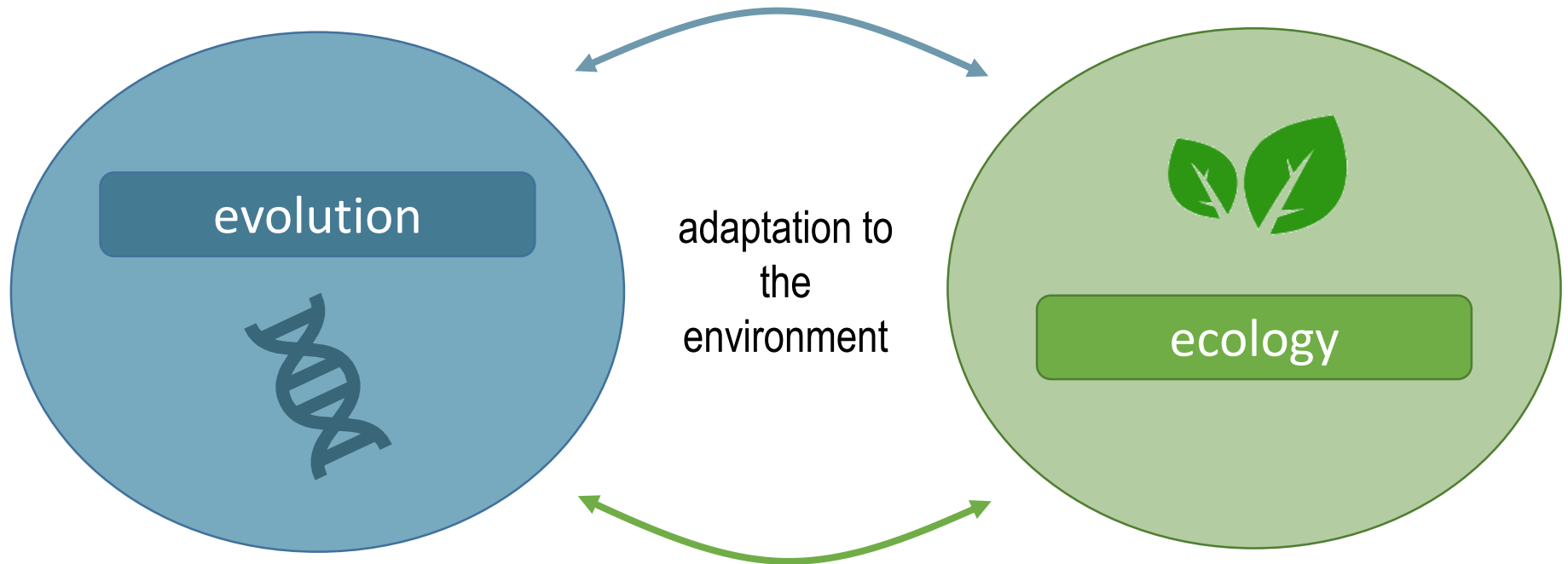




# A practical perspective on HOW to use GEA to study adaptation to the environment

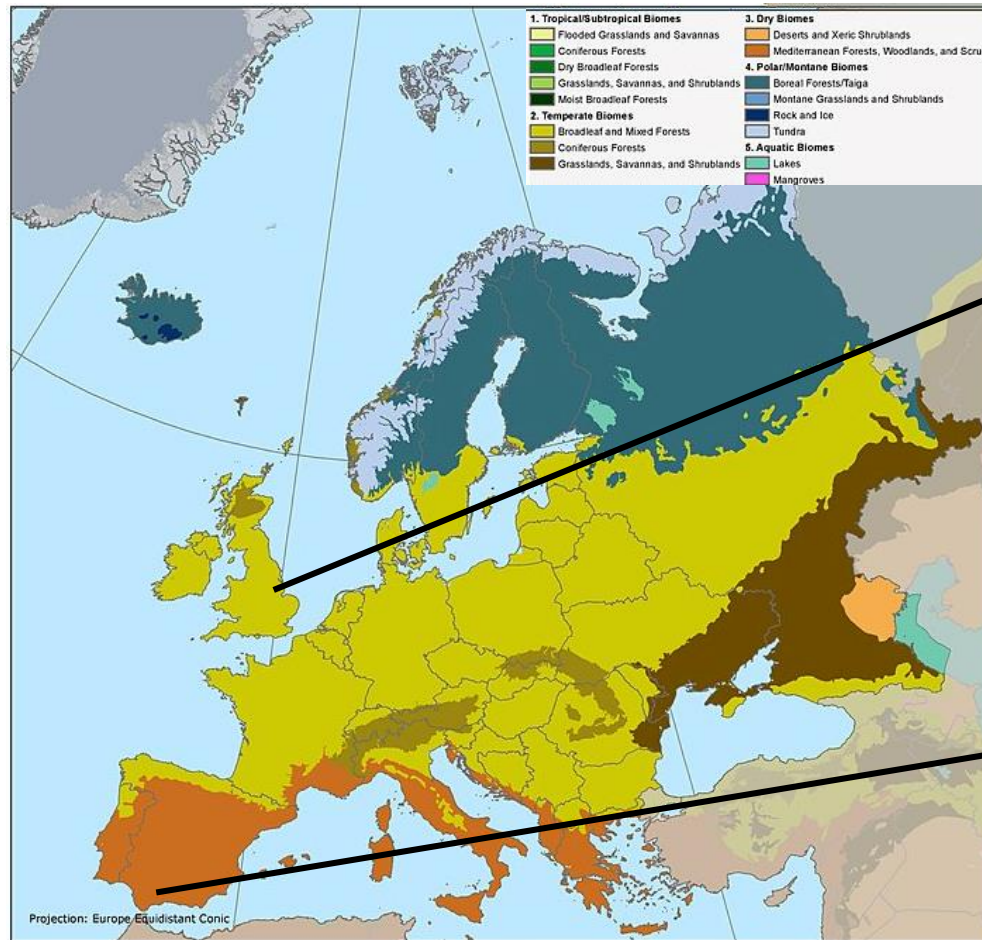
# “Ecology sets the context for evolution while genetic variation sets the opportunity”

Joan Roughgarden





# Opportunity ~ context: across bioms



*Quercus ilex*



Center for International Earth  
Science Information Network  
CIESIN | COLUMBIA UNIVERSITY

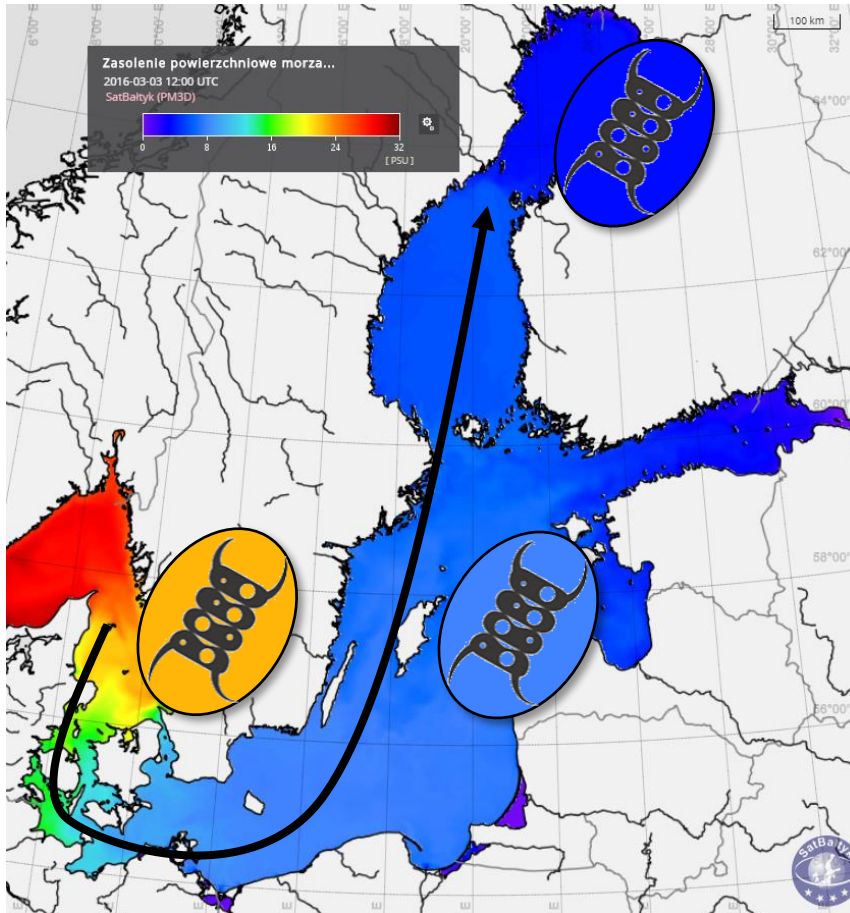


© 2012. The Trustees of Columbia University in the City of New York. Center for International Earth Science Information Network (CIESIN)/Columbia University. 2012. National Aggregates of Geospatial Data Collection: Population, Landscape, and Climate Estimates, Version 3 (PLACE III). Palisades, NY: NASA Socioeconomic Data and Applications Center (SEDAC). <http://sedac.ciesin.columbia.edu/data/set/hagdo-population-landscape-climate-estimates-v3>.

Publication Date:  
March 2012



# Opportunity ~ context: along env gradient



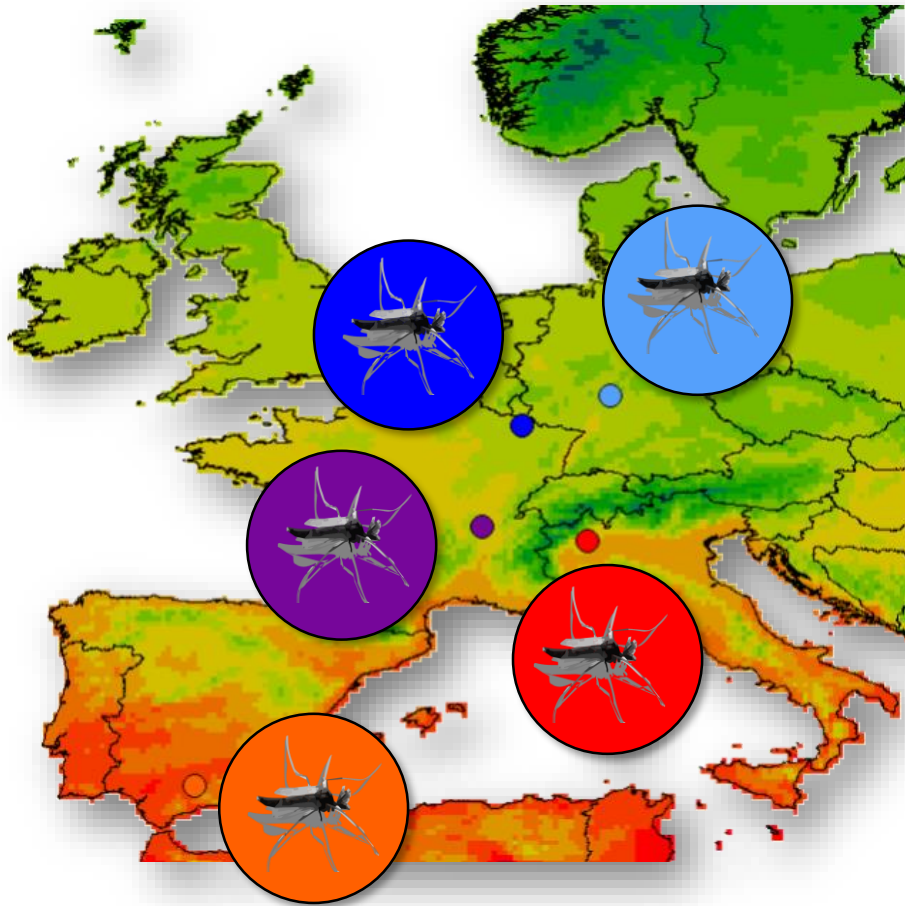
Distribution and adaptation of diatoms along salinity gradient in the North and Baltic Seas.

*Kowalewski 1997, Oceanol. Stud.*  
*Sjöqvist et al. 2015, Mol Ecol*





# Opportunity ~ context: along clim gradient

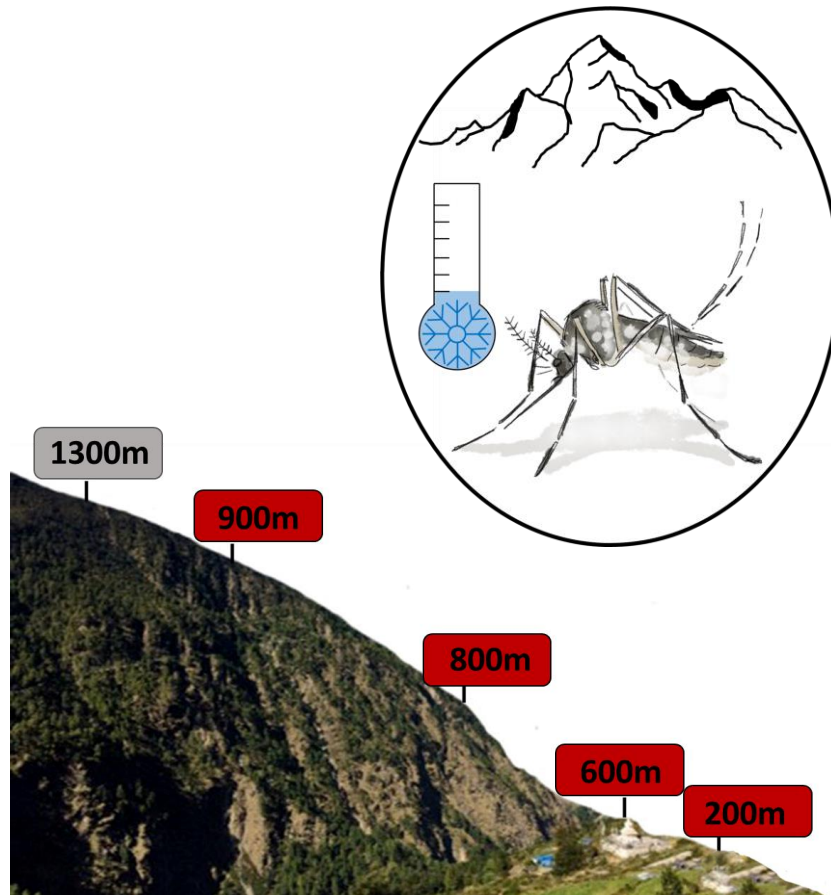


Distribution and adaptation of non-biting midges along climate gradient.

*Waldvogel et al. 2018, Mol Ecol*



# Opportunity ~ context: along alt. gradient



Invasion of Yellow fever mosquito *Aedes aegypti* towards higher altitudes in the Himalayan mountains of Nepal.

Kramer et al. (under review)  
Phuyal, Kramer et al. (in prep)

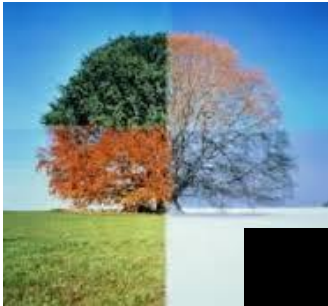


# Plasticity versus adaptation

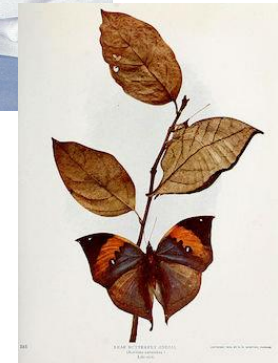
phenotypic  
plasticity

?

genetic  
adaptation

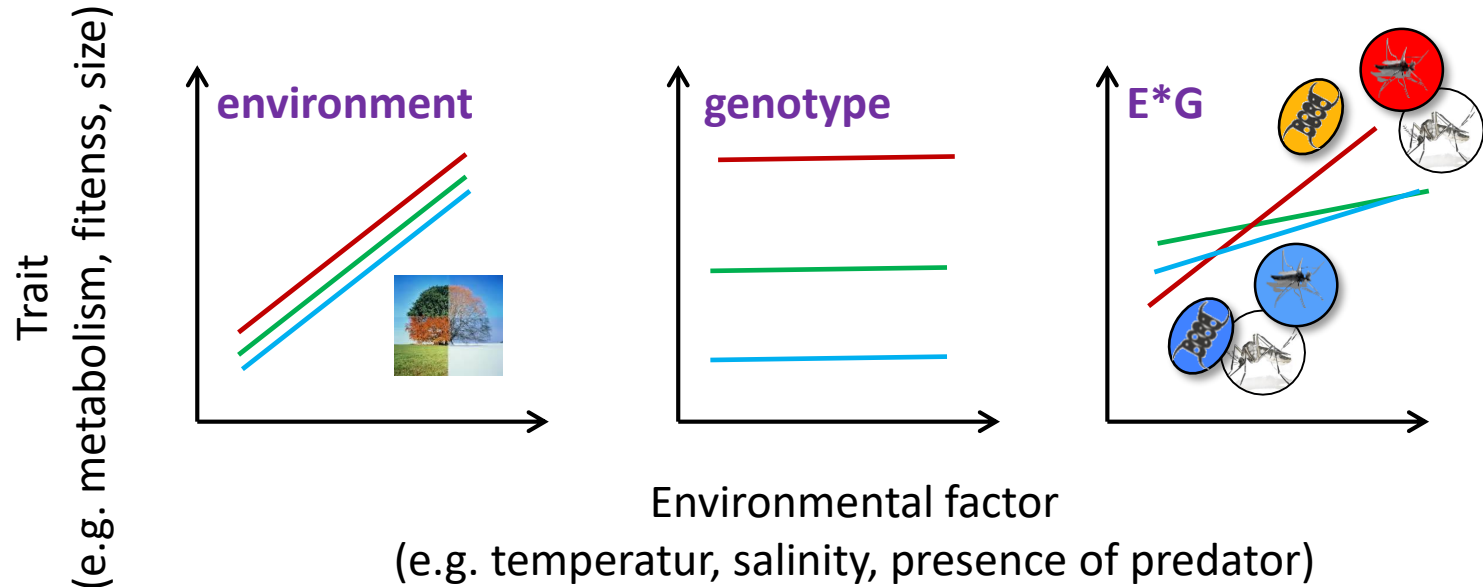


?





# Ecological reaction norms



complex  
traits

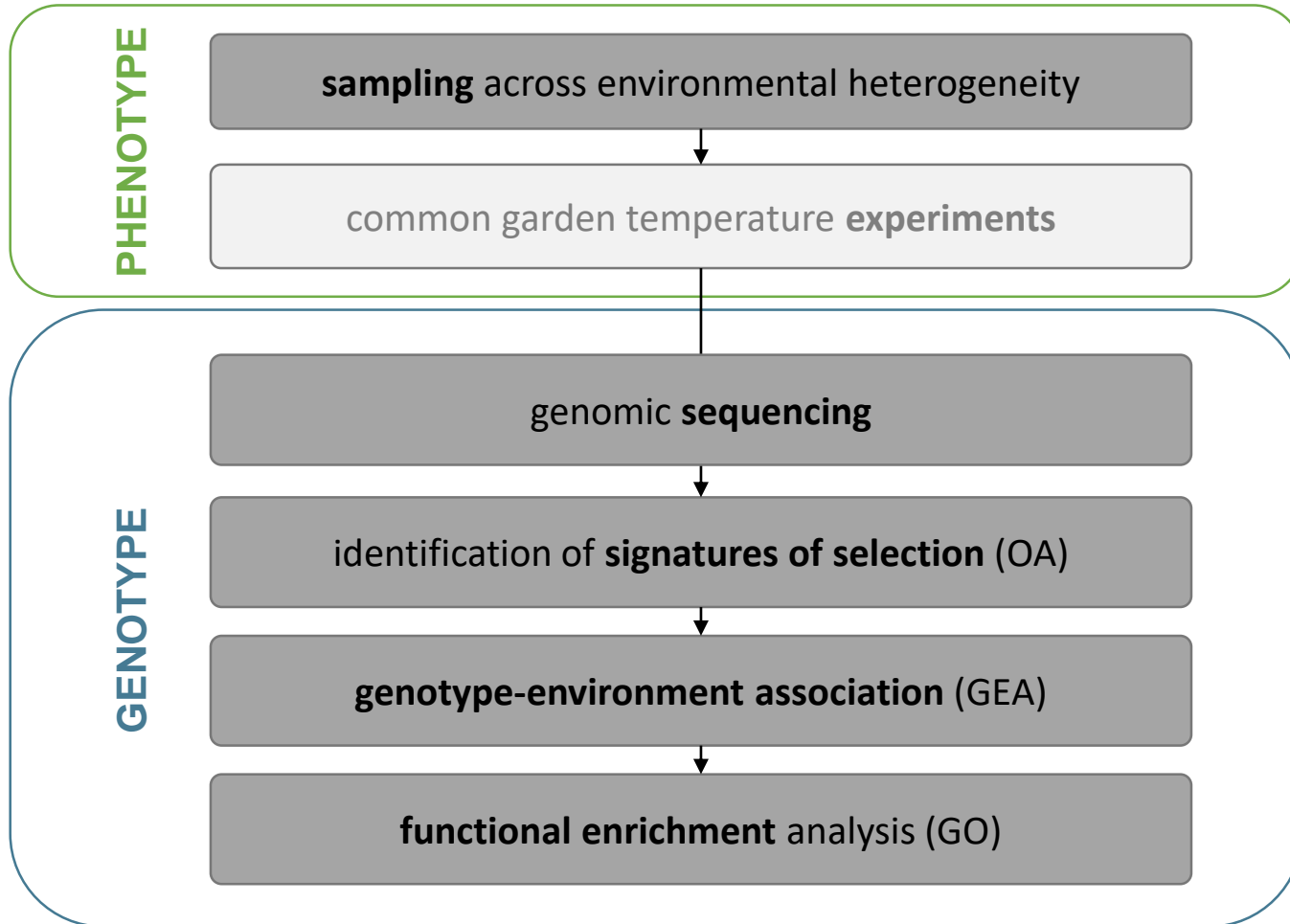
impossible  
cultivation

long  
generation time



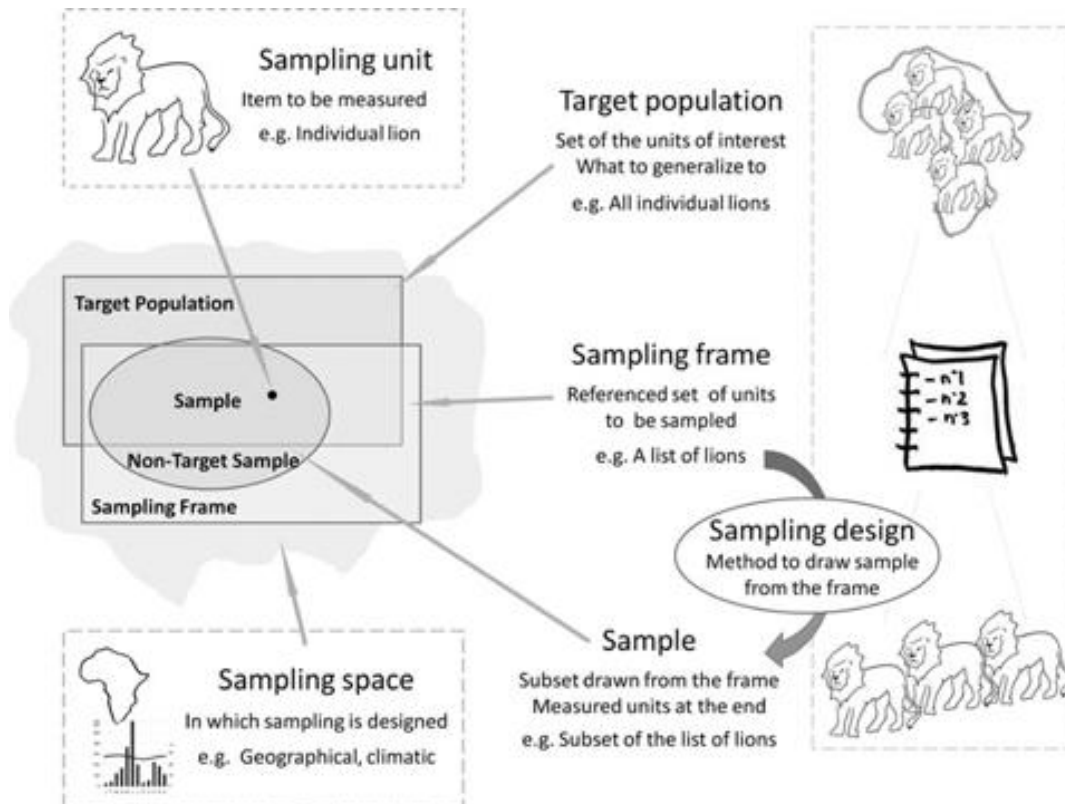


# From phenotype to genotype with natural populations of any species

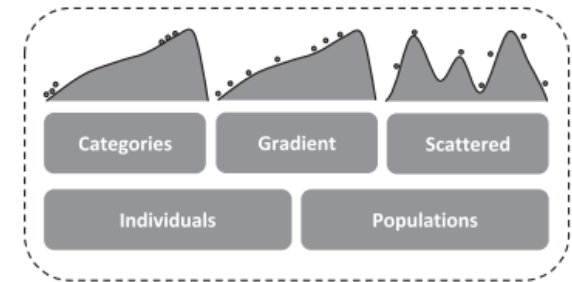




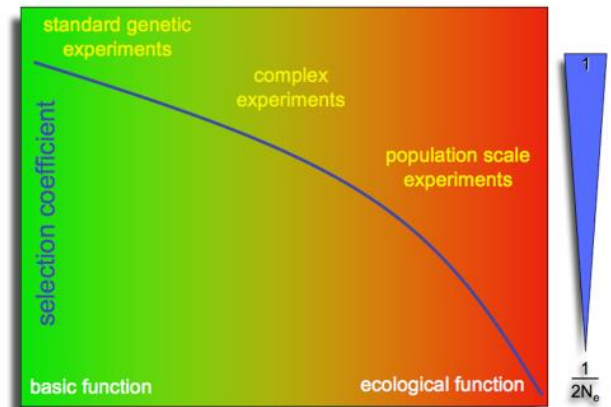
# Sampling



Manel et al. 2012



Reilstab et al. 2015, Mol Ecol

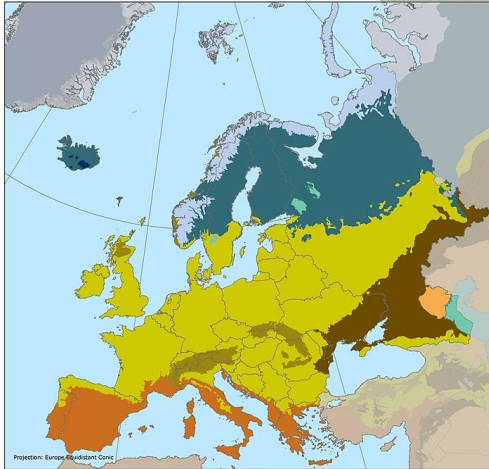


[Weigel&Tautz](#)

Inclusion of ecological and evolutionary context requires comprehensive population-scale sampling across ranges, categories, or gradients.



# Sampling along env gradients



## The GEA hypothesis

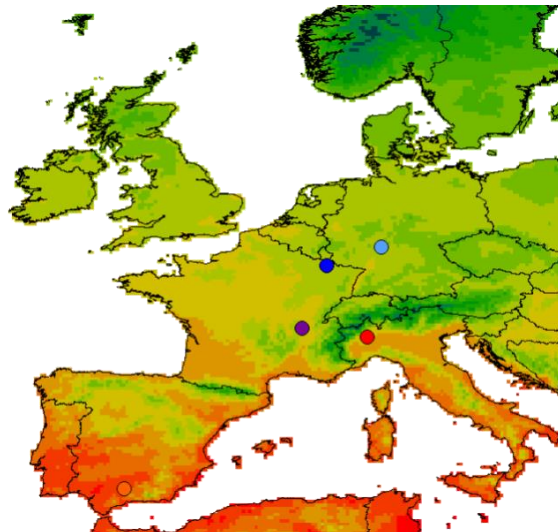
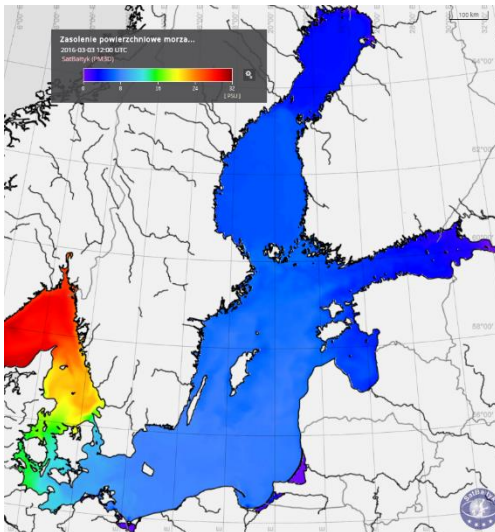
adaptation to the  
environment



local env conditions



population occurrence as  
trait proxies



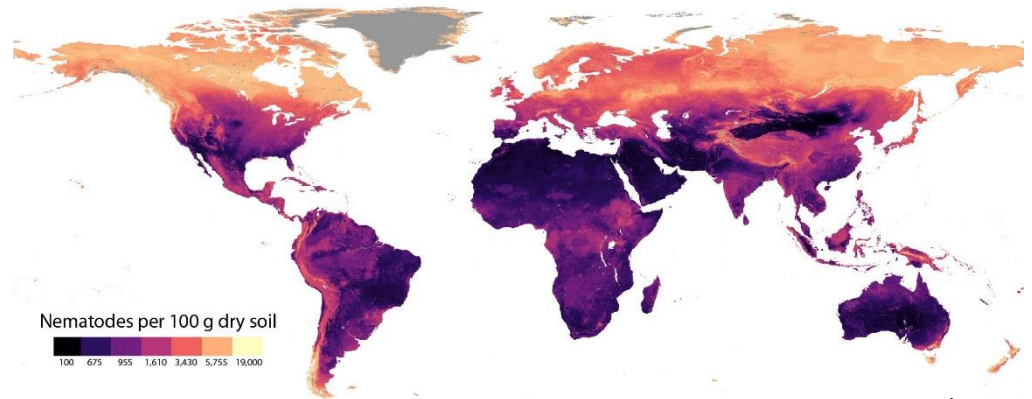


# Sampling and appropriate sequencing

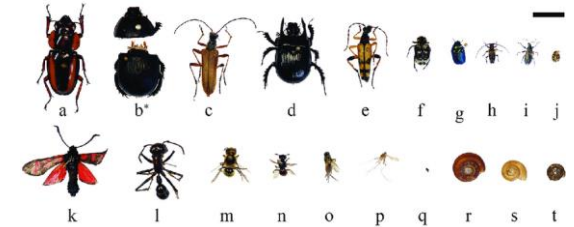
geographic distribution

abundance  
accessability  
body size

genome size

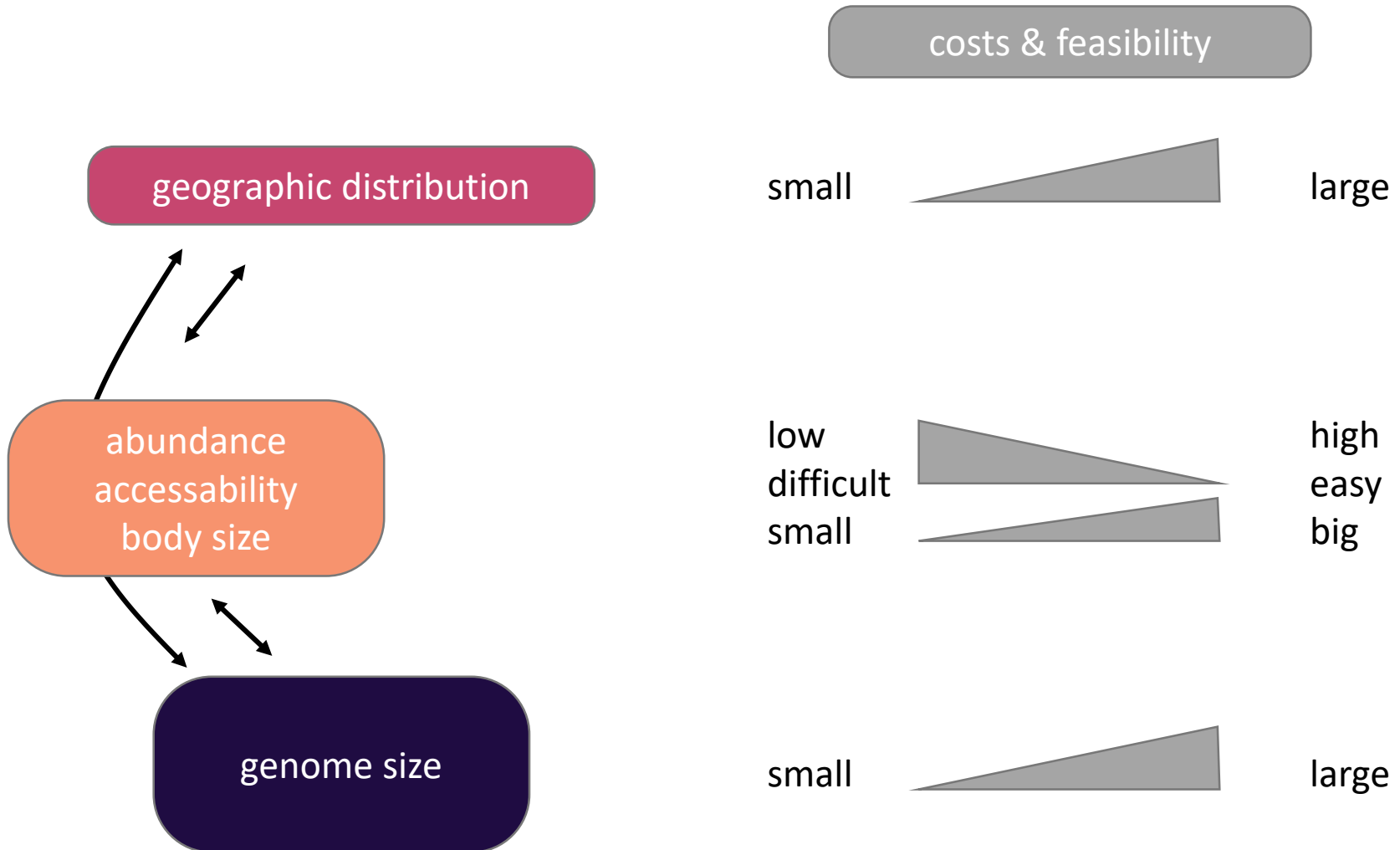


Hoogen et al. 2019





# Sampling and appropriate sequencing







# Strategies for genome sequencing

## Whole genome sequencing:

Indiv-Seq

### Guideline for standard pre-processing of genome data

Ann-Marie Waldvogel, University of Cologne

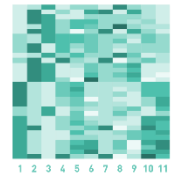
19/09/2022

→ pooled individuals of the same population

metagenomics



```
aacgtccaaaggagt
gttacctacggctaa
aacgtccaaaggagt
ttcagacatacgact
cacgtcgaatgagt
attacgtacggglaa
tacgtgcttacgagt
tacgtgcttacgagt
atcgaaggctagctat
atcgaaggctagctat
```



→ entire samples with individuals of many species



# Strategies for genome sequencing

## Whole genome sequencing:

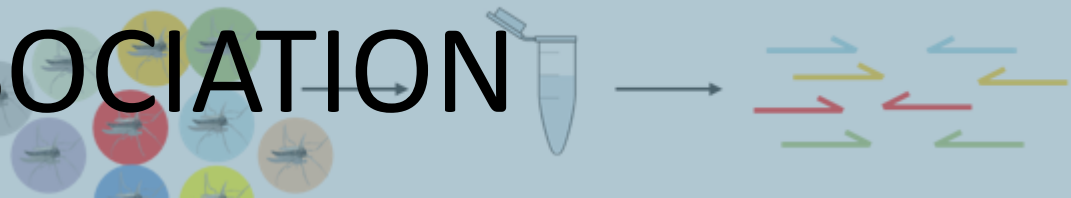
Indiv-Seq



→ single individual

# GENOTYPE-ENVIRONMENT ASSOCIATION

Pool-Seq

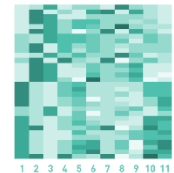


→ pooled individuals of the same population

metagenomics



aacgtccaaaggagt  
gttacctacggctaa  
aacgtccaaaggagt  
ttcagcatatcgact  
cacgtcgaatgagt  
attacgtacggglaa  
tacgtgcttacgagt  
tacgtgcttacgagt  
atcgaaggctagctat  
atcgaaggctagctat



→ entire samples with individuals of many species





# Environmental data



*Climatologies at high resolution for the earth's land surface areas*

<https://chelsa-climate.org/>

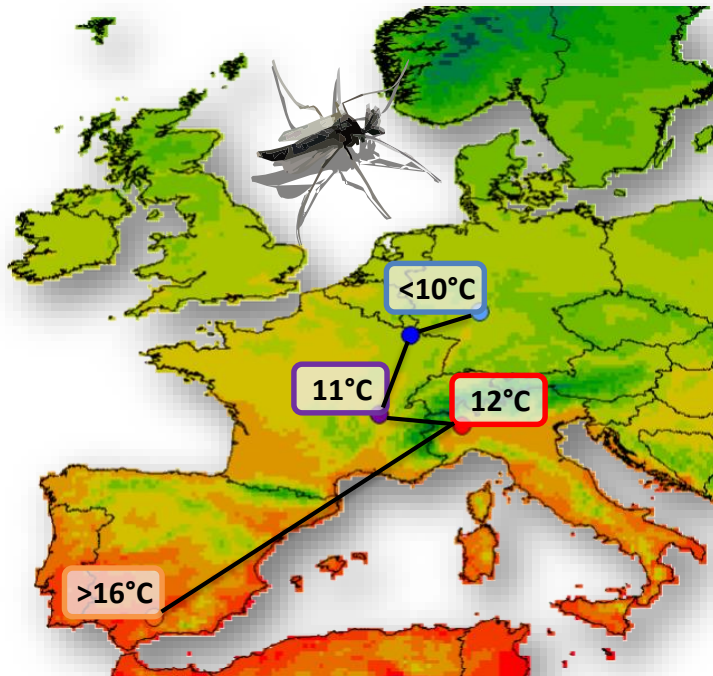
Logging of microhabitat conditions...  
Remote sensing...



*Theoria cum praxis...*

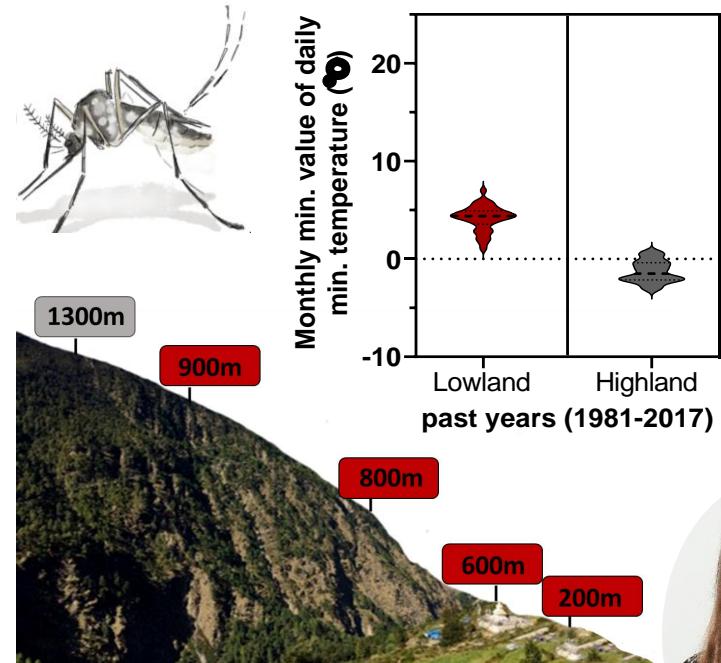


# Studying temperature as a selection factor along environmental gradients



across climate zones

Waldvogel et al. 2018, Mol Ecol



along altitudinal clines

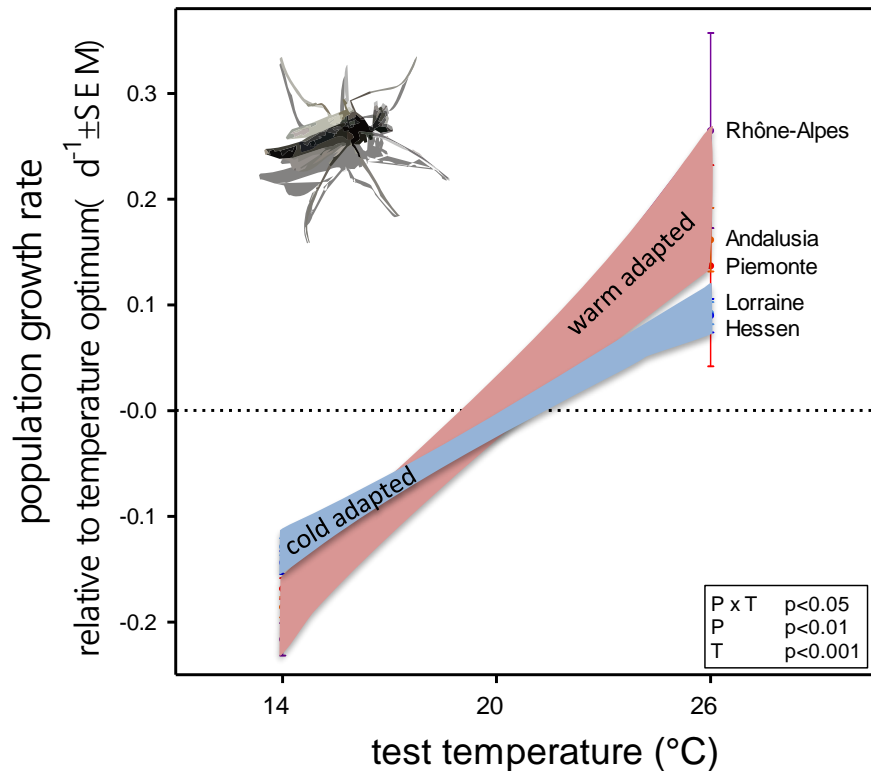
Phuyal, Kramer et al. (in prep)



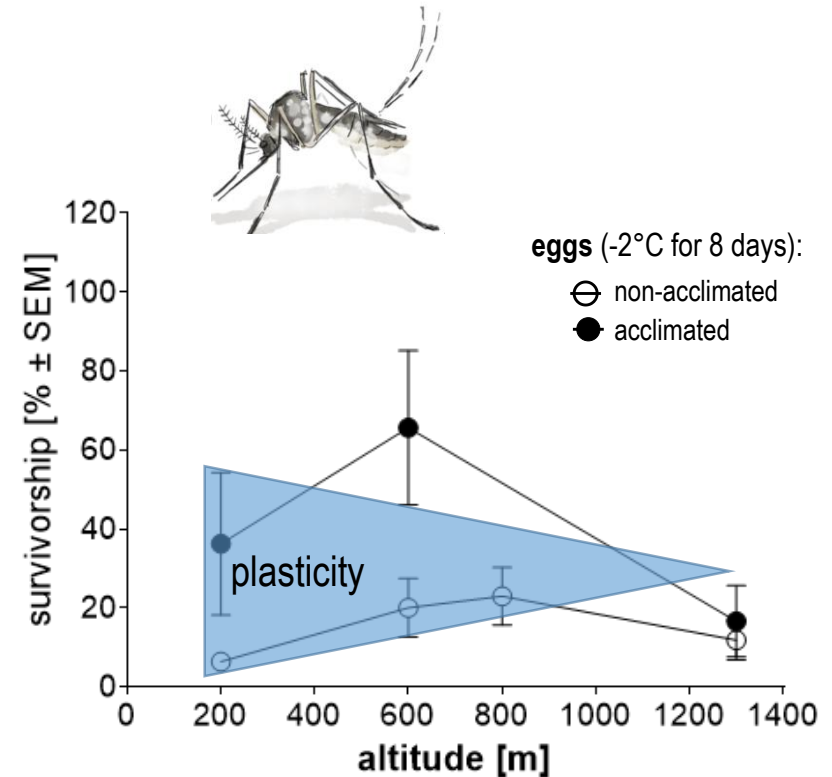




# Phenotypic evidence as prerequisite to study the genomic basis of adaptation



Waldvogel et al. 2018, Mol Ecol



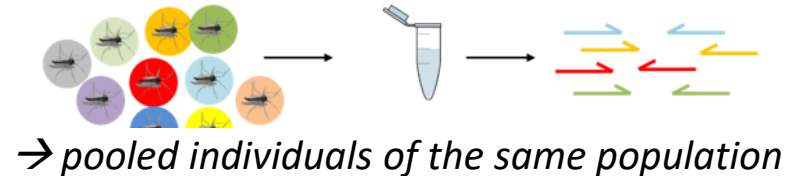
Kramer et al. 2021, STOTEN

Heritable phenotypic adaptation to local temperature regime reflects the gradient (climate zone / altitude).



# WGS of natural populations as pooled sampled

Pool-Seq



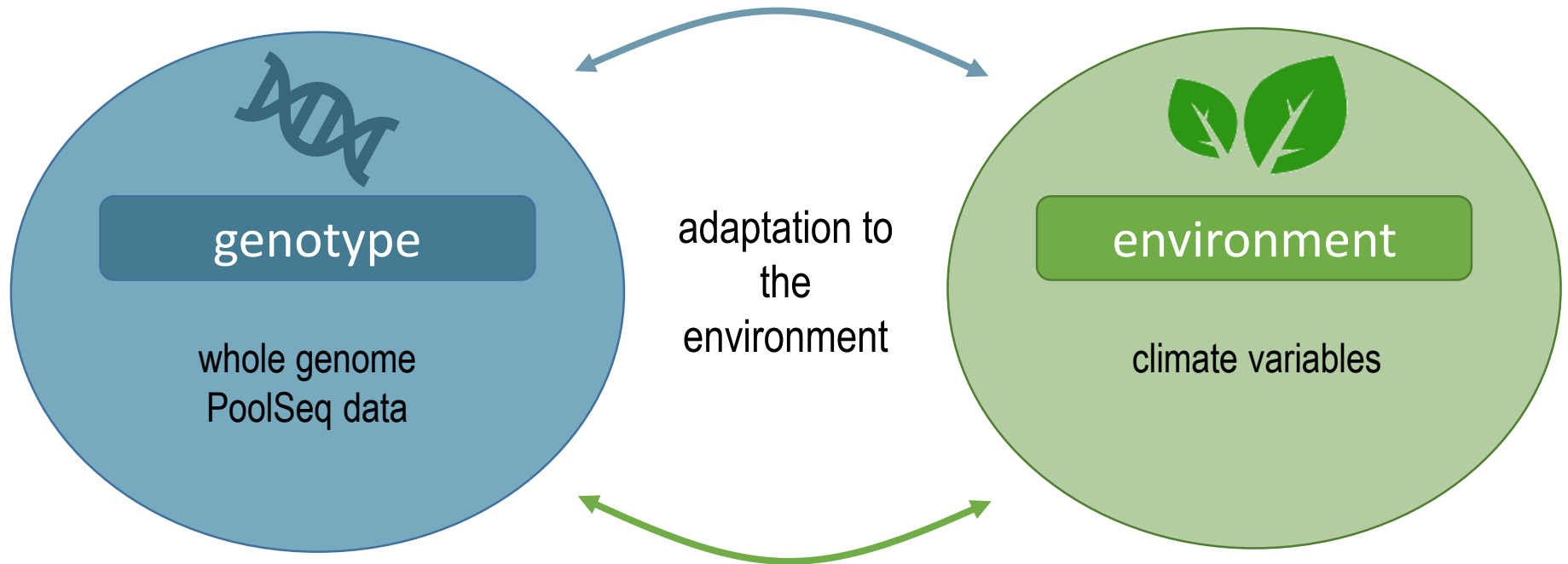
5 natural populations  
à ~100 individuals  
(=200 chromosomes)



5 natural populations  
à ~100 individuals  
(=200 chromosomes)

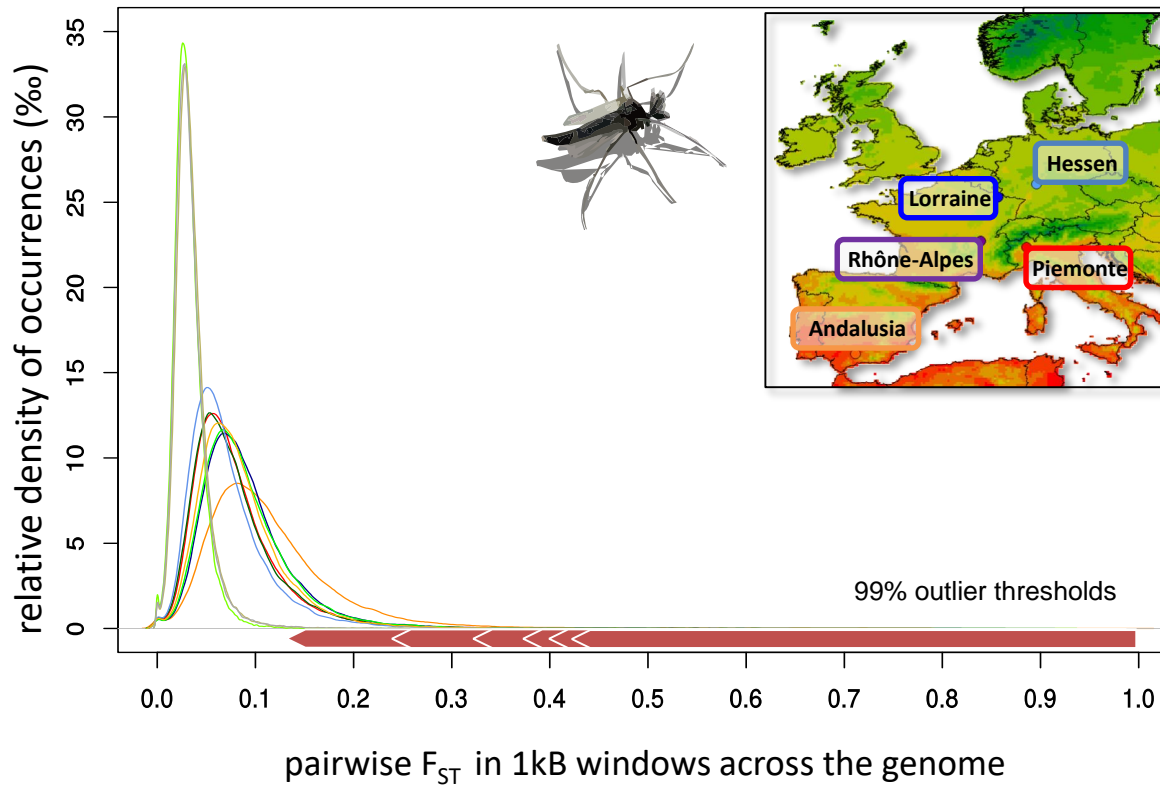


# Integrating approaches





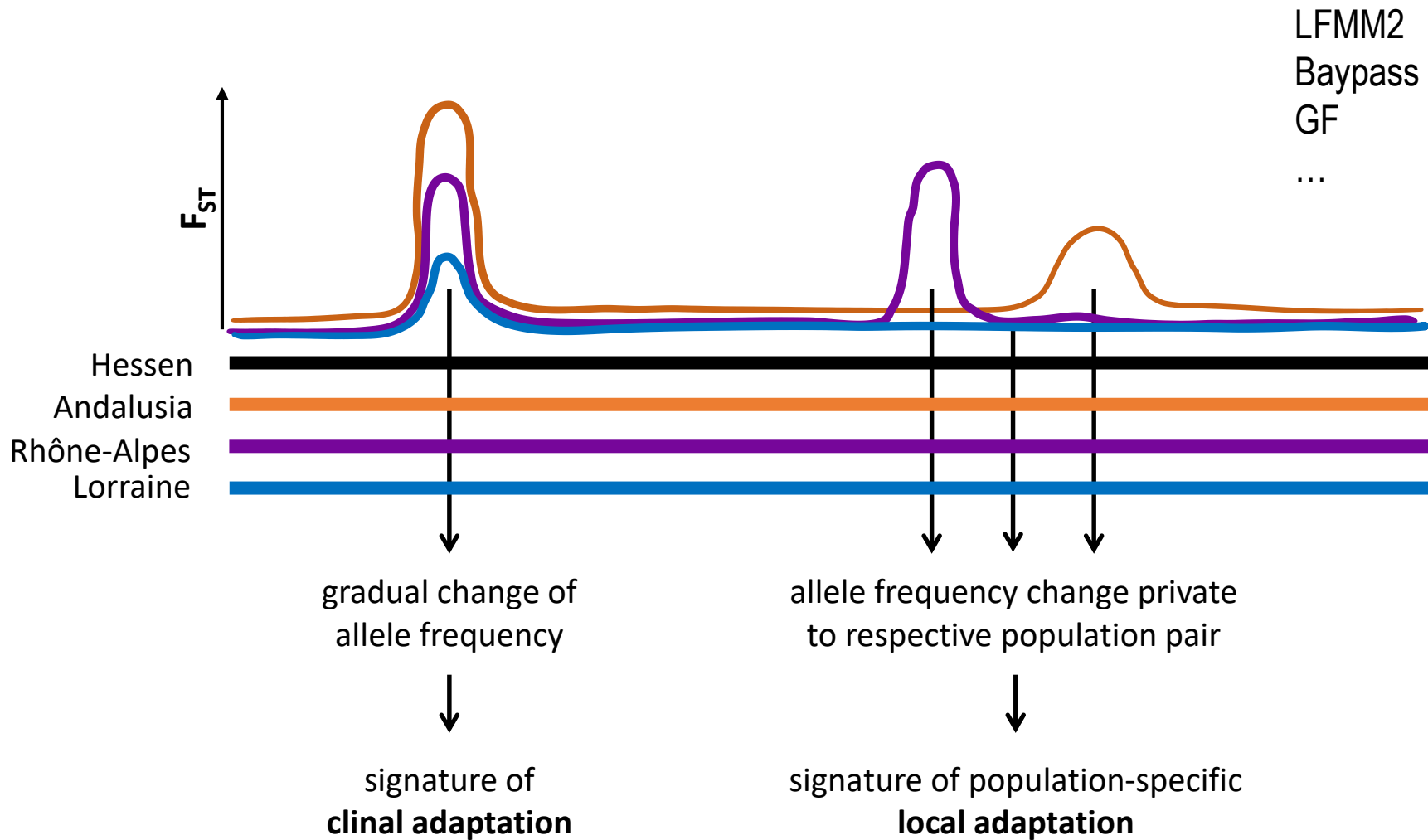
# Genome-wide population differentiation and signatures of selection



Simple but stringent: outlier approach



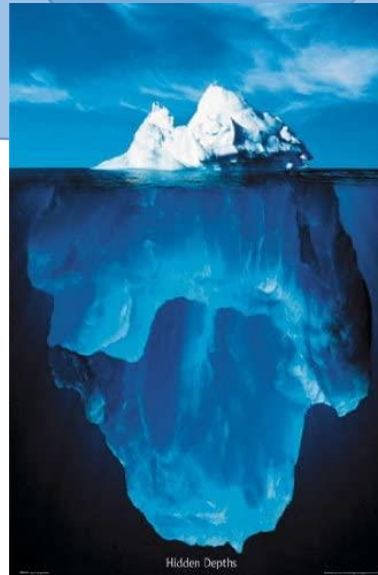
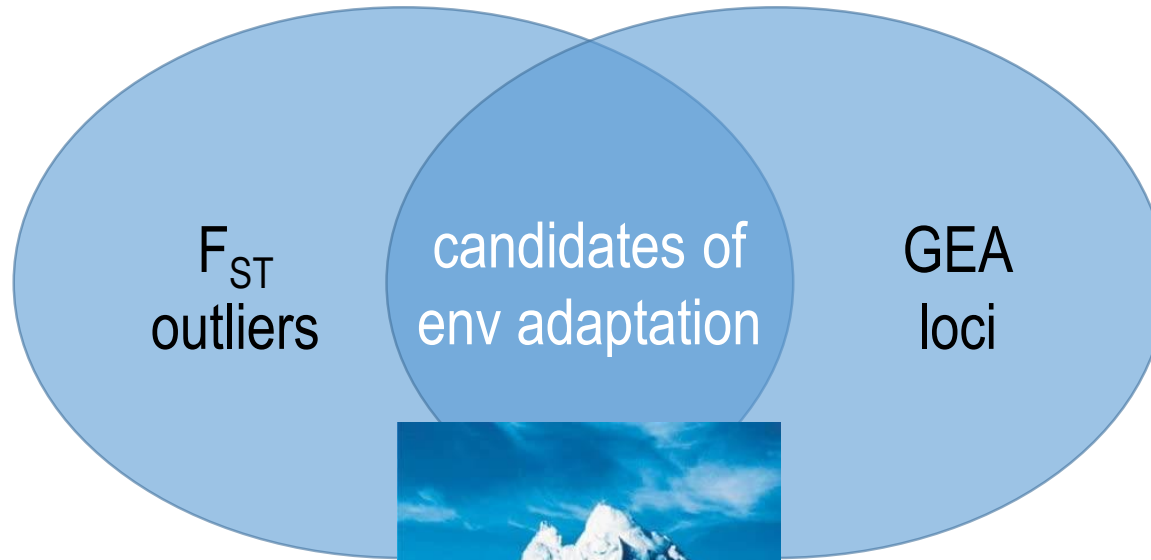
# Genotype-environment association







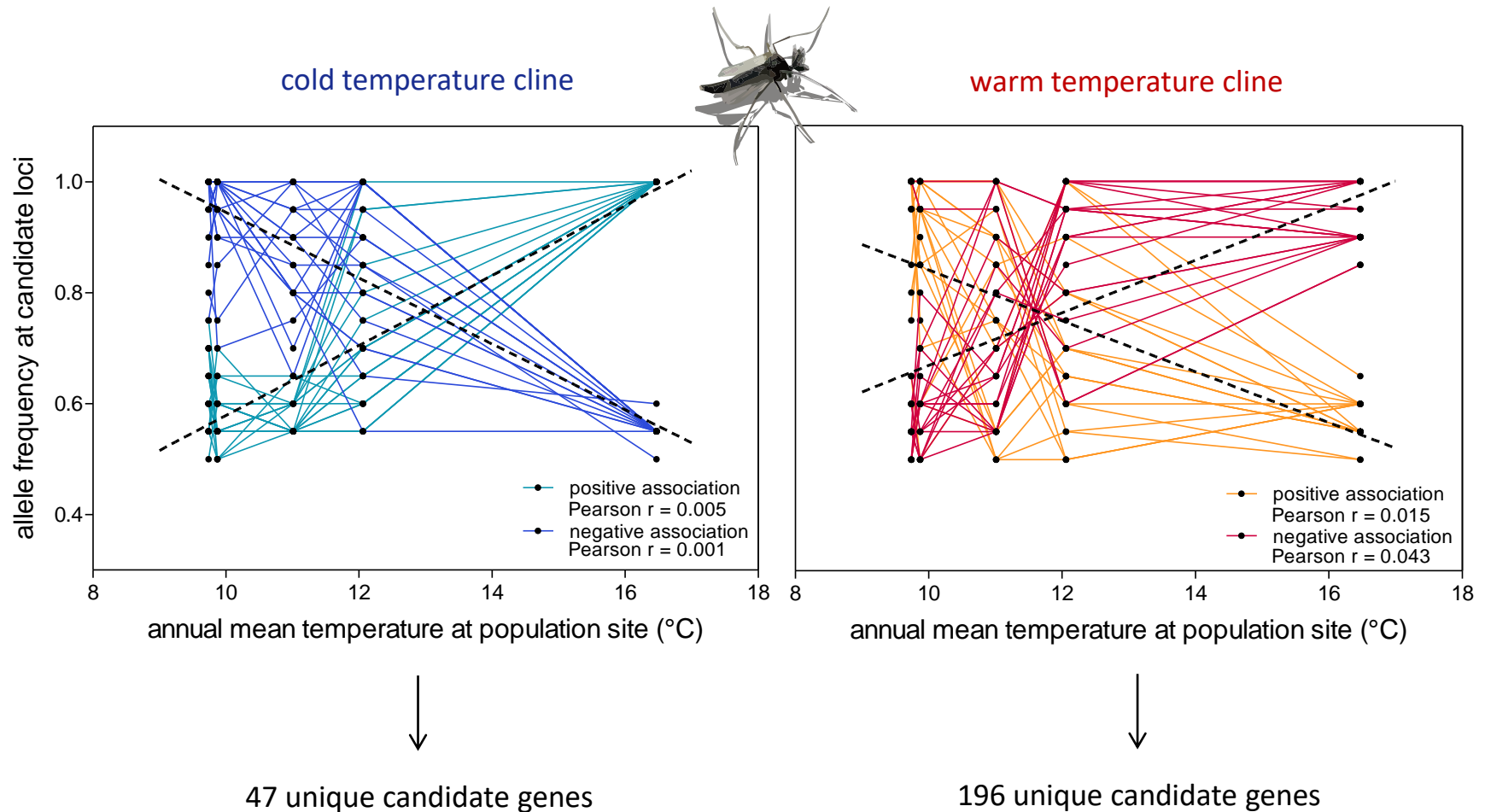
# Integrating approaches



→ time-series data??

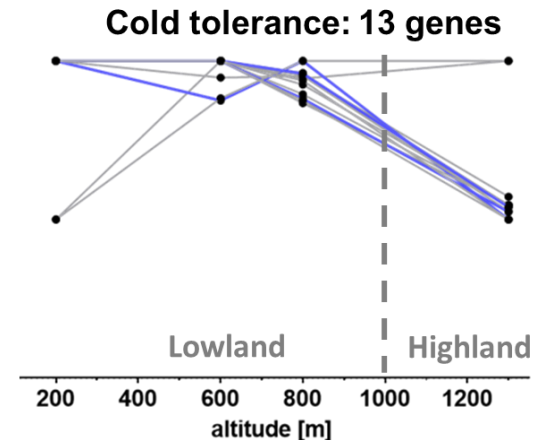
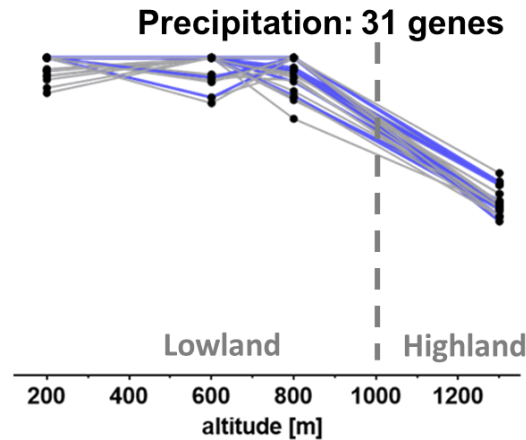
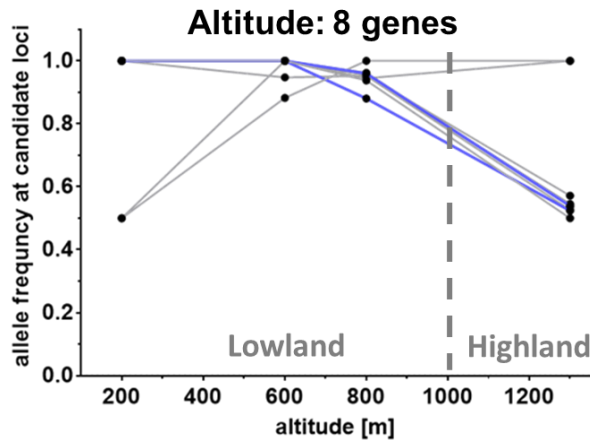


# Gradual AFC across climate zones





# Non-gradual AFC along altitudinal gradient



Kramer et al. (under review)

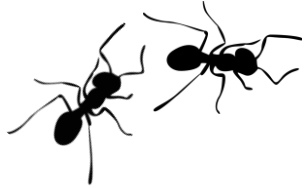


Isolation-by-environment  
versus population/invasion  
history?!

→ Meet Isabelle at her poster for details!



# Flexibility of GEAs: you define the environment

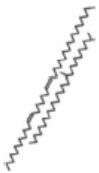


Genotype association  
to **climate factors** and  
to **cuticular hydrocarbon profiles**

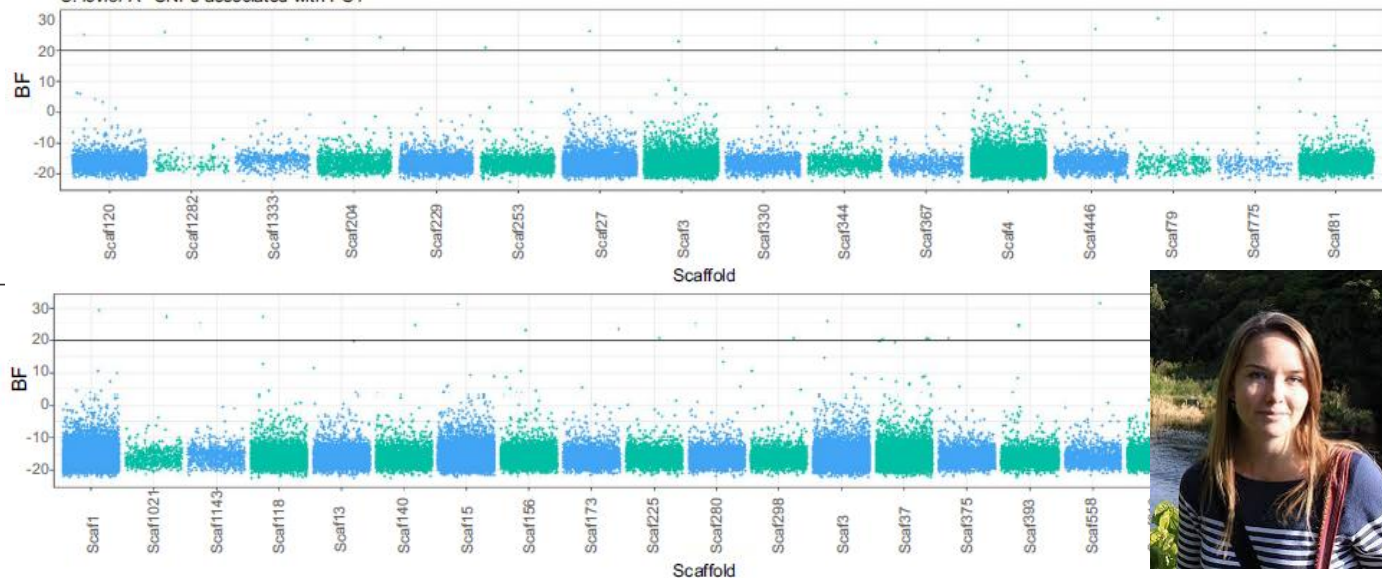
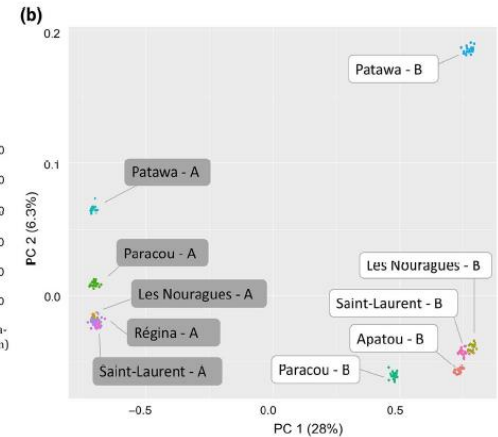
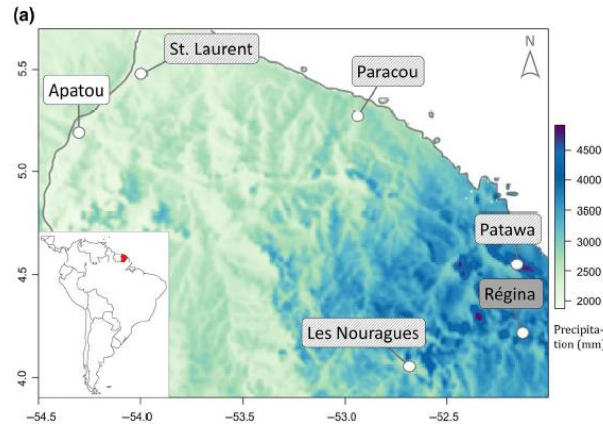
Analysis



Environmental association



Chemical association





# How to proceed with candidates loci/genes of environmental adaptation?

space-for-time  
approaches / genomic  
offset predictions

structural and  
functional annotation /  
enrichment analysis

**GO!!!**





# Functional annotation and its relevance

| GO term                                 | Interesting gene hits  | Biological plausibility   |
|---|--|---|
| Signatures of local adaptation          |  |   |
| Ion transport (associated with Golgi)   | Link transporter 1 (Q60738), metal transporter CNIM2 (Q9HBM5), Golgi-fucose transporter 1 (Q9VNF4)   | Golgi vesicles play important detoxification processes, esp transformation and exocytosis shown for a wide range of insect species (Sinkin & Taylor, 1998)  |
| Protein phosphorylation                 | Protein phosphatase 1 (Q9VNF4), PDPR (Q8NC01)  | During cellular detoxification several intermediate steps in phosphorylation or dephosphorylation of proteins (Quistad, Zhang, Sp 2000), though this broad bio currently cannot be interpreted mechanistically  |
| Methylation                             | Trimethylguanine synthase (Q96RS0), TRMT61A (Q96FX7)   | Evidence suggests that insect in insects might be regulates mechanisms involving DNA (Oppold et al., 2015) and chromatin modifications (Hu et al., 2011 Reports 7:41255). Genetic interacting with the epigenome might be a response to insect local scale  |
| ATP-dependent chromatin remodelling     | Iswi (Q24368)  |   |
| Toll signalling pathway                 | TOLLIP (Q9H0E2)  | In <i>Drosophila</i> , Toll receptors a embryonic development and (Valanne, Wang, & Ramet, 2009)  |
| Ecdysone-receptor signalling            | Ecr (P49882)   | Ecdysone receptor signalling is coordination of development metamorphosis. Adult lifespan to unfavourable environment influenced by ecdysone sign & Carney, 2012)   |
| Signatures of clinal climate adaptation |  |   |
| Apoptotic process                       | Serine/threonine-protein kinase hippo (Q8T0S6); human cell division cycle & apoptosis regulator protein 1 CCAR1 (Q8IX12); E3 ubiquitin-protein ligase HUWE1 (Q7TMY8) | Considering the physiological impact of temperature in particular, the necessity to adapt the programmed cell death under stress conditions seems reasonable for ectotherms in general  |
| Response to heat                        | Transient receptor potential channel pyrexia (Q9W0T5)  | Involves any process to change state and activity of molecular processes. The herewith associated gene "transient receptor potential channel pyrexia" is responsive to high temperatures and involved in protection and tolerance from high temperature stress in <i>D. melanogaster</i> (Lee et al., 2005). With the general temperature dependence of |

**Table 4.** Details on gene function of the nine characterized candidate genes associated to environmental variables. ENV1 ~ altitude. ENV2 ~ precipitation, ENV4 = cold tolerance. Three other uncharacterized genes are not included in this list

| ENV1 | ENV2 | ENV4 | Gene description                           | Isoform | Function   | Overall functional description | Species analyzed                        | Reference                  |
|------|------|------|--|---------|--|--------------------------------|---|----------------------------|
|      |      |      |  |         | 1. insecticide resistance - regulating resistance-related gene expression  | Insecticide resistance         | <i>Culex quinquefasciatus</i>           | (T. Li & Liu, 2019)        |
|      |      |      |  |         | 2. insecticide resistance - regulating resistance-related gene expression  |                                | <i>Drosophila melanogaster</i>          |                            |
|      |      |      |  |         | 3. highly expressed in the brain of mosquito signaling transcription and regulation genes at the different life stages of mosquito |                                | <i>C. quinquefasciatus</i>              | (T. Li & Liu, 2017)        |
|      |      |      | adenylate cyclase type 9                   | X1, X2  | 4. ROS is mainly related to the ATP binding pathway  | Lifecyle: development          | <i>Somia cynthia vicini</i> (butterfly) | (S. Z. Zhang et al., 2018) |
|      |      |      |  |         | 5. ROS were up-regulated - response of haemolymph to 1-decaypirimycin  |                                |   |                            |
|      |      |      |  |         | 6. suggested development   |                                | <i>Drosophila</i>                       | (Acquaviva et al., 2009)   |
|      |      |      | proto-oncogene tyrosine-protein kinase ROS | X1-X4   | 7. larval development and metamorphosis formation of sense organs (including the   |                                |   |                            |
|      |      |      |  |         | 8. larval development and metamorphosis formation of sense organs (including the   |                                |   |                            |
|      |      |      |  |         | 9. larval development and metamorphosis formation of sense organs (including the   |                                |   |                            |

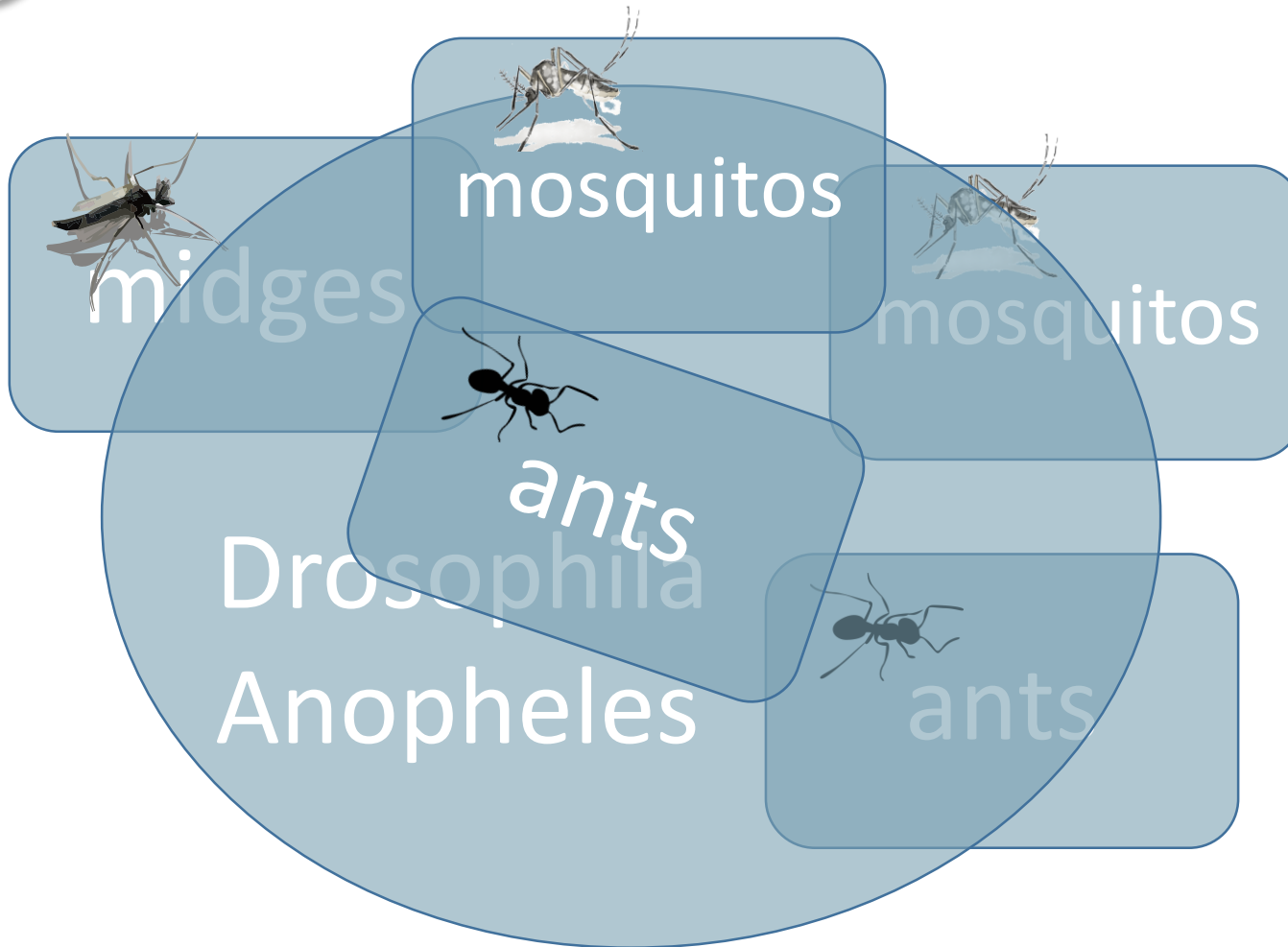
**TABLE 3** GO terms that were significantly enriched in the environmental association analysis in *C. levior A* and *C. levior B*

| <i>C. levior A</i> |   |
|--------------------|---|
| PC1                | DNMT initiation<br>histone H3-K27 demethylation   |
| PC3                | ammonium transport and transport<br>phosphatidylinositol-mediated signaling<br>vesicle docking involved in exocytosis<br>phosphatidylinositol phosphorylation |
| <i>C. levior B</i> |   |
| PC1                | chitin metabolic process  |
| PC2                | homophilic cell adhesion via plasma membrane adhesion molecules<br>response to metal ion<br>transmembrane receptor protein tyrosine kinase signaling pathway  |
| PC3                | ATP hydrolysis coupled proton transport   |





# Taxonomic validation approach





# Towards comparative studies

## Climate Change Genomics Calls for Standardized Data Reporting

Ann-Marie Waldvogel<sup>1,2</sup>, Dennis Schreiber<sup>1,3</sup>, Markus Pfenninger<sup>1,3,4\*</sup> and Barbara Feldmeyer<sup>1</sup>

**TABLE 1** | Suggested standards for deposition of GEA input and results data.

| Step in GEA pipeline  | Data type  | Data format                             | Deposition platform   |
|-----------------------|--|---|---|
| Tool implementation   | Matrix of environmental input (sample ID,  | Processable text-table format (not pdf) | Dryad; gfbio; supplement; <i>intended integration</i>   |
| Tool                  |  |   | (EMBL-EBI)  |
| Tool                  |  |   | ect   |
| Tool                  |  |   | ect   |
| Tool                  |  |   | ENA   |
| Tool                  |  |   | tion<br>(EBI)   |
| Stru                  |  |   | tion<br>(EBI)   |
| Functional annotation | Full set of protein sequences corresponding to the structural annotation of the reference genome | Fasta format                            | Integration in NCBI BioProject or ENA Project (EMBL-EBI)  |
| Validation            | Experimentally or phylogenetically validated gene with association to an environmental factor    |   | <i>Intended integration in GO database referring to novel GO domain "environmental association"</i> |

Join us to proceed the idea of this meta-analysis aiming for the GO category „environmental association“

Waldvogel et al. 2020, Front Ecol Evol



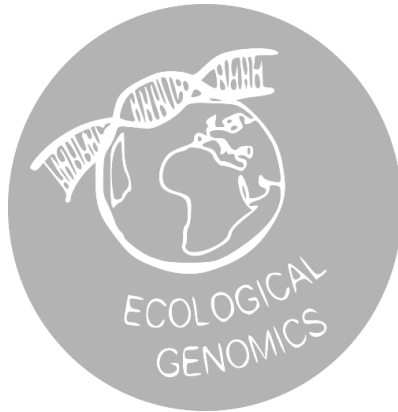



# Open challenges



Community level:  
metagenome ~ environment association

Integrating estimators of adaptive capacity:  
time-series data, rates of phenotypic trait change,  
rates of AFC

# Acknowledgements



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@UniCologne

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 @AmWaldvogel



Senckenberg BIK-F  
Markus Pfenninger with the  
Molecular Ecology Group



Institute of Tropical Medicine  
Ruth Müller



Isabelle Kramer



SENCKENBERG  
world of biodiversity

