

keggorthology: the KEGG orthology as graph

VJ Carey

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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 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] "K0.Feb10root"           "Metabolism"
[3] "Carbohydrate Metabolism" "Glycolysis / Gluconeogenesis"
[5] "Citrate cycle (TCA cycle)"
```

The upper component of the hierarchy is:

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

$K0.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")

$`K0.Feb10root:PPAR signaling pathway`
$`K0.Feb10root:PPAR signaling pathway`$length
[1] 3

$`K0.Feb10root:PPAR signaling pathway`$path_detail
[1] "K0.Feb10root"           "Organismal Systems"      "Endocrine System"
[4] "PPAR signaling pathway"

$`K0.Feb10root:PPAR signaling pathway`$length_detail
$`K0.Feb10root:PPAR signaling pathway`$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 4.3.1 (2023-06-16 ucrt)
Platform: x86_64-w64-mingw32/x64 (64-bit)
Running under: Windows Server 2022 x64 (build 20348)

Matrix products: default

locale:
[1] LC_COLLATE=C
```

```
[2] LC_CTYPE=English_United States.utf8
[3] LC_MONETARY=English_United States.utf8
[4] LC_NUMERIC=C
[5] LC_TIME=English_United States.utf8
```

```
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_1.43.0      RBGL_1.78.0      keggorthology_2.54.0
[4] hgu95av2.db_3.13.0  org.Hs.eg.db_3.18.0  AnnotationDbi_1.64.0
[7] IRanges_2.36.0     S4Vectors_0.40.0    Biobase_2.62.0
[10] graph_1.80.0      BiocGenerics_0.48.0
```

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

```
[1] crayon_1.5.2      vctrs_0.6.4      httr_1.4.7
[4] cli_3.6.1         rlang_1.1.1      DBI_1.1.3
[7] png_0.1-8         bit_4.0.5        RCurl_1.98-1.12
[10] Biostrings_2.70.0  KEGGREST_1.42.0  bitops_1.0-7
[13] fastmap_1.1.1     GenomeInfoDb_1.38.0  memoise_2.0.1
[16] compiler_4.3.1    RSQLite_2.3.1     blob_1.2.4
[19] pkgconfig_2.0.3    XVector_0.42.0     R6_2.5.1
[22] GenomeInfoDbData_1.2.11 tools_4.3.1       bit64_4.0.5
[25] zlibbioc_1.48.0    cachem_1.0.8
```