

AUTOMATIC SEGMENTATION OF HUMAN BRAIN TRACTOGRAPHY DATA

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Monday October 25, 2010

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White and Gray Matter



Figure: Matter

DTI

- Diffusion of water molecule probes tissue structure at the smallest *i.e.* voxel resolution.
- Water diffusion in oriented fibrous structures (as white matter and muscles) is anisotropic (varies with direction).
- Tensors are used to model diffusion. Major eigen vectors of the tensor (Principle Directions) gives the fiber tract direction.

Neuronal Cell Structure

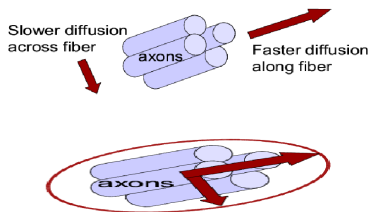
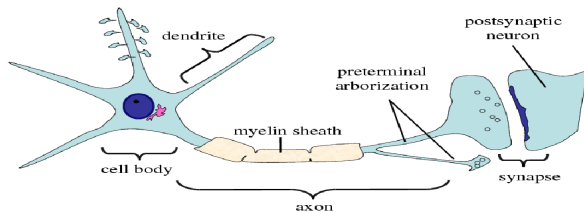


Figure: Diffusion

Tractography

- Streamline Tractography estimates white matter tract trajectories following the most likely tract direction. It locally chooses the most likely fiber trajectory.
- Entire brain tractography is estimated by stepping along the major eigen vector direction using RK method.

DTI with Tractography gives us the white matter fiber orientation.

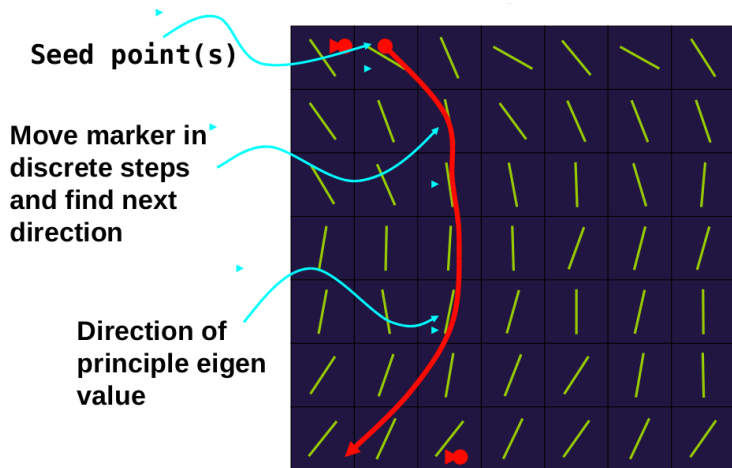
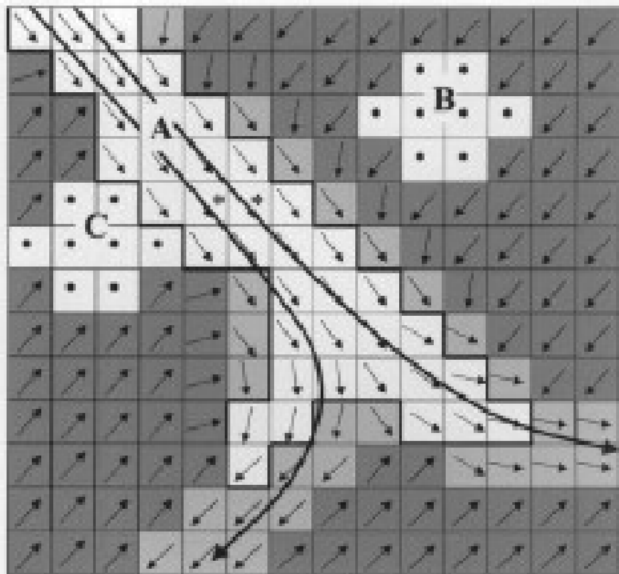


Figure: Tractography through seed

Tractography Cont



Tractography Data

The fiber trajectories are colored with random colors. This data is the input to the segmentation algorithm.

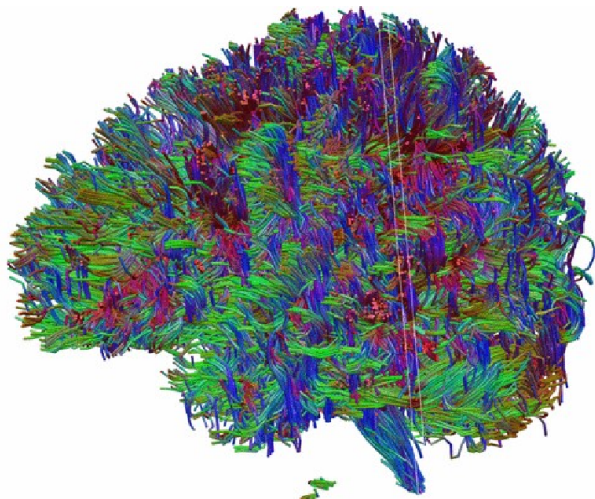


Figure: An example of whole brain white matter tractography

- A fiber is represented as a set of points in 3D space (typically 20 to 30 points per fiber).
- Tractography produces thousands of fiber trajectories per subject (250K).
- Tractography can be seen as a 3D point cloud but that is not very useful.
- Useful information can be extracted only when they are organized into anatomically meaningful structure.

Automatically Tractography Segmentation

- Given the tractography data of a human brain, Segment it automatically into tracts having “similar” fibers which are anatomically meaningful.

Eight Major Tracts
Arcuate
Cingulum
Corticospinal
Forceps Major
Fornix
Inferior Occipitofrontal Fasciculus
Superior Longitudinal Fasciculus
Uncinate



Figure: Major fiber tracts

- Localization of specific tracks for surgical planning.
- Surgery planning with minimum damage to the fibers.



Figure: Some Applications

Atlas creation

- Learn common white matter structure present across the subjects and build white matter atlas.
- Project the fibers into a high dimensional space where each fiber can be seen as a point.
- Cluster the points in that space using any central clustering technique (as K-mean or GMM).
- Label the clusters formed using experts knowledge (allot anatomical names).
- This constitutes the anatomical model of white matter structure (High Dimensional White Matter Atlas).

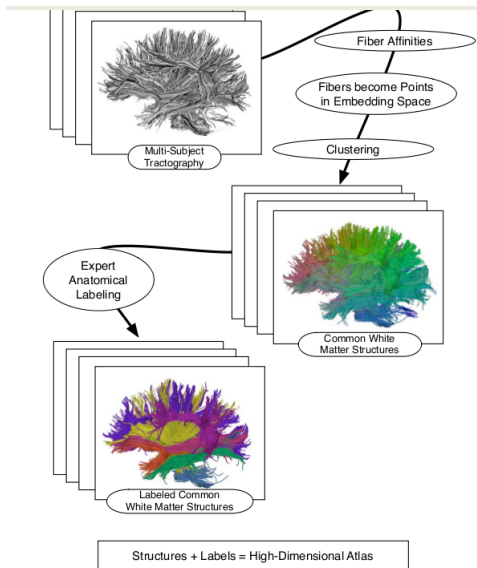


Figure: A concept map for atlas creation

Automatic Segmentation

- Novel subjects can be segmented by embedding new fiber trajectory as a point in the high dimensional white matter atlas space.
- Label fiber according to the nearest cluster centroid.

Automatic Segmentation

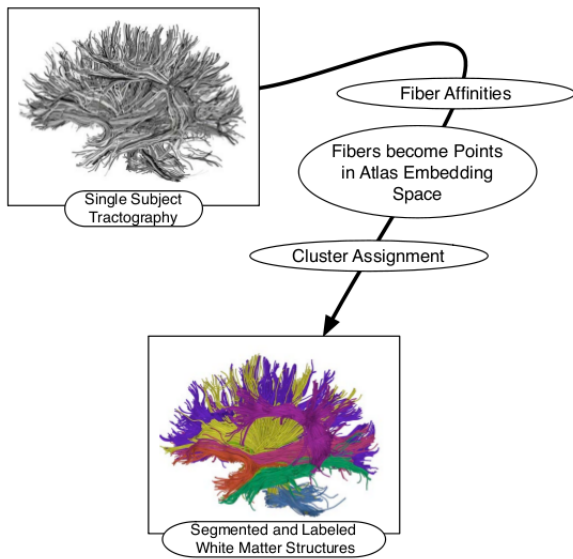


Figure: A cmap to segment a novel brain

Diagrammatically

Shape information is automatically extracted and used for clustering.

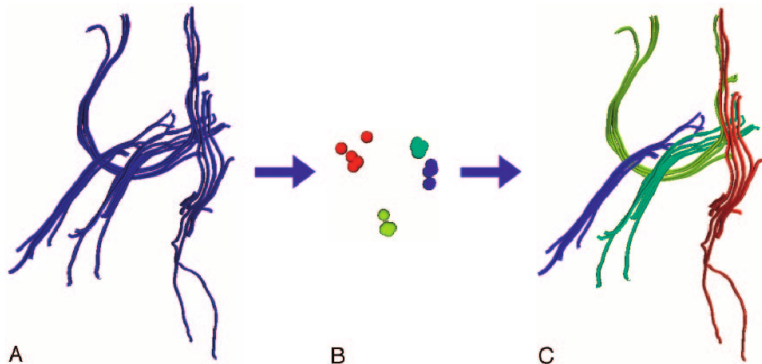


Figure: [A] Shows input fiber tracts, [B] Shows Clustering Step: Each point represents the similarity relationships of a fiber (points are coming from the highest eigenvectors of affinity matrix), [C] Shows the tracts with different colors

Three modes of Segmentation

- Interactive.
- Automatic Clustering.
- Automatic Atlas Based.

Interactive (Virtual Dissection)

- Labeling is done by experts knowledge.
- Select fibers passing through user defined ROI.
- Partridge [1] defined pyramidal tract ROI instead of manual.
- Commonly used but requires extensive knowledge of 3D white matter fiber tract anatomy.

Automatic Clustering

- Clustering algorithms are used to organise fiber trajectories into fiber bundles or tracts.
- Attach Anatomical label to the cluster.
- Mathematically define a fiber similarity measure.
- Calculate pairwise distances and calculate Affinity matrix.
- Calculate the principle components and use them for segmentation.

Assumption Exploited

Fiber trajectories that begin near each other follow similar path and terminates near each other should belong to the same anatomical structure.

Fiber Similarity Measures

- Brun [13] considered distances between fiber end points.
- Brun [10] further used a 9D shape descriptor vector defined as mean and lower triangular part of the covariance matrix of the points on fiber and computed euclidean distance between shape descriptor.
- Gerig [8, 9] *et.al* proposed mean closest point distance.
- Jonasson *et.al* [11] used a similarity measure based on the number of times 2 trajectories shared the same voxel.

Convergence of literature with respect to the fiber distance measure is on mean closest point distances as used by [7, 8, 9, 12, 14, 15].

Automatic Atlas Based

- Madah [16] proposed a manual interaction method to create a tractography atlas and gave an algorithm for transferring its labels to novel subjects.
- Madah [17] further proposed an atlas creation method for corpus callosum using labeled tractography from several subjects and then used Expectation Maximization (EM) framework to classify fibers of novel subjects.

Atlas Generation

- 1 Registration.
- 2 Whole Brain Tractography.
- 3 Fiber Affinity Calculation.
- 4 Fiber Embedding.
- 5 Fiber Clustering.
- 6 Expert Anatomical labeling.

[1] Registration

All subject tractography must be in same co-ordinate system. Unbiased group registration congealing algorithm is used for rotation, translation, scaling [19].

[2] Whole Brain Tractography

- Generate Tractography of the entire white matter of brain using RK method of order 2 using fixed step size 0.5mm
- Every voxel have a C_L value associated to it.
- $C_L = \frac{\lambda_1 - \lambda_2}{\lambda_1}$, where λ_1 and λ_2 are first 2 eigen values of diffusion tensor for any voxel.

Threshold

T_{seed} : Initiate tractography in voxels having C_L value greater than T_{seed} .

T_{stop} : Stop tractography if C_L falls below T_{stop} , indicating gray matter (area of planar anisotropy).

T_{length} : Higher (for major tracts), Lower (to see everything).

- Depending on subject, thresholds and seeding resolution brain tractography produces 10000 to 100000 fibers per subject.
- Picking up randomly 10000 fibers per subject is reasonable.

[3] Fiber Affinity Calculation

Assumption: Fibers following similar trajectories belongs to the same anatomical structure.

- Mean closest point a variant of Hausdorff distance is used for calculating the pairwise fiber distances because it captures the degree of similarity through the shape trajectory.

Mean Closest Point ($d_{mcp}(i, j)$)

- For each point on fiber i find the closest point on fiber j and compute the distance between them.
- The distance for all the points on fiber i , giving you the corresponding distances d_i .
- $$d_{mcp}(i, j) = \frac{1}{n} \sum_{k=1}^n d_k$$

Fiber Distance

Represent each fiber using 15 to 10 equi-distant points, including end points (distances are calculated along the trajectory). Sample points are represented as yellow points.

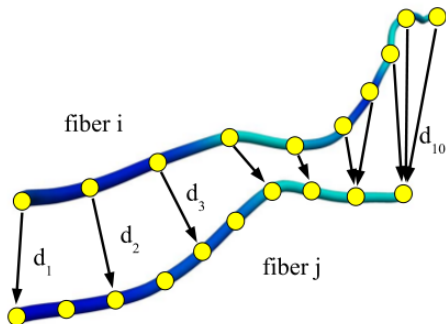


Figure: Illustration of computation of mean closest point between 2 fibers.

Directed closest point distances from fiber i to j are represented with black arrows.

Properties

- $d_{mcp}(i, j) \neq d_{mcp}(j, i)$

Symmetry

- $d_{ij} = \text{Min}(d_{mcp}(i, j), d_{mcp}(j, i))$. Taking *Min* encourages grouping of shorter fibers with longer fibers, if they run parallel for some distance.
- $d_{ij} = d_{ji}$
- $d_{ii} = 0$

Pairwise fiber distances are converted into pairwise fiber affinity through Gaussian kernel.

Finally, fiber distances are converted into fiber affinity using the Gaussian kernel to get the *Affinity Matrix* (W)

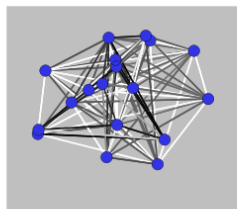
Affinity Matrix (W)

- $W[i][j] = e^{\frac{-d_{ij}^2}{\sigma^2}}$.
- σ defines the size scale of the problem by setting the distance over which fibers can be considered similar.
- W contains affinities for all pairs of fibers across all brain.

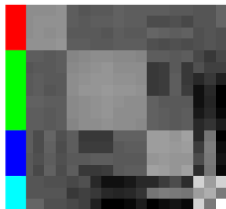
Problem: W is huge hence cannot be computed. We use an approximation called Nystrom method for eigen analysis of W , with explicitly computing it completely.



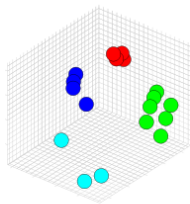
1. Input Paths



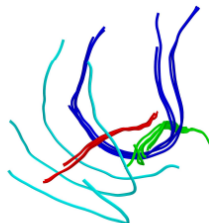
2. Weighted Graph and Affinity Matrix (A)



3. Normalized Affinity Matrix (A)



4. Embedding Vectors



5. Clusters

Figure: Atlas Creation

Overall Approach

Nystrom Analysis [18]

- Randomly choose a subset of fiber trajectory.
- Compute affinities of them from all the fibers, dividing W into A, B, C matrices (as in figure).
- A = Pairwise affinities of randomly chosen subset.
- B = Pairwise affinities of rest of the fibers to that subset.
- C = Huge matrix and is not required to be calculated.

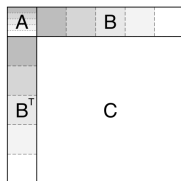


Figure: Multi subject fiber affinity matrix

[4] Fiber Embedding

- In embedding space each fiber is represented as a point and nearby points generally corresponds to similar fiber trajectories.
- Similarity relationships are represented spatially to facilitates the clustering.
- Embedding is done using the eigen vectors of fiber affinity matrix.

3 steps of fiber embedding

- Normalization of W to get W' .
- Estimating Eigen vector and values of W' .
- Calculating Embedding vector for each fiber.

3 steps of fiber embedding

[1] Normalization

- $W'[i][j] = \frac{W[i][j]}{\sqrt{d_i \times d_j}}$, where d_i is the row sum of i^{th} row.
- $W' = D^{-\frac{1}{2}} \cdot W \cdot D^{-\frac{1}{2}}$, here D is the diagonal matrix having d_i 's as diagonal elements. $\begin{bmatrix} 2 & 14 \\ 5 & 4 \end{bmatrix} \rightarrow \begin{bmatrix} \frac{2}{4 \cdot 4} & \frac{14}{4 \cdot 3} \\ \frac{5}{3 \cdot 4} & \frac{4}{3 \cdot 3} \end{bmatrix}$

A	a_r	B	b_r
B^T	b_c	$C \approx B^T A^{-1} B$	$B^T A^{-1} b_r$

Column vector

- $d = \begin{bmatrix} a_r + b_r \\ b_c + B^T A^{-1} b_r \end{bmatrix}$, here d is a column matrix such that d_i is the sum of i^{th} row.

[2] Estimating Eigen vector and values of W' .

- The eigen vector matrix U' of W' are required for the fiber embedding.
- U' is estimated by projecting A' and B' onto the eigen vector basis from A (i.e. $U\Lambda^{-1}$) [18].

$$U' = \begin{bmatrix} U \\ B'^T U \Lambda^{-1} \end{bmatrix} = \begin{bmatrix} A'^T U \Lambda^{-1} \\ B'^T U \Lambda^{-1} \end{bmatrix}$$

where

U : Eigen Vector Matrix of A'

Λ : Eigen Value Diagonal Matrix of A'

A' and B' are normalized version of matrices A and B respectively.

[2] Estimating Eigen vector and values of W' . Continued

- Let N is the total number of fibers and n is the fibers selected randomly for the Nystrom estimation.

Matrix Name	Dimension
A	$n \times n$
B	$n \times (N - n)$
B^T	$(N - n) \times n$
$C \approx B^T A^{-1} B$	$(N - n) \times (N - n)$
U	$n \times n$
$B^T U \Lambda^{-1}$	$(N - n) \times n$
U'	$N \times n$

- U' contains N dimensional top n eigen vectors of huge normalized affinity matrix W' .

[3] Calculating Embedding vector for each fiber

- Normalize the matrix U' to get E matrix. Each row corresponds to the embedding vector.
- $E_j = \frac{1}{\sqrt{d_j}}(U'_{j,1}, U'_{j,2}, \dots, U'_{j,n})$

Atlas information can be used to segment novel brain. New tractography path is embedded in the same space in which the clustering was performed originally. Cluster labels and anatomical informations are assigned according to the nearest cluster centroid.

Transfer Atlas Information to new subject

- **STEP 1:** Affinity Computation
- **STEP 2:** Matrix Normalization
- **STEP 3:** Embedding New Data
- **STEP 4:** Classification and Labeling

Automatic Segmentation

[1] Affinity Computation

- S holds the pairwise affinities between all the trajectories (in novel brain) and each path in the random subset of paths that was chosen during atlas creation.
- Distances are symmetrized and converted to affinities.

A	B	S
B^T	C	D
S^T	D^T	

[2] Matrix Normalization

- Each element is normalized by the row and column sums at that location. Required row sums are estimates of row sums of $[S^T D^T]$
- $d_{row} = [s_c + S^T A^{-1} b_r]$
- $d_{col} = [a_r + b_r]$
- $S'^T [i][j] = \frac{S^T [i][j]}{\sqrt{d_{row}[i] \cdot d_{col}[j]}}$

Reasons

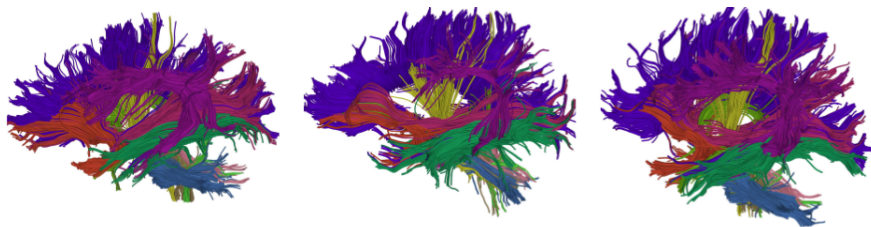
- Re-embedding of already seen path mapped to same location in the embedding space.
- S^T will not change the column sum significantly.
- Hence, scaling applied to a novel path is basically the same as that which have been applied if it were part of the original clustering problem.





[3] Embedding New Data

- From normalized S matrix i.e S' , eigen vectors are estimated using *Nystrom method* as:
$$\hat{U}_s = S^T U \Lambda^{-1}$$
- Embedding vectors are given as the rows of \hat{U}_s , each divided by the square root of the corresponding row sum from d_{row} .
- This processes is exactly same as that employed for the matrix B in atlas creation.

[4] Classification and Labeling

- New subject's embedding vectors are labelled according to the nearest cluster centroid, giving a cluster label for each path.
- Per cluster anatomical label and any addition (say color) informations are transferred to the novel subject.



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Integral Transform

- Integral and Inverse Integral Transforms are defined as:

$$\int_{t_1}^{t_2} K(t, u) \cdot f(t) dt = T(f(u)) = g(u)$$

$$\int_{u_1}^{u_2} K^{-1}(t, u) \cdot T(f(u)) du = f(t)$$

- K Kernel defines the transform which maps an equation from its original domain into another domain.
- Such mappings are useful when manipulating and solving the equation in the target domain is much easier than manipulating in original domain.
- Finally solution is mapped back to original domain with the inverse of integral transform.

Definition

- 1 Given a kernel there are some special functions ϕ which only got scaled up by a scalar λ after transformation. Such functions are called Eigen functions and corresponding λ 's are called Eigen values.

- 2
$$\int_a^b W(x, y) \cdot \phi(y) dy = \lambda\phi(x) = T(\phi(x)).$$

- 3 Approximating above integral by evaluating it over a set of evenly spaced points $y_1, y_2, y_3, \dots, y_n$ on interval $[a, b]$ using quadrature rule as:

$$\frac{b-a}{n} \sum_{j=1}^n W(x, y_j) \cdot \hat{\phi}(y_j) = \lambda\hat{\phi}(x)$$

where $\hat{\phi}(x)$ is the approximation of true $\phi(x)$.

- 4 If we sample x also on the interval $[a, b]$ over same points then W can now be seen as a square matrix. We solve the above equation by setting:
 $(x = y_i) \forall i \in \{1 \text{ to } n\}.$

Continued..

- 5 We got the system of equations $\forall i \in \{1 \text{ to } n\}$ as:

$$\frac{1}{n} \sum_{j=1}^n W(y_i, y_j) \cdot \hat{\phi}_i(y_j) = \lambda_i \hat{\phi}_i(y_i)$$

- 6 Above system can be seen as :

$$A \cdot \Phi = n \cdot \Phi \cdot \Lambda$$

where $A[i][j] = W(y_i, y_j)$, $\Phi = [\phi_1, \phi_2, \dots, \phi_n]$ are n eigen vectors of A and Λ is diagonal corresponding eigen value matrix.

- 7 Natural Nystrom extension for each $\hat{\phi}_i$ that allow us to extend an eigenvector computed for a set of sample points to any arbitrary point x is:

$$\hat{\phi}_i(x) = \underbrace{\frac{1}{n \cdot \lambda_i}}_{\Lambda^{-1}} \sum_{j=1}^n \underbrace{W(x, y_j)}_{B'^T} \cdot \underbrace{\hat{\phi}_i(y_j)}_{\text{columns of } U}$$

- 8 Hence, $U' = \begin{bmatrix} U \\ B'^T U \Lambda^{-1} \end{bmatrix} = \begin{bmatrix} A'^T U \Lambda^{-1} \\ B'^T U \Lambda^{-1} \end{bmatrix}$ where U is $(n \times n)$, $B'^T U \Lambda^{-1}$ is $((N - n) \times n)$ and U' is $(N \times n)$ matrix.

Continued..

9 $W = \begin{bmatrix} A & B \\ B^T & C \end{bmatrix}$, where A is a $(n \times n)$, B is a $(n \times (N - n))$ and C is a $((N - n) \times (N - n))$ Matrices.

10 Let us denote U' a $(N \times n)$ matrix as the approximate eigen vector of W' using Nystrom extension as :

$$U' = \begin{bmatrix} U \\ B'^T U \Lambda^{-1} \end{bmatrix}$$

11

$$W' = U' \Lambda U'^T \tag{1}$$

$$= \begin{bmatrix} U \\ B'^T U \Lambda^{-1} \end{bmatrix} \Lambda \begin{bmatrix} U^T & \Lambda^{-1} \cdot U^T \cdot B' \end{bmatrix} \tag{2}$$

$$= \begin{bmatrix} U \Lambda U^T & B \\ B^T & B^T A^{-1} B \end{bmatrix} = \begin{bmatrix} A & B \\ B^T & C \approx B^T A^{-1} B \end{bmatrix} \tag{3}$$

Thanks.

Thank You.