Development of a noisy brain

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Baycrest
Enriching Care
Enhancing Knowledge
Enlightening Minds

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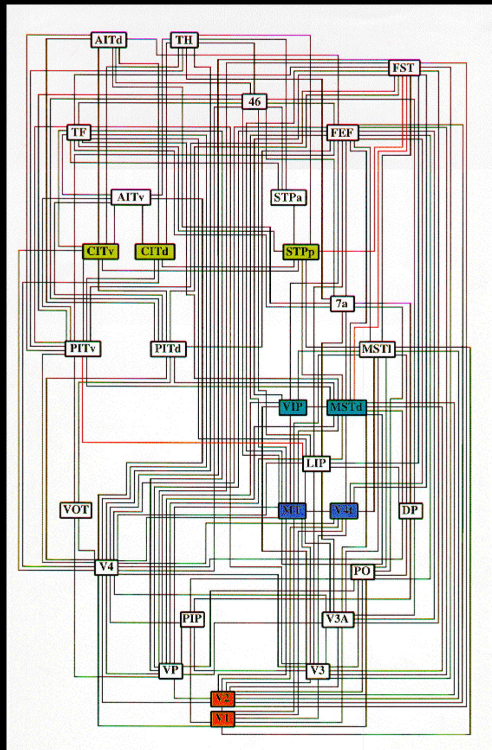
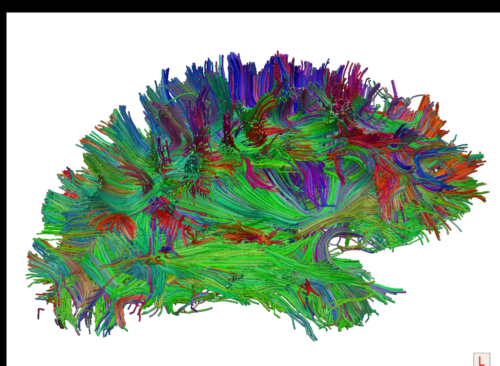
University of Toronto

Outline

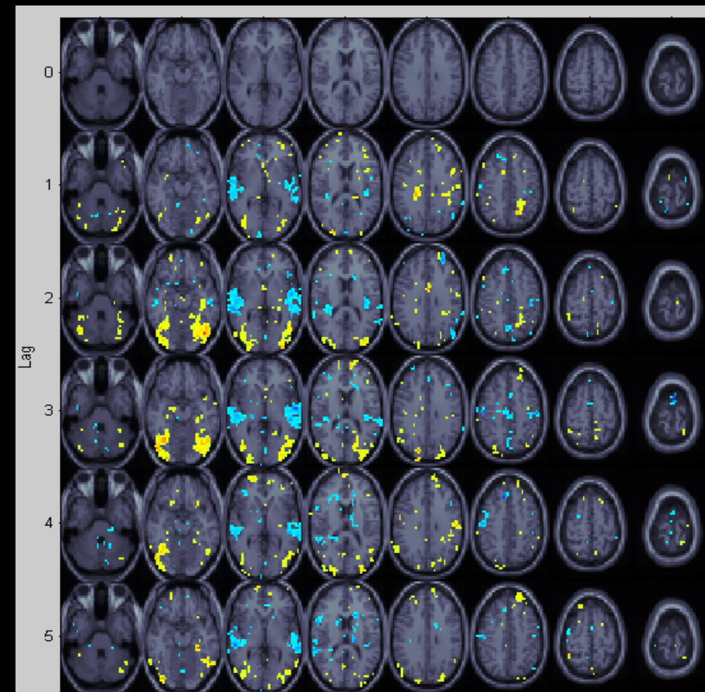
- Functional network dynamics
  - Network concepts
  - What is brain noise?
    - Pure noise vs. information
- Noise & Variability in the brain
  - Large-scale network models
  - Brain maturation
  - Healthy aging
  - Clinical conditions

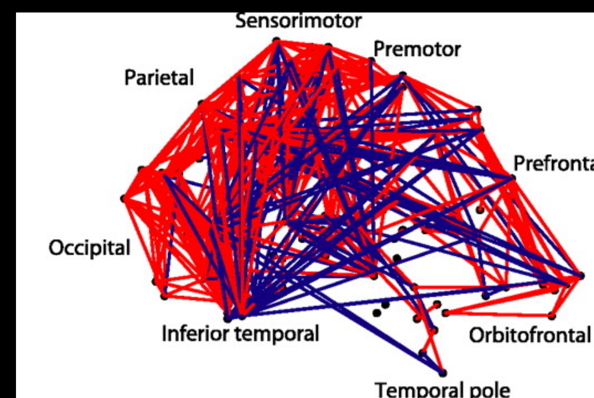




Anatomy

conduit





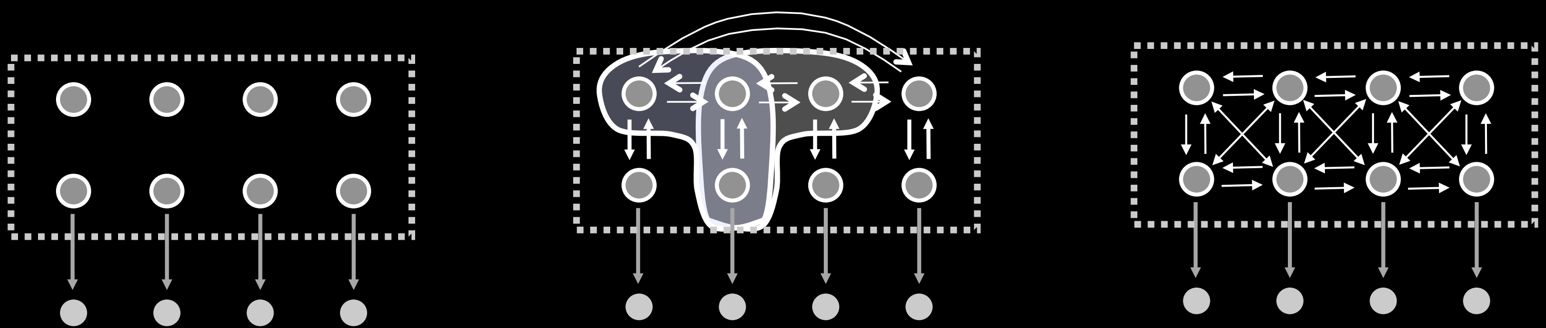
Function/dynamics

communication

The Language of Networks

- Key principles that help discuss networks
  - Small-world architecture
  - Connector & Provincial Hubs
  - Complexity
  - Integration & Segregation
  - Neural context and embeddeness

Functional and anatomical features



Independent Degenerate Redundant

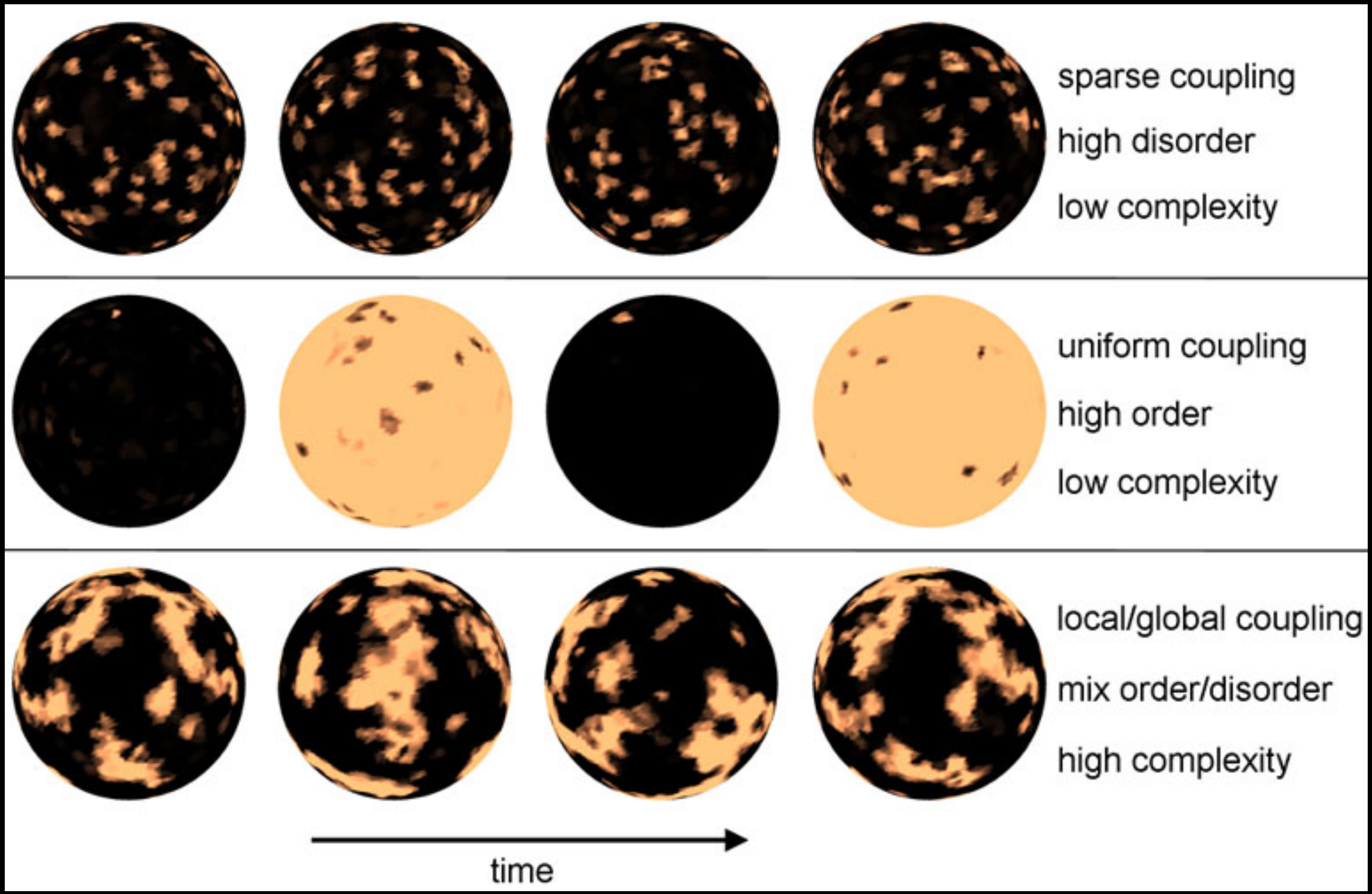
Maximum Complexity

Optimal ability to

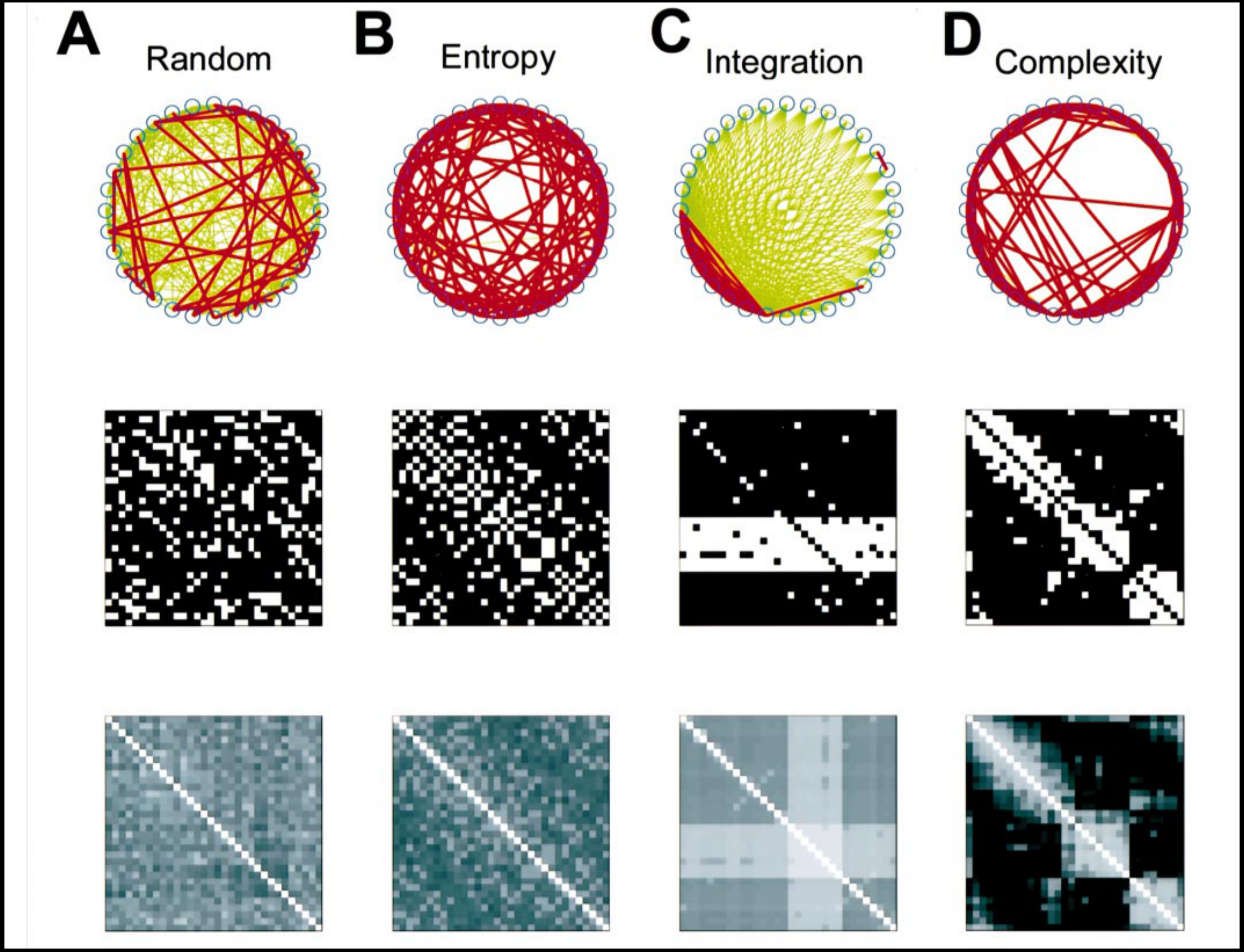
differeniate and integrate

Tononi, Sporns & Edelman, PNAS, 1999

Function, anatomy, complexity

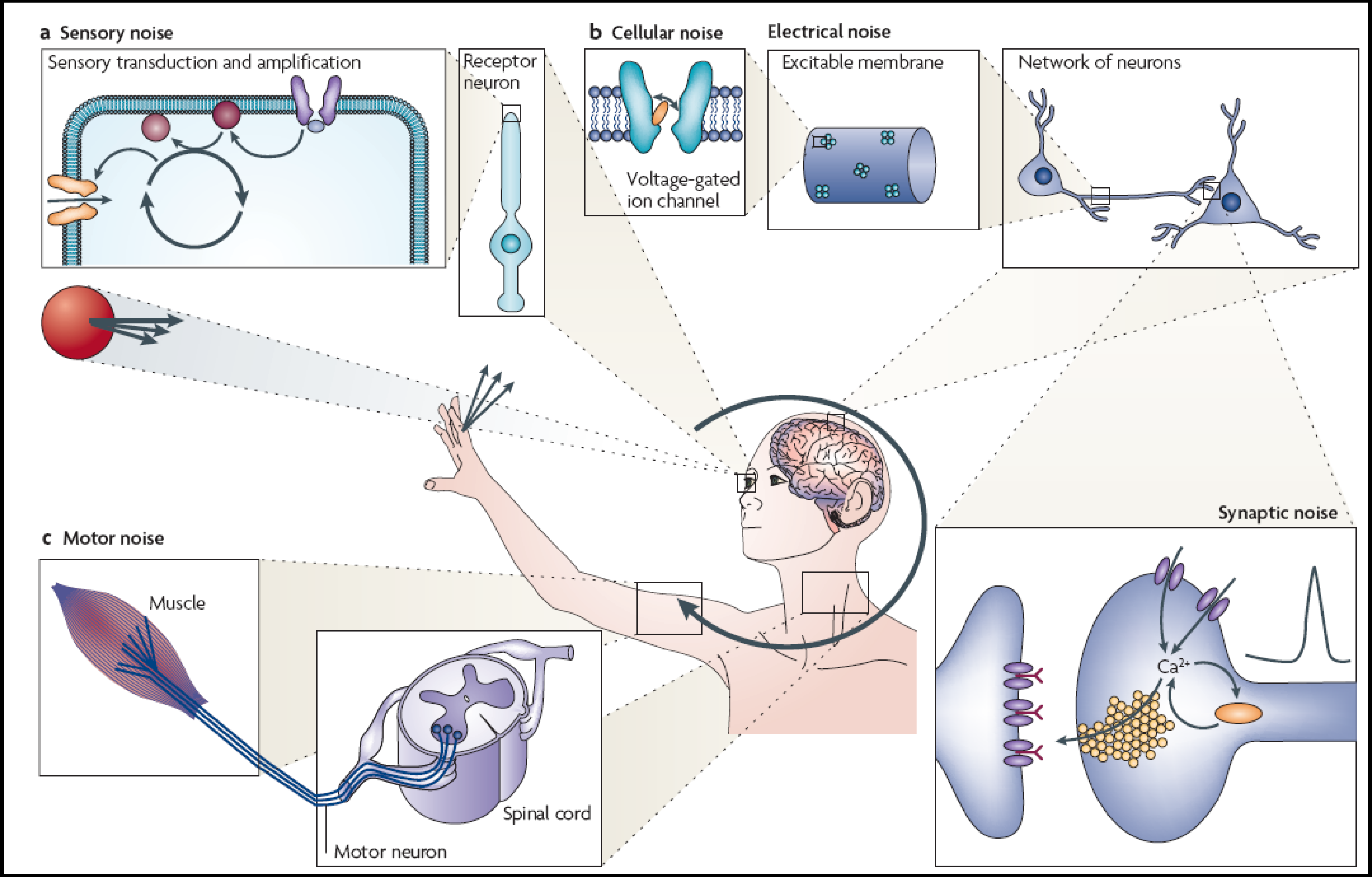


Optimizing complexity



Sporns, Tononi & Edelman, Cerebral Cortex, 2000

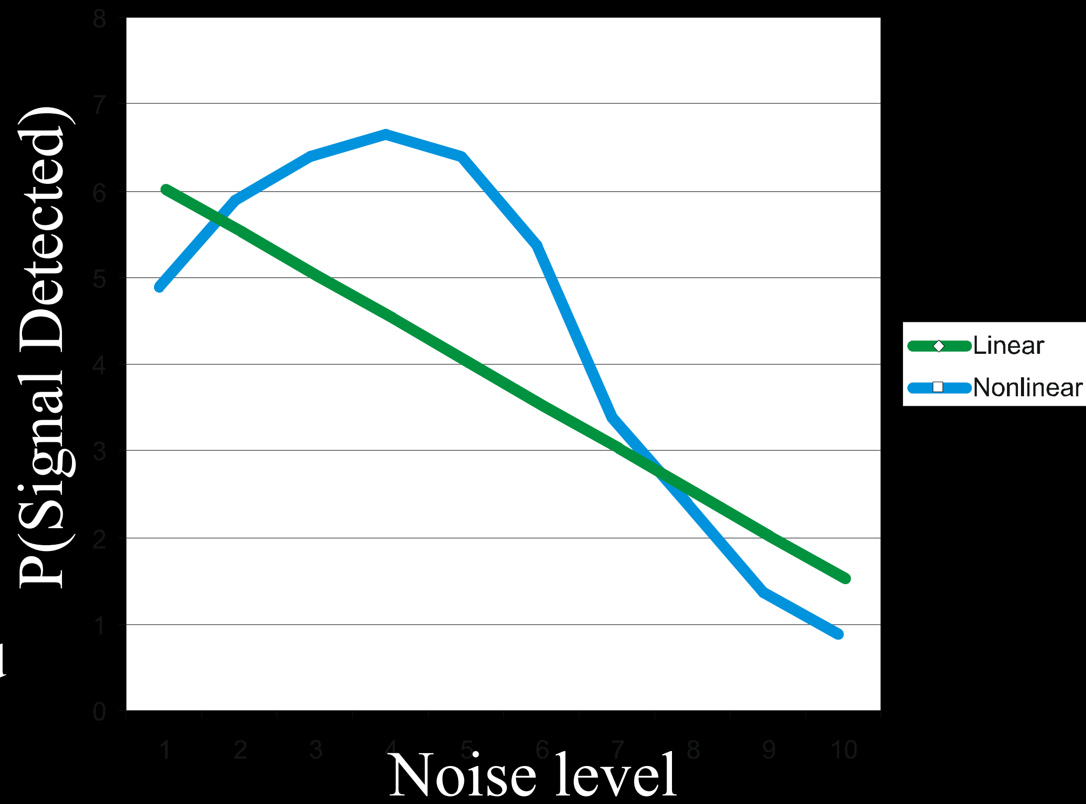
Sources of noise in the brain



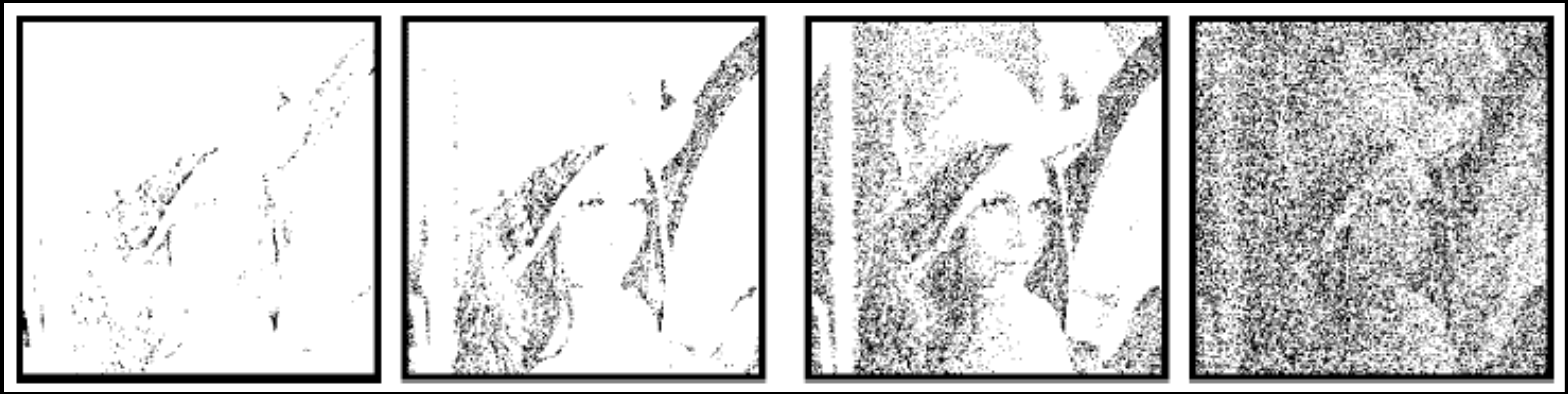
Faisal, Selen, & Wolpert, Nature Rev Neuro, 2008

Stochastic Resonance
Linear vs Nonlinear Systems

- A small amount of noise is beneficial in detecting weak signals
- Noise also beneficial in transmitting signals between neurons
- For dynamic systems, optimal noise necessary to maintain multistable state
  - *Complexity* & noise are related
  - Behavioural/cognitive repertoire

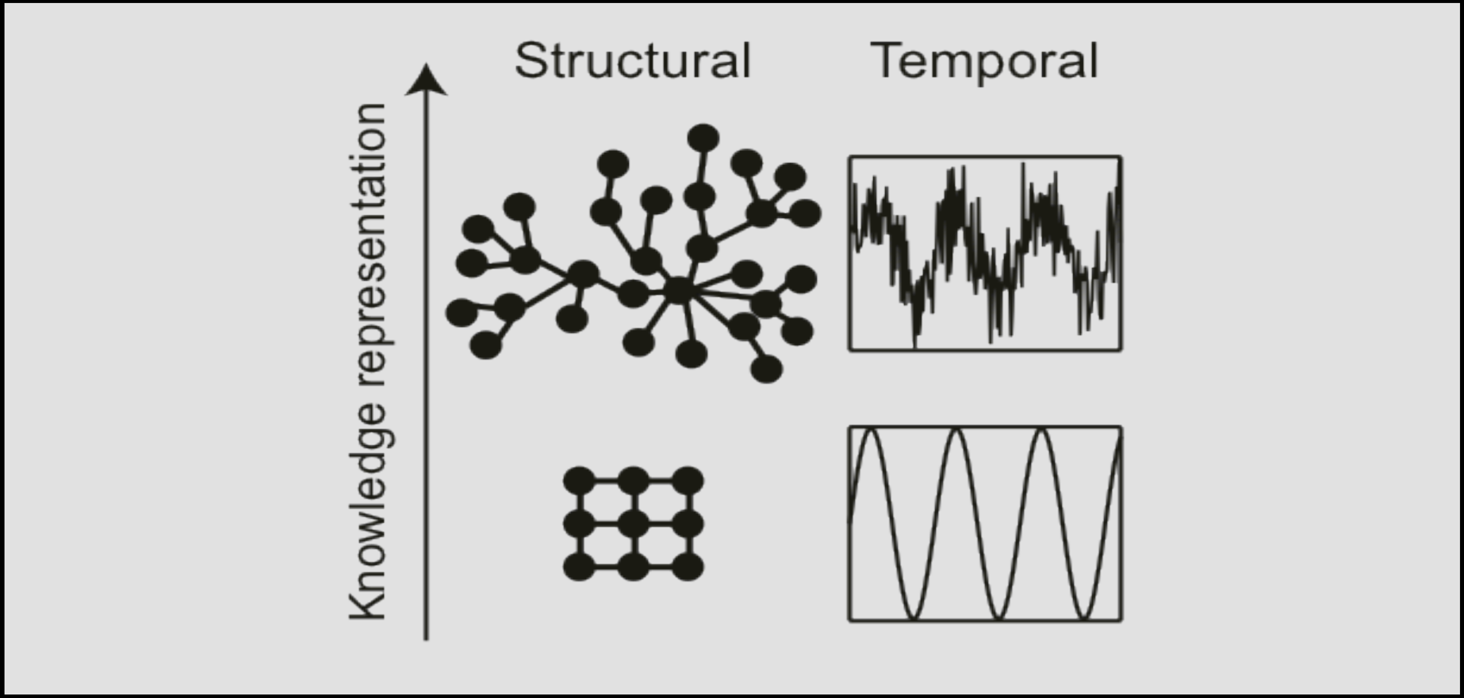


Stochastic Resonance
"Lena" & white noise



Mitaim & Kosko, Proc IEEE, 1998

Systems with complex structure generate "noisier" signals



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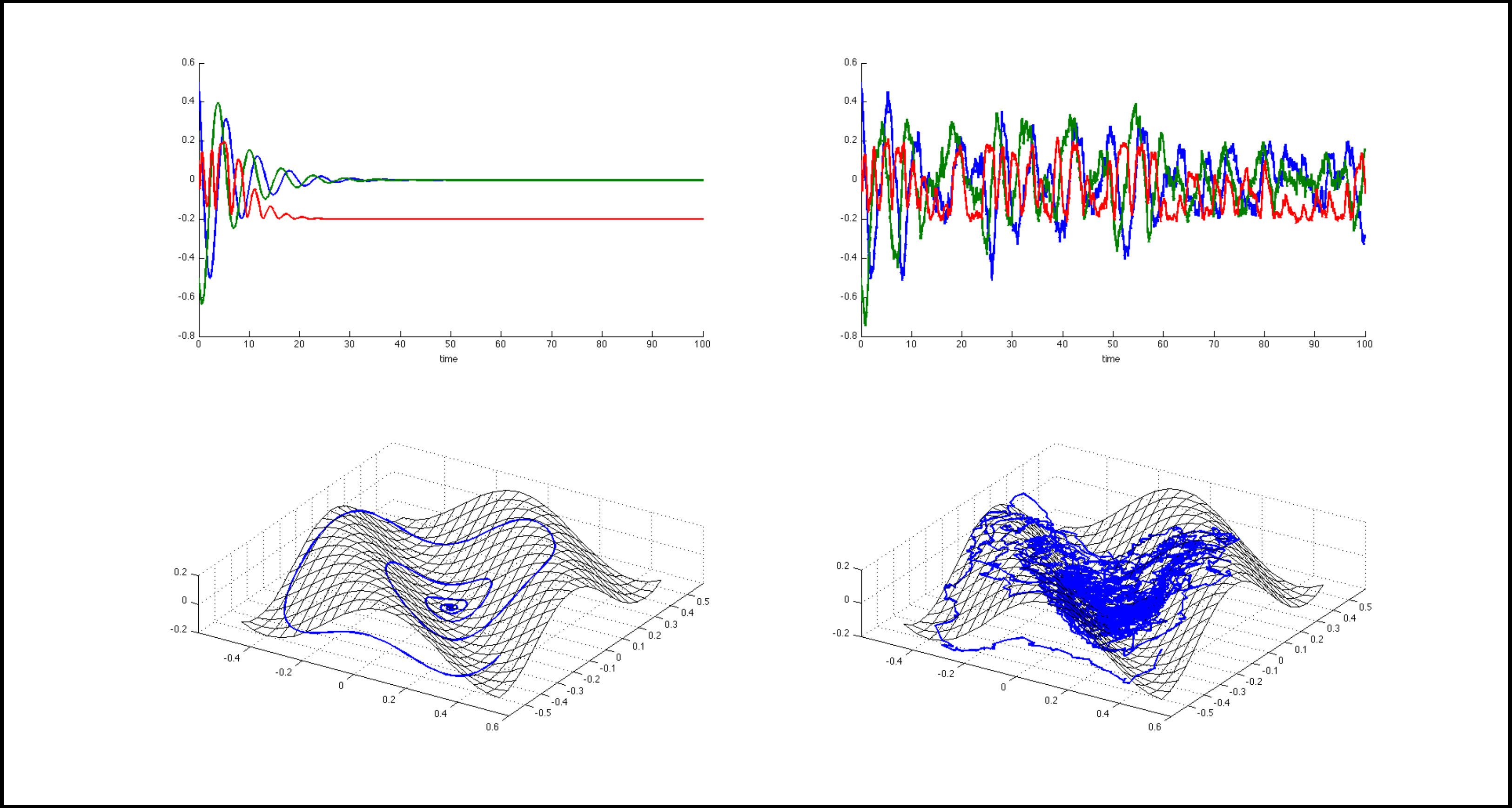
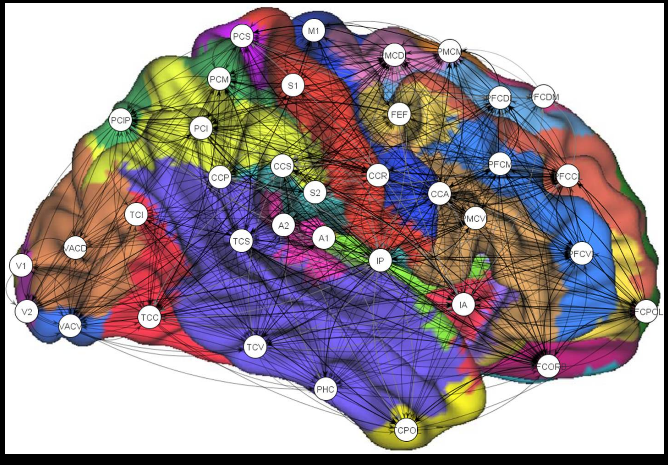
“Noisy” nodes

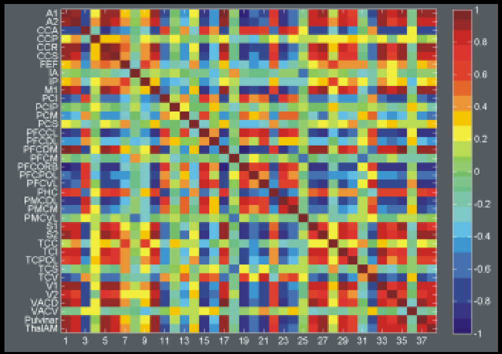

0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
0 10 20 30 40 50 60 70 80 90 100
time
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
0 10 20 30 40 50 60 70 80 90 100
time
0.2
0
-0.2
-0.4 -0.2 0 0.2 0.4 0.6
-0.5 -0.4 -0.3 -0.2 -0.1 0 0.1 0.2 0.3 0.4 0.5
0.2
0
-0.2
-0.4 -0.2 0 0.2 0.4 0.6
-0.5 -0.4 -0.3 -0.2 -0.1 0 0.1 0.2 0.3 0.4 0.5

Towards the virtual brain: network modeling of the intact and the damaged brain

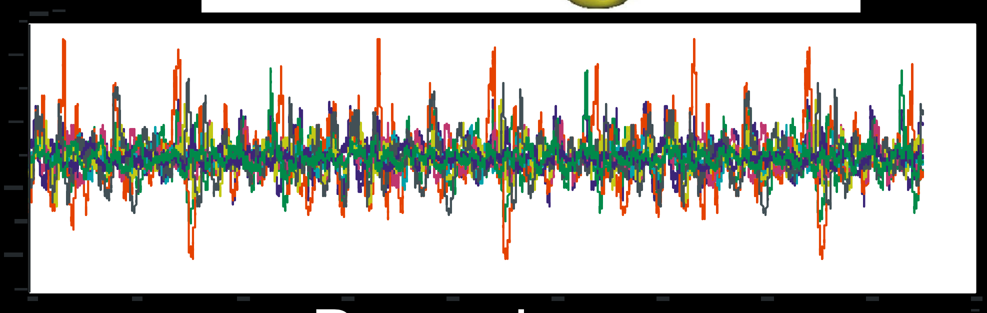
V.K. JIRSA[1], O. SPORNS[2], M. BREAKSPEAR[3,4], G. DECO[5], A.R. MCINTOSH[6]

- Nodes connections & placement based on neuroanatomy
- Nonlinear equations characterize dynamics at each node
- Model produces realistic activity measures such as EEG and fMRI





Network Interactions



Dynamics

THEVIRTUALBRAIN.

http://www.thevirtualbrain.org

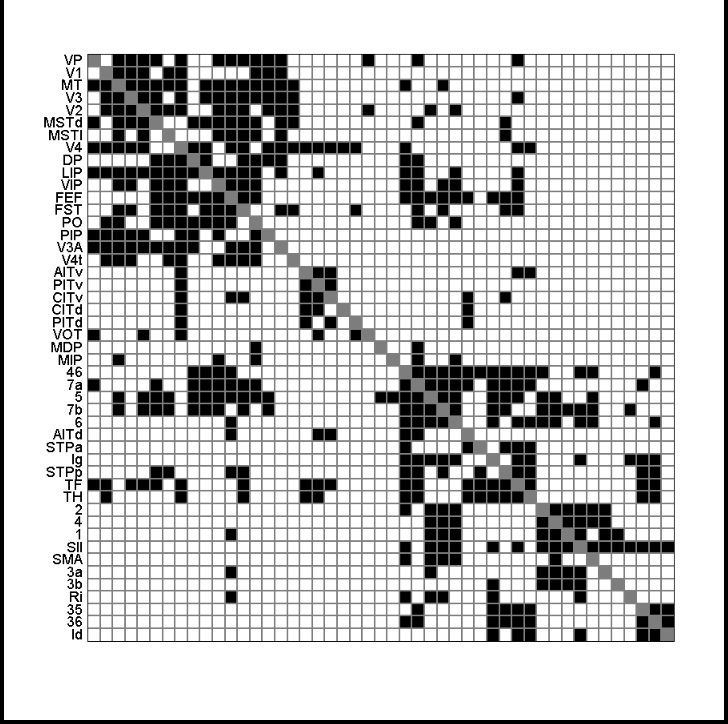
Intrinsic Dynamics (Resting State) Model

Connectivity

Structural connection matrix of regions of *macaque neocortex* connected by inter-regional pathways.

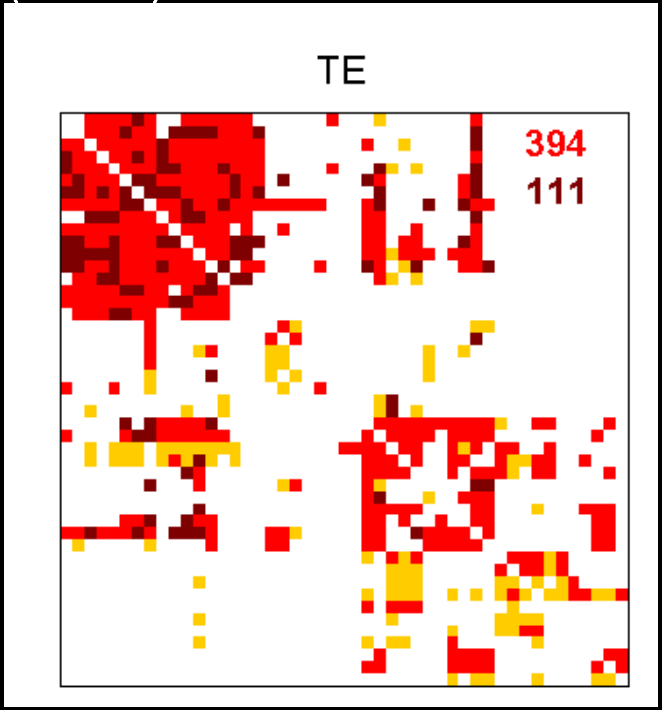
Dynamics

Neural mass model



Extracting Functional Networks

When using long samples (~240 secs.), transfer entropy functional networks show high overlap with the underlying structural network (~80%).

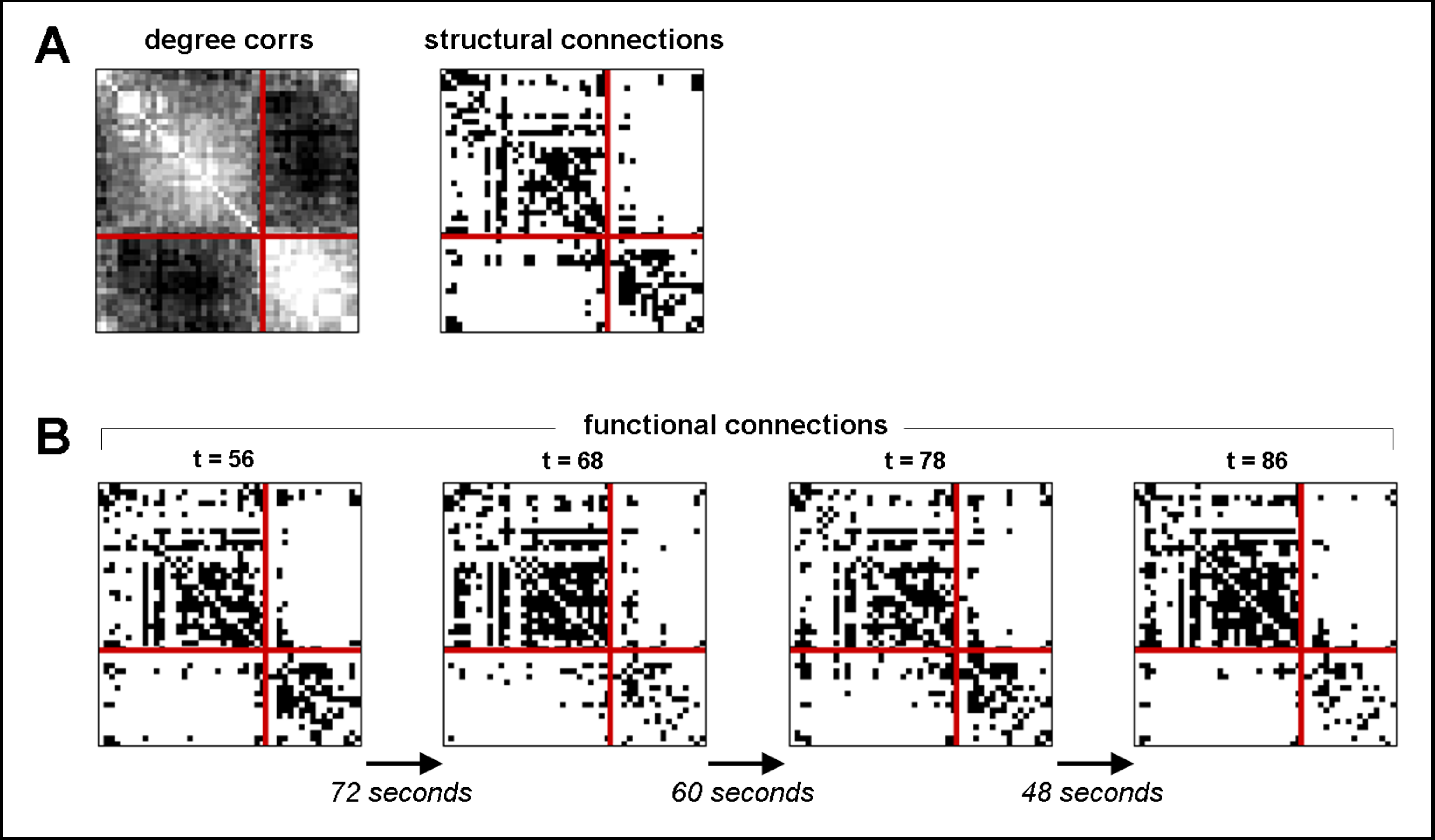


Honey, Breakspear, Kötter, Sporns (2007) PNAS

Intrinsic Dynamics (Resting State) Model

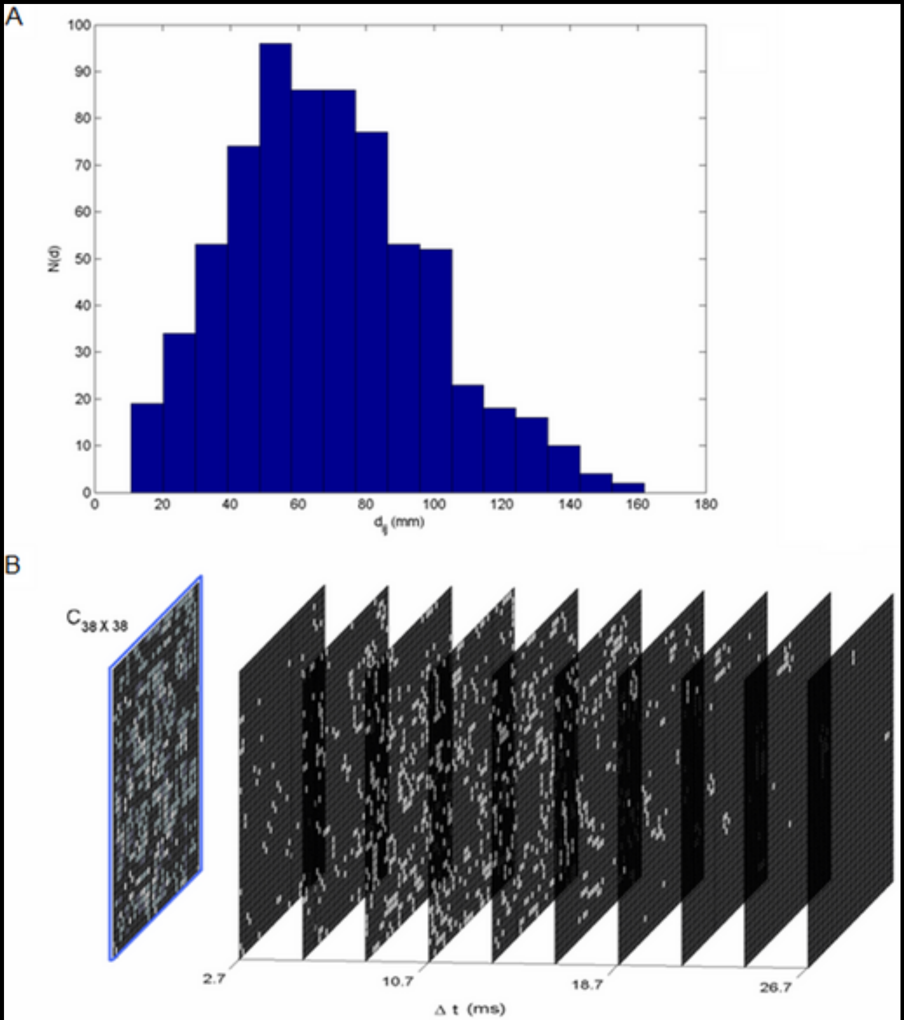
Functional Networks form a Variable Repertoire

Over shorter time scales, functional connectivity patterns show significant variations



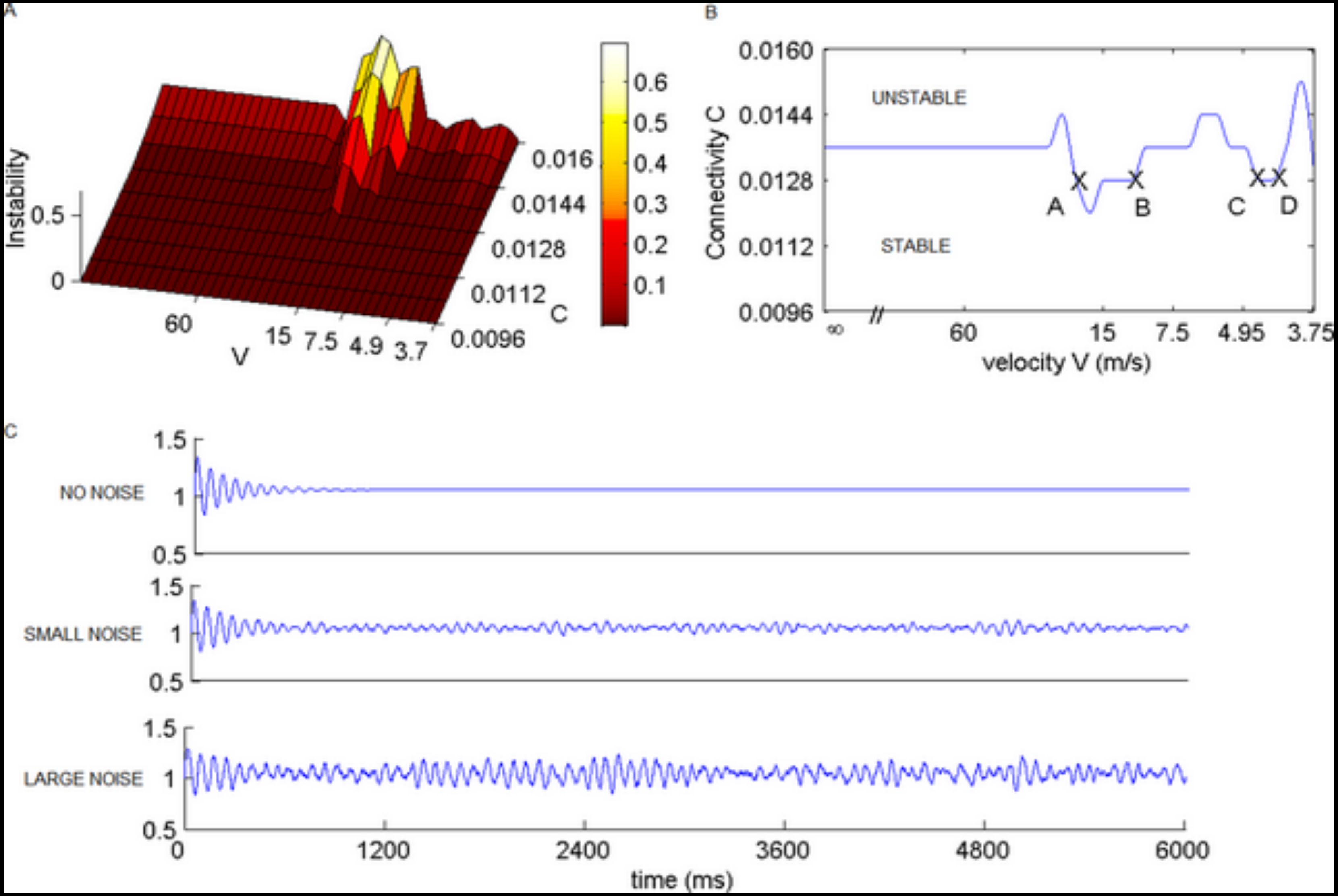
Honey, Breakspear, Kötter, Sporns (2007) PNAS

Space time structure of couplings.

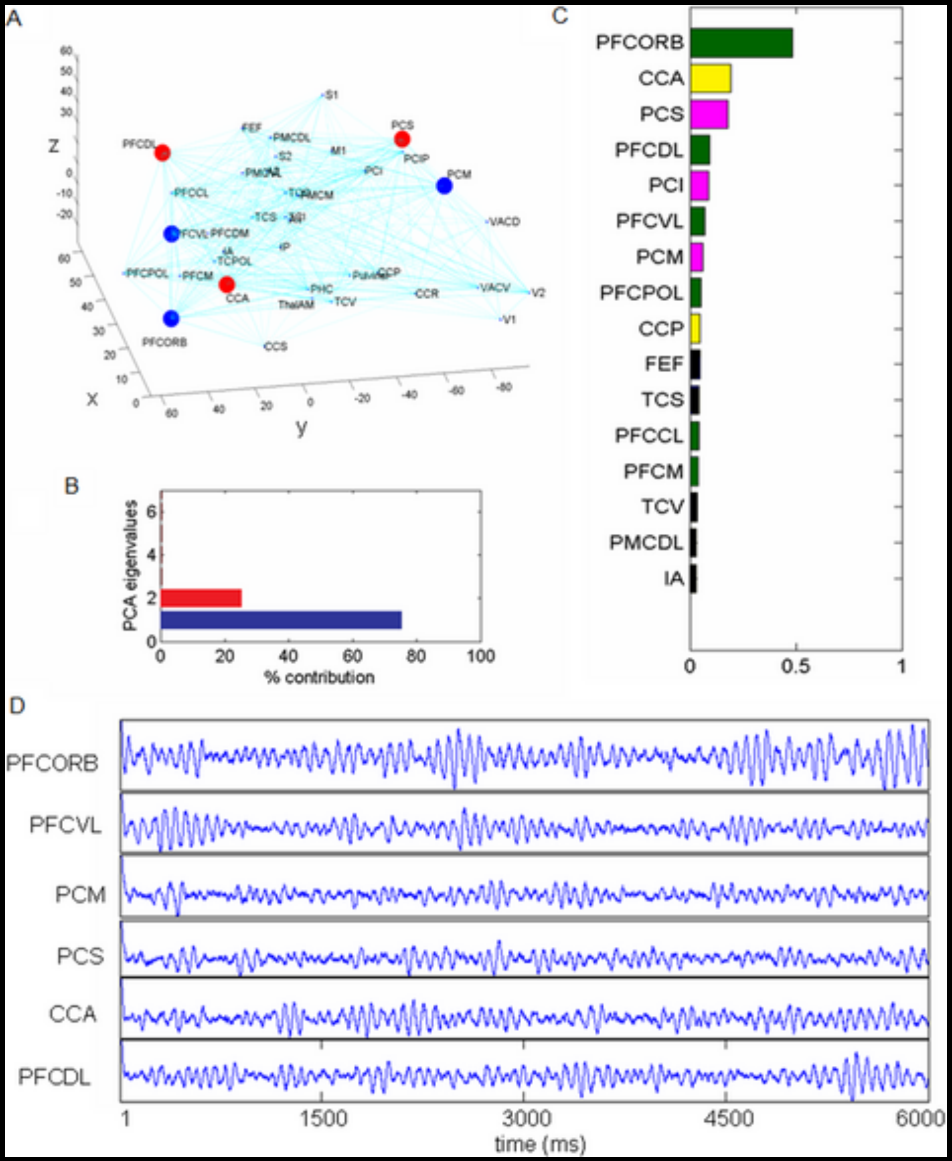


Ghosh A, Rho Y, McIntosh AR, Kötter R, et al. (2008)

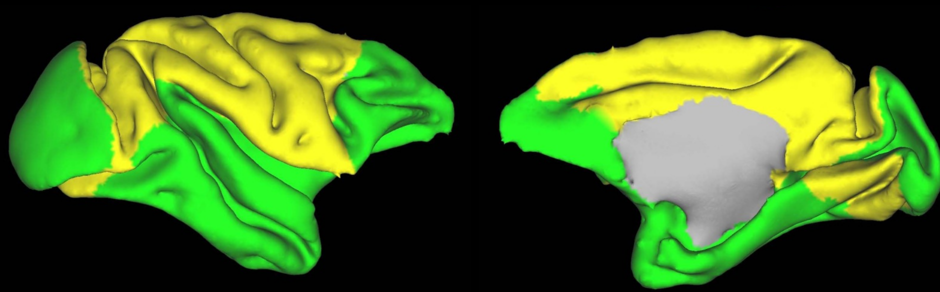
Stability regimes

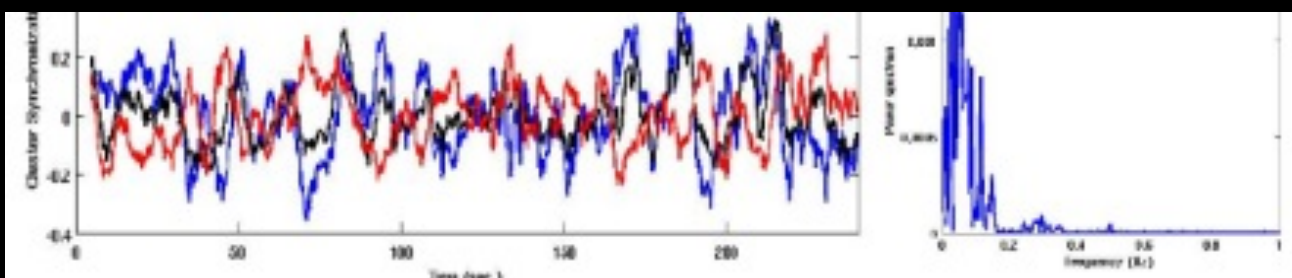


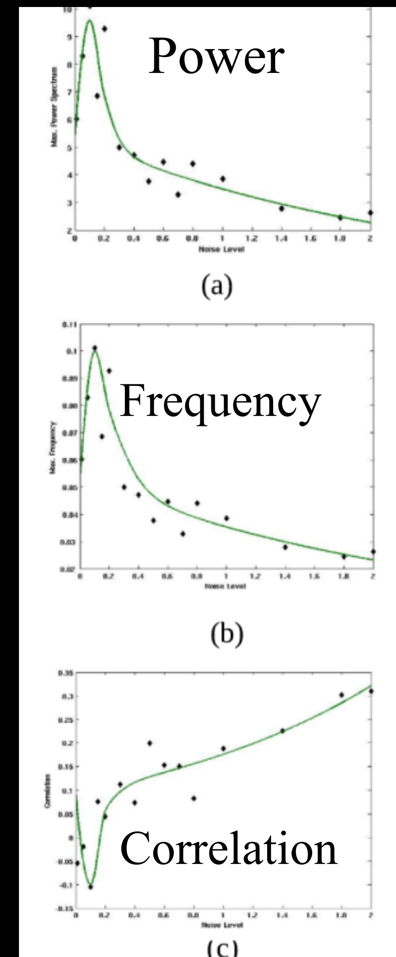
PCA of the network dynamics close to the instability



Influence of noise on intrinsic activity and large-scale oscillations

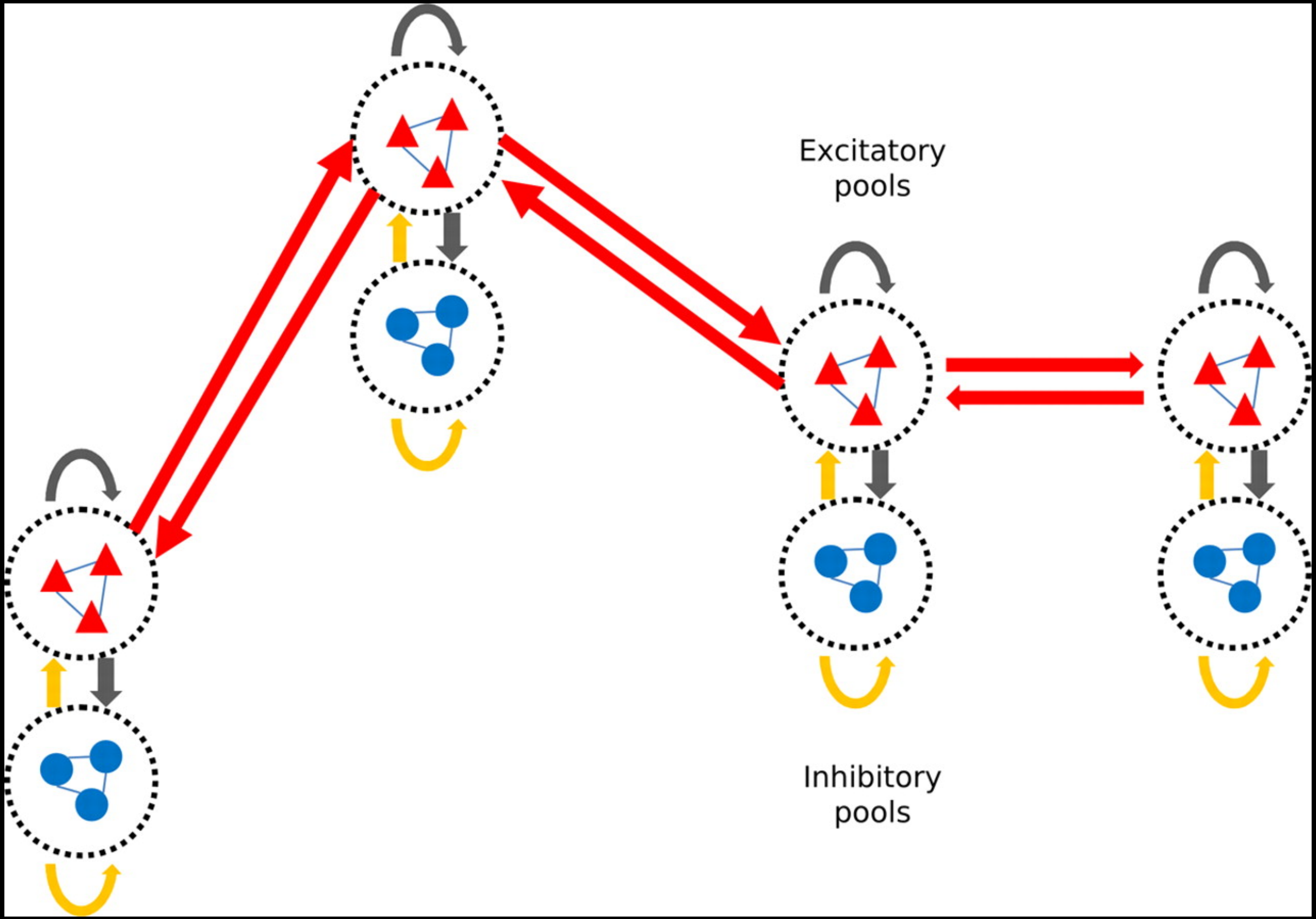






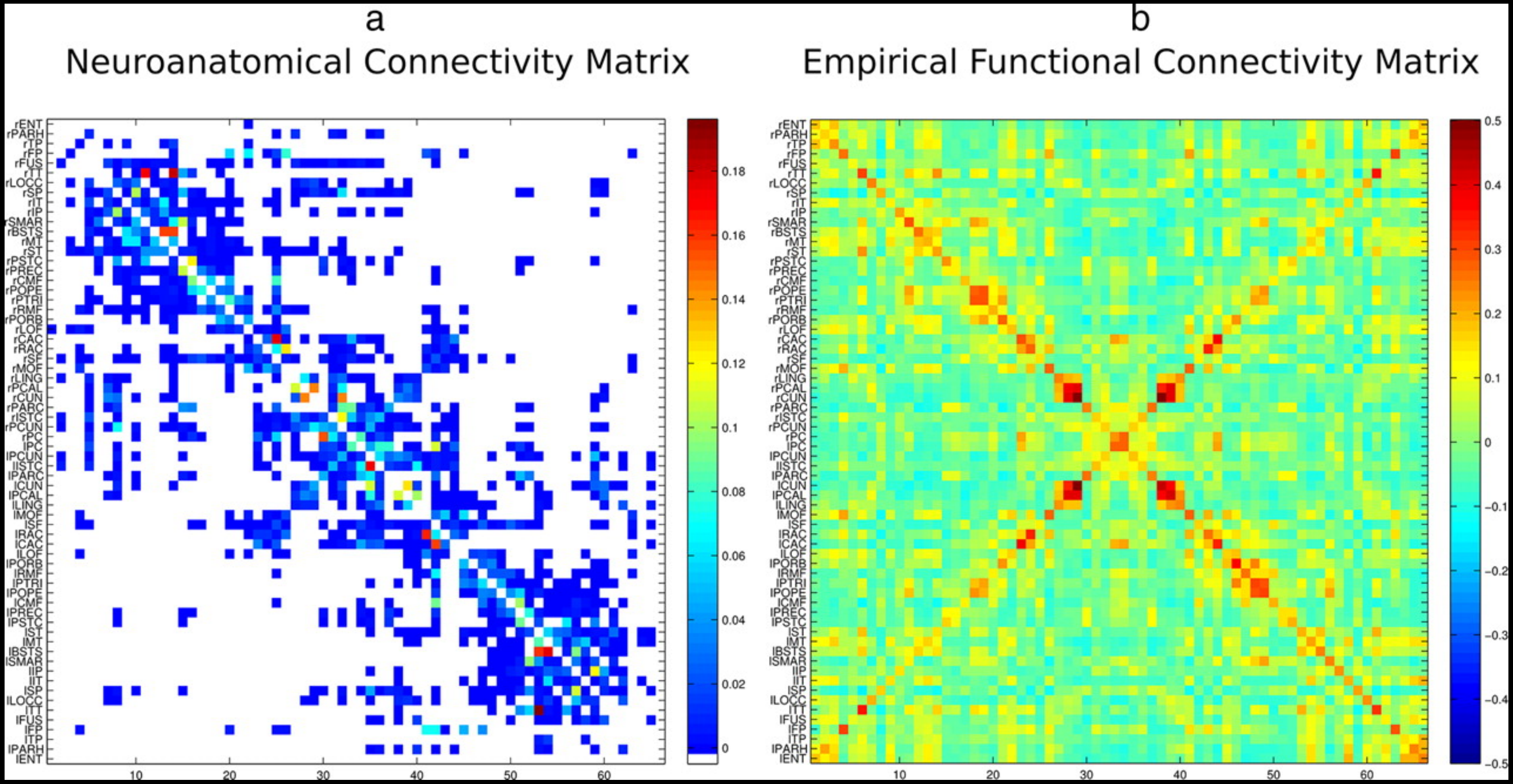
Deco, Jirsa, McIntosh, Sporns & Kotter, PNAS, 2009
Deco, Jirsa & McIntosh, Nature Rev Neurosci, 2011

Ongoing Cortical Activity at Rest: Criticality, Multistability, and Ghost Attractors



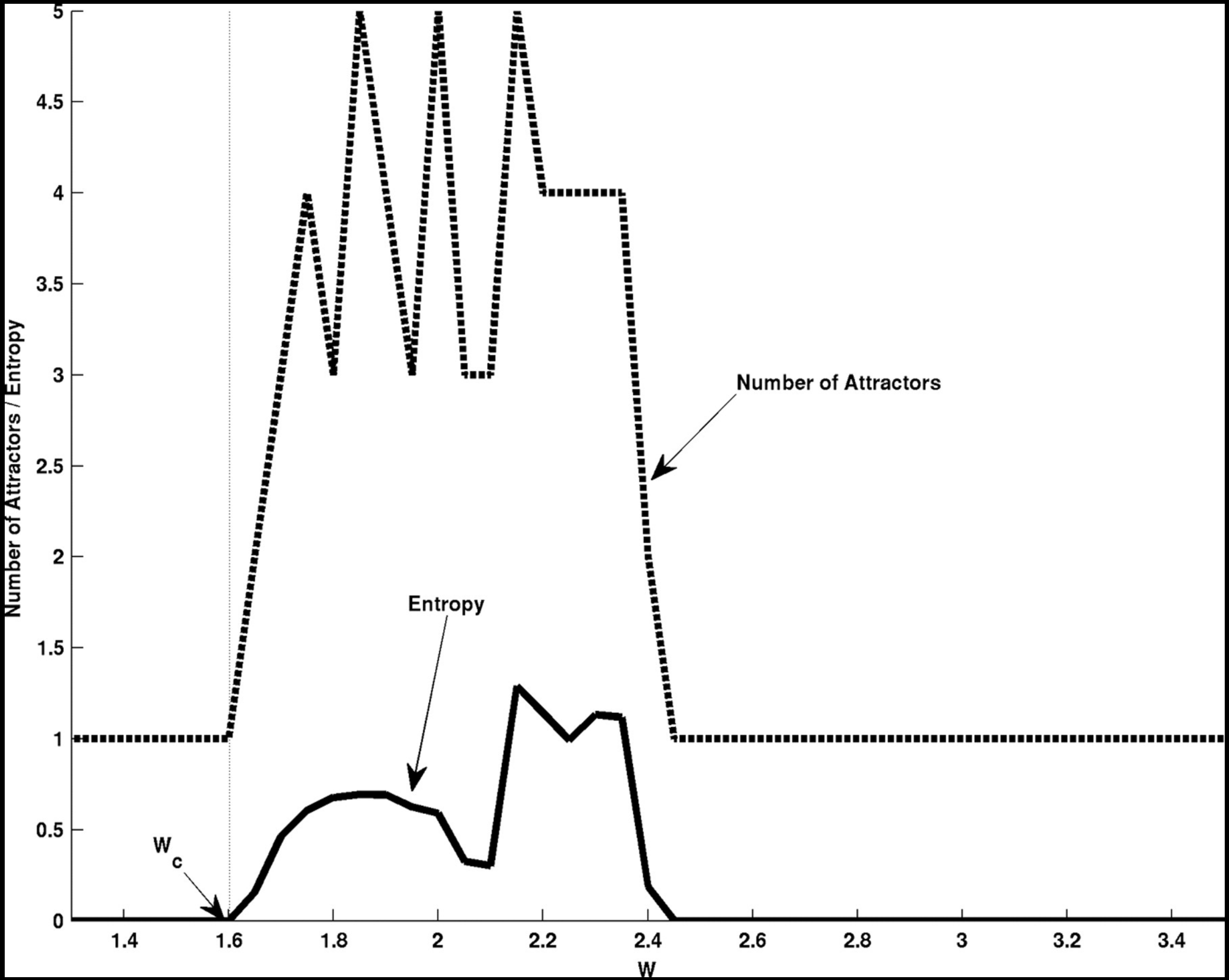
Deco G , Jirsa V K J. Neurosci. 2012;32:3366-3375

Empirically-derived Neuroanatomical Connectivity matrix obtained by DSI tractography and functional connectivity matrix



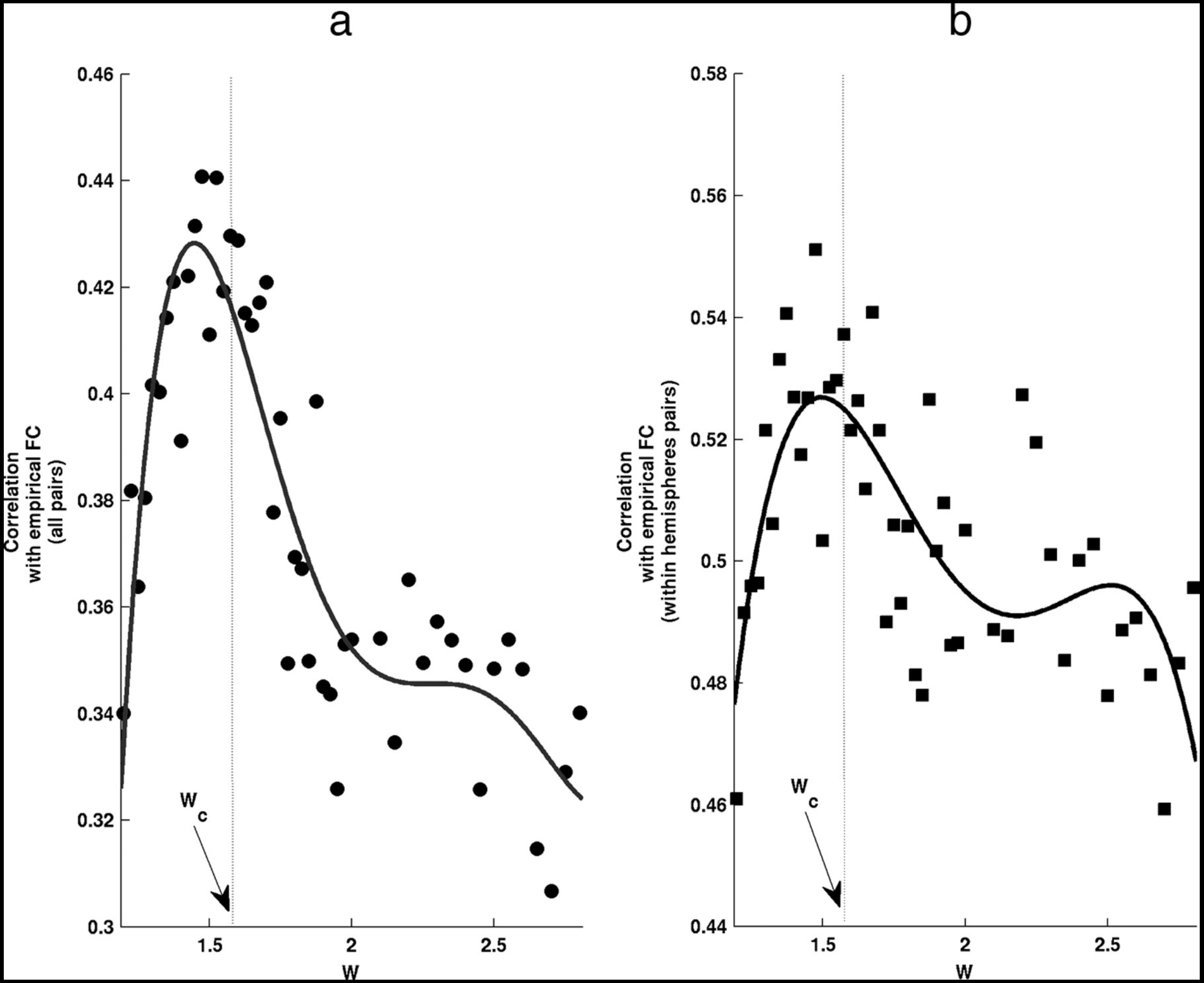
Deco G , Jirsa V K J. Neurosci. 2012;32:3366-3375

Mean-field analyses of the attractor landscape as a function of the global inter-areal coupling strength.



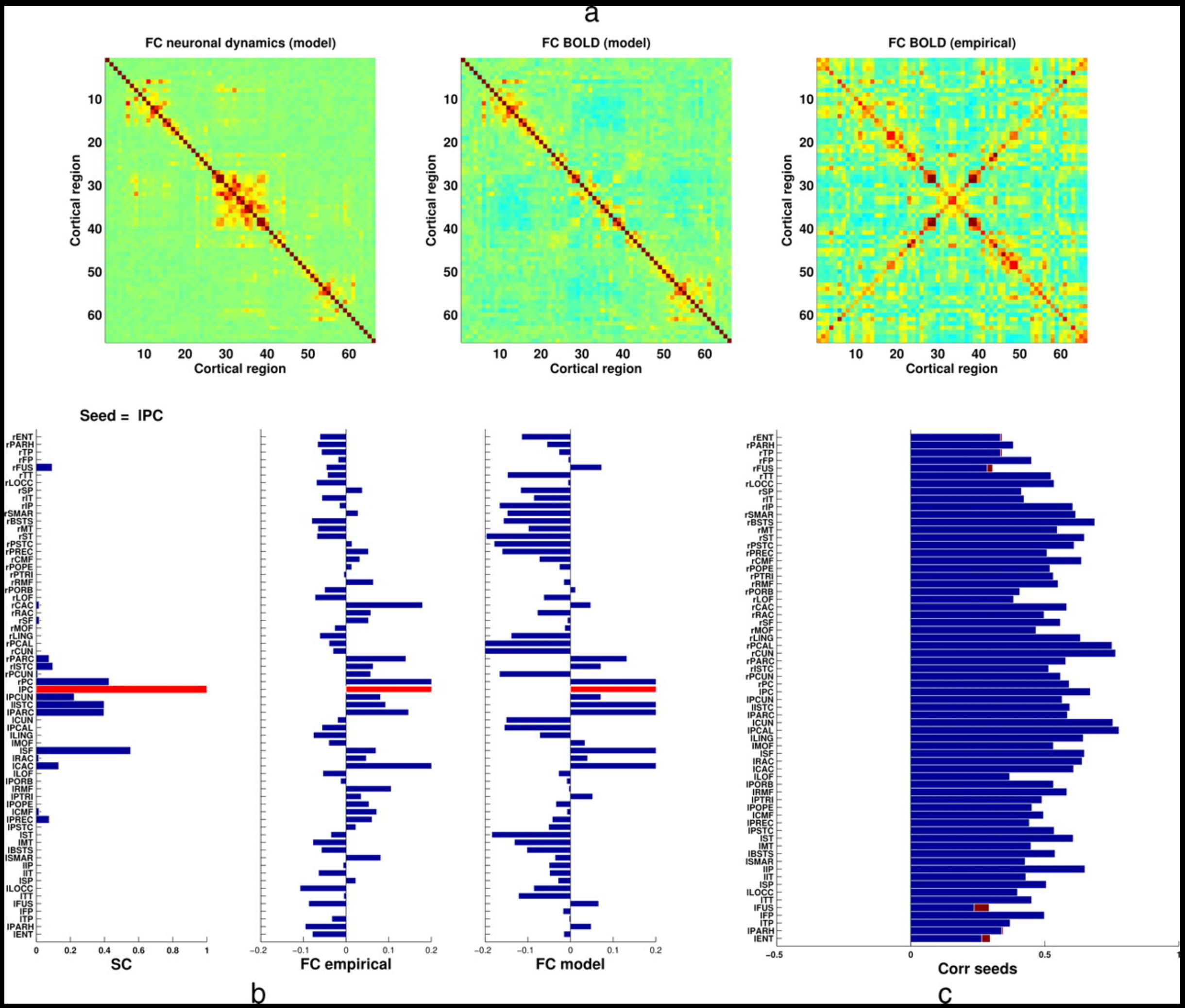
Deco G , Jirsa V K J. Neurosci. 2012;32:3366-3375

Fitting of empirical data as measured by the correlation of functional connectivity as a function of the global coupling parameter W.



Deco G , Jirsa V K J. Neurosci. 2012;32:3366-3375

Detailed comparison between the neuroanatomical connectivity matrix, the empirical and the simulated functional connectivity for the working point W = Wc = 1.6 at the edge of the bifurcation. a, Left, Functional connectivity matrix based on the firing rates...



Deco G , Jirsa V K J. Neurosci. 2012;32:3366-3375

SfN SOCIETY FOR NEUROSCIENCE The Journal of Neuroscience

Beneficial effects of brain noise is not a new idea

- 46 years ago: Lawrence Pinneo (PsychReview, 1966)
  - Neural **variability "is not merely noise "** (p 245); it enables the stabl and functional output of a neural system = TONIC activity!
  - **...variability** is in fact, the **"functional substrate of the brain"** (p242)

Psychological Review
1966, Vol. 73, No. 3, 242–247

ON NOISE IN THE NERVOUS SYSTEM [1]

LAWRENCE R. PINNEO
Delta Regional Primate Research Center, Tulane University

Treisman and Hebb have suggested that "spontaneous," "random," or "background" activity in the nervous system constitutes "noise" in discrimination and learning; that is, this type of activity has no functional value to the organism. This paper attempts to show that tonic activity, a term including all of the types of activity listed above, is rather the functional substrate of the brain. Examples are cited for the skeletal and autonomic motor systems, the primary sensory systems, and the diffuse ascending and descending reticular activating systems to show that the tonic activity in the entire brain enters into all discrimination and learning, and, in agreement with Lashley, represents the neural basis of behavior.

Two recent theoretical papers have argued that "noise" in the nervous system has interfering effects in discrimination and learning. In one, Treisman (1964) has suggested that three sources of noise limit discrimination: (*a*) the irreducible physical variability of the stimulus, (*b*) the "spontaneous" neural background activity to which a stimulus is added, and (*c*) the neural noise arising from variation in the pathways transmitting messages centrally. Based on these three sources of noise, Treisman has worked out a complicated signal-detection theory to explain the form of the Weber function for visual intensity discrimination and for other sense dimensions.

In the other paper, Hebb (1961) raised the question of the interfering effects of random activity in the nervous system during learning of a specific task. By learning he meant the modification of the direction of transmission in the central nervous system (CNS) at the synapse. He pointed out that a large brain such as a mammal's has many more neurons present than are necessary for learning a specific task. Therefore, random activity in the neurons not involved in learning the task constitutes noise, which Hebb felt must interfere with learning.

[1] This work was supported by National Institutes of Health, United States Public Health Service Grants FR-00164-03 and NB-04951-01.

These two papers illustrate a widely held misconception of brain function, namely, that the spontaneous, random, or background discharge of neurons has little or no functional value; that is, this activity has no information value for the organism and therefore is noise in the communications sense of the word. In this theoretical note I attempt to show that the *neural* noise to which Treisman and Hebb refer (leaving out Treisman's first category) is not noise at all, that this neural activity does not limit discrimination nor interfere with learning, and that in fact this activity is essential to discrimination and learning.

Arduini (1963) has suggested that there are fundamentally two types of nervous discharge, and he has carefully defined them; his definitions will be used in this paper. Borrowing from the terminology applied to muscle activity, Arduini defines "phasic" activity as a transient increase or decrease in impulse firing rates of neurons that is time locked to a particular stimulus. A familiar example is the evoked response. "Tonic" activity on the other hand is nontransient, or continuous, neural discharge in which the average firing rate is random and constant and is *not* time locked to a stimulus. So-called spontaneous activity (a dubious term at best since it implies the discharge of neurons without benefit of influences external to the neurons),

Tonic vs. phasic activity

- "Phasic" or stimulus-driven activity argued to operate on existing tonic activity to allow behaviours of interest.
  - This conceptualization reaches back at least to **Lashley (1951)**.

Tonic activity is the basis of the human mind!

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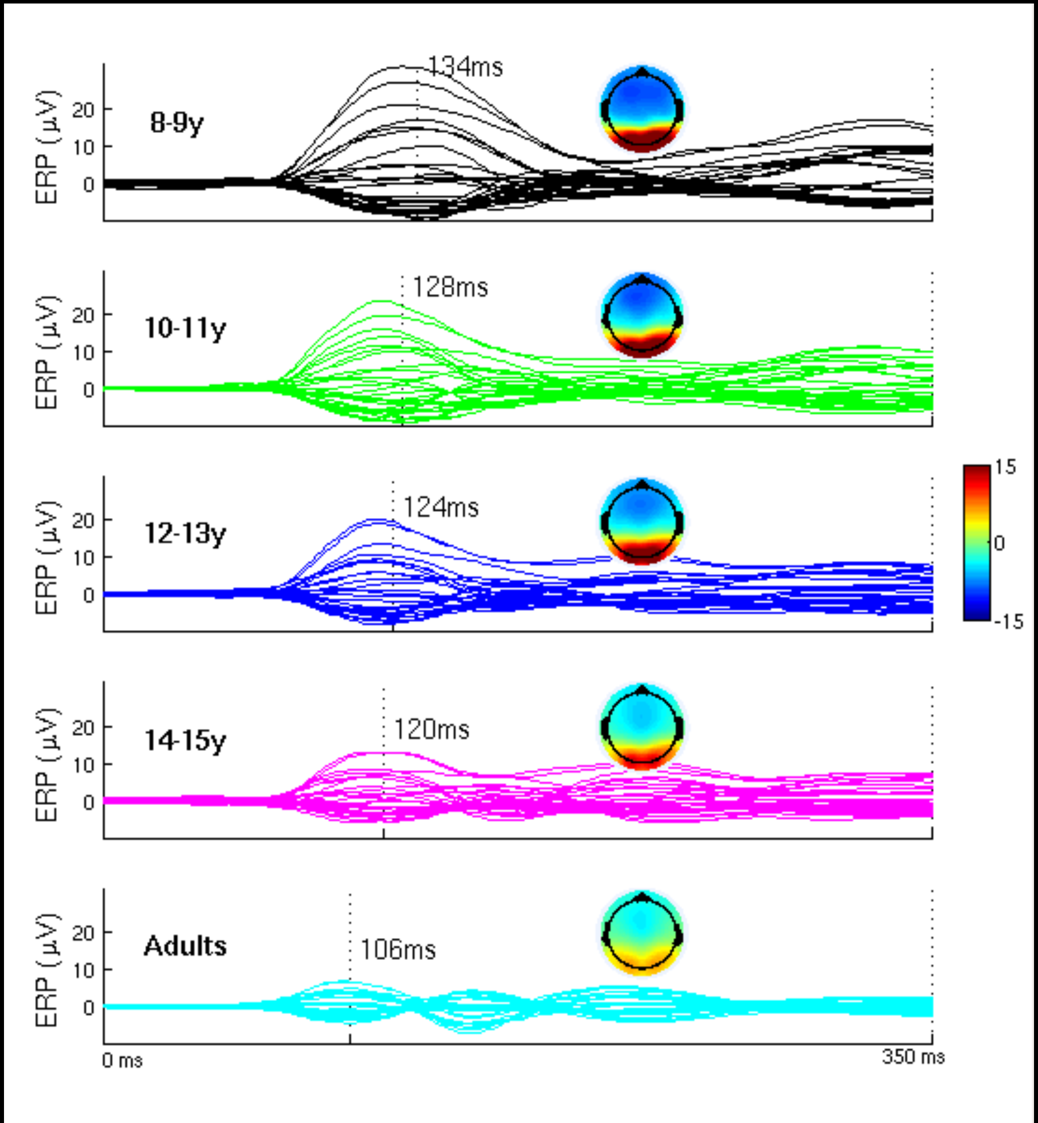
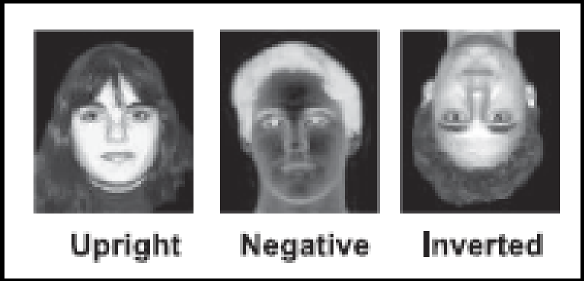
  - Large-scale network models
  - Brain maturation
  - Healthy aging
  - Clinical conditions

Noise & Variability in the Brain

- If "brain noise" reflect the brain' s repertoire, it should change with maturation
  - Can developmental changes be partly accounted for by changing noise structure?
- Hypothesis:
  - Early maturation may lead to an *increase* in internal noise
  - The behavior of the aging nervous system is consistent with a *reduction* in internal noise.

Maturation & Brain Variability





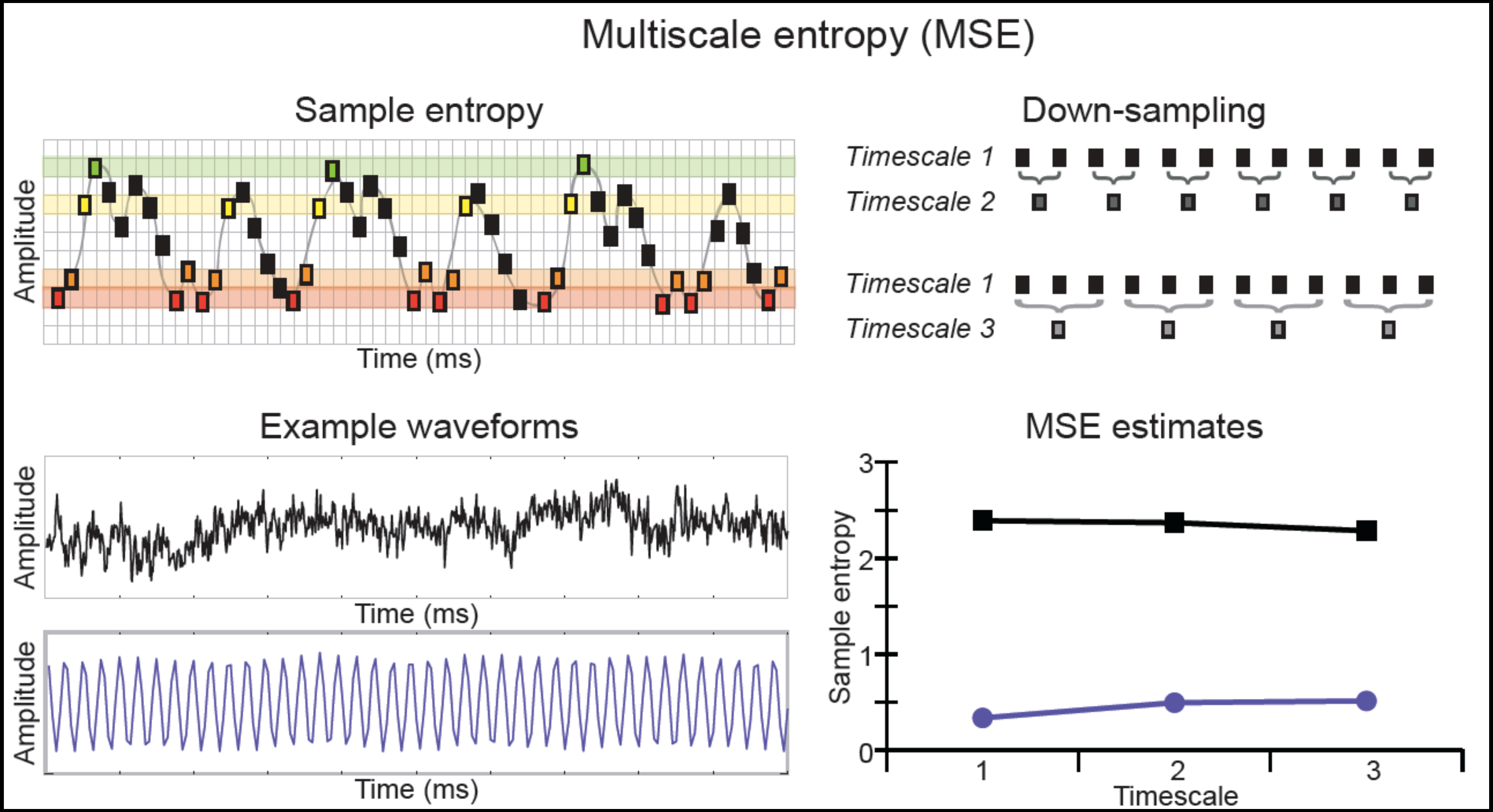
McIntosh, Kovacevic & Itier, PLoS Comp Biol, 2008

How do we measure variability?

- Reduced internal noise should relate to reduced variance in measured physiological signal

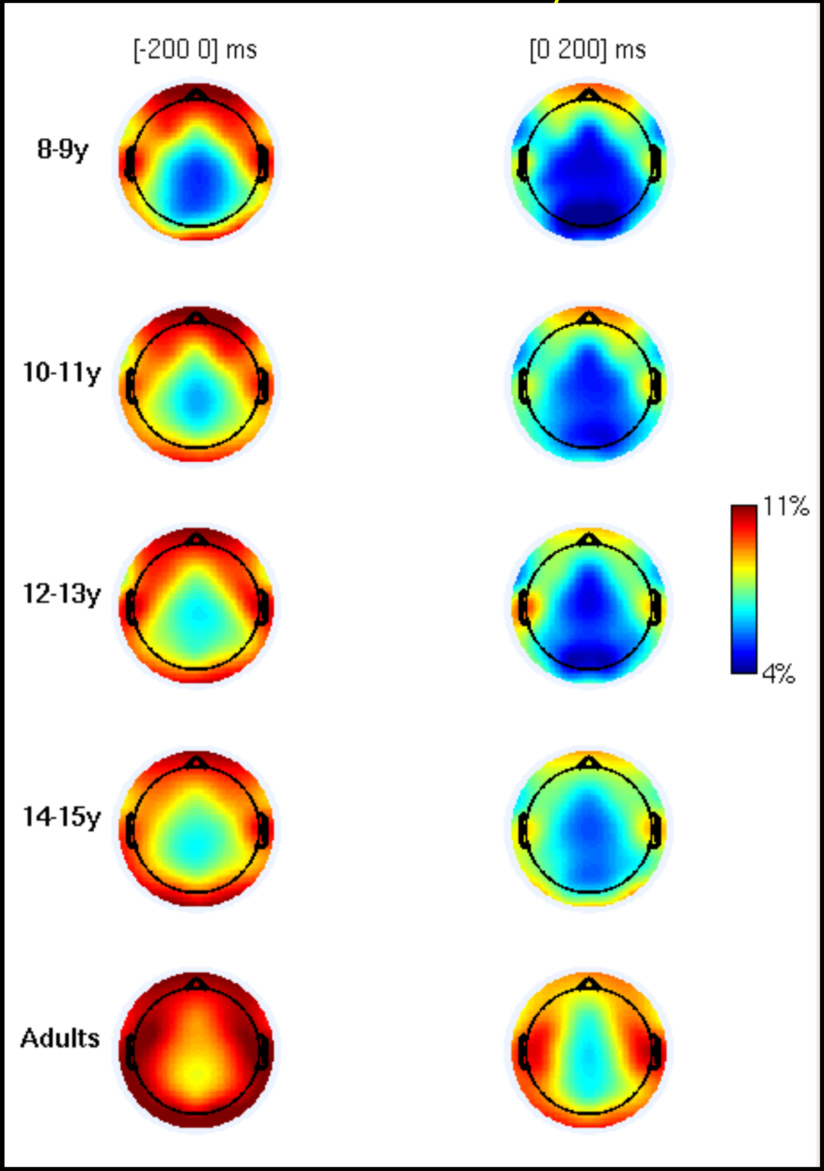
1. Look at number of dimensions (PCA) needed to capture ~90% variance in an individual's brain data
   - How predictable is the signal across trials?
2. Look at temporal dependency - multiscale entropy (MSE)
   - How predictable is the signal at different timescales?

Multiscale Entropy



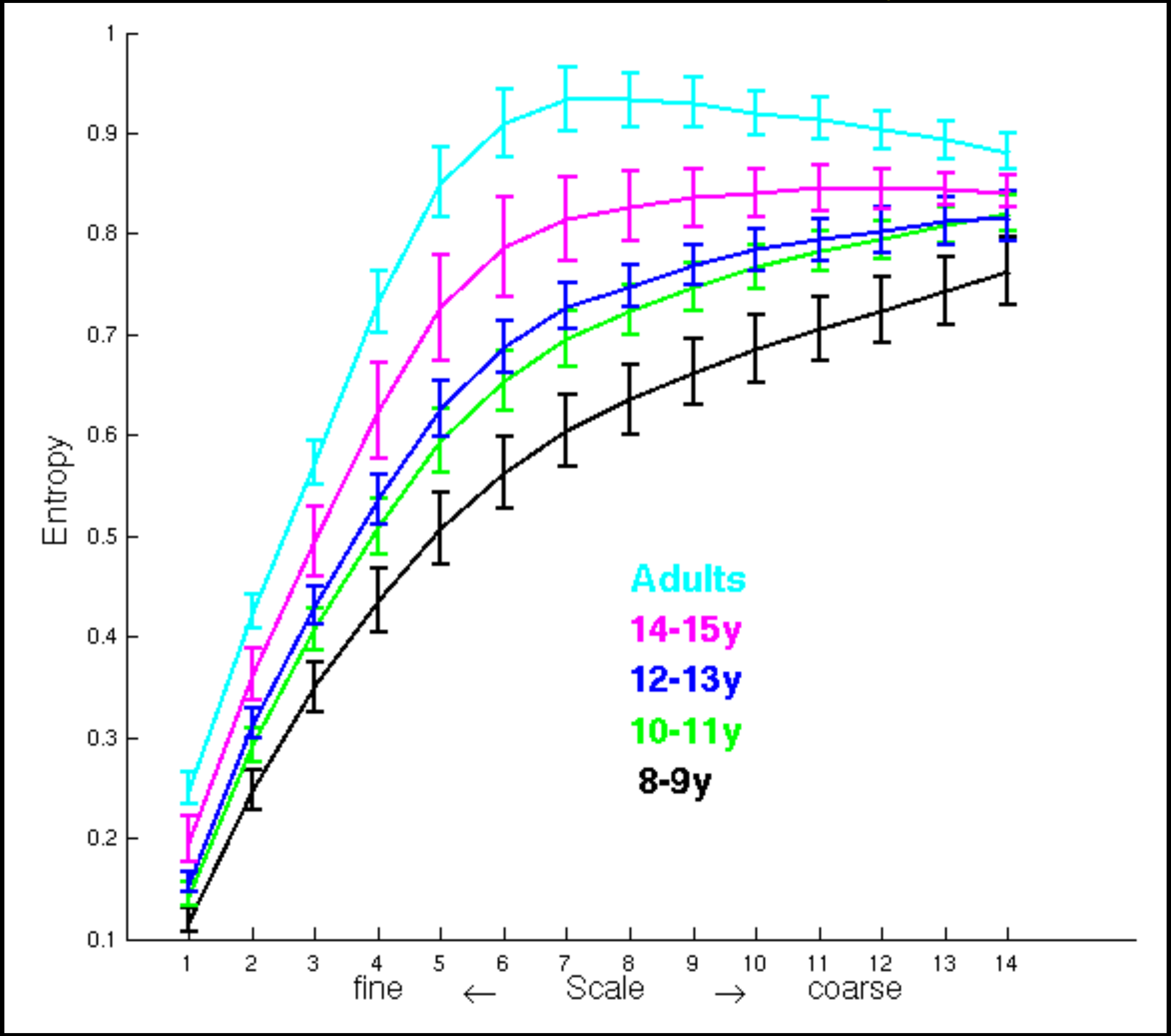
Costa, Goldberger & Peng, Phys Rev Lett, 2002
http://www.physionet.org/physiotools/mse/tutorial/

Maturation & Brain Variability
PCA dimensionality estimation



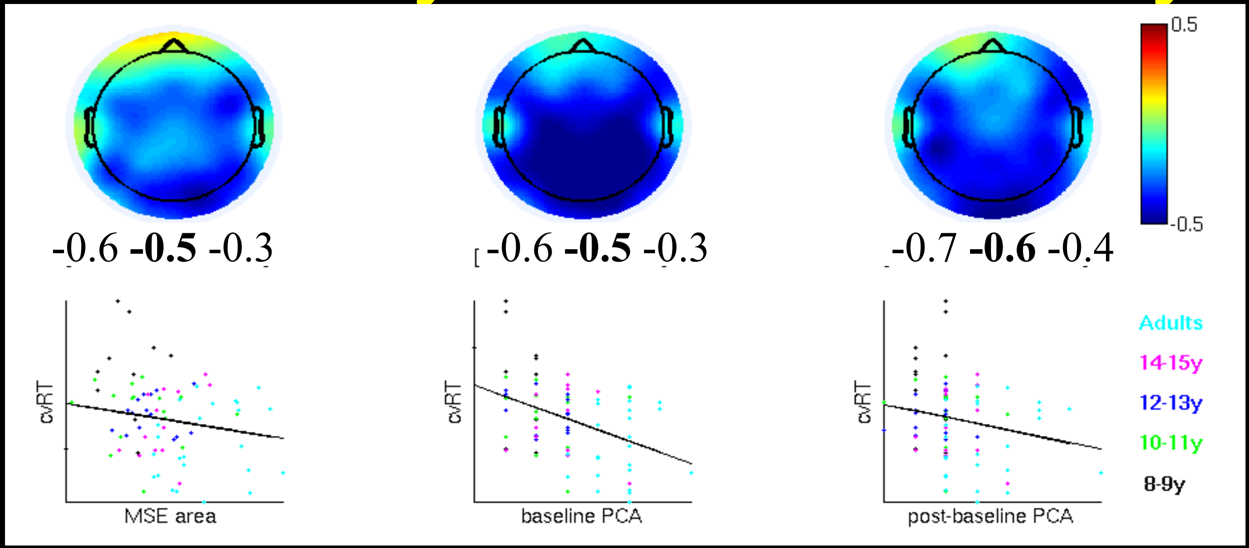
Note drop in dimensionality post-stimulus

Maturation & Brain Complexity
Multiscale Entropy

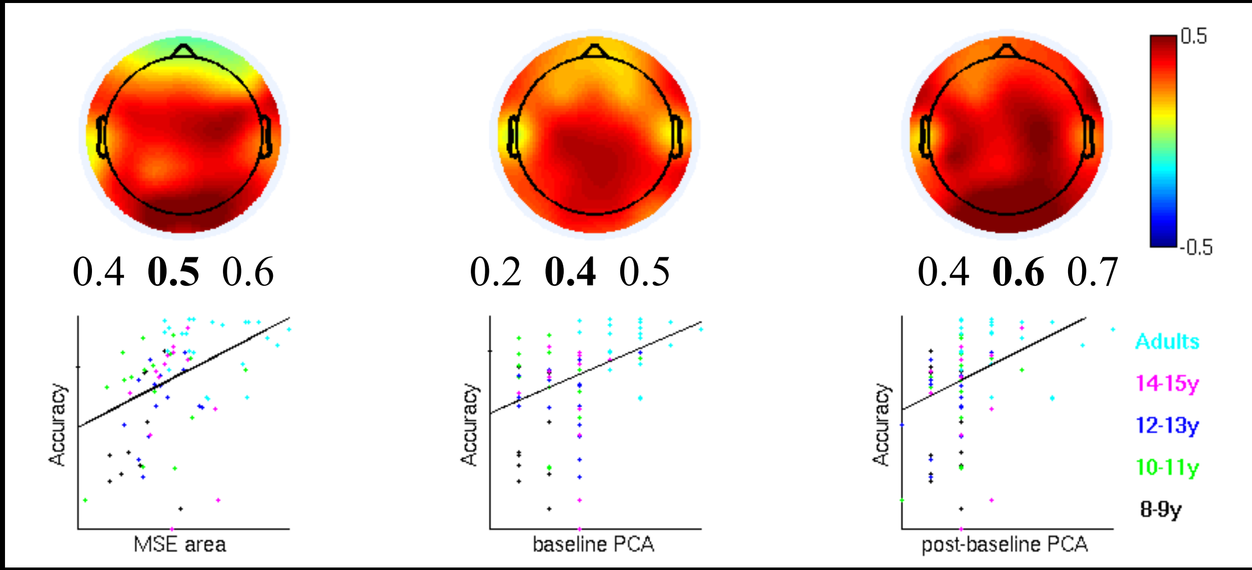


Behavioural stability & brain variability

Negative correlation between brain variability and stable RT
(no correlation with mean RT)

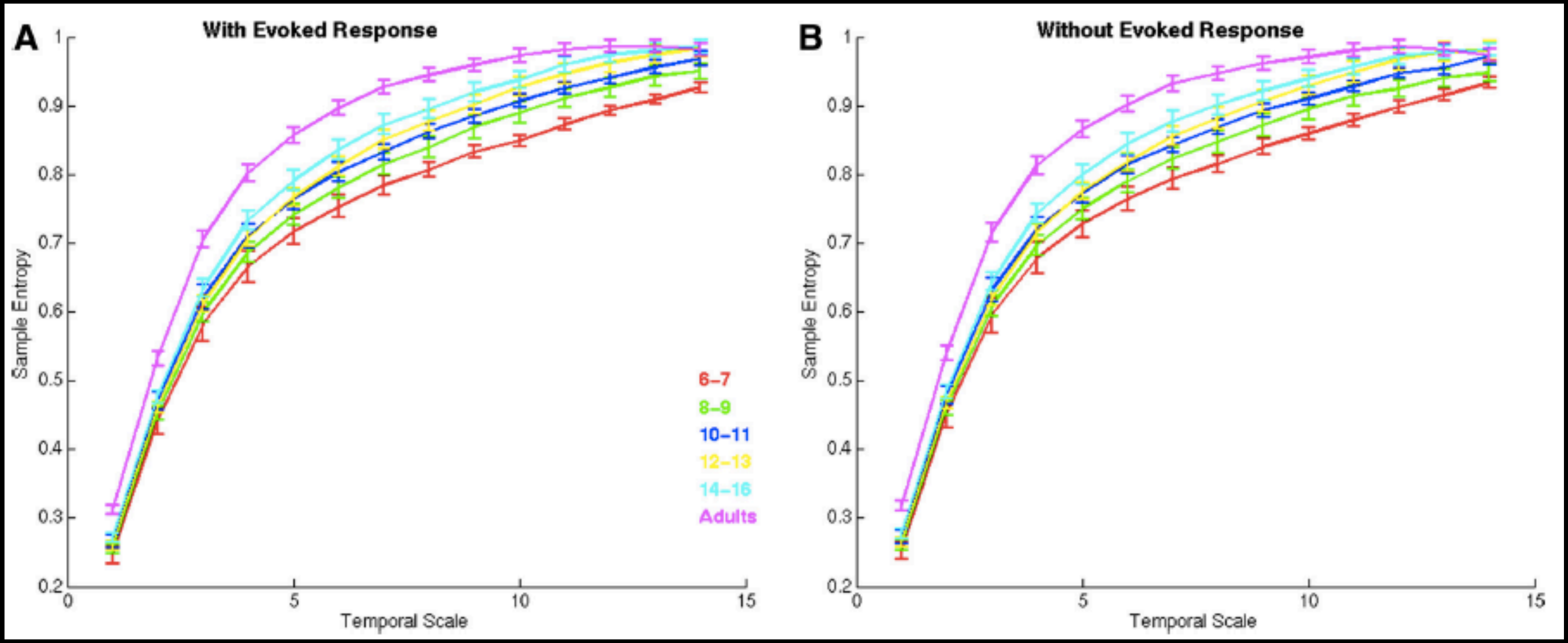


Positive correlation between brain variability and accuracy



Face perception & Maturation

MEG data show same developmental trend and relation to behavior



Misic et al, J Neurophys, 2010

Face perception & Maturation

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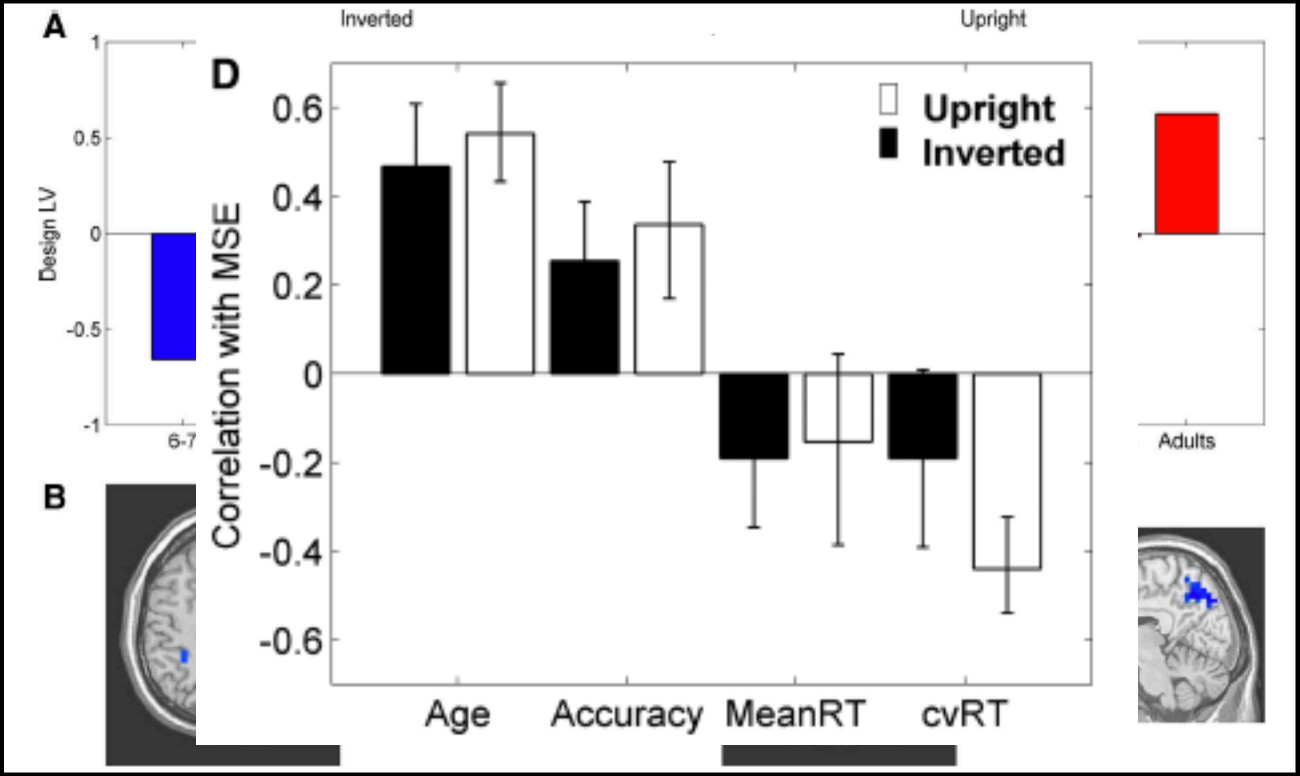
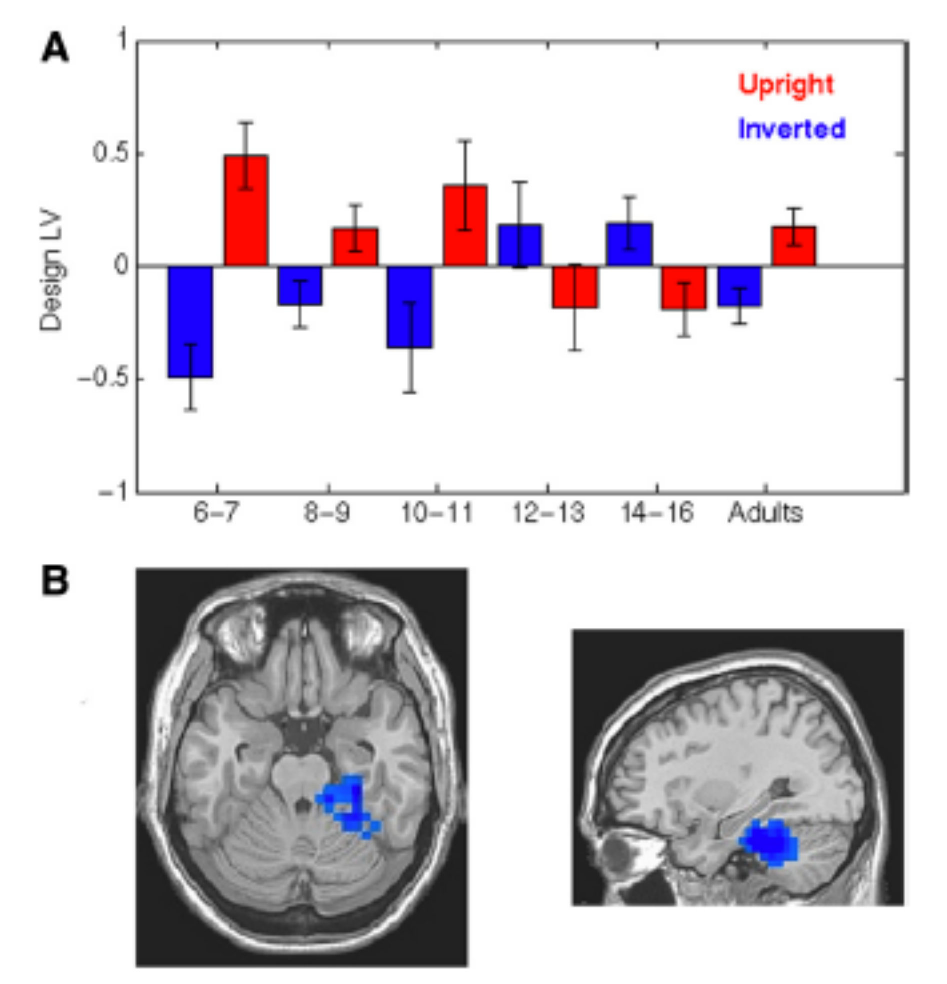


Misic et al, J Neurophys, 2010

Stimulus-dependent differences in MSE



What about babies?

Participants

- 1 week to 5 ½ years
- 75 infants and children
- 15 adults

Lippé S, Kovacevic N, McIntosh AR, Front Neuro, 2009

Babies
Entropy increases with age

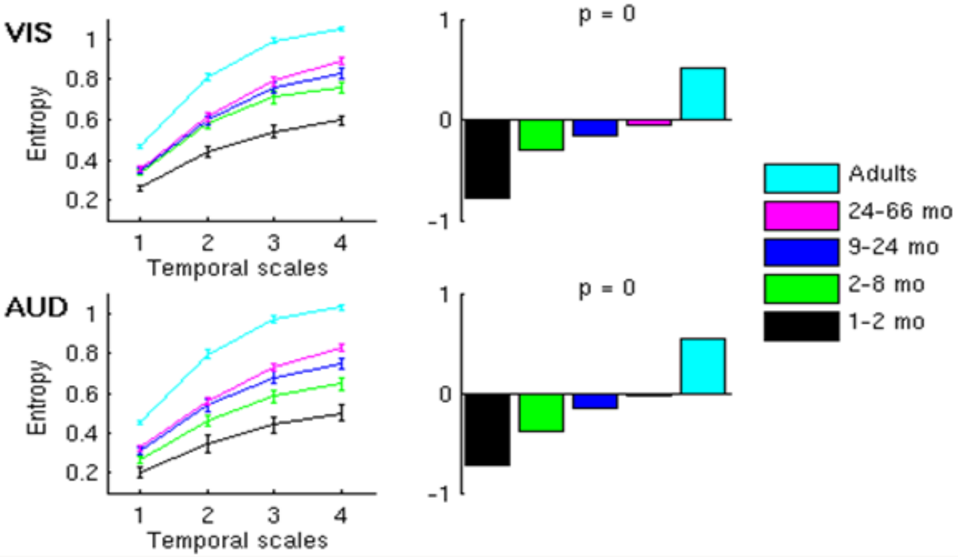
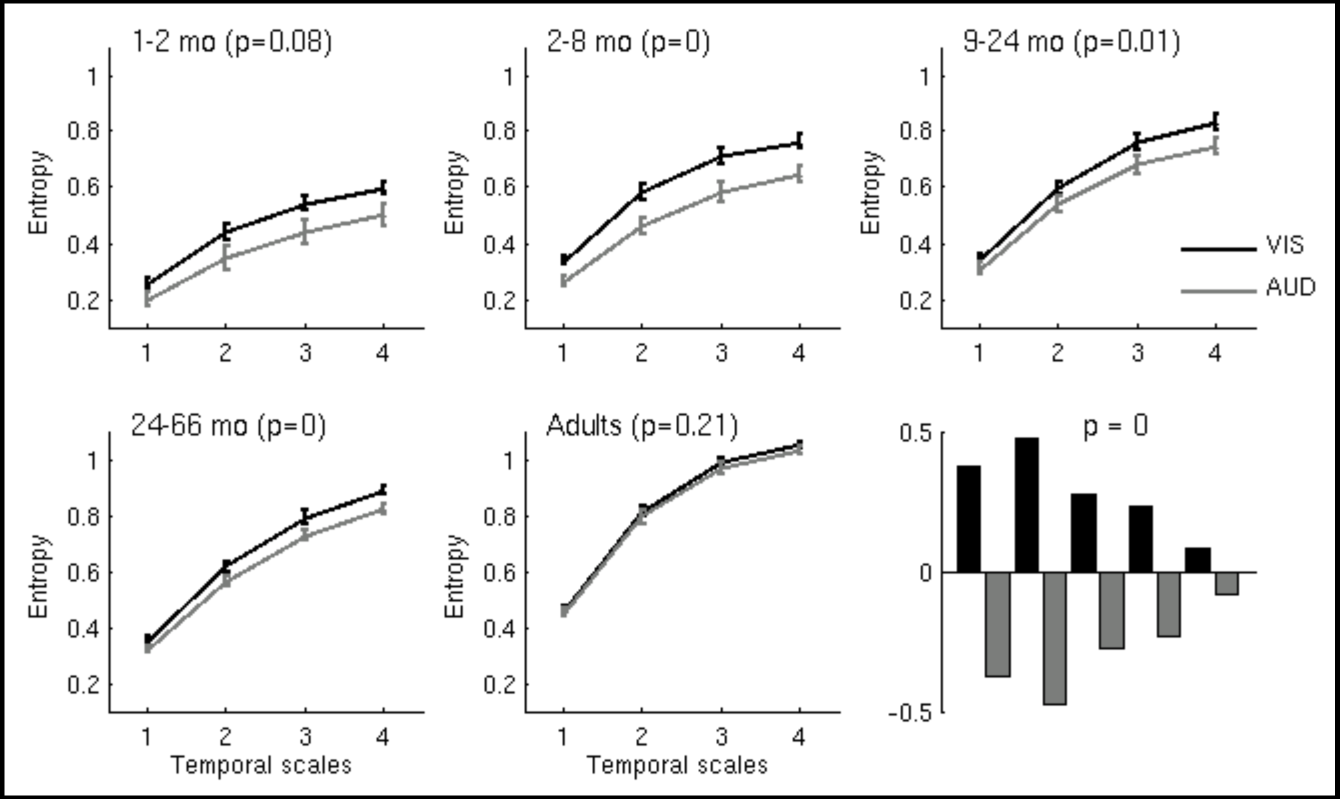


Fig.2

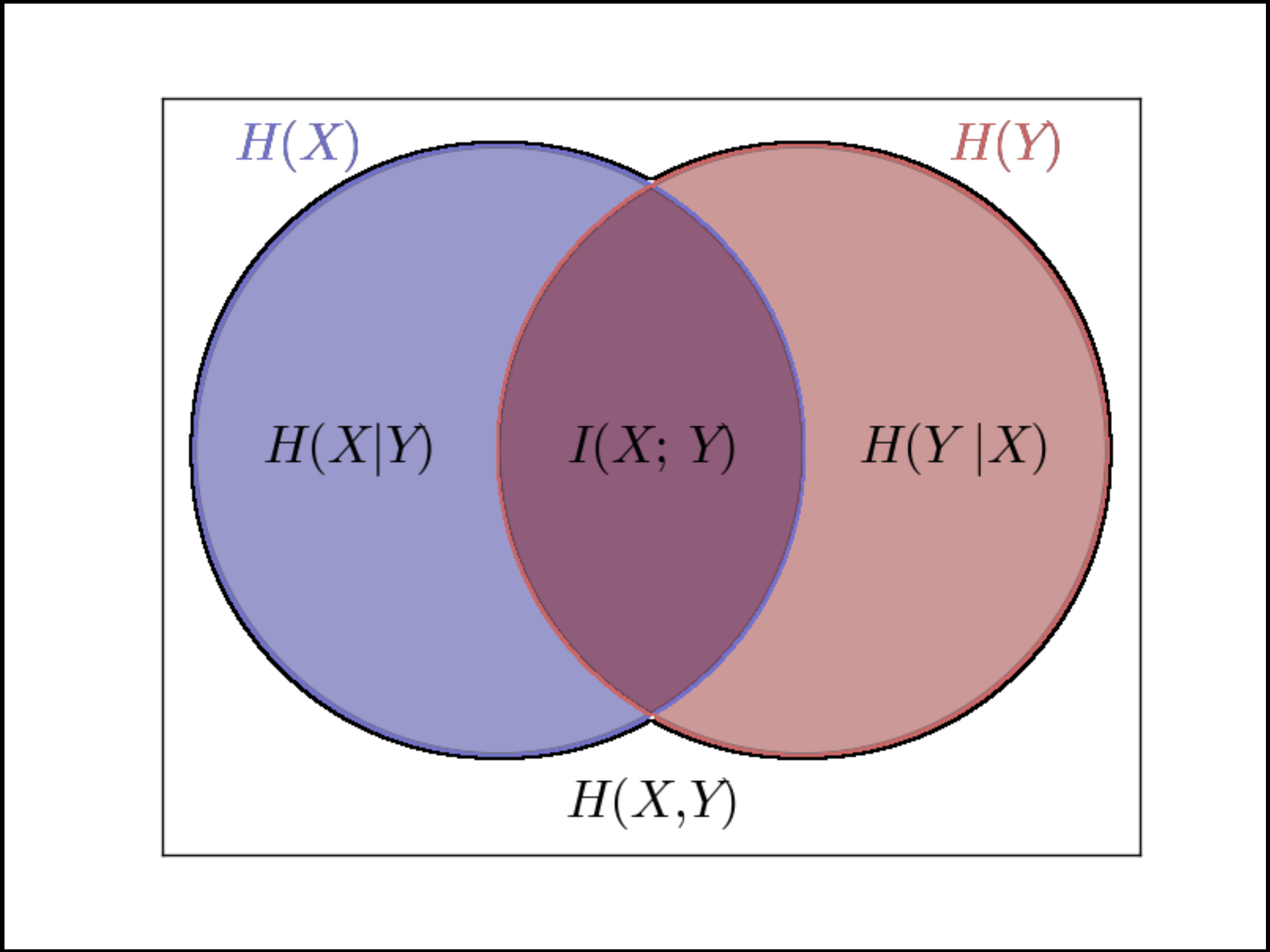
Lippé S, Kovacevic N, McIntosh AR, Front Neuro, 2009

Babies
Entropy increases with age differentially by sensory modality



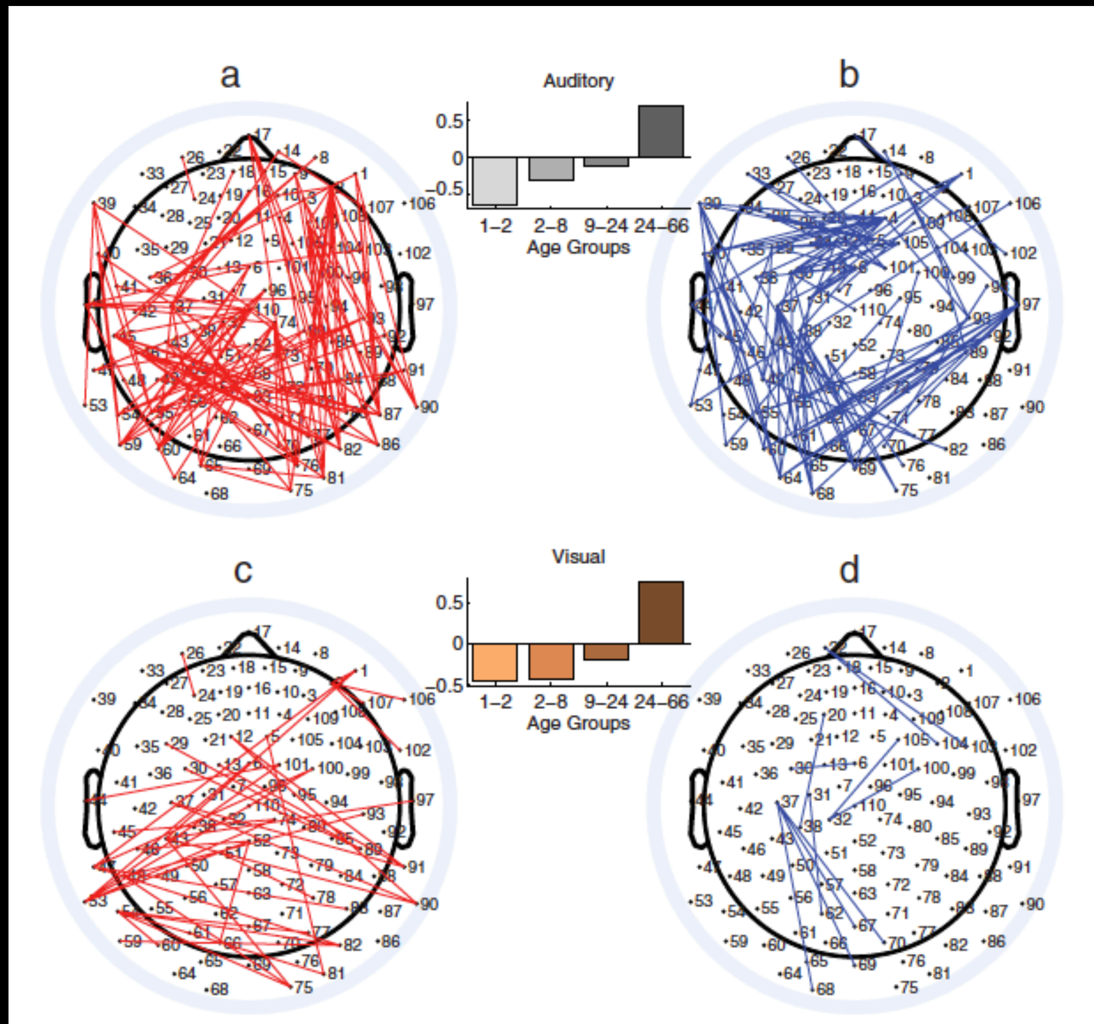
Lippé S, Kovacevic N, McIntosh AR, Front Neuro, 2009

Can we parse entropy into local and distributed sources?



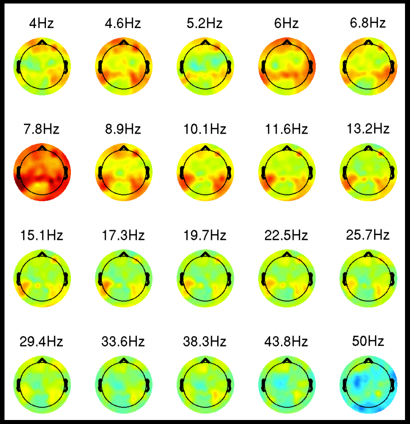
Variability of Brain Signals Processed Locally Transforms into Higher Connectivity with Brain Development

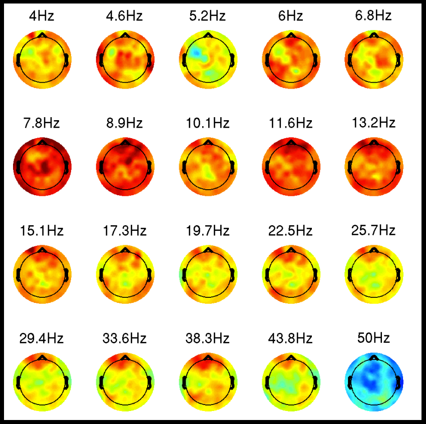
Vasily A. Vakorin,[1] Sarah Lippé,[2] and Anthony R. McIntosh[1,3]

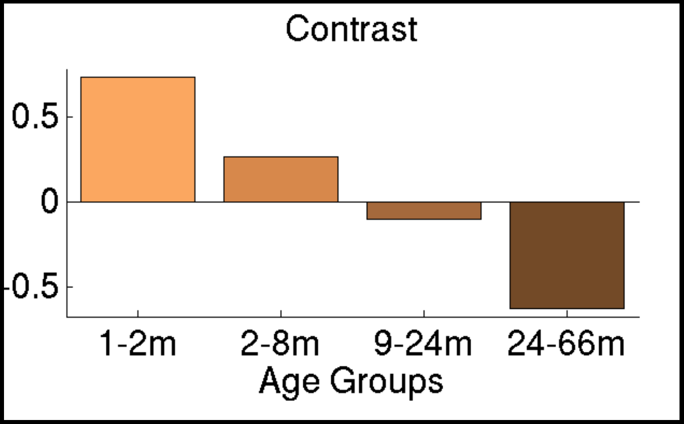


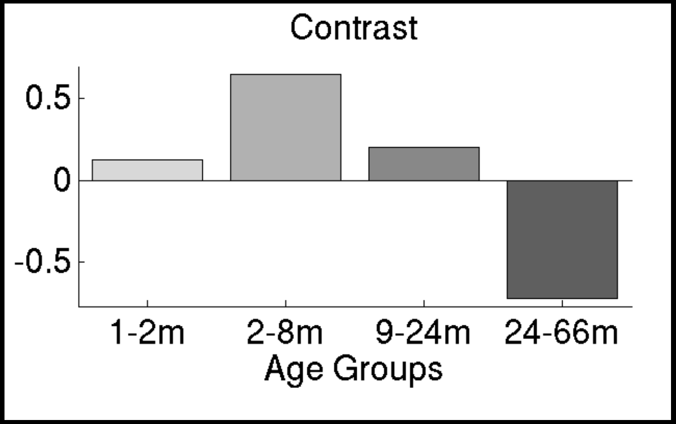
J Neuroscience, 2011

Local entropy









Vakorin, Lippé et McIntosh, 2011 Journal of Neuroscience

Network dynamics and maturation
Behavioral stability & brain noise

- Behavior stability increases with maturation
- Neurophysiological variability also increases with maturation
- Development brings a transition from a brain that is deterministic to one that is more stochastic, but adaptive
  - Paradoxical negative correlation between behavioral and brain variability

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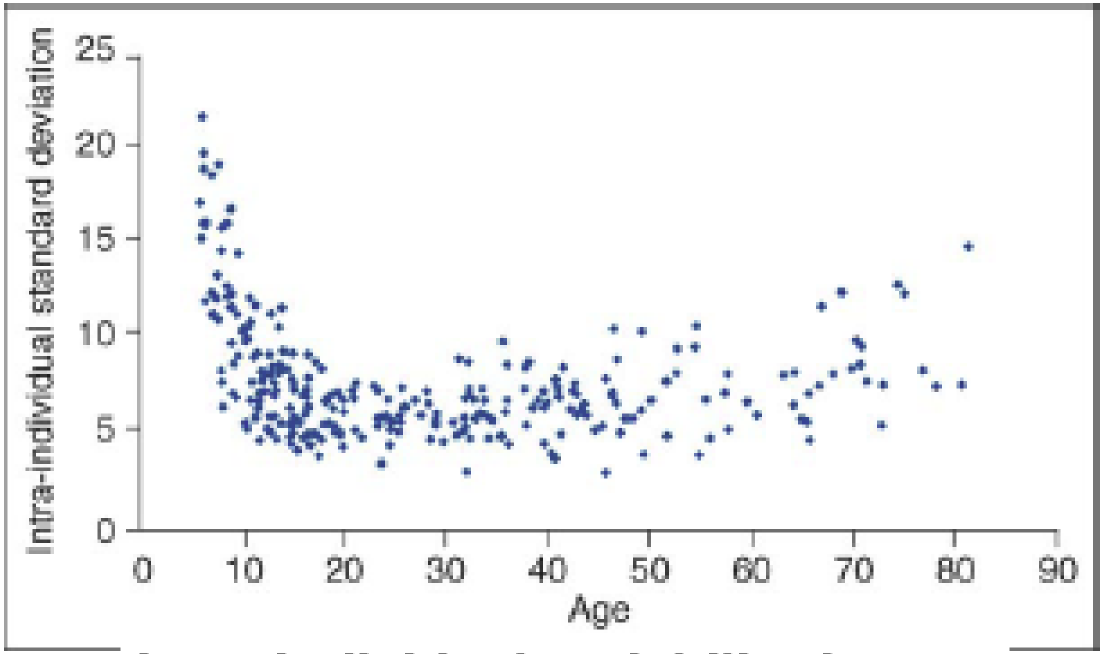
  - Clinical conditions

Aging & Brain Noise

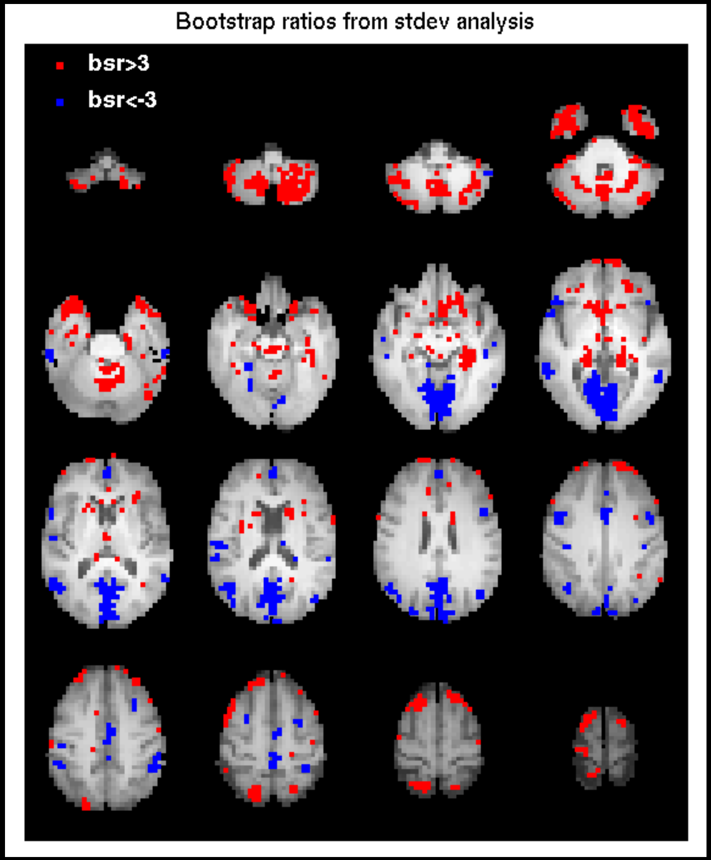


Intra-individual variability in behavior: links to brain structure, neurotransmission and neuronal activity

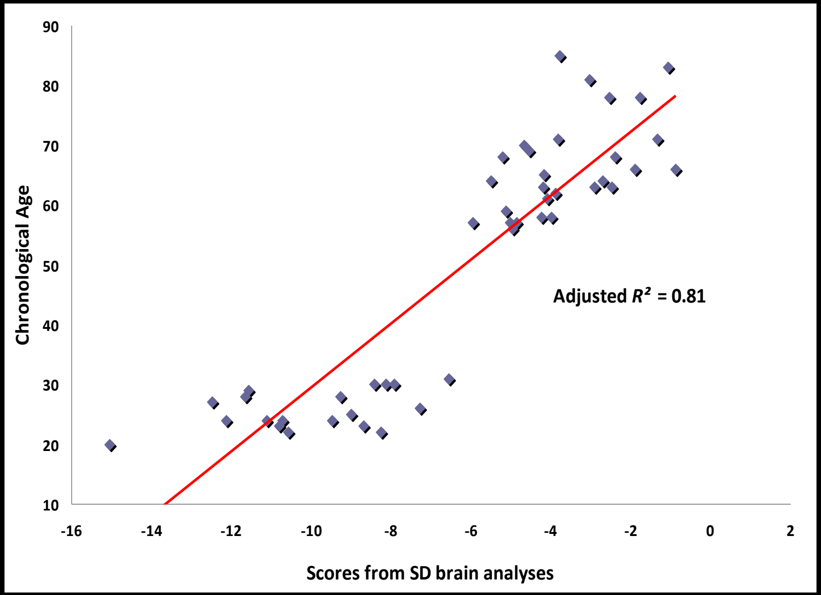
Stuart W.S. MacDonald[1], Lars Nyberg[2,3] and Lars Bäckman[1]

Trends Neurosci, 29, 2006

Age-related changes in BOLD variability: regional specificity



Standard Deviation



Regions show age-related decreases in standard deviation also correlate with stable reaction time

Garrett et al, J Neurosci, 2010

Normal Aging & Brain Noise
EEG data

1. *Tasks*: Simple perceptual matching & Delayed match to sample
2. *Stimuli*: Bandpass filtered white noise (subject-specific thresholds).
3. *Duration of visual stimuli*: 1.4 to 2 sec (4 sec delay for DMS)

Participants:

- **Young (N=16):** 20-35yrs (10 females; mean age = 22 yrs)
- Middle (N=16): 36-55 yrs (11 females; mean age = 45 yrs)
- **Old (N=16):** 60-78yrs (11 females; mean age = 66 yrs)

McIntosh, Vakorin, Wang, Diaconescu & Kovacevic in prep

Normal Aging & Brain Noise MEG data

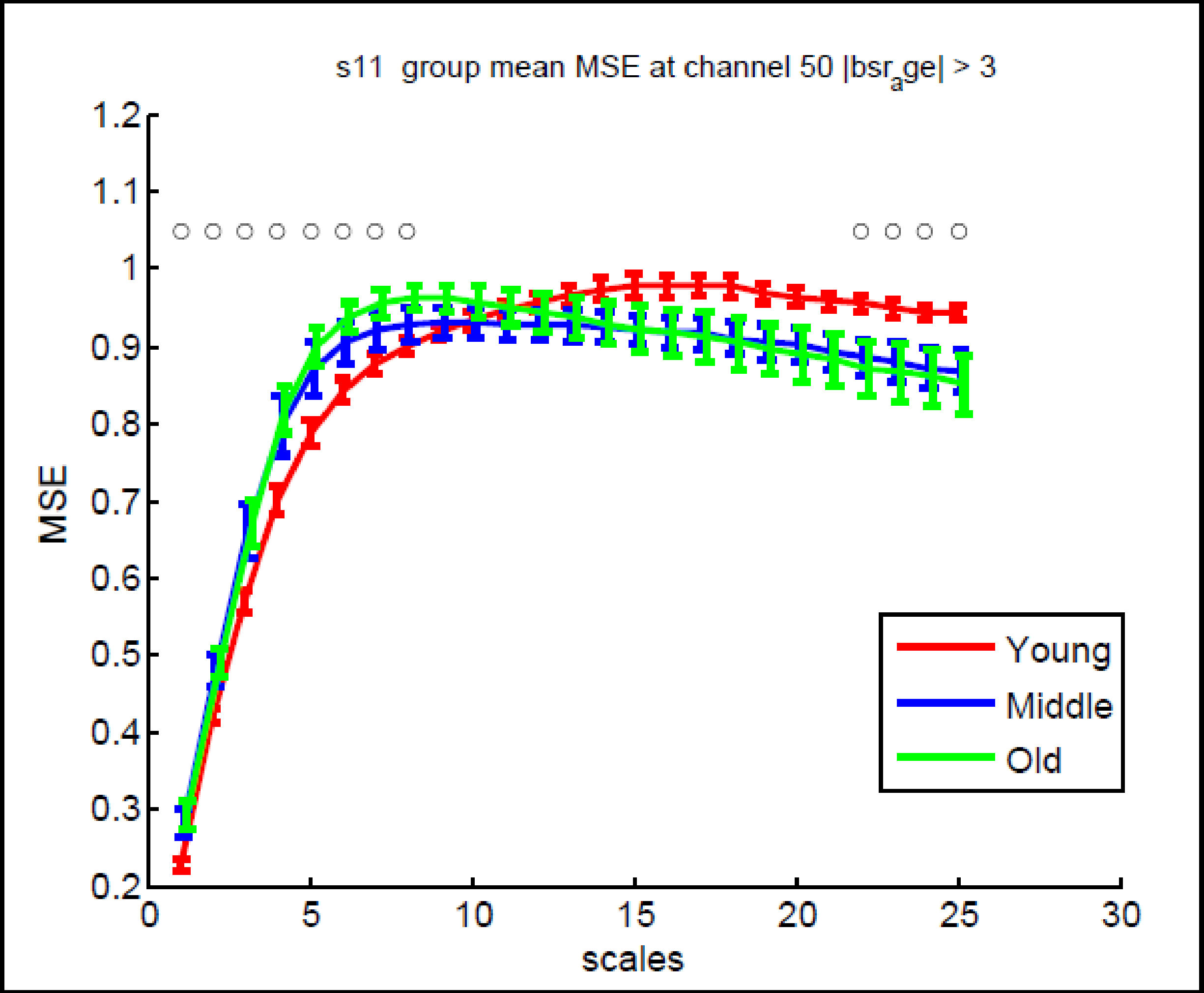
1. *Task*: Simple reaction time
2. *Stimuli*: Black-and-white line drawings selected from the Snodgrass and Vanderwart (1980) database. All visual stimuli were matched according to size (in pixels), brightness, and contrast.
3. *Duration of visual stimuli*: 400ms
4. Left Hand Response

Participants:

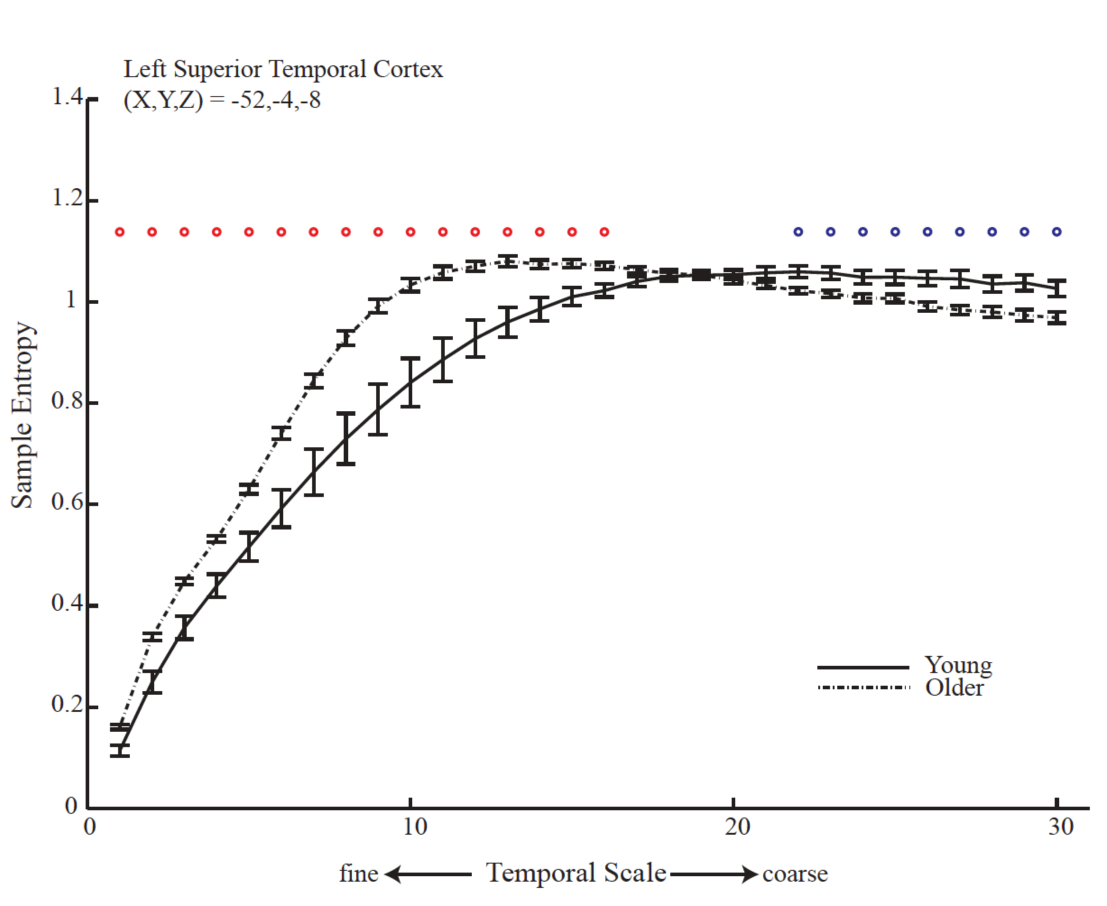
- **Young (N=15):** 20-30yrs (8 females; mean age = 23.46 years)
- **Old (N=16):** 60-78yrs (6 females; mean age = 69.93 years)

McIntosh, Vakorin, Wang, Diaconescu & Kovacevic in prep

EEG data – Multiscale entropy
Visual Match-to-sample task



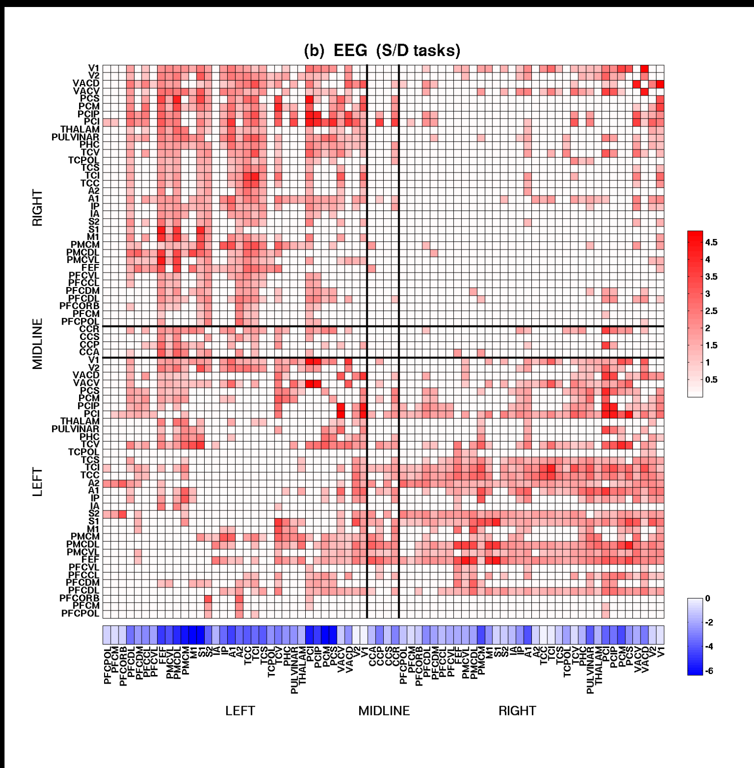
MEG data Multiscale Entropy Auditory detection



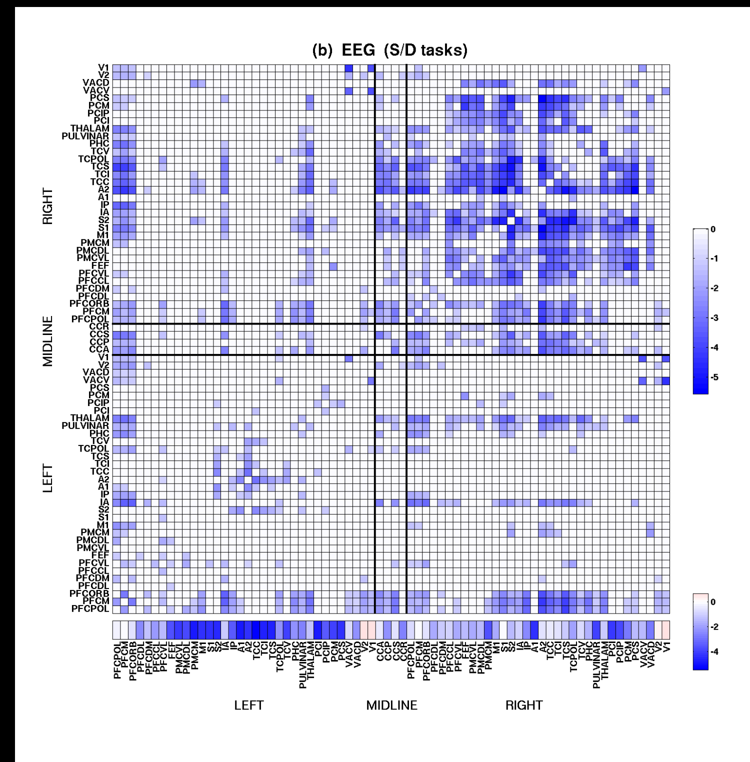
Age-related changes are time scale dependent

Local vs Distributed Entropy
EEG Data

Distributed entropy decreases across hemispheres



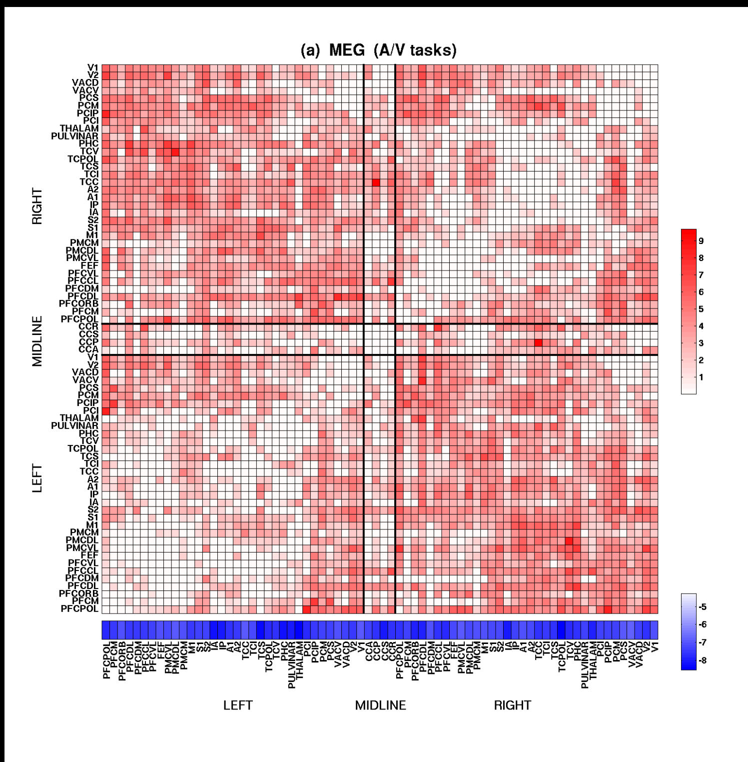
Distributed entropy increases within hemispheres



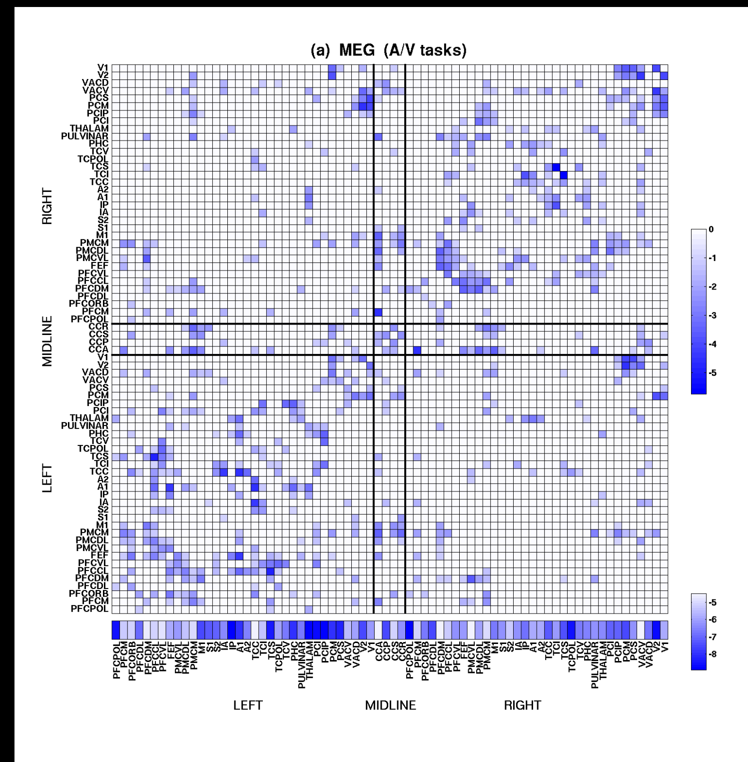
Local entropy increases with age

Local vs Distributed Entropy
MEG Data

Distributed entropy decreases across hemispheres



Distributed entropy increases within hemispheres



Local entropy increases with age

Outline

- Functional network dynamics
  - Network concepts
  - What is brain noise?
    - Pure noise vs. information
- Noise & Variability in the brain
  - Large-scale network models
  - Brain maturation
  - Healthy aging
  - Clinical conditions

Noise & Clinical Conditions

Schizophrenia: reduced signal-to-noise ratio and impaired phase-locking during information processing

G. Winterer[b,*], M. Ziller[a], H. Dorn[a], K. Frick[a], C. Mulert[a], Y. Wuebben[a], W.M. Herrmann[a], R. Coppola[b]

Clin Neurophysiol 2000

Fluctuations in Cortical Synchronization in Pediatric Traumatic Brain Injury

VERA NENADOVIC,[1,2,3] JAMES S. HUTCHISON,[1,3,4] LUIS GARCIA DOMINGUEZ,[3] HIROSHI OTSUBO,[5] MARTIN P. GRAY,[1] ROHIT SHARMA,[5] JASON BELKAS,[3] and JOSE LUIS PEREZ VELAZQUEZ[2,3,5]

J Neurotrauma, 2008

Dynamic Range Enhancement for Cochlear Implants

Robert S. Hong, Jay T. Rubinstein, Dan Wehner, and David Horn

Otology & Neurology, 2003

Applied Biodynamics Laboratory

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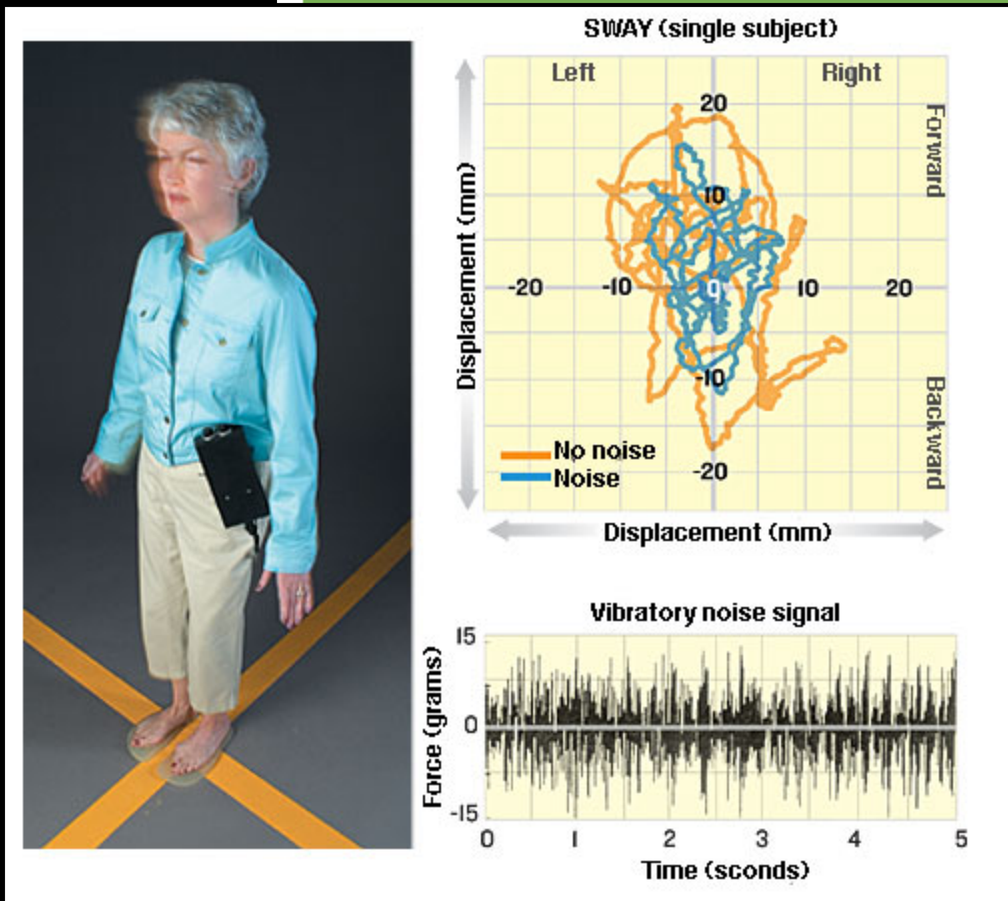
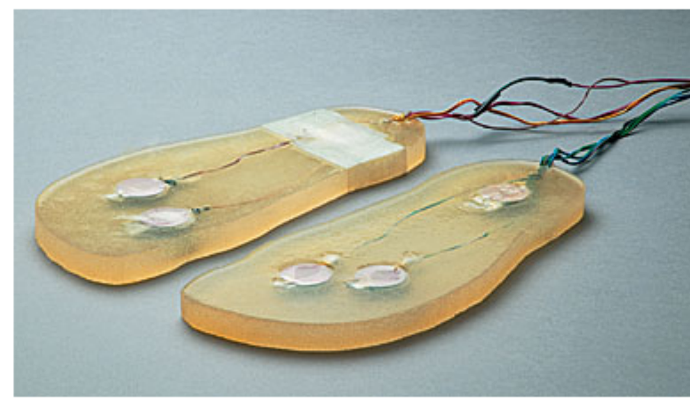
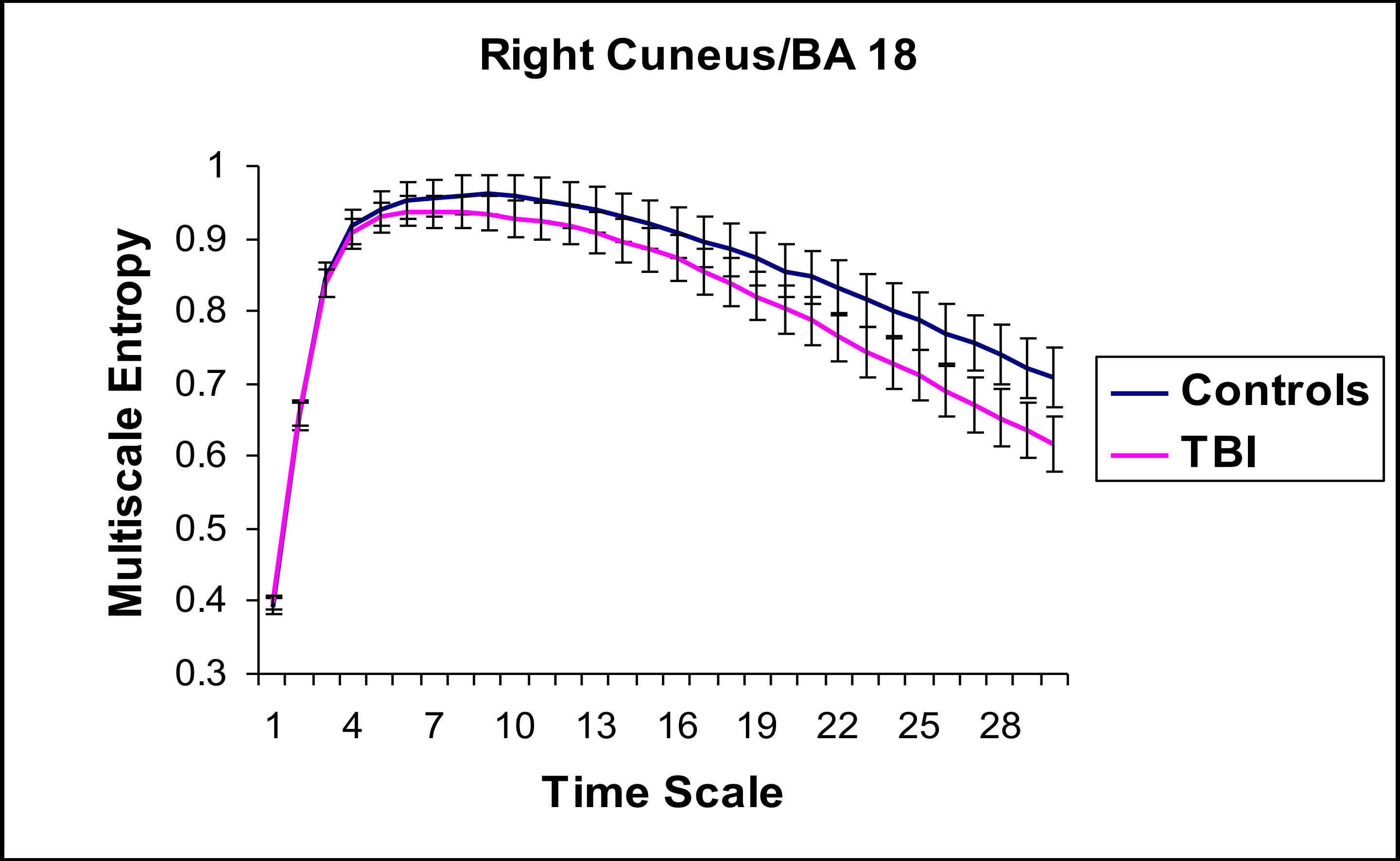




VIBRATING SOLES: Electric motors embedded in gel insoles produce noisy vibrations that improve balance.

Group Differences in Multiscale Entropy

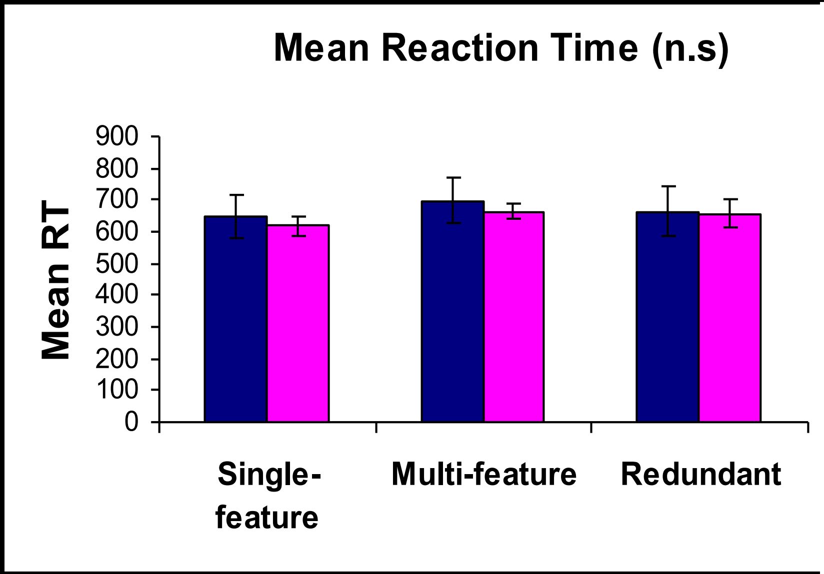
- Traumatic Brain Injury & attention
  - TBI patients show lower entropy at coarser time scales compared to controls

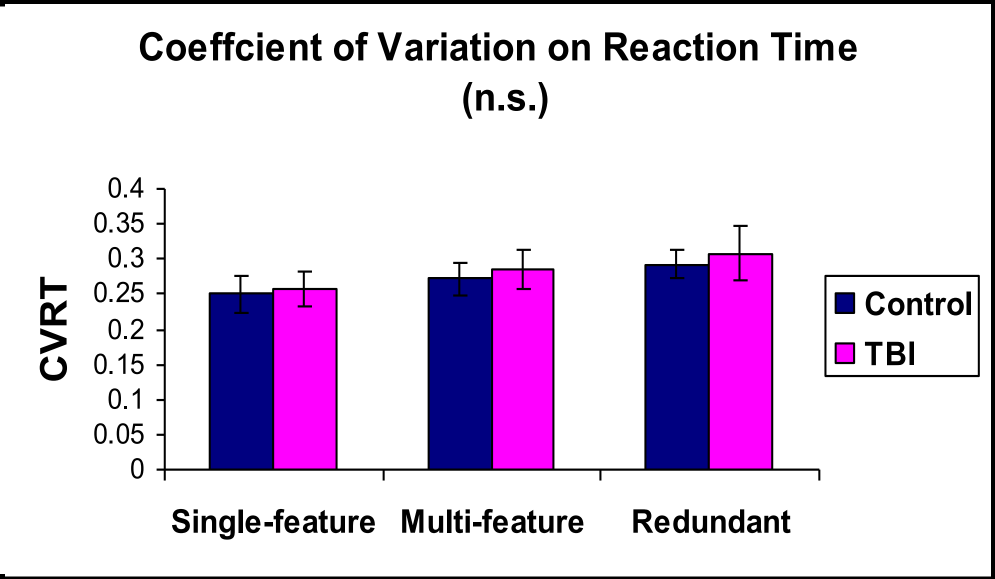


Raja, et al, Neuroimage, 2012

Brain-Behavior Analysis

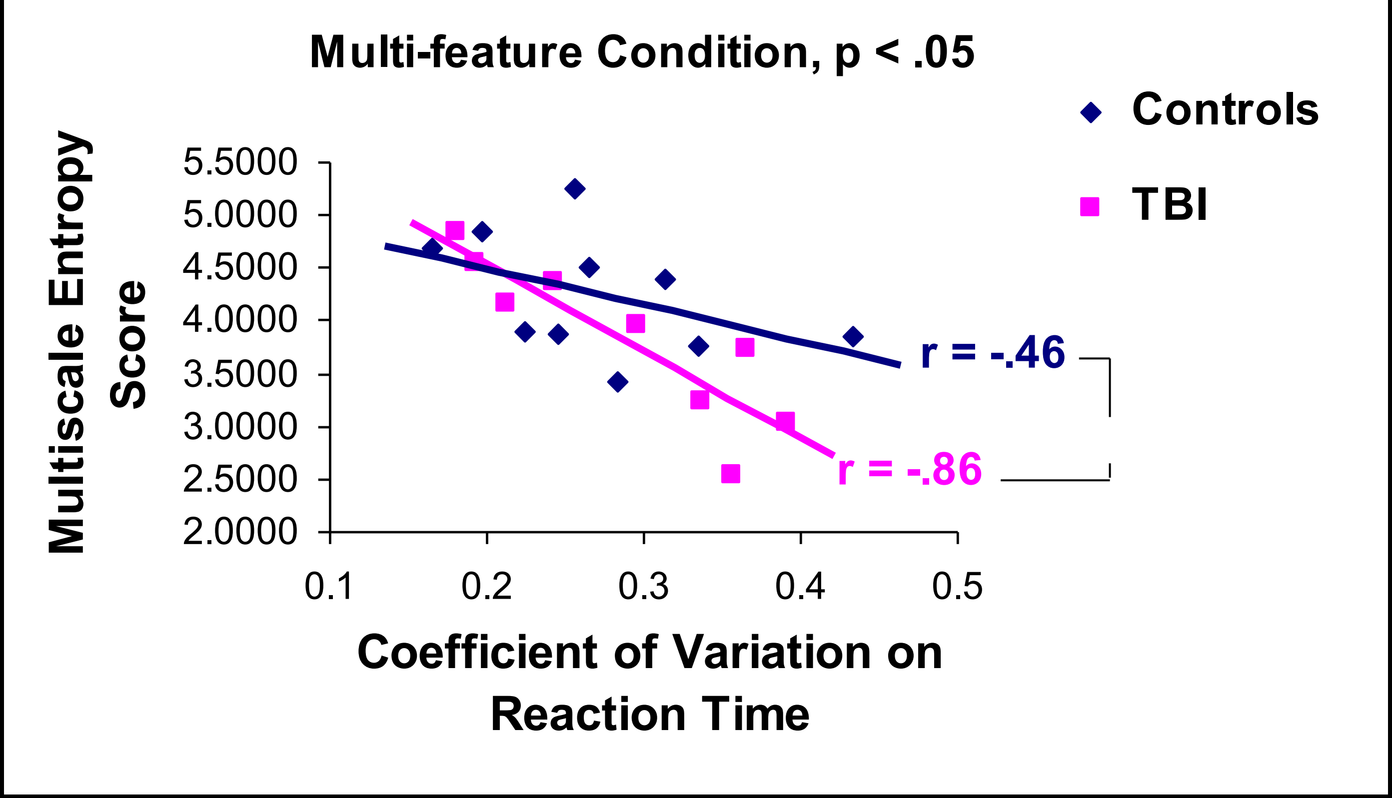
- No difference between TBI and controls in mean and coefficient of variation of reaction time





Brain-Behavior Analysis

- Significant negative correlation between entropy variability in RT
  - more strongly expressed in TBI patients than controls

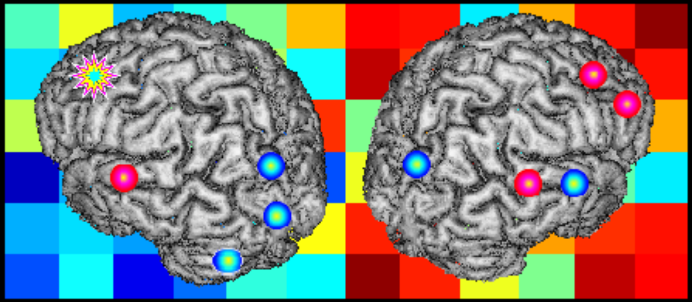


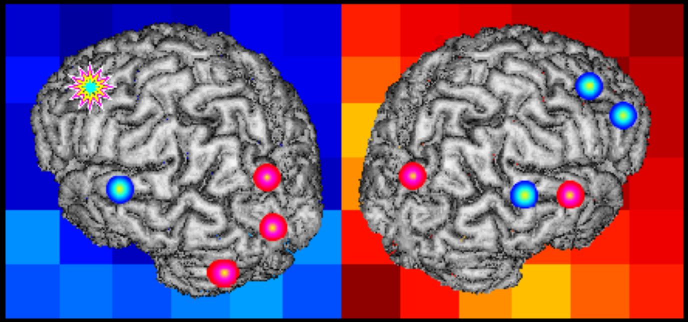
General Conclusions

- Functional network dynamics
  - Brain operates through networks not regions
  - The interplay of structural and functional architecture makes for a “noisy” complex system
    - Noise enables multistability – *Dynamic repertiore*
    - Different temporal and spatial signatures in the dynamic repertoire
- Noise & Variability in the brain
  - A *certain amount* of noise seems important for normal function
  - Emergence of “noise” with maturation
    - Scale dependency emphasized in normal aging
    - May be useful in assessing clinical conditions
  - Interplay of noise and function (direction unclear)

- *The brain, through its unique network architecture and multiscale noise, is in a constant state of exploring what is possible*

Thank You





THEVIRTUALBRAIN.