

keggorthology: the KEGG orthology as graph

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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 K0graph

```
> library(keggorthology)
> library(graph)
> data(K0graph)
> K0graph
```

A graphNEL graph with directed edges

Number of Nodes = 358

Number of Edges = 357

```
> nodes(K0graph)[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: 30 features, 128 samples
  element names: exprs
protocolData: none
phenoData
  sampleNames: 01005 01010 ... LAL4 (128 total)
  varLabels: cod diagnosis ... date last seen (21 total)
  varMetadata: labelDescription
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 4.4.0 Patched (2024-04-24 r86482)
Platform: aarch64-apple-darwin20
Running under: macOS Ventura 13.6.6
```

```
Matrix products: default
```

```
BLAS: /Library/Frameworks/R.framework/Versions/4.4-arm64/Resources/lib/libRblas.0.dylib
LAPACK: /Library/Frameworks/R.framework/Versions/4.4-arm64/Resources/lib/libRlapack.dylib
```

```
locale:
```

```
[1] C/en_US.UTF-8/en_US.UTF-8/C/en_US.UTF-8/en_US.UTF-8
```

```
time zone: America/New_York  
tzcode source: internal
```

```
attached base packages:
```

```
[1] stats4      stats      graphics  grDevices  utils      datasets  methods  
[8] base
```

```
other attached packages:
```

```
[1] ALL_1.45.0          RBGL_1.79.0          keggorthology_2.55.0  
[4] hgu95av2.db_3.13.0  org.Hs.eg.db_3.19.1  AnnotationDbi_1.65.2  
[7] IRanges_2.37.1      S4Vectors_0.41.7     Biobase_2.63.1  
[10] graph_1.81.1        BiocGenerics_0.49.1
```

```
loaded via a namespace (and not attached):
```

```
[1] crayon_1.5.2          vctrs_0.6.5          httr_1.4.7  
[4] cli_3.6.2             rlang_1.1.3          DBI_1.2.2  
[7] png_0.1-8             UCSC.utils_0.99.7     jsonlite_1.8.8  
[10] bit_4.0.5             Biostrings_2.71.6     KEGGREST_1.43.1  
[13] fastmap_1.1.1         GenomeInfoDb_1.39.14  memoise_2.0.1  
[16] compiler_4.4.0        RSQLite_2.3.6         blob_1.2.4  
[19] pkgconfig_2.0.3       XVector_0.43.1       R6_2.5.1  
[22] GenomeInfoDbData_1.2.12 tools_4.4.0           bit64_4.0.5  
[25] zlibbioc_1.49.3       cachem_1.0.8
```