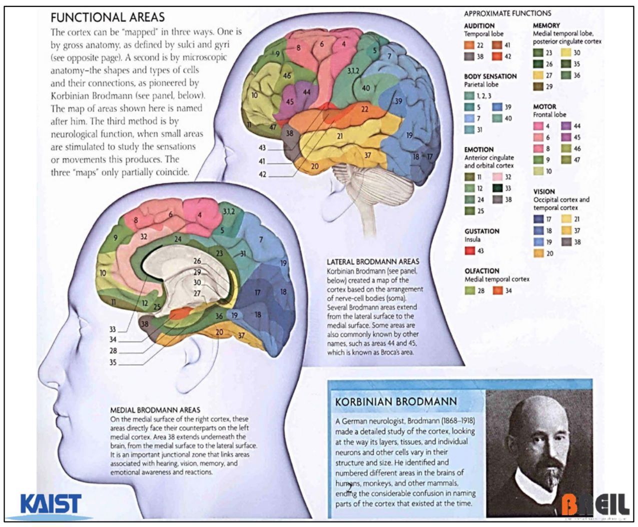
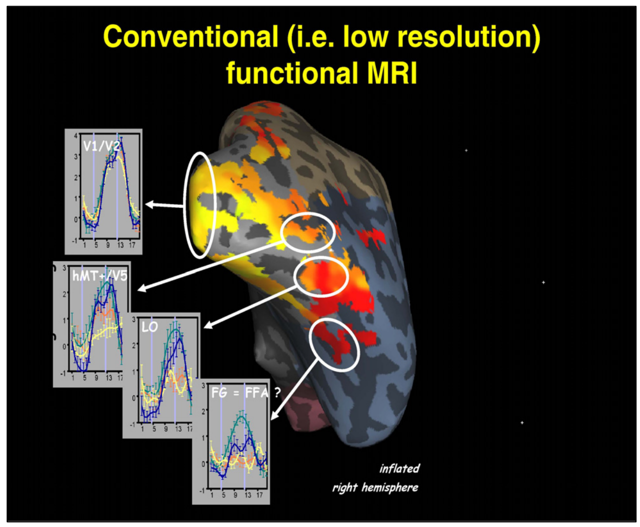
대뇌피질의 구조와 기능의 관계: 분산인가 극소화인가?

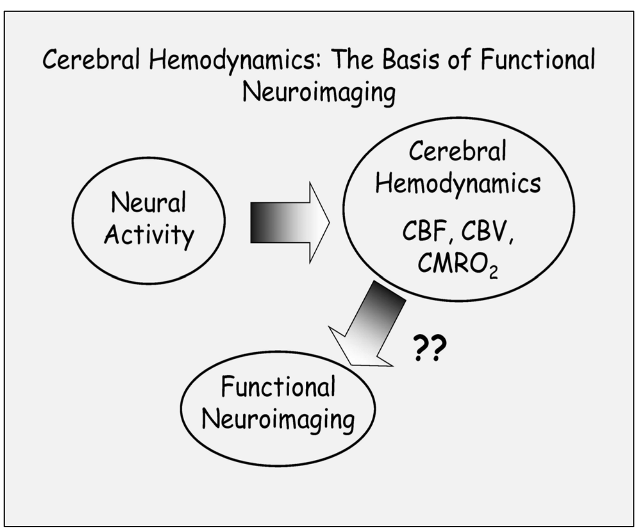
김 대 식
KAIST 전기 및 전자공학과

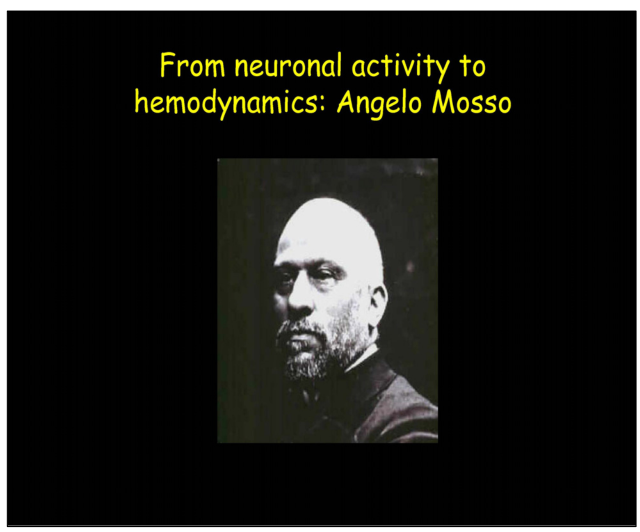
Distributed or Localized?: Structure-Function Relation in Mammalian cortex

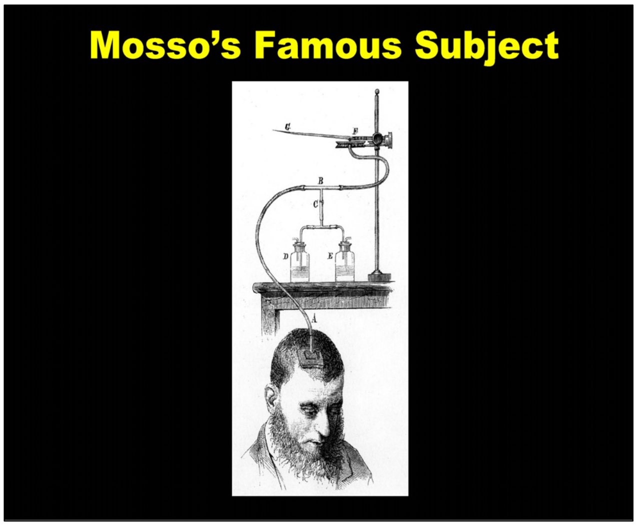
Dae-Shik Kim, PhD
Department of Electrical Engineering, KAIST

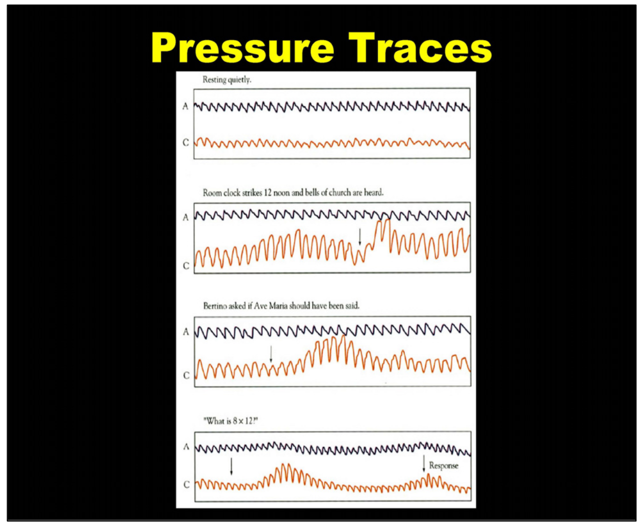


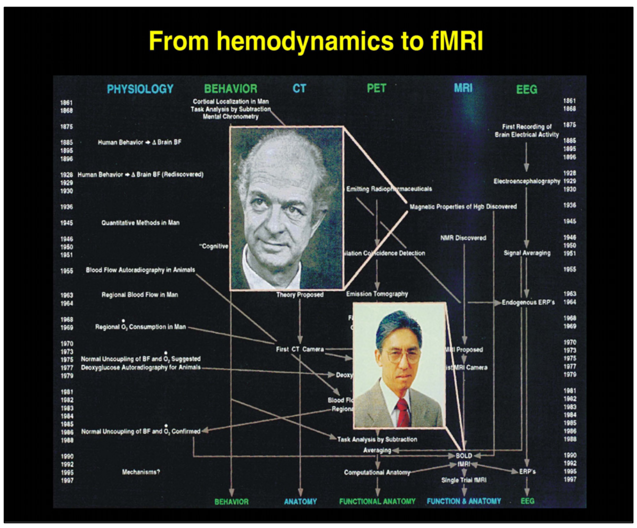


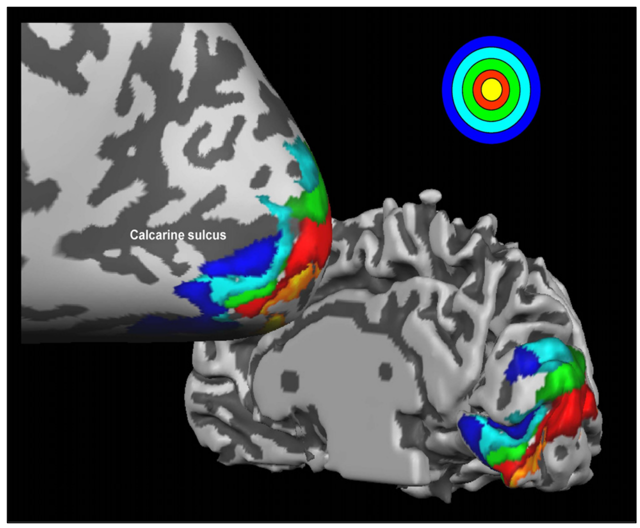


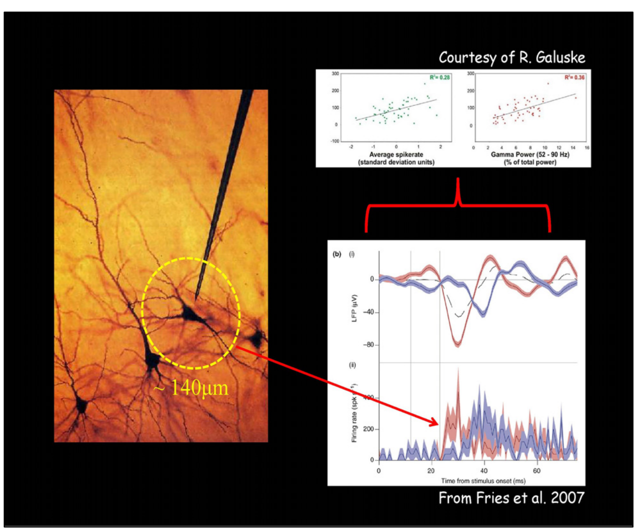


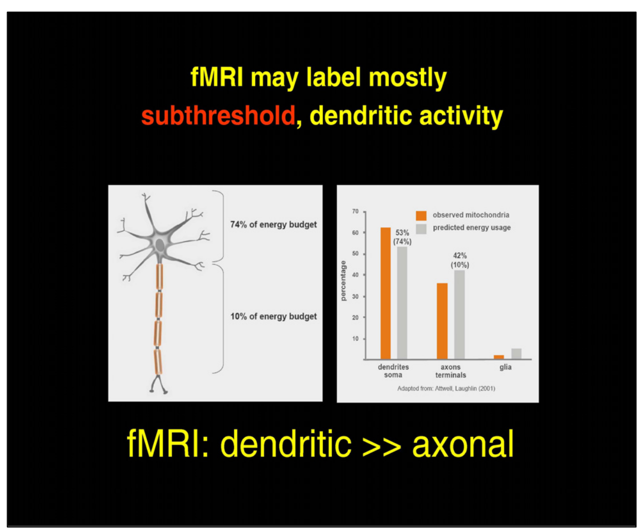

Mosso's Famous Subject

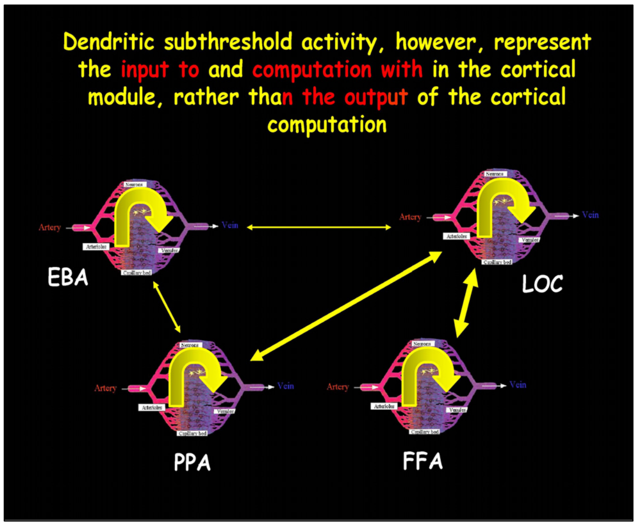

Pressure Traces
Resting quietly.
Room clock strikes 12 noon and bells of church are heard.
Bertino asked if Ave Maria should have been said.
"What is 8 x 12?"
Response

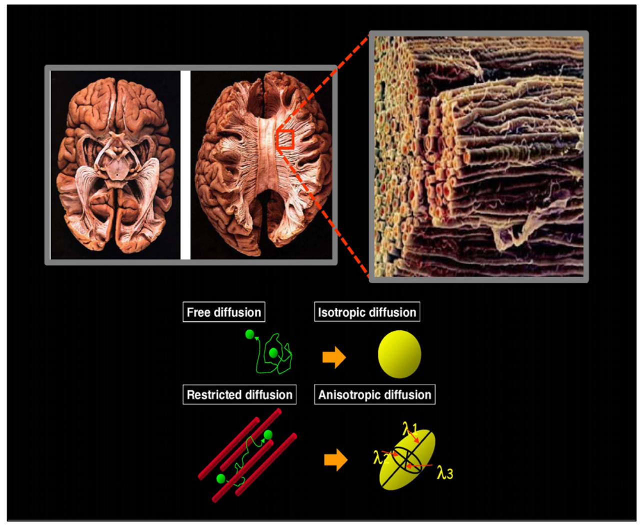

From hemodynamics to fMRI
PHYSIOLOGY
BEHAVIOR
CT
PET
MRI
EEG
BEHAVIOR
ANATOMY
FUNCTIONAL ANATOMY
FUNCTION & ANATOMY
EEG

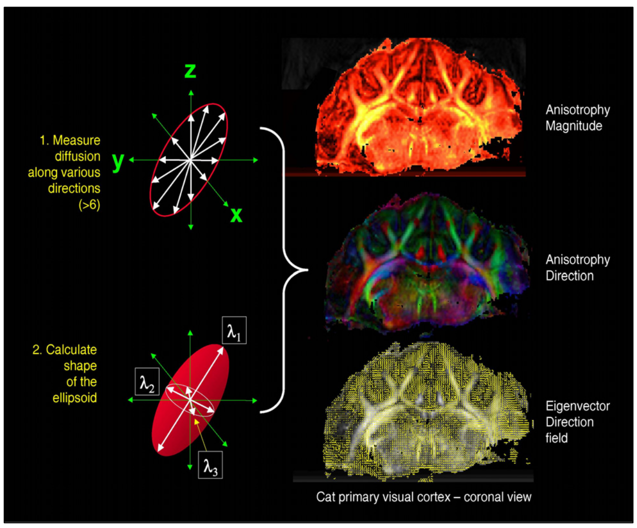

Calcarine sulcus

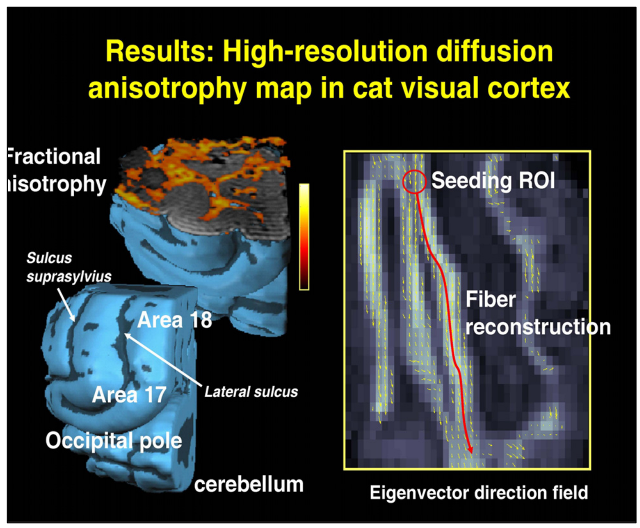

Courtesy of R. Galuske
Average spikerate (standard deviation units)
Gamma Power (52 - 90 Hz) (% of total power)
~ 140µm
Time from stimulus onset (ms)
From Fries et al. 2007

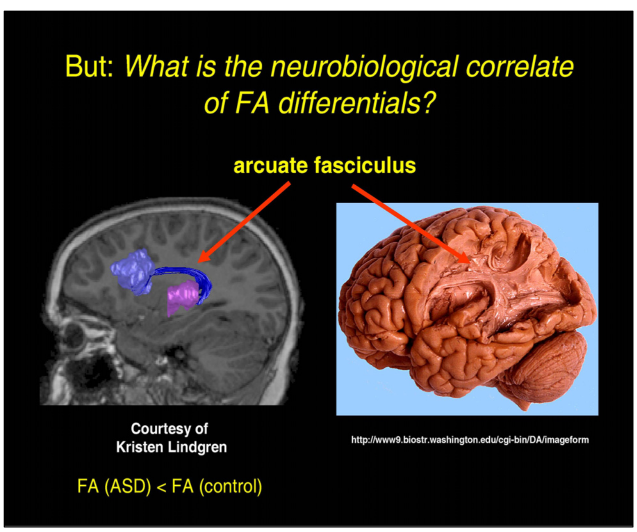

fMRI may label mostly
subthreshold, dendritic activity
74% of energy budget
10% of energy budget
observed mitochondria
predicted energy usage
dendrites soma
axons terminals
glia
Adapted from: Attwell, Laughlin (2001)
fMRI: dendritic >> axonal

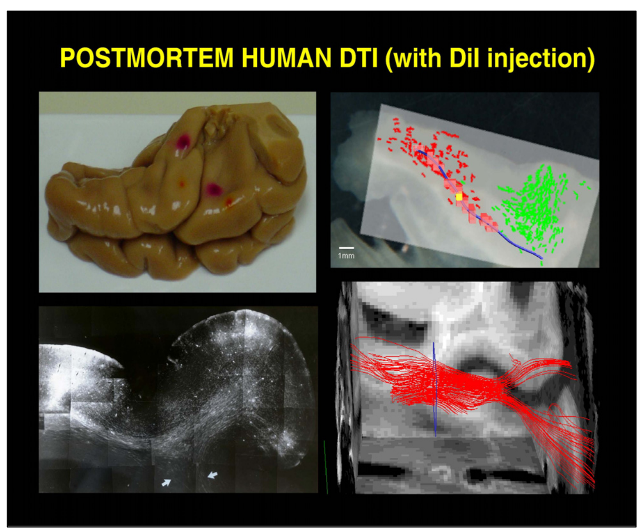

Dendritic subthreshold activity, however, represent the input to and computation with in the cortical module, rather than the output of the cortical computation
EBA
LOC
PPA
FFA

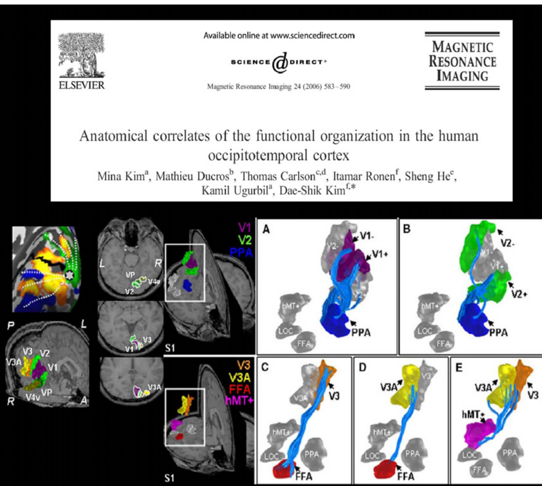

Free diffusion
Isotropic diffusion
Restricted diffusion
Anisotropic diffusion
λ1
λ2
λ3


z
y
x
1. Measure diffusion along various directions (>6)
2. Calculate shape of the ellipsoid
λ1
λ2
λ3
Anisotrophy Magnitude
Anisotrophy Direction
Eigenvector Direction field
Cat primary visual cortex – coronal view

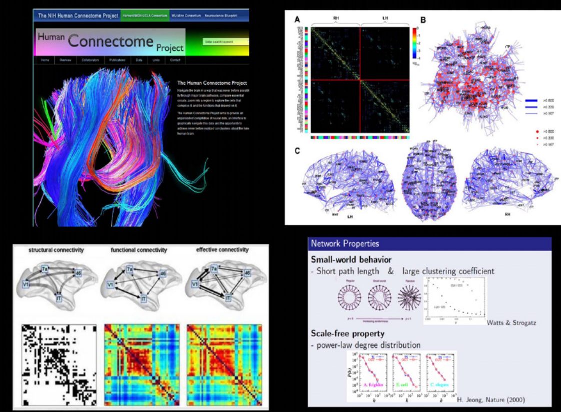

Results: High-resolution diffusion anisotrophy map in cat visual cortex
Fractional
Anisotrophy
Sulcus suprasylvius
Area 18
Area 17
Lateral sulcus
Occipital pole
cerebellum
Seeding ROI
Fiber reconstruction
Eigenvector direction field


But: What is the neurobiological correlate of FA differentials?
arcuate fasciculus
Courtesy of Kristen Lindgren
http://www9.biostr.washington.edu/cgi-bin/DA/imageform
FA (ASD) < FA (control)

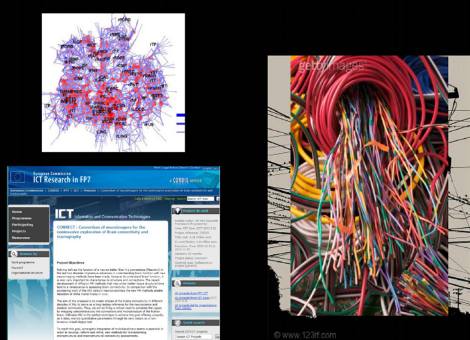

POSTMORTEM HUMAN DTI (with DiI injection)
1mm



The Human Connectome



CONNECT: EU F7 FET Project



Microstructural Diffusion Imaging

Water diffusion in tissue

- "True" brownian motion gives rise to a Gaussian diffusion process – the Displacement Distribution Function is a gaussian whose width (displacement RMS) increases with the square root of the diffusion time Δ and the diffusion coefficient D:

$$R_{RMS} = \sqrt{6\Delta D}$$

- Gaussian diffusion process gives is well described by a single diffusion coefficient, related to the DW experiment in the following way:

$$S_b = S_{b=0} e^{-bD}$$

- A gaussian diffusion process, as measured by DW-MRI will give rise to a signal that decays monoexponentially with respect to the b-value. That is the implicit assumption in most of the diffusion analysis, from ADC measurements to DTI.

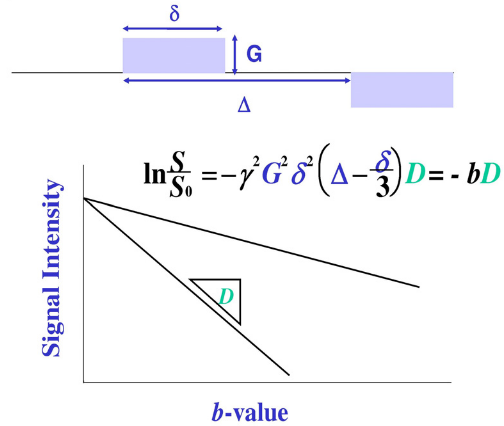
…But cortical diffusion is more complicated…

- Diffusion of water molecules occurs
  - In Intracellular Space
  - In Extracellular Space
  - Exchange between Intracellular and Extracellular spaces
  - Between Layers of Myelin Sheath
- Intricate and Heterogeneous Extracellular Space
  - Glia cells and Astrocytes
  - Organized Macromolecules (Myelin)
  - Randomly Oriented Macromolecules
- Intricate and Heterogeneous Intracellular Space
  - Microfilaments, Microtubules, Neurofilaments
- Water exchanges with hydrophilic binding sites of macromolecules

And the implications:

- Fundamental lack of understanding of the relationship between the DWI contrast and the microscopic structure of tissue in health and disease.
- BAD: Potential misinterpretation of DTI parameters.
- GOOD: Novel DTI which is highly specific to microstructural tissue environment!!! => however: "conventional" (single b-value) DTI results can be ambiguous.

Equation for the diffusion attenuation



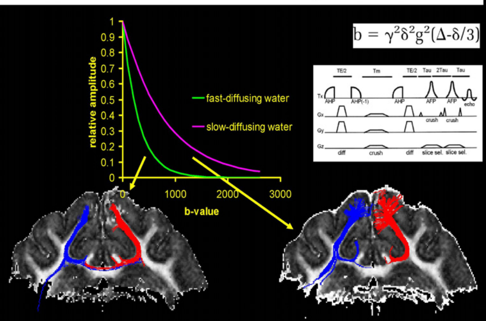
$$\ln\frac{S}{S_0} = -\gamma^2 G^2 \delta^2 \left(\Delta - \frac{\delta}{3}\right) D = -bD$$

COMMUNICATIONS

Magnetic Resonance in Medicine 49:785–790 (2003)

Conventional DTI vs. Slow and Fast Diffusion Tensors in Cat Visual Cortex

Itamar Ronen,* Keun-Ho Kim, Michael Garwood, Kamil Ugurbil, and Dae-Shik Kim



However, it is not guaranteed that D_slow = intracellular only!!

Decrease the number of variables associated with diffusion by decreasing the number of compartments.

↓

How? → Look for biological marker for intracellular Space

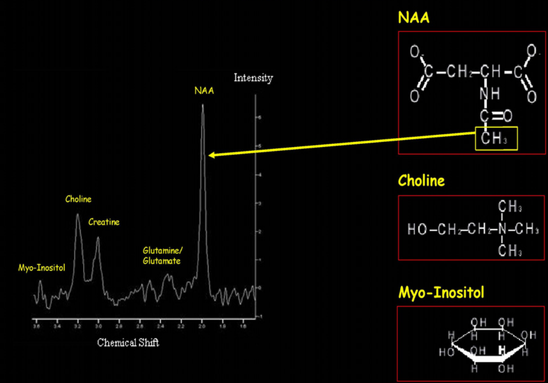
↓

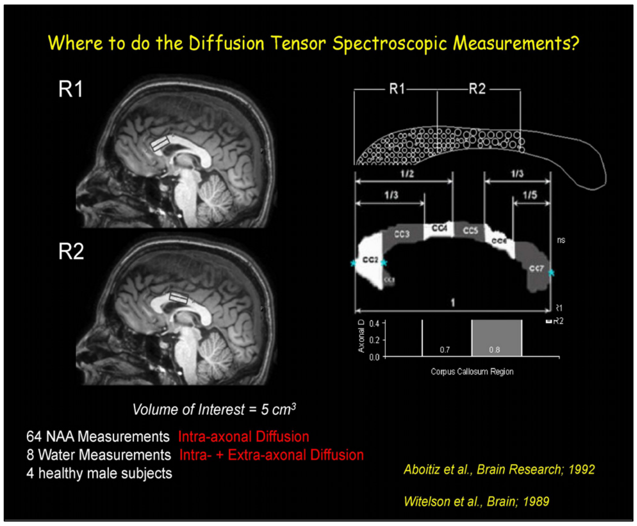
What? → *N*-Acetyl Aspartate (NAA)

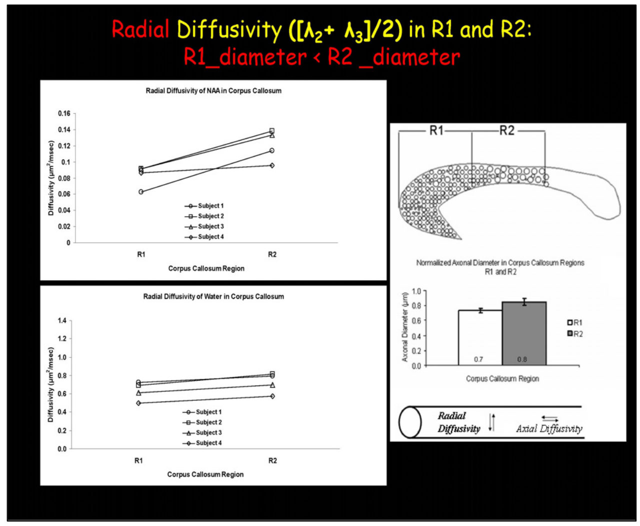
Potential candidate - NAA

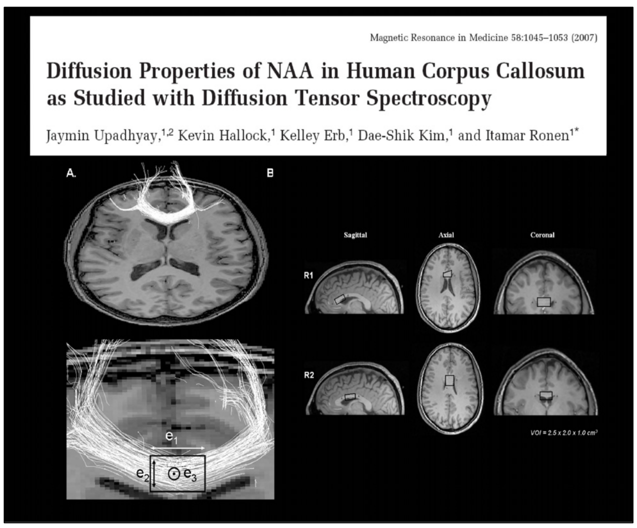
- N-acetyl aspartate is the most abundant intraneuronal metabolite (10mM). [compare to water - 55M!]
- [NAA] is too low to provide signal for a high-resolution image.
- The tool of choice - localized MR spectroscopy (MRS) on a volume of interest (VOI) or Chemical Shift Imaging.

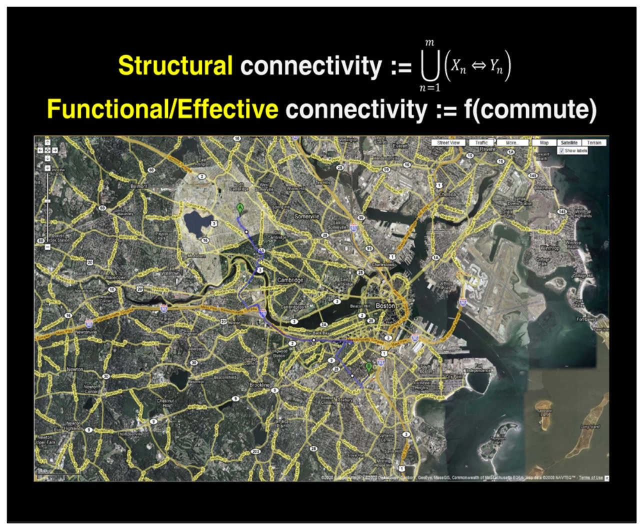
Proton MRS of a VOI located on brain tissue

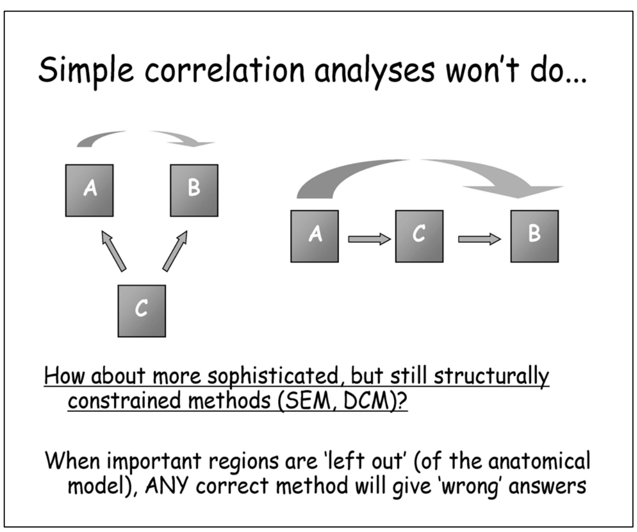


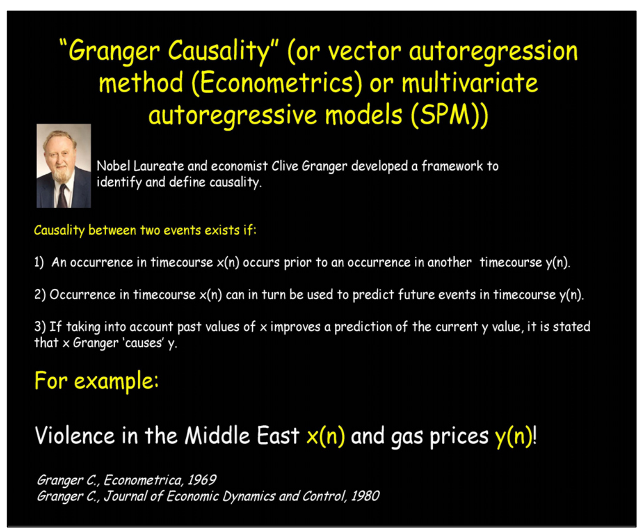

Where to do the Diffusion Tensor Spectroscopic Measurements?
R1
R2
R1
R2
1/2
1/3
1/3
1/5
CC3
CC4
CC5
CC6
CC2
CC7
Axonal D
Corpus Callosum Region
Volume of Interest = 5 cm³
64 NAA Measurements Intra-axonal Diffusion
8 Water Measurements Intra- + Extra-axonal Diffusion
4 healthy male subjects
Aboitiz et al., Brain Research; 1992
Witelson et al., Brain; 1989

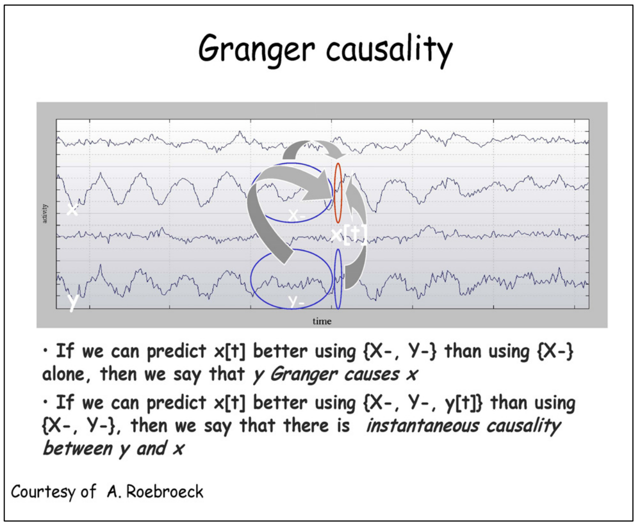

Radial Diffusivity ([λ2+ λ3]/2) in R1 and R2:
R1_diameter < R2 _diameter
Radial Diffusivity of NAA in Corpus Callosum
Diffusivity (μm²/msec)
Subject 1
Subject 2
Subject 3
Subject 4
R1
R2
Corpus Callosum Region
Radial Diffusivity of Water in Corpus Callosum
Diffusivity (μm²/msec)
Corpus Callosum Region
R1
R2
Normalized Axonal Diameter in Corpus Callosum Regions R1 and R2
Axonal Diameter (μm)
Corpus Callosum Region
Radial Diffusivity
Axial Diffusivity

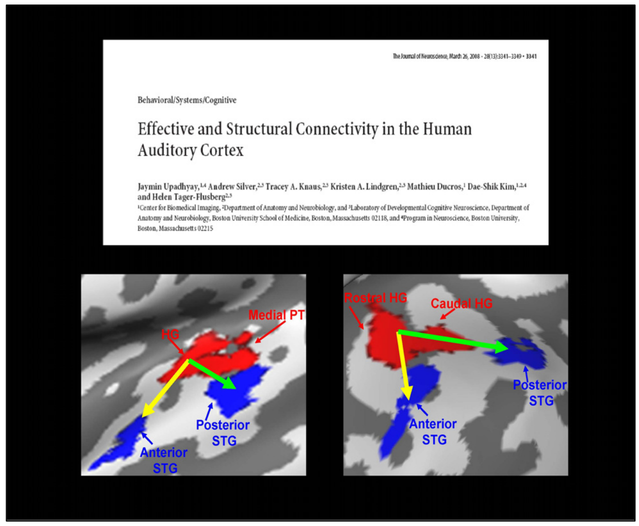

Magnetic Resonance in Medicine 58:1045–1053 (2007)
Diffusion Properties of NAA in Human Corpus Callosum as Studied with Diffusion Tensor Spectroscopy
Jaymin Upadhyay,1,2 Kevin Hallock,1 Kelley Erb,1 Dae-Shik Kim,1 and Itamar Ronen1*
A.
B
Sagittal
Axial
Coronal
R1
R2
e1
e2
e3

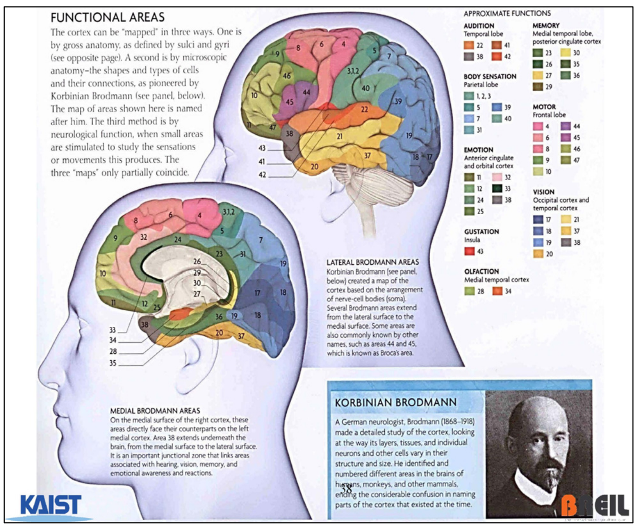

Structural connectivity := $\bigcup_{n=1}^{m}(X_n \Leftrightarrow Y_n)$
Functional/Effective connectivity := f(commute)

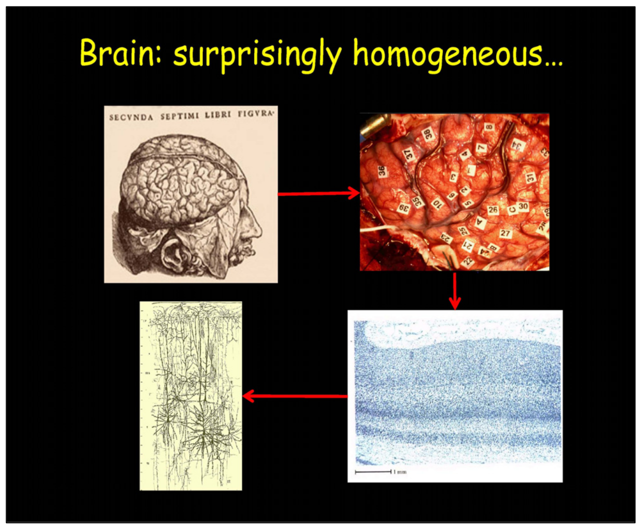

Simple correlation analyses won't do...
A
B
C
A
C
B
How about more sophisticated, but still structurally constrained methods (SEM, DCM)?
When important regions are 'left out' (of the anatomical model), ANY correct method will give 'wrong' answers

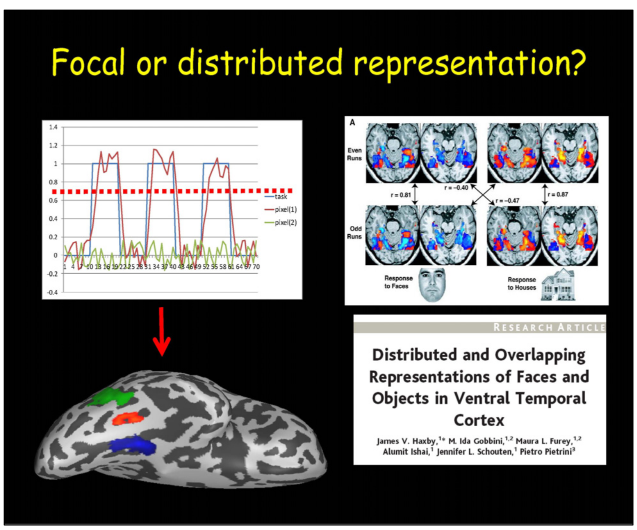

"Granger Causality" (or vector autoregression method (Econometrics) or multivariate autoregressive models (SPM))
Nobel Laureate and economist Clive Granger developed a framework to identify and define causality.
Causality between two events exists if:
1) An occurrence in timecourse x(n) occurs prior to an occurrence in another timecourse y(n).
2) Occurrence in timecourse x(n) can in turn be used to predict future events in timecourse y(n).
3) If taking into account past values of x improves a prediction of the current y value, it is stated that x Granger 'causes' y.
For example:
Violence in the Middle East x(n) and gas prices y(n)!
Granger C., Econometrica, 1969
Granger C., Journal of Economic Dynamics and Control, 1980

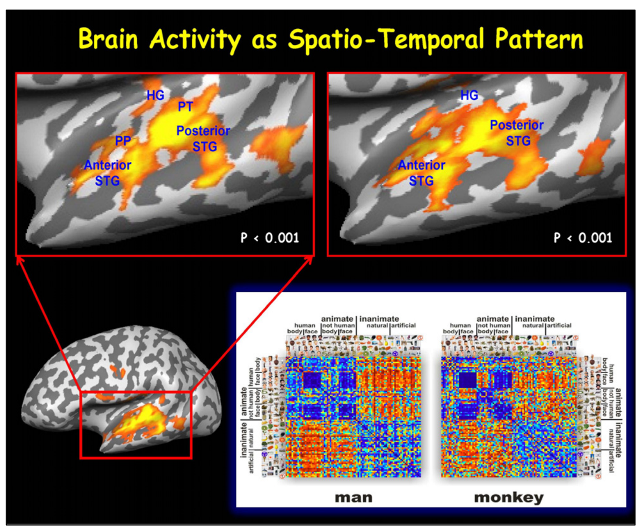

Granger causality
time
• If we can predict x[t] better using {X-, Y-} than using {X-} alone, then we say that *y Granger causes x*
• If we can predict x[t] better using {X-, Y-, y[t]} than using {X-, Y-}, then we say that there is *instantaneous causality between y and x*
Courtesy of A. Roebroeck

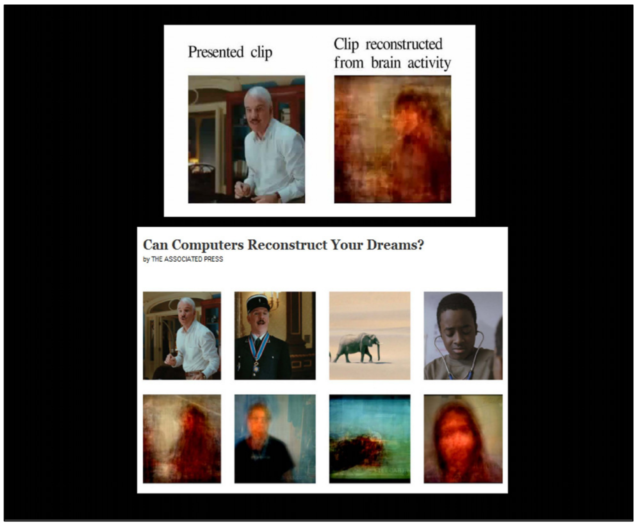

Behavioral/Systems/Cognitive
Effective and Structural Connectivity in the Human Auditory Cortex
HG
Medial PT
Posterior STG
Anterior STG
Rostral HG
Caudal HG
Posterior STG
Anterior STG

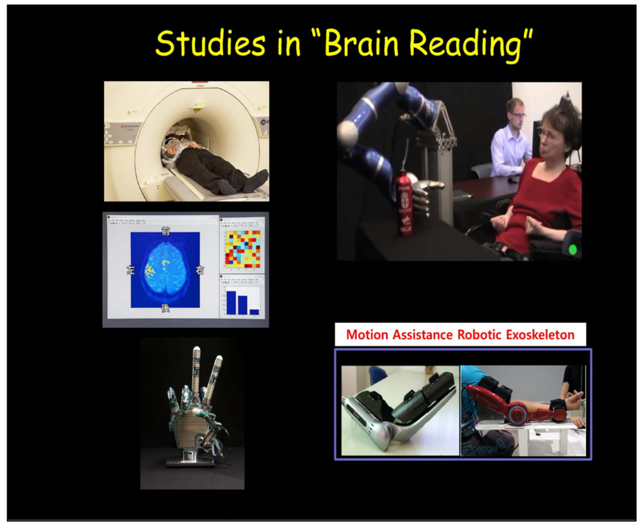

FUNCTIONAL AREAS
APPROXIMATE FUNCTIONS
LATERAL BRODMANN AREAS
MEDIAL BRODMANN AREAS
KORBINIAN BRODMANN
KAIST

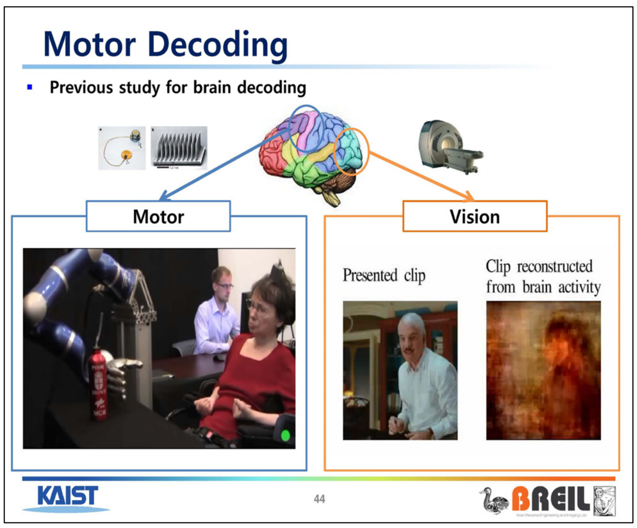

Brain: surprisingly homogeneous...
SECVNDA SEPTIMI LIBRI FIGVRA

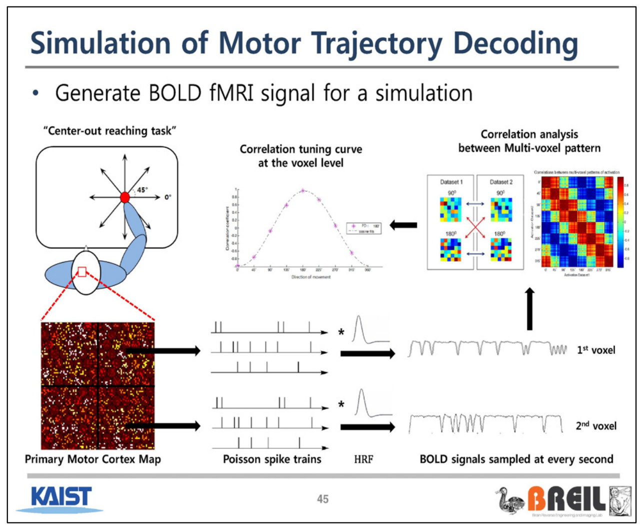

Focal or distributed representation?
Distributed and Overlapping Representations of Faces and Objects in Ventral Temporal Cortex

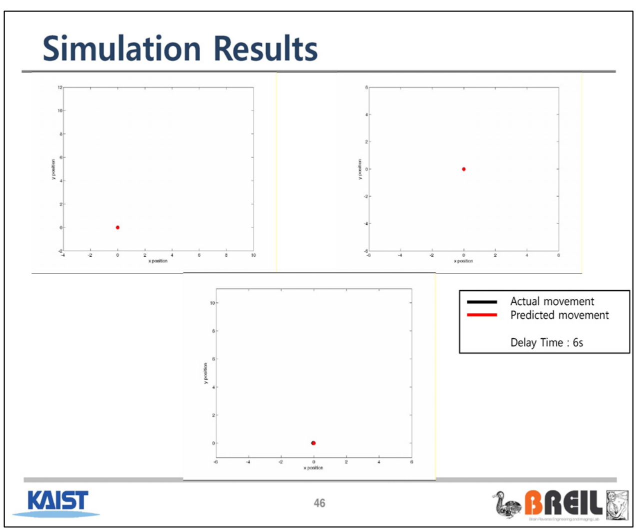

Brain Activity as Spatio-Temporal Pattern
HG
PT
PP
Posterior STG
Anterior STG
P < 0.001
HG
Posterior STG
Anterior STG
P < 0.001
animate
inanimate
man
monkey

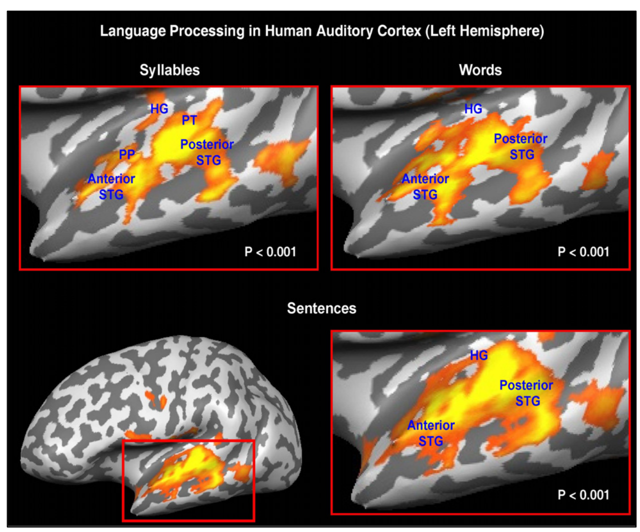

Presented clip
Clip reconstructed from brain activity
Can Computers Reconstruct Your Dreams?
by THE ASSOCIATED PRESS

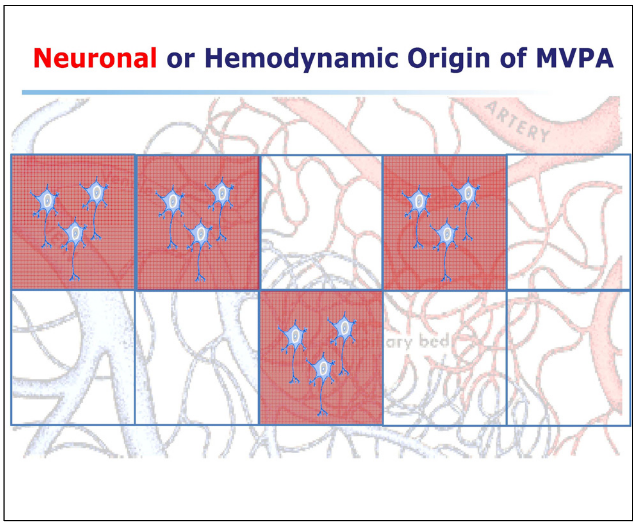

Studies in "Brain Reading"
Motion Assistance Robotic Exoskeleton

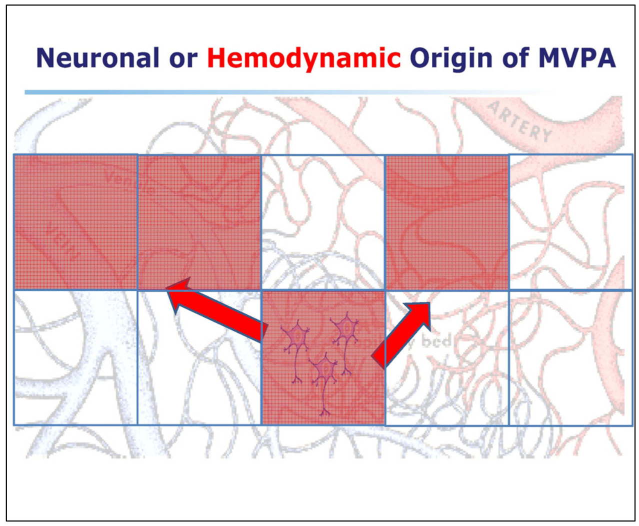

Motor Decoding
Previous study for brain decoding
Motor
Vision
Presented clip
Clip reconstructed from brain activity
KAIST
44
BREIL

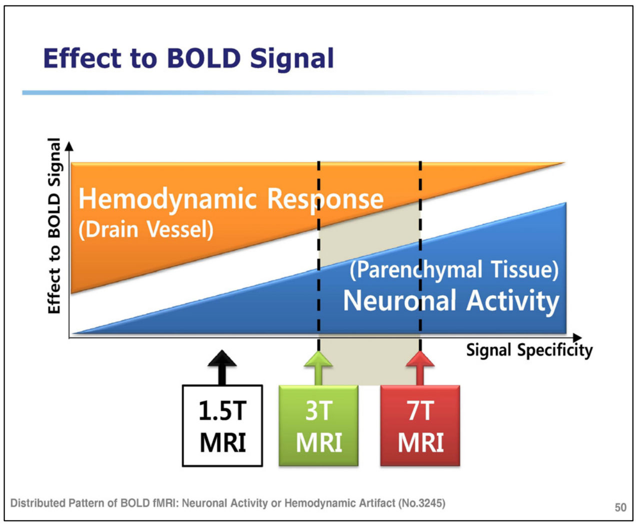

Simulation of Motor Trajectory Decoding
Generate BOLD fMRI signal for a simulation
"Center-out reaching task"
Correlation tuning curve at the voxel level
Correlation analysis between Multi-voxel pattern
Dataset 1
Dataset 2
1st voxel
2nd voxel
Primary Motor Cortex Map
Poisson spike trains
HRF
BOLD signals sampled at every second
KAIST
45
BREIL

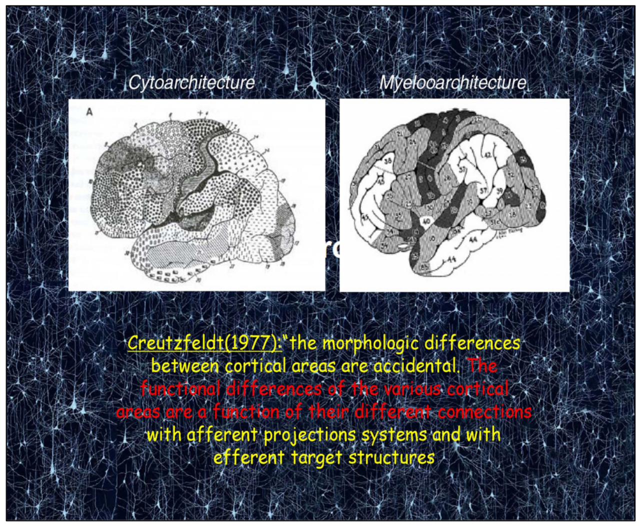

Simulation Results
Actual movement
Predicted movement
Delay Time : 6s
KAIST
46
BREIL

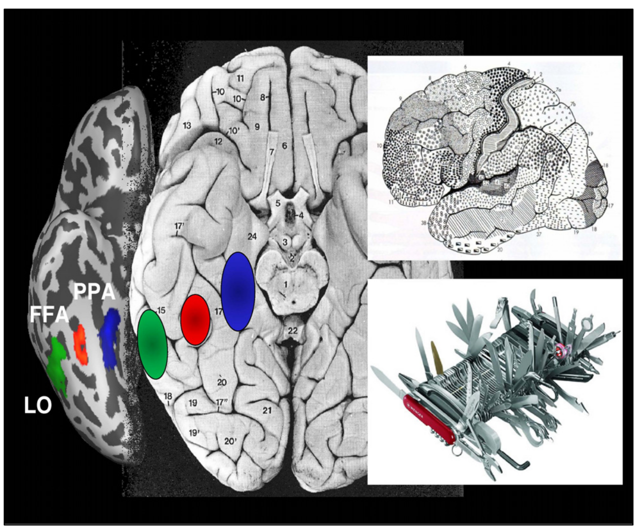

Language Processing in Human Auditory Cortex (Left Hemisphere)
Syllables
Words
HG
PT
PP
Posterior STG
Anterior STG
P < 0.001
Sentences

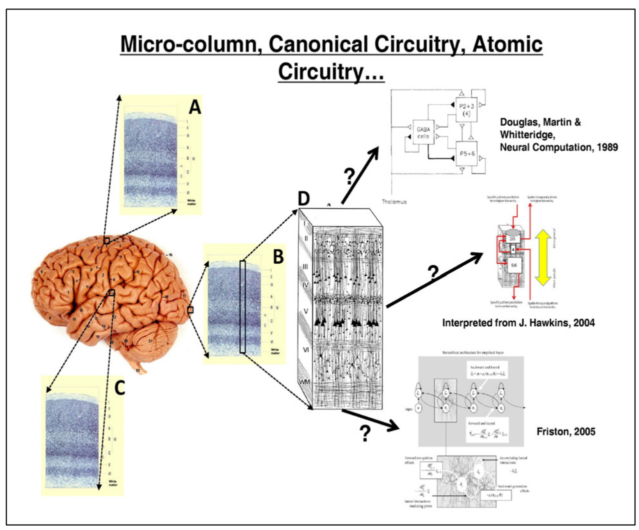

Neuronal or Hemodynamic Origin of MVPA
ARTERY
ary bed

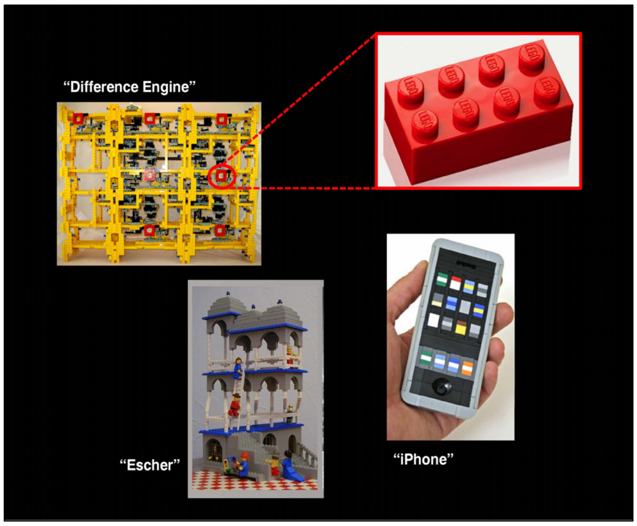

Neuronal or Hemodynamic Origin of MVPA
ARTERY
bed


Effect to BOLD Signal
Effect to BOLD Signal
Hemodynamic Response
(Drain Vessel)
(Parenchymal Tissue)
Neuronal Activity
Signal Specificity
1.5T MRI
3T MRI
7T MRI
Distributed Pattern of BOLD fMRI: Neuronal Activity or Hemodynamic Artifact (No.3245)
50


Cytoarchitecture
Myelooarchitecture
Creutzfeldt(1977): "the morphologic differences between cortical areas are accidental. The functional differences of the various cortical areas are a function of their different connections with afferent projections systems and with efferent target structures


PPA
FFA
LO


Micro-column, Canonical Circuitry, Atomic Circuitry…
A
B
C
D
Douglas, Martin & Whitteridge, Neural Computation, 1989
Interpreted from J. Hawkins, 2004
Friston, 2005


"Difference Engine"
"Escher"
"iPhone"