Physics in Brain Research

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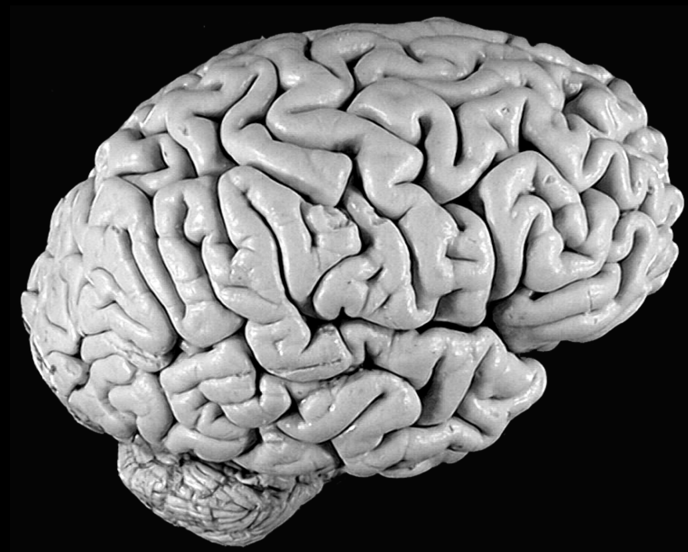
Complexity of the Brain



open
dissipative
adaptive

Structure ↔ Function

Fluctuations

Order ↔ Disorder

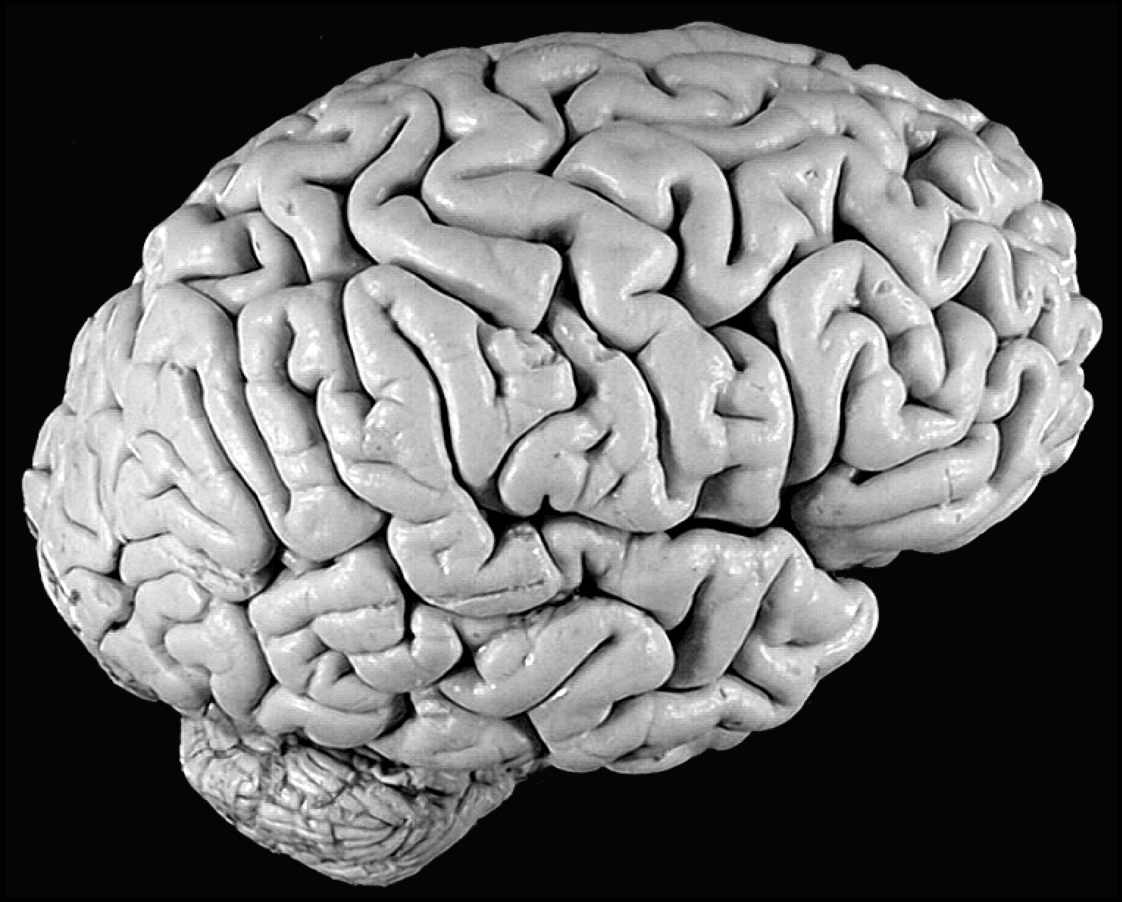
Complexity of the Brain: Structure

number of neurons: ~ 10^{10}
number of synapses/neuron: ~ 10^3 - 10^4
total number of connections: ~ 10^{14}
length of all connections: ~ 10^7- 10^9 m
connectivity factor: ~ 10^{-6} (adult) - 10^{-4} (juvenile)
(number of connections present out of all possible)
ion channel types / neuron ~ 10^2 - 10^3
neurotransmitter and other
active substances ~ 50

- brain networks are not random, but form highly specific patterns.
- neurons tend to connect with other neurons in local groups.

Murre & Sturdy. Biol Cybern 73, 529, 1995

Complexity of the Brain: Function

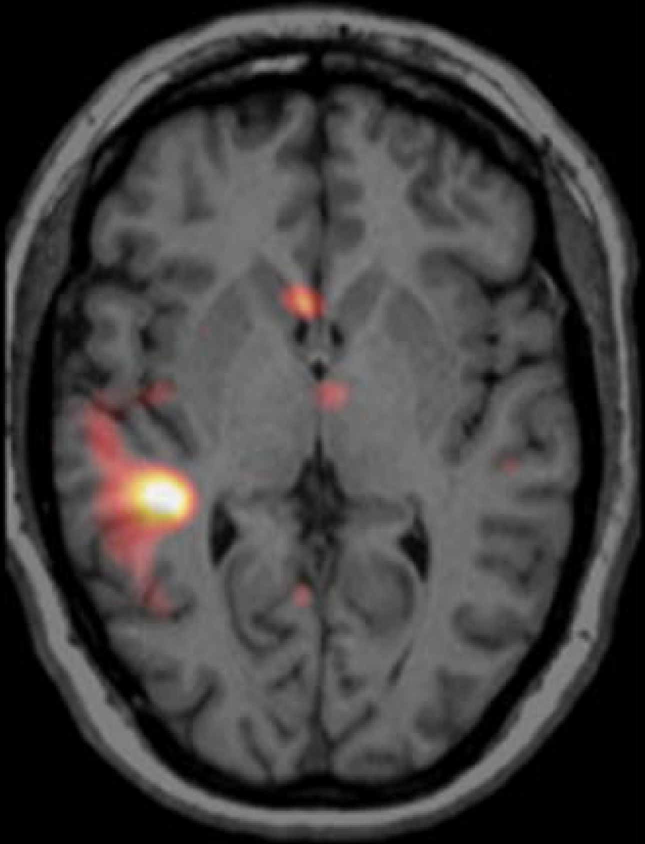


control (body functions)
movement
perception
attention
learning
memory
knowledge
emotions
motivation
language
thinking
planning
personality
self-identity
consciousness
dysfunctions

Understanding Functional and Structural Complexity of the Brain

non-destructive measurement of structure and function of the living brain from the outside

Andreas Vesalius
Anatomist
1514-1564



Understanding Functional and Structural Complexity of the Brain

… requires multidisciplinarity !!

structure:
anatomy, histology,
cytology, biochemistry,
molecular biology, …

function:
cognitive neurosciences,
psychology, neurophysiology,
electrophysiology, ….

physics
+
mathematics
engineering
computer science

Imaging Techniques in Brain Research

"passive" or "direct" imaging measure signals generated by the brain		"active" or "indirect" imaging measure interactions between some appropriate energy and matter			
neuro- electricity	magnetism	x-ray CT	PET	SPECT	nuclear magnetic resonance
el. fields	mag. fields	μ	γ (511 keV)	γ	e. m. fields HF
function / (morphology)		morphology	metabolism		function / morphology
EEG ECoG, SEEG LFP, AP, MP	MEG	PET-CT			MRI, fMRI MRS DTI

Structural Imaging Techniques in Brain Research

Historical overview

1895 Discovery of x-rays

1946 NMR principles

1948 Nuclear medicine scan

1952 Ultrasound imaging

1953 Positron tomography

1971 Single Photon Emission Tomography

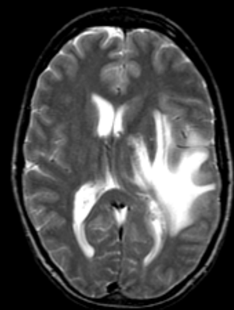
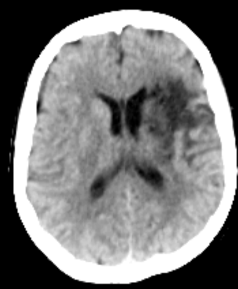
1972 Development of x-ray CT

1976 NMR Imaging

Nobel Prizes

- Röntgen (1901, x-rays)
- Rabi (1944, MR)
- Bloch, Purcell (1952, MR)
- Hounsfield, Cormack (1979, CT)
- Ernst (1991, NMR)
- Wuthrich (2002, NMR)
- Lauterbur, Mansfield (2003, MRI)

Structural Imaging Techniques in Brain Research

spatial resolution			soft tissue	bones	volumes	physical load
1 mm	**MRI**		++	+	++	low
0.1 mm	**CT**		-	+++	++	high
0.01 mm	**x-ray film**		+/-	+++	-	high

Structural Imaging Techniques in Brain Research

Limiting factors

Physical limits

x-ray/CT:	number of γ-quanta
MRI:	proton density/volume

Technical limits

x-ray/CT:	tubes, detectors, ionizing radiation
MRI:	field strength, coils

Noise, Artifacts

Structural Imaging Techniques in Brain Research

Possible improvements

Measurement techniques

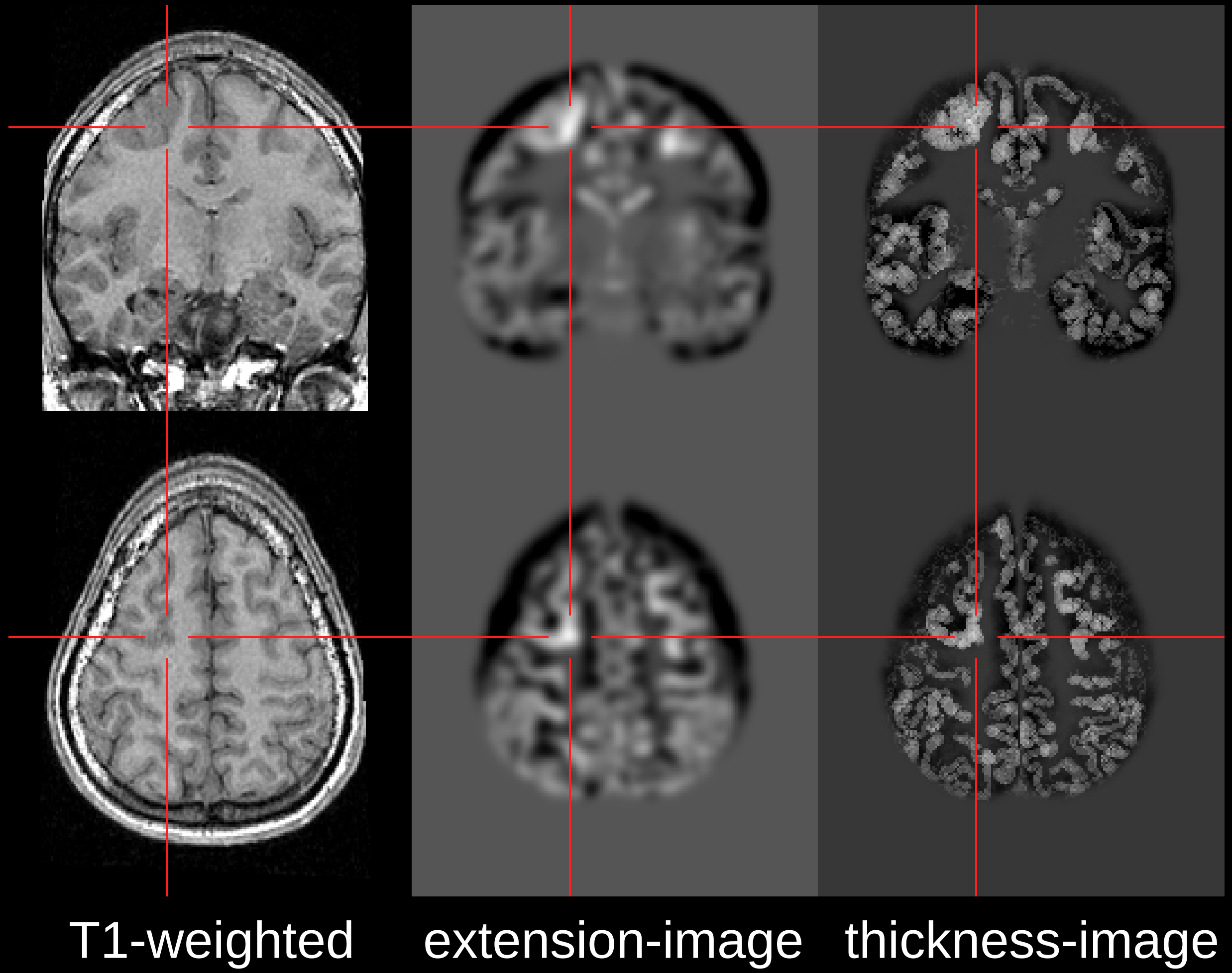
Advanced post-processing techniques

Contrast agents, magnetic nanoparticles, ferrofluids

Combined techniques (PET-CT, PET-MRT)

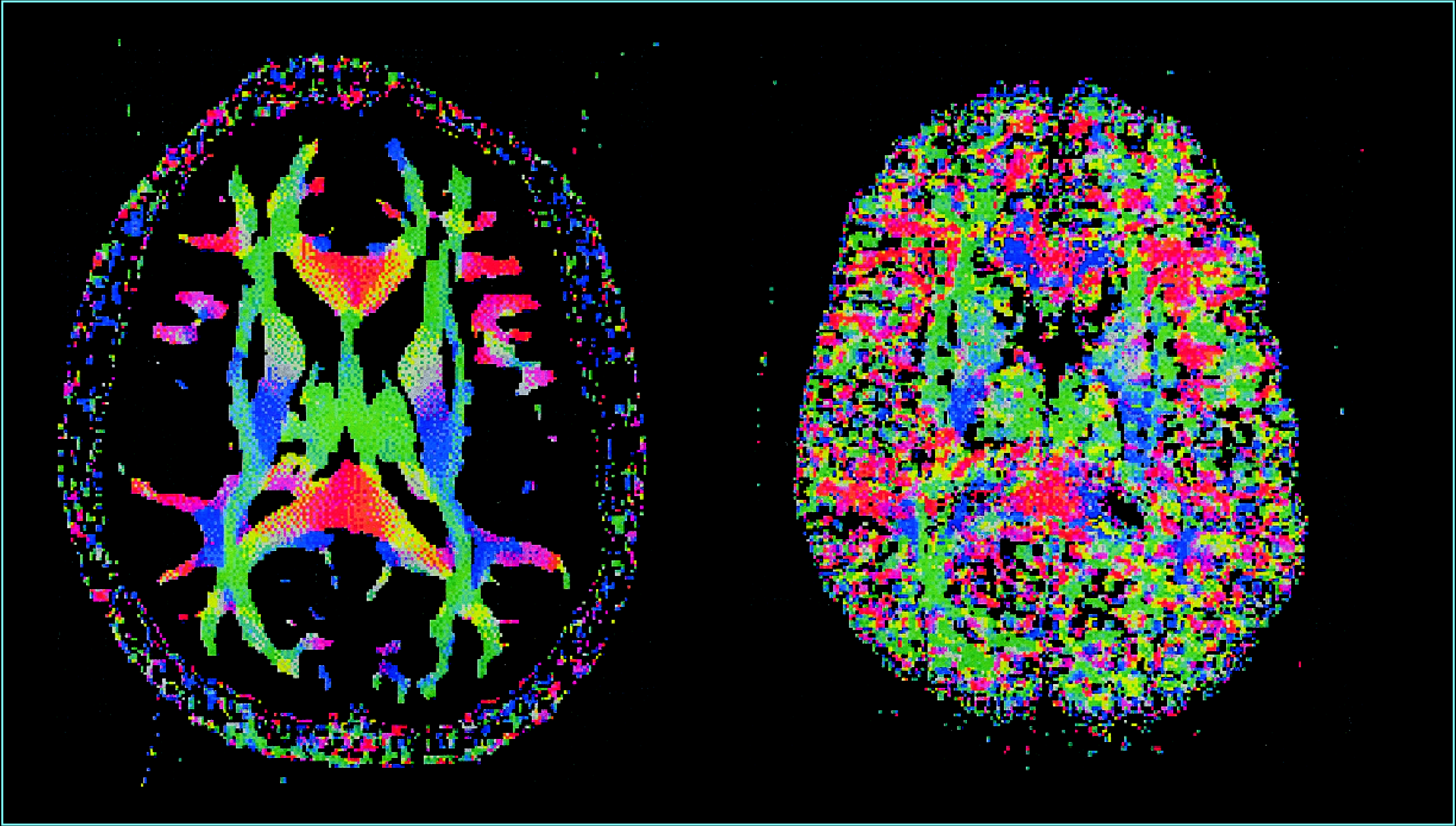
Structural Imaging in Focal Cortical Dysplasia

- Visualization of Blurred Gray–White Matter Junctions -



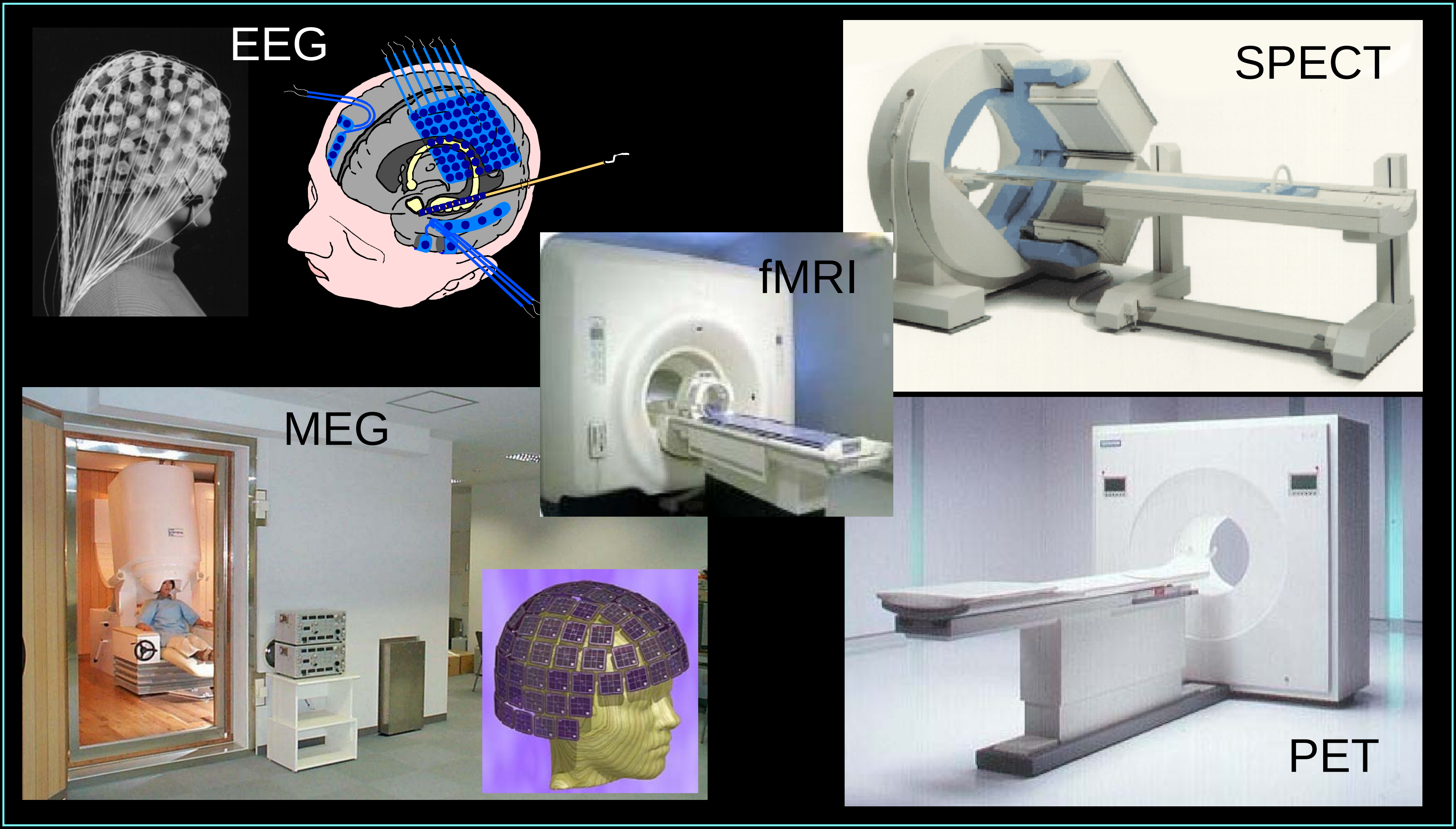
B. Fischl & A.M. Dale, Proc. Natl. Acad. Sci., 97, 11050, 2000;   J. Kassubek et al., Epilepsia, 43, 596, 2002

Fiber Tracking with Diffusion Tensor Imaging

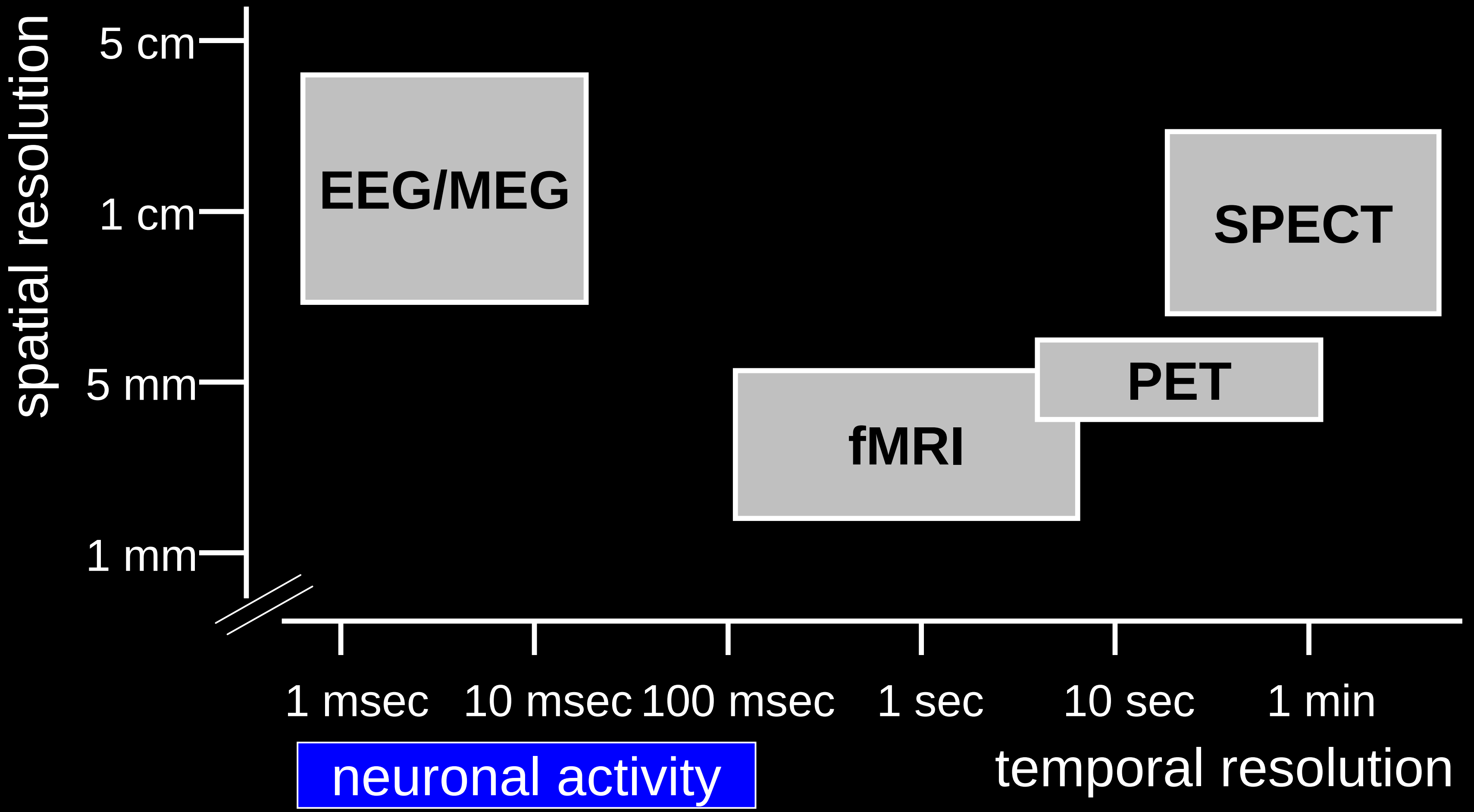


from: Clark et al., Magnetic Resonance in Medicine 47:623–628, 2002

Functional Imaging Techniques in Brain Research



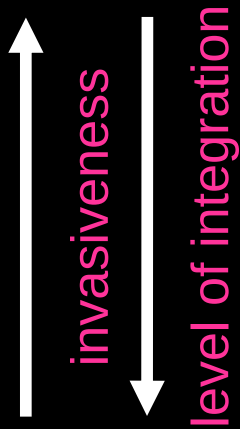
Functional Imaging Techniques in Brain Research



Functional Imaging Techniques in Brain Research

- Measurement Techniques -

neuronal activity	spatial resolution	temporal resolution
direct measurements		
- single/multiple unit recordings	high	high
- local field potentials (LFP)		
- stereo-electro-encephalogram (SEEG)		
- electrocorticogram (ECoG)		
- electroencephalogram (EEG)	low	
- magnetoencephalogram (MEG)		
indirect measurements		
- PET / SPECT	low	low
- fMRI	high	



Functional Imaging

Specific Aims

- analysis of information processing in the brain
- alterations due to pathologies of central nervous system

temporal information: what, when, and why?

spatial information: what, where?

- modeling, prediction

Functional Imaging Techniques in Brain Research

Historical overview

1929 electroencephalogram

1947- evoked potentials

1953 Positron tomography

1971 Single Photon Emission Tomography

1975 magnetoencephalogram

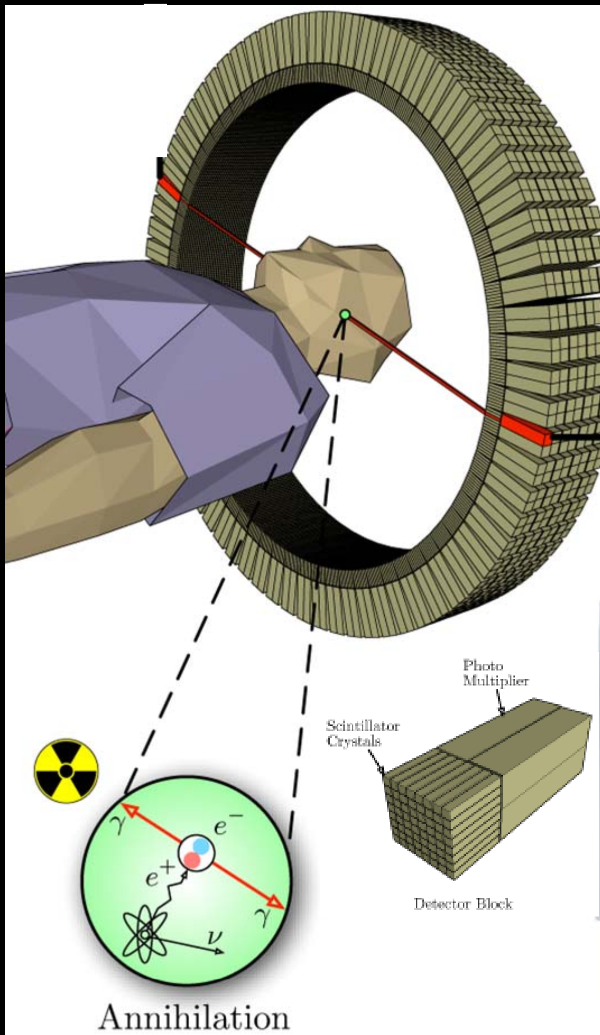
1976 NMR Imaging

1990 BOLD-Effect

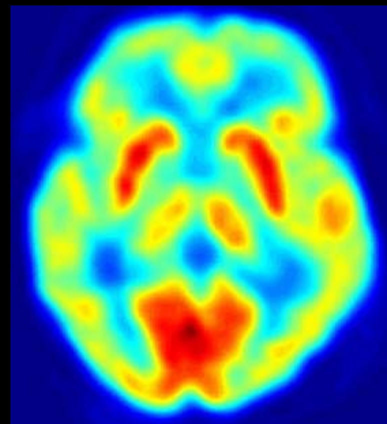
Nobel Prizes

- Sherrington, Adrian - 1932
  function of neurons
- Eccles, Hodgkin, Huxley - 1963
  ionic mechanism in neurons
- Bardeen, Cooper, Schrieffer - 1972
  superconductivity
- Sperry, Hubel, Wiesel - 1981
  information processing visual system
- Lauterbur, Mansfield - 2003
  magnetic resonance imaging

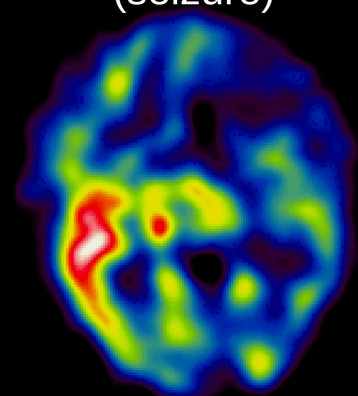
Functional Imaging Techniques: PET/ SPECT

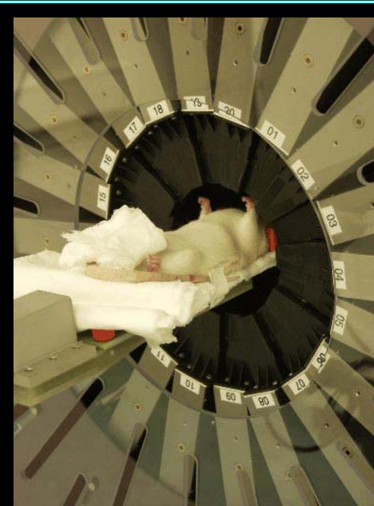


^{18}F FDG-PET (normal)

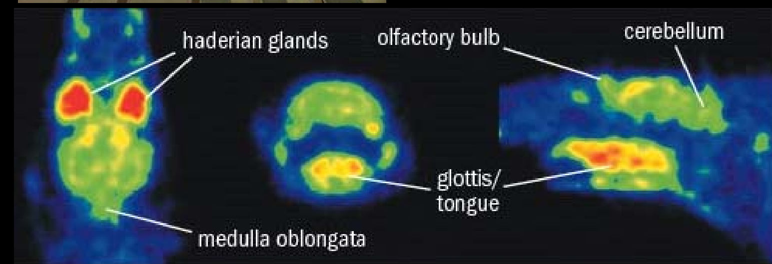


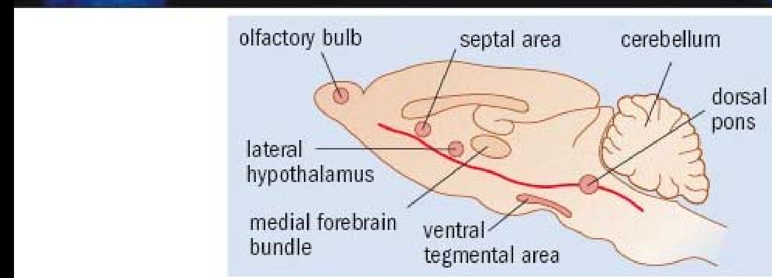
^{99m}Tc HMPAO-SPECT (seizure)





ClearPET©
Small Animal
PET System
2 mm resolution



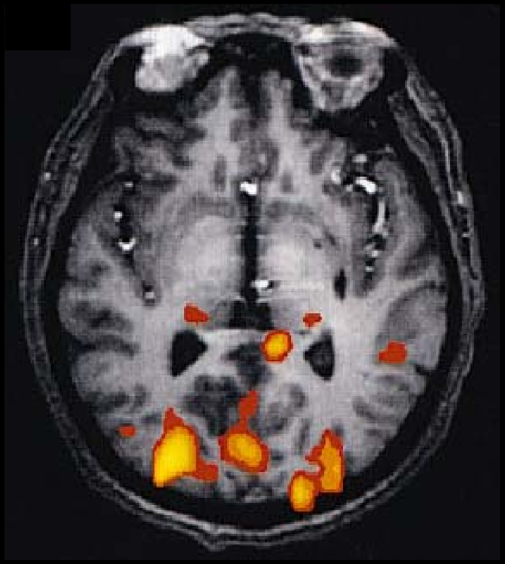


Source: Cern Courier, 45, 27, 2005

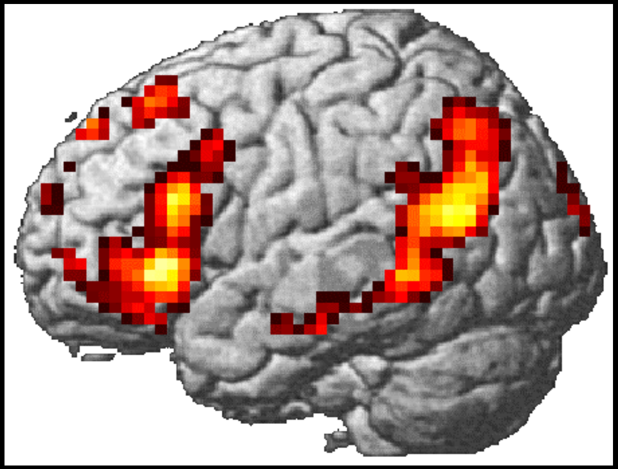
Functional Imaging Techniques: fMRI

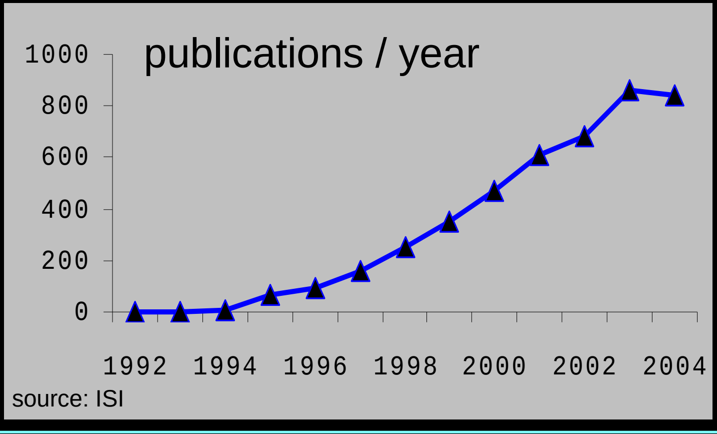
sensory

visual



language



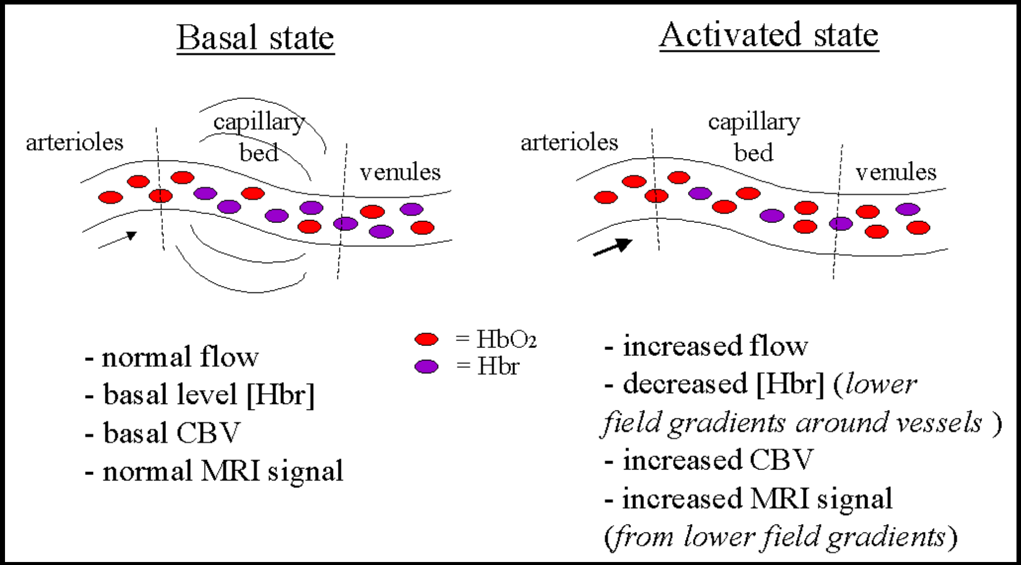


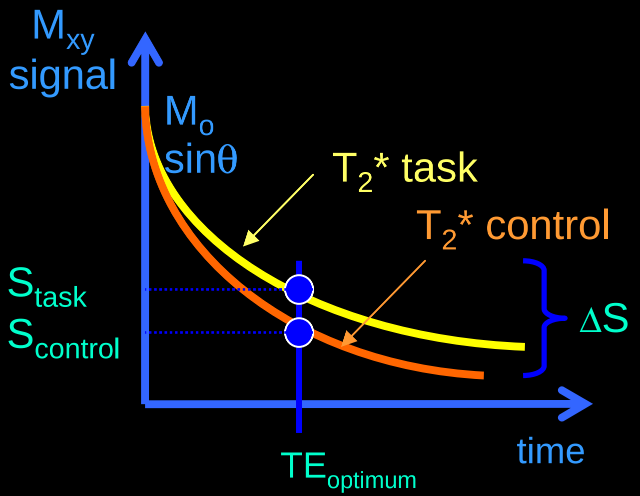
Functional Imaging Techniques: fMRI

IDEA: use Hemoglobin (Hgb) as *intrinsic tracer*:
- oxy-Hgb is diamagnetic, deoxy-Hgb is paramagnetic (local field inhomogeneities)

BOLD (Blood **O**xygen **L**evel **D**ependent**) Effect:**

↑neural activity ➔ ↑ blood flow ➔ ↑ oxy-Hgb ➔ ↑ T2* ➔ ↑ MR signal

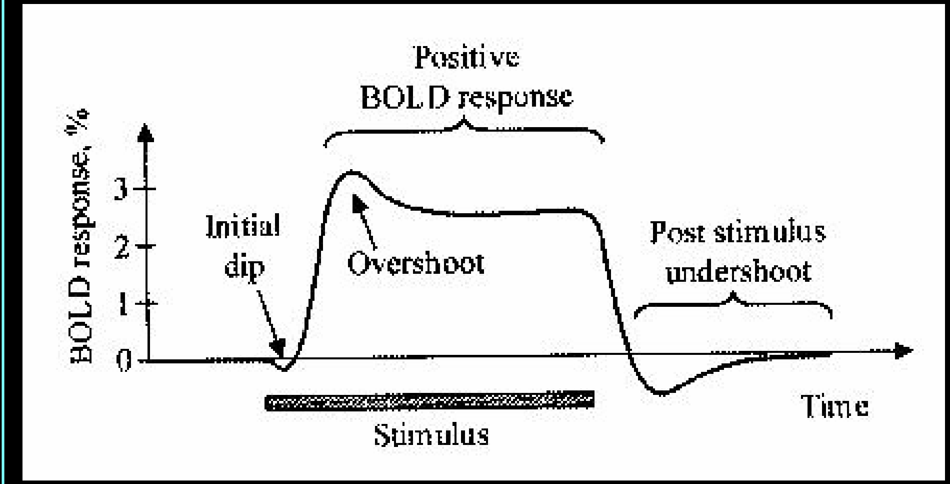




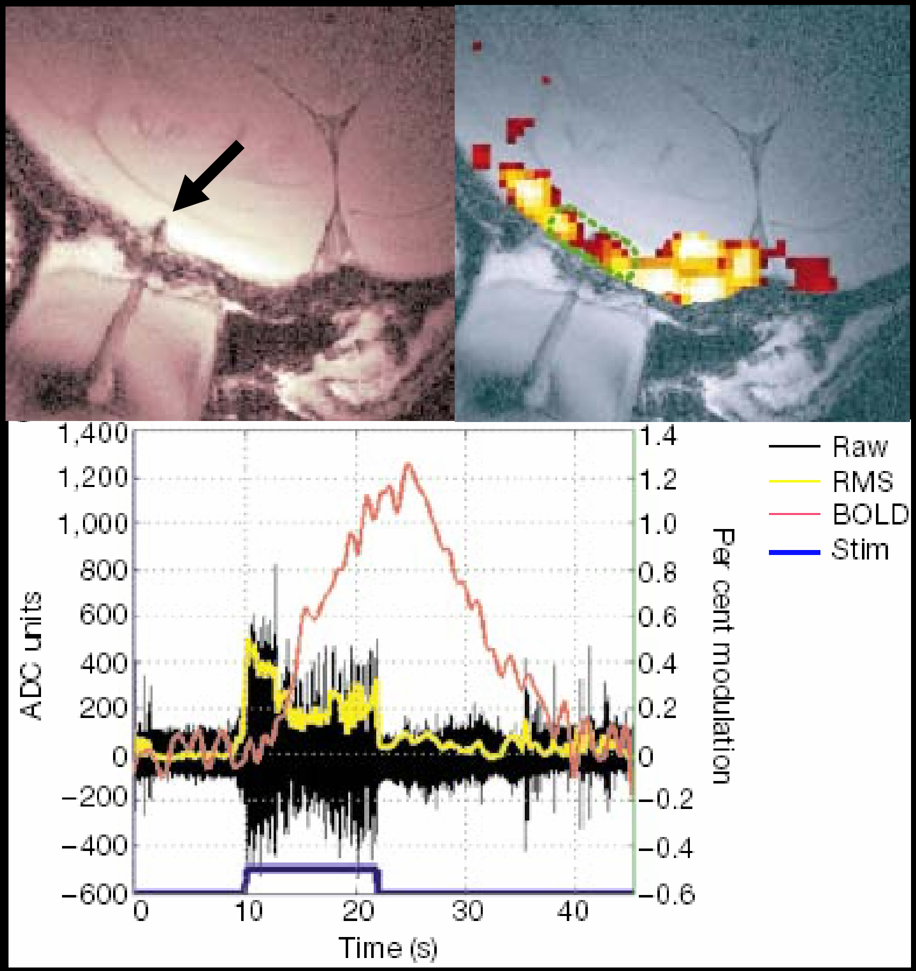
ΔS ~ 3-5 % !!

Functional Imaging Techniques: fMRI

hemodynamic response function

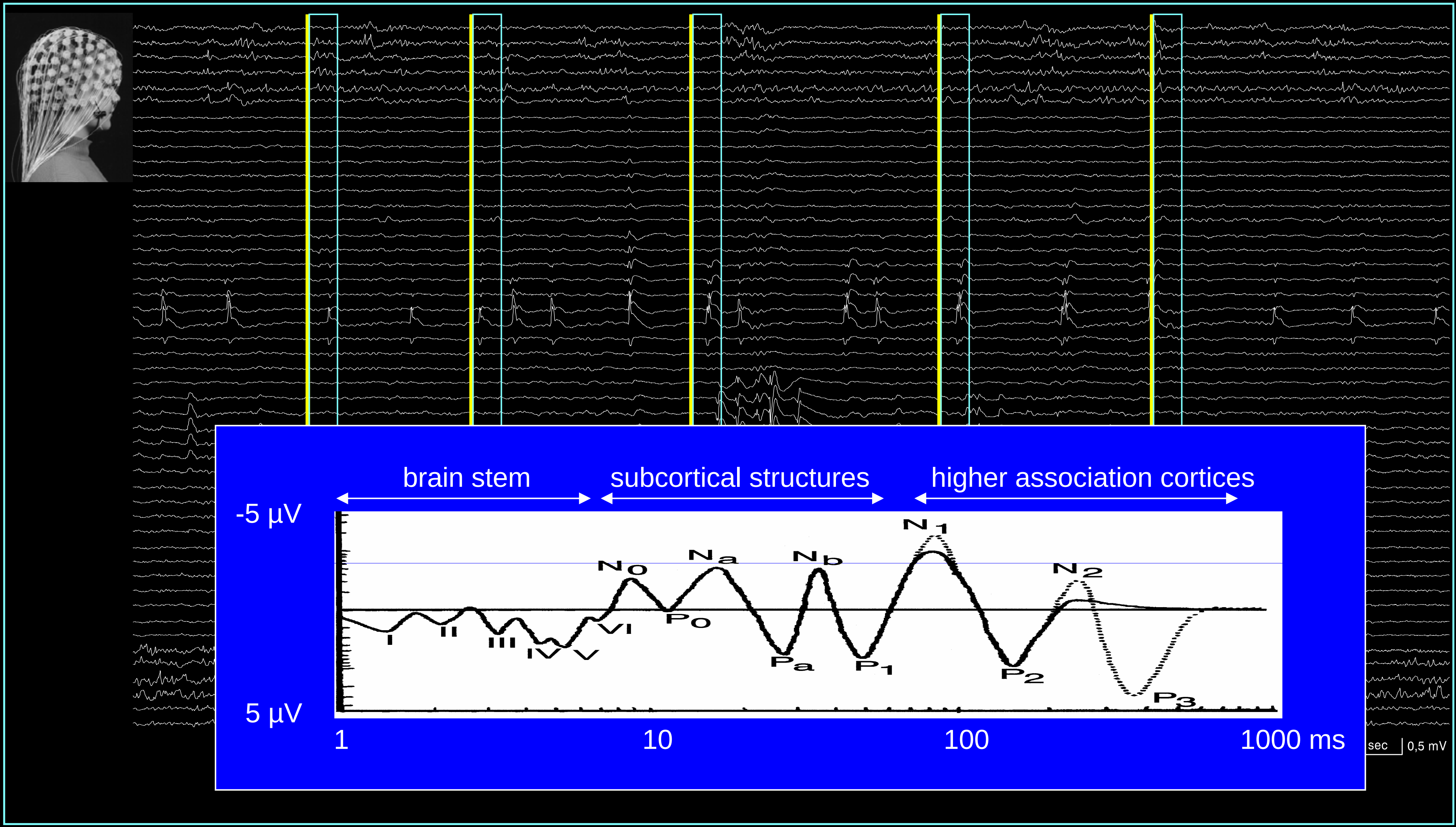


BOLD-effect and neuronal activity:
- monotonous but nonlinear relationship
- neurovascular coupling ?
- initial dip ?
- time scales ?



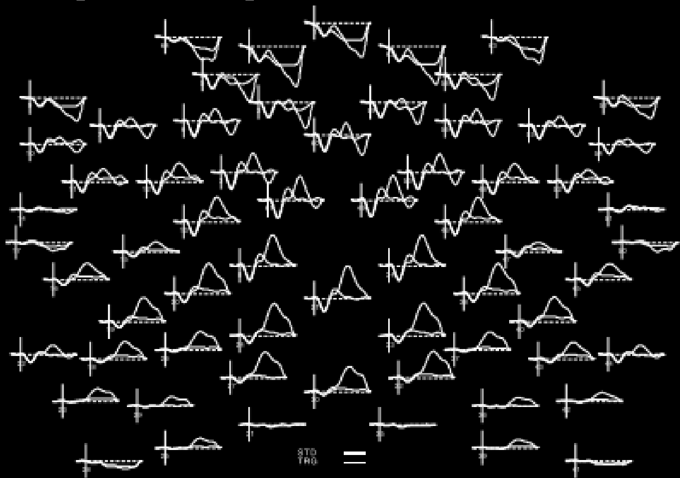
from: Logothetis et al., Nature, 412, 2001

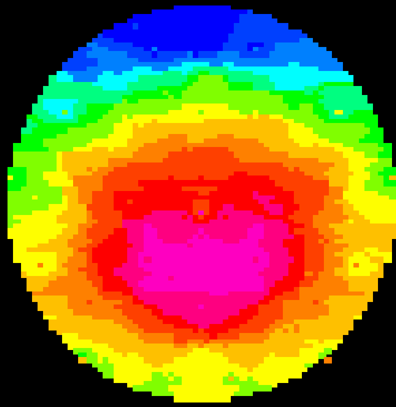
Functional Imaging Techniques: EEG/MEG

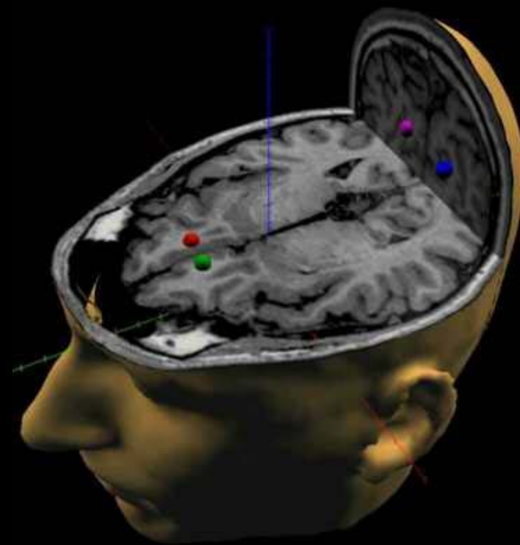


Functional Imaging Techniques: EEG/MEG

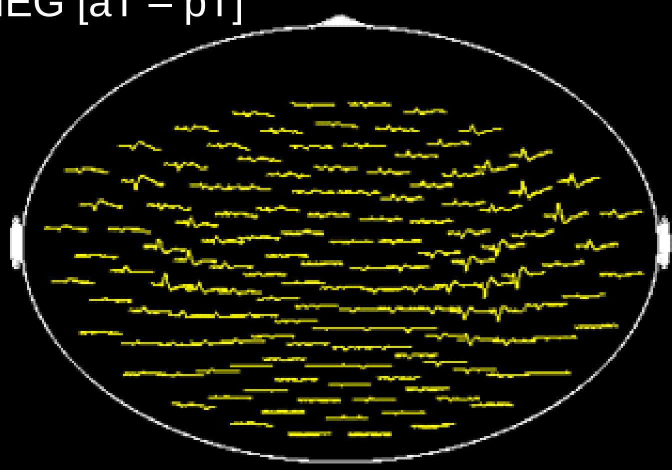
EEG [nV – mV]

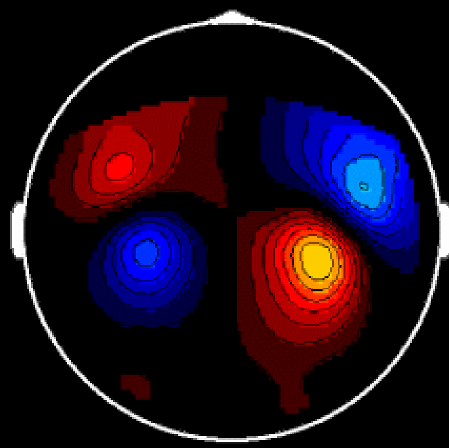


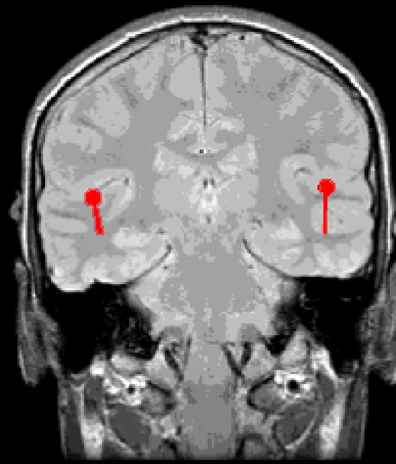




MEG [aT – pT]

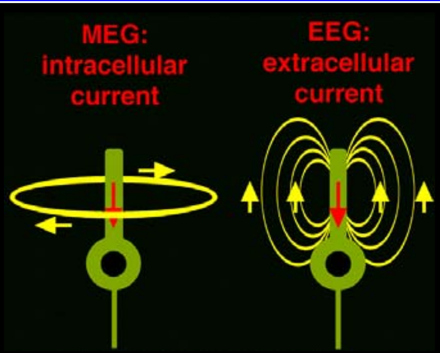






Functional Imaging Techniques: EEG/MEG

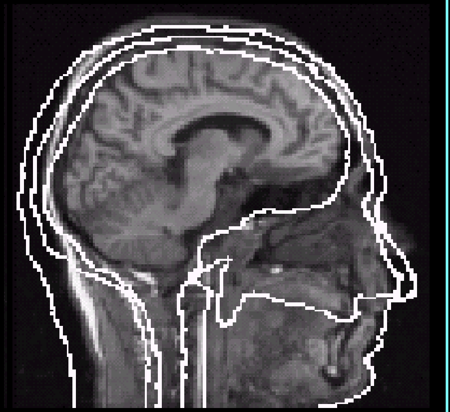
source modeling



single/multiple dipoles, multipole expansion, current density distr., ….

volume conductor modeling

half space
sphere
ellipsoid
realistic models
…



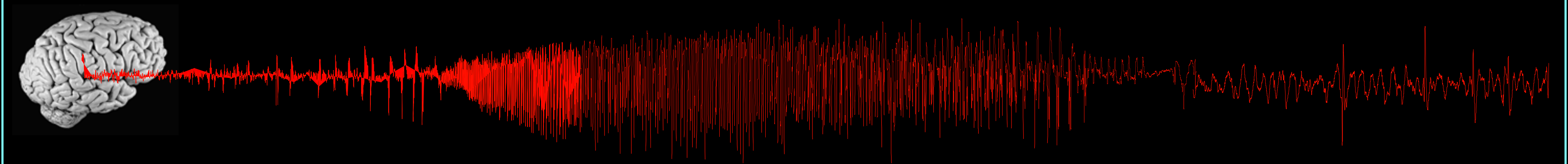
inverse problem

$$\vec{B}(\vec{r}) = \frac{\mu_0}{4\pi} \int j(\vec{r}\,') \times \frac{\vec{r} - \vec{r}\,'}{|\vec{r} - \vec{r}\,'|^3} dr'$$

$$V(\vec{r}) = \frac{\sigma_0}{\sigma_{\vec{r}}} V_0(\vec{r}) - \frac{1}{4\pi} \sum_{i,j} \frac{(c_i - c_j)}{\sigma_{\vec{r}}} \int_{S_{i,j}} V(\vec{r}\,') \frac{(\vec{r} - \vec{r}\,')}{\|\vec{r} - \vec{r}\,'\|^3} x\, dS' \qquad V_0(\vec{r}) = \frac{1}{4\pi\sigma_0} \int \frac{\nabla' \cdot j(\vec{r})}{\|\vec{r} - \vec{r}\,'\|^3} dv'$$

3D localization of neuronal activity

Functional Imaging Techniques: EEG/MEG

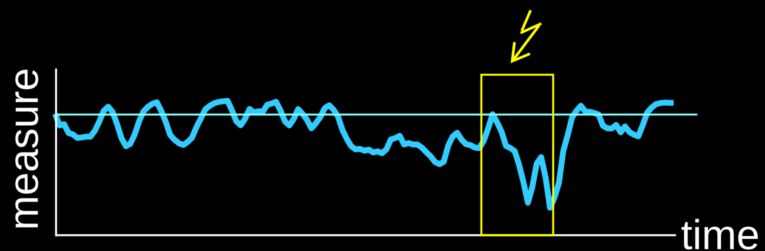


time series analysis

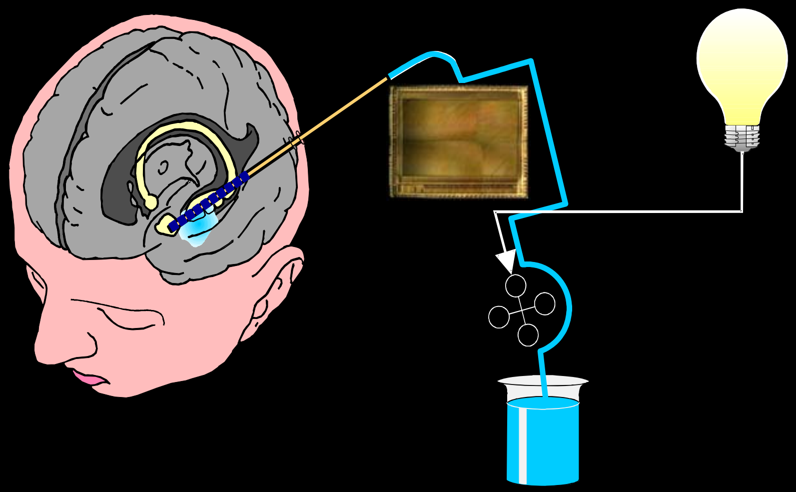
statistical physics

complex system theory

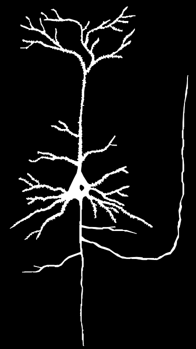
nonlinear dynamics

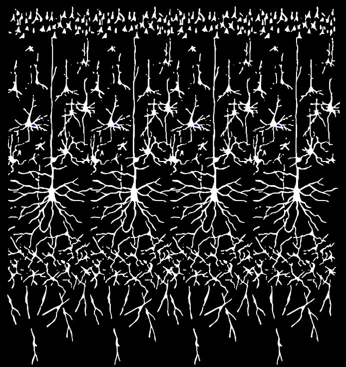


anticipation ⇒control



Understanding Functional and Structural Complexity of the Brain: Modeling





integrate-and-fire
FitzHugh-Nagumo
Hodgkin-Huxley

ion channels
neurotransmitter
synapses

branching structure

network size
connectivity

inhibition/excitation
feed back/ feed forward
coupling

interneurons / glia cells

?

Understanding Functional and Structural Complexity of the Brain

medical/biological physics

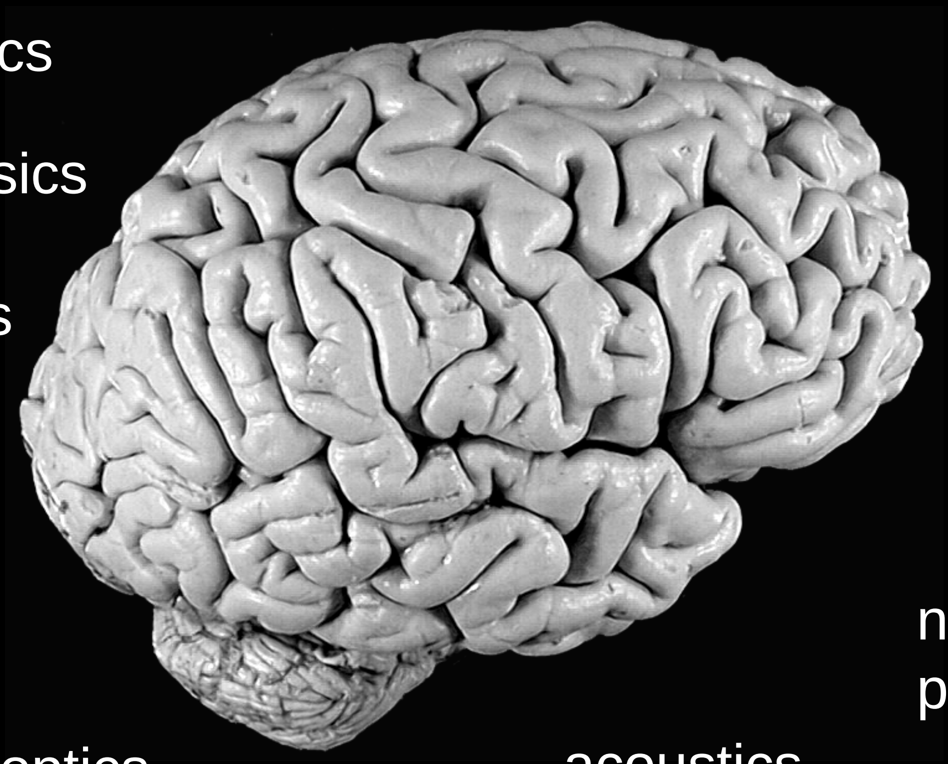
statistical physics

condensed matter physics

computational physics

low temperature physics

nonlinear dynamics



thermodynamics

detector physics

electrodynamics

nuclear/atomic physics

optics

acoustics

Understanding Functional and Structural Complexity of the Brain

Medical imaging celebrated its centennial anniversary in 1995, and today it continues to push the frontiers of research and clinical applications forward. It is an excellent example of what can be done through a multidisciplinary effort, in this case involving physicists, engineers, and physicians.
Many research opportunities are available, as much remains to be done in further improving the applications of medical imaging to reducing human disease and disability.

W. R. Hendee
Physics and applications of medical imaging
Rev. Mod. Phys., Vol. 71(2), pp. S444, Centenary 1999

•**How to Reduce Noise**

•• Head motion artifacts are the worst

•– Test experienced subjects

•– Give your subjects clear instructions (e.g., try not to swallow)

•– Consider motion correction algorithms (Jody's opinion: garbage in, garbage

•out, when in doubt throw it out; exception: rare subjects such as patients)

•• Spatially smooth the data

•– Tradeoff: lose resolution

•• Choose your signal power in a frequency with low noise

•– high noise at low frequencies (so don't use long epochs: optimum epoch

•duration is 16 sec)

•– try to have multiple repetitions of conditions within each run

•– high noise at breathing frequency (once every 4-10 seconds)

•• Temporal smoothing

•– At a minimum, perform linear trend removal

•– Consider filtering out low frequencies (high-pass filter)

•– Jody advises against filtering out high frequencies (temporal Gaussian)

•because it artificially inflates your stats

•Go with a stronger magnet (4T rules!)

•• Go with a better coil (surface coil)

•– Tradeoff: lose other areas

•• Take bigger voxels

•– Tradeoff: lose spatial resolution, if voxels are too big, you

•lose signal

•• Make sure your subject is paying attention to the

•stimuli/task

•– e.g., "1 back" task: hit button after every stimulus repetition

•– Tradeoff: Attention itself can distort the activation

•– Caveat: need to be sure attention is comparable across

•conditions