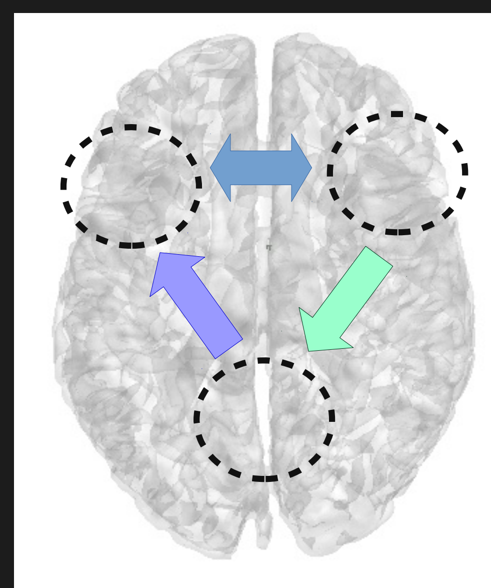
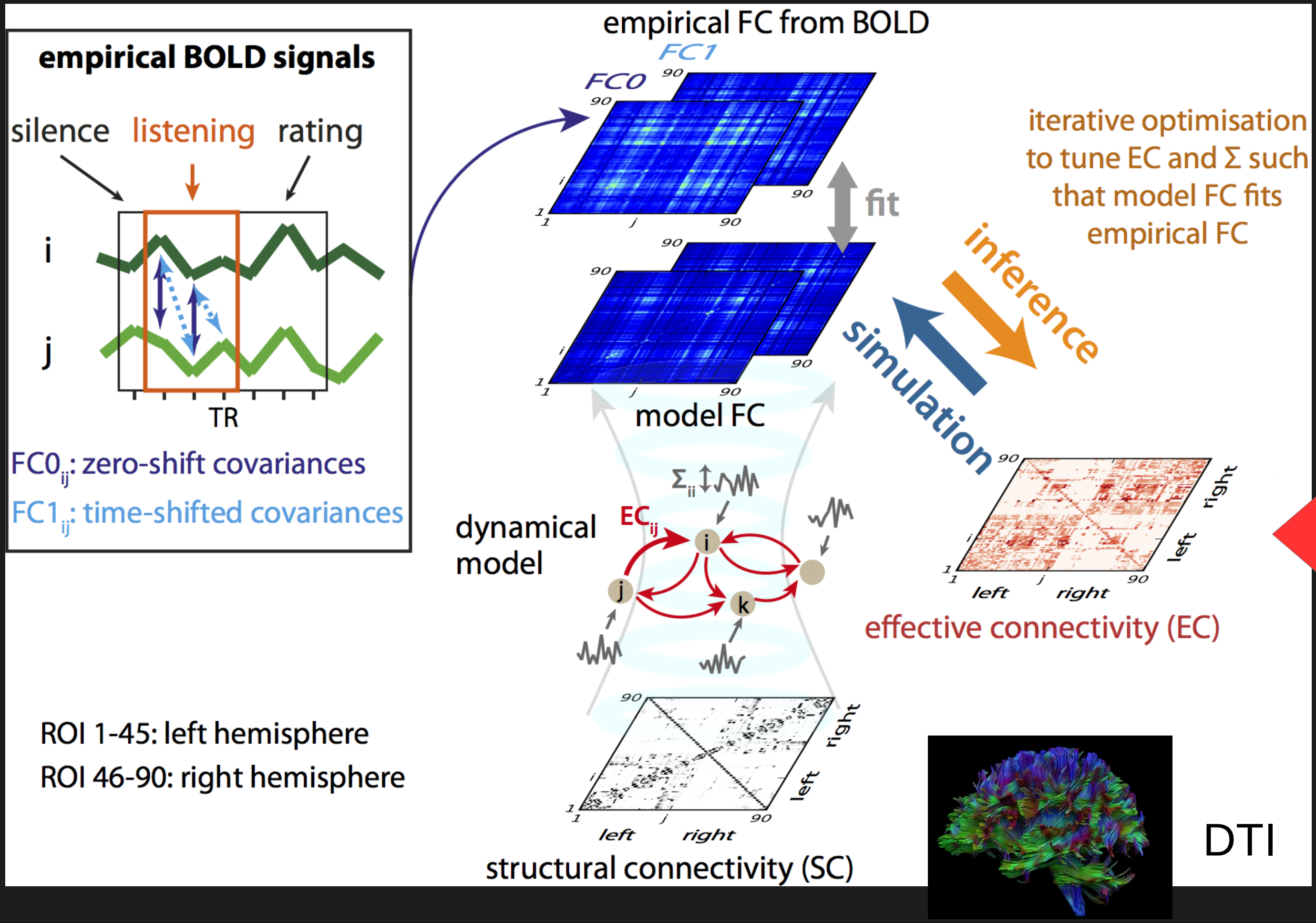
Estimation of effective dynamics and network analysis from whole-brain fMRI data

M Gilson, A Tauste Campo, G Zamora-López, N Kouvaris, G Deco

Universitat Pompeu Fabra (Barcelona, Spain)



Analysis of whole-brain effective connectivity

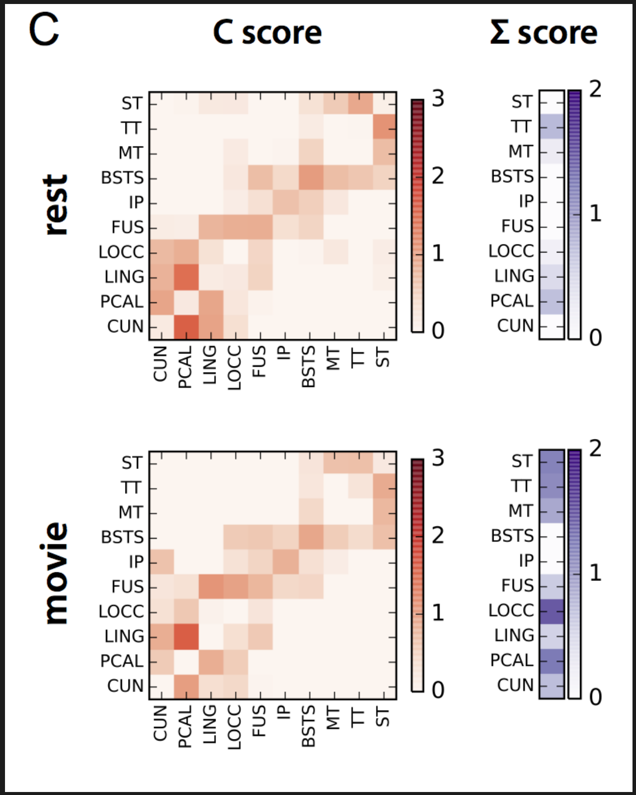


Effective connectivity ~ signature of brain dynamics
(related to transitions of BOLD activity between ROIs)

Analysis of whole-brain effective connectivity

Matrix of effective connectivity:

- Changes across conditions



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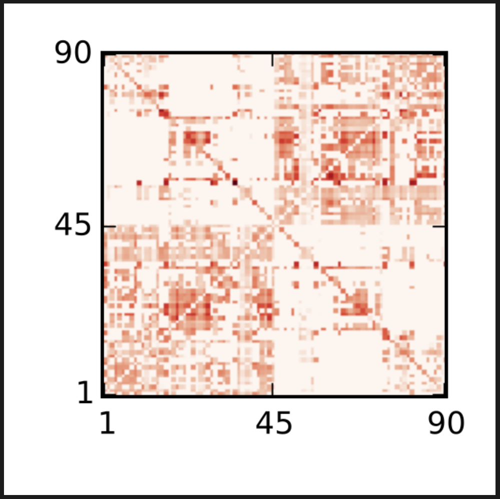
Analysis of whole-brain effective connectivity

Matrix of effective connectivity:

- Changes across conditions
- Important and strong links



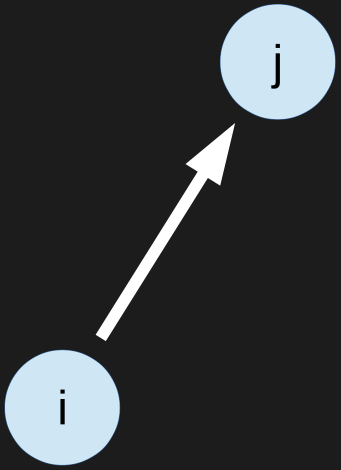
Weight significantly different from 0

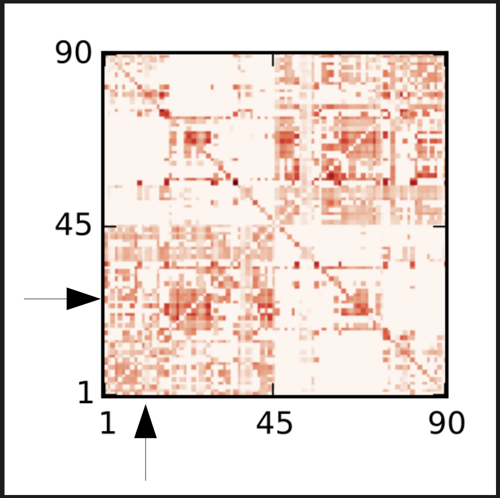
~ Granger causality analysis

Analysis of whole-brain effective connectivity

Matrix of effective connectivity:

- Changes across conditions
- Important and strong links
- Network effect





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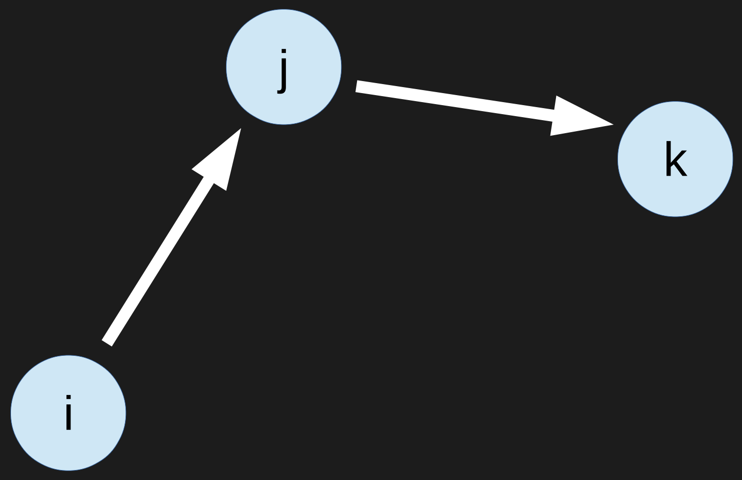

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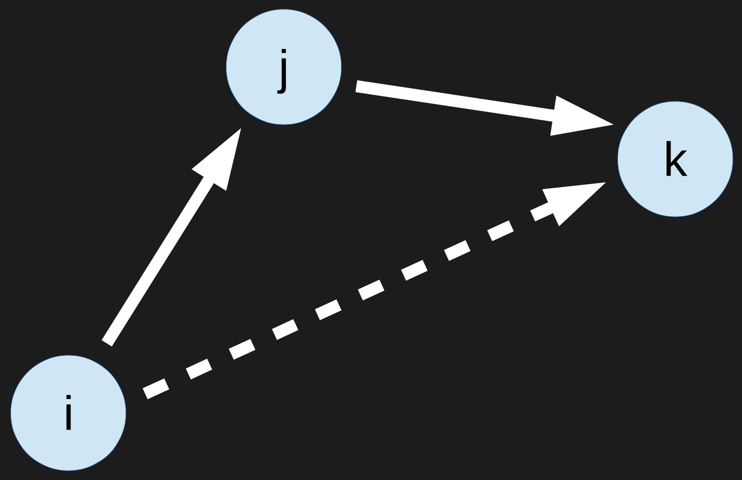

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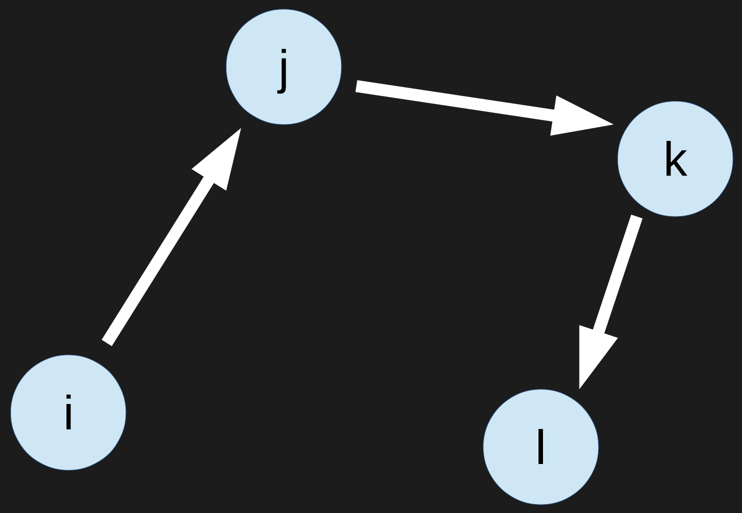

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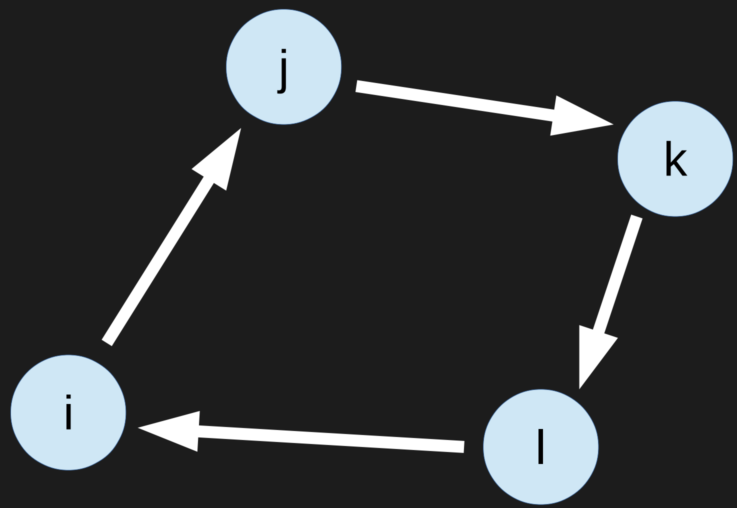

Analysis of whole-brain effective connectivity

Matrix of effective connectivity:

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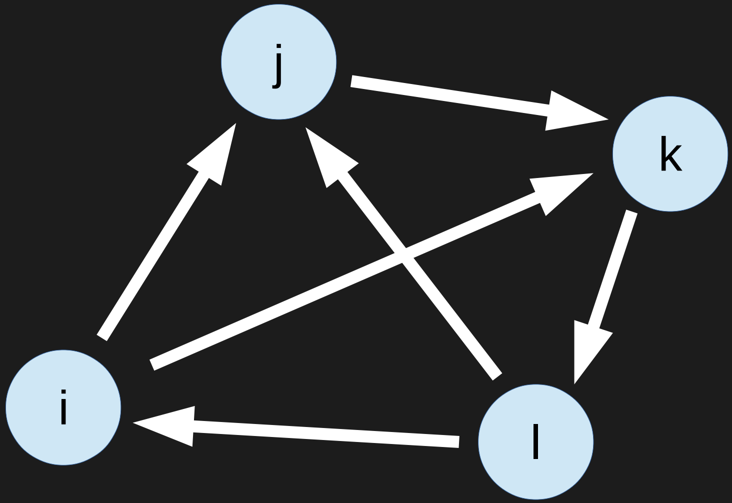
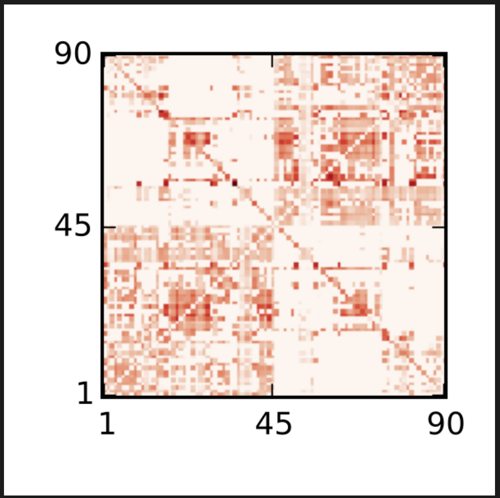
How to make sense of the multiple superposed paths for the network dynamics?





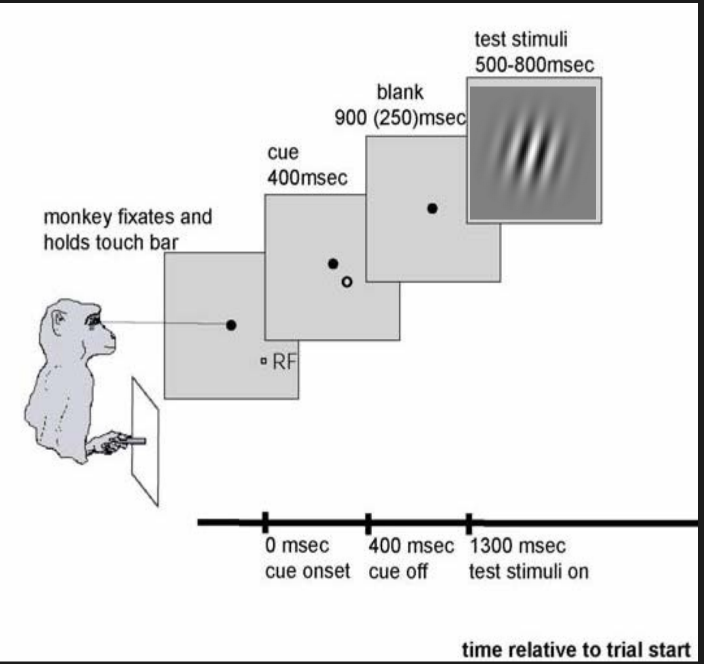
Outline

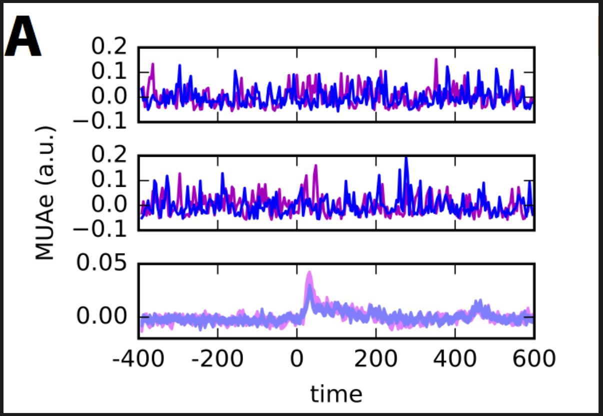
- Non-parametric method to evaluate significance of estimated weights
  - multivariate autoregressive process (discrete time)
  - www.biorxiv.org/content/early/2017/06/26/100669

- Communicability to quantify network effect
  - multivariate Ornstein-Uhlenbeck process (continuous time)

How to detect significantly strong interactions?

- Estimated connectivity from multiunit activity from UTAH electrode array (in monkey V1) from Alex Thiele (U Newcastle)
- Visual stimulus in a bottom-up attention task





trial #1

trial #2

average over 200 trials

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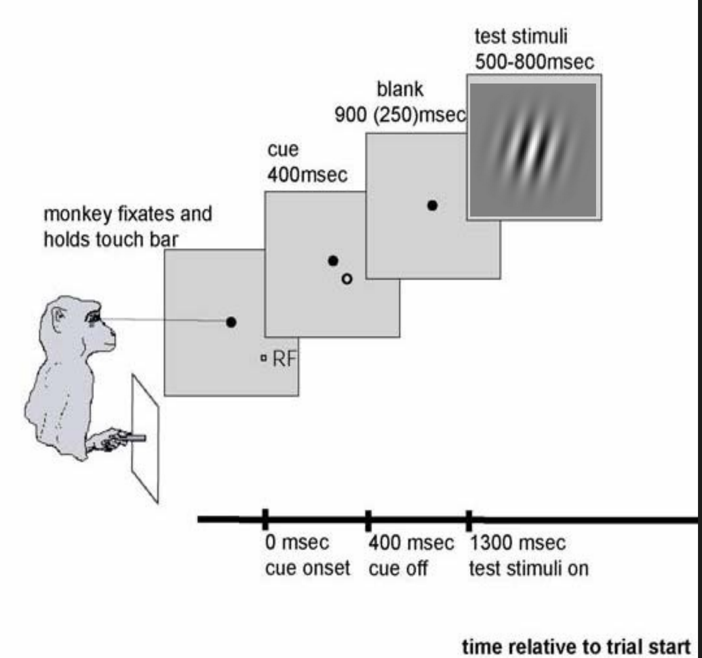

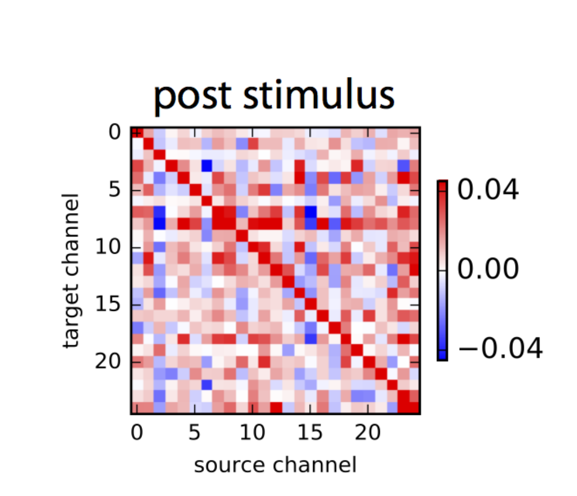

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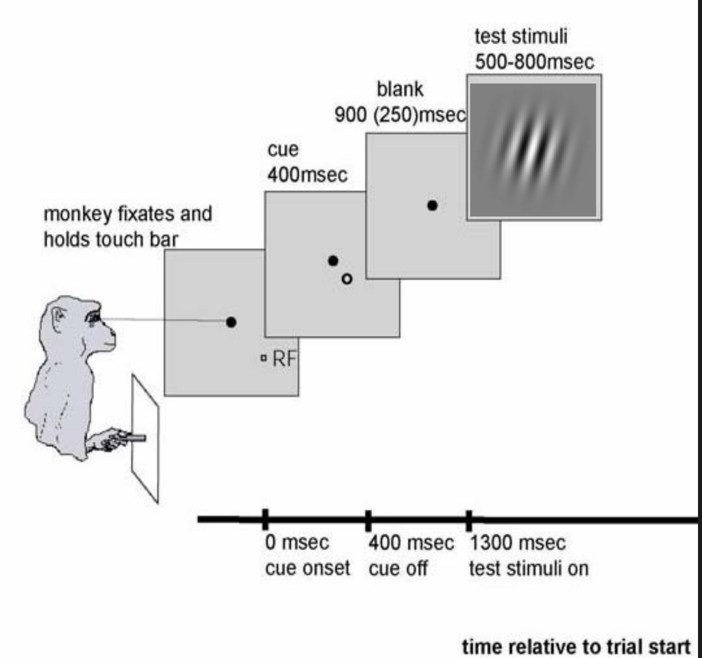

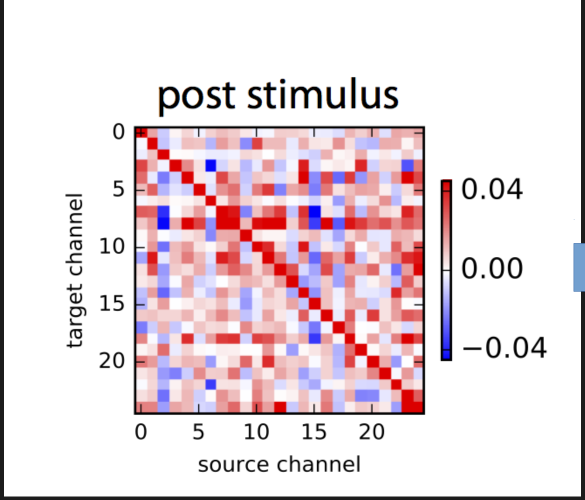

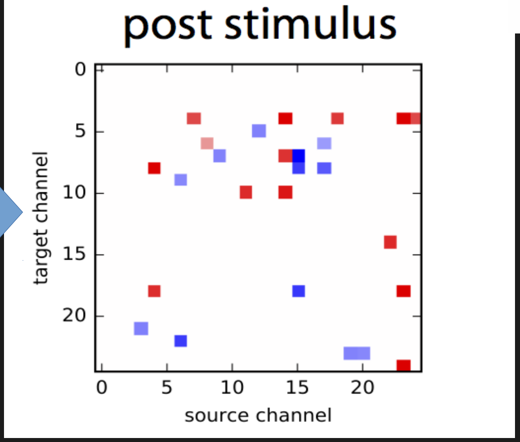

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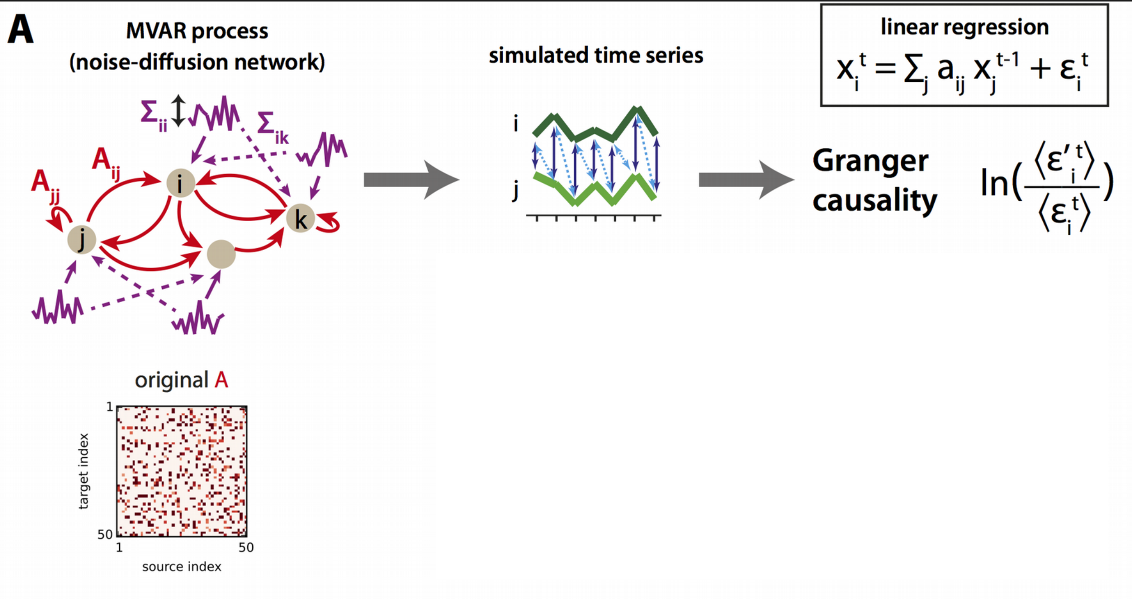
Theoretical study with synthetic networks



Generative model: multivariate autoregressive model (linear feedback with discrete time)

$$x^t = Ax^{t-1} + \zeta^t \ ,$$

Parametric testing for Granger causality analysis

Autoregression from observed time series

$$x_i^t = \sum_{j \in \mathcal{S}} A_{ij} x_j^{t-1} + \epsilon^t$$

Residual noise

$$\epsilon\left(x_i^{2 \le t \le T} | x_i^{1 \le t \le T-1}\right) = \sqrt{\sum_t (\epsilon^t)^2}$$

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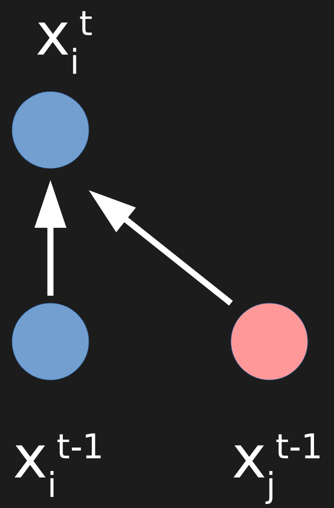
Log ratio

$$\mathrm{GRu}(x_j \to x_i) \quad = \quad \ln\left[\frac{\epsilon\left(x_i^{2 \le t \le T} | x_i^{1 \le t \le T-1}\right)}{\epsilon\left(x_i^{2 \le t \le T} | x_{i,j}^{1 \le t \le T-1}\right)}\right];$$

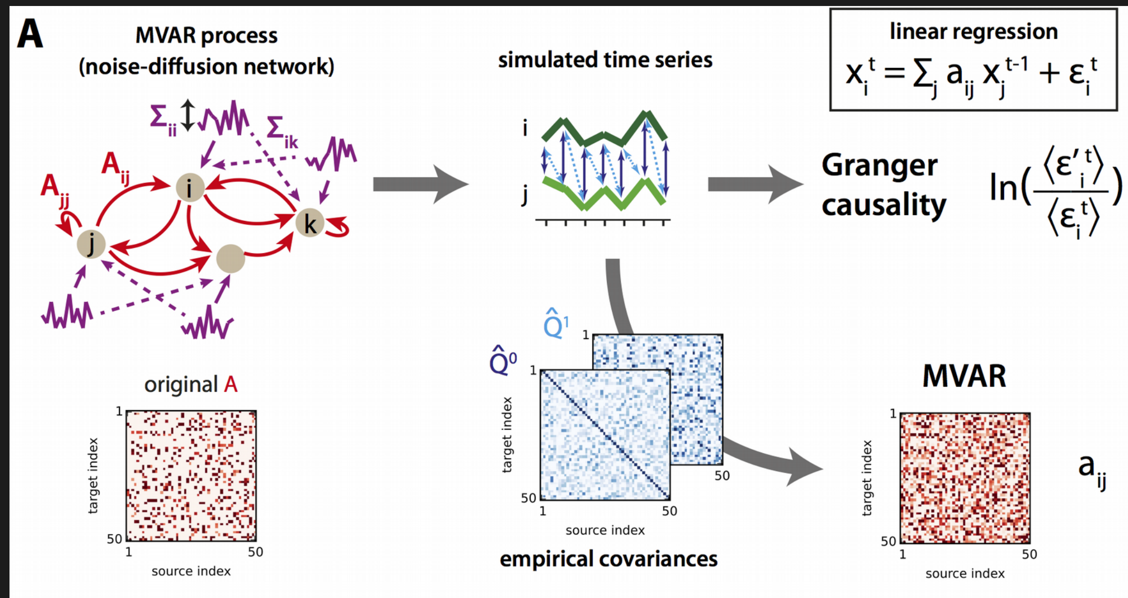
F test for significance (T samples)

$$[\exp(\mathrm{GRu}_{ij}) - 1] > \frac{\phi(\alpha, 1, T-3)}{T-3}$$

Is x_j useful to predict x_i?



Non-parametric test for estimated MVAR coefs?



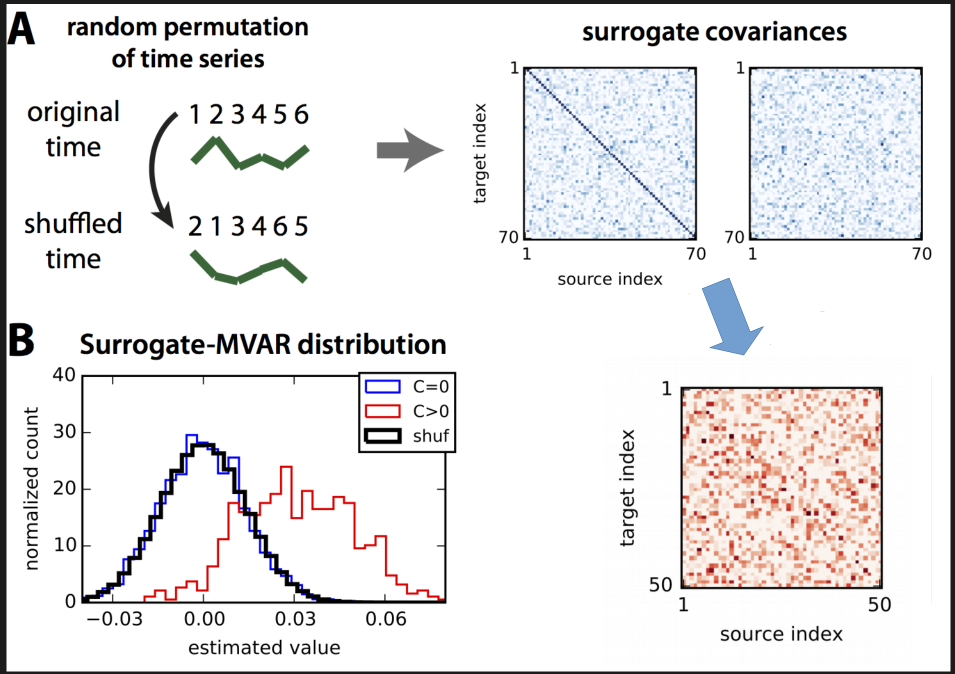
Maximum likelihood estimate
obtained from covariances
(simpler than continuous time)

$$A = \widehat{Q}^1 (\widehat{Q}^0)^{-1}$$

Shuffling the observed time series

- Destroys covariance structure to build surrogate
- Distribution of estimated MVAR coefficients for absent connections (blue) is matched by surrogate distribution (black)

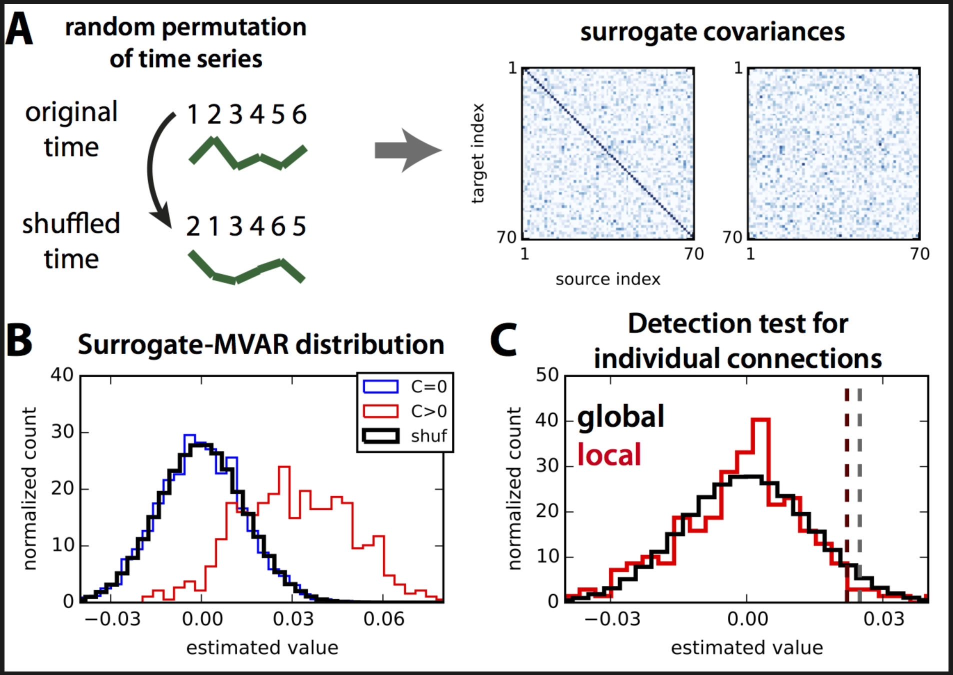
control of false alarms



$$A = \widehat{Q}^1 (\widehat{Q}^0)^{-1}$$

Local versus global surrogate distribution

- Local: each connection has its surrogate distribution
- Global: pooling all surrogate matrix elements



local/global significance threshold
(p=0.01 ↔ 1%-tail of the distribution)

Local versus global surrogate distribution

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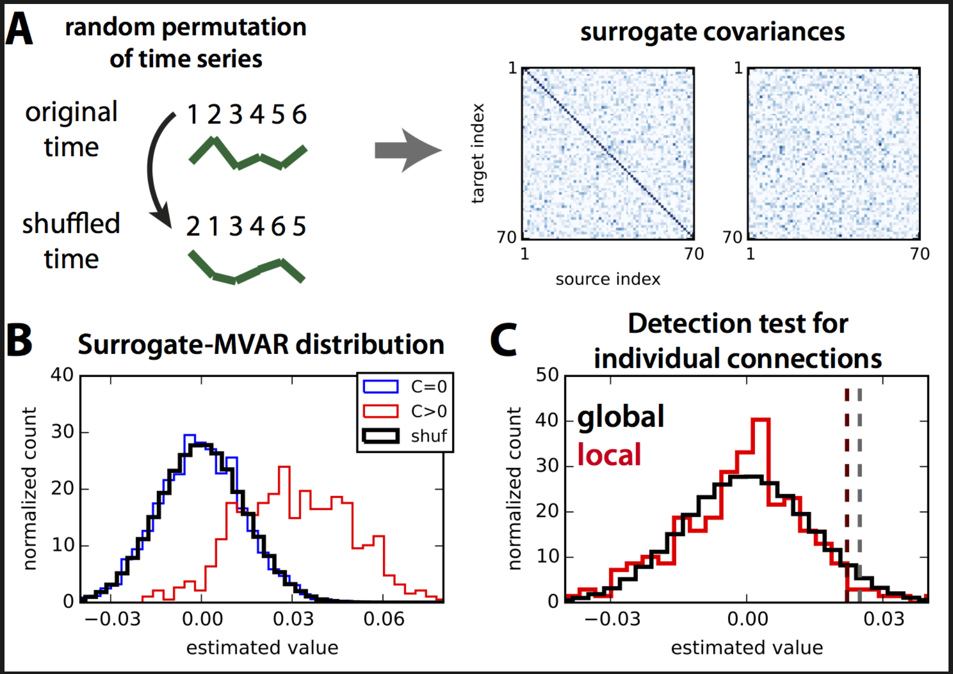
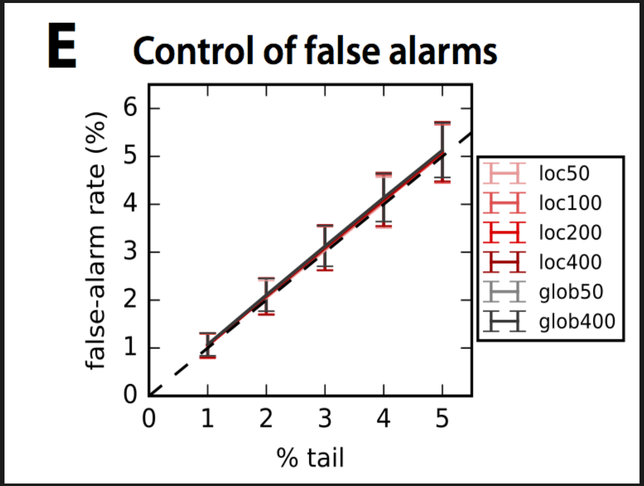


- **false alarm:** wrong detection of absent connection

network with N=100 nodes and 5-30% density: 1% false alarms corresponds to 70-95 connections!



Local versus global surrogate distribution

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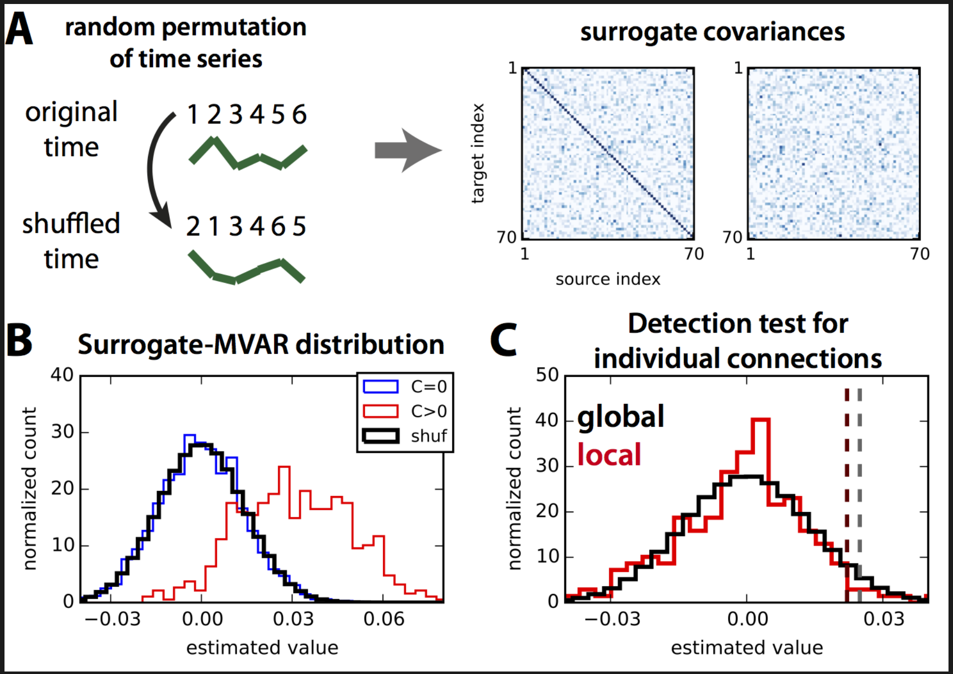
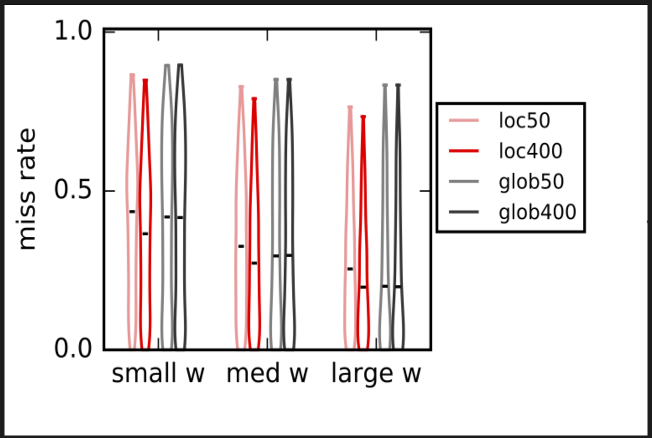


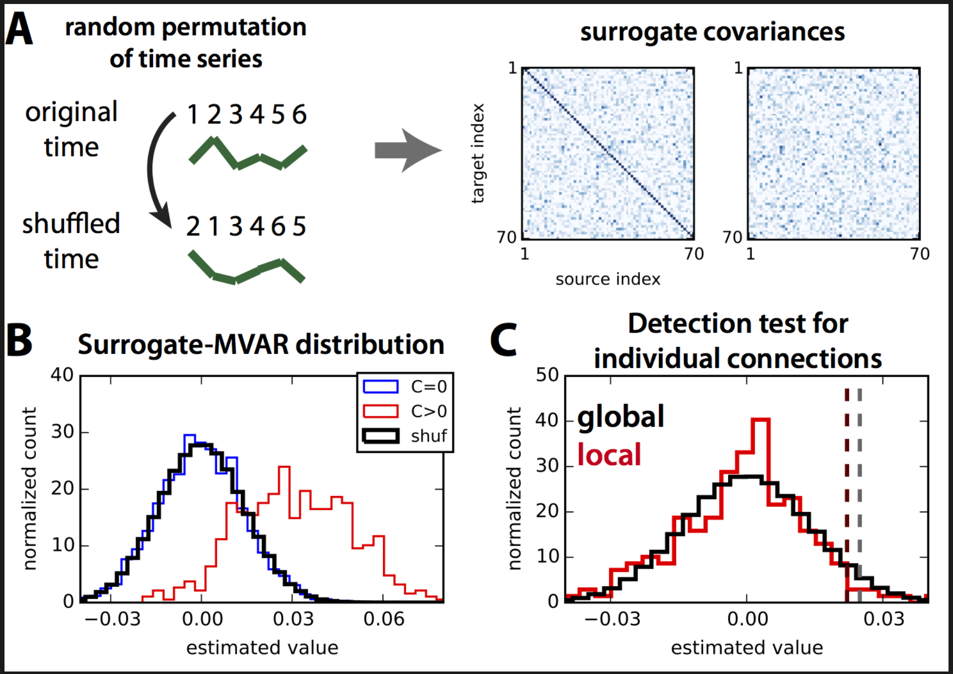
- **false alarm:** wrong detection of absent connection
- **miss:** fail to detect existing connection



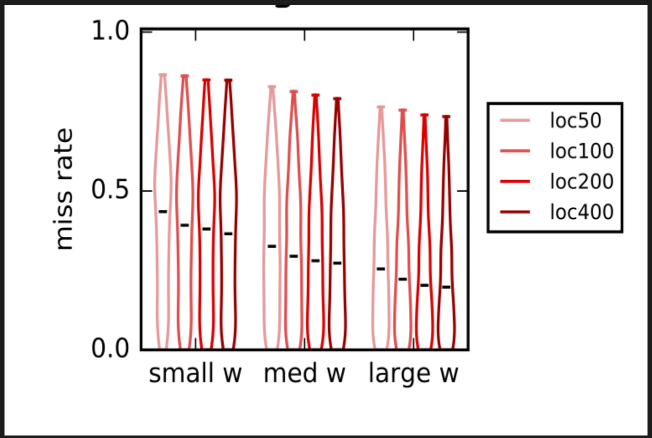
50 versus 400 surrogates

Local versus global surrogate distribution

- Local: each connection has its surrogate distribution
- Global: pooling all surrogate matrix elements

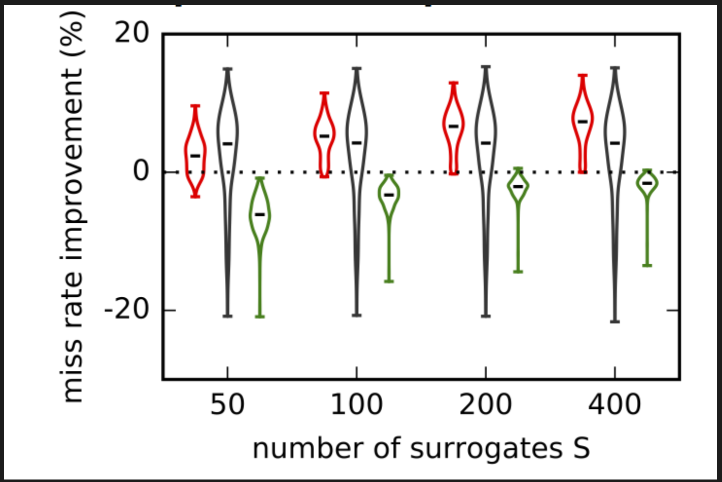


With local test, more surrogates (darker red) reduce the miss rate (especially for small weights, left violin plots)



Comparison with Granger causality analysis

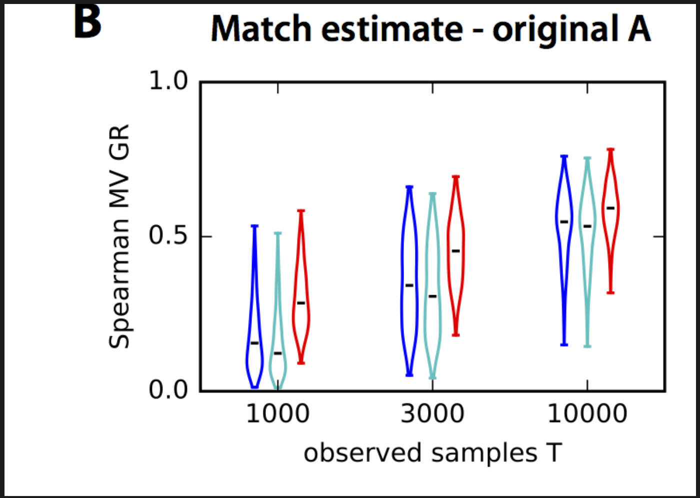
- Local test (red) and global test (gray)
- Comparison with conditional Granger causality analysis:
  - parametric test (reference in B, zero on y-axis)
  - non-parametric test (green)



- Local test always better for S>100 surrogates
- Conditional Granger causality analysis doesn't work well in network with redundant information (Stramaglia et al. 2014)
  - high feedback due to density

- Blue: unconditional Granger residuals
- Cyan: conditional Granger residuals
- Red: MVAR coefficients

For the considered dense networks, estimated MVAR coefficients are better aligned with the original weights (Spearman correlation)



Summary for detection of significant connections

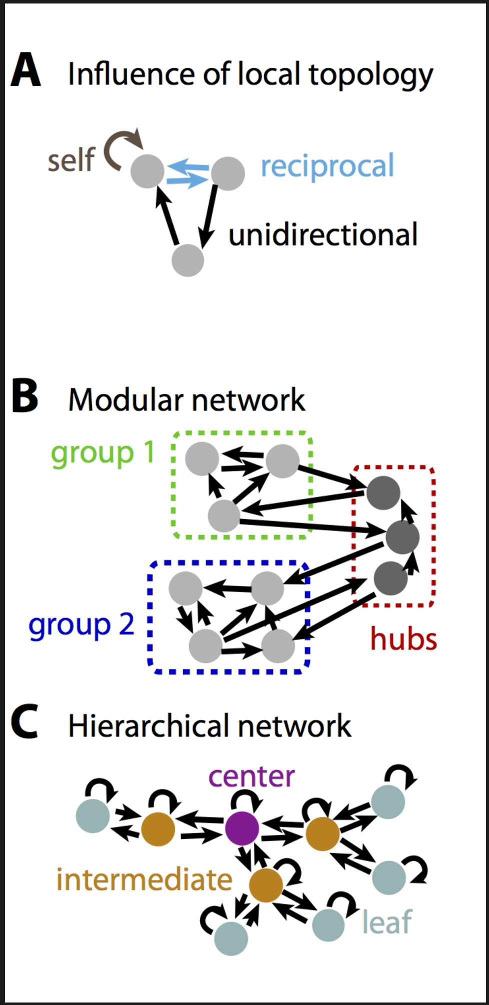
- Surrogates generated by shuffling observed time series can be used to perform statistical testing for MVAR estimates

- Robust to network topology, works with 2nd-order MVAR

- Computational cost is reasonable

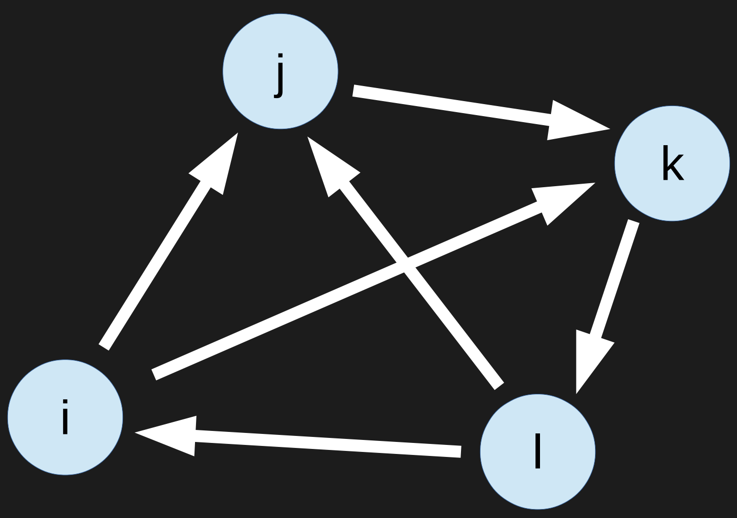
- Future work:

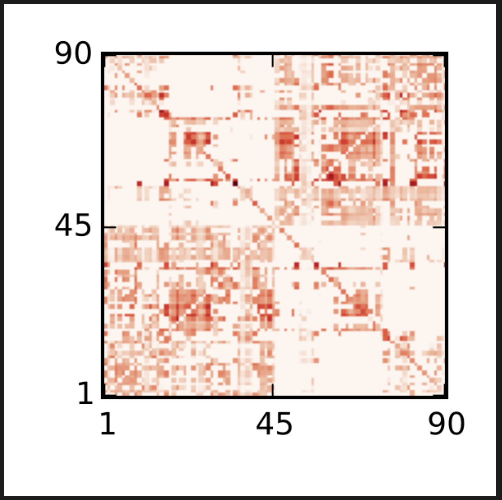
- Also: better characterize what information is extracted from MUAe (monkey data)



www.biorxiv.org/content/early/2017/06/26/100669
(accepted in Network Neuroscience)

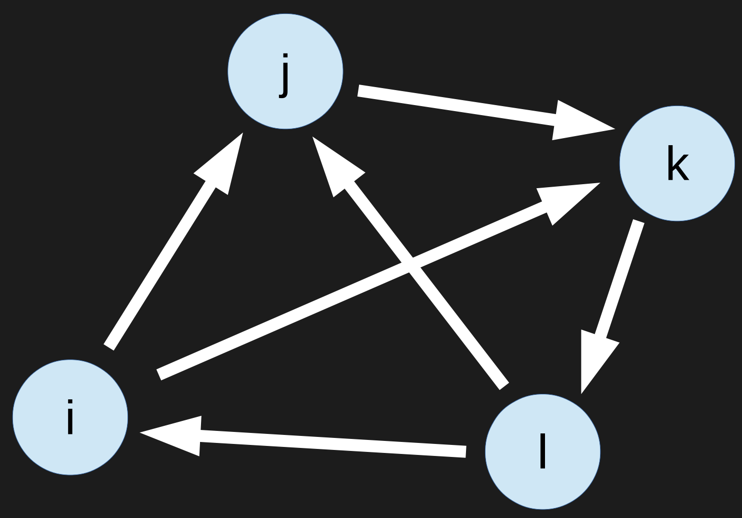
How to make sense of the multiple superposed paths for the network dynamics?





Communicability for graphs (structure→function)

- Measures indirect interactions
- Involves both shortest paths and longer paths (Estrada and Hatano 2008)



number of paths between i and k of lengths 1, 2, 3, etc. from adjacency matrix A:

$$A_{ik}, \left(A^2\right)_{ik}, \left(A^3\right)_{ik}, \ldots$$

Communicability for graphs (structure→function)

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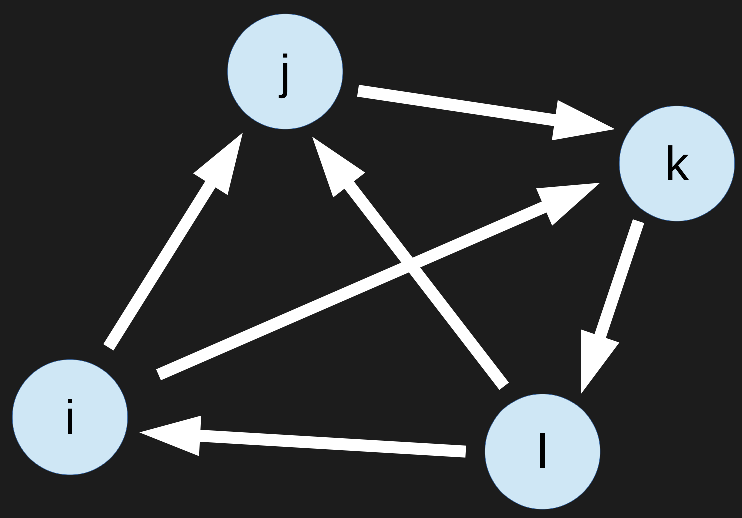


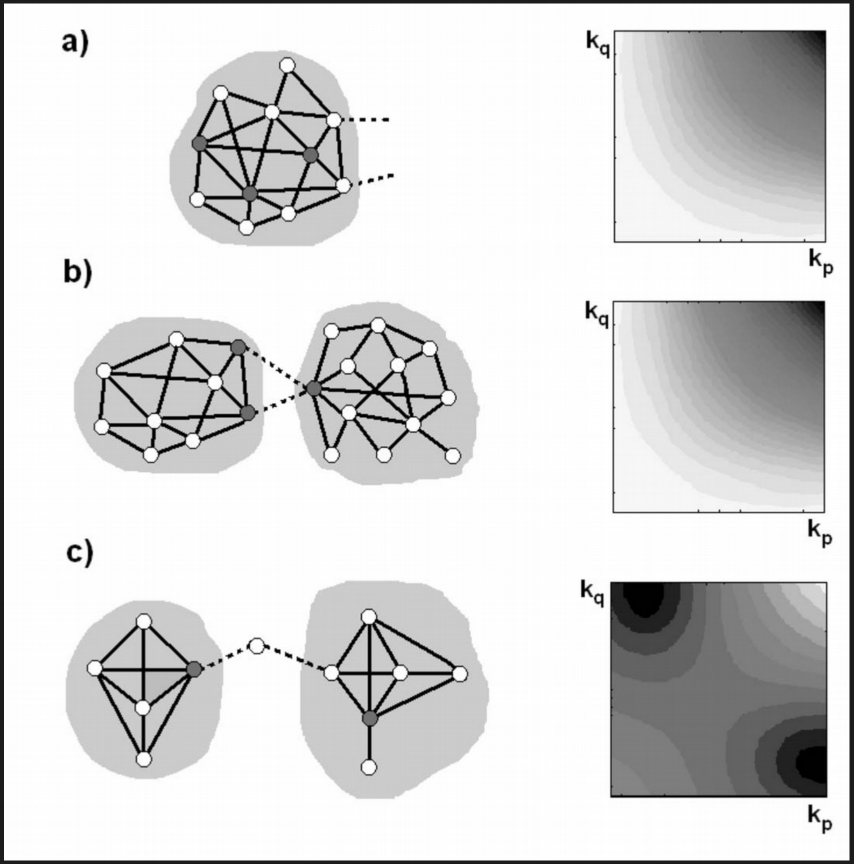
decay for longer paths

$$e^A = 1 + \frac{A}{1!} + \frac{A^2}{2!} + \frac{A^3}{3!} + \dots$$

from i to k: $\left(e^A\right)_{ki}$

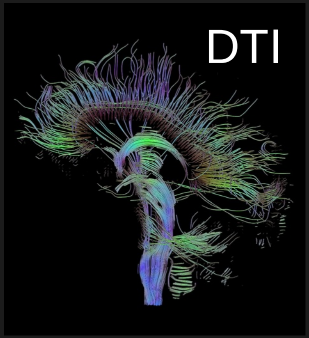
Communicability for static networks

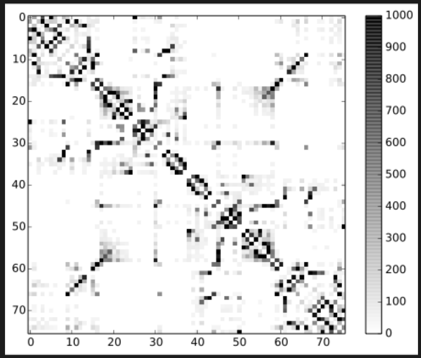
- Initially used to detect communities in undirected graphs
  - communicability for pairs of nodes as a function of their degrees (k_p, k_q)



Estrada and Hatano 2008

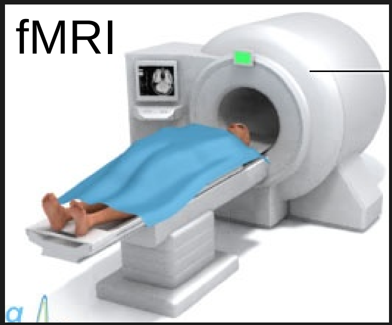
Communicability for static networks

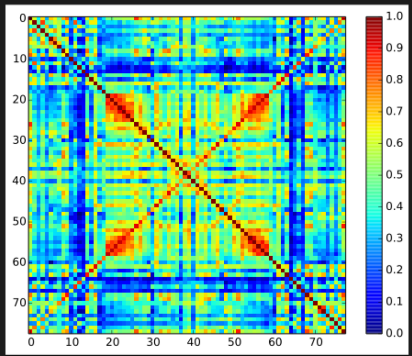




- Initially used to detect communities in undirected graphs
  - communicability for pairs of nodes as a function of their degrees (k_p, k_q)
- Also used to relate brain structure to function
  - anatomical (DTI) → functional (fMRI) connectivity

Bettinardi, Deco, Zamora-López et al., Chaos (2017)





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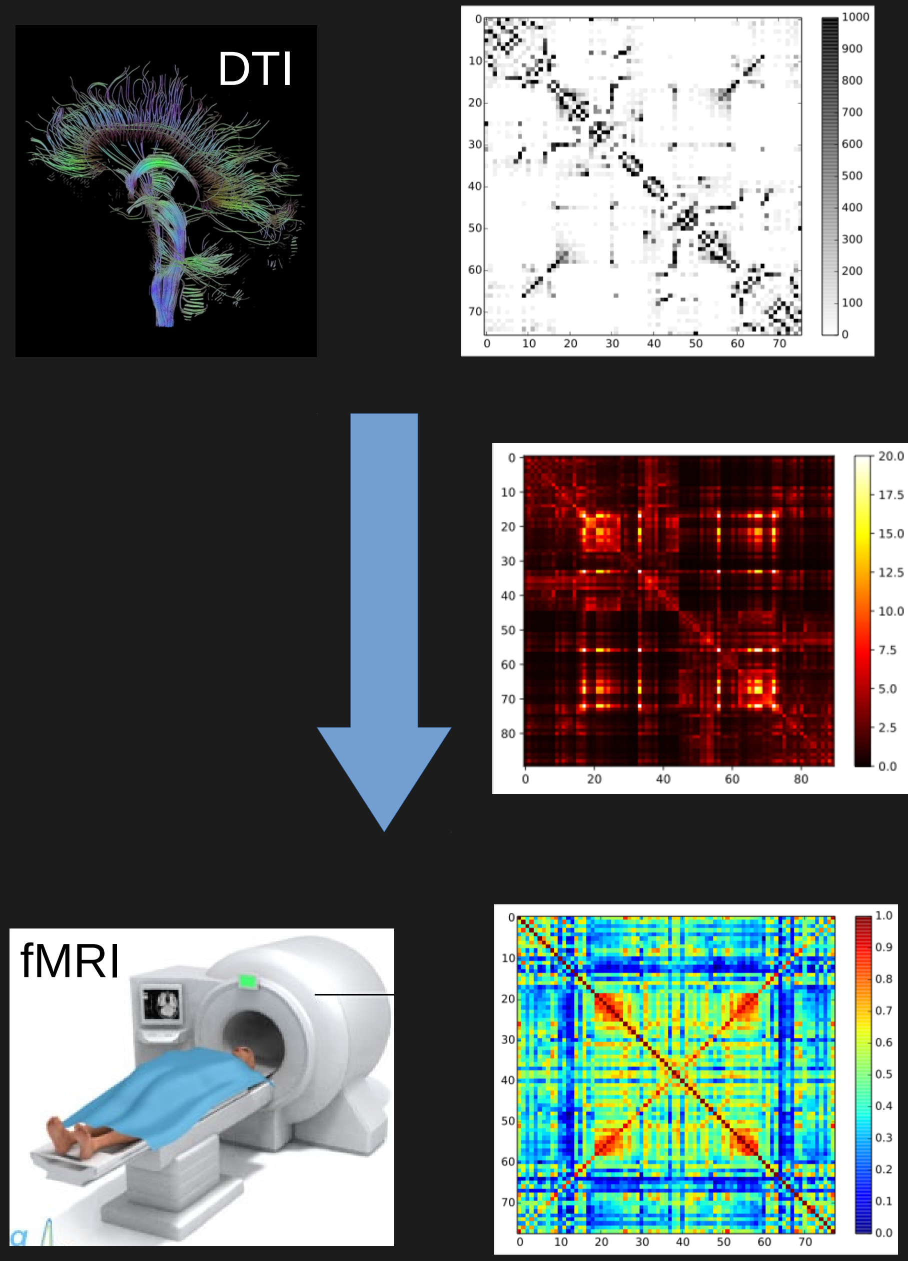

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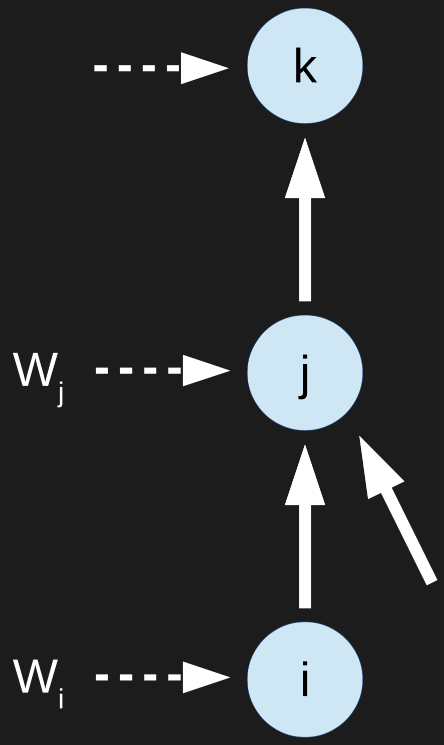
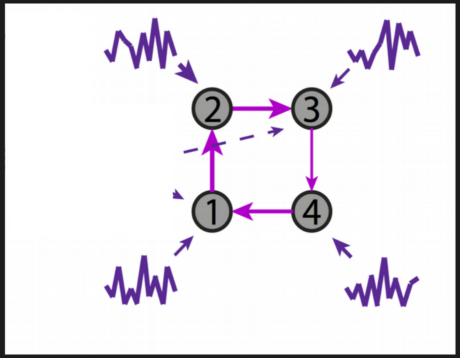
Formal relationship with noise-diffusion model

multivariate Ornstein-Uhlenbeck process

$$dx = \left(\frac{-x}{\tau} + Cx\right)dt + dW$$



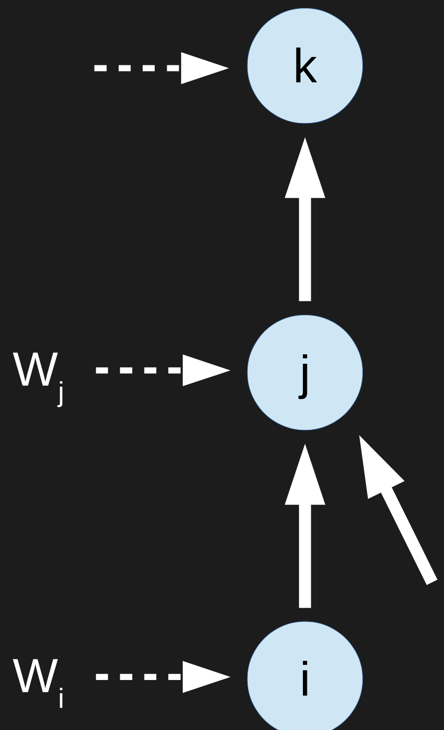
- Effective connectivity matrix C (transition matrix)
- Decay time constant τ
- Wiener process W (white noise)



Formal relationship with noise-diffusion model

multivariate Ornstein-Uhlenbeck process

$$dx = \left(\frac{-x}{\tau} + Cx \right) dt + dW \longrightarrow J_{ij} = \frac{-\delta_{ij}}{\tau} + C_{ij}$$



- Effective connectivity matrix C (transition matrix)
- Decay time constant τ
- Wiener process W (white noise)
- Jacobian J = propagator of dynamics

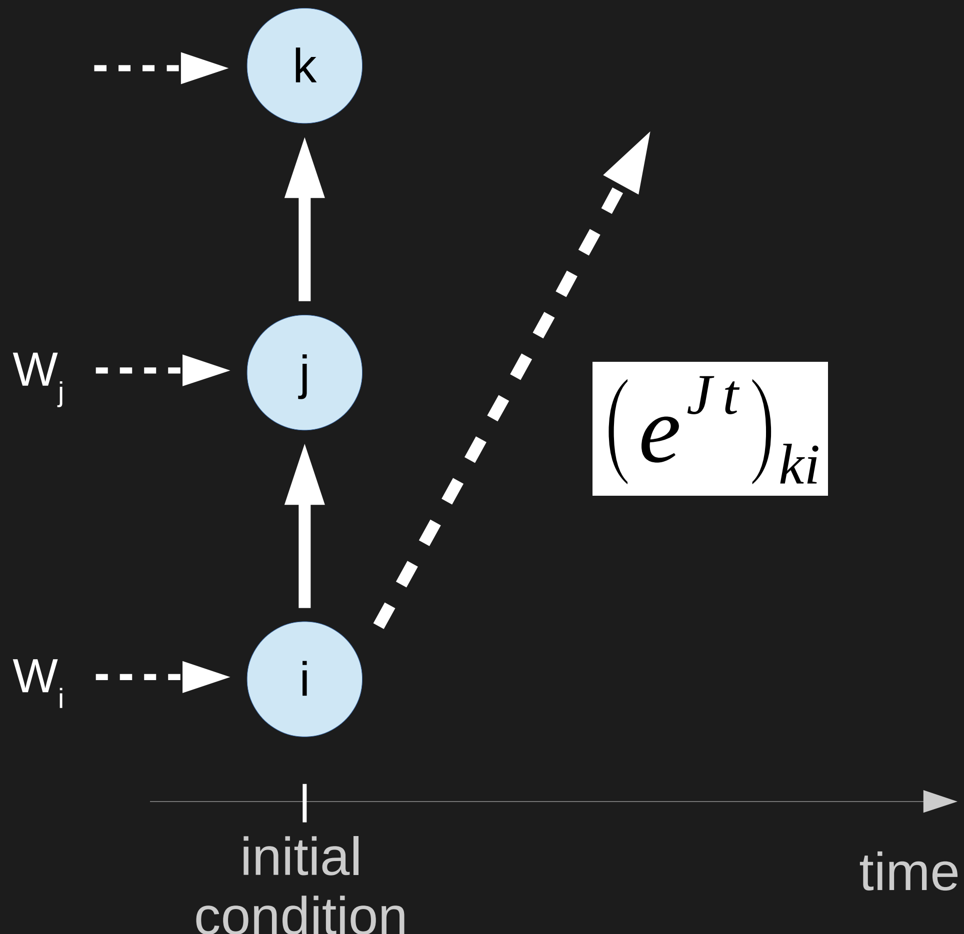
Forward equation to predict future state:

$$x(t) = e^{Jt} x(0) + \int_0^t e^{J(t-s)} dW(s)$$

Formal relationship with noise-diffusion model

multivariate Ornstein-Uhlenbeck process

$$J_{ij} = \frac{-\delta_{ij}}{\tau} + C_{ij}$$



$$\left(e^{J\,t}\right)_{ki}$$

- EC ~ transition matrix
- Matrix exponential is Green function of network dynamics
- Estrada and Hatano (2008): static viewpoint (t=1)

Dynamic communicability for noise-diffusion network

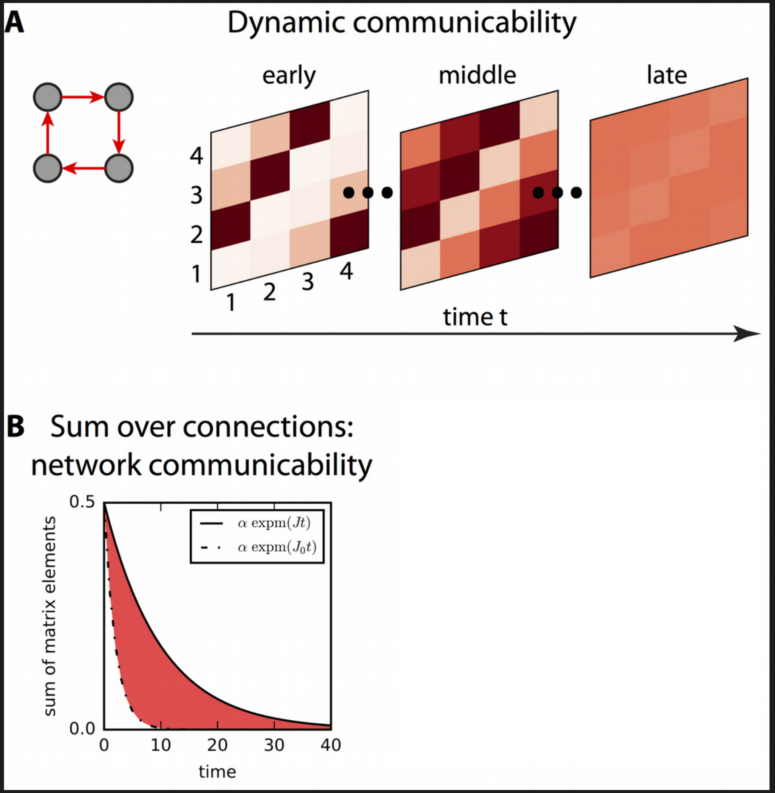
Comparison to null model with no connectivity (only local dynamics)

$$K^t = \frac{e^{Jt} - e^{J^0 t}}{\left\| \left(J^0 \right)^{-1} \right\|}$$

Jacobian for null model

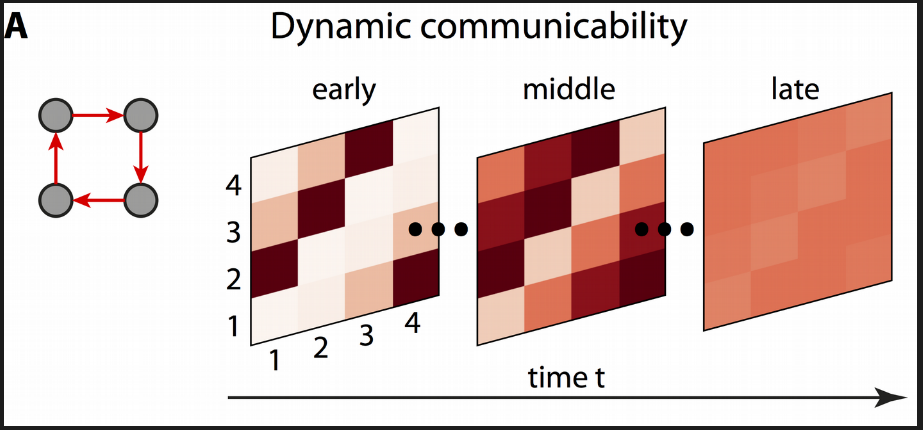
$$J_{ij} = \frac{-\delta_{ij}}{\tau} + C_{ij}$$

$$J^0_{ij} = \frac{-\delta_{ij}}{\tau}$$



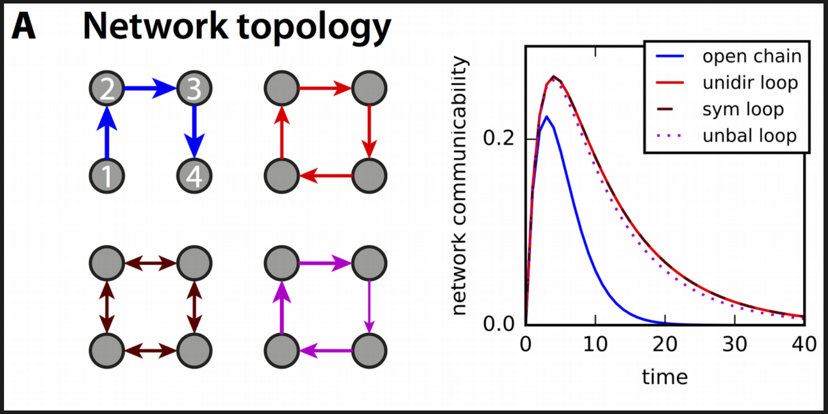
Time-dependent analysis of communicability

Network communicability	$\sum_{ij} K_{ij}^t$	global
Input communicability	$\sum_{j} K_{ij}^t$	integrating
Output communicability	$\sum_{i} K_{ij}^t$	broadcasting



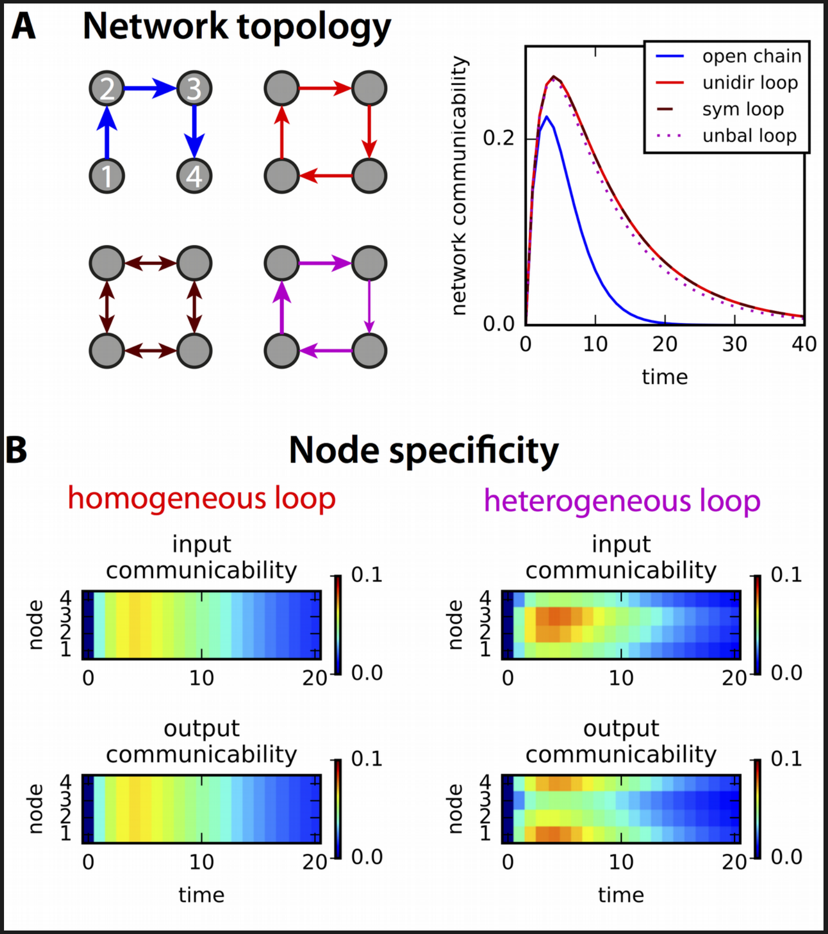
Quantification of network feedback

- Open loop < closed loops



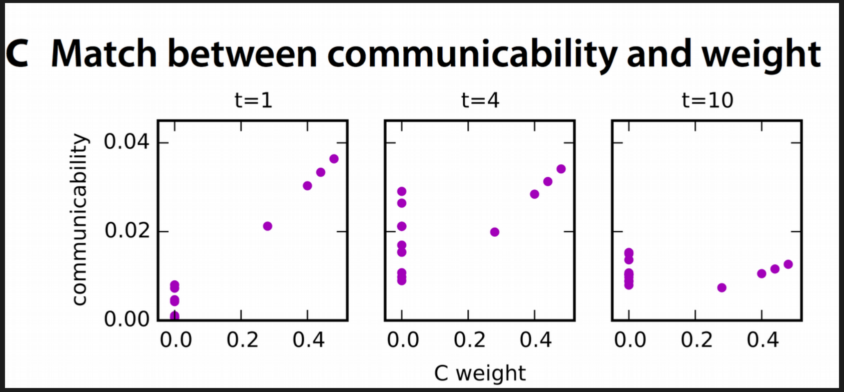
Quantification of network feedback

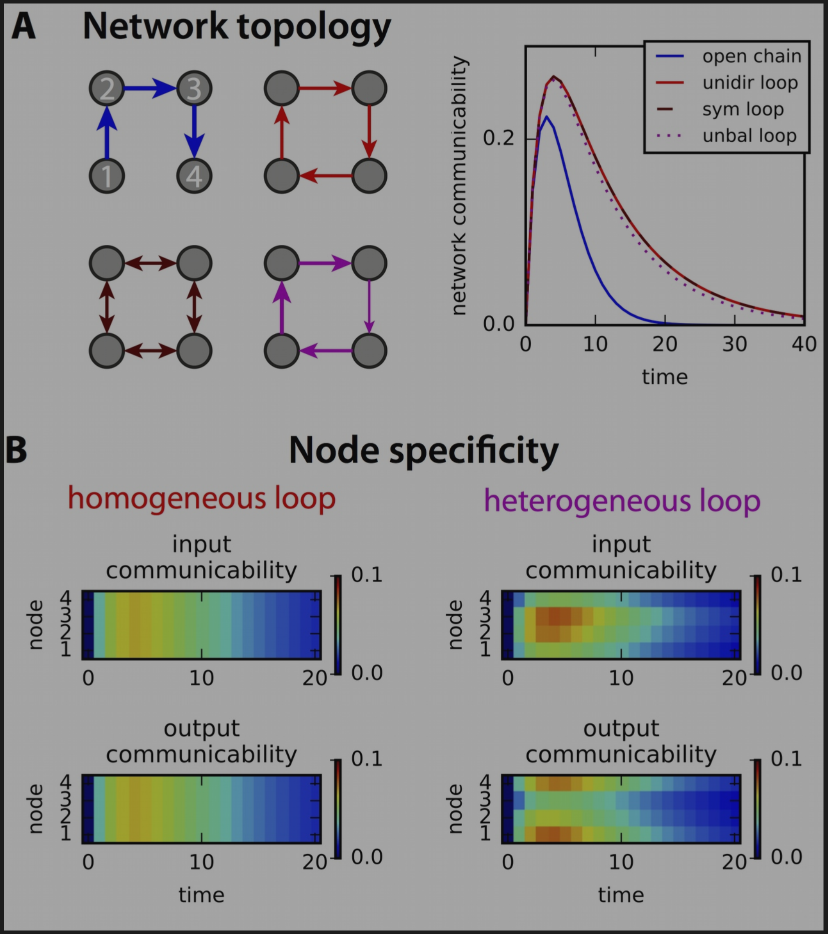
- Open loop < closed loops
- Dynamic communicability captures heterogeneities between nodes



Quantification of network feedback

- Open loop < closed loops
- Dynamic communicability captures heterogeneities between nodes
- Homogenization over time

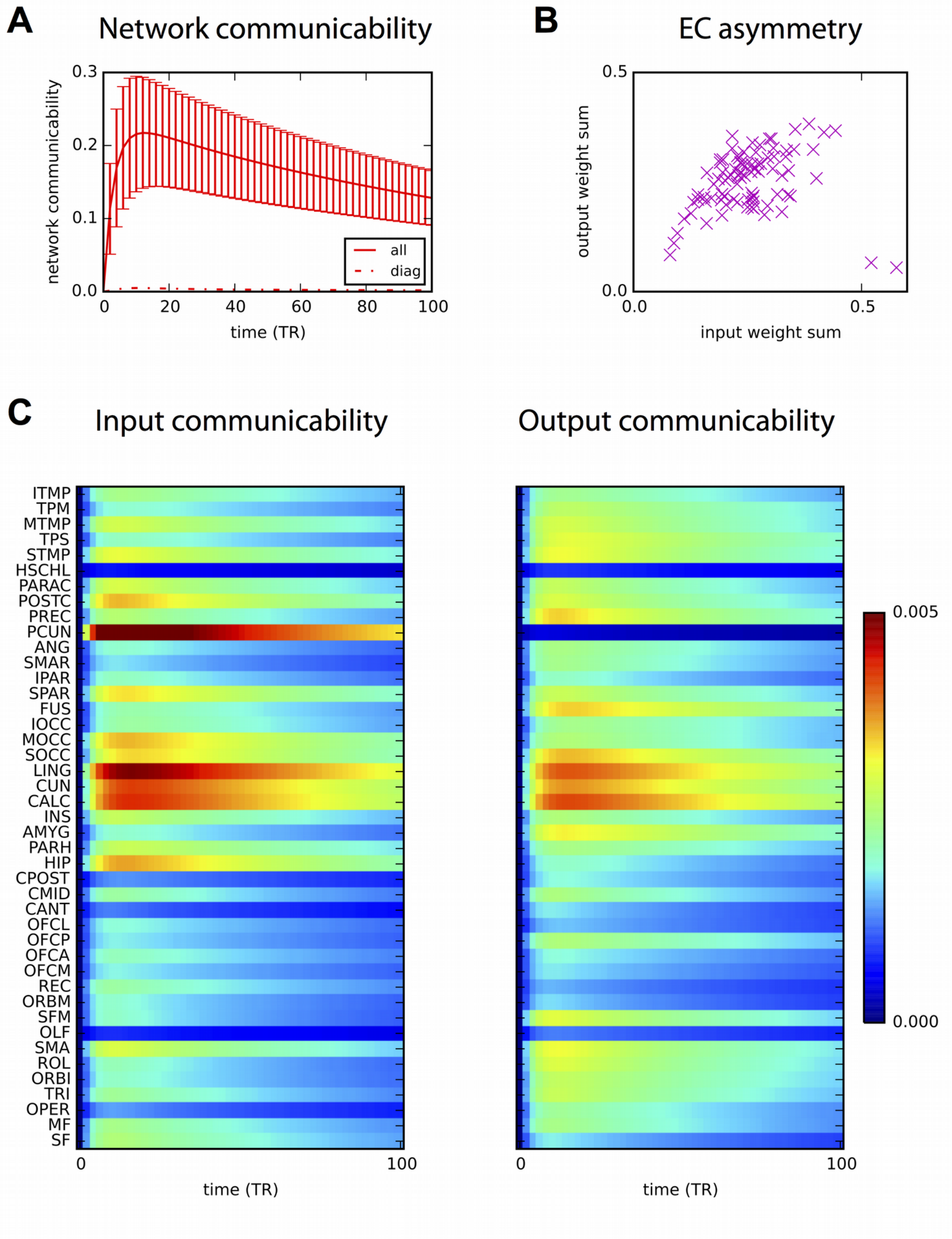




Application to resting-state fMRI

- Data from JF Mangin (Neurospin)
- 57 subjects
- AAL90 parcellation
- TR = 2 seconds

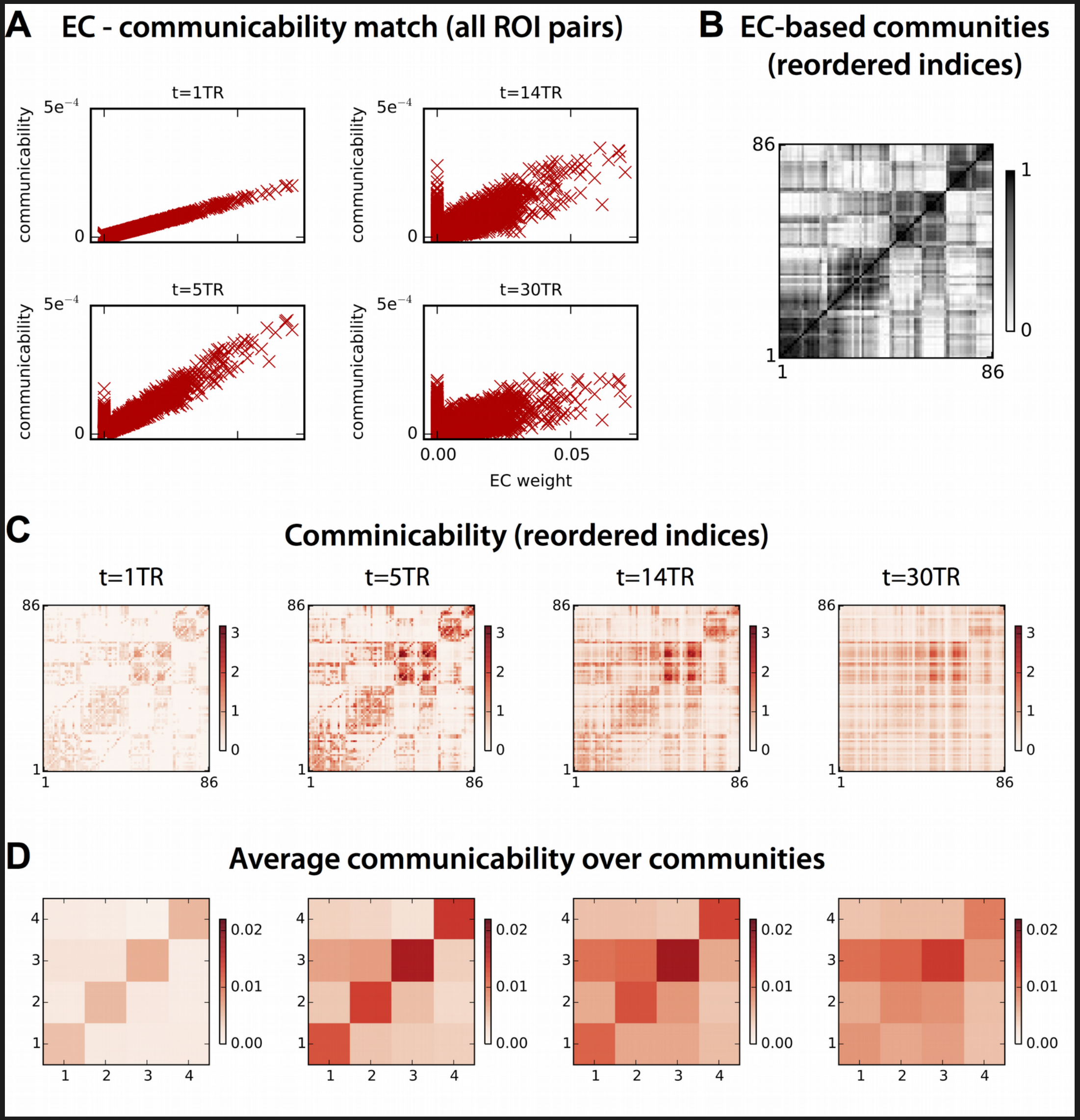
- Strong network effect (long lasting)
  - close to criticality
- Input-output heterogeneities across nodes
  - e.g., precuneus listens but does not broadcast



From segregated to global integration

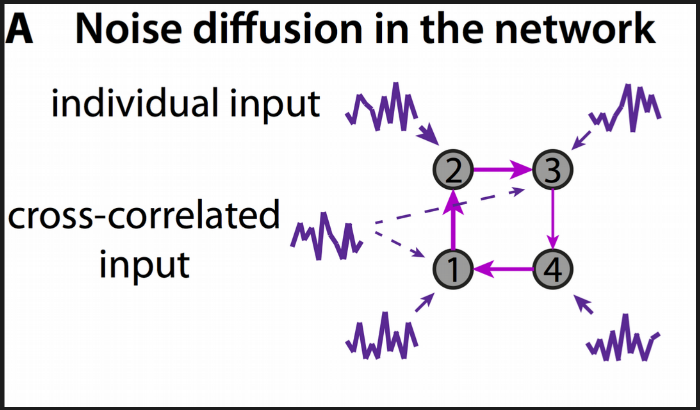
- Panel B: 4 communities detected from EC weights using the Louvain method (Newman modularity)

- Communicability initially increases within communities, then spreads (cf. off-diagonal blocks)
  - link with Laplacian-flow to detect communities (Rosvall and Bergstrom; Lambiotte, Bahorona)



Summary for dynamic communicability

- It quantifies network interactions across time
- Time-dependent measures (e.g., to compare distinct conditions)
  - global network effect
  - integration and broadcast strengths for each node
  - segregated → global integration (community merging over time)
- Definition of flow to take the input statistics (variances) into account in the noise-diffusion process



Conclusions

- We aim to develop an analysis framework for complex network dynamics estimated from data (e.g., fMRI, MUAe)
  - extend graph theory for static network
  - beyond mean-field approaches for dynamic systems
  - adequate statistical tests
- Code for EC estimation available online (matthieugilson.eu)

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