PCAone Manual

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Contents

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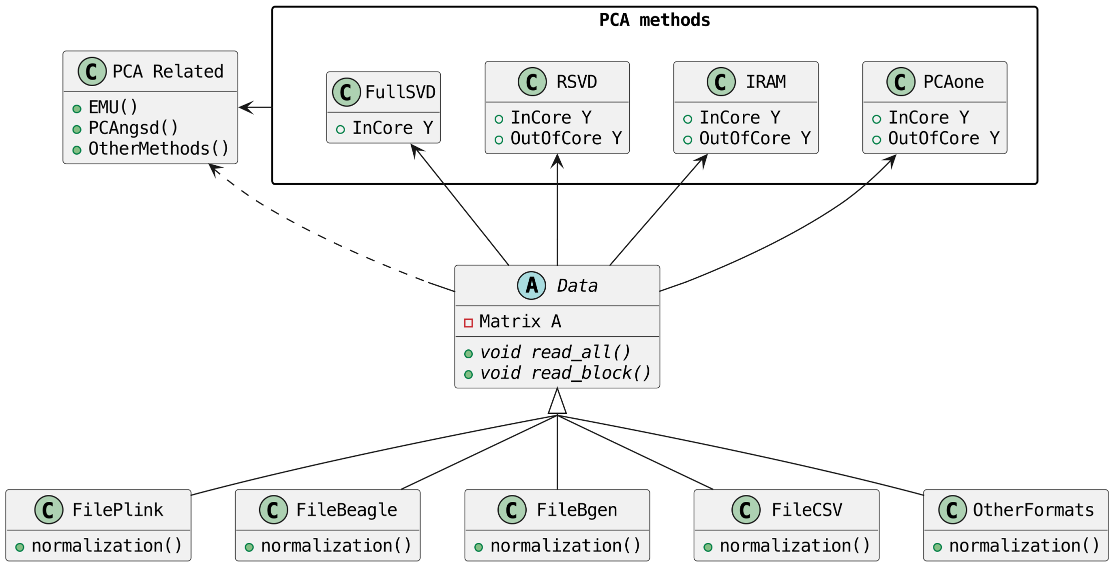
PCAone is a fast and memory efficient PCA tool implemented in C++ aiming at providing comprehensive features and algorithms for different scenarios. PCAone implements 3 fast PCA algorithms for finding the top eigenvectors of large datasets, which are Implicitly Restarted Arnoldi Method (IRAM, PCAoneArnoldi), single pass Randomized SVD but with power iteration scheme (RSVD, Algorithm1 in paper) and our own RSVD method with window based power iteration scheme (PCAone, Algorithm2 in paper). All have both in-core and out-of-core implementation. There is also an R package here but without out-of-core implementation. PCAone supports multiple different input formats, such as PLINK, BGEN, Beagle genetic data formats and a general comma separated CSV format for other data, such as scRNAs and bulk RNAs. For genetics data, PCAone also implements EMU and PCAngsd algorithm for data with missingness and uncertainty.



1 Quickstart

We can run the following on Linux to have a quick start.

```
pkg=https://github.com/Zilong-Li/PCAone/releases/latest/download/PCAone-avx2-Linux.zip
wget $pkg
unzip -o PCAone-avx2-Linux.zip
wget http://popgen.dk/zilong/datahub/pca/example.tar.gz
tar -xzf example.tar.gz && rm -f example.tar.gz
# in default calculating top 10 PCs with in-core mode if having enough RAM
./PCAone --bfile example/plink -k 10
R -s -e 'df=read.table("pcaone.eigvecs", h=F);plot(df[,1:2], xlab="PC1", ylab="PC2");'
```

We will find those files in your current directory.

```
.
 PCAone             # program
 Rplots.pdf         # pca plot
 example            # folder of example data
 pcaone.eigvals     # eigenvalues
 pcaone.eigvecs     # eigenvectors, the PCs you need to plot
 pcaone.perm.bed    # the permuted bed file, only for PCAone
 pcaone.perm.bim    # the permuted bim file, only for PCAone
 pcaone.perm.fam    # the permuted fam file, only for PCAone
 pcaone.log         # log file
```

1.1 Download PCAone

1.1.1 Linux

```
pkg=https://github.com/Zilong-Li/PCAone/releases/latest/download/PCAone-avx2-Linux.zip
wget $pkg || curl -LO $pkg
unzip -o PCAone-avx2-Linux.zip
```

If the server is too old to support `avx2` instruction, one can download the following version.

```
pkg=https://github.com/Zilong-Li/PCAone/releases/latest/download/PCAone-x64-Linux.zip
wget $pkg || curl -LO $pkg
unzip -o PCAone-x64-Linux.zip
```

1.1.2 Mac

```
pkg=https://github.com/Zilong-Li/PCAone/releases/latest/download/PCAone-avx2-Mac.zip
curl -LO $pkg || wget $pkg
unzip -o PCAone-avx2-Mac.zip
```

1.2 Download example dataset

```
pkg=http://popgen.dk/zilong/datahub/pca/example.tar.gz
wget $pkg || curl -LO $pkg
tar -xzf example.tar.gz && rm -f example.tar.gz
```

We should find a fold named `example` with some example data.

2 Features

See change log here.

- Has both Implicitly Restarted Arnoldi Method (IRAM) and Randomized SVD (RSVD) with **out-of-core** implementation.
- Implements our new fast window based Randomized SVD algorithm for tera-scale dataset.
- Quite fast with multi-threading support using high performance library MKL or OpenBLAS as backend.
- Supports the PLINK, BGEN, Beagle genetic data formats.
- Supports a general comma separated CSV format for single cell RNA-seq or bulk RNA-seq data compressed by zstd.
- Supports EMU algorithm for scenario with large proportion of missingness.
- Supports PCAngsd algorithm for low coverage sequencing scenario with genotype likelihood as input.

3 Installation

There are 3 ways to install PCAone.

3.1 Download compiled binary

There are compiled binaries provided for both Linux and Mac platform. Check the releases page to download one.

3.2 Via Conda

PCAone is also available from bioconda.

```
conda config --add channels bioconda
conda install pcaone
PCAone --help
```

3.3 Build from source

`PCAone` can be running on a normal computer/laptop with `x86-64` instruction set architecture. `PCAone` has been tested on both `Linux` and `MacOS` system. To build PCAone from the source code, the following dependencies are required:

- GCC/Clang compiler with C++11 support
- GNU make
- zlib
- llvm or libomp for MacOS

We **recommend** building the software from source with MKL as backend to maximize the performance. For MacOS users, we recommend using `llvm` or `gcc` by `brew install llvm gcc` instead of the default `clang` shipped with MacOS. One should run `export CC=$(find $(brew --prefix)/bin/ -name "gcc-[0-9]*" | tail -1); export CXX=$(find $(brew --prefix)/bin/ -name "g++-[0-9]*" | tail -1)` and check the similar mac workflow.

3.3.1 With MKL or OpenBLAS as backend

Build PCAone dynamically with MKL can maximize the performance since the faster threading layer `libiomp5` will be linked at runtime. One can obtain the MKL by one of the following option:

- install `mkl` by conda

```
conda install -c conda-forge -c anaconda -y mkl mkl-include intel-openmp
git clone https://github.com/Zilong-Li/PCAone.git
cd PCAone
# if mkl is installed by conda then use ${CONDA_PREFIX} as mklroot
make -j4 MKLROOT=${CONDA_PREFIX}
./PCAone -h
```

- download `mkl` from the website

After having `mkl` installed, find the `mkl` root path and replace the path below with your own.

```
# if libiomp5 is not in the mklroot path, please link it to $MKLROOT/lib folder
make -j4 MKLROOT=/path/to/mklroot
```

Alternatively, for advanced user, modify variables directly in `Makefile` and run `make` to use MKL or OpenBlas as backend.

3.3.2 Without MKL or OpenBLAS dependency

If you don't want any optimized math library as backend, just run:

```
git clone https://github.com/Zilong-Li/PCAone.git
cd PCAone
make -j4
./PCAone -h
```

If this doesn't work because the server is too outdated, run `make clean && make -j4 AVX=0` instead.

4 Documentation

4.1 Options

run `./PCAone --help` to see all options. Below are some useful and important options.

```
Main options:
-h, --help                print list of all options including hidden advanced options
-d, --svd arg (=2)        svd method to be applied. 0 is the recommended for big data
                          0: the implicitly restarted arnoldi method
                          1: the yu's single-pass randomized svd with power iterations
                          2: the proposed window-based randomized svd method
                          3: the full singular value decomposition.
-b, --bfile arg           prefix to PLINK .bed/.bim/.fam files
-B, --binary arg          path of binary file
-c, --csv arg             path of comma seperated CSV file compressed by zstd
-g, --bgen arg            path of BGEN file
-G, --beagle arg          path of BEAGLE file
-k, --pc arg (=10)        top k components to be calculated
-m, --memory arg (=0)     specify the RAM usage in GB unit. default [0] uses all RAM
-n, --threads arg (=10)   number of threads for multithreading
-o, --out arg (=pcaone)   prefix to output files. default [pcaone]
-p, --maxp arg (=40)      maximum number of power iterations for RSVD algorithm
-S, --no-shuffle          do not shuffle the data if it is already permuted
-v, --verbose             verbose message output
-w, --batches arg (=64)   number of mini-batches to be used by PCAone (algorithm2)
-C, --scale arg (=0)      do scaling for input file.
                          0: do just centering
                          1: do log transformation eg. log(x+0.01) for RNA-seq data
                          2: do count per median log transformation(CPMED) for scRNAs
--emu                     use EMU algorithm for genotype data with missingness
--pcangsd                 use PCAngsd algorithm for genotype likelihood input
--maf arg (=0)            skip variants with minor allele frequency below maf
-V, --printv              output the right eigen vectors with suffix .loadings
```

4.2 Input formats

PCAone is designed to be extensible to accept many different formats. Currently, PCAone can work with SNP major genetic formats to study population structure. such as PLINK, BGEN and Beagle. Also, PCAone supports a comma delimited CSV format compressed by zstd, which is useful for other datasets requiring specific normalization such as single cell RNAs data.

4.3 Output files

4.3.1 Eigen vectors

Eigen vectors are saved in file with suffix `.eigvecs`. Each row represents a sample and each col represents a PC.

4.3.2 Eigen values

Eigen values are saved in file with suffix `.eigvals`. Each row represents the eigenvalue of corresponding PC.

4.3.3 Features Loadings

Features Loadings are saved in file with suffix `.loadings`. Each row represents a feature and each col represents a PC. need to use `--printv` option to print it.

4.4 Running mode

PCAone has both **in-core** and **out-of-core** mode for 3 different partial SVD algorithms, which are IRAM (`--svd 0`), Yu+Halko RSVD (`--svd 1`) and PCAone window-based RSVD (`--svd 2`). Also, PCAone supports full SVD (`--svd 3`) but with only **in-core** mode. Therefore, there are **7** ways in total for doing PCA in PCAone. In default PCAone uses **in-core** mode with `--memory 0`, which is the fastest way to do calculation. However, in case the server runs out of memory with `in-core` mode, the user can trigger `out-of-core mode` by specifying the amount of memory using `--memory` option with a value greater than 0.

4.4.1 run the window-based RSVD method (algorithm2) with in-core mode

```
./PCAone --bfile example/plink --svd 2
```

4.4.2 run the window-based RSVD method (algorithm2) with out-of-core mode

```
./PCAone --bfile example/plink --svd 2 -m 2
```

4.4.3 run the Yu+Halko RSVD method (algorithm1) with in-core mode

```
./PCAone --bfile example/plink --svd 1
```

4.4.4 run the Yu+Halko RSVD method (algorithm1) with out-of-core mode

```
./PCAone --bfile example/plink --svd 1 -m 2
```

4.4.5 run the IRAM method with in-core mode

```
./PCAone --bfile example/plink --svd 0 -m 2
```

4.4.6 run the IRAM method with out-of-core mode

```
./PCAone --bfile example/plink --svd 0 -m 2
```

4.4.7 run the Full SVD method with in-core mode

```
./PCAone --bfile example/plink --svd 3
```

4.5 Normalization

PCAone will automatically apply the standard normalization for genetic data. Additionally, there are 3 different normalization method implemented with `--scale` option.

- 0: do just centering by substracting the mean
- 1: do log transformation (usually for count data, such as bulk RNA-seq data)
- 2: do count per median log transformation (usually for single cell RNA-seq data)

One should choose proper normalization method for specific type of data.

4.6 Examples

Let's download the example data first.

```
wget http://popgen.dk/zilong/datahub/pca/example.tar.gz
tar -xzf example.tar.gz && rm -f example.tar.gz
```

4.6.1 Genotype data (PLINK)

We want to compute the top 10 PCs for this genotype dataset using 4 threads and only 2GB memory. We will use the proposed window-based RSVD algorithm with default setting `--svd 2`.

```
./PCAone --bfile example/plink -k 10 -n 4 -m 2
```

Then, we can make a PCA plot in R.

```
pcs <- read.table("pcaone.eigvecs",h=F)
fam <- read.table("example/plink.fam",h=F)
pop <- fam[,1]
plot(pcs[,1:2], col=factor(pop), xlab = "PC1", ylab = "PC2")
legend("topright", legend=unique(pop), col=factor(unique(pop)), pch = 21, cex=1.2)
```

4.6.2 Genotype dosage (BGEN)

Imputation tools usually generate the genotype probabilities or dosages in BGEN format. To do PCA with the imputed genotype probabilities, we can work on BGEN file with `--bgen` option instead.

```
./PCAone --bgen example/test.bgen -k 10 -n 4 -m 2
```

Then, we can make a PCA plot in R.

```
pcs <- read.table("pcaone.eigvecs",h=F)
fam <- read.table("example/plink.fam",h=F)
pop <- fam[,1]
plot(pcs[,1:2], col=factor(pop), xlab = "PC1", ylab = "PC2")
legend("topright", legend=unique(pop), col=factor(unique(pop)), pch = 21, cex=1.2)
```

4.6.3 Single cell RNA-seq data (CSV)

In this example, we run PCA for the single cell RNAs-seq data using a different input format with a normalization method called count per median log transformation (CPMED).

```
./PCAone --csv example/BrainSpinalCord.csv.zst -k 10 -n 20 -m 4 --scale 2 --svd 1
```

It should take around 5 minutes.

5 Citation

- If you are using PCAone algorithm, please cite our paper PCAone: fast and accurate out-of-core PCA framework for large scale biobank data.
- If using EMU algorithm, please also cite Large-scale inference of population structure in presence of missingness using PCA.
- If using PCAngsd algorithm, please also cite Inferring Population Structure and Admixture Proportions in Low-Depth NGS Data.

6 Acknowledgements

PCAone use Eigen for linear algebra operation. The IRAM method is based on yixuan/spectra. The bgen lib is ported from jeremymcrae/bgen. The EMU and PCAngsd algorithms are modified from @Jonas packages.