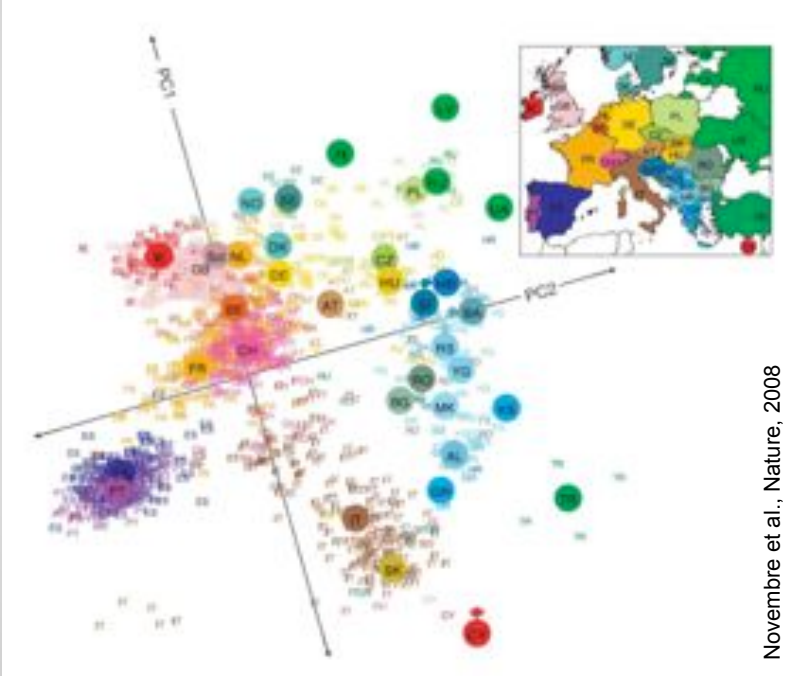
# Advanced data analysis in population genetics

# Demographic inference under isolation by distance




Novembre et al., Nature, 2008

Raphael Leblois

INRA, Center for population biology and management

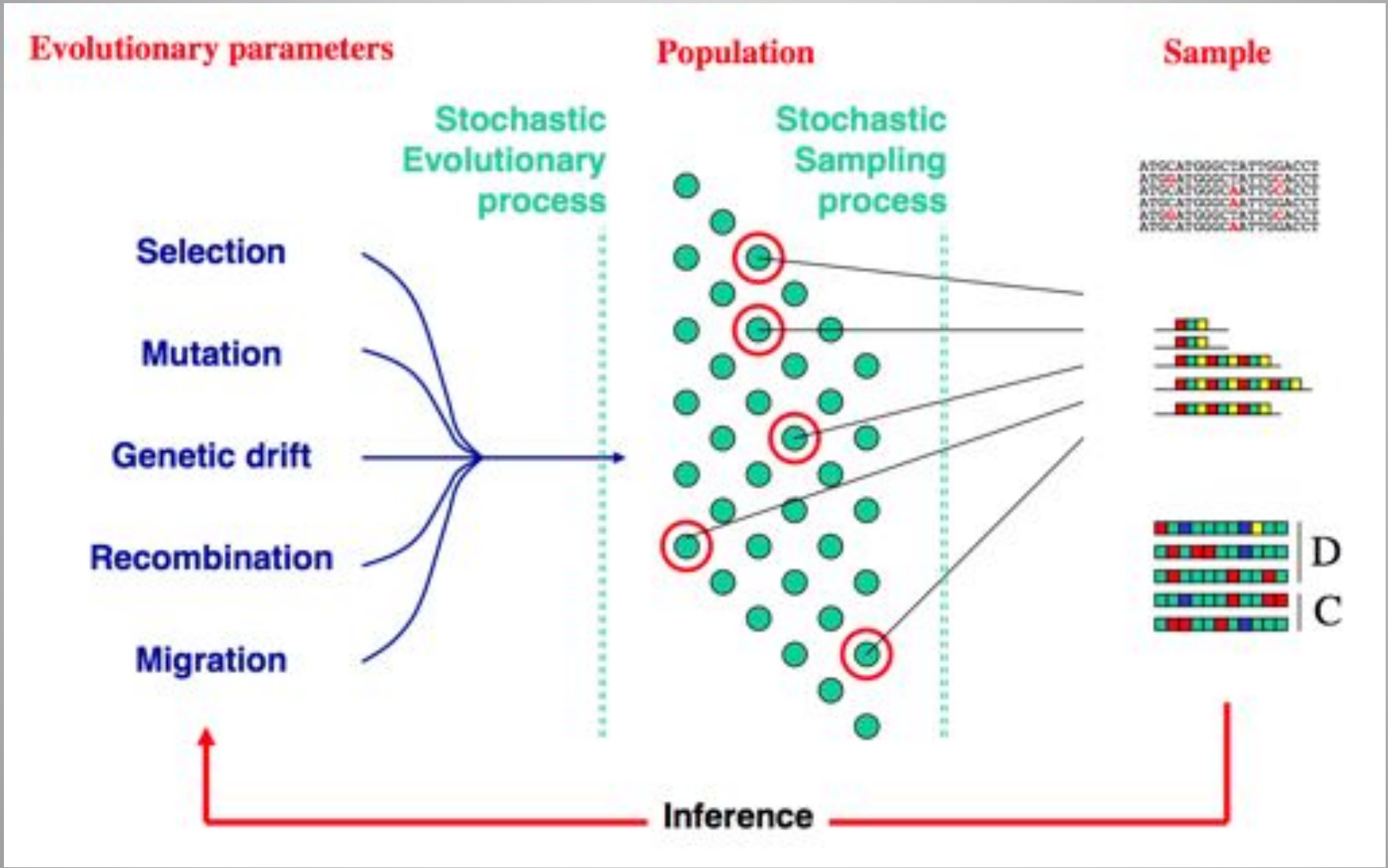
MEME master 2010-2011

# Advanced data analysis in population genetics

## Demographic inference under isolation by distance

1. Demographic inference and population genetic models
2. IBD models and mathematical analyses
3. A simple inference method : Rousset's regression
4. Examples : some real data sets analyses (Pygmies and Damselflies)
5. Testing inference methods : application to the regression method
6. IBD between two habitats
7. Landscape genetics based on IBD

# Inference in population genetics




From McVean Courses : http://www.stats.ox.ac.uk/~mcvean/pgindex02.html

# Demographic inference in population genetics

Demographic parameters (DP) are:

pop sizes, migration rates, dispersal distances, divergence times, etc …

- General interest in evolutionnary biology because DP are important factors for local adaptation of organisms to their environment

- Great interest also in ecology et population managments (Molecular ecology : conservation biology, study of invasive species,…)

# How to do demographic inferences?

- Direct methods, i.e. strictly demographic
  - ✓ tracking individuals: radio, GPS,…
  - ✓ Capture – Mark – Recapture studies (CMR)

  but do not account for temporal variability difficult and needs lots of time

- Indirect methods: neutral polymorphism and population genetics
  - ✓ more and more powerful because of recent advances in molecular biology

  and population genetic statistical analyses

**Are those methods equivalent ?**

# How to make demographic inferences?

- Direct methods, i.e. strictly demographic

- Indirect methods: neutral polymorphism and population genetics

It is generally considered that :

**Direct methods → "present-time and census" parameters**

**Indirect methods → "past and effective" parameters**

# How to make demographic inferences?

- Direct methods, i.e. strictly demographic

- Indirect methods:  neutral polymorphism and population genetics

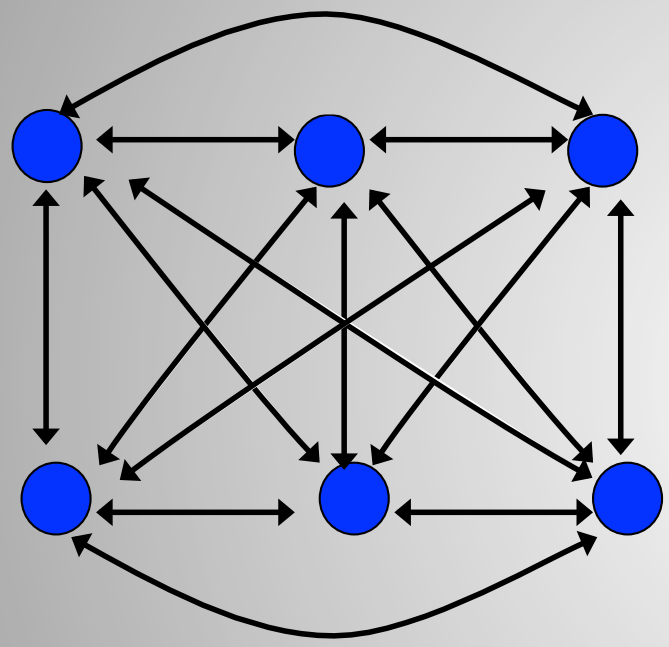
**Direct methods → "present-time and census" parameters**

**Indirect methods → "~~past~~ and effective" parameters**

not always true… as we will see under IBD

# Models for structured populations:

# 1 – the island model



Most simple structured model

2 to 3 demographic parameters :

*d* = sub-population number (or ∞)

*N* = sub-population size

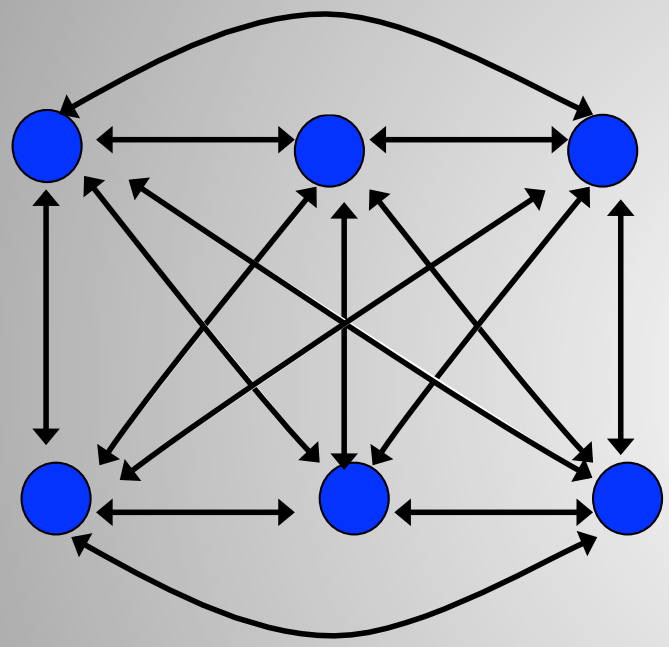
*m* = migration rate

**Fully homogeneous and non-spatial**

$$Fst=1/(1+4Nm)$$

# Models for structured populations:

# 1 – the island model



Most simple structured model

**Fully homogeneous and non-spatial**

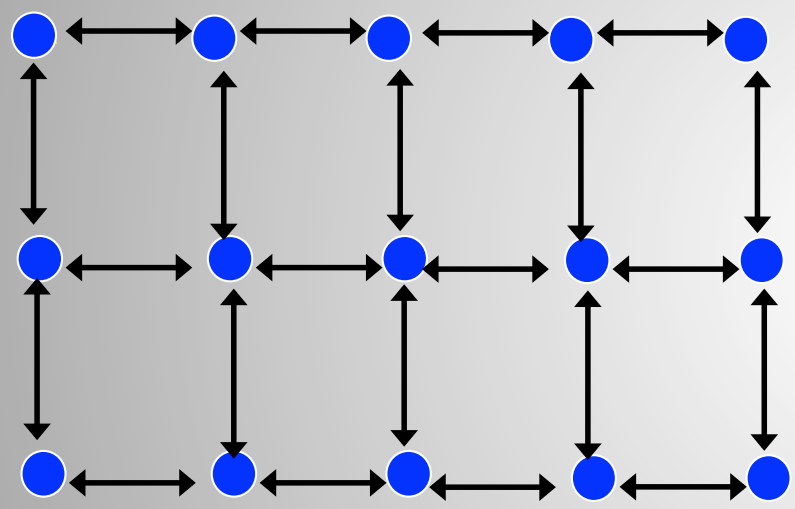
**Extremely useful to study theoretical evolutionary effects of migration**

**but generally not realistic enough to allows precise demographic inferences**

## In practice Fst ≠ 1/(1+4Nm)

# Models for structured populations:

# 2 – the stepping stone model



also simple structured model but with

localized dispersal (1D, 2D or 3D)

the same 2 to 3 DP :

*d* = sub-population number (or ∞)

*N* = sub-population size

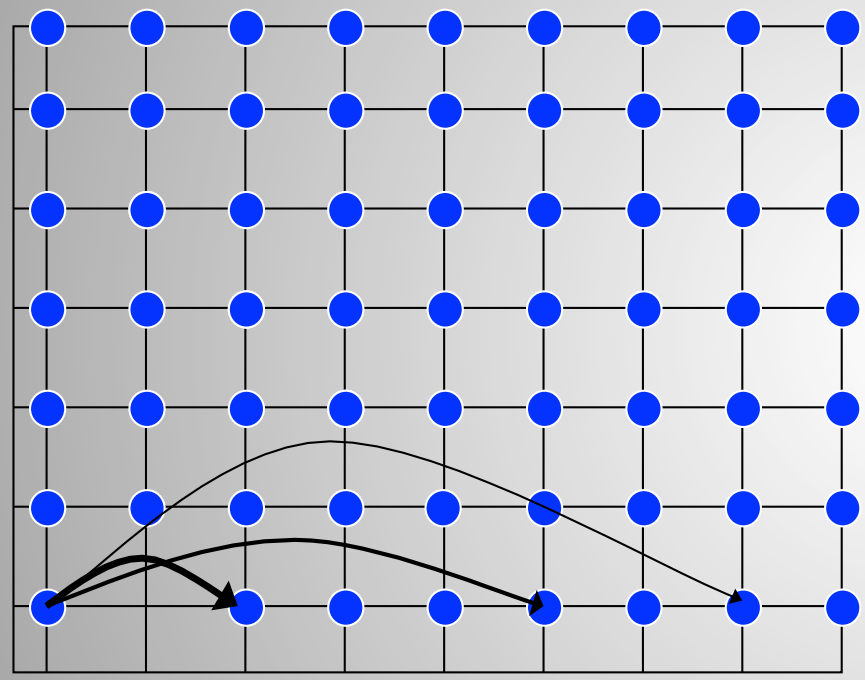
*m* = migration rate

**Fully homogeneous and "spatial"**

**Also extremely useful to study theoretical evolutionary effects of localized dispersal but generally not realistic enough to allows precise demographic inferences**

# Models for structured populations:

# 3 – the general isolation by distance model



Based on the simple property that dispersal is localized in space

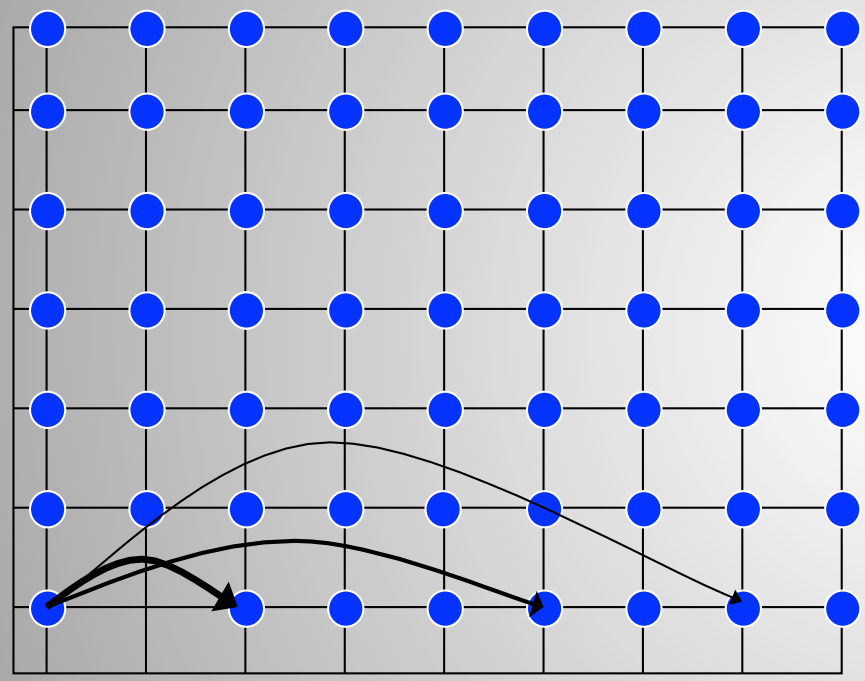
i.e., 2 individuals are more likely to mate if they live geographically close to each other

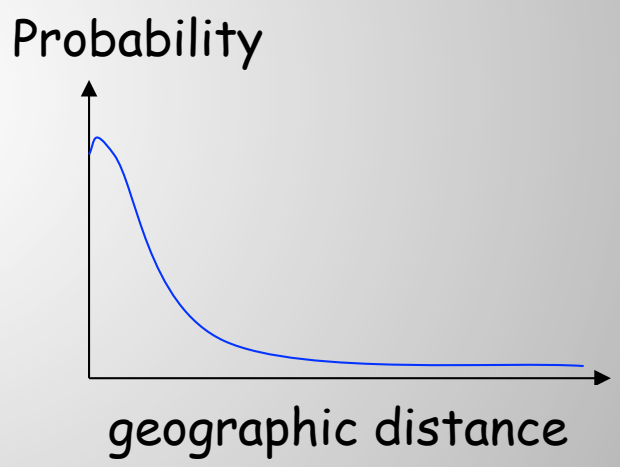
Endler (1977) first showed in a review that

the vast majority of species has geographically localized dispersal

# Models for structured populations:

# 3 – the general isolation by distance model



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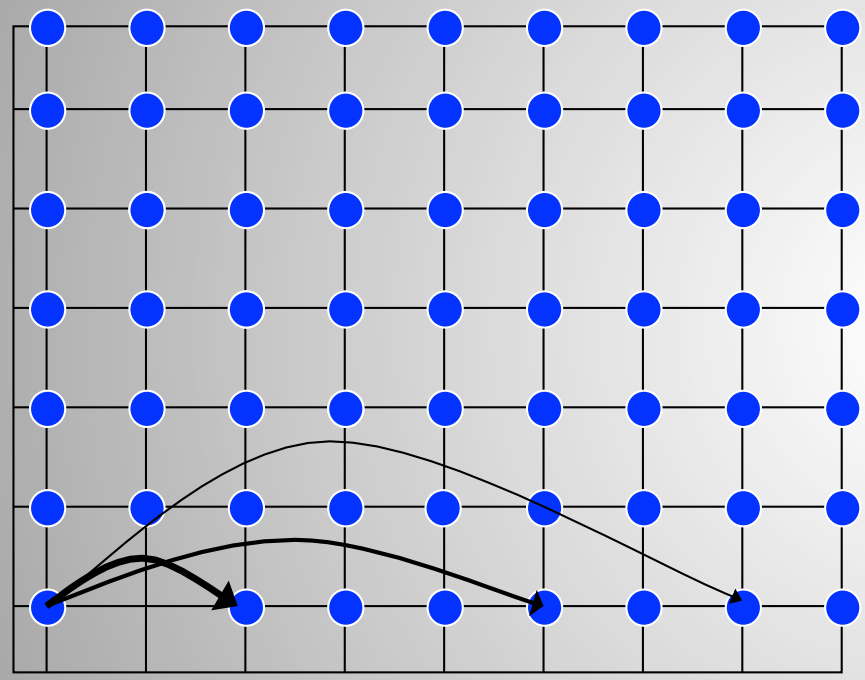
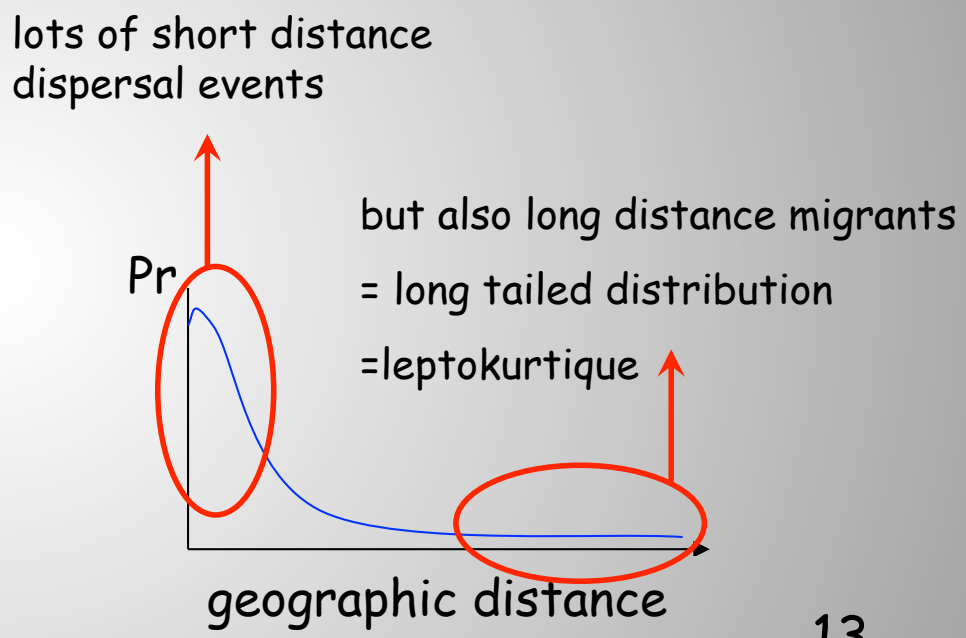
**the migration rate between sub-populations is function of the geographic distance through a dispersal distribution**

# Models for structured populations:

# 3 – the general isolation by distance model



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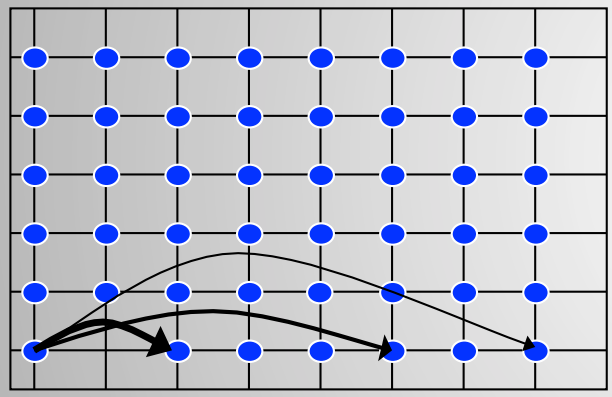
**the migration rate between sub-populations is function of the geographic distance through a dispersal distribution**

# Models for structured populations:

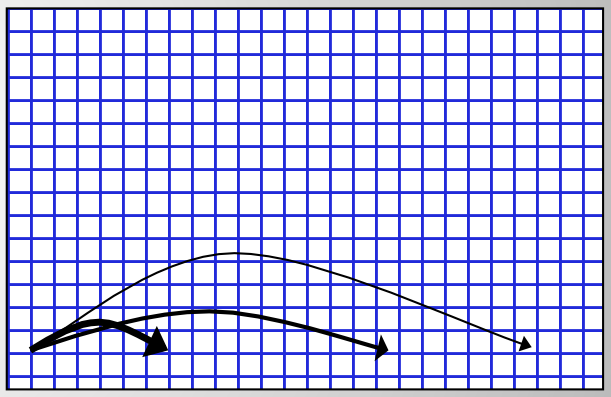
# 3 – the general isolation by distance model

**2 models depending on individual spatial distribution in the landscape**



**Population with a demic structure**

each node of the lattice corresponds to a panmictic sub-population of size N individuals



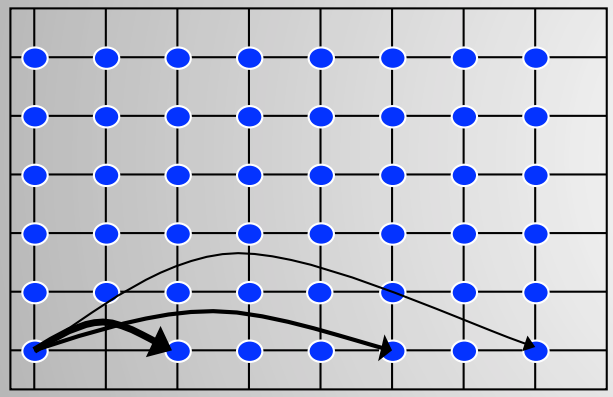
**"continuous" population**

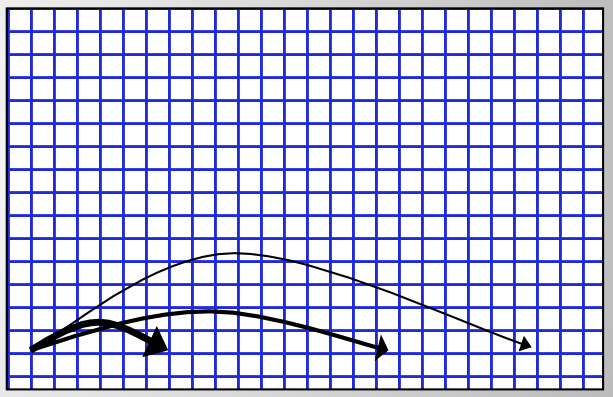
each node of the lattice is a single individual (N=1)

# Models for structured populations:

# 3 – the general isolation by distance model

**2 models depending on individual spatial distribution in the landscape**





**Fully homogeneous model :**

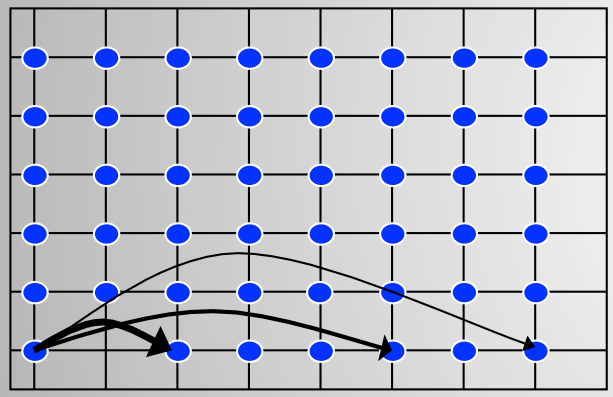
deme size or density of individuals is constant on the lattice

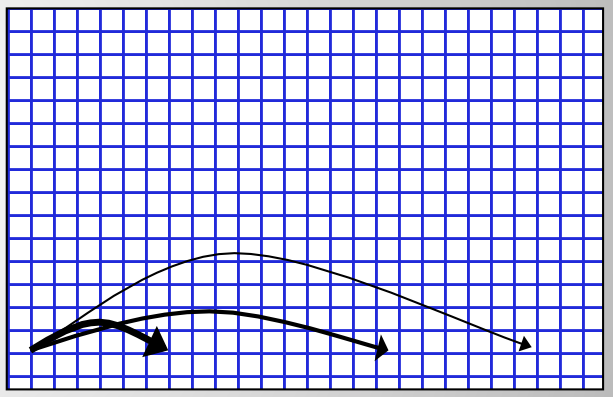
dispersal distribution is the same for all lattice nodes

# Models for structured populations:

# 3 – the general isolation by distance model

**2 models depending on individual spatial distribution in the landscape**





**2 (or more) demographic parameters :**

*N* or *D* : sub-population size or density of individuals

$\sigma^2$ : mean squared parent-offspring dispersal distance

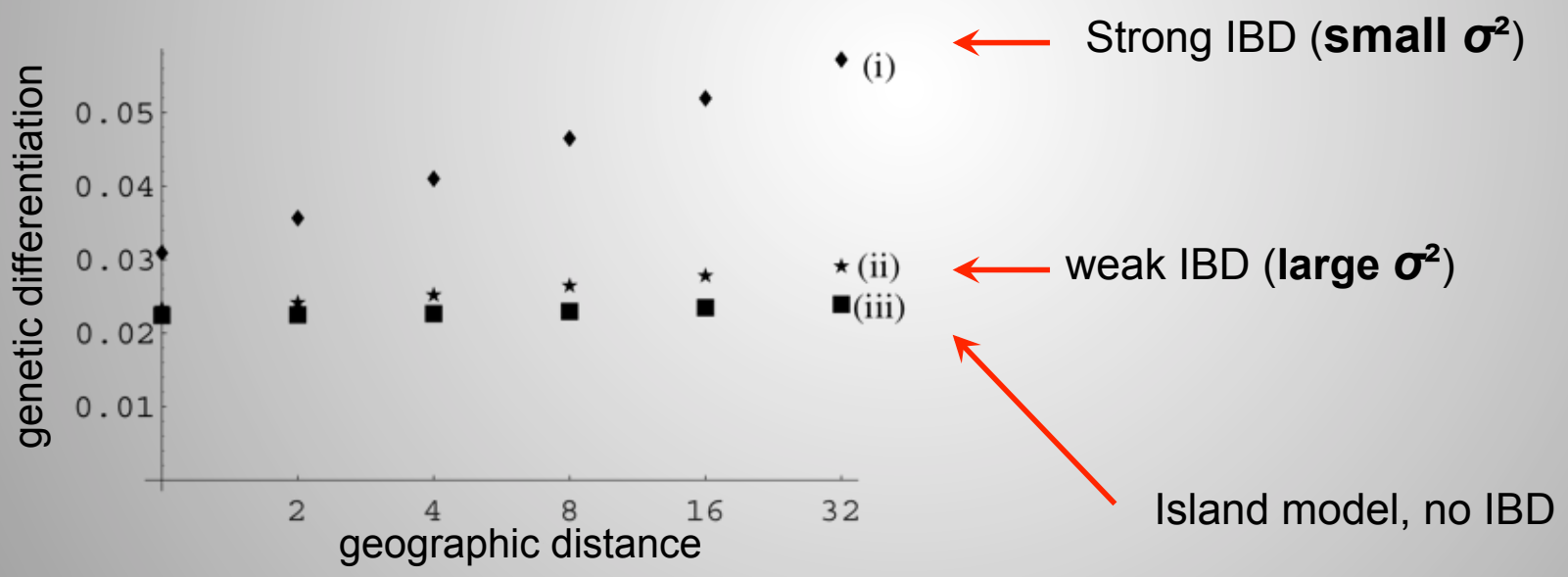
: inverse of the "strength of IBD"

# Models for structured populations:

# 3 – the general isolation by distance model

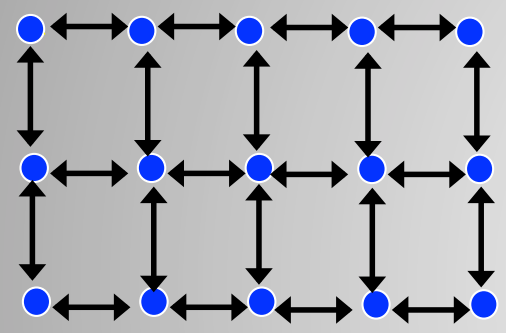
The main characteristic of IBD models is that

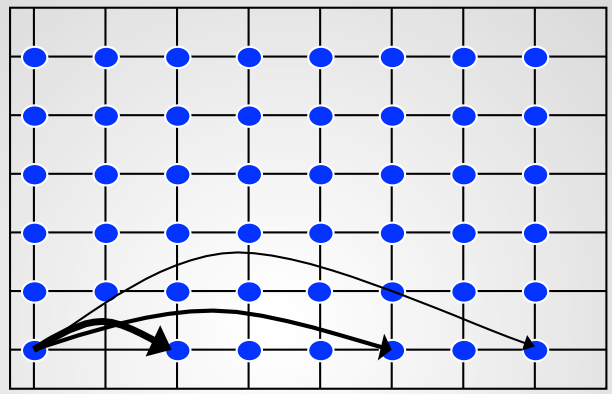
**genetic differentiation increases with geographic distance**

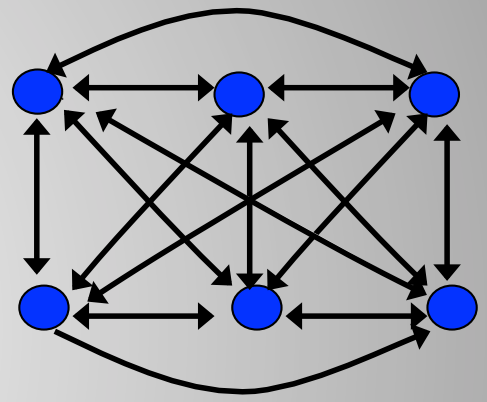


# Models for structured populations:

# 3 – the general isolation by distance model







IBD models are quite general depending on how localized dispersal is :

| | | | | |
|---|---|---|---|---|
| **Stepping stone** | **>** | **IBD** | **>** | **Island Model** |
| $\sigma^2 = m < 1$ | | $1 < \sigma^2 << \infty$ | | $\sigma^2 \approx \infty$ |

# Dispersal inference under isolation by distance:

## 1 – the differentiation parameter : $F_{ST}/(1-F_{ST})$

The mathematical analysis is done in terms of Probability of Identity (cf? Vitalis) and then expressed as combination of F-statistics
For the demic model :

$Q_1$ is the probability of identity of two genes taken within a single deme,
$Q_2, Q_r$ are probabilities of identity of two genes taken in different demes,

$$\boxed{\frac{Q_1 - Q_r}{1 - Q_1} = \frac{F_{ST}}{1 - F_{ST}} \text{computed between demes at geographical distance } r}$$

with

$$F_{ST} \equiv \frac{Q_1 - Q_2}{1 - Q_2}$$ and $Q_2 \Leftrightarrow Q_r$ to take distance into account

# Dispersal inference under isolation by distance:

## 1 – the differentiation parameter : $F_{ST}/(1-F_{ST})$

The mathematical analysis is done in terms of Probability of Identity (cf? Vitalis) and then expressed as combination of F-statistics

For the "continuous" model :

$$a_r \equiv \frac{Q_1 - Q_r}{1 - Q_1} \text{ computed between individuals at geographical distance } r$$

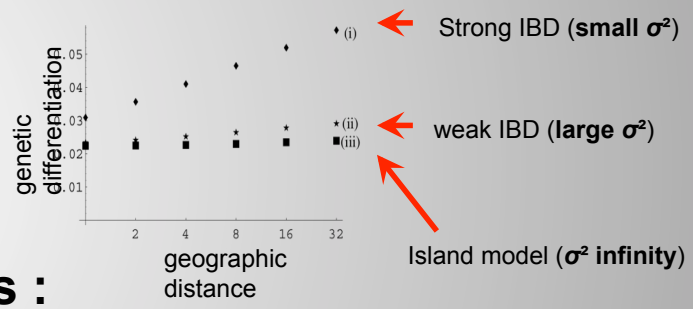
with $Q_1$ the probabiilty of identity of two genes taken within a single individual and $Q_r$ the probability of identity of two genes taken in two individuals separated by a distance *r*

$$a_r \equiv \frac{Q_1 - Q_r}{1 - Q_1} \text{ is analoguous to } \frac{F_{ST}}{1 - F_{ST}} \text{ between individuals}$$

# Dispersal inference under isolation by distance:

## 2 – relationship between differentiation and distance

The main result of the analysis of IBD models in terms of probabilities of identity is the following relationship between the differentiation parameter and the geographic distance and the different assumptions leading to it :




**RECALL : 2 (or more) demographic parameters :**

*N* or *D* : sub-population size or density of individuals

$\sigma^2$ : mean squared parent-offspring dispersal distance

: inverse of the "strength of IBD"

+ μ the mutation rate (per locus per generation)

# Dispersal inference under isolation by distance:

## 2 – relationship between differentiation and distance

The main result of the analysis of IBD models in terms of probabilities of identity is the following relationship between the differentiation parameter and the geographic distance and the different assumptions leading to it :

in one dimension IBD models with demes :

$$a_r \text{ or } \frac{F_{ST}}{1-F_{ST}} = \frac{Q_1 - Q_r}{1-Q_1} \approx \frac{1-e^{\frac{-\sqrt{2\mu r}}{\sigma}}}{4N\sigma\sqrt{2\mu}} + \text{constant}$$

$$a_r \text{ or } \frac{F_{ST}}{1-F_{ST}} \approx \text{r et } \mu \text{ petit} \; \frac{r}{4N\sigma^2} + \text{constant}$$

**Simple linear relationship between differentiation and distance but only for small distances and low mutation rates**

# Dispersal inference under isolation by distance:

## 2 – relationship between differentiation and distance

The main result of the analysis of IBD models in terms of probabilities of identity is the following relationship between the differentiation parameter and the geographic distance and the different assumptions leading to it :

in one dimension IBD models with continuous distribution :

$$a_r \text{ or } \frac{F_{ST}}{1 - F_{ST}} \approx^{\text{r et } \mu \text{ petit}} \frac{r}{4N\sigma^2} + \frac{A_1}{4N\sigma}$$

$$\approx^{N \to D} \frac{r}{4D\sigma^2} + \frac{A'_1}{4D\sigma}$$

similar relationship for the continuous model

**Simple linear relationship between differentiation and distance but only for small distances and low mutation rates**

# Dispersal inference under isolation by distance:

## 2 – relationship between differentiation and distance

The main result of the analysis of IBD models in terms of probabilities of identity is the following relationship between the differentiation parameter and the geographic distance and the different assumptions leading to it :

in two dimension IBD models :

$$\frac{Q_1 - Q_r}{1 - Q_1} \approx^{\text{r et } \mu \text{ petit}} \frac{\ln(r)}{4\pi N\sigma^2} + \text{constant}$$

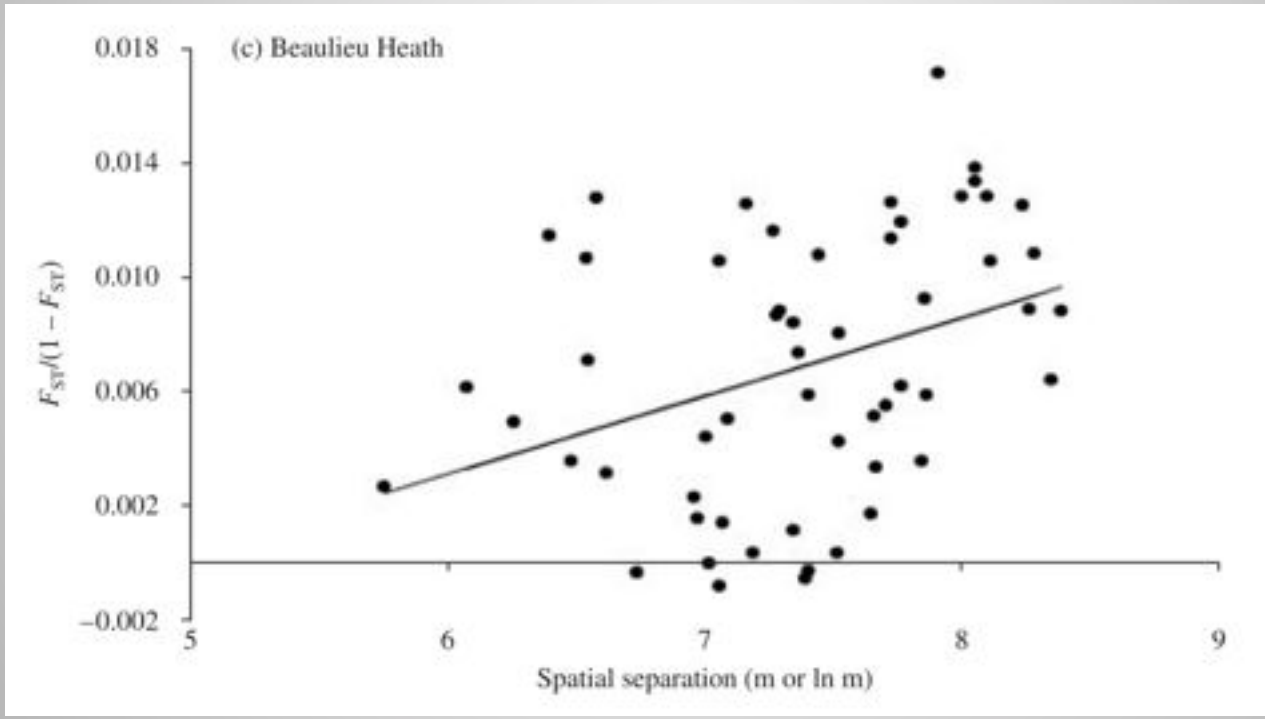
$$\approx^{\text{N} \rightarrow \text{D}} \frac{\ln(r)}{4\pi D\sigma^2} + \text{constant}$$

**Simple linear relationship between differentiation and the logarithm of the distance**
**but only for small distances and low mutation rates**

# Dispersal inference under isolation by distance:

## 3 – the regression method of Rousset (1997, 2000)

The regression slope is expected to be $4\pi D\sigma^2$, thus a simple method to infer $D\sigma^2$ is to do the regression on the data and estimate the slope




➔ **1/slope is an estimator of $D\sigma^2$**

# Dispersal inference under isolation by distance: 3 – the regression method of Rousset (1997, 2000)

The regression slope is expected to be $4\pi D\sigma^2$, thus a simple method to infer $D\sigma^2$ is to do the regression on the data and estimate the slope

In practice :

1 – go to field and sample 80-500 individuals on a given surface

2 – genotype them using a dozen or more of microsatellite markers

3 – Use Genepop : option IBD between individuals or demes

- it estimates $F_{ST}/(1-F_{ST})$ or $a_r$ for all pairs of demes or individuals
- it regresses them against the geographic distance or its logarithm
- it infer the slope of the regression

# Inference of $D\sigma^2$ under isolation by distance:

# 3 – the regression method of Rousset (1997, 2000)

- Point estimate : 1/slope ➔ estimate of $4\pi D\sigma^2$

- Significance :
  - ✓ **Mantel Test** (by permutations) :

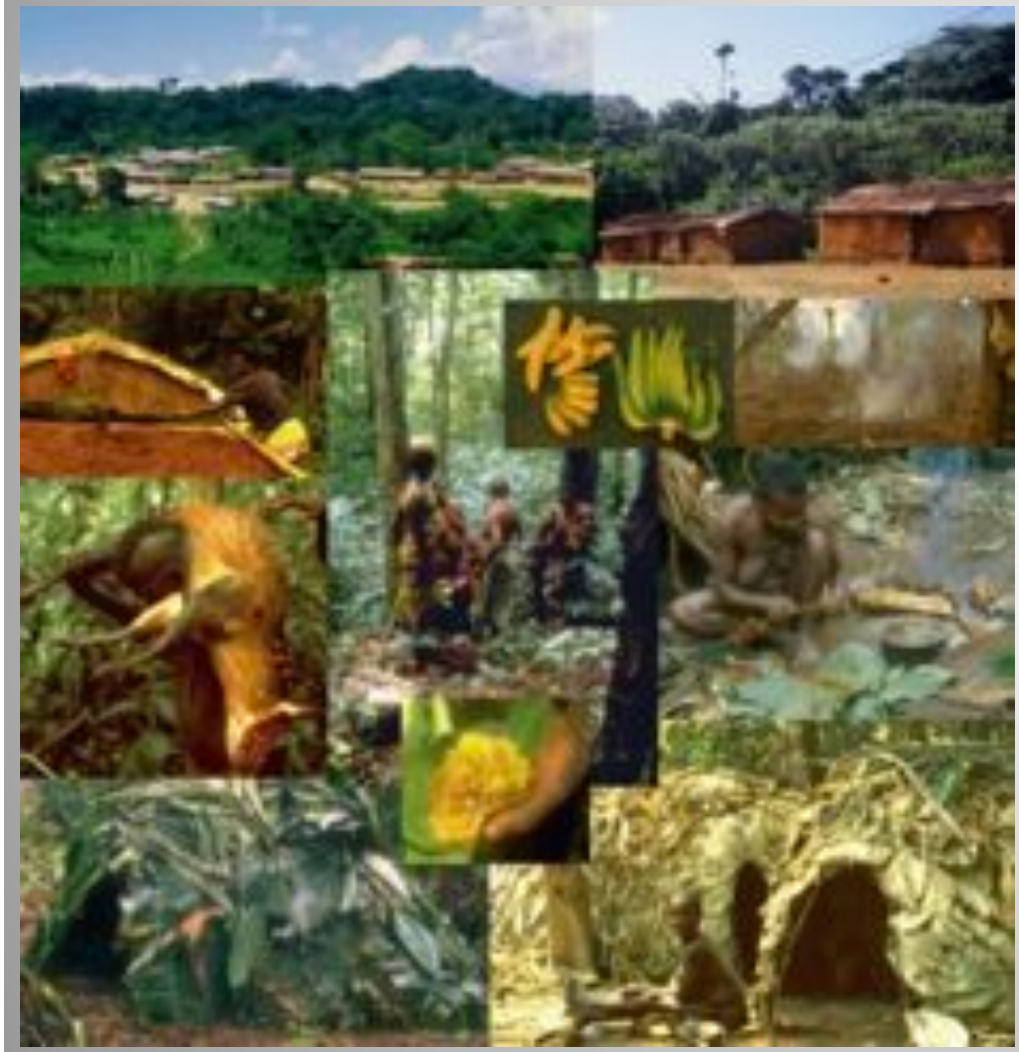
    Test the correlation between the genetic and the geographic matrices by permuting rows and columns from one of the two matrices

    -> significant if the initial correlation is greater than the correlation on permuted matrices (e.g. in the higher 5%)
  - ✓ **Bootstrap** : re-sampling of loci (ok because they are independent) gives Confidence Intervals (CI) for the slope

    -> significant if the CI does not contain 0 (null slope, infinite $D\sigma^2$)

# Inference of $D\sigma^2$ under isolation by distance:

## 4 – example on a Pygmy population



Paul Verdu PhD

National Museum of Natural History,

Paris :

**History of the pygmy populations from Western Africa**

# Inference of $D\sigma^2$ under isolation by distance:

## 4 – example on a Pygmy population

biology letters

Biol. Lett.
doi:10.1098/rsbl.2010.0192
Published online

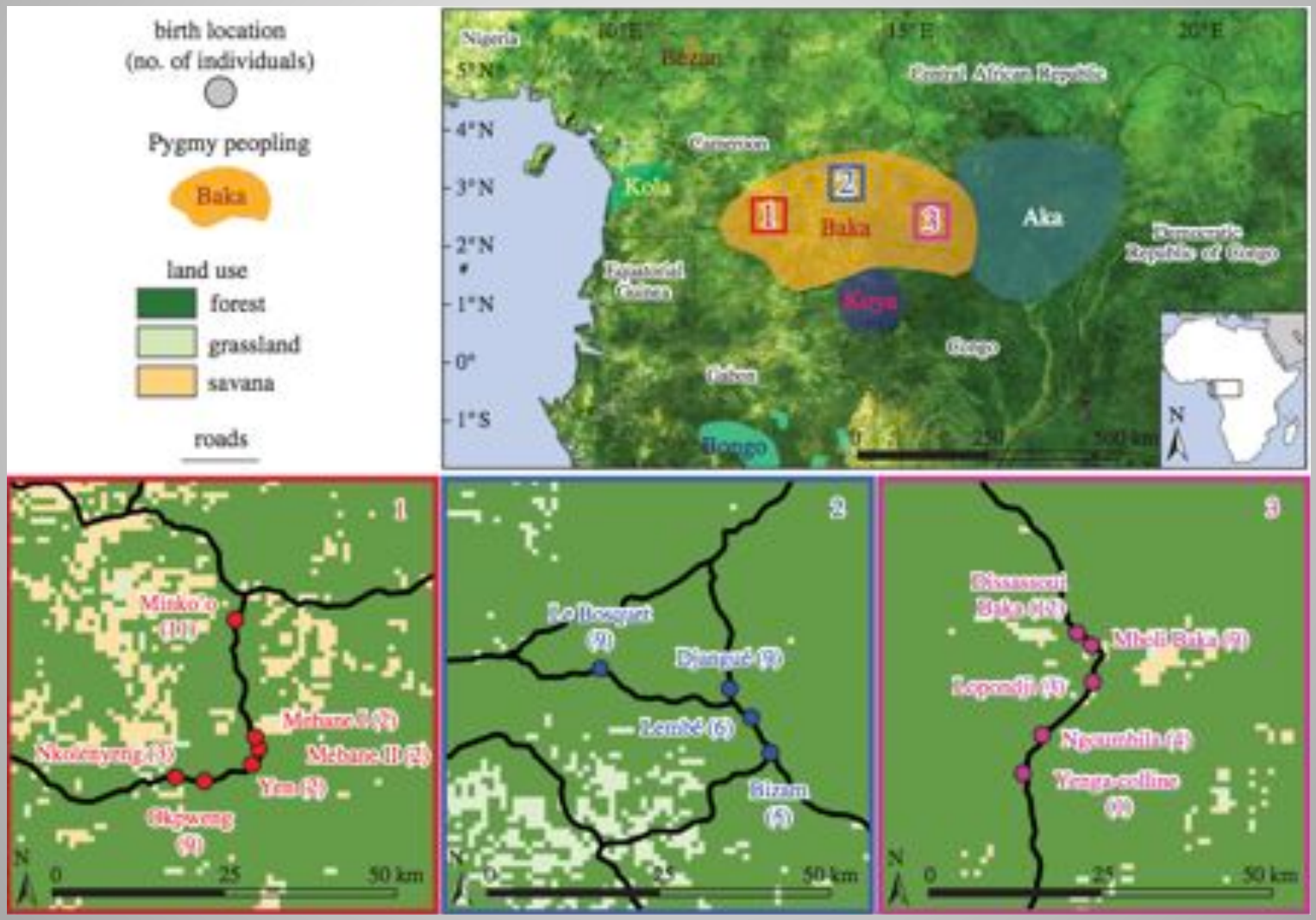
Population genetics

**Limited dispersal in mobile hunter–gatherer Baka Pygmies**

Paul Verdu[1,2,*], Raphaël Leblois[3], Alain Froment[4], Sylvain Théry[2], Serge Bahuchet[2], François Rousset[5], Evelyne Heyer[2] and Renaud Vitalis[2,†]

# Inference of $D\sigma^2$ under isolation by distance:

## 4 – example on a Pygmy population



# Inference of $D\sigma^2$ under isolation by distance:

## 4 – example on a Baka Pygmy population

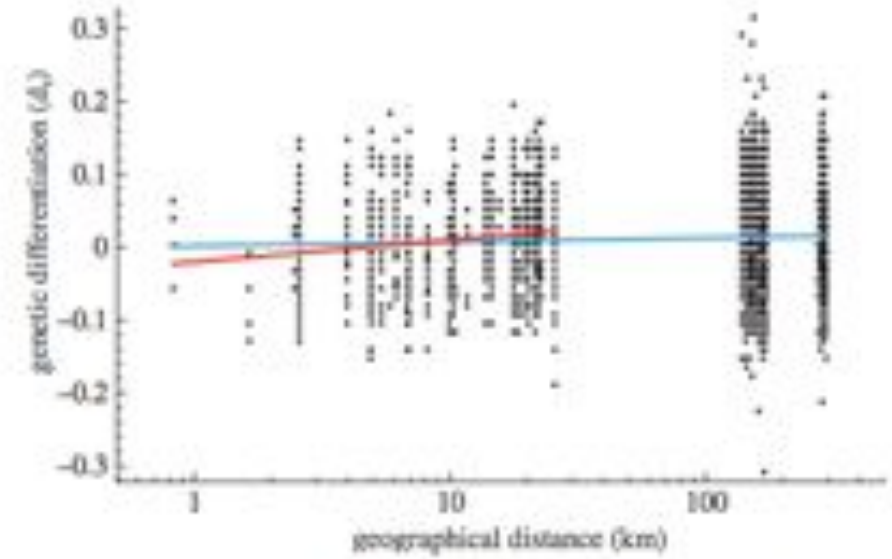



Figure 2. Correlation between genetic differentiation and the logarithm of geographical distances among Baka Pygmies. Multilocus estimates of pairwise differentiation ($\hat{d}_c$) are plotted against the logarithm of geographical distances (in kilometres). The linear regression considering all pairs of individuals is $y = 0.0027x - 0.0153$ (in blue). The linear regression considering only pairs of individuals born within the same group is $y = 0.0137x - 0.1138$ (in red).

Total sample : $4\pi D\sigma^2 = 373$

within group (small scale) : $4\pi D\sigma^2 = 73$

**using D=0.47 ind/km$^2$**

**we have $12.4 < \sigma^2 < 63.2$ km$^2$**

Cavalli-Sforza & Hewlett (1982) found
$\sigma^2 \approx 3683$ km$^2$
from a ethnological survey
in Aka pygmies !

# Inference of $D\sigma^2$ under isolation by distance:

## 4 – example on a Pygmy population

<u>indirect genetic estimate</u> (regression method) : **$12.4 < \sigma^2 < 63.2$ km$^2$**

<u>indirect ethnologic estimate</u> (questionnaire) **$\sigma^2 \approx 3683$ km$^2$**

<u>Those discrepancies can be explained by:</u>

- demographic/ethnologic data (distances between birthplaces and places of residence) may reflects exploration behavior rather than parent-offspring dispersal
- the two studies done in different pygmy groups (Aka vs Baka) which may have different dispersal behavior

<u>Conclusions</u> :

Although our results do not challenge the view that hunter–gatherer Pygmies have frequent movements in their socio- economic area, we demonstrate that extended individual mobility does not necessarily reflect extended dispersal across generations

# Testing inference methods

## 1 – How to test an inference method ?

- Tests by simulations:

  = how close are estimates / values specified in simulations

  - simulations under the right model (i.e. the one used for inference)

  ➠ gives the precision of the inference in the best cases

  - simulations under a model that does not respect some assumptions

  ➠ gives the robustness / model assumptions

- Tests on real data sets for which we have "independent expectations"

  = For demographic parameter inference from genetic data, the only solution is to compare our indirect estimates with direct estimates obtain with demographic methods (CMR, tracking, …)

# Testing inference methods

## 2 – Simulation test of the regression method

**(1)** Choice of mutational and demographic parameter values for simulations

↓

**(2)** Simulation : 1000 runs for 10 loci

↓

**(3)** Analysis of the 1000 simulated multilocus data sets

→1000 estimates of the regression slope

↓

**(4)** Comparison with the "expected" value of the slope :

Relative bias = $\sum$(Est-Exp)/Exp

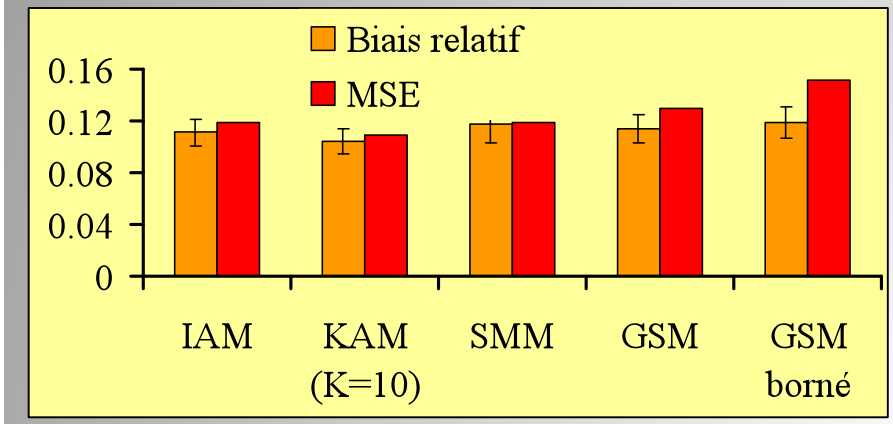
Mean squarre error MSE = $\sum(\text{Est-Exp})^2/\text{Exp}^2$

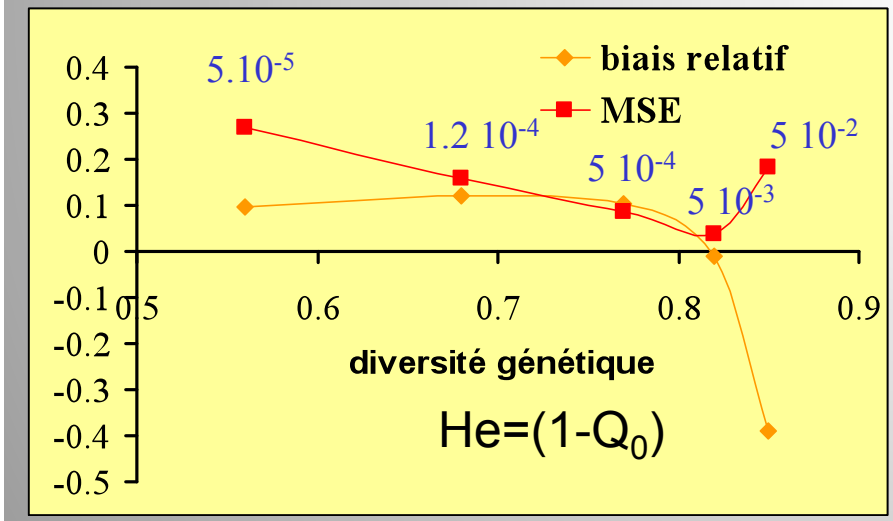
Proportion of estimates within a factor 2 from the expected value

i.e. in $[D\sigma^2_{exp} / 2 ; 2 \times D\sigma^2_{exp}]$

# Testing inference methods

## 2 – Simulation test of the regression method




**Influence of mutational processes**

Method based on Identity by Descent (IBD)

Marker information is not by descent but by state: e.g. Stepwise mutations for microsats

Simulation results ➠ very robust method : small effects of different mutational models

**Influence of mutation rate (genetic diversity)**

Assumption: low $\mu$ ; but diversity is needed to have enough "genetic information"

Simulation results:

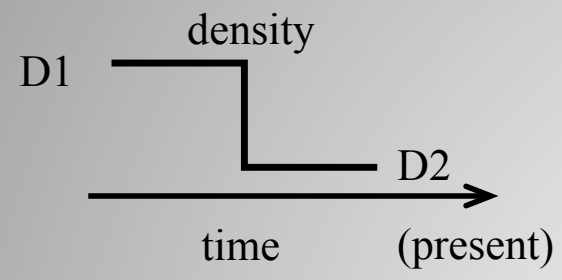
➠ better precision with high diversity (0.7-0.8)

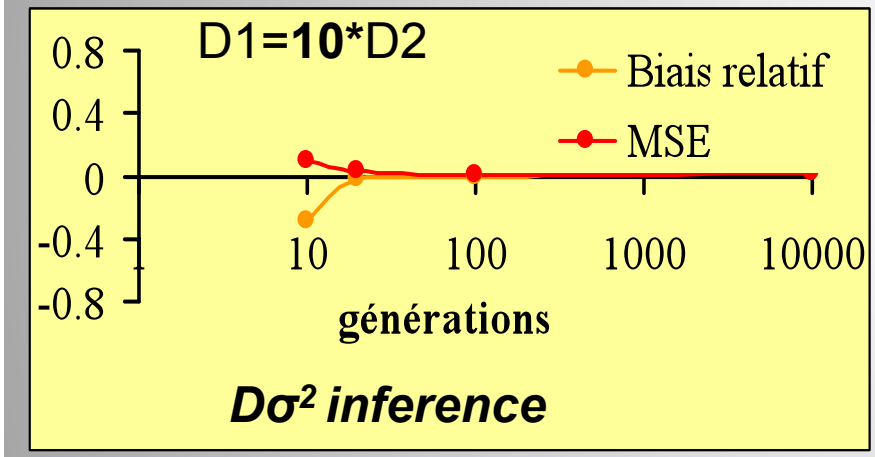
➠ strong bias for very high mutation rates

**Microsatellites are good markers despite their complex mutational processes because they show high genetic diversity**

# Testing inference methods

## 2 – Simulation test of the regression method




**Influence of past demographic processes:**

Ex 1 : past decrease in density (bottleneck)

Simulations results ➠ robust method because the influence of past density is very weak

**Other tests**:

- past density increase
- spatial expansion
- spatial heterogeneity in density

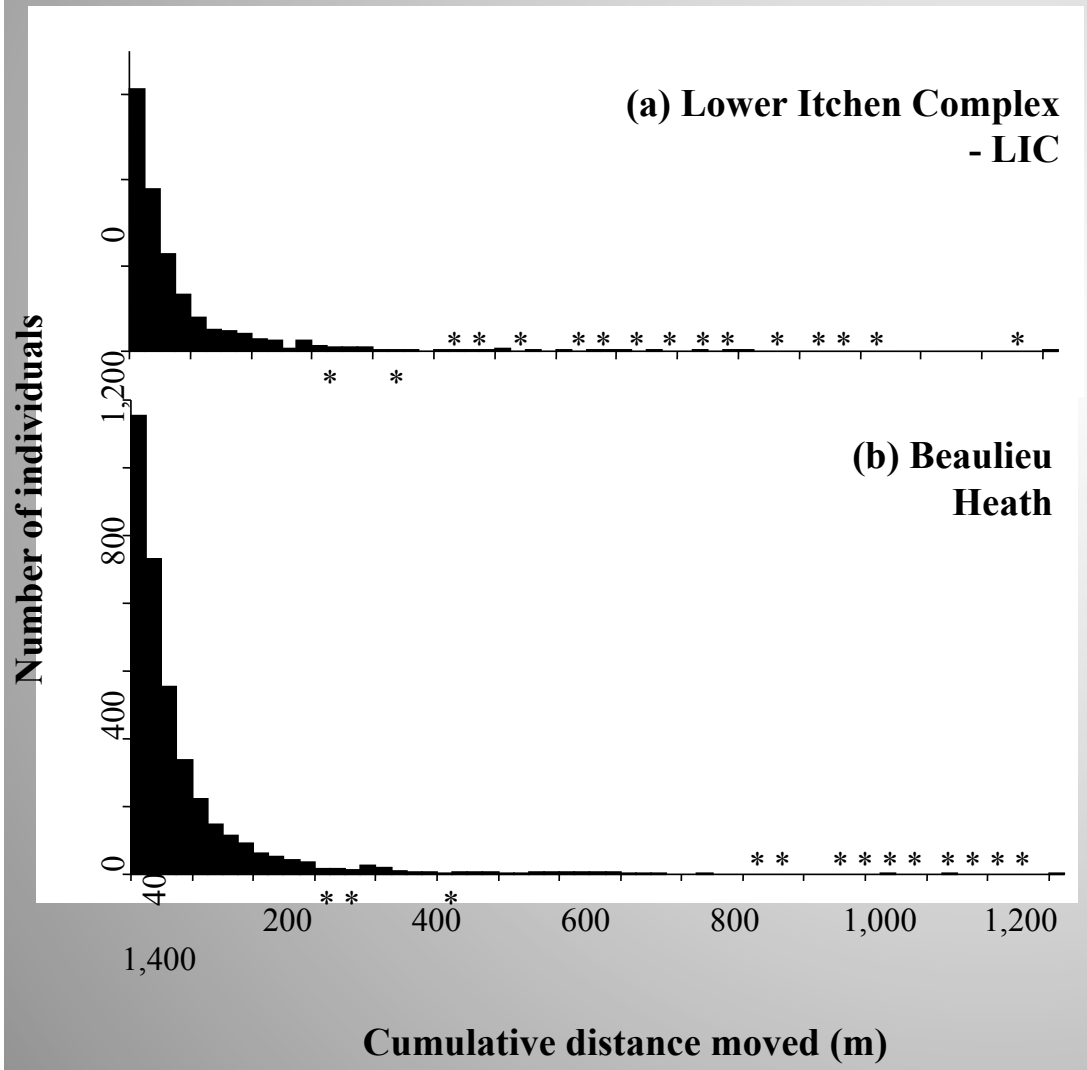
**All simulation tests** ➠ Global robustness of the regression method to temporal and spatial heterogeneities of demographic parameters :

➠ **the regression method infer the present-time and local *Dσ²* of the population sampled**

# Testing inference methods

## 3 – Comparisons between genetic and demographic estimates

- example on damselfly populations (Watt et al. 2007 Mol.Ecol.)




**Demographic data (CMR)**

➠ Census density and distribution of dispersal

# Testing inference methods

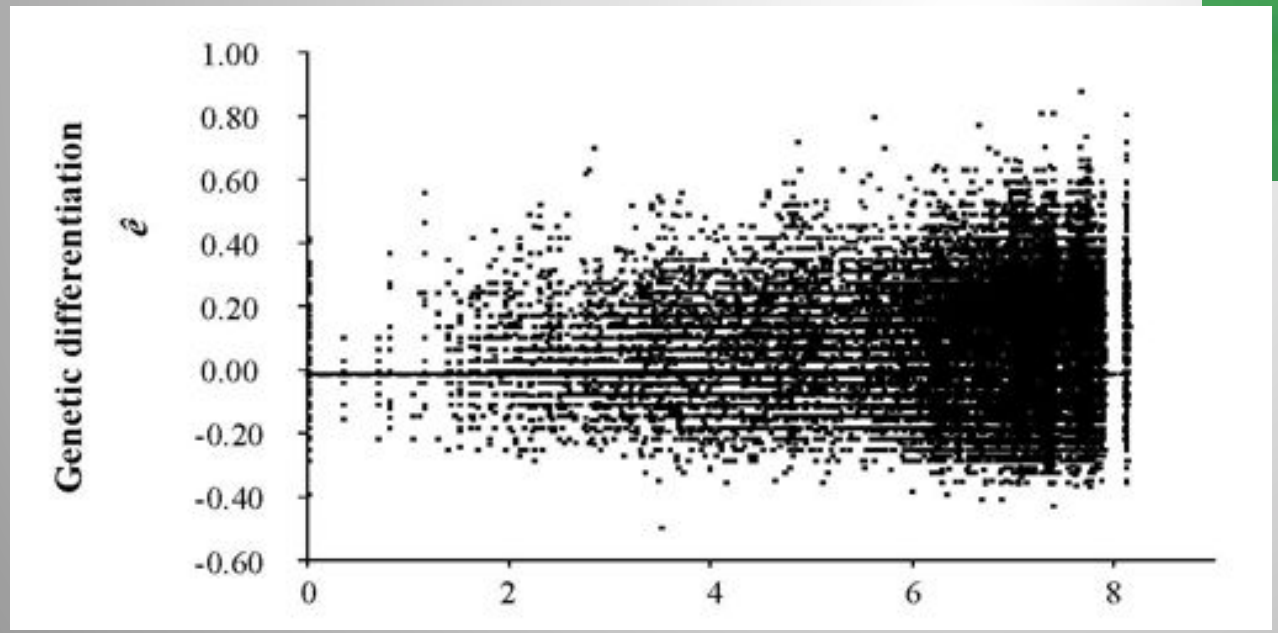
## 3 – Comparisons between genetic and demographic estimates

- example on damselfly populations (Watt et al. 2007 Mol.Ecol.)

**Genetic data : 700 individuals genotyped**

**at 13 microsatellite loci**

➠ indirect estimates of $D\sigma^2$



# Testing inference methods

## 3 – Comparisons between genetic and demographic estimates

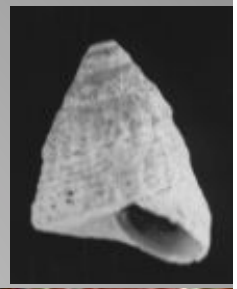
- example on damselfly populations (Watt et al. 2007 Mol.Ecol.)

| | $D\sigma^2$ estimates | |
|---|---|---|
| | Direct (demographic) | Indirect (genetic) |
| Site 1 | 277 | 222 |
| Site 2 | 249 | 259 |
| Site 3 | 555 | 606 |

**very good agreement between demographic and genetic estimates**

# Testing inference methods

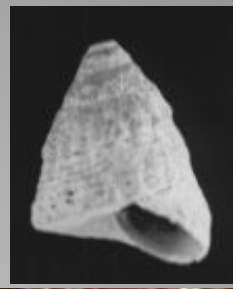
## 3 – Comparisons between genetic and demographic estimates



| | Direct (Demography) | Indirect (genetic) |
|---|---|---|
| **American Marten** (Martes americana) | **7.5** | **3.8** |
| **Kangaroo rats** (Dipodomys) | **1.43** | **2.58** |
| **intertidal snails** (Bembicium vittatum) | **2.4** | **3.6** |
| **Forest lizards** (Gnypetoscincus queenslandiae) | **11.5** | **5.5** |
| **Humans in the rainforest** (Papous) | **29.3** | **21.1** |
| **Legumin** (Chamaecrista fasciculata) | **9.6** | **13.9** |

# Testing inference methods

## 3 – Comparisons between genetic and demographic estimates



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| Legumin | 9.6 | 13.9 |

very good agreement between demographic and genetic estimates for all available data sets with demographic and genetic data at a local geographical scale

➠ **validate the regression method and isolation by distance models**

# Usual (and often justified) critics on indirect demographic inferences

Main critics on demographic parameter inference from genetic data (Hasting et Harrison 1994, Koenig et al. 1996, Slatkin 1994) :

- Demo-genetic models are not realistic enough, especially dispersal modeling in the island model
- Natural population are often inhomogeneous and at disequilibrium, whereas most demo-genetic models assume spatial homogeneity and time equilibrium
- Assumptions on mutation rates and mutational models are oversimplified regarding complex mutational processes of genetic markers
- neutral markers do not really exist, there is always a form of selection

➠ Whitlock & McCauley (1999, Heredity) :

Indirect measure of gene flow and migration : $Fst \neq 1/(1+4Nm)$

# Usual (and often justified) critics on indirect demographic inferences

Main critics on demographic parameter inference from genetic data (Hasting et Harrison 1994, Koenig et al. 1996, Slatkin 1994) :

- no realistic models of dispersal
- too many assumptions on spatial homogeneity and time equilibrium
- oversimplified mutational models
- genetic markers are not neutral

➠ Whitlock & McCauley (1999, Heredity) :

Indirect measure of gene flow and migration : Fst ≠1/(1+4Nm)

**So why do we have good results for $D\sigma^2$ inferences using the regression method on IBD models ?**

# Why $D\sigma^2$ inferences using the regression method on IBD models seems to work so well ?

- **The model : Isolation by Distance is a "relatively realistic" model**
  - Dispersal is well modeled (allows localized but also leptokurtic dispersal)
  - "Continuous" IBD models allows the consideration of continuous spatial distribution of individuals ➠ no need to a priori define sub-populations/demes
- **The inference method : the regression methods of Rousset (1997, 2000) is well designed, precise and robust**
  - the relationship between $F_{ST}/(1-F_{ST})$ and the distance is easier to interpret in terms of demographic parameters than Fstatistics alone (simple linear relationship)
  - No assumptions on the shape of the dispersal (allows leptokurtic distributions)
  - only valid for sampling at a local geographical scale (small distance assumption)
    ➠ less demographic and selective spatial heterogeneities
- **The genetic markers : microsatellites are good highly informative markers**

# Why $D\sigma^2$ inferences using the regression method on IBD models seems to work so well ?

- **The model : Isolation by Distance is a "relatively realistic" model**
- **The inference method : the regression methods of Rousset (1997, 2000) is well designed, precise and robust**
- **The genetic markers : microsatellites are good highly informative markers**

➠ Both the demo-genetic model, the inference method, the sampling strategy and the genetic markers are important for the inference of demographic parameters to be accurate, i.e. to obtain precise and robust estimation of local and present-time demographic parameters

# Why $D\sigma^2$ inferences using the regression method on IBD models seems to work so well ?

**Quick interpretation of the robustness of the regression method to mutational processes and past demographic changes using the coalescent theory :**

- small deme/sub-population sizes
- high migration rates
- sampling at small geographical scale

} short coalescence times

➠ **short coalescence times (i.e. most of the coalescent tree is in a recent past) decrease the influence of past factors acting on the distribution of polymorphism, such as past mutation processes et past demographic fluctuations**

Note that this effect is even more pronounced for the "continuous" IBD model because deme size is one individual and migration rates are very high (>0.3)

# Extensions to classic isolation by distance models

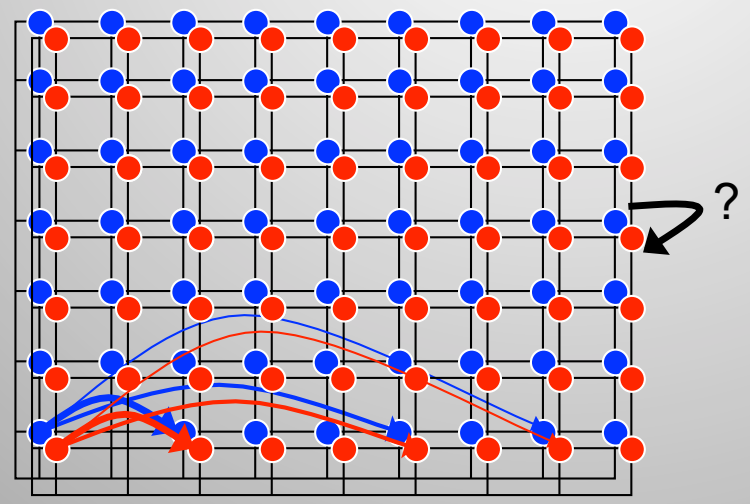
## 1 – IBD within and bewteen two habitats or groups

Using IBD models to test for potential gene flow between populations of organisms living in different habitats in sympatry (Rousset 1999)

Different habitats can be, for example :

- different hosts for a parasite
- agricultural vs natural populations

IBD within each habitat, but what could the signal of the differentiation between the habitats tell us about gene flow between those habitats



# Extensions to classic isolation by distance models

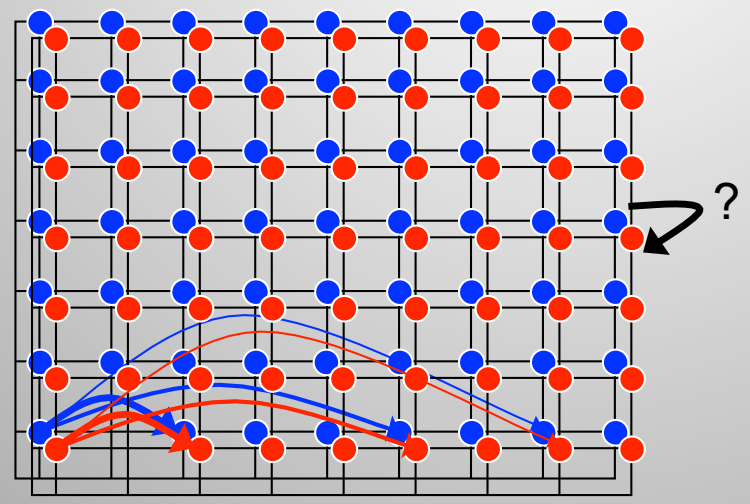
## 1 – IBD within and bewteen two habitats or groups

Using IBD models to test for potential gene flow between populations of organisms living in different habitats in sympatry (Rousset 1999)

Assumption : IBD in at least one of the habitats

The theory showed that if there is enough gene flow between the two habitats ($m$>0.001) then IBD should be observed between habitats, with a "intermediate" IBD pattern compared to IBD patterns within each habitat

if there is no gene flow between the two habitats ($m$<0.001) then the differentiation between habitats should be independent of the distance



# Extensions to classic isolation by distance models

## 1 – IBD within and between two habitats or groups

Ex: European Corn Borer (Ostrinia Nubilalis), a major pest for corn plantations

Native in Europe, introduced in North America

# Extensions to classic isolation by distance models

## 1 – IBD within and between two habitats or groups

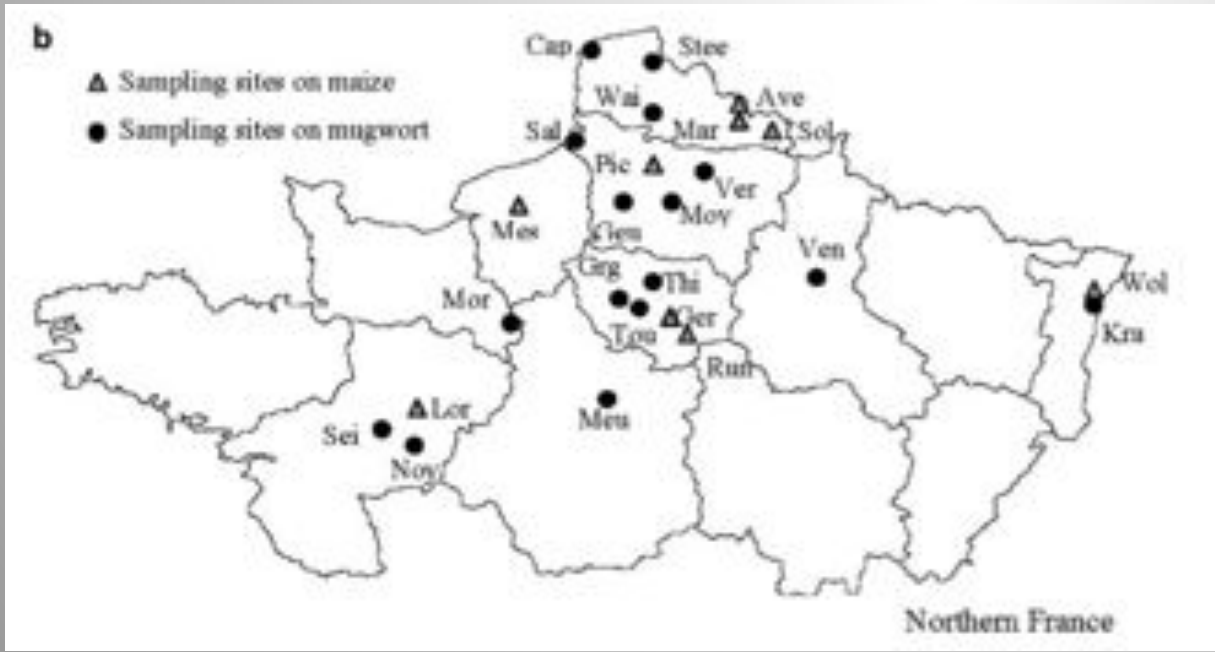
The European Corn Borer (Ostrinia Nubilalis)

naturaly feeds on mugwort (Asteraceae) in Europe

# Extensions to classic isolation by distance models

## 1 – IBD within and between two habitats or groups

- GMO "Bt" maize plants are resistant to the European Corn Borer, but to manage the evolution of resistance to the B. thuringiensis toxins in the pest, there is a need to keep "refuge habitats" near the GMO plantations
- Refugia can theoretically be plant on which the insect can feed and reproduce, however, to be efficient, there should be enough gene exchanges between pest populations living on plantations and refuges




Martel et al (2003, Heredity) tested the usefulness of using mugwort natural populations as refuges

# Extensions to classic isolation by distance models

## 1 – IBD within and between two habitats or groups

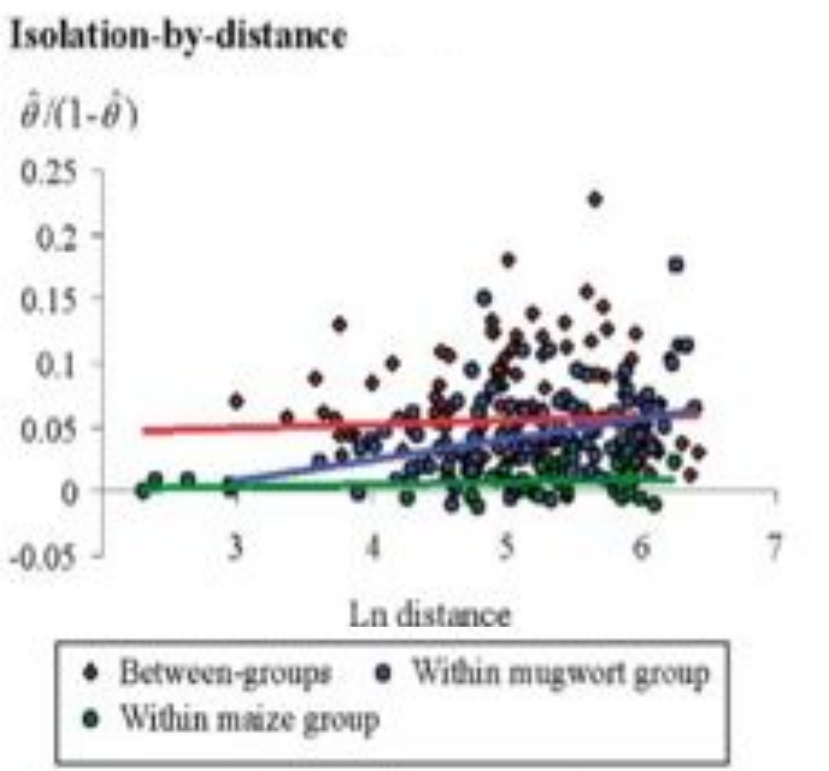



**Figure 2** Regressions of $\hat{\theta}/(1-\hat{\theta})$ against ln (geographical distances) (km) for populations collected on *Artemisia vulgaris* (within mugwort), on *Zea mays* (within maize) and between populations collected on the two host plants (between-group). Regressions are given for all loci and for all loci except the *Mpi* locus.

**Expectation :**

No gene flow between habitats (m<0.01)

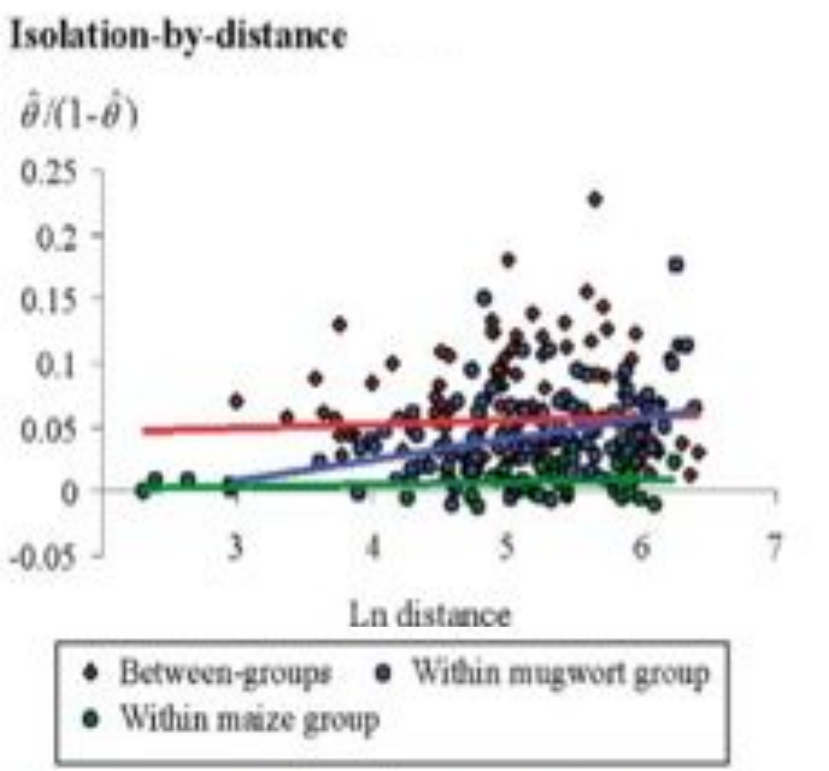
➠ differentiation between habitats independent of geographic distance

**What is observed :**

- Within mugwort-feeding pops ➠ slope is 0.0163 (significantly ≠ 0) and $D\sigma^2$=5 moths
- Within maize-feeding pops ➠ slope is 0.0020. (not ≠ 0) and $D\sigma^2$=40 moths
- Between Maize & Mugwort-feeding pops ➠ slope is 0.0029, (not ≠ 0)
- Differentiation is always higher between habitats than within each habitat

# Extensions to classic isolation by distance models

## 1 – IBD within and between two habitats or groups

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**Conclusions :**

1. Difference in $D\sigma^2$ between the two host-plant groups probably due to higher densities in maize-feeding populations rather than differences in dispersal
2. there is clearly a strong barrier to gene flow between mugwort and maize-feeding populations of the European corn borer

➠ natural mugwort populations should not be used as refuges because it will not limit evolution of resistance within maize-feeding populations but only within mugwort-feeding populations

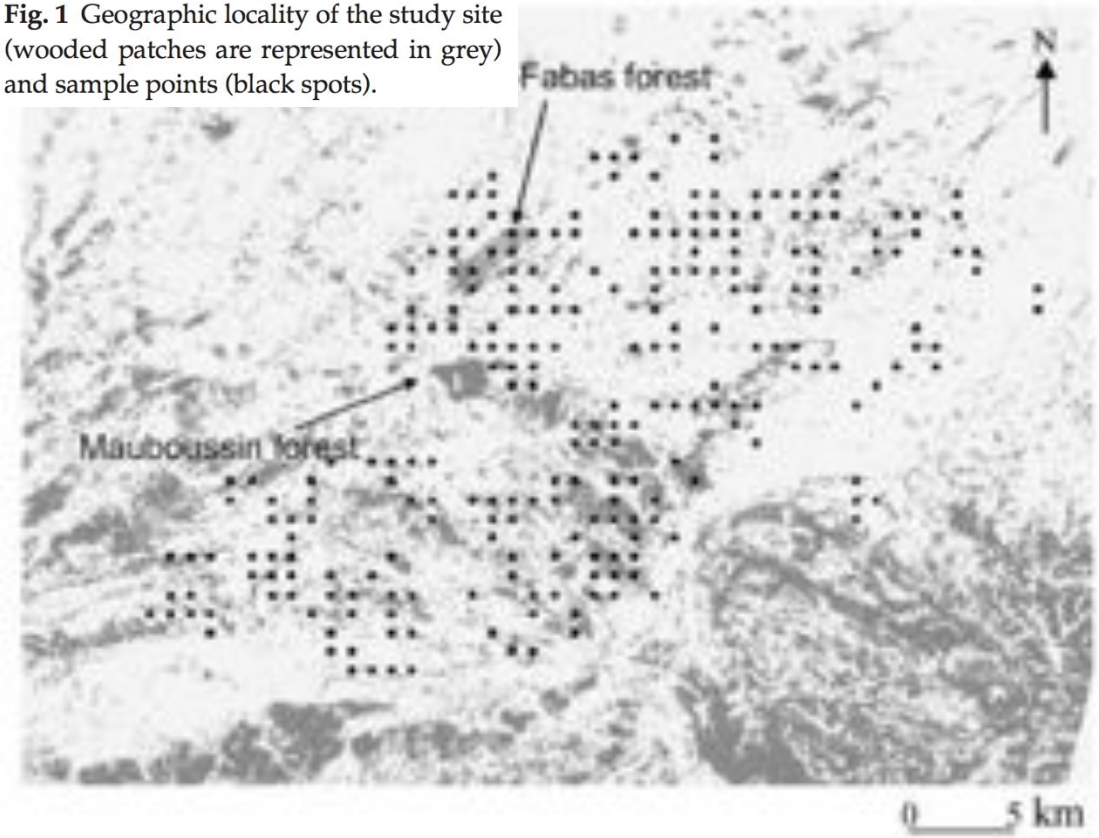
# Extensions to classic isolation by distance models

## 2 – euclidian distance vs "least cost distance"

Habitat connectivity is often not homogeneous in space but strongly depends on landscape feature ➠ **using euclidian distance may not be optimal**

ex : Roe deers (*Capreolus capreolus*) in a patchy landscape (Coulon et al. 2004)

**Fig. 1** Geographic locality of the study site (wooded patches are represented in grey) and sample points (black spots).

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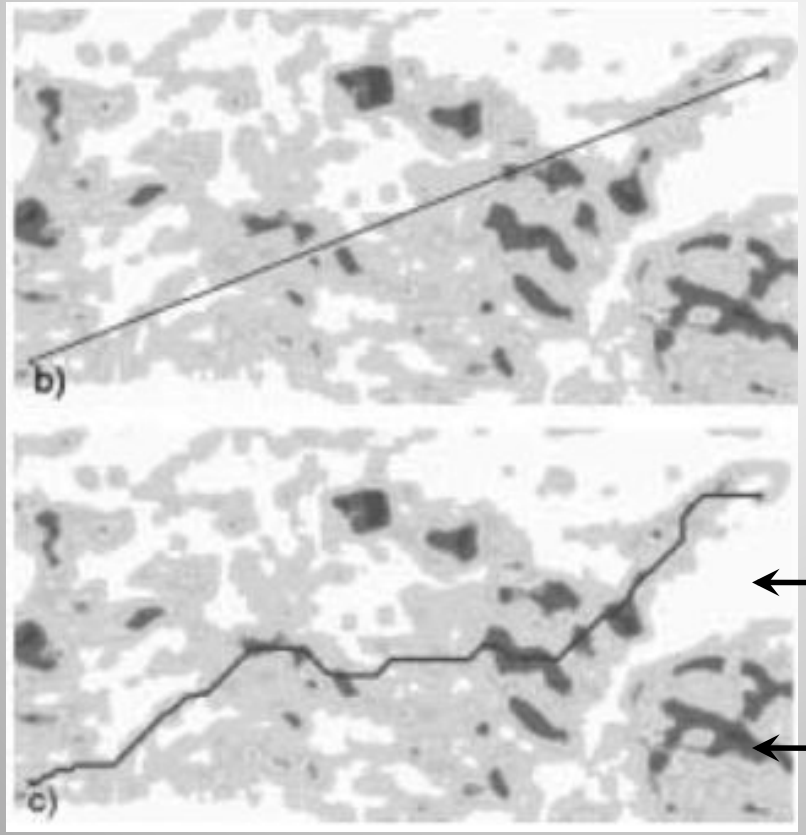
# Extensions to classic isolation by distance models

## 2 – euclidian distance vs "least cost distance"

**ex : Roe deer population in a patchy landscape (Coulon et al. 2004)**

the least cost distance is the trajectory that maximizes the use of wooded corridors

Euclidian distance




Least cost distance

Open land

Forest patches

# Extensions to classic isolation by distance models

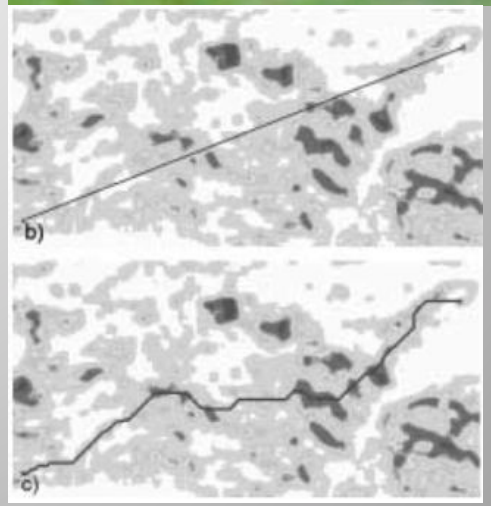
## 2 – euclidian distance vs "least cost distance"

**ex : Roe deer population in a patchy landscape (Coulon et al. 2004)**

**Table 2** Correlations between genetic and (logarithmic) geographical distances for females and males roe deer. Values of the statistics $r$ for Mantel tests are given for each relationship between genetic and geographical distances and the associated probabilities (in brackets) were calculated by carrying out 10 000 permutations of lines or columns of one of the two half-matrices

| | Females | Males |
|---|---|---|
| ln Euclidean distance | 0.019<br>(0.118) | −0.0001<br>(0.5) |
| ln least cost distance | 0.031<br>(0.005)** | 0.003<br>(0.401) |

**$P < 0.01$.




✓ Better correlation between genetic differentiation and least cost distance

✓ IBD is only significant for females when considering the least cost distance

# Extensions to classic isolation by distance models

## 2 – euclidian distance vs "least cost distance"

**ex : Roe deer population in a patchy landscape (Coulon et al. 2004)**

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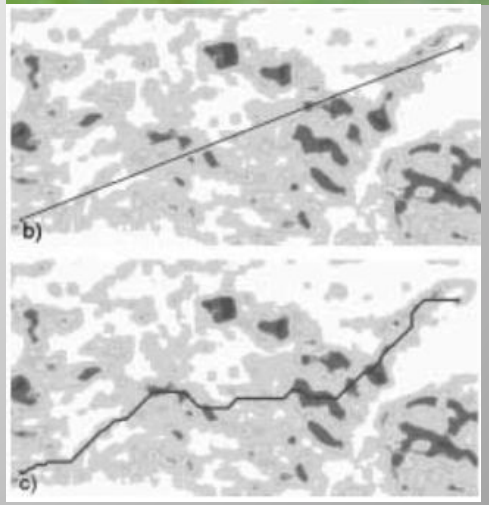



**Limits and problems:**

✓ What cost should we attribute to different landscape features?

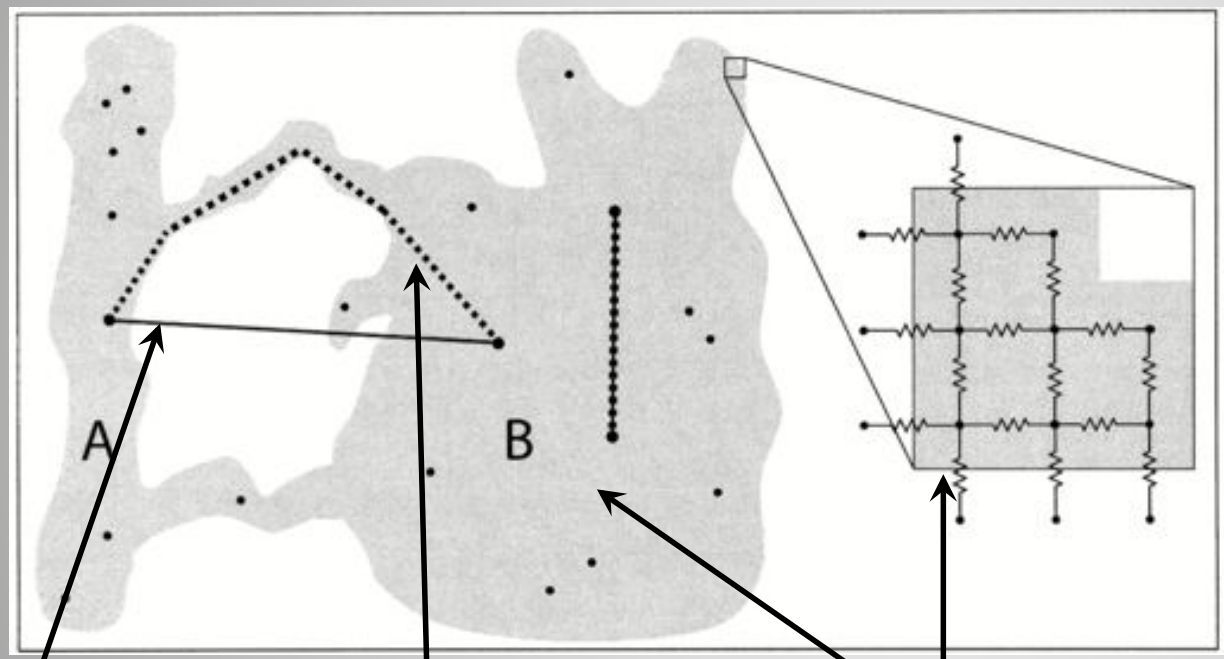
✓ Inference of the cost from genetic data may be really difficult (too many parameters)

✓ Does a better correlation really means a better model under IBD models?

# Extensions to classic isolation by distance models

## 2 – euclidian distance vs resistance distance

**Isolation by resistance (McRae 2006 Evolution) :** analogy with circuit theory




euclidian distance

Least cost distance

Resistance surface

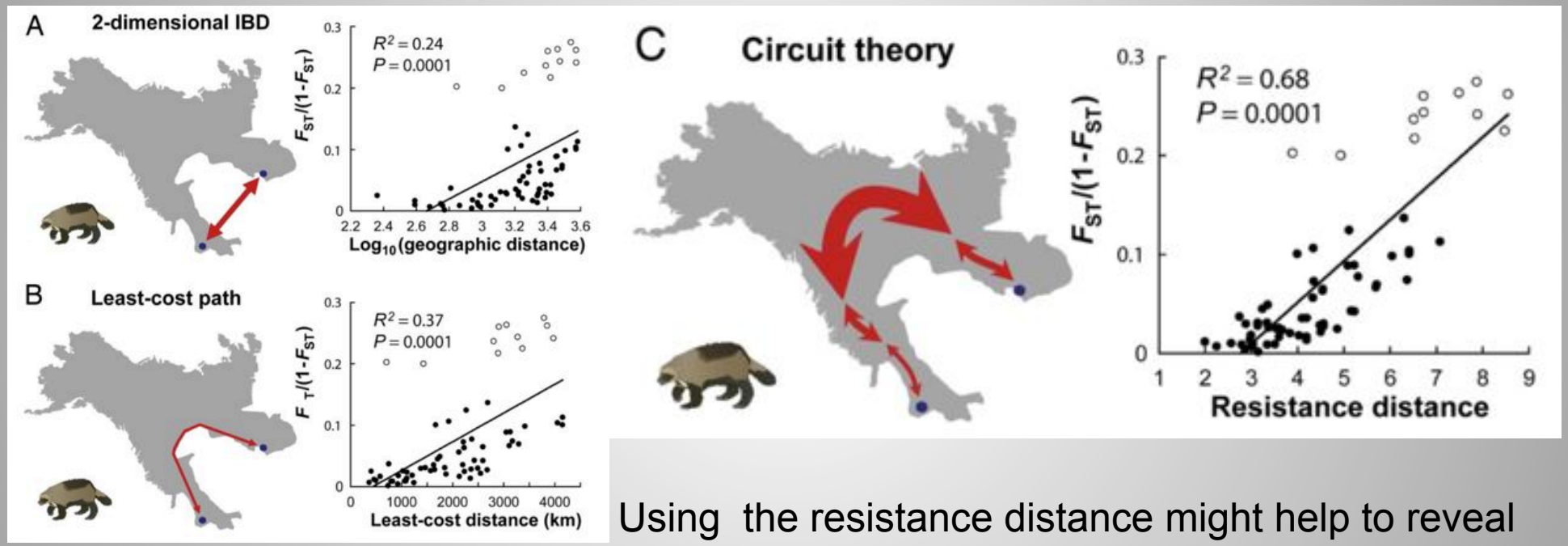
Not a single path but all potential paths across the whole landscape surface

This "distance" is defined as the effective resistance that would oppose a conductive material displaying a topology similar to that of the study area.

# Extensions to classic isolation by distance models

## 2 – euclidian distance vs resistance distance

**Isolation by resistance (McRae 2006 Evolution)**




Using the resistance distance might help to reveal patterns of IBD in heterogeneous landscapes that would not have appeared with the use of Euclidean or least cost distances

However, as for the least cost methods, it is not straightforward to assign a resistance value for each of the different landscape features

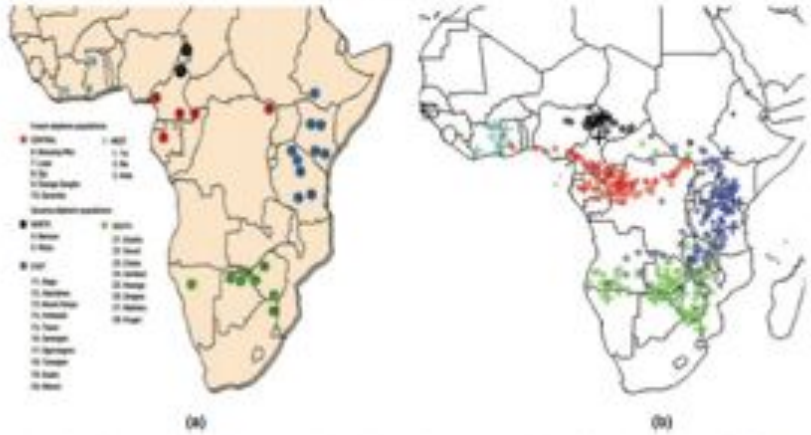
# Extensions to classic isolation by distance models

**Box 1: Using isolation-by-distance patterns to perform spatially continuous assignment**

Random genetic drift under IBD tends to produce smooth spatial variations of allele frequencies. Inferred maps of allele frequencies can be used to perform geographically explicit individual assignments. Wasser *et al.* (2004) and Wasser *et al.* (2007) developed a method that jointly estimates such maps and estimates the unknown geographic origin of a DNA sample by comparing its alleles with estimated allele frequencies. Rather than simply assigning individuals to predefined populations, the method can, in principle, assign individuals to any spatial location whose inferred allele frequencies best explains the genotype of the sample. Using this method, Wasser *et al.* (2007) showed that a large shipment of contraband ivory originated from a narrow region centred on Zambia. The accuracy of the assignment depends on the accuracy of the allele frequency map implicitly generated during the inference step, which in turn depends on the size of the training data set and on how much allele frequencies characterize a given region.

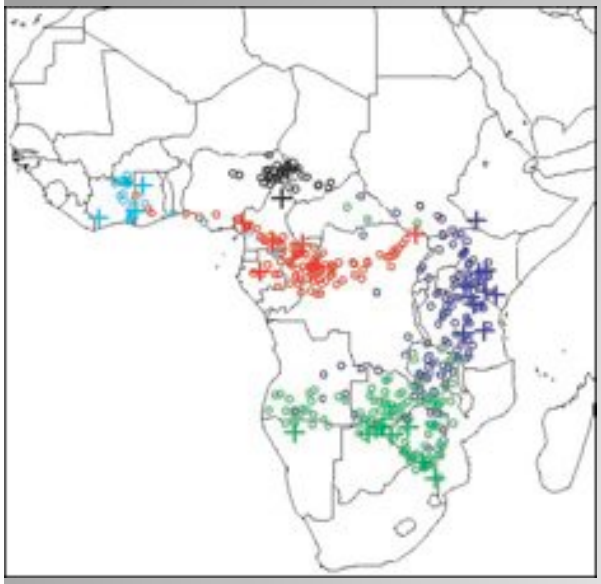
Pope *et al.* (2007) found that the individual spatial assignments generated by the method proposed by Wasser *et al.* (2004) could give ambiguous results (many possible locations). This might result from: (i) a lack of differentiation in the data; (ii) uncertainty about allele frequencies due in particular to the use of data with individuals continuously sampled over space; (iii) departure of data from the underlying statistical model; (iv) overparametrization compared with sample size; (v) MCMC convergence flaw. Pope *et al.* (2007) devised a simpler method based on the same rationale. They used their method to compare the movement of individual badgers before and after a culling operation performed in the context of bovine tuberculosis (*Mycobacterium bovis*) control. Even though they showed that the badgers moved, on average, further post- than pre-cull, it yet remains to be seen how accurate Pope *et al.*'s method is in the assignment of individuals to specific geographic localities.

In a study in human genetics, modelling allele frequencies as a linear function of spatial coordinates as the synoptic scale, Amos & Manica (2006) were capable of assigning individuals with an accuracy of 1200 miles. Novembre & Stephens (2008) proposed a method based on a PCA suitable for large SNPs data that predict spatial origin through a linear regression on the first two principal components.




(a) Map of Africa showing the collection sites divided into five regions: West Africa (cyan), Central forest (red), and Central (black), South (green) and East (blue) savanna. (b) Estimated locations of elephant tissue and faecal samples from across Africa when assignments are allowed to vary anywhere within the elephants' range. All tissue and scat samples ($n = 399$) were successfully amplified at seven or more loci. Sampling locations are indicated by a cross and are colour coded according to actual broad geographic region of origin: West Africa, Central forest, and Central, South and East savanna [colour coded as in (a)]. Assigned location of each individual sample is shown by a circle and is colour coded according to its actual region of origin. The closer each circle is to crosses of the same colour, the more accurate is that individual's assignment (figures and caption reprinted from Wasser *et al.* 2004).

# Extensions to classic isolation by distance models



## 3 –

Assignment results for 37 tusks from a large seizure in Singapore. Circles represent the estimated origin of the 37 tusks analyzed. Plus signs coincide with the those in the figure above. [from Wasser et al. 2007]