A practical tutorial on S4 programming

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1 Introduction

Here we introduce R object-oriented (OO) programming using microarrays as a use case. The introduction is purely practical and does not aim for an exhaustive guide to R object-oriented programming. We will concentrate on the S4 system and only mention the older S3 system and the recent S4 reference class infrastructure here.

In section 2, we present a solution on how to represent microarray data in R using basic data types and conclude with some issues and limitations of this implementation. In section 3, we introduce fundamental concepts of OO programming and present how OO programming is implemented in the S4 system.

In sections 4 and 5, we implement the S4 class and methods of an microarray example. Section 6 briefly shows how to learn about existing classes and methods.

2 An microarray example

We assume the students are familiar with microarrays and the type of data that is obtained from such experiments. Before embarking in any serious programming task, in particular when modelling data and defining data structures (using an OO class system or not), one should carefully think about how to best represent and store the data.

Exercise 1: Based on your understanding of microarrays, the nature of data their produce and the kind of computational analysis the data fill undergo, think of what is going to be needed to describe an experiment and what the type(s) of data structure available in R (data.frame, matrix, vector, ...) are most appropriate. Ideally, one would want everything (data, meta-data, ...) to be stored together as a single variables.

There are of course multiple valid solutions to the above question. Below are three pieces of information that we consider essential along with their respective R data structure.

- We choose to represent the microarray results as a matrix of size $n \times m$, where n is the number of probes on the microarray and m is the number of samples. The matrix that stores the intensities (these could also be fold-changes) is named marray.
- The sample annotation (meta-data) is described using a data.frame with exactly m rows and any number of columns. It is named pmeta.

• The feature (probe) annotation (meta-data) is described using a data.frame with exactly n rows and any number of columns. Let's call it fmeta.

We will also use the same names for the marray columns and the pmeta rows as well as the marray and fmeta rows.

Finally, to link these related pieces of information together, marray, pmeta and fmeta will all be combined into a list that will represent our microarray experiment.

```
> maexp <- list(marray = marray,</pre>
+
                fmeta = fmeta,
                pmeta = pmeta)
> rm(marray, fmeta, pmeta) ## clean up
> str(maexp)
List of 3
 $ marray: num [1:10, 1:6] 6.87 10.92 5.82 17.98 11.65 ...
  ..- attr(*, "dimnames")=List of 2
  ....$ : chr [1:10] "probe1" "probe2" "probe3" "probe4" ...
  ....$ : chr [1:6] "A" "B" "C" "D" ...
 $ fmeta :'data.frame': 10 obs. of 2 variables:
  ..$ geneId : int [1:10] 1 2 3 4 5 6 7 8 9 10
  ..$ pathway: Factor w/ 8 levels "E", "F", "L", "M", ..: 8 4 4 1 7 3 5 2 2 6
 $ pmeta :'data.frame': 6 obs. of 2 variables:
  ..$ sampleId : int [1:6] 1 2 3 4 5 6
  ..$ condition: Factor w/ 2 levels "MUT", "WT": 2 2 2 1 1 1
```

We can access and manipulate the respective elements of our microarray experiment with the \$ operator.

```
> maexp$pmeta
  sampleId condition
Α
          1
                    WT
          2
В
                    WT
С
          3
                    \mathbb{W}\mathbb{T}
          4
D
                   MUT
Ε
          5
                   MUT
F
          6
                   MUT
> summary(maexp$marray[, "A"])
   Min. 1st Qu.
                   Median
                              Mean 3rd Qu.
                                                Max.
  5.822
           7.269
                  11.280
                            10.660
                                   12.770
                                             17.980
> wt <- maexp$pmeta[, "condition"] == "WT"</pre>
> maexp$marray["probe8", wt]
                    В
13.691624 14.719181 2.646238
> maexp[["marray"]]["probe3", !wt] ## different syntax
       D
                 Ε
11.93836 13.48482 11.70560
```

The above solution does not provide a clean syntax. As a user, we have to know the names or positions of the respective elements of the microarray list elements to directly access the parts of interest.

> boxplot(maexp\$marray)

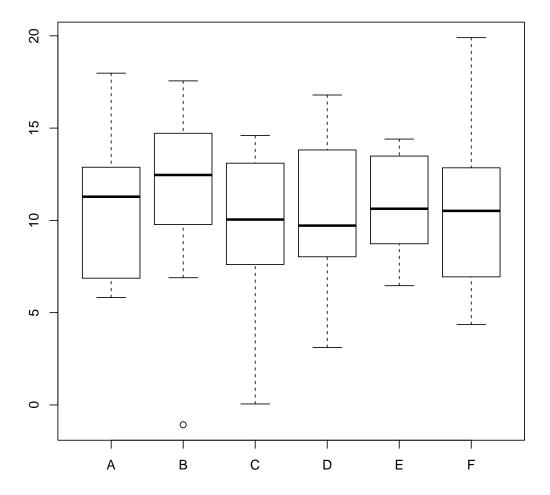


Figure 1: Boxplot representing the intensity distributions of the 10 probes for the 6 samples.

Exercise 2: But what if we want to subset the experiment. How would we extract the 10 first probes for the 3 first samples?

We have to manually subset the individual elements of our list, making sure that the number of rows of the marray and fmeta elements remain identical as well as the number of columns of marray and the number of columns of pmeta.

```
> x <- 1:5
> y <- 1:3
> marray2 <- maexp$marray[x, y]</pre>
> fmeta2 <- maexp$fmeta[x, ]</pre>
> pmeta2 <- maexp$pmeta[y, ]</pre>
> maexp2 <- list(marray = marray2,</pre>
                  fmeta = fmeta2,
+
                  pmeta = pmeta2)
> rm(marray2, fmeta2, pmeta2) ## clean up
> str(maexp2)
List of 3
 $ marray: num [1:5, 1:3] 6.87 10.92 5.82 17.98 11.65 ...
  ..- attr(*, "dimnames")=List of 2
  ....$ : chr [1:5] "probe1" "probe2" "probe3" "probe4" ...
  ....$ : chr [1:3] "A" "B" "C"
 $ fmeta :'data.frame': 5 obs. of 2 variables:
  ..$ geneId : int [1:5] 1 2 3 4 5
  ..$ pathway: Factor w/ 8 levels "E", "F", "L", "M", ..: 8 4 4 1 7
 $ pmeta :'data.frame': 3 obs. of 2 variables:
  ..$ sampleId : int [1:3] 1 2 3
  ..$ condition: Factor w/ 2 levels "MUT", "WT": 2 2 2
```

A simple operation like sub-setting the microarray experiment is very cumbersome and prone to errors. If we were to use this implementation for further work, we would of course want to write a custom function to perform the above.

3 Object-oriented programming

Object-oriented programming is based on two important concepts, abstraction and encapsulation. We want to represent the microarray concept in a way that makes most sense to the users without distracting them with unnecessary technicalities. These technicalities refer to the underlying implementation. Do users really need

to know that we used a list and that the first element, called marray is the matrix? We want the users to comprehend microarrays in R like they know them in real life, i.e. manipulate the abstract concept microarray while keeping all the underlying technical details, the implementation, hidden, or encapsulated.

These goals are achieved in two steps. First, we defined a *class* that represents (abstracts) the concept of a microarray. This is very similar to what we have done with the list above (the S3 system does use lists), but we will use a more elaborated approach that, although more verbose, provides numerous benefits that will be described in the next sections.

The class represents a data container and is defined on its own. An instance of a specific class, that contains data arranged in the specific container, is called an object.

Once we have created a class, we will want to define a set of specific behaviours, that make sense in the eyes of the users. These behaviours will be implemented by special functions, called *methods*. Methods are functions that tune their behaviour based on the class of their input. You have already observed this in your every day usage of R: whether we ask to produce the boxplot of a matrix (for example boxplot(maexp[[1]])) or provide a data.frame and a formula like boxplot(sampleId ~ condition, data = maexp[[3]]), R automatically does the right thing.

From the above, it transpires that we have now two different kind of roles. The developer is the person who creates the class and knows the implementation while the user is the one who uses the class without knowing, or needing to know, the actual underlying representation.

4 The MArray class

We can define a class with the setClass function. Our class is defined by a name, MArray, and a content structure. The different elements/fields of an S4 class are called slots¹. When defining the slots, we provide their respective names and classes as a (named) vector or list. It will only be possible to create objects with exactly these types of slots.

```
> MArray <- setClass("MArray",
+ slots = c(marray = "matrix",</pre>
```

¹Note that the usage of slots to define the representation of the class is the preferred way to define a class; the representation function is deprecated from version 3.0.0 and should be avoided.

```
+ fmeta = "data.frame",
+ pmeta = "data.frame"))
```

The setClass function returns a special function called a constructor, that can be used to create an instance of the class.

```
> MArray() ## an empty object
An object of class "MArray"
Slot "marray":
<0 x 0 matrix>
Slot "fmeta":
data frame with 0 columns and 0 rows
Slot "pmeta":
data frame with 0 columns and 0 rows
> MArray(marray = 1:2) ## not allowed
Error in validObject(.Object): invalid class "MArray" object: invalid
object for slot "marray" in class "MArray": got class "integer", should
be or extend class "matrix"
> ma <- MArray(marray = maexp[[1]],</pre>
               pmeta = maexp[["pmeta"]],
               fmeta = maexp[["fmeta"]])
> class(ma)
[1] "MArray"
attr(,"package")
[1] ".GlobalEnv"
> ma
An object of class "MArray"
Slot "marray":
                Α
                          В
                                      C
                                                 D
       6.867731 17.558906 14.59488686 16.793398
probe1
probe2 10.918217 11.949216 13.91068150 9.486061
       5.821857 6.893797 10.37282492 11.938358
probe3
```

```
probe4 17.976404 -1.073499 0.05324152 9.730975
probe5 11.647539 15.624655 13.09912874 3.114702
probe6 5.897658 9.775332 9.71935630 7.925027
probe7 12.437145 9.919049 9.22102247 8.028550
probe8 13.691624 14.719181 2.64623808 9.703433
probe9 12.878907 14.106106 7.60924972 15.500127
probe10 8.473058 12.969507 12.08970780 13.815879
               Ε
                         F
probe1 9.177382 11.990529
probe2 8.733192 6.939868
probe3 13.484817 11.705598
probe4 12.783316 4.353185
probe5 6.556222 17.165119
probe6 6.462524 19.901999
probe7 11.822910 8.163893
probe8 13.842665 4.779327
probe9 9.438269 12.848598
probe10 14.405539 9.324727
Slot "fmeta":
        geneId pathway
            1
probe1
             2
                    M
probe2
probe3
            3
                    M
probe4
                    Ε
                    Τ
probe5
            5
            6
probe6
                    L
probe7
            7
                    N
            8
                    F
probe8
probe9
            9
                    F
           10
                    Р
probe10
Slot "pmeta":
  sampleId condition
Α
         1
                 WT
В
         2
                 WT
С
         3
                 WT
D
         4
                MUT
```

```
E 5 MUT
F 6 MUT
```

To access individual slots, we need to use the **@**. This is equivalent to using the **\$** for a list.

```
> ma@pmeta
  sampleId condition
           1
Α
                      WT
           2
В
                      WT
C
           3
                      WT
D
           4
                     MUT
           5
Ε
                     MUT
           6
                     MUT
```

But this is something we do not want a user to do. To access a slot like this, one needs to know its name, i.e. the underlying plumbing of the class. This breaks the notion of encapsulation. Instead, the developer will provide the user with specific accessor methods (see section 5.2) to extract (or update using a replace method, section 5.5) specific slots.

5 MArray methods

Before proceeding, we need to explain the concept of generic function. A generic function, or generic for short, is a function that *dispatches* methods to their appropriate class-specific implementation. A method do will implement behaviour for a specific class A, while another implementation of do, will define another behaviour for class B. The generic do is the link between the class and its dedicated implementation. If we have do(a) (where a is of class A), than the generic will make sure that the A-specific code of do will be executed.

Before we define a method with **setMethod**, we will always want to first check if such a method does not exists (in which case there is already a generic function), as illustrated with the **show** method in section 5.1. If it is the case, we write our new methods. If not, we first create the generic and then proceed with the method.

5.1 The show method

The **show** method (it is a method, as it exhibits custom behaviour depending on the class of its argument) is a very helpful one. It allows to define custom summary

view of an object when we type its name in the console, instead of having all its (possibly very long content) displayed.

```
> show
standardGeneric for "show" defined from package "methods"

function (object)
standardGeneric("show")
<bytecode: 0x25bb040>
<environment: 0x18254c0>
Methods may be defined for arguments: object
Use showMethods("show") for currently available ones.
(This generic function excludes non-simple inheritance; see ?setIs)
> isGeneric("show")

[1] TRUE
> hasMethod("show")
```

As there is already a show generic function, we can immediately proceed with the method definition using the setMethod function. To do so we need a few things. First, we need to know for what class we implement the specific show method; this is the MArray class and will be passed as the signature argument in setMethod. We also need to know the argument names that are defined in the generic. These must match exactly, as we write a method for that specific generic. The arguments can be found by just typing the name of the generic (as in the previous) code chunk, look at its documentation or directly ask for the arguments with args(show). We see that there is only one argument, object (naming the first argument of a generic object is a widely applied convention). This is the same name that we will have to use when writing the definition of our method.

```
+ ncol(object@marray), " samples.\n", sep = "")
+ invisible(NULL)
+ })

[1] "show"
> ma

An object of class MArray
10 features by 6 samples.
```

5.2 Accessors

As mentioned above, we want to provide customised and controlled access to the class slots. This does not prevent us, as developers, to use the @ accessor, but does not force others to know the implementation details.

Let's create an accessor for the marray slot and call the accessor marray. There is no harm in naming the slot and its accessor with the same name but there is no constrain in doing so. There is no such method or generic; just typing marray with tell you that no such object is found. Below, we create a new generic function with setGeneric. We define the name of our new generic as well as the name of the argument(s) that will have to be re-used when defining class-specific method.

```
> setGeneric("marray", function(object) standardGeneric("marray"))
[1] "marray"
```

In general, it is considered good practice to add a . . . in the signature of a generic function. It provides the flexibility for other methods to use more arguments.

```
> setGeneric("marray", function(object, ...) standardGeneric("marray"))
[1] "marray"
```

We now proceed in the same way as above, using **setMethod**. The definition of our method (i.e. the actual code that will be executed) is very short and of course uses **@** to access (and return) the slot content.

```
> setMethod("marray", "MArray",
+ function(object) object@marray)
```

```
[1] "marray"
> marray(ma)
                Α
                                       C
                                                 D
         6.867731 17.558906 14.59488686 16.793398
probe1
probe2
        10.918217 11.949216 13.91068150
                   6.893797 10.37282492 11.938358
probe3
         5.821857
        17.976404 -1.073499 0.05324152
probe4
                                         9.730975
probe5
        11.647539 15.624655 13.09912874
                                          3.114702
                                         7.925027
         5.897658
                  9.775332 9.71935630
probe6
        12.437145
                   9.919049 9.22102247
probe7
                                          8.028550
probe8
        13.691624 14.719181
                             2.64623808
                                         9.703433
probe9
        12.878907 14.106106 7.60924972 15.500127
         8.473058 12.969507 12.08970780 13.815879
probe10
                E
         9.177382 11.990529
probe1
         8.733192 6.939868
probe2
probe3
        13.484817 11.705598
probe4
        12.783316 4.353185
probe5
         6.556222 17.165119
probe6
         6.462524 19.901999
probe7
        11.822910
                  8.163893
probe8
        13.842665
                   4.779327
probe9
         9.438269 12.848598
probe10 14.405539
                   9.324727
```

If we change the underlying implementation by changing the name of the slot or using an environment instead of a matrix, the ma@marray is going to break. However, when providing accessors, we can echo the changes in the accessor implementation without affecting the users' behaviour or existing scripts.

Exercise 3: Implement the fmeta and pmeta accessors.

5.3 The sub-setting operation

Let's now encapsulate the sub-setting of an MArray object in a proper method to facilitate this simple operation. In R, the default subsetting operator is [. Although its syntax looks like it is special, the operator is just a normal function with a bit of extra syntactic sugar.

```
> letters[1:3]
[1] "a" "b" "c"
> `[`(letters, 1:3)
[1] "a" "b" "c"
```

If you type '[' in you R console, you will see that this is a primitive function. These internally implemented functions have a special property that, although not explicitly generic functions, they get automatically promoted to generics when a method of the same name is defined. In other words, we we must not create a generic (this would break [is all the other cases) and can directly proceed with implementing a specific behaviour of [for the MArray class.

The documentation help("[") shows that, in addition to x, the object to be subset, we also have to take the i and j indices into account and the drop argument. When an argument is not relevant, we specify this by declaring that it is "missing".

5.4 The validity method

While discussing the design of our microarray data structure in section 2, we have implicitly stated the following validity constrains, schematically represented in figure 2. In terms of dimensions, the number of rows of the expression matrix must be equal to the number of rows in the feature meta-data data frame and the number

of columns in the expression matrix must be equal to the number of rows in the sample meta-data data frame. In terms of names, we have also implied that the row names of the expression matrix and feature meta-data data frame were identical and that the column names of the expression matrix and the row names of the sample meta-data data frame were identical. The latter is a good check to make sure that the order in these respective data structures are the same.

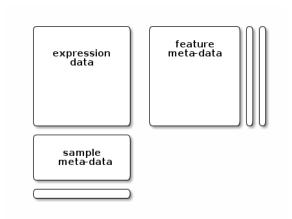


Figure 2: Dimension requirements for the respective expression, feature and sample meta-data slots. (Figure from the pRoloc package vignette.)

It is possible to create a validity method for S4 classes to check that the assumptions about the data are met. This validity method is created using the setValidity function and the validity of an object can be checked with validObject.

```
> setValidity("MArray", function(object) {
      msg <- NULL
      valid <- TRUE
+
      if (nrow(marray(object)) != nrow(fmeta(object))) {
          valid <- FALSE
          msg <- c(msg,
                   "Number of data and feature meta-data rows must be identical.")
      }
+
      if (ncol(marray(object)) != nrow(pmeta(object))) {
+
          valid <- FALSE
          msg <- c(msg,
+
                   "Number of data rows and sample meta-data columns must be identi
+
      }
      if (!identical(rownames(marray(object)), rownames(fmeta(object)))) {
+
          valid <- FALSE
+
          msg <- c(msg,
```

```
"Data and feature meta-data row names must be identical.")
      }
+
      if (!identical(colnames(marray(object)), rownames(pmeta(object)))) {
          valid <- FALSE
+
          msg <- c(msg,
                   "Data row names and sample meta-data columns names must be ident
      }
+
      if (valid) TRUE else msg
+ })
Class "MArray" [in ".GlobalEnv"]
Slots:
Name:
                  fmeta
          marray
Class:
          matrix data.frame data.frame
> validObject(ma)
[1] TRUE
```

Exercise 4: Try to create a new invalid MArray object using the constructor MArray.

```
> x <- matrix(1:12, ncol = 3)
> y <- fmeta(ma)
> z <- pmeta(ma)
> MArray(marray = x, fmeta = y, pmeta = z)

Error in validObject(.Object): invalid class "MArray" object: 1: Number
of data and feature meta-data rows must be identical.
invalid class "MArray" object: 2: Number of data rows and sample meta-data
columns must be identical.
invalid class "MArray" object: 3: Data and feature meta-data row names
must be identical.
invalid class "MArray" object: 4: Data row names and sample meta-data
columns names must be identical.
```

5.5 A replacement method

The following section describes how to write a method that is dedicated to the replacement or update of the content of slots. It is of course possible to perform such an operation by accessing the slot content directly, as illustrated below.

As discussed in previous sections, this is not advised as it violates the encapsulation of our data and makes it possible to break the validity of an object. Note also that it is not possible to overwrite any slot with data that is not of the expected class.

```
> ma@marray <- 1</pre>
Error in checkAtAssignment(structure("MArray", package = ".GlobalEnv"),
   assignment of an object of class "numeric" is not valid for @'marray'
in an object of class "MArray"; is(value, "matrix") is not TRUE
> (broken <- ma)</pre>
An object of class MArray
 10 features by 6 samples.
> broken@marray <- matrix(1:9, 3)</pre>
> broken
An object of class MArray
 3 features by 3 samples.
> validObject(broken)
Error in validObject(broken): invalid class "MArray" object: 1:
                                                                     Number
of data and feature meta-data rows must be identical.
invalid class "MArray" object: 2: Number of data rows and sample meta-data
columns must be identical.
invalid class "MArray" object: 3: Data and feature meta-data row names
must be identical.
invalid class "MArray" object: 4: Data row names and sample meta-data
columns names must be identical.
```

There is a special type of method, called a *replacement method*, that can be implemented to obtain the desired behaviour in a clean and controlled way. A replacement method provides the convenient slot(object)<- syntax.

Replacement method are always named by concatenating the name of the method and the arrow assignment operator. If we wish to write a method to replace the slot that can be accessed with the marray accessor (again, the slot itself is called marray, but that does not need to be the case), the corresponding replacement method would be called marray<-2.

Another important specificity of replacement methods is that they always take (at least) two arguments; the object to be updated, that we will name object and the replacement data, always called value.

Finally, as marray<- is going to be a method (and there is no existing generic), we first need to define a generics.

```
> setGeneric("marray<-",
+ function(object, value) standardGeneric("marray<-"))
[1] "marray<-"</pre>
```

In the definition of the replacement method, we check that the user-provided value does not break the validity of object with the validObject method (see section 5.4) before returning it.

Below, we firs try to replace the expression matrix with an invalid value and then test out new replacement method with a valid matrix.

```
> tmp <- matrix(rnorm(n*m, 10, 5), ncol = m)
> marray(ma) <- tmp

Error in validObject(object): invalid class "MArray" object: 1: Data
and feature meta-data row names must be identical.
invalid class "MArray" object: 2: Data row names and sample meta-data
columns names must be identical.
> colnames(tmp) <- LETTERS[1:m]
> rownames(tmp) <- pasteO("probe", 1:n)
> head(marray(ma), n = 2)
```

²It could actually be called anything followed by <-, but that would be confusing for the user.

```
В
probe1 6.867731 17.55891 14.59489 16.793398 9.177382
probe2 10.918217 11.94922 13.91068 9.486061 8.733192
               F
probe1 11.990529
probe2 6.939868
> marray(ma) <- tmp</pre>
> head(marray(ma), n = 2)
                          В
                                              D
probel 10.9439615 11.457231 11.66475 12.792432
probe2 0.9752069
                  7.783541 15.31550 3.617039
              Ε
probe1 18.83644 8.035960
probe2 13.58354 8.400036
```

Exercise 5: Implement the fmeta and pmeta replacement methods and show that it works with the following replacement.

```
> pmeta(ma)$sex <- rep(c("M", "F"), 3)</pre>
> pmeta(ma)
  sampleId condition sex
Α
                     WT
                           Μ
          2.
В
                           F
                     WT
С
          3
                     WT
D
          4
                    MUT
                           F
Ε
          5
                    MUT
                           М
F
           6
                    MUT
                           F
```

5.6 The dim method

Let's also implement a dim method that will tell us the dimensions of the marray matrix. Let's start by looking at dim to see if it is a method at all.

```
> dim
function (x) .Primitive("dim")
```

6 Introspection

To find out more about a class you are using without reading its source code, one can use the following functions to get the slot names and the complete class definition.

```
> slotNames(ma)

[1] "marray" "fmeta" "pmeta"

> getClass("MArray")

Class "MArray" [in ".GlobalEnv"]

Slots:

Name: marray fmeta pmeta
Class: matrix data.frame data.frame
```

To obtain all the methods that are available for a given function name of for a given class class, one can use showMethods.

```
object="MArray"

Function: marray<- (package .GlobalEnv)
object="MArray"

Function: pmeta (package .GlobalEnv)
object="MArray"

Function: pmeta<- (package .GlobalEnv)
object="MArray"

Function: show (package methods)
object="MArray"</pre>
```

To obtain the code for a specific method, one can use getMethod with the name of the method and the name of the class.

```
> getMethod("marray", "MArray")

Method Definition:

function (object, ...)
{
     .local <- function (object)
     object@marray
     .local(object, ...)
}

Signatures:
     object
target "MArray"
defined "MArray"</pre>
```

7 Conclusion

The Bioconductor project provides S4 implementations for microarray data. As a conclusion to our exercise, let's use the class introspection tools seen in section 6 to study the ExpressionSet implementation available in the Biobase package.

```
> library("Biobase")
> getClass("ExpressionSet")
Class "ExpressionSet" [package "Biobase"]
Slots:
Name:
           experimentData
                                    assayData
Class:
                    MIAME
                                    AssayData
Name:
                phenoData
                                  featureData
Class: AnnotatedDataFrame AnnotatedDataFrame
Name:
               annotation
                                 protocolData
                character AnnotatedDataFrame
Class:
        .__classVersion__
Name:
Class:
                 Versions
Extends:
Class "eSet", directly
Class "VersionedBiobase", by class "eSet", distance 2
Class "Versioned", by class "eSet", distance 3
```

There are of course many more slots, to support description of the experiment itself as well as the microarray platform. The expression data is stored in the assayData slot and is of class AssayData. In practice, this generally equates to an environment that contains one or multiple expression matrices. The feature and sample annotations are stored in the featureData and phenoData slots, both of class AnnotatedDataFrame. An AnnotatedDataFrame is a data.frame that supports additional variable annotation. Each of these S4 classes can in turn be inspected with getClass or, better, by reading the respective documentation.

We also see that the ExpressionSet class extends the eSet class, i.e. ExpressionSet is a sub-class of the eSet. See the contains field in ?setClass to read more about sub/super-class hierarchies.

Although the verbosity of the S4 system might seem like a little overhead in the beginning, it provides improved stability and usability for the future. The design and usage of an efficient class system requires one to think about the needs of the user role before writing code, as it involves some commitment in the design decisions

and the resulting interface.

Session information

All software and respective versions used to produce this document are listed below.

- R version 3.2.2 (2015-08-14), x86_64-pc-linux-gnu
- Locale: LC_CTYPE=en_US.UTF-8, LC_NUMERIC=C, LC_TIME=zh_CN.UTF-8, LC_COLLATE=en_US.UTF-8, LC_MONETARY=zh_CN.UTF-8, LC_MESSAGES=en_US.UTF-8, LC_PAPER=zh_CN.UTF-8, LC_NAME=C, LC_ADDRESS=C, LC_TELEPHONE=C, LC_MEASUREMENT=zh_CN.UTF-8, LC_IDENTIFICATION=C
- Base packages: base, datasets, graphics, gr
Devices, methods, parallel, stats, utils
- Other packages: Biobase 2.28.0, BiocGenerics 0.14.0, knitr 1.11
- Loaded via a namespace (and not attached): evaluate 0.8, formatR 1.2.1, highr 0.5.1, magrittr 1.5, stringi 1.0-1, stringr 1.0.0, tools 3.2.2