Rendering pathways to convey quantitative genomic relationships

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1 Introduction

Given an R graph representing a biological pathway and a vector of numbers (e.g., estimated levels of gene expression, or quantile of gene expression value in a distribution over samples) linked to the nodes of the pathway (e.g., genes), we wish to display the graph with nodes colored to convey the relationships among the numbers.

Our primary tool for rendering graphs is *Rgraphviz*. This package uses AT&T graphviz to compute layouts, and various aspects of R graphics to create renderings.

Our primary tools for creating pathway graphs are the *graph* and *pathRender* packages.

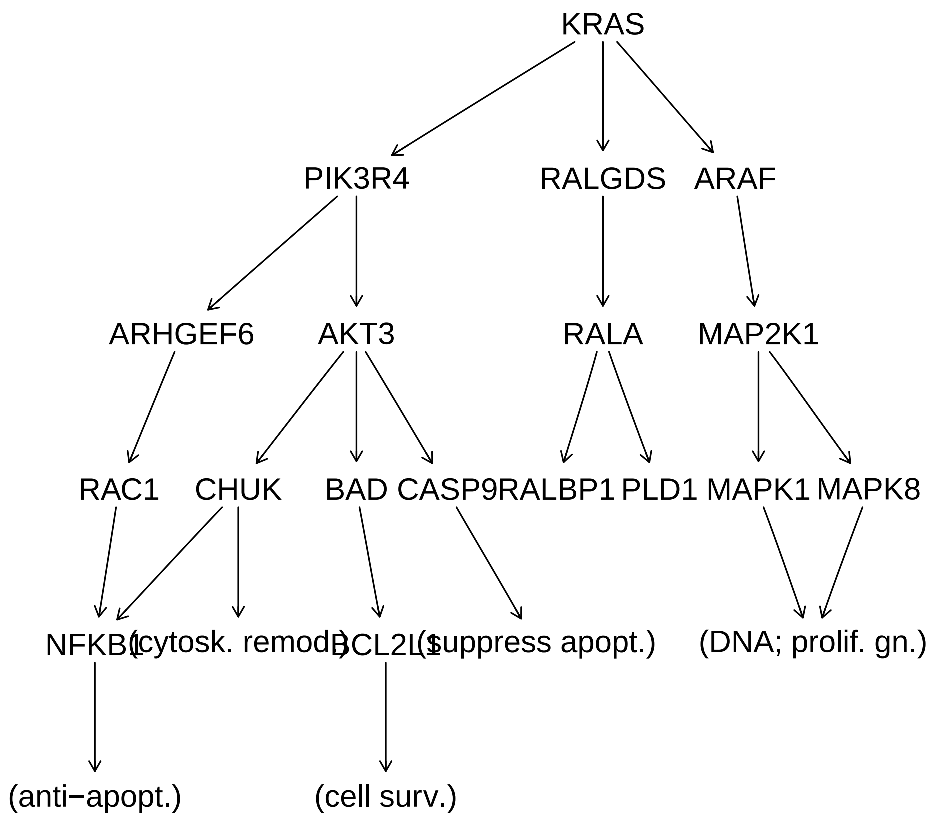
In this vignette and associated code, we aim to simplify the use of software in these components to allow the intended renderings to be created in a flexible way.

2 An example

2.1 A pathway graph

The *graph* package contains a custom-made graph representing the pancreatic cancer initiation pathway. First we render it in isolation from data:

```
> library(graph)
> library(pathRender)
> library(Rgraphviz)
> data(pancrCaIni)
> plot(pancrCaIni, nodeAttrs=pwayRendAttrs(pancrCaIni))
```



Note that the default rendering of the pathway graph is hard to read; we use the new `pwayRendAttrs` function to generate attributes that improve readability.

2.2 An ExpressionSet and its reduction

We will work with ALL.

```
> library(ALL)
> if (!exists("ALL")) data(ALL)
```

A basic problem is to reduce the information obtained using the whole-genome microarray to a set of numbers relevant to the pathway we wish to render. The `reduceES` function helps with this. Given a vector of annotation tokens (e.g., HUGO gene symbols) and a map from symbols to associated microarray probes, `reduceES` restricts the assay data to relevant probes. The map parameter can be either an AtomicAnnDbBimap as created in the *.db annotation packages, or a list with annotation tokens as element names and vectors probe identifiers as elements. Here we illustrate the use of the Bimap:

```
> if ("package:hgu95av2" %in% search()) detach("package:hgu95av2")
> library(hgu95av2.db)
> red1 = reduceES( ALL, nodes(pancrCaIni), revmap(hgu95av2SYMBOL), "symbol" )
> red1

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
  featureNames: 1940_at 32159_at ... 34006_s_at (30 total)
  fvarLabels: symbol
  fvarMetadata: labelDescription
experimentData: use 'experimentData(object)'
  pubMedIds: 14684422 16243790
Annotation: hgu95av2

> pData(featureData(red1))

             symbol
1940_at        KRAS
32159_at       KRAS
37901_at     PIK3R4
34254_at     RALGDS
37543_at    ARHGEF6
40781_at       AKT3
1706_at        ARAF
1707_g_at      ARAF
1876_at        RALA
1877_g_at      RALA
39253_s_at     RALA
2050_s_at      RAC1
40864_at       RAC1
33770_at       CHUK
1861_at         BAD
486_at        CASP9
487_g_at      CASP9
1130_at      MAP2K1
1844_s_at    MAP2K1
```

```
36628_at    RALBP1
177_at        PLD1
1377_at      NFKB1
1378_g_at    NFKB1
38438_at     NFKB1
1615_at     BCL2L1
34742_at    BCL2L1
976_s_at     MAPK1
2070_i_at    MAPK8
2071_s_at    MAPK8
34006_s_at   MAPK8
```

Note that the reduceES creates a featureData variable and that there are repetitions of values of this variable. We can specify that we want to collapse repetitions by specifying a function for the collapseFun parameter. We will use mean.

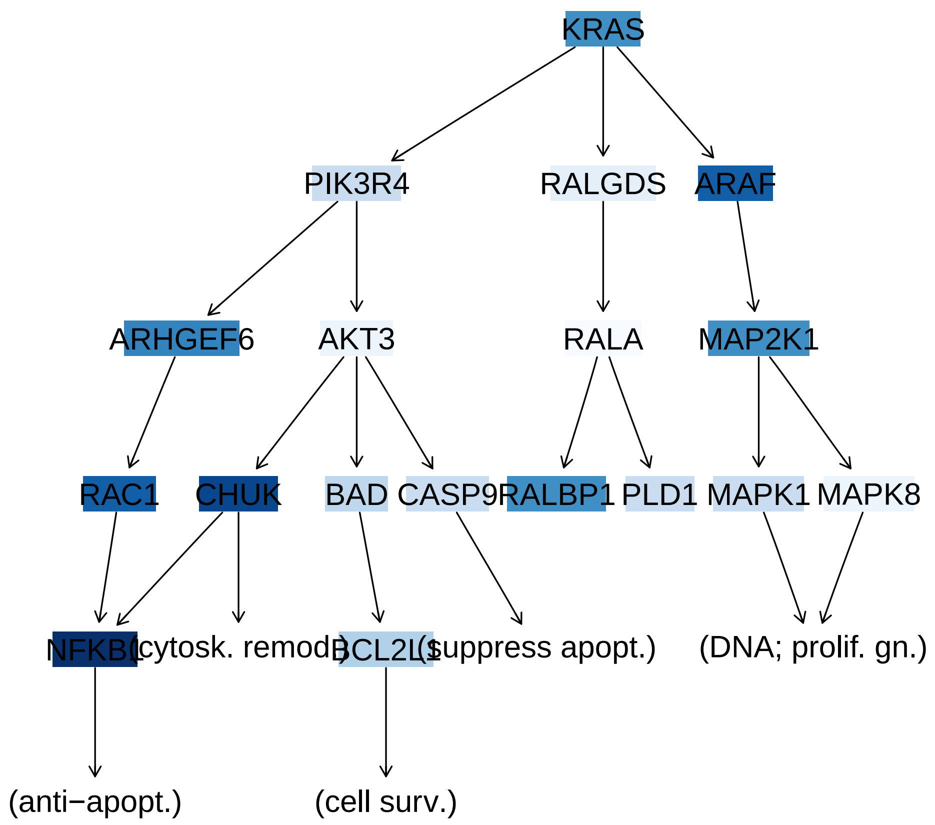
```
> collap1 = reduceES( ALL, nodes(pancrCaIni), revmap(hgu95av2SYMBOL), "symbol", mean
> collap1
```

```
ExpressionSet (storageMode: lockedEnvironment)
assayData: 18 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
  featureNames: AKT3 ARAF ... RALGDS (18 total)
  fvarLabels: symbol
  fvarMetadata: labelDescription
experimentData: use 'experimentData(object)'
Annotation:
```

2.3 A rendering

Now we will render information on one sample from the reduced data.

```
> library(RColorBrewer)
> plotExGraph(pancrCaIni, collap1, 1)
```


KRAS
PIK3R4
RALGDS
ARAF
ARHGEF6
AKT3
RALA
MAP2K1
RAC1
CHUK
BAD
CASP9
RALBP1
PLD1
MAPK1
MAPK8
NFKB1
(cytosk. remod.)
BCL2L1
(suppress apopt.)
(DNA; prolif. gn.)
(anti−apopt.)
(cell surv.)