

Rendering pathways to convey quantitative genomic relationships

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April 23, 2010

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.

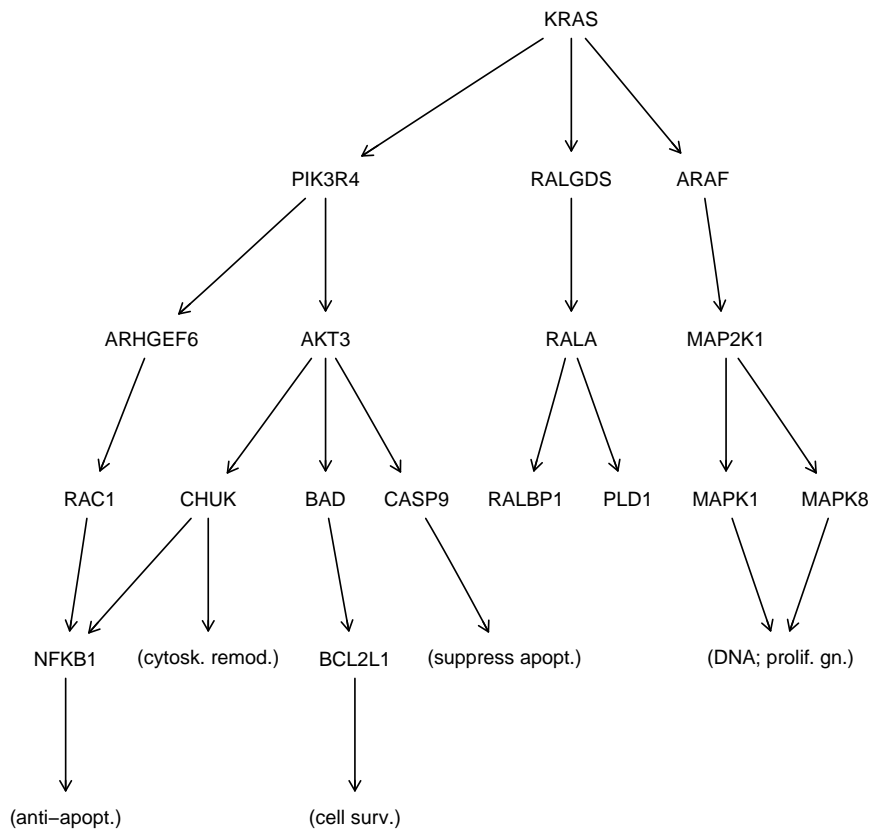
In this vignette and associated code, we aim to simplify the use of software in these components to allow the intended renderings to be created in a flexible way.

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(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 and varMetadata description:
    cod: Patient ID
    diagnosis: Date of diagnosis
    ...: ...
    date last seen: date patient was last seen
    (21 total)
featureData
  featureNames: 1940_at, 32159_at, ..., 34006_s_at (30 total)
  fvarLabels and fvarMetadata description:
    symbol: NA
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 and varMetadata description:
    cod: Patient ID
    diagnosis: Date of diagnosis
    ...: ...
    date last seen: date patient was last seen
    (21 total)
featureData
  featureNames: AKT3, ARAF, ..., RALGDS (18 total)
  fvarLabels and fvarMetadata description:
    symbol: NA
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)
```

