Relevance Network Approach to Network Reconstruction

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Network Reconstruction Task

- Also network inference task

Given time-series data

Find network links
Applications and Methods

• Example applications by domain
  • Bioinformatics: from expression data to gene regulatory networks
  • Social networks: from time-series of number of retweets to Twitter influence networks
  • Collaborative environments: from number of article edits to information propagation networks in Wikipedia
  • Climate: from time-series data measured at a regular grid over the globe, identify geographical regions affected by El Nino

• Methods and approaches to network reconstruction
  • Operate on various target formal representation of the networks
  • Methods for Bayesian networks, more general graphical models
  • This talk: Relevance Network Approach
Relevance Network Approach

- Assumption: (high) similarity between the time series observed in two nodes indicate a presence of network link between them
  - Thus: the focus is on **measuring similarity** between time series
  - Problem: **Similarity** often **symmetric**, leading to undirected nets
  - Solution: **symmetry-breaking** scoring schemes

\[ n \text{ Time Series} \rightarrow \text{Similarity Matrix } M^{n \times n} \rightarrow \text{Scoring Scheme} \rightarrow \text{Weights Matrix } W^{n \times n} \rightarrow \text{Thresholding } W_{ij} > \tau \rightarrow \text{Adjacency Matrix } A^{n \times n} \]
What is this Talk About?

- Brief survey of the relevance network approaches
  - Similarity measures and scoring schemes
  - Spoiler alert: in sum, there are (too) many of them

- So: which similarity measure and scoring scheme should be used?
  - Michelangelo’s answer: all of them at the same time
  - We rephrase the question into: What works where?

- Ideally, we would be able to provide recommendations
  - You should use similarity measure X and scoring scheme Y, since
  - There is a large number of nodes in the network, and
  - The time series are long
Talk Outline

- Introduction and motivation

- Relevance network (RN) approach
  - Similarity measures
  - Scoring schemes

- Empirical comparison of the RN variants
  - Experimental setup: networks, data sets, performance measures
  - Comparison methodology
  - Empirical results: what works where?

- Conclusion and further work
Similarity Measures (SM)

- Similarity measure $m: \mathbb{R}^n \times \mathbb{R}^n \rightarrow \mathbb{R}$
  - Detects (non)linear relation between two given time series

- Many different measures proposed; can be clustered in 5 classes
  - Distances
  - Dynamic Time Warping
  - Correlations
  - Mutual Information
  - Symbolic
SM: Distances (Norns)

- Distance-based similarities **regard time series as vectors**

- Distance between $x$ and $y$ defined as a $p$-norm of the vector $x-y$:
  - $d_p(x,y) = \left( \sum_i |x_i-y_i|^p \right)^{1/p}$
  - $p=1$: Manhattan distance
  - $p=2$: Euclidean distance
  - Often used (please do not ask why) $p=10$

- From **distance to similarity**?
  - Many ways, most simple $m(x,y) = - d_p(x,y)$
  - Or, if you are afraid of negative numbers $m(x,y) = 1 / d_p(x,y)$
SM: Dynamic Time Warping

- Optimal mapping between two time series $x$ and $y$, such that
  - Points from $x$ are linked to points in $y$
  - Each point should participate in at least one link
  - The sum of the link lengths is minimal

- Finding the optimal mapping: **dynamic programming** formula
  - Different variants of the formula lead to different DTW measures
SM: Correlation Coefficients

- Regard time series as random variables $X$ and $Y$
  - Pearson $r_p(X,Y) = \frac{E[(X-E[X])(Y-E[Y])]}{(E[(X-E[X])^2]E[(Y-E[Y])^2])}$

- More robust to non-normal distributions
  - Spearman $r_s(X,Y) = r_p(\text{ranks}(X), \text{ranks}(Y))$
  - Kendall $r_k(X,Y) = \frac{2(n_c-n_d)}{(n(n-1))}$
    - $n_c$: number of concordant pairs of time points
    - $n_d$: number of dis-concordant pairs of time points

- Often squared values used
  - Since we are not inferring the direction of the relationship (positive, negative), but only to its degree
  - We are not referring here to the causal direction, which could have been interpreted as a link direction
SM: Mutual Information

- Treat the time series as random variables X and Y
  - $MI(X,Y) = H(X) + H(Y) - H(X,Y)$, where H denotes entropy

- Requires discretization of the numeric variables; hence different variants corresponding to different discretization methods
  - Equal-frequency or equal-width bins
  - Various techniques for determining the number of bins
SM: Simple Qualitative/Symbolic Distance

- Comparing simple pairwise increase/decrease trends
  - \((t_1, t_2): X \uparrow Y \uparrow, (t_1, t_3): X \uparrow Y \uparrow, (t_1, t_4): X \uparrow Y \uparrow, (t_1, t_5): X \uparrow Y \uparrow\)
  - \((t_2, t_3): X \downarrow Y \downarrow, (t_2, t_4): X \downarrow Y \uparrow, (t_2, t_5): X \uparrow Y \uparrow\)
  - \((t_3, t_4): X \uparrow Y \uparrow, (t_3, t_5): X \uparrow Y \uparrow\)
  - \((t_4, t_5): X \uparrow Y \uparrow\)

- 1 difference in 10 pairwise comparisons: \(d(X, Y) = 1/10 = 0.1\)
SM: Symbolic Dynamics

- Transformation of time series to a vector of order patterns
- Calculating distances or mutual information on symbolic vectors

<table>
<thead>
<tr>
<th>Order patterns for 3 time points</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Order patterns" /></td>
</tr>
<tr>
<td>( P_1 )</td>
</tr>
<tr>
<td>( P_2 )</td>
</tr>
<tr>
<td>( P_3 )</td>
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<tr>
<td>( P_4 )</td>
</tr>
<tr>
<td>( P_5 )</td>
</tr>
<tr>
<td>( P_6 )</td>
</tr>
</tbody>
</table>

\[
(t_{1}, t_{2}, t_{3}): P_2 \quad (t_{1}, t_{2}, t_{4}): P_2 \quad (t_{1}, t_{2}, t_{5}): P_1 \\
(t_{1}, t_{3}, t_{4}): P_1 \quad (t_{1}, t_{3}, t_{5}): P_1 \quad (t_{2}, t_{3}, t_{4}): P_4 \\
(t_{2}, t_{3}, t_{5}): P_5 \quad (t_{2}, t_{4}, t_{5}): P_5 \\
(t_{3}, t_{4}, t_{5}): P_1
\]

Symbolic vector \((P_2, P_2, P_1, P_1, P_1, P_4, P_5, P_5, P_1)\)
Symmetry Breaking Scoring Schemes

- **Time shifting (TS)**
  - Common way to **infer** the **directionality of causal relationships**
  - Observing the trend of **correlation change** when shifting one time **series**, provides a hint on the direction of the causal relationship
  - $X \rightarrow Y$: shifting $X$ (the cause) to the right (forward in time) will **increase the similarity/correlation** between $X$ and $Y$

- **Asymmetric Weighting (AWE)**
  - Similarity matrix elements divided by the sum of the elements in the corresponding column, i.e., $W_{ij} = \frac{M_{ij}}{\sum_k M_{kj}}$
  - Can be used alone or in combination with TS
Other Scoring Schemes

• **Must be combined with time shifting** to identify causal direction

• Context Likelihood of Relatedness (CLR)
  - Uses the distribution of the values in the matrix $M$ for
  - Normalization using the averages and standard deviations of the values in the columns and rows of $M$

• Identifying and discriminating indirect links
  - Algs for Reconstruction of Accurate Cellular Networks (ARACNE)
  - Heuristic for identification of indirect links: $M_{ik} \leq \min(M_{ij}, M_{jk})$

• Maximum Relevance / minimum redundancy Network (MRNET)
  - Assigns higher ranks to direct links, lower ranks to indirect links
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Networks and Data: Yeast

- Four Yeast networks (size: #nodes, #links, density)
  - YN1: 42, 61, 1.1E-2
  - YN2: 75, 135, 4.1E-3
  - YN3: 300, 448, 1.5E-3
  - YN4: 188, 283, 2.4E-3

- 13 time-series data sets that only partially cover network nodes
- Real measurements that only partially cover network nodes
- For each network data sets selected that cover at least 95% nodes
  - YN1: 6 data sets, YN2: 2, YN3: 5, and YN4: 3 data sets

- Total of 20 network reconstruction tasks
Networks and Data: Dream5

- Two Dream5 NR-challenge networks (size: #nodes, #links, density)
  - DN1: 4511, 2066, 1.1E-03
  - DN2: 5950, 3940, 3.8E-04

- Four synthetic (simulated) data sets that cover all network nodes
  - DN1: 2 data sets, DN2: 2 data sets

- Total of 4 network reconstruction tasks
Methods and Performance Measures

• 114 (=19*6) Relevance Network Approach Variants
  • 19 similarity measures: 3 distances, 3 DTW variants, 3 correlation coefficients, 4 mutual-information variants, 6 symbolic variants
  • 6 scoring schemes: TS, AWE, AWE+TS, CLR+TS, ARACNE+TS, MRNET+TS

• 2,736 (=114*(20+4)) experiments

• Three performance measures

AuROC, AuPRC, AuPRC-20
Comparison Methodology

- One sample Student’s t-test (p-value < 0.05)
  - Identify well-performing methods that on average perform significantly better than the default/random NR
- WRT at least one performance measure: AUROC default 0.5, AUPRC default 0.5, AUPRC-20% default 0.1
- The average calculated on the 20 network reconstruction problems

- Compare the average rankings of the well-performing methods
  - Pareto fronts in the 3D performance space
  - Observing method ranks (can be also performances)
- Which methods are in the first three Pareto fronts:
  - Similarity measures? Scoring schemes?
Methods Selection: T-Test

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Pareto Fronts in the Performance Space

6.3–13.3
SymQD-AWE
SymQD-AWE-TS
SymQD-CLR-TS

8.1–13.8
CorrP-TS
MI-ARACNE-TS
SymQD-TS

10.6–14.3
CorrP-AWE
CorrP-AWE-TS
MI-ARACNE-TS

MDS of the performance space, 27 methods
Pareto Fronts Analysis

- Similarity measures (left-hand graph)
  - Mostly symbolic (dark green; 4, all 3 in the first Pareto front)
  - Some based on mutual-information (light green; 3)
  - Others based on correlation (yellow; 3)

- Scoring schemes (right-hand graph)
  - Majority AWE weighting scheme (dark and light green), no MRNET
Comparison: Yeast vs. Dream5 (YvD)
YNvDN: Similarity Measures

- In both cases: **symbolic measures** (dark green) **perform best**
- Yeast: also mutual-information (light green) based measures
- Yeast: all the best symbolic performers use the **simple QD measure**
- Dream5: the best performers use **complex symbolic measures**
YNvDN: Scoring Schemes

- Difficult to generalize
  - Yeast: five schemes among top performers; only MRNET missing
  - Dream5: MRNET is the only scheme used by the top performers
Network Size: Similarity Measures

- Again, symbolic measures prevail; Pearson correl (yellow) for small and medium networks
  - Small: symbolic (4; all simple QD), mutual info (1) and Pearson (1)
  - Medium: mutual info (5), symbolic (3 simple QD) and Pearson (3)
  - Large networks = Dream5 networks: complex symbolic

- Network size important factor for selecting the similarity measure
Network Size: Scoring Schemes

- Scoring scheme selection more important for non-small networks
  - Small and medium: 4 and 5 different scoring schemes; no MRNET
  - Large networks = Dream5 networks: MRNET only

- No obvious relation
Time Series Length: Similarity Measures

- Time series length important factor for selecting similarity measure
  - **Short**: symbolic (QD) and **mutual-information** based
  - **Medium**: symbolic (mostly QD, also complex) and **Pearson corr.**
  - **Long**: plain distances (L10 and Euclidean; red) **perform best**

- **Symbolic measures perform well for not-too-long time series only**
Time Series Length: Scoring Schemes

- TS length not important when selecting the scoring scheme
  - Small: no MRNET
  - Medium: no AWE (dark orange)
  - Large: AWE and MRNET
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Conclusion: What Works Where?

- Most successful similarities: based on symbolic dynamics
  - The simple qualitative distance measure best overall performer; top performer for small/med networks and short/mid-length time series
  - Complex symbolic measures better for large networks
- Pearson correlation seems to work well for medium networks
  - No other correlations among the top performers
- Distances work well for long time series
  - Distances based on $p=10$ and Euclidian norm top performers
- Mutual-info top performers for short time series
- No DTW among the top performers
Further Work

- Open issue: similarity measure and scoring scheme combo
  - Which combination work well and which are broken?

- More experiments and benchmarks
  - These might be performed for additional GRN benchmarks
  - Other domains: Social Networks? Collaborative Environments?

- General methodology for comparing methods performance
  - Taking into account multiple perf criteria
  - In contrast with current *average rank diagrams* that are limited to comparing methods wrt one performance criterion
  - Extend the methodology with quantifying and testing the significance of the differences between Pareto fronts
Collaboration and Acknowledgements

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