# "I have a dream"

## 1 Introduction

## 1.1 What are fitness landscapes and where do they come from?

#### 1.1.1 Definition

- Topographic metaphor
- Link between a phenotypic or a genetotypic landscape

### 1.1.2 Wright vs Fisher

- Wright : Genotype to fitness with multipics
- Fisher: Phenotype to fitness with a single pic
- 2 "shape" of landscape (Gravilets 2010) and a link between them

## 1.2 Fisher's idea of adaptation

### 1.2.1 Small mutations in a complex organism and adaptation towards an optimum

- Micro-mutationnism, gradual adaptation
- Single pic with balancing selection
- Pervasive epistasis

#### 1.2.2 The geometry of the model

- The function of fitness
- The complexity
- The distribution of fitness effects

## 1.3 A renewed interest for a simple but powerful tool

- Kimura, Lande, Orr, Waxman and Welch, Martin...
- Distribution of fitness effects
- Distribution of epistasis
- Speciation
- Species repartition
- Moving optimum (Gradual/abrupt environmental change)
- Dominance
- Sexe conflicts
- Senescence...

## 2 Basic version of the FGM

### 2.1 Detailed description of the landscape

### 2.1.1 Population genetic concepts and hypotheses and parameters

- Height of the pic and unicity of the optimum
- Complexity and pleiotropy
- Variance of selective/mutationnnal effects and isotropy

#### 2.1.2 The geometry of the model across environments and genotypes

- Fitness function
- Phenotypic and fitness distances

#### 2.2 Inference in the FGM

#### 2.2.1 The distribution of fitness effects

- DFE in the FGM
- Fitting DFE from mutation accumulation experiments or "designed mutations"
- Fitting DFE from fluctuation assays
- Fitting DFE from drift load

### 2.2.2 The distribution of epistasis

- Diminishing return epistasis and constant curvature
- Pairwise epistasis
- Empirical fitness landscape

#### **2.2.3** Autres

- Rate of adaptation
- A preciser

### 2.3 Mapping genotypes and environments to the landscape

#### 2.3.1 Example from the litterature

- Hietpas 2013
- Harmand 2017

#### 2.3.2 Version simplifiée du FGM

• Reprendre précédent document

### 2.4 Probability of fixation of a compensatory mutation

### 2.4.1 "Cost of resistance" and "compensation"

- The concept of cost of resistance (Lenormand et al. 2018)
- The definition of compensation here

#### 2.4.2 Probability of emergence of a mutation considering two envs

- Joint-DFE in two environments (Martin & Lenormand 2015)
- Angle between the environments' optima

## 2.4.3 Probability of fixation

- SSWM regime (Extension autour du "2s")
- WSSM regime (Compliqué ?)

## 3 Extended version of the FGM

## 3.1 Limits in the basic model and its "simplified" version

## 3.1.1 Complexity and pleiotropy

- Origin of the differences observed in the dimension of the phenotypic landscape between DFE fitting
- Lmitation of universal pleiotropy

#### 3.1.2 Parallel evolution and anisotropy

- Definition of parallel evolution and examples
- Different sort of anisotropy and link with pleiotropy
- Example of Harmand 2017

## 3.2 Extensions for a single environment

### 3.2.1 Anisotropy

- Modelling (Chevin et al. 2010)
- Inferring (Chevin et al. 2010)

#### 3.2.2 Retsricted pleiotropy

- Modelling (Chevin et al. 2010, Lourenço 2011)
- Inferring (Chevin et al. 2010, Voir autres refs)

## 3.3 Dealing with multiple environments

#### 3.3.1 Which parameters stay constant across environments?

- Inferring n
- Inferring rmax in each environments

### 3.3.2 Anisotropy between environments

- Module and directionnality
- Problem for the mapping for the computation of the phenotypic distances

## 4 Conclusion

### 4.1 Summary of the main results available depending on the data

• Table with datas and inference possible

### 4.2 Extrapolation from the results

#### 4.2.1 Prediction of risk of resistance of a mutation in new environment

#### 4.2.2 Prediction of the risk of evolving a compensatory mutations