

# PECA 2.0 manual

Zhana Duren

[durenzn@gmail.com](mailto:durenzn@gmail.com)

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# 1. Getting started.

## 1.1 About PECA

The rapid increase of genome-wide data sets on gene expression, chromatin states and transcription factor (TF) binding locations offers an exciting opportunity to interpret the information encoded in genomes and epigenomes. This task can be challenging as it requires joint modeling of context specific activation of cis-regulatory elements (RE) and the effects on transcription of associated regulatory factors. To meet this challenge, we propose a statistical approach based on paired expression and chromatin accessibility (PECA) data across diverse cellular contexts. In our approach, we model 1) the localization to REs of chromatin regulators (CR) based on their interaction with sequence-specific TF, 2) the activation of REs due to CRs that are localized to them, 3) the effect of TFs bound to activated REs on the transcription of target genes (TG). The transcriptional regulatory network inferred by PECA provides a detailed view of how trans- and cis-regulatory elements work together to affect gene expression in a context specific manner.

PECA is a statistical tool for gene regulatory network inference from paired gene expression and chromatin accessibility data. If you use PECA software, please cite:

Duren, Zhana, et al. "Modeling gene regulation from paired expression and chromatin accessibility data." *Proceedings of the National Academy of Sciences* 114.25 (2017): E4914-E4923.

## 1.2 Installation

PECA is a software for inferring context specific gene regulatory network from paired gene expression and chromatin accessibility data. PECA software source code can be downloaded from Github: <https://github.com/SUwonglab/PECA>.

To run PECA, you need to install following:

Matlab, Macs2, Homer, Samtools and Bedtools.

Download and install PECA on Linux:

```
wget https://github.com/SUwonglab/PECA/archive/master.zip
```

```
unzip master.zip
```

```
cd PECA-master/
```

```
bash install.sh
```

## 1.3 PECA software

There are three tools included in PECA 2.0 software: network inference, comparison of two networks and comparison of two groups of networks. To run network comparison, you need to run network inference first.

## 2. Network inference

To run PECA network inference tool, you need to do following two steps: i) prepare input data and ii) run PECA network inference.

### 2.1 Prepare input data

Put the input files into folder named *./Input*. PECA network require following three input files: *\${SampleName}.txt*, *\${SampleName}.bam*, *\${SampleName}.bam.bai*.

*\${SampleName}.txt* is gene expression file containing two columns (tab delimited), gene Symbol and FPKM (or TPM). *\${SampleName}.bam* is chromatin accessibility data, DNase-seq or ATAC-seq. *\${SampleName}.bam.bai* is the index file of bam file.

Note that all the three files should have same before-dot-file-name *\${SampleName}*, only difference is after dot ".txt", ".bam" or ".bam.bai". Please see the example of RAd4 in the *./Input* directory (*RAd4.txt*, *RAd4.bam*, and *RAd4.bam.bai*).

### 2.2 Run PECA network inference

After the input data is prepared, please run following script do network inference.

```
sh PECA.sh $sampleName $genome
```

Example: *sh PECA.sh RAd4 mm9*

The results will be *./Results/\${SampleName}/*. Please see the description of the output files:

*\${SampleName}\_network.txt* is the tissue specific network. Each row represent one regulation. The first two columns are TF and TG. The third column is regulation

score. Higher value represents higher possibility of regulation. Rows are ranked by regulation score. The Forth column is FDR. The Fifth column is List of Regulatory elements (REs, including promoter, enhancers,...) which regulating TG and contain accessible motif binding site of TF .

*TFTG\_score.txt* is regulation strength for the all TF to TG. Each row represents one TF and each column represents one target gene. Higher value represents higher possibility of regulation.

*CRB\_pval.txt* is the Chromatin regulators' (CR) binding site matrix, each column represents one CR, each row represents one region, the values are p-values.

### 3. Comparison of two networks

If you have two samples and want to compare the two samples at network level, please run network comparison tool by following steps:

#### 3.1 Prepare input data

Prepare two networks: Run PECA network inference tool on two samples one by one. (Script: *sh PECA.sh \$sampleName \$genome* )

#### 3.2 Run PECA network comparison

2, Run: *sh PECA\_compare\_dif.sh \$Sample1 \$Sample2 \$Organism*

Examples: *sh PECA\_compare\_dif.sh K562 GM12878 human*

*sh PECA\_compare\_dif.sh mESC Rad4 mouse*

Note that \$Sample1 and \$Sample2 **must be consistent with** the file names in Input directory.

The results will be *./Results/Compare\_\${Sample1}\_\${Sample2}/*. Please see the description of the output files:

Specific network of two samples: *\${Sample1}\_specific\_network.txt* and *\${Sample2}\_specific\_network.txt*

Common network of two samples: *\${Sample1}\_\${Sample2}\_common\_network.txt*

Specific module of two networks: *\${Sample1}\_specific\_module.txt* and *\${Sample2}\_specific\_module.txt*

Common module of two samples: *\${Sample1}\_\${Sample2}\_common\_module.txt*

Files *PooledNetwork.txt* or *PooledModule.txt* can be used to visualize the networks by Cytoscape, and the node label is given in file *Node\_label.txt*. "1" and "-1" in *PooledNetwork.txt* or *PooledModule.txt* represent "Activation" and "Repression" respectively. "1" and "2" in *Node\_label.txt* represent the gene is Sample1 specific or Sample2 specific.



## 4. Comparison of two groups of networks

If you have two conditions (multiple samples in each conditions) and want to compare the two conditions at network level, please do it by following steps:

### 4.1 Prepare input data

1, Run PECA network inference tool on all the samples from two conditions one by one. (Script: *sh PECA.sh \$sampleName \$genome* )

2, Construct labels: Write the sample names of Group1 and Group2 into text files named *\$Group1* and *\$Group2*, respectively. (eg. create one text file named "*Control*" and put the sample names of one condition to this file, create other text file named "*Case*" and put the names of the other condition to this file. Note that *sample names must be consistent with* the file names in Input directory. Note that the sample name files contain one sample name per line.)

### 4.2 Run PECA multiple network comparison

3, Run: *sh PECA\_compare\_dif\_multiple.sh \$Group1 \$Group2 \$Organism*

Example: *sh PECA\_compare\_dif\_multiple.sh Control Case human*

The results will be *./Results/CompareGroup\_{\$Group1}\_{\$Group2}* . Please see the description of the output files:

Specific network of two conditions: *{\$Group1}\_specific\_network.txt* and *{\$Group2}\_specific\_network.txt*

Common network of two conditions: *{\$Group1}\_{\$Group2}\_common\_network.txt*

Specific module of two conditions:  $\text{\textit{\$ \{Group1\}_specific\_module.txt}}$  and  $\text{\textit{\$ \{Group2\}_specific\_module.txt}}$

Common module of two conditions:  $\text{\textit{\$ \{Group1\}_\$ \{Group2\}_common\_module.txt}}$

Files *PooledNetwork.txt* or *PooledModule.txt* can be used to visualize the network by Cytoscape, and the node label is given in file *Node\_label.txt*. "1" and "-1" in *PooledNetwork.txt* or *PooledModule.txt* represent "Activation" and "Repression" respectively. "1" and "2" in *Node\_label.txt* represent the gene is Group1 specific or Group2 specific.