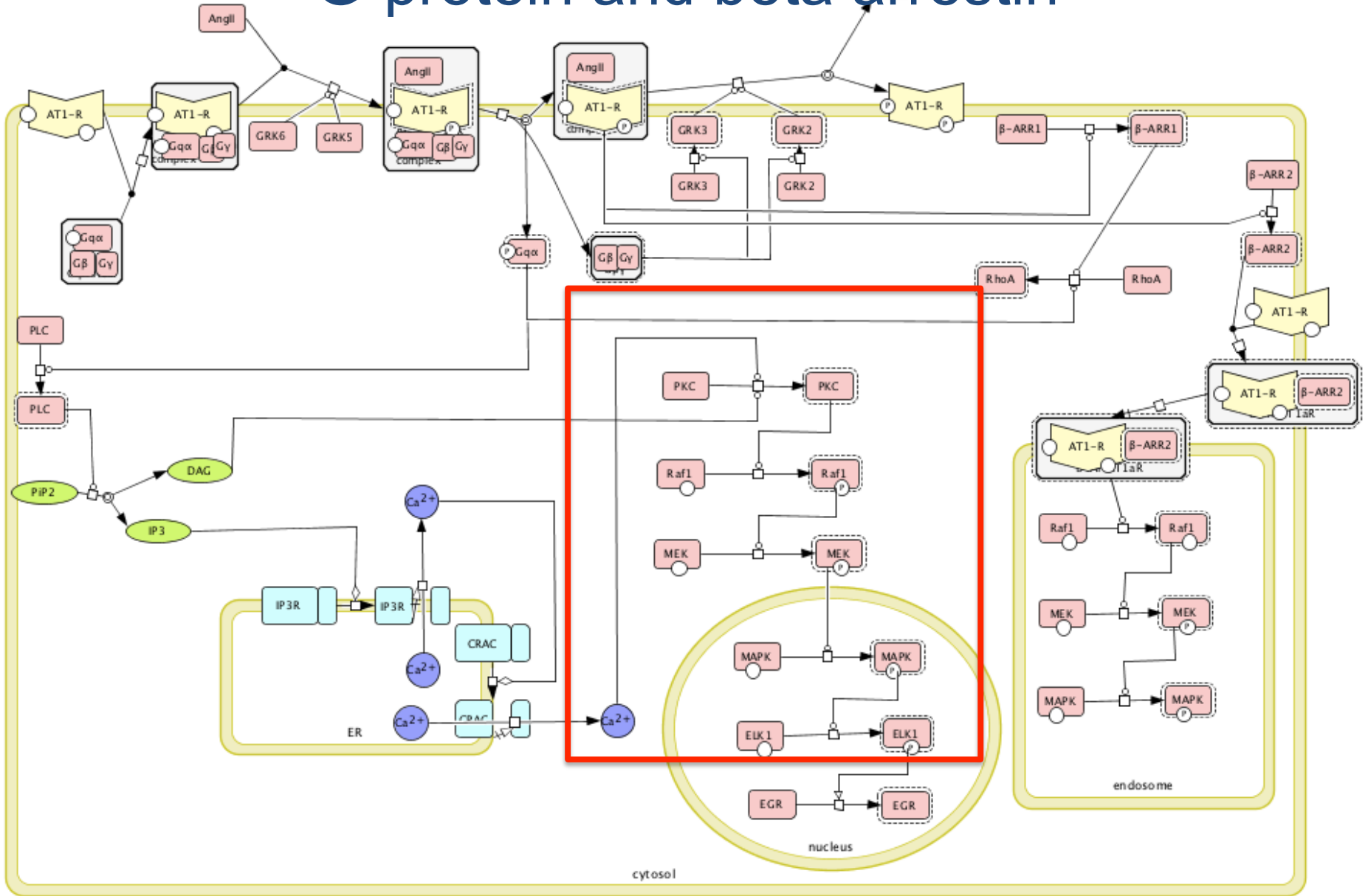
reaction 2 is BiochemicalReaction
has left Raf1.1
has right Raf1.2
is left-to-right

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

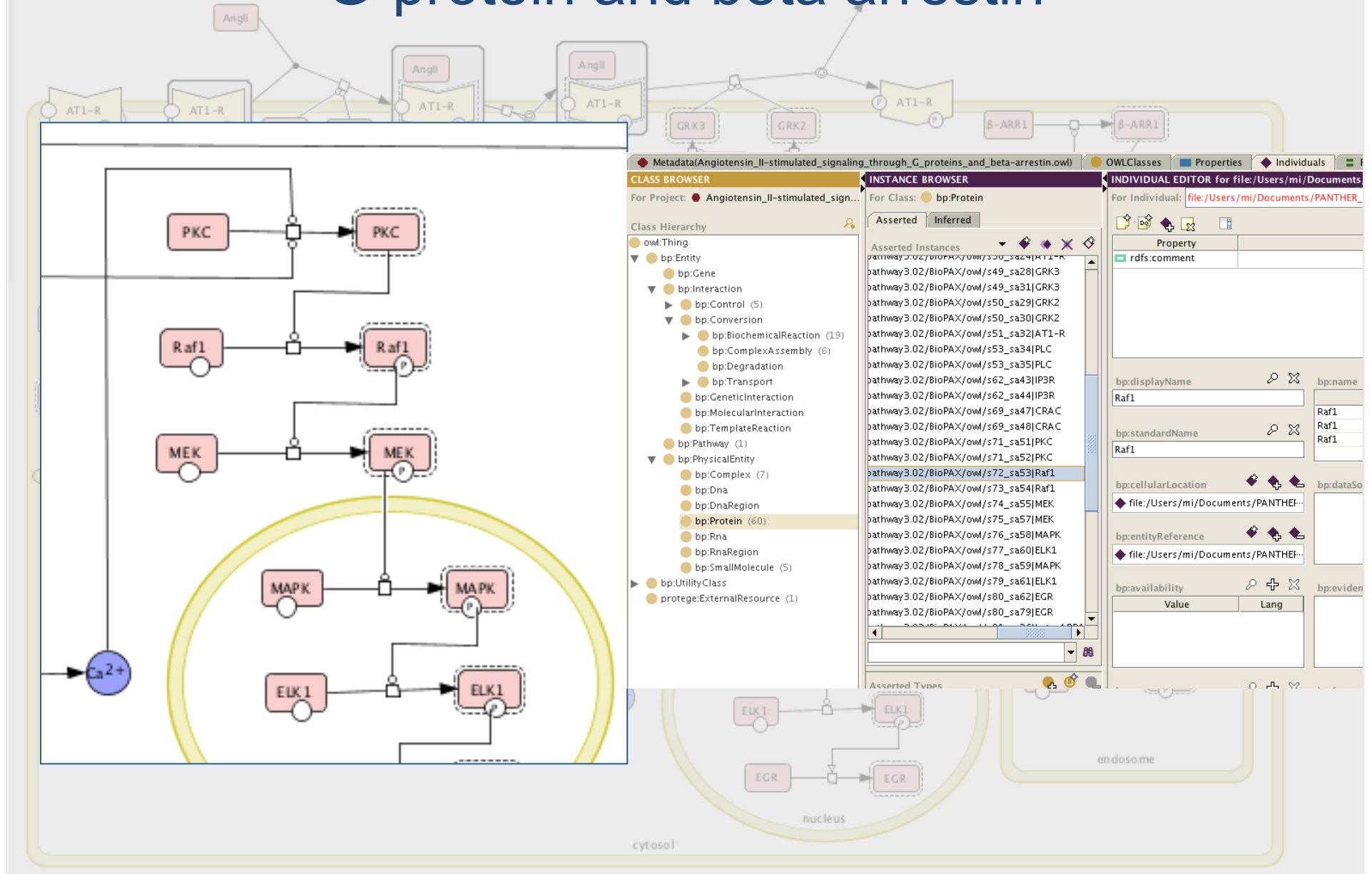
Angiotensin-II stimulating signaling through G-protein and beta arrestin



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 shows the CellDesigner 4.1 interface. The 'File' menu is open, and the option 'Export BioPAX Level 3...' is highlighted with a red arrow. The main workspace displays 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**: The initial stimulus, shown as a pink box.
- AT1-R**: The Angiotensin II receptor, shown as a yellow box with a 'P' (phosphorylation) and 'COOH' label.
- Gqα, Gβ, Gy**: G proteins, shown as pink boxes. The Gqα subunit is phosphorylated (P-Gqα).
- GRK6, GRK5, GRK3, GRK2**: G protein-coupled receptor kinases, shown as pink boxes.
- PLC**: Phospholipase C, shown as a pink box.
- PKC**: Protein kinase C, shown as a pink box.

The diagram shows AngII binding to AT1-R, which activates the Gqα subunit. This leads to the activation of GRK6 and GRK5, which in turn phosphorylate Gqα. The phosphorylated Gqα subunit then activates PLC, which leads to the activation of PKC. Additionally, AT1-R is phosphorylated, which activates GRK3 and GRK2. GRK3 and GRK2 then phosphorylate Gβ and Gy, leading to the activation of PKC. The diagram also shows AngII binding to another AT1-R, which activates GRK3 and GRK2, leading to the activation of PKC.

BioPAX is supported by PANTHER Pathway



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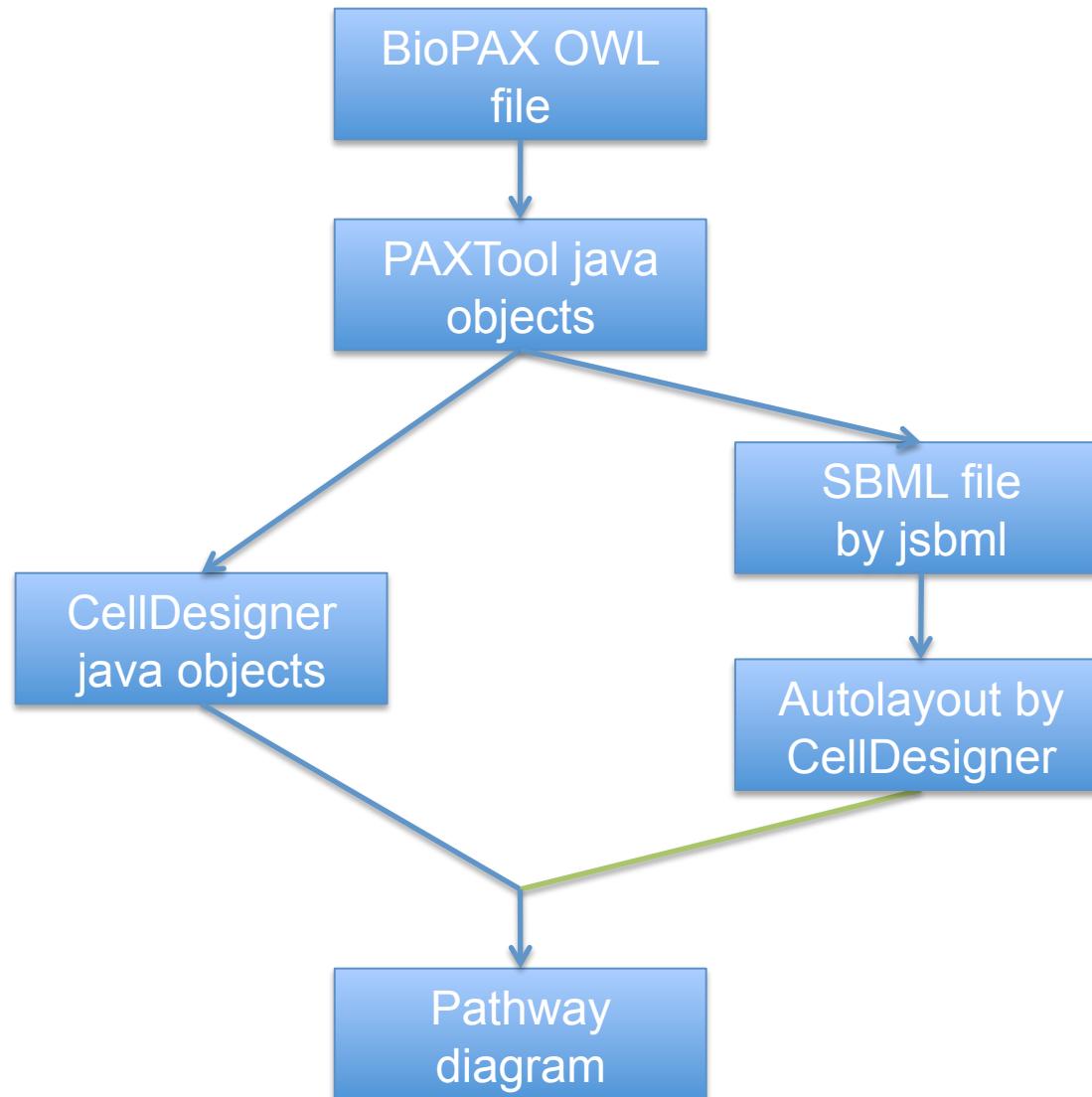
Enter your Email:

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



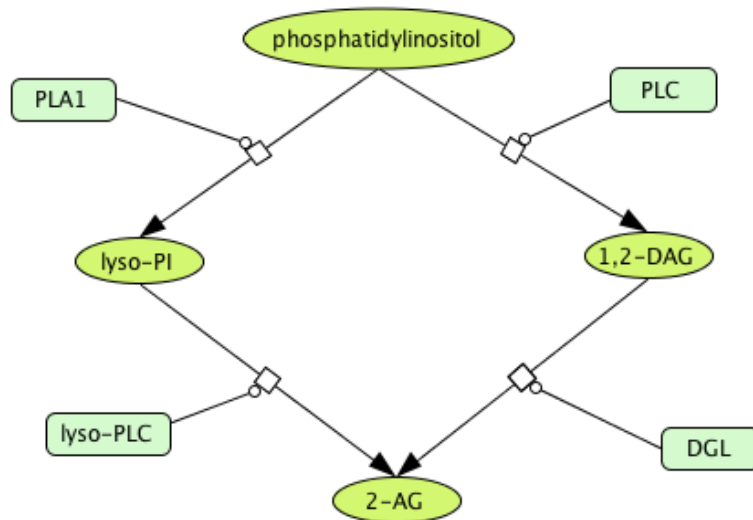
Tests

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

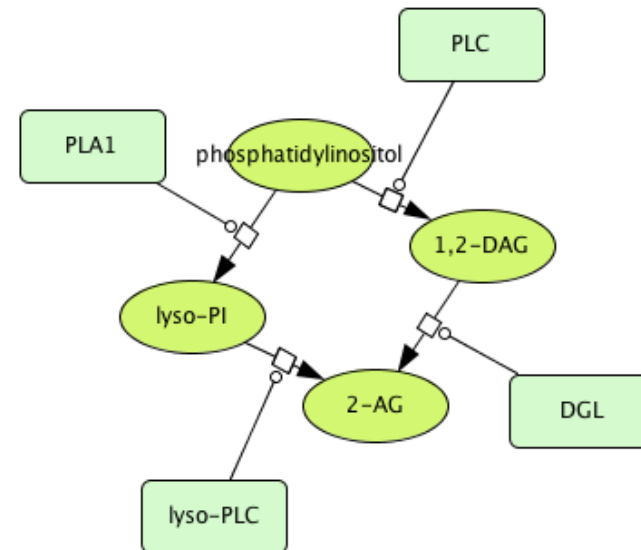
Example

-2-arachidonylglycerol biosynthesis

Curated



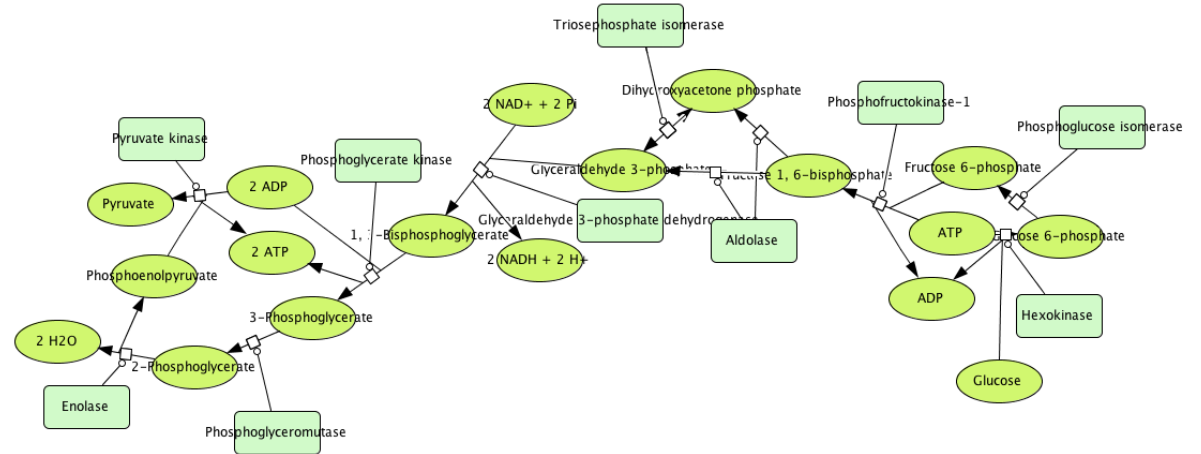
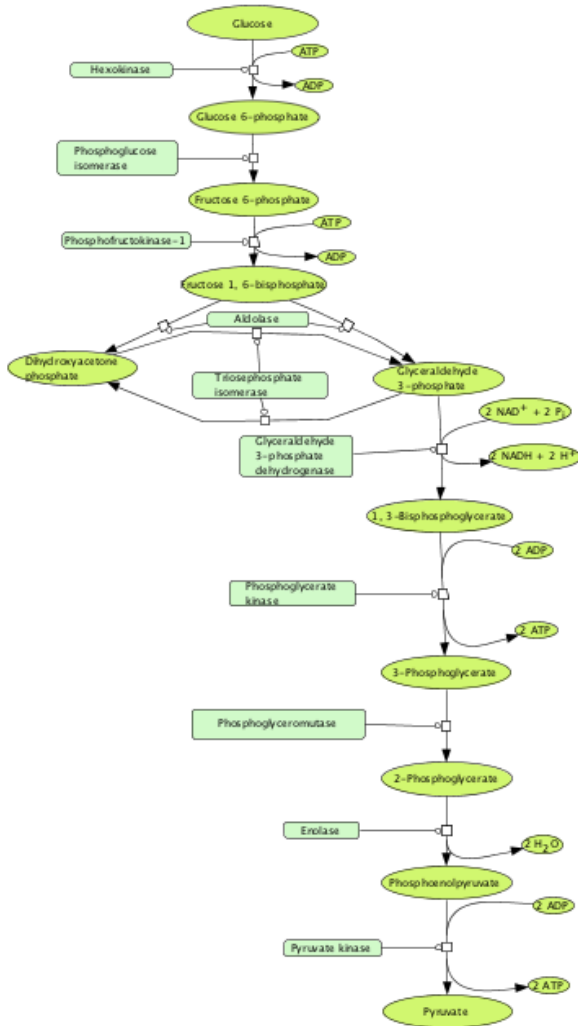
Autolayout



Example -glycolysis

Curated

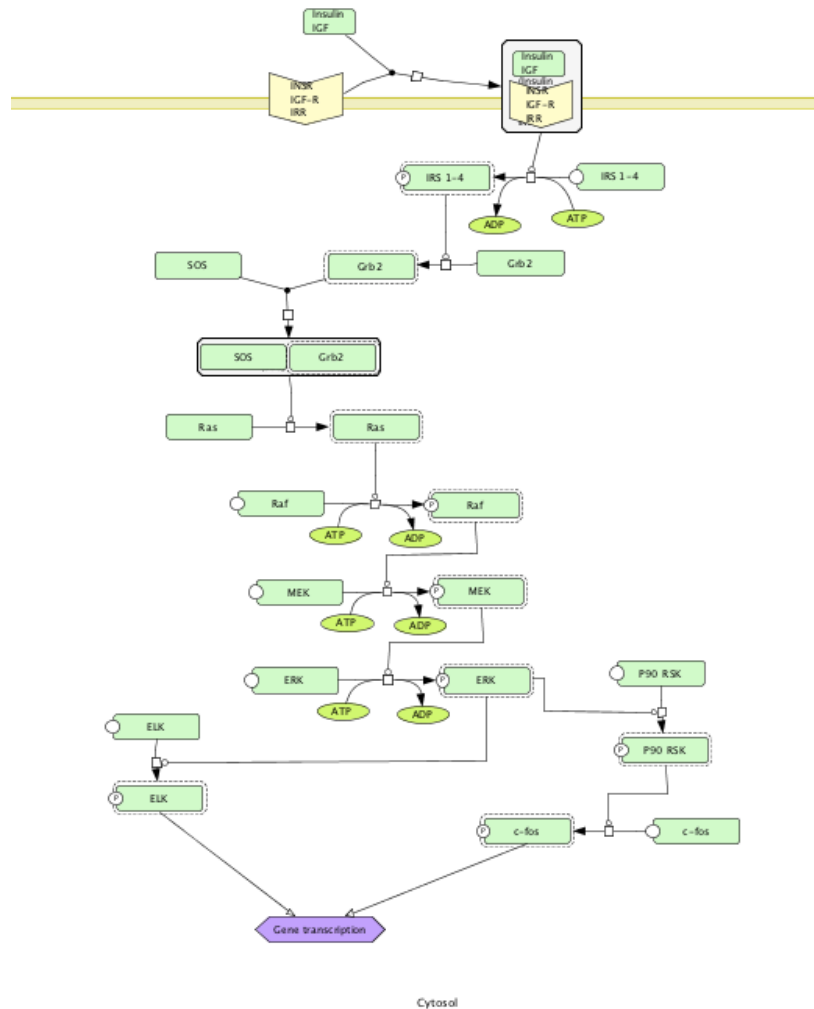
Autolayout



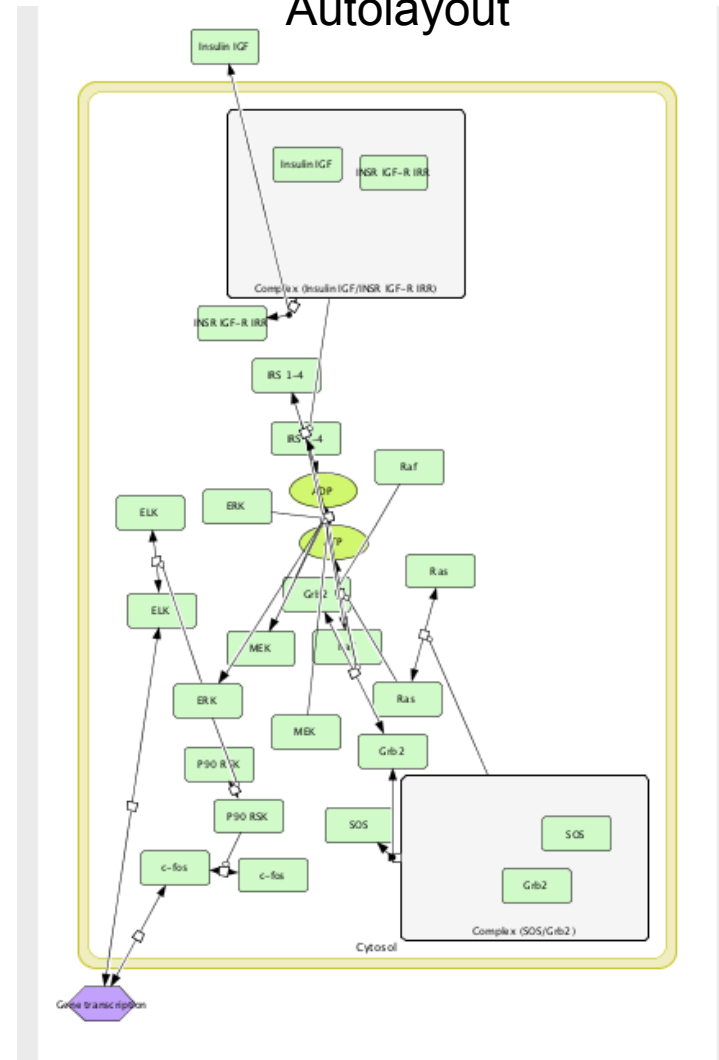
Example

- Insulin/IGF pathway MAP kinase cascade

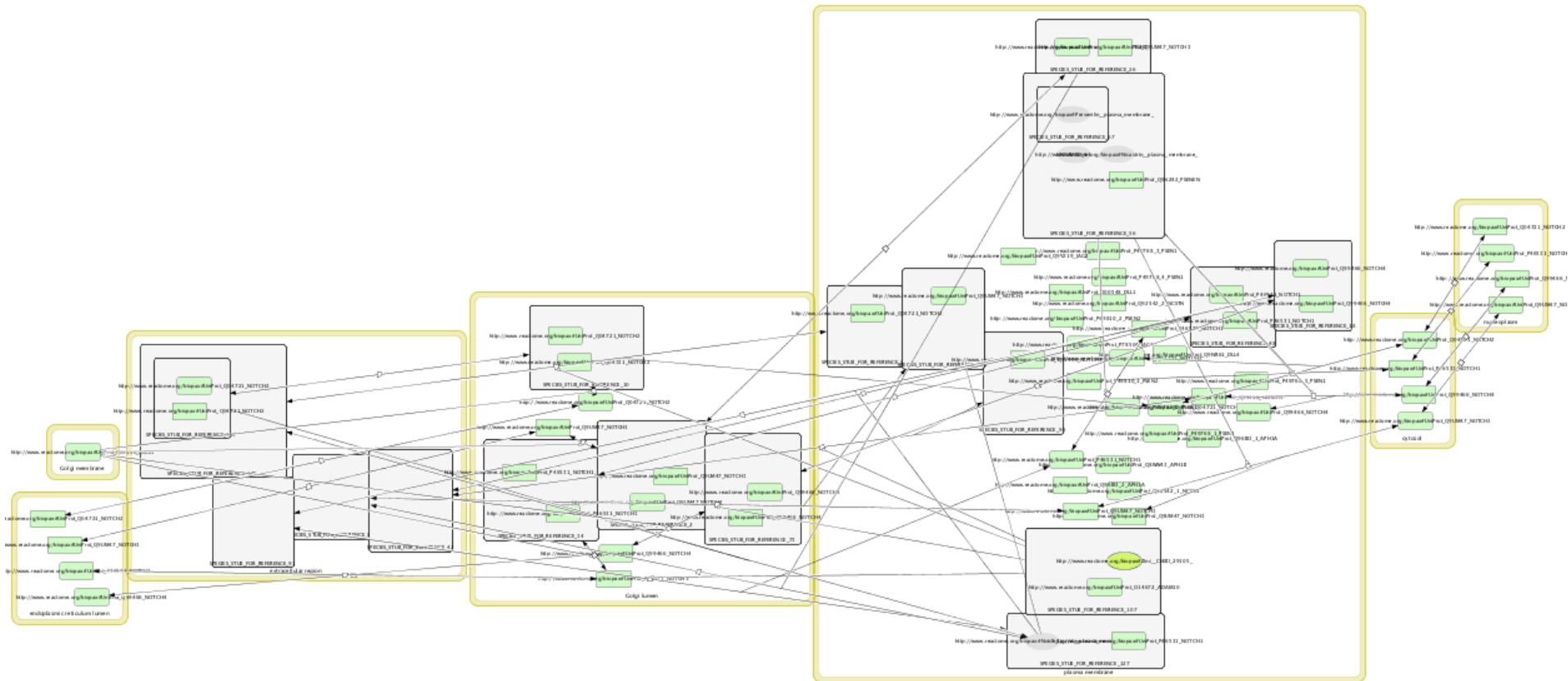
Curated



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

- SRI
 - Anushya Muruganujan
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