# A suite of R packages for the analysis of DNA copy number microarray experiments
# Application in cancerology

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The R User Conference 2009
Rennes




# Outline


1. Biological / clinical context
2. R packages description
3. End-user interfaces / automatic workflow

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1 Biological / clinical context

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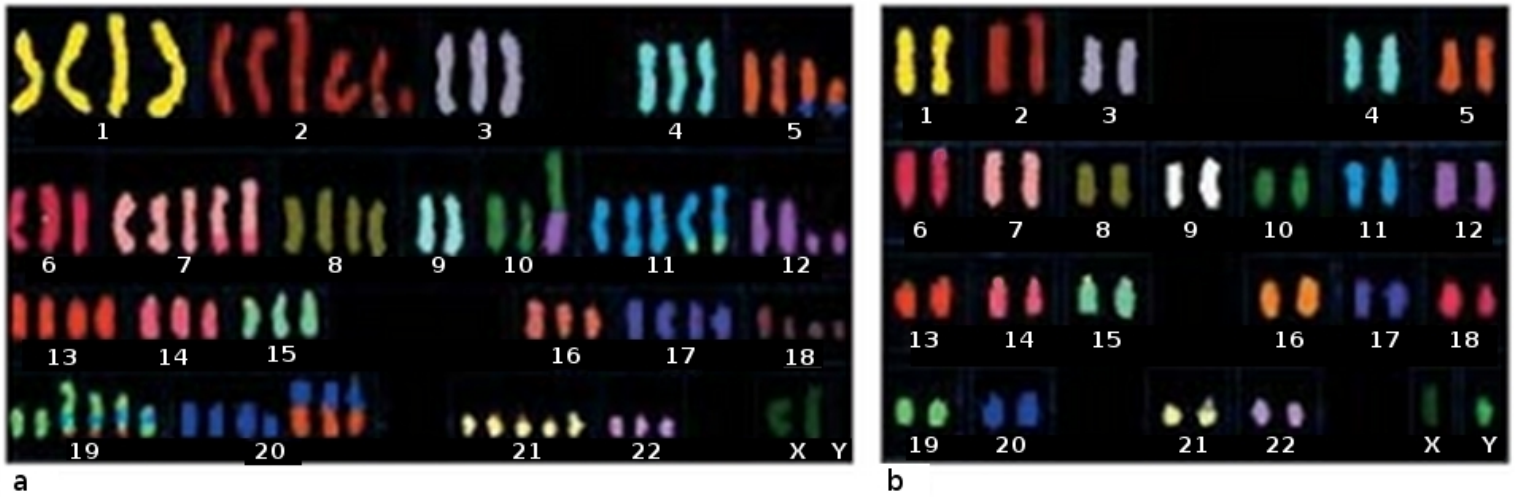
# DNA copy number alteration in tumour




tumoral cell

normal cell

## Chaos in cancer cells

gain, loss or amplification of chromosomes or pieces of chromosomes.

## Molecular profiling of tumours

- Identification of DNA copy number alterations in each patient
- Is the pattern of alterations is related to patient outcome (e.g. relapse, metastasis)?

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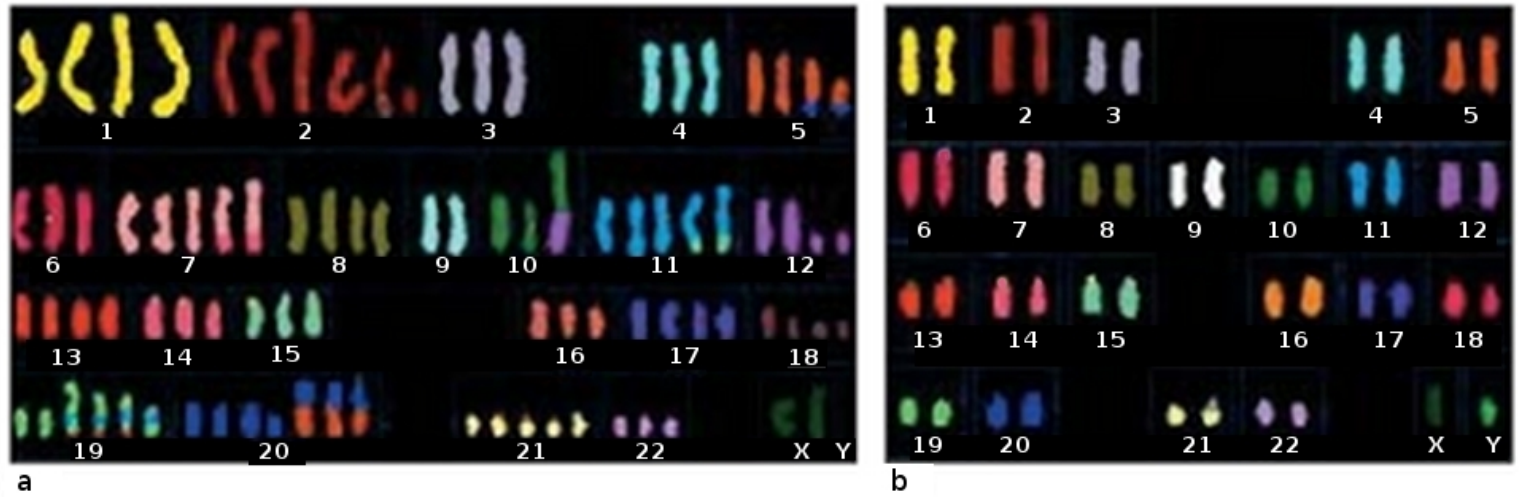


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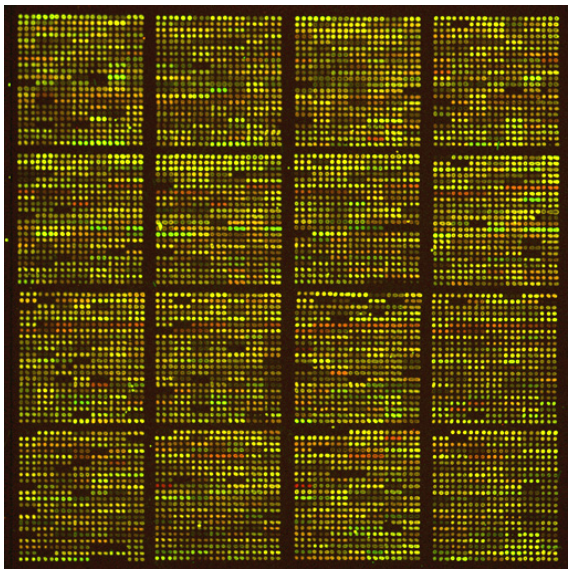
# High-throughput quantification of DNA copy number

## Microarray technology

- DNA copy number for $5 \times 10^3$ up to $2 \times 10^6$ genomic loci
- Probes spotted on a glass array (i.e. the microarray)



microarray

Colour study: squares with concentric circles

*Wassily Kandinsky*, 1913

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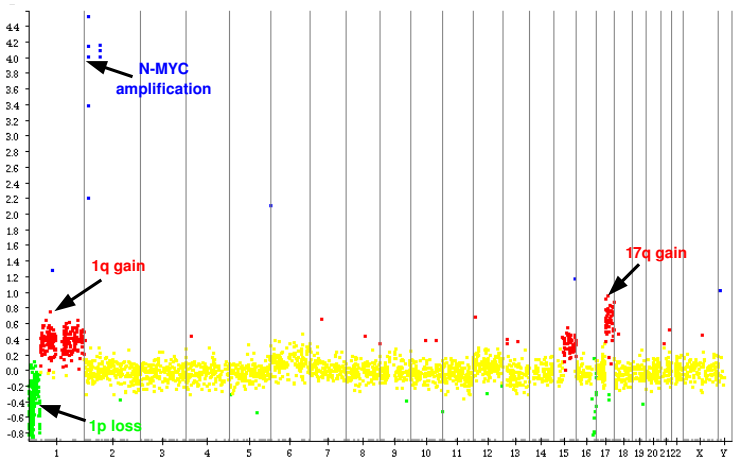
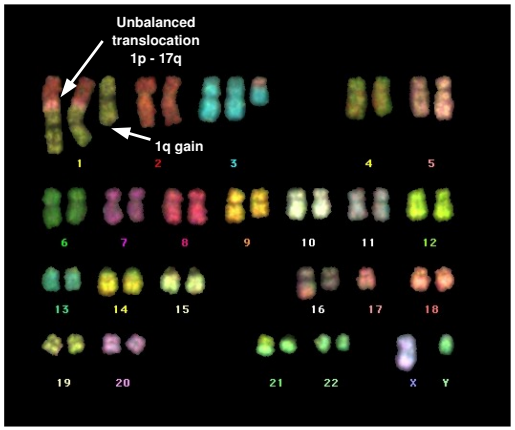



DNA copy number profile of the tumour




Karyotype of the tumour

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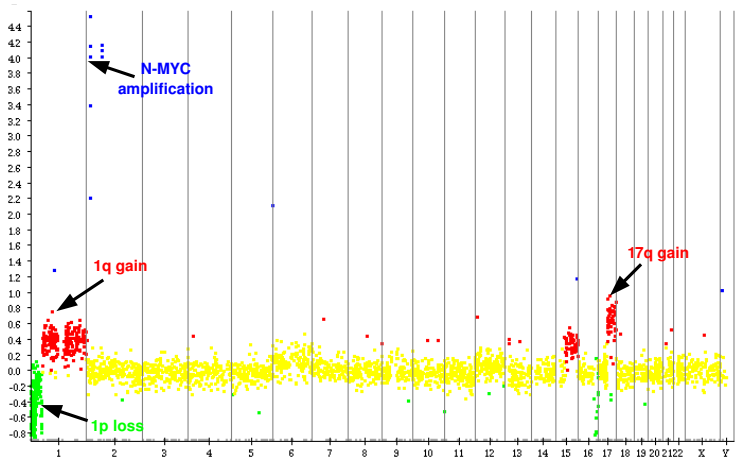


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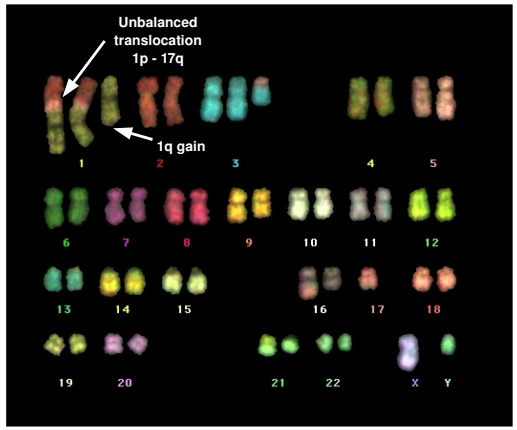
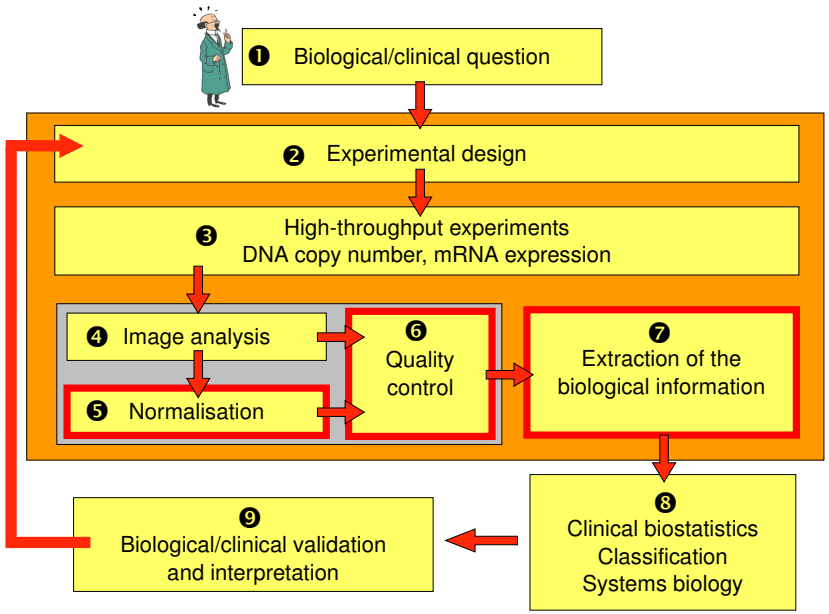



Karyotype of the tumour

## Huge amount of data ($\sim 2 \times 10^6$ variables for each patient)

Need for biostatistical algorithms and automatic bioinformatic pipelines

# Biostatistical workflow




## R packages available from www.bioconductor.org

- MANOR: spatial normalisation
- GLAD: extraction of the biological information
- ITALICS: normalisation + extraction of the biological information

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2 R packages description

3 End-user interfaces / automatic workflow

# MANOR: an algorithm to detect spatial bias

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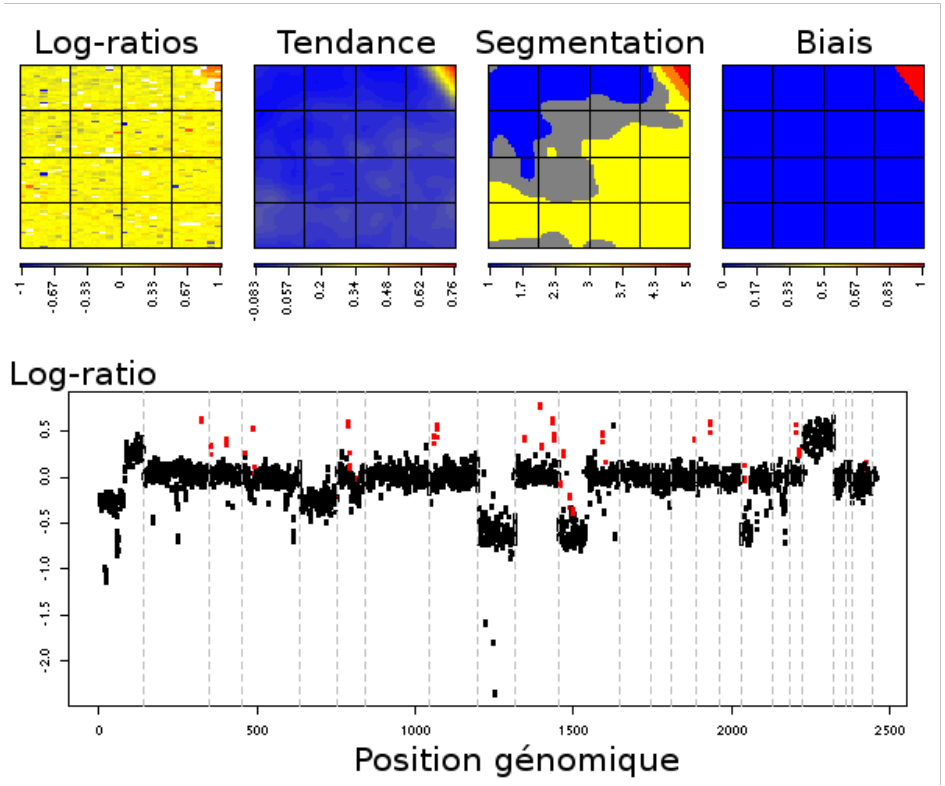


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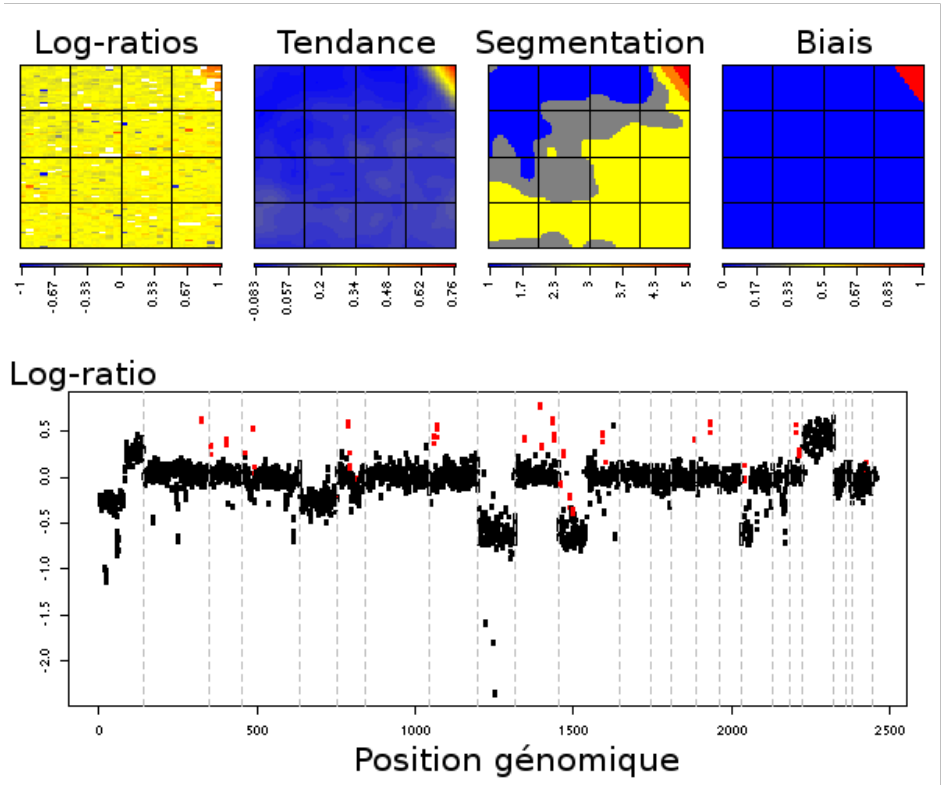


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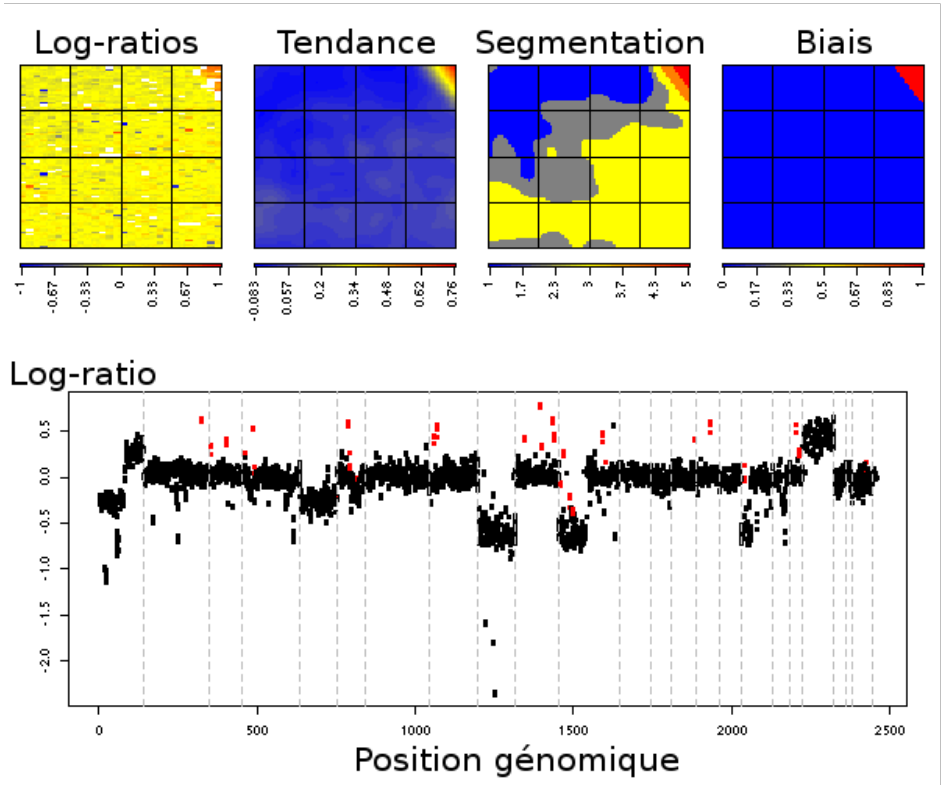


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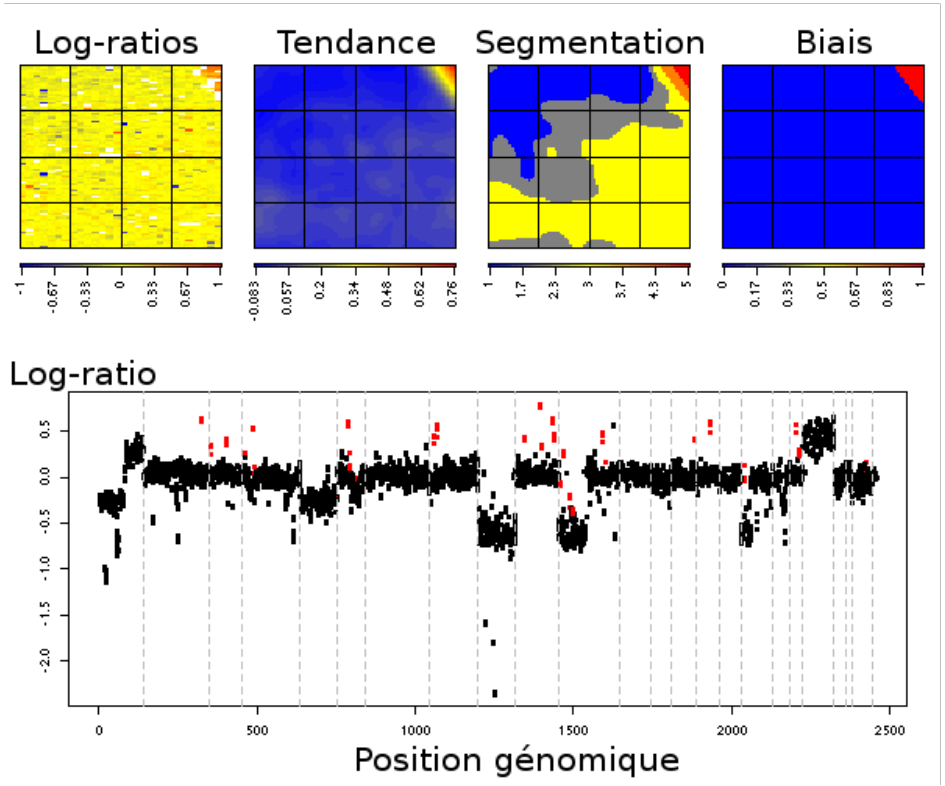


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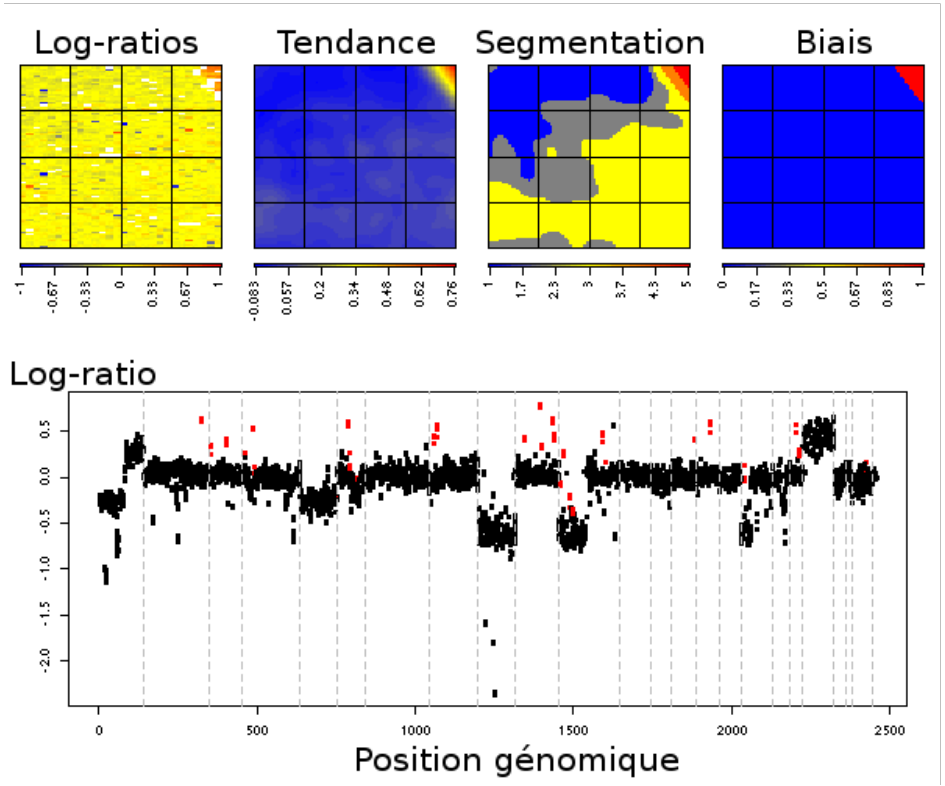


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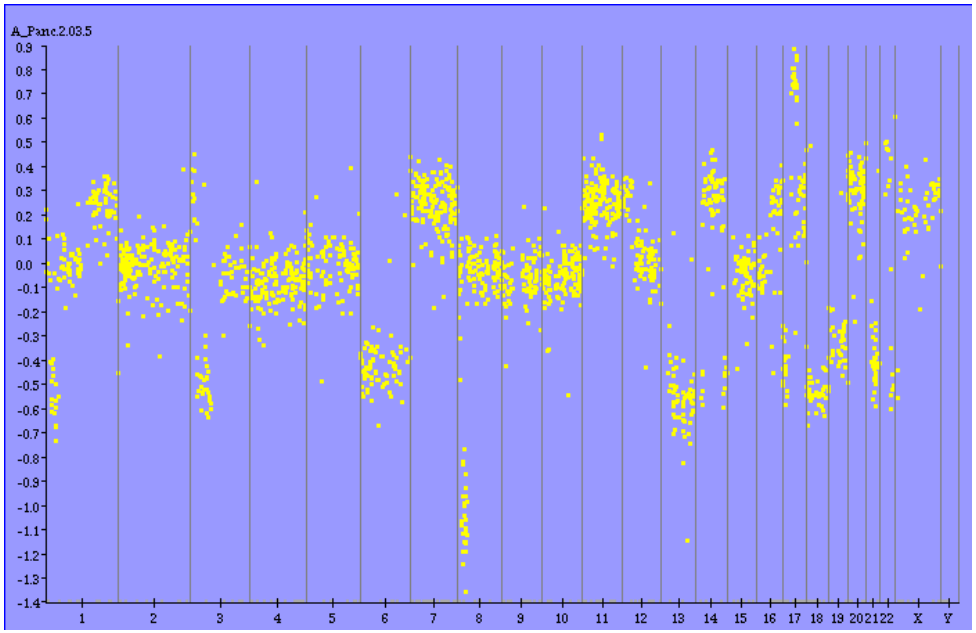
## Profile segmentation

- The GLAD algorithm aims at identifying chromosomal regions with identical DNA copy number.

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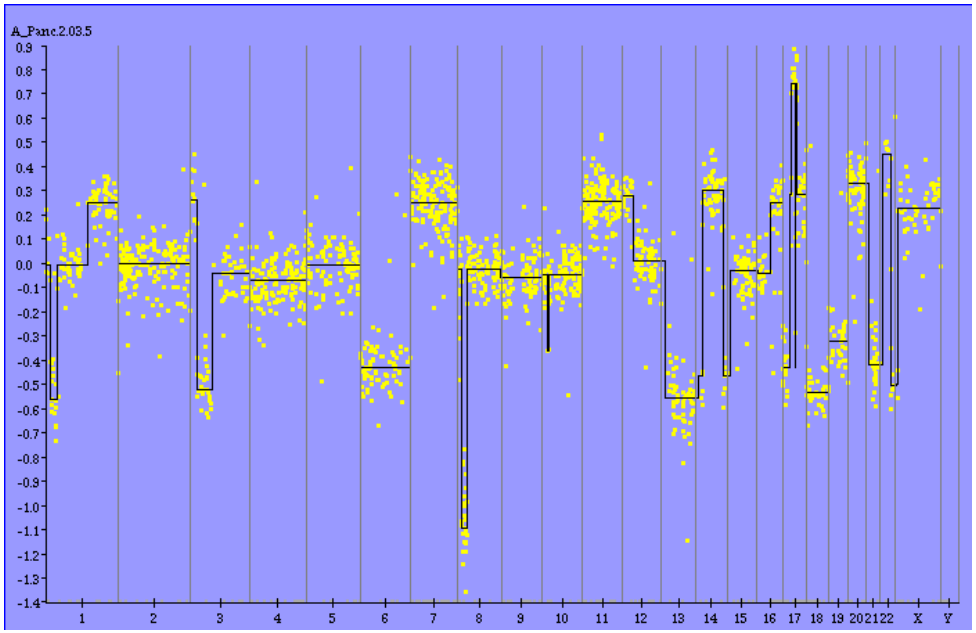


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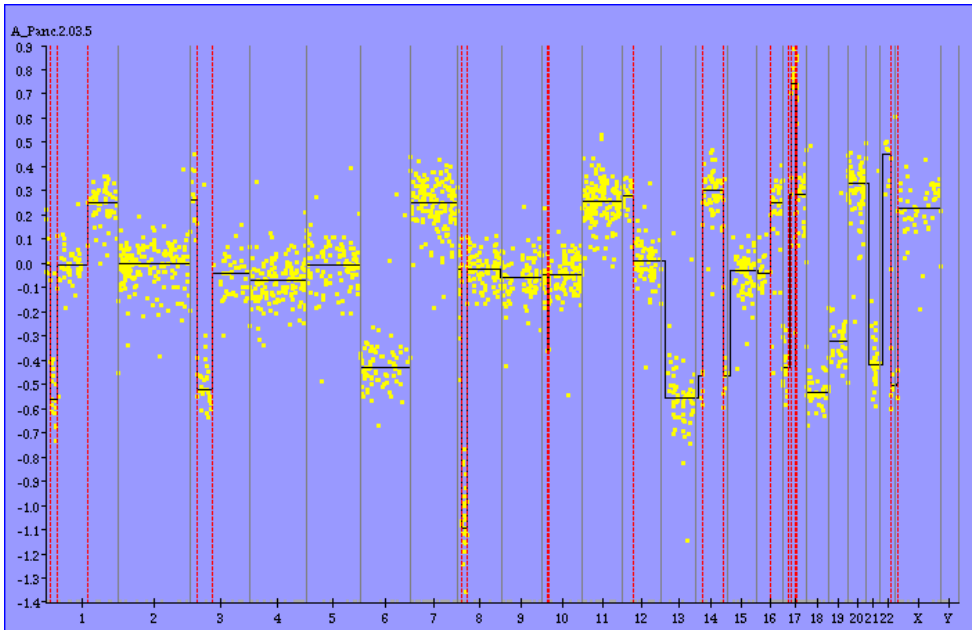


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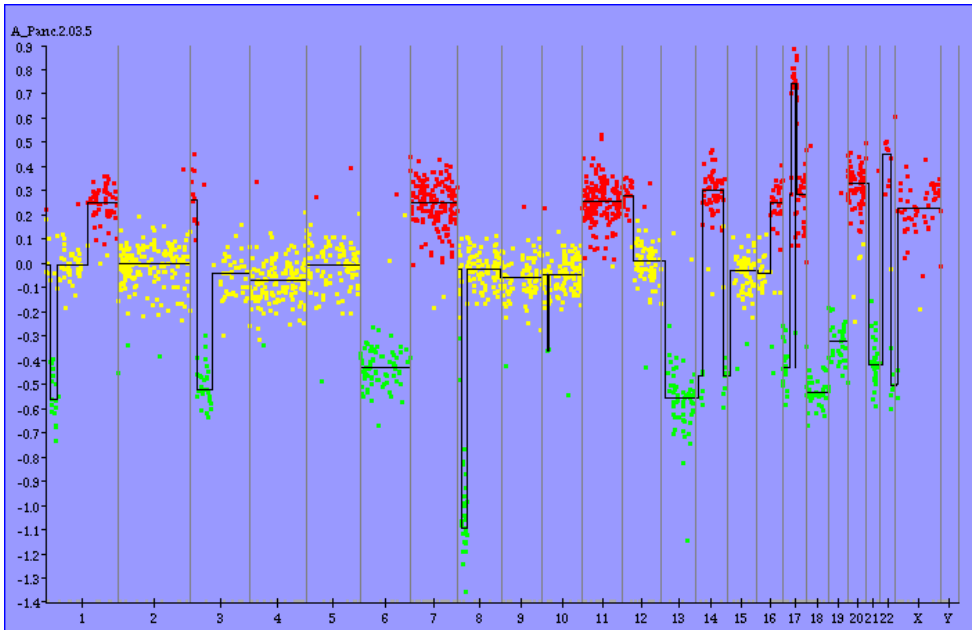


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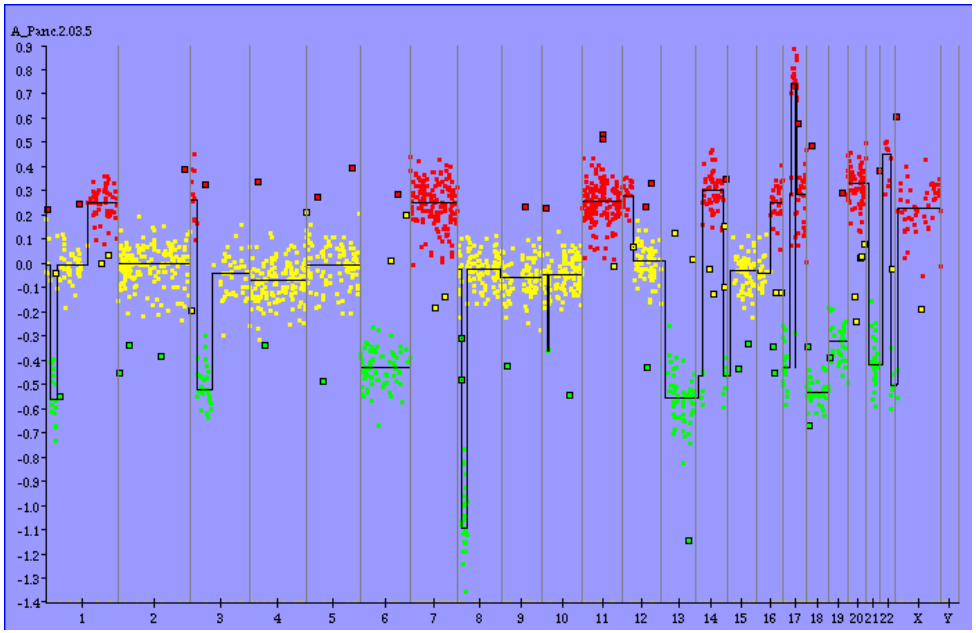


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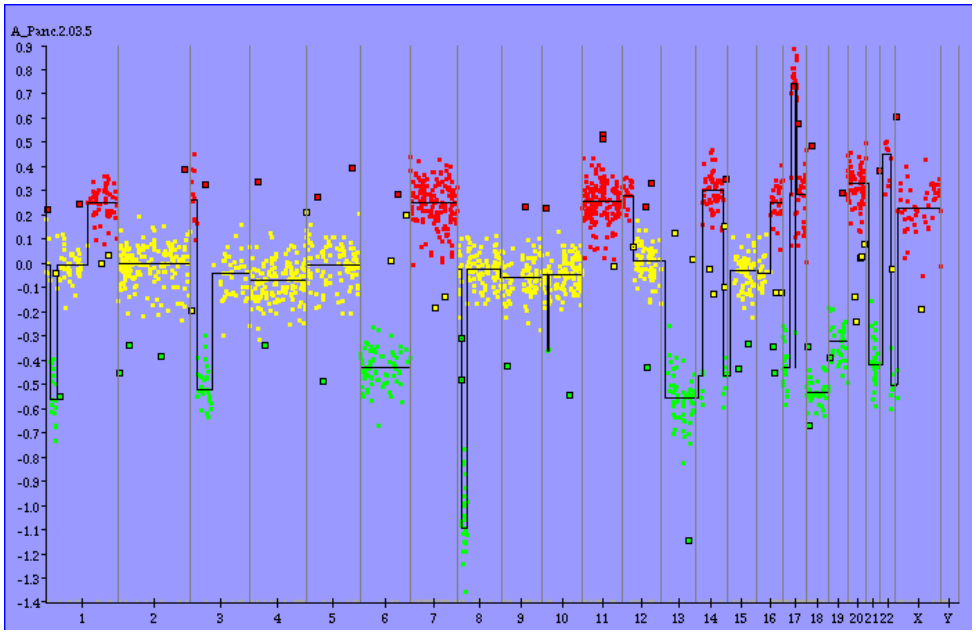


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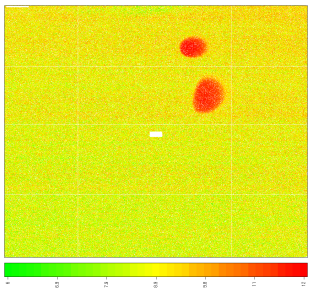
## ITALICS: ITerative and Alternative normaLIzation of Copy number Snp array

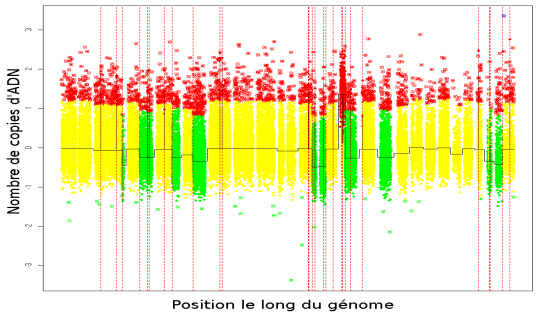
Rigaill et al., Bioinformatics, 2008

## Devoted to the analysis of Affymetrix Genome-Wide SNP chip

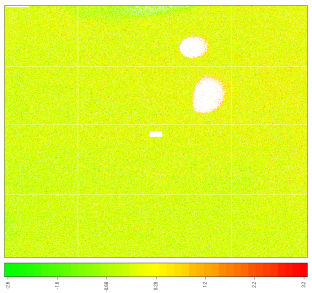
- the specificities of the affymetrix technology are taken into account in the algorithm
- the signal to noise ratio is better
- the breakpoint location is more accurate

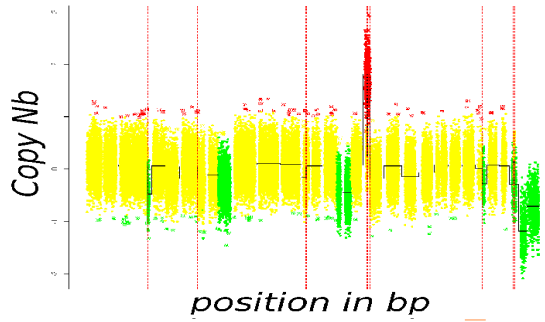
Spatial artifact $\Rightarrow$ 1600 aberrant values






ITALICS $\Rightarrow$ 90 aberrant values, 13 SNP discarded





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- need to visualise their data
- biological interpretation of their data
- not necessarly familiar with R programing language
- no biostatistician/bioinformatician in their lab
- need easy-to-use interfaces

**Diffusion of statistical methods within the scientific community**

If we want our statistical methods to be used, we need to package them properly.

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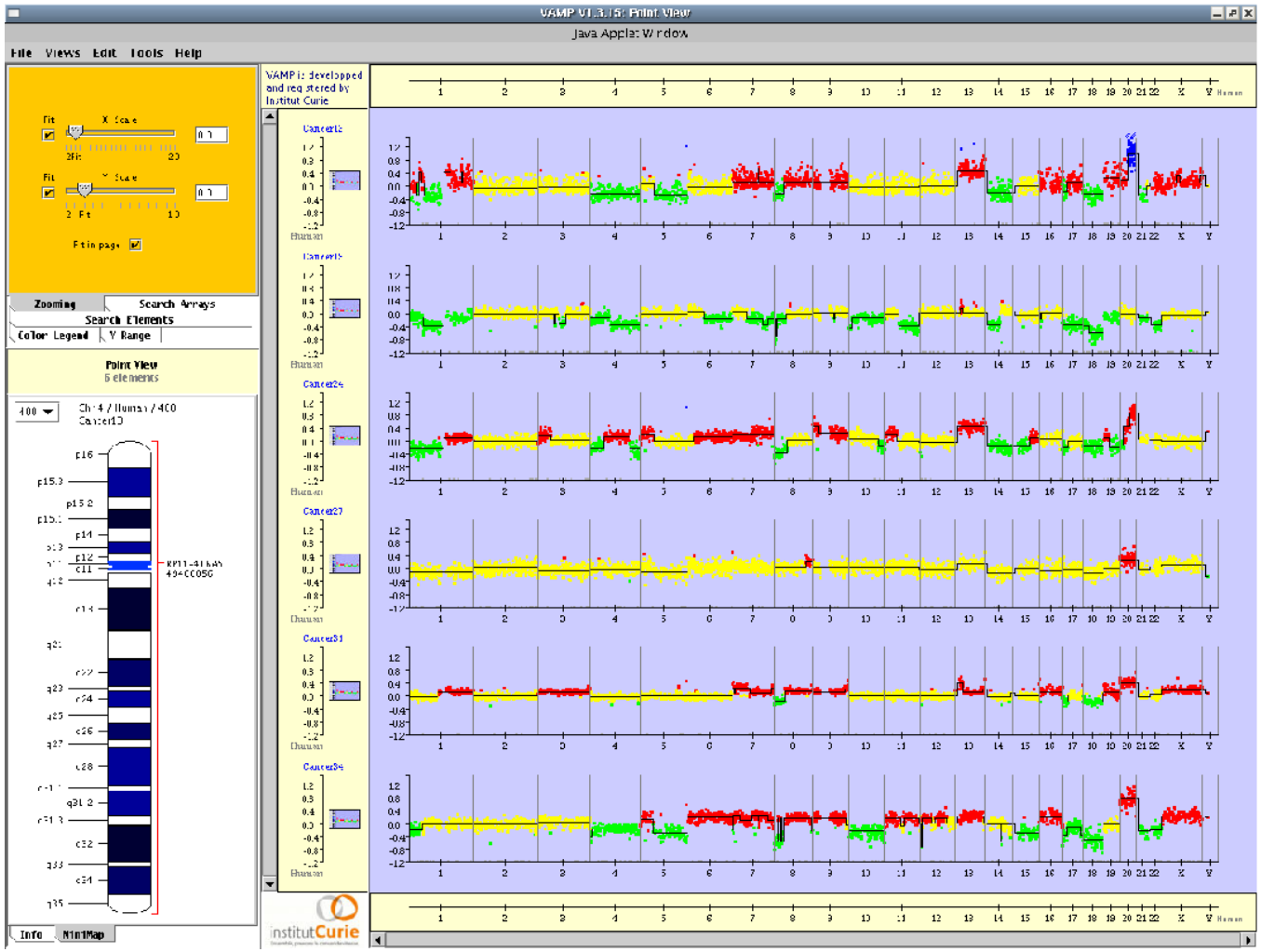
# VAMP: a software to visualise and analyse data

## La Rosa et al., Bioinformatics, 2006




http://bioinfo.curie.fr/vamp

# Our tools fo DNA copy number experiments

- R packages (MANOR, GLAD, ITALICS) for biostatistical analysis
- VAMP java software for visualisation (and analysis)

**Need for an integrated environment**

CAPweb is a web interface which allows the use of all the previous tools.

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# CAPweb: an end-user web platform

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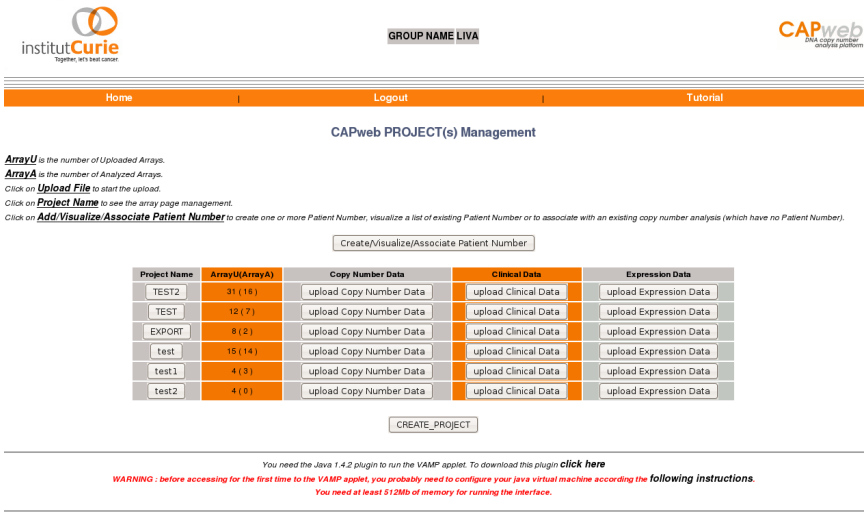


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- breakpoint detection: GLAD
- summary report
- visualise the data with VAMP
- array technology: BAC, cDNA, Agilent, Affymetrix (100K, 500K) (Illumina, Nimblegen soon)
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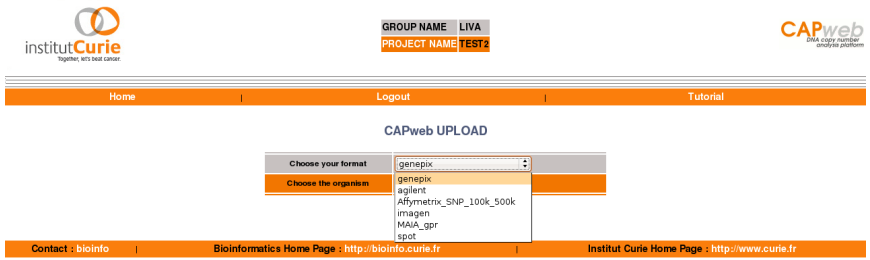


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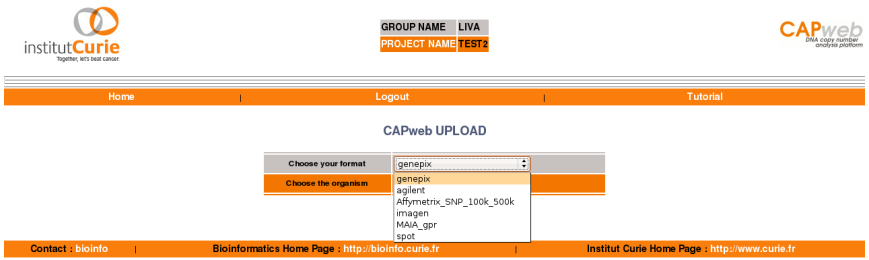


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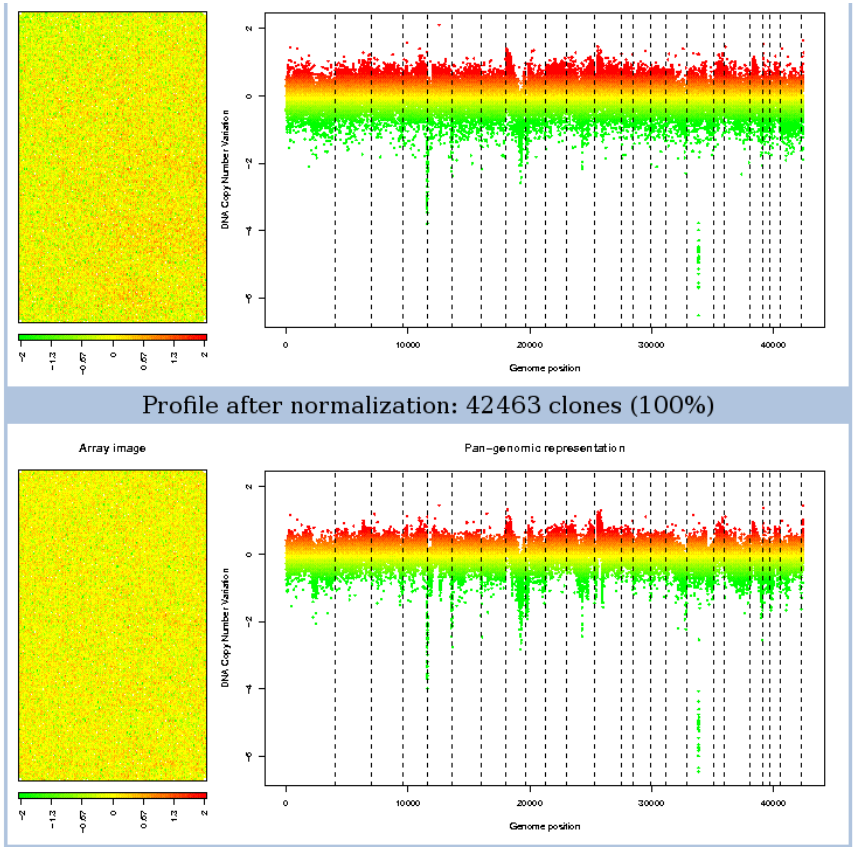


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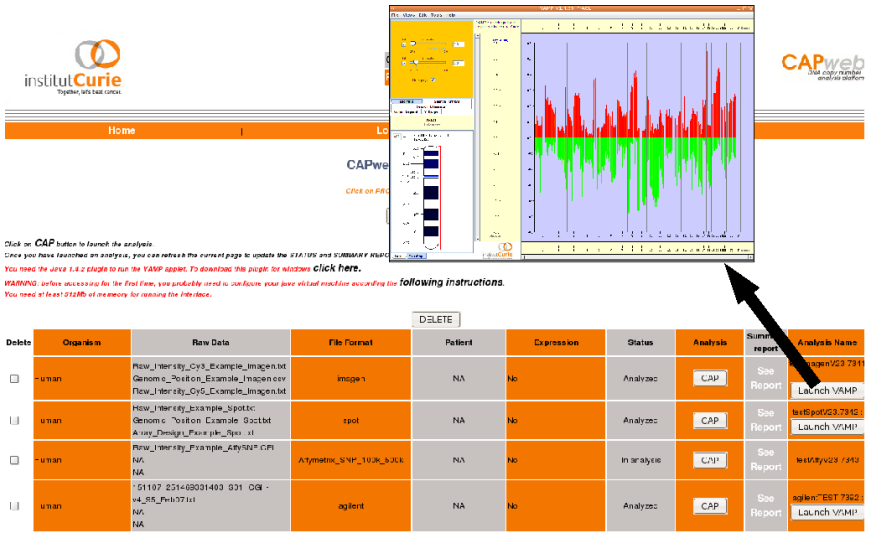


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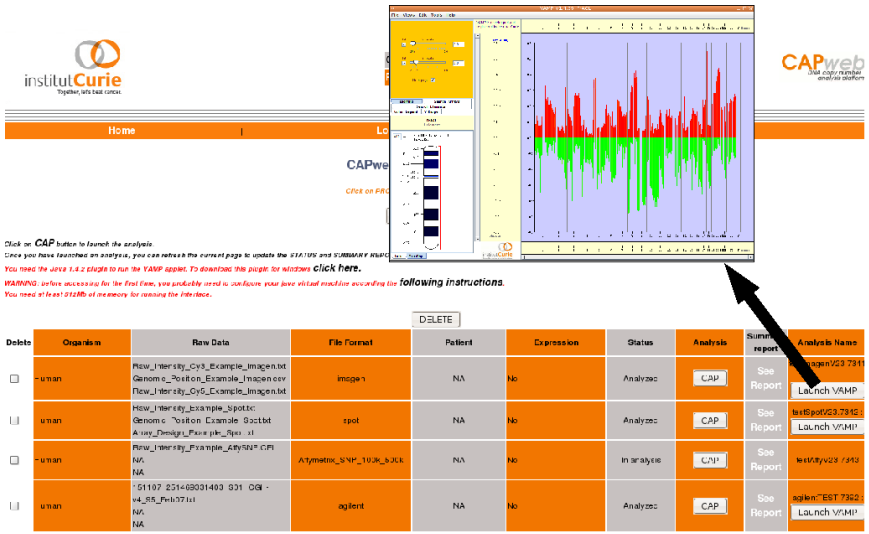


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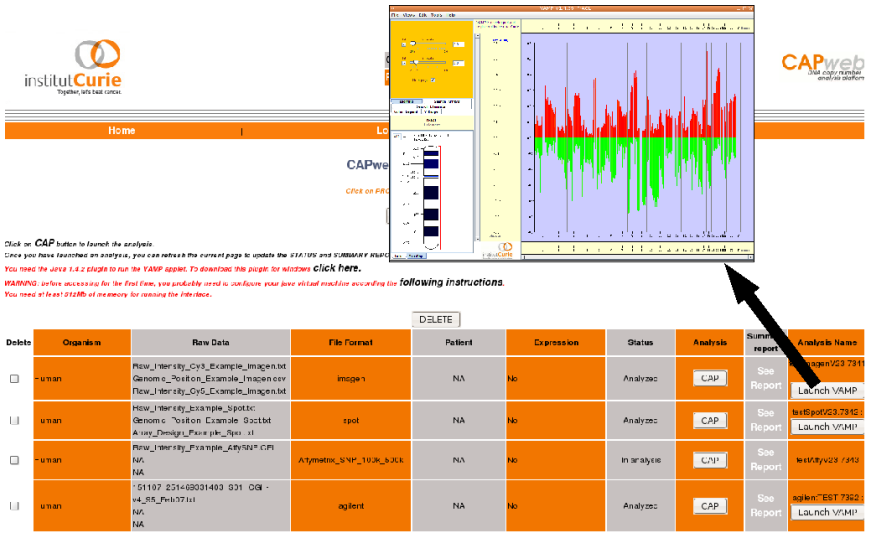


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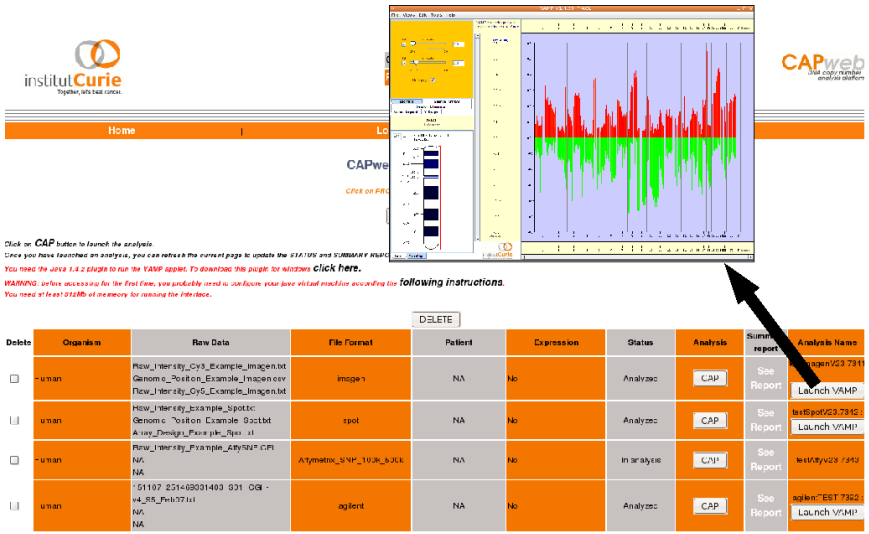


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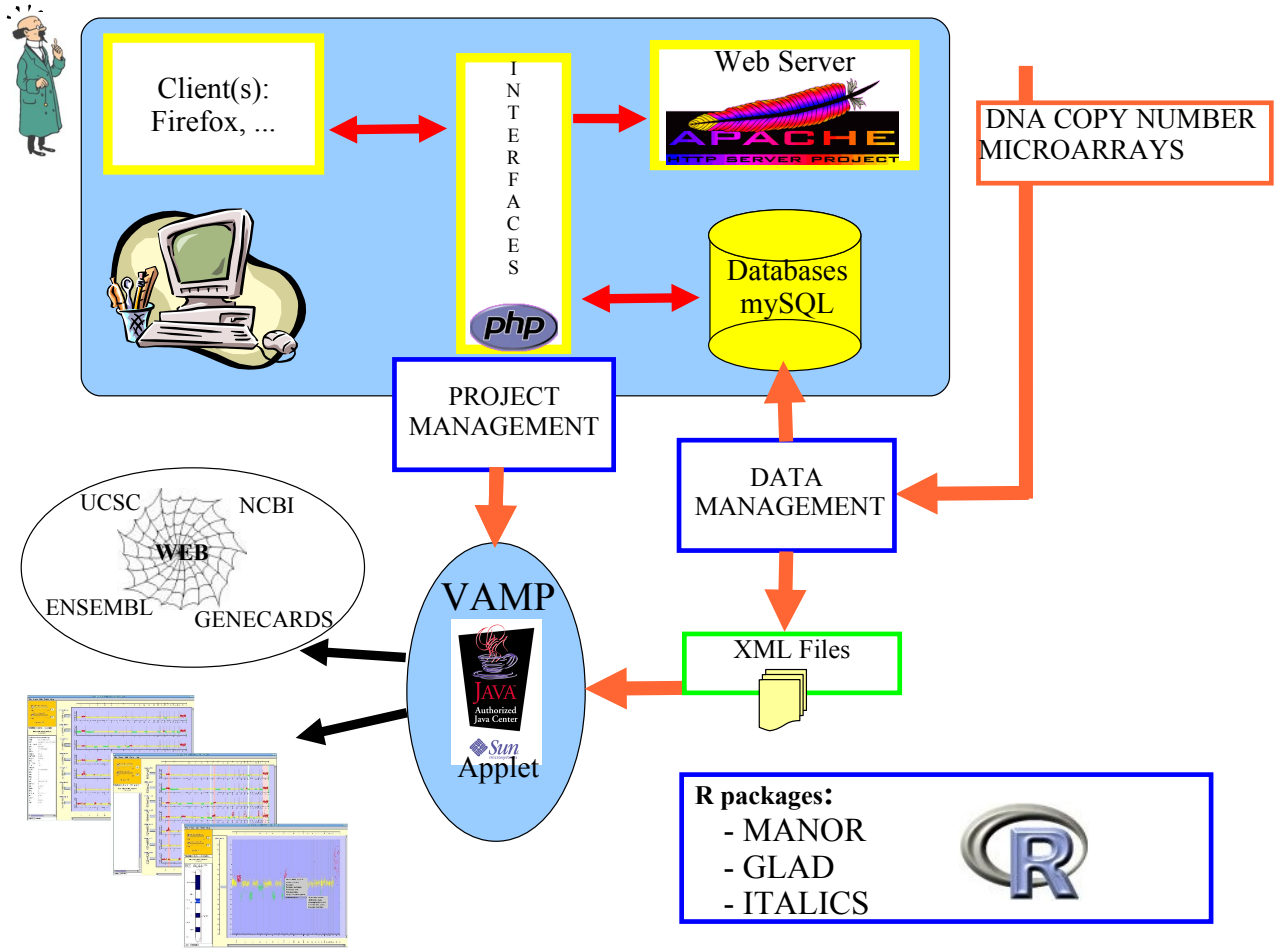


Our R packages are used calling CGI from any web browser

# Recent evolutions and perspectives

## Recent changes

- Possibility to use HaarSeg algorithm (Ben-Yaacov and Eldar, Bioinformatics, 2008) in GLAD $\rightarrow$ 2 millions genomic profiles can be analysed within 1 minute
- Use C/C++ in order to reduce computing time

## On-going work

- Improvement of ITALICS in order to analyse Affymetrix Genome Wide SNP 6.0
- Extension to Next-Generation Sequencing technologies (Terabytes of data!!)

aroma.affymetrix (Bengtsson et al.) R package offers many functionalities for affymetrix data analysis

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aroma.affymetrix (Bengtsson et al.) R package offers many functionalities for affymetrix data analysis

# Recent evolutions and perspectives

## Recent changes

- Possibility to use HaarSeg algorithm (Ben-Yaacov and Eldar, Bioinformatics, 2008) in GLAD $\rightarrow$ 2 millions genomic profiles can be analysed within 1 minute
- Use C/C++ in order to reduce computing time

## On-going work

- Improvement of ITALICS in order to analyse Affymetrix Genome Wide SNP 6.0
- Extension to Next-Generation Sequencing technologies (Terabytes of data!!)

aroma.affymetrix (Bengtsson et al.) R package offers many functionalities for affymetrix data analysis

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