Climate associated genetic variation in *Fagus sylvatica* and potential responses to climate change in the French Alps.

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ABSTRACT

Local adaptation patterns have been found in many plants and animals, highlighting the genetic heterogeneity of species along their range of distribution. In the next decades, global warming must induce a change in the selective pressures that drive this adaptive variation, forcing a reshuffling of the underlying adaptive allele distributions. For species with low dispersion capacity and long generation time such as trees, the rapidity of the change could imped the migration of beneficial alleles and lower their capacity to track the changing environment. Identifying the main selective pressures driving the adaptive genetic variation is thus necessary when investigating species capacity to respond to global warming. In this study, we investigate the adaptive landscape of *Fagus sylvatica* along a gradient of populations in the French Alps. Using a ddRAD-seq approach, we identified 7,000 SNPs from 570 individuals across 36 different sites. An RDA-derived method allowed us to identify several SNPs that were strongly associated with climatic gradients; moreover, we defined the primary selective gradients along the natural populations of *F. sylvatica* in the Alps. Strong effects of elevation and humidity, which contrast north-western and south-eastern site, were found and were believed to be important drivers of genetic adaptation. Finally, simulations of future genetic landscapes that used these findings predicted a severe range contraction and a shift towards higher altitudes for *F. sylvatica* in the Alps and allowed to identify populations at risk, which could be helpful for future management plans.

24 **KEYWORDS:**

25 Climate change – trees - RDA - Landscape genetics - *Fagus sylvatica*.

26

27 **INTRODUCTION**

28   The long-term survival and the distribution of species are triggered by

29 their ability to grow and reproduce in a given set of environmental conditions

30 (Hutchinson 1957). When populations of the same species experience different

31 environments, adaptation to the local conditions may occur. As a result,

32 individuals have a better fitness in their local environment than individuals from

33 other populations (Rehfeldt et al. 2002). Patterns of local adaptation are

34 commonly studied to better understand adaptation and especially the

35 equilibrium between natural selection and gene flow within a set of intra-specific

36 connected populations (Kawecki and Ebert 2004). Better assessing the genetic

37 selective pressure encompassed by the different populations of a species leads to

38 a better understanding of the ecology and distribution of the species and can help

39 refine our vision of species homogeneity over space and time (Poncet *et al.* 2010,

40 Manel *et al.* 2012, Alberto *et al.* 2013a, De Kort *et al.* 2013, Fitzpatrick and Keller

41 2015).

42   Recent projections predict major environmental changes by the end of the

43 century (IPCC, 2007 and 2013), and these changes are already impacting

44 biodiversity (Thuiller *et al.* 2005, Bellard *et al.* 2012). This prediction is especially

45 true for mountainous plant and tree species (Pauli *et al.* 2012, Thuiller *et al.* 2014,

46 Duputié *et al.* 2015, Trumbore *et al.* 2015), which are expected to undergo a shift

47   towards higher elevations (Penuelas *et al.* 2003, Walther *et al.* 2005, Parmesan

48   2006, Beckage *et al.* 2008, Lenoir 2008, Shaw and Etterson 2012). When

49   projections of species' responses to climate change have been investigated, the

50   studies have frequently been conducted using presence/absence with habitat

51   suitability modelling (Bakkenes *et al.* 2002, Thuiller *et al.* 2005). In such models,

52   in most cases, the species has been considered as a homogeneous unit, and any

53   potential heterogeneous genetic adaptations across populations have been

54   neglected (Alberto *et al.* 2013a, Bay et al. 2017a). Nonetheless, in the last decade,

55   it has been proposed that genetic heterogeneity should be considered when

56   studying species diversity and distribution (Jay *et al.* 2012, Alsos *et al.* 2012,

57   Steane *et al.* 2014, Razgour *et al.* 2018). To do so, the goal would be to translate

58   the genomic information into spatially explicit predictions of genetic and

59   especially adaptive variation (Schoville et al. 2012, Fitzpatrick and Keller 2015).

60   Furthermore, some authors have suggested that local adaptation must be

61   integrated into estimates of the risk of species' range losses under climate change

62   scenarios (Morin *et al.* 2007, Benito Garzon *et al.* 2011, Mouquet *et al.* 2015, Bay

63   et al. 2017b, Bay et al. 2018, Exposito-Alonso *et al.* 2018, Martins *et al.* 2018).

64   The adaptive genetic heterogeneity could largely impact species response

65   to climate change in the next decades (Aitken *et al.* 2008, Jump & Penuelas 2005,

66   Rehfeld *et al.* 2002). A changing environment induces a continuous modification

67   of the selective pressure across the landscape and could create a distortion

68   between population phenotypes and newly optimal ones (Hoffmann & Sgro 2011,

69   Aitken *et al.* 2008). It would result in a need for the populations to change their

70   adaptive genetic component accordingly and track the new optima across the

71   landscape. An emerging field of research aims at estimating the magnitude of the

72   deviance between the current and future optimal genetic composition (Steane *et*

73   *al.* 2014, Fitzpatrick & Keller 2015, Bay *et al.* 2018, Exposito-Alonso *et al.* 2018,

74   Martins *et al.* 2018). To do so they investigate the relationship among genetic,

75   phenotypic and environmental variability and extrapolate these relations across

76   a landscape. By looking at the deviance between optimal genetic composition in

77   current and future conditions they estimate a potential genetic offset (Fitzpatrick

78   & Keller 2015) that the populations would have to reduce to ensure their

79   survival. These new methods have been facilitated by the recent development of

80   next-generation sequencing (NGS) techniques, which have created the possibility

81   to access a large amount of genetic variation across the genome (da Fonseca *et al.*

82   2016, Hoban *et al.* 2016).

83   The present study uses a RDA-based approach and a large matrix of

84   genomic data to investigate the genetic-environment relationship and estimate

85   the potential deviance between current and future genetic composition optima in

86   common beech (*Fagus sylvatica*) along the French Alps. *F. sylvatica* is a tree

87   species commonly found in European mountain ecosystems, covering large

88   environmental gradients, with a distribution from the Pyrenees Mountains to

89   Scandinavia (Frydl *et al.* 2011). In the Alps, the species is distributed at altitudes

90   ranging from 600 to 1800 m. This distribution spans a variety of environmental

91   conditions, sometimes at very small geographical scales (e.g., along altitudinal

92   gradients), which makes beech populations likely to be affected by local

93   adaptation. A recent study by Garate-Escamilla *et al.* (2019) identified local

94   adaptation to variation in potential evapotranspiration in beech populations

95   across Europe. Furthermore, two other studies by Csilléry *et al.* (2014) and

96   Pluess *et al.* (2016) found evidence for local adaptation to climate, as the authors

97   identified adaptive variation at very short spatial scales (< 10 km) in the south of

98   the French Alps and at a regional scale across Switzerland (> 100 km),

99   respectively. Thus, beech appears to be an appropriate species to identify the

100   adaptive component of genetic variability, determine the environmental factors

101   shaping this component variation in populations, and explore the potential

102   impact of climate change on the future adaptive landscape of the species.

103   Here, we aimed to i) identify the environmental constraints partially

104   shaping the genetic differentiation of beech along the French Alps; ii) isolate the

105   genetic variation associated with environmental gradients; and iii) consider

106   genetic heterogeneity to estimate the species' capacity to respond to climate

107   change. To answer these questions, we based our investigations on a single-

108   nucleotide polymorphism (SNP) dataset obtained through a double-digest

109   restriction-site associated DNA sequencing procedure (ddRADseq, Peterson *et al.*

110   2012). We used a large number of SNPs genotyped in our sampling to combine

111   analyses of genetic differentiation, genetic variance decomposition and genome

112   scans. This approach allowed us to identify the main climatic drivers of *F.*

113   *sylvatica* genetic variation and to extrapolate the contemporary and future

114   adaptive potential of this species along the French Alps.

115

MATERIALS AND METHODS

1. Material and genetic data acquisition

We sampled 36 populations of *F. sylvatica* along the western front of the French Alps (Fig. 1 and Table S1) during the summer of 2016. The complete sampling included 570 individuals distributed in 19 different mountain ranges located from the Jura to the Mediterranean Alps. This sampling covered most of the distribution of *Fagus sylvatica* in the French Alps.

ddRADseq protocol - DNA was extracted from one or two leaves of each individual using the DNeasy Plant kit (QIAgen) according to the manufacturer's instructions, and samples were stored at -20°C. A double-digested RAD (restriction site associated DNA) experiment was conducted on the 570 individuals (using 12 different libraries) using a modified version of the protocol described in Peterson *et al.* (2012). The enzymes used were PstI and MspI; for more details on the experimental protocol, see Capblancq et al. (2015). The 12 libraries were then sequenced on a complete lane of Illumina Hi-Seq 2500 2x 125 (Fasteris SA, Switzerland). DNA reads (~250 million reads) resulting from the sequencing were used to genotype single-nucleotide polymorphism (SNP).

Sequences treatment - We demultiplexed the sequences with the program *STACKS* (Catchen *et al.* 2013) using a Phred score of 10 for reads filtering (*process_radtags* function). We mapped the reads against the newly assembled beech genome (Mishra *et al.* 2018) using BWA software (Li and Durbin 2009) and the BWA-MEM algorithm. We processed the mapped sequences with the *gstacks*

139   function of *STACKS* pipeline using a minimum mapping quality of 20. Finally, only

140   SNPs on tags present in at least 60% of the 570 individuals and with a frequency

141   higher than 0.5% (~3 individuals) were used for further analyses.

142   Using the *ProcessMyRAD* scripts (https://github.com/cumtr/PmR, Cumer

143   *et al.* 2018), we also produced graphical outputs at the filtering step of the

144   treatment, which allowed an evaluation of the experimental success for each

145   library and individual. This method provides the proportion of retained reads

146   after the first step of filtering, the number of reads by individuals, the quality of

147   the sequencing and the proportion of the different nucleotides along the reads.

148

149   **2.   Genetic variation among the populations**

150   We estimated individual grouping and population differentiation using

151   principal component analysis (PCA) that was conducted on the ddRADseq SNPs

152   dataset using the *adegenet* R package (Jombart 2008). We also estimated the

153   population structure using a constrained method of genetic clustering: sNMF

154   (Frichot *et al.* 2014). This analysis was performed using the R package *LEA*

155   (Frichot and François 2015), with the number of genetic clusters (K) ranging

156   from 2 to 6.

157

158   **3.   Testing genetic-environment relationship**

159   To detect genetic-environment association in alpine populations of *Fagus*

160   *sylvatica*, we tested the link between a set of climatic variables and the genetic

161   variability across the sampled populations. Specifically, we used a series of partial

162   redundancy analysis (RDA) performed using the function *rda* of the *vegan*

163   package in R (Oksanen *et al.* 2015). The genetic dataset (e.g., allelic frequencies in

164   populations in our case) was used as response matrix Y, and a set of

165   environmental variables was used as explanatory matrix X. A third matrix of

166   geographic variables and "neutral" genetic composition was used as a

167   conditioning matrix to avoid confounding associations between genetic

168   variability and geography and/or evolutionary history. This conditioning matrix

169   allowed the consideration of a potential pattern of isolation caused by distance or

170   a genetic differentiation due to lineage splitting rather than adaptation to the

171   environment. All the different combinations of the explanatory and conditioning

172   variables have been used in the RDA model to partition the percentage of genetic

173   variance explained by each specific set of variables (e.g., climatic, geography or

174   "global/neutral" genetic composition).

175   The geographic variables used in the partial RDA models are typically the

176   coordinates of the population (longitude: x and latitude: y), and the "neutral"

177   genetic composition is the ancestry coefficient obtained from the sNMF analysis

178   for K=2 (see section *Genetic variation among the populations*). We used longitude

179   and latitude without any correction for the curved surface of the planet because

180   of the small geographic scale considered here. The set of climatic variables used

181   in this study came from Thuiller *et al.* (2014), and these variables are known to

182   be drivers of plant distribution over an area, such as the French Alps. These

183   variables include the annual sum of degree-days above 0°C (*degg0*), the annual

184   mean potential evapotranspiration (*etp_mean*), a moisture index (*mind_mean*),

185 the sum of the annual precipitation (*prec_sum*), the maximum temperature

186 (*tmax_mean*) and the minimum temperature (*tmin_mean*). These variables were

187 available at 250m-resolution in the studied area (see Thuiller *et al.* 2014 for more

188 details). To avoid multi-collinearity between variables, only variables that were

189 not overly correlated (i.e., R-squared < 0.8) were included in the final analysis,

190 which avoids overfitting due to redundant information (Fig. S2).

191

192 **4.   Signature of adaptation**

193   Specific loci associated with environmental adaptation were searched

194 using a method derived from RDA and following the procedure proposed in

195 Capblancq *et al.* (2018). The approach uses RDA to identify loci that are

196 extremely linked to environmental variables and are likely under selection in the

197 sampled population (see Lasky *et al.* 2012, Forester *et al.* 2016 & 2017, Capblancq

198 *et al.* 2018). This method starts using a classical RDA procedure, and an outlier

199 locus is detected when its projection in the K first axis of the RDA (principal

200 component) does not follow the projection of the majority of the loci along the

201 same K principal component. More precisely, outliers correspond to loci for

202 which the Mahalanobis distance (i.e., the distance estimated between the z-scores

203 of the locus on the K first principal component and the mean of all the loci z-

204 scores on the same set of principal components) is extreme relative to the

205 distribution of the Mahalanobis distances of all loci (Luu *et al.* 2017, Capblancq *et*

206 *al.* 2018). A p-value is then obtained for each locus after a transformation of the

207 Mahalanobis distances (see the procedure in Luu et al. (2017)).

208 In this study, we used the population allelic frequencies as the genetic

209 matrix (response matrix Y) rather than individual genotypes; this avoided biases

210 due to a non-equal number of samples in the genotyped populations. Only the

211 SNP with a minor allele frequency superior to 10% of the complete sampling (> 5

212 indidivuals). Furthermore, we wanted to consider the past evolutionary history

213 of the population during the RDA, and thus, we conditioned the analysis using the

214 global genetic structure observed in the sampling. To do so, we used the ancestry

215 coefficient obtained from the sNMF analysis for K=2 (see section *Genetic variation*

216 *among the populations*). We assumed here that the ancestry is a pertinent proxy

217 to catch the neutral genetic differentiation due to both isolation caused by

218 distance among populations and demographic history of the populations (*i.e.* post

219 glacial colonization history). The use of ancestry as a conditioning variable could

220 remove any variation linked to both geography and environment. We resolved

221 this issue by sampling multiple populations showing strong environmental

222 differentiations (*i.e.* differences in altitude, see Figure 1) at very short distance.

223 Finally, we controlled for a false discovery rate (FDR) by transforming the p-

224 values into q-values using the procedure of the *qvalue* R package (Storey, 2002).

225 We kept the loci with q-values less than 10^{-4}, which corresponds to a false

226 discovery rate of 0.01%.

227

228 **5. Spatial extrapolation of the adaptive landscape**

229 **Adaptive indices -** We performed a second RDA with only the loci

230 previously found as outliers (*q.values* < 0.0001). This set of outliers provides an

231 "adaptively enriched genetic space" (Steane *et al.* 2014), and a second RDA on

232 these specific loci allows the identification of environmental variables that are the

233 most correlated with putative adaptive variation. Thus, we used the scores of the

234 different environmental variables along the first two RDA axes to build composite

235 indices that predicted the adaptive score of individuals in the environment

236 following the formula:

237 $$\text{RDA index} = \sum a_i b_i$$

238 where *a* is the variable score (loading) along the concerned RDA axis, *b* is the

239 value of the standardized environmental variable in the concerned location, and *i*

240 refers to the different variables used in the RDA model (Steane *et al.* 2014).

241 Adaptive indices were estimated in the entire study area for both RDA1 and

242 RDA2. A map representation of these indices allows for a better understanding of

243 the adaptive landscape of *F. sylvatica* in the French Alps.

244 **Future predictions -** The same climatic variables previously used were

245 projected for 2050-2080 following the A1B emission scenario (see Thuiller *et al.*

246 2014 for more details). In the same way as it was conducted for the current

247 climatic conditions, we used these projected variables to spatially predict the

248 RDA1 and RDA2 indices in the future. We then used the present occurrences of *F.*

249 *sylvatica* in the French Alps (data came from the French National Alpine Botanic

250 Conservatory, CBNA, and the National Mediterranean Botanic Conservatory,

251 CBNMED) to extract the current favourable range of the RDA1 and RDA2 indices

252 and to compare them to the indices values predicted in 2080 using the A1B

253 scenario.

254   **Assessing the capacity of species' responses to climate change –** For

255   each pixel included in the current range of *Fagus sylvatica* in the French Alps, we

256   estimated a need of adaptive score change, equivalent to the genetic offset

257   proposed by Fitzpatrick and Keller (2015). To do so, we subtracted for both

258   RDA1 and RDA2 the value of the index predicted with the present climatic

259   conditions and the value of the index predicted with the future climatic

260   conditions. We thus obtained a specific genetic offset for each of the two RDA axis

261   and sum them to obtain an estimate of the global genetic offset. Moreover, for

262   each future favourable pixel, we measured the distance to the closest population

263   showing an equivalent adaptive score under the current climatic conditions. For

264   this purpose, we looked for both RDA1 and RDA2 the closest pixel showing an

265   index being in the same quartile under the current climatic conditions and

266   averaged for each pixel the two distances obtained (RDA1 and RDA2). With this

267   index we wanted to estimate a resistance of adaptation potentially occurring if

268   the alleles favourable in the future climatic conditions have to migrate long

269   distances to reach the focal location. Finally, we investigate the levels of adaptive

270   standing genetic variation (SGV) in the populations by calculating the mean of the

271   outlier loci allele frequency variances ($p \ x \ q$), as an index of within population

272   adaptive variation (Chhatre *et al.* 2019). In the same way, we estimated the

273   Population Adaptive Index (PAI) of each population as proposed by Bonin et al.

274   (2007). PAI is calculated by measuring the absolute difference between the

275   adaptive allele frequencies of a specific population and the mean adaptive allele

276   frequencies of the complete sampling. When the estimation of allele frequency

277   variance gives a measure of the availability of the adaptive alleles in the

278   population (Standing Genetic Variation), the PAI gives an estimate of the

279   extremeness of the population along the gradient of genetic adaptation.

280

281   **RESULTS**

282   **1.   *Fagus sylvatica* genetic variability along the French Alps**

283   The double-digested RAD libraries produced a mean of 11,588 fragments,

284   with a mean coverage of 22.6 reads/fragment for the 569 samples that were

285   analysed. The polymorphism in the RAD fragments allowed the scoring of 7,010

286   independent SNPs with 19% of missing data at the end. PCA on these SNPs

287   succeeded in differentiating the sampled populations of *Fagus sylvatica*. The

288   differentiation was mostly carried by the first PC axis, which exhibited a clear

289   north-south differentiation pattern with high scores for the Mediterranean

290   populations (e.g., Prealpes-Azur or Verdon) and negative scores for the northern

291   populations (Fig. 2). These results were congruent with the results of genetic

292   clustering analysis using sNMF. The sNMF analysis showed a progressive

293   gradient of assignation when two clusters were constrained with the same north-

294   south pattern of differentiation (Fig. 2). When looking at higher values of K, we

295   can see that new cluster assignations did not identify clear genetic groups of

296   individuals and/or were not really consistent with geography (Fig. S3).

297

298   **2.   *Genetic-environment association***

299 The different partial RDAs performed on the population allelic frequencies

300 allowed the identification of the proportion of genetic variance independently

301 explained by the climatic variables, geography or ancestry of the populations. The

302 climatic variables used in the analysis included the mean evapotranspiration

303 (*etp_mean*), the maximum and minimum temperature (*tmax_mean, tmin_mean*),

304 the sum of the annual precipitation (*prec_sum*) and the moisture index

305 (*mind_mean*). We removed the other variables because they were strongly

306 correlated with the previous ones (Fig. S4). For all the RDAs and to avoid

307 potential correlation bias due to rare values, we removed all the loci with minor

308 allele frequencies inferior to 1% of the sampling, leaving us with 6,857 loci for

309 which allele frequencies were calculated for all of the populations.

310 The model that considered all the variables (e.g., climatic variables,

311 geographic variation and ancestry) produced a strong significant association

312 between these variables and the allelic frequencies in the populations. This model

313 explained 35.2% of the total genetic variability (Table 1). The different partial

314 RDAs identified that 47.1% of this global explained variance was associated with

315 climatic variation only (16.6% of the total genetic variance), 19.4% was due to

316 geographic variations (geographic coordinates), 13.9% was due to the ancestry of

317 the individuals and 19.6% was not distinguishable among these different

318 parameters. The five climatic variables used were able to explain a considerable

319 and significant part of the genetic variability, suggesting that environmental

320 conditions have constrained a portion of the genetic composition in *F. sylvatica*

321 populations along the Alps.

322   Building on these results, we conducted the RDA-based genome scan

323   procedure using the same five non-correlated climatic variables and the ancestry

324   of the individuals for $K = 2$ (averaged by population), as a conditioning matrix. We

325   retained the 3 first axes to process the genome scan, as indicated by the

326   screeplots (Fig. S4). The analysis with an FDR of 10^{-4} retains 65 loci as outliers

327   among the 6,857 tested SNPs (Fig. 3A). The part of the genetic sampling

328   represented by these 65 loci (0.01% of the SNPs) showed a strong association

329   with environmental variation and was hypothesized to represent genomic

330   regions associated with environmental selection in *F. sylvatica*. This set of 65

331   highly significant loci was then considered as the "adaptively enriched genetic

332   space" of *Fagus sylvatica* in the Alps. They served as a base to extrapolate the

333   adaptive constraints encompassed by the species in the sampling area and to

334   analyse the adaptive landscape.

335

336   **3.   *Adaptive landscape***

337   When we performed a new RDA on the 65 outlier SNPs constituting the

338   adaptively enriched genetic space, we found that the two first axes explained

339   most of the adaptive genetic variance among the populations (*i.e.*, 35 and 20%,

340   respectively). RDA1 was correlated with most of the environmental variables

341   used in the analysis and contrasted high maximum temperatures from high

342   values of minimum temperature, precipitation and moisture index (Fig. 3B). Such

343   gradient contrasts the populations from northern locations in the pre-alps where

344   the minimum temperatures are not very low and the precipitation are important

345   with the southern mountainous populations where the minimum temperature is

346   usually lower but with a drier climate. In the other side, the RDA2 was correlated

347   with another part of the variation that contrasted high values of maximum and

348   minimum temperature to high values of precipitation or moisture index. Thus,

349   RDA2 was clearly associated with the altitudinal constraints.

350   In the same way, the correlation between the different outlier SNPs and the

351   RDA axes showed interesting patterns (Fig. 3A and Fig. S5). Some of the 65

352   outliers were specifically associated with one of the two RDA axes, demonstrating

353   that the genetic variation associated with RDA1 and RDA2 was partially

354   supported by different loci (Fig. S5). The RDA procedure orientated ordination

355   axes in the direction of orthogonal environmental gradients. The two observable

356   sets of adaptive loci were thus "independently" associated with the two different

357   environmental constraints experienced by *F. sylvatica* in the French Alps.

358   Nonetheless, many loci were associated with both RDA1 and RDA2. Finally, the

359   variation in the allelic frequencies across the different sampled locations was

360   high for all 65 outlier SNPs (Fig. S5). The frequency differential varied from at

361   least 0.50% and up to 0.8%, showing that outlier identification was not based

362   only on small variations.

363   We extrapolated the adaptive genetic variation to the entire French Alps by

364   estimating the RDA1 and RDA2 scores in the entire range of *F. sylvatica* in the

365   French Alps (Fig. 4). The two gradients showed some similarities but the RDA1

366   index was mainly differentiating the mountain ranges receiving more

367   precipitation in the northern Alps (i.e., Chartreuse, Bauges, Aravis, Chablais, Jura)

368   from the rest of the study area, especially the valleys (i.e., Durance valley, Haute-

369   Maurienne) and the hinterland of the Provence region (Fig. 4) that are typically

370   much drier. On the other side, the RDA2 index was mostly impacted by the

371   altitude of the location. The highest values of this index corresponded to high

372   elevations, and the lowest values were found near the Mediterranean Sea or in

373   lowlands along the Rhone River. 99% of the current occurrences of *F. sylvatica*

374   had an RDA2 index value ranging between -0.93 and 5.99 (Fig. 5). These two

375   values probably represented the limits of the favourable range for *F. sylvatica*

376   along this adaptive constraint.

377

378   **4.   *Potential capacity of response to climate change***

379   Regarding the future predictions made for 2080 using the A1B scenario of

380   climate change, we found a change in the RDA1 index would especially concern

381   the southern areas of the range where the future index values (pixels with a value

382   >2 in Fig. 4) would exceed the values observed for the current climatic conditions

383   (Fig. 4 and Fig. 5). However, we found that the predicted change of the RDA2

384   index was even more dramatic. According to the predictions, almost one-quarter

385   of the current location of *F. sylvatica* would be beyond the RDA2 index favourable

386   range in 2080 (Fig. 5). In this case, the change would mainly affect the lowland

387   parts of the range where the RDA2 values would go under the lower limit of the

388   index in the current climatic conditions (values < -2 in Fig. 4 and Fig. 5).

389   Different proxies have been measured to investigate the capacity of *F.*

390   *sylvatica* to respond to climate change across the French Alps. The need of

391 adaptive score change between the current and future climatic conditions (Fig.

392 6A) and the distance of populations showing current adaptive scores equivalent

393 to the future adaptive needs (Fig. 6B) have been estimated by combining the

394 RDA1 and RDA2 indexes (see Materials and Methods). These two proxies,

395 respectively called genetic and geographic offset, have been estimated across the

396 current range of *F. sylvatica* in the French Alps, not taking into account potential

397 future colonization of newly favourable locations. We first observed that none of

398 them were homogeneous across the studied area, the genetic offset being greater

399 in mountains areas (Fig. 6A), while the highest values for the geographic offset

400 were found in the valleys and at low elevations (Fig. 6B).

401 Finally, when looking at the actual adaptive genetic variation in the

402 sampled populations, we found that the locations sampled in the southern part of

403 the Alps showed a combination of low rate of standing genetic variation and high

404 value of PAI (Fig. 6C). The six populations sampled in the Chartreuse and Bauges

405 mountains also showed weak level of SGV, but a relatively low PAI. One

406 population sampled at relatively high elevation in the Devoluy mountains

407 showed, at the opposite, a combination of high SGV and PAI.

408

DISCUSSION

410 *Fagus sylvatica genetic variability and evidence of association between genetic and*

411 *environmental variation*

412 Benefitting from the large genetic matrix obtained through ddRADseq

413 sequencing, we found a substantial genetic variability across the *Fagus sylvatica*

414   populations of the French Alps. We observed a gradual genetic differentiation

415   between the northern locations (i.e., Jura or Chablais mountain ranges) and the

416   locations close to the Mediterranean Sea (Fig. 2). This latitudinal gradient of

417   genetic composition suggests a pattern of isolation by distance without a clear

418   geographical barrier to gene flow among *F. sylvatica* populations. The absence of

419   discrete genetic groups is also congruent with the history of postglacial

420   colonization proposed for *F. sylvatica* by Magri and colleagues (2006) and by

421   Magri (2008). In these studies, the authors suggested that the north-western

422   French Alps would have served as a refuge for *Fagus sylvatica* during the Last

423   Glacial Maximum (LGM). The species would have colonized all the French Alps

424   from this particular location since the end of the glacial period.

425   Disentangling the signatures of isolation by distance (IBD), local adaptation

426   and demographic history in the genetic variation of a species can be tricky

427   (Nadeau et al. 2016). IBD is largely known to induce neutral genetic gradients

428   that are strongly correlated to the distance among populations (Meirmans 2012,

429   Orsini *et al.* 2013), and postglacial colonization is able to produce allele frequency

430   gradients similar to IBD as a result of repeated founder events along the

431   colonization front (De Lafontaine et al. 2013). Thus, it is difficult to separate the

432   effects of geography, environment and demographic history when they are

433   spatially correlated, as seems to be the case for *F. sylvatica* in the French Alps. The

434   use of partial RDAs allowed us to tackle this issue by decomposing the portion of

435   genetic variance explained by each group of variables when any potential

436   associations with the other variables have been removed (Legendre and

437   Legendre 2012). Our results showed that a proportion of *F. sylvatica* genetic

438   variation was explained by geographic distance (7%), demographic history (5%)

439   and climate (17%). A confounding effect of the three factors was also found (7%

440   of the variation), attesting the difficulty of completely disentangling these

441   variables (Table 1).

442   A great portion of the genetic variation was explained by climate (17%),

443   which suggests that environmental variables partially shaped the genetic

444   composition of *F. sylvatica* populations across the sampling area. We suggest here

445   that local adaptation occurs in *F. sylvatica* populations along the French Alps, as

446   has already been evidenced in Mount Ventoux (France, Csilléry *et al.* 2014), in

447   Switzerland (Pluess *et al.* 2016) and at very short geographic scales along an

448   altitudinal gradient in two adjacent valleys of the Pyrenees (Vitasse *et al.* 2009).

449   At larger geographic scale, provenance trials across whole Europa have revealed

450   population differentiations suggesting local adaptation (Gömöry & Paule 2011,

451   Kreyling *et al.* 2014) and a recent study investigating at the same time the effects

452   of plasticity and genetically driven adaptation also found evidence of local

453   adaptation to potential evapotranspiration across the whole range of *F. sylvatica*

454   in Europe (Garate-Escamilla *et al.* 2019). Our results are therefore

455   complementary to these previous works, confirming the idea that this species is a

456   good model to further investigate the factors driving species adaptation and

457   distribution.

458

459   *The factors driving adaptive genetic variation in F. sylvatica*

460   The statistical approach we used to investigate the drivers of local adaptation in

461   *F. sylvatica* is based on redundancy analysis (RDA) and is just starting to show its

462   potential in the field of genetics of adaptation (Lasky et al. 2012, De Kort *et al.*

463   2014, Steane *et al.* 2014, Forester *et al.* 2016 and 2017, Capblancq *et al.* 2018).

464   RDA has shown great potential in identifying the signatures of selection and

465   adaptive loci, both in comparison with other genome scan methods (Forester *et*

466   *al.* 2017, Capblancq *et al.* 2018) and in different types of environments (Forester

467   *et al.* 2016). Such multivariate approaches are thought to be more efficient in

468   detecting multi-loci selection since they consider the potential co-variation

469   among genetic markers (Rellstab *et al.* 2015). This fact is important to highlight

470   because we know that traits involved in local adaptation seem to be triggered by

471   many genes that generally have weak effects (Aitken *et al.* 2008, Savolainen *et al.*

472   2013, Yeaman 2015, Bay *et al.* 2017a). Moreover, by allowing the identification of

473   the environmental gradients that are associated with adaptive genetic variation,

474   this approach can be used to spatially predict a landscape of species adaptive

475   capacity under current or future environmental conditions (Steane *et al.* 2014,

476   Fitzpatrick and Keller 2015, Capblancq *et al.* 2018).

477   Here, we found that two principal environmental gradients have triggered two

478   relatively independent adaptive genetic responses in the French alpine

479   populations of *Fagus sylvatica* (Figs. 3 & 4). The first adaptive genetic variation

480   identified was associated with both humidity and minimum and maximum

481   temperatures variations (RDA1 in Fig. 3). This gradient contrasts the northern

482   mountainous locations (*i.e.* high elevation) with the southern and valleys

483   locations (*i.e.* low elevation) of the sampling zone (Fig. 4). Previous studies have

484   described that southern and internal zones (*e.g.* Maurienne valley) of the Alps

485   receive less rainfall that impact the survival of beech populations (Ozenda 1985,

486   Courbaud *et al.* 2011). These regions showed the highest RDA1 index values (Fig.

487   4), with values very close the extreme edge of the species range in term of

488   survival capacities (Fig. 5). Furthermore, this constraint is not the only one

489   exercising a selective pressure on the *F. sylvatica* genetic variation. We found a

490   second adaptive genetic gradient linked to environmental variations induced by

491   the altitudinal gradient (RDA2 in Fig. 3 & Fig. 4). Such finding strongly suggests

492   that the identified outlier genetic markers are close to genomic regions involved

493   in *F. sylvatica* adaptation to the differential climatic conditions between lowlands

494   and high altitudes. A signature of genetic adaptation correlated with the

495   altitudinal gradient has similarly been found by Csilléry and colleagues (2014) in

496   one population of the south-western French Alps (Mount Ventoux).

497   To temper our results, it is important to note that, given a genome size of 535

498   Mbp (Kremer 2012), the 6,857 genotyped SNPs would be spaced at about 78, 000

499   bp on average. Linkage disequilibrium probably decays much more rapidly, even

500   around selected sites. We are thus aware that we certainly missed genomic

501   regions associated with environmental selection. More genomic data such as

502   whole genome sequencing would be interesting to produce an analysis at finer

503   scale. In the same way, because of data availability, we only included climatic

504   variables in our analysis and possibly missed some other environmental factors

505   that could have played a role in *F. sylvatica* local adaptation. However, climate is

506   known to be the main causal factor shaping the distribution of tree species in

507   temperate areas (Svenning and Skov 2004, Morin *et al.* 2007). Moreover, the two

508   environmental pressures identified as drivers of the adaptation of *F. sylvatica* are

509   congruent with the main environmental constraints driving other tree species'

510   distributions (e.g., *Picea glauca*, Andalo *et al.* 2005; *Picea mariana*, Beaulieu *et al.*

511   2004).

512

513   *Future of the species in the Alps*

514   All general atmospheric circulation models predict that there will be major

515   changes in temperature and rainfall by the turn of the century (IPCC 2007 and

516   2013). These predictions are likely to induce dramatic changes in most

517   ecosystems around the globe and are of special concern for mountainous

518   ecosystems (Thuiller *et al.* 2005, Thuiller *et al.* 2014, Duputié *et al.* 2015). In this

519   context, *Fagus sylvatica* could be severely impacted (Magri 2008, Meier *et al.*

520   2011). According to the A1B scenario of climate change used in our simulations,

521   the favourable zone for the survival of *F. sylvatica* in the French Alps would

522   indeed change substantially (Fig. S6). The model predicted a drastic loss of

523   favourable zones in lowlands and valleys and a species range shift towards higher

524   altitudes, a pattern already observed for many plant species (Pauli *et al.* 2012,

525   Steinbauer *et al.* 2018). This first model basically assumes a genetic homogeneity

526   and a full dispersion of adaptive alleles. Nonetheless, we found evidence of

527   significant co-variation between environmental and genetic gradients in the

528   populations of beech in the French Alps. Assuming that the genetic variation

529   identified here is indeed involved in species adaptation to climate, the species'

530   sensitivity to climate change could spatially vary depending on the strength of the

531   environmental change experienced by the local populations and the availability of

532   adaptive alleles nearby (Franks and Hoffmann 2012).

533   Investigating the capacity of populations' response to climate change, we

534   found that beech populations in high mountainous areas would need a greater

535   change in adaptive genetic composition than would lowland or valley populations

536   (Fig. 6A). The important changes in the climatic conditions in these areas would

537   constrain a consequent change in the adaptive genetic component. In contrast,

538   lowlands and valleys exhibited a weaker genetic offset but will host populations

539   the farthest from the current locations showing the genetic composition that will

540   be required under the future environmental conditions (geographic offset in Fig.

541   6B). Considering the very short time scale studied here (<100 years), we can

542   assume that its adaptation to climate change will be mostly promoted by the

543   genetic variation already existing between the different populations (standing

544   genetic variation) (Barrett and Schluter 2008, Savolainen et al. 2013). Thus, any

545   genetic adaptation would rely on either the frequency increase of alleles already

546   present in the population or the migration of new alleles coming from locations

547   already adapted (Jump et al. 2006, Barrett and Schluter 2008, Jump *et al.* 2009,

548   Franks and Hoffmann 2012).

549   When looking more precisely at the levels of adaptive standing genetic

550   variation in the populations, we found that some populations in the Chartreuse,

551   Bauges and Chablais mountains currently show very low level of SGV, which

552   would also correspond to populations where the adaptive genetic component is

553   supposed to change the most in the next century (Fig. 6C). The small SGV found in

554   those populations could be explained by a recent founder effect linked to the

555   recent reforestation of the high elevation areas in the Alps. Fortunately, those

556   populations are also strongly connected to large populations of beech in the

557   lowland nearby from where lacking adaptive alleles could potentially migrate to

558   balance the predicted genetic offset. In general, it seems that high mountainous

559   populations will be able to find the needed adaptive genetic material more easily

560   than the lowland locations, although they also show the highest need of genetic

561   change (Fig. 6A and 6B). Such pattern is due to the geographic proximity of

562   populations that have already adapted along the altitudinal gradient (Jump et al.

563   2009). In contrast, the valleys, separated from each other by high mountain

564   ranges, could be less prompt to receive the needed adaptive genetic material. The

565   situation is probably even more problematic for the two southernmost sampled

566   populations (Prealpes-Azur or Verdon) where the levels of SGV are very low and

567   the PAI very high. Those populations are already at the extreme bound of the

568   potential genetic adaptation (high PAI) and most of the adaptive alleles are

569   already fixed or almost fixed (low SGV), impeding their frequencies to increase

570   even more in the future. In those circumstances, they might not be able to balance

571   the predicted genetic offset, yet relatively weak, and track the change of climate

572   predicted for the next decades.

573   By integrating together an appropriate genome scan approach, the

574   spatially explicit estimation of future change in adaptive selective pressure and a

575　measure of the adaptive standing genetic variation already present in the

576　populations we have given a global picture of the potential of *Fagus sylvatica* to

577　respond to future climate change in the French Alps. This type of integrated

578　analyses, more and more common in the literature (Fitzpatrick and Keller 2015,

579　Bay et al. 2018, Martins et al. 2018, Exposito-Alonso et al. 2018) is very promising

580　to better understand the role intra-specific adaptive genetic variation can play in

581　constraining species ability to track climate change (Jay *et al.* 2012, Alberto *et al.*

582　2013) and could largely benefit management strategies and conservation efforts

583　in the future (Aitken and Whitlock 2013, Steane et al. 2014, Aitken and Bemmels

584　2016).

585

586　**ACKNOWLEDGEMENTS**

596

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809

DATA ACCESSIBILITY STATEMENT

811
812 • *Fagus sylvatica* sequences data will be available on Dryad

813 • Scripts and SNP dataset are available on Github:
814 https://github.com/Capblancq/LocalAdaptationFagus

815

AUTHOR CONTRIBUTIONS

817 E. Bazin, X. Morin and S. Lobreaux designed the study. T. Capblancq
818 performed the analysis and treatments with the help of M. Gueguen and J.
819 Renaud. T. C. wrote the manuscript and all authors contributed to revisions.

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TABLES AND FIGURES

822
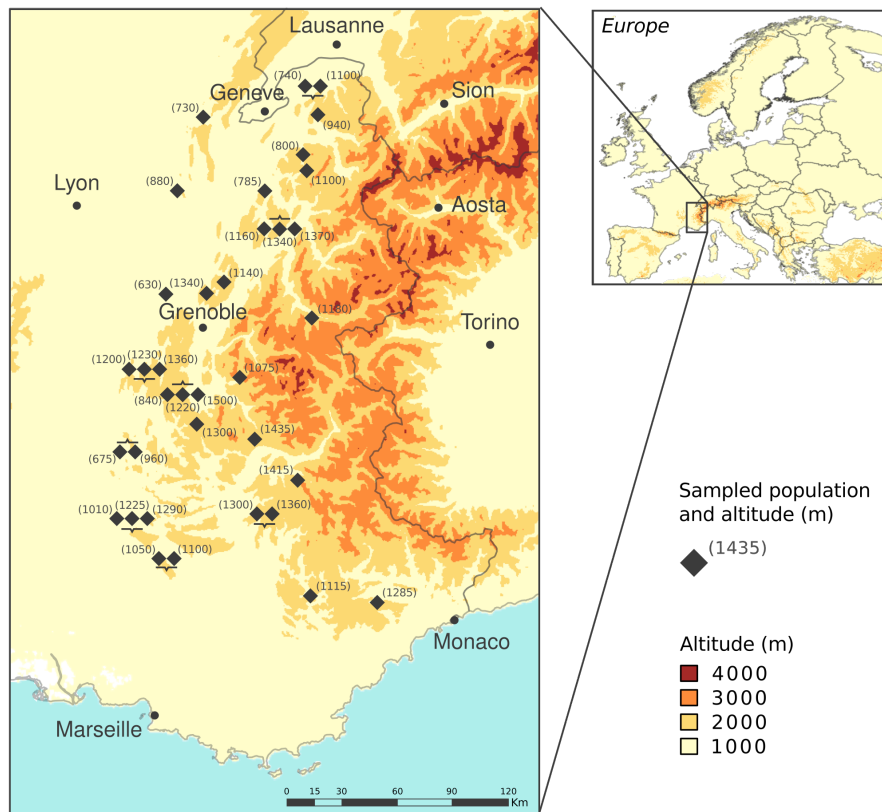
Figure 1: Map of the study area with locations of sampled population. The numbers give the number of sampled individuals in each population.
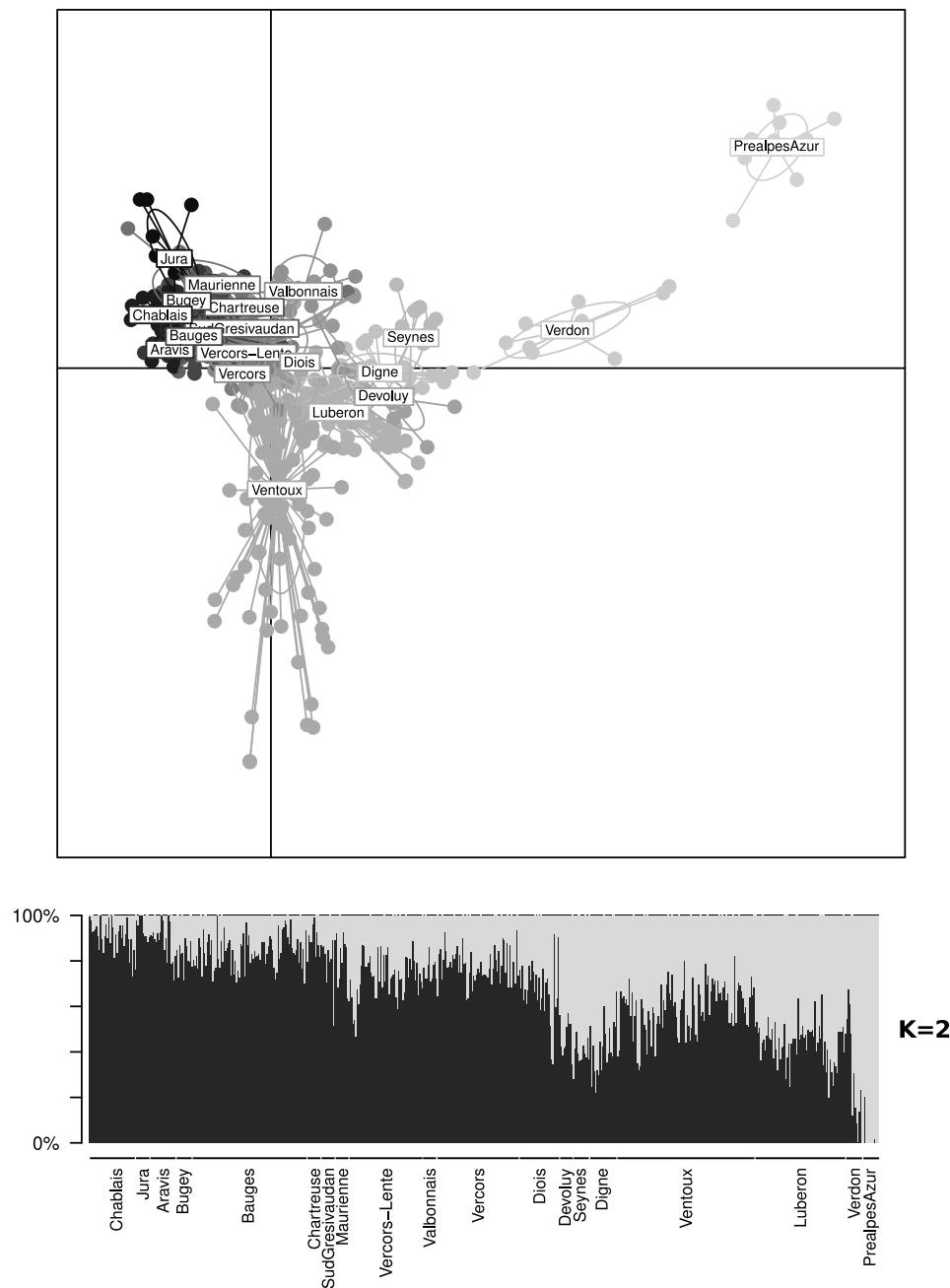
Figure 2: Principal component analysis (top) and sNMF clustering (bottom) obtained from the ddRADseq genetic data set. On the PCA plot, the first two PCs are represented; they caught 2% of the total variance (1.16% for PC1 and 0.81% for PC2). The ellipse gathered the different populations and the colour of the points and ellipses are linked to their latitude with black points coming from northern populations and grey points coming from the populations close to the Mediterranean Sea. The sNMF results are shown for K = 2, the samples are ordered depending on their latitudinal coordinates with northern locations in the left of the plot.

	Inertia	p(>F)	Proportion of total Variance
Total explainable : *F ~ clim. + anc. + geog.*	**21.92**	*0.001* ***	0.333
Pure climate : *F ~ clim. | (geog. + anc.)*	11.136	*0.001* ***	0.169
Pure geography : *F ~ geog. | (clim. + anc.)*	6.04	*0.001* ***	0.092
Pure ancestry : *F ~ anc. | (clim. + geog.)*	1.95	*0.001* ***	0.03
Confounded climate/geography/ancestry	2.794		0.043
Total unexplained	**43.82**		0.667
Total inertie	**65.74**		1

835

836 **Table 1:** Table of partial redundancy analysis results. The influences of each set
837 of variables (climate, geography and ancestry variables) have been tested
838 separately and together. The percentage of explained total genetic variance is
839 given for each of the model together with the significance of the test and the
840 percentage of variance explainable by the complete set of variables.

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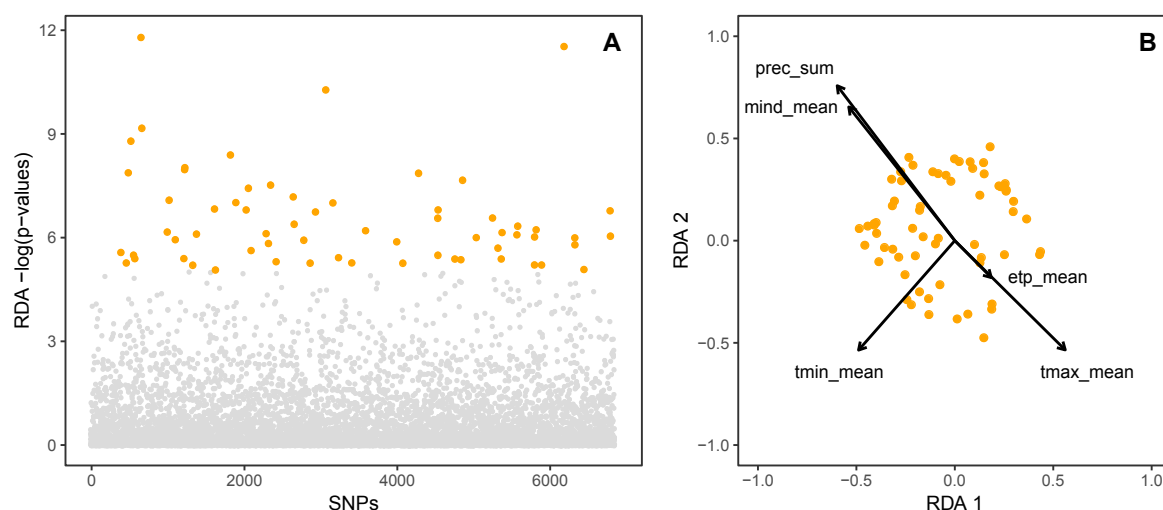
844 **Figure 3:** (**A**) Manhattan plots of the RDA results. Loci with a q-value superior to
845 0.1 % are colored in orange. The ddRADseq loci are not localised in the genome,
846 in this way the x-axis is not informative on loci proximities. (**B**) Projection of loci
847 and environmental variables into the adaptively enriched genetic RDA space. The
848 two first axes are represented; they explain respectively 36% and 20% of the
849 total variance.
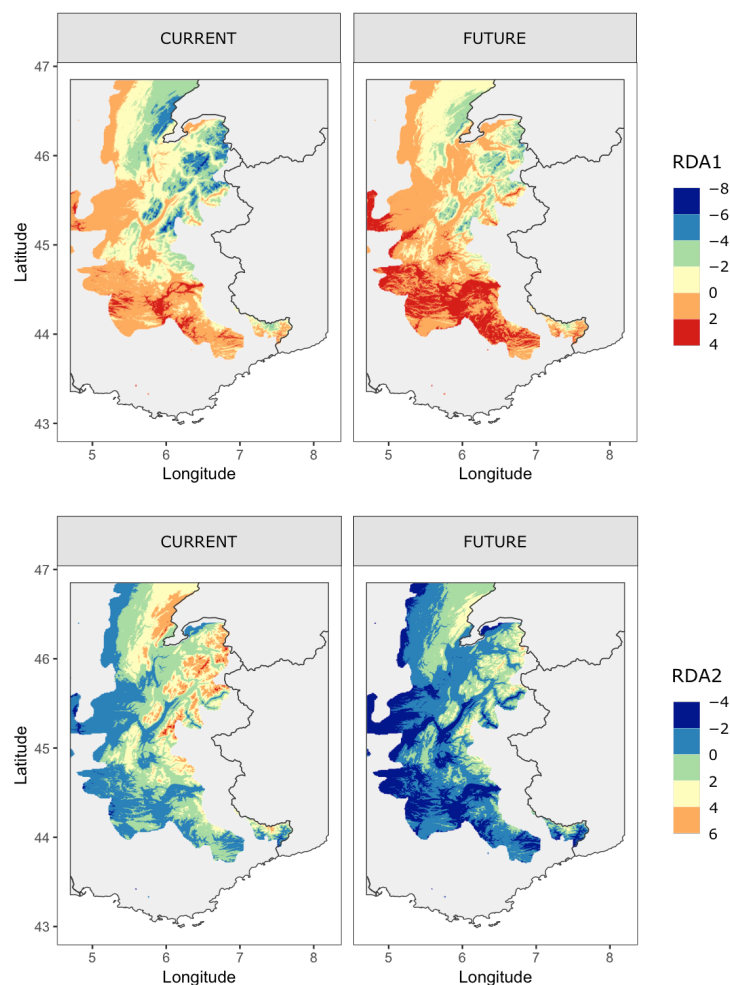
Figure 4: Spatial extrapolation of RDA1 and RDA2 gradients in the French Alps for the current climatic conditions and with future climatic conditions predicted by A1B scenario. The bottom panels show the impact of climate change in *Fagus sylvatica* genetic landscape along the French Alps.
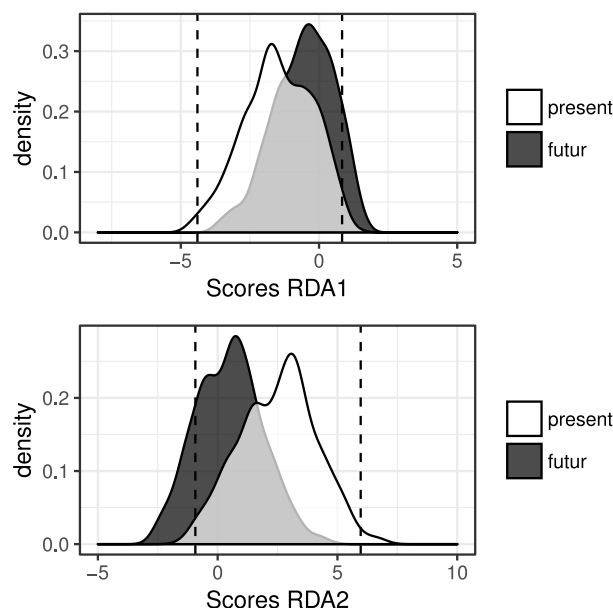
Figure 5: Distribution of RDA1 and RDA2 scores in present occurrences of *Fagus sylvatica* in the French Alps. The distribution of RAD scores is given with actual climatic conditions (top) and future estimated climatic values (bottom). The dashed lines represent the 95% interval of present RDA scores distribution. The black points indicate the actual scores of the sampled populations.
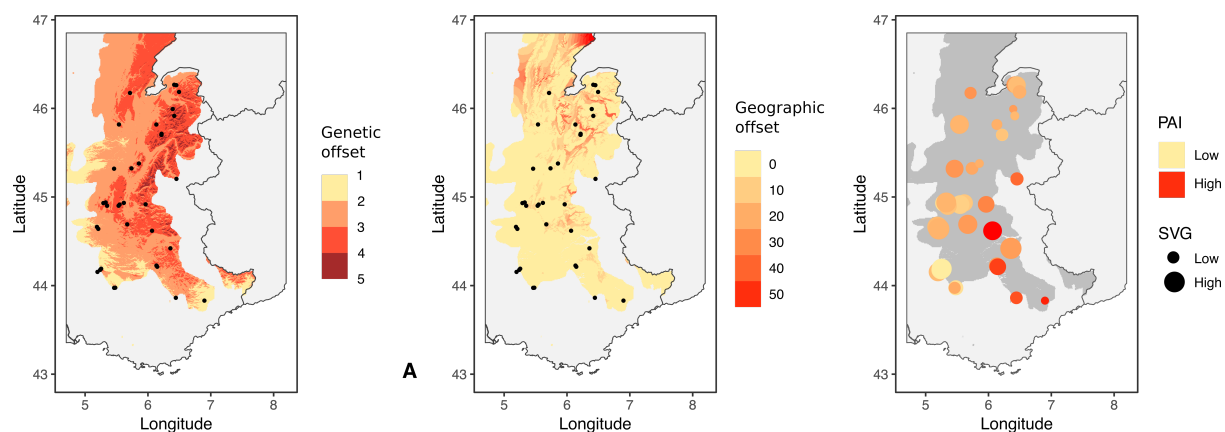
Figure 6: Spatial representation, in the future favourable locations for *F. sylvatica,* of (A) RDA1 index difference between current and future climatic conditions, (B) distances from populations currently showing a RDA1 score equivalent to the future adaptive needs and (C) a composite index taking the two previous factors into account.

SUPPORTING INFORMATION

Table S1: Description of sampled populations.
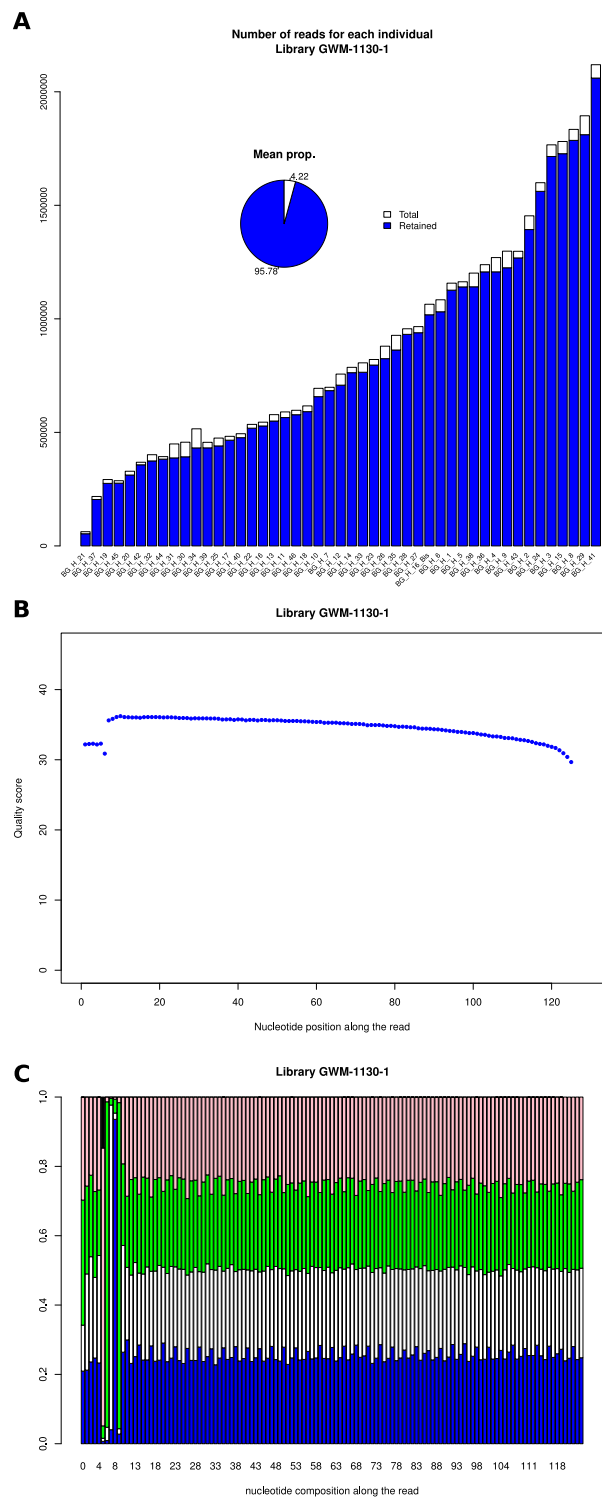
**Figure S1:** Impact of M values on polymorphism rate in ddRADseq results. M value ranges from 1 to 15.

874
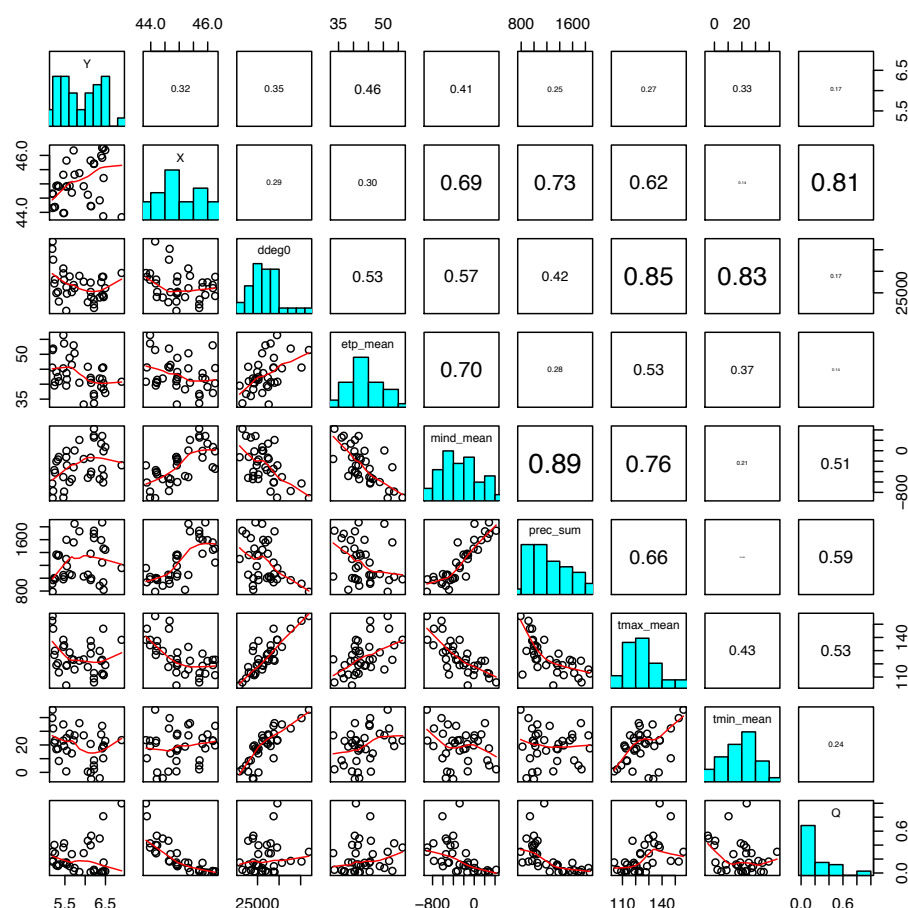
Figure S2: Correlations between pairs of climatic, geographic and ancestry variables. Y: latitude; X: longitude; ddeg0: the annual sum of degree-days above 0°C (degg0), the annual mean potential evapotranspiration (etp_mean), a moisture index (mind_mean), the sum of the annual precipitation (prec_sum), the maximum temperature (tmax_mean) and the minimum temperature (tmin_mean). The panels above the diagonal show the R-squared of the correlation and the panels below the diagonal show the value plot of each pair of variables.

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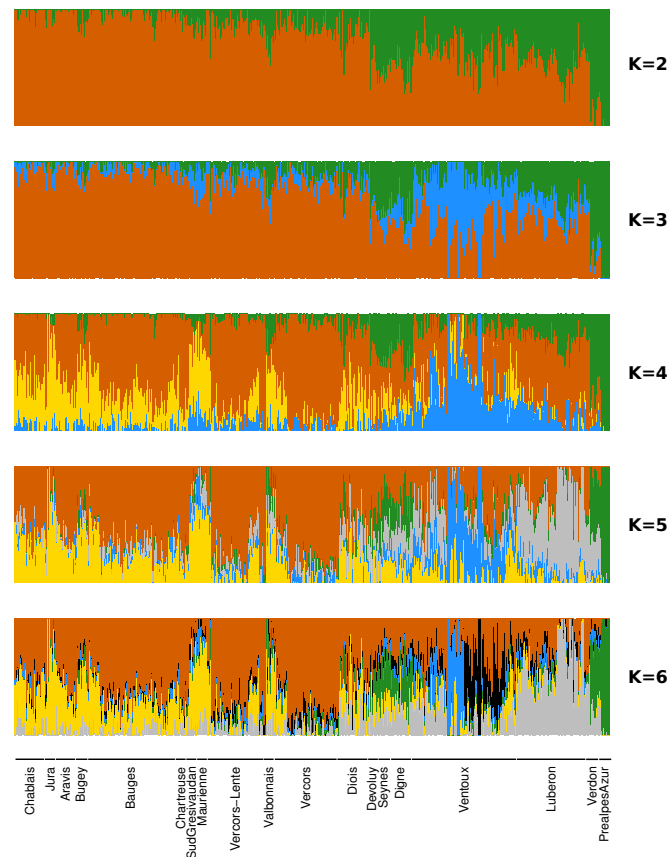
Figure S3: sNMF results with K ranging from 2 to 6

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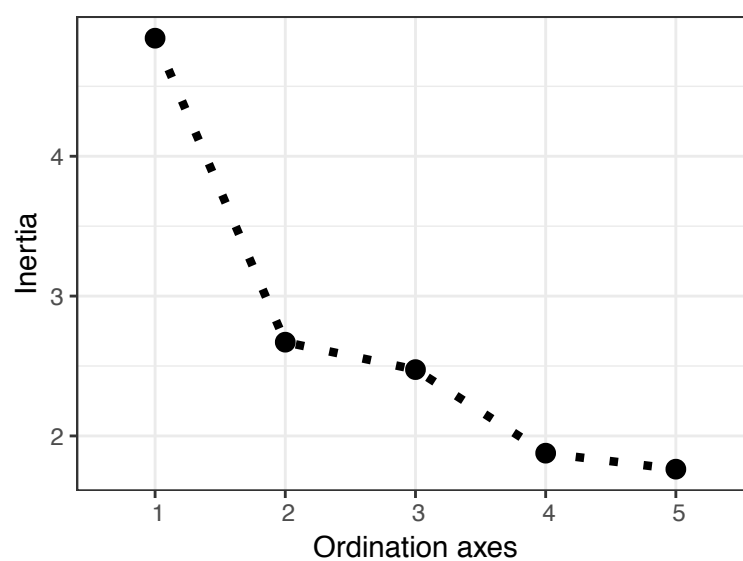
Figure S4: Scree plot for RDA analysis of the complete *Fagus* genetic dataset.
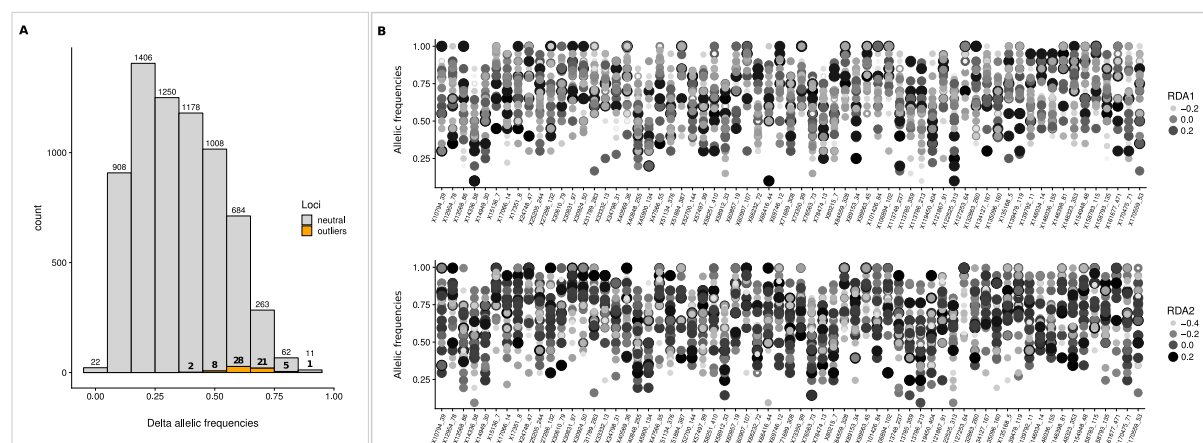
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Figure S5: Distribution of delta between maximum and minimum allele frequencies in sampled populations for the 4577 SNPs considered during RDA-based procedure (A). Variation of outlier loci allelic frequencies across the sampled populations (B). The stars above the points represent the significance of the correlation between population RDA scores and allelic frequency for each locus and independently with RDA1 and RDA2 (* < 0.1; ** < 0.05; *** < 0.01).
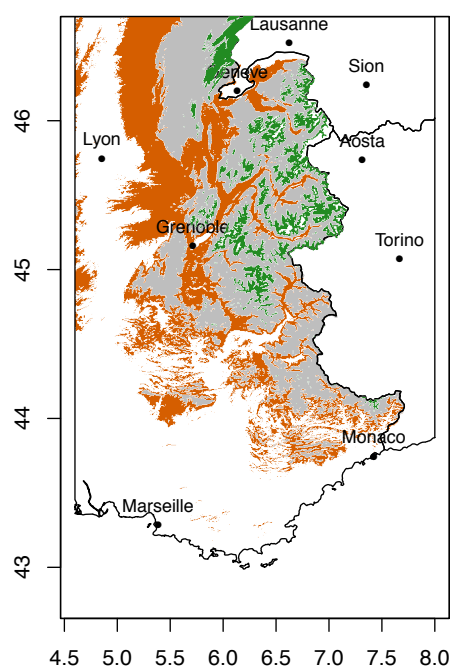

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Figure S6: Decrease (orange) and increase (green) of favourable climatic areas for *Fagus sylvatica* in 2080. Grey pixels are favourable now and remain favourable in the future.