SBF vignette

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1 Background

Joint matrix factorization facilitates the comparison of expression profiles from different species without using gene mapping. Transforming gene expression profiles into reduced eigengene space using singular value decomposition (SVD) has been shown to capture meaningful biological information (Alter, Brown, and Botstein 2000). Tamayo et al. (2007) used a non-negative matrix factorization approach to learn a low-dimensional approximation of the microarray expression datasets and used the reduced space for comparisons. Matrix factorization-based methods are commonly used for gene expression analysis (Alter, Brown, and Botstein 2000; Tamayo et al. 2007). An orthology independent matrix factorization framework based on generalized singular value decomposition [GSVD; Van Loan (1976)] was used by Alter, Brown, and Botstein (2003) to compare gene-expression profiles from two species. This framework was later extended to develop higher-order generalized singular value decomposition (HO GSVD) to analyze data from more than two species (Ponnapalli et al. 2011).

This study developed a joint diagonalization approach called approximate shared basis factorization (A-SBF) for cross-species expression comparisons. This approach extends the exact factorization approach we developed called shared basis factorization (SBF). We discuss the details of the two methods in the following sections.

2 Shared basis factorization

Consider a set of real matrices $D_i \in \mathbb{R}^{m_i \times k}$ $(i = 1, \ldots, N)$ with full column rank. We define shared basis factorization (SBF) as

$$D_1 = U_1 \Delta_1 V^T,$$
$$D_2 = U_2 \Delta_2 V^T,$$
$$\vdots$$
$$D_N = U_N \Delta_N V^T.$$

Here each $U_i \in \mathbb{R}^{m_i \times k}$ is a dataset-specific left basis matrix, each $\Delta_i \in \mathbb{R}^{k \times k}$ is a diagonal matrix with positive values δ_{ik}, and V is a square invertible matrix.

2.1 Estimating the shared right basis matrix

Let M be the scaled sum of the $D_i^T D_i$. We define M is defined as

$$M = \frac{\sum_{i=1}^N D_i^T D_i / w_i}{\alpha}.$$

The scaling factor w_i is the total variance explained by the column vectors of D_i, and α is the inverse sum of the total variance of D_i, for $i = 1 \cdots N$. The weights w_i and α are defined as

$$w_i = \sum_{j=1}^k \sigma_{jj}^{2\ (i)} \text{ and}$$

$$\alpha = \sum_{i=1}^N \frac{1}{\sum_{j=1}^k \sigma_{jj}^{2\ (i)}}.$$

Here $\sum_{j=1}^k \sigma_{jj}^{2\ (i)} = \mathrm{tr}(D_i^T D_i) = \mathrm{tr}(A_i)$. Using the w_i and α, individual $D_i^T D_i$ are standardized. If all the variances are equal, M becomes the arithmetic mean of the sum of $D_i^T D_i$. The shared right basis matrix V is then determined from the eigenvalue decomposition of M, where $M = V\Theta V^T$. The shared right basis matrix V is an orthogonal matrix as M is symmetric. Given V, we compute U_i and Δ_i by solving the linear system $D_i V = U_i \Delta_i = L_i$. By normalizing the columns of L_i, we have $\delta_{ik} = \|l_{ik}\|$ and $\Delta_i = \mathrm{diag}(\delta_{i1}, \ldots, \delta_{ik})$.

3 Approximate shared basis factorization

Consider a set of matrices $D_i \in \mathbb{R}^{m_i \times k}$ $(i = 1, \ldots, N)$, each with full column rank. We define approximate shared basis factorization (A-SBF) as

$$D_1 = U_1 \Delta_1 V^T + \epsilon_1,$$
$$D_2 = U_2 \Delta_2 V^T + \epsilon_2,$$
$$\vdots$$
$$D_N = U_N \Delta_N V^T + \epsilon_N.$$

Each $U_i \in \mathbb{R}^{m_i \times k}$ is a species-specific left basis matrix with **orthonormal** columns (eigengenes), $\Delta_i \in \mathbb{R}^{k \times k}$ is a diagonal matrix with positive values Δ_{ik} and V is a non singular square matrix. The right basis matrix V is identical in all the N matrix factorizations and defines the common space shared by all species. We learn the factorization such that the learned V is closest to that in the exact decomposition and by minimizing the total decomposition error $\sum_{i=1}^N \epsilon_i = \sum_{i=1}^N \|D_i - U_i \Delta_i V^T\|_F^2$.

4 Usage cases

4.1 SBF examples

```
# load SBF package
library(SBF)
```

Let us create some random matrices using the `createRandomMatrices` function from SBF package. We will create four matrices, each with three columns with rows varying from 4 to 6.

```
set.seed(1231)
mymat <- createRandomMatrices(n = 4, ncols = 3, nrows = 4:6)
sapply(mymat, dim)
#>      mat1 mat2 mat3 mat4
#> [1,]    5    6    4    5
#> [2,]    3    3    3    3
```

Rank of each of this matrices

```
sapply(mymat, function(x) {
  qr(x)$rank
  })
#> mat1 mat2 mat3 mat4
#>    3    3    3    3
```

Let us compute SBF using different approaches.

- Estimate V using sum of $D_i^T D_i / N$
- Estimate V using sum of $D_i^T D_i / N$ with inverse variance weighting
- Estimate V using inter-sample correlation

```
sbf <- SBF(matrix_list = mymat)
sbf_inv <- SBF(matrix_list = mymat, weighted = TRUE)
sbf_cor <- SBF(matrix_list = mymat, transform_matrix = TRUE)
```

When D_i's are transformed to compute inter-sample correlation, we do not need to scale it using inverse-variance weighting anymore. We recommend using inverse variance weights, giving a more robust estimate of V when noisy datasets are present. We estimate V using inter-sample correlation when dealing with gene expression data sets.

`?SBF` help function shows all arguments for the SBF function. Let us inspect the output of the `SBF` call.

```
names(sbf)
#> [1] "v"      "lambda" "u"      "delta"  "m"
```

`sbf$u`, `sbf$v`, and `sbf$delta` correspond to the estimated left basis matrix, shared right basis matrix, and diagonal matrices.

The estimated $V \in R^{k \times k}$ has a dimension of $k \times k$, where k is the number of columns in D_i.

```
sbf$v
#>           [,1]       [,2]       [,3]
#> [1,] 0.4793022  0.8669998  0.1363110
#> [2,] 0.7027353 -0.2860780 -0.6514004
#> [3,] 0.5257684 -0.4080082  0.7463892
```

The delta values for each matrix for the three cases are shown below.

```
printDelta <- function(l) {
  for (eachmat in names(l$delta)) {
```

```
    cat(eachmat, ":", l$delta[[eachmat]], "\n")
  }
}
cat("sbf\n");printDelta(sbf)
#> sbf
#> mat1 : 205.4915 29.6746 71.43295
#> mat2 : 206.5816 71.72548 55.682
#> mat3 : 189.9136 52.6758 42.36825
#> mat4 : 192.6911 80.22868 58.57913
cat("sbf_inv\n");printDelta(sbf_inv)
#> sbf_inv
#> mat1 : 205.5109 22.4888 73.95623
#> mat2 : 206.5963 77.00352 48.05638
#> mat3 : 189.8719 58.60394 33.92988
#> mat4 : 192.6942 72.41955 67.98802
cat("sbf_cor\n");printDelta(sbf_cor)
#> sbf_cor
#> mat1 : 200.4197 44.25134 77.99852
#> mat2 : 199.8621 80.34494 67.23723
#> mat3 : 176.1738 76.95449 60.64485
#> mat4 : 185.4579 67.51833 89.69184
```

The $V \in R^{k \times k}$ estimated in SBF is orthogonal. So $V^T V = V V^T = I$.

```
zapsmall(t(sbf$v) %*% sbf$v)
#>      [,1] [,2] [,3]
#> [1,]    1    0    0
#> [2,]    0    1    0
#> [3,]    0    0    1
```

The estimated V is an invertible matrix.

```
qr(sbf$v)$rank
#> [1] 3
```

The U_i matrices estimated in the SBF do not have orthonormal columns. Let us explore that.

```
sapply(sbf$u, dim)
#>      mat1 mat2 mat3 mat4
#> [1,]    5    6    4    5
#> [2,]    3    3    3    3
```

Let us take the first matrix $U_i \in R^{m_i \times k}$ to check this. For this matrix, $U_i^T U_i$ will be $k \times k$ matrix where $k = 3$.

```
t(sbf$u[[names(sbf$u)[1]]]) %*% sbf$u[[names(sbf$u)[1]]]
#>              [,1]        [,2]       [,3]
#> [1,]  1.00000000 -0.07071457  0.1405487
#> [2,] -0.07071457  1.00000000 -0.6201468
#> [3,]  0.14054867 -0.62014676  1.0000000
```

The estimated M matrix is stored **sbf$m** and **sbf$lambda** gives the eigenvalues in the eigenvalue decomposition $(M = V \Theta V^T)$.

```
sbf$lambda
#> [1] 39524.940  3809.127  3357.434
```

SBF is an exact factorization. Let compute the factorization error for the three cases using **calcDecompError**

function.

```
calcDecompError(mymat, sbf$u, sbf$delta, sbf$v)
#> [1] 1.851693e-26
calcDecompError(mymat, sbf_inv$u, sbf_inv$delta, sbf_inv$v)
#> [1] 1.894292e-26
calcDecompError(mymat, sbf_cor$u, sbf_cor$delta, sbf_cor$v)
#> [1] 2.835482e-26
```

The errors are close to zero in all three cases.

4.1.1   Adding new dataset

The total column variance of matrix 1-4 in mymat is approximately in the same range.

```
sapply(mymat, function(x) sum(diag(cov(x))))
#>    mat1    mat2    mat3    mat4
#> 2076.80 2273.50 2375.25 2860.40
```

Now, let us create two new matrix lists containing our mymat matrix list. We will add a dataset with a similar variance to the first list and a high variance to the second.

```
mat5 <- matrix(c(130, 183, 62, 97, 147, 94, 102, 192, 19), byrow = T,
                    nrow = 3, ncol = 3)
mat5_highvar <- matrix(c(406, 319, 388, 292, 473, 287, 390, 533, 452),
                        byrow = T, nrow = 3, ncol = 3)

mymat_new <- mymat
mymat_new[["mat5"]] <- mat5
sapply(mymat_new, function(x) sum(diag(cov(x))))
#>     mat1     mat2     mat3     mat4     mat5
#> 2076.800 2273.500 2375.250 2860.400 2299.667
mymat_new_noisy <- mymat
mymat_new_noisy[["mat5"]] <- mat5_highvar
sapply(mymat_new_noisy, function(x) sum(diag(cov(x))))
#>     mat1     mat2     mat3     mat4     mat5
#>  2076.80  2273.50  2375.25  2860.40 22915.00
```

Let us compute SBF with the new datasets.

```
sbf_new <- SBF(matrix_list = mymat_new)
sbf_inv_new <- SBF(matrix_list = mymat_new, weighted = TRUE)


sbf_new_noisy <- SBF(matrix_list = mymat_new_noisy)
sbf_inv_new_noisy <- SBF(matrix_list = mymat_new_noisy, weighted = TRUE)
```

Let us take the newly estimated values U_i, Δ_i, and V for the four initial matrices in mymat. We will then compare the decomposition error for the two cases with and without inverse variance weighting.

```
e1 <- calcDecompError(mymat, sbf_new$u[1:4], sbf_new$delta[1:4], sbf_new$v)
e2 <- calcDecompError(mymat, sbf_new_noisy$u[1:4], sbf_new_noisy$delta[1:4],
                    sbf_new_noisy$v)
e2 / e1
#> [1] 3.887268

e3 <- calcDecompError(mymat, sbf_inv_new$u[1:4], sbf_inv_new$delta[1:4],
                    sbf_inv_new$v)
```

```
e4 <- calcDecompError(mymat, sbf_inv_new_noisy$u[1:4],
                      sbf_inv_new_noisy$delta[1:4], sbf_inv_new_noisy$v)
e4 / e3
#> [1] 1.657059
```

With inverse variance weighting, the deviation is smaller.

4.2 A-SBF examples

```
set.seed(1231)
mymat <- createRandomMatrices(n = 4, ncols = 3, nrows = 4:6)
sapply(mymat, dim)
#>      mat1 mat2 mat3 mat4
#> [1,]    5    6    4    5
#> [2,]    3    3    3    3
```

Now Let us compute Approximate-SBF for the same datasets.

- A-SBF
- A-SBF with inverse variance weighting
- A-SBF with inter-sample correlation

```
asbf <- SBF(matrix_list = mymat, approximate = TRUE)
asbf_inv <- SBF(matrix_list = mymat, weighted = TRUE, approximate = TRUE)
asbf_cor <- SBF(matrix_list = mymat, approximate = TRUE, transform_matrix = TRUE)

names(asbf)
#> [1] "v"       "lambda" "u"       "u_ortho" "delta"   "m"       "error"
```

A-SBF is not an exact factorization. A-SBF output has two additional values. `asbf$u_ortho` is the left basis matrix with orthonormal columns and `asbf$error` gives the decomposition error.

```
asbf$error
#> [1] 2329.73
asbf_inv$error
#> [1] 1651.901
asbf_cor$error
#> [1] 14045.99
```

The same error can also be computed using the `calcDecompError` function.

```
calcDecompError(mymat, asbf$u_ortho, asbf$delta, asbf$v)
#> [1] 2329.73
calcDecompError(mymat, asbf_inv$u_ortho, asbf_inv$delta, asbf_inv$v)
#> [1] 1651.901
calcDecompError(mymat, asbf_cor$u_ortho, asbf_cor$delta, asbf_cor$v)
#> [1] 14045.99
```

In A-SBF factorization, U_i has orthonormal columns, and V is orthogonal.

```
zapsmall(t(asbf$u_ortho[[names(asbf$u_ortho)[1]]]) %*%
           asbf$u_ortho[[names(asbf$u_ortho)[1]]])
#>      [,1] [,2] [,3]
#> [1,]    1    0    0
#> [2,]    0    1    0
#> [3,]    0    0    1
```

```
zapsmall(t(asbf$v) %*% asbf$v)
#>      [,1] [,2] [,3]
#> [1,]    1    0    0
#> [2,]    0    1    0
#> [3,]    0    0    1
```

5 Reduce A-SBF factorization error

Let us optimize the factorization error using the `optimizeFactorization` function for the three cases of A-SBF computation shown before. Depending upon the mymat and initial values, optimization could take some time.

```
myopt <- optimizeFactorization(mymat, asbf$u_ortho, asbf$delta, asbf$v)
myopt_inv <- optimizeFactorization(mymat, asbf_inv$u_ortho, asbf_inv$delta,
                                   asbf_inv$v)
myopt_cor <- optimizeFactorization(mymat, asbf_cor$u_ortho, asbf_cor$delta,
                                   asbf_cor$v)
```

The number of iteration taken for optimizing and new factorization error:

```
cat("For asbf, # iteration =", myopt$error_pos, "final error =", myopt$error)
#> For asbf, # iteration = 220 final error = 1411.555
cat("\nFor asbf inv, # iteration =", myopt_inv$error_pos, "final error =",
    myopt_inv$error)
#>
#> For asbf inv, # iteration = 202 final error = 1411.555
cat("\nFor asbf cor, # iteration =", myopt_cor$error_pos, "final error =",
    myopt_cor$error)
#>
#> For asbf cor, # iteration = 196 final error = 1411.555
```

```
#> After optimization, for all three A-SBF factorizations, the final error
#> is the same (up to 2 decimals).
#> The final error is 1411.56
```

6 Cross-species gene expression analysis using A-SBF

For cross-species gene expression datasets, we learn the common space V based on correlation (R_i) between column phenotypes (such as tissues, cell types, etc.) within a species. In our study, we have shown that the inter-tissue gene expression correlation is similar across species. Let $X_i \in \mathbb{R}^{m_i \times k}$ be a standardized gene expression matrix where $X_i = C_i D_i S_i^{-1}$. Here $C_i = I_{m_i} - m_i^{-1} 1_{m_i} 1_{m_i}{}^T$ is a centering matrix and $S_i = \text{diag}(s_1, \ldots, s_k)$ is a diagonal scaling matrix, where s_p is the standard deviation of p-th column of D_i. The matrix X_i is a matrix with columns of D_i mean-centered and scaled by the standard deviation. The correlation between expression profiles of k tissue types in species i is given by $R_i = X_i^T X_i / m_i$. We then define an expected correlation matrix ($\mathbb{E}(R_i)$) across N species as M, where M is defined as

$$M = \frac{\sum_{i=1}^{N} R_i}{N}.$$

The shared right basis matrix V capturing the inter-tissue gene expression correlation is determined from the eigenvalue decomposition of M, where $M = V \Theta V^T$. Once the V and Δ_i are learned using the SBF factorization, we compute U_i with orthonormal columns using proposition I. The estimated V space captures inter-tissue gene expression correlation relationship. For gene expression analysis, we do not update/change

V while optimizing the factorization error as we may not be able to interpret the new V space. So in the `optimizeFactorization` function, we set `optimizeV = FALSE` while reducing the factorization error.

6.1 Proposition I

Let $A \in \mathbb{R}^{m \times n}$ with rank n and SVD of $AQ^T = X\Sigma Y^T$. Among all matrices $B \in \mathbb{R}^{m \times n}$ with orthonormal columns, the Forbenius norm $\|A - BQ\|_F^2$ is minimized when $B = XY^T$.

$$\min \|A - BQ\|_F^2 = \text{tr}\,(A - BQ)^T\,(A - BQ)$$
$$= \text{tr}(A^T A) + \text{tr}(Q^T Q) - 2\text{tr}(AQ^T B^T).$$

This is equivalent to maximizing $\text{tr}(AQ^T B^T)$. Let SVD of $AQ^T = X\Sigma Y^T$, where $X \in R^{m \times m}$ is left singular matrix, $\Sigma \in R^{m \times n} = \begin{bmatrix} \Sigma_n \\ 0 \end{bmatrix}$ with $\Sigma_n = \text{diag}(\sigma_1, \ldots, \sigma_n)$, and $V \in R^{m \times n}$ is the right singular matrix. Let $Z = Y^T B^T X$. Now Z is a rectangular matrix with orthonormal rows ($ZZ^T = I$) as $B^T B = I$. Now we have,

$$\text{tr}(AQ^T B^T) = \text{tr}(X\Sigma Y^T B^T) = \text{tr}(Y^T B^T X\Sigma) = \text{tr}(Z\Sigma)$$

$$= \sum_{i=1}^{n} z_{ii}\sigma_i \leq \sum_{i=1}^{n} \sigma_i.$$

The upper bound is obtained when $Z = I$ and thus $B = XY^T$.

6.2 Usage examples

Let us load the SBF package's in-built gene expression dataset. The dataset contains the average gene expression profile of five similar tissues in three species.

```
# load dataset
avg_counts <- SBF::TissueExprSpecies
# check the names of species
names(avg_counts)
#> [1] "Homo_sapiens"   "Macaca_mulatta" "Mus_musculus"
```

```
# head for first species
avg_counts[[names(avg_counts)[1]]][1:3, 1:3]
#>                hsapiens_brain hsapiens_heart hsapiens_kidney
#> ENSG00000000003         2.3109         1.9414          5.2321
#> ENSG00000000005         0.0254         0.2227          0.5317
#> ENSG00000000419         5.2374         5.3901          5.5659
```

The number of genes annotated in different species is different. As a result, the number of rows (genes) in the expression data will be different for different species.

```
sapply(avg_counts, dim)
#>      Homo_sapiens Macaca_mulatta Mus_musculus
#> [1,]        58676          30807        54446
#> [2,]            5              5            5
```

Let us compute A-SBF with inter-tissue correlation.

```
# A-SBF call using correlation matrix
asbf_cor <- SBF(matrix_list = avg_counts, check_col_matching = TRUE,
                col_index = 2, approximate = TRUE, transform_matrix = TRUE)
# decomposition error
asbf_cor$error
#> [1] 65865.92
```

Optimize factorization to reduce decomposition error but by not updating V.

```
myopt_gef <- optimizeFactorization(avg_counts, asbf_cor$u_ortho, asbf_cor$delta,
                                   asbf_cor$v, optimizeV = FALSE)
names(myopt_gef)
#> [1] "u"          "v"          "d"          "error"      "error_pos" "error_vec"
```

```
# new error
myopt_gef$error
#> [1] 63540.08
# number of iterations
myopt_gef$error_pos
#> [1] 10
```

The number of iterations taken to optimize = 10.

```
identical(asbf_cor$v, myopt_gef$v)
#> [1] TRUE
```

Check estimated Ui's have orthonormal columns.

```
zapsmall(t(as.matrix(myopt_gef$u[[names(myopt_gef$u)[1]]])) %*%
           as.matrix(myopt_gef$u[[names(myopt_gef$u)[1]]]))
#>      [,1] [,2] [,3] [,4] [,5]
#> [1,]    1    0    0    0    0
#> [2,]    0    1    0    0    0
#> [3,]    0    0    1    0    0
#> [4,]    0    0    0    1    0
#> [5,]    0    0    0    0    1
```

References

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