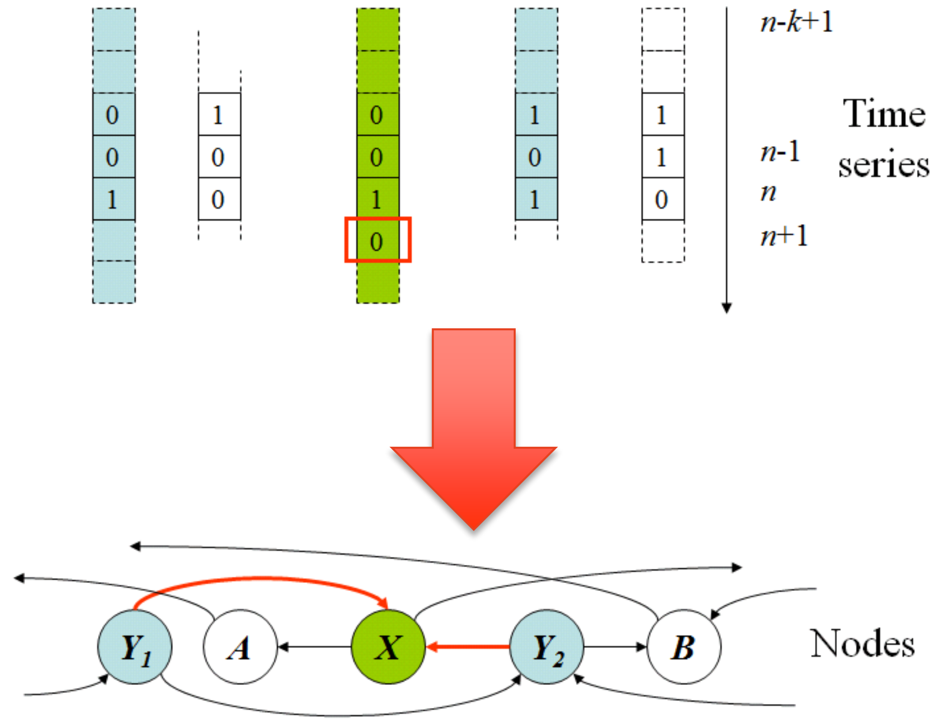
Inferring network models from multivariate time-series data:

Philosophy, approaches and considerations



A/Prof. Joseph Lizier

School of Computer Science
Centre for Complex Systems

THE UNIVERSITY OF SYDNEY

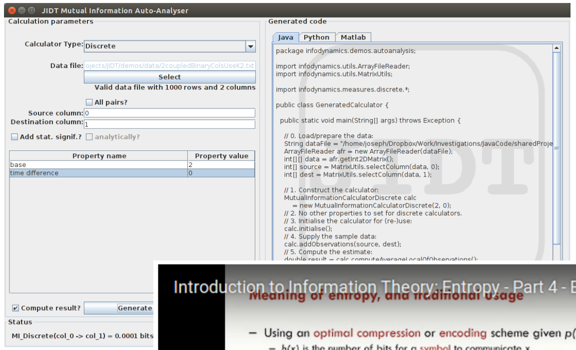
https://github.com/jlizier/netinf_tutorial

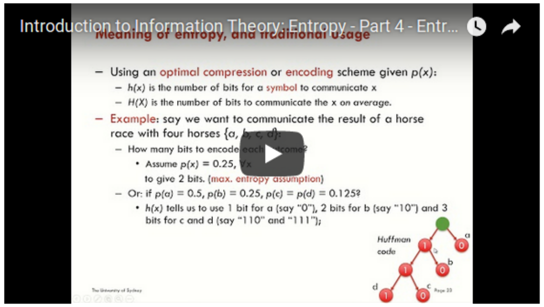
Inferring network models

Session outcomes:

1. Understand **philosophy** of different goals in network inference from time-series data
2. Understand **measures** and **approaches** (and how to access them)
3. Understand key **considerations** to incorporate

- Primary references:
  - Github:
    - https://github.com/jlizier/netinf_tutorial
    - JIDT http://github.com/jlizier/jidt/
    - IDTxl https://github.com/pwollstadt/idtxl
  - Short course: http://bit.ly/jidt-course-alpha
    - Lecture slides (“course” branch, module 12)
    - Youtube videos
    - Tutorial



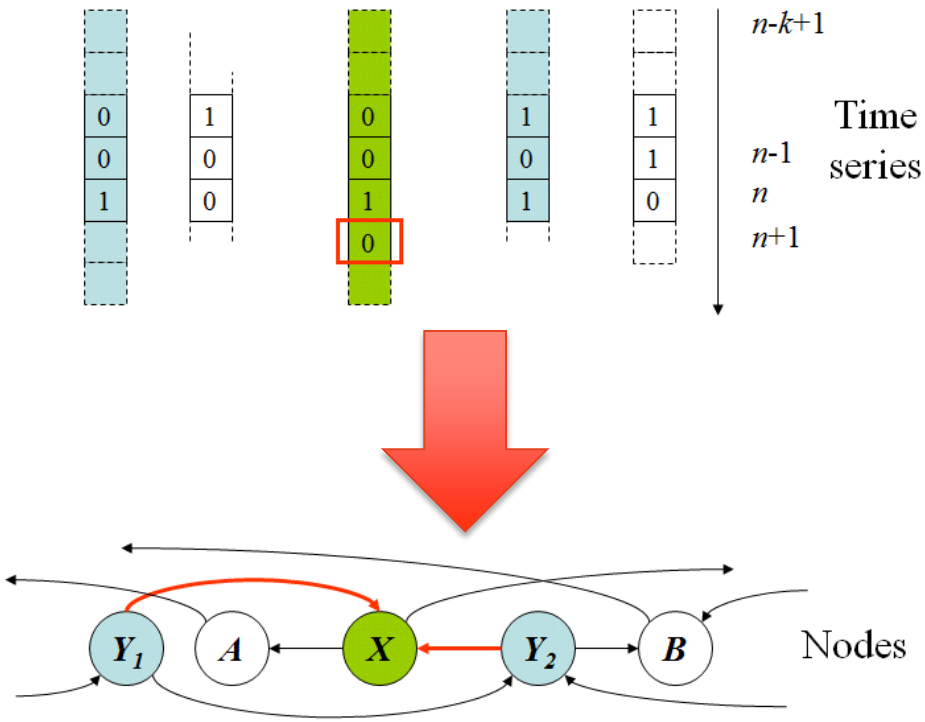


Scope

- Many, many approaches
  - Cannot cover all
- Focus on:
  - Linear regression models
  - Information-theoretic measures
- Application areas:
  - Neural recordings
  - Financial market data sets
  - Gene regulatory networks
  - Sport analytics
  - …

Inferring network models

– Key question: *given only time series for each of a set of variables, how can we build a network* ***model*** *which represents the* ***relationships*** *between these variables?*



Complex system as a multivariate time-series of activity of variables. Examples?

Options, philosophically:

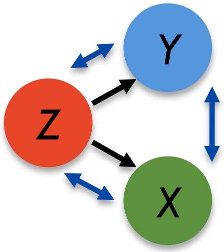
1. Functional connectivity

2. Effective connectivity

3. Structural connectivity

Functional network inference

- Constructs (**undirected**) networks to represent **pairwise statistical relationships** between nodes
- Usually using a measure of correlation or mutual information (MI) to provide pairwise edge weights
- Trade-off: fast and simple, but does not explain dynamics



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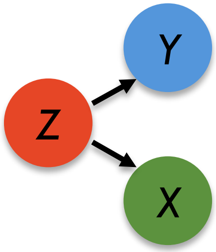
K. J. Friston. Functional and effective connectivity in neuroimaging: A synthesis. *Human Brain Mapping*, 2(1-2):56–78, 1994.

Structural network inference

- Constructs **directed** networks to represent the physical, directed (**causal**) connections
- *Generally* only possible via interventional techniques but not directly from large (observational) multivariate time-series sets alone.
- Does not tell us about time or experimentally modulated changes in how the variables are interacting
- Trade-off: full picture (?), but isn't generally achievable.



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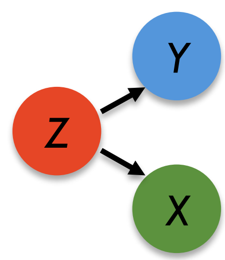
K. J. Friston. Functional and effective connectivity in neuroimaging: A synthesis. *Human Brain Mapping*, 2(1-2):56–78, 1994.

J. Pearl, Causality: Models, Reasoning, and Inference. Cambridge: Cambridge University Press, 2000.

Bossomaier, Barnett, Harré, Lizier, "An Introduction to Transfer Entropy: Information Flow in Complex Systems", Springer, Cham, 2016; section 7.2

Effective network inference

- Constructs **directed** networks to provide "*minimal neuronal circuit model*" which can replicate and indeed explain the time series of the nodes
- Not strictly causal, but aims at providing best **generative model** possible from data.
- Hybrid approach, and aligns with dynamical systems/computational views
- Trade-off: multivariate model, data/runtime requirements



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Functional connectivity

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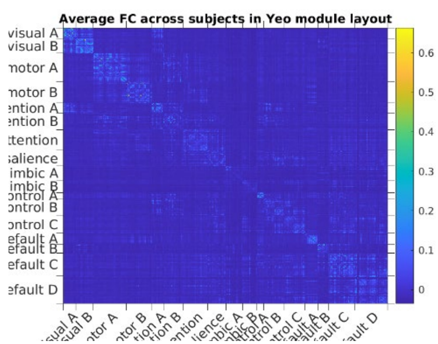
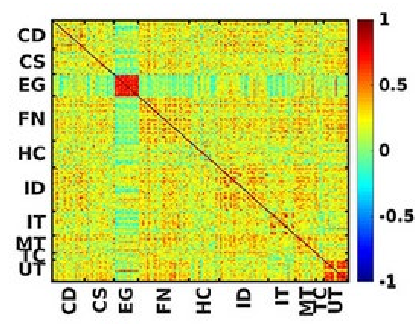
Functional connectivity

- Constructs **undirected** networks to represent **pairwise statistical relationships** between nodes
- Pros:
  - Easy and fast to implement and run (e.g. correlation)
  - Simple to interpret
  - Good at identifying network modules with community detection [1,2]





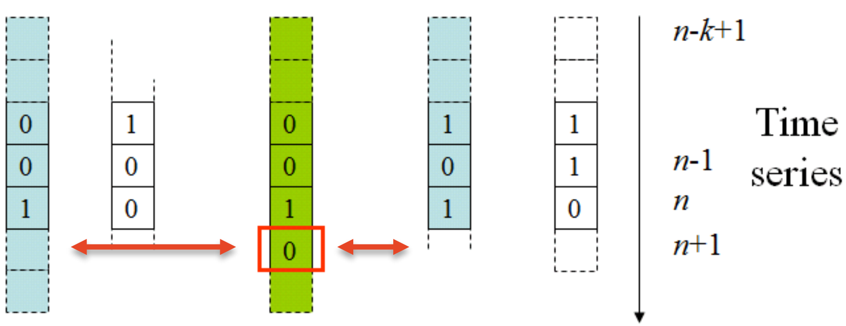
  - Sensitive to changes in the underlying dynamics
    - E.g. changes under conditions such as Alzheimer's disease [3]
    - Even if structure does not change

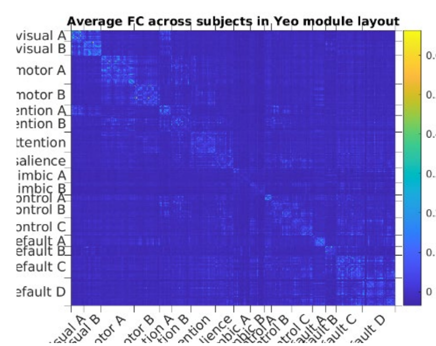
1. After: B. T. T. Yeo et al., J. Neurophys., 106(3), 1125, (2011)
2. Kukreti et al (2020) *Front. Phys.* 8:323. doi: 10.3389/fphy.2020.00323 (Figure used under CC BY)
3. J. A. Contreras et al., Neuroimage Clin., 22, 101687, (2019)

Functional connectivity: measures

– Correlation (Pearson)
  – $r_{xy} = \frac{\sum_{i=1}^{N}(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_{i=1}^{N}(x_i - \bar{x})^2 \sum_{i=1}^{N}(y_i - \bar{y})^2}}$
– Spearman correlation
– Mutual information
  – $I(X;Y) = \sum_{x,y} p(x,y) \log \frac{p(x|y)}{p(x)}$
  – Captures **non-linear** statistical relationships
    • More powerful, but requires more data

https://github.com/jlizier/jidt





Consideration 1: data preprocessing

- Important to:
  - remove noise / artifacts
  - "stationarise" the data
    - Better goal – ergodic:
      - Want comparable samples, and
      - Good sampling of the whole state space to estimate probabilities
- But it changes the question that you're asking, and may make investigating relationships more difficult.

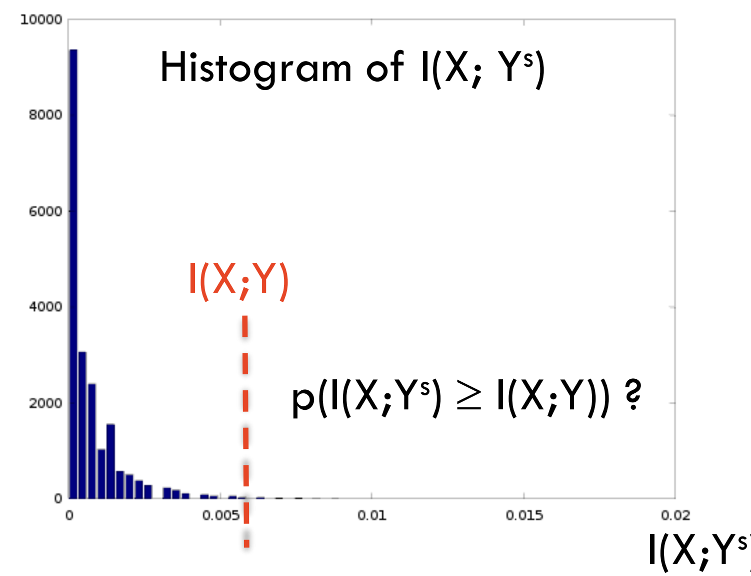
Examples:

- Brain fMRI BOLD recordings: detrending, band-pass filtering, global signal regression, deconvolution
- Equity prices in financial markets: log-differences

G.-R. Wu et al., Med. Image Anal., 17(3), 365, (2013).

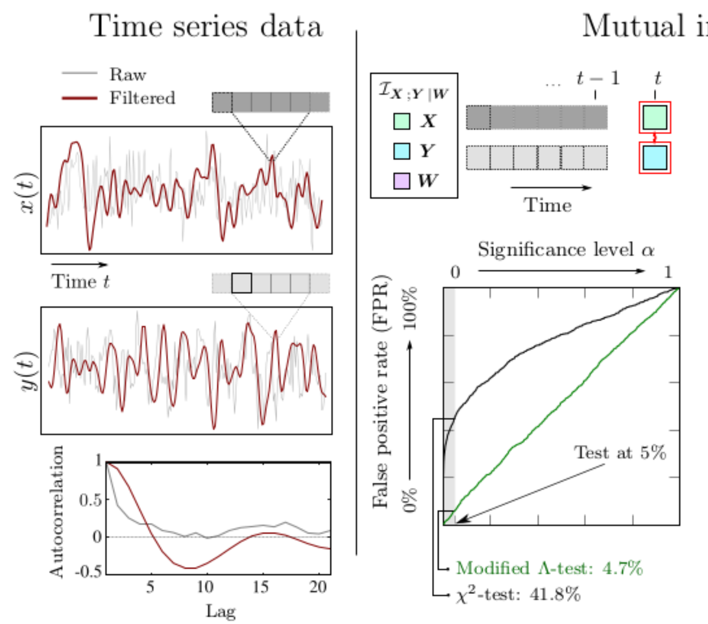
Consideration 2: thresholding / statistical significance

- Stay with raw values as edge weights, or:
  - Threshold edges in network (whether remaining weighted or not):
    - By raw value (how to choose?), or
    - Computing statistical significance against a threshold α
      - E.g. p-value of a correlation (as a function of N)
  - Bias correct the statistics
- Family-wise error-rate correction
  - Bonferroni correction
    - If making N(N-1) comparisons, correct $\alpha \rightarrow \alpha / N(N-1)$
- Enhance potential significance with:
  - Larger effects
  - More samples
  - Less nodes



Consideration 3: autocorrelated data

- Becomes very important for auto-correlated time-series:
  - Autocorrelation renders our samples non-independent
  - Which increases the variance of our estimates
  - Which can make more of them appear significant
  - Exacerbated by digital filtering!



- Handle via:
  - Correlation: compute the effective number of samples
    - https://github.com/olivercliff/exact-linear-dependence
  - MI (non-linear estimators): use dynamic correlation exclusion

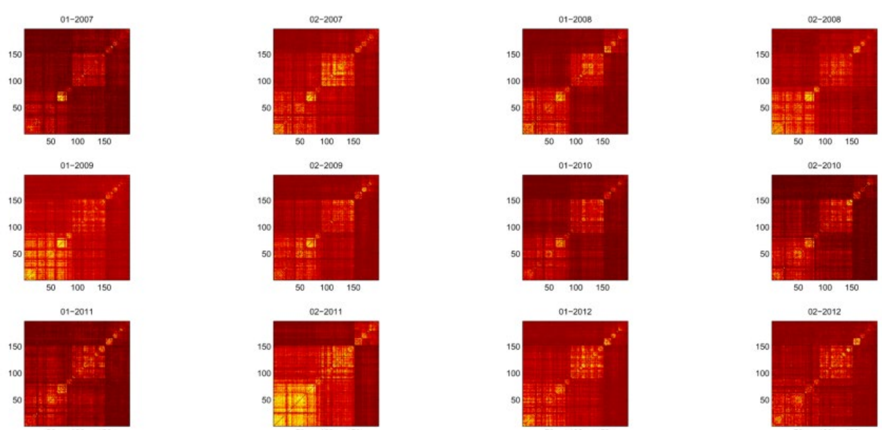
S. Afyouni, S. M. Smith, and T. E. Nichols, "Effective degrees of freedom of the Pearson's correlation coefficient under autocorrelation", NeuroImage 199, 609 (2019).

Cliff et al, "Assessing the significance of directed and multivariate measures of linear dependence between time series", *Physical Review Research*, 3, 013145 (2021)

Consideration 4: combining / splitting time series

- If you have multiple time series realisations (e.g. trials for different subjects in neuroscience experiments), can/should you:
  - Combine time-series into a single analysis
    - (assumes common statistics across them)
  - Run network analysis separately and combine for group level result

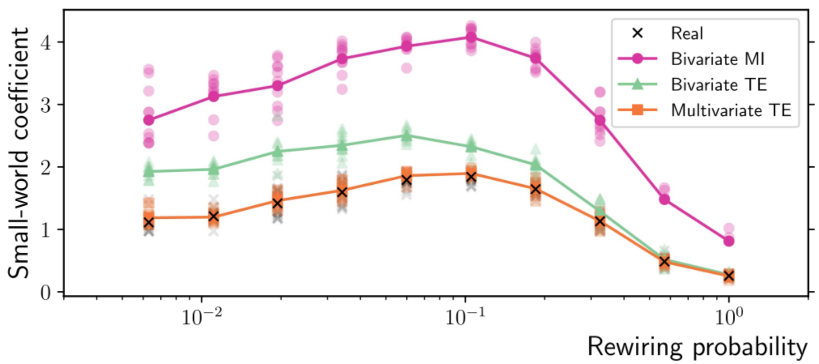
- If you have long and non-stationary time series (e.g. equities over decades), can/should you:
  - Run a single analysis, or partition into different periods?



L. Sandoval, "Structure of a Global Network of Financial Companies Based on Transfer Entropy," *Entropy*, vol. 16, no. 8, pp. 4443–4482, 2014.

Consideration 5: application of network measures?

- Be careful on interpreting network measures on FC networks:
  - Edges are not determined independently, and e.g. clustering is elevated
  - Tend to be a poor reflection of underlying structure and network measures on it
  - E.g. eigenvalues describe persistence of modes in how dynamics are forward propagated; what do eigenvalues of FC matrix mean?
  - Maybe consider network measures (pragmatically) to highlight different structure of statistical relationships in two conditions, but not interpret mechanistically



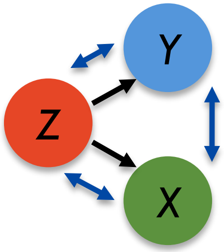
Novelli & Lizier, Inferring network properties from time series using transfer entropy and mutual information: Validation of multivariate versus bivariate approaches, *Network Neuroscience*, 5(2), 373–404. doi:10.1162/netn_a_00178

Langford, E., Schwertman, N., & Owens, M. (2001). Is the property of being positively correlated transitive? *The American Statistician*, 55(4), 322–325.

Zalesky, A., Fornito, A., & Bullmore, E. (2012). On the use of correlation as a measure of network connectivity. NeuroImage, 60(4), 2096–2106

Functional connectivity

- Constructs **undirected** networks to represent **pairwise statistical relationships** between nodes
- Pros: easy to implement, run and interpret, and sensitive
- Cons:
  - Do not describe directed relationships
  - Do not describe higher-order relationships
  - Do not model/explain how dynamics are generated
  - Need to limit interpretation of network measures



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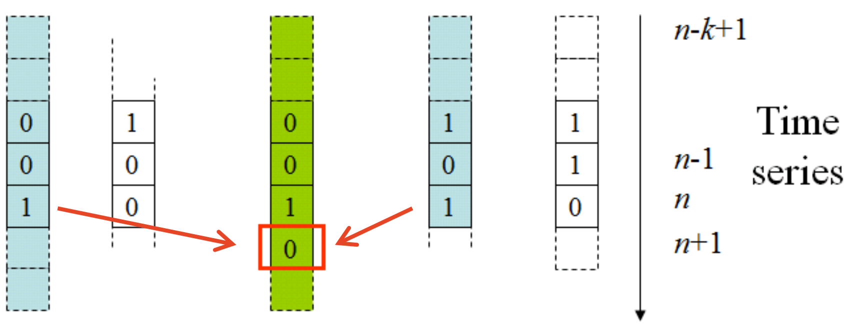
Directed functional connectivity

– Constructs **directed** networks to represent **pairwise statistical relationships** between nodes
– Pros: easy to implement, run and interpret , and sensitive
  – Describes directed relationships



Directed functional connectivity: measures

– Lagged correlation
– Lagged mutual information $I(X(n); Y(n+1))$

JIDT

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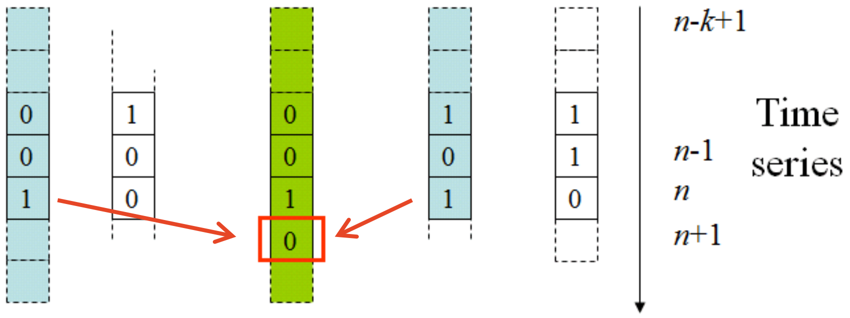

Directed functional connectivity: measures

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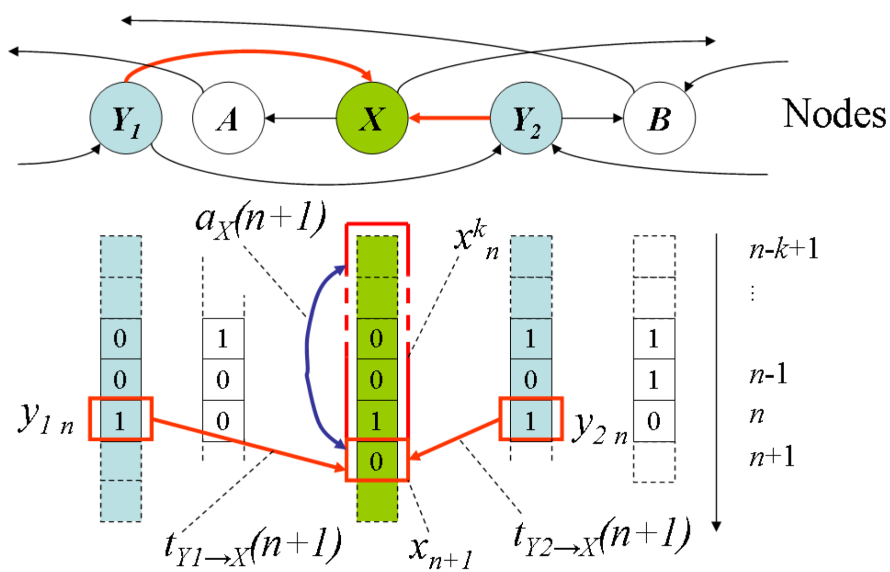
Dynamical systems models:

- Granger causality
- Transfer entropy $I(Y(n); X(n+1) \,|X(n)^{(k)}))$

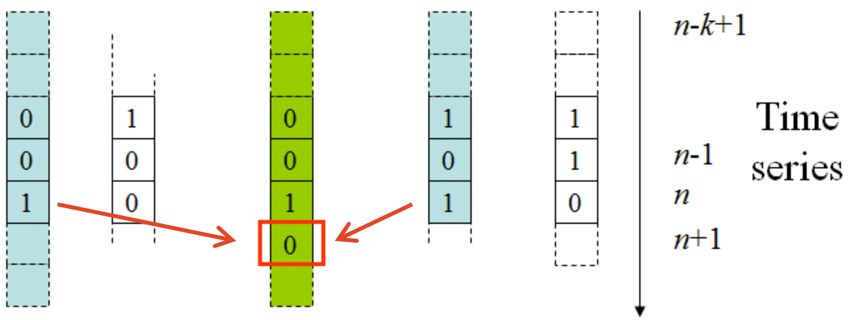


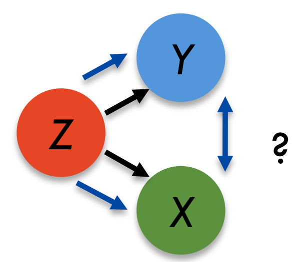
- How much information about the next observation X_n of process X can be found in observation Y_n of process Y, in the context of the past state $\boldsymbol{X}_n^{(k)} = \{X_{n-k+1}, \dots, X_{n-1}, X_n\}$?
- Or, in modelling the dynamics of the target, how much information transfer does the source add to that model (after already including target past)
- Directed and dynamic

T. Schreiber, "*Measuring Information Transfer*", Physical Review Letters, 85(2), pp. 461-4, 2000.
Bossomaier, Barnett, Harré, Lizier, "An Introduction to Transfer Entropy: Information Flow in Complex Systems", Springer, Cham, 2016

Directed functional connectivity

- Constructs **directed** networks to represent **pairwise statistical relationships** between nodes
- Pros: easy to implement, run and interpret , and sensitive
  - Describes directed relationships
- Cons:
  - Goes part of way to explain how dynamics are generated
  - Better interpretation of network measures
  - Do not describe higher-order relationships





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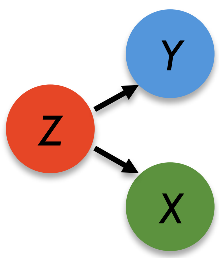
Directed functional connectivity

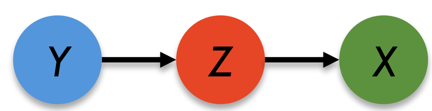
Pairwise approaches, even dynamic ones, do not describe multivariate or higher order relationships

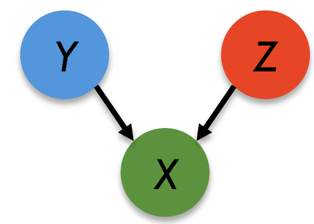
– Because they do not handle redundancies or synergies between sources.



Common driver

Pathway





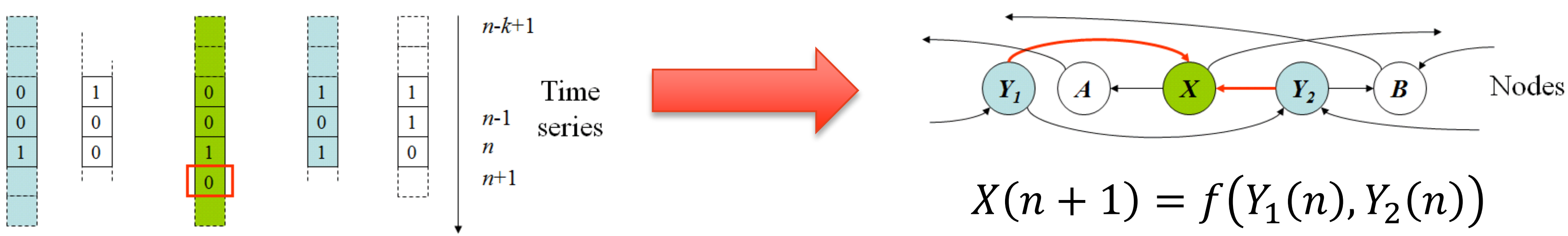
Synergy

Bossomaier, Barnett, Harré, Lizier, "An Introduction to Transfer Entropy: Information Flow in Complex Systems", Springer, Cham, 2016; section 7.2

Effective connectivity

Effective connectivity

- Constructs **directed** networks to provide a "*minimal neuronal circuit model*" [1] which can replicate and indeed explain the time series of the nodes
- Not strictly causal, but aims at providing best **generative model** possible from data.
- Pros:
  - Provides a (directed) generative model that **explains** the dynamics

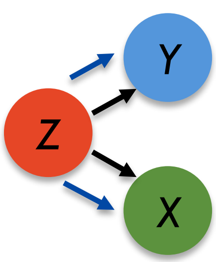


$$X(n+1) = f\big(Y_1(n), Y_2(n)\big)$$
$$Y_2(n+1) = g(Y_1(n), \dots)$$
$$etc.$$

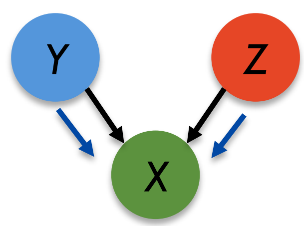
[1] K. J. Friston. Functional and effective connectivity in neuroimaging: A synthesis. *Human Brain Mapping*, 2(1-2):56–78, 1994.
[2] O. Sporns. *Networks of the Brain*. MIT Press, Cambridge, Massachusetts, USA, 2011

Effective connectivity

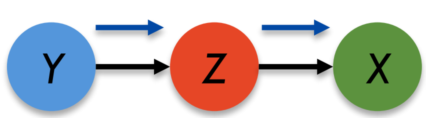
– Pros:
  – Provides a (directed) generative model that **explains** the dynamics
  – Inferring the **multivariate set** of parents that provide the best minimal model for dynamics of each target.
    - Higher order network inference!
  – Incorporates multivariate effects:
    - Removes redundancies, includes synergies



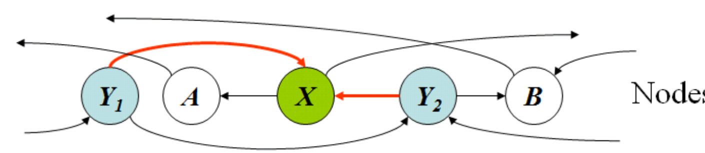
Common driver



Synergy



Pathway



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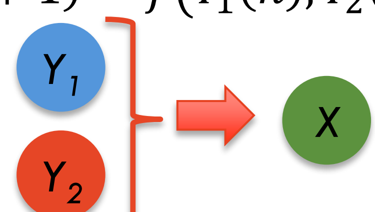

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J. T. Lizier and M. Rubinov. Techn Report Preprint 25/2012, Max Planck Institute for Mathematics in the Sciences, 2012.

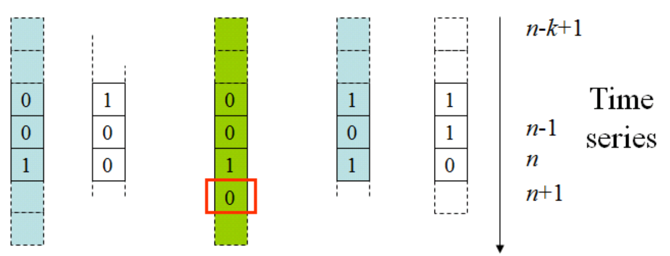
Effective connectivity

- Pros:
  - Provides a (directed) generative model that **explains** the dynamics
  - Inferring the **multivariate set** of parents that provide the best minimal model for dynamics of each target.
    - Higher order network inference!
  - Incorporates multivariate effects:
    - Removes redundancies, includes synergies
  - Like FC, sensitive to change in dynamics.
  - In principle (*more on this later*):
    - Leads to models faithful to underlying structure *
    - More sensible to apply network measures to EC than FC

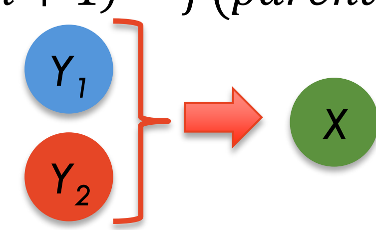
Novelli & Lizier, Inferring network properties from time series using transfer entropy and mutual information: Validation of multivariate versus bivariate approaches, *Network Neuroscience*, 5(2), 373–404. doi:10.1162/netn_a_00178

Effective connectivity: approaches (general)

- Inferring the **multivariate set** of parents that provide the best minimal model for dynamics of each target
- Goal, in language of *dynamic Bayesian networks*: given data *D*, maximise posterior probability of network model *G*: *p(G |D)*
- Bayesian inversion to consider:
  - $p(G|D) \propto p(D|G)p(G)$
  - *p*(*G*) Encodes any constraints / priors on the network (can make it model based)
  - Problem becomes computing likelihood of data given network model
  - For any given target X, this means maximising *p()* given constraints of network model *p*(*G*), and model of dynamics *f* which informs how we evaluate *p(X(n+1)|parents(n))*



$$X(n+1) = f\big(parents(n)\big)$$

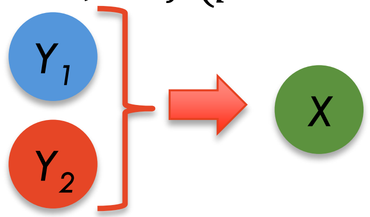


O.M. Cliff et al., An Information Criterion for Inferring Coupling of Distributed Dynamical Systems. Frontiers in Robotics & AI, 3, 71, (2016).
L. Barnett et al., Transfer Entropy as a Log-Likelihood Ratio. Physical Review Letters, 109, 138105, (2012).

Model-based vs model-free approaches

- For any given target X, this means maximising *p()* given constraints of network model *p(G)*, and model of dynamics *f* which informs how we evaluate $p(X(n+1)\,|\,parents(n))$
- "Model-based" may mean placing constraints on:
  - Network structure, e.g.:
    - Biologically feasible brain structures
    - Stochastic block models
  - Dynamics, e.g.:
    - Linear dynamics
    - Biologically realistic models

$$X(n+1) = f\big(parents(n)\big)$$



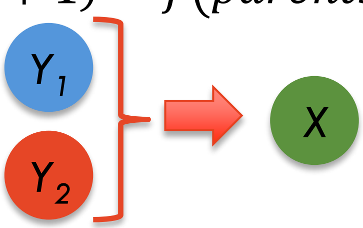
- Model-based approaches are:
  - Faster runtime (particularly linear)
  - More efficient *if* the model is correct
  - Specific to model domain

- Model-free approaches are:
  - Slower runtime
  - Less efficient (more data hungry)
  - Generalisable outside domain and applicable if model unknown

Model likelihood

- For any given target X, this means maximising *p()* given constraints of network model *p(G)*, and model of dynamics *f* which informs how we evaluate $p(X(n+1) \mid parents(n))$
- Evaluating $p(G \mid D)$ may be via
  - log-likelihood log $p(G \mid D)$, or
  - prediction error
- Returning to consideration 2 (statistical significance):
  - Score may include penalty for model complexity (number of parents):
    - explicitly (AIC/BIC style) or
    - implicitly (statistical significant test being harder to pass for multivariate models)
  - Should use family-wise error correction if selecting between many models

$$X(n+1) = f\big(parents(n)\big)$$



Approach 1: Least squares regression

– Model for dynamics: Linear vector autoregressive dynamics (VAR) with temporally uncorrelated Gaussian noise:

$$\underline{x}(n+1) = C\underline{x}(n) + \underline{r}(n)$$

– Compute lagged covariance matrices from time-series samples:

$$\Omega_\tau = \left\langle \underline{x}(n+\tau)\underline{x}(n)^T \right\rangle$$

– Infer [1]:

$$\hat{C} = \Omega_1 \Omega_0^{-1}$$

– Very fast; assumes linearity.

– Various extensions, e.g. for optimisation approaches for continuous time dynamics [2,3], or via SVD

– Questions: statistical significance / autocorrelation handling?

[1] P.-Y. Lai, Reconstructing network topology and coupling strengths in directed networks of discrete-time dynamics, Physical Review E, vol. 95, no. 2, 2017.
[2] M. Gilson et al., Estimation of Directed Effective Connectivity from fMRI Functional Connectivity Hints at Asymmetries of Cortical Connectome, PLOS CB, vol. 12, no. 3, e1004762, 2016
[3] R. F. Galán, "On How Network Architecture Determines the Dominant Patterns of Spontaneous Neural Activity, PLOS ONE, vol. 3, no. 5, e2148, 2008

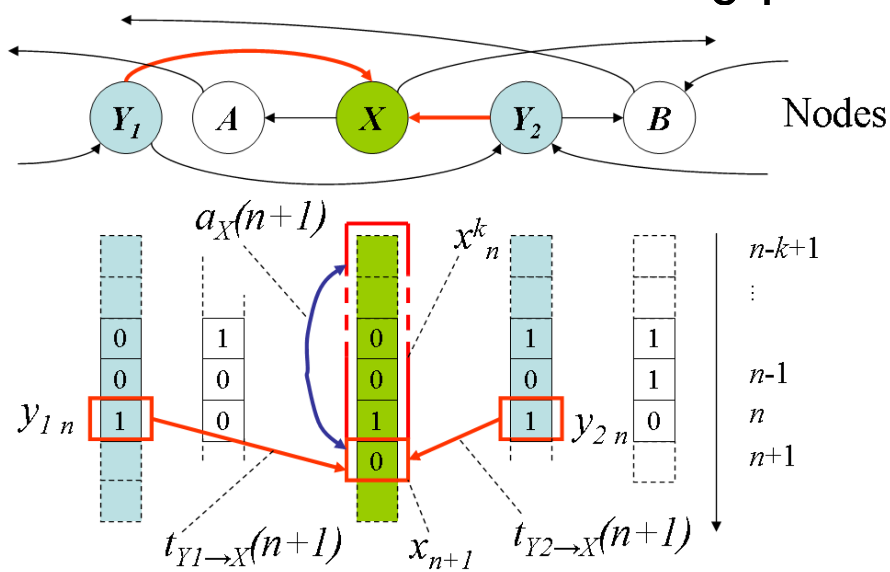
Approach 2: Dynamic causal modelling (DCM)

- Designed for brain imaging data but general framework may be extended
- Computes log probabilities by combining:
  - Biologically realistic dynamics and mapping to imaging for $p(D|G)$, with
  - Biological constraints on connectivity $p(G)$
- Model comparison focus then:
  - Compares log-likeihoods of models in an exhaustive search
    - Causes an issue for scaling number of nodes but are enhancements, e.g. [3]

[1] K. J. Friston. Functional and effective connectivity in neuroimaging: A synthesis. *Human Brain Mapping*, 2(1-2):56–78, 1994.
[2] K. J. Friston et al., Dynamic causal modelling, NeuroImage, 19(4), 1273, (2003).
[3] A. Razi et al., Large-scale DCMs for resting-state fMRI, Net. Neurosci., 1(3), 222, (2017)

Approach 3: Multivariate transfer entropy

- Maximise transfer from **set** of sources $I(\underline{Y}(n); X(n+1) | X(n)^{(k)})$
- Uses log probabilities of $p(D|G)$ behind the scences
  - Equivalently Bayesian [3], but
  - Model-free in terms of dynamics and network structure
- Would still have a scaling problem if exhaustive search

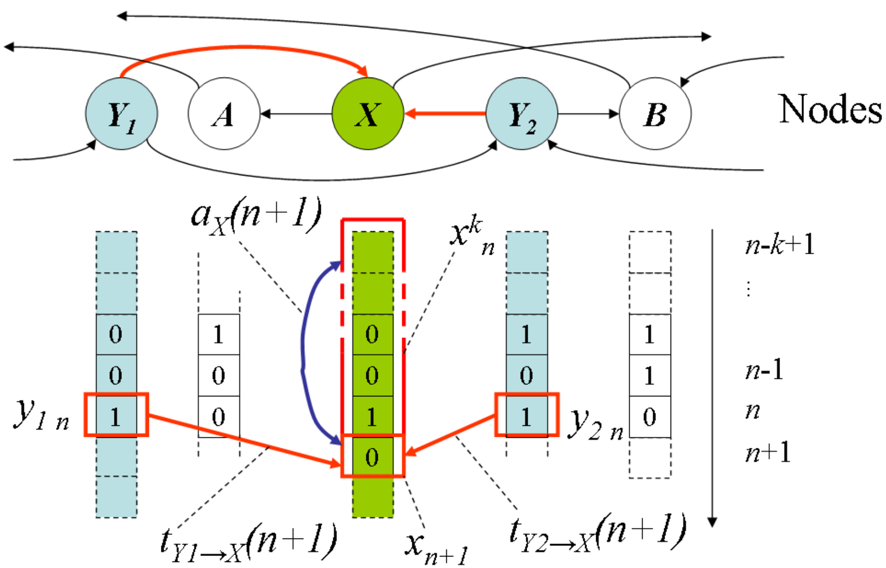


- And difficult to conclude on statistical significance of difference between models.

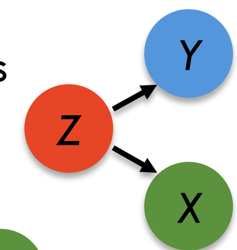
[1] J. T. Lizier and M. Rubinov. Techn Report Preprint 25/2012, Max Planck Institute for Mathematics in the Sciences, 2012.
[2] Bossomaier, Barnett, Harré, Lizier, "An Introduction to Transfer Entropy", Springer, Cham, 2016; section 7.2
[3] O.M. Cliff et al., An Information Criterion for Inferring Coupling of Distributed Dynamical Systems. Frontiers in Robotics & AI, 3, 71, (2016).

Conditional Transfer entropy

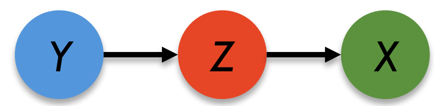
- $I(Y\ (n); X(n+1)\ |X(n)^{(k))}, \underline{Z}(n))$
- Building a model: Marginal benefit (log probability) of adding *Y* into the parent set **Z**.



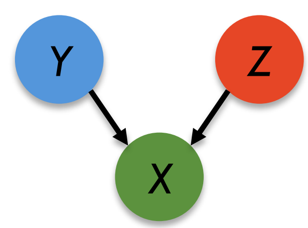
- Removes redundancies between Y and Z, e.g.
  - Common driver effects



  - Pathway effects



- Includes synergies between Y and Z, e.g.
  - Gated effects

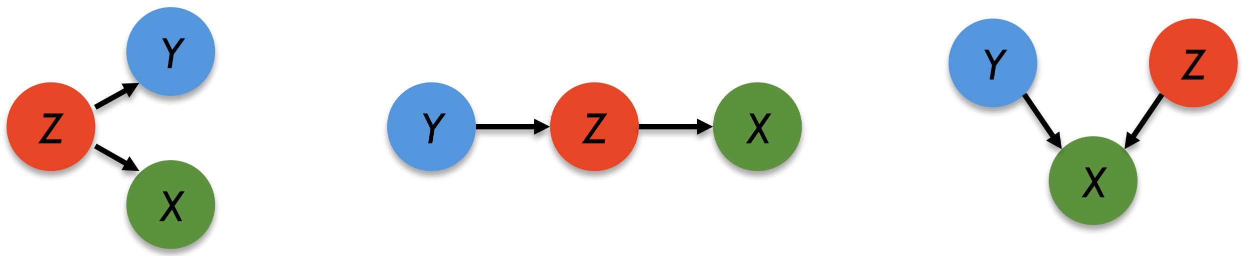


J. T. Lizier, M. Prokopenko, & A. Y. Zomaya. "*Local information transfer as a spatiotemporal filter for complex systems*". Physical Review E, 77(2):026110, 2008.
J. T. Lizier, M. Prokopenko, & A. Y. Zomaya. "*Information modification and particle collisions in distributed computation*", Chaos, 20(3), 037109, 2010.

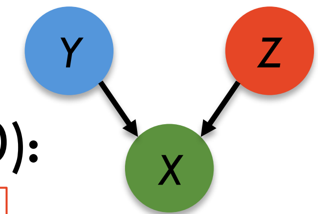
Approach 3: Multivariate transfer entropy

- Hinted that conditional TE:
  - Computes marginal benefit of adding another parent to the model
  - Address redundancy and synergy

- But what to condition on …? And how to use it?
  - If we condition on all other variables:
    - We can undersample too easily
    - We can eliminate too many links from our model
- Key: we're going to iteratively build a parent set…



Approach 3: Multivariate information regression



- Modelling the information processing in X.
- Consider two sources to X. (General case in Lizier 2010):

Real goal here: to infer this parent set $\{Y, Z\}$ for X

$$H(X_{n+1}) = I\left(\boldsymbol{X}_n^{(k)}; X_{n+1}\right) + I\left(Y_n, Z_n; X_{n+1} \middle| \boldsymbol{X}_n^{(k)}\right) + H\left(X_{n+1} \middle| \boldsymbol{X}_n^{(k)}, Y_n, Z_n\right)$$

$$H(X_{n+1}) = I\left(\boldsymbol{X}_n^{(k)}; X_{n+1}\right) + I\left(Y_n; X_{n+1} \middle| \boldsymbol{X}_n^{(k)}\right) + I\left(Z_n; X_{n+1} \middle| \boldsymbol{X}_n^{(k)}, Y_n\right) + H\left(X_{n+1} \middle| \boldsymbol{X}_n^{(k)}, Y_n, Z_n\right)$$

$$H(X_{n+1}) = I\left(\boldsymbol{X}_n^{(k)}; X_{n+1}\right) + I\left(Z_n; X_{n+1} \middle| \boldsymbol{X}_n^{(k)}\right) + I\left(Y_n; X_{n+1} \middle| \boldsymbol{X}_n^{(k)}, Z_n\right) + H\left(X_{n+1} \middle| \boldsymbol{X}_n^{(k)}, Y_n, Z_n\right)$$

1. Active information storage

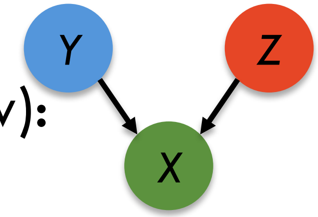
2-. Multivariate transfer entropy

2. Pairwise/apparent transfer entropy

3+. Conditional transfer entropy

J. T. Lizier, M. Prokopenko, & A. Y. Zomaya. "*Local information transfer as a spatiotemporal filter for complex systems*". Physical Review E, 77(2):026110, 2008.
J. T. Lizier, M. Prokopenko, & A. Y. Zomaya. "*Information modification and particle collisions in distributed computation*", Chaos, 20(3), 037109, 2010.

Approach 3: Iterative/greedy information regression



– Maths for two sources to X. (General case in refs below):

Real goal: to infer this parent set $\{Y, Z\}$ for X

$$H(X_{n+1}) = I\left(\boldsymbol{X}_n^{(k)}; X_{n+1}\right) + \boxed{I\left(Y_n, Z_n; X_{n+1} \middle| \boldsymbol{X}_n^{(k)}\right)} + H\left(X_{n+1} \middle| \boldsymbol{X}_n^{(k)}, Y_n, Z_n\right)$$

– Inferring whole parent set at once is combinatorially difficult.

– Instead, infer parent set one by one in a greedy fashion:

1. Start with empty parent set P
2. Evaluate TE from each source to target, conditioning on P.
3. Add the source with max conditional TE to P if p-value is statistically significant.
4. Go back to step 2 if a new parent was added, else terminate.

$$H(X_{n+1}) = I\left(\boldsymbol{X}_n^{(k)}; X_{n+1}\right) + I\left(Y_n; X_{n+1} \middle| \boldsymbol{X}_n^{(k)}\right) + I\left(Z_n; X_{n+1} \middle| \boldsymbol{X}_n^{(k)}, Y_n\right) + H\left(X_{n+1} \middle| \boldsymbol{X}_n^{(k)}, Y_n, Z_n\right)$$

$$H(X_{n+1}) = I\left(\boldsymbol{X}_n^{(k)}; X_{n+1}\right) + I\left(Z_n; X_{n+1} \middle| \boldsymbol{X}_n^{(k)}\right) + H\left(X_{n+1} \middle| \boldsymbol{X}_n^{(k)} \quad Z_n\right)$$

Synthesis: **L. Novelli et al, "Large-scale directed network inference with multivariate transfer entropy …," *Network Neuroscience*, 3(3), 827–847, 2019.**

J. T. Lizier and M. Rubinov. Technical Report Preprint 25/2012, Max Planck Institute for Mathematics in the Sciences, 2012.

L. Faes, G. Nollo, and A. Porta, "Information-based detection of nonlinear Granger causality …," Physical Review E, 83, 051112, 2011

J. Sun, D. Taylor, E.M. Bollt, Causal network inference by optimal causation entropy. SIAM Journal on Applied Dynamical Systems, 14(1), 73–106, 2015

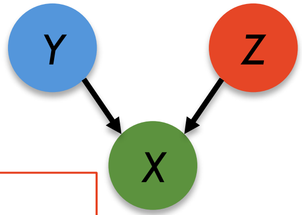
I. Vlachos and D. Kugiumtzis, "Nonuniform state-space reconstruction and coupling detection", Physical Review E, 82, 016207, 2010

J. Runge, et al, "Escaping the curse of dimensionality in estimating multivariate transfer entropy. *Physical Review Letters*, 108(25), 258701, 2012

A. Montalto, L. Faes, D. Marinazzo, MuTE: A MATLAB toolbox to compare established and novel estimators of the multivariate TE. PLoS ONE, 9(10), e109462, 2014

T. Bossomaier, L. Barnett, M. Harré, J. Lizier, "An Introduction to Transfer Entropy: Information Flow in Complex Systems", Springer, Cham, 2016; section 7.2

Approach 3: Multivariate transfer entropy



- Instead, infer parents one by one in a greedy fashion:
  0. Embed target past
  1. Start with empty parent set *P*
  2. Evaluate TE from each source to target, conditioning on *P*.
  3. Add the source with max cond. TE to *P* if p-value is statistically significant.
  4. Go back to step 2 if a new parent was added, else go to step 5.
  5. Prune redundant links in context of final set *P*.
  6. Perform statistical test of whole parent set *P*.

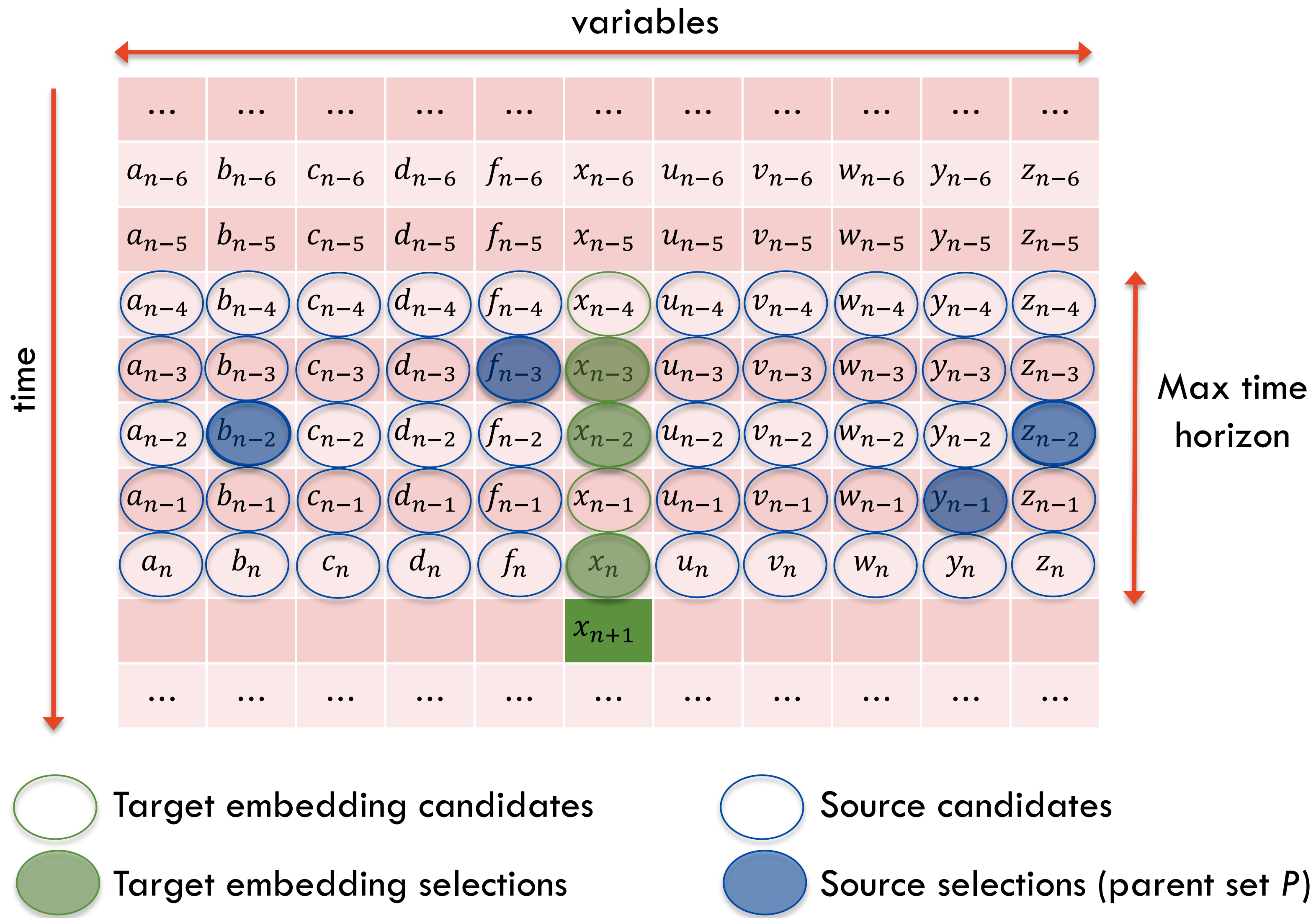
$$H(X_{n+1}) = I\left(\boldsymbol{X}_n^{(k)}; X_{n+1}\right) + I\left(Y_n, Z_n; X_{n+1} \middle| \boldsymbol{X}_n^{(k)}\right) + H\left(X_{n+1} \middle| \boldsymbol{X}_n^{(k)}, Y_n, Z_n\right)$$

- More efficient than brute force search for parent set.
- Handles redundancies and synergies between parents.
- Could scan for multiple samples from each source (non-uniform embedding)
- Statistical tests provide "automatic brake" when statistical power of data is exhausted.
- Can add additional tests.
- Must control for multiple comparisons (e.g. max statistics)
- End result is the parent set. Order that nodes were inferred in is no longer relevant.

L. Novelli et al, "Large-scale directed network inference with multivariate transfer entropy and hierarchical statistical testing," *Network Neuroscience*, 3(3), 827–847, 2019.
P. Wollstadt, J.T. Lizier, R. Vicente, C. Finn, M. Martinez-Zarzuela, P. Mediano, L. Novelli and M. Wibral, "IDTxl: The Information Dynamics Toolkit xl: a Python package for the efficient analysis of multivariate information dynamics in networks", *Journal of Open Source Software*, 4(34), 1081, 2019

Iterative/greedy approaches

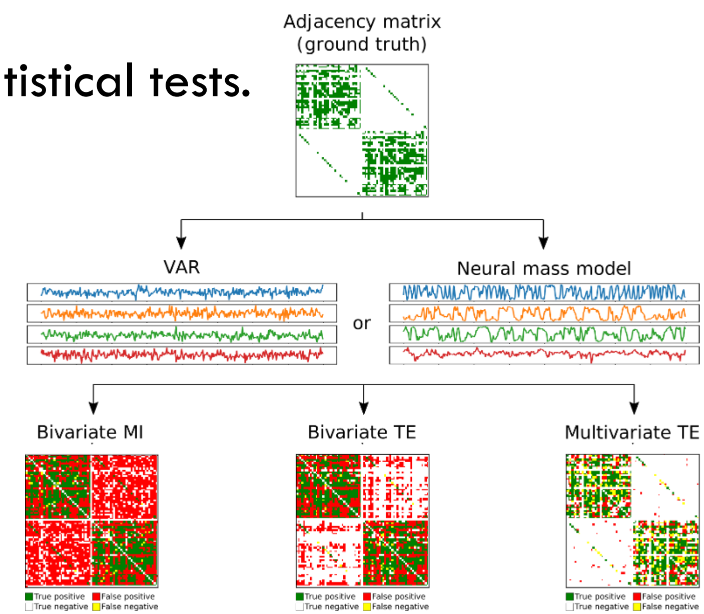
- Instead, infer parents one by one in a greedy fashion:
  0. Embed target past
  1. Start with empty parent set *P*
  2. Evaluate TE from each source to target, conditioning on *P*.
  3. Add the source with max cond. TE to *P* if p-value is statistically significant.
  4. Go back to step 2 if a new parent was added, else go to step 5.
  5. Prune redundant links in context of final set *P*.
  6. Perform statistical test of whole parent set *P*.



Using iterative/greedy approaches

https://github.com/pwollstadt/IDTxl

- IDTxl (which uses JIDT as an internal information-theoretic engine) implements the greedy algorithm, including:
  - "Max statistics" for multiple comparison correction in parent selection;
  - Handles TE parameter selection, non-uniform embedding / delay selection of sources;
  - Adds additional steps (pruning step) and statistical tests.
- Validation studies confirm convergence to structure under idealised conditions

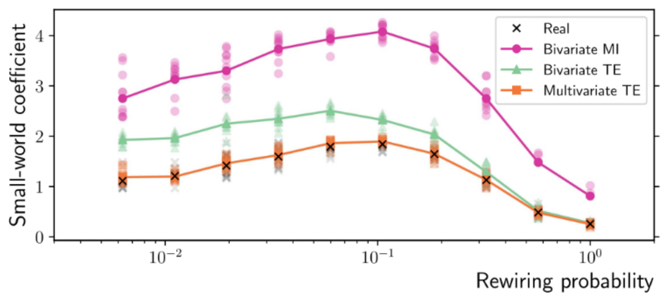


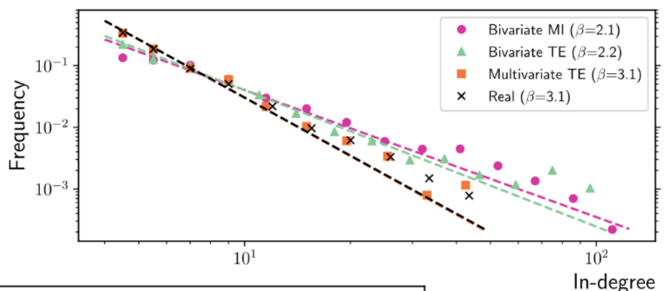
P. Wollstadt, et al, "IDTxl: The Information Dynamics Toolkit xl…", *Journal of Open Source Software*, 4(34), 1081, 2019
L. Novelli et al, "Large-scale directed network inference with multivariate transfer …," *Network Neuroscience*, 3(3), 827–847, 2019.
L. Novelli and J. T. Lizier, "Inferring network properties from time series using TE and MI: …," *Network Neuroscience*, 5(2), 373–404, 2021
D. Shortem et al, "Inferring effective networks of spiking neurons using a continuous-time estimator of transfer entropy", bioRxiv:2024.09.22.614302, 2024

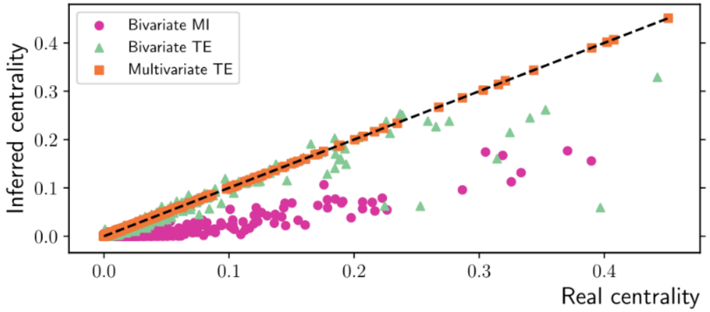
Effective connectivity

Pros (continuing from earlier)

- Leads to models faithful to underlying structure:
  - Without hidden nodes
  - With exploration of whole state space
- More sensible to apply network measures to EC than FC







Novelli & Lizier, Inferring network properties from time series using transfer entropy and mutual information: Validation of multivariate versus bivariate approaches, *Network Neuroscience*, 5(2), 373–404. doi:10.1162/netn_a_00178

Effective connectivity

Cons:

- Data requirements
  - Pairwise methods may be more useful in low data situations?
- Runtime and scaling
- Convergence to underlying structure? *(do we always really want this anyway?)*
  - Depends on hidden nodes
  - Data exploring full space?

Network inference from time-series data: summary

1. Understand **philosophy** of different goals in network inference from time-series data:
   – Functional, effective and structural connectivity
2. Understand **measures and approaches** (and how to access them)
   – Model-based and model-free measures
   – Linear and information-theoretic families
   – Pairwise and multivariate (and algorithms serving the latter)
3. Understand key **considerations** to incorporate
   1. Data pre-processing
   2. Thresholding / statistical significance
   3. Handling autocorrelation
   4. Combining / splitting realisations
   5. Applying network measures

Questions