

Lag Penalized Weighted Correlation (LPWC)

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Biological Time Series

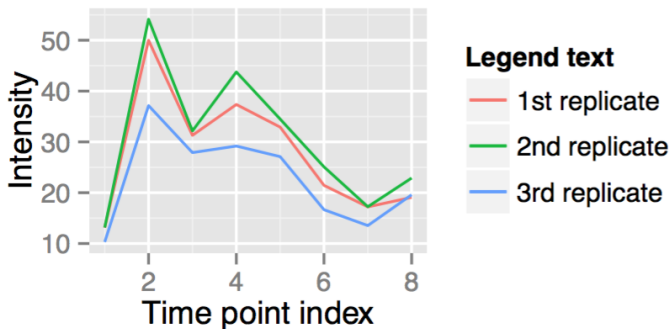


Figure 1: Simple time series plot with 8 time points and 3 replicates

Toy Example: Intuitive Clustering

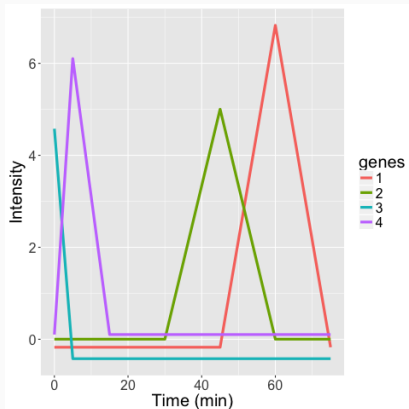
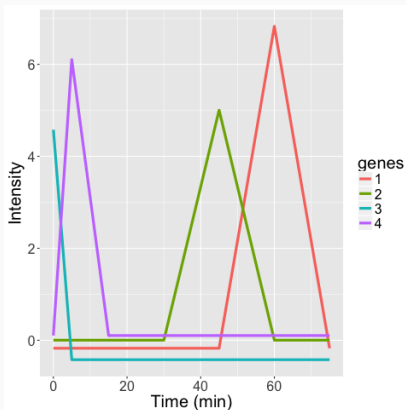


Figure 2: Hypothetical example with 4 genes

Toy Example: Algorithmic Clustering



(a) Hypothetical example with 4 genes

Clustering Algorithm	Cluster 1	Cluster 2
hLPWC/ILPWC	● ●	● ●
DTW	●	● ● ●
STS	●	● ● ●
heuc	●	● ● ●

(b) Cluster assignment of the 4 genes

Figure 3: Existing methods do not group early and late genes

Motivation

Irregular time sampling

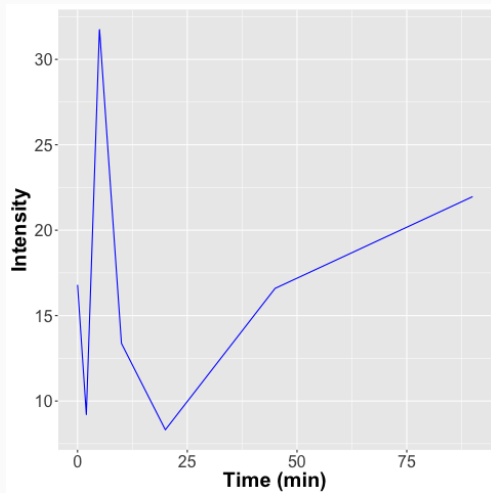


Figure 4: Irregularly sampled time series data

Motivation

Delayed response (lags)

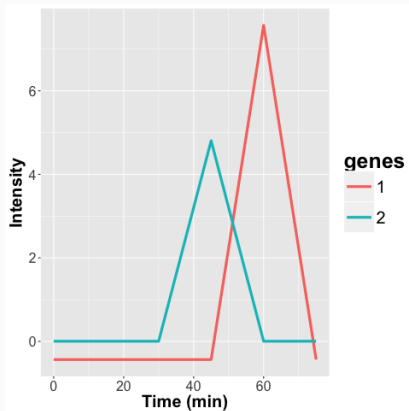


Figure 5: Gene 1 spikes after gene 2

What is a Lag?

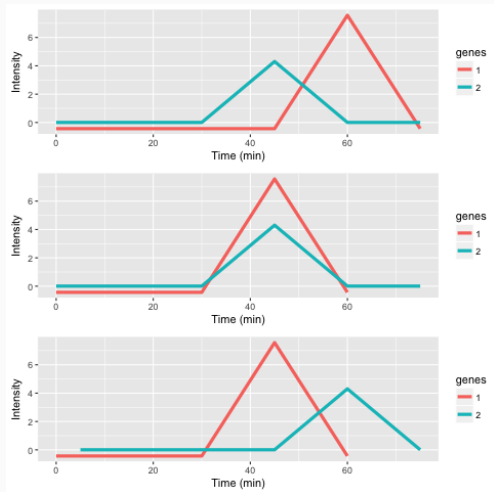


Figure 6: An example of the effects of applying different lags to genes 1 and 2. Genes 1 and 2 are not lagged (top). Gene 1 with lag -1, gene 2 with no lags (middle). Gene 1 with lag -1 and gene 2 with lag 1 (bottom).

Method Overview

LPWC is composed of two steps:

- computing optimal lags for each gene
- computing final correlation matrix for all gene

General Formula

$$\text{corr}_{LPWC}(i, j, X_i, X_j) = \underbrace{\exp\left(\frac{-E(w)}{C}\right)}_{\text{penalty}} * \underbrace{\text{corr}_w(L^{X_i} Y_i, L^{X_j} Y_j, \exp\left(\frac{-w}{C}\right))}_{\text{weighted correlation}}$$

$$w = (L^{X_i} T_i - L^{X_j} T_j)^2$$

- Adjusted Rand Index (ARI): similarity between two data clusterings and adjusted for chance
- ARI score close to 1 indicates similar clusterings, score close to 0 otherwise

Simulated Data

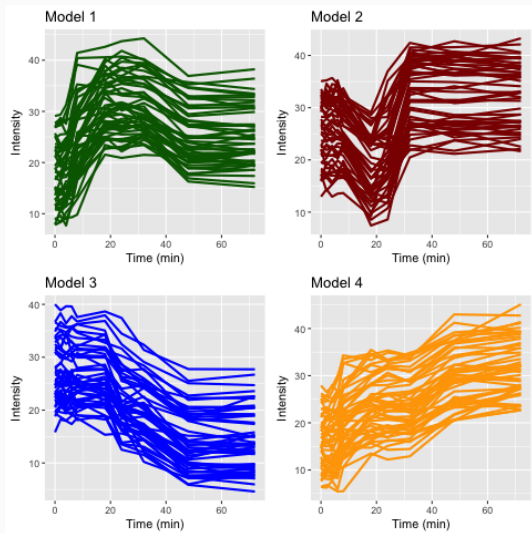


Figure 7: Four models simulated using ImpulseDE. Random noise was added to the model parameters to induce variation around a common trend.

ARI Score for Simulated Data

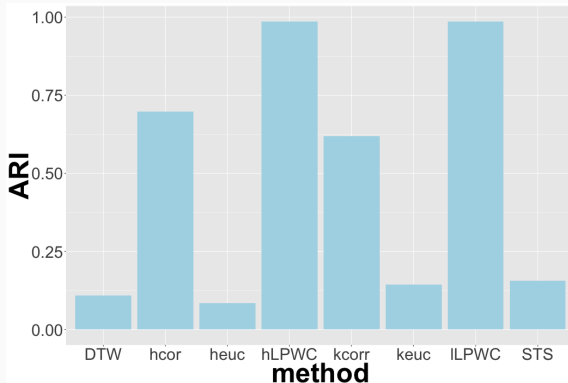


Figure 8: ARI score for different clustering methods for the simulated data where the real clusters are known.

Yeast Osmotic Stress Response Data

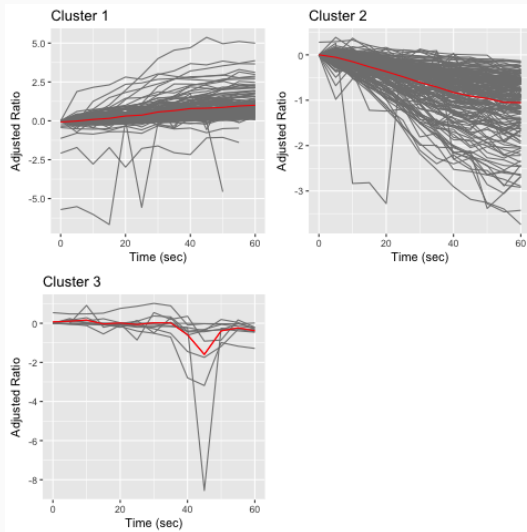


Figure 9: Clustering 344 phosphopeptides in yeast osmotic stress into 3 different clusters.

Conclusion & Future Work

- Algorithm tackles the issue of irregular time samples and delayed responses
- R package available on CRAN (LPWC) and preprint on bioRxiv
- Allow missing data (imputation) and support mixed dataset with different time points
- Improve the optimal lag assignments

Acknowledgements

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