Applications to modelling and landscape genomics

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  → Highly complex modeling approaches, hardly testable, and whose predictions therefore remain highly uncertain.

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- Predicting the **adaptive potential** of the populations, i.e. the potential for an evolutionary change in the next few generations.

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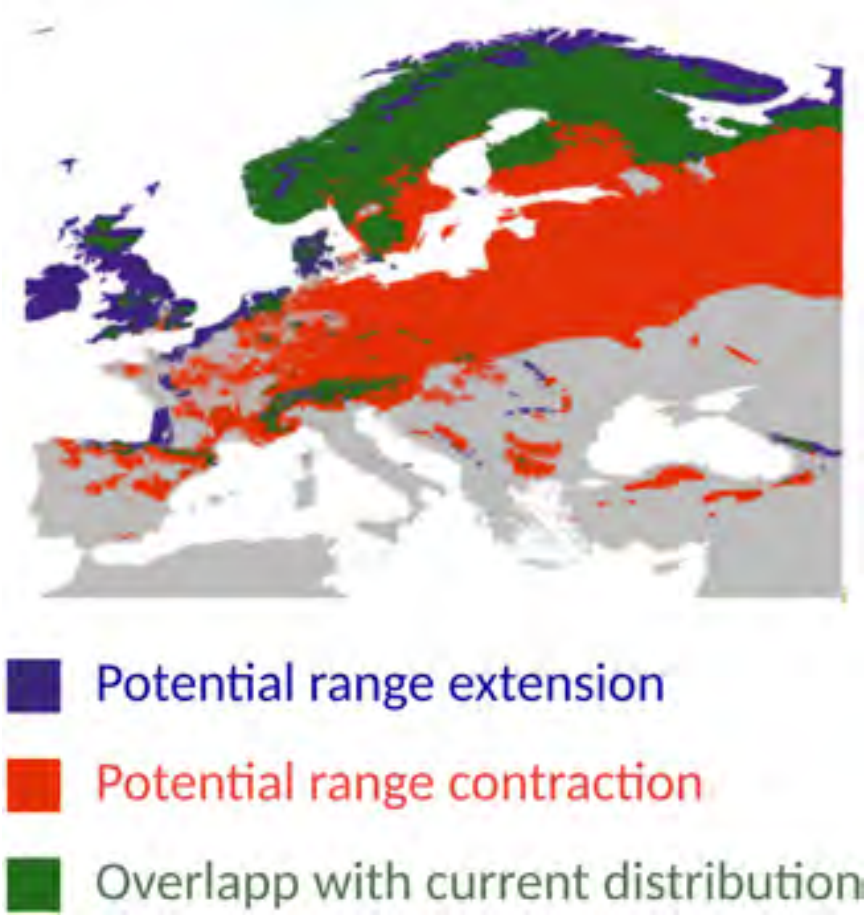
Species distribution models (SDMs)

Based on occurrence data.

Assume **uniformity of climate responses** below the species level.



Predicted future distribution of Scots pine under the (pessimistic) scenario RCP8.5.

Dyderski *et al.* 2017

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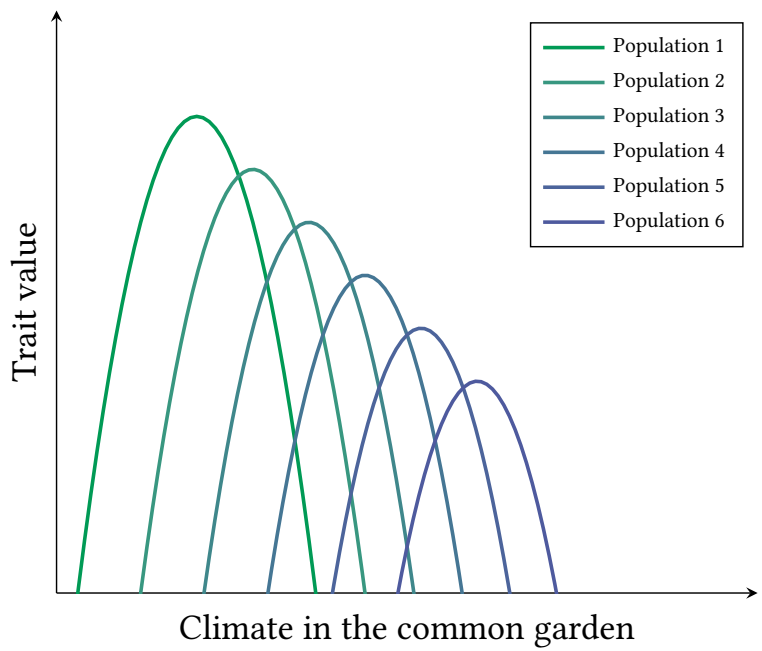

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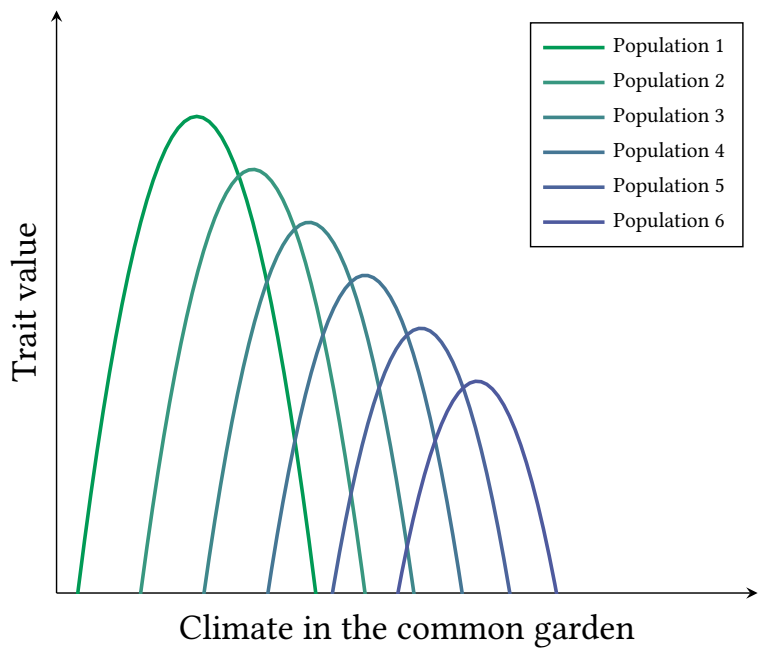

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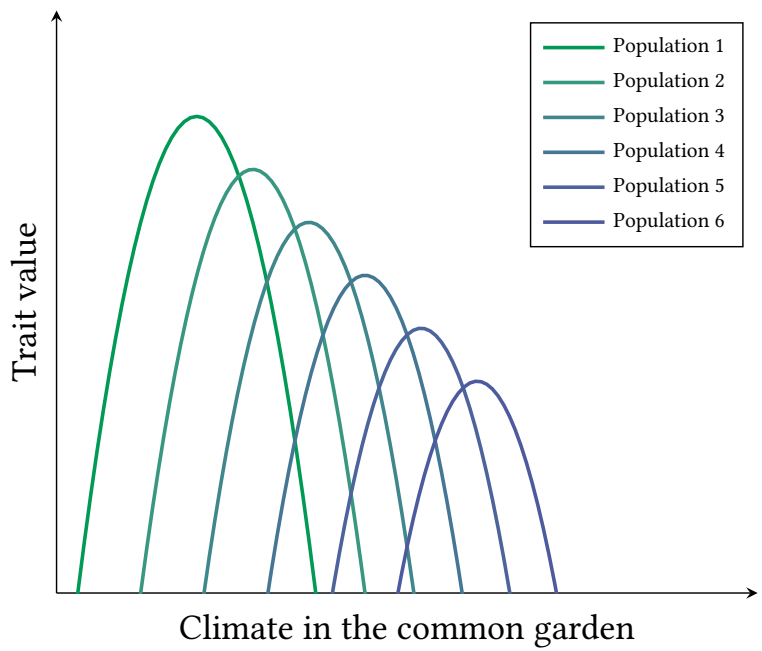

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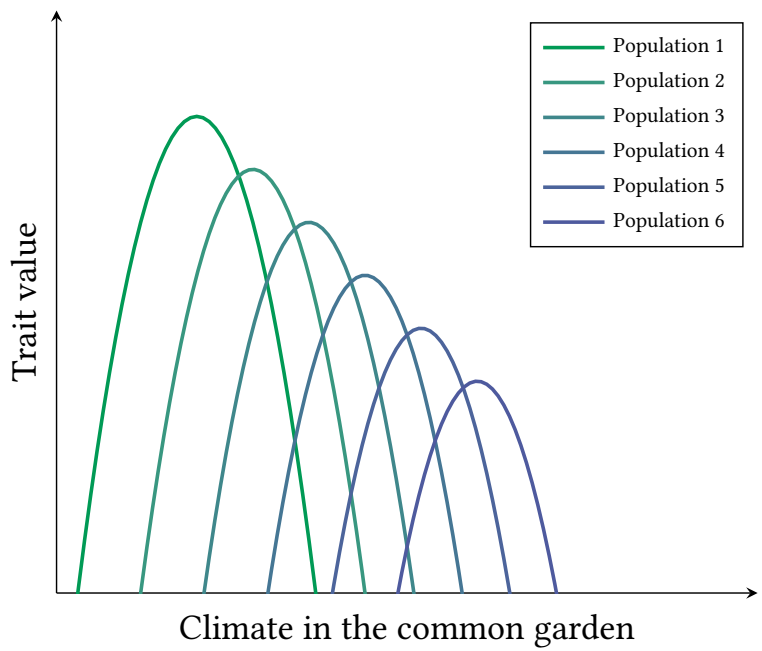

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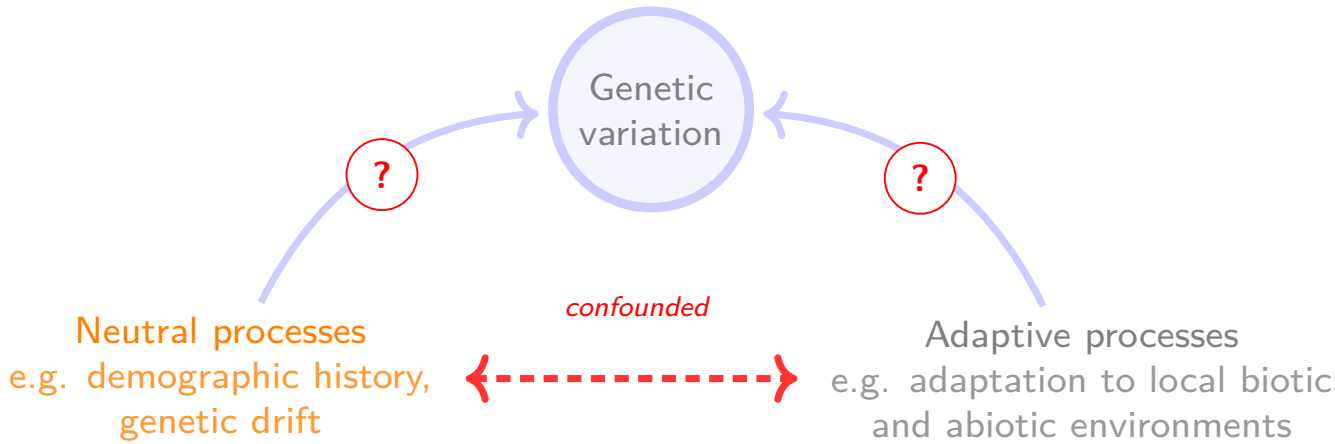

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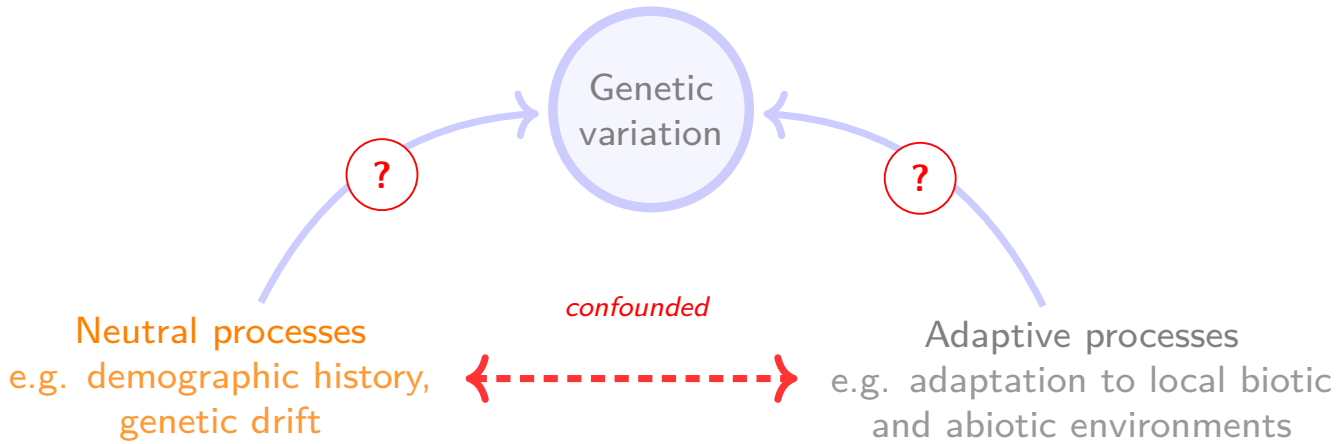

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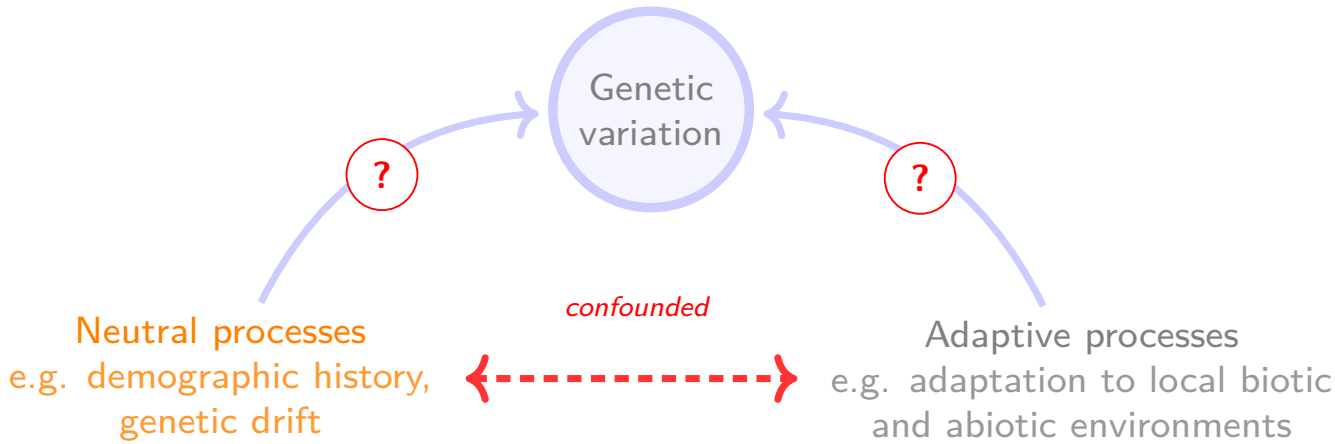

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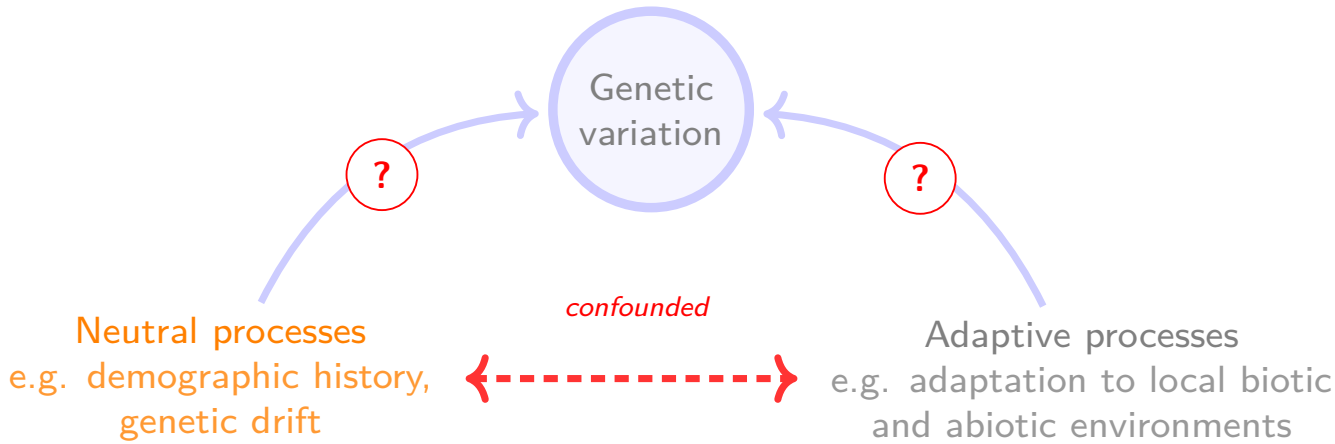

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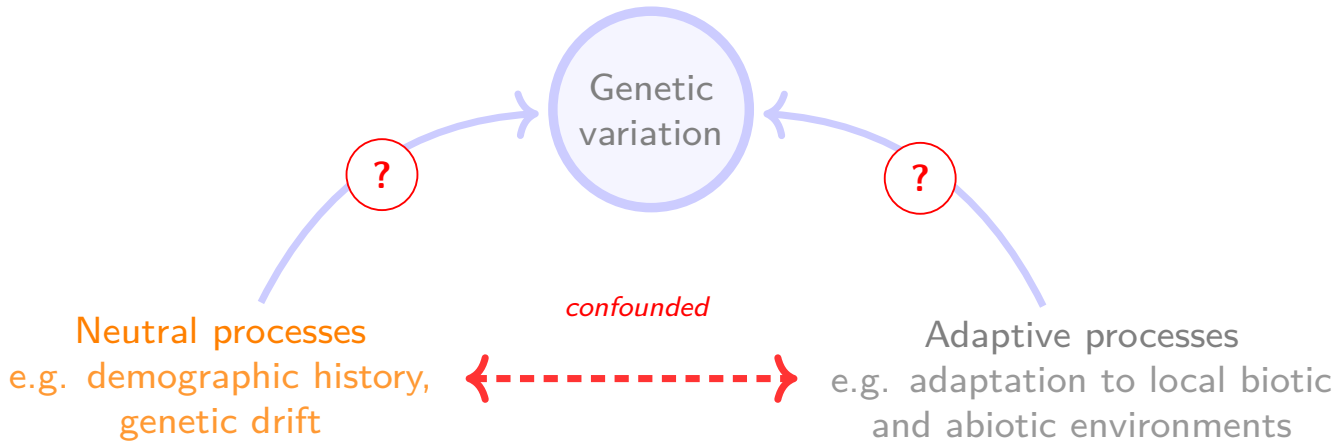

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- increasing the chances of **fast-adaptive decision** making.

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Landscape genomics: the study of the processes shaping the geographical patterns of adaptive genetic variation across the landscape.

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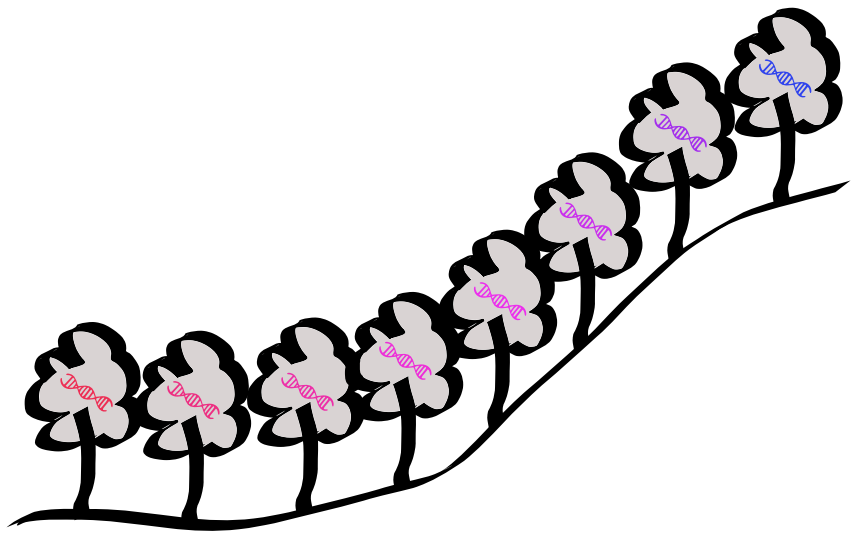

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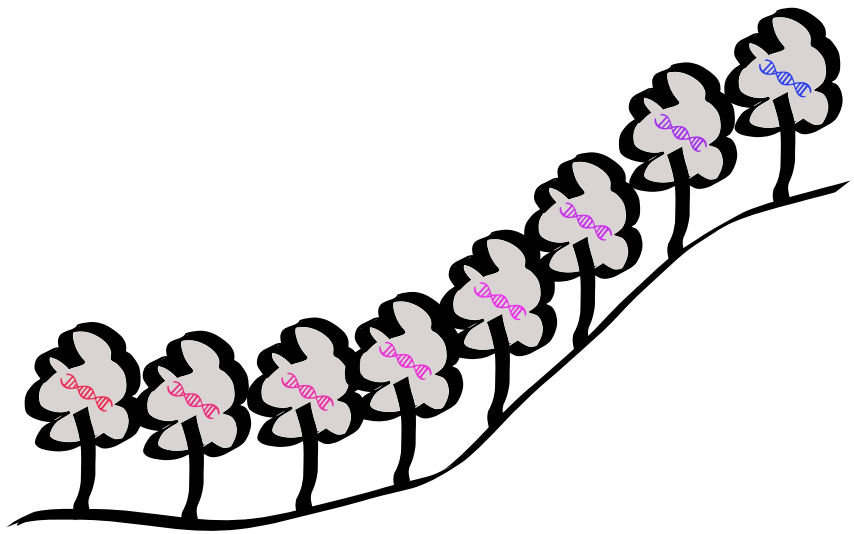

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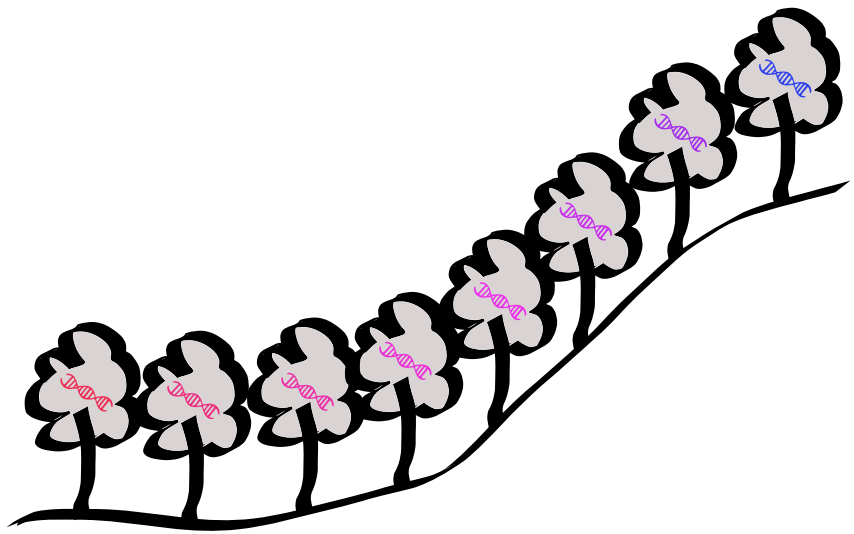

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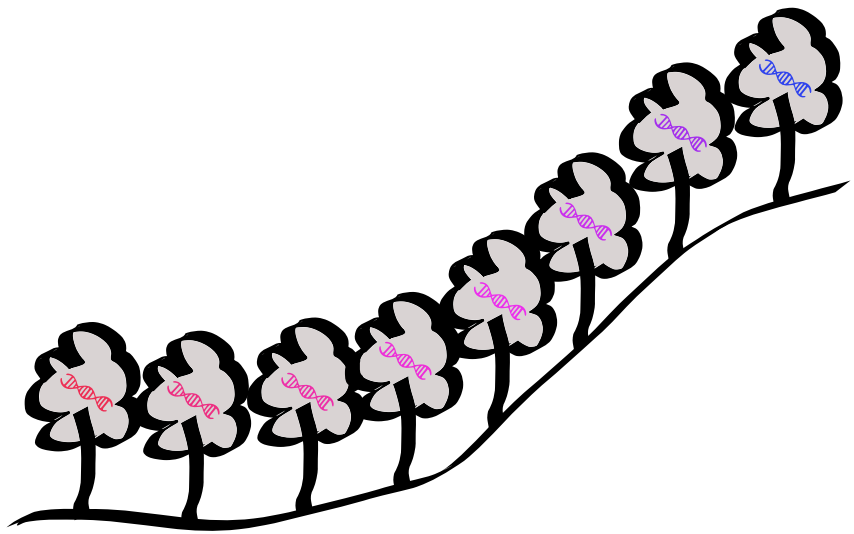

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Methods and limits in predicting phenotypes based on genotypes

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$$y_i = \mu + a_i + e_i$$

y_i is the phenotype of the individual i.
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a_i is the **breeding value** of the individual i, i.e. its **aggregate additive genetic value**, of which the individual passes on average half to its offspring.
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V_A is the additive genetic variance.
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Breeding values are calculated as the **sum of the additive effects** of the markers (previously estimated), such as:

$$a_i = \sum (SNP_{ij}\gamma_j)$$

SNP_{ij} is the genotype of the individual i at the locus j.
γ_j is the effect of the SNP on the phenotype.

Estimating **breeding values**: two main types of statistical models

$$y_i = \mu + a_i + e_i$$

y_i is the phenotype of the individual i.
μ is the average population phenotype.
a_i is the **breeding value** of the individual i, i.e. its **aggregate additive genetic value**, of which the individual passes on average half to its offspring.
e_i is the residual variation.

• Animal model

Henderson 1975

Breeding values are estimated from the **covariance among relatives** in **additive genetic effects**, such as:

$$a_i \sim \mathcal{N}(0, \mathbf{A}V_A)$$

V_A is the additive genetic variance.
A is the relatedness matrix.

A can either be estimated from a pedigree or from genomic markers (genomic relationship matrix).

• Genome regression

Meuwissen *et al.* 2001

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Known as **polygenic risk scores** (PRS) in humans.

Methods and limits in predicting phenotypes based on genotypes

Estimating **breeding values**: from marker-assisted to genomic selection

Jannink *et al.* 2010, Meuwissen *et al.* 2016

- **Marker-assisted selection (MAS)**

Using a **subset of SNPs** the most associated with the phenotypes.

Likely more accurate for **oligonenic** traits.

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In natural populations of **large effective population size**, GS methods still have slightly lower predictive accuracy than pedigree-based approaches.

e.g. in Beaulieu *et al.* 2014. When predicting wood and growth traits in a large undomesticated population of related white spruces (within-family predictions, i.e. with known relatedness between training and testing data sets), GS methods achieved between 68 and 89% of the accuracy obtained with pedigree information.

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But, **weak predictive accuracy** across:

Methods and limits in predicting phenotypes based on genotypes

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e.g. in Resende Jr *et al.* 2012. GS models developed for early growth traits (diameter and height at age 1 or 2 yr) had limited accuracy in predicting phenotypes at age 6 yr in loblolly pine.

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→ Can be explained by the presence of **shared ancestry** (with the relatedness picked up by the markers) and **historical LD** (likely if the sampled populations are from the same glacial lineage).

So, how to incorporate **genomic information** in phenotypic predictions encompassing **multiple natural populations**?

Introduction: from species-level to genome-informed modelling

Predicting short-term performance with trait-based approaches

- Methods and limits in predicting phenotypes based on genotypes
- Predicting phenotypes based on genotypes in natural populations
- Predicting phenotypes from gene-environment associations

Predicting the adaptive potential of populations under climate change

- Incorporating intraspecific climatic adaptations into ENMs
- The genomic offset framework
- Extending the genomic offset framework
- Potential applications

Predicting phenotypes based on genotypes in natural populations

Some examples from forest tree research:

Predicting phenotypes based on genotypes in natural populations

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- Using **genomic estimated breeding values** (GEBVs; the sum of the effects of genome-wide markers on the trait of interest), i.e. **polygenic scores**.

Browne L., Wright J. W., Fitz-Gibbon S., Gugger P. F., and Sork V. L. (2019). Adaptational lag to temperature in valley oak (Quercus lobata) can be mitigated by genome-informed assisted gene flow. *Proceedings of the National Academy of Sciences* **116**.50: 25179– 25185.

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Mahony C. R., MacLachlan I. R., Lind B. M., Yoder J. B., Wang T., and Aitken S. N. (2020). Evaluating genomic data for management of local adaptation in a changing climate: A lodgepole pine case study. *Evolutionary Applications* **13**.1: 116– 131.

MacLachlan I. R., McDonald T. K., Lind B. M., Rieseberg L. H., Yeaman S., and Aitken S. N. (2021). Genome-wide shifts in climate-related variation underpin responses to selective breeding in a widespread conifer. *Proceedings of the National Academy of Sciences* **118**.10.

Archambeau, J., Garzón, M. B., Barraquand, F., Miguel, M. D., Plomion, C., & González-Martínez, S. C. (2022). Combining climatic and genomic data improves range-wide tree height growth prediction in a forest tree. *The American Naturalist*.

Predicting phenotypes based on genotypes in natural populations

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Goal: evaluate the potential for a *genome-informed* assisted gene flow strategy to mitigate the negative impact of rising temperatures on growth rates in valley oak.

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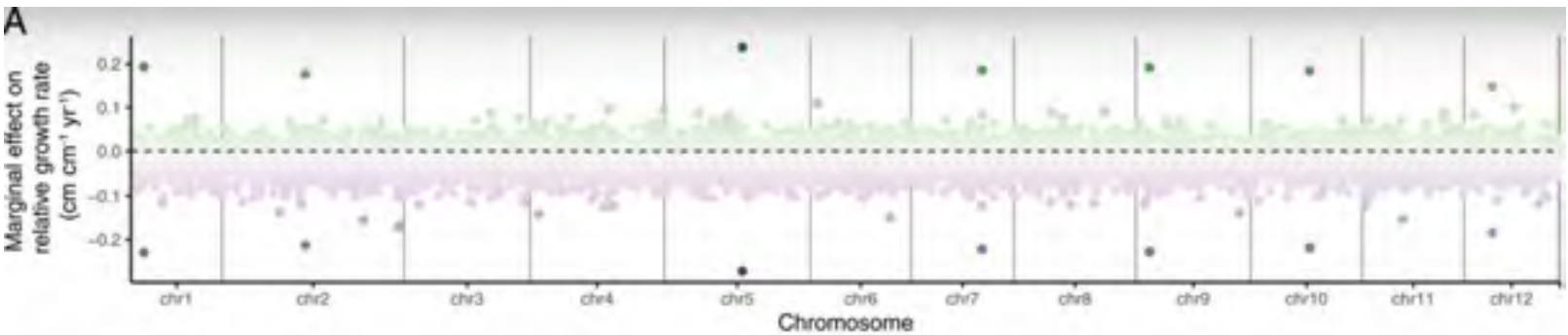
Goal: evaluate the potential for a *genome-informed* assisted gene flow strategy to mitigate the negative impact of rising temperatures on growth rates in valley oak.

1. A **genome-wide association study** (GWAS) framework was used to estimate allelic effects on **relative growth rates** after controlling for potential confounding factors.



Predicting phenotypes based on genotypes in natural populations

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2. Genomic estimated breeding values (GEBVs) indicate the **genetic value** of each maternal tree (i.e. maternal genotype of each seedling) and were estimated as the **average progeny performance** (i.e. the predicted adjusted progeny relative growth rates) when grown in **warmer temperatures**.

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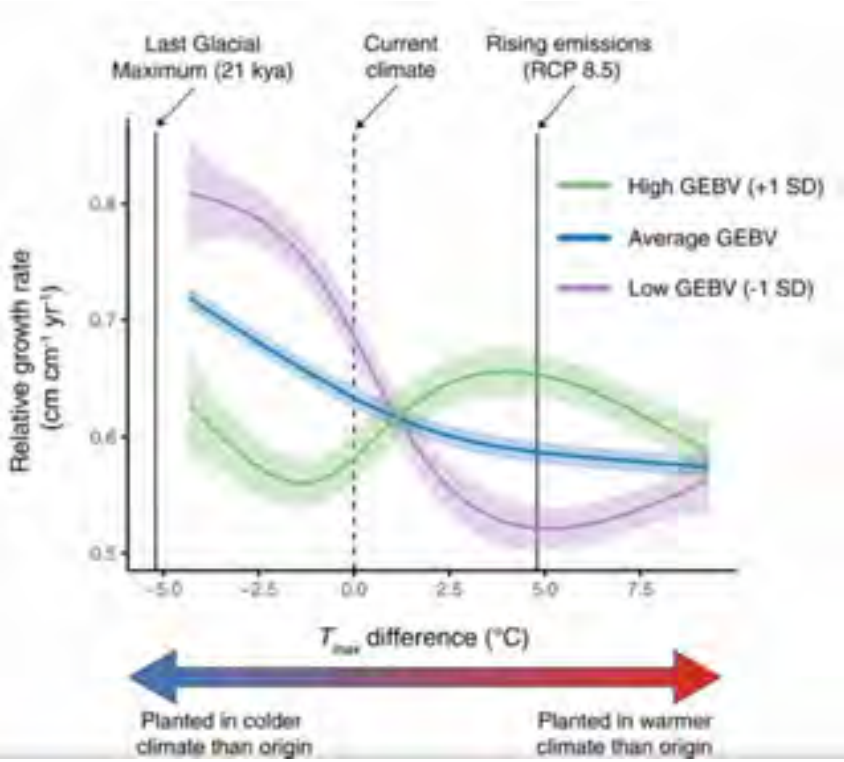

Predictions:

→ Progeny of maternal trees with high GEBVs were **preadaptated to warmer temperatures**.

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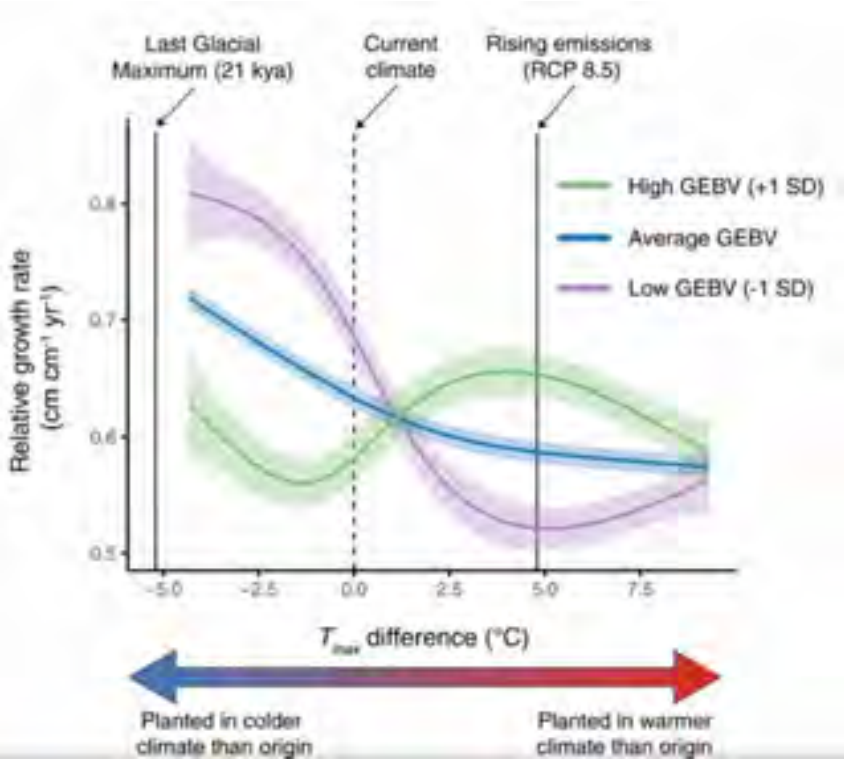

Predictions:

→ Progeny of maternal trees with high GEBVs were **preadaptated to warmer temperatures**.

→ At a 4.8 °C increase in temperature (predicted under RCP-8.5 by 2070 to 2099), progeny of maternal trees with high GEBVs have 11% and 25% higher relative growth rates than the progeny of maternal trees with average GEBVs or low GEBVs, respectively.

Predicting phenotypes based on genotypes in natural populations

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3. Progeny growth rates under **warmer temperatures** were predicted for four hypothetical sets of seedlings used as **seed source**.

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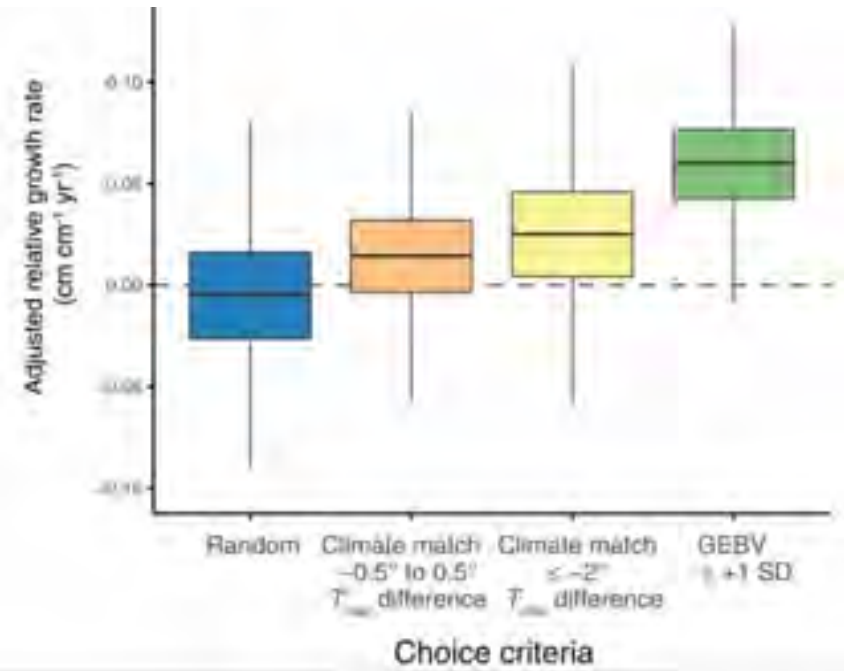

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→ Choosing individuals with the highest GEBVs as seed sources leads to substantial increases in predicted progeny growth rates under warmer temperatures.

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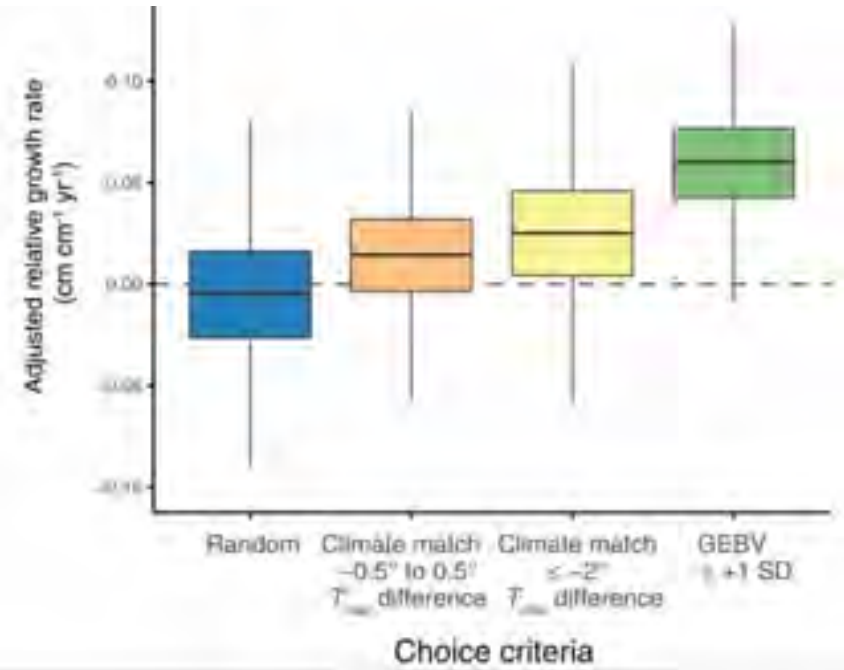

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Conclusion:

→ This study shows the potential of genome-informed assisted gene flow to mitigate the negative effects of future increases in temperature by selecting for genotypes predicted to have relatively high productivity in future climate scenarios.

Predicting phenotypes based on genotypes in natural populations

Mahony *et al*. 2020

Goal: evaluate genomic data, relative to phenotypic and climatic data, as a basis for assisted gene flow and genetic conservation in lodgepole pine.

Predicting phenotypes based on genotypes in natural populations

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For four **seedling traits** measured in common gardens, they compared the **proportion of phenotypic variance explained** by:

- the **geographic location** of the populations
- the **climate-of-origin** of the populations
- several sets of **genomic markers**:
  - the full SNP array
  - candidate SNPs identified with genotype–phenotype associations (GPAs)
  - candidate SNPs identified with genotype–environment associations (GEAs)
  - candidate SNPs identified with GPAs and GEAs.
  - control set of SNPs.

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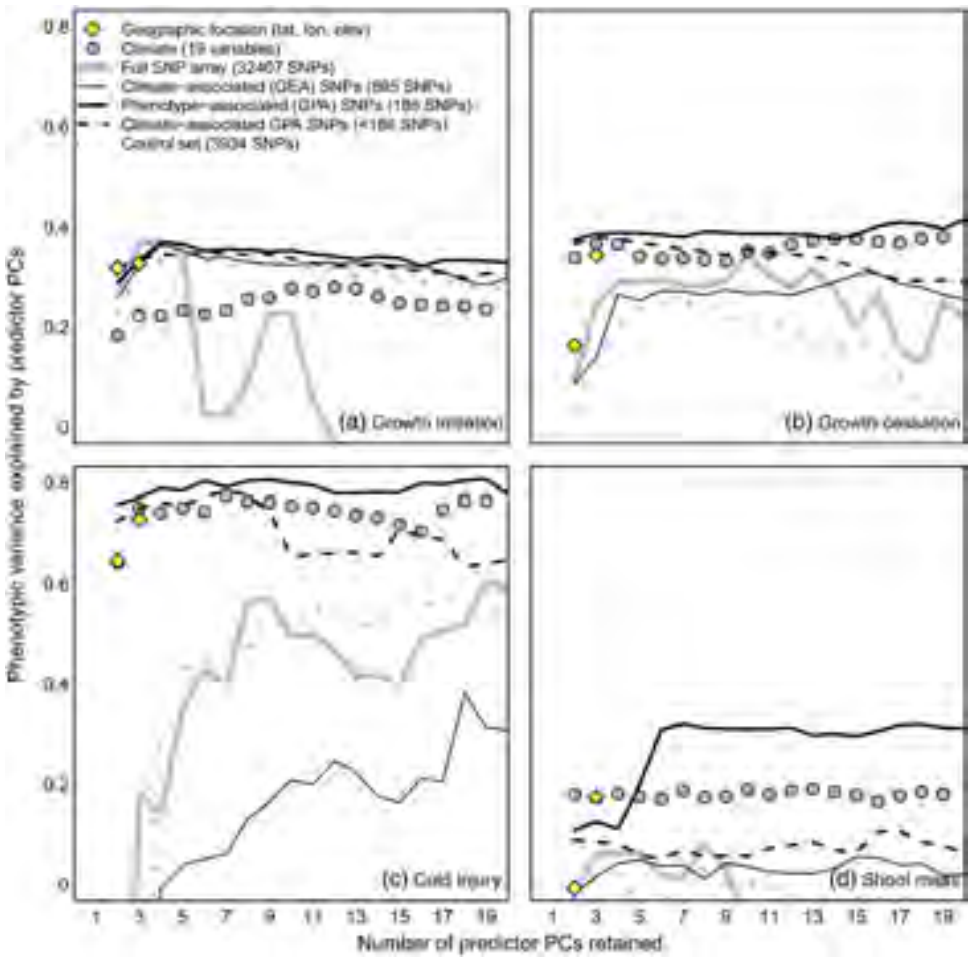

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The **predictive power** of climate variables, geography, and genotypes varied greatly among seedling traits.

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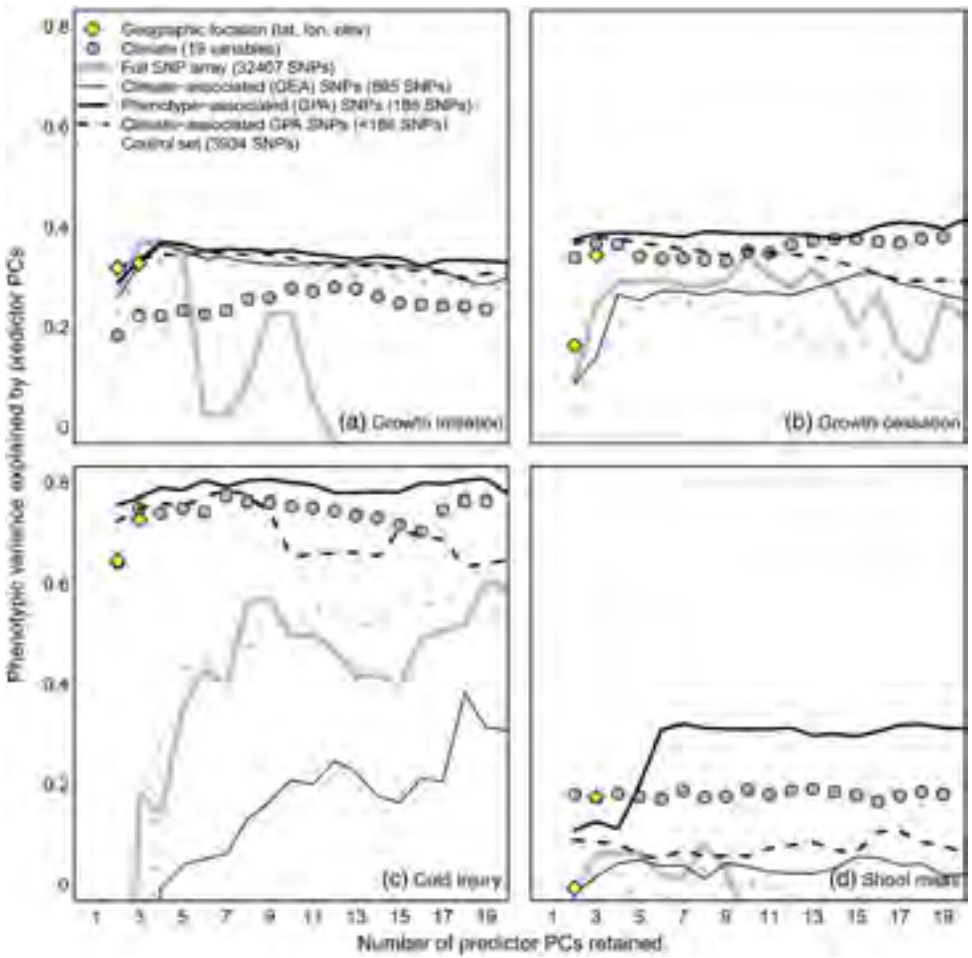

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Can be explained by:

→ link between phenotype and fitness

→ degree of polygenicity

→ epistatic and pleiotropic interactions

→ relative importance of natural selection vs demographic history

→ method shortcomings

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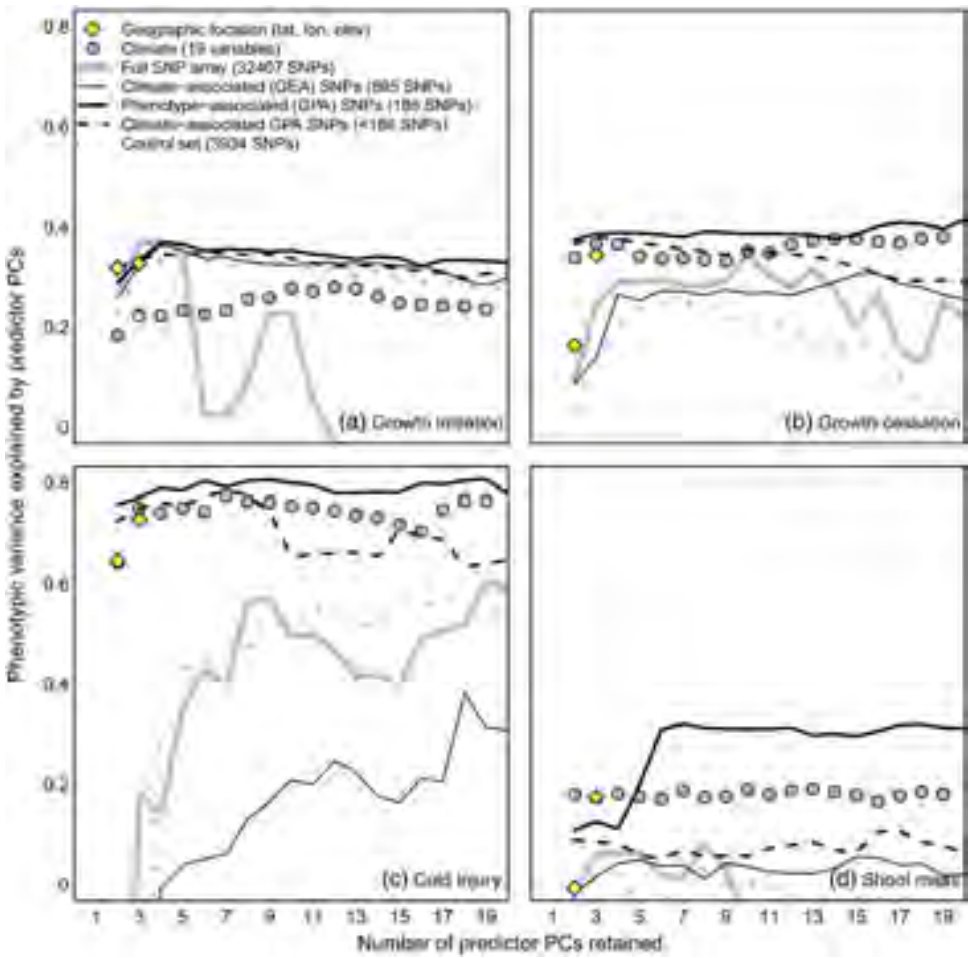

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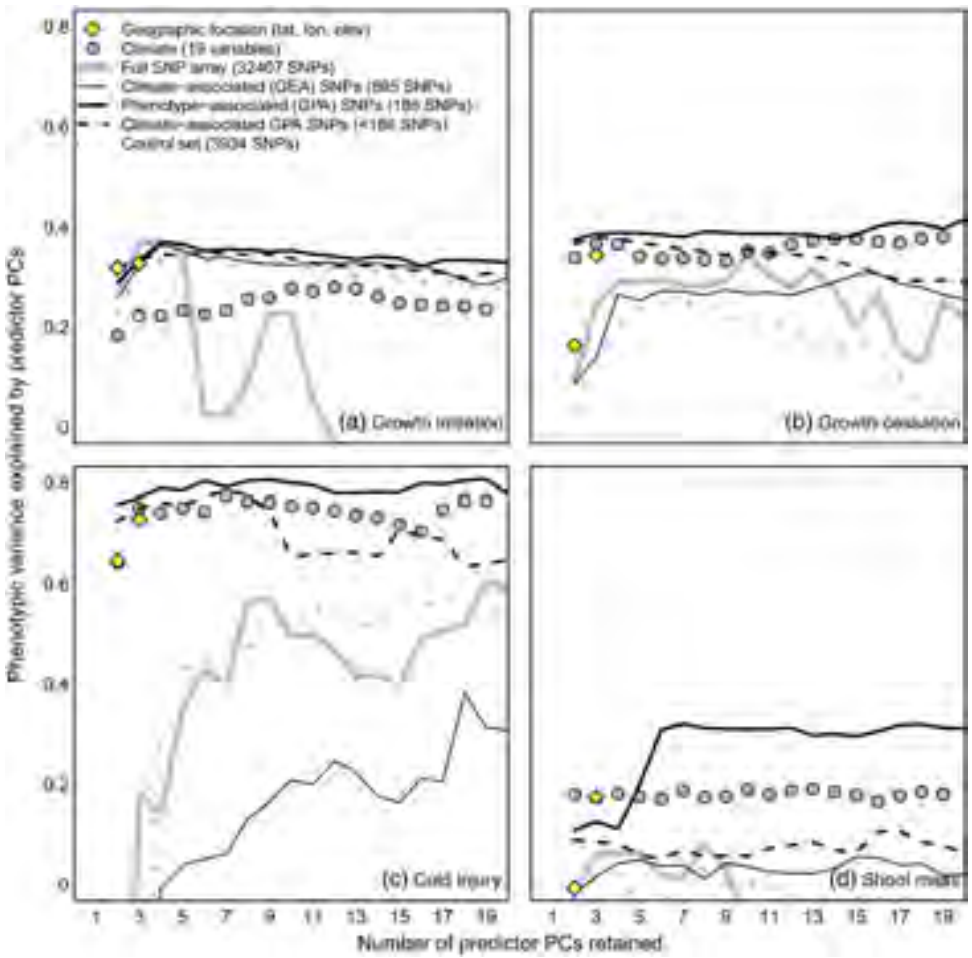

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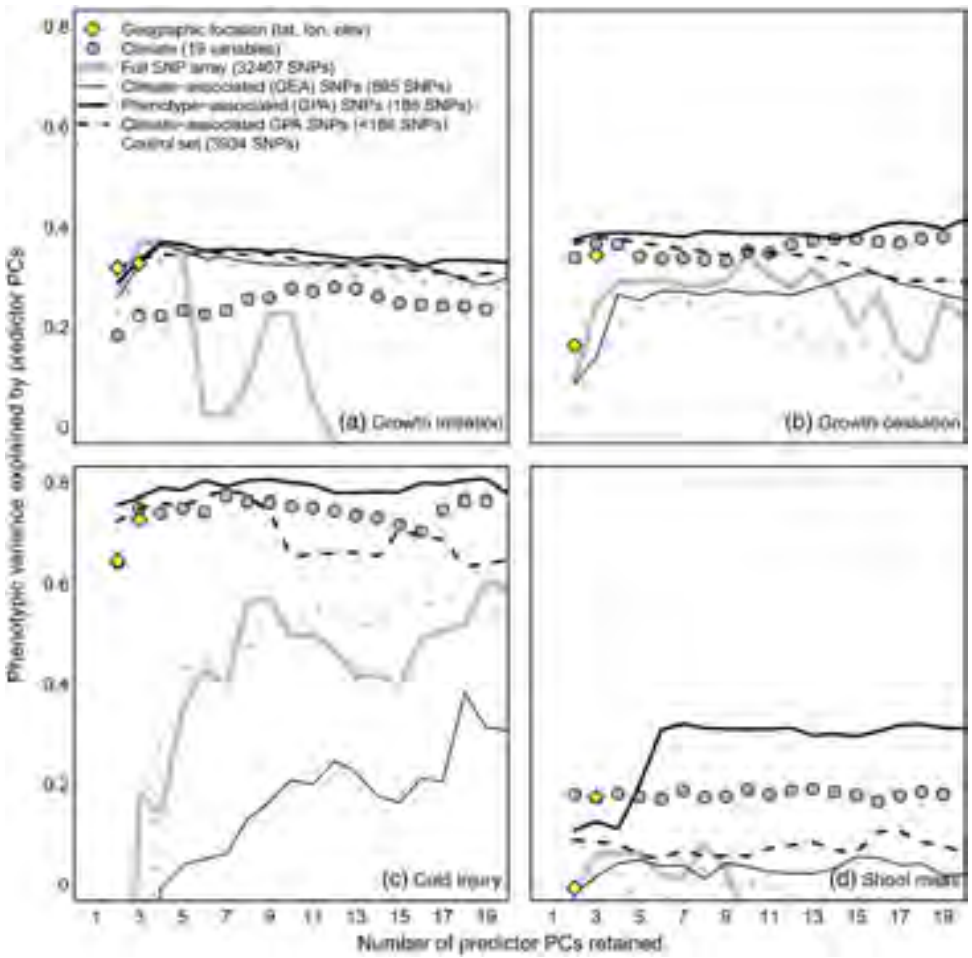

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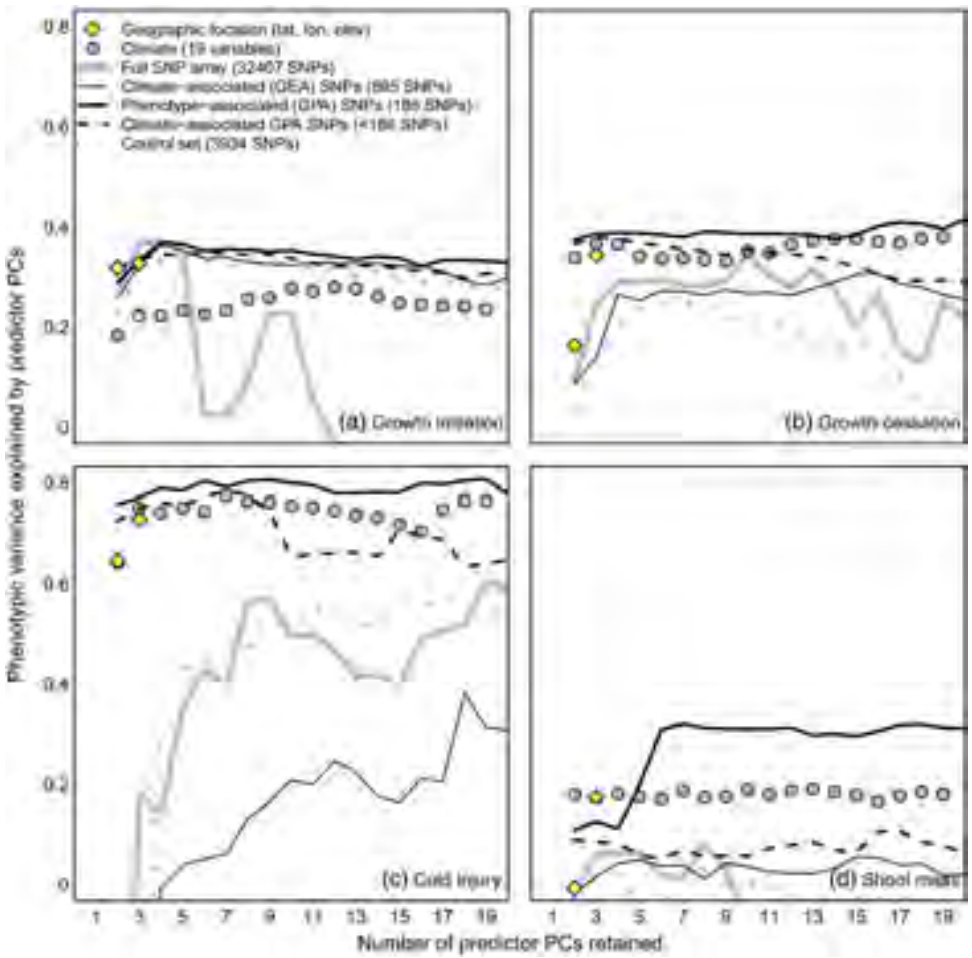

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GPA SNPs may play an effective role in designing assisted gene flow strategies.

Predicting phenotypes based on genotypes in natural populations

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Goal: evaluate genomic data, relative to phenotypic and climatic data, as a basis for assisted gene flow and genetic conservation in lodgepole pine.

- Counts of **positive-effect alleles** (PEAs), i.e. alleles that are positively associated with the trait of interest.

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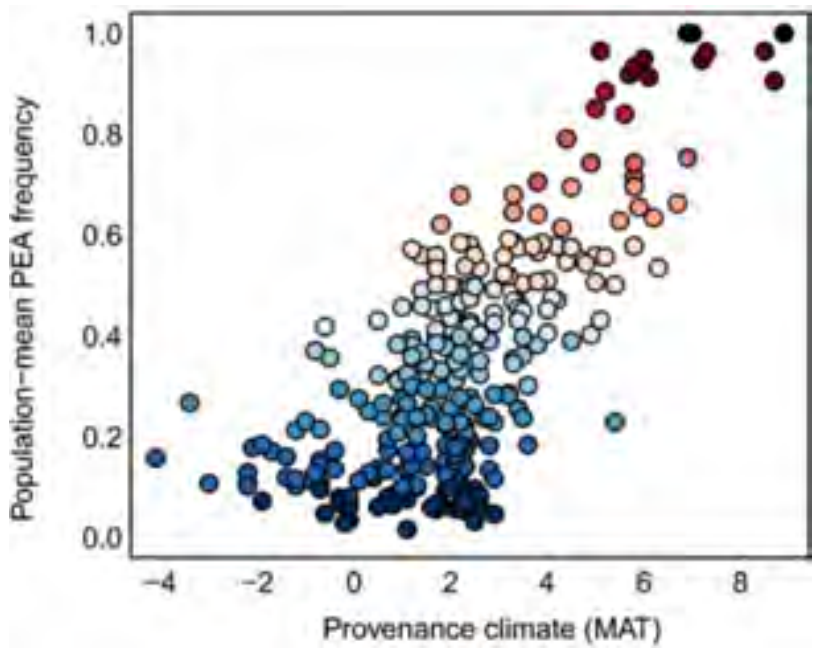
- To characterize the spatial scale of the genetic clines associated with the traits of interest (here, autumn cold injury).



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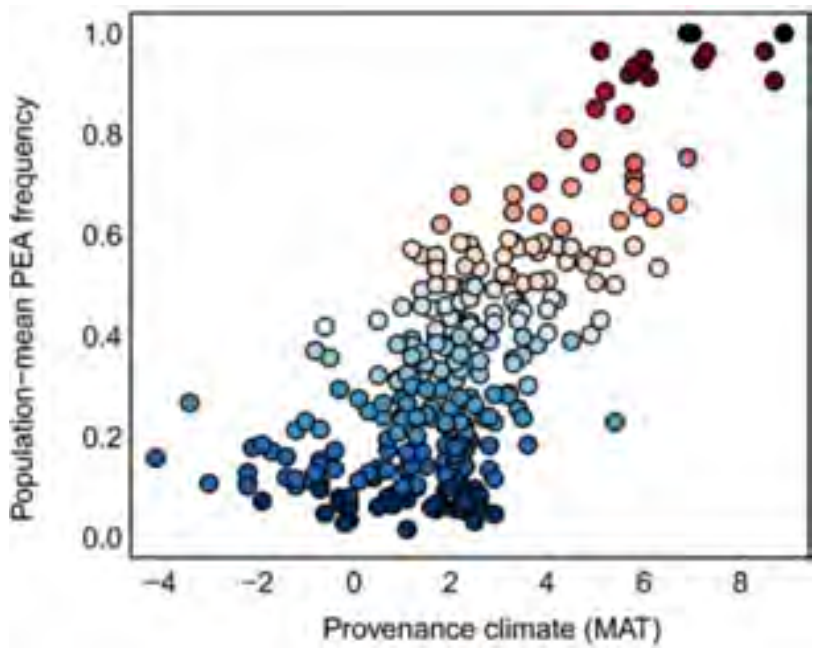

→ **No evidence for highly localized genetic clines** at scales that would constrain local seed transfer to scales finer than those indicated by phenotypic data or necessitate geographically small genetic conservation units.

Predicting phenotypes based on genotypes in natural populations

MacLachlan *et al.* 2021

Goal: evaluate the effect of artificial selection for faster growth on climatically adaptive genes and traits in lodgepole pine.

Predicting phenotypes based on genotypes in natural populations

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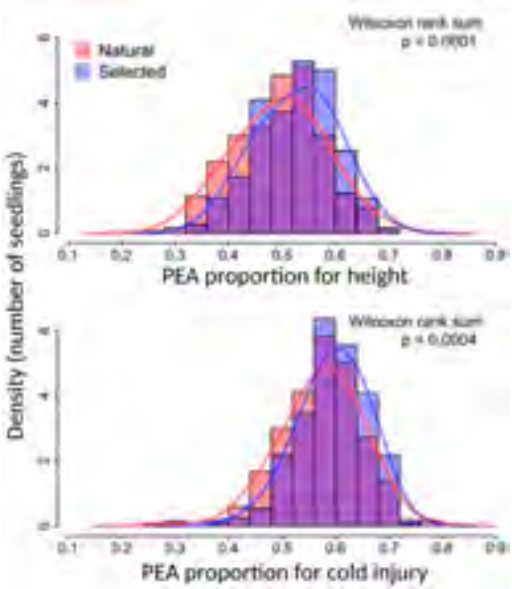
Goal: evaluate the effect of artificial selection for faster growth on climatically adaptive genes and traits in lodgepole pine.

$\rightarrow$ Identify **positive-effect alleles** (PEAs), i.e. alleles that are positively associated with the traits of interest (growth, cold injury, growth initiation and growth cessation) in natural populations.



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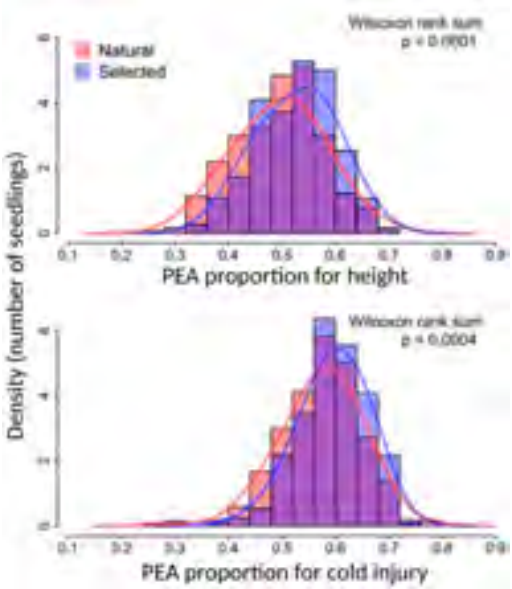

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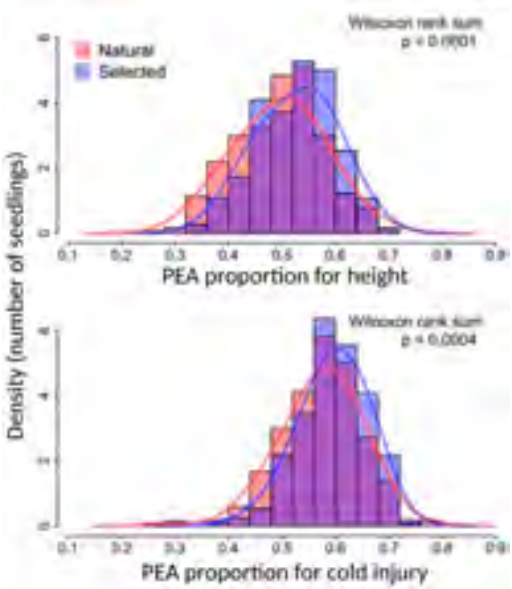

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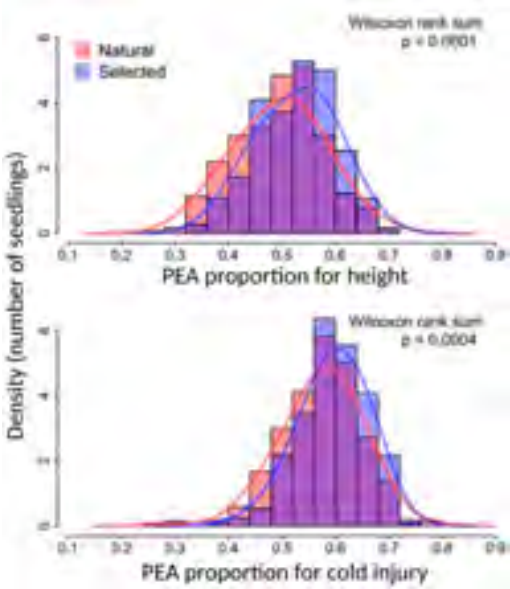

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→ By affecting trait-associated genetic variation involved in climate adaptation, artificial selection for tree growth may compromise future adaption in a changing climate and assisted gene flow strategies.

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Goal: predicting height growth of populations with no phenotypic information in maritime pine.

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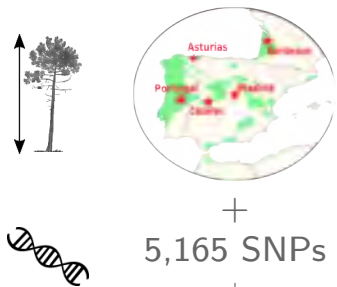

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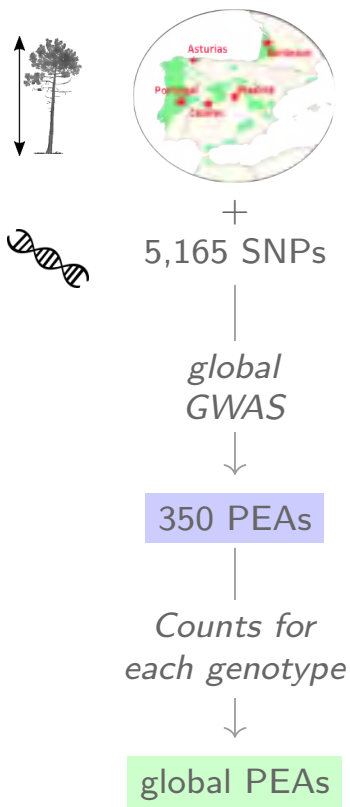

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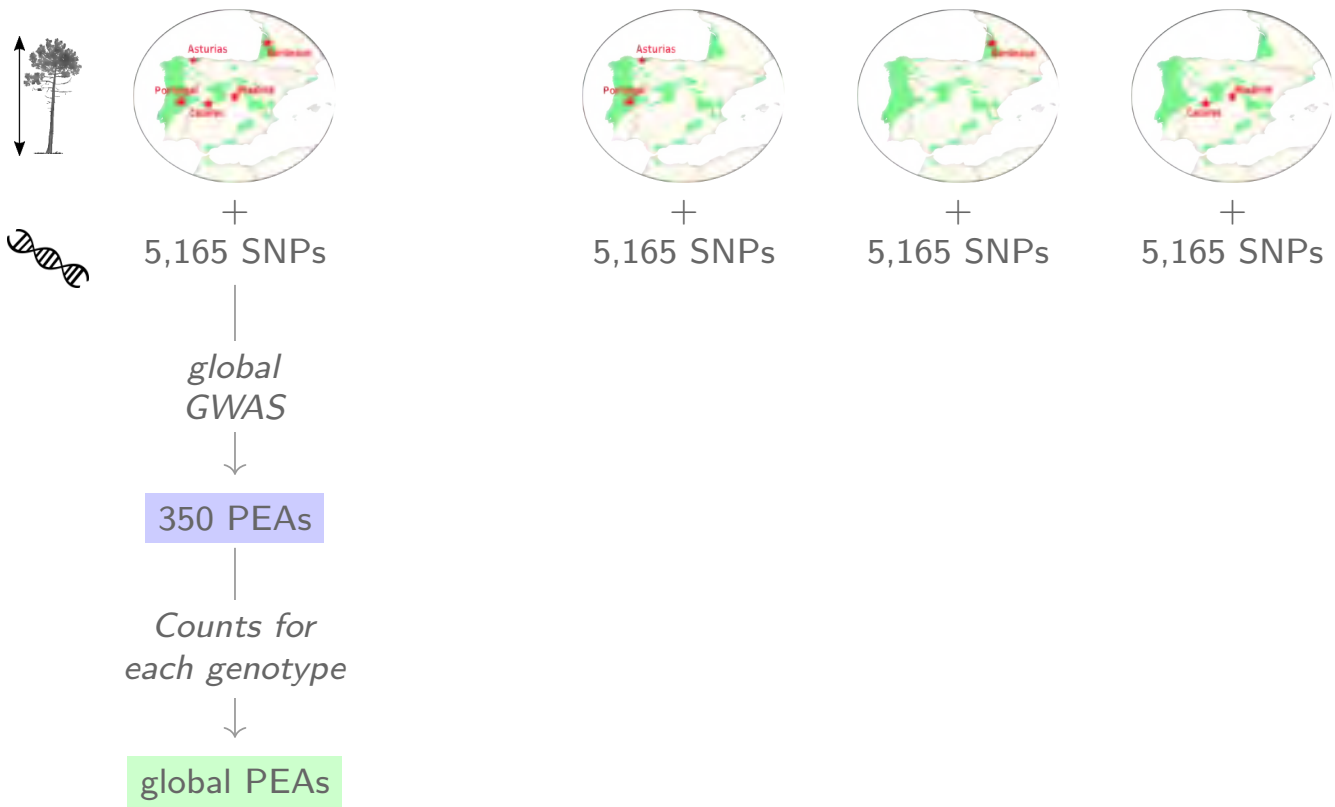

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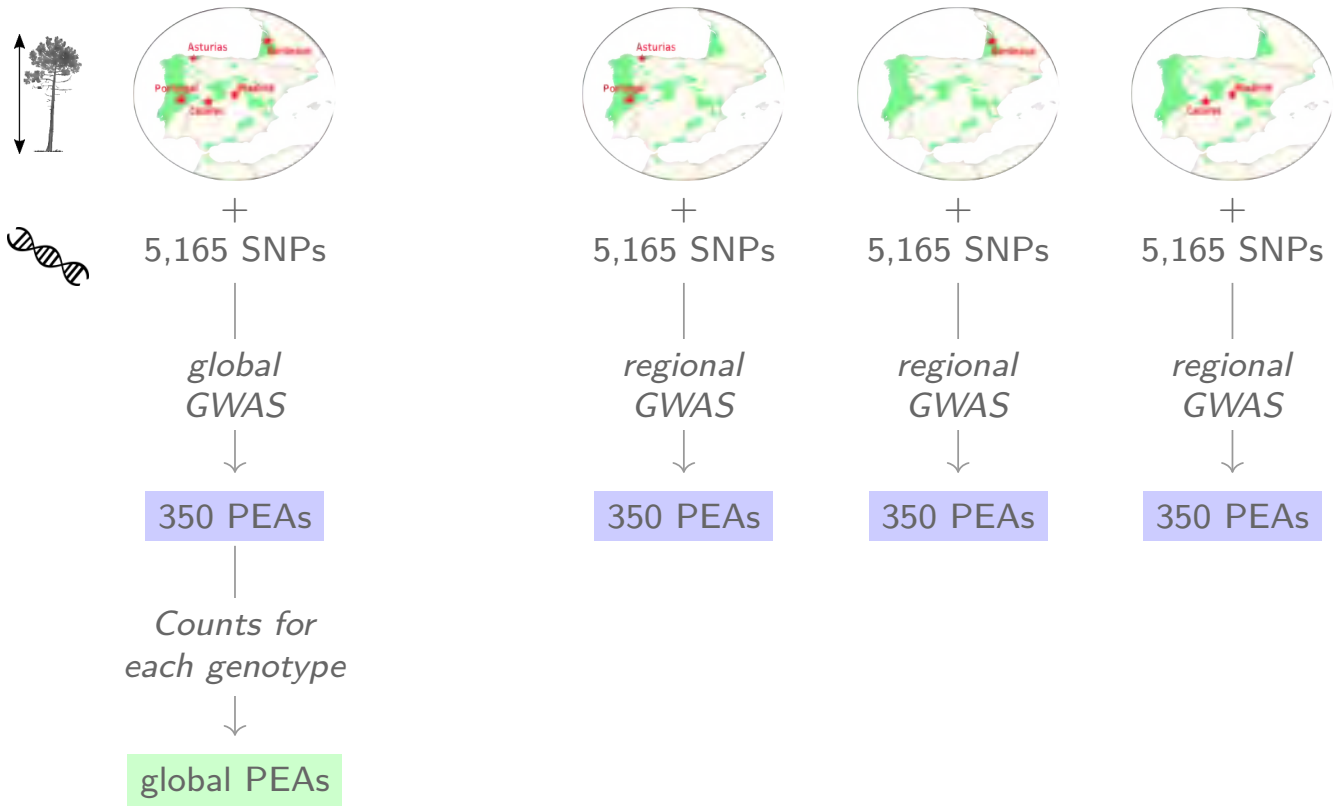

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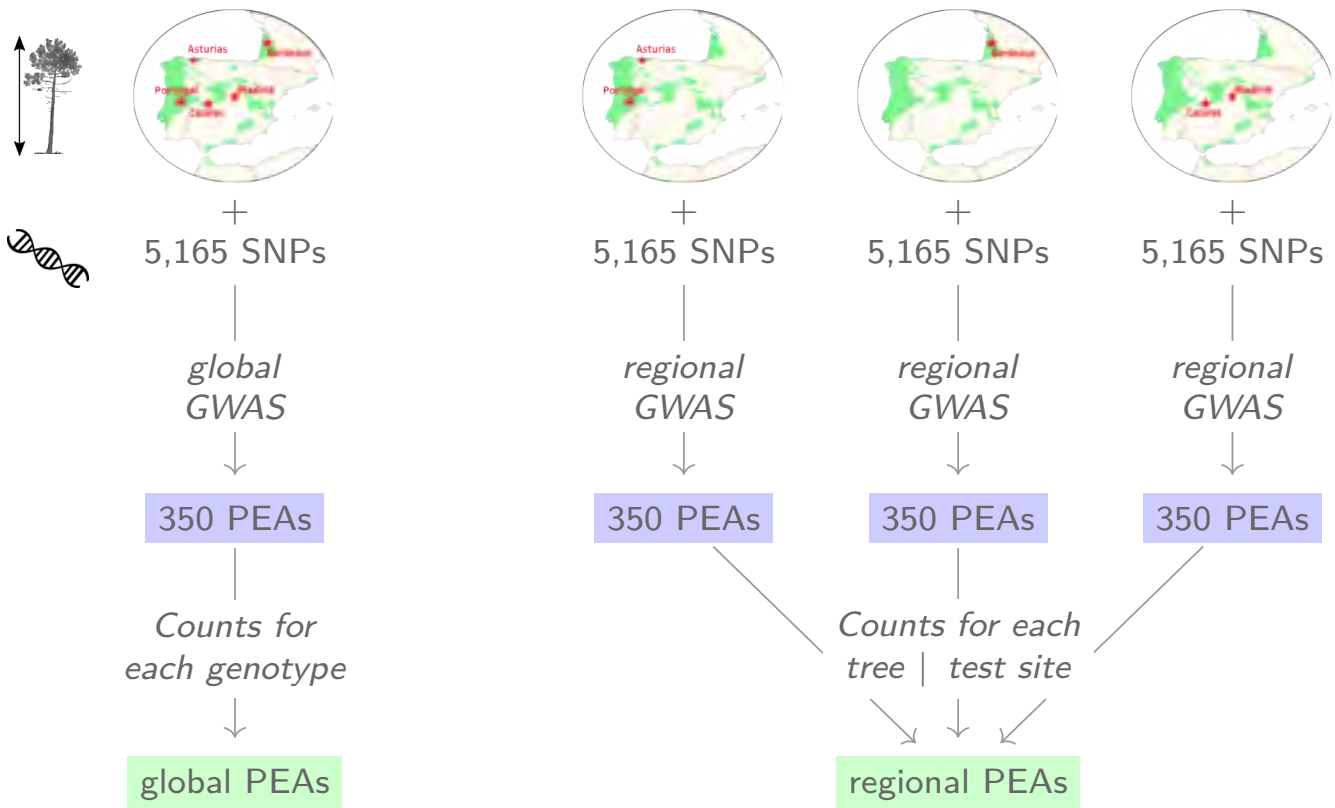

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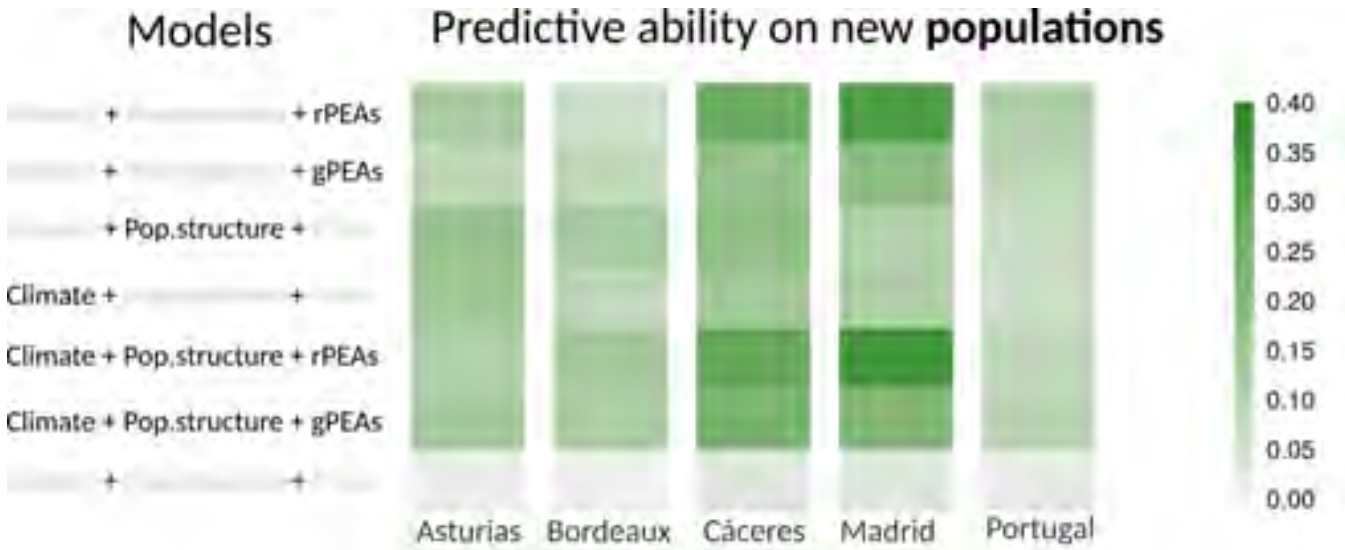

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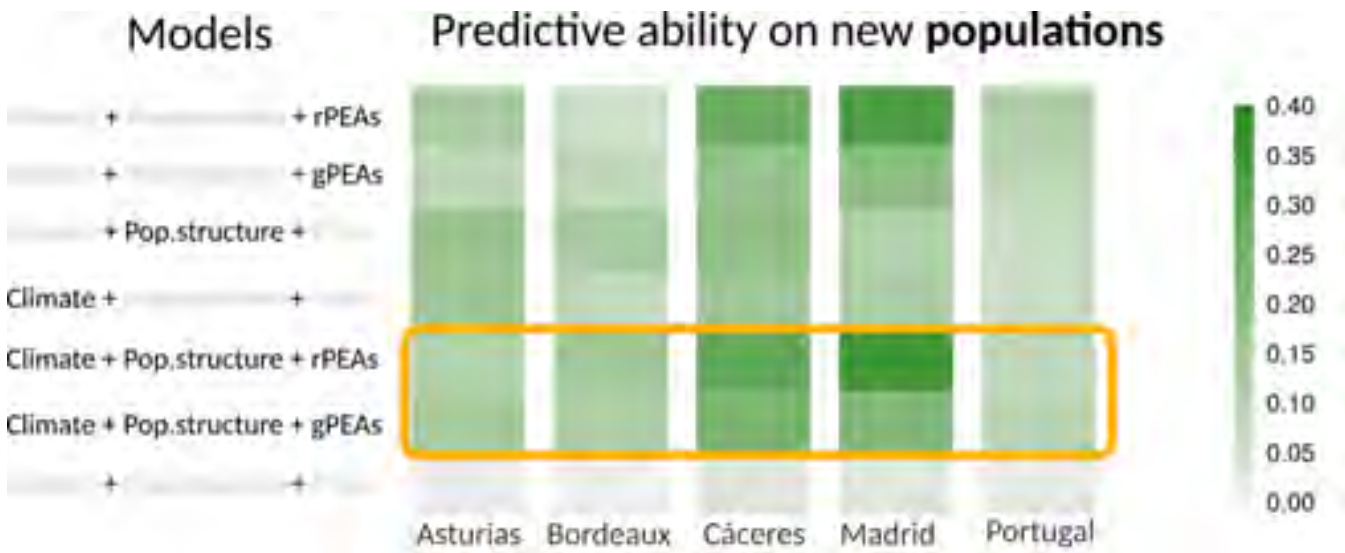

Models **combining climatic and genomic information** had the best out-of-sample predictive ability.

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Models **combining climatic and genomic information** had the best out-of-sample predictive ability.

Better predictive ability of **regionally-selected PEAs (rPEAs)** than globally-selected PEAs (gPEAs).

Predicting phenotypes based on genotypes in natural populations

So, **GEBVs** or **PEA counts**, which one to use in **natural populations**?

Genomic estimated breeding values (GEBVs)

Counts of alleles associated with the phenotype **weighed** by their phenotypic effects

Equivalent to polygenic risk scores (PRS)

✓ Likely more precise within genetic groups (i.e. family, population)

✗ Less precise for highly polygenic traits?

✓ More precise for olygogenic traits?

✗ Low transferability across genetic groups (inconsistent allelic effects)

Positive-effect allele (PEA) counts

Counts of alleles positively associated with the phenotype

✗ Less precise within genetic groups

✗ Less precise for olygogenic traits

✓ More precise for highly polygenic traits?

✓ Higher transferability across genetic groups? (remains to be tested)

✓ More robust to small stochastic SNP sampling effects (whether a large effect alleles is included or not)

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Lasky *et al.* 2015

A huge dataset

— 1943 georeferenced sorghum landraces genotyped at 404,627 SNPs
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– Predicting **average phenotypes** across relatively benign and stressful environments.
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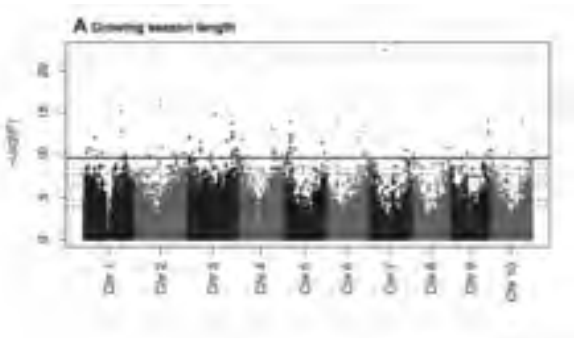
Approaches to predict the genomic breeding values

– **Marker-assisted selection** (MAS) approach:



- Identifying SNPs with the **strongest environmental associations**.
- Filtering the SNPs with low LD.
- Predicting phenotypes using the **summed SNP-environment associations**.

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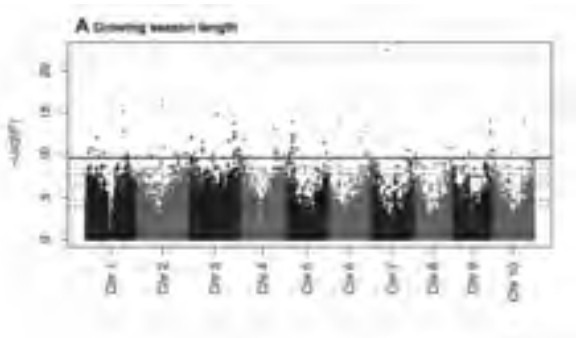

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Predicting phenotypes based on **environmental associations** with estimated **genome-wide kinship**.

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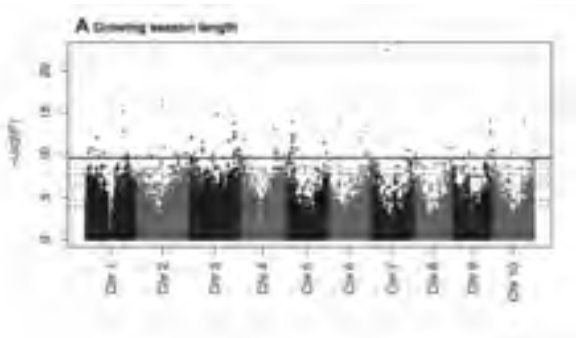

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– **Hybrid** approach combining MAS and GS approaches.

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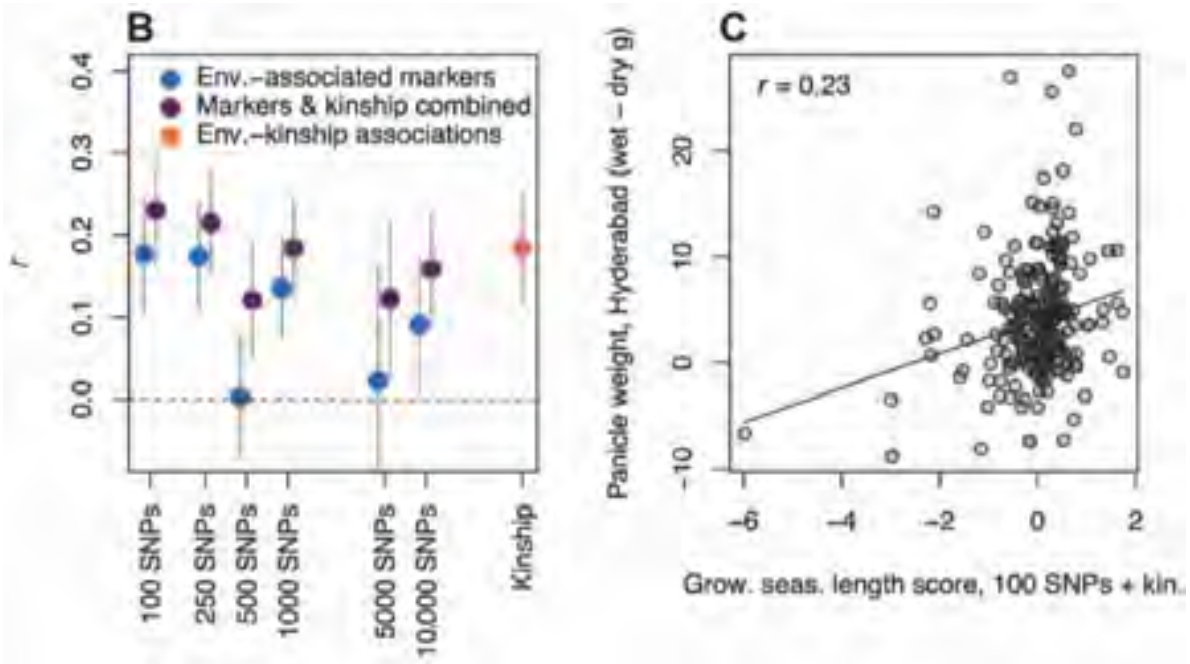
→ Environment-associated SNPs are good predictors of **genotype-by-environment interactions**.

e.g. reductions in panicle height under drought conditions best predicted by SNPs with the strongest associations with growing season length.



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→ A case study on aridity tolerance in sugar beet (Manel *et al.* 2018)

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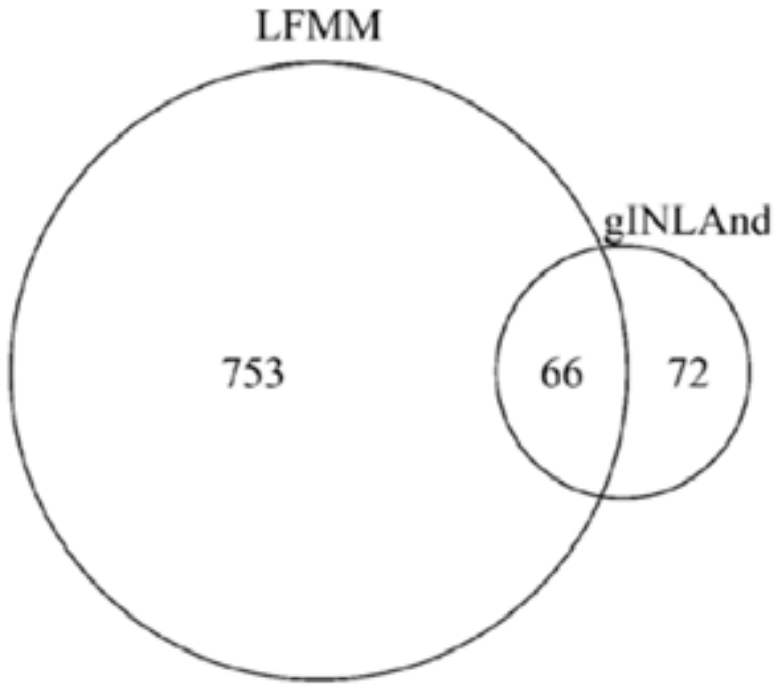
1. 66 SNPs were significantly associated with aridity in two gene-environment association (GEA) methods.



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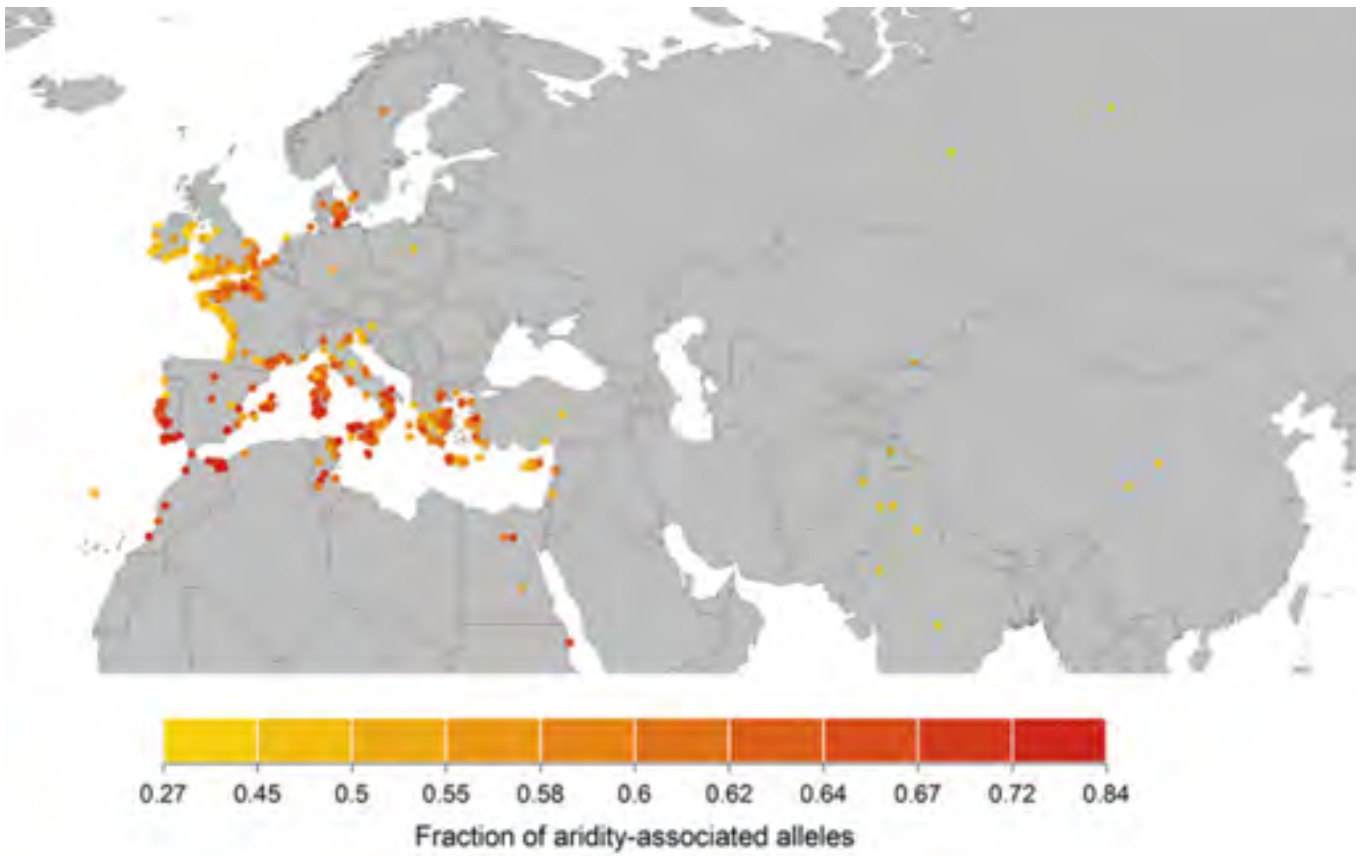
2. The fraction of SNPs positively associated with aridity was calculated for each individual.



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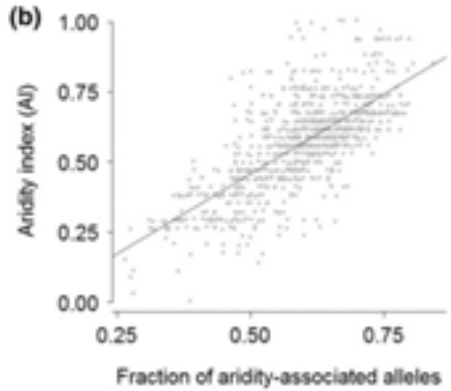
3. The association between the aridity index and the fraction of aridity-associated alleles was estimated in the training dataset,



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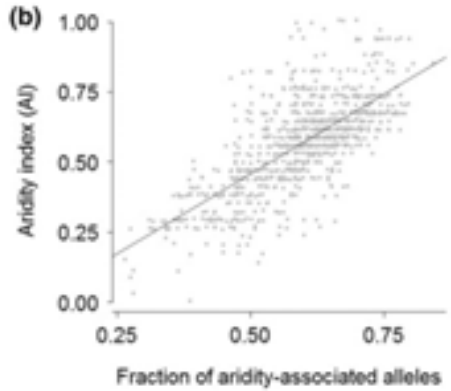
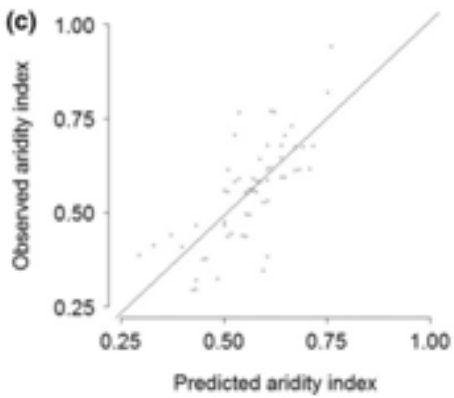


4. and validated in an independent dataset.



Predicting phenotypes from gene-environment associations

Predicting the **environmental range** of the genotypes

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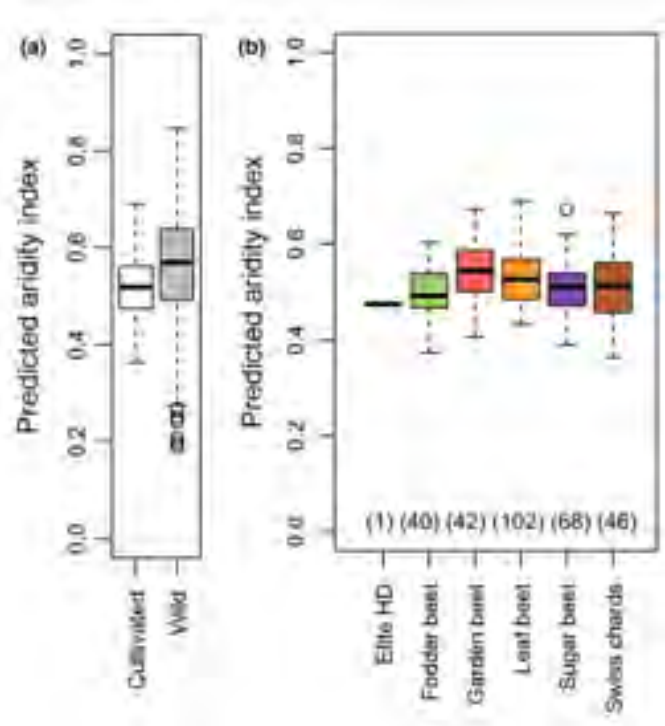
5. This approach can be used to predict the **environmental range** of individuals for which only the genotype is known.

e.g. the aridity range of cultivated beets



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Predicting **locally adapted genotypes** for a given site

→ A case study in *Arabidopsis thaliana* (Gienapp *et al.* 2017)

1. Estimating a **genomic-relationship matrix** (GRM) based on **average allelic correlation** with more than 200,000 SNPs.

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→ This approach **does not require** experiments or phenotypic measurements: predictions are based solely on the **relationship** between **GRM** and **native environments**.

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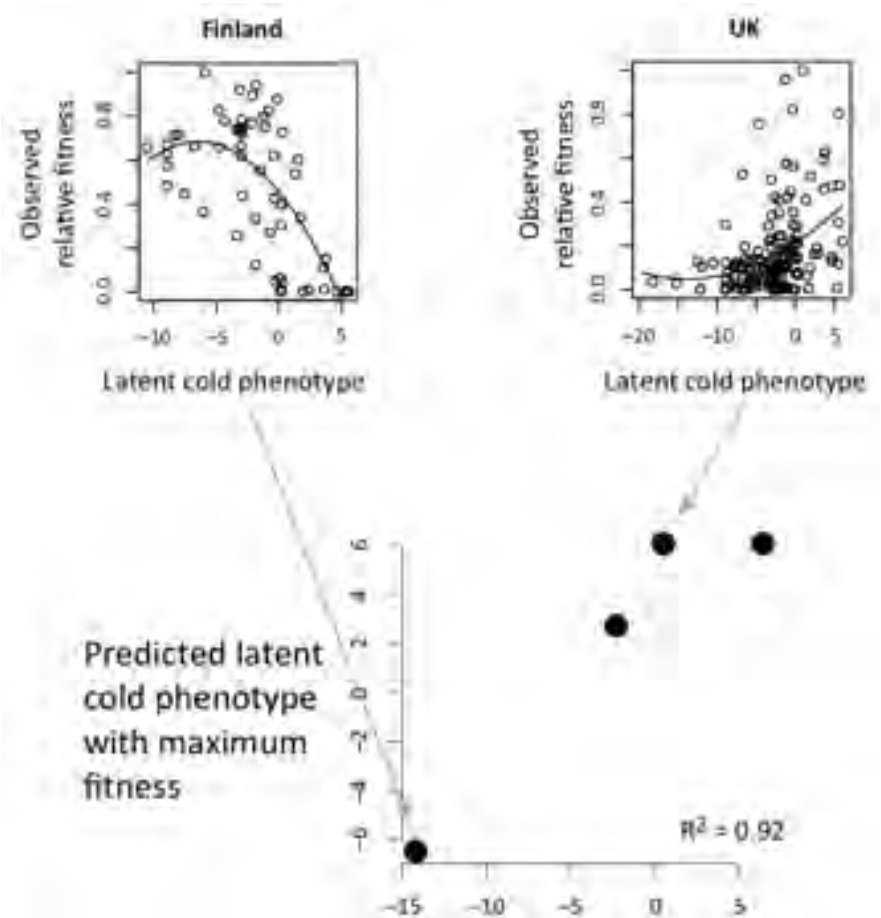
4. Validating the predictions with experimental data (individual relative fitness of 157 ecotypes) from four common gardens.

- Identifying the **expected most locally adapted phenotype** in each common garden based on the association between the observed relative fitness and the predicted latent cold-adapted phenotypes.
- Predicted latent cold-adapted phenotypes in the four common gardens were **strongly associated** with temperature conditions in the common gardens.

→ This approach can be used to **predict locally adapted genotypes** in a **given environment**, which is particularly useful to guide conservation and restoration strategies.



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Razgour *et al.* 2017: an innovative integrated framework

Goal: identify populations under **threat** from **climate change** in a bat species with limited dispersal abilities.

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Exposure: captures **changes in climatic suitability** as predicted by the ENMs and the **extent of environmental dissimilarity** between present and future conditions.

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Range shift potential: captures the **degree of connectivity** to **other populations** under future conditions or to **areas** predicted to be **climatically suitable**.

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Population	Exposure	Sensitivity (adaptive; neutral)	Range shift	Risk level
Lisboa	1	− (−; 0)	+	Low
Bizkaia	1	+ (++; −)	+	Low
Granada	2	− (−; 0)	−	Medium
Girona	3	0 (+; −)	−	Medium
Valladolid	3	− (−; −)	−	Medium-high
Albacete	4	− (−; −)	−	Medium-high
Valencia	4	+ (++; −)	−	High

Implications: Assigned levels of threat can help prioritize and inform conservation action under climate change, such as:

- **rescuing high-risk populations** (through translocation of the entire population or of individuals with relevant adaptive variation into the population)
- **increasing landscape connectivity** to facilitate range shifts and the spread of adaptive genetic variation to reduce threats to medium- and medium–high-risk populations.

Razgour *et al.* 2019: incorporating directly climate-adaptive genetic variation into ENMs

Goal: assess the **vulnerability** of populations to **climate change** in two cryptic bat species with limited long-distance dispersal abilities.

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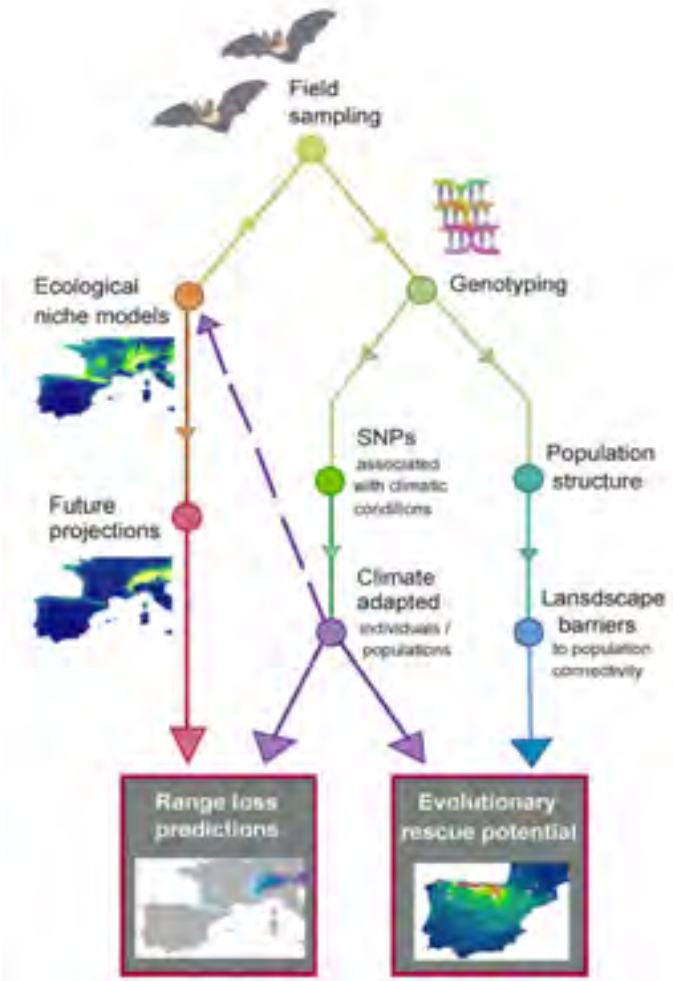
1. Identifying local climatic adaptations in wild populations by using genotype–environment association (GEA) analysis.

2. Incorporating this information into:

- forecasts of **range changes** under future climate.
- assessment of population persistence through the spread of climate-adaptive genetic variation (**evolutionary rescue potential**).



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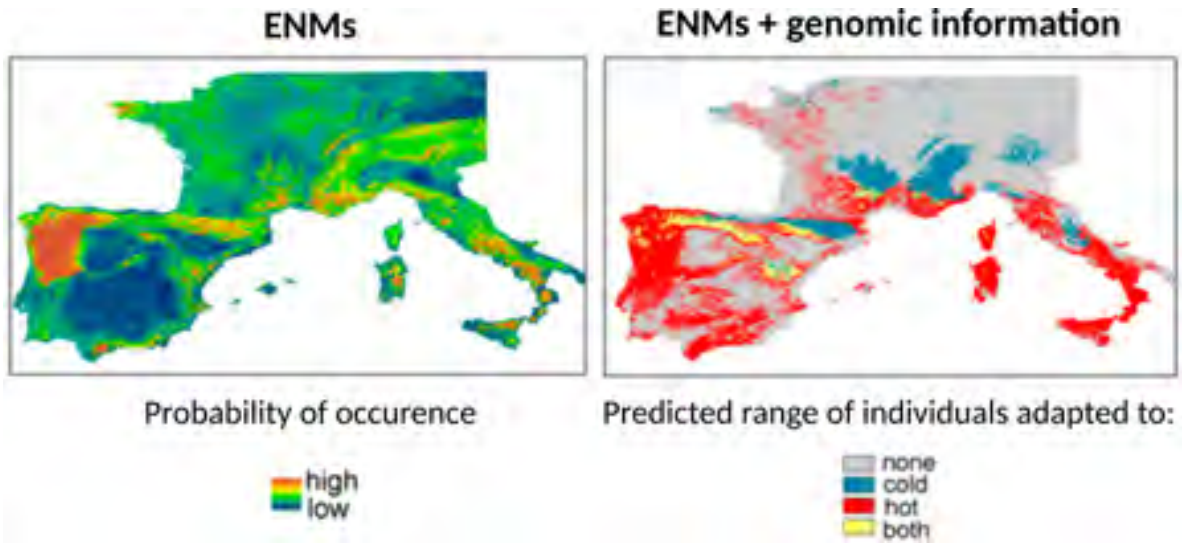

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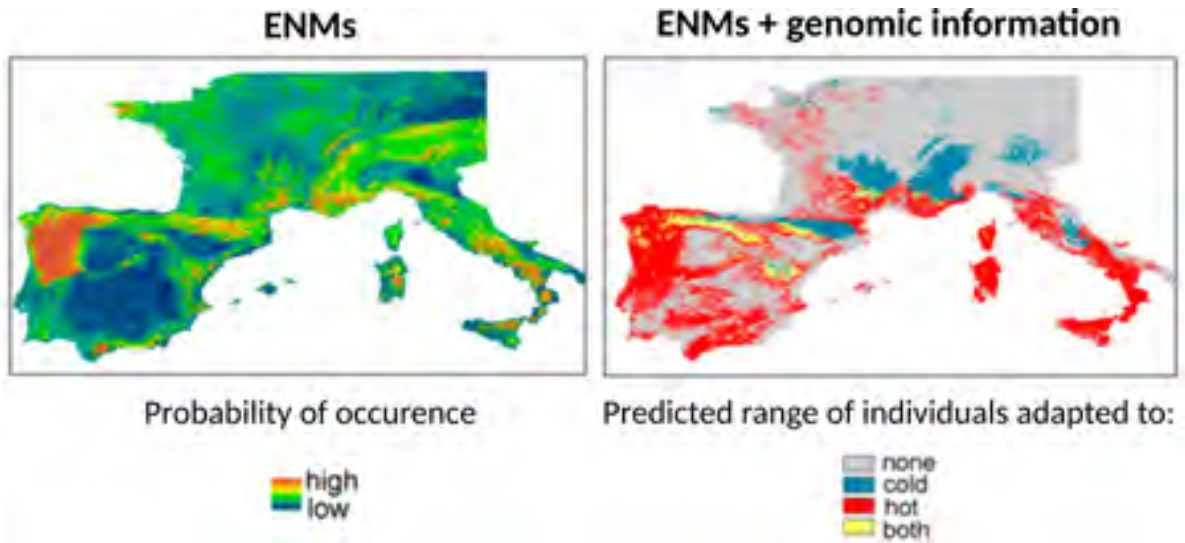

→ Hot–dry genotypes are predicted to expand their range at the expense of cold–wet genotypes.

→ Considering local climatic adaptations in ecological niche models (ENMs):

- reduces future range loss projections.
- **increases** the predicted potential for interspecific competition, through increased range overlap.

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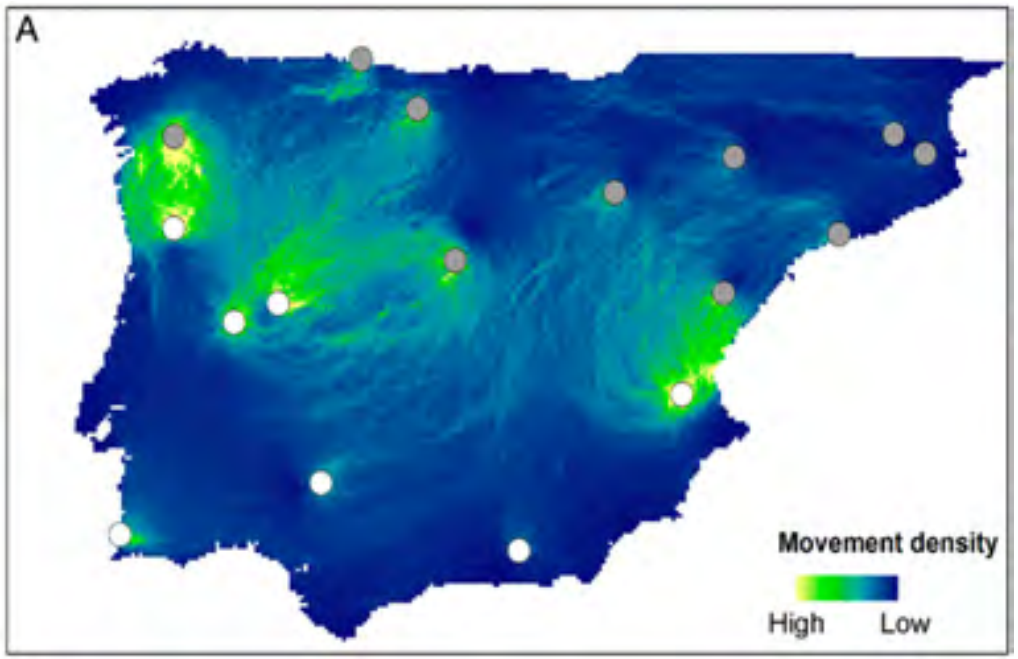

Evolutionary rescue potential under future climate change = predicted density of movement from populations or individuals adapted to hot–dry conditions (white circles) to those adapted to cold–wet conditions (gray circles) based on the effect of slope and tree/forest cover (landscape resistance) on movement.

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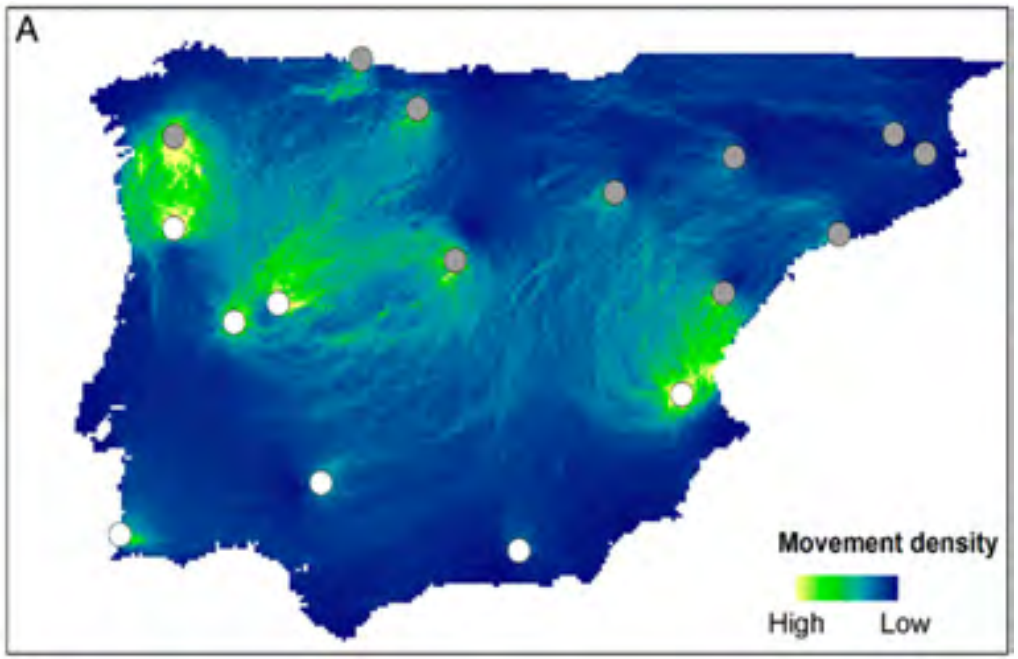

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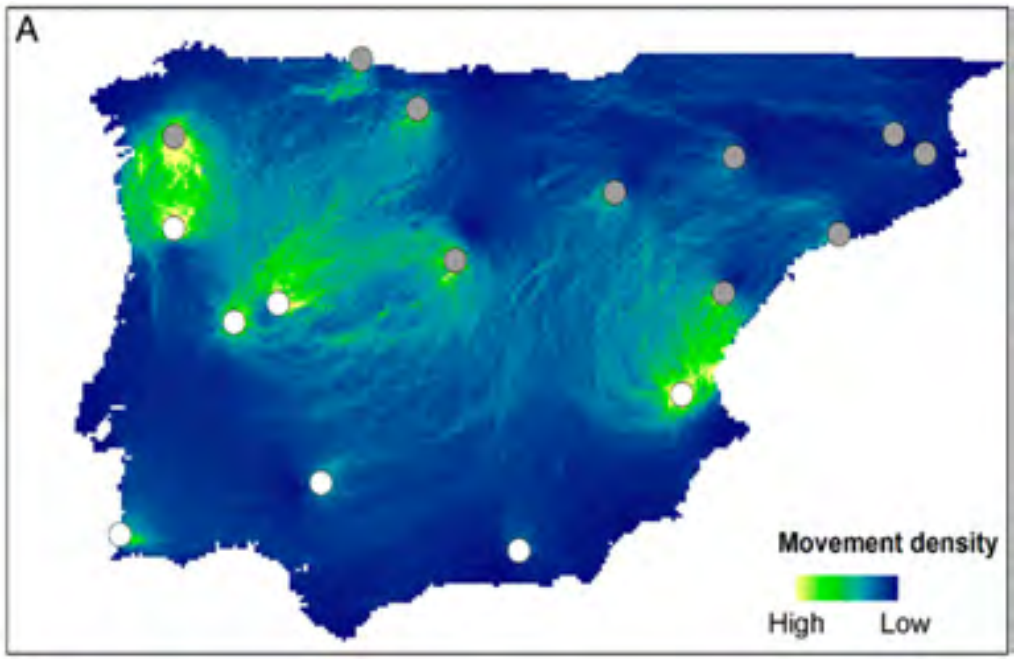

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→ In the other species, evolutionary rescue **may not be necessary** as most areas will remain suitable to cold-adapted individuals.

Introduction: from species-level to genome-informed modelling

Predicting short-term performance with trait-based approaches
- Methods and limits in predicting phenotypes based on genotypes
- Predicting phenotypes based on genotypes in natural populations
- Predicting phenotypes from gene-environment associations

Predicting the adaptive potential of populations under climate change
- Incorporating intraspecific climatic adaptations into ENMs
- The genomic offset framework
- Extending the genomic offset framework
- Potential applications

The genomic offset framework

Landmark papers

Fitzpatrick, M. C., & Keller, S. R. (2015). Ecological genomics meets community-level modelling of biodiversity: Mapping the genomic landscape of current and future environmental adaptation. *Ecology letters*, *18*(1), 1-16.

Rellstab, C., Zoller, S., Walthert, L., Lesur, I., Pluess, A. R., Graf, R., ... & Gugerli, F. (2016). Signatures of local adaptation in candidate genes of oaks (Quercus spp.) with respect to present and future climatic conditions. *Molecular Ecology*, *25*(23), 5907-5924.

Important reviews

Capblancq, T., Fitzpatrick, M. C., Bay, R. A., Exposito-Alonso, M., & Keller, S. R. (2020). Genomic prediction of (mal)adaptation across current and future climatic landscapes. *Annual Review of Ecology, Evolution, and Systematics*, *51*(1).

Rellstab, C., Dauphin, B., & Exposito-Alonso, M. (2021). Prospects and limitations of genomic offset in conservation management. *Evolutionary Applications*, *14*(5), 1202-1212.

The genomic offset framework

The genomic offset framework

Genomic data

Climatic data

Phenotypic data

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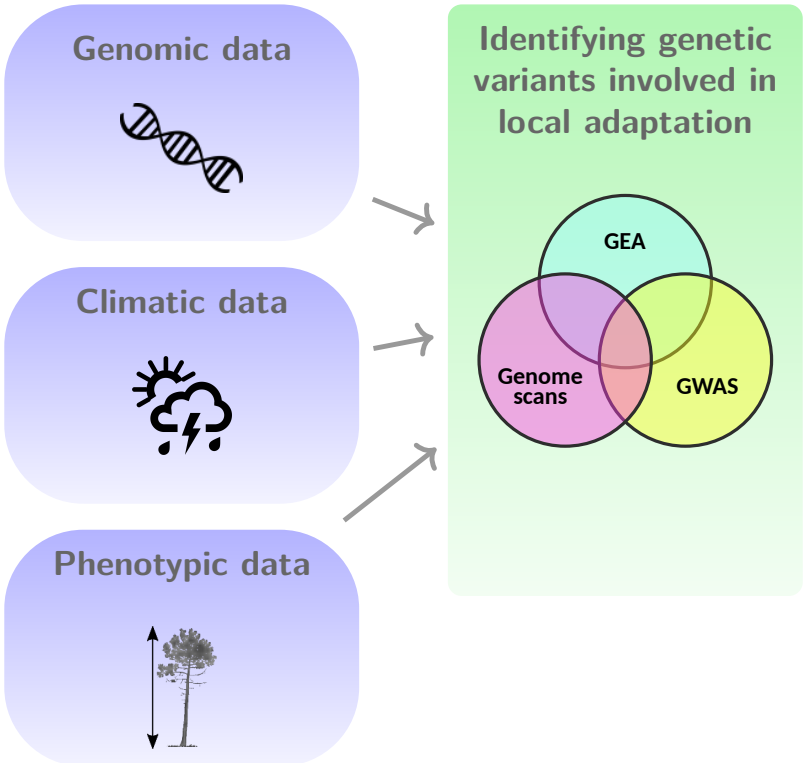

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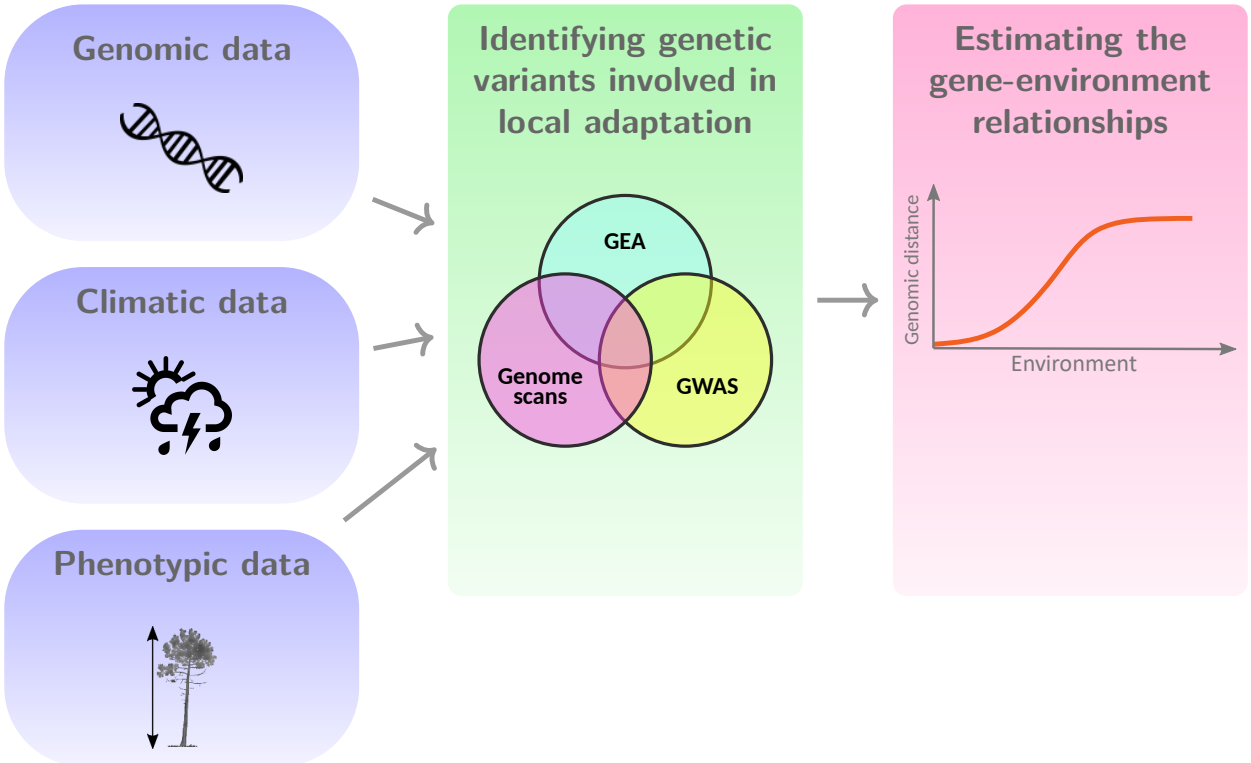

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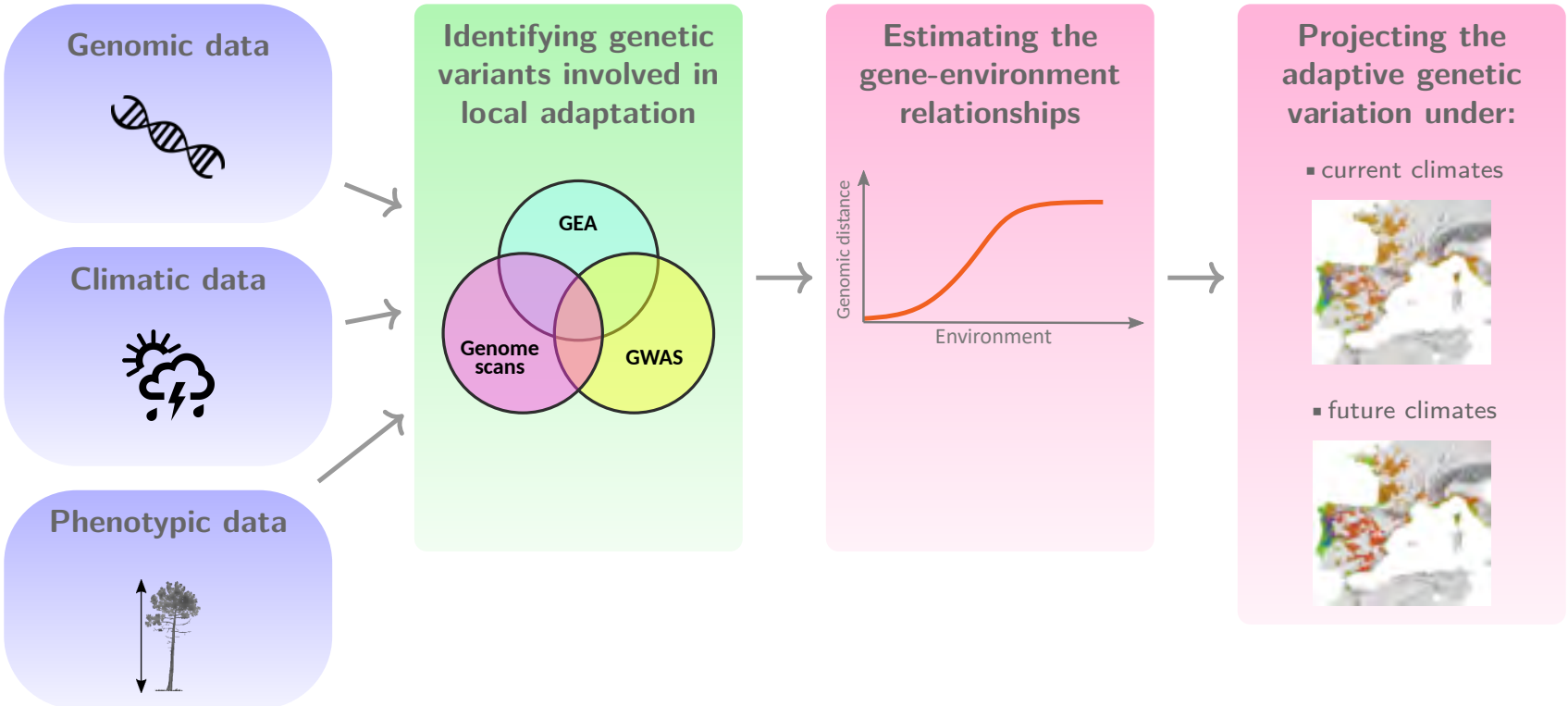

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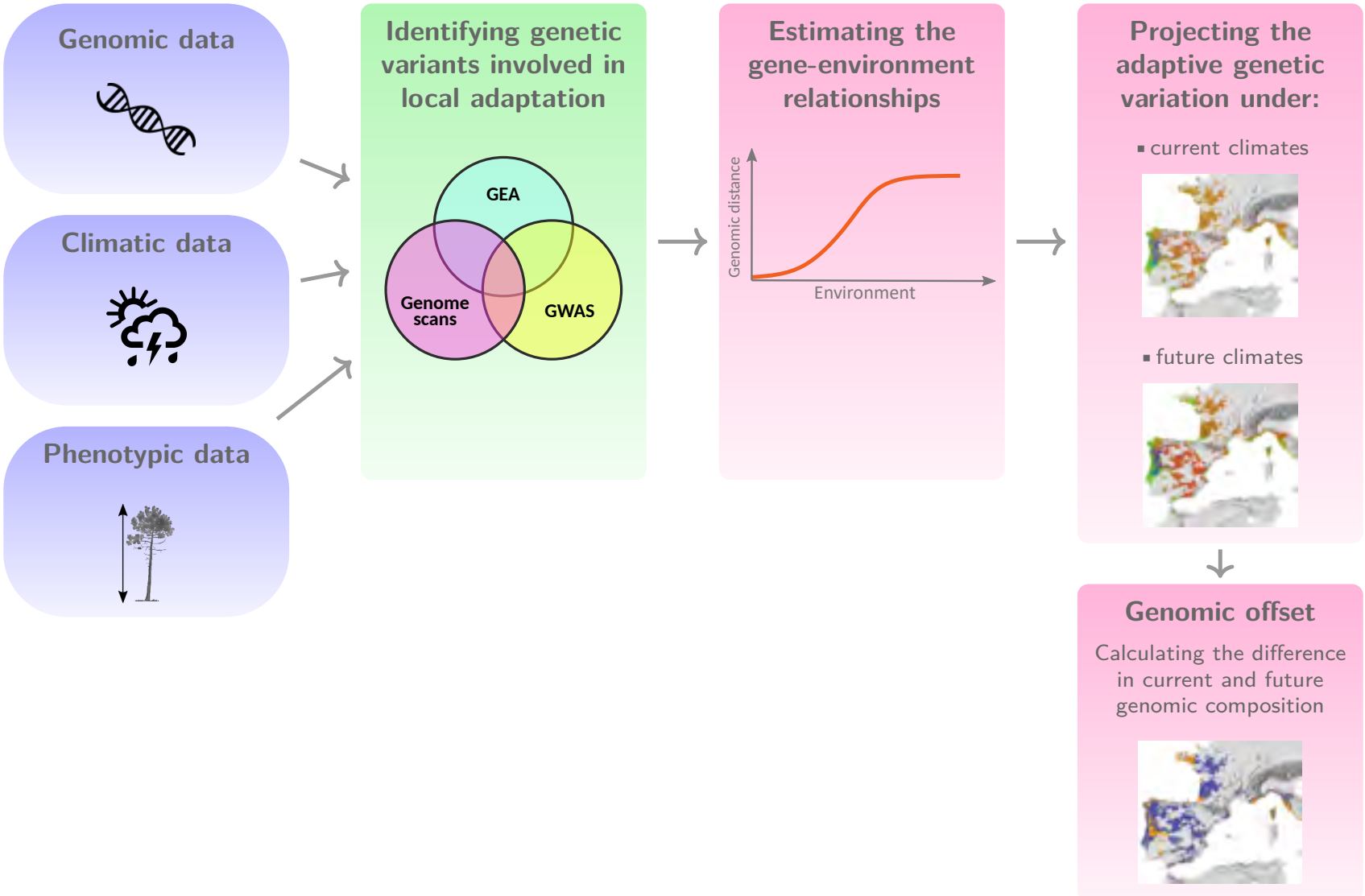

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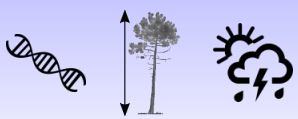
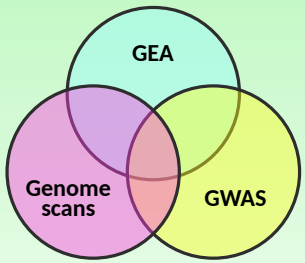
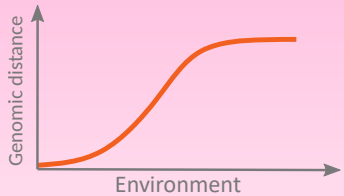


Identifying genetic variants involved in local adaptation



Estimating the gene-environment relationships



Projecting the adaptive genetic variation under:

- current climates

- future climates

Genomic offset

Calculating the difference in current and future genomic composition

Validating the assumptions and predictions

e.g. Testing whether populations with lower genomic offset exhibit relative fitness declines

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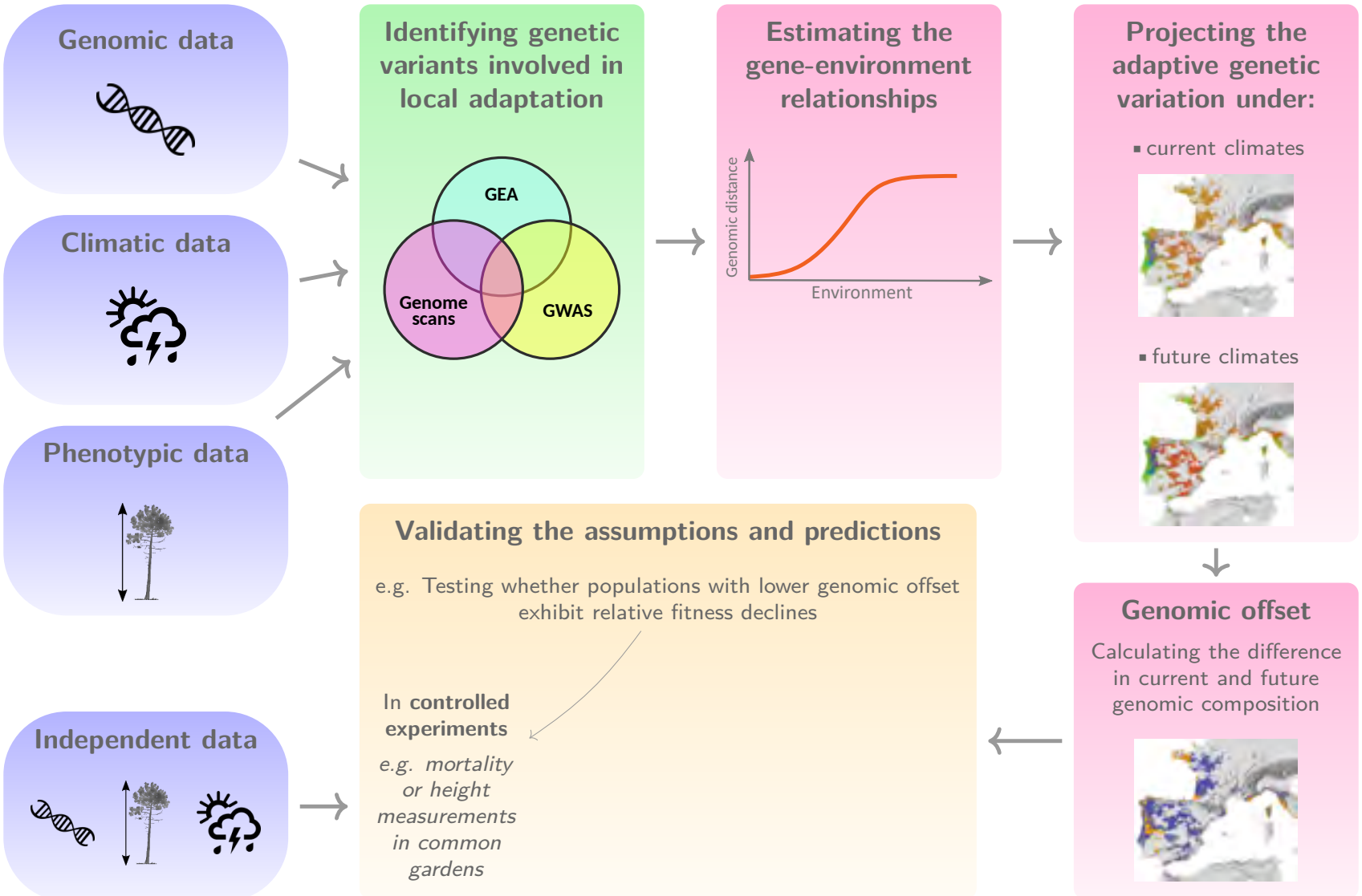

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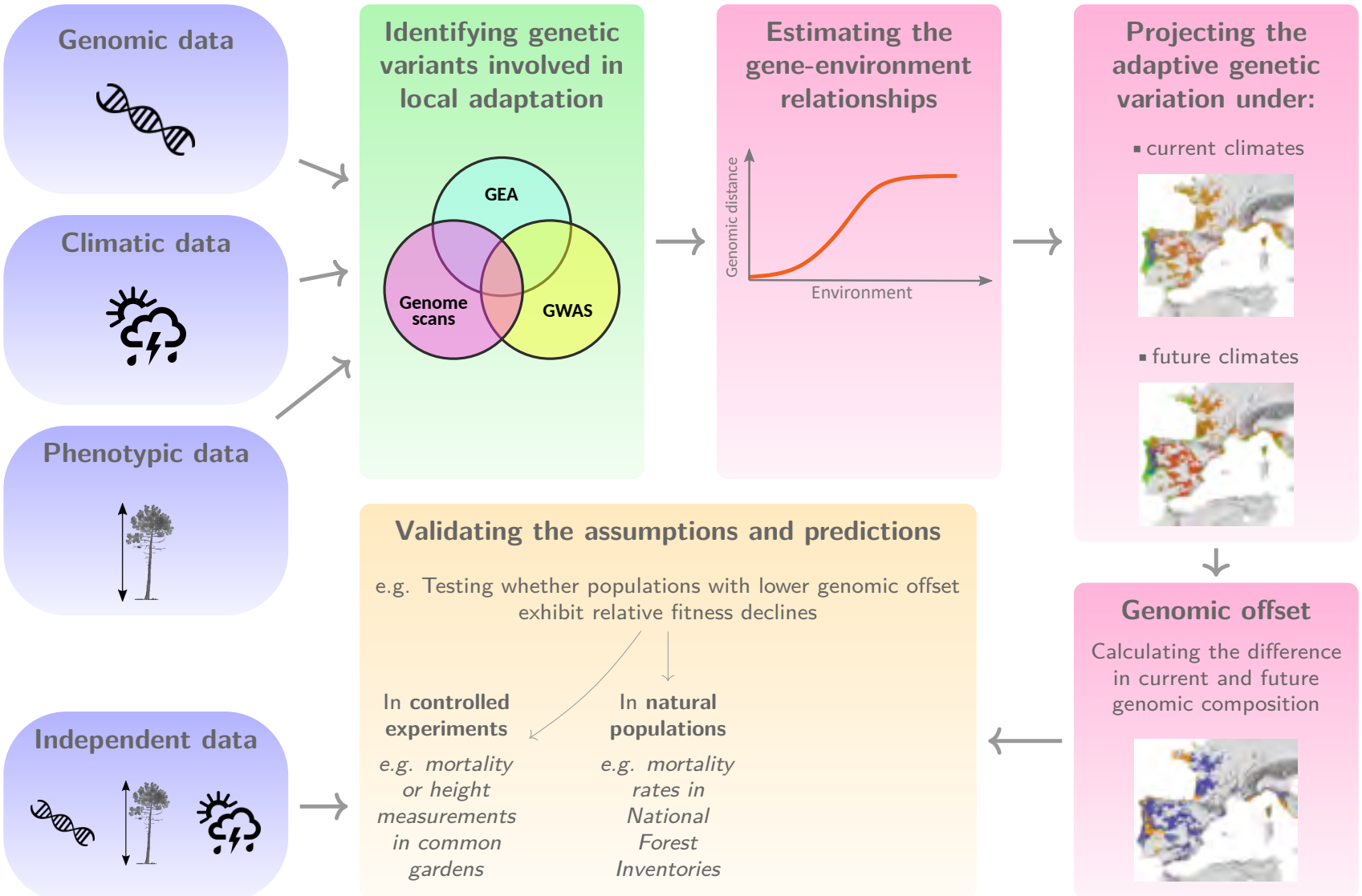

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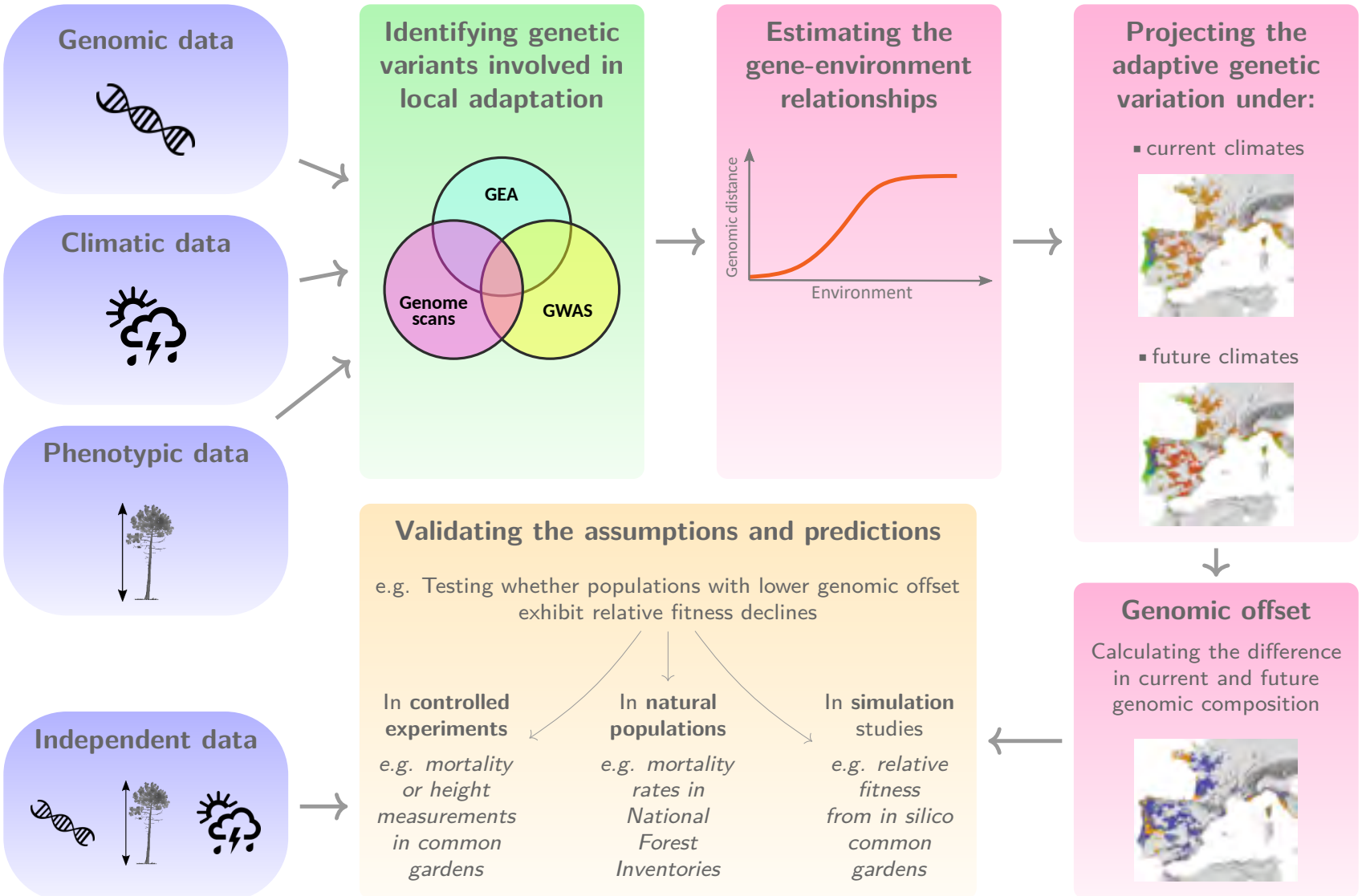
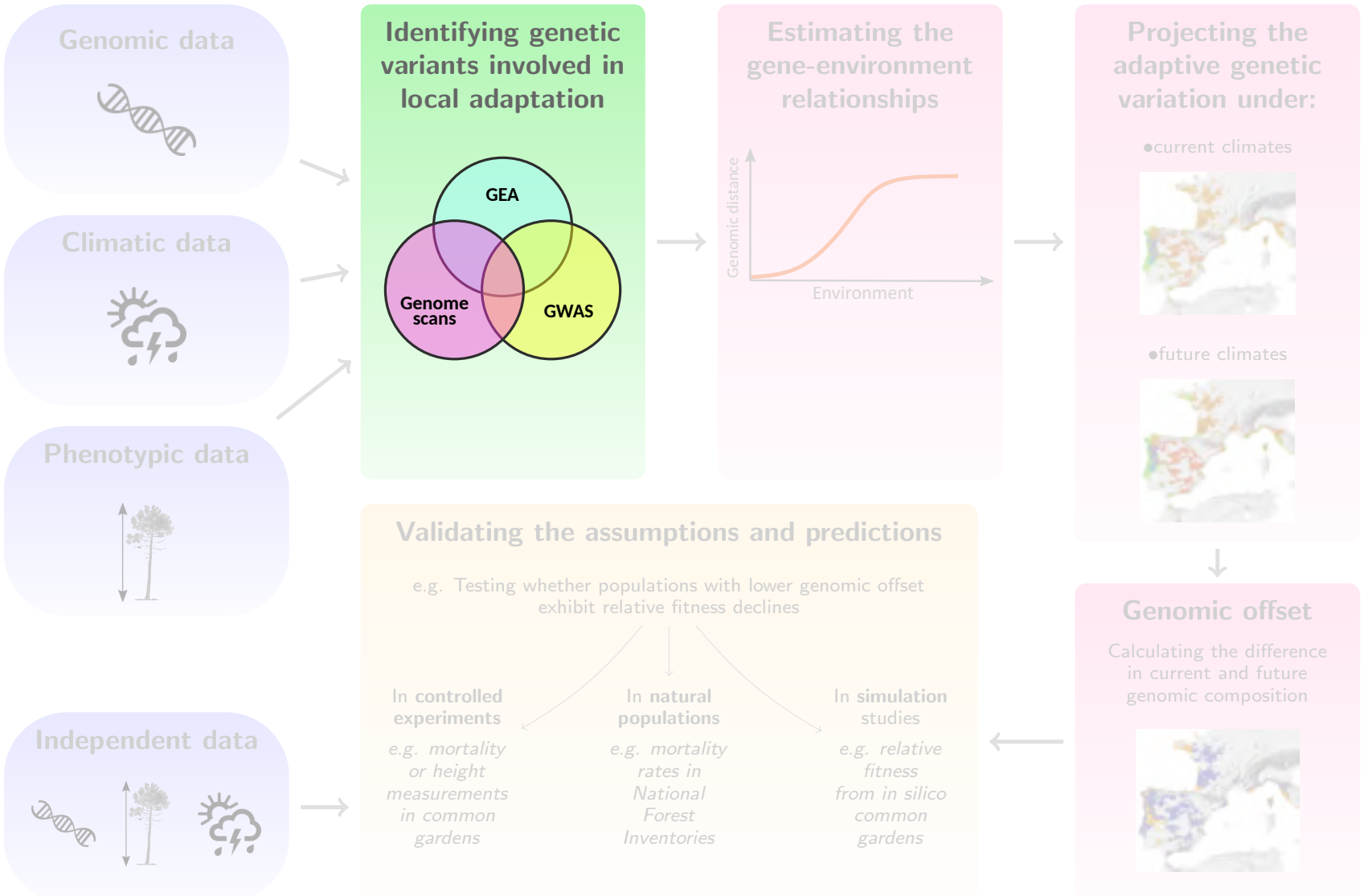


Discovery phase



Identifying genetic variants involved in local adaptation

Genome scans (outlier tests)

Identification of loci **deviating** from the **neutral distribution** of genetic variation.

F_{ST}-based methods: Arlequin and Bayescan.

Method based on selective sweeps: SweepFinder2.

Other methods: SelEstim.

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Identification of loci whose frequencies are associated with **climatic gradients**.

Single-locus methods: Bayenv, Bayescenv, LFMM, gINLAnd, Samβada

Multi-loci methods: RDA

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Genome-wide association studies (GWAS)

Identification of loci whose frequencies are associated with **adaptive traits**.

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- ✗ Choosing a set of climate variables and appropriate spatial and temporal scales to capture the most likely drivers of selection is challenging.

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Lotterhos and Witlock 2015, Forester *et al.* 2018, Ahrens *et al.* 2021

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✓ Can be relevant in **exploratory analyses** or when the **selective gradients** are **unknown**.

✗ Too conservative when **selection is well understood** and uninformative predictors are not used, and when the goal is to detect **weakly selected loci**.

Identifying genetic variants involved in local adaptation

Multiple confounding factors...

- **Demographic history**

Excoffier *et al.* 2009, Bonhomme *et al.* 2010, Lotterhos and Witlock 2014, Ahrens *et al.* 2018.

- **Population genetic structure** reflecting gene flow levels and population isolation

Vasemägi 2006, Le Corre and Kremer 2012.

- Gene surfing

Bierne *et al.* 2011, Ahrens *et al.* 2018.

- Background selection

Bierne *et al.* 2011, Lotterhos and Witlock 2015.

- Endogenous genetic barriers

Bierne *et al.* 2011, de Mita *et al.* 2013

- Genomic variation in the recombination rate

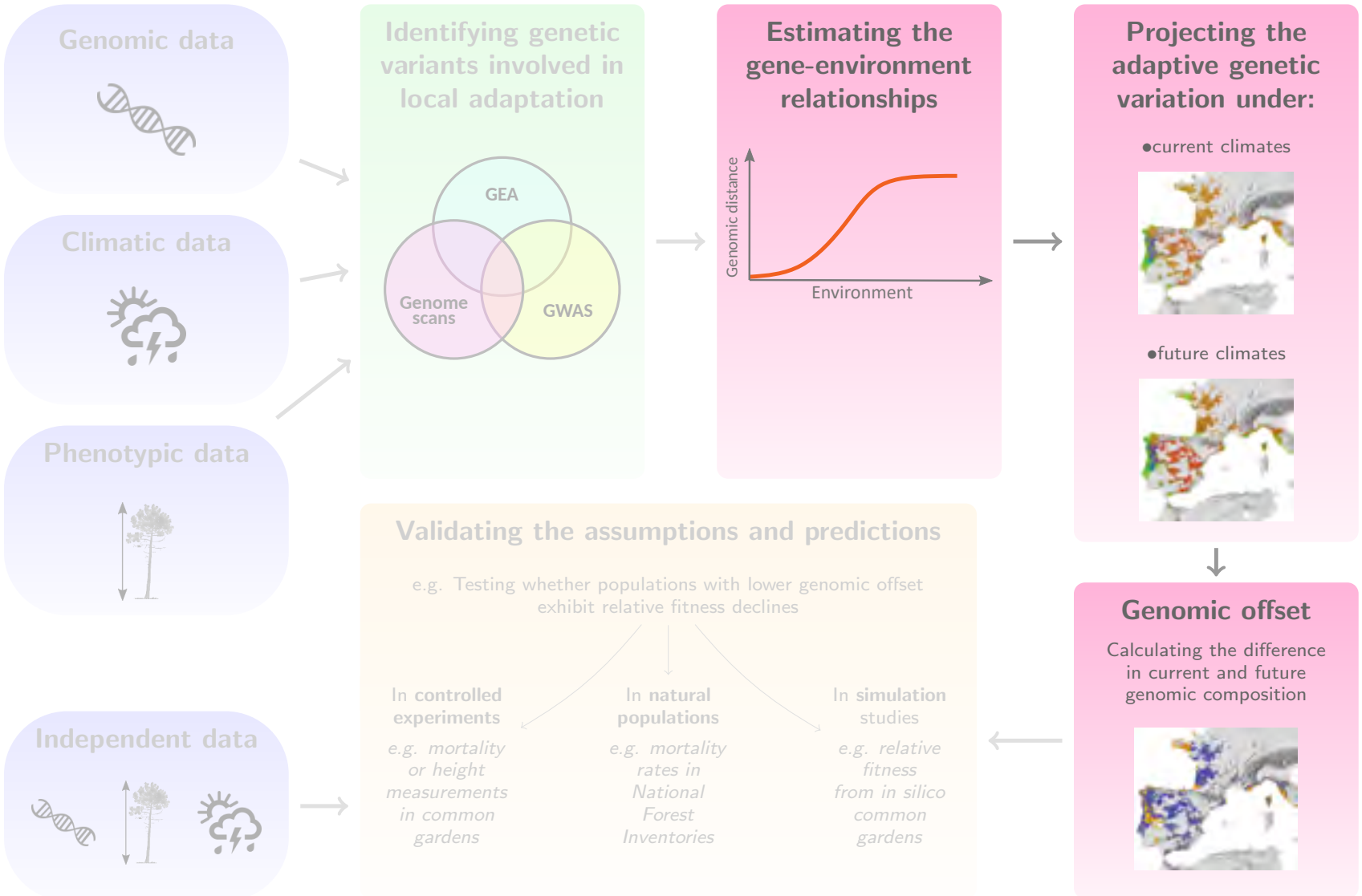
Noor and Bennett 2009, Roesti *et al.* 2012, Cruickshank and Hahn 2014.

- Genetic hitchhiking

Oleksyk *et al.* 2010, Pritchard and Di Rienzo 2010, Tiffin and Ross-Ibarra 2014.

...

Prediction phase



Predicting the genomic offset with GDM and GF

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- **Nonlinear multivariate** approaches that model the **turnover in allele frequencies** along **environmental gradients**.

- **Increasingly used** in **forest trees**, as particularly well suited to long-lived and sessile organisms.

  e.g. Fitzpatrick *et al.* 2021, Gougherty *et al.* 2020, Keller *et al.* 2018, Lu *et al.* 2019, Supple *et al.* 2018, Vanhove *et al.* 2021.

Predicting the genomic offset with GDM and GF

Modelling the turnover in allele frequency along environmental gradients.

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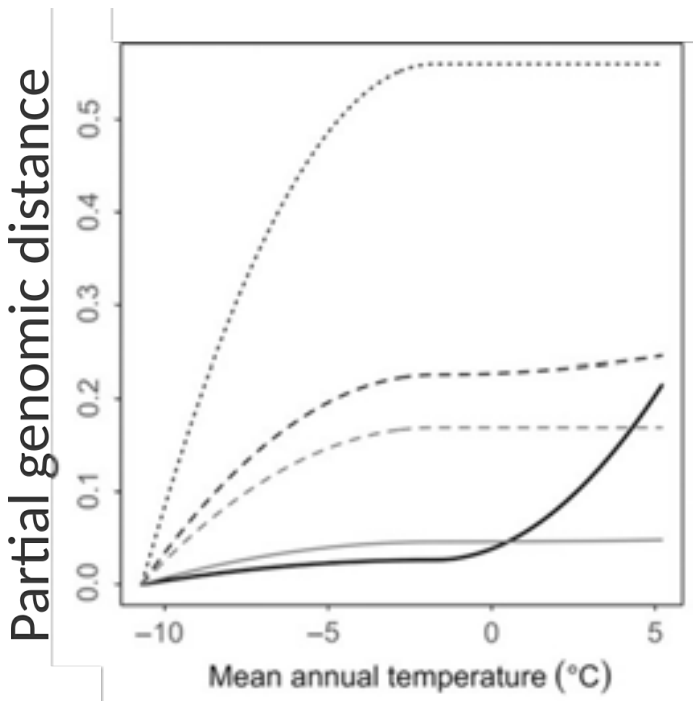
Generalized Dissimilarity Modelling

Models **pairwise genetic dissimilarity** among populations as a function of **pairwise population differences** in **environmental** and **geographic** variables.

→ **I-spline turnover functions**



Predicting the genomic offset with GDM and GF

Modelling the turnover in allele frequency along environmental gradients.

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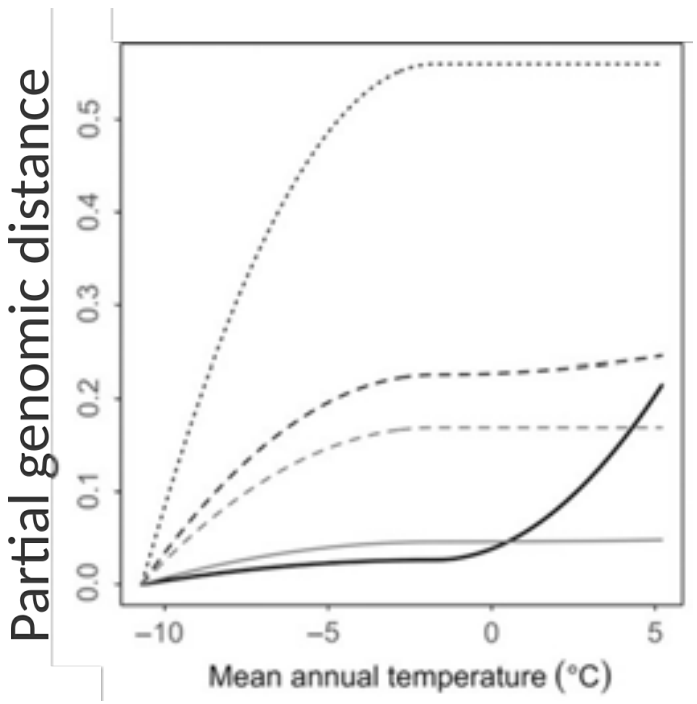
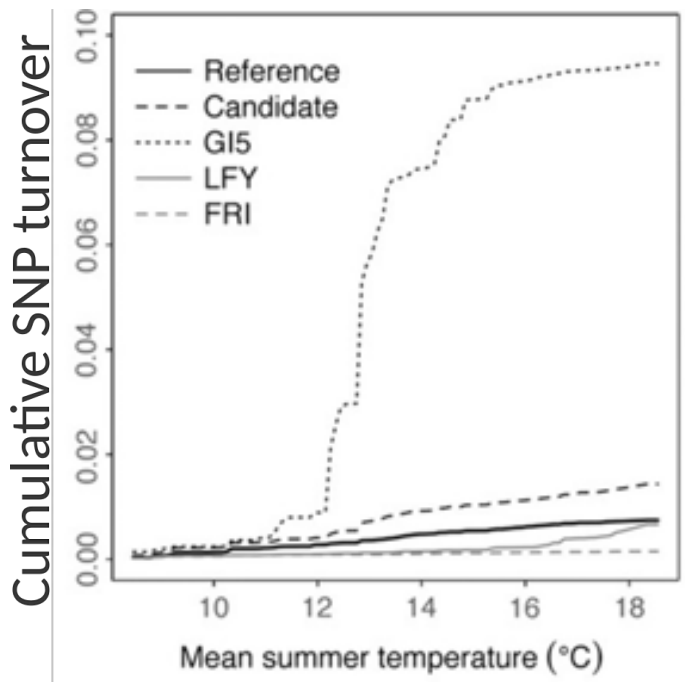


Gradient Forests

Fits an ensemble of **decision trees** that determine how well **partitions** distributed at numerous **split values** along each gradient explain **changes in allele frequencies** on either side of a split.

→ **Cumulative importance turnover functions**



Predicting the genomic offset with GDM and GF

Projecting the genomic composition under current and future climates

The GDM and GF turnover functions are used to **transform** the current and future values of the environmental covariates into **genetic importance values**, thus which allows to project the **current** and **future genomic composition** across the area of interest (e.g the species range).

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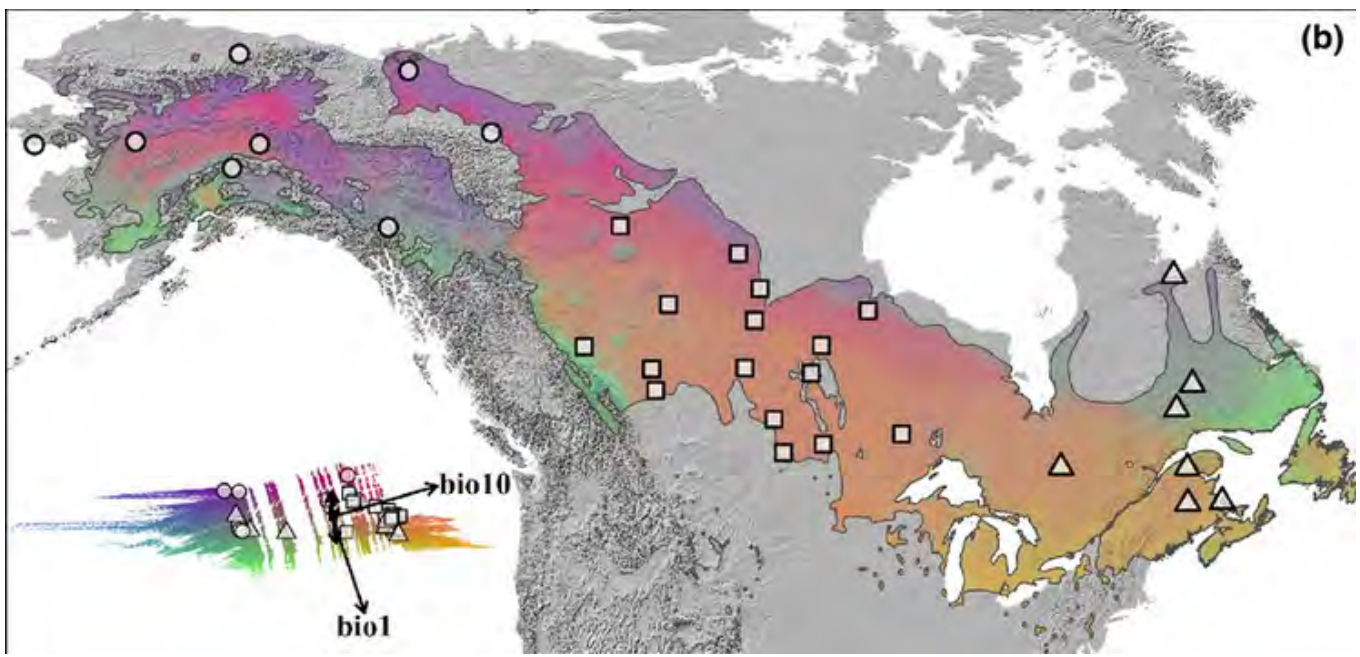
To aid visualisation, a principal component analysis (PCA) is used to reduce the dimensionality of the transformed environmental covariates and a RGB colour palette is assigned to the first three PCs, with resulting **similar colour** for **similar expected patterns of genomic composition**.



From Fitzpatrick and Keller (2015)

Predicting the genomic offset with GDM and GF

Predicting the genomic offset across the landscape

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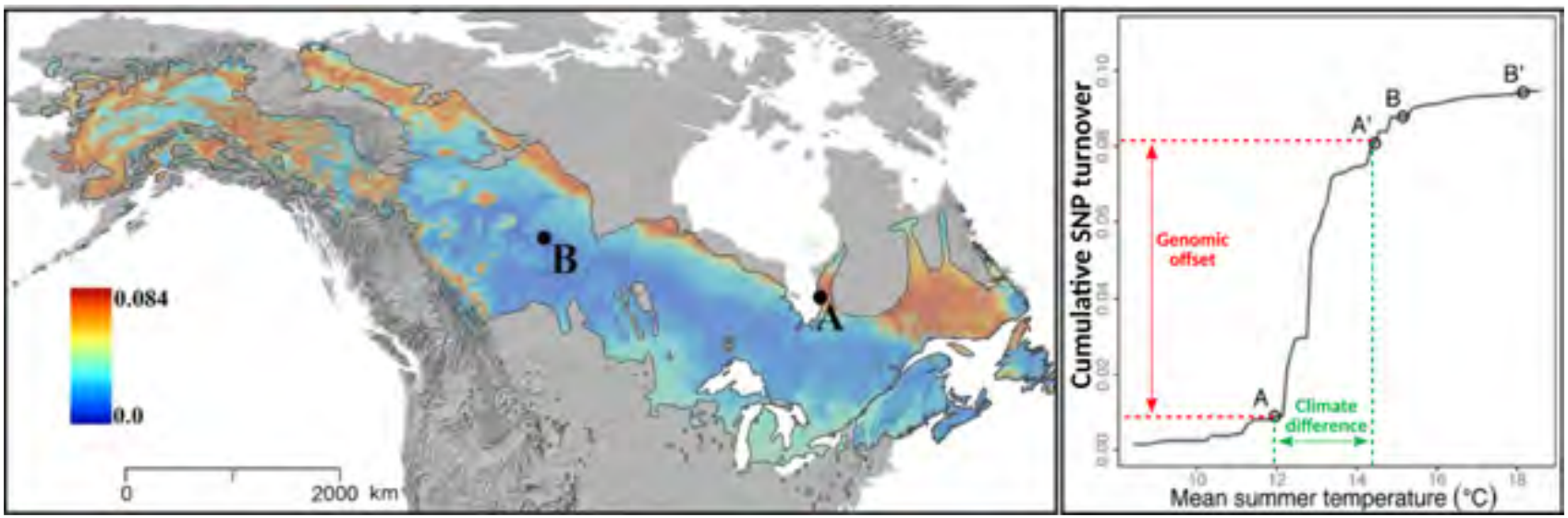
It is expected to indicate how much the **genomic composition** would have to **change** to **maintain** the **gene-environment associations** observed under **current** environmental conditions.



From Fitzpatrick and Keller (2015)

Predicting the genomic offset with linear regression (RONA)

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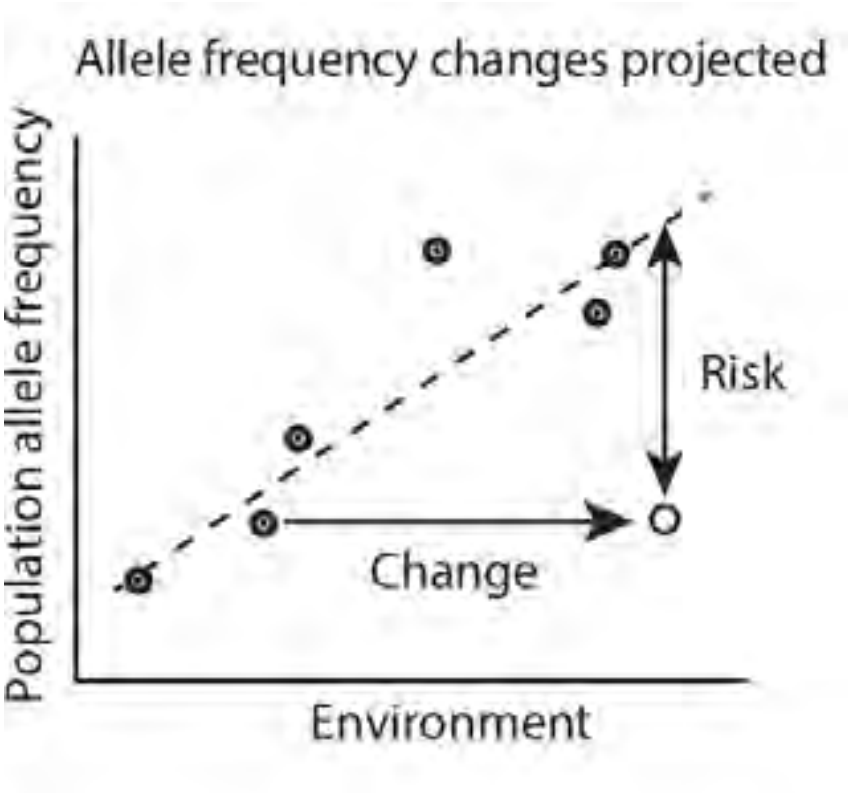

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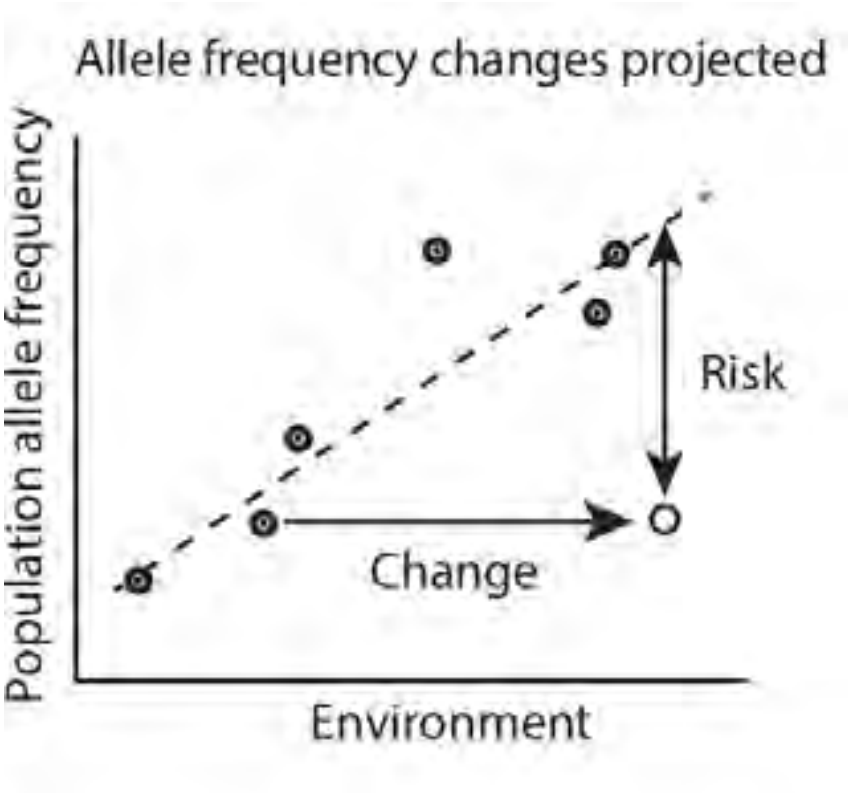

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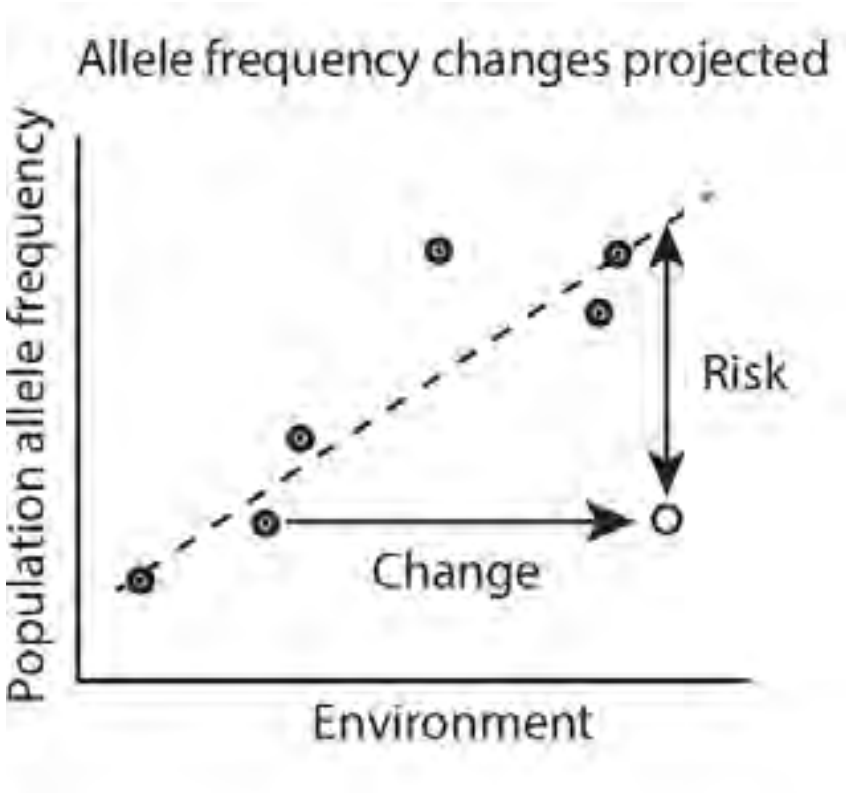

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Risk of nonadaptedness (RONA) = average difference across the selected loci between the observed allele frequencies under current climates and the expected allele frequencies under future climates.

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Capblancq and Forester 2021. Genotype-environment associations

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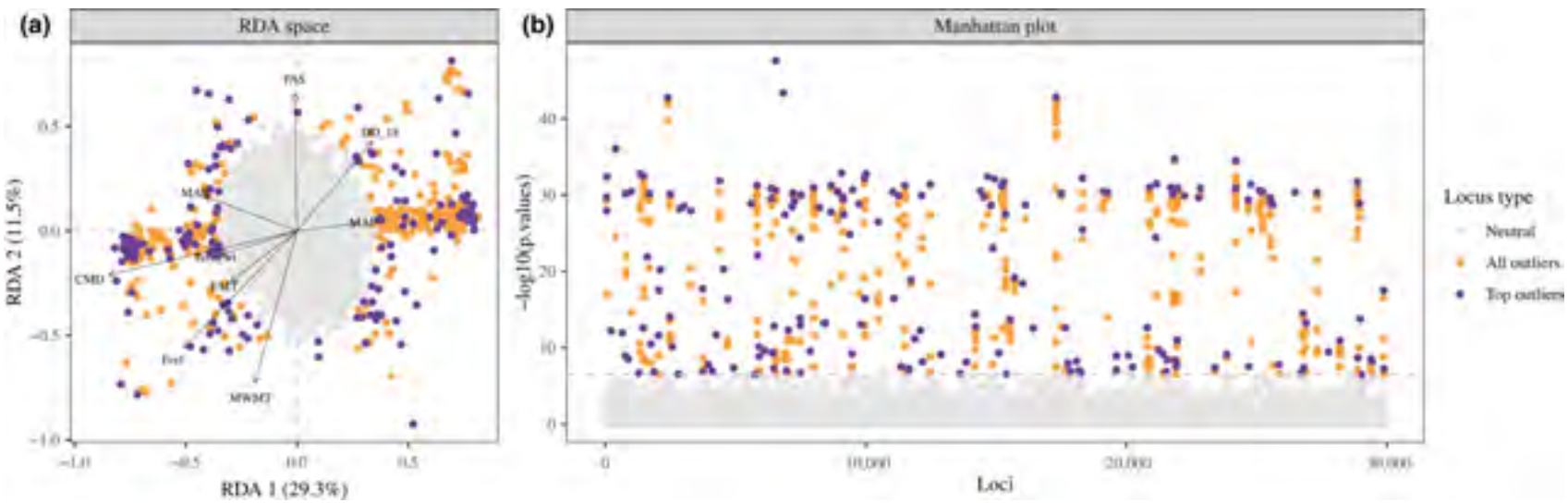

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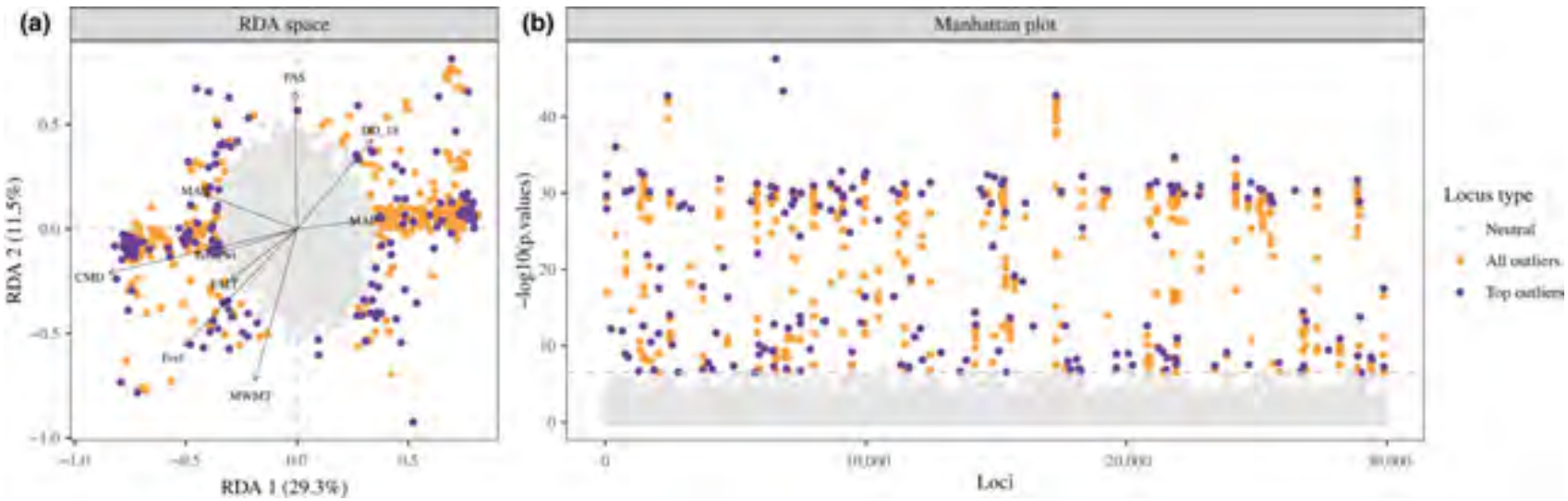

→ The **constrained ordination axes** consist of covarying sets of genotypes that are correlated with the multivariate environment.

→ The **loci putatively under selection** are the markers showing **extreme loadings** (i.e. score) along one or multiple axes.

Predicting the genomic offset with Redundancy analysis (RDA)

Capblancq and Forester 2021. Spatial projections of adaptive gradient(s)

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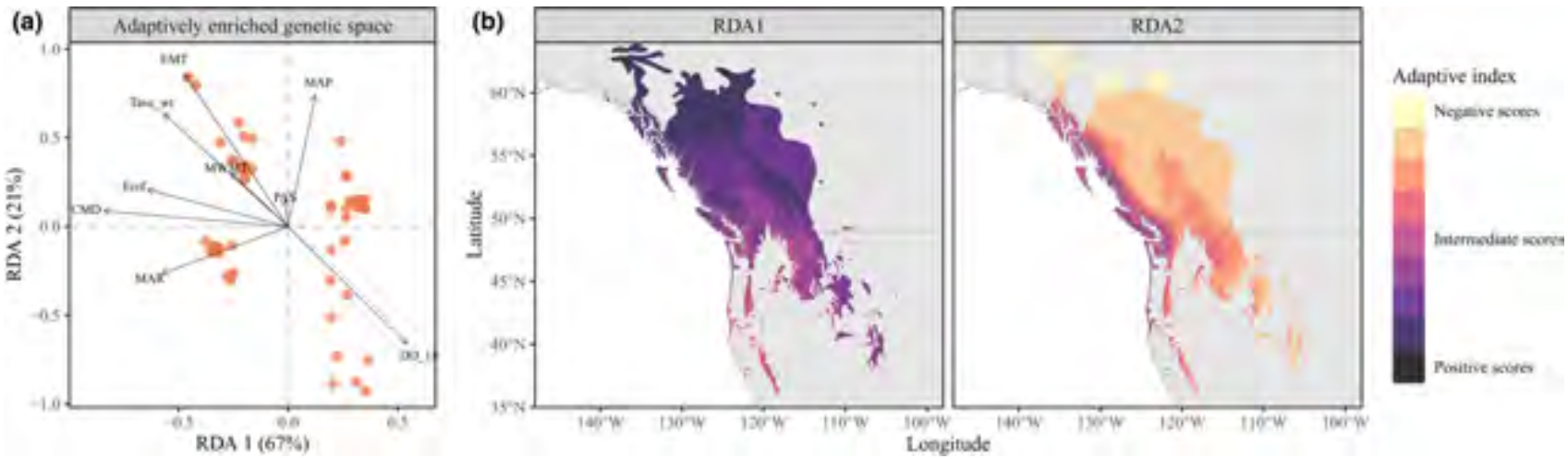

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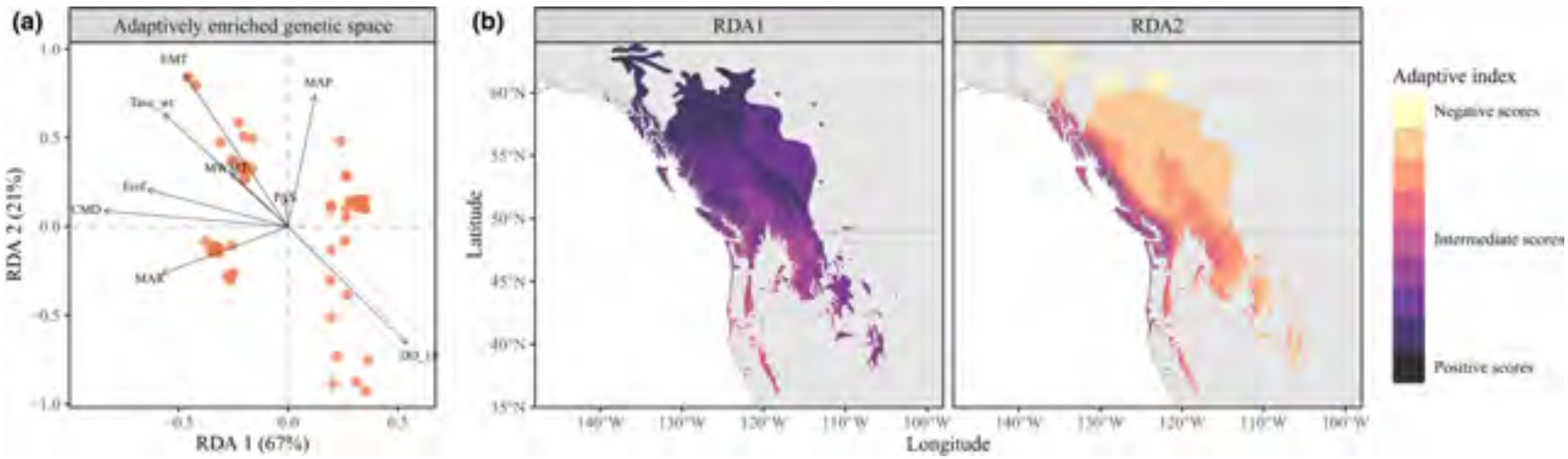

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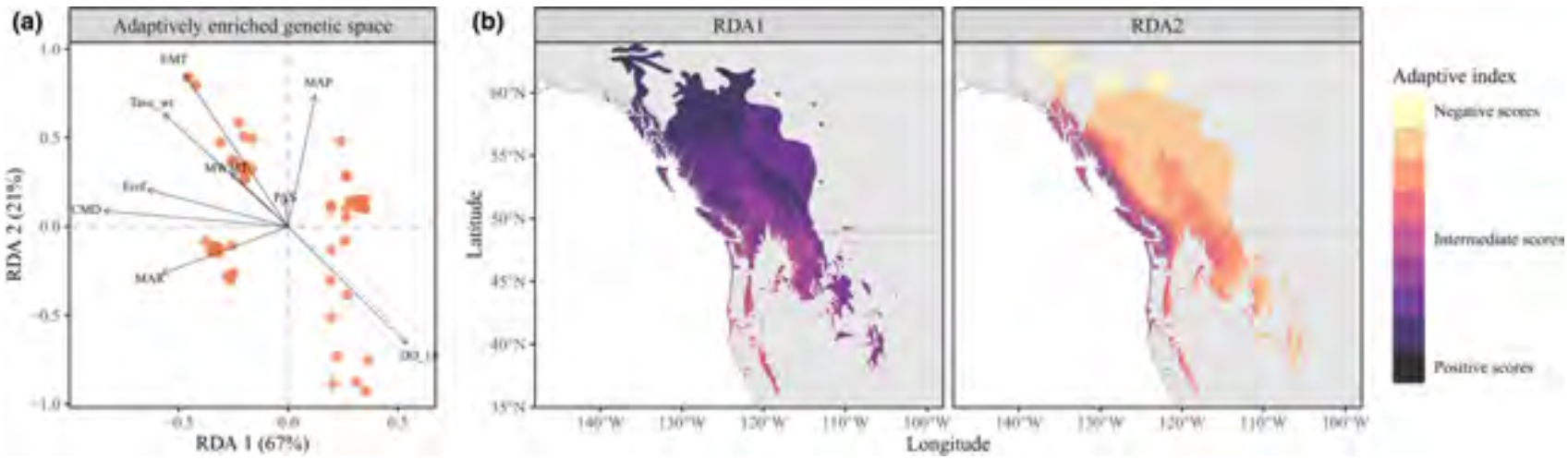

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→ In this example, the **spatial projection** of the **adaptive gradient** across the landscape shows how RDA1 index contrasts southern/low elevation areas from northern/high elevation areas, and how RDA2 index contrasts coastal/southern areas from inland/mountainous areas.

Predicting the genomic offset with Redundancy analysis (RDA)

Capblancq and Forester 2021. Predicting the genomic offset

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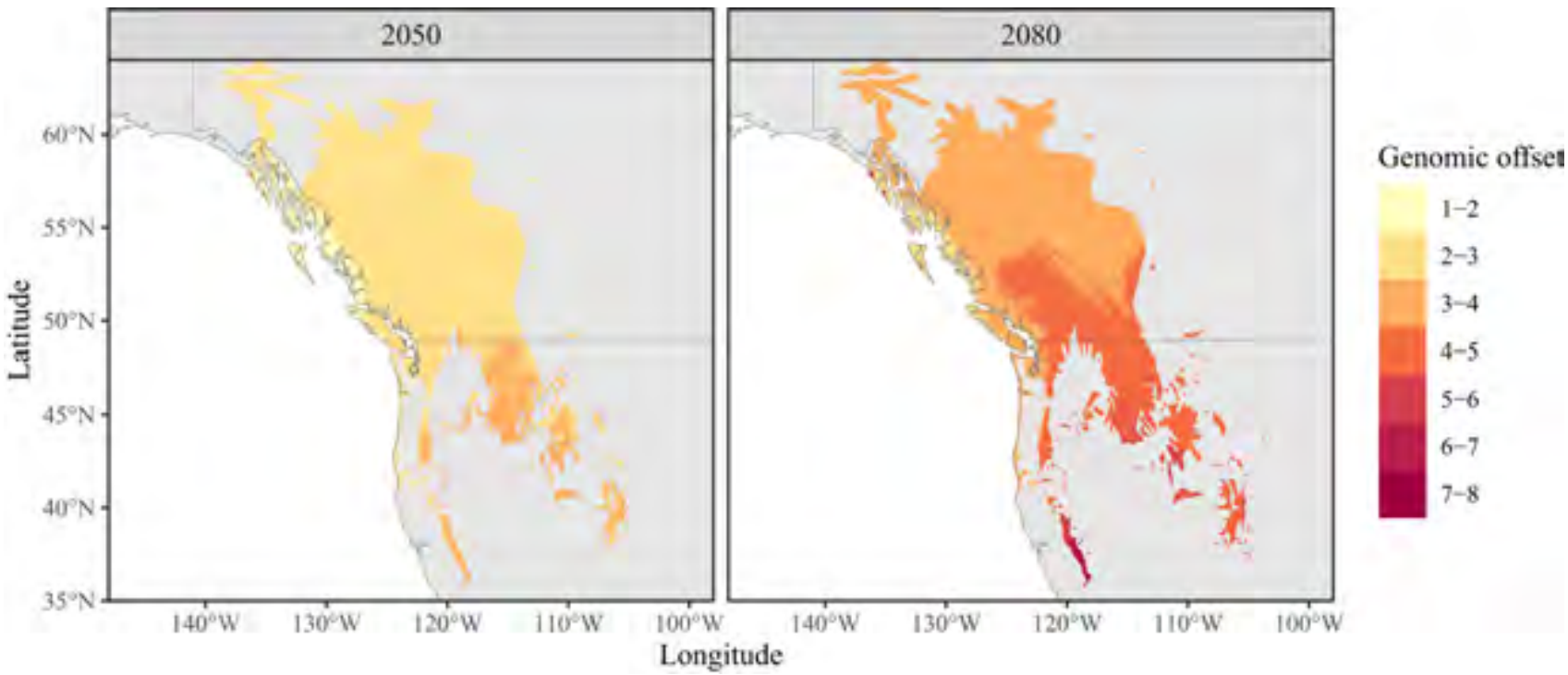
The **genomic offset** is calculated as the difference between the two predictions, and provides an estimate of the **shift in adaptive index** that would be required to track climate change.



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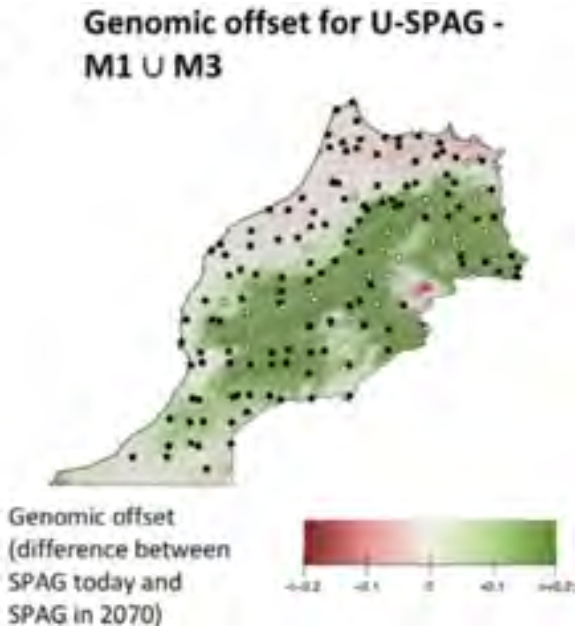

Union SPAGs (U-SPAGs) = probabilities of finding at least one of the adaptive single-locus genotypes of interest.

→ **epistatic situation** where the presence of an adaptive single-locus genotype is sufficient for securing the selective advantage, while additional adaptive genotypes do not confer additional advantages.

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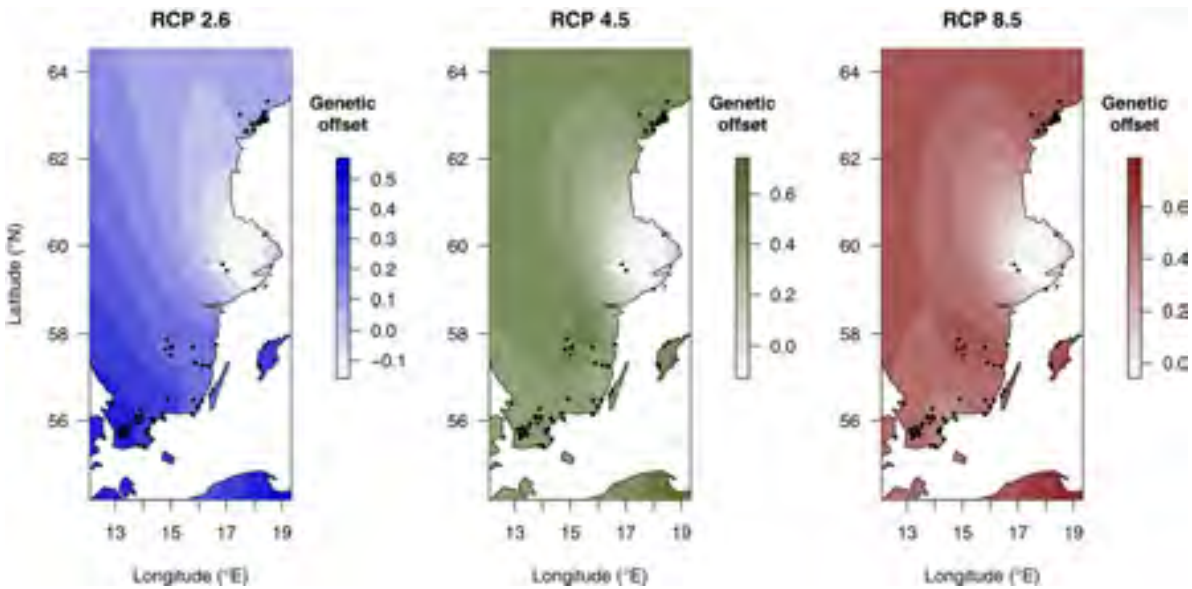

Predicting the genomic offset

To sum-up:

$\rightarrow$ Genomic offset approaches are in their infancy of development and applications.

$\rightarrow$ A growing number of methods, each with different pros and cons.

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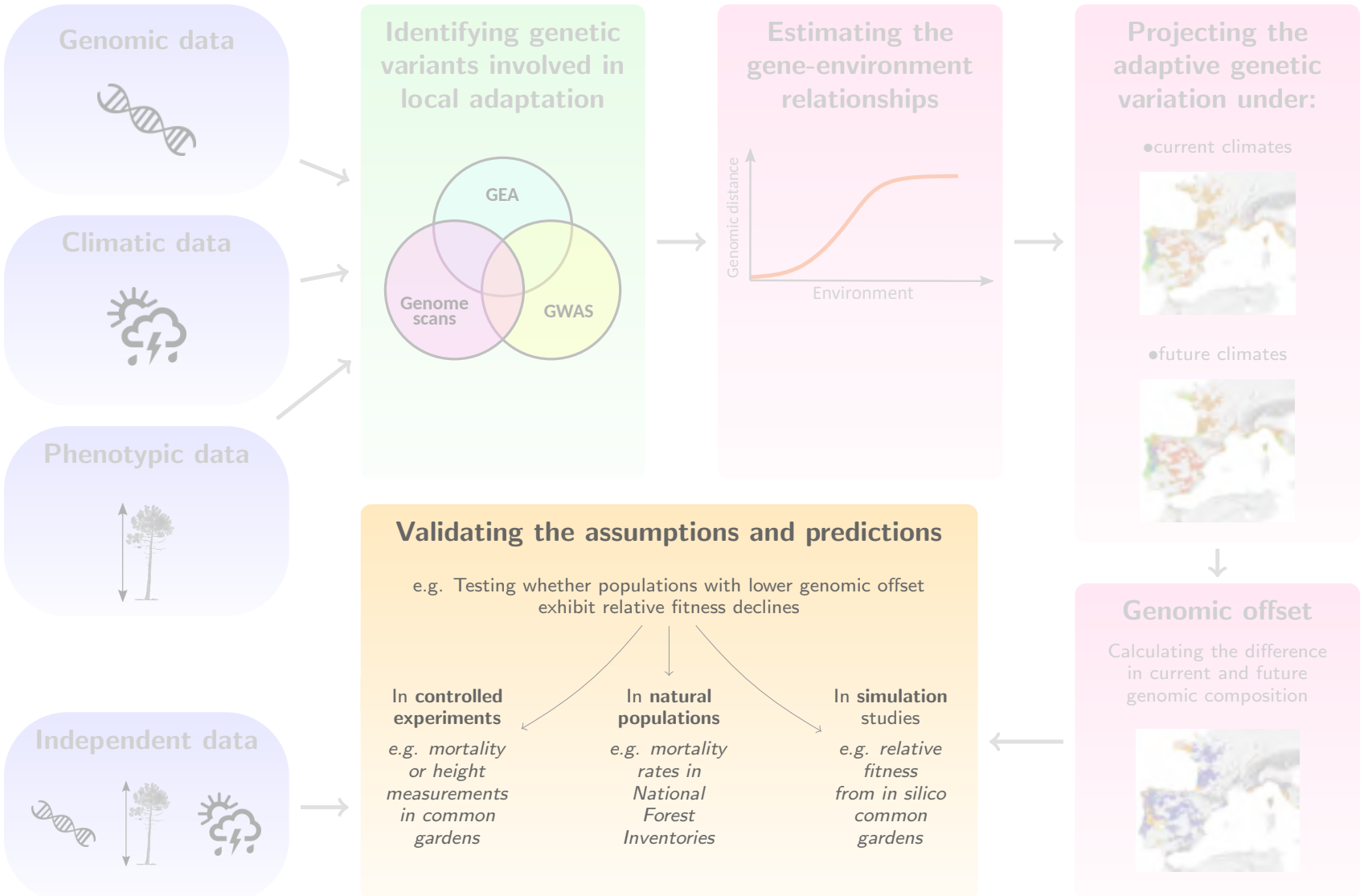

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→ a inherent assumption of **space-for-time substitution approaches**.

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- verifying the **phenotypic effects** of the candidate genes under **controlled conditions** or via **functional validation**, e.g. through genetic transformation into specific mutant backgrounds, gene editing of putatively causal sites, or by knocking back gene expression.

e.g. Exposito-Alonso et al. 2019, Yoder et al. 2014, Curtin et al. 2017, Monroe et al. 2018, Rohde et al. 2018

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• **Adaptation lags** to temperature observed in valley oak, with fastest growth rates occurring at cooler temperatures than populations are currently experiencing.

→ may be caused by the **rapid rate** of **current climate change** to which populations **are not adapting fast enough**.

Browne *et al.* 2019

Validation phase

Are populations at their adaptive equilibrium?

Validation phase

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Can be tested with the genomic offset approach itself!

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Borell *et al.* 2019

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The **risk of non-adapteness** (RONA; equivalent to the genomic offset) was calculated for **specific populations**.

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$\rightarrow$ measures the **mismatch** between their **current** genomic composition and the **required** genomic composition to be adapted to their current environment (based on the gene-environment associations measured in the other populations).

$\rightarrow$ is proportional to the variation in allele frequency that would be required for the population to optimally adapt to its local environment.

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Do populations with **higher predicted genomic offset** show **lower relative fitness**?

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Can be evaluated with:

- controlled experiments such as common gardens.
- observational data.
- *in silico*.

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Informs on model robustness in the face of:

- **demographic** and **stochastic processes** that might also affect the spatial variation in allele frequencies (e.g. expansion history, gene flow, genetic drift, mutation).
- **genetic architecture** of climate adaptation (polygenic trait architectures, G×E interactions, nonadditive genetic variance).

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*Validating genomic offset predictions in **common gardens***

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The turnover functions are used to predict the genomic offset of populations when transplanted from their environment of origin to the environment of the common garden.

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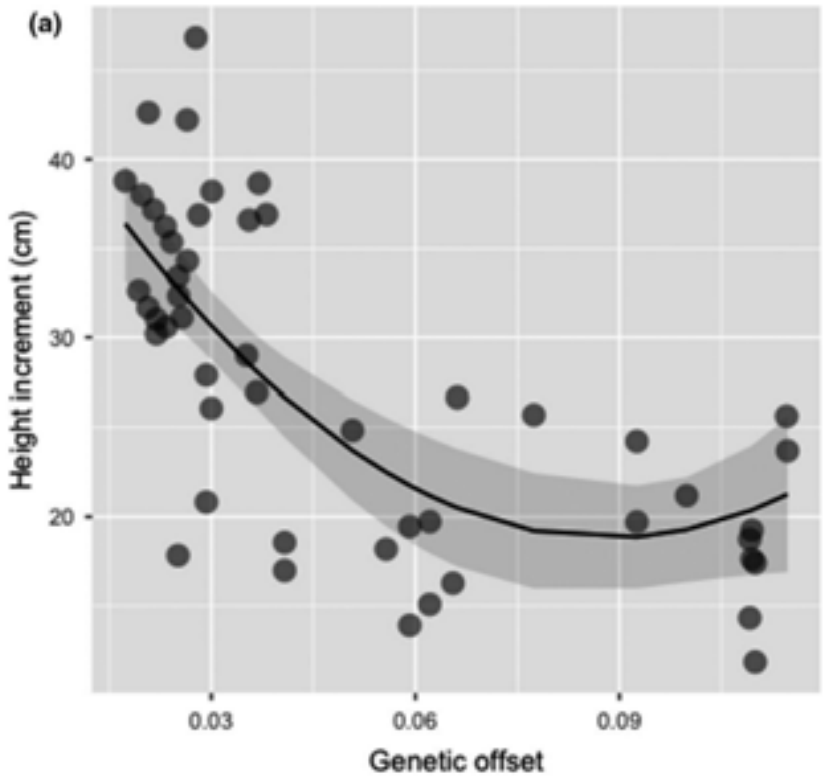

Fitzpatrick *et al.* 2021.

→ As expected, the predicted genomic offset was negatively associated with height growth increment measured in common gardens.

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Validating genomic offset predictions in ***common gardens***

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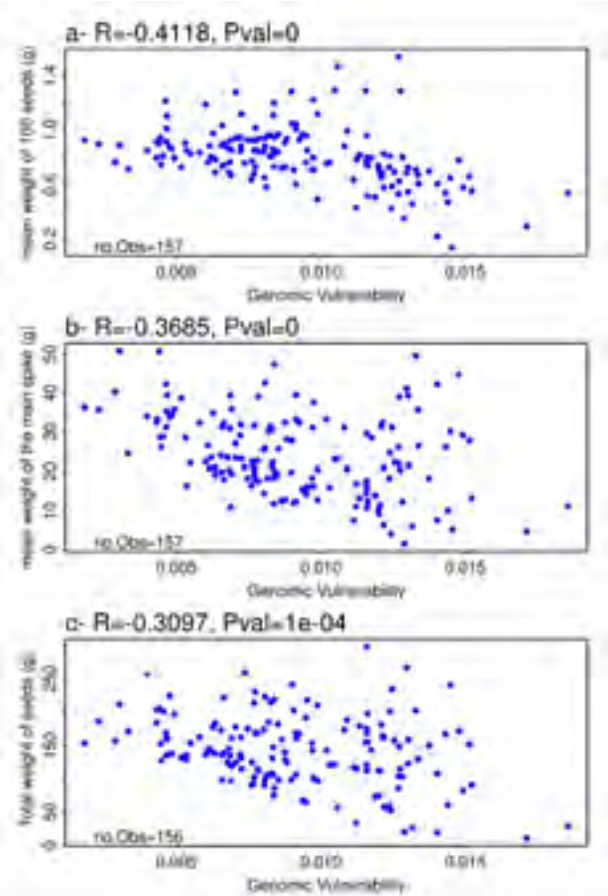

Rhoné *et al.* 2021.

A study investigating the patterns of potential maladaptation in 173 pearl millet landraces of agronomic importance in West Africa.

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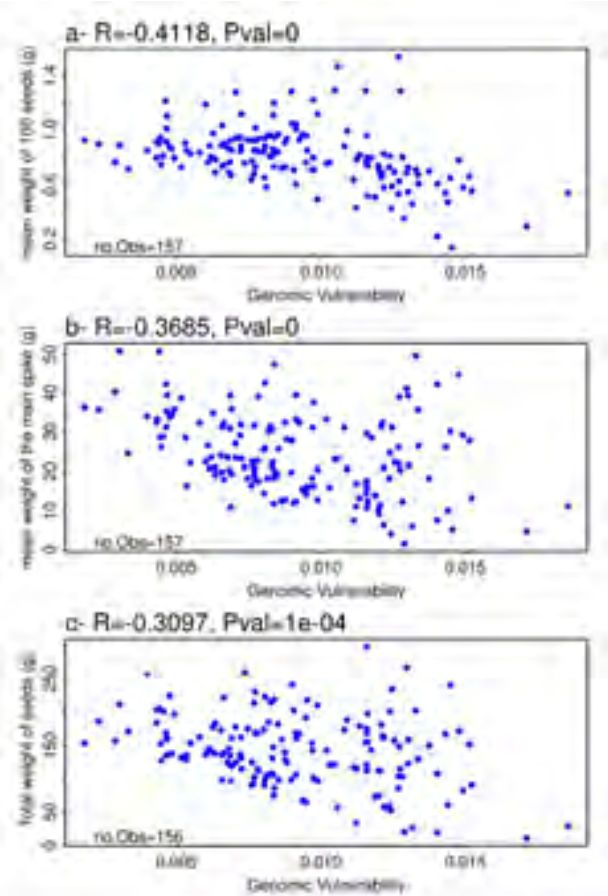

Rhoné *et al.* 2021.

A study investigating the patterns of potential maladaptation in 173 pearl millet landraces of agronomic importance in West Africa.

→ As expected, the predicted genomic offset is **negatively associated** with **yield-related traits** in a common garden experiment in Niger.

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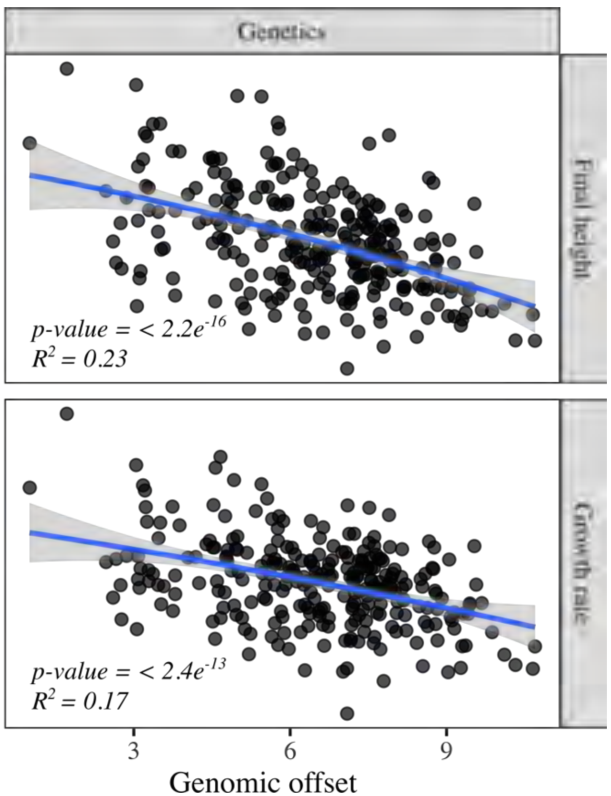

Capblancq and Forester 2021.

1,594 seedlings (from 281 provenances) of lodgepole pine planted in a common garden in Vancouver and genotyped for 29,941 SNPs (after filtering).

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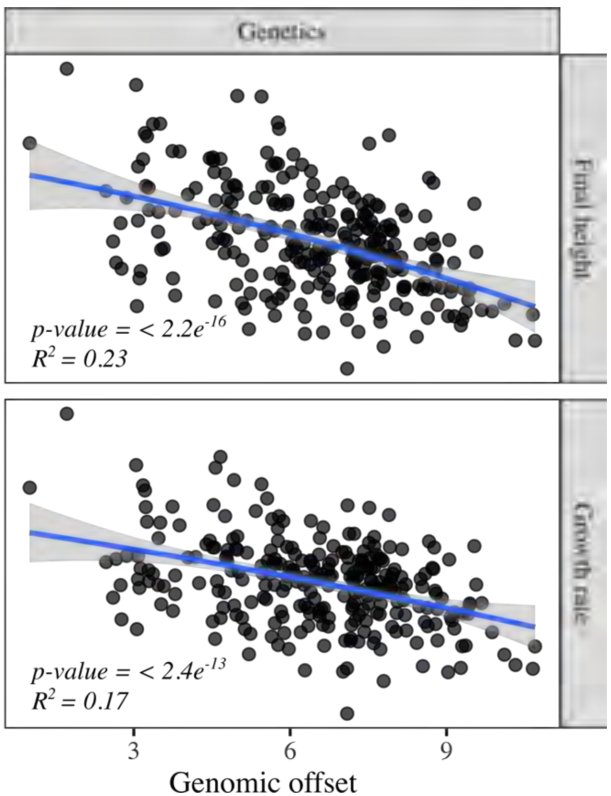

Capblancq and Forester 2021.

1,594 seedlings (from 281 provenances) of lodgepole pine planted in a common garden in Vancouver and genotyped for 29,941 SNPs (after filtering).

→ Strong negative relationship between genomic offset and seedling fitness (i.e. height and growth rate) in the common garden.

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*Validating genomic offset predictions in **observational studies***

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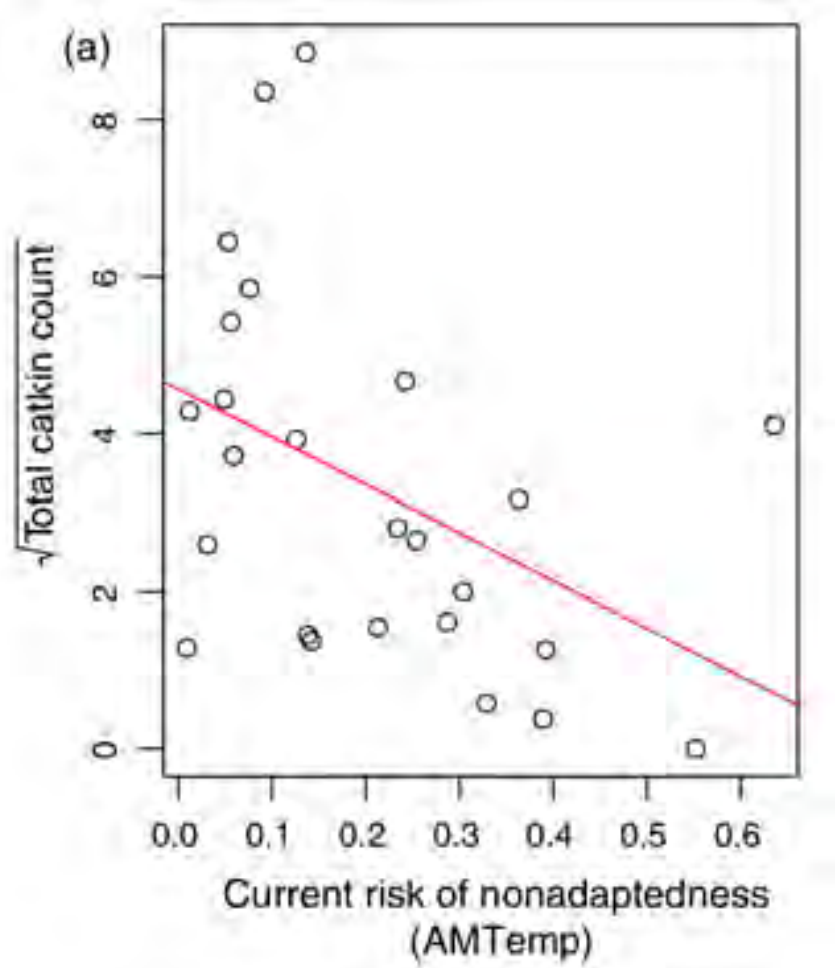

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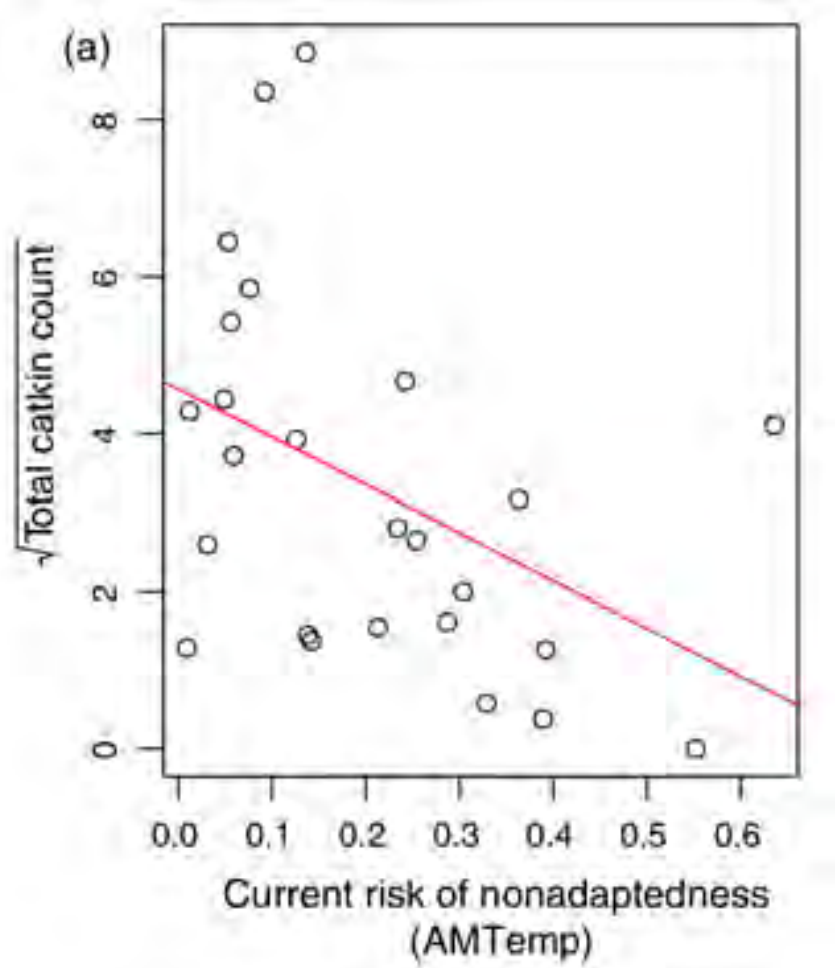

Borell *et al.* 2019.

Evaluating maladaptation in Scottish populations of the montane plant dwarf birch.

→ Populations predicted to be currently maladapted (i.e. with a mismatch between their allele frequencies at loci associated with annual mean temperature and their local environment) had reduced catkin production.

Comment: the possibility that reduced reproductive output could be an adaptive response to a poorer environment cannot be excluded, but this seems unlikely given the short timescales involving a handful of generations.

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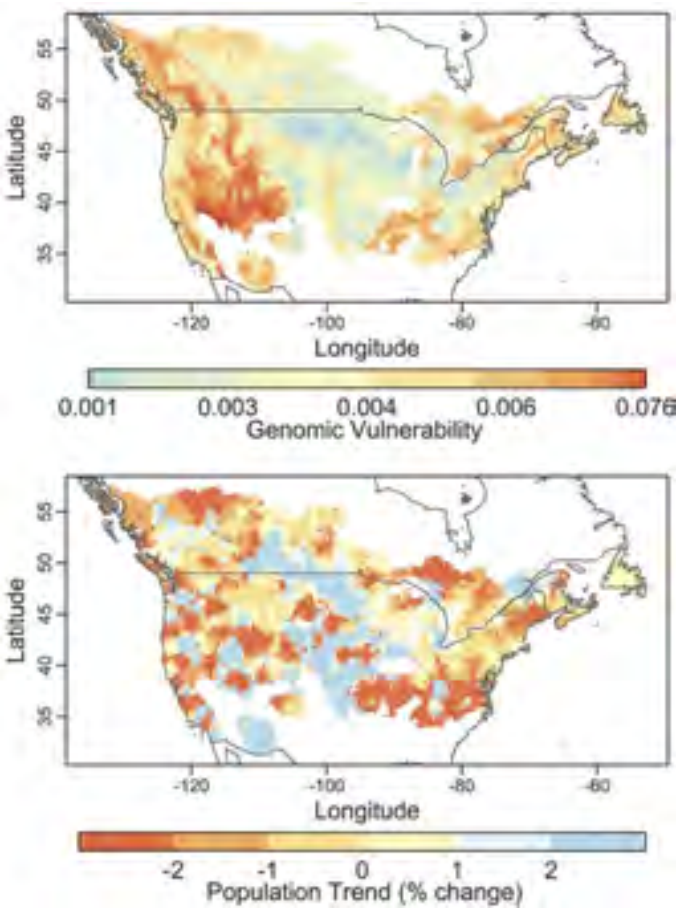


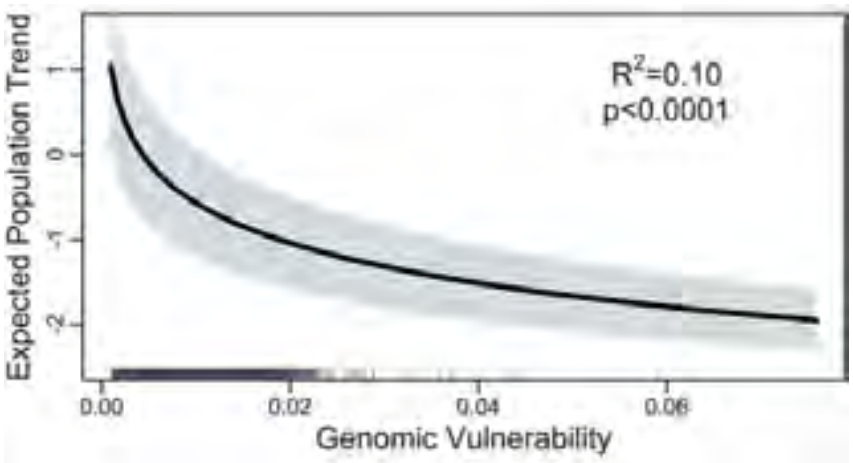
Bay *et al*. 2018.

Compared **genomic offset predictions** in a migratory bird species (yellow warbler) to spatial extrapolations of **population declines** over the past half century.

Validation phase

Do populations with **higher predicted genomic offset** show **lower relative fitness**?

Validating genomic offset predictions in ***observational studies***



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→ Populations with highest genomic offset have experienced the largest population declines.

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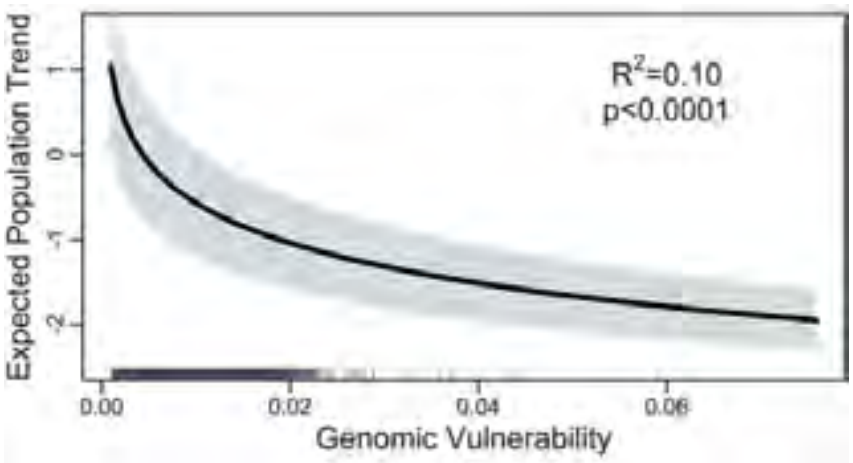

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Authors' interpretation: populations already in decline are most vulnerable to future climate change and a mismatch between genomic variation and climate may have already negatively affected populations.

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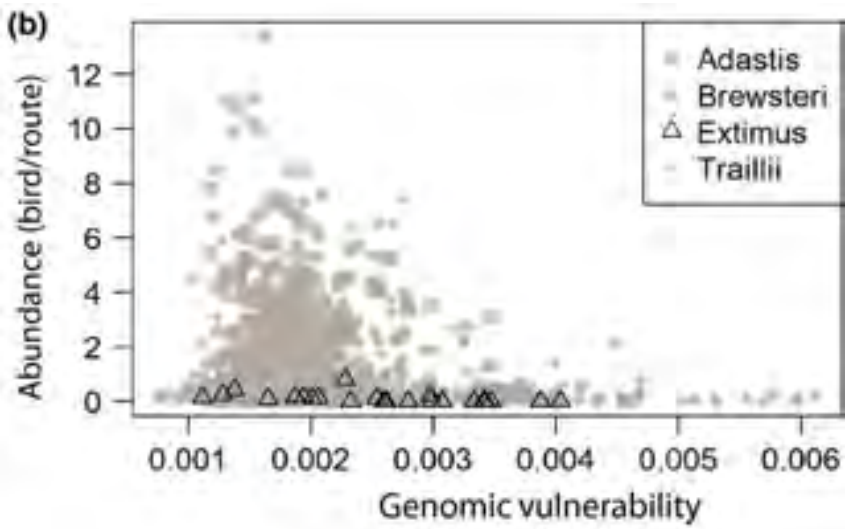

Ruegg *et al*. 2018.

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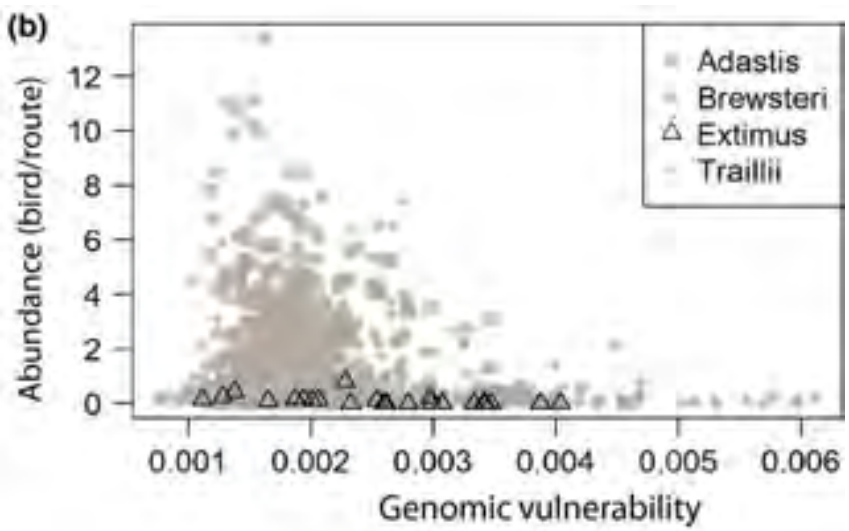

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→ Genomic offset predictions were negatively associated with abundance, which was mostly due to the especially low abundance in sites with the highest genomic offset.

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However, according to **Fitzpatrick *et al.* 2018**, the statistical analyses and interpretation of the genomic offset proposed in Bay et al. 2018 have severe problems:

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$\rightarrow$ **Initiated a debate** on the conditions and assumptions underlying the genomic offset approach for reliable estimates of vulnerability to climate change.

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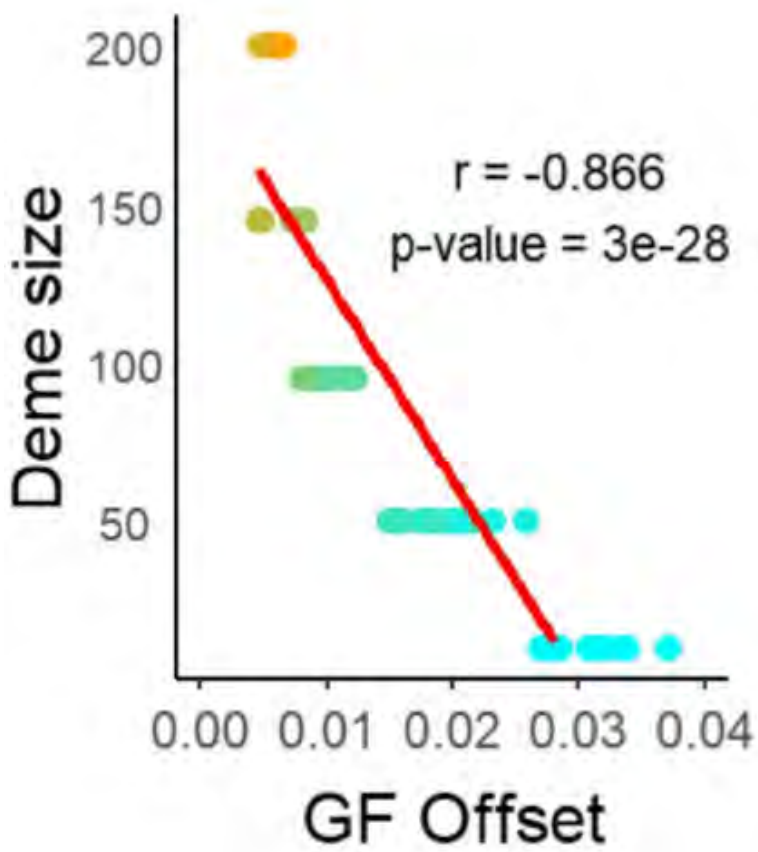

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→ Genomic offset at neutral loci **negatively associated** with **population size** varying along an environmental gradient.

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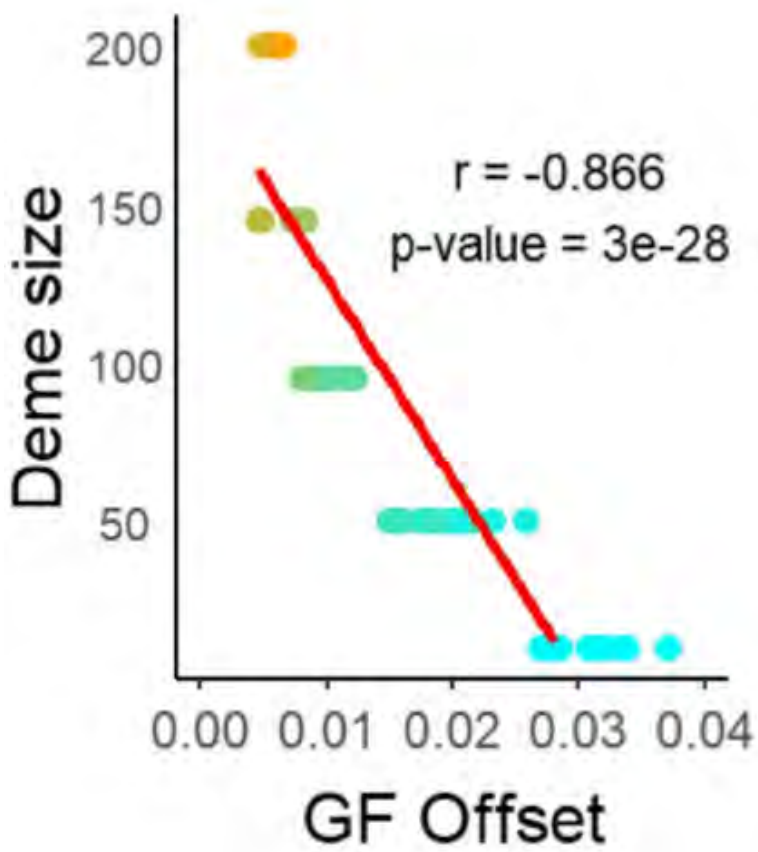

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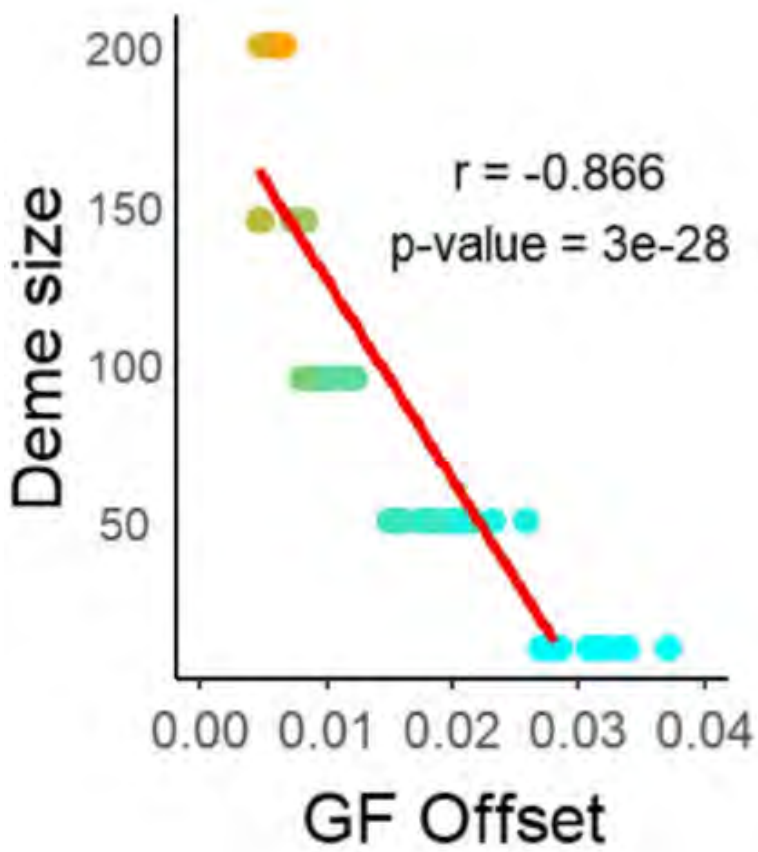

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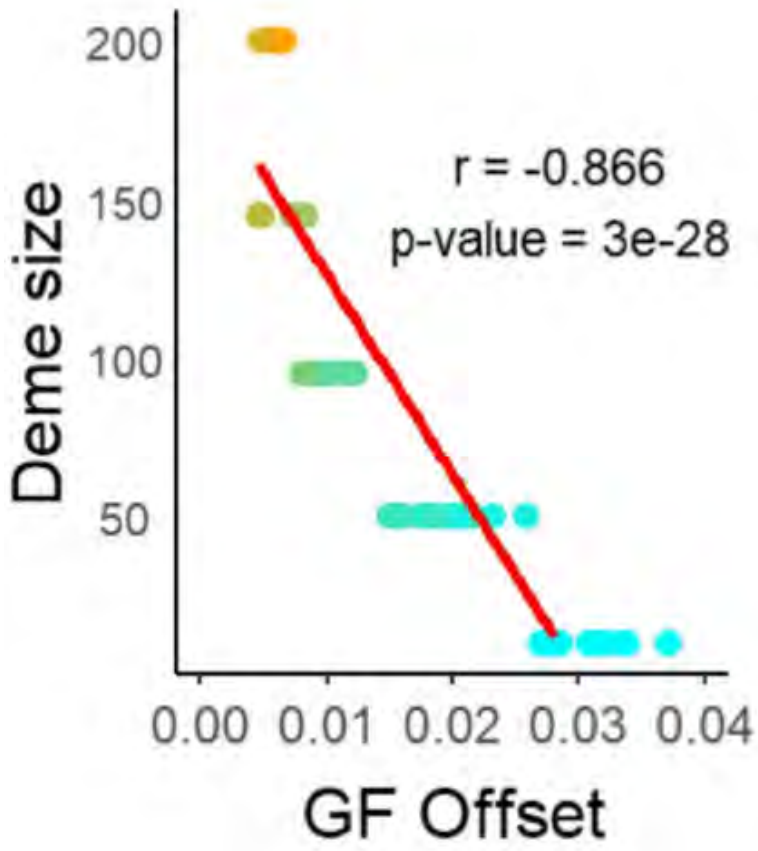

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Implications: The negative associations between genomic offset and population size found in some studies (Bay et al. 2018, Ruegg et al. 2018) may originate from **neutral genetic drift** and not natural selection as assumed.

→ **Empirical studies** identifying an association between population size and genomic offset predictions **should not be considered** as validation of the genomic offset concept.

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Genomic offset predictions were also sensitive to **sampling schemes**.

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Is the space-for-time substitution assumption valid?

- A first major source of uncertainty comes from how **current adaptive genetic variation** may recombine into **novel genotypic combinations**, in particular under **novel climates** (i.e. novel combinations of climatic variables).

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Space-for-time substitution approaches are **correlative**, and therefore do not account for potential **plastic** or **adaptive responses** to climate change or other **evolutionary processes** shaping future patterns of **genetic variation** (e.g. gene flow).

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• Another great deal of uncertainty around the future climate conditions that populations will have to face, as climate forecasts vary strongly among existing general circulation models (GCMs).

→Therefore, **space-for-time substitution approaches** has to be used **with caution** and further work is needed to **integrate** these **uncertainties** into the **predictions**.

Validation phase

Evaluating some **interpretations** of the turnover functions ***in silico***.

Láruson *et al.* 2021

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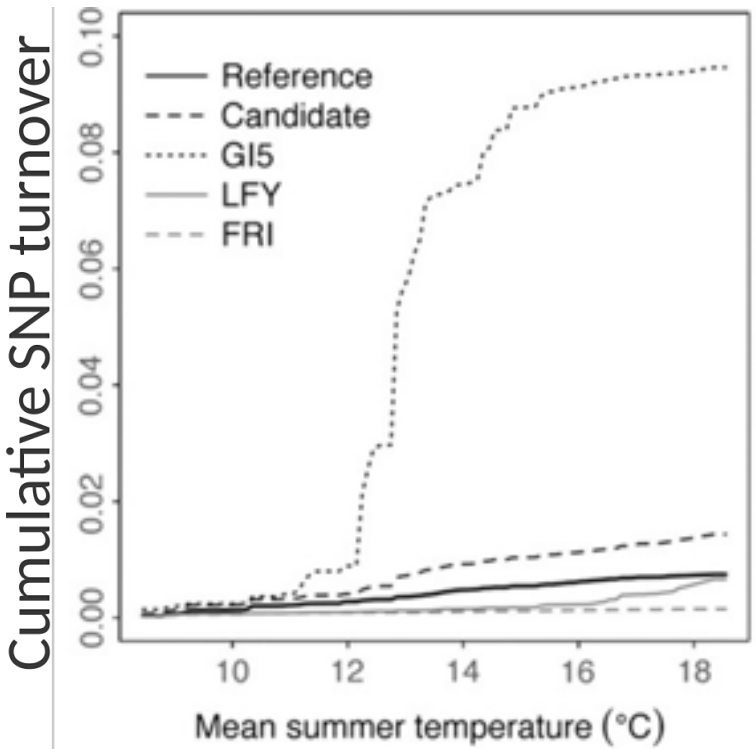
Láruson *et al.* 2021



Proposed interpretations:

• 'The **maximum height** of each curve indicates the **total amount of turnover in allele frequencies** associated with that variable, and by extension, the **relative importance** of that variable in explaining changes in allele frequency, holding all other variables constant.'

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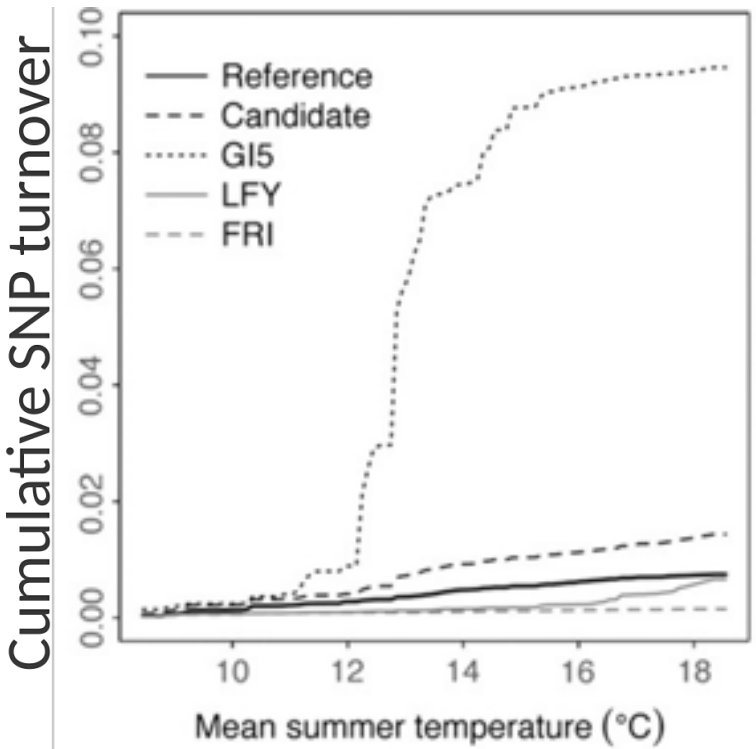
Evaluating some **interpretations** of the turnover functions ***in silico***.

Láruson *et al.* 2021



Proposed interpretations:

- 'The **maximum height** of each curve indicates the **total amount of turnover in allele frequencies** associated with that variable, and by extension, the **relative importance** of that variable in explaining changes in allele frequency, holding all other variables constant.'
- 'The **shape** of each function indicates how the **rate of change in allele frequencies** varies along the gradient.'

From Fitzpatrick and Keller (2015)

Validation phase

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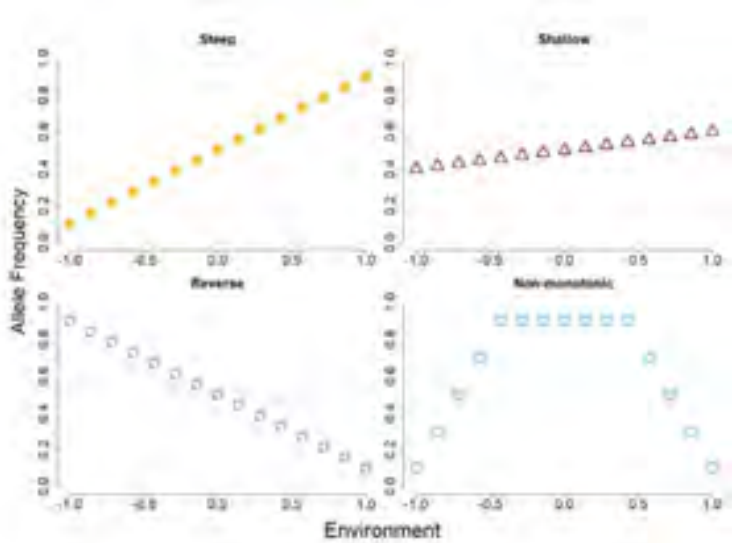

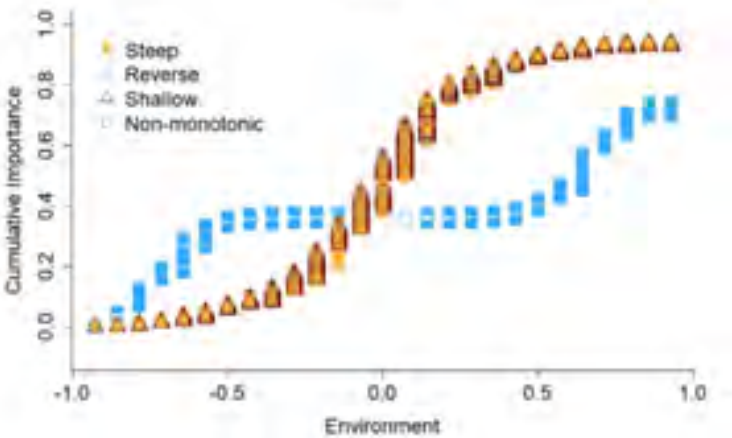

- For **linear** allele frequency clines, the **steepness** of the turnover function **does not reflect** the **rate** of allele frequency change.

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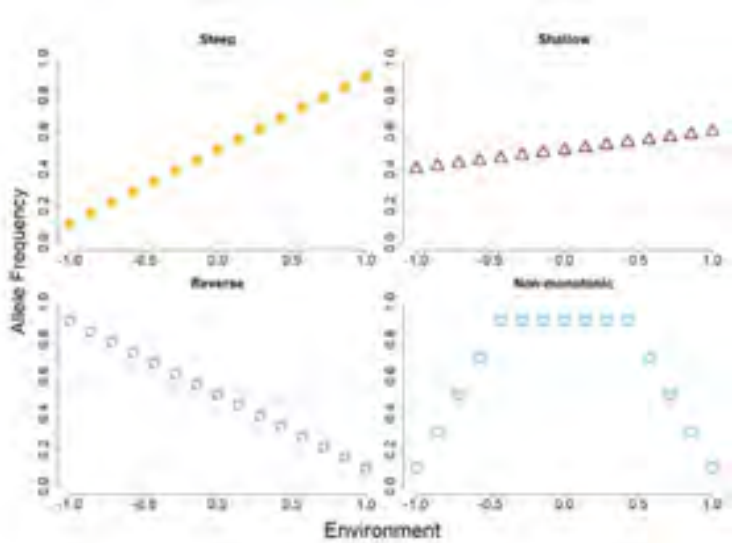

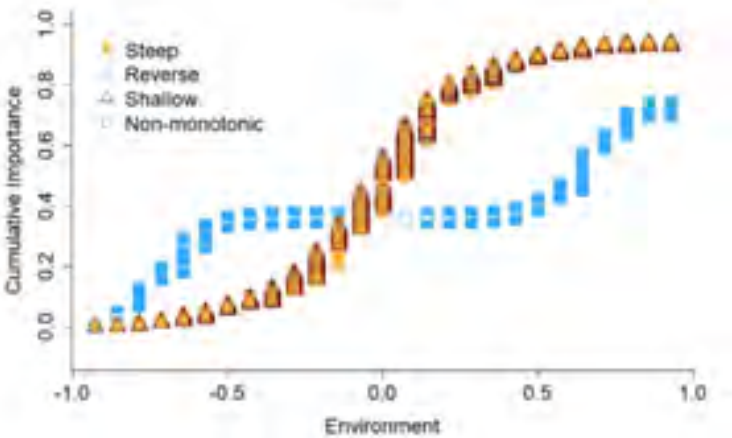

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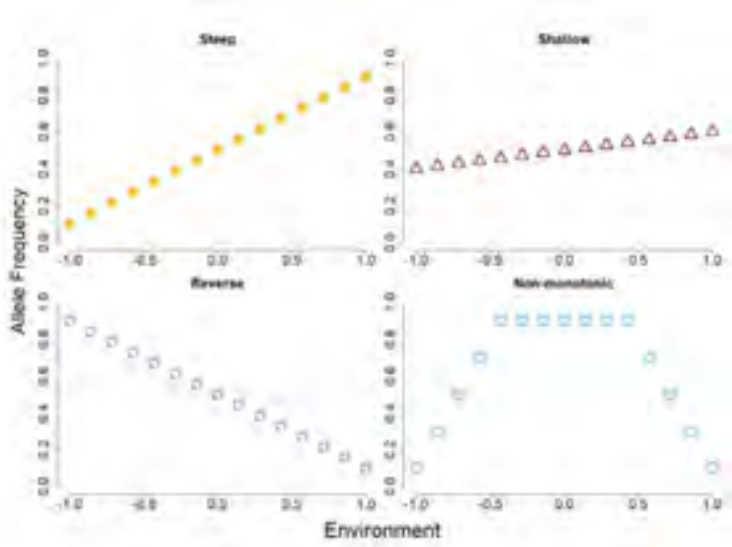

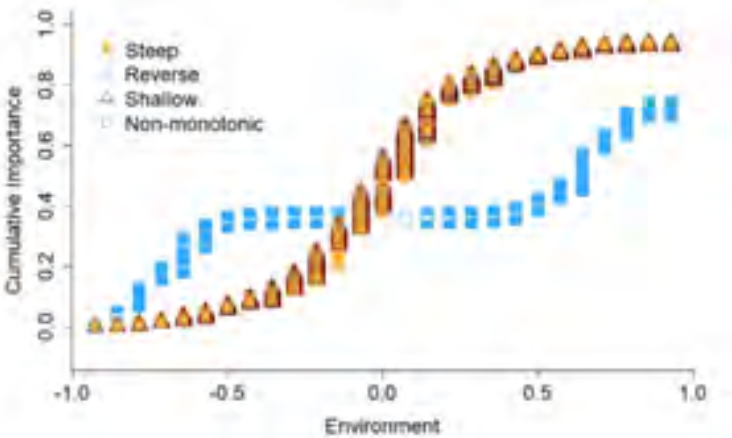

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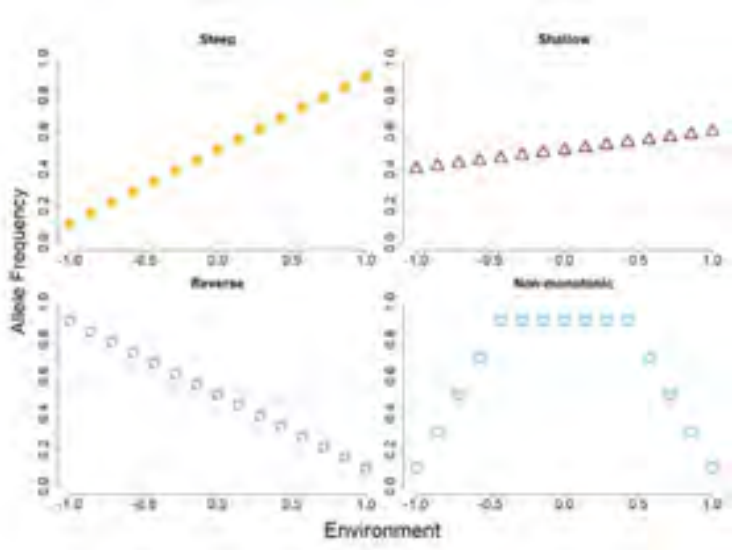
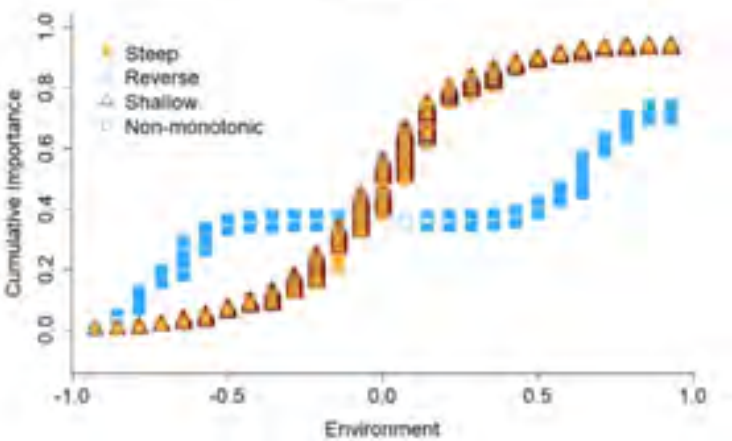
Láruson *et al.* 2021





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Comment: In the nonmonotonic case, although the allele frequencies are the same at the environmental extremes (-1 and 1), a population would be predicted to have a nonzero genomic offset for an environmental shift from -1 to 1 for that locus.

Validation phase

More **empirical** and **simulation** studies are clearly needed to determine:

- the validity of the genomic offset predictions
- the limits of the interpretation of the genomic offset approach, i.e. in which cases and to what extent the genomic offset reflects future maladaptation.

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Introduction: from species-level to genome-informed modelling

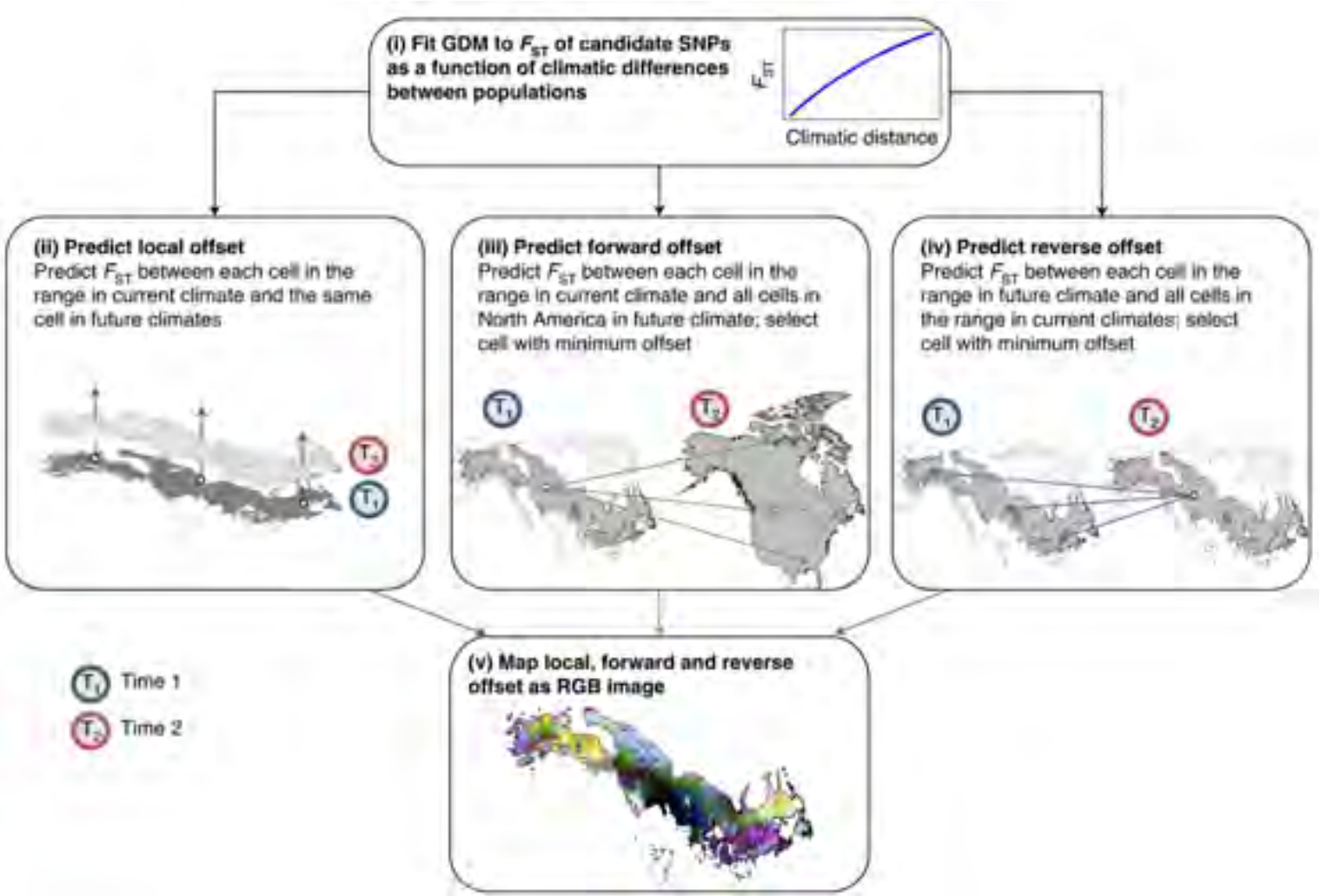
Predicting short-term performance with trait-based approaches
- Methods and limits in predicting phenotypes based on genotypes
- Predicting phenotypes based on genotypes in natural populations
- Predicting phenotypes from gene-environment associations

Predicting the adaptive potential of populations under climate change
- Incorporating intraspecific climatic adaptations into ENMs
- The genomic offset framework
- Extending the genomic offset framework
- Potential applications

Extending the genomic offset framework

Incorporating migration distances and genotype-climate novelty

Gougherty *et al.* 2021.



Extending the genomic offset framework

Incorporating migration distances and genotype-climate novelty

Gougherty *et al.* 2021.

Local offset: may be the most relevant metric of vulnerability for **long-lived sessile organisms** with long generation times.

Forward offset: assumes that populations have **unlimited migration ability**.

$\rightarrow$ The current genotype-climate associations of populations with high forward offset may disappear from the landscape.

Reverse offset: captures the possibility that some populations in the current range may be preadatpated to the future climates at a particular location.

$\rightarrow$ Locations with high reverse offset may correspond to areas to which no populations will be adapted in the future, and in which we might expect some changes along existing gradients of genotype-climate associations.

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Potential applications

Spatially explicit predictions of potential maladaptation to climate can help highlight the relative vulnerability of populations to climate change, which may serve to guide conservation policies.

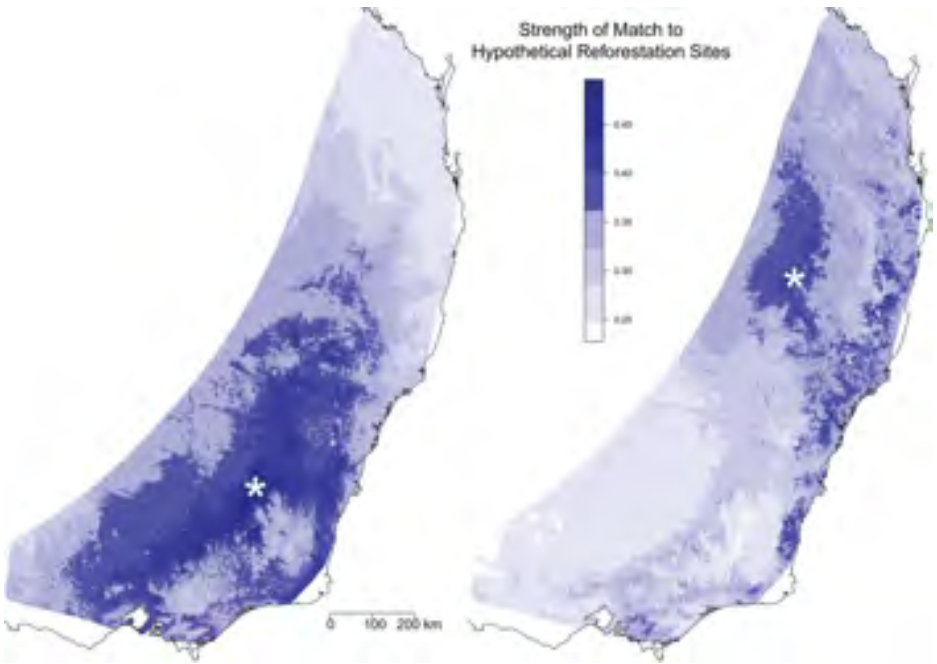
Potential applications

Providing recommendations for seed sourcing

Stupple *et al.* 2018.

Yellow box (*Eucalyptus melliodora*) is an emblematic Australian tree, essential to many native ecosystems, and **critically endangered**.

Can be difficult for reforestation practitioners to decide which seeds to plants in a given area as they have to select the ones with the highest chances of surviving now and in the future.



Genetic material from 275 *E. melliodora* trees at 36 different sites.

The genomic offset approach was used to match **hypothetical reforestation sites** (white asterisks) with the **seeds that will perform the best** in those sites under future climates.

Dark blue areas indicate **seed sourcing areas** predicted to **best match** future conditions at the hypothetical reforestation sites.