Prediction of protein-to-protein interactions

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1. Method

1.1 Smoothing

We create a smoothed version of our original signal h, which removes noise and effectively captures the properties of the signal at a higher scale (Figure 1b). We obtain such a smoother signal by convolving the original signal h with the Gaussian function:

\[ h(t) \ast k(t) = \int h(t - r)k(r) \, dr \]  

where k(t) is the Gaussian function:

\[ k(t, m, s) = \frac{1}{\sqrt{2\pi s^2}} e^{\frac{-(t - m)^2}{2s^2}} \]

By varying s, we can vary the scale level (and thus the smoothing) of the scale-space representation.

1.2 Discretisation

We compute the regularized (smoothed) derivative of the gene expression time signal by convolution with the first-order derivative of the Gaussian function as:

\[ \Delta h + k(t) = (h + \Delta h)(t) - (\Delta h + k)(t) \]

1.3 Similarity function

We distinguish four kinds of possible relations and the associated relation between the discrete time patterns, as shown in Figure 5. We find putative relations by comparing discrete gene patterns using these similarity functions (Figure 1d).

1.4 Integration of data sets

Many patterns are similar by mere chance. We remove these chance findings by combining the results of two independent data sets using a logical AND (Figure 1e).

1.5 Confidence intervals

For each detected local extrema (i) in a gene pattern we calculate the probability of a type I error, P(i). The total confidence for a gene Q with n extrema is then calculated by the geometric mean:

\[ C_Q = \left( \prod_{i=1}^{n} (1 - P(i)) \right)^{1/n} \]

We rank predictions according to their confidence (Figure 1f). For any relation consisting of genes Q and R the confidence measure becomes:

\[ C_{QR} = C_Q \cdot C_R \]

2. Results

We applied the method to two yeast datasets of Spellman et al. and validated the resulting predictions by using a public Gold standard protein-to-protein interaction database. We compared the results to a similar approach where discretisation was based on per gene thresholding as shown in Figure 4.

3. Conclusion

Local extrema are a feature in time-series gene expression data that can be used for finding biologically relevant interactions (e.g., protein-to-protein interactions). The applied method is invariant under scaling and shifting and can be adjusted for the amount of experimental noise.