# Introduction to Pathway Commons

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# Topics to be Covered

- Overview of BioPAX and Pathway Commons
- Accessing Pathway Commons (PC) using `paxtoolsr`
  - Searching PC
  - Visualizing PC Data
  - Overlaying Experimental Data on PC Networks
  - Getting Network Statistics
  - Gene Set Enrichment with PC
  - ID Mapping

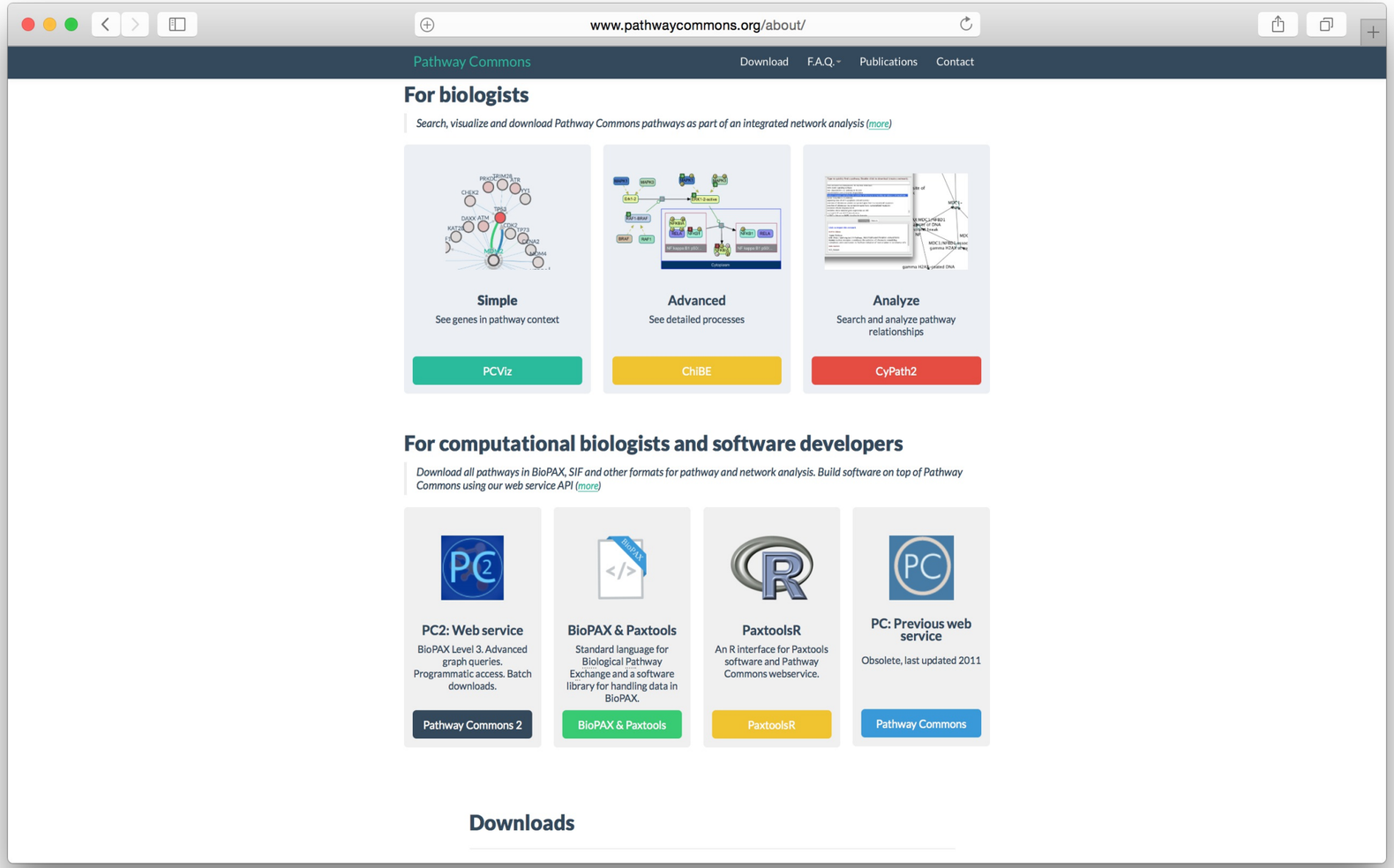
# What is Pathway Commons?

- Website: http://www.pathwaycommons.org/
- An aggregation of public pathway database information
- Provides data in multiple formats
  - Biological Pathway Exchange (BioPAX) Format
  - Simple Interaction Format (SIF)
  - Gene sets as Gene Matrix Transposed (GMT) Format
- Provides infrastructure for searching the aggregated pathway data

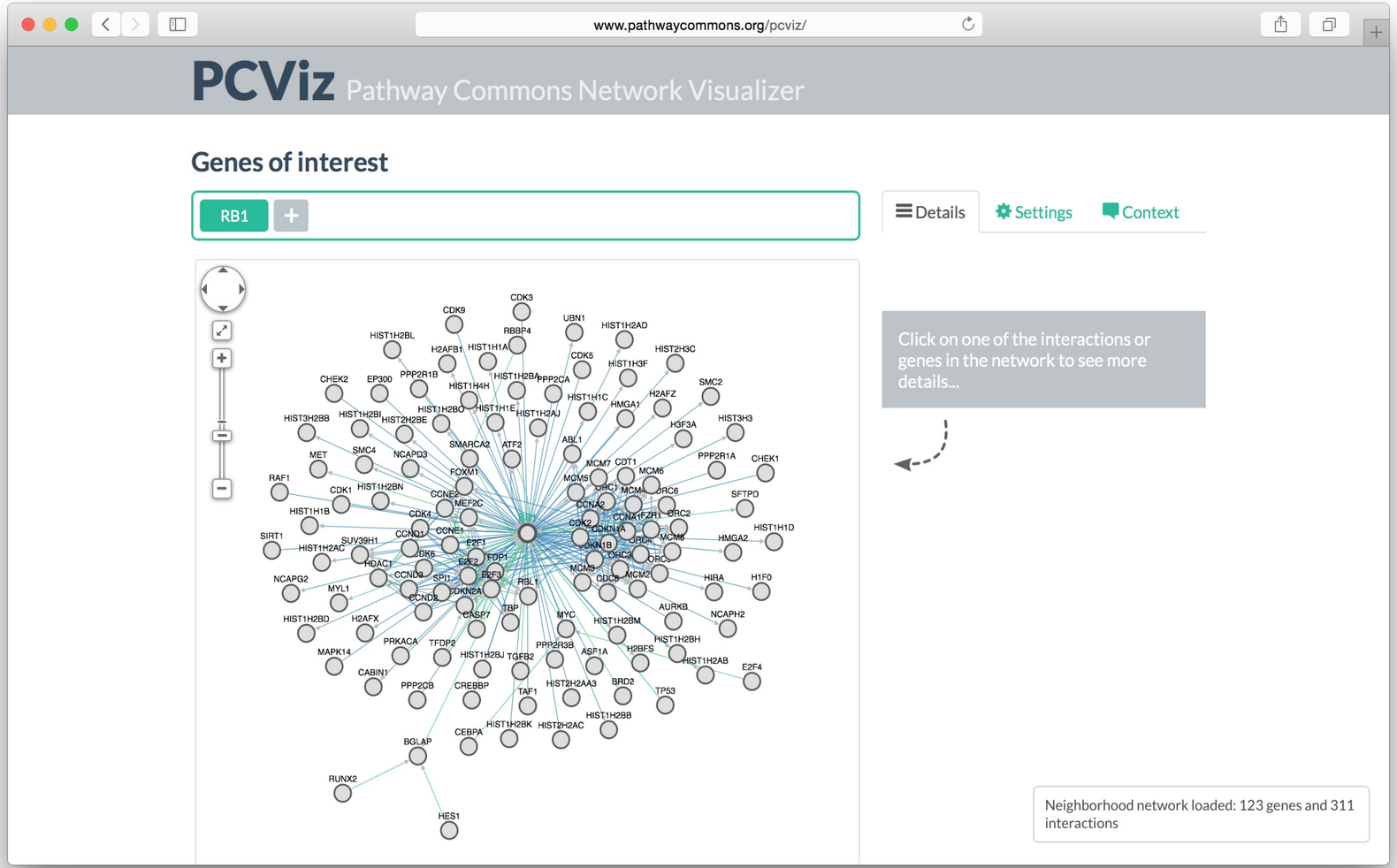
# Biological Pathway Exchange (BioPAX) Format

- BioPAX: http://biopax.org/
- Community-wide effort to represent biological pathways
  - Pathways are collections of interactions that biologists have found useful to group together for organizational, historic, biophysical or other reasons
- Types
  - Metabolic pathways
  - Signaling pathways
  - Protein-protein interactions
  - Gene regulatory pathways
- Advanced tutorial on BioPAX
  - https://github.com/cannin/biopaxTutorial

# Pathway Commons Homepage



# Pathway Commons Visualizer



# Pathway Commons Datasets

| Database | Interaction Count |
|---|---|
| Reactome | 11924 |
| NCI PID | 16017 |
| PhosphoSitePlus | 13642 |
| HumanCyc | 7024 |
| HPRD | 40618 |
| PantherDB | 5282 |
| DIP | 7102 |
| BioGRID | 244843 |

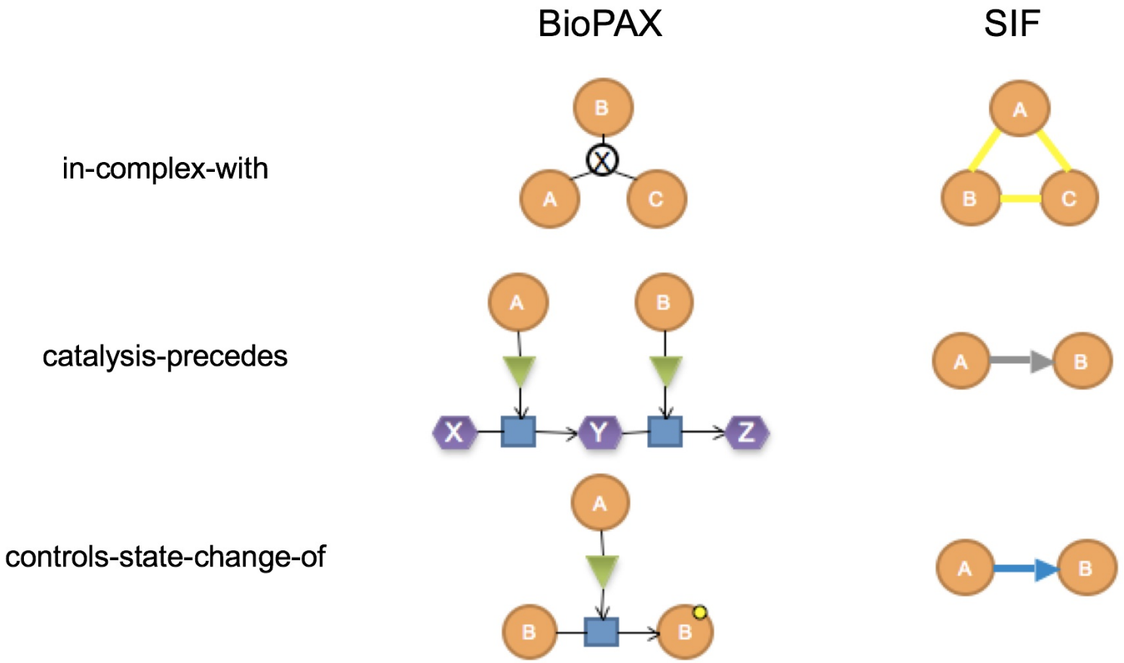
| Database | Interaction Count |
|---|---|
| InAct | 98347 |
| BIND | 35566 |
| TRANSFAC | 261624 |
| mirTarBase | 51214 |
| DrugBank | 19159 |
| Recon X | 10910 |
| CTD | 313174 |
| KEGG | 4472 |

# Simple Interaction Format (SIF)

- An edgelist with interaction type: 3 columns
  - PARTICIPANT_A, INTERACTION_TYPE, PARTICPANT_B
- Expected representation for many network analyses
- Extracted using graph queries that detect biologically interesting interaction patterns in Pathway Commons data
  - Complexes, metabolic, modification, control interactions
  - Generates binary interactions and integrates them across databases

# SIF Interaction Types

- Complete list of interaction types in Google Docs
- Examples of conversions from BioPAX to SIF




14 Interaction Types Total

# Gene Set (GMT) Format

| Gene Set | Description | Gene 1 | Gene 2 | Gene 3 | … |
|---|---|---|---|---|---|
| KEGG_GLYCOLYSIS_GLUCONEOGENESIS | KEGG | GCK | PGK2 | PGK1 | … |
| REACTOME_SIGNALING_BY_EGFR_IN_CANCER | Reactome | AKT3 | ADAM10 | SPRY1 | … |

# What is paxtoolsr?

- Website and Tutorial (Vignette):
  - https://bioconductor.org/packages/release/bioc/html/paxtoolsr.html
- Publication:
  - http://www.ncbi.nlm.nih.gov/pubmed/26685306
- Read and write
  - Biological Pathway Exchange (BioPAX)
  - Binary Simple Interaction Format (SIF)
  - Extended SIF: Includes additional information about SIF network
  - Gene Set (GMT)
  - Systems Biology Graphical Notation Markup Language (SBGN-ML)
- Search and summarize local BioPAX files
- Search Pathway Commons

# Enrichment Analysis with Pathway Commons and CellMiner

- Example on conducting an enrichment analysis on CellMiner cell line data using gene sets from Pathway Commons

```
# Load libraries
library(paxtoolsr); library(rcellminer)

# Load data
geneSets <- downloadPc2("Pathway Commons.7.Reactome.GSEA.hgnc.gmt.gz")
mutData <- getAllFeatureData(rcellminerData::molData)[["mut"]]

hiMutGenes <- head(sort(rowSums(mutData), decreasing=TRUE), 25)

# Initialize variable
pvals <- NULL

for(set in geneSets) {
  #set <- hiMutGenes
  sampleSize <- length(hiMutGenes) # size drawn
  hitInSample <- length(which(hiMutGenes %in% set)) # black drawn
  hitInPop <- length(which(rownames(mutData) %in% set)) # all black
  failInPop <- nrow(mutData)-hitInPop # number of red
  # Calculate over-enrichment for current gene set
  pval <- phyper(hitInSample-1, hitInPop, failInPop, sampleSize, lower.tail= FALSE)
  # Add current result
  pvals <- c(pvals, pval)
}

# Adjust p-values
pvals <- p.adjust(pvals, method="fdr")
length(pvals[pvals < 0.05])
```

```
[1] 0
```

# Getting Help

- BioPAX Google Group
  - http://groups.google.com/group/biopax
- Biostars
  - https://www.biostars.org
- Online Contact Form
  - http://www.pathwaycommons.org/pc/get_feedback.do