Bachelor Thesis

Using Approximate Bayesian Computation to Infer the Number of Populations from SNP Genotype Data

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1 Introduction

A central objective in population genetics is to evaluate population structure. Genetic differences of member individuals are analysed to detect systematic genetic similarities and dissimilarities that could indicate the presence of various populations. The biological definition of a population generally follows the lines of: a population is a "group of organisms of the same species living within a sufficiently restricted geographical area so that any member can potentially mate with any other member of the opposite sex". However, as only a theoretical setting is assumed without any further context, like geography, social hierarchy and other factors that could hinder genetic exchange, individuals will be associated with one another upon to what extent their genetic information is sufficiently homogeneous. In reality population structure usually possesses a hierarchical form, in the sense that within each group until solely the individual remains further structure usually can be observed. Therefore, every group of sufficiently genetic homogeneous individuals in the highest highest population structure level will subsequently be considered as a population.
An allele is a variant of a gene found at a specific location on a chromosome (locus), and consequently alleles are responsible for the appearance of genetic variation in a species. An allele frequency describes the probability $p(a|k)$ that an individual from population k has the allele a. Since individuals in a population possess similar genotypes (their genetic make-up), so some alleles are encountered more frequently in these individuals than others and what therefore in total sets the population apart, the allele frequencies sufficiently summarise the population.
The ampleness of information usually found in a genom poses a challenge dimensionality wise if all of it were to be captured. For tasks that solely involve the analysis of genetic variation between individuals and groups of individuals it suffices to rely on the evaluation of a limited amount of genes. Mostly genes are chosen that are known to be subject to genetic variation, these particular genes are called markers. The allele frequencies at markers will consequently be used to approximate the genetic variance found in a set of to be analysed individuals. Followingly it is assumed that biallelic SNP markers are used, so there are two possible alleles at every marked locus.
A challenging task that arises with in the domain of assessing population structure, is to infer the number populations K. The difficulty stems from the often encountered ambiguity of distinguishing the hierarchical levels of population structure from another. Many models in population genetics demand the specification of the number of populations as hyperparameter in the given data. The assessability and comparability of models utilising K as hyperparameter is undermined should no realistic value for K be priorly determined. For e.g. a model with faulty underlying model assumptions could not be easily rejected since a goodness of fit evaluation would be skewed for an unrealisticly specified value of K.
So far no single best solution for determinig K has been established, probably because of the manifold of existing population scenarios. However one promising method that yielded reliable results was based on a generative model proposed by Pritchard, Stephens, and Donnelly 2000; Falush, Stephens, and Pritchard 2003. Although they implemented an MCMC algorithm in the software package STRUCTURE for determining all parameters of the generative model, their algorithm has also been widely applied for a reasonable estimation of the hyperparameter K. The most common approach involves an adhoc heuristic for detecting the "elbow" in the plotted likelihood outputs of the MCMC algorithm for different values of K. However, as the process of retrieving genetic information has been refined and thus the dimensions of genetic data have dramatically increased, the implemented MCMC algorithm has not proven to be scalable. **mention ADMIXTURE?** Also running an MCMC algorithm for inferring the number of

populations seems computationally a bit too elaborate.
Further propositions for calculating the number of populations involve the insight that population structure in given data is also conveyed through a certain pattern in the eigenvalues of the corresponding covariance matrix. In summary, for K populations K distinguishable (linearly independnt) clusters can be observed, that yield $K-1$ significantly larger eigenvalues.
Subsequently approximate bayesian computation is used by constructing a summary statistics with the eigenvalues of the covariance matrix from SNP genotype data to efficiently handle the dimensional challange. In addition, the generative model proposed by Pritchard, Stephens, and Donnelly 2000; Falush, Stephens, and Pritchard 2003 will be used to generate synthetic data, where the ground truth for the number of populations is known. Then a supervised learning method attempts to generalise a connection between the calculated summary statistics of the synthetic data instances and its ground truth values for K, to yield a model that estimates the number of populations for highly dimensional SNP genotype data with the same model assumptions as the model implemented in STRUCTURE. As supervised learning method gradient boosting with decision trees will be used.

1.1 Reframing the Problem

With the established biological framework, the task can be formulated more specific: Given the SNP genotype data of individuals from the same species, each entry from $\{0, 1, 2\}$, organised in a matrix X where each row corresponds to an individual and each column to a locus, the task is to infer how many populations K are present in the data X. If the markers sufficiently captures the genetic variation of the sampled individuals, it is expected for members of the same population to cluster together in the feature space spanned by the parametarised alleles of the selected SNP markers. A cluster is a set of data points that are similar enough (by some means of evaluation) to be grouped together, which coenciedes with the given definition for a population. So for the K populations K different clusters should be observable in the feature space. Each cluster corresponding to a specific population, where the position of the cluster should be determined by the allele frequencies of the respective population.

1.2 Approaches currently used

Clustering problems have been well invstigated and many methods for solving these problems have been proposed. The methods can predominantly be apportioned among two groups.
One group compares the similarities between datapoints by the means of a distance measure. Structure is attempted to be recognized by evaluating the distance of every datapoint to every other datapoint. Examples of distance based clustering methods are centroid based clustering, hierarchical clustering, etc.
The other group contains methods that are based on statistical model assumptions. Every datapoint is considered to be a random draw of a probability distribution. The parameters of the distributions are inferred via common statistical methods, such as maximum likelihood or baysian methods.
For a long time model based approaches were favored and used for determining desired parameter values. A widely applied (Rosenberg, Pritchard, et al. 2002; Harter et al. 2004; Rosenberg, Burke, et al. 2001) implementation of a model based method is the software package STRUCTURE first developed by (Pritchard, Stephens, and Donnelly 2000; Falush, Stephens, and Pritchard 2003). In short, at core lies the modelling of K unobserved populations by assigning them specific allele frequencies, where it is assumed that the genotype of an individual is

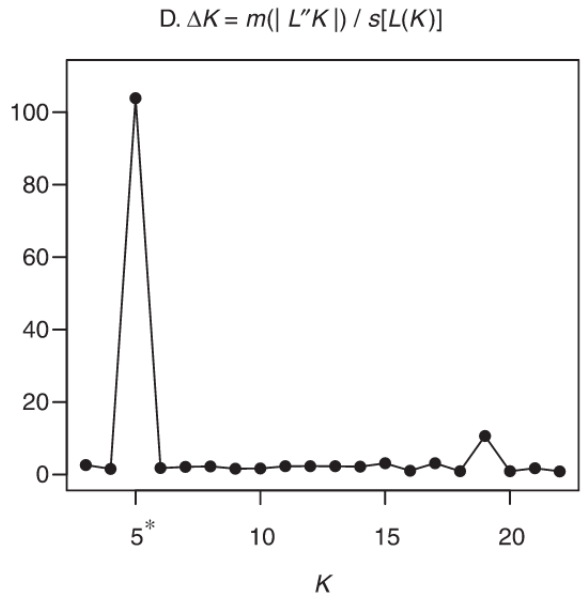
drawn according to its population allele frequencies. Furtherly the whole is embedded into a bayesian framework, where priors are set over the population membership of each individual and the allele frequencies of each population, in order to include scenario specific conditions like geography into the model and thus increasing model flexibility. Given some genotype data, the parameters of the model are inferred via a Markov Chain Monte Carlo (MCMC) algorithm with Gibbs sampling.
For the matter of determining the number of populations K present in the data the posterior $P(K|X)$ distribution is approximated for various K, where X is the given data. As only the maximum posterior of the selected K values is to be determined following reduced relation is received

$$P(K|X) \propto P(X|K)P(K)$$

(For further information on Bayes' theorem see section about Approximate Bayesian Computation)
The likelihood $P(X|K)$ is estimated by making a gaussian assumption about the distribution of the deviance D of the parameters model parameters conditioned on the data X. The assumption allows for determining the gaussian distribution by only calculating the mean and variance of D with the MCMC samples of the stationary distribution. **further information appendix** However, even Pritchard, Stephens, and Donnelly (2000) themselves describe this as a "dubious" assumption rendering the method as only a supportive argument for picking K.
Nonetheless, STRUCTURE is widely used for inferring the number of populations, however in a different way than originally intended. Most often the decision of K follows a heuristic based on the likelihood $P(X|K)$, which is calculated with the implemented Monte Carlo algorithm in STRUCTURE. The heuristic most commonly applied, investigated and proposed by Evanno, Regnaut, and Goudet 2005, relies on the search for the largest jump in the second derivative of a composed loglikelihood function. The likelihood function $L(K)$ is calculated by averaging the loglikelihood of each MCMC step and further subtracting half of the variance off that mean **(a penalisation for unstable models)**. The second derivative is defined as $L''(K|X) = L'(K+1) - L'(K)$ with of course $L'(K) = L(K+1) - L(K)$. Several runs are completed and therefore also several results for $L(K)$ received. The selection criteria then is $\Delta K = \frac{m(L''(K))}{s(L(K))}$, where m is the mean and s the standard deviation.

The method offers reasonable results, even for hierarchical clusters (the population structure in the highest hierarchy layer is the expected result), however it was conceived only as an ad-hoc solution strongly reliant on the results outputted by the STRUCTURE algorithm. Furthermore, there are indications that the method is biased towards lower Ks if not several exhaustive sampling rounds with the MCMC algorithm is completed, which tends to be at least computationally very time consuming as the dimension of genotype data has rapidly expanded with the introduction of more modern genome sequencing equipment.

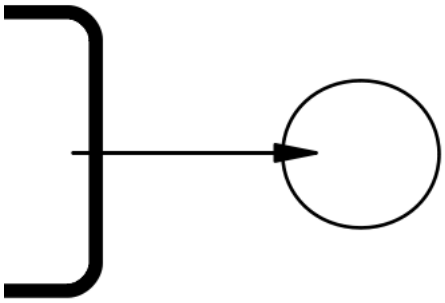
add snmf - crossentropy
A more recent approach involves the insight that cluster structure is also resembled in a structured form in the spectrum of the covariance matrix from the respective data. The connection between the spectrum of a matrix and its clustering structure has been subject to research for a fair amount of time. It was first discovered in graph theory Donath and Hoffman 1973 Fiedler 1973 and later introduced into machine learning (Shi and Malik 2000; Meila and Shi 2001; Ng, Jordan, and Weiss 2002) for further information see Von Luxburg 2007. In general the relevant insight states that: suppose K clusters can be observed in the data matrix X (w.l.o.g. X is a square matrix), then the first $k-1$ eigenvalues $\lambda_1 \geq \lambda_2 \geq \cdots \geq \lambda_{k-1}$ are significantly larger



than the remaining eigenvalues, also the corresponding eigenvectors. The number of clusters can thus be inferred by examining the eigenvalues of the data.
the In the context of inferring the number of populations by exploiting the appearence of population structure in the eigenvalues was firstly applied by Patterson, Price, and Reich 2006. They used insights from random matrix theory, which state that (under various assumptions, like the covariance matrix has properties of a random Wishart matrix) the significant $K-1$ eigenvalues are approximately Tracy-Widom distributed. The Tracy-Widom distribution describes the distribution of the largest eigenvalue for varoius random gaussian matrix ensembles, like the Gaussian orthogonal ensemble ($\beta = 1$) to which the Wishart-matrix belongs. A statistical test is constructed where the eigenvalues are checked with a chosen p-value if there is substantial evidence for the eigenvalue to be Tracy-Widom distributed.

Further research has been made with random matrix theory (RMT) to concretise the behaviour of the first $k-1$ eigenevalues, including, under certain assumptions, a mathematicaly quantifieable threshhold that destinguishes significantly larger eigenvalues from lower ones. K. Bryc, W. Bryc, and Silverstein 2013, indicating further that it is only necessary to detect the jump point in the eigenvalues to infer the number of populations. Therefore, instead of relying on ad hoc heuristics or attempting to formulate specific mathematical methods with multiple underlying assumptions which in turn have trouble with real data, the use of a machine learning technique that generalises the connection between the number of populations present in genotype data and the correlating structure observed in the eigenvalues.

Patterson, Price, and Reich 2006 regards the eigenvalues approach as a black-box method, nonetheless it could also be categorised as distance method as it is dictated by the second central moment (variance), which is determined by the distance of the samples from the mean. The following presented supervised learning approach, using a model to generate synthetic training data and then summarising it by its eigenvalues, can therefore be viewed as a synthesis of model based and distance based clustering.



2 The Generative Model

The subsequently presented model resembles the hierarchical model implemented in STRUCTURE. A first layer, referred to subsequently as the F-layer, originates from Falush, Stephens, and Pritchard 2003 to introduce the possibility of adjusting the correlation of allele frequencies between populations. The F-layer is responsible for determining the allele frequencies of the populations. The second layer, from now on referred to as the admixture layer, stems from Pritchard, Stephens, and Donnelly 2000 and allows for individuals to have admixed genotypes. In other words, the frequencies of several populations are partially contributing to the pool from which the genotype of an admixed individual is sampled from. Thus, the admixture layer samples the genotypes of the individuals, whereby controlling the proportions every population contributes to the genotype of an individual.
Alleles captured from SNP markers are biallelic, for the SNP markers locate a mutation in a single nucleotide base pair. That a base pair is effected by several mutations and these mutations assert themselves in the population is, because of the low chances of single nucleotide being affected by a mutation, very unlikely and therefore the possibilities of more than two alleles at an SNP marker is neglected. This allows for a notation simplification of the allele frequencies. Let subsequently p_{kl} determine the probability that an individual from population k has a mutation at locus l. Of course the existence of mutant variants is always relative to some reference genome from which over sufficiently long amount of time mutations formed and were able to gather some share in the allele frequencies of a population.

2.1 F-Layer

further informations, reader can consult textbooks The motivation for introducing correlation between allele frequencies of populations is that populations often originate from a common ancestral population, so each population stems from the same starting allele frequencies. Reasons for the emergence of new populations are numerous, ranging from geographical divides to social structure impacting the genetic make-up, the component common to all is that a group of individuals excludes themselves sufficiently from mating with the rest of the population and thus practices inbreeding. Schematically in population genetics these scenarios of fragmentation are often abstracted as a set of K secluded islands to which some individuals of an ancestral population A migrated and interbreeding on each island occurs.
The formation of populations on the islands with distinct allele frequencies is due to a phenomenon called random genetic drift. From a simplified view point, excluding all the biological idiosyncrasies and only looking at the alleles at a single locus, random genetic drift can be seen

as an urn model, where the alleles at the locus make up the balls that are drawn from the urn. The proportions of the balls should represent the allele frequencies of the population. The alleles that the offspring receives are sampled from the urn (with replacement). However, since the amount of individuals in the offspring is finite, the offspring will most likely not possess exactly the same allele frequencies as the parents did. This causes the allele frequencies of a population to vary until one allele achieves fixation. Fixation occurs when by chance only one specific allele is sampled from the urn, thus eliminating all its competing alleles.

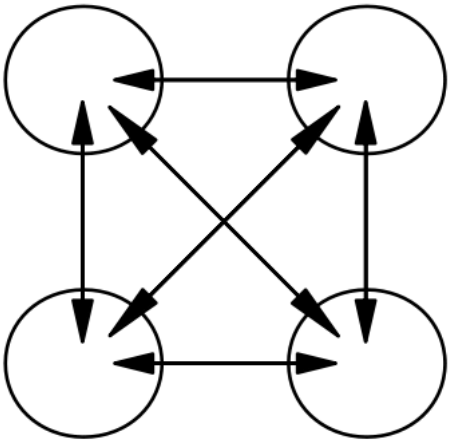
Repeated over time and expanded to the continuous case, genetic drift can be formulated mathematically as a stochastic process on the change of allele frequencies, where the total dominance of an allele is an absorbing state (**crow1970introduction**). Therefore, after a sufficient amount of time a decrease in genetic diversity will be observed in inbreeding populations as more alleles tend to fixation. Wright's F-statistic is a widely used measure for evaluating the divergence of allele frequencies of populations from the mean. It consists of a single value F_{ST} and is calculated as $F_{ST} = Var(p_a)/\overline{p_a}(1-\overline{p_a})$, where $Var(p_a)$ is the variance of the allele frequencies for allele a across the evaluated populations and $\overline{p_a}$ the mean. Once all alleles are fixed in (considering an infinite amount of populatoins), it is expected for a proportionate amount according to $\overline{p_a}$ to have fixed the allele a. The variance would consequently conclude to $\overline{p_a}(1-\overline{p_a})$ making the equation equal to one and indicating total fixation. If the variance is near zero all populations would still most likely have not diverged far from the overall starting allele frequency.

The model will employ an analogous adoption of the F-statistic. The ancestral allele frequency p_{Al} acts as the mean from which all other frequencies originate. Instead of a single parameter F_{st}, a hyperparameter F_k for each population k is introduced that controls the magnitude of its divergence from the ancestral population.

The alleles frequencies for a population k are sampled from a beta distribution, with following parametrisation:

$$p_{kl} = beta(p_{Al}\frac{1-F_k}{F_k}, (1-p_{Al})\frac{1-F_k}{F_k}) \tag{1}$$

The parametrisation arises when the mean of a the beta distribution is set equal to p_{Al} and the variance equal to $F_{ST}p_{Al}(1-p_{Al})$. The choice of using a beta distribution is motivated by the fact that it is the stationary distribution that is received for the stochastic process if a counter force working against allele fixation is added, such as accounting for a steady stream of migrants from the ancestral population or further mutations that sustain an allele.
(**balding2003likelihood**)
It is assumed that the loci are independent from one another, as a consequence factors like linkage disequilibrium can not be respected, however it allows for the independent sampling at each locus with the same F_k value.
Proceeding, the allele frequencies for a population k are joined together to a vector p_k and then merged with all other K populations to a matrix $\mathbf{F} = [p_1 p_2 \dots p_K]^T$ of size $K \times L$, where L is the number of loci. Each column of $\mathbf{F}$ gives the allele frequency for each population at a specific locus l.



2.2 Admixture Layer

Apart from populations drifting from another apart, individuals of populations also migrate and mate with other individuals of other populations, which results in individuals having a genotype that exhibits the shared ancestry of different populations. The admixture layer introduces the prospect of modelling diverse ancestry according to the admixture model presented in Pritchard, Stephens, and Donnelly 2000, whereby the flexibility is achieved by sampling the proportions of admixture from a Dirichlet distribution. Its hyperparameters allow for the finetuning of the probabilities over the potential admixing proportions of the populations. Section 3.6 provides a more thorough look of the modelling with the Dirichlet distribution.
Before translating the admixture proportions to the genotypes of individuals, another matrix $\mathbf{Q}$ is created that contains the admixture proportions of every individual. Mathematically, for an individual i the mixture weights q_i are sampled from a Dirichlet distribution with K, according to the number of populations, influencing hyperparameters $\alpha 1, \alpha 2, \ldots, \alpha_K$. A "non admixed" individual j also receives admixture proportions with the speciality that the only non-zero value is a one at the kth position (with a lenient notation), indicating that the individual belongs to population k, so $q_j = [0_1, \ldots, 1_k, \ldots, 0_K]^T$. All N individuals are combined to a mixing matrix $\mathbf{Q} = [q_1, q_2, \ldots q_M]^T$ of dimensions $N \times K$.

2.3 Combining the Layers

The admixture proportions of an individual act upon each locus by weighing the allele frequency of each population at the locus according to the respective proportions and subsequently summing them. Since this accords to a linear operation, the matrix multiplication with both established matrices $\mathbf{P} = \mathbf{QF}$ yields a matrix $\mathbf{P}$ of dimension $N \times L$ that holds the allele frequencies at each locus for all individual from which their genotypes are sampled. In a final step each entry of $\mathbf{P}$ is used to sample twice from a Bernoulli distribution (binomial - two tries), as it is assumed that individuals are diploidic. Each individual consequently has at each locus a value of $0, 1, 2$, according to how many mutations in total their both of their chromosomes exhibit.

Further assumptions that the model expresses include random mating and thus the absence of further lower level population structure within the populations and that the alleles captured by

the markers are neutral, meaning that they have no impact on the fitness of an individual and are therefore (with the allele independence assumption) exempt from natural selection.

2.4 Summary

In summary the generation of a new population setting for which the number of populations K is known proceeds as following:

1. Sample the ancestral allele frequencies $p_A(l) \sim Uniform(0,1)$
2. Determine the F-values F^k
3. For each of the K populations:
   (i) Sample $p^k(l) \sim beta(p_l^A \frac{1-F^k}{F^k}, (1-p_l^A)\frac{1-F^k}{F^k})$
   (ii) Combine allele probabilities into matrix $\mathbf{F}$
4. For each individual i:
   (i) Choose admixture coefficients $q_i \sim Dir(\alpha_1, \ldots, \alpha_k)$
   (ii) Combine admixture coefficients into matrix $\mathbf{Q}$
5. Calculate admixture $\mathbf{P} = \mathbf{QF}$
6. Convert each value p of $\mathbf{P}$ by sampling $bernoulli(p)$

2.5 Looking at Admixture

The admixture of an individual is determined by the Dirichlet distribution. The Dirichlet distribution is parametrised by K hyperparameters $\alpha_1, \alpha_2, \ldots, \alpha_k$. K corresponds to the desired dimension of the output. The probability density function

$$f(x_1, \ldots, x_K, \alpha_1, \ldots, \alpha_K) = \frac{1}{B(\alpha)} \prod_{i=1}^{K} x_i^{\alpha_i - 1}$$

where $\sum_{i=1}^{K} x_i = 1$ and all $x_1 \geq 0$. So the Dirichlet distribution defines a probability density on the $K-1$-simplex and is therefore a natural choice for sampling admixture coefficients.
Of particular interest for the described model are the hyperparameters, also called concentration parameters, as they control the mode and the variance around it. For values $a_i \geq 1$ the distribution has a single mode, whose coordinates at the maximum x is given by Bishop 2006:

$$x_i = \frac{\alpha_i - 1}{\sum_{k=1}^{K} a_k - K}$$

The mode moves therefore more towards those directions, simplex vertices that have a relatively higher valued corresponding hyperparameter compared to the other hyperparameters. In addition, the variance σ, given by

$$\sigma_i = \frac{\alpha_i(\alpha_0 - \alpha_i)}{\alpha_0^2(\alpha_0 + 1)}$$

where $\alpha_0 = \sum_{i=1}^{K} \alpha_i$, reveals that higher values of hyperparameters leads to a decrease of the variance, meaning a higher concentration around the mode.
These two properties can be exploited to control the probability of sampling certain admixture coefficients. Furthermore, by sampling from the same Dirichlet distribution one is able to simulate various population scenarios, such as a detached admixed cluster, which would correspond to a mode with high concentration parameters, or a population that experienced migration originating from another population, which would coincide with a degenerated Dirichlet distribution that only has two non-zero, concentration values for the two involved population, which is in the end a beta distribution.

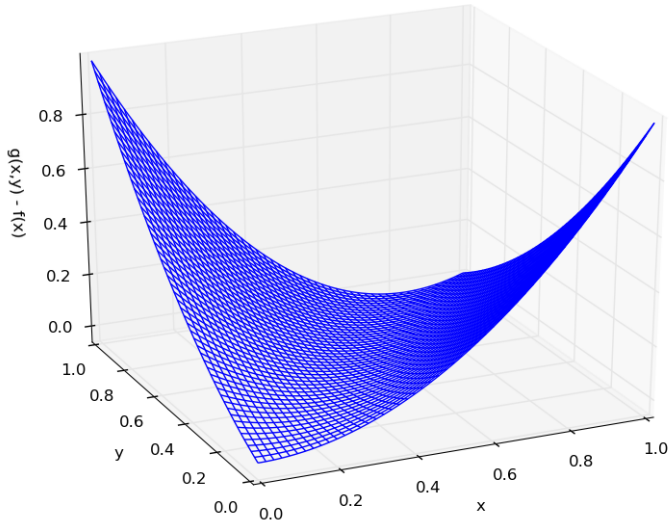
2.6 Further Analysis of the Model

The population centroids given by the population allele frequencies (they are the probabilities used for the Bernoulli sampling and thus the mean) construct the vertices of a simplex in which the individuals approximately lie. Outliers are solely due to the natural variance created by sampling at the end from a Bernoulli distribution. The probabilities the genetic information from each individual is sampled from, nonetheless always combine to a vector that lies within the simplex, for the probabilities are through the admixture coefficients a linear combination of the population allele frequencies or, in other words, of the simplex vertices. From another perspective, the matrix $\mathbf{F}$ that holds the centroids of the populations as rows, then the matrix maps every vector s from the support of an L dimensional Dirichlet distribution accordingly on to the simplex spanned by the centroids (so $\mathbf{F}s$). The matrix $\mathbf{F}$ linearly transforms the L-simplex to the desired population simplex.
As presented the allele frequencies, from which the genotype of an individual is sampled, are constructed by a linear combination of the population allele frequencies, whereby the coefficients in the $K-1$ simplex lie. The $K-1$ simplex is defined by its vertices given by the K unit vectors. The sampling space from which the allele frequencies for a locus l are determined corresponds to a simplex that moved the $K-1$ simplex vertices to the allele frequencies of the populations. From another perspective one can interpret the allele frequencies as constructing a change of basis transformation through the diagonal matrix $\mathbf{D} = diag(p_{1l}, \ldots, p_{Kl})$ that squishes the unit vectors to the allele frequencies. Therefore, the allele frequencies from which the genotype is sampled could be determined by sampling a vector v from the $K-1$ simplex and transforming it into the allele frequency simplex through $\mathbf{D}v$. The transformation $\mathbf{FQ}$ given above generalises this idea for all L loci.

For further assessment a mean of quantifying the genetic dissimilarity between two individuals is necessary. As a measure of genetic distance between two individuals i and j a natural choice is to use a normalised Manhattan distance because the possible genotype values $0, 1, 2$ are discrete and already reflect dissimilarity appropriately. More concretely, let N be the number of loci used as genetic markers, then $\{0,1,2\}^N \subseteq \mathbb{R}^N$ is the set containing all possible values for the genetic information of an individual. The measure of genetic distance is

$$D = \frac{1}{2N} \sum_{n=1}^{N} |l_n^i - l_n^j|$$

where l_n^i and l_n^j are the values of individual i and j respectively at locus l_n. The normalisation keeps the measure invariant to the number of loci used, as recovering more genetic information should not increase the genetic distance per se, as well es calculating out the diploidity. The



measure ranges from 0, as two individuals are genetically similar, to 1, meaning genetic dissimilarity.
Suppose two individuals i and j are generated by the described model, so sampling from a Bernoulli distribution for each loci l with the respective allele frequencies $p_i(l)$ and $p_j(l)$. The expected genetic difference of both individuals then is:

$$\begin{aligned}\mathbb{E}[D] &= \frac{1}{2N}\sum_{n=1}^{N}\mathbb{E}[|l_n^i - l_n^j|] \\ &= \frac{1}{2N}\sum_{n=1}^{N}\sum_{(x,y)\in\{(j,i),(i,j)\}} p_x(l)(1-p_x)(1-p_y(l))^2 \\ &+p_x(l)^2 p_y(l)(1-p_x(l)) \\ &+2p_x(l)^2(1-p_y(l))^2\end{aligned}$$

For individuals sampled from the same allele frequencies the expectation equates to:

$$\begin{aligned}&\frac{1}{N}\sum_{n=1}^{N} p(l)(1-p(l))(p(l)+(1-p(l))^2 \\ &= \frac{1}{N}\sum_{n=1}^{N} p(l)(1-p(l))\end{aligned}$$

This lends further justification to the choice of the distance measure for diploid individuals. It corresponds to the expected genetic variance found in a population without any further underlying substructure, as also used in the calculation of the F_{ST} value.

Let the expected distance of two individuals with arbitrary allele frequencies at a locus l be given by the function $g(p_i, p_j)$ and for two individuals sampled from the same allele frequencies $f(p_i)$. Figure **insert tag** illustrates that it is expected that the genetic distance for individuals sampled from different allele frequencies possess a greater genetic dissimilarity, therefore

it is expected for individuals from the same population to cluster together and the generative model. Furthermore, it should be expected that populations that have not diverged much from the ancestral population are more difficult to distinguish.

Apart from establishing that individuals from different clusters are distinguishable, another clustering quality that would be advantageous to assess is the clustering density. As presented, individuals are sampled from probabilities located in the allele frequency simplex, however the resulting genotype could very much lie outside of the simplex due to the necessary discretization and thus the consequently induced variance of the binomial sampling. By determining the variance of two individuals from the same population and therefore sampled from the same allele frequencies a better impression of the cluster (population) density can be obtained. Also the expected severity of individuals lying outside the simplex can be assessed.
But before calculating the variance, for simplicity reasons the expectation of the genetic difference squared is calculated:

$$\begin{aligned}
\mathbb{E}[D^2|i,j\in k] &= \frac{1}{4N^2}\mathbb{E}[(\sum_{n=1}^{N}|l_n^i - l_n^j|)^2] \\
&= \frac{1}{4N^2}\sum_{n=1}^{N}\sum_{m=1}^{N}\mathbb{E}[|l_n^i - l_n^j||l_m^i - l_m^j|] \\
&= \frac{1}{4N^2}(\sum_{n=1}^{N}\mathbb{E}[|l_n^i - l_n^j|^2] + \sum_{n=1}^{N}\sum_{\substack{m=1\\m\neq n}}^{N}\mathbb{E}[|l_n^i - l_n^j||l_m^i - l_m^j|]) \\
&= \frac{1}{4N^2}(\sum_{n=1}^{N}2p(l_n)^4 - 2p(l_n)^3 + p(l_n)^2 + p(l_n) + \sum_{n=1}^{N}\sum_{\substack{m=1\\m\neq n}}^{N}4p(l_n)(1-p(l_n)p(l_m)(1-p(l_m)))
\end{aligned}$$

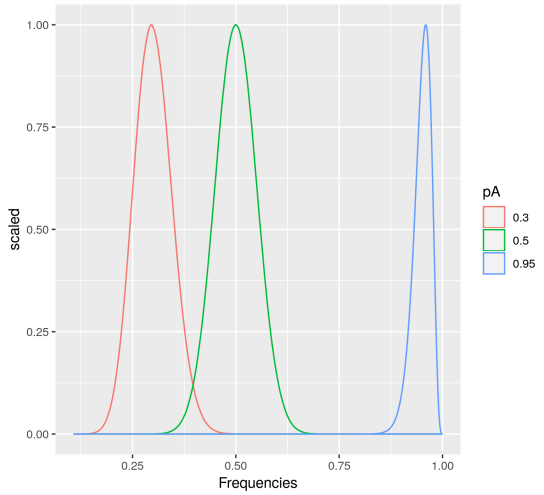
and since

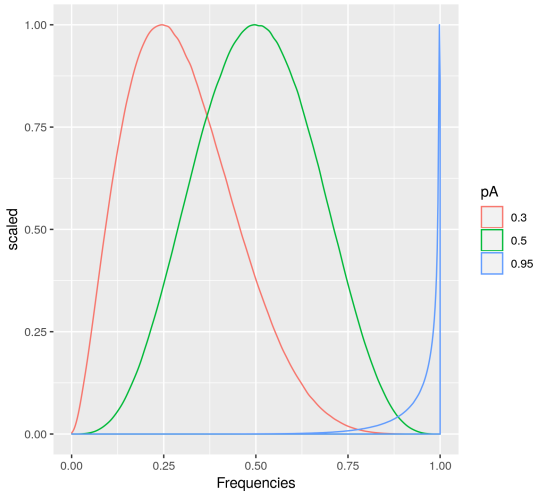
$$\mathbb{E}[D|i,j\in k]^2 = \frac{4}{4N^2}(\sum_{n=1}^{N}\sum_{m=1}^{N}p(l_n)(1-p(l_n)p(l_m)(1-p(l_m)))$$

The variance simplifies to

$$\begin{aligned}
Var(D) &= \mathbb{E}[D^2] - \mathbb{E}[D]^2 \\
&= \frac{1}{4N^2}(\sum_{n=1}^{N} -p(l_n)^4 + 4p(l_n)^3 - 3p(l_n)^2 + p(l_n))
\end{aligned}$$

This reveals that the variance decreases significantly of the order $\mathcal{O}(N^{-2})$ with the number of loci. Therefore, less severe outliers and better observable clusters are to be expected the more loci are simulated. Furthermore, the terms in the summation possess a single maximum at 0.5, so a higher variance exists the further alles are from fixation.
mention maximum entropy?


1.00
0.75
0.50
0.25
0.00
scaled
0.25
0.50
0.75
1.00
Frequencies
pA
0.3
0.5
0.95


1.00
0.75
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scaled
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1.00
Frequencies
pA
0.3
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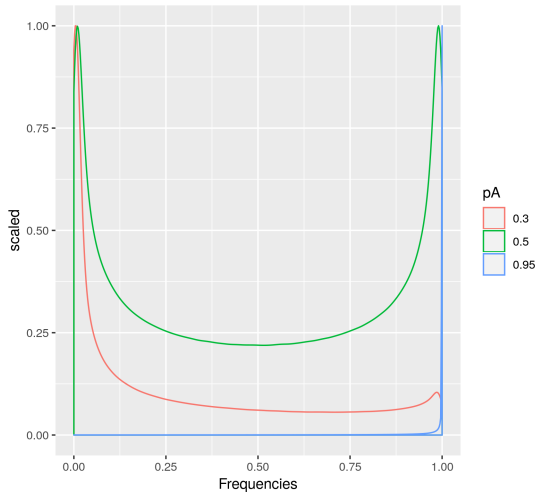
0.95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0.50
0.75
1.00
Frequencies
pA
0.3
0.5
0.95

2.7 Relationship to LDA

The presented model is strongly related to a model more commonly known under the name latent Dirichlet allocation (LDA) Blei, Ng, and Jordan 2003. LDA uses in the setting of natural language processing (NLP) an ensemble of words that are probabilistically associated with certain topics, in order to determine which topics are exhibited by analysed documents, that preferably possess some associated words. Since not all existing words are associated with topics but only a selection, the selected words can be perceived as reasonable indicators of the topic context, as are the used genetic markers to determine population affiliation. A one hot encoding of whether a word is present in a document or not is the respective equivalent of whether an individual possess a gene variant at a genetic maker or not. The encoding of the selected words or respectively of the genetic markers span the feature space in which the topics/populations lie. The topics/populations then span a simplex in which the documents/individuals are mapped according to the admixture.

3 Theoretical Background of Summary Statistics

The prior described model will serve as generative model for constructing a training data set that will be used in a supervised learning scheme. Since the dimensionality of SNP genotype data poses as a challenge, approximate Bayesian computation (ABC) approaches will be employed. The core approximation is the construction of a summary statistics composed of the ordered eigenvalues of the covariance matrix from the genotype data. The chosen supervised learning technique, gradient boosting with decision trees, attempts to generalise the connection between the patterns found in the ordered eigenvalues to the numbers of populations in the respective original genotype data.

3.1 Approximate Bayesian Computation

At heart of approximate Bayesian computation (ABC) lies the inference of a desired parameter value θ for given data D by relating the conditional probability of that data given the parameter value $P(D|\theta)$ to the symmetric counter part, the conditional probability of the parameter given the data $P(\theta|D)$. This is done by exploiting Bayes' rule:

$$P(\theta|D) = \frac{p(D|\theta)P(\theta)}{P(D)}$$

Where $P(D|\theta)$ is often called the likelihood, $P(\theta|D)$ the posterior, $P(\theta)$ the prior and $P(D)$ the evidence which is used in Bayes' rule solely for normalisation purposes.
For many problems the problem space is intractable or dimensionally too large to compute the likelihood. ABC intends to circumvent these problems.

3.1.1 Rejection Algorithm

The rejection algorithm is naturally derived from a certain perspective on conditional probability. Let A, B be a probability spaces and $P(x \subseteq A|y \subseteq B)$ the to be determined conditional probability. By infinitely sampling an event from A and from B and in addition always recording if the produced events correspond to x and y, then the desired conditional probability is computable by taking the past unsuccessful sampling iterations into consideration. Algorithmically this can be expressed as:

Algorithm 1 Conditional Probability $P(x \subseteq A | y \subseteq B)$

```
1: i ← 1
2: for ∞ do
3:     repeat
4:         x_i ← event sampled from A
5:         i ← i + 1
6:     until sample y from B
7:     output x_i
```

And the computation amounts to:

$$\begin{aligned} P(x \subseteq A | y \subseteq B) &= \sum_{i=1}^{\infty} P((x = x_i) \cap y)(1 - P(y))^{i-1} \\ &= P(x \cap y) \sum_{i=1}^{\infty} (1 - P(y))^{i-1} \\ &= \frac{P(x \cap y)}{P(y)} \end{aligned}$$

The rejection algorithm employs a basic approach for finding the posterior distribution of the desired parameter θ for specific data D. Given a known prior distribution of θ, the algorithm samples values $\hat{\theta}$ from the prior and then inputs $\hat{\theta}$ into an appropriate model to simulate some data $\hat{D}$. If the simulated data lies with in a margin of error $\epsilon \geq 0$ from data D for a chosen metric ρ , so $\rho(D, \hat{D}) \leq \epsilon$, then the sampled prior value $\hat{\theta}$ is accepted by adding it to the final sample of parameter values for θ. The final sample should approximate the desired posterior. For further information and possible refinements such as using linear or non linear regression to counter a low acceptance rate or using Sequential Monte Carlo - ABC to sample from areas with higher posterior density the reader is referred to Csilléry et al. 2010.
If the task is for example to compare different models concerning a specific data set, For tasks that only require a good point estimate of θ that fits well to the data D, like the maximum a posteriori (MAP), the rejection algorithm might be too elaborate. Also, the algorithm demands to be run multiple times which could be computationally costly.

3.1.2 In Context of Supervised Learning

A supervised learning method attempts to find a general connection between any given input data D and its desired output θ by training a malleable model. The model is instructed to infer the general connection by adapting itself in such a way that it minimises the empirical risk (for some chosen loss function) when solving a finite training set of size N, which is a data set with "presolved" values $((D_1, \theta_1), \dots (D_N, \theta_N))$. From another perspective, a supervised learning algorithm attempts to forge a model in such a way that it perfects the approximation of the desired mapping from the input space described by D into the output space, which is desirably the correct value for θ. With a uniformly distributed training dataset a supervised learning model will approximate the maximum likelihood (maximise $P(D|\theta)$ w.r.t. θ). By changing the proportions of θ in the training data, a prior $P(\theta)$ can be implicitly set and the trained model will consequently attempt to approximate the maximum a posteriori value (MAP) (maximise $P(D|\theta)P(\theta)$ w.r.t. θ).

The task of choosing K can be viewed as a model selection problem. A rejection algorithm variant usually constitutes a reasonable choice for choosing a model for a particular data set, by for example using posterior ratios. Since the rejection algorithm produces an approximate posterior distribution a broader choice for the selection criterion exists. However, the parameter space is, even with taking summary statistics into account, because of the large dimensionality of snp genotype data seems rather daunting to tame computationally. Out of this reason one settles with the MAP value as sufficient selection criterium for the exchange of the posterior density calculation being waived. The supervised learning technique is subject to the same assumptions through the generative model and uses the same summary statistics just like a rejection algorithm.

3.1.3 Summary Statistics

Large dimensionality of a data set can undermine the practicability of an ABC-method. By summarising the data one attempts to reduce dimensionality, while still sustaining a good approximation of the posterior. So if $S(D)$ is a summary statistics of some data D then the acceptance criterion for the rejection algorithm converts to $\rho(S(D), S(\hat{D})) \leq \epsilon$, whereby $P(\theta|D) \approx P(\theta|S(D))$ holds sufficiently. The use of summary statistics is not confined to the rejection algorithm, rather it is a general tool that allows for a trade off between reduction of dimensionality and the goodness of the approximation, since each summarisation usually forfeits some of the principal information. If no information is lost, so $P(\theta|D) = P(\theta|S(D))$ applies, then the summary statistics is called sufficient. bfHowever, only exponential families have finite sufficient summary statistics, for they are maximum entropy distributions???. A good informative choice of summary statistics is highly task and data set dependent Matthew A Nunes and Balding 2010. An overview of common heuristics and algorithms for choosing summary statistics can be found in Blum et al. 2013.
To infer the number of populations K expressed in a given dataset X the conditional probability $P(K|X)$ with respect to K is maximised. Since the large dimensionality of the used datasets pose substantial computational difficulties, the datasets are summarised in an effective manner, such that the approximation $P(K|X) \approx P(K|sum(X))$ is sufficient for the intended inference. Bayes' theorem then yields

$$P(K|sum(X)) = \frac{P(sum(X)|K)P(K)}{P(sum(X))}$$

3.2 Choosing the Summary Statistics

The choice of adequate summary statistics is essential to obtain significant results. Large dimensional data often times demands it to be summarised, so the intended methods a reasonably applicable. In doing so, the manner summary is of great importance because each summarisation usually forfeits some of the principal information. So one is confronted with the problem of how to effectively manage the trade off between the practicability the method and the loss of information that could endanger desired results.
The entropy of a distribution measures the existing uncertainty about which event appears if one samples from the distribution. It is defined mathematically for a given continuous probability mass function $P(X)$ as

$$h(x) = -\int_{supp(P)} P(x)\log(P(x))dx$$

The principal of maximum entropy states that given some prior information about the underlying probability distribution, such as already drawn samples or a constraining property, the maximum entropy distribution that incorporates the prior information is the best distribution to respect the remaining uncertainty Jaynes 1957. In other words, the maximum entropy distribution is the best distribution to fit the already obtained information if no further assumptions are to be added.
For a given mean μ and covariance Σ the multivariate continuous distribution that maximises the entropy is the multivariate Gaussian, for a proof the reader is referred to Cover and Thomas 2012. The entropy of the multivariate Gaussian is derived as following:

$$\begin{aligned}
h(x) &= -\int_{-\infty}^{\infty} N(x|\mu,\Sigma)\ln(N(x|\mu,\Sigma))dx \\
&= E[\ln(N(x|\mu,\Sigma)] \\
&= E[\ln(det(2\pi\Sigma)^{-\frac{1}{2}}e^{-\frac{1}{2}(x-\mu)^T\Sigma^{-1}(x-\mu)})] \\
&= \frac{1}{2}\ln(det(2\pi\Sigma)) + \frac{1}{2}E[(x-\mu)^T\Sigma^{-1}(x-\mu)] \\
&= \frac{1}{2}\ln(det(2\pi\Sigma)) + \frac{1}{2}E[trace(\Sigma^{-1}(x-\mu)^T(x-\mu))] \\
&= \frac{1}{2}\ln(det(2\pi\Sigma)) + \frac{1}{2}E[trace(I)] \\
&= \frac{1}{2}\ln(det(2\pi e\Sigma))
\end{aligned}$$

The only non-constant factor influencing the entropy of a multivariate Gaussian is the determinant of the respective covariance matrix. Since any real symmetric matrix is diagonalisable, $det(\Sigma)$ breaks down to $det(\Sigma) = det(\mathbf{Q}^{-1})\cdot det(\mathbf{\Lambda})\cdot det(\mathbf{Q}) = \prod_{i=1}\lambda_i$, thus revealing that actually the eigenvalues of the covariance matrix are responsible for the magnitude of the entropy. In conclusion, by summarising the data by its covariance matrix, one implicitly approximates the data as being Gaussian and secondly it suffices for the summary to only take the eigenvalues into consideration.

3.2.1 Principal Component Analysis

Principle component analysis (PCA) is a statistical method that performs a basis transformation on a given data set, such that no linear correlations are any more present in the data. Since the direction of a linear correlation corresponds to the direction of the highest variance in a concerning subspace, a new axis must be aligned according that particular direction. This construction of the axes is done by requiring in an iterative manner each new axis to align with the direction that captures the most variance in the data, which however has not been captured by previous axes.
The variance and the magnitude of variety found in a data set form a duality. Decreasing the variance in a data set by projecting it into a subspace decreases the variety, thus it endangers distinguishability between data points, which is the information. The amount of sustained variance after projecting the data into a subspace can therefore act as an indicator for how

much information was retained. So by always maximizing the captured variance of a newly added axis to the transformation, which is a subspace of the principal data set, the highest possible amount of information is retained for a projection into a subspace with a particular rank K (under the assumption that variance corresponds to information). The subspace is spanned by the K largest eigenvectors of the empirical covariance matrix, as is subsequently shown.
Let $S = \frac{1}{N} XX^T - \overline{XX}^T$ denote the empirical covariance matrix of the data matrix X. Then the expression $u^T Su$ is the empirical variance of $u^T X$, which is the data X projected on to the vector u.

$$\begin{aligned} u^T Su &= \frac{1}{N} u^T XX^T u - u^T \overline{XX}^T u \\ &= \frac{1}{N} u^T X (u^T X)^T - \overline{u^T X} (\overline{u^T X})^T \\ &= \frac{1}{N} (u^T X)^2 - (\overline{u^T X})^2 \end{aligned}$$

The empirical variance is maximised with the restriction $\parallel u \parallel = 1$ because u is supposed to be part of a new standard basis. By using a Lagrange multiplier to add this restriction, the equation $\max_u u^T \Sigma u - \lambda(u^T u - 1)$ is obtained.

$$\begin{aligned} \frac{d}{du}(u^T \Sigma u - \lambda(u^T u - 1)) &= 0 \\ \Sigma u - \lambda u &= 0 \\ \Sigma u &= \lambda u \end{aligned}$$

The solution coincides with the definition of the Eigenvectors, where λ is the eigenvalue of u. Since u should be maximised, the overall solution is the eigenvector belonging to the largest eigenvalue. Solving the eigenproblem on a semi-definite matrix such as the covariance matrix Σ, yields the following factorisation:

$$\Sigma = Q \Lambda Q^T$$

Where Q is an orthogonal matrix that has the eigenvectors of Σ as its columns, and λ a diagonal matrix with the corresponding eigenvalues on its diagonal.

3.2.2 In context to clustering

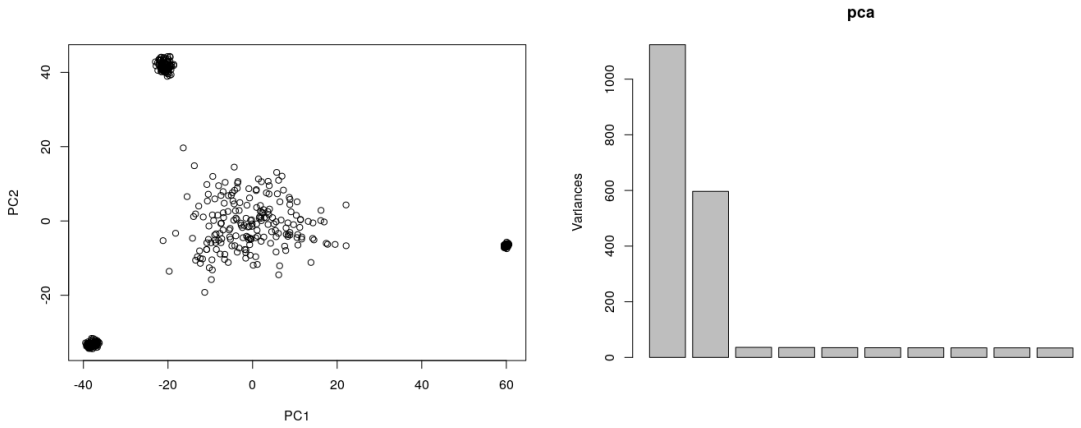
The reason for the clustering structure in data being also expressed in the eigenvalues of the covariance matrix is quite intuitive. Subsequently the term "within variance" will describe the highest possible variance received when a single cluster is projected on to a vector and the term "in-between variance" the highest possible variance received when multiple clusters are projected onto a vector.
The within variance of a set of clusters will usually be greater than in-between variance of any of the considered clusters, because more . Of course several clustering assumptions, such as about the spread and the density of individual clusters, are implied in this statement. The assumption made in the previously described generative model that a population k can be summarised by its allele frequencies which determines the centroid in the generative model around the individuals of a population cluster. The centroid c_k for diploid organisms would be given by a vector where

each entry corresponding to a locus l would be the Bernoulli mean $2p_{kl}$ (or close to it for a finite amount of population members). Also the Bernoulli distribution exhibits a single mode around its mean (usually not exactly because of the discretization). With sufficient distance between the population clusters and sufficient amount of members it is assumable that the in-between variance of a set of population clusters generated by the proposed generative model is significantly greater than the within variance of each population cluster. Furthermore, the Bernoulli sampling can be regarded as noise that adds no further structure.
Since the eigenvectors align themselves along the biggest possible variance, it is to be expected that their orientation is greatly dominated by the with-in variance and thus their eigenvalues are significantly larger. The allele frequencies are from which genotypes are sampled stem from a simplex where the population allele frequencies compose the vertices. As discussed the simplex can be seen as the squishing of the $(K-1)$-simplex, that implements the constraint of all vectors having their values sum to 1. The constraint inhibits a degree of freedom, such that the simplex can be fully spanned by $K-1$ vectors. So it is to be expected that exactly $K-1$ eigenvectors will be needed to fully capture all the in-between variances of K population clusters. Therefore, the according eigenvalues of the first $K-1$ eigenvectors should be significantly greater than the remaining.
Admixed individuals have minimal impact on the magnitude
Another more intuitive argumentation could look like following. Consider the allele frequencies of a population as the origin. Then $K-1$ linearly independent vectors are needed to be able to reach the allele frequencies of every other population. If less would be needed, then the allele frequencies would not be independent and some population would not be considered a population, but a group of admixed individuals that are sampled from a linear combination from other population frequencies. The $K-1$ linearly independent vectors could consequently be composed of direction vectors pointing to the population allele frequencies from origin. This implies that the space between the allele frequencies is spanned by the direction vectors and thus they capture all the in between variance. The first $K-1$ eigenvectors orient themselves along the greatest variance and are linearly independent, therefore it is to be expected that they approximately span the space spanned by the direction vectors. What remains is the smaller within variance found in the clusters, concluding that the first $K-1$ eigenvalues should be significantly greater than the remaining.

3.3 Examples

A synthetic problem instance generated by the model, could look like shown in Figure 1, where three populations that span the simplex are observable. The populations have fairly distinct F-values (meaning they drifted away from the ancestral population at quite different magnitudes), therefore the clusters are well separable from one another. Within the simplex is a cluster of several admixed individuals located. They were all sampled from the same Dirichlet distribution $Dir(8,8,8)$, with uniform hyperparameters, so they are concentrated around a central mode and all populations participate on average the same amount to the admixture.
Just by looking at the corresponding biggest eigenvalues, it is fairly easy, with the use of the previously insights, to infer the number of populations. The first two eigenvalues are significantly larger than the rest, thus the number of populations should be three.
Figure 2 shows a similar scenario as Figure 1, whereby the only difference consists of a different admixture of the admixed individuals. In this example admixed individuals are sampled from three different dirichlet distributions. In turn one of the hyperparameters is set to zero, thus always on population does not partake in the admixture of an individual. As a consequence the individuals are spread along the edges of the simplex, also because the non-zero hyperparameters

Figure 1: Projection of three populations and one admixed on to the firs two PCs and corresponding eigenvalues



Three populations with F-values of $0.1, 0.5, 0.9$ and 100 individuals each were sampled. The admixed population derived the proportional weightings for its allele probabilities by sampling for each allele from a $Dir(8, 8, 8)$ distribution. 200 individuals were sampled for the admixed. For this simulation 10000 loci were simulated.

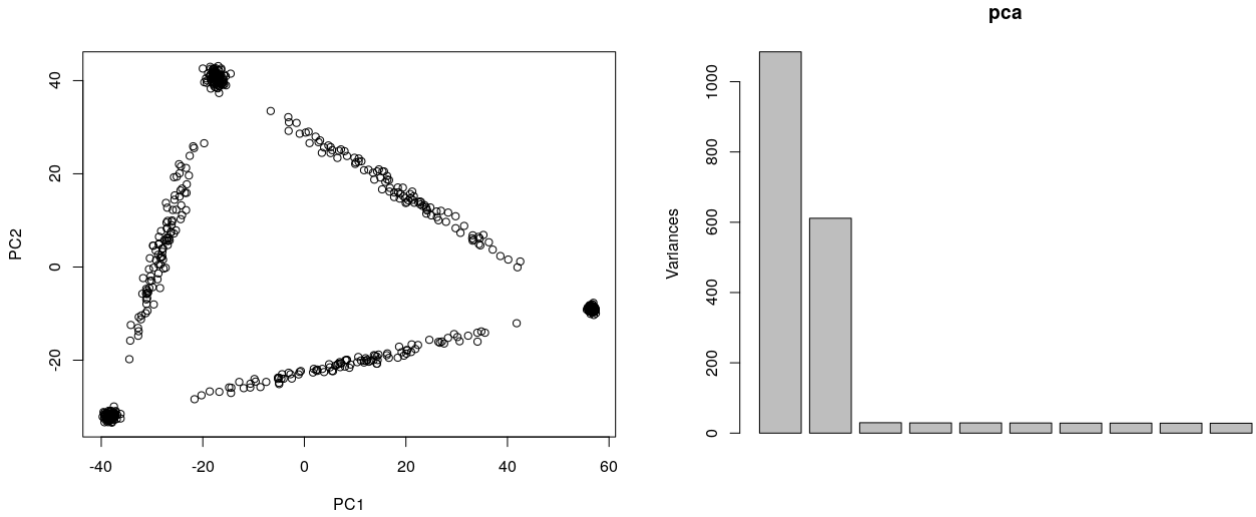
model a lower concentration than in Figure 1.
Again the eigenvalues feature two significant large eigenvalues, making the inference of the number of populations using solely the eigenvalues once again a simple task. The natural variance of the discretization of the allele values through the Bernoulli distribution, which would allow individuals to lie outside the simplex, only has a neglectable marginal effect on the eigenvalues.

3.3.1 Difficulties

The past examples only demonstrate fairly simple problem instances, for which even a human recognition capabilities suffice. It is also possible to construct more difficult problem instances. Figure 3 is an example of such. The ploy is to simulate a setting where most of the variance is already captured by less than $k - 1$, hence making it more difficult to recognise the cut-off for significant and insignificant eigenvalues. In figure 3 there are two populations that have similar allele frequencies (F-values 0.05 and 0.1) and one population that has been subject to strong genetic drift and therefore is genetically completely distinct (F-value 0.99). Furthermore, most individuals are distributed over one of the two close populations and the one very far apart. This introduces high a high incentive for the eigenvalues to try to capture the variance of the individuals of the two populations, since a bigger distance accounts for higher variance. Inversely, because the population that holds a fewer amount of individuals is not very far away from the positioning of the first eigenvector, such that the second eigenvector, which has to orient itself perpendicular to the first, does not capture very much variance. Also the low amount of individuals in the smaller population makes the orientation of the second eigenvector susceptible to the variance of the other populations or to any outliers. An admixed population also resides between the two greater populations, giving the first eigenvalue even more weight.

The graph with the biggest eigenvalues reveals the described dilemma. The first eigenvector accounts for almost all of the variance between the populations, rendering the other significant

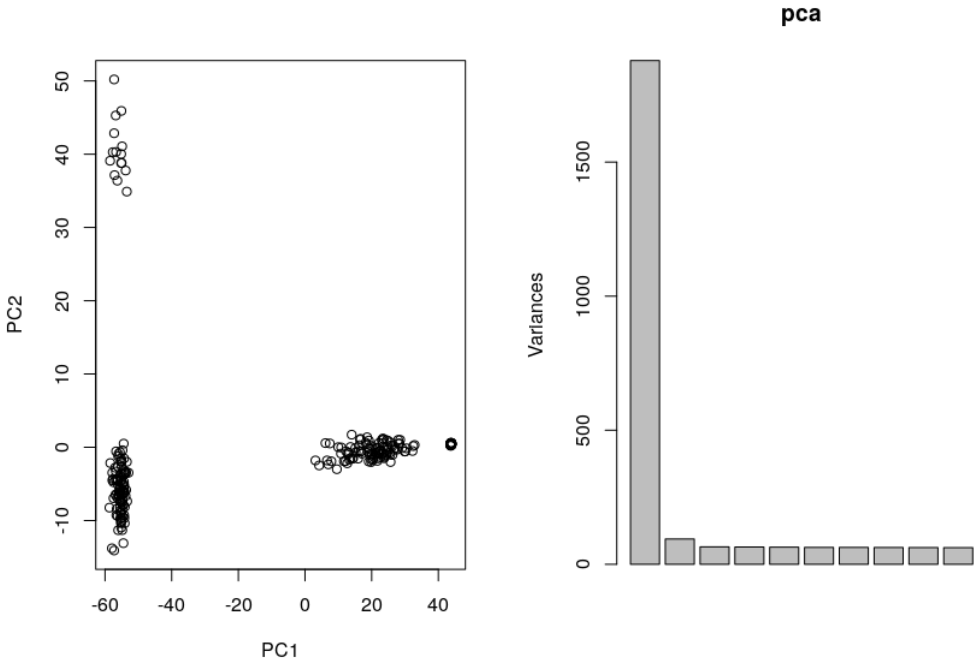
Figure 2: Projection of three populations and one admixed on to the firs two PCs



Three populations with F-values of $0.1, 0.5, 0.9$ and with 100 individuals each were sampled. Between each pair of population clusters lies an admixed population sampled from a Dirichlet with 5s and a 0 for not involved populations, which corresponds to a $beta(5, 5)$. Each admixed cluster holds 200 individuals. The simulation used again 10000 loci.

eigenvalue almost insubstantial and indiscernible from the other insignificant eigenvalues. In different scenarios the distance between the populations and the distribution of the individuals over the populations could be even more disadvantageous (although the question could more be of the nature to decide what is considerable to be a population, **this is part of the discussion???**). In addition, the situation becomes even more difficult if even more populations are simulated with "extreme" F-values.

Figure 3: Example of a difficult case



Three populations with F-values of $0.05, 0.01, 0.99$. The first population with the smallest F-value has 15 members, while the others have a 100 each. The mixture proportions of the admixed population were sampled from a $Dir(0, 10, 30)$. 10000 loci were simulated.

4 Boosting Decision Trees

Subsequently a concise overview of gradient boosting and decision trees is presented. For further details and idiosyncrasies of the methods the reader should consult more elaborate literature, like Trevor, Robert, and JH 2009.

4.1 Gradient Boosting

Gradient boosting is a supervised learning method for classification and regression, that iteratively adds basis learners to a linear combination to reduce an arbitrary differentiable loss function.

Let χ denote the input space. The task then is to approximate the function $f^*(x)$ that maps an arbitrary input $x \in \chi$ to the desired output $y \in \mathbb{R}$. An ensemble of M different basis learners $g_1, g_2, \ldots, g_M : \chi \to \mathbb{R}$ can be used to generalise over a training set $((x_1, y_1), (x_2, y_2), \ldots, (x_N, y_N))$ of N training pairs in a linear fashion as following:

$$f(x) = \sum_{m=1}^{M} \phi_m g_m(x)$$

where $\phi_i \in \mathbb{R}$ are the weights for each basis learner. Linear models for a set of given basis learners can be fitted via conventional methods such as least squares, lasso, ridge Bishop 2006. $f(x)$ can be used as an approximation for various tasks like regression, classification (by for

example using a threshold).

The model is limited by the explicit choice of the basis learners. Instead an algorithm that finds the best base learners from a hypothesis space $\mathcal{H}$ would increase the adaptive potential of the model. Thus, for a given differentiable loss function $l(x, f(x))$, an algorithm should find the best M base learners $h_1, h_2, \ldots, h_m \in \mathcal{H} : \chi \to \mathbb{R}$ and corresponding weights such that the empirical risk is minimised:

$$\underset{\phi_i, h_i}{\operatorname{argmin}} \frac{1}{N} \sum_{i=1}^{N} l(y_i, \sum_{m=1}^{M} \phi_m h_m(x_i)) \tag{2}$$

Solving this task is an optimisation problem usually beyond practicability. A common optimisation technique is too update the parameters through the use of gradient descent. Several problems arise in the case of differentiating over the hypothesis space:

- Firstly, the hypothesis space would need to be parametrised with finite dimensions. In the face of a countless manifold of possible base learners a rather daunting task. One is far better off by confining the possibilities of base learners, by choosing a subset $H \subset \mathcal{H}$ like decision trees or neural networks.
- Many modelling frameworks such as neural networks (e.g. number of hidden layers) and decision trees (e.g. tree depth) have to be parametrised at least partly discretely. Of course all discrete model features could be fixed to a constant, but that would greatly degrade the modelling capabilities.
- Lastly, some base learners do not model a differentiable functions. For e.g. decision trees model functions that possess jump discontinuities.

Gradient boosting algorithms, firstly developed and described by Freund and Schapire 1997; J. H. Friedman 2001; J. H. Friedman 2002, circumvent the necessity of differentiability by growing the ensemble of base learners iteratively that minimises the empirical risk with respect to so called pseudo residuals.
The backbone of an gradient boosting algorithm is constituted by forward stagewise additive modelling, which works as following: Let $H \subset \mathcal{H}$ be the chosen set of possible base learners.

1. Initialise with constant like $f_0(x) = 0$
2. For each stage $m \in 1, \ldots, M$:
   (i) solve
   $$\underset{\phi_i, h_i}{\operatorname{argmin}} \frac{1}{N} \sum_{i=1}^{N} l(y_i, f_{m-1}(x_i) + \phi_m h_m(x_i))$$
   (ii) Set $f_m(x) = f_{m-1}(x) + \phi_m h_m(x)$

The optimisation step, although the amount of parameters is reduced compared to (3), only possess closed viable solving techniques for a limited amount of loss functions, like L2-loss or exponential loss. More information is provided in J. Friedman, Hastie, Tibshirani, et al. 2000. To expand the optimisation step to any arbitrary differentiable loss function, the numerical

optimisation via gradient boosting is used.

The optimisation procedure fixates at stage m the current estimates made by $f_{m-1}(x)$ of the training data in a vector $\mathbf{f}_m = [f_{m-1}(x_1), f_{m-1}(x_2), \dots f_{m-1}(x_N)]^T$.

The loss function then can be reformulated as:

$$L(\mathbf{f}) = \sum_{i=1}^{N} l(y_i, \mathbf{f}_i)$$

Then the gradient of the loss function is calculated w.r.t $\mathbf{f}$.

$$\begin{aligned}\hat{h}_m &= \nabla_{\mathbf{f}_m} L(\mathbf{f}_m) \\ &= [\partial_{\mathbf{f}_1} l(y_1, \mathbf{f}_1), \dots, \partial_{\mathbf{f}_N} l(y_N, \mathbf{f}_N)]^T\end{aligned}$$

Like in conventional gradient descent algorithms the model is adjusted in a manner that the empirical risk is minimised along the direction of steepest descent. The direction of steepest descent corresponds to the negative of the gradient, which is $-\hat{h}_m$. Base learners that output differentiable function approximations can express the gradient via chain rule through the adjustable parameters of the model itself (like the weights in a neural network) and hence these are reciprocally changed to minimise the loss. Other base learners on the other hand have to resort to a different strategy.
The embedding in the forward additive model allows for the negative gradient $-\hat{h}_m$ to be approximated directly by a base learner. The objective of the new base learner $h_m(x)$ consequently concludes therein to approximate

$$h_m(x) \approx -\hat{h}_m$$

as well as possible. A possible approach would be to train a base learner on the training data, but where the labels are exchanged by $-\hat{h}_m$.
Intuitively, a base learner $h_m(x)$ should be considered as an approximate step in the direction of steepest descent of the empirical risk. Following this setup, the weight $\phi_m > 0$ can be considered as the corresponding step size to be adjusted to ones taste. As a conclusion the iterative construction of the final linear model with gradient boosting

$$f(x) = \sum_{m=1}^{M} f_{m-1}(x) + \phi_m h_m(x)$$

is a sequence of gradient descent steps towards a minimum of the empirical risk.

4.2 Decision Trees

Typical decision trees are a supervised learning method that solve a regression or classification problem by segmenting the feature space in to distinct regions, whereby all data points lying in the same region are assigned the same value by the tree.

Let $(x_1, y_1), (x_2, y_2), \dots, (x_N, y_N)$ be the training data. The input dimension of a point x_i is D.

Suppose a tree T partitions the featurespace $X_1, X_2, \ldots, X_D$ into M regions $R_1, R_2, \ldots, R_M$. The response function outputed by T is given by:

$$f_T(x) = \sum_{m=1}^{M} c_m I(x \in R_m)$$

where I is an indicator function signalling if the input x is part of a particular region. c_m is the response for a region R_m. The optimal value of c_m depends on a chosen loss function that should be minimised w.r.t c_m over all the training points assigned to region R_m. As an example, for square loss in a regression setting this would accord to the empirical average of the label values from the training points lying in the region R_m.

A far more challenging optimisation task is finding the optimal tree that partitions the feature space into M regions, for a given loss function l.

$$\underset{R_m, c_m}{\operatorname{argmin}} \sum_{i=1}^{N} l(y_i, \sum_{m=1}^{M} c_m I(x_i \in R_m))$$

The possibilities of partitioning feature space grows exponentially with the number of features, rendering the encounter of an optimal tree in most cases computationally infeasible.

As an alternative, a greedy approximation approach can be used (CART add citation). The greedy algorithm chooses the best dimension X_d and splitting point s that minimises the loss for the two new regions that arise (w.l.o.g. only binary trees will be considered). The two new regions are defined as:

$$R_1(d, s) = \{X | X_d \leq s\} \qquad R_2(d, s) = \{X | X_d > s\}$$

The feature space is divided by a plane that is orthogonal to the axis corresponding to feature X_j. The plane cuts the value of s on that axis.
The optimisation objective thus reduces to the choice of positioning the best partitioning plane orthogonal to an axis:

$$\underset{s,d}{\operatorname{argmin}}[\underset{c_1}{\operatorname{argmin}} \sum_{x_i \in R_1(d,s)} l(y_i, x_i) + \underset{c_2}{\operatorname{argmin}} \sum_{x_j \in R_2(d,s)} l(y_j, x_j)]$$

The optimisation step yields, for a naive implementation that checks for every dimension the splitting value of a plane between every two neighbouring data points, a worst case running time of $\mathcal{O}(D \cdot Nlog(N))$ ($Nlog(N)$ for sorting feature values), which is computationally much more feasible. However between two neighbouring data points x_1 and x_2 there are infinitely many positions to place the splitting plane that evaluate to the same empirical risk. As a convention the splitting value s that lies in the middle of x_1 and x_2, when they are projected on the axis X_d, is chosen by convention. The reasoning is that no further assumptions are to be added through the positioning of the plane and since the splitting of the feature space can be viewed as a Bernoulli experiment (data point either lies left or right of plane) the Bernoulli distribution with expected value of 0.5 is the maximum entropy Bernoulli.

After finding the best split, the procedure is repeated on the newly constructed regions until the desired depth of the tree is reached. Regression and classification trees differ from one another

only through the selection of a different loss function. For regression standard loss functions like square loss would be reasonable choices. Classification trees have revealed better results for loss function that reward node purity, so to which degree does a node hold data points of a single class. Such loss functions are for example the Gini index or cross entropy loss for classification. From an information theory perspective, node purity leads to a greater reduction in entropy.

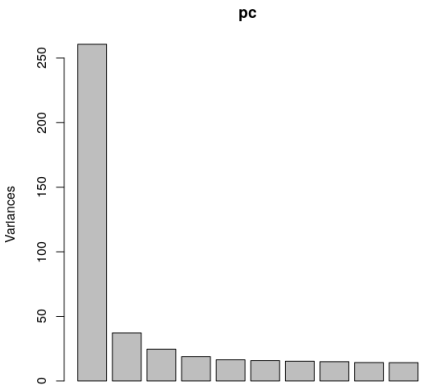
Growing a too big tree T_0 is susceptible to overfitting. A regularisation technique that aids in the construction of a well generalising tree is cost-complexity pruning. The goal of pruning is to find a sub-tree $T \subseteq T_0$, by conflating all hierarchically lower nodes that lead off an internal node into that internal nodes, that minimises:

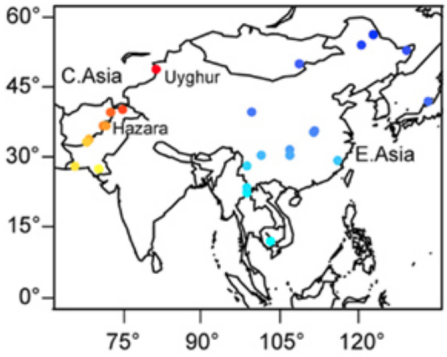
$$C_\alpha(T) = \sum_{i=1}^{N} l(y_i, f_T(x_i)) + \alpha|T|$$

where $f_T(x)$ is the estimate of Tree T for input x and $|T|$ denotes the number of terminal nodes of T. The tuning parameter $\alpha \geq 0$ punishes larger more complex trees according to its value. It resembles the regularisation term of ridge regression.
The optimal sub-tree corresponding to a particular tuning parameter T_α can be found using weakest link pruning. Weakest link pruning conflates those terminal nodes into an internal node to which the terminal nodes are all adjacent, such that the empirical risk increases minimally. Continuing with this procedure until only the root stub remains gives a sequence of subtrees $T_1, T_2, \ldots, T_n$ in which with a probability of 1 the optimal subtree T_α can be found Breiman et al. 1984. Cross validation can be used to find the optimal value for α.

Decision trees exhibit high variance, meaning that completely different splits occur and thus the output prediction rules change considerably when there are minor changes added to the training data. The reason resides inherently with how the splits are chosen in a greedy fashion. For example, two promising features could reduce the loss almost equally much, but just the best of both is considered for the next split. Adjusting the training data slightly by for example adding new data points could possibly change the value of the loss function enough to choose the other feature for a split the hierarchical nature consequently propagates the difference further down the tree. This behaviour reveals that the confinement to the greedy perspective when constructing a tree to some degree neglects the goal of generalisation in return for tractability.

Remedies that address model stability involve the introduction of bias. The bias-variance trade off possess an eminent role in machine learning as its a principle that is prominent for many models. In summary, it describes the forfeit of expected accuracy in return for decreasing the variance of an estimated parameter when the training sample is being varied. Creating an ensemble of decision trees is a widely used and fruitful approach. Ensemble approaches for decision trees include bagging, random forests and as well gradient boosting. Several further refinements improve the quality of an ensemble tree models, including randomly masking different features and training data entries for each tree, as this generates differing trees that place their splits differently and therefore deliver more uncorrelated predictions.





5 Results

5.1 Training

The training data set is composed of 30.000 synthetically generated instances, with the population sizes evenly distributed ranging from $2-16$. The number of loci was uniformly randomly varied ranging from 2000 to 40000 as well as the sample size, which could include from 100 to 5000 individuals. The $F-values$ are sampled from a beta .... The eigenvalues $\lambda_1 \dots \lambda_K$ are determined by first calculating the singular value decomposition of the simulated genotype matrix and then setting $\lambda_i = s_i^2/(n-1)$ where $s_1, \dots, s_K$ are the singular values.

For training the mlogloss function ...?

5.2 Real World Instances

6 Discussion

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