TV-DCT: Method to impute Gene Expression data using DCT based Sparsity and Total Variation Denoising

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Introduction

- High dimensional genomics data such as microarray gene expression data and RNA sequencing data, generally suffers from missing values.
- Incomplete data can adversely affect the downstream analysis for diagnostics and treatment.
- Several methods to impute missing values in gene expression data have been developed, but most of these work at high levels of observability.
- Interdependence between the expression levels of genes in gene expression data leads to a highly correlated data matrix (of subjects versus genes). Gene expression matrix can be considered as a low rank matrix embedded into a lower dimensional linear subspace. Further, missing value imputation in genomics can be viewed as a matrix completion problem.
- We propose a novel 2-stage method, namely, TV-DCT method for predicting missing values in gene expression data using Discrete Cosine Transform DCT based sparsity in Stage-1 and Total Variation (TV) denoising in Stage-2 .

Proposed Method

Proposed TV-DCT method for completing the gene expression matrix is a 2-stage method.

Stage-1: Compressive Sensing Framework

- Columns of gene expression matrix are highly sparse in the DCT domain because every column represents the expression values of a particular gene across subjects that would be biologically similar and hence, data within any column would be slowly varying in nature.
- Hence, we propose to recover missing data column-wise, i.e., by applying CS framework on each column of the matrix **Y**. The sensing matrix Φ_i of size $r_i \times m$ is constructed for every i^{th} column, where r_i denotes the number of observed entries in that column.
- Every i^{th} column of matrix **Y** using the CS-based reconstruction with the sparsity constraint on the column in the DCT domain as

$$\underset{\tilde{\mathbf{x}}_i}{min}(||\mathbf{y}_i - \Phi_i \tilde{\mathbf{x}}_i||_2^2 + \lambda_1 ||\mathbf{D}\tilde{\mathbf{x}}_i||_1) \quad (1)$$

- Since DCT is an orthogonal transform, we transformed it to synthesis prior formulation as

$$\underset{\tilde{\mathbf{z}}_i}{min}(||\mathbf{y}_i - \Phi_i \mathbf{D}^T \mathbf{z}_i||_2^2 + \lambda_1 ||\mathbf{z}_i||_1) \quad (2)$$

Stage-2: Denoising Framework

- Recovered matrix from stage-1 is assumed to be the noisy version of the original matrix and denoising is used in Stage-2. Total Variation (TV) based denoising is used in Stage-2 and is formulated as-

$$\underset{\mathbf{x}_i}{min}(||\mathbf{x}_i - \tilde{\mathbf{x}}_i||_2^2 + \lambda_2 ||\mathbf{A}\mathbf{x}_i||_1) \quad (3)$$

where i ranges from 1 to n (number of columns/ genes).

- **A** is a difference operator defined as

$$\mathbf{A} = \begin{bmatrix} -1 & 1 & & \\ & -1 & 1 & \\ & & \ddots & \\ & & -1 & 1 \end{bmatrix}$$

- It maps a vector x_i to

$$(\mathbf{A}\mathbf{x}_i^k) = \mathbf{x}_i^k - \mathbf{x}_i^{k+1} \quad (4)$$

- Dual formulation of above is used to solve the optimization framework (because of non-differentiability of L_1-norm) as

$$\underset{\mathbf{x}_i}{min}\ \underset{|\mathbf{w}_i| \leq 1}{max}\ (||\mathbf{x}_i - \tilde{\mathbf{x}}_i||_2^2 + \lambda_2 \mathbf{w}_i^T \mathbf{A}\mathbf{x}_i) \quad (5)$$

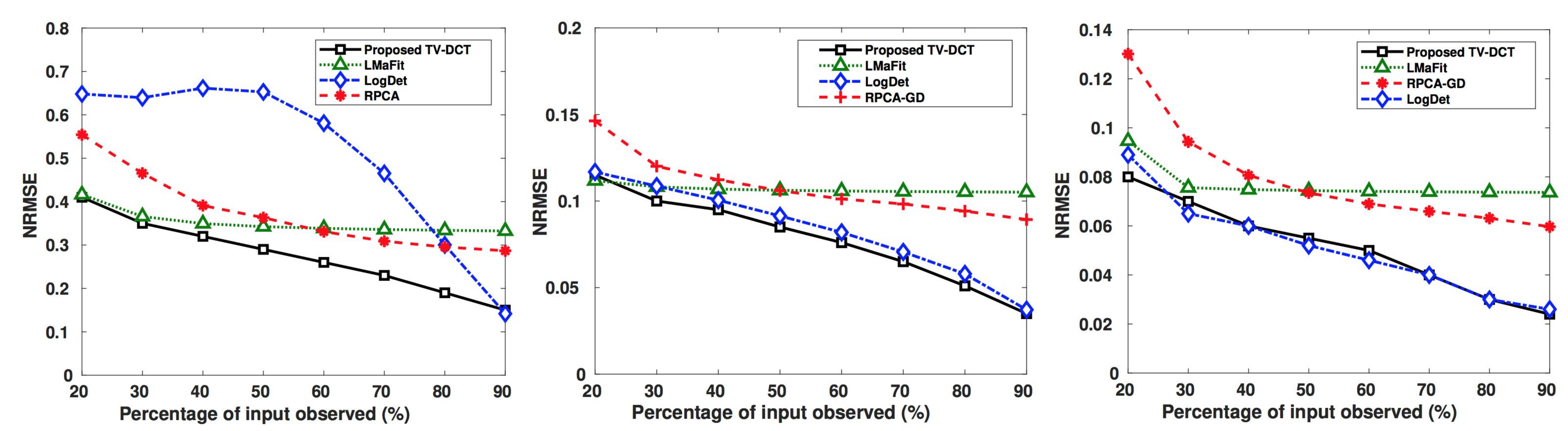
where w_i is an auxiliary vector such that

$$||\mathbf{x}_i||_1 = \underset{|\mathbf{w}_i| \leq 1}{max}\ (\mathbf{w}_i^T \mathbf{x}_i) \quad (6)$$

- TV denoising problem is minimized using iterative clipping algorithm with update equations as given in algorithm where,

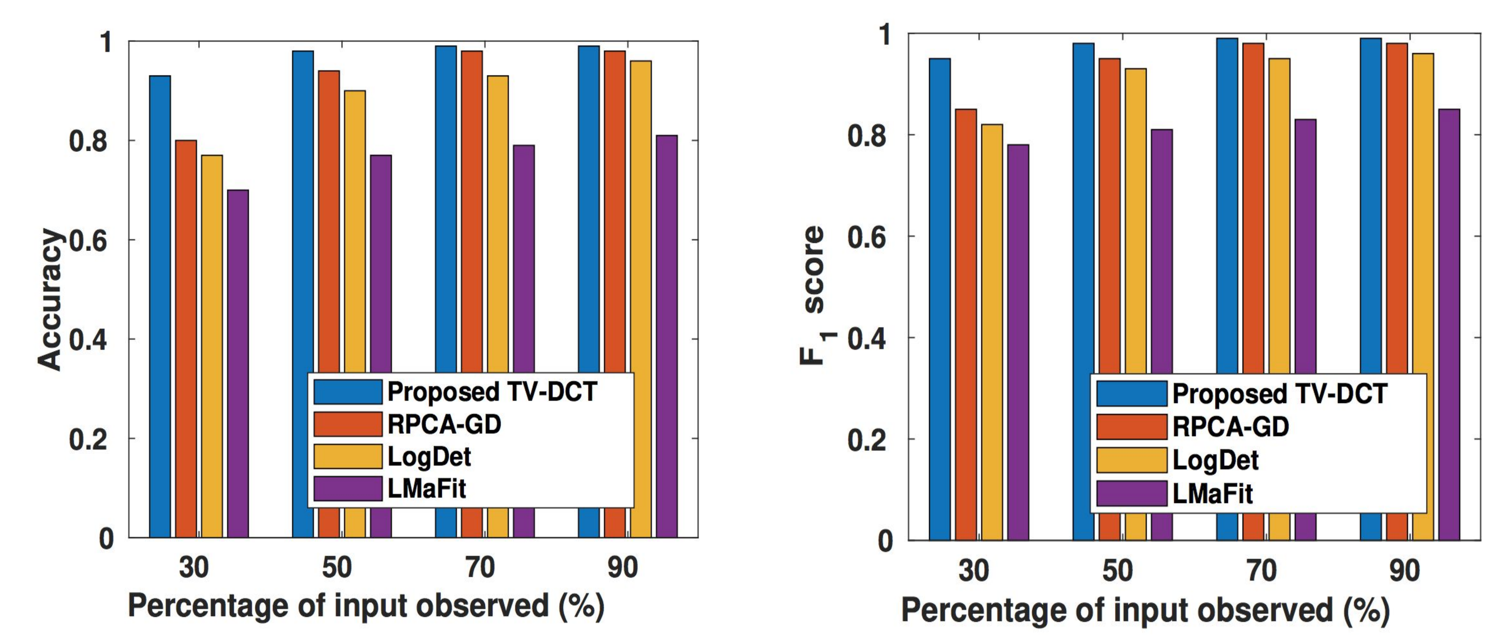
$$\mathbf{w}^{(0)} = \mathbf{0} \text{ and } \alpha \geq \text{maxeig}(\mathbf{A}\mathbf{A}^T)$$

Results



(a) ALLAML dataset (b) lung dataset (c) Myeloma dataset

Fig. 1: Comparison of proposed TV-DCT method with other methods at different percentage of observed input.



(a) Classification Accuracy (a) F_1 score

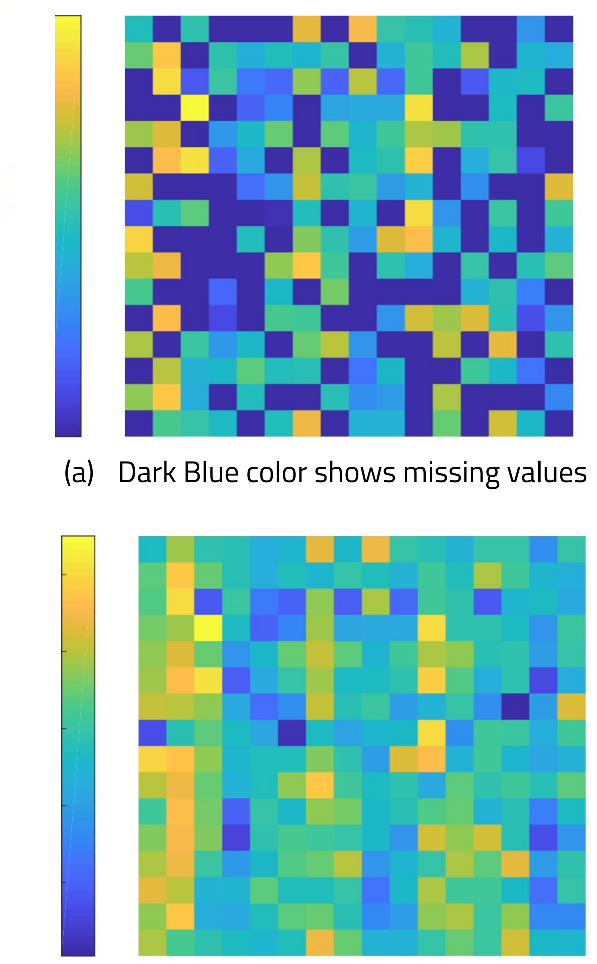
Fig. 2: Classification Accuracy and F_1 score obtained on imputed matrices of ALLAML dataset at varying sampling ratios.

Table 1:. Classification accuracy and F_1 scores on different sampling percentage of incomplete matrix and the recovered/imputed matrix using proposed TV-DCT method for ALLAML dataset

	Classification Accuracy				F_1 score			
Classifier	Random Forest		Linear SVM		Random Forest		Linear SVM	
SR	Observed	Imputed	Observed	Imputed	Observed	Imputed	Observed	Imputed
20	0.65	**0.96**	0.67	**0.90**	0.77	**0.96**	0.79	**0.90**
30	0.65	**0.96**	0.67	**0.93**	0.77	**0.96**	0.80	**0.95**
40	0.69	**0.97**	0.72	**0.94**	0.79	**0.97**	0.82	**0.95**
50	0.71	**0.97**	0.74	**0.97**	0.80	**0.97**	0.83	**0.98**
60	0.75	**0.97**	0.81	**0.98**	0.83	**0.97**	0.87	**0.99**
70	0.77	**0.96**	0.86	**0.99**	0.84	**0.97**	0.90	**0.99**
80	0.80	**0.95**	0.91	**0.99**	0.86	**0.96**	0.93	**0.99**
90	0.85	**0.95**	0.94	**0.99**	0.88	**0.96**	0.96	**0.99**

Algorithm

Stage 1 - Matrix Recovery
Input: **Y** (Input incomplete matrix), DCT matrix **D**
for loop from $i = 1........n$
Calculate Φ_i for all i using $\mathbf{y}_i$
while converge:
$\mathbf{z}_i^{k+1} = soft\left\{\mathbf{z}_i^k + \frac{1}{\alpha}(\mathbf{D}\Phi_i^T)(\mathbf{y}_i - \Phi_i \mathbf{D}^T \mathbf{z}_i^k), \frac{\lambda_1}{2\alpha}\right\}$
end while
$\tilde{\mathbf{x}}_i = \mathbf{D}^T \mathbf{z}_i$
end for
Obtain $\tilde{\mathbf{X}}$ from $\tilde{\mathbf{x}}_i$
Output: $\tilde{\mathbf{X}}$ (Recovered Matrix)
Stage 2 - Denoising
Input: $\tilde{\mathbf{X}}$(Noisy matrix), **A** (Difference Operator)
for loop from $i = 1........n$
while converge:
$\mathbf{x}_i^{k+1} = \tilde{\mathbf{x}}_i - \mathbf{A}^T \mathbf{w}_i^k$
$\mathbf{w}_i^{k+1} = clip\left\{\mathbf{w}_i^k + (\frac{1}{\alpha})\mathbf{A}\mathbf{x}_i^{k+1}, \frac{\lambda_2}{2}\right\}$
end while
end for
Obtain **X** from $\mathbf{x}_i$
$\mathbf{x}_{j,i} = \hat{\mathbf{x}}_{j,i}, \ \ if \ \ \Omega_{j,i} = 1$
Output: **X** (Recovered Matrix)



(a) Dark Blue color shows missing values

(b) Imputed Matrix

Fig. 1: 16x16 patch of Incomplete and Imputed matrix.

Evaluation metric is Normalized Root Mean Square Error defined as

$$\text{NRMSE} = \frac{||\hat{\mathbf{X}}(original) - \mathbf{X}(recovered)||_F}{||\hat{\mathbf{X}}(original)||_F} \quad (7)$$

Conclusion

- In this study, we have presented novel TV-DCT method that is a 2-stage matrix imputation method and we have investigated the performance of our proposed method at low as well as high observability of data.
- The comparative performance of TV-DCT method is observed to be superior to three state-of-the-art matrix completion methods in terms of NRMSE and classification accuracy.

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