Multivariate analysis of genetic data
— an introduction —

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Population genomics in R
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23 Aug 2016

Outline

Multivariate analysis in a nutshell

Applications to genetic data

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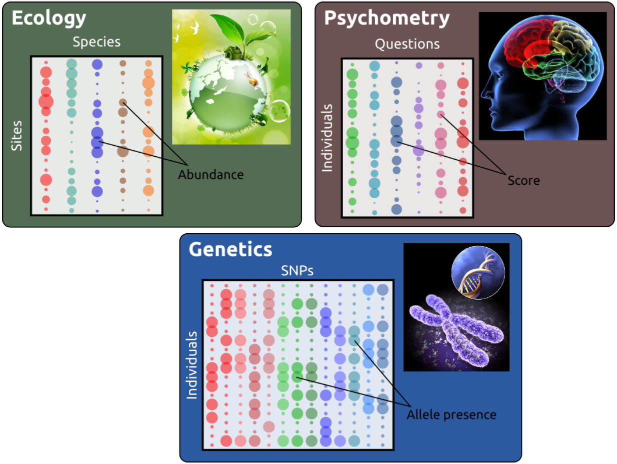
Applications to genetic data

Multivariate data: some examples



Association between individuals? Correlations between variables?

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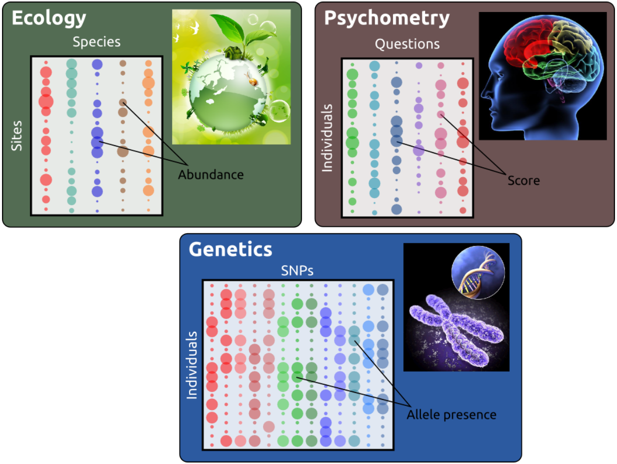

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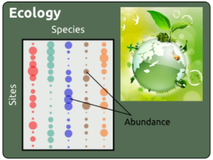
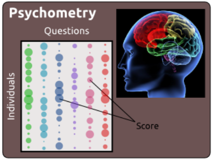
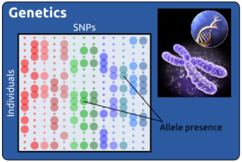
Multivariate analysis to summarize diversity







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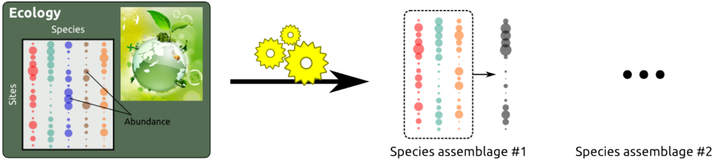

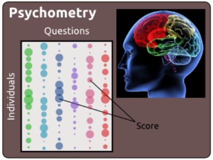

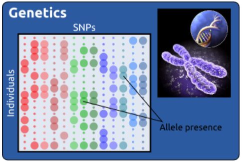

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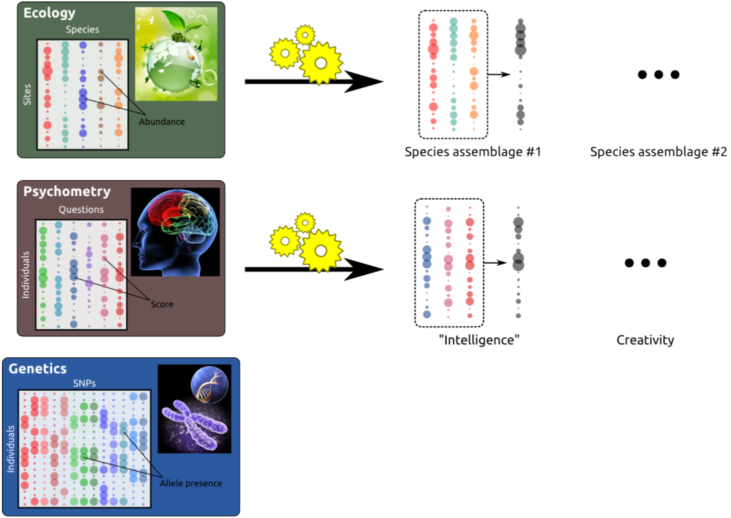

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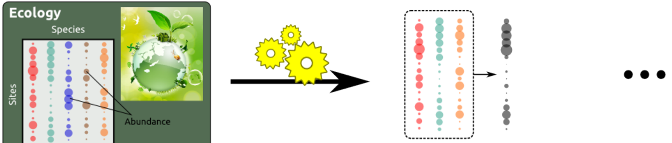
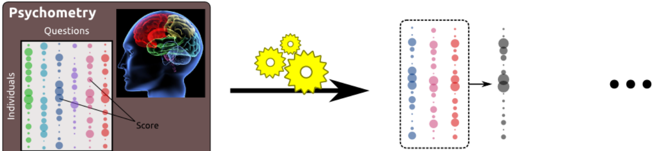


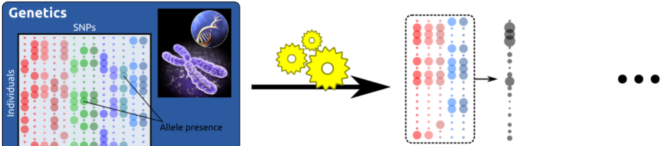
Species assemblage #1

Species assemblage #2



"Intelligence"

Creativity



Two populations

Resistant/susceptible strains

Multivariate analysis: an overview

Multivariate analysis, a.k.a:

- "*dimension reduction techniques*"
- "*ordinations in reduced space*"
- "*factorial methods*"

Purposes:

- summarize diversity amongst observations
- summarize correlations between variables

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Most common methods

Differences lie in input data:

- quantitative/binary variables: *Principal Component Analysis* (PCA)
- 2 categorical variables: *Correspondance Analysis* (CA)
- $>$2 categorical variables: *Multiple Correspondance Analysis* (MCA)
- Euclidean distance matrix: *Principal Coordinates Analysis* (PCoA) / *Metric Multidimensional Scaling* (MDS)

Many other methods for ≥ 2 data tables, spatial analysis, phylogenetic analysis, etc.

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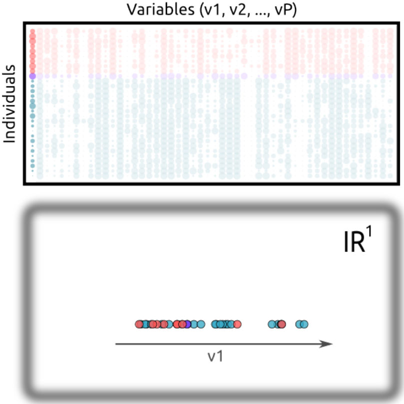
1 dimension, 2 dimensions, P dimensions



Need to find most informative directions in a P-dimensional space.

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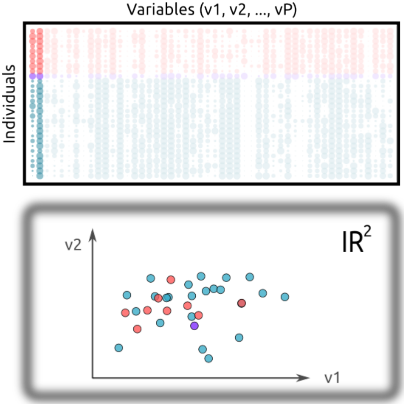

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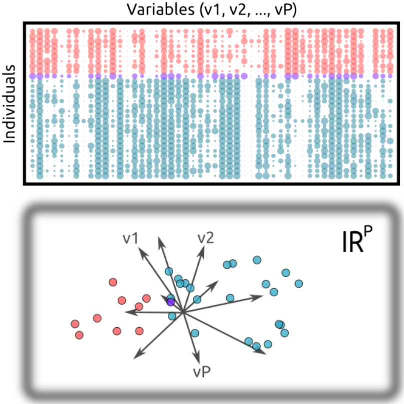

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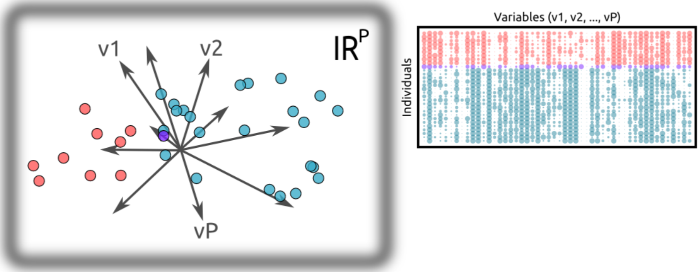
Reducing P dimensions into 1



- $\mathbf{X} \in \mathbb{R}^{N \times P}$; $\mathbf{X} = [\mathbf{x}_1 | \dots | \mathbf{x}_P]$: data matrix
- $\mathbf{u} \in \mathbb{R}^P$; $\mathbf{u} = [u_1, \dots, u_P]$: **principal axis** $(\|\mathbf{u}\|^2 = \sum_{j=1}^{P} u_j^2 = 1)$
- $\mathbf{v} \in \mathbb{R}^N$; $\mathbf{v} = \mathbf{X}\mathbf{u} = \sum_{j=1}^{P} u_j \mathbf{x}_j$: **principal component**

→ find $\mathbf{u}$ so that $\frac{1}{N}\|\mathbf{v}\|^2 = \text{var}(\mathbf{v})$ is maximum.

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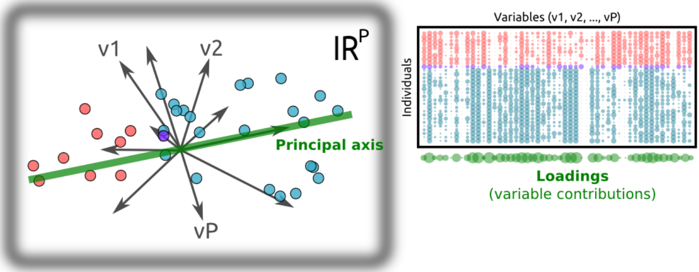

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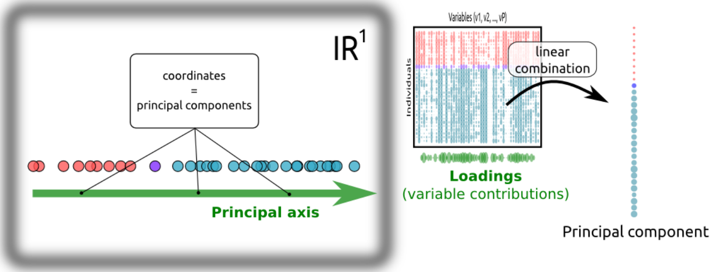

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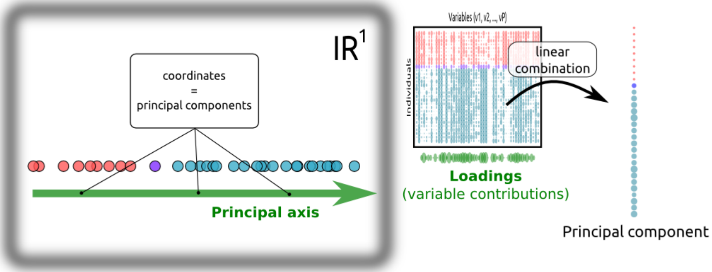

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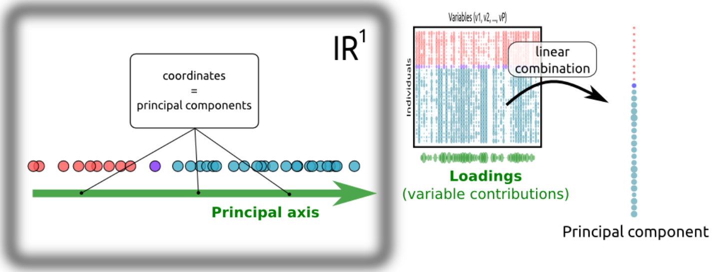
Keeping more than one principal component



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- $\mathbf{u}_2$ and $\mathbf{v}_2$: **2nd principal axis and component**

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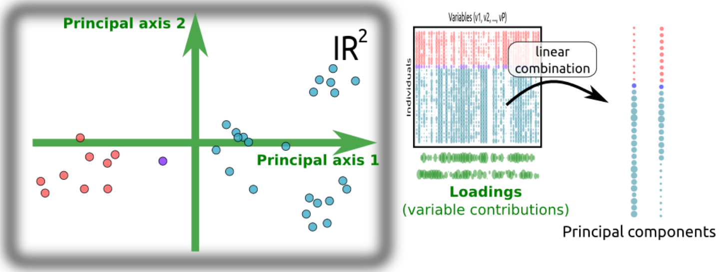

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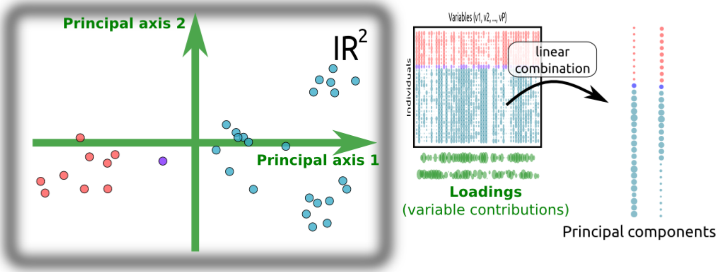

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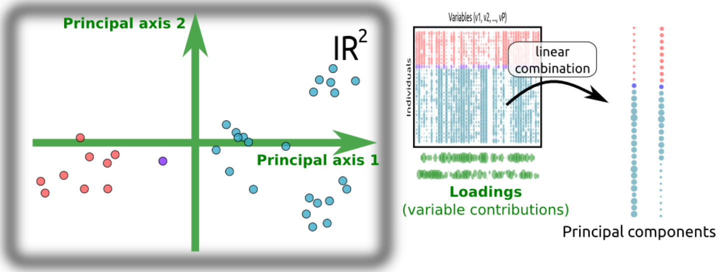

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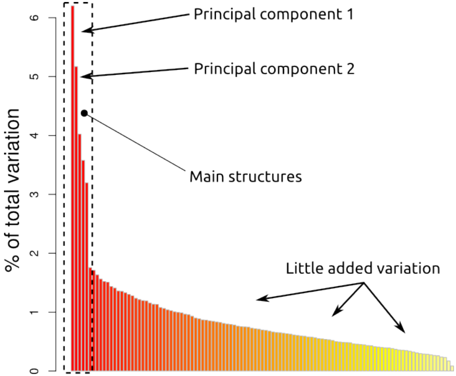
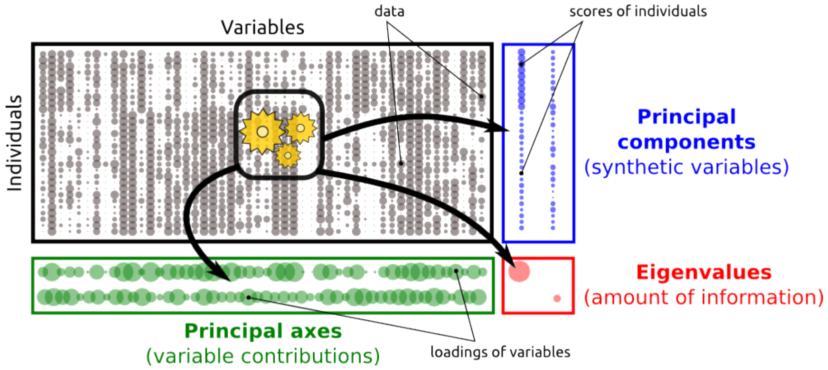
How many principal components to retain?

Choice based on "**screeplot**": barplot of eigenvalues



Retain only "significant" structures... but not trivial ones.

Outputs of multivariate analyses: an overview



Main outputs:

- **principal components**: diversity amongst individuals
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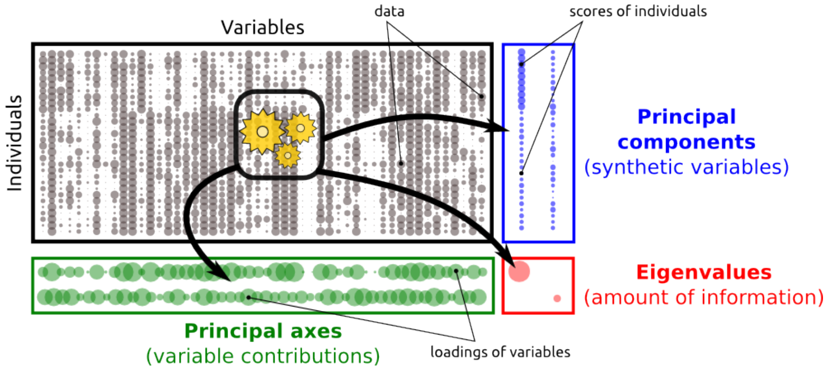

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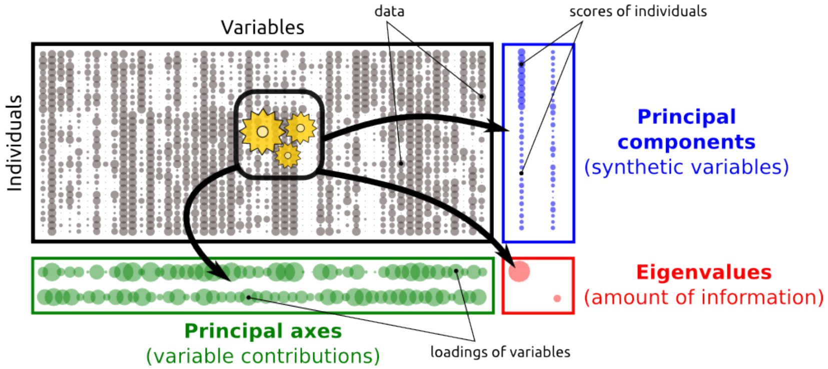

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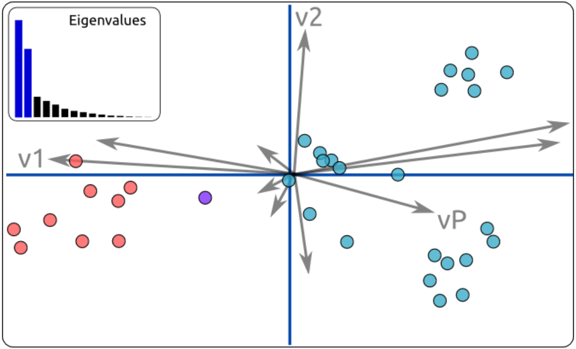
Usual summary of an analysis: the biplot



Biplot: principal components (points) + loadings (arrows)

- groups of individuals
- discriminating variables (longest arrows)
- magnitude of the structures

Multivariate analysis in a nutshell

- **variety of methods** for different types of variables
- **principal components** (PCs) summarize diversity
- **variable loadings** identify discriminating variables
- other uses of PCs: **maps** (spatial structures), **models** (response variables or predictors), ...

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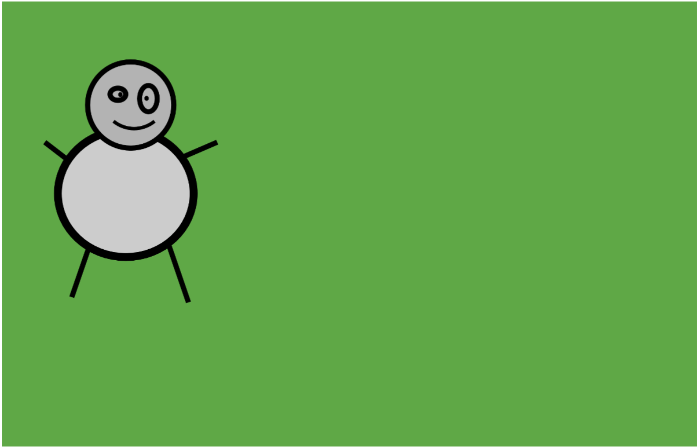
From DNA sequences to patterns of biological diversity



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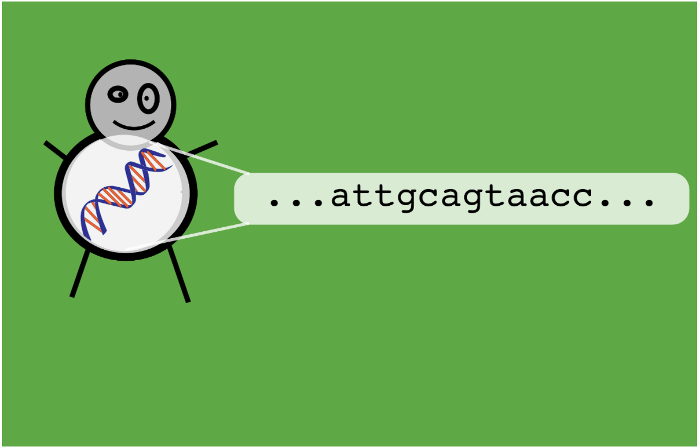

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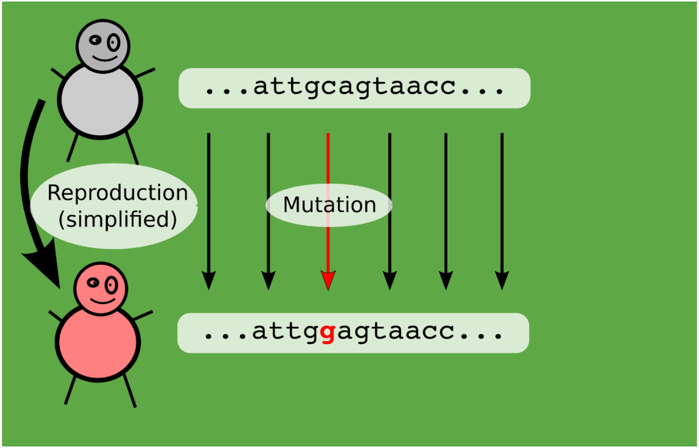

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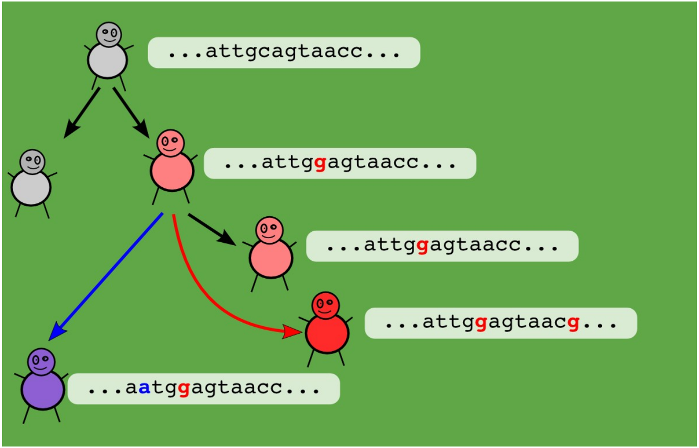

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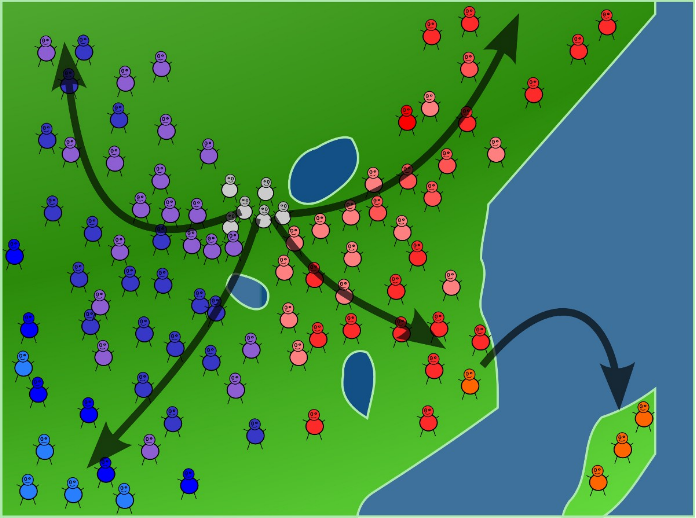

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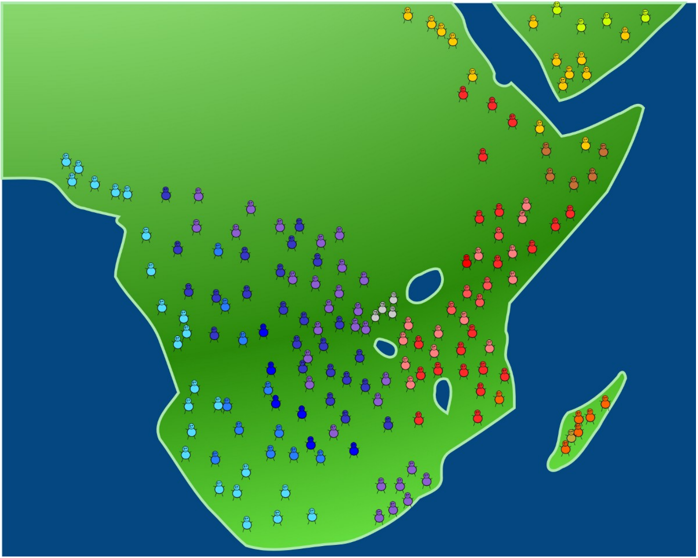

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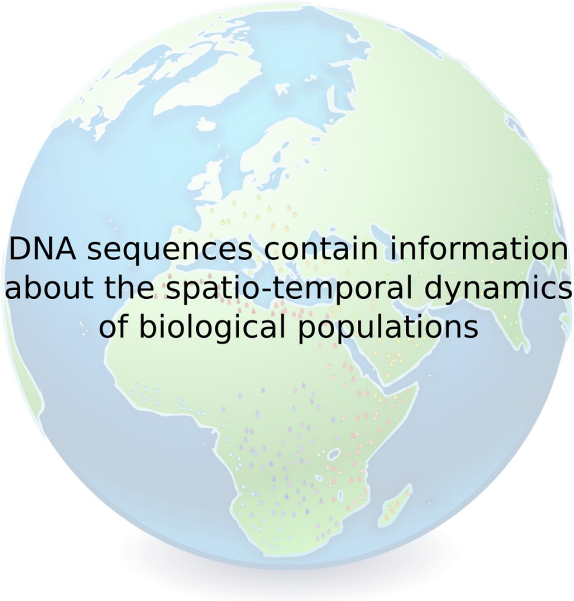
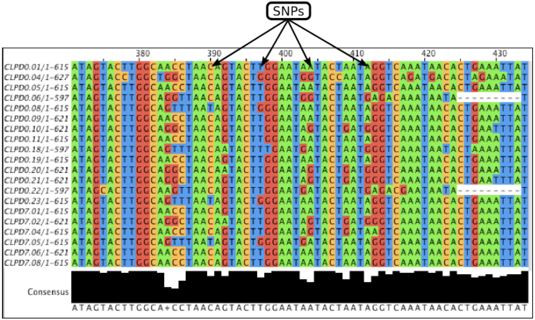


DNA sequences contain information
about the spatio-temporal dynamics
of biological populations

DNA sequences: a rich source of information



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- up to millions of single nucleotide polymorphism (SNPs)

⇒ **Multivariate analysis use to summarize genetic diversity.**

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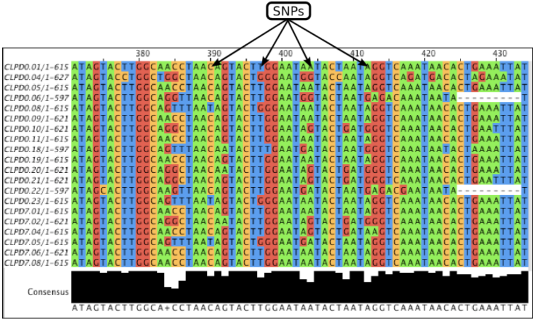

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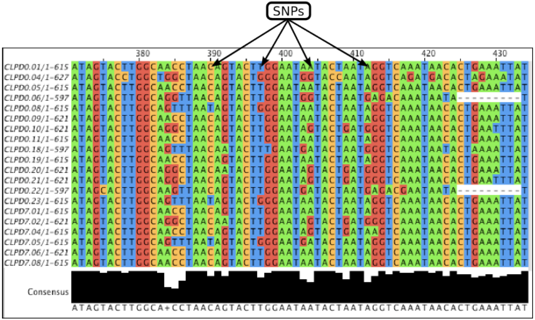

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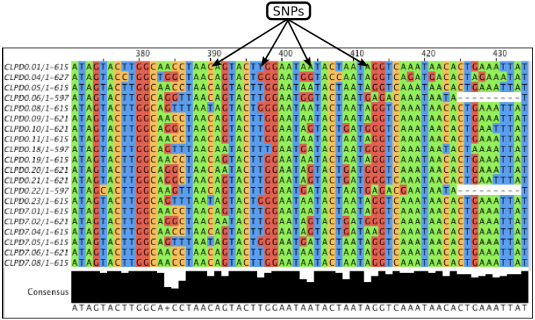

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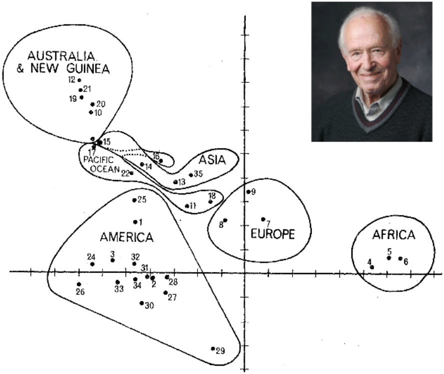
First application of multivariate analysis in genetics

PCA of genetic data, native human populations (Cavalli-Sforza 1966, *Proc B*)



First 2 principal components separate populations into continents.

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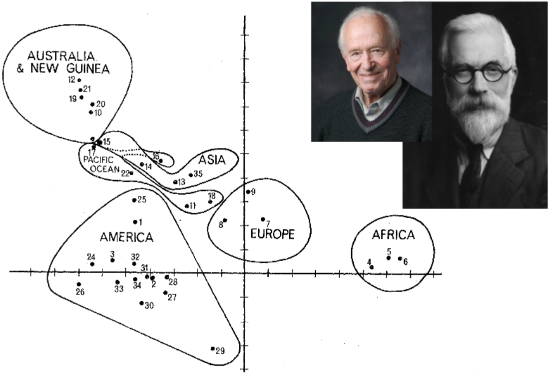

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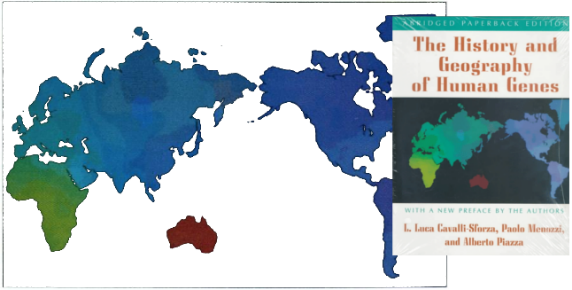
Applications: some examples

PCA of genetic data + colored maps of principal components

(Cavalli-Sforza et al. 1993, *Science*)



Signatures of Human expansion out-of-Africa.

Since then...

Multivariate methods used in genetics

- Principal Component Analysis (PCA)
- Principal Coordinates Analysis (PCoA) / Metric Multidimensional Scaling (MDS)
- Correspondance Analysis (CA)
- Discriminant Analysis (DA)
- Canonical Correlation Analysis (CCA)
- ...

Since then...

Applications

- reveal spatial structures (historical spread)
- explore genetic diversity
- identify cryptic species
- discover genotype-phenotype association
- ...
- review in Jombart et al. 2009, *Heredity* **102**: 330-341

In practice

Multivariate analysis of genetic data using R

Usual workflow

1. read data in (*adegenet*)
2. convert data into numeric values (*adegenet*)
3. replace missing values (*adegenet*)
4. use "classical" methods (*ade4*/*adegenet*)
5. graphics and interpretation (*ade4*/*adegenet*)

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Multivariate analysis of genetic data using R

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Recoding data numerically

- Presence/absence (e.g. RFLP, AFLP) and SNPs: binary coding
- Multiallelic data (e.g. microsatellites) are recoded as counts/frequencies

Example using microsatellites:

Raw data:

```
  locus1 locus2
1  80/80  30/30
2  50/55  30/30
3  80/50  29/30
4  50/50  30/30
5  50/50  29/29
```

Recoded data (allele counts):

```
  locus1.50 locus1.55 locus1.80 locus2.29 locus2.30
1         0         0         2         0         2
2         1         1         0         0         2
3         1         0         1         1         1
4         2         0         0         0         2
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How are data handled in *adegenet*?

Types of data:

- codominant markers (e.g. microsatellites) with any ploidy level → allele counts
- dominant markers (e.g. RAPD) → presence/absence
- nucleotide / amino-acids variation → allele counts
- purely biallelic SNPs → binary data (bits)

Formats:

- software: *GENETIX*, *Fstat*, *Genepop*, *STRUCTURE*, *PLINK*
- `data.frame` of raw allelic data
- `data.frame` of allelic frequencies
- SNPs/amino-acids extracted from DNA/protein alignments

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(Almost) time to get your hands dirty!

And after lunch, the pdf of the practical is online:

`http://adegenet.r-forge.r-project.org/`

or

Google → adegenet → documents → "Lausanne August 2016"