Preprocessing-and-Filtering

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Overview

SLIDE uses the feature-feature correlation structure in the data to create latent factors. Input data does not need to be autoscaled (meaning each feature has `mean = 0` and `std dev = 1`), as this is done when calculating the latent factors. However, there are a few important considerations:

- **The goal is to get down to approximately ≤ 5000 features for SLIDE to run smoothly**
- **Be sure to remove features with `std deviation = 0` before starting - these will cause errors in SLIDE**
- Normalization is still recommended (such as normalizing for read-depth or library size); other transformations (log, power,etc) may be recommended for specific data types.
- `thresh_fdr` argument sets the threshold below which correlations (in the scaled correlation matrix) will be removed. The default is `0.2`, but use a lower value to get more diverse latent factors.
  - Occasionally, `thresh_fdr` and `delta` will cause the algorithm to fail because the remaining correlations in the data are too sparse and more than `delta` apart from each other. Consider lowering both if you encounter problems.

The sections below outline:

1. Load Sample data
2. Remove features with `std dev = 0`
3. Handling missing values
   - data repair
   - imputation
4. Filtering
   - sparsity
   - variance

Load Sample Data

Below are some examples using example data (note, download these files from the examples folder on the SLIDE repo at jishnu-lab/SLIDE):

```r
unfiltered_x = as.matrix(read.csv("SLIDE/Data_Scripts/CD4_Expansion/x.csv",
    row.names = 1))
unfiltered_y = as.matrix(read.csv("SLIDE/Data_Scripts/CD4_Expansion/y.csv",
    row.names = 1))
```

Remove features with `standard dev = 0`

First things first: remove all features that have a `std dev = 0` because these are uninformative and will cause errors in calculating the correlation matrix in SLIDE.

```r
# find columns with sd = 0
zero_sd_features = which(apply(unfiltered_x, 2, sd) == 0)

filtered_x = unfiltered_x[, -zero_sd_features]
```

Handling Missing Values

SLIDE requires that the input sample-feature data be a numeric matrix and contain no characters or `NA`/`NAN`/`Inf` values.

Data repair - Find `NA`/`NAN`/`Inf` values

```r
# this will give you a vector with positions in the flattened matrix
bad_values = which(is.na(unfiltered_x) | is.nan(unfiltered_x) | is.infinite(unfiltered_x))

# you can replace the bad values with zeros or see below for
# imputation
repaired_x = unfiltered_x[bad_values] = 0
```

Imputation

If you wish to impute values (for example, by using the mean), you can do so similarly

```r
# same as above
bad_values = which(is.na(unfiltered_x) | is.nan(unfiltered_x) | is.infinite(unfiltered_x))

# go through each column and replace bad values with the mean of that
# column
imputed_x = apply(unfiltered_x, MARGIN = 2, function(x) x[which(is.na(x) |
    is.nan(x) | is.infinite(x))] = mean(x, na.rm = TRUE))
```

Filtering

- **Sparsity**: both in features and samples will create problems. Consider removing features, then samples based on sparsity (generally, any sample filtering should come after feature filtering).
    - A good initial check is to see how many features have `median = 0` (50% of feature are zeros) - if there are a significant number of these features, instead of removing all of them consider removing features that have more than 50% zeros (e.g. remove features that are 90% zeros or 75% zeros). Afterwards, do the same for samples (although we are generally more conservative and only remove samples that have a significant proportion of zeros).
- **Variance**: Low variance features are less informative, so Consider filtering these out.

  - Remove features with `std dev = 0`, because these are uninformative
- **Coefficient of Variation**: Ratio of feature `std dev / mean`. Features with high coefficient of variation may be noise and features with low coefficient of variation may be uninformative.

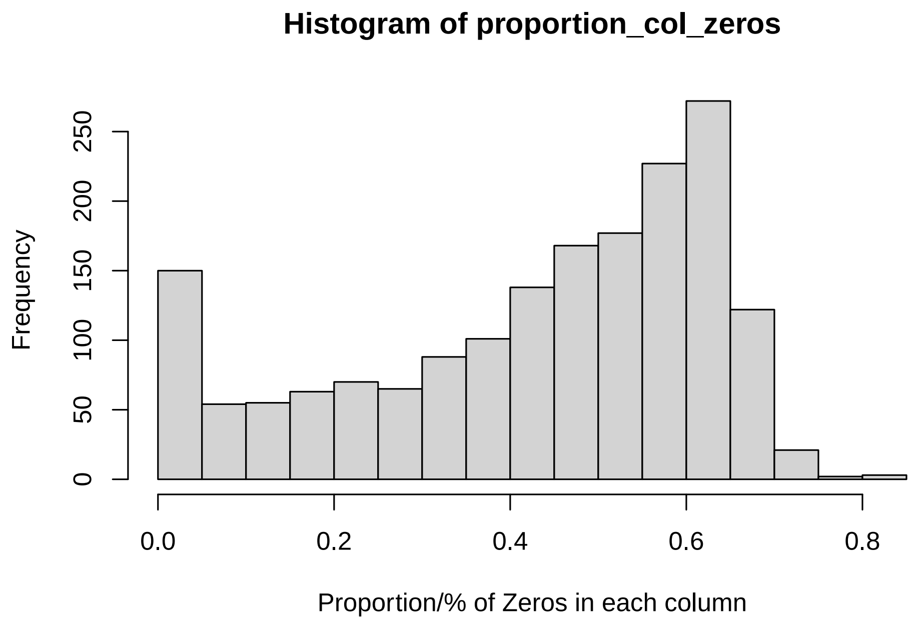
Sparsity Filtering

Filtering features (columns)

You can measure the proportion of zeros in each row/column. Start by filtering out features, then filter samples

```
proportion_col_zeros = apply(unfiltered_x, MARGIN = 2, function(x) length(which(x ==
    0))/length(x))

hist(proportion_col_zeros, xlab = "Proportion/% of Zeros in each column")
```



We can now remove any column that has more than `0.9` (90%) zeros.

```
filtered_x = unfiltered_x[, -which(proportion_col_zeros > 0.9)]
```

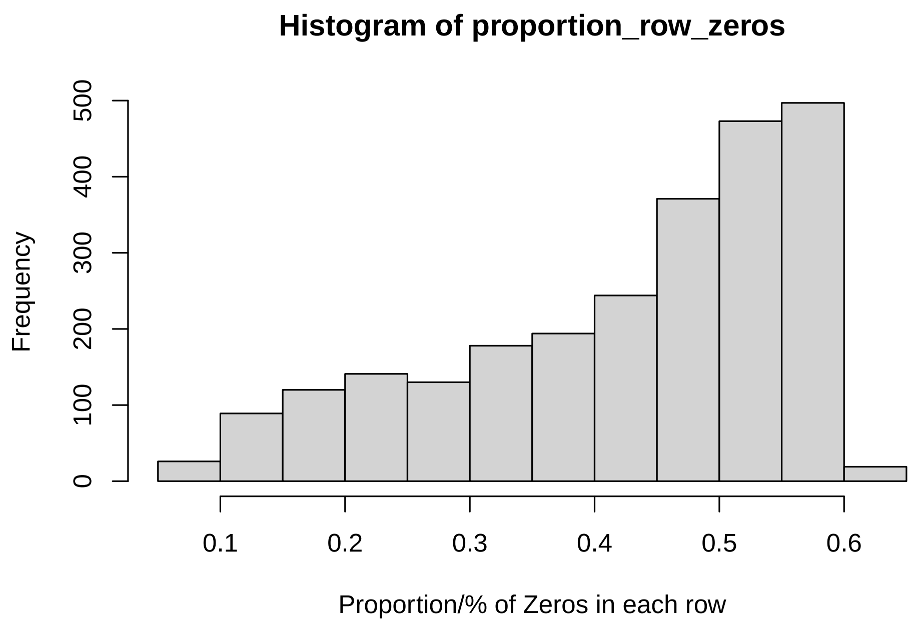
Note: we can use these vectors with the quantile function to set a threshold for percentage of zeros - note: you can also use the quantile function.

Filtering samples (rows)

We can do the same for rows (**remember to remove the corresponding rows from your response vector as well!**)

```
# Get indices for rows that are the top 10% sparse
proportion_row_zeros = apply(unfiltered_x, MARGIN = 1, function(x) length(which(x ==
    0))/length(x))

hist(proportion_row_zeros, xlab = "Proportion/% of Zeros in each row")
```



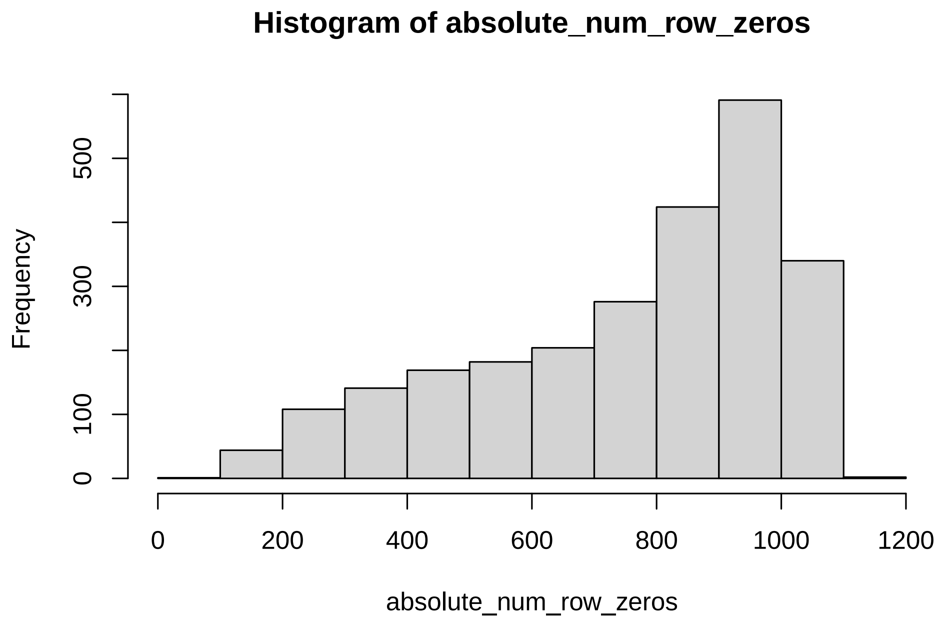
```
rows_above_zero_threshold = which(proportion_row_zeros > 0.9)

filtered_x = unfiltered_x[-rows_above_zero_threshold, ]
filtered_y = unfiltered_y[-rows_above_zero_threshold]
```

Note: you may want to filter out zeros based on absolute number (versus just filtering out by quantile); in this case, your apply function will not normalize for length:

```
absolute_num_col_zeros = apply(unfiltered_x, MARGIN = 2, function(x) length(which(x ==
    0)))
absolute_num_row_zeros = apply(unfiltered_x, MARGIN = 1, function(x) length(which(x ==
    0)))

# should look the same as hist for row % above
hist(absolute_num_row_zeros)
```



Alternatively, you can use the `zeroFiltering` function in the SLIDE package: - Features with more than `col_thresh` zeros will be filtered out - Samples with more than `row_`thresh‘ zeros will be filtered out

```
# this will remove all features and samples that have more than 50%
# zeros (any feature or column with median = 0)
col_thresh = nrow(unfiltered_x)/2
row_thresh = ncol(unfiltered_x)/2

# columns with more than col_thresh number of zeros will be filtered
# rows with more than row_thresh number of zeros will be filtered
filtered_mats = SLIDE::zeroFiltering(unfiltered_x, unfiltered_y, col_thresh = nrow(unfiltered_x)/2,
    row_thresh = ncol(unfiltered_x)/2)
#> Original dataframe dimension is  2482  by  1776
#> Filtered dataframe dimension is  1493  by  952
filtered_x = filtered_mats$filtered_x
filtered_x = filtered_mats$filtered_y
```

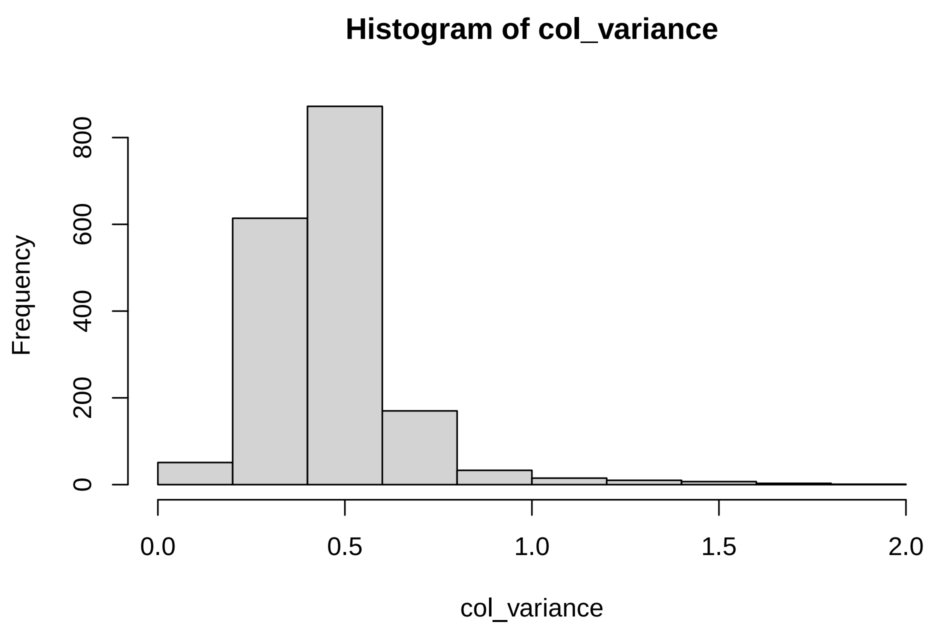
Variance Filtering

We use similar functions to filter by variance; generally speaking, you will want to look at the variance of mean-centered data (although your input data does not need to be centered or scaled, as that is done in SLIDE)

```
# mean center each column
scaled_x = apply(unfiltered_x, MARGIN = 2, function(x) scale(x, center = TRUE,
    scale = FALSE))

# get the variance of each column
col_variance = apply(scaled_x, MARGIN = 2, var)
```

```
hist(col_variance)
```



Next, using this histogram, we want to filter out features with low variance. It looks like `0.20` is a good choice to remove the lowest variance features

```
# we can filter out features with very low variance (typically we use
# somewhere between the 25th-45th percentiles). We use 25th
# percentile below
low_var_cols = which(col_variance < 0.2)

filtered_x = unfiltered_x[, -low_var_cols]
```

Alternatively, we filter out the bottom 25th percentile by variance. We can also use the `quantile` function to control the number of features we filter, and so that we don't need to explicitly pick a variance threshold (e.g. filtering out the 25th percentile removes the lowest 25% of features by variance)

Note, you can repeat this same process for rows by changing the `MARGIN` argument in the apply function - e.g. for columns, `MARGIN = 2` `apply(unfiltered_x, MARGIN = 2, var)` and for rows, `MARGIN = 1` `apply(unfiltered_x, MARGIN = 1, var)`

```
# we can filter out features with very low variance (typically we use
# somewhere between the 25th-45th percentiles). We use 25th
# percentile below
low_var_cols = which(col_variance < quantile(col_variance, 0.25))

filtered_x = unfiltered_x[, -low_var_cols]
```