

Multivariate analysis of genetic data — an introduction —

Thibaut Jombart, Caitlin Collins

MRC Centre for Outbreak Analysis and Modelling
Imperial College London

Genetic data analysis using , University of Leuven
28-10-2014

Outline

Multivariate analysis in a nutshell

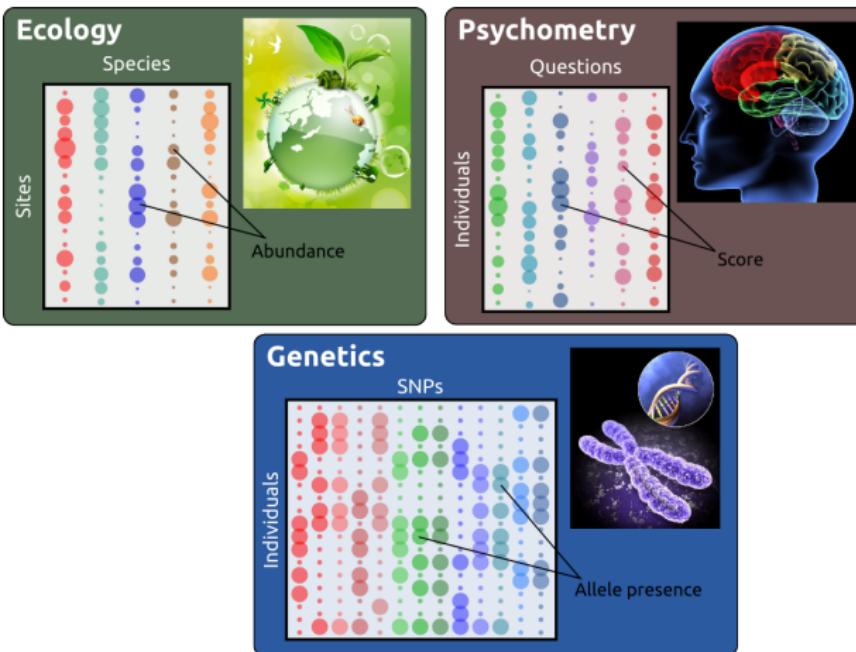
Applications to genetic data

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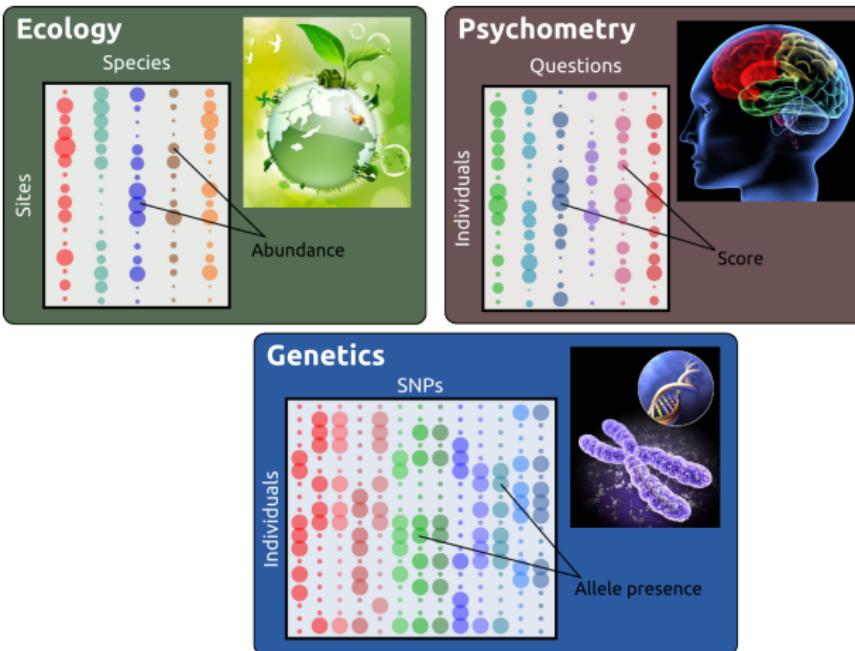
Applications to genetic data

Multivariate data: some examples



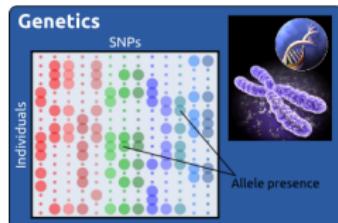
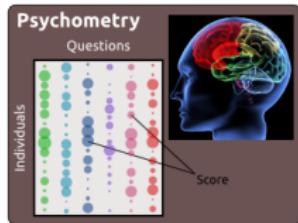
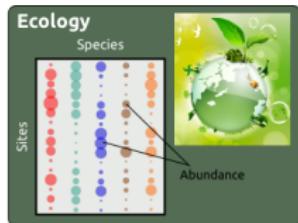
Association between individuals? Correlations between variables?

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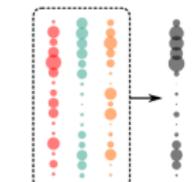
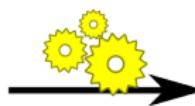
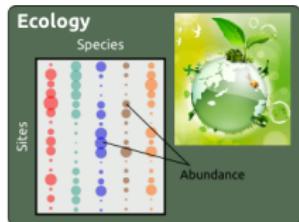


Association between individuals? Correlations between variables?

Multivariate analysis to summarize diversity

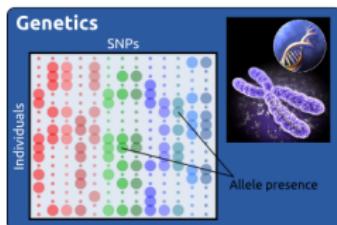
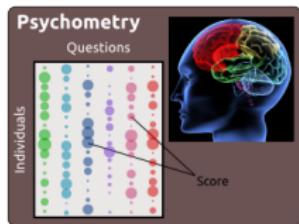


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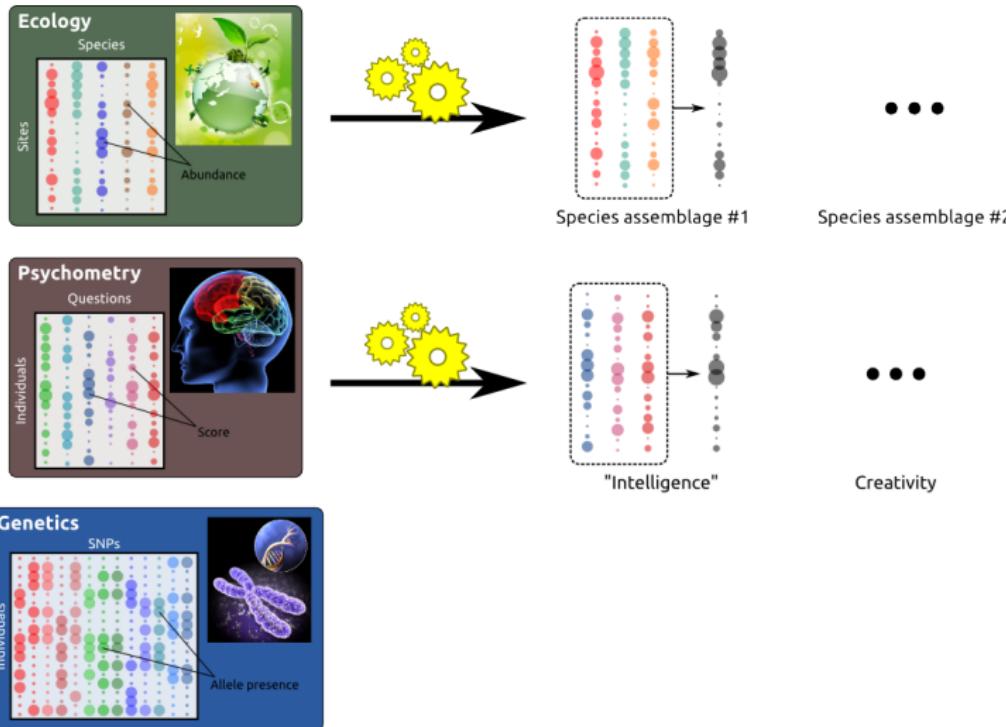


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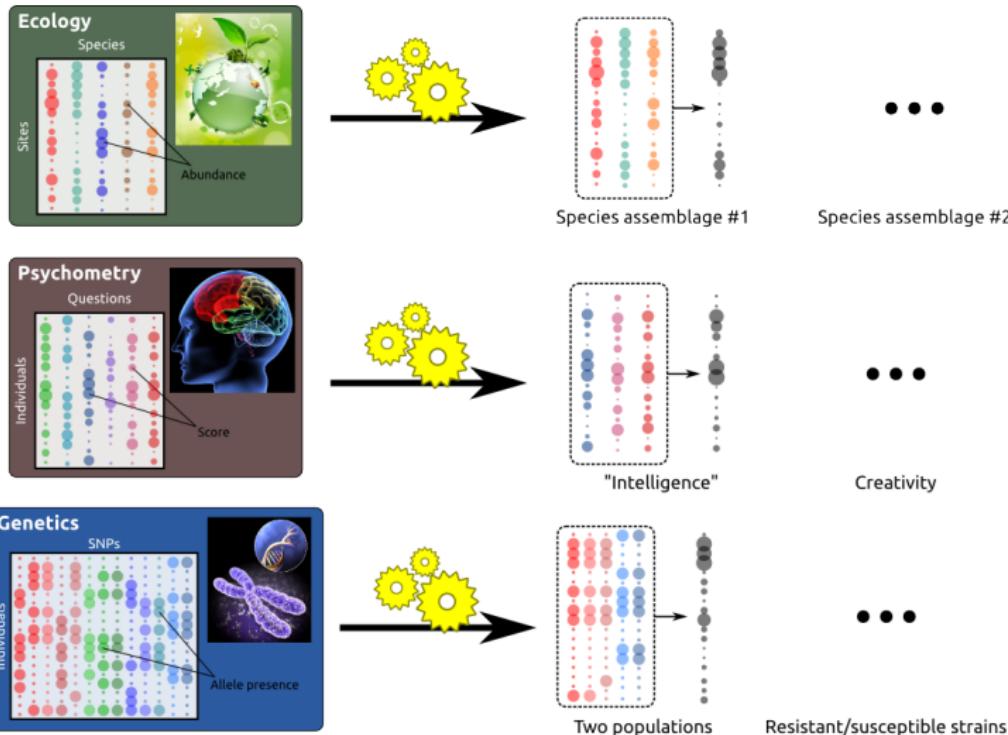
Species assemblage #2



Multivariate analysis to summarize diversity



Multivariate analysis to summarize diversity



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)

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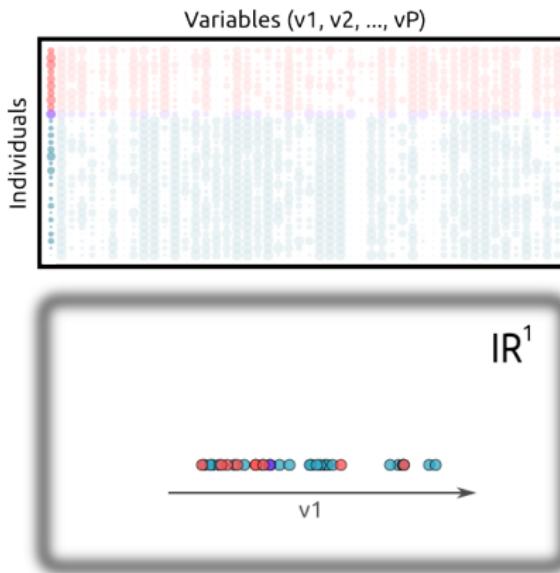
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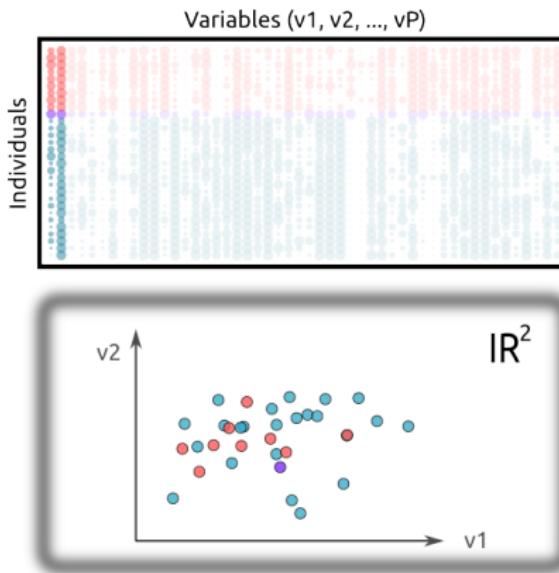
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1 dimension, 2 dimensions, P dimensions



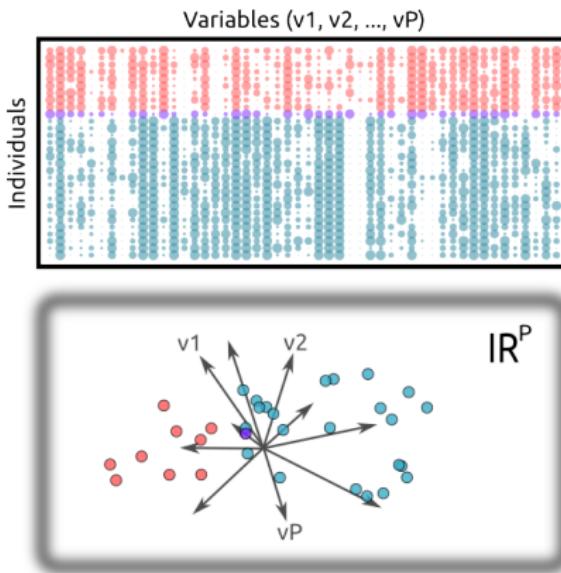
Need to find most informative directions in a P -dimensional space.

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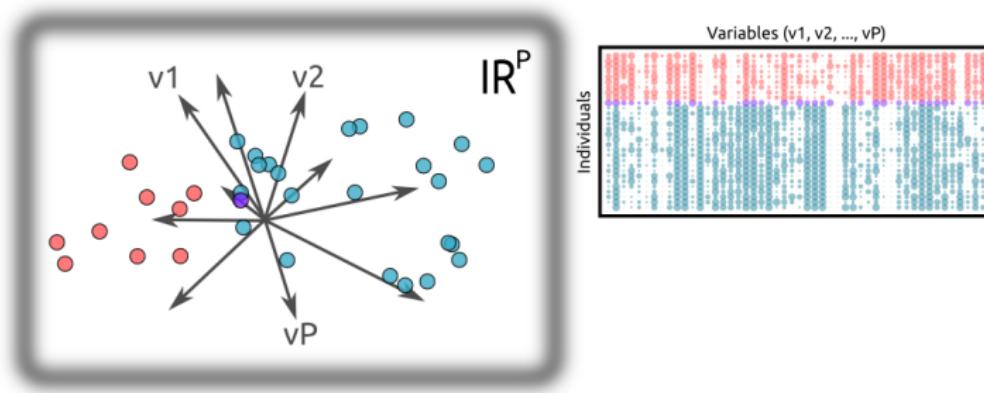


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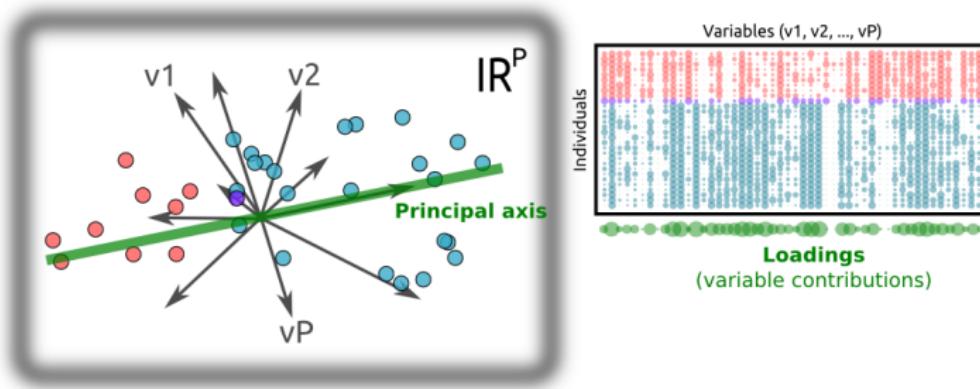


Need to find most informative directions in a P -dimensional space.

Reducing P dimensions into 1

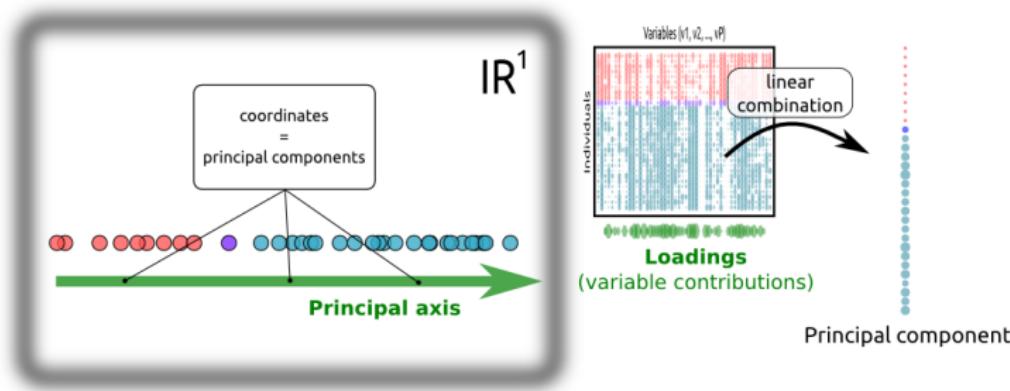
- $\mathbf{X} \in \mathbb{R}^{N \times P}; \mathbf{X} = [\mathbf{x}_1 | \dots | \mathbf{x}_P]$: data matrix
- $\mathbf{u} \in \mathbb{R}^P; \mathbf{u} = [u_1, \dots, u_P]$: principal axis
($\|\mathbf{u}\|^2 = \sum_{j=1}^P u_j^2 = 1$)
- $\mathbf{v} \in \mathbb{R}^N; \mathbf{v} = \mathbf{X}\mathbf{u} = \sum_{j=1}^P u_j \mathbf{x}_j$: principal component
→ find \mathbf{u} so that $\frac{1}{N} \|\mathbf{v}\|^2 = \text{var}(\mathbf{v})$ is maximum.

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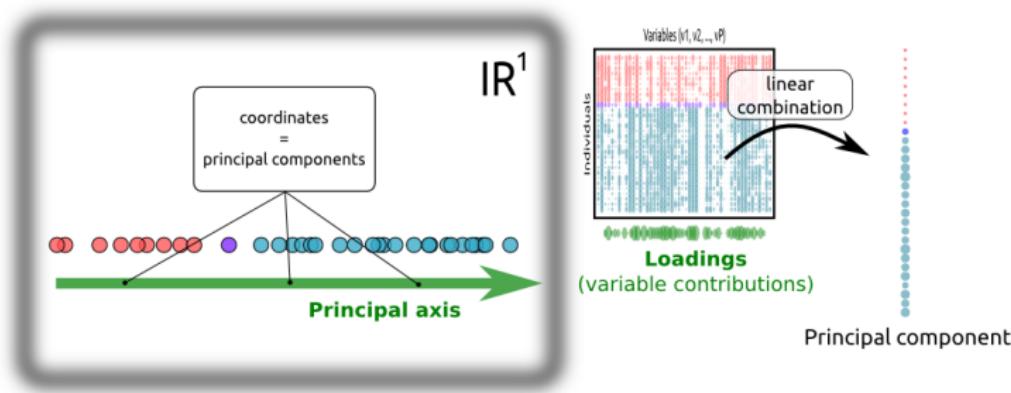
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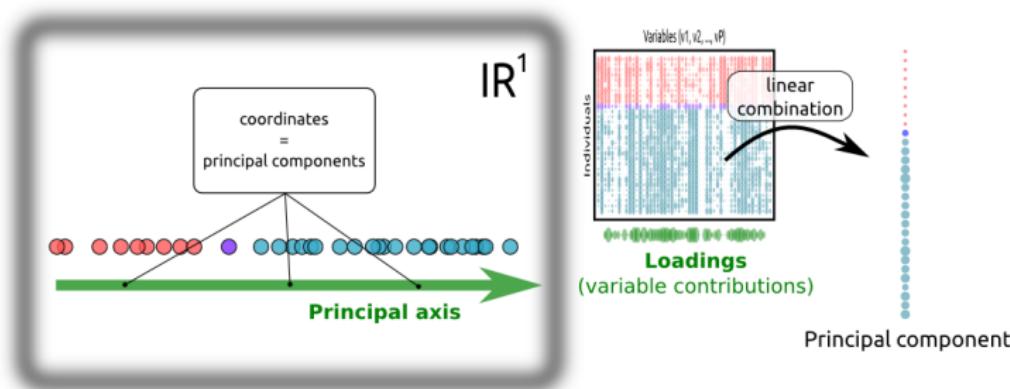
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Keeping more than one principal component

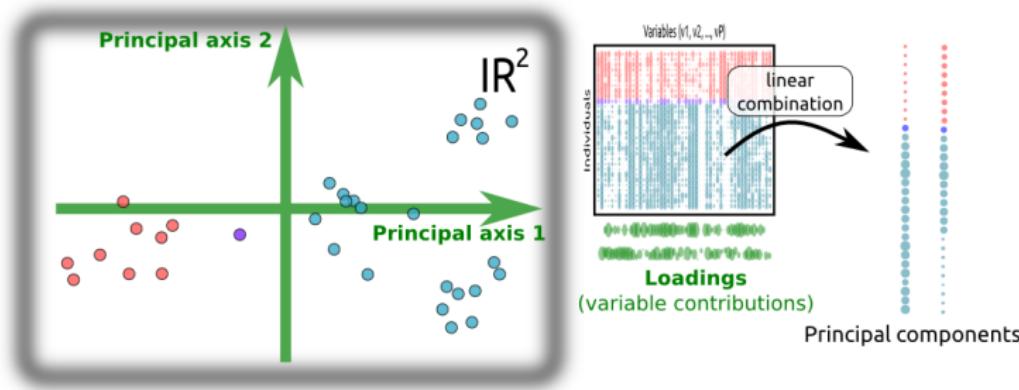


- u_1 and v_1 : **1st principal axis and component**
- u_2 and v_2 : **2nd principal axis and component**

→ constraint: $u_1 \perp u_2 (\iff \text{cor}(v_1, v_2) = 0)$

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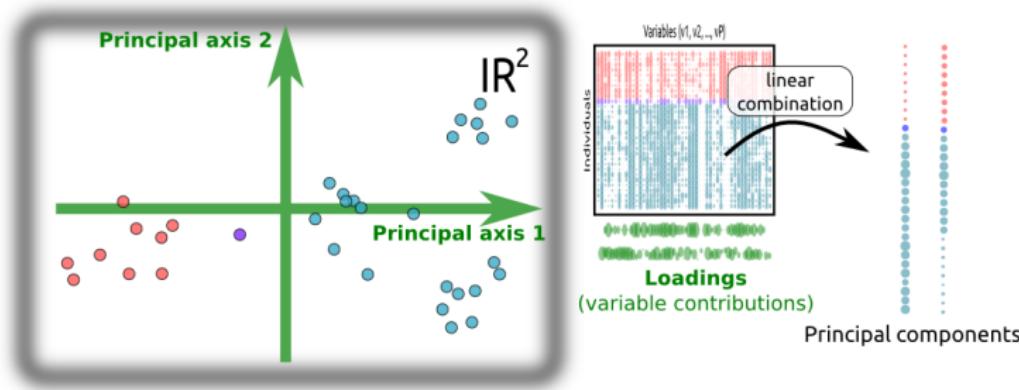


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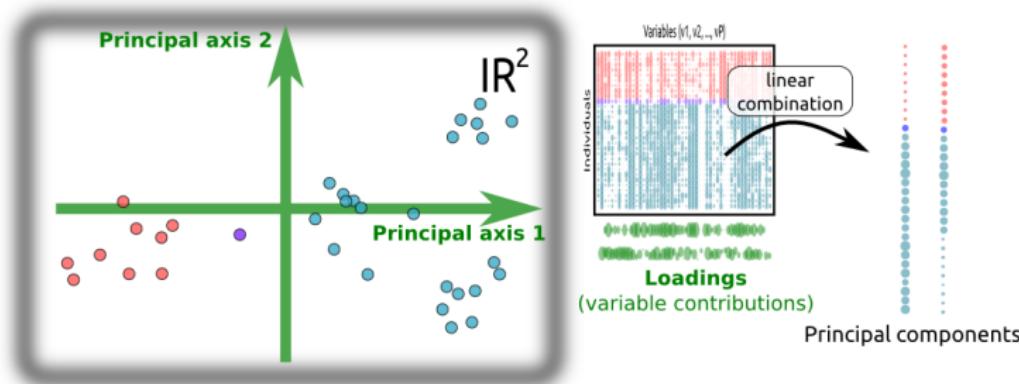


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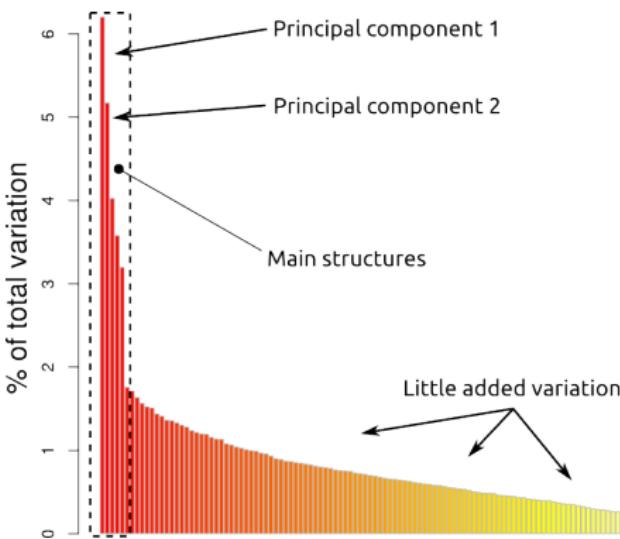
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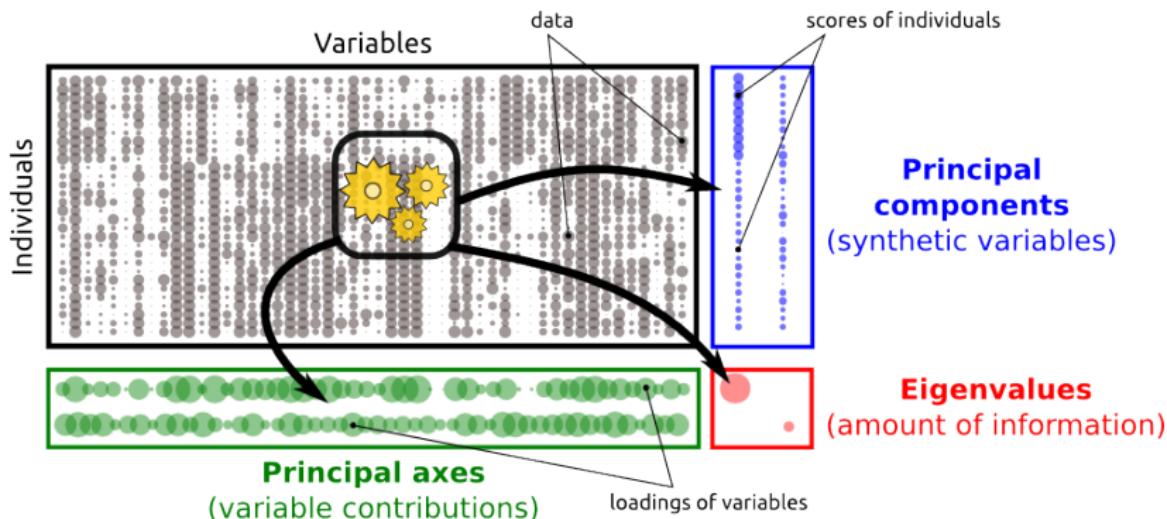
How many principal components to retain?

Choice based on “**screeplot**”: barplot of eigenvalues



Retain only “significant” structures... but not trivial ones.

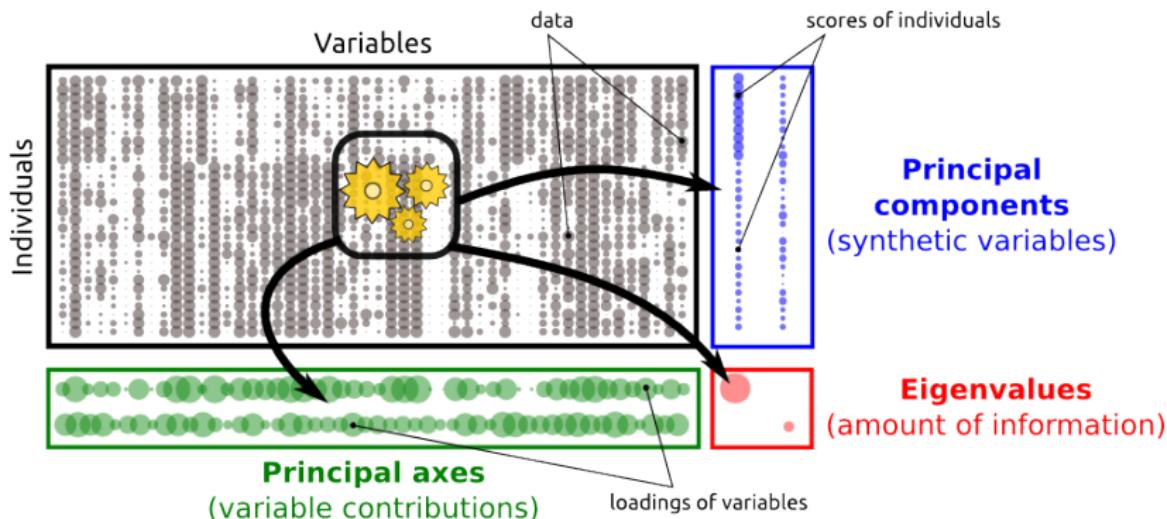
Outputs of multivariate analyses: an overview



Main outputs:

- **principal components:** diversity amongst individuals
- **principal axes:** nature of the structures
- **eigenvalues:** magnitude of structures

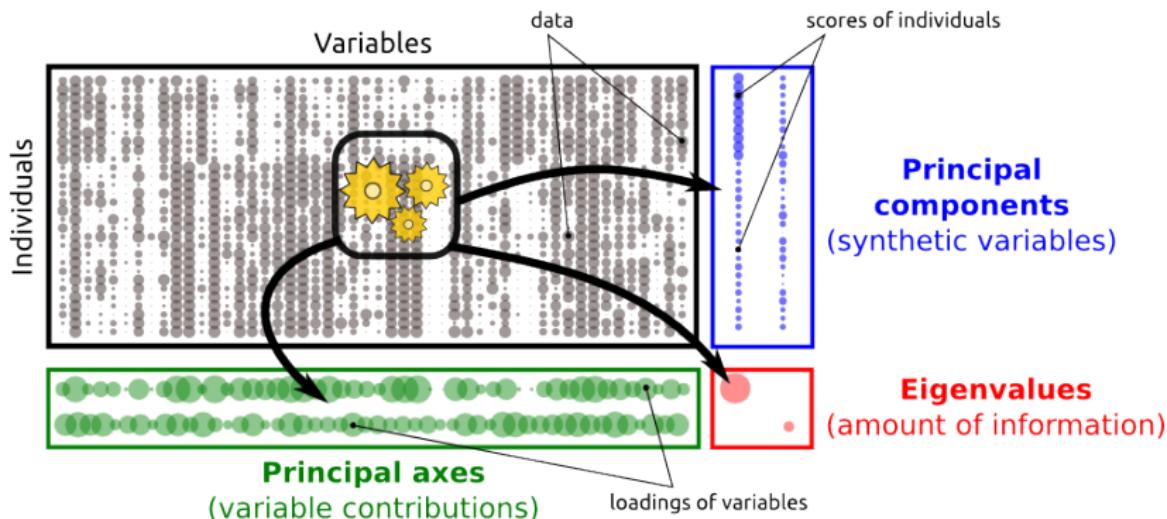
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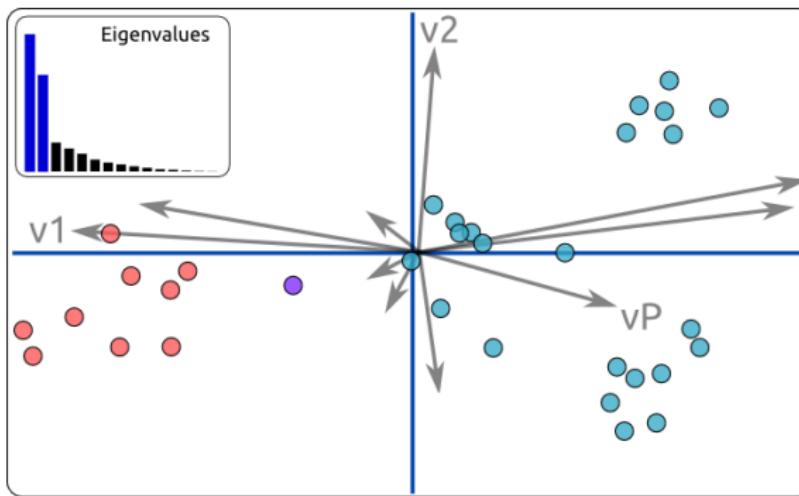
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Usual summary of an analysis: the biplot



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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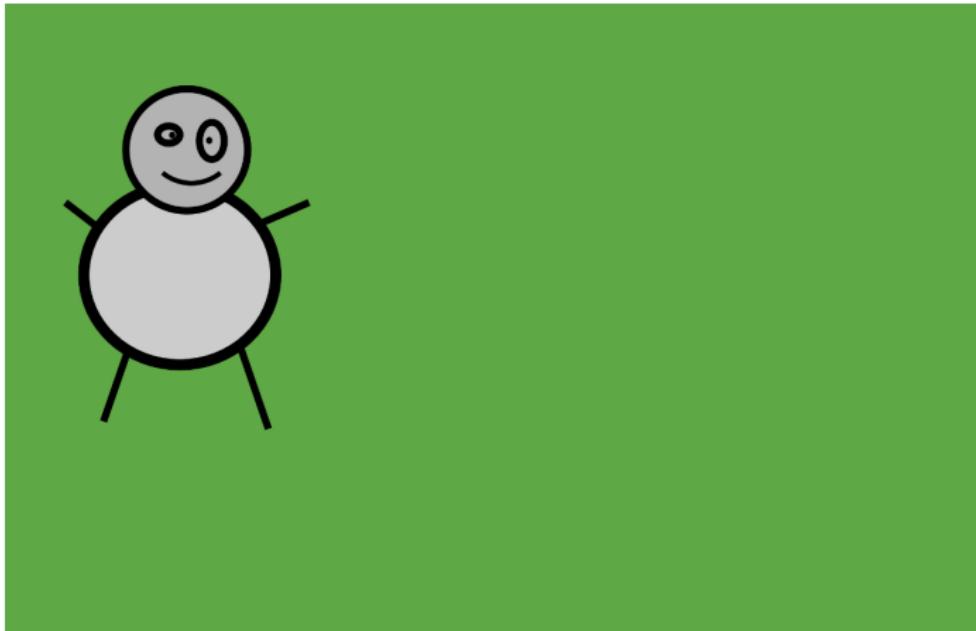
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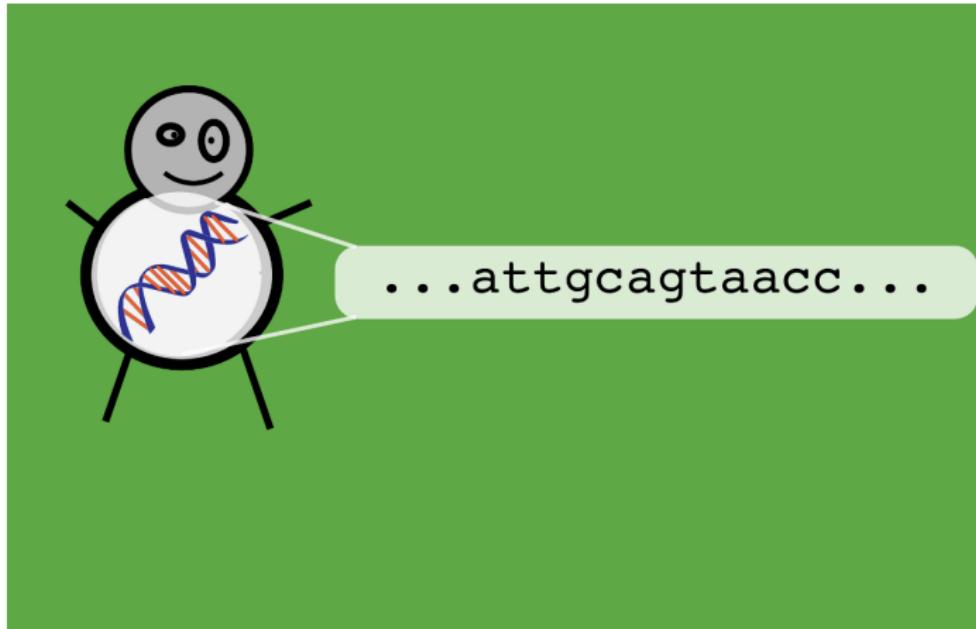
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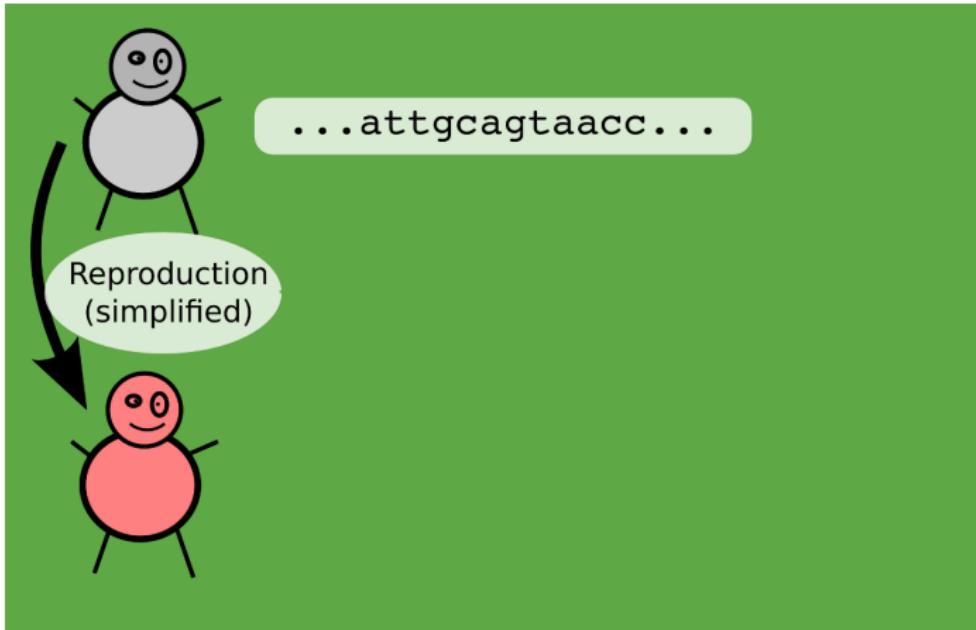
From DNA sequences to patterns of biological diversity



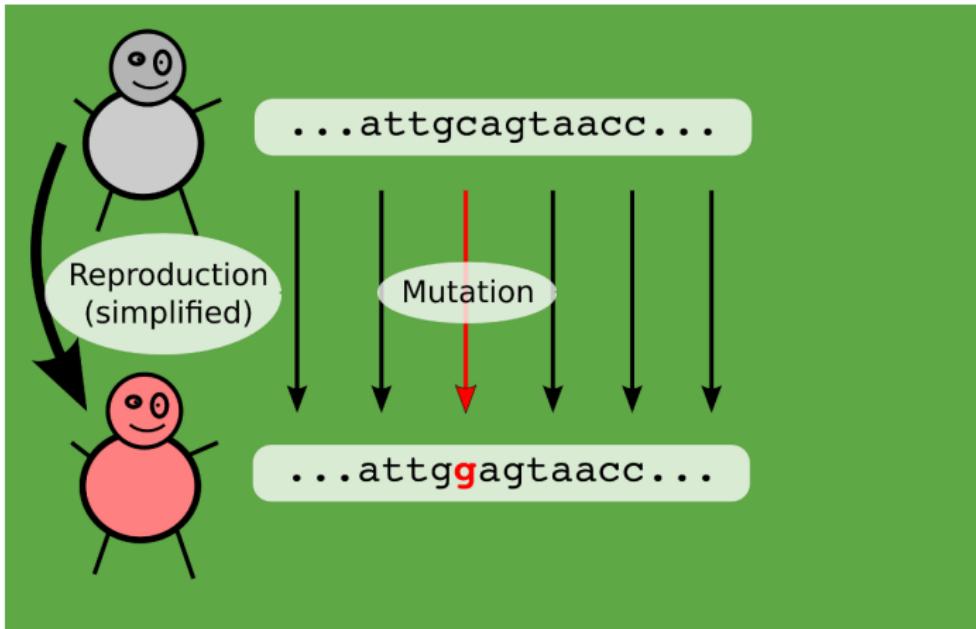
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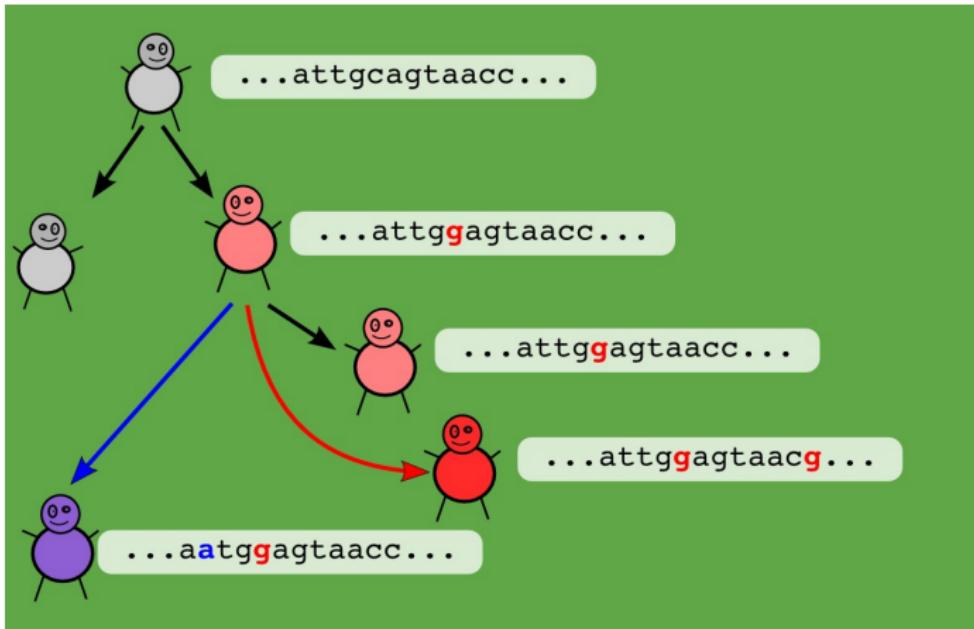
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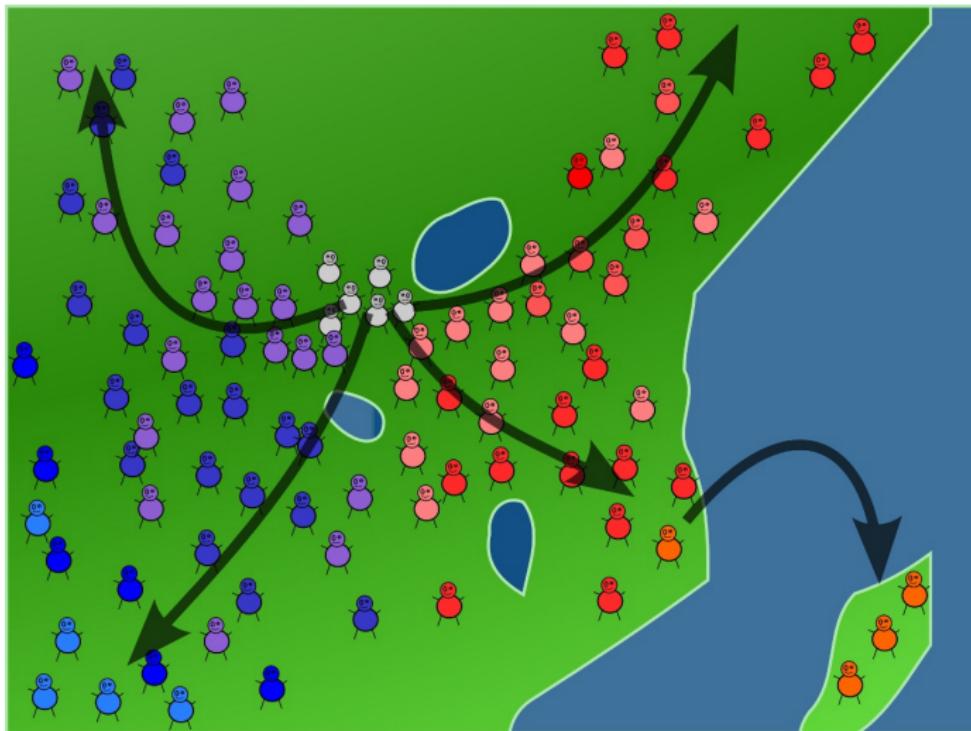
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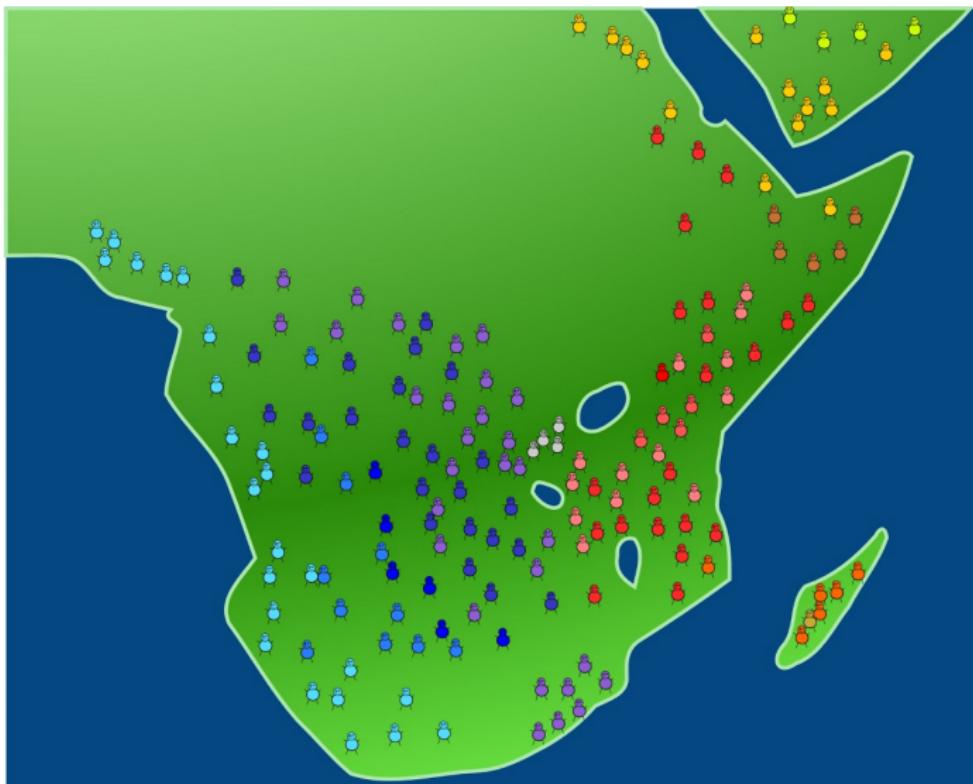
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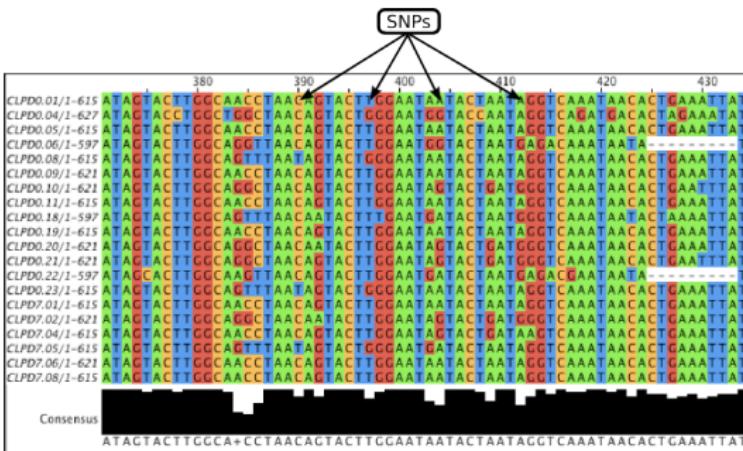


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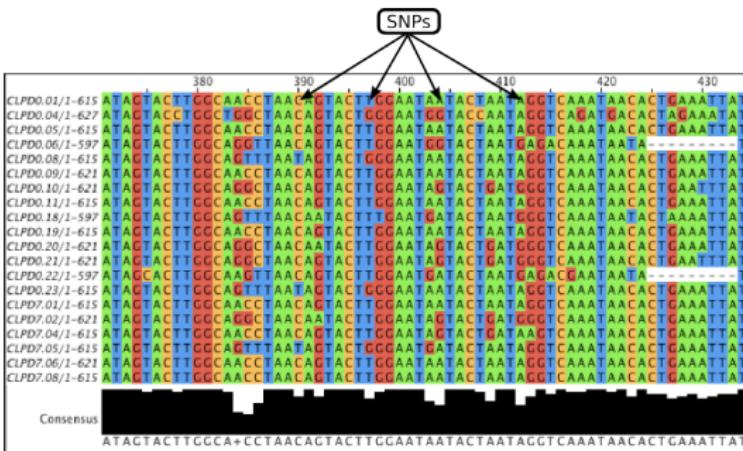
DNA sequences contain information about the spatio-temporal dynamics of biological populations

DNA sequences: a rich source of information



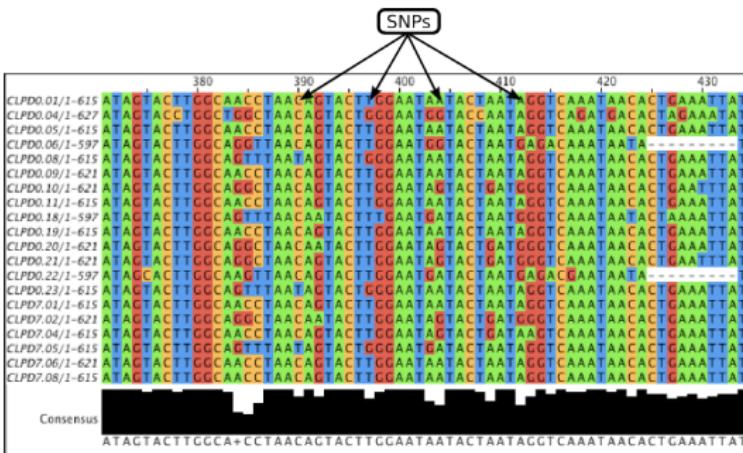
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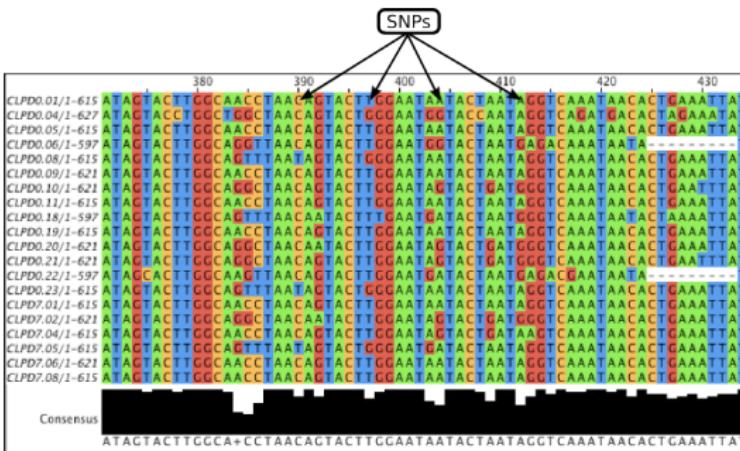
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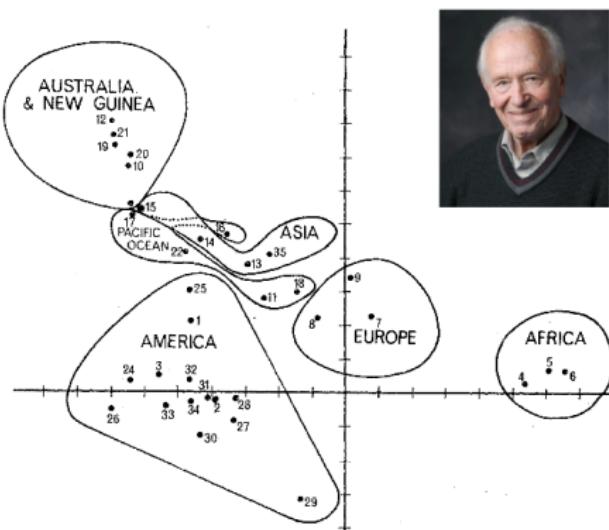
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First application of multivariate analysis in genetics

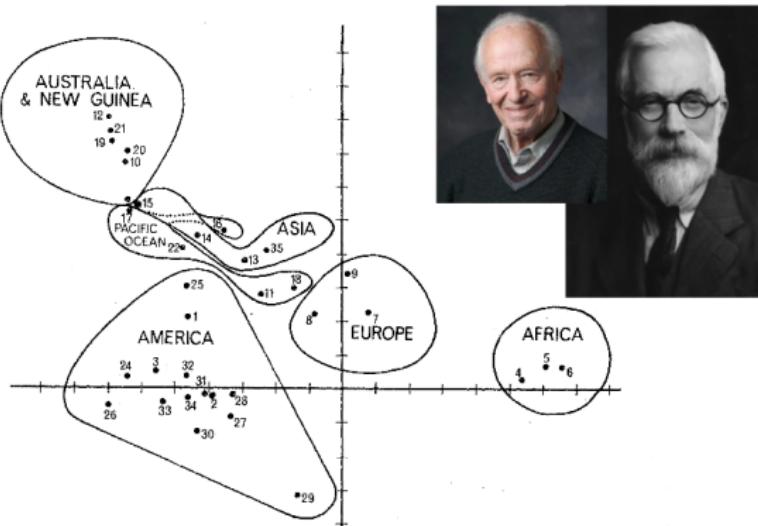
PCA of genetic data, native human populations (Cavalli-Sforza 1966, *Proc B*)



First 2 principal components separate populations into continents.

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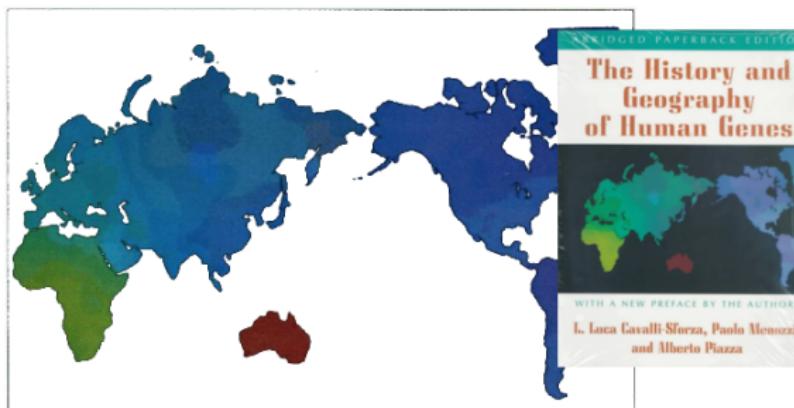


First 2 principal components separate populations into continents.

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 

Usual pipeline

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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Recoding data numerically

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

Example using microsatellites:

Raw data: Recoded data:

	locus1	locus2		locus1.50	locus1.55	locus1.80	locus2.29	locus2.30
1	80/80	30/30	1	0.0	0.0	1.0	0.0	1.0
2	50/55	30/30	2	0.5	0.5	0.0	0.0	1.0
3	80/50	29/30	3	0.5	0.0	0.5	0.5	0.5
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2	50/55	30/30	2	0.5	0.5	0.0	0.0	1.0
3	80/50	29/30	3	0.5	0.0	0.5	0.5	0.5
4	50/50	30/30	4	1.0	0.0	0.0	0.0	1.0
5	50/50	29/29	5	1.0	0.0	0.0	1.0	0.0

Recoding data numerically

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

Example using microsatellites:

Raw data: Recoded data:

	locus1	locus2		locus1.50	locus1.55	locus1.80	locus2.29	locus2.30
1	80/80	30/30	1	0.0	0.0	1.0	0.0	1.0
2	50/55	30/30	2	0.5	0.5	0.0	0.0	1.0
3	80/50	29/30	3	0.5	0.0	0.5	0.5	0.5
4	50/50	30/30	4	1.0	0.0	0.0	0.0	1.0
5	50/50	29/29	5	1.0	0.0	0.0	1.0	0.0

How are data handled in *adegenet*?

Types of data:

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

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 → “Workshop Leuven, October 2014”