Challenges for graph theory in human neuroscience

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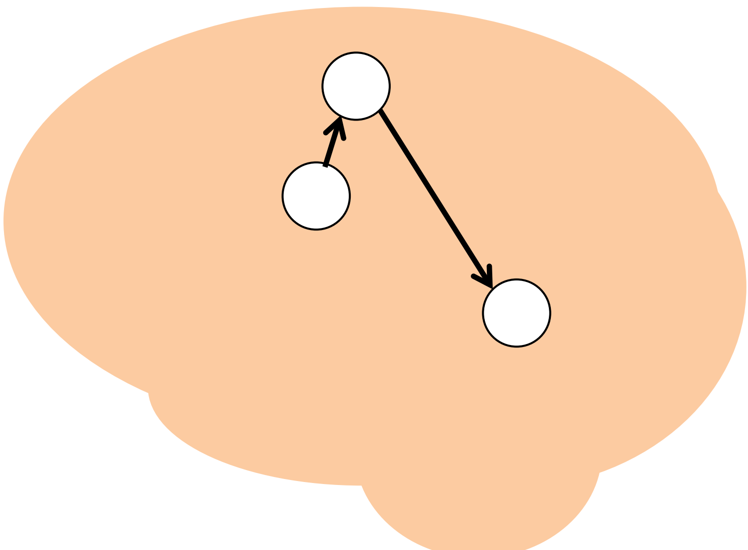
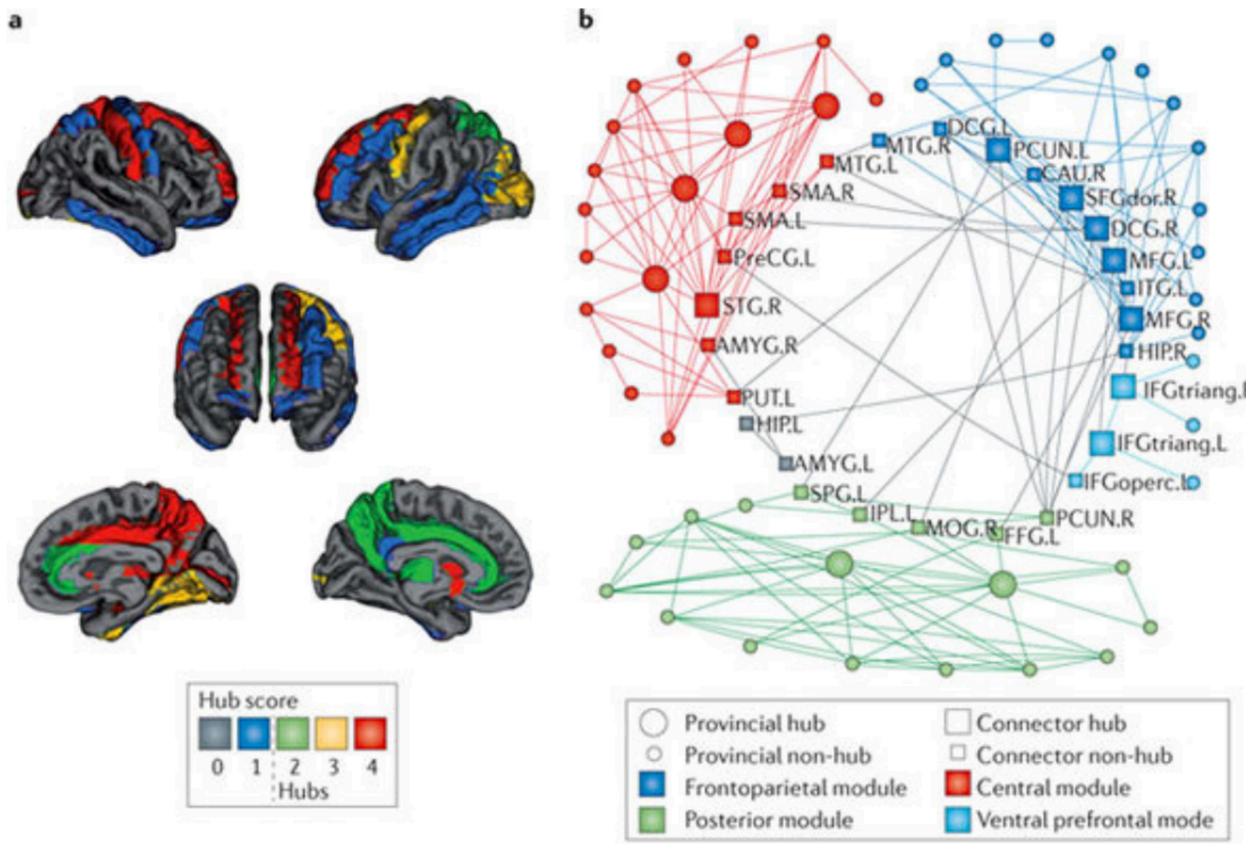
Motivation for graph theory in human neuroscience

- Conceptualizing the brain as a network has revolutionized the way we think about and study brain function



Motivation for graph theory in human neuroscience

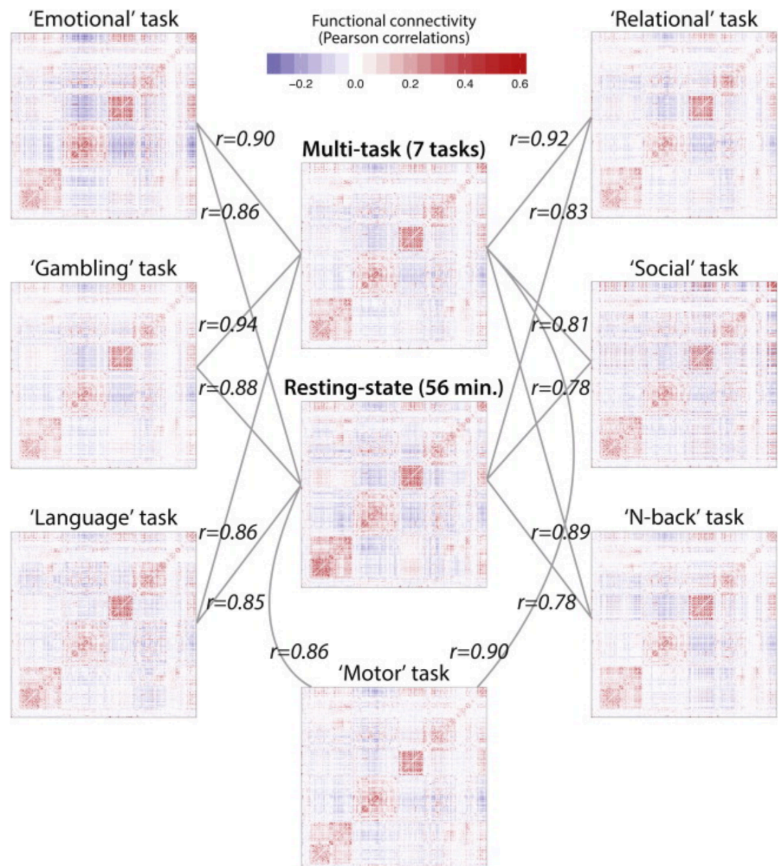
- Network topology of brain structure/function



(Bullmore and Sporns, 2010)

Motivation for graph theory in human neuroscience

- Human cognition

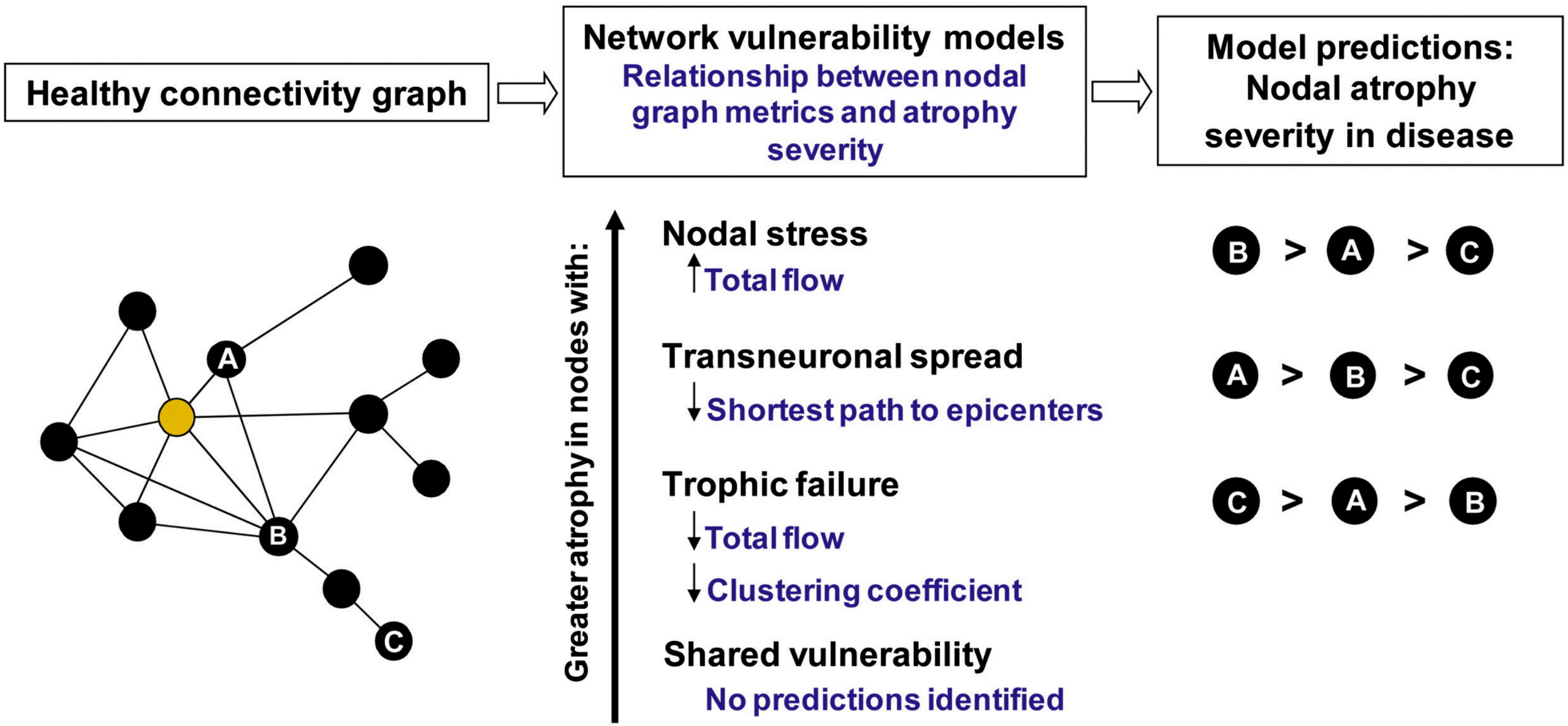


(Cole et al., 2014)

Motivation for graph theory in human neuroscience

- Neurological disease

  (Seeley et al., 2009; Raj et al., 2012)



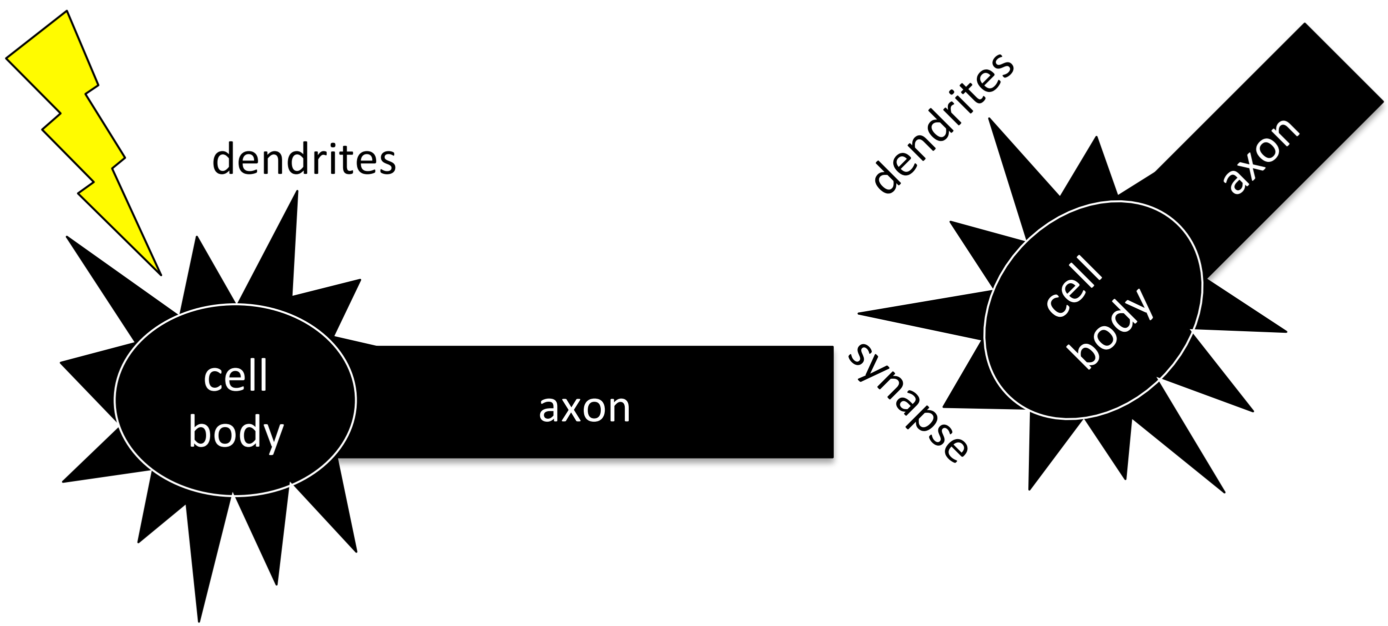
(Zhou et al., 2012)

Challenges for graph theory in human neuroscience

- Determining elements of a brain graph
- Comparing graphs
- Graph properties and algorithms

Challenges for graph theory in human neuroscience

- Healthy brain function requires coordination across distributed areas of the brain



Determining elements of a brain graph: the nodes

- Nodes are typically defined by:
  - units being measured (e.g. voxels or electrodes)
  - regions of interest (ROIs) – units grouped based on similar anatomical or functional features

Key challenges:

- ROIs can be defined in many different ways
  (Desikan et al., 2006; Tzourio-Mazoyer et al., 2002; Craddock et al., 2012; Power et al., 2011; Glasser et al., 2016; Kong et al., 2018)
- We don't always know and/or can't always obtain the ideal "level" of measurement
  - synapses vs cells vs columns vs larger ROIs
- Inconsistent/variable structure and/or brain coverage

Determining elements of a brain graph: the edges

- Defining an edge
  - Correlation, partial correlation, GLASSO, etc
  - Pairwise relationship of units over time (fMRI, dMRI, EEG, ECog, MEG) or across individuals (sMRI, PET)

Key challenges:

- Interdependence of measurements
- Inferring direction
- Determining a threshold
- Binary vs. weighted edges

Comparing graphs

- Heterogeneous approaches to define graphs
  – different definitions of nodes/edges
  – different brain measurements (e.g. EEG, ECog, MEG, fMRI, dMRI, sMRI, PET)
- Inherent differences across populations/individuals
  – different numbers of nodes/edges
  – different distributions of weights

Key challenges:

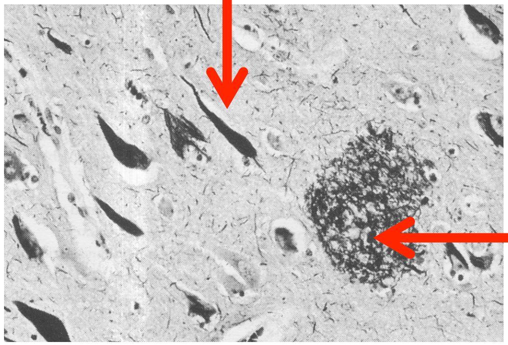
- Comparing metrics across heterogeneous graphs
- Combining information from graphs across modalities

Graph properties and algorithms

- There are both challenges faced by broader field of graph theory and challenges due to graph properties/algorithms designed to address problems in other disciplines
  - Detecting multiple epicenters/sources

Alzheimer's disease primer

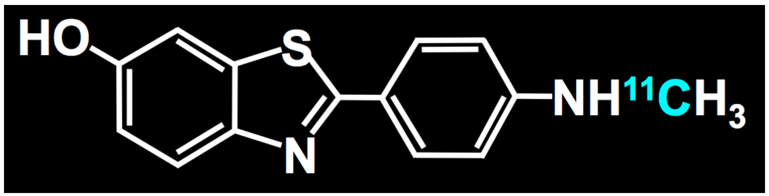
neurofibrillary
tangles (tau)



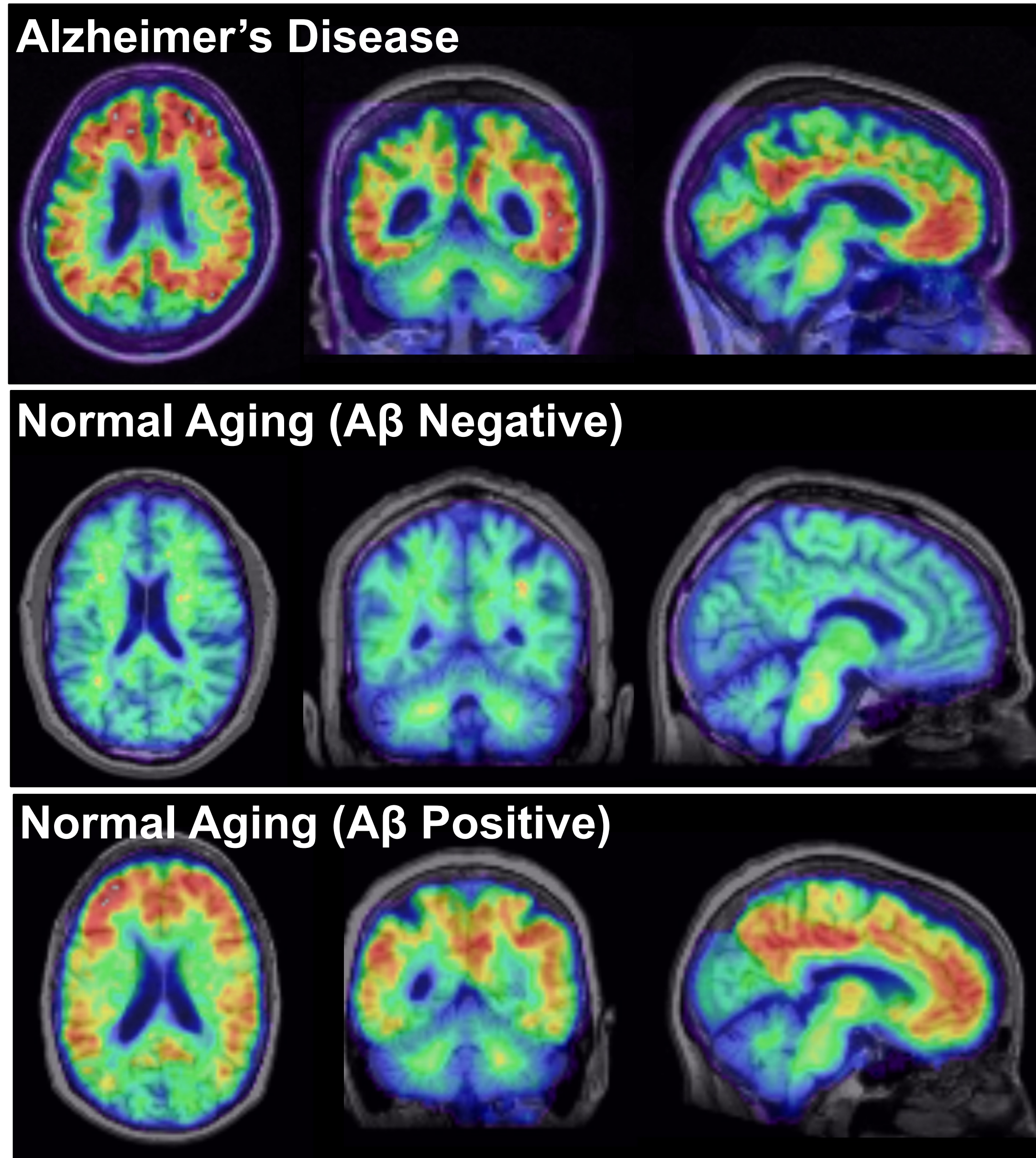
amyloid-β
plaques (Aβ)

Aβ PET Imaging

PET Imaging -
[^{11}C]6-OH-BTA-1 (PIB)



- PET revealed that ~30% of cognitively normal older adults aged 70+ have substantial Aβ



Large-scale brain structure/function shapes neurodegeneration

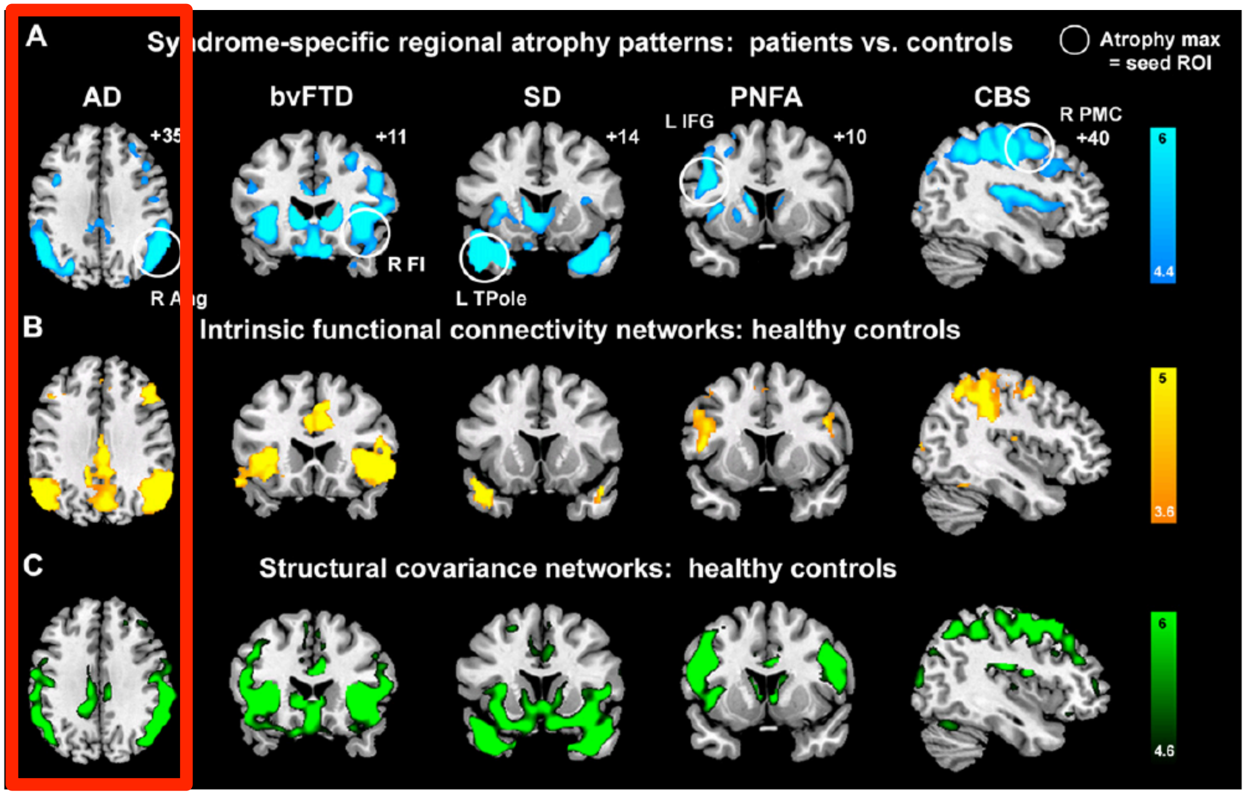


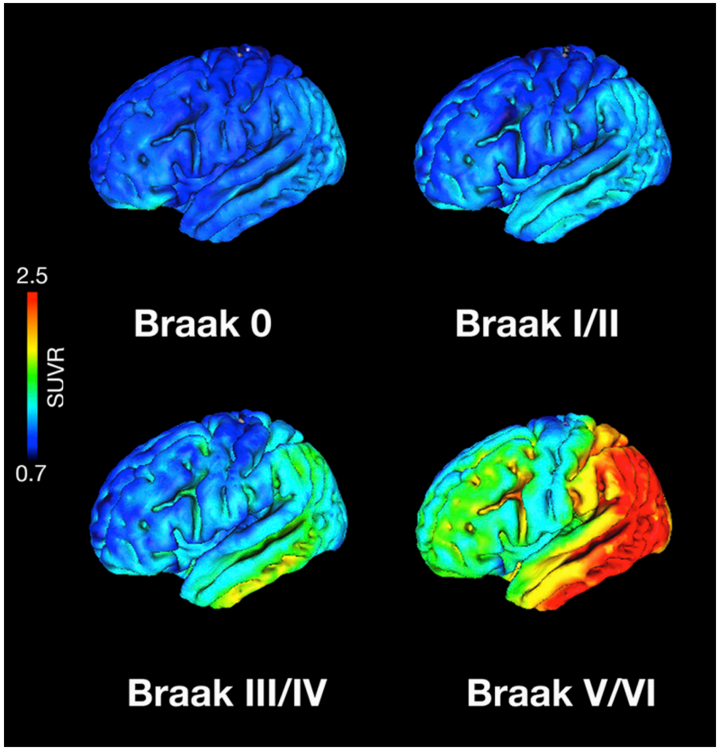
Figure 2. Convergent Syndromic Atrophy, Healthy ICN, and Healthy Structural Covariance Patterns

(A) Five distinct clinical syndromes showed dissociable atrophy patterns, whose cortical maxima (circled) provided seed ROIs for ICN and structural covariance analyses. (B) ICN mapping experiments identified five distinct networks anchored by the five syndromic atrophy seeds. (C) Healthy subjects further showed gray matter volume covariance patterns that recapitulated results shown in (A) and (B). For visualization purposes, results are shown at $p < 0.00001$ uncorrected (A and C) and $p < 0.001$ corrected height and extent thresholds (B). In (A)–(C), results are displayed on representative sections of the MNI template brain. Color bars indicate t-scores. In coronal and axial images, the left side of the image corresponds to the left side of the brain. ANG, angular gyrus; FI, frontoinsula; IFGoper, inferior frontal gyrus, pars opercularis; PMC, premotor cortex; TPole, temporal pole.

Seeley et al., Neuron, 2009

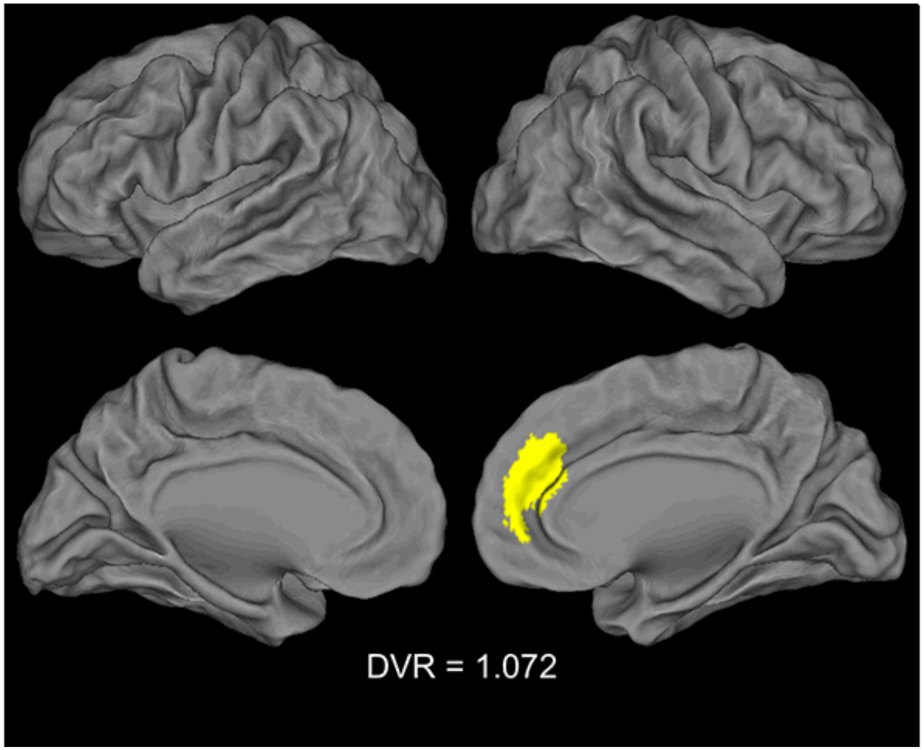
Spatiotemporal pattern of pathology with Alzheimer's disease progression

Tau (AV1451-PET)



(adapted from Scholl et al., 2015)

Amyloid-β (Aβ, PIB-PET)

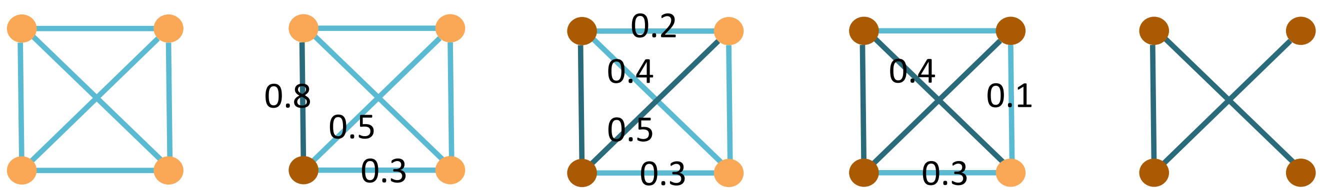


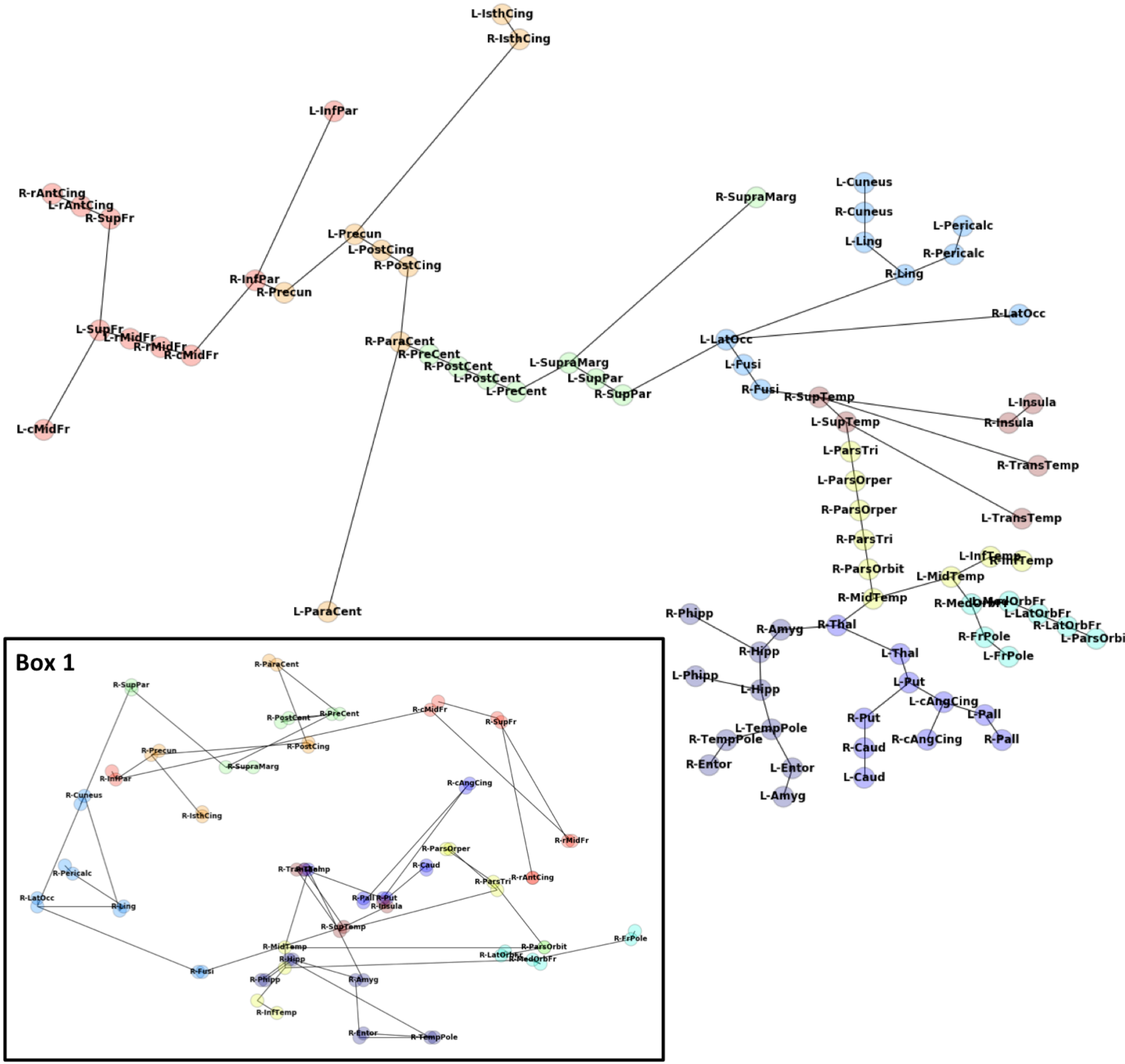
(Villeneuve et al., 2015)

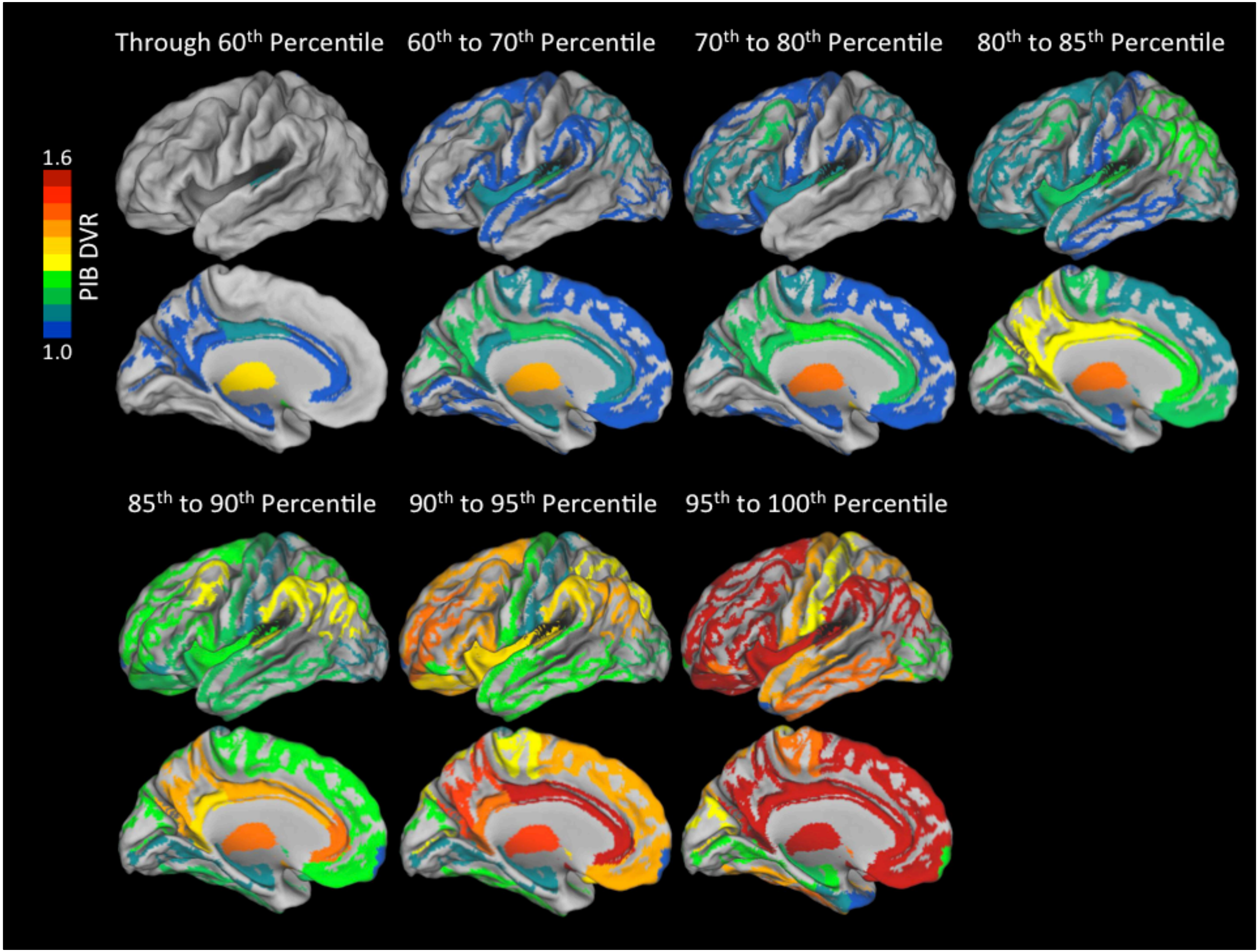
→Differences across the brain in vulnerability to Aβ and tau pathology

Minimum Spanning Tree (MST)

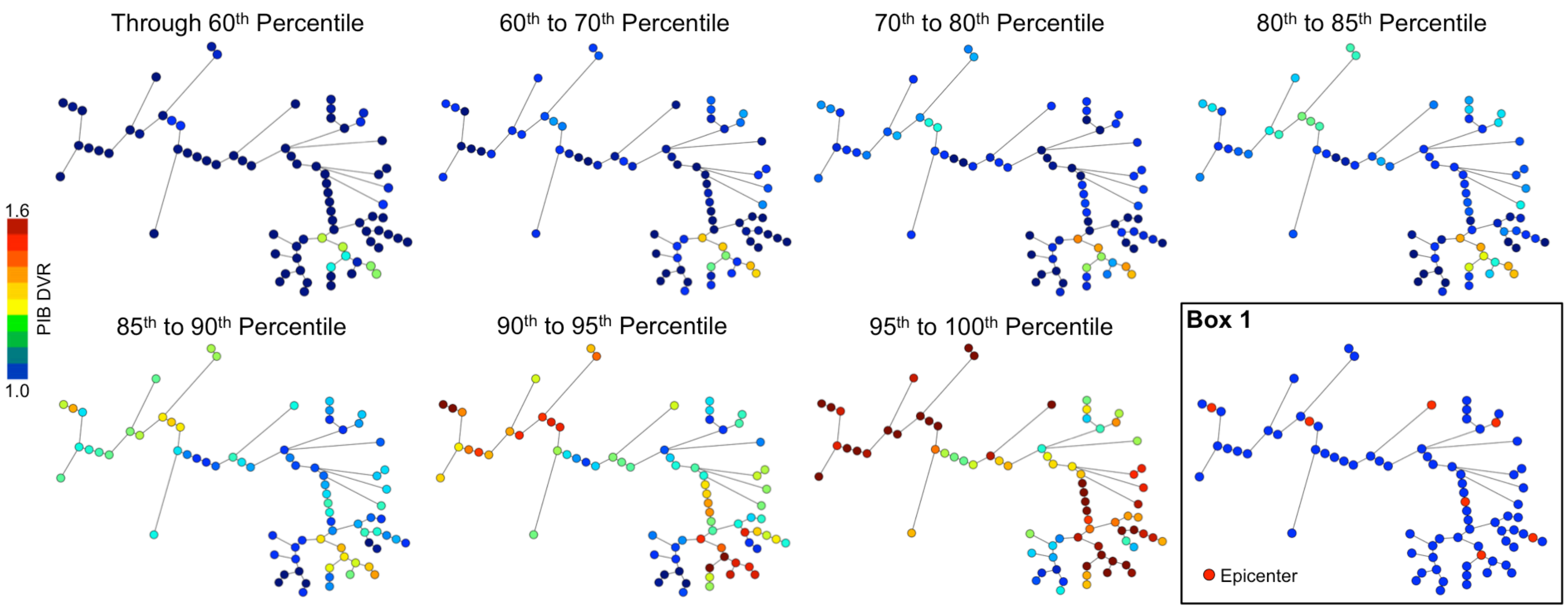
- MST: *a unique, acyclic graph minimally connecting all nodes* (Jackson & Read, Phys Rev E, 2010a/b)
  - → Path of maximal information flow through the brain (Stam et al., Int J Psychophysiol, 2014)
  - → Amyloid-β spread?



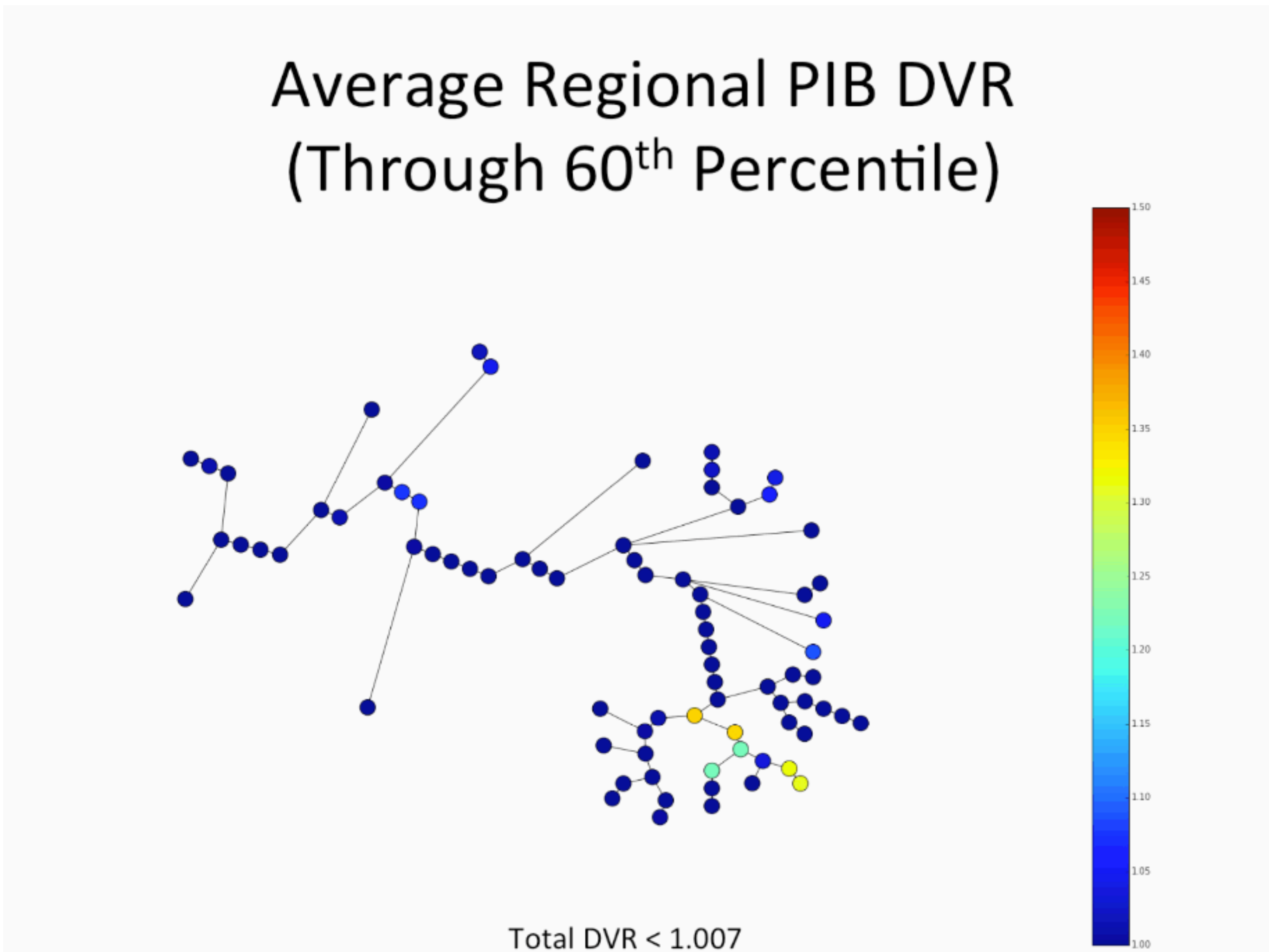

L-IsthCing
R-IsthCing
L-InfPar
R-rAntCing
L-rAntCing
R-SupFr
L-Precun
L-PostCing
R-PostCing
R-InfPar
R-Precun
L-SupFr
L-rMidFr
R-rMidFr
R-cMidFr
L-cMidFr
R-ParaCent
R-PreCent
R-PostCent
L-PostCent
L-PreCent
L-SupraMarg
L-SupPar
R-SupPar
R-SupraMarg
L-ParaCent
L-Cuneus
R-Cuneus
L-Ling
L-Pericalc
R-Pericalc
R-Ling
R-LatOcc
L-LatOcc
L-Fusi
R-Fusi
R-SupTemp
L-SupTemp
L-Insula
R-Insula
R-TransTemp
L-TransTemp
L-ParsTri
L-ParsOrper
R-ParsOrper
R-ParsTri
R-ParsOrbit
L-InfTemp
R-InfTemp
L-MidTemp
R-MidTemp
L-LatOrbFr
R-LatOrbFr
L-ParsOrbit
R-FrPole
L-FrPole
R-Phipp
R-Amyg
R-Thal
R-Hipp
L-Thal
L-Phipp
L-Hipp
L-Put
L-cAngCing
L-Pall
R-Put
R-Pall
L-TempPole
R-TempPole
R-Caud
R-cAngCing
R-Entor
L-Entor
L-Caud
L-Amyg
Box 1
R-ParaCent
R-SupPar
R-PostCent
R-PreCent
R-cMidFr
R-SupFr
R-Precun
R-PostCing
R-InfPar
R-SupraMarg
R-cAngCing
R-Cuneus
R-IsthCing
R-rMidFr
R-ParsOrper
R-Caud
R-Pericalc
R-rAntCing
R-ParsTri
R-LatOcc
R-Ling
R-Pall
R-Put
R-Insula
R-SupTemp
R-MidTemp
R-ParsOrbit
R-LatOrbFr
R-MedOrbFr
R-FrPole
R-Hipp
R-Fusi
R-Phipp
R-Amyg
R-InfTemp
R-Entor
R-TempPole


Through 60th Percentile
60th to 70th Percentile
70th to 80th Percentile
80th to 85th Percentile
1.6
PIB DVR
1.0
85th to 90th Percentile
90th to 95th Percentile
95th to 100th Percentile

Directed progression of Alzheimer's disease pathology



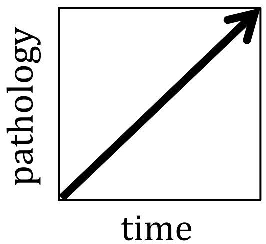
Directed progression of Alzheimer's disease pathology



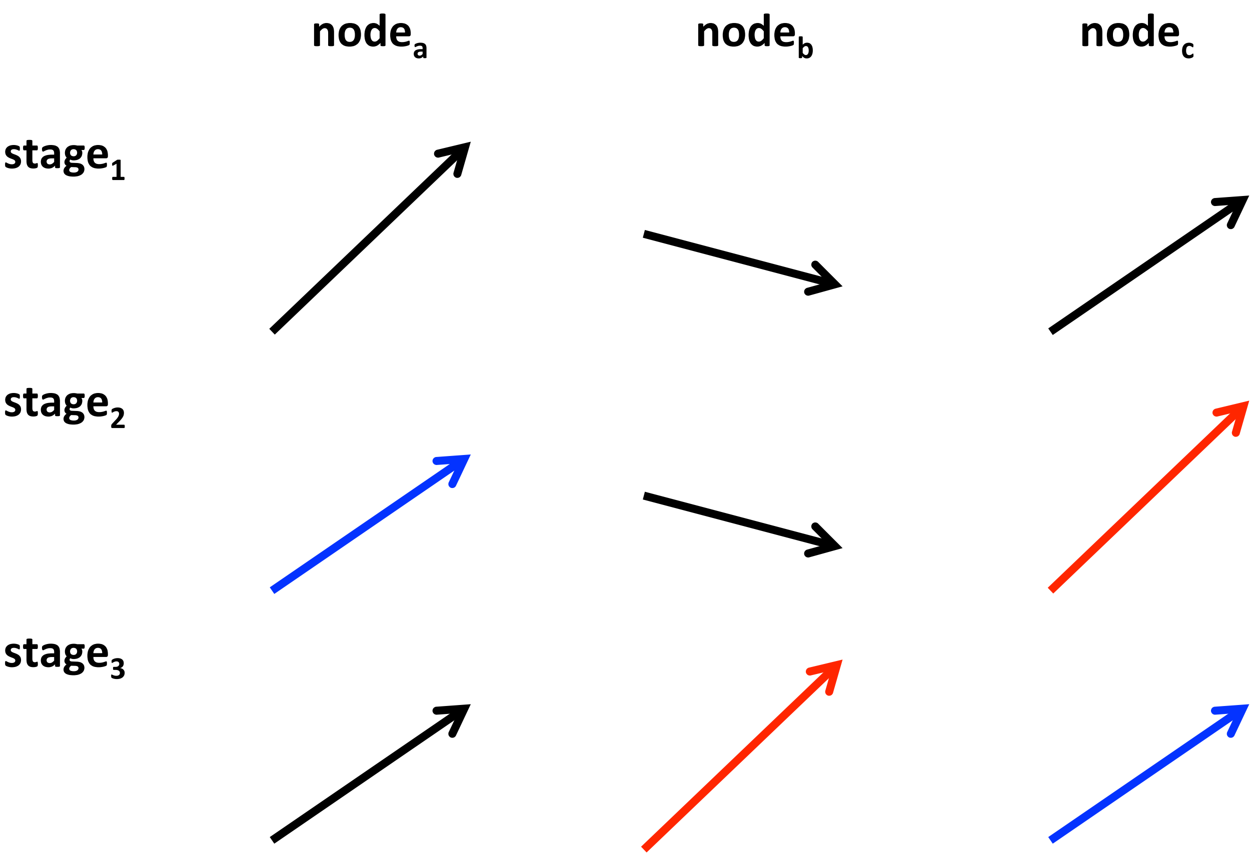
Directed progression graphs

node$_a$

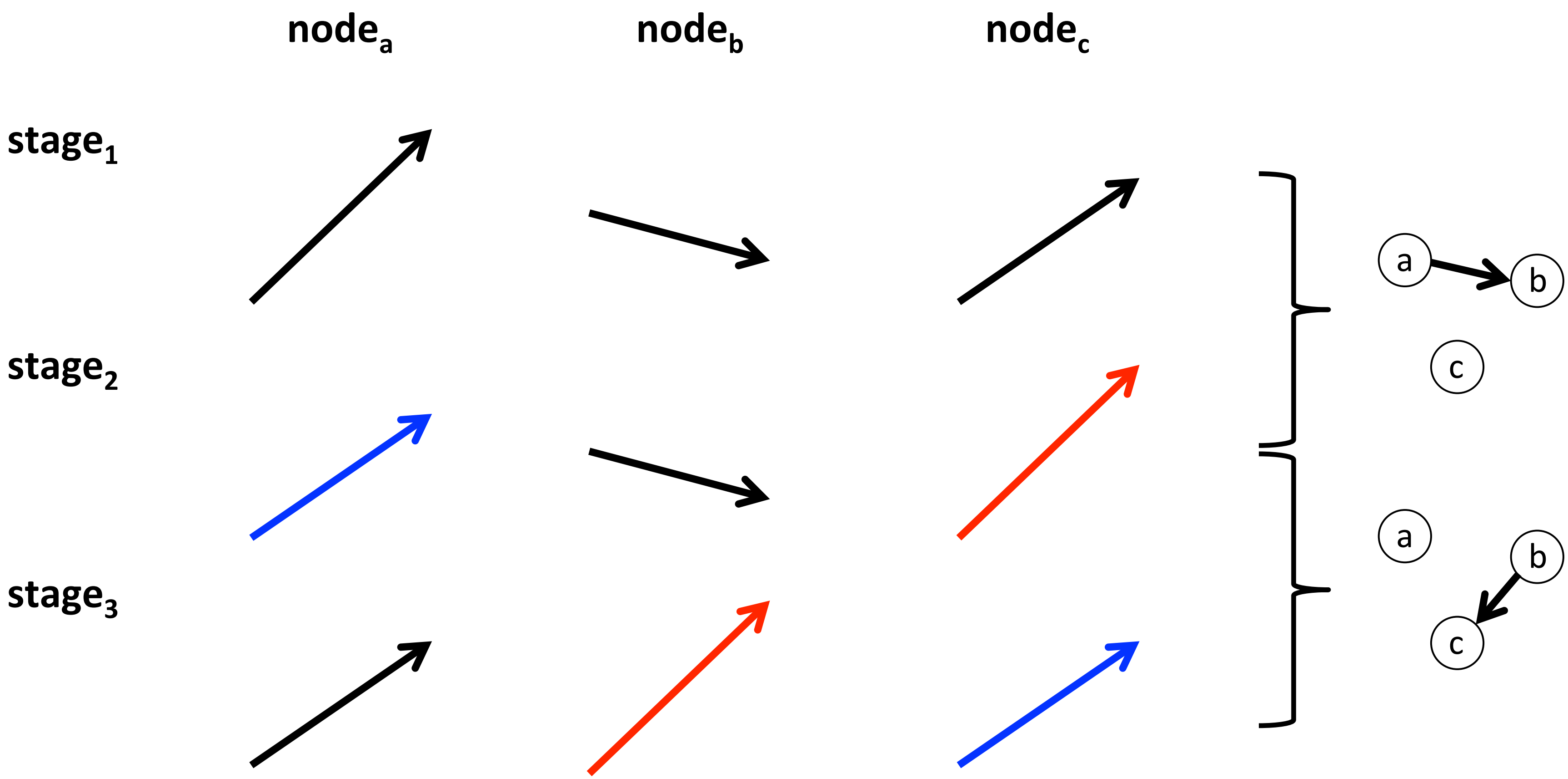
stage$_1$



Directed progression graphs

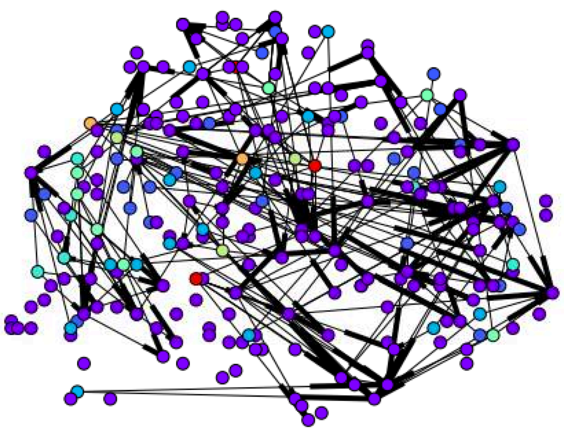


Directed progression graphs

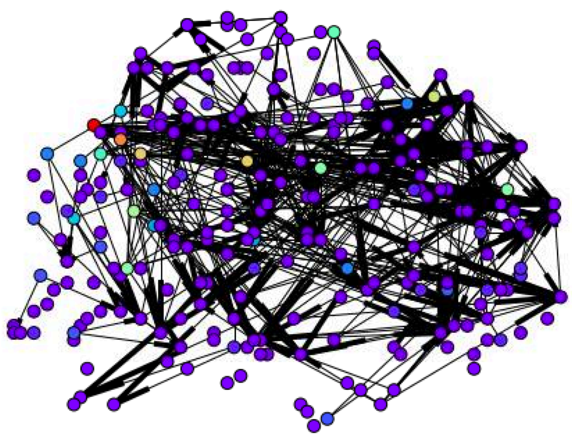


Directed progression graphs

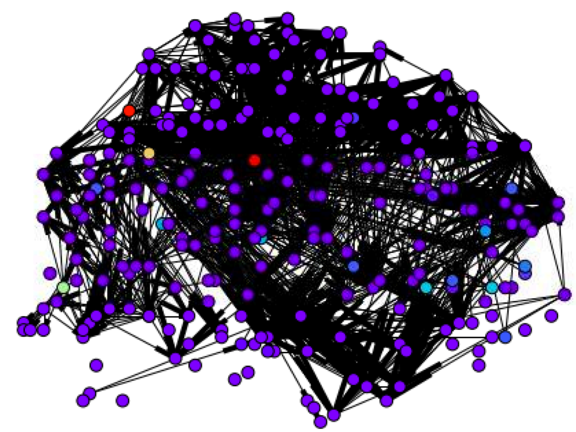
Low PIB- to High PIB-

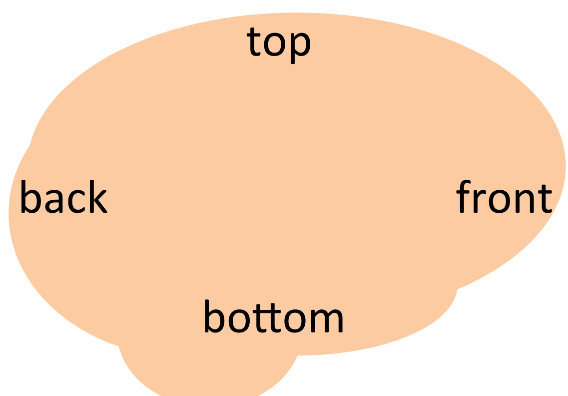


High PIB- to Low PIB+



Low PIB+ to High PIB+

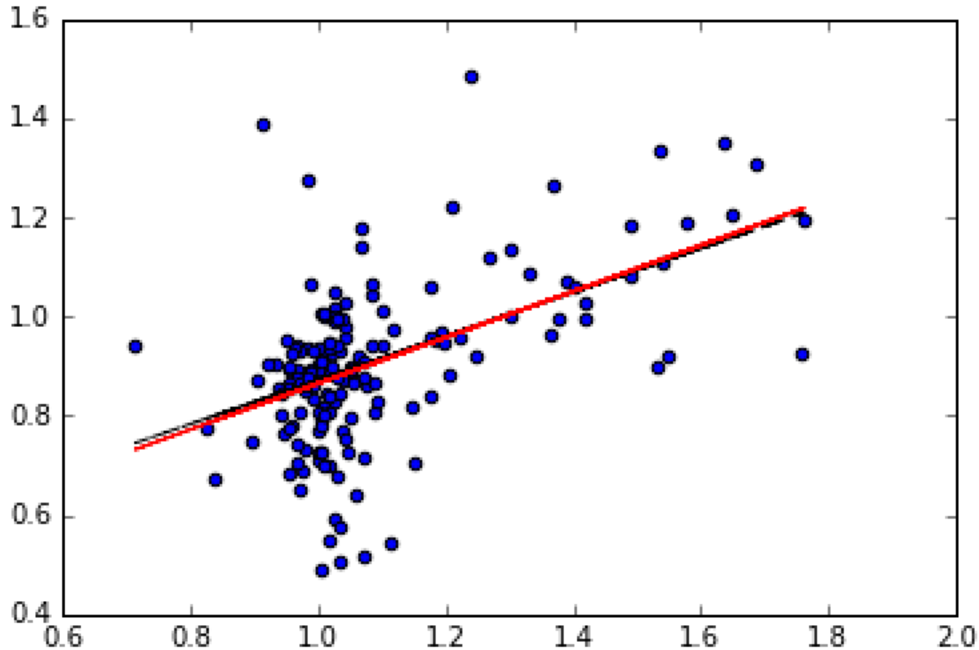




Directed progression graph

- Data-driven stages?

ROI Load
(PIB DVR)



Total Load
(PIB Index)

Acknowledgements

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