

A quantitative theory for genomic offset statistics

Clément Gain¹, Bénédicte Rhoné^{2,3}, Philippe Cubry², Israfel Salazar⁴,
Florence Forbes⁴, Yves Vigouroux², Flora Jay⁵, Olivier François^{1,4}

Authors' affiliations:

¹ Université Grenoble-Alpes, Centre National de la Recherche Scientifique, Grenoble INP, TIMC UMR 5525, 38000 Grenoble, France.

² DIADE, Université de Montpellier, Institut de Recherche pour le Développement, French Agricultural Research Centre for International Development (CIRAD), Montpellier, France

³ CIRAD, UMR AGAP Institut, F-34398 Montpellier, France, and UMR AGAP Institut, Univ Montpellier, CIRAD, INRAE, Institut Agro, Montpellier, France

⁴ Université Grenoble-Alpes, Centre National de la Recherche Scientifique, Grenoble INP, Inria Grenoble - Rhône-Alpes, LJK UMR 5224, 655 Avenue de l'Europe, 38335 Montbonnot, France.

⁵ Université Paris-Saclay, Centre National de la Recherche Scientifique, Inria, Laboratoire Interdisciplinaire des Sciences du Numérique, UMR 9015 Orsay, France.

Corresponding author: `olivier.francois@univ-grenoble-alpes.fr`

Abstract

Genomic offset statistics predict the maladaptation of populations to rapid habitat alteration based on association of genotypes with environmental variation. Despite substantial evidence for empirical validity, genomic offset statistics have well-identified limitations, and lack a theory that would facilitate interpretations of predicted values. Here, we clarified the theoretical relationships between genomic offset statistics and unobserved fitness traits controlled by environmentally selected loci, and proposed a geometric measure to predict fitness after rapid change in local environment. The predictions of our theory were verified in computer simulations and in empirical data on African pearl millet (*Cenchrus americanus*) obtained from a common garden experiment. Our results proposed a unified perspective on genomic offset statistics, and provided a theoretical foundation necessary when considering their potential application in conservation management in the face of environmental change.

Keywords: Predictive Ecological Genomics, Genomic Offset, Climate Change, Local Adaptation, Pearl Millet.

17 Introduction

18 **Maladaptation across environmental changes.** Predicting maladaptation re-
 19 sulting from traits that evolved in one environment being placed in an altered envi-
 20 ronment is a long-standing question in ecology and evolution, originally termed as
 21 evolutionary traps or mismatches (Schlaepfer *et al.*, 2002; Cook and Saccheri, 2013).
 22 With the increasing availability of genomic data, a recent objective is to determine
 23 whether those shifts could be predicted from the genetic loci that control adaptive
 24 traits and the fitness effects of these loci in spatially varying environments, bypassing
 25 any direct phenotypic measurements (Capblancq *et al.*, 2020; Waldvogel *et al.*, 2020).
 26 This question is crucial to understand whether sudden changes in the species ecolog-
 27 ical niche, *i.e.*, the sum of the habitat conditions that allow individuals to survive
 28 and reproduce, can be sustained by natural populations (Grinnell, 1917; Hutchinson,
 29 1957; Sork *et al.*, 2010; Jay *et al.*, 2012; Aitken and Whitlock, 2013; Schoville *et al.*,
 30 2012; Foden *et al.*, 2019). To this aim, several approaches have incorporated genomic
 31 information on local adaptation into predictive measures of population maladaptation
 32 across ecological changes, called genomic offset (or genomic vulnerability) statistics
 33 (Fitzpatrick and Keller, 2015; Capblancq *et al.*, 2020; Waldvogel *et al.*, 2020).

34 **Genomic offset statistics and their limitations.** Genomic offset statistics first
 35 estimate a statistical relationship between environmental gradients and allelic fre-
 36 quencies using genotype-environment association (GEA) models (Forester *et al.*,
 37 2018). The inferred relationship is then used to evaluate differences in predicted
 38 allelic frequencies at pairs of points in the ecological niche (Fitzpatrick and Keller,
 39 2015; Rellstab *et al.*, 2016; Gougherty *et al.*, 2021). The central hypothesis is that

those statistics are predictive of changes in fitness traits that occur under altered environmental conditions (Capblancq *et al.*, 2020). Recent efforts combining trait measurements in common garden experiments or natural population censuses with landscape genomic data have shown that the loss of fitness due to abrupt environmental shift correlates well with genomic offset predictions (Bay *et al.*, 2018; Ruegg *et al.*, 2018; Rhoné *et al.*, 2020; Ingvarsson and Bernhardsson, 2020; Fitzpatrick *et al.*, 2021; Chen *et al.*, 2022; Sang *et al.*, 2022). Experiments in which organisms are placed into an environment that differs from the one in which the traits evolved are, however, not always feasible (or efficient). Genomic offsets – that can be calculated in field studies – offer then a reasonable alternative to common garden experiments in a wide spectrum of applications to model and non-model organisms.

Despite substantial evidence for empirical validity, the proposed measures of genomic offset have well-identified limitations due to migration and gene flow (but see Gougherty *et al.* (2021)), population structure or genomic load. They also have difficulties to account for polygenic effects or correlated predictors (Rellstab *et al.*, 2021; Aguirre-Liguori *et al.*, 2021; Hoffmann *et al.*, 2021). More importantly, different types of genomic offset statistics have been proposed in recent years (Fitzpatrick and Keller, 2015; Rellstab *et al.*, 2016; Capblancq and Forester, 2021), and the inferred values for each of those statistics have not been explicitly linked to fundamental measures in quantitative and population genetics. The proposed measures lack theoretical foundations that would clarify how those different statistics are related to fitness and to each other. Thus, there is an urgent need to propose theoretical developments that will facilitate biological interpretations of genomic offset statistics. Here, we developed a theoretical framework that links genomic offset statistics to adaptive trait

64 values controlled by ecological conditions, unifies existing approaches and addresses
65 their limitations.

66 Results

67 **Geometry of the ecological niche.** We developed a geometric approach to the
68 concept of genomic offset (GO) by defining a dot product of ecological predictors
69 built on effect sizes of those predictors on allelic frequencies. Effect sizes, $(\mathbf{b}_\ell) = (b_{\ell j})$,
70 were obtained from a GEA model of centered allelic frequencies on scaled predictors
71 observed at a set of sampling locations. In that notation, ℓ stands for a locus,
72 and j stands for a predictor. Effect sizes were corrected for the confounding effects
73 of population structure and missing predictors (Methods: “GEA studies”). Given d
74 ecological predictors, recorded in vector $\mathbf{x}$, and their altered versions based on some
75 change in time or space, recorded in $\mathbf{x}^*$, we defined a geometric GO – implemented
76 as *genetic gap* in the computer package LEA – as a quadratic distance between the
77 two vectors $\mathbf{x}$ and $\mathbf{x}^*$

$$G^2(\mathbf{x}, \mathbf{x}^*) = (\mathbf{x} - \mathbf{x}^*) \mathbf{C}_\mathbf{b} (\mathbf{x} - \mathbf{x}^*)^T, \quad (1)$$

78 where $\mathbf{C}_\mathbf{b} = \mathbb{E}[\mathbf{b}^T \mathbf{b}]$ is the empirical covariance matrix of environmental effect sizes.
79 Here the notation $\mathbb{E}[\cdot]$ stands for the empirical mean across genomic loci in the analy-
80 sis, ideally the number of loci controlling adaptive traits. Because the reference allele
81 defining the genotype at a particular locus can be changed without any impact on
82 the GEA analysis, we assume that the average value of effect sizes across all genomic
83 loci is null, $\mathbb{E}[\mathbf{b}] \approx 0$. Considering allelic frequencies predicted from the GEA model,
84 $f(\mathbf{x}) = \mathbf{x} \mathbf{b}^T + \sum_{k=1}^K \mathbf{u}_k \mathbf{v}_k^T$ and $f(\mathbf{x}^*) = \mathbf{x}^* \mathbf{b}^T + \sum_{k=1}^K \mathbf{u}_k \mathbf{v}_k^T$, where the $\mathbf{u}_k$ represents

85 K confounding factors and $\mathbf{v}_k$ their loadings, we have

$$G^2(\mathbf{x}, \mathbf{x}^*) = \mathbb{E}[(\mathbf{x} - \mathbf{x}^*)\mathbf{b}^T]^2 = \mathbb{E}[(f(\mathbf{x}) - f(\mathbf{x}^*))^2]. \quad (2)$$

86 Thus the geometric GO has a dual interpretation as a quadratic distance in environ-
 87 mental and in genetic space. The population genetic interpretation of the geometric
 88 GO is as the average value of Nei's $D_{ST}/2$ ($= F_{ST} \times H_T/2$) for the set of loci assumed
 89 to be involved in local adaptation (Nei, 1973; François and Gain, 2021). As a genomic
 90 offset, the D_{ST} statistic can be calculated between pairs of population in space, but
 91 also in time, and it evaluates the genetic diversity between the populations in which
 92 $\mathbf{x}$ and $\mathbf{x}^*$ are measured or forecasted.

93 **Quantitative theory for genomic offset.** We developed a quantitative theory
 94 for the geometric GO and for other GO statistics under the hypothesis of local stabi-
 95 lizing selection (Kimura, 1965; Lande, 1975). Under this hypothesis, observed allelic
 96 frequencies have reached local equilibria in which polygenic or quantitative charac-
 97 ters are under natural selection for intermediate optimum phenotypes. The theory
 98 relies on a statistical model for an unobserved fitness trait for which a large number
 99 of small allelic effects mediate the effects of ecological predictors on fitness.

100 We defined $\omega(\mathbf{x}, \mathbf{x}^*)$ to be the relative fitness value of a trait at equilibrium in
 101 environment $\mathbf{x}$ being placed in the altered environment $\mathbf{x}^*$. Under local Gaussian
 102 stabilizing selection, we found that the value of the logarithm of altered fitness varies
 103 in proportion with the geometric GO (Figure 1, Box 1)

$$-\log \omega(\mathbf{x}, \mathbf{x}^*) \propto G^2(\mathbf{x}, \mathbf{x}^*)/2V_s, \quad (3)$$

where the V_s coefficient depends on the inherited variance and on the strength of stabilizing selection. In addition, the above equation remains valid when environmental predictors are indirectly related to the factors that influence the traits under selection, for example when those predictors are built on linear combinations of causal predictors for selection (Supporting Information: “Linear combination of predictors”). The geometric GO is thus robust to correlation in causal effects, and Eq. (3) extends to known and unknown linear combinations of those effects.

Unifying genomic offset statistics. Beyond defining a new geometric measure of genomic offset, the quantitative theory provides a unified framework for GO statistics based on redundancy analysis (RDA, Capblancq and Forester (2021)), the risk of nonadaptedness (Rona, Rellstab *et al.* (2016)), and gradient forests (GF, Fitzpatrick and Keller (2015)) (Supporting Information: “Relationships to other GO statistics”). The main result is that all GO statistics predict the logarithm of fitness, but not for the same shape of the (within-locality) selection gradient. When RDA is performed on both environmental and latent predictors, the RDA GO is theoretically equivalent to the geometric GO, and thus predicts relative fitness under the hypothesis of Gaussian selection within localities. The risk of nonadaptedness, which is defined as the average of allelic frequency differences instead of squared differences, makes the implicit assumption that the selection gradient is built upon an exponential (Laplace) curve. When the distribution of effect sizes is Gaussian, Rona is then related to the square root of the geometric GO (times $\sqrt{2/\pi}$). Like most machine learning techniques, GF is a nonparametric approach. In GF, no selection gradient is modelled a priori, but may be thought of as being estimated from the observed data. This might

127 be one reason for which GF require more information than linear approaches based on
 128 low-dimensional parameters. The GF GO nevertheless follows a construction similar
 129 to the geometric GO and the RDA GO.

Box 1. Genomic offset theory. Consider an (unobserved) fitness trait, z , for which a large number of genes mediate the effects of ecological predictors on organismal viability. Using Eq. (7) in (Barton *et al.*, 2017), the trait value is assumed to be controlled by L mutations each having infinitesimally small allelic effect of equal size, $a_\ell \approx \pm a/\sqrt{L}$, defining the trait value as a polygenic score, $z = \sum_{\ell=1}^L a_\ell y_\ell + e$. Here, y_ℓ is the allelic frequency at locus ℓ , expressed as deviation from the population mean, a_ℓ has random sign, a^2 controls the additive genetic variance, and the random term e models the non-genetic variance. The definition is equivalent to the more traditional decomposition of variance into inherited and non-inherited components (Figure S1). Assuming a local Gaussian stabilizing selection model, the relative fitness of the trait in environment $\mathbf{x}$ is equal to $\omega(z|\mathbf{x}) = \exp(-(z - z_{\text{opt}}(\mathbf{x}))^2/2V_S)$, where $1/V_S$ represents the strength of stabilizing selection. Conditional on local environment, the optimum, $z_{\text{opt}}(\mathbf{x})$, corresponds to the mean (or predicted) value of the trait, $\bar{z} = \sum_{\ell=1}^L a_\ell f_\ell(\mathbf{x})$. The logarithm of fitness for a trait at equilibrium in environment $\mathbf{x}$ being placed in the altered environment $\mathbf{x}^*$ is thus equal to

$$-\log \omega(\mathbf{x}, \mathbf{x}^*) = (\bar{z} - \bar{z}^*)^2/2V_S \quad (4)$$

where $\bar{z}^* = \sum_{\ell=1}^L a_\ell f_\ell(\mathbf{x}^*)$. The difference in fitness traits, $(\bar{z} - \bar{z}^*)$, is equal to $a(\mathbf{x} - \mathbf{x}^*) \sum_{\ell=1}^L \mathbf{b}_\ell^T/\sqrt{L}$. According to the central limit theorem, the conditional distribution of $(\bar{z} - \bar{z}^*)$ is Gaussian $N(0, a^2 \mathcal{G}^2(\mathbf{x}, \mathbf{x}^*))$, where $\mathcal{G}^2(\mathbf{x}, \mathbf{x}^*)$ is defined from the theoretical – instead of empirical – effect size covariance matrix. The distribution of $(\bar{z} - \bar{z}^*)^2$ is a non-standard chi-squared distribution with one degree of freedom

$$(\bar{z} - \bar{z}^*)^2 \sim a^2 \mathcal{G}^2(\mathbf{x}, \mathbf{x}^*) \chi_1^2. \quad (5)$$

Since $G^2(\mathbf{x}, \mathbf{x}^*) \approx \mathcal{G}^2(\mathbf{x}, \mathbf{x}^*)$ for large L , the value of the logarithm of altered fitness varies in proportion with the geometric GO, where the proportionality coefficient is equal to $a^2 \chi_1^2/2V_S$. The expected value is thus approximately equal to $\mathcal{G}^2(\mathbf{x}, \mathbf{x}^*)/2V_s$, where $V_s = V_S/a^2$. Consideration of traits that are not at equilibrium in environment $\mathbf{x}$ adds an intercept term to the expected value, equal to $a^2 \sigma_\epsilon^2/2V_S + \sigma_e^2/2V_S$, where σ_ϵ^2 is the residual variance in the GEA model and σ_e^2 is the non-inherited variance (Supporting Information: “Logarithm of altered fitness for non-optimal traits”).

Validation of the theory. To illustrate the above theory, we analyzed simulated data in which adaptive traits were matched to ecological gradients by local Gaussian stabilizing selection (Figure 2A, Methods: “Simulation study”, Supporting Information: “Extended simulation study”) (Haller and Messer, 2019). Two environmental predictors playing the role of temperature and precipitation in the studied range were considered, as well as two additional non-causal predictors correlated to the first ones (Figure 2B). The median values of temperature and precipitation determined four broad types of environments from *dry/warm* to *wet/cold* conditions. As an outcome of the simulation, the genetic groups resulting from selection, drift and gene flow matched the environmental classes, generating high levels of correlation between environmental predictors and population structure in the GEA analysis (Figure S2). As predicted by equation (3), the values of the geometric GO computed according to equation (1) varied linearly with the logarithm of fitness after alteration of local conditions ($r^2 \approx 78\%$, $P < 0.001$, Figure 2C-D). The predictive power of the geometric GO was much higher than the predictive power of squared Euclidean environmental distance between predictors and their altered values ($r^2 \approx 45\%$, $J = 11.3$, $P < 0.001$). Although it was calculated on both causal and non-causal predictors, the GO adjusted almost perfectly to the quadratic function that determines the intensity of local Gaussian stabilizing selection ($r^2 = 97\%$, $P < 0.001$, Figure S3). The first two eigenvalues of the covariance matrix of environmental effect sizes were much larger than the last ones (Figure 2C). We found that the loadings on the first axes gave more weight to predictors associated with natural selection, while the loadings on the last axes weighted predictors that did not play a role in the simulated evolutionary process. Uninformative predictors were given only low weights in the calculation of

155 the GO statistic. Those results provided evidence that the largest eigenvalues that
156 characterize the geometric GO contain useful information about local adaptation.

157 **Extended simulation study.** Expanding our case analysis, additional simulation
158 scenarios were considered with traits under local stabilizing selection having dis-
159 tinct levels of polygenicity. Some cases were complicated by a strong correlation of
160 environmental predictors with population structure. To overcome this complication,
161 correction based on latent factors were included in all GO calculations (Methods: “GO
162 computations”). As predicted by the theory, the values of the squared correlation
163 between the GO statistic and the logarithm of fitness were very close to each other
164 in all investigated cases (Figure 3, Figure S4). As expected, methods that did not
165 use correction (undercorrection) or include population structure covariates (overcor-
166 rection) worked less well than methods with latent factor correction (Figures S5-S6).
167 Once corrected, the GO statistics ranked similarly in all simulation scenarios. The
168 ability of the geometric GO to predict the logarithm of fitness was equal to that of
169 corrected RDA GO. It was slightly superior to that of Rona and to that of the GF
170 GO. All GO statistics were highly correlated with the geometric GO (Figure S7).
171 The geometric GO also exhibited high correlation with the quadratic distance be-
172 tween causal predictors explaining the traits under local stabilizing selection in the
173 simulation model (Figure S8). This result supported the evidence of near-optimal
174 fitness prediction by the GO statistics in all simulated evolutionary scenarios. When
175 all genomic loci in the genotype matrix were included in the GO calculations, the
176 predictions stayed close to those based on subsets of loci identified in the GEA anal-
177 ysis, GF GO reaching then performances similar to the other GO statistics (Figure

178 [S9](#)).

179 **Evaluating the bias of linear allelic frequency predictions.** An approxima-
 180 tion made by the geometric and other GO statistics is that allelic frequencies are
 181 predicted by unconstrained linear functions of environmental predictors. To evalu-
 182 ate the impact of this approximation, we compared linear predictions to those of a
 183 logistic regression model, which are constrained between zero and one. For small en-
 184 vironmental change, the effect sizes in the linear GEA model could be approximated
 185 by the effect sizes in the logistic regression multiplied by the heterozygosity at each
 186 locus (Supporting Information: “Bias of linear predictors”). The geometric GO was
 187 then accurately approximated by the squared distance between constrained genetic
 188 predictors, $\mathbb{E}[(f_c(\mathbf{x}) - f_c(\mathbf{x}^*))^2]$ ([Figure S10](#)). Using a nonlinear machine learning
 189 model (Supporting Information: “Variational autoencoder GO”), we found again that
 190 the squared genetic distance between constrained genetic predictors strongly cor-
 191 related with the geometric GO, supporting the approximation of fitness in altered
 192 environment using linear models ([Figure S11](#)).

193 **Pearl millet common garden experiment.** We hypothesized that GO statistics
 194 could predict the logarithm of fitness in pearl millet, a nutritious staple cereal culti-
 195 vated in arid soils in sub-Saharan Africa (Rhoné *et al.*, 2020). Pearl millet is grown
 196 in a wide range of latitudes and climates with wide variety of ecotypes (landraces).
 197 The geometric GO and other measures of GO were estimated from 138,948 single-
 198 nucleotide polymorphisms for 170 Sahelian landraces in a two-year common garden
 199 experiment conducted in Sadoré (Niger) using loci identified in the GEA study ([Fig-
 200 ure 4A](#), Methods: “Pearl millet experiment”). For each landrace grown in the common

garden, the total weight of seeds was measured as a proxy of landrace fitness, which was explained by a Gaussian selection gradient (Figure S12). Including latent factor correction, GO statistics were computed using the climate condition at the location of origin of the landrace and the climate at the experimental site. All GO statistics displayed a consistent relationship with the logarithm of seed weight (Figure 4B, Figure 5). Loci identified in the GEA study increased the performance of GO statistics compared to using whole genomic data, and the improvements were substantial compared to methods that did not include correction for confounding factors (Figures S13-S14 and Table S1). The best predictions of fitness in the common garden were obtained with the geometric GO and with the corrected version of Rona ($r^2 = 61\%$, $P < 0.001$, Figure 5). The eigenvalues and eigenvectors of the covariance matrix of environmental effect sizes suggested that climatic conditions could be summarized in three axes. Temperature predictors were given higher importance in driving fitness variation than precipitation and solar radiation predictors (Figure S15).

Discussion

Quantitative theory. The geometric theory presented in our study provided a unified framework that not only explains why and when a GO statistic differs from the standard Euclidean environmental distance, but also allowed for a better understanding of previous measures of genomic offset. Based on models of local selection gradients, a theoretical analysis of GO statistics relying on Fisher’s infinitesimal trait model was developed. In this framework, the geometric GO decays linearly with the logarithm of fitness in the altered environment. Although of much lower computational complexity, the geometric GO was proved to be equivalent to a GO based on

224 RDA, which justifies the use of RDA approaches under local Gaussian selection. The
225 square root of the geometric GO was connected to Rona, and justifies the use of
226 absolute differences in allele frequencies under exponential selection gradient.

227 **Improving GO statistics.** According to Rellstab *et al.* (2021), current GO statis-
228 tics may provide wrong predictions due to the correlation between population struc-
229 ture at selectively neutral loci and environmental predictors. Built on unbiased effect
230 sizes, the geometric GO, which is based on a unique model for GEA estimation and
231 for GO prediction, addressed this problem by including latent factors as covariates
232 in the prediction model. Latent factor corrections were then incorporated into all
233 considered GO statistics, which increased their predictive performance compared to
234 their traditional usage. Our versions of RDA GO and Rona – that slightly differ from
235 original proposals – were implemented in the R package LEA. Although those changes
236 led to improved statistics, the geometric GO reached higher predictive performance
237 than the other GO approaches. Next, the geometric GO addressed the problem of
238 correlated predictors by modeling the covariance of their effect sizes. The impor-
239 tance of predictors could be assessed by examining the eigenvalues and eigenvectors
240 of the environmental effect size covariance matrix. The eigenvalues provide a natural
241 ranking of the importance of each axis, similar to the cumulative importance curves
242 in GF. When a statistical analysis includes redundant predictors, reproducing infor-
243 mation already present in a reduced set of predictors, the geometric GO gave lower
244 weight to those redundant predictors, and differed substantially from the Euclidean
245 environmental distance. Generally, the principal benefit of genomic offset over purely
246 environmental distances in predicting maladaptation comes from the weighting of en-

247 vironmental predictors by their effect sizes (Làruson *et al.*, 2022). All proposed GO
248 approaches share the principle of weighting the environmental predictors by their
249 strength of genetic association. For the vast majority of organisms where the most
250 important predictors are unknown or for which common garden experiments are not
251 efficient or unfeasible, genomic offset therefore provides a useful means for weighting
252 the environmental predictors based on the information contained in allele frequencies.

253 **Limitations.** Our simulation models and our theoretical developments relied upon
254 a model of genotype $\times$ environment interaction for fitness related to antagonistic
255 pleiotropy, whereby native alleles are best adapted to local conditions (Kawecki, 2004;
256 Anderson *et al.*, 2011). While antagonistic pleiotropy is an important mechanism for
257 local adaptation, there are other types of interactions for fitness. If local adapta-
258 tion is caused by conditional neutrality at many loci, where alleles show difference in
259 fitness in one environment, but not in a contrasting environment, the predictive per-
260 formances of GO statistics remain to be explored. In addition, GO statistics (except
261 GF) are based on linear models for the relationship between genotype and environ-
262 ment. Linear models generate GO statistics that are invariant under translation in
263 the niche, making predictions relevant at the center of the species distribution, but
264 perhaps less relevant at margins of the range. While translational invariance could
265 be corrected for by defining the offset as the average of squared differences between
266 allelic frequencies in nonlinear models, we found that the results were very close to
267 the linear models. An explanation may be that nonlinear machine learning models
268 offer more flexible GO statistics than linear models, but that linear models achieve a
269 better bias-variance trade-off than machine learning models, likely because less data

are needed for their application. Other conceptual limitations include gene flow and constraints on adaptive plasticity that might mitigate the effect of environmental change on fitness (Aguirre-Liguori *et al.*, 2021; Kawecki, 2004). As they do not use any observed information on fitness traits, GO statistics provide measures of expected fitness loss based on the indirect effects of environment mediated by loci under selection (Baron and Kenny, 1986). GO statistics are more accurate when non-genetic effects do not covary with environmental predictors. Lastly, we found that using candidate loci based on statistical significance in GEA improved prediction of fitness in altered conditions both in simulation and in real data analysis. We think that this happens because those studies may generally be underpowered, *i.e.*, a much larger sample size would increase the predictive power of GO statistics. Using a liberal threshold in GEA studies was considered as a trade-off between polygenicity and statistical significance, so that the GO measures could actually be based on polygenic scores while not erasing or blurring the genomic signals of local adaptation.

Pearl millet experiment. To compare predictions of local adaptation with empirical data, GO statistics were estimated in a common garden experiment on pearl millet landraces in sub-Saharan Africa. Using GF, the original study reported a squared correlation of $r^2 \approx 9.5 - 17\%$ for seed weight, indicating that higher genomic vulnerability was associated with lower fitness under the climatic conditions at the experimental site (Rhoné *et al.*, 2020). In our reanalysis, signals of local adaptation were consistent across all GO statistics, and improved fitness prediction substantially, up to a value of squared correlation equal to $r^2 \approx 61\%$. The results strengthened the conclusions of (Rhoné *et al.*, 2020), and supported the use of GO statistics in

293 predictions of fitness values across the sub-Saharan area.

294 **Conclusions.** Considering a duality between genetic space and environmental space,
 295 we developed a theoretical framework that linked GO statistics to a non-Euclidean
 296 geometry of the ecological niche. The geometric GO, as well as the modified Rona
 297 statistic, were implemented in the genetic gap function of the R package LEA (Gain
 298 and François, 2021). As a result of the quantitative theory, interpretations in terms
 299 of fitness in the altered environment were proposed, unifying several existing ap-
 300 proaches, and addressing some of their limitations. Based on extensive numerical
 301 simulations and on data collected in a common garden experiment, our study indi-
 302 cated that GO statistics are important tools for conservation management in the face
 303 of climate change.

304 Materials and Methods

305 **GEA studies.** GEA studies and estimates of environmental effect sizes were per-
 306 formed based on LFMMs in the computer package LEA v3.9 (Caye *et al.*, 2019; Gain
 307 and François, 2021). In LFMMs, allelic frequencies are modelled at each genomic
 308 locus of a genotype matrix as a mixed response of observed environmental variables
 309 with fixed effects and K unobserved latent factors. The number of latent factors
 310 was estimated from the screeplot of a principal component analysis of the genotype
 311 matrix. Loci with minor allele frequency less than 10% were filtered out the analysis.
 312 Statistical significance was determined by using the R package `qvalue` at a level of
 313 false discovery rate equal to 10%.

GO computations. RDA was performed by using principal components of fitted values of the GEA regression model. Rona was computed as the average value of the absolute distance between predicted allelic frequencies across genomic loci (de Aquino *et al.*, 2022; Rellstab *et al.*, 2016). GF computations were performed using the R package `gradientForest` version 0.1. For consistency, we reported squared values of GO statistics in RDA and GF. Unless specified, GO statistics were computed on the loci detected in the GEA study, i.e., a same set of loci for all methods. To correct statistics for the confounding effect of population structure, all analyzes were performed conditional on the factors estimated in the LFMM analysis (Supporting Information: “GO computations”).

Simulation study. Spatially-explicit individual-based simulations were performed using SLiM 3.7 (Haller and Messer, 2019) (Supporting Information: “Extended simulation study”). Each individual genome contained neutral mutations and quantitative trait loci (QTLs) under local stabilizing selection from a two-dimensional environment. The probability of survival of an individual genome in the next generation was computed as the product of density regulation and fitness. We designed four classes of scenarios, including weakly or highly polygenic traits, and weak or high correlation of environment with population structure. In scenarios with high polygenicity, traits controlled by 120 mutations with additive effects were matched to each environmental variable by local stabilizing selection. In weakly polygenic scenarios, the traits were controlled by 10 mutations. Scenarios with high confounding effects were initiated in a demographic range expansion process, creating correlation between environment and allelic frequencies at the genome level. For each scenario, thirty replicates were

run with distinct seed values of the random generator. At the end of a simulation, individual geographic coordinates, environmental variables and individual fitness values before and after instantaneous environmental change were recorded. Paired t -tests were used to test statistical differences in the mean of predictive performances for the geometric GO and the other GO statistics.

Empirical study. Methods regarding the common garden experiment on Pearl millet landraces conducted in Sadoré (13° 14' 0" N, 2° 17' 0" E, Niger, Africa) were described by Rhoné *et al.* (2020). For each of 170 landraces grown in the common garden, the total weight of seeds was measured by harvesting the main spike in ten plants per landrace sown during two consecutive years and was used as a proxy of landrace fitness. For each landrace grown in the common garden, environmental predictors, $\mathbf{x}$, were obtained at the location of origin of the landrace, and $\mathbf{x}^*$ corresponded to the local conditions in Sadoré. We made the hypothesis that the mean total weight of seeds for a landrace was proportional to $\omega(\mathbf{x}, \mathbf{x}^*)$ in the common garden. Using 100 plants per landrace in a pool-sequencing design, allelic frequencies were inferred at 138,948 single-nucleotide polymorphisms. Climate data were used to compute 157 metrics in three categories, precipitation, temperature (mean, maximum and minimum near surface air temperature), and surface downwelling shortwave radiation, that were reduced by principal component analysis (27 axes). GO statistics were computed using the climate condition ($\mathbf{x}$) at the location of origin of the landrace and the climate conditions ($\mathbf{x}^*$) at the experimental site. For each GO statistic, we estimated a linear relationship with the logarithm of the mean total weight of seeds and used Pearson's squared correlation to evaluate the goodness of fit. The J -test

was used to test differences between predictive performances, corresponding to R -squared for distinct regression models, of the geometric GO and other GO statistics (Davidson and MacKinnon, 1981).

Data Availability. The pearl millet data have already been published, and have permissions appropriate for fully public release.

Code Availability. The codes necessary to reproduce the simulations and data analyses of this study are available at <https://github.com/bcm-uga/geneticgap> under GNU General Public License v3.0 The geometric GO is implemented in the genetic gap function of the R package LEA (version number > 3.9.5) available from the public repository bioconductor and <https://github.com/bcm-uga/LEA> (latest version).

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484 **Author contributions**

485 B.R., P.C., Y.V., I.S., F.F. contributed analyzes and helped drafting the manuscript.
 486 C.G., F.J. and O.F. conceived the study, developed the method, carried out analyzes,
 487 and wrote the manuscript.

488 **Competing Interests**

489 The authors declare no competing interests.

490 **Additional information**

491 Supporting methods and materials, supplementary figures and tables, are available
 492 online.

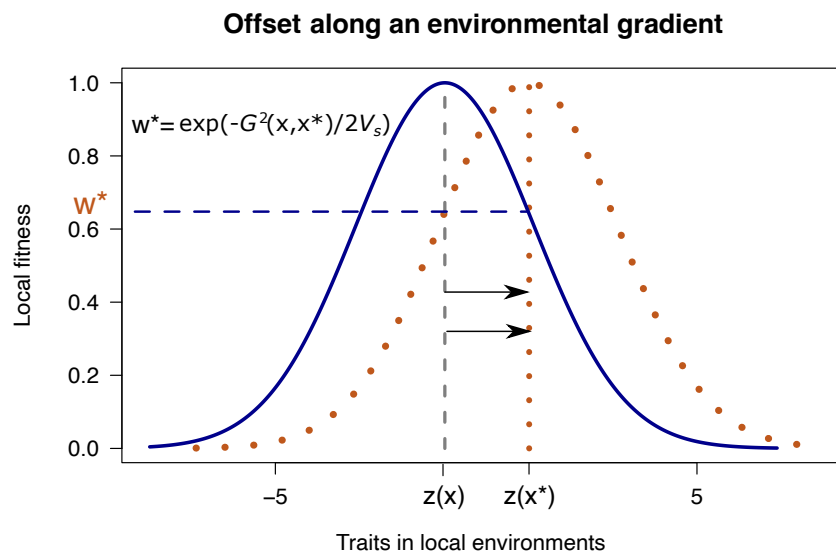


Figure 1. Geometric offset (genetic gap) under local Gaussian stabilizing selection. The two points, $z(\mathbf{x}) = \bar{z}$ and $z(\mathbf{x}^*) = \bar{z}^*$, represent locally optimal values of an adaptive trait in respective environments $\mathbf{x}$ and $\mathbf{x}^*$. The curves display the fitness values for the trait in each environment. An organism with trait $z(\mathbf{x})$, optimal in environment $\mathbf{x}$, being placed in altered environment $\mathbf{x}^*$, has a fitness value equal to $w^* = \exp(-G^2(\mathbf{x}, \mathbf{x}^*)/2V_s)$, where $G^2(\mathbf{x}, \mathbf{x}^*)$ is the genomic offset (horizontal dashed line), and V_s is defined in text.

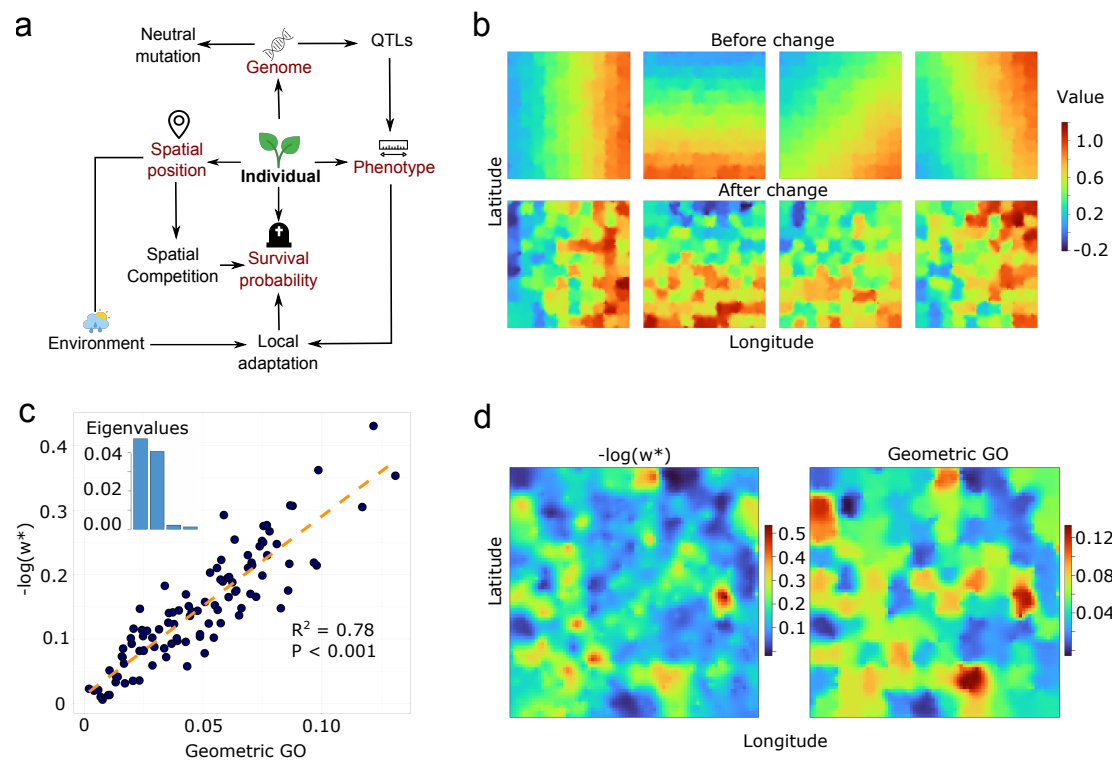


Figure 2. Simulation of fitness traits and geometric offset. **a)** Spatial individual-based forward simulations: Adaptive traits were matched to ecological gradients by local Gaussian stabilizing selection. **b)** Geographic maps of four environmental predictors before and after change. **c)** Logarithm of altered fitness values as a function of geometric offset. The eigenvalues of the covariance matrix of environmental effect sizes are displayed in the top left corner. **d)** Geographic maps of the logarithm of altered fitness values (left) and geometric offset (right).

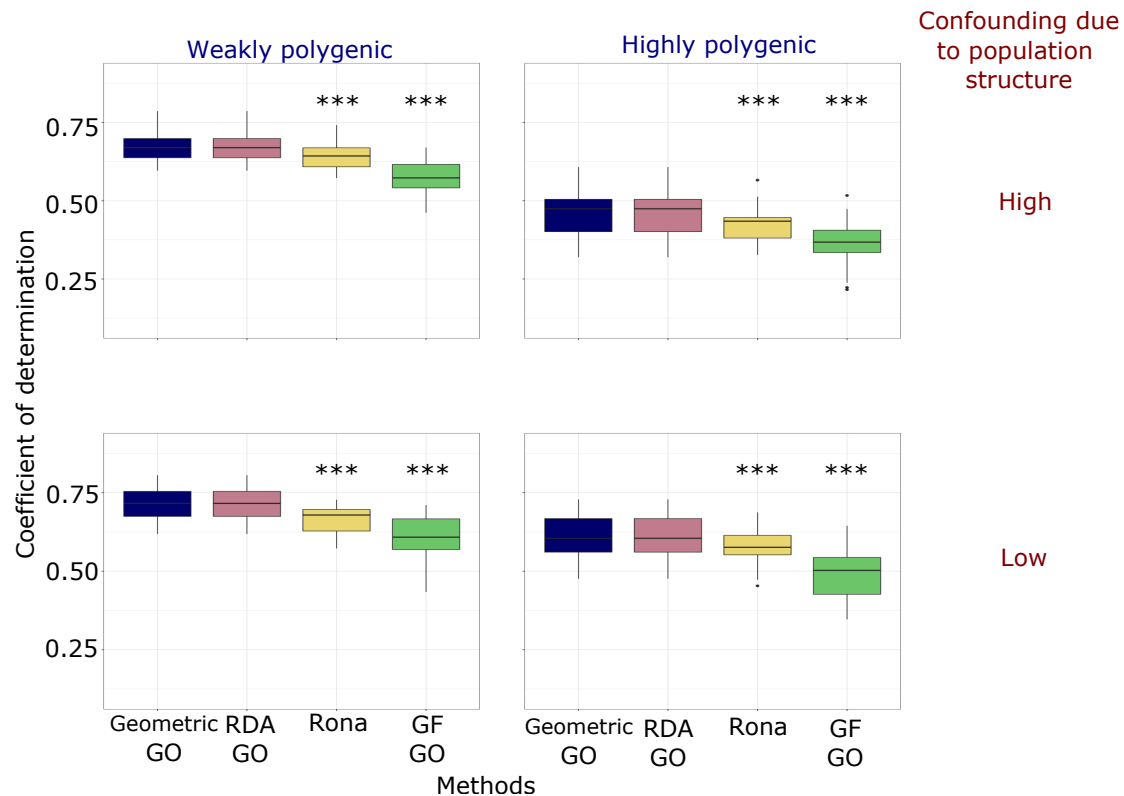


Figure 3. Predictive performances of GO statistics. Proportion of variance of fitness in the altered environment explained by GO statistics (coefficient of determination). Four scenarios with distinct levels of polygenicity in adaptive traits and correlation of environmental predictors with population structure were implemented. Significance values were based on paired t-tests of the difference in mean performance for each GO statistic relative to the geometric GO (***: $P < 0.001$). Boxplots display the median, the first quartile, the third quartile, and the whiskers of distributions. The upper whisker extends from the hinge to the largest value no further than 1.5 inter-quartile range (IQR) from the hinge. The lower whisker extends from the hinge to the smallest value at most 1.5 IQR of the hinge. Extreme values are represented by dots.

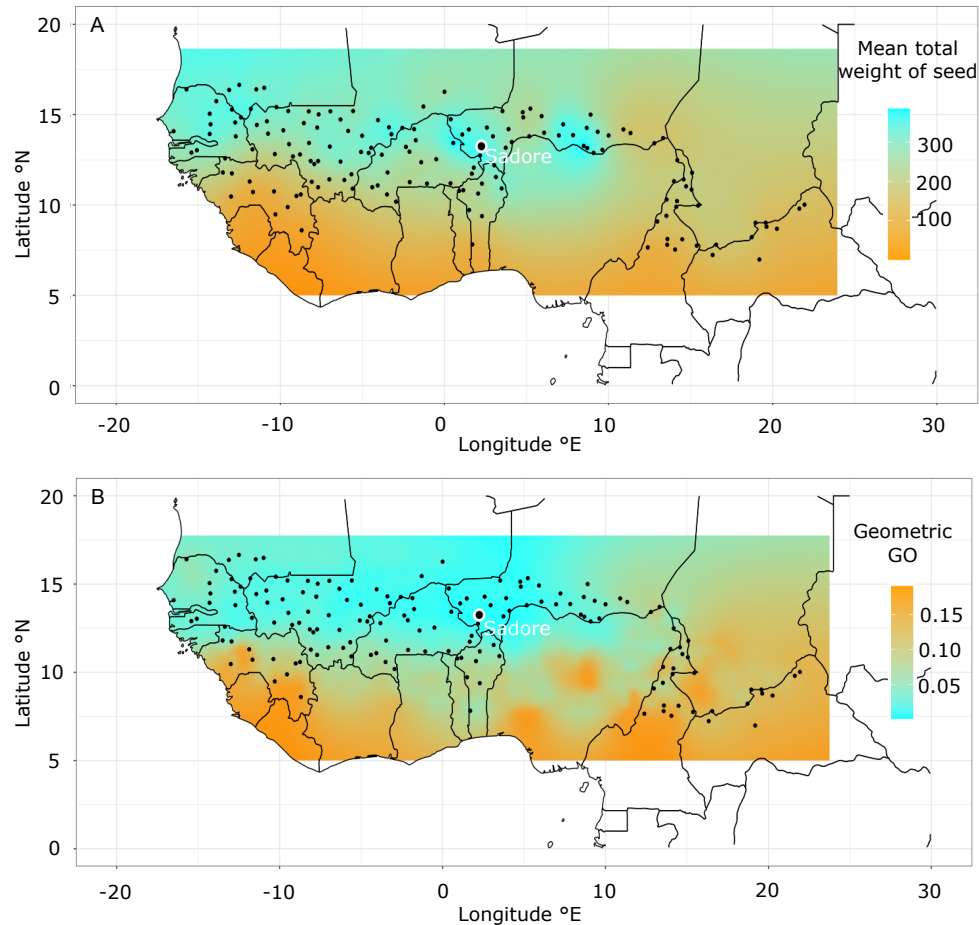


Figure 4. Interpolated fitness gradient and genomic offset for pearl millet landraces. A) Fitness values (log) measured as the mean total seed weight for each pearl millet landrace in the common garden experiment located in Sadoré (Niger). B) Values of the geometric genomic offset. Locations of landrace origin are represented as dots. Values at unsampled locations were interpolated from the nearest sampled location using the inverse distance weighting method.

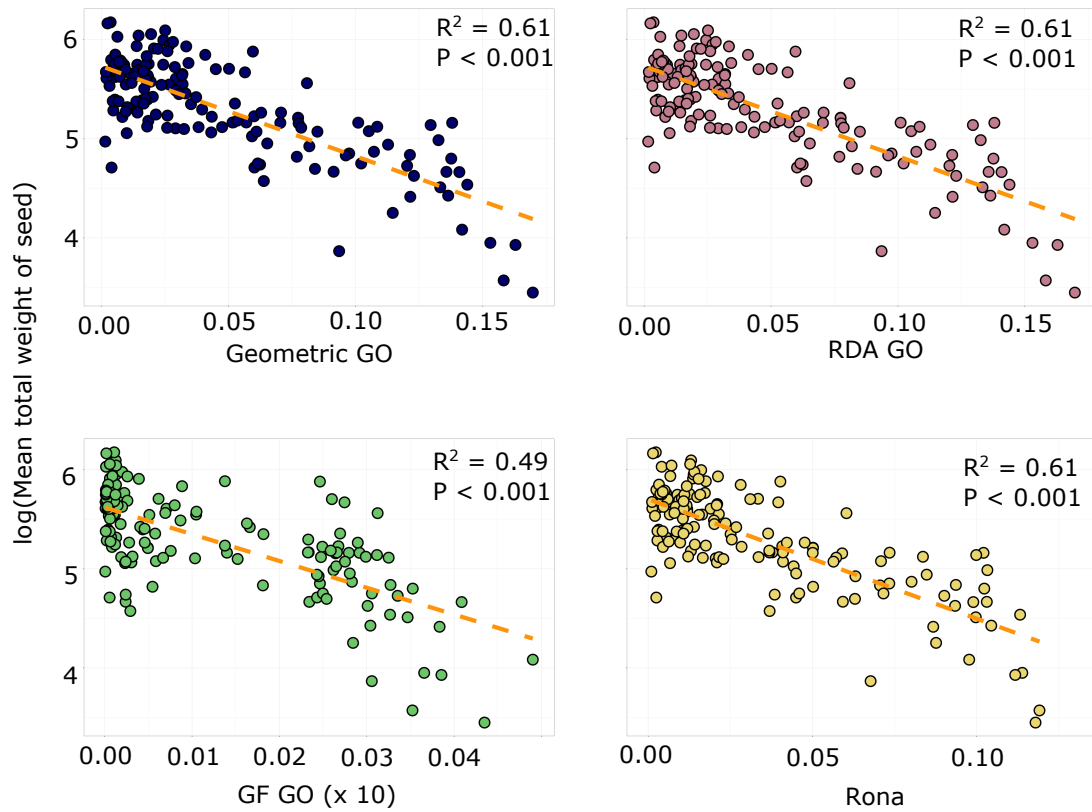


Figure 5. Logarithm of fitness in the common garden as a function of the GO statistic. Latent factor corrections were included in the calculation of all GO statistics (ten factors). Fitness was evaluated as the mean total weight of seed for 170 pearl millet landraces. GO values for GF were multiplied by a factor of ten.