The CGDS-R library

Anders Jacobsen

June 20, 2012

Contents

1 Introduction

This package provides a basic set of R functions for querying the Cancer Genomic Data Server (CGDS) hosted by the Computational Biology Center (cBio) at the Memorial Sloan-Kettering Cancer Center (MSKCC). This service is a part of the cBio Cancer Genomics Portal, `http://www.cbioportal.org/`.

In summary, the library can issue the following types of queries:

- `getCancerStudies()` : What cancer studies are hosted on the server? For example, TCGA glioblastoma or TCGA ovarian cancer.
- `getGeneticProfiles()` : What genetic profile types are available for cancer study X? For example, mRNA expression or copy number alterations.
- `getCaseLists()` : what case sets are available for cancer study X? For example, all samples or only samples corresponding to a given cancer subtype.

- `getProfileData()`: Retrieve slices of genomic data. For example, a client can retrieve all mutation data for PTEN and EGFR in TCGA glioblastoma.
- `getClinicalData()`: Retrieve clinical data (e.g. patient survival time and age) for a given cancer study and list of cases.

Each of these functions will be briefly described in the following sections. The last part of this document includes some concrete examples of how to access and plot the data.

The purpose of this document is to give the reader a quick overview of the `cgdsr` package. Please refer to the corresponding R manual pages for a more detailed explanation of arguments and output for each function.

2 The CGDS R interface

2.1 `CGDS()` : Create a CGDS connection object

Initially, we will establish a connection to the public CGDS server hosted by Memorial Sloan-Kettering Cancer Center. The function for creating a CGDS connection object requires the URL of the CGDS server service, in this case `http://www.cbioportal.org/public-portal/`, as an argument.

```
> library(cgdsr)
> # Create CGDS object
> mycgds = CGDS("http://www.cbioportal.org/public-portal/")
```

The variable `mycgds` is now a CGDS connection object pointing at the URL for the public CGDS server. This connection object must be included as an argument to all subsequent interface calls. Optionally, we can now perform a set of simple tests of the data returned from the CGDS connection object using the `test` function:

```
> # Test the CGDS endpoint URL using a few simple API tests
> test(mycgds)

getCancerStudies...  OK
getCaseLists (1/2) ...  OK
getCaseLists (2/2) ...  OK
getGeneticProfiles (1/2) ...  OK
getGeneticProfiles (2/2) ...  OK
getClinicalData (1/1) ...  OK
getProfileData (1/7) ...  OK
getProfileData (2/7) ...  OK
getProfileData (3/7) ...  OK
getProfileData (4/7) ...  OK
getProfileData (5/7) ...  OK
getProfileData (6/7) ...  OK
getProfileData (7/7) ...  OK
```

2.2 getCancerStudies() : Retrieve a set of available cancer studies

Having created a CGDS connection object, we can now retrieve a data frame with available cancer studies using the `getCancerStudies` function:

```
> # Get list of cancer studies at server
> getCancerStudies(mycgds)[,c(1,2)]
```

```
   cancer_study_id                                                    name
1        blca_tcga          Bladder Urothelial Carcinoma (TCGA, Provisional)
2         lgg_tcga              Brain Lower Grade Glioma (TCGA, Provisional)
3        brca_tcga             Breast Invasive Carcinoma (TCGA, Provisional)
4        cesc_tcga      Cervical Squamous Cell Carcinoma (TCGA, Provisional)
5    coadread_tcga       Colon and Rectum Adenocarcinoma (TCGA, Provisional)
6         gbm_tcga                                        Glioblastoma (TCGA)
7        hnsc_tcga Head and Neck Squamous Cell Carcinoma (TCGA, Provisional)
8        kirc_tcga     Kidney Renal Clear Cell Carcinoma (TCGA, Provisional)
9        kirp_tcga Kidney Renal Papillary Cell Carcinoma (TCGA, Provisional)
10       lihc_tcga        Liver Hepatocellular Carcinoma (TCGA, Provisional)
11       luad_tcga                  Lung Adenocarcinoma (TCGA, Provisional)
12       lusc_tcga          Lung Squamous Cell Carcinoma (TCGA, Provisional)
13       paad_tcga             Pancreatic Adenocarcinoma (TCGA, Provisional)
14       prad_tcga               Prostate Adenocarcinoma (TCGA, Provisional)
15      prad_mskcc                                  Prostate Cancer (MSKCC)
16      sarc_mskcc                                    Sarcoma (MSKCC/Broad)
17         ov_tcga                               Serous Ovarian Cancer (TCGA)
18       stad_tcga                Stomach Adenocarcinoma (TCGA, Provisional)
19       thca_tcga                     Thyroid Carcinoma (TCGA, Provisional)
20       ucec_tcga Uterine Corpus Endometrioid Carcinoma (TCGA, Provisional)
```

Here we are only showing the first two columns, the cancer study ID and short name, of the result data frame. There is also a third column, a longer description of the cancer study. The cancer study ID must be used in subsequent interface calls to retrieve case lists and genetic data profiles (see below).

2.3 getGeneticProfiles() : Retrieve genetic data profiles for a specific cancer study

This function queries the CGDS API and returns the available genetic profiles, e.g. mutation or copy number profiles, stored about a specific cancer study. Below we list the current genetic profiles for the TCGA glioblastoma cancer study:

```
> getGeneticProfiles(mycgds,'gbm_tcga')[,c(1:2)]
```

```
                   genetic_profile_id
1                   gbm_tcga_gistic
2                  gbm_tcga_cna_rae
3              gbm_tcga_cna_consensus
4                    gbm_tcga_mrna
```

```
5  gbm_tcga_mrna_merged_median_Zscores
6                        gbm_tcga_mirna
7                      gbm_tcga_log2CNA
8          gbm_tcga_mrna_median_Zscores
9                  gbm_tcga_methylation
10       gbm_tcga_mirna_median_Zscores
11                  gbm_tcga_mutations
12           gbm_tcga_RPPA_protein_level
                                                    genetic_profile_name
1                  Putative copy-number alterations (GISTIC, 501 cases)
2                     Putative copy-number alterations (RAE, 203 cases)
3  Putative copy-number alterations (Consensus, GBM Pathways, 206 cases)
4                                                          mRNA expression
5                              mRNA/miRNA expression Z-scores (all genes)
6                                                       microRNA expression
7                                                  Log2 copy-number values
8                                      mRNA Expression z-Scores (microarray)
9                                                             Methylation
10                                          microRNA expression Z-scores
11                                                             Mutations
12                                       RPPA protein/phosphoprotein level
```

Here we are only listing the first two columns, genetic profile ID and short name, of the resulting data frame. Please refer to the R manual pages for a more extended specification of the arguments and output.

2.4 getCaseLists() : Retrieve case lists for a specific cancer study

This function queries the CGDS API and returns available case lists for a specific cancer study. For example, within a particular study, only some cases may have sequence data, and another subset of cases may have been sequenced and treated with a specific therapeutic protocol. Multiple case lists may be associated with each cancer study, and this method enables you to retrieve meta-data regarding all of these case lists. Below we list the current case lists for the TCGA glioblastoma cancer study:

```
> getCaseLists(mycgds,'gbm_tcga')[,c(1:2)]
```

```
                   case_list_id                          case_list_name
1         gbm_tcga_3way_complete                  All Complete Tumors
2                   gbm_tcga_all                              All Tumors
3        gbm_tcga_expr_classical            Expression Cluster Classical
4      gbm_tcga_expr_mesenchymal          Expression Cluster Mesenchymal
5           gbm_tcga_expr_neural              Expression Cluster Neural
6        gbm_tcga_expr_proneural            Expression Cluster Proneural
7                 gbm_tcga_gcimp                           G-CIMP samples
8             gbm_tcga_manuscript                     Manuscript Tumors
9               gbm_tcga_nongcimp                  non G-CIMP samples
10            gbm_tcga_sequenced                     Sequenced Tumors
```

```
11            gbm_tcga_seq_paper           Sequenced Tumors, GBM Manuscript
12    gbm_tcga_sequenced_nohyper                Sequenced, No Hypermutators
13 gbm_tcga_sequenced_nottreated                     Sequenced, Not Treated
14    gbm_tcga_sequenced_treated                         Sequenced, Treated
15                gbm_tcga_acgh                                Tumors aCGH
16             gbm_tcga_log2CNA                   Tumors log2 copy-number
17          gbm_tcga_methylation               Tumors with methylation data
18             gbm_tcga_microrna   Tumors with microRNA data (microRNA-Seq)
19                 gbm_tcga_mrna Tumors with mRNA data (Agilent microarray)
20                 gbm_tcga_rppa                        Tumors with RPPA data
21               gbm_tcga_cnaseq       Tumors with sequencing and aCGH data
```

Here we are only listing the first two columns, case list ID and short name, of the resulting data frame. Please refer to the R manual pages for a more extended specification of the arguments and output.

2.5 getProfileData() : Retrieve genomic profile data for genes and genetic profiles

The function queries the CGDS API and returns data based on gene(s), genetic profile(s), and a case list. The function only allows specifying a list of genes and a single genetic profile, or oppositely a single gene and a list of genetic profiles. Importantly, the format of the output data frame depends on if a single or a list of genes was specified in the arguments. Below we are retrieving mRNA expression and copy number alteration genetic profiles for the NF1 gene in all samples of the TCGA glioblastoma cancer study:

```
> getProfileData(mycgds, "NF1", c("gbm_tcga_cna_rae","gbm_tcga_mrna"), "gbm_tcga_all")[c(1

             gbm_tcga_cna_rae gbm_tcga_mrna
TCGA.02.0001                0    -0.2404532
TCGA.02.0002              NaN     1.3338257
TCGA.02.0003                0     0.2362541
TCGA.02.0004              NaN    -0.2083863
TCGA.02.0006                0     1.3945620
```

We are here only showing the first five rows of the data frame. In the next example, we are retrieving mRNA expression data for the MDM2 and MDM4 genes:

```
> getProfileData(mycgds, c("MDM2","MDM4"), "gbm_tcga_mrna", "gbm_tcga_all")[c(1:5),]

                  MDM2       MDM4
TCGA.02.0001 -0.1062067 -1.0838320
TCGA.02.0002  2.3479364  1.0459768
TCGA.02.0003 -0.1150306 -1.0204845
TCGA.02.0004 -0.6583829 -1.4602322
TCGA.02.0006  3.8872395  0.6589751
```

We are again only showing the first five rows of the data frame.

2.6 `getClinicalData()` : Retrieve clinical data for a list of cases

The function queries the CGDS API and returns available clinical data (e.g. patient survival time and age) for a given case list. Results are returned in a data frame with a row for each case and a column for each clinical attribute. The available clinical attributes are:

- `overall_survival_months`: Overall survival, in months.
- `overall_survival_status`: Overall survival status, usually indicated as "LIVING" or "DECEASED".
- `disease_free_survival_months`: Disease free survival, in months.
- `disease_free_survival_status`: Disease free survival status, usually indicated as "DiseaseFree" or "Recurred/Progressed".
- `age_at_diagnosis`: Age at diagnosis.

Below we retrieve clinical data for the TCGA ovarian cancer dataset (only first five cases/rows are shown):

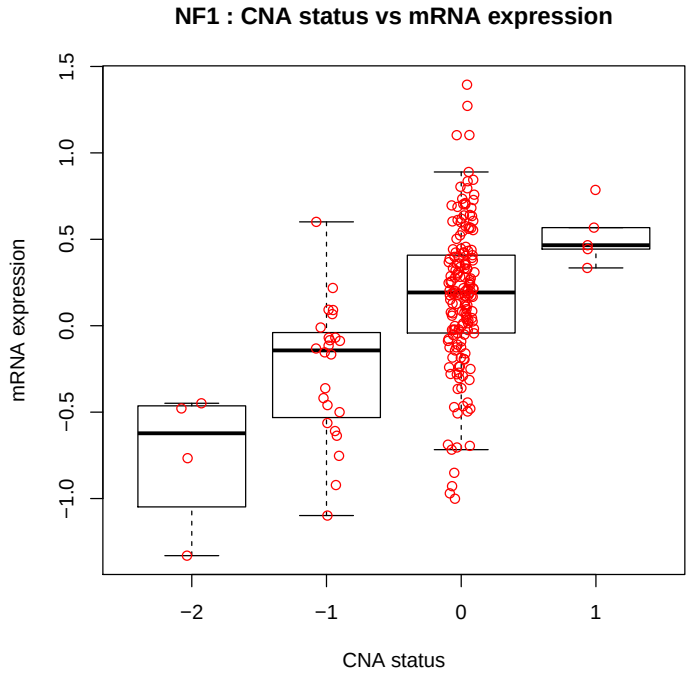
```
> getClinicalData(mycgds, "ova_all")[c(1:5),]

data frame with 0 columns and 5 rows
```

3 Examples

3.1 Example 1: Association of NF1 copy number alteration and mRNA expression in glioblastoma

As a simple example, we will generate a plot of the association between copy number alteration (CNA) status and mRNA expression change for the NF1 tumor suprpressor gene in glioblastoma. This plot is very similar to Figure 2b in the TCGA research network paper on glioblastoma (McLendon et al. 2008). The mRNA expression of NF1 has been median adjusted on the gene level (by globally subtracting the median expression level of NF1 across all samples).

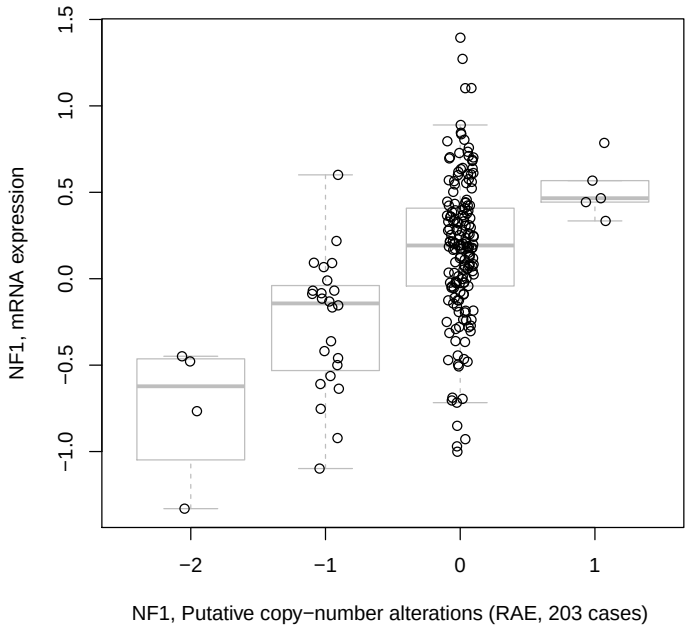
```
> df = getProfileData(mycgds, "NF1", c("gbm_tcga_cna_rae","gbm_tcga_mrna"), "gbm_tcga_all"
> head(df)

             gbm_tcga_cna_rae gbm_tcga_mrna
TCGA.02.0001                0    -0.2404532
TCGA.02.0002              NaN     1.3338257
TCGA.02.0003                0     0.2362541
TCGA.02.0004              NaN    -0.2083863
TCGA.02.0006                0     1.3945620
TCGA.02.0007                0     0.3064915

> boxplot(df[,2] ~ df[,1], main="NF1 : CNA status vs mRNA expression", xlab="CNA status",
> stripchart(df[,2] ~ df[,1], vertical=T, add=T, method="jitter",pch=1,col='red')
```



Alternatively, the generic `cgdsr plot()` function can be used to generate a similar plot:

```
> plot(mycgds, "gbm_tcga", "NF1", c("gbm_tcga_cna_rae","gbm_tcga_mrna"), "gbm_tcga_all", s
```

```
[1] TRUE
```



3.2 Example 2: MDM2 and MDM4 mRNA expression levels in glioblastoma

In this example, we evaluate the relationship of MDM2 and MDM4 expression levels in glioblastoma. mRNA expression levels of MDM2 and MDM4 have been median adjusted on the gene level (by globally subtracting the median expression level of the individual gene across all samples).

```
> df = getProfileData(mycgds, c("MDM2","MDM4"), "gbm_tcga_mrna", "gbm_tcga_all")
> head(df)
```

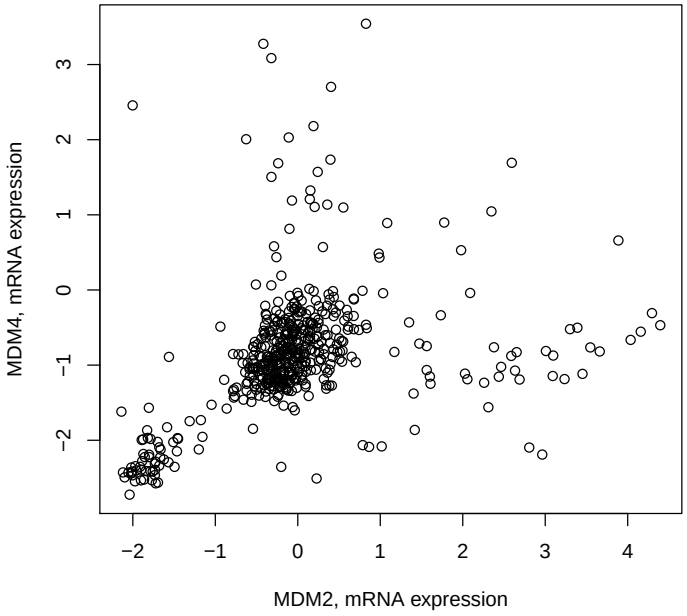
```
                   MDM2       MDM4
TCGA.02.0001 -0.1062067 -1.0838320
TCGA.02.0002  2.3479364  1.0459768
TCGA.02.0003 -0.1150306 -1.0204845
TCGA.02.0004 -0.6583829 -1.4602322
TCGA.02.0006  3.8872395  0.6589751
TCGA.02.0007 -0.2883431  0.5814032
```

```
> plot(df, main="MDM2 and MDM4 mRNA expression", xlab="MDM2 mRNA expression", ylab="MDM4 m
```

Alternatively, the generic `cgdsr plot()` function can be used to generate a similar plot:

```
> plot(mycgds, "gbm_tcga", c("MDM2","MDM4"), "gbm_tcga_mrna" ,"gbm_tcga_all")
```

```
[1] TRUE
```



3.3 Example 3: Comparing expression of PTEN in primary and metastatic prostate cancer tumors

In this example we plot the mRNA expression levels of PTEN in primary and metastatic prostate cancer tumors.

```
> df.pri = getProfileData(mycgds, "PTEN", "prad_mskcc_mrna", "prad_mskcc_primary")
> head(df.pri)
```

```
            PTEN
PCA0001 9.467183
PCA0002 9.041528
PCA0003 8.511305
PCA0004      NaN
PCA0005 9.413217
PCA0006      NaN
```

```
> df.met = getProfileData(mycgds, "PTEN", "prad_mskcc_mrna", "prad_mskcc_mets")
> head(df.met)
```

```
            PTEN
PCA0182 7.486938
PCA0183      NaN
PCA0184 7.578755
PCA0185      NaN
PCA0186      NaN
PCA0187 8.756132
```

```
> boxplot(list(t(df.pri),t(df.met)), main="PTEN expression in primary and metastatic tumor
> stripchart(list(t(df.pri),t(df.met)), vertical=T, add=T, method="jitter",pch=1,col='red'
```