

keggorthology: the KEGG orthology as graph

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Contents

1	Introduction	1
2	KOgraph	1
3	Application to gene filtering	3
4	Infrastructure considerations	4
5	Session info	4

1 Introduction

KEGG is the Kyoto Encyclopedia of Genes and Genomes. An important product of the KEGG group is a catalog of pathways. The KEGG Orthology (KO) organizes the pathways into a conceptual hierarchy. This package encodes the hierarchy as a graph, and provides some support for deriving sets of array feature identifiers from the hierarchy.

2 KOgraph

```
> library(keggorthology)
> library(graph)
> data(KOgraph)
> KOgraph
```

```
A graphNEL graph with directed edges
Number of Nodes = 358
Number of Edges = 357
```

```
> nodes(KOgraph)[1:5]
```

```
[1] "KO.Feb10root"           "Metabolism"
[3] "Carbohydrate Metabolism" "Glycolysis / Gluconeogenesis"
[5] "Citrate cycle (TCA cycle)"
```

The upper component of the hierarchy is:

```
> adj(KOgraph, nodes(KOgraph)[1])

$KO.Feb10root
[1] "Metabolism"
[2] "Genetic Information Processing"
[3] "Environmental Information Processing"
[4] "Cellular Processes"
[5] "Organismal Systems"
[6] "Human Diseases"
```

Graph operations can be used to explore the orthology. For example, the context of the PPAR signaling pathway is found as follows:

```
> library(RBGL)
> sp.between(KOgraph, nodes(KOgraph)[1], "PPAR signaling pathway")

$`KO.Feb10root:PPAR signaling pathway`
$`KO.Feb10root:PPAR signaling pathway`$length
[1] 3

$`KO.Feb10root:PPAR signaling pathway`$path_detail
[1] "KO.Feb10root"           "Organismal Systems"     "Endocrine System"
[4] "PPAR signaling pathway"

$`KO.Feb10root:PPAR signaling pathway`$length_detail
$`KO.Feb10root:PPAR signaling pathway`$length_detail[[1]]
      KO.Feb10root->Organismal Systems
                        1
      Organismal Systems->Endocrine System
                        1
Endocrine System->PPAR signaling pathway
                        1
```

Fixed-length identifiers are used to label pathways. These are available as the 'tag' nodeData attribute.

```
> nodeData(KOgraph, , "tag")[1:5]
```

```
$KO.Feb10root
[1] "NONE"
```

```
$Metabolism
[1] "01100"
```

```
$`Carbohydrate Metabolism`
[1] "01101"
```

```
$`Glycolysis / Gluconeogenesis`
[1] "00010"
```

```
$`Citrate cycle (TCA cycle)`
[1] "00020"
```

The depth of each term is also available.

```
> nodeData(KOgraph, , "depth")[1:5]
```

```
$KO.Feb10root
[1] 0
```

```
$Metabolism
[1] 1
```

```
$`Carbohydrate Metabolism`
[1] 2
```

```
$`Glycolysis / Gluconeogenesis`
[1] 3
```

```
$`Citrate cycle (TCA cycle)`
[1] 3
```

3 Application to gene filtering

Several functions are available for retrieving relevant information from the orthology. If you know a substring of the pathway name of interest, you can obtain the numerical tag(s).

```
> getKOtags("insulin")
```

```
Insulin signaling pathway
      "04910"
```

We can get probe set identifiers corresponding to a term. The default chip annotation package used is hgu95av2.db.

```
> library(hgu95av2.db)
> mp = getK0probes("Methionine")
> library(ALL)
> data(ALL)
> ALL[mp, ]
```

```
ExpressionSet (storageMode: lockedEnvironment)
assayData: 32 features, 128 samples
  element names: exprs
protocolData: none
phenoData
  sampleNames: 01005, 01010, ..., LAL4 (128 total)
  varLabels and varMetadata description:
    cod: Patient ID
    diagnosis: Date of diagnosis
    ...: ...
    date last seen: date patient was last seen
    (21 total)
featureData: none
experimentData: use 'experimentData(object)'
  pubMedIds: 14684422 16243790
Annotation: hgu95av2
```

4 Infrastructure considerations

Based on keggorthology read of KEGG orthology, March 2 2010. Specifically, we run wget on ftp://ftp.genome.jp/pub/kegg/brite/ko/ko00001.keg and use parsing and modeling code given in inst/keggHTML to generate a data frame respecting the hierarchy, and then keggDF2graph function in keggorthology package to construct the graph.

5 Session info

```
> sessionInfo()
```

```
R version 2.11.0 (2010-04-22)
x86_64-unknown-linux-gnu
```

```
locale:
 [1] LC_CTYPE=en_US          LC_NUMERIC=C            LC_TIME=en_US
```

```
[4] LC_COLLATE=en_US      LC_MONETARY=C          LC_MESSAGES=en_US
[7] LC_PAPER=en_US         LC_NAME=C              LC_ADDRESS=C
[10] LC_TELEPHONE=C         LC_MEASUREMENT=en_US  LC_IDENTIFICATION=C
```

attached base packages:

```
[1] tools      stats      graphics  grDevices  utils      datasets  methods
[8] base
```

other attached packages:

```
[1] ALL_1.4.7          RBGL_1.24.0          keggorthology_2.0.1
[4] hgu95av2.db_2.4.1  org.Hs.eg.db_2.4.1  RSQLite_0.9-0
[7] DBI_0.2-5          AnnotationDbi_1.10.1 Biobase_2.8.0
[10] graph_1.26.0
```