AwesomePackage: A Valid R Package for Ancestry Inference

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Abstract

We use the classical PSD model for ancestor inference, which has been widely used, such as STRUCTURE (MCMC), FRAPPE (EM), ADMIXTURE (SQP), fastSTRUCTURE (VI), TeraStructure (SVI). We illustrate the close relationship between the PSD model, the Poisson NMF model, the multinomial topic model and the LDA model, which can optimize the algorithm. We use Expectation-Maximization algorithm (EM), sequential quadratic programming algorithm (SQP), variational inference algorithm (VI) and stochastic variational inference algorithm (SVI) to fit the model, then illustrate the relationships and differences between these algorithms through simulation experiments and real data experiments.

***K*eywords** PSD model · EM algorithm · SQP algorithm · VI algorithm · SVI algorithm

1 Introduction

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1.1 Ancestor inference

PSD model

PCA-based methods

model-based approaches

1.2 Algorithms

STRUCTURE (MCMC) (Pritchard, Stephens, and Donnelly 2000)

FRAPPE (EM) (Tang et al. 2005)

ADMIXTURE (SQP) (Alexander, Novembre, and Lange 2009)

fastSTRUCTURE (VI) (Raj, Stephens, and Pritchard 2014)

TeraStructure (SVI) (Gopalan et al. 2016)

1.3 Data

TGP (Abecasis et al. 2012)

HGDP (Cann et al. 2002; Cavalli-Sforza 2005; Lu et al. 2011; Li et al. 2008)

2 Models and Methods

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2.1 PSD model

observed variable: genotype matrix G

latent variable: matrix Z of the true origin of genes

parameters: population scale matrix P, gene scale matrix F

hyperparameter: population number K

2.2 EM algorithm

E-step: compute the expectation a_{ijk} and b_{ijk}

M-step: compute the maximization and update the parameters p_{ik} and f_{kj}

convergence criterion: the log-likelihood of incomplete data $\mathcal{L}(G|P, F)$ converges

2.3 SQP algorithm

update parameters: update P and F block by block alternately

convergence criterion: the log-likelihood of incomplete data $\mathcal{L}(G|P, F)$ converges

2.4 VI algorithm

update parameters: update variational parameters $z_{ij}^{\tilde{a}}$, $\tilde{p_i}$, $f_{kj}^{\tilde{1}}$, $f_{kj}^{\tilde{2}}$

convergence criterion: the ELBO converges

2.5 SVI algorithm

sample: sample a SNP

update parameters: iteratively update local parameter F_j at the SNP until it converges, then update global parameter P

convergence criterion: the log-likelihood at the validation set converges

2.6 Relationships with other models

Poisson NMF model (Carbonetto et al. 2021)

multinomial topic model

LDA model

3 Applications

We fit the PSD model on simulated data set, TGP data set and HGDP data set.

3.1 Simulated data set

To evaluate the performance of the different learning algorithms, we generated two groups of simulated genotype data sets. In simulated data set A, we focus on the influence of the strength of population structure and the choice of parameter `K` on the performance of different algorithms. In simulated data set B, we focus on the performance of different algorithms when the mixing ratio gap between different individuals is small.

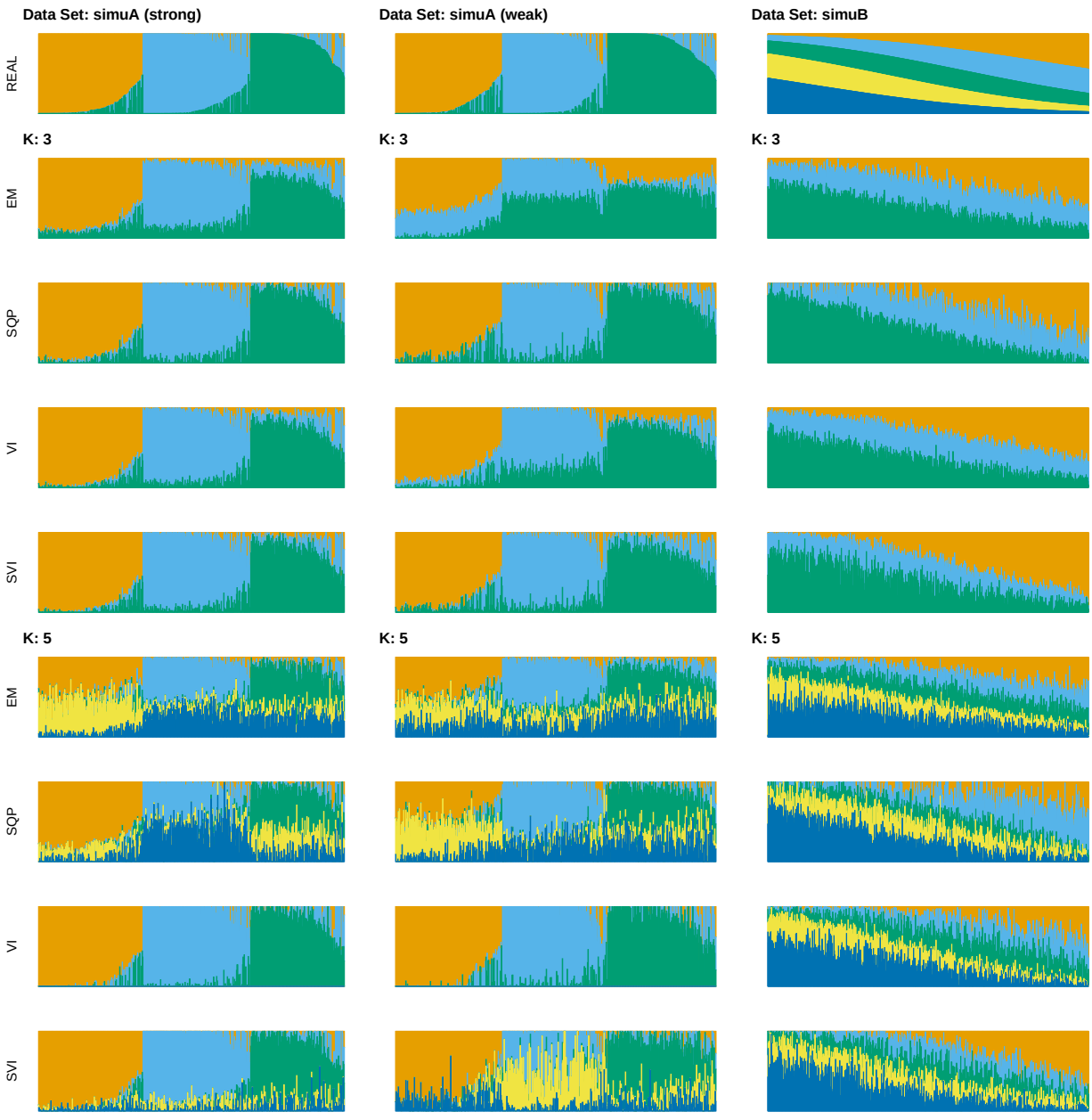

Figure 1: The structure plot of simulated data sets.

3.1.1 Simulated Data Set A

We generated the simulated data set A (Raj, Stephens, and Pritchard 2014) in three steps. First, generate the population scale matrix P using the Dirichlet distribution; In the second step, the gene scale matrix F is generated using beta distribution. The third step is to generate the genotype matrix G using the binomial distribution. We set the number of individuals I to 600, the number of SNPs J to 2500, and the number of populations K to 3.

Step 1. The population scales for each sample are drawn from a symmetric Dirichlet distribution to simulate small amounts of gene flow between the three populations. Here we use $Dirichlet(\frac{1}{10}\mathbf{1}_3)$, of course, in the implementation code, we can adjust the parameters of the Dirichlet distribution.

Step 2. The ancestral allele frequencies $\bar{f}_j$ for each SNP are drawn from a natural data set to simulate allele frequencies in natural populations. Here we use the HGDP data set. First, $\bar{f}_j$ is equal to the total number of suballeles observed at the jth SNP divided by twice the number of individuals. Then, we assume that the samples are drawn from a three-population demographic model. The edge weights correspond to the parameter F_k (Wright 1949) [1] in the model that quantifies the genetic drift of each of the three current populations from an ancestral population. Here we choose $(F_1, F_2, F_3) = (0.1, 0.05, 0.01)$ to simulate strong structure and $(F_1, F_2, F_3) = 0.5 \times (0.1, 0.05, 0.01)$ to simulate weak structure. Thus, the allele frequency at a given locus for each population is drawn from a beta distribution (Balding and Nichols 1995) $f_{kj} \sim Beta\Big(\frac{1-F_k}{F_k}\bar{f}_j, \frac{1-F_k}{F_k}(1-\bar{f}_j)\Big)$.

Step 3. According to the PSD model, each element g_{ij} of the matrix G follows a binomial distribution with probability $(PF)_{ij} = \sum_{i=1}^{K} p_{ik} f_{kj}$ and number of trials 2.

3.1.2 Simulated Data Set B

We also use three steps to generate simulated data set B. In the second step, we set all F_k to 0.1. The third step is the same as for data set A. We just consider the first step. We set a Gaussian density for each ancestral population centered at its location and normalizing each individual such that all proportions sum to 1 (Gopalan et al. 2016). In this case, each ancestral population is placed at a location evenly spaced along a line. Individuals are also positioned evenly on the line, and their proportions p_{ik} are a function of their proximity to each population's location. We set the number of individuals I to 1000, the number of SNPs J to 5000, and the number of populations K to 5.

3.1.3 Results

The main purpose of simulated data set A is to study the influence of the strength of population structure and the choice of parameter `K` on the performance of different algorithms.

For EM and SQP algorithms, they tend to reveal details, that is, they are sensitive to parameter `K` and structure strength. With the appropriate parameter `K`, this may be an advantage, as it reveals a finer structure. However, when the parameter `K` is too large, the phenomenon of overfitting is easy to occur. In addition, SQP algorithm is more accurate than EM algorithm.

For the VI algorithm, we notice that the results of VI are almost consistent for both parameter `K` and structure strength changes. This means that the VI algorithm only tends to reveal the main factors, thereby ignoring some smaller contributions. This is both a strength and a weakness.

The SVI algorithm is an ideal choice in many cases, because it can both highlight the main parts like VI, and react acutely when the structure is not obvious like EM and SQP.

The main purpose of simulated data set B is to study the performance of different algorithms when the mixing ratio gap between different individuals is small. In this case, EM algorithm and SQP algorithm can more faithfully reflect the structure of the dataset (the former is better), while VI algorithm and SVI algorithm will overemphasize some features (the former is worse).

[1] In population genetics, F-statistics (also known as fixation indices) describe the statistically expected level of heterozygosity in a population; more specifically the expected degree of (usually) a reduction in heterozygosity when compared to Hardy–Weinberg expectation.

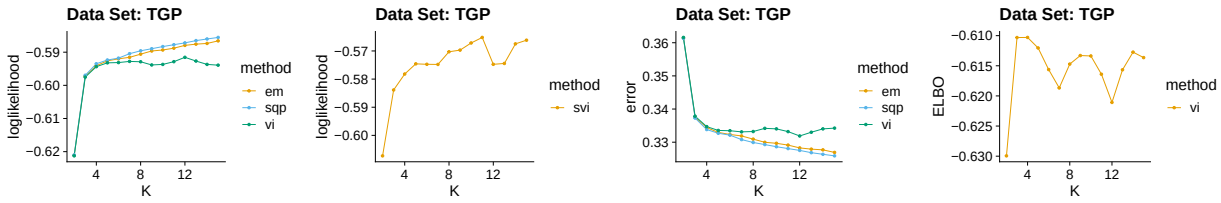

Figure 2: The evaluation indicators of TGP data set.

3.2 TGP data set

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3.2.1 Choose K

Criteria for choosing K: When there is no obvious gap in indicators, the smaller K is preferred. See Figure 2. We notice that the log-likelihood curves of EM and SQP have a continuous upward trend, which is due to the fact that there is no prior distribution constraint, which is prone to overfitting. The log-likelihood curves of EM and SQP slow down from K equals 4. The log-likelihood curve of VI flattens out from about K equals 4, and shows that the optimal K is 12. The log-likelihood curve of SVI is relatively irregular for three reasons. First, we use different training and validation sets to fit different K. Although we finally fixed the validation set when calculating the log-likelihood on the validation set, this was based on the assumption that the data are equivalent. Second, our convergence criterion may be relatively loose, resulting in some cases that do not really converge to the optimal value. Third, the sensitivity of the algorithm to the initial value leads to large errors in a single measurement. The log-likelihood curve of SVI shows that the optimal K is 11, and 8, 9, 10, and 11 are all good choices for K. The error curves of EM, SQP and VI are almost identical with the log-likelihood curves of EM, SQP and VI. The ELBO curve of VI shows the curve oscillating from K equals 3.

In conclusion, we note that when K is around 4, the fit is already doing very well. The optimal K should be reached around 11, but from the structure diagram, the populations appear redundant at this time.

For the **best** K (equals 4 and 11), we draw more subtle structures. We can compare with the results in the article (Gopalan et al. 2016), and the structure diagram is almost the same. See Figure 3.

3.3 HGDP data set

Todo

3.3.1 Choose K

Criteria for choosing K: When there is no obvious gap in indicators, the smaller K is preferred. See Figure 4. We notice that the log-likelihood curves of EM and SQP have a continuous upward trend, which is due to the fact that there is no prior distribution constraint, which is prone to overfitting. The log-likelihood curves of EM and SQP slow down from K equals 7. The log-likelihood curve of VI flattens out from about K equals 6, and shows that the optimal K is 8 and 11. The log-likelihood curve of SVI is relatively irregular for three reasons. First, we use different training and validation sets to fit different K. Although we finally fixed the validation set when calculating the log-likelihood on the validation set, this was based on the assumption that the data are equivalent. Second, our convergence criterion may be relatively loose, resulting in some cases that do not really converge to the optimal value. Third, the sensitivity of the algorithm to the initial value leads to large errors in a single measurement. The log-likelihood curve of SVI shows that the optimal K is 11 and 14, and 8, 9, 10, and 11 are all good choices for K. The error curves of EM, SQP and VI are almost identical with the log-likelihood curves of EM, SQP and VI. The ELBO curve of VI shows the curve oscillating from K equals 7.

In conclusion, we note that when K is around 7, the fit is already doing very well. The optimal K should be reached around 11, but from the structure diagram, the populations appear redundant at this time.

For the **best** K (equals 7 and 11), we draw more subtle structures. We can compare with the results in the articles (Li et al. 2008; Raj, Stephens, and Pritchard 2014; Gopalan et al. 2016), and the structure diagram is almost the same. See Figure 5.

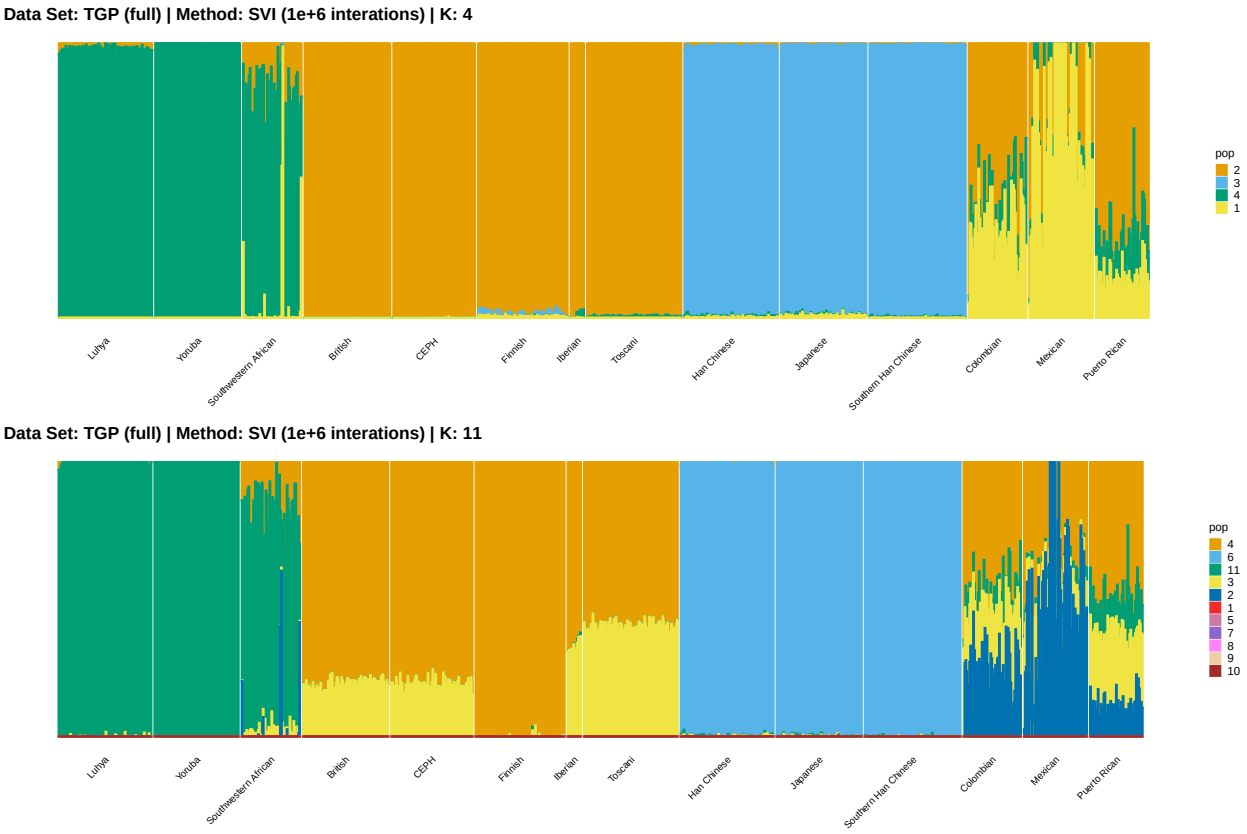

Figure 3: The structure plot of TGP data set.

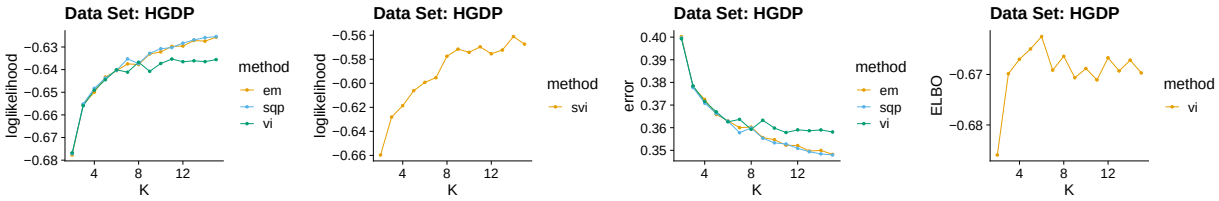

Figure 4: The evaluation indicators of HGDP data set.

4 Discussion

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4.1 Algorithm evaluation

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4.1.1 Convergence accuracy

For suitable `K`, the SVI algorithm and SQP algorithm perform best in terms of convergence accuracy, followed by VI algorithm and finally EM algorithm. We can see this clearly in Section 3.1.

For the unknown `K`, due to the lack of prior constraints, the EM algorithm and SQP algorithm are prone to overfitting when the population number is redundant. Therefore, we had better use VI algorithm and SVI algorithm to select the appropriate `K`. See **Article** in AwesomePackage for details.

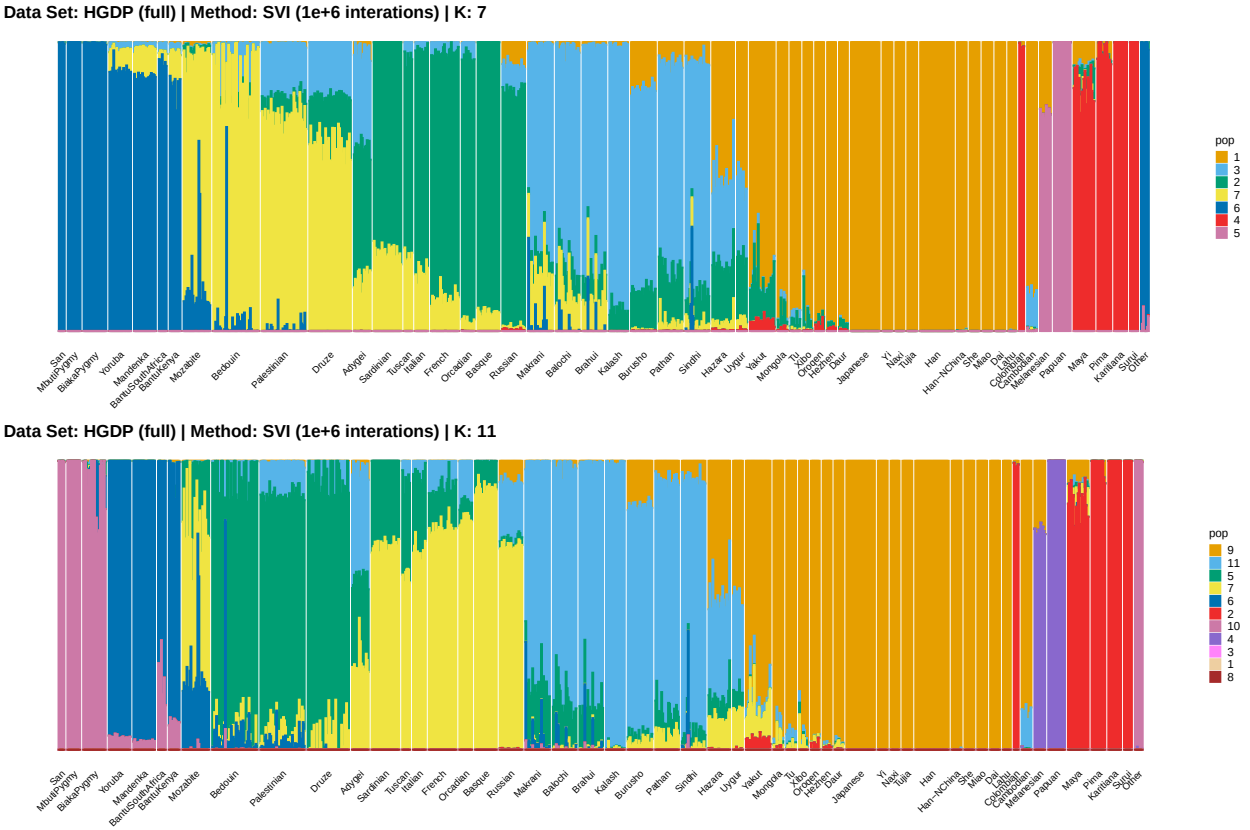

Figure 5: The structure plot of HGDP data set.

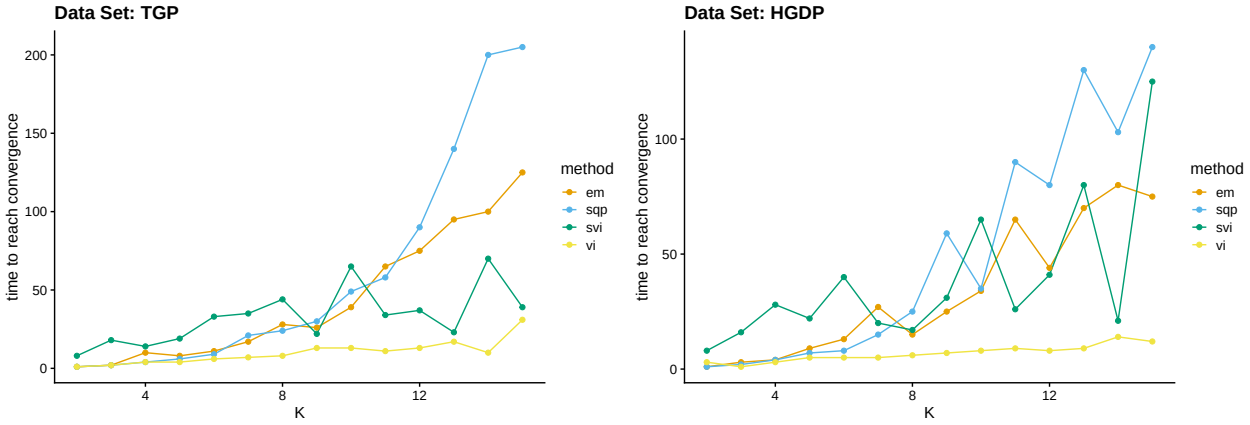

Figure 6: Convergence time. Since we only recorded integer values, we made a modest estimate of the value in integer hours.

4.1.2 Convergence efficiency

In addition to measuring the accuracy of convergence, we still need to consider the efficiency of convergence. We have two indicators to measure the convergence efficiency, which are convergence speed (the number of iterations required to achieve convergence) and convergence time (the time required for a single iteration). We can see the convergence time plots in Figure 6, and we can see the convergence speed plots in Appendix A.

EM algorithm is poor in terms of convergence time and convergence speed, and the convergence time increases rapidly with the increase of `K`.

Although SQP algorithm has a good performance in terms of convergence speed, the convergence time of the unaccelerated SQP algorithm is extremely slow, which increases rapidly with the increase of `K`.

VI algorithm has similar convergence speed with EM algorithm (both of them have poor performance), but in terms of convergence time, VI algorithm has excellent performance, especially with the increase of `K`, the required time increases slowly.

Due to different principles, we only consider the convergence time for the SVI algorithm. Although the performance of convergence time of SVI algorithm is poor on small data sets, the time of SVI algorithm is almost only related to the length of single sampling (the number of individuals), that is to say, for complete data sets, the convergence time of SVI is almost unchanged. This means that SVI has irreplaceable advantages for large data sets. Meanwhile, similar to VI algorithm, the change of convergence time of SVI algorithm is relatively insensitive to `K`. By the way, compared with other algorithms, the convergence time of SVI algorithm is irregular due to the randomness of sampling.

4.1.3 Algorithm selection criteria

In conclusion, we should consider both algorithm accuracy and algorithm efficiency. For small data sets, we can get good results by using VI directly. Or we can first use VI algorithm to reach the vicinity of the optimal value, and then use SQP algorithm to improve the convergence accuracy. The reason why the SQP algorithm is not directly used here is that the unaccelerated SQP algorithm is inefficient and the SQP algorithm is extremely easy to converge to local minima. For large data sets, we use the SVI algorithm without question. Of course, if `K` is unknown, we should pick `K` first, in the same way as above.

4.2 Others

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Acknowledgments

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Appendix A

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Appendix B

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