Part III. Overview of the Bioconductor project

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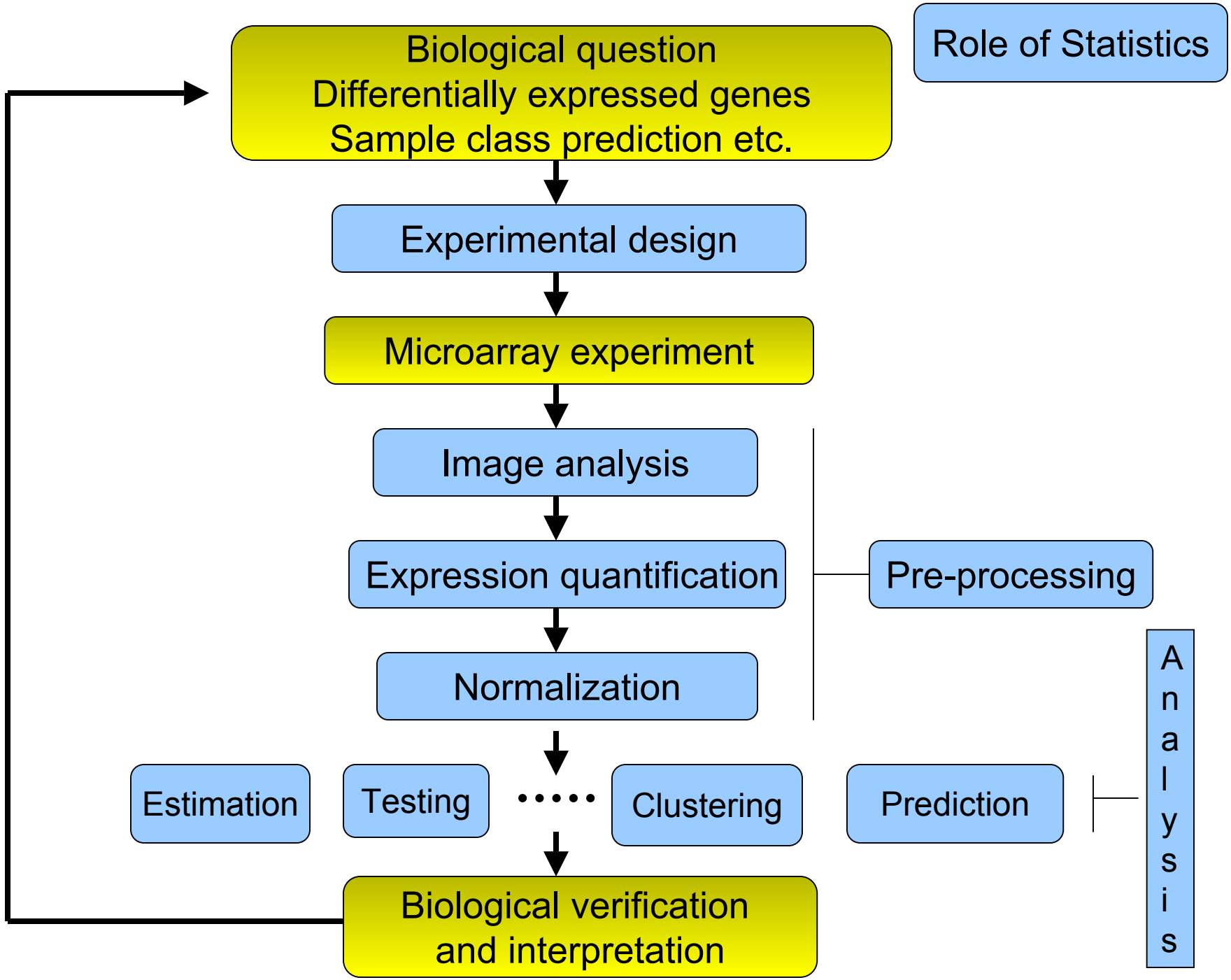
Role of Statistics
Biological question
Differentially expressed genes
Sample class prediction etc.
Experimental design
Microarray experiment
Image analysis
Expression quantification
Normalization
Pre-processing
Estimation
Testing
.....
Clustering
Prediction
Analysis
Biological verification
and interpretation

Statistical computing

Everywhere …

- Statistical design and analysis:
  - image analysis, normalization, estimation, testing, clustering, prediction, etc.

- Integration with biological information resources, in house and external databases:
  - gene annotation (GenBank, LocusLink);
  - literature (PubMed);
  - graphical (pathways, chromosome maps).

Computing needs

- Access to a broad range of statistical and graphical methods:

  diagnostic plots, linear and non-linear modeling, survival analysis, multiple testing, model selection, prediction, cluster analysis, resampling, etc.
- Tools for integrating biological metadata in the analysis of microarray data.
- Extensible, scalable, and interoperable software.

Bioconductor

- Bioconductor is an open source and open development software project for the analysis and comprehension of genomic data.

- Software and documentation are available from www.bioconductor.org.

Bioconductor

The broad goals of the project are

- to enable sound and powerful statistical analyses in genomics;
- to provide a computing platform that allows the rapid design and deployment of high-quality software;
- to develop a computing environment for both biologists and statisticians.

Bioconductor

- The project was started in the Fall of 2001 by Robert Gentleman, at the Biostatistics Unit of the Dana Farber Cancer Institute.
- There are currently 21 core developers.
- The first release of 15 packages occurred on May 2nd, 2002.

R

- Most of the early developments are in the form of R packages.

- R is a widely used open source language and environment for statistical computing and graphics

  - GNU's S-Plus.

R

- R is available from www.r-project.org.
- R is available for Unix, Windows, and Macintosh computers.
- Comprehensive R Archive Network - CRAN - www.cran.r-project.org: repository of software packages for a broad range of statistical and graphical techniques.

Bioconductor packages

Release 1.0, May 2nd, 2002

- General infrastructure:
  `Biobase`, `rhdf5`, `tkWidgets`.
- Annotation:
  `annotate`, `AnnBuilder`.
- Graphics:
  `geneplotter`.
- Pre-processing for Affymetrix oligonucleotide chip data:
  `affy`.
- Pre-processing for cDNA microarray data:
  `marrayClasses`, `marrayInput`, `marrayNorm`, `marrayPlots`.
- Differential gene expression:
  `edd`, `genefilter`, `multtest`, `ROC`.

Bioconductor

- Object-oriented class/method design. Allows efficient representation and manipulation of large and complex biological datasets of multiple types.
- Widgets. Small-scale graphical user interfaces, allowing point & click access to specific analysis tasks.
- E.g. File browsing and selection for data input.

Bioconductor

- Interactive tools for linking experimental results to annotation and literature WWW resources in real time.

  E.g. PubMed, GenBank, LocusLink.

- Scenario. For a list of differentially expressed genes obtained from **`multtest`** or **`genefilter`**, use the **`annotate`** package
  - to retrieve and search PubMed abstracts for these genes;
  - to generate an HTML report with links to LocusLink for each gene.

Bioconductor training

Extensive documentation and training resources for R and Bioconductor are available on the WWW.

- R manuals and tutorials are available from CRAN.
- R help system
  - detailed on-line documentation, available in text, HTML, PDF, and LaTeX formats;
  - e.g. **`help(genefilter), ?pubmed.`**
- R demo system
  - user-friendly interface for running demonstrations of R scripts;
  - e.g. **`demo(marrayPlots)`**, **`demo(affy).`**

Bioconductor training

- R vignette system
  - comprehensive repository of step-by-step tutorials covering a wide variety of computational objectives in `/doc` subdirectory;
  - documents generated using the **`Sweave`** function from the **`tools`** package;
  - integrated statistical documents intermixing text, code, and code output (textual and graphical);
  - documents can be automatically updated if either data or analyses are changed.

- Bioconductor short courses
  - modular training segments on software and statistical methodology;
  - lectures and computer labs available on WWW for self-instruction.

R programming

- In order to deliver high quality software, the Bioconductor project relies on a few programming techniques that might not be familiar
  - environments and closures;
  - object oriented programming.

- We review these here for interested programmers (understanding them is not essential but is often very helpful).

Environments and closures

- An environment is an object that contains bindings between symbols and values.
- It is very similar to a hash table.
- Environments can be accessed using the following functions
  - get a listing of objects in the environment **`e`**

    ```
    ls(env=e)
    ```
  - get the value of the object with name **`x`** in the environment **`e`**

    ```
    get("x", env=e)
    ```
  - assign to the name **`x`** the value **`y`** in the environment **`e`**

    ```
    assign("x",y,env=e)
    ```

Environments and closures

- Since these operations are used a great deal in Bioconductor we have provided two helper functions
  - **`multiget`**
  - **`multiassign`**

- These functions get and assign multiple values into the specified environment.

Environments and closures

- Environments can be associated with functions.
- When an environment is associated with a function, then that environment is used to obtain values for any unbound variables.
- The term closure refers to the coupling of the function body with the enclosing environment.
- The **`annotate`**, **`genefilter`**, and other packages take advantage of environments and closures.

Environments and closures

```
x <- 4

e1 <- new.env()
assign("x",10, env=e1)
f <- function() x
environment(f) <- e1

x   # returns 4
f() # returns 10!
```

Object oriented programming

- The Bioconductor project has adopted the OOP paradigm presented in *Programming with Data*, J. M. Chambers, 1998.

- Tools for programming using the class/method mechanism are provided in the `methods` package.

OOP

- A class provides a software abstraction of a real world object. It reflects how we think of certain objects and what information these objects should contain.
- A class defines the structure, inheritance, and initialization of objects.
- Classes are defined in terms of slots which contain the relevant data.
- An object is an instance of a class.

OOP

- A method is a function that performs an action on data (objects).
- A generic function is a dispatcher, it examines its arguments and determines the appropriate method to invoke.
- Examples of generic functions include **`plot`**, **`summary`**, **`print`**.

OOP

- It is important to realize that when calling a generic function (such as `plot`), the actions performed depend on the class of the arguments.
- Methods define how a particular function should behave depending on the class of its arguments.
- Methods allow computations to be adapted to particular data types, i.e., classes.

OOP

- The **`methods`** package contains a number of functions for defining new classes and methods (e.g. **`setClass`**, **`setMethod`**) and for working with these classes and methods.

- A tutorial is available at http://www.omegahat.org/RSMethods/index.html

OOP

- To obtain documentation (on-line help) about
  - a class: `class?classname`

    so, **`class?exprSet`**, will display the help file for the **`exprSet`** class.
  - a method: `methods?methodname`

    so, **`methods?print`**, will display the help file for the **`print`** methods.

OOP

```
> x <- 1:10
> y <- 2*x + 1 + rnorm(10)

> class(x)
[1] "integer"
> plot(x,y)

> fit <- lm(y ~ x)
> class(fit)
[1] "lm"
> plot(fit)
```

OOP

```
> setClass("simple",
     representation(x="numeric",y="matrix"),
     prototype = list(x=numeric(),y=matrix(0)))
> z <- new("simple", x=1:10,
                  y=matrix(rnorm(50),10,5))
> z@x
 [1]  1  2  3  4  5  6  7  8  9 10
> setMethod("plot",
    signature(x="simple", y="missing"),
    function(x, y,...)
     plot(slot(x,"x"),slot(x,"y")[,1]))
> plot(z)
```