S4 System Development in Bioconductor

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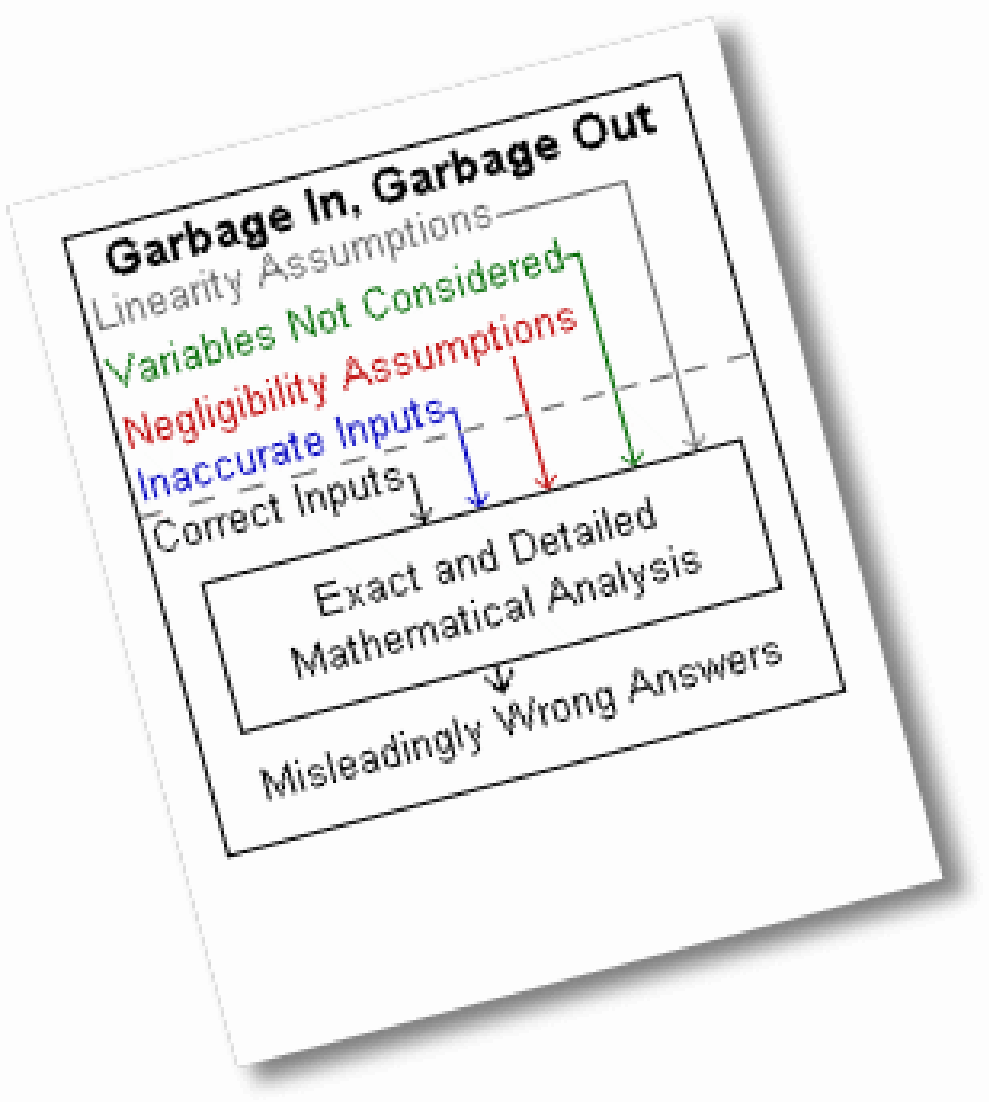
20-21 May, 2010

BioC Motivation for OOP

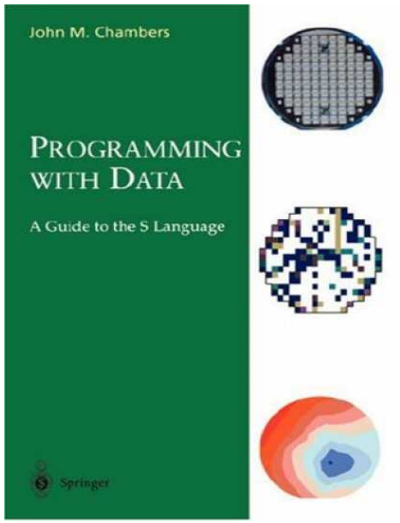


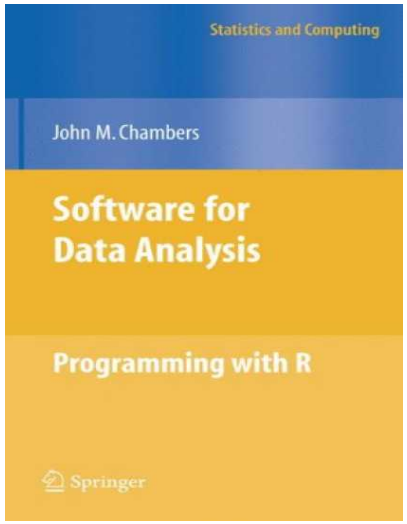
OOP: Minimizing inaccurate inputs & modularizing inputs and outputs.

Outline

Two Programming Systems in R

- R is an implementation of the S3 language by Chambers and Hastie (1992).
- S3 uses a *"class" attribute* to mimic aspects of OOP.
- S4 is a formal OOP system.
- The methods package implements the S4 system as described in Chambers (1998) and Chambers (2008).





Main Features of Bioconductor

S4 superiority to S3 in realizing BioC features

- The R project for statistical computing
- Documentation and **reproducible research**
- Statistical and graphical **methods for genomic data**
- **Genomic annotations**
- Open source
- **Open development**

Reasons

- Explicit representation of classes
- Validity checking of instances
- Methods registered with generics

Use of S4 in Bioconductor

Statistics on packages in BioC 2.6

- 197 of 389 (51%) BioC packages define S4 classes
- 97 use inheritance
  - traditional parents: *ExpressionSet* and *eSet* from Biobase
  - newer prolific parent: *Sequence* from IRanges
  - common off-beat parent: *list*, an S3 type
- 30 define virtual classes
- 14 use multiple inheritance

Outline

S4 Framework

S4 Components

Class

- is virtual?
- slots (properties)
- contains (inherits)
- prototype
- validity function

Generic Function

- dispatch signature
- dispatch method

*Methods**

- signature mapping
- function definition

* Grouped in methods list

Important differences with Java and C++

1. Classes don't own methods.
2. Design goal: Be "vectorized".
   (a) Class slots ideally vectors and matrices.
   (b) Methods avoid unnecessary looping.

S4 Class Creation

`setClass` function arguments

- `Class` – the class name.
- `representation` – the slot definitions.
- `contains` – the parent classes.
- `prototype` – the slot values for a default instance.
- `validity` – a function that checks instance validity.

`new` constructor arguments

- `Class` – the class name.
- `...` – typically, slot values.

Canonical Example in S4 (1/2)

Class definition

```
> setClass("Greeting",
+          representation =
+          representation(phrase = "character"),
+          prototype = prototype(phrase = "Hello world!"))
```

Default instantiation

```
> new("Greeting")
```

```
An object of class "Greeting"
Slot "phrase":
[1] "Hello world!"
```

Customized instantiation

```
> new("Greeting", phrase = "ciao")
```

```
An object of class "Greeting"
Slot "phrase":
[1] "ciao"
```

Canonical Example in S4 (2/2)

Validity method

```
> setValidity("Greeting",
+     function(object) {
+         if (length(object@phrase) != 1)
+             "'phrase' not a single string"
+         else if (!nzchar(object@phrase))
+             "'phrase' is empty"
+         else
+             TRUE
+     })
```

Invalid object instantiation

```
> new("Greeting", phrase = "")
Error in validObject(.Object) :
  invalid class "Greeting" object: 'phrase' is empty
```

Creating New S4 Objects from Old

`initialize` function arguments

- `.Object` – an S4 object.
- `...` – typically, new slot values.

Creation via `initialize`

```
> nametag <- new("Greeting")
> nametag <- initialize(nametag, phrase = "Welcome")
> nametag

An object of class "Greeting"
Slot "phrase":
[1] "Welcome"
```

S4 Generic Function & Method Creation

`setGeneric` function arguments

- `name` – the generic function name.
- `def` – the generic definition, typically of the form

  `function(<<ARG_LIST>>) standardGeneric("<<GEN_NAME>>"))`
- `signature` – the method dispatch signature.

`setMethod` function arguments

- `f` – the generic function name.
- `signature` – the mapping of arguments in dispatch signature to classes.
- `definition` – the method definition.

Generic Function & Method for Canonical Example (1/2)

Generic function definition

```
> setGeneric("words", signature = "x",
+     function(x) standardGeneric("words"))
```

Method definition

```
> setMethod("words", c("x" = "Greeting"),
+     function(x)
+     {
+         ans <- strsplit(x@phrase, "\\W")[[1L]]
+         sort(unique(ans[nzchar(ans)]))
+     })
```

Method invocation

```
> words(new("Greeting"))

[1] "Hello" "world"
```

Generic Function & Method for Canonical Example (2/2)

Method definition

```
> setMethod("words", c("x" = "character"),
+     function(x)
+     {
+         ans <- unlist(strsplit(x, "\\W"),
+                       use.names = FALSE)
+         sort(unique(ans[nzchar(ans)]))
+     })
> setMethod("words", c("x" = "Greeting"),
+     function(x) callGeneric(x@phrase))
```

Method invocation

```
> words(new("Greeting"))
```

```
[1] "Hello" "world"
```

Implicit Generic Method for Canonical Example

Non-S4 generic function

```
> showMethods("nchar")

Function: nchar (package base)
x="AlignedXStringSet0"
x="ANY"
x="character"
    (inherited from: x="ANY")
x="CompressedCharacterList"
x="CompressedRleList"
x="MaskedXString"
x="PairwiseAlignedFixedSubjectSummary"
x="PairwiseAlignedXStringSet"
x="Rle"
x="SimpleCharacterList"
x="SimpleRleList"
x="XString"
x="XStringSet"
x="XStringViews"
```

Implicit Generic Not Always Available

```
> showMethods("nzchar")

Error in genericForPrimitive(f) :
  methods may not be defined for primitive function
"nzchar" in this version of R
```

```
> setMethod("nzchar", c("x" = "Greeting"),
+           function(x) nzchar(x@phrase))

Error in genericForPrimitive(f) :
  methods may not be defined for primitive function
"nzchar" in this version of R
```

S4 Coerce and Replace Method Creation

`setAs` function arguments; produces `coerce` methods

- `from` – the old object's class.
- `to` – the new object's class.
- `def` – the method definition.

`setReplaceMethod` function; produces `"<-"` methods

- A wrapper for `setMethod` that adds suffix `"<-"` to argument `f`.
- e.g. `"names<-"`, usage: `names(x) <- letters`.

Coercion Method for Canonical Example

Method definition

```
> setAs("Greeting", "character",
+       function(from) from@phrase)
```

Display coerce methods

```
> showMethods("coerce", classes = "Greeting")
```

```
Function: coerce (package methods)
from="Greeting", to="character"
```

Perform coercion

```
> as(new("Greeting"), "character")
```

```
[1] "Hello world!"
```

Slot Accessor and Replacer in Canonical Example (1/2)

Accessor generic and method

```
> setGeneric("phrase", signature = "x",
+     function(x) standardGeneric("phrase"))
> setMethod("phrase", "Greeting",
+     function(x) x@phrase)
```

Replacer generic and method

```
> setGeneric("phrase<-", signature = "x",
+     function(x, value) standardGeneric("phrase<-"))
> setReplaceMethod("phrase", "Greeting",
+     function(x, value) initialize(x, phrase = value))
```

Slot Accessor and Replacer in Canonical Example (2/2)

Accessor invocation

```
> silentBob <- new("Greeting")
> phrase(silentBob)

[1] "Hello world!"
```

Replacer invocation

```
> phrase(silentBob) <- ""

Error in validObject(.Object) :
  invalid class "Greeting" object: 'phrase' is empty
```

Motivation for Replacement Methods

Slot replacement methods don't validity check

```
> silentBob <- new("Greeting")
> silentBob@phrase <- ""

> validObject(silentBob)
Error in validObject(silentBob) :
  invalid class "Greeting" object: 'phrase' is empty
```

`initialize` function does

```
> initialize(silentBob, phrase = "")
Error in validObject(.Object) :
  invalid class "Greeting" object: 'phrase' is empty
```

Object Display in Canonical Example

`show` method definition

```
> setMethod("show", "Greeting",
+     function(object)
+     {
+         cat("A ", class(object), ": \"", phrase(object),
+             "\"\n", sep = "")
+     })
```

`show` method invocation

```
> new("Greeting")

A Greeting: "Hello world!"
```

Finding Methods for an S4 Class

`showMethods` function wrapper

```
> s4Methods <- function(class)
+ {
+     methods <-
+       showMethods(classes = class, printTo = FALSE)
+     methods <- methods[grep("^Function:", methods)]
+     sapply(strsplit(methods, " "), "[", 2)
+ }
```

Using custom function

```
> s4Methods("Greeting")
```

```
[1] "coerce"     "initialize" "nchar"      "phrase"
[5] "phrase<-"   "show"       "words"
```

Outline

S4 Classes for Exercises

Virtual Class

```
> setClass("Sample",
+          representation("VIRTUAL",
+                         description = "character"))
```

Subclasses

```
> setClass("OneSample", contains = "Sample",
+          representation(one = "numeric"))

> setClass("TwoSample", contains = "Sample",
+          representation(one = "numeric",
+                         two = "numeric"))
```

S4 Exercises

1. Create a *PairedSample* class that inherits from *TwoSample*.
   (a) Same slots as *TwoSample*.
   (b) Validity method checks slots `one` and `two` to be of equal length.
2. Create a `tTest` generic and methods using `t.test` function from the stats package.
   (a) Generic signature
   ```
   (x, alternative = c("two.sided", "less",
   "greater"), mu = 0, conf.level = 0.95, ...)
   ```
   (b) *OneSample* and *PairedSample* method signature
   ```
   (x, alternative = c("two.sided", "less",
   "greater"), mu = 0, conf.level = 0.95)
   ```
   (c) *TwoSample* method signature
   ```
   (x, alternative = c("two.sided", "less",
   "greater"), mu = 0, conf.level = 0.95, var.equal =
   FALSE)
   ```
3. Create `show` methods and any other features you find interesting.

Outline

S4 Objects Always Copied on Modification

S4 object copy-on-change

```
> setClass("DotDash", representation =
+          representation(dot = "raw", dash = "integer"))
> aDotDash <- new("DotDash", dot = as.raw(1), dash = 1:1e8)
> system.time(aDotDash@dot <- as.raw(2))
   user  system elapsed
  0.254   0.333   0.603
```

Best practices

- Use one `initialize` call instead of multiple `"@<-"`/`"slot<-"` calls.
- Vectorize (e.g. inherit from IRanges's *CompressedList* class).

S4 Object Overhead

S4 object instantiation timing & size

```
> setClass("DotDash", representation =
+          representation(dot = "raw", dash = "integer"))

> system.time(dd <- lapply(1:1e4, function(i) new("DotDash")))
   user  system elapsed
  0.740   0.003   0.745

> print(object.size(dd), units = "Mb")
4.2 Mb
```

Best practice

- Vectorize (e.g. inherit from IRanges's *CompressedList* class).

S4 Method Dispatch

S4 method dispatch

```
> setClass("DotDash", representation =
+          representation(dot = "raw", dash = "integer"))
> aDotDash <- new("DotDash")
> setMethod("show", "DotDash", function(object) cat())
> system.time(lapply(1:1e4, function(i) show(aDotDash)))
   user  system elapsed
  0.424   0.004   0.441
```

Best practice

```
> chosenFun <- selectMethod("show", "DotDash")
> system.time(lapply(1:1e4, function(i) chosenFun(aDotDash)))
   user  system elapsed
  0.084   0.001   0.094
```

Outline

Slot-Oriented Virtual Class (eSet)

Biobase's *eSet*

```
> library(Biobase)

> isVirtualClass("eSet")

[1] TRUE

> getSlots("eSet")

           assayData
         "AssayData"
           phenoData
"AnnotatedDataFrame"
         featureData
"AnnotatedDataFrame"
      experimentData
             "MIAME"
          annotation
         "character"
        protocolData
"AnnotatedDataFrame"
   .__classVersion__
          "Versions"
```

limma's *MAList*

```
> library(limma)

> isVirtualClass("MAList")

[1] FALSE

> getSlots("MAList")

 .Data
"list"
```

Method-Oriented Virtual Class (Sequence)

IRanges's *Sequence*

```
> library(IRanges)
> isVirtualClass("Sequence")
[1] TRUE
> getSlots("Sequence")
elementMetadata     elementType        metadata
          "ANY"     "character"          "list"
> getSlots("Rle")
          values            lengths  elementMetadata
"vectorORfactor"          "integer"             "ANY"
     elementType           metadata
     "character"             "list"
> length(s4Methods("Sequence"))
[1] 42
> head(s4Methods("Sequence"), 8)
[1] "!="        "["          "[<-"        "[["
[5] "$"         "aggregate" "append"     "as.env"
```

Method-Oriented Virtual Class (Sequence)

Sequence subclass defines

`"["`, `c`, `length`, `window`, `seqselect`, `"seqselect<-"`

Sequence subclass inherits

`head`, `tail`, `append`, `subset`, `rep`, `rev` (optimize?), `"window<-"`, `"[<-"`

```
setMethod("head", "Sequence",
    function(x, n = 6L, ...)
    {
        stopifnot(length(n) == 1L)
        if (n < 0L)
            n <- max(length(x) + n, 0L)
        else
            n <- min(n, length(x))
        if (n == 0L)
            x[integer(0)]
        else
            window(x, 1L, n)
    })
```

Multiple Inheritance & Vectorization (CompressedIRangesList)

CompressedIRangesList

```
setClass("CompressedIRangesList",
         prototype = prototype(elementType = "IRanges",
                               unlistData = new("IRanges")),
         contains = c("IRangesList", "CompressedList"))
```

IRanges's *List* paradigm

- *IRangesList* – a method-oriented virtual class
- *CompressedList* – a slot-oriented virtual class
- *SimpleIRangesList* – a sibling class to *CompressedIRangesList*

Build or Reuse? (CompresssedIRangesList)

IRanges's *CompressedIRangesList*

```
> library(IRanges)

> is(new("CompressedIRangesList"))

[1] "CompressedIRangesList"
[2] "IRangesList"
[3] "CompressedList"
[4] "RangesList"
[5] "Sequence"
[6] "Annotated"

> length(s4Methods("RangesList"))

[1] 34

> head(s4Methods("RangesList"), 8)

[1] "as.data.frame" "coerce"
[3] "countOverlaps" "coverage"
[5] "disjoin"       "end"
[7] "end<-"         "findOverlaps"
```

Biostrings's *MIndex*

```
> library(Biostrings)

> isVirtualClass("MIndex")

[1] TRUE

> s4Methods("MIndex")

[1] "coerce"     "countIndex"
[3] "coverage"   "length"
[5] "names"      "names<-"
[7] "unlist"     "width0"

> s4Methods("ByPos_MIndex")

[1] "[["         "endIndex"
[3] "show"       "startIndex"
```

Class Union & Group Generic (Rle)

IRanges's *Rle*

```
setClassUnion("vectorORfactor", c("vector", "factor"))

setClass("Rle", contains = "Sequence")
         representation(values = "vectorORfactor",
                        lengths = "integer"),
         <<REMAINING DEFINITION>>)

setMethod("Summary", "Rle",
    function(x, ..., na.rm = FALSE)
        switch(.Generic,
               all =, any =, min =, max =, range =
               callGeneric(runValue(x), ..., na.rm = na.rm),
               sum = sum(runValue(x) * runLength(x), ...,
                         na.rm = na.rm),
               prod = prod(runValue(x) ^ runLength(x), ...,
                           na.rm = na.rm)))
```

Outline

Resources

Books

- John M. Chambers. *Software for Data Analysis: Programming with R*. Springer, New York, 2008. ISBN-13 978-0387759357.
- Robert Gentleman. *R Programming for Bioinformatics*. Chapman & Hall/CRC, New York, 2008. ISBN-13 978-1420063677.

Documents on the Web

- John M. Chambers. "How S4 Methods Work", `http://developer.r-project.org/howMethodsWork.pdf`
- Friedrich Leisch, "S4 Classes and Methods", `http://www.ci.tuwien.ac.at/Conferences/useR-2004/Keynotes/Leisch.pdf`
- "S4 Classes in 15 pages, more or less", `http://www.stat.auckland.ac.nz/S-Workshop/Gentleman/S4Objects.pdf`