I see a solution

Makoto Miyakoshi

Swartz Center for Computational Neuroscience
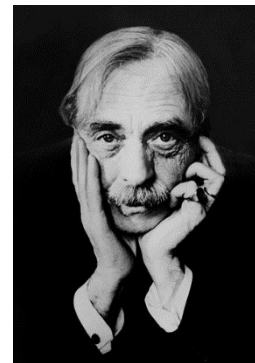
Institute for Neural Computation

University of California San Diego

Last update: 10/26/2018

Part 1

- Future of EEG—Makoto's pessimism
- Present of EEG—Vacation of ground truth and adolesc-i-ence
- Past of EEG—Popperian defense in *cul-de-sac*

We enter the future backwords.
Paul Valéry

http://www.aphorism4all.com/images/1355814906.jpg

Introduction: Complex mind to read

- Key Question: Does EEG have capacity to represent complexity of mind?

Ghost in the Shell (1996)

https://myanimelist.net/featured/993/13_Cyberpunk_GIFs_from_Ghost_in_the_Shell

The true degrees of freedom in EEG

256 ch EEG

Active saccade task

PCA
To obtain 95% variance
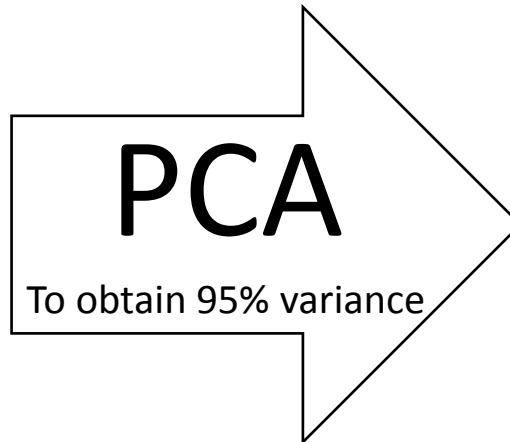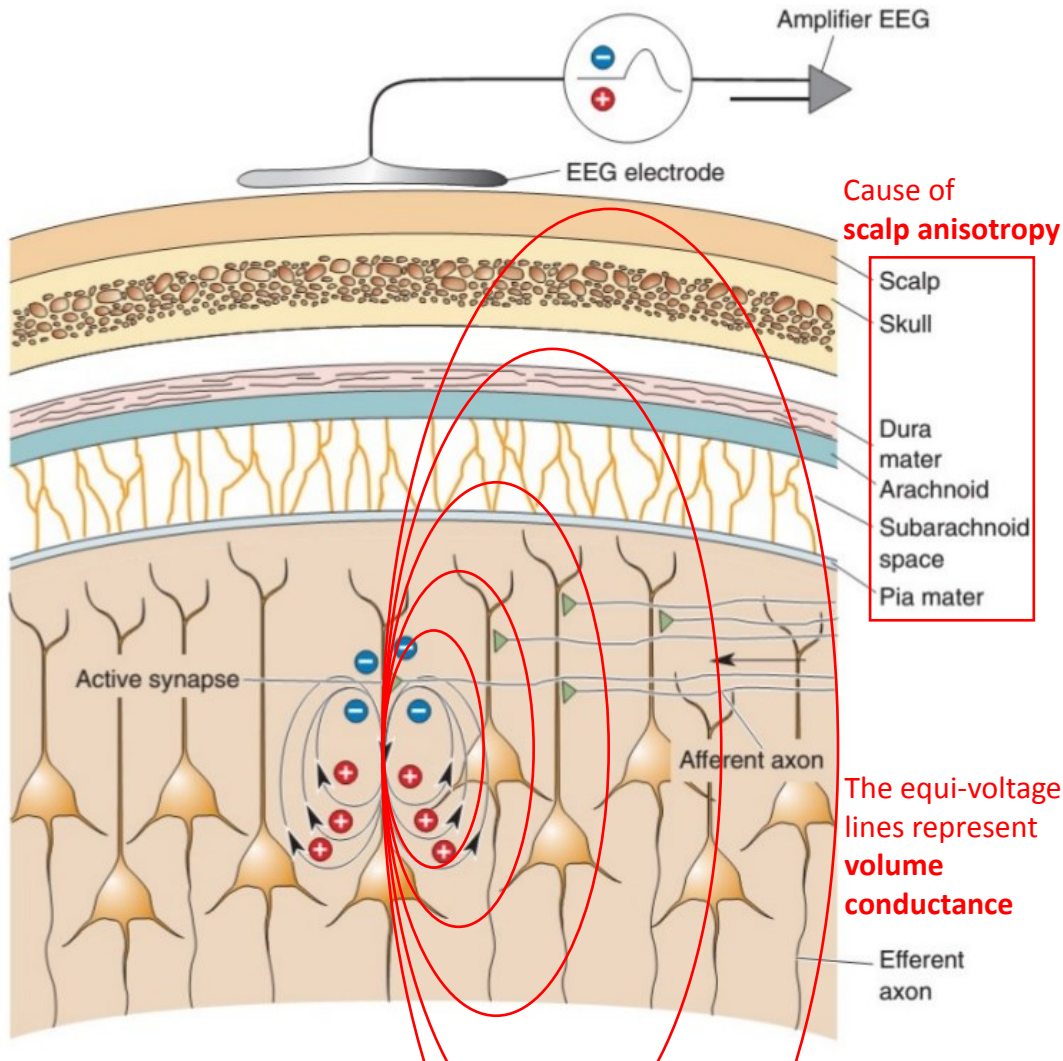
9

- Does EEG has capacity to represent complexity of mind? [-> *Nein*]

How is EEG's true degrees of freedom determined

Amplifier EEG

EEG electrode

Cause of **scalp anisotropy**

Scalp
Skull

Dura mater
Arachnoid
Subarachnoid space
Pia mater

Active synapse

Afferent axon

The equi-voltage lines represent **volume conductance**

Efferent axon

- There are *favorable* conditions for source activity to be scalp-measurable.
  - Cyto-architecture
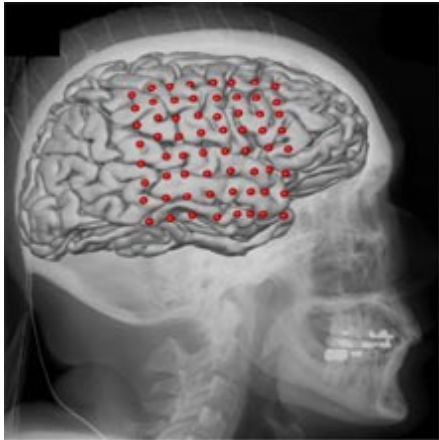 - Chrono-architecture

Figure by Dr. Mayank Agarwal
https://www.slideshare.net/drmayankmanu/eeg-69533120

Which neuron is more scalp-measurable?
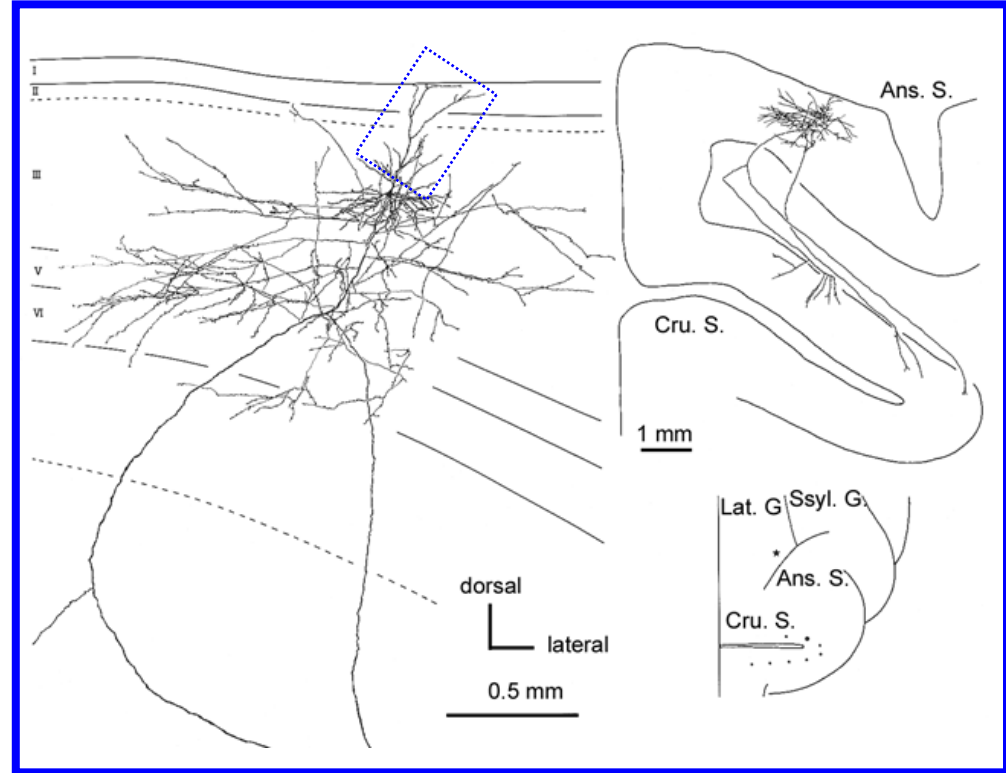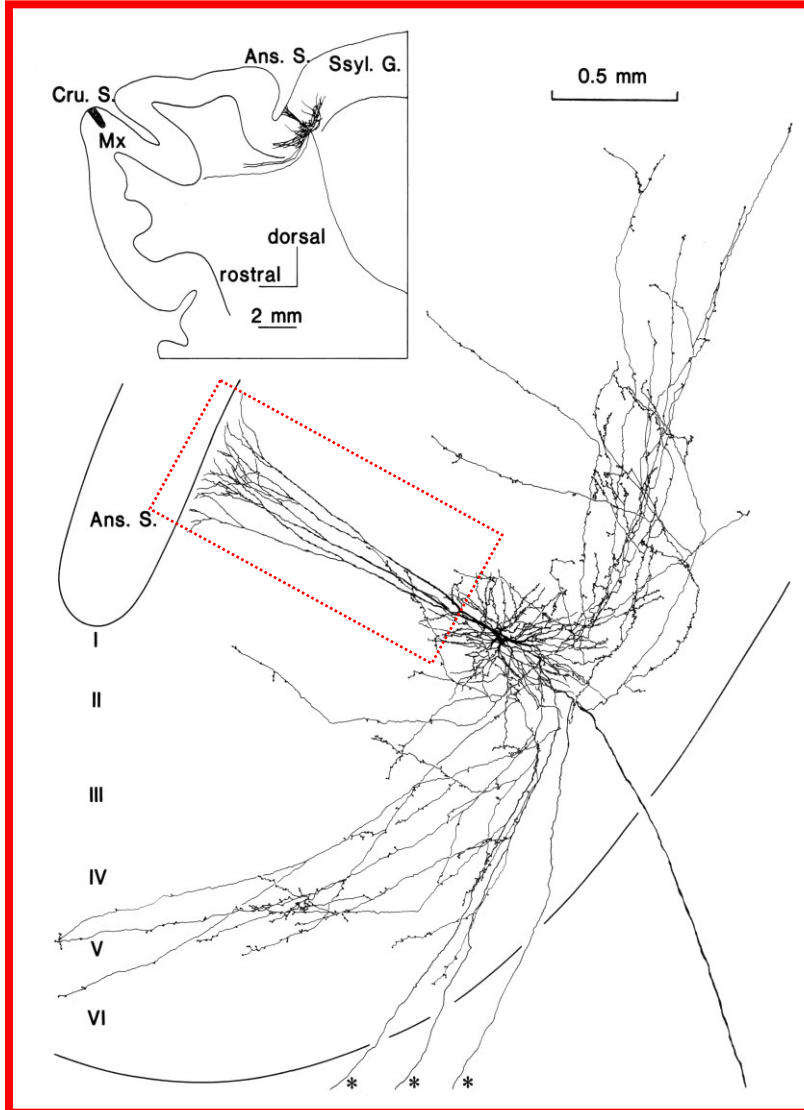
Shinji Kakei at SCCN
(June 26, 2017)

Figures courtesy of Shinji Kakei and Yoshikazu Shinoda

The true degrees of freedom in ECoG

137 ch ECoG

Resting state

PCA

To obtain 95% variance
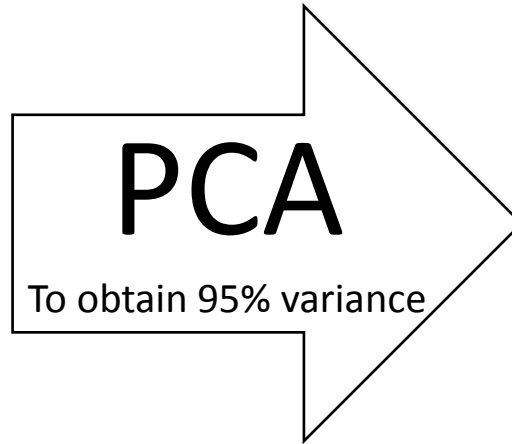
78
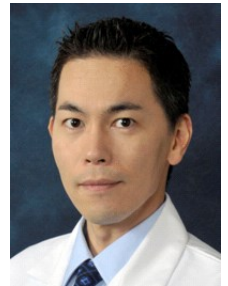
(ECoG: Electrocorticogram)

Data courtesy of Eishi Asano

Functional *channel* mapping?

ECoG!?

ECoG implantation

von Ellenrieder et al. (2016)
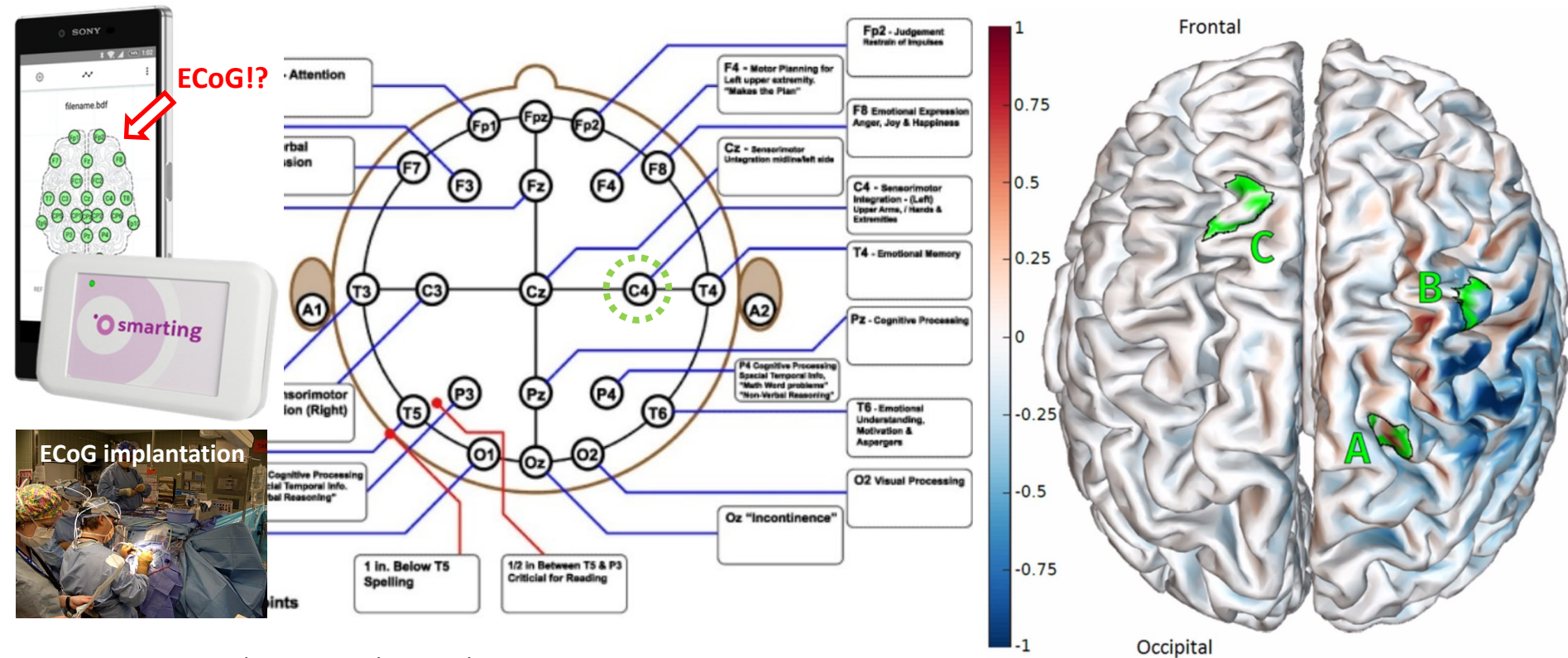
Figure by Dr. Mayank Agarwal
https://www.slideshare.net/drmayankmanu/eeg-69533120
https://mbraintrain.com/smarting/
http://www.schalklab.org/sites/default/files/pics/IMGP1752_0.JPG

8

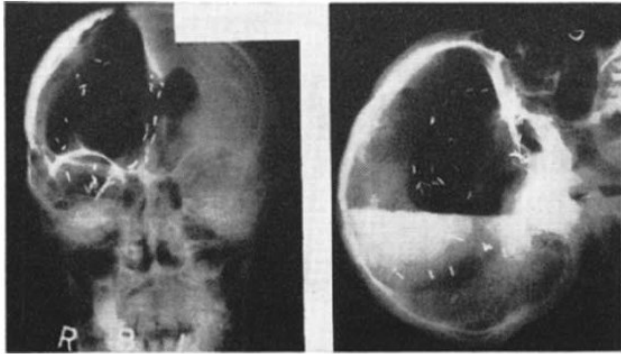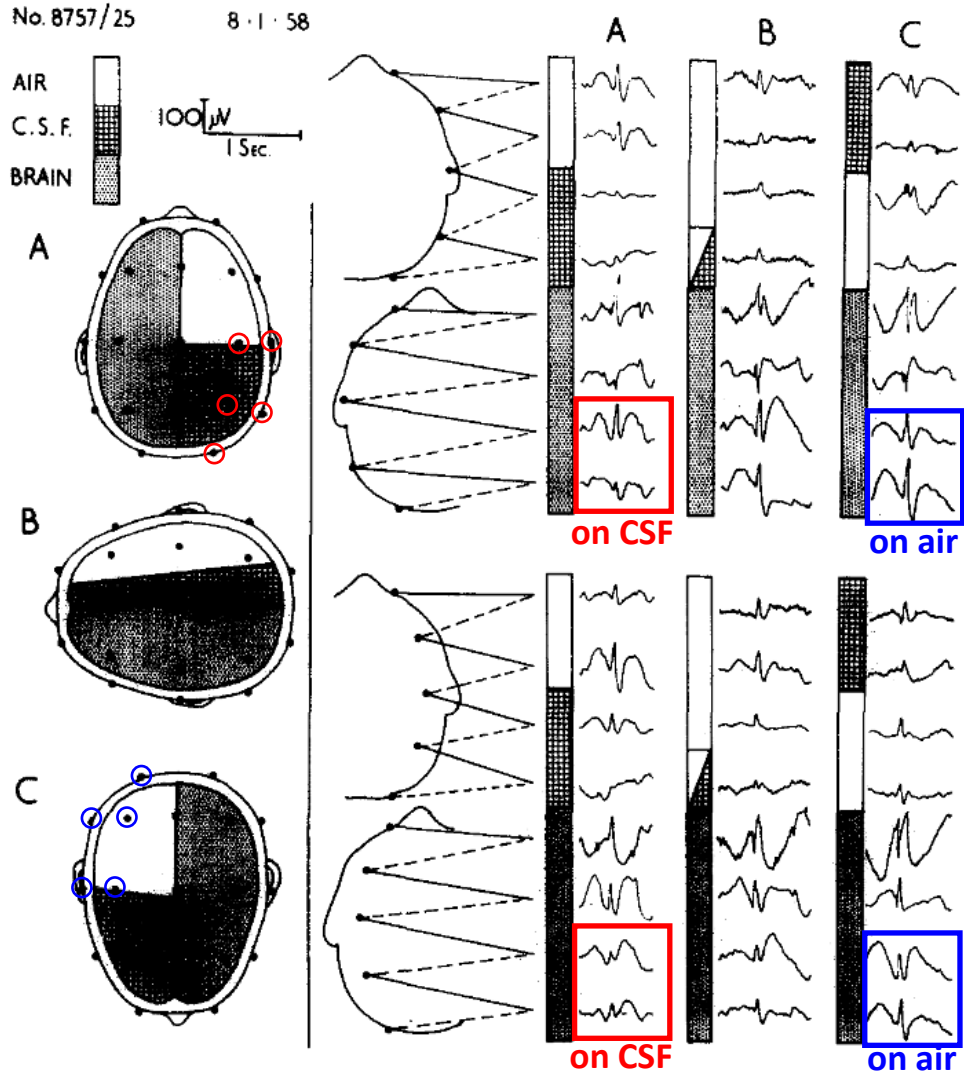# Channels above CSF (A) < above air (C)!

Fig. 5

Case 4. A-P and right lateral X-rays after replacement of about half of the C.S.F. by air. Brow-up, showing fluid level and enlarged left ventricle.

Cobb and Sears (1960)

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Spatial smoothness difference between Scalp EEG and ECoG

- *...It is well known that, with present techniques and methods of analysis, decreasing the distance between scalp electrodes below a few centimetres does not give additional useful EEG information because the electrical activities recorded from closely spaced electrodes are very similar. In marked contrast, recordings from intracerebral and cortical electrodes can show differences from millimetre to millimetre. (Cooper et al., 1965)*

# Part 1 Summary
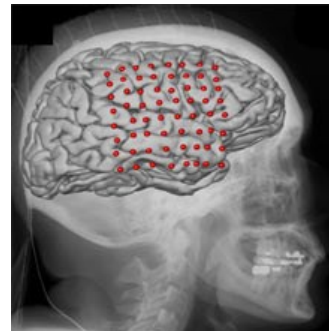
9/256 (96.5% reduction)   78/137 (56.9% reduction)

- *Makoto's pessimism*—the true degrees of freedom in scalp EEG is limited.
  - This is probably why ICA always returns only 10-20 usable ICs even if we use >100 or > 200 channel EEG data.
- ECoG has more degrees of freedom. More possibility!
- Functional *channel* mapping is quite naive.

Interlude: ECoG in science fiction

- Micro machines are injected to cerebrospinal fluid to establish ultra high-density ECoG connection.
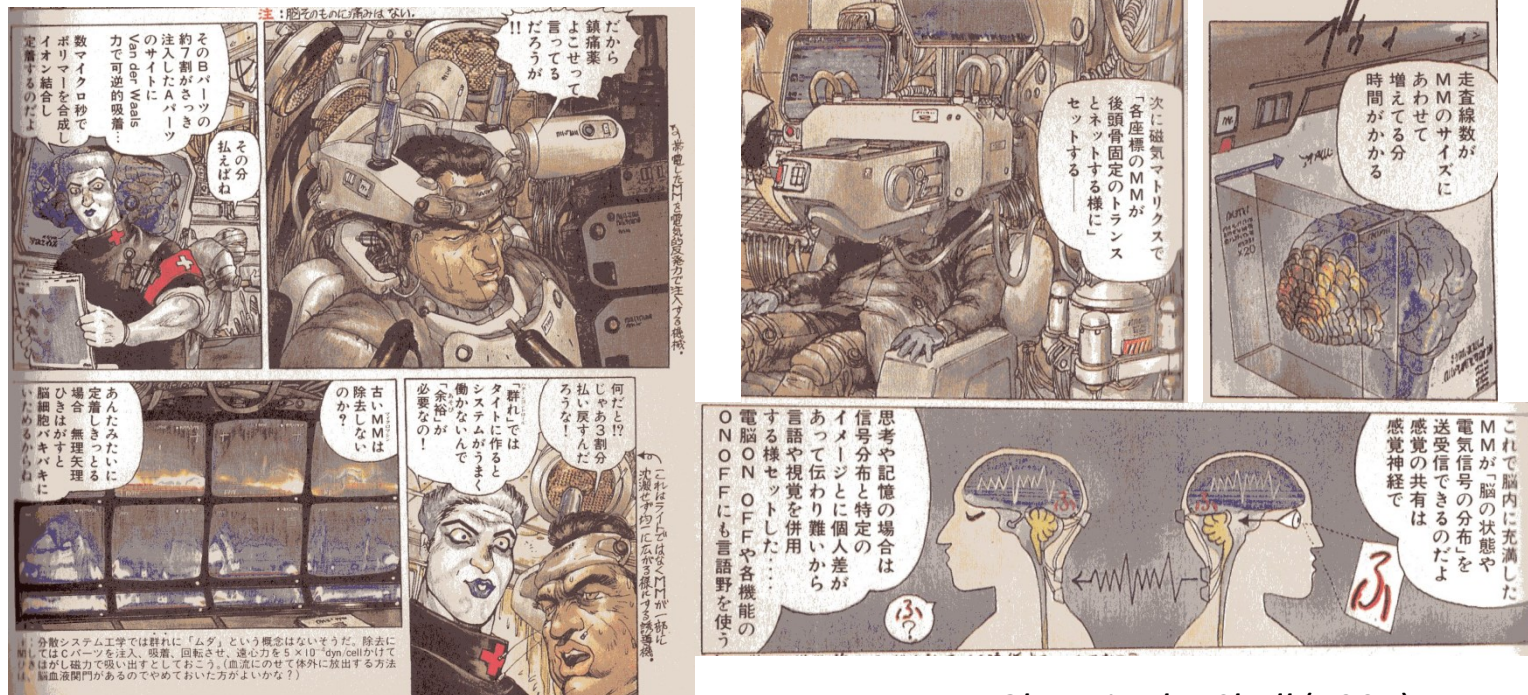
Ghost in the Shell (1991)

Part 2

- Future of EEG—Makoto's pessimism
- Present of EEG—Vacation of ground truth and adolesc-i-ence
- Past of EEG—Popperian defense in a *cul-de-sac*

The soul of a true poet predicts the past and remembers the future.
Shigenobu Takayanagi

https://s-media-cache-ak0.pinimg.com/564x/39/71/5f/39715f9d481828bd0b945588f5a7eb3f.jpg

Let's measure the potential!

- Key Question: What can EEG do today?

BRAIN.

PART 3, VOL. 58.

THE ORIGIN OF THE BERGER RHYTHM.

BY E. D. ADRIAN AND K. YAMAGIWA.

IN a recent paper Adrian and Matthews (1934b) have discussed the origin of the Berger rhythm, the characteristic oscillation of electric potential on the surface of the head reported by Hans Berger in 1929. It consists of a series of waves with a frequency of about 10 a second, and an amplitude of 0·05-0·1 millivolts, appearing when the subject is at rest with eyes closed and disappearing when the eyes are opened or when the attention is fully engaged. Berger (1929-35) has shown that the potential waves originate in the brain and has made a detailed study

Crawford Sams
Brigadier general in occupied Japan

'The United States have penicillin and EEG recorder.'

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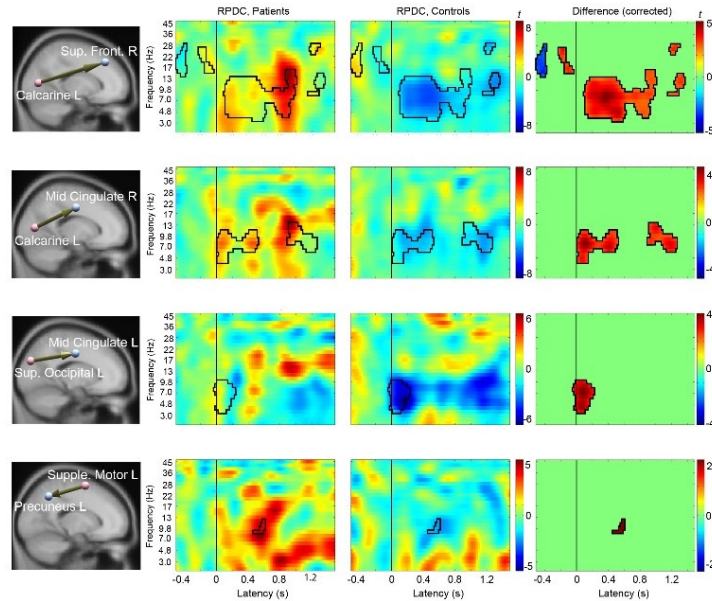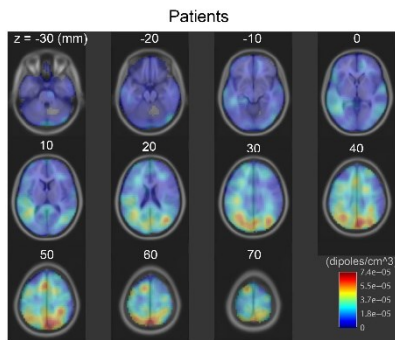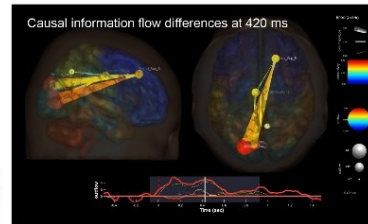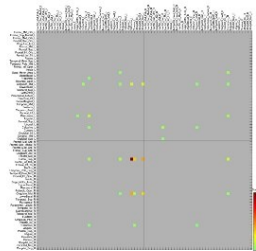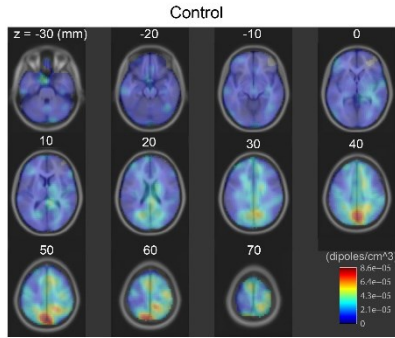# Demo 1: Our classic analysis (since early 2000's)
ICA clustering and 'envtopo' analysis on Left vs. Right M1 TMS-ERP
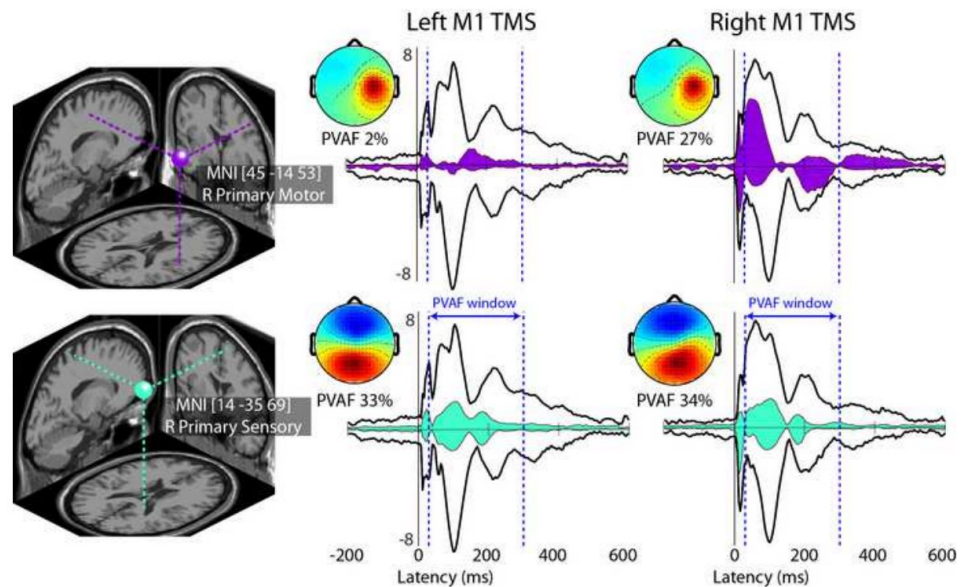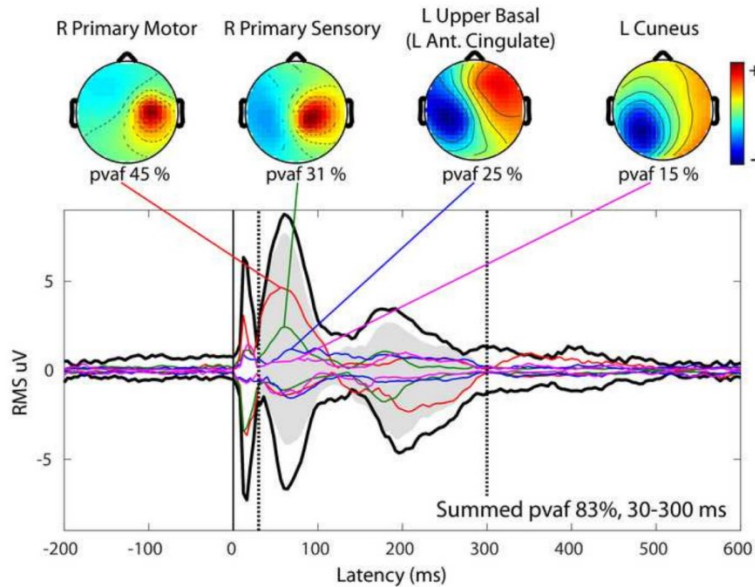
Miyakoshi et al. (*rejected*)
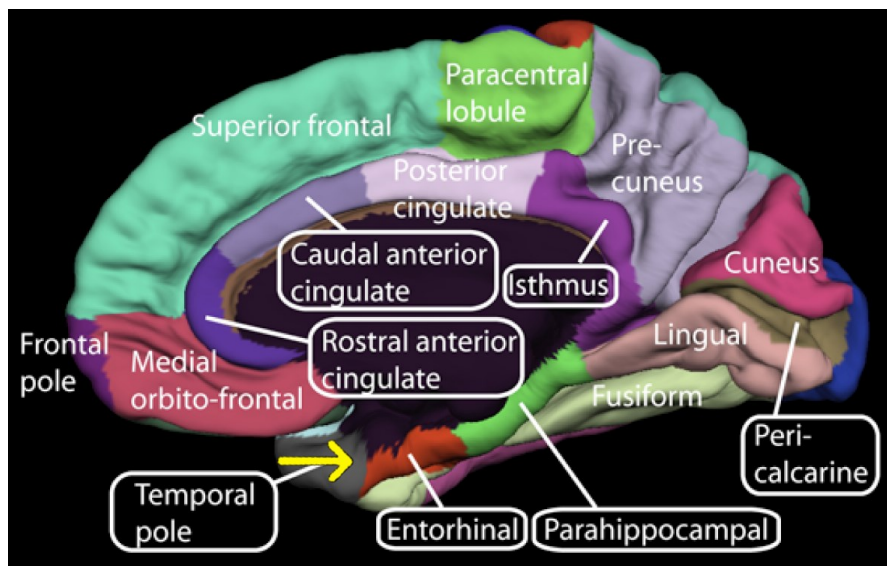
Demo 2: Our new analysis
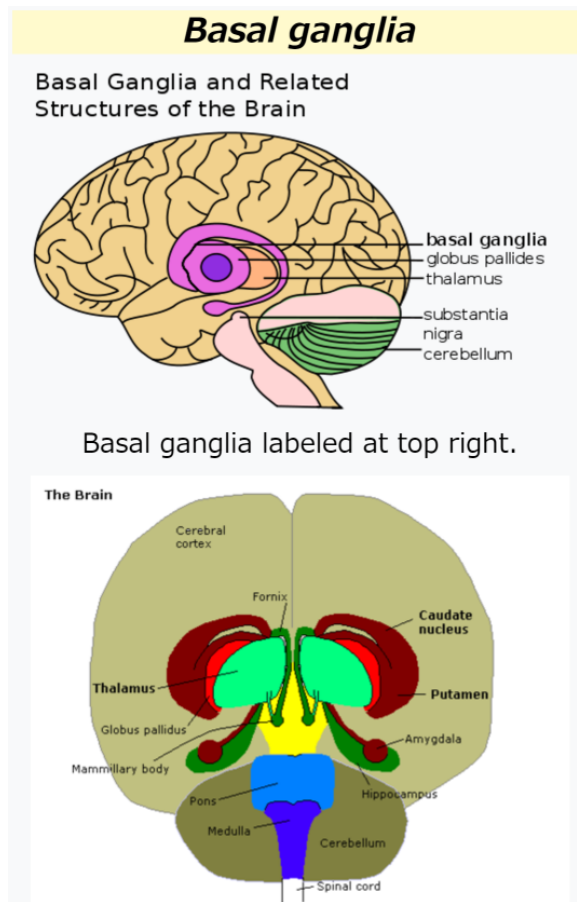# Information flow across effective EEG sources
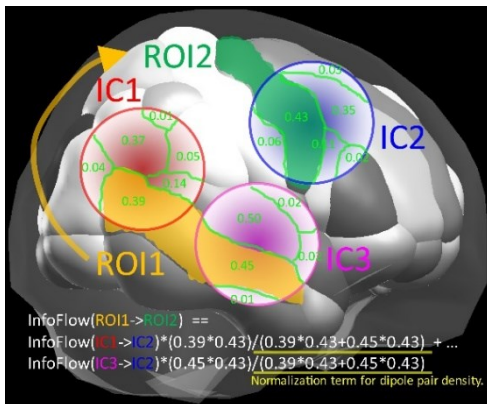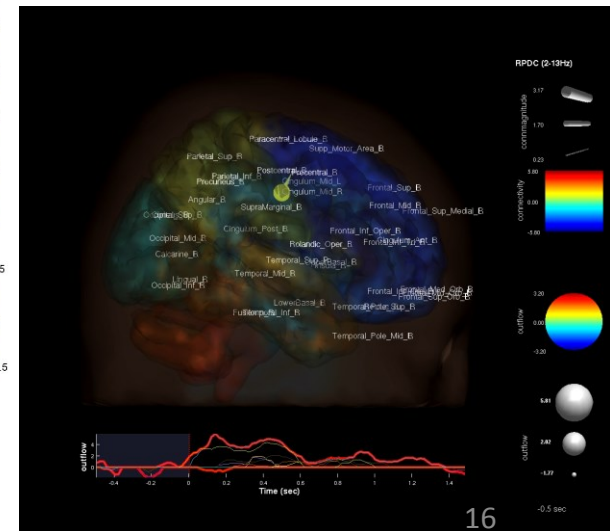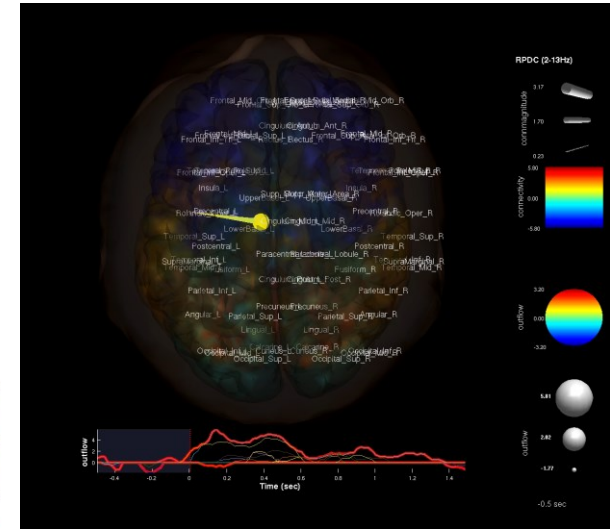
Miyakoshi et al. (*in prep.*)

Loo et al. (*in prep.*)
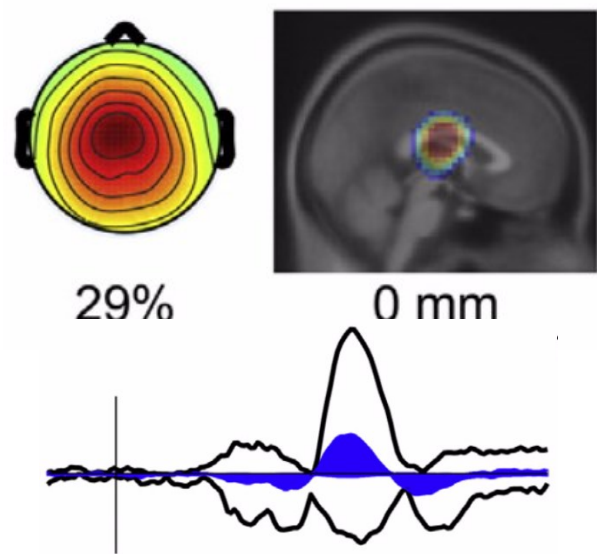
Limitation 1: No sensitivity to basal ganglia
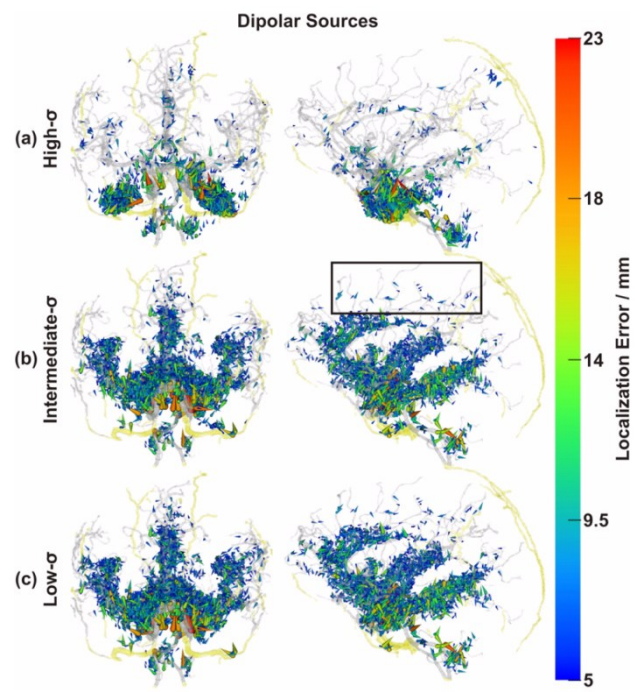

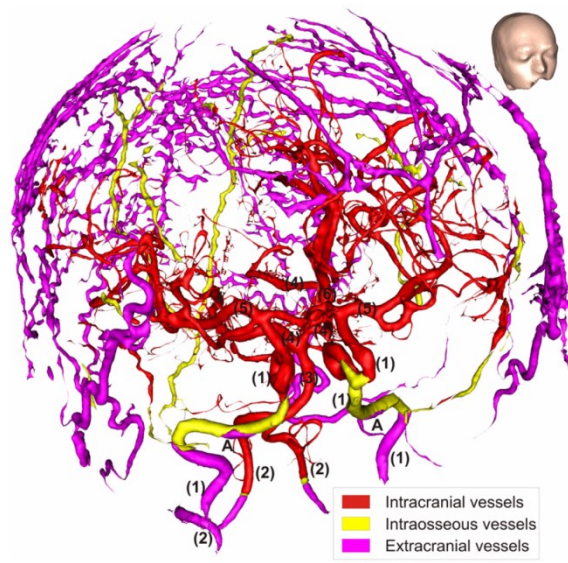EEG <u>CAN</u> measure cortical activity.

EEG <u>CANNOT</u> measure subcortical activity.

(From Wikipedia)

Limitation 2: Poor source localization (poor electric forward model)


(Rissling et al., 2014)

(Fiederer et al., 2016)

Emissary veins: A skull has more than one hole

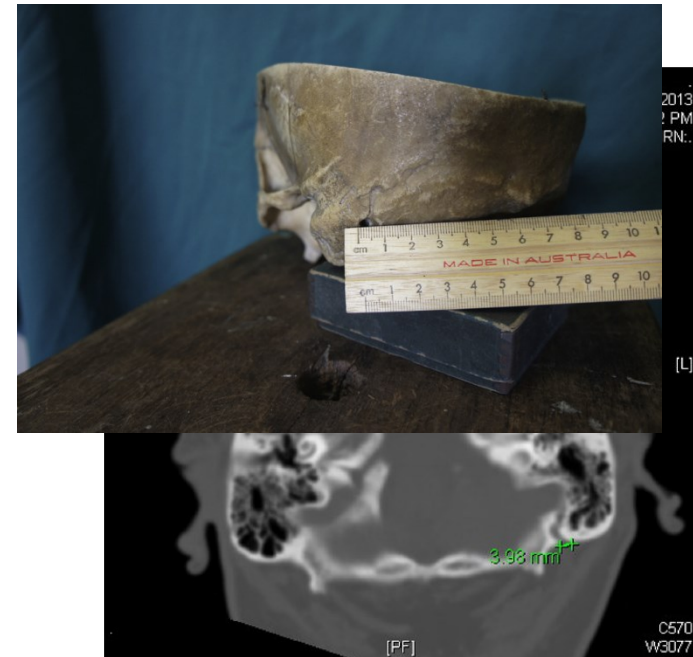The **emissary veins** connect the extracranial venous system with the intracranial venous sinuses. They connect the veins outside the cranium to the venous sinuses inside the cranium. They drain from the scalp, through the skull, into the larger meningeal veins and dural venous sinuses. (Wikipedia)

Parietal foramen
(wikipedia)
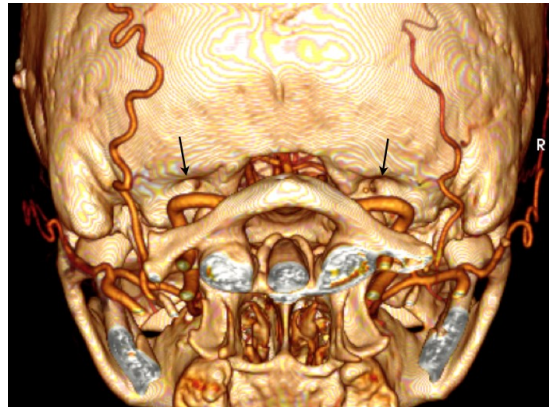
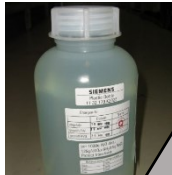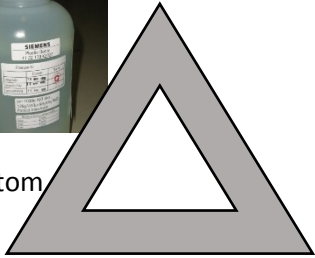Condylar canal
(wikipedia)

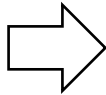Mastoid foramen
(Kim et al., 2014)

Fundamental limitation: Vacation of the ground truth

MRI
Phantom

Ground truth to scan

Imaging device
(X-ray, MRI)
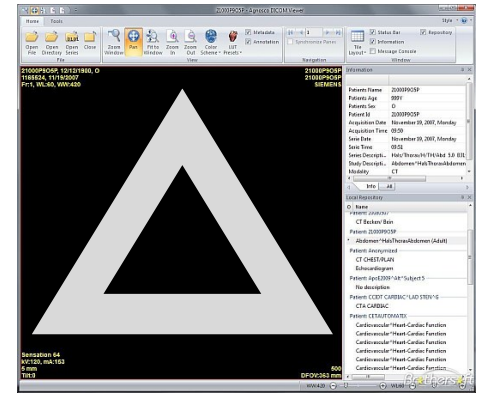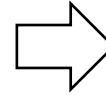
Image
(reconstructed truth)
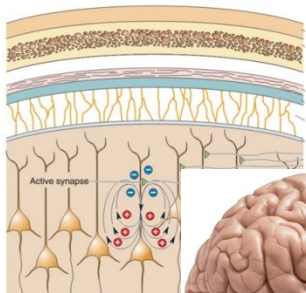
Unknown ground truth
shuttered into micro (single
unit), meso (LFP), and macro
(ECoG/EEG) scales.
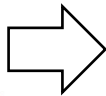
Recording device
(ECoG/EEG)
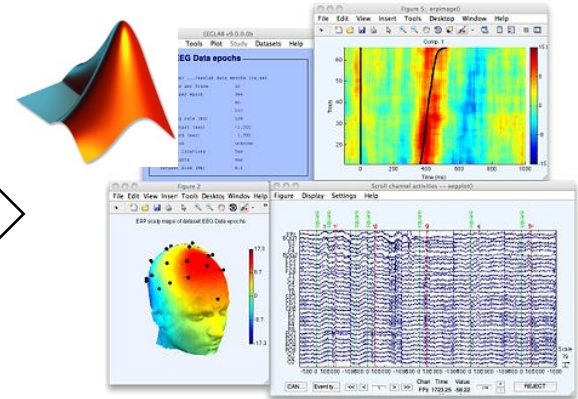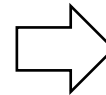
'Colorful' visualizations;
Is this reconstructed truth?

fMRI as 'X-ray of the effects significance'

- "…The ensuing SPM can be thought of as an X-ray of the effects significance."

- It detects neural correlate, which serves for box models.
- Do we not tend to compensate the lack of the ground truth by signal processing?

http://www.fil.ion.ucl.ac.uk/spm/doc/history.html
Figure taken from Nakane et al. (2015)

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PhD dissertation of Makoto Miyakoshi

EEG is closer to X-ray than MRI?

2-D FT

Unit: HU
(Hounsfield)
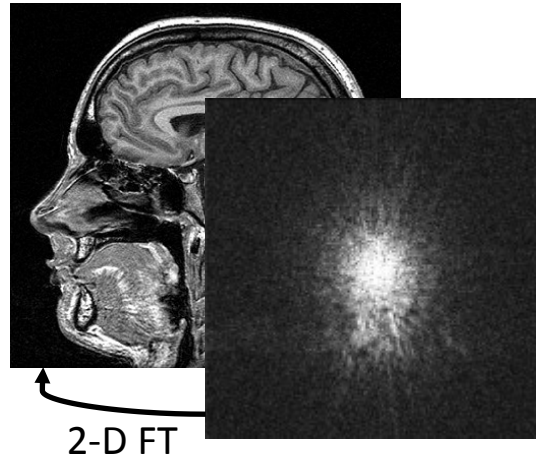
Unit: None
(signal strength is relative)
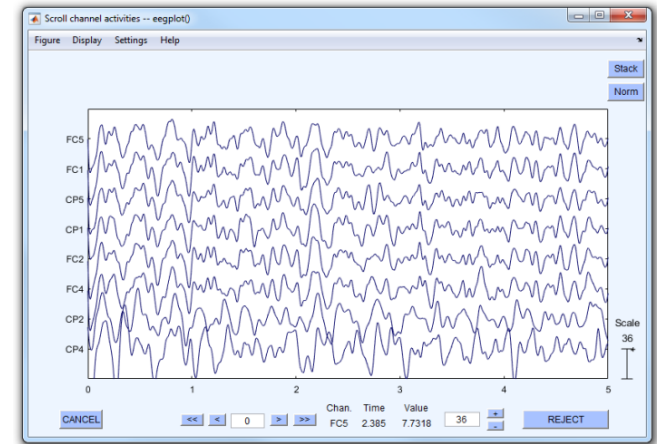
Unit: μV
(microvolt)

EEG is a measurement of *physical quantity* like an X-ray—but who knows this is a *strength*?

Toshiki Nakane
May 12, 2011 at Montreal

22

Active vs. Passive imaging

Active

Passive
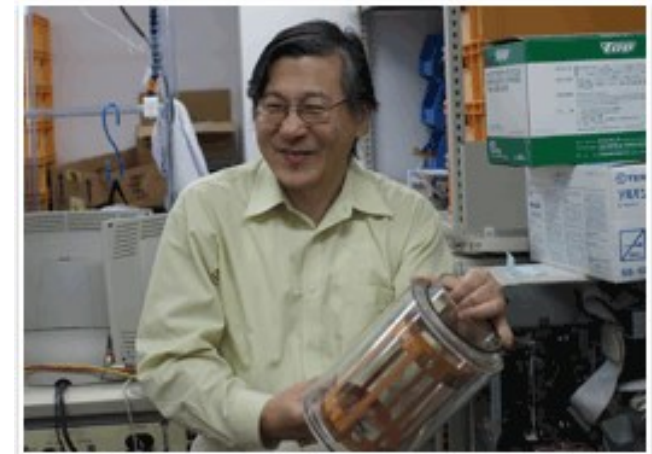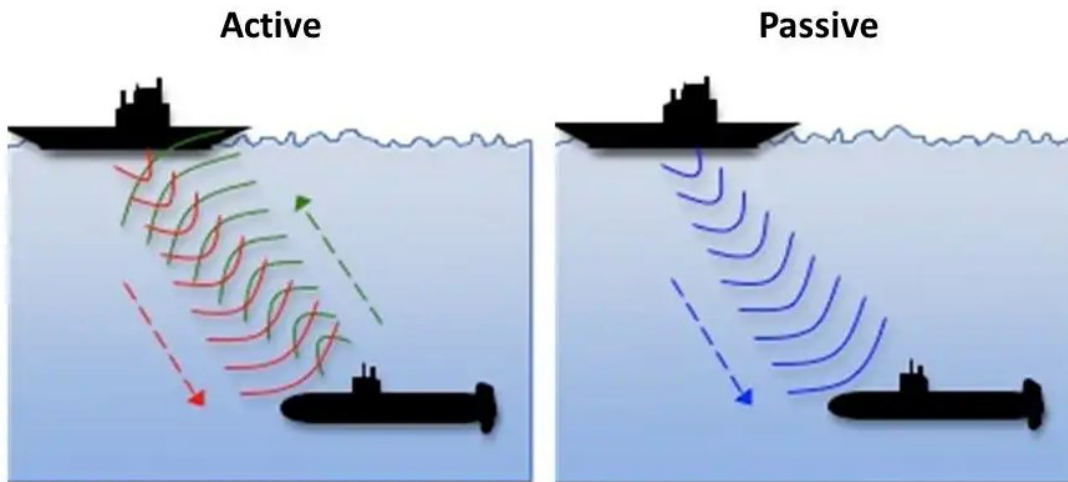
Toshiharu Nakai, my mentor in MRI

http://slideplayer.com/slide/6447603/22/images/27/Sonar+Active+Passive.jpg

One more degree of freedom in active imaging

Can radiate various pulse sequences to 'active-image' different properties

'Passive imaging' = Just listening.
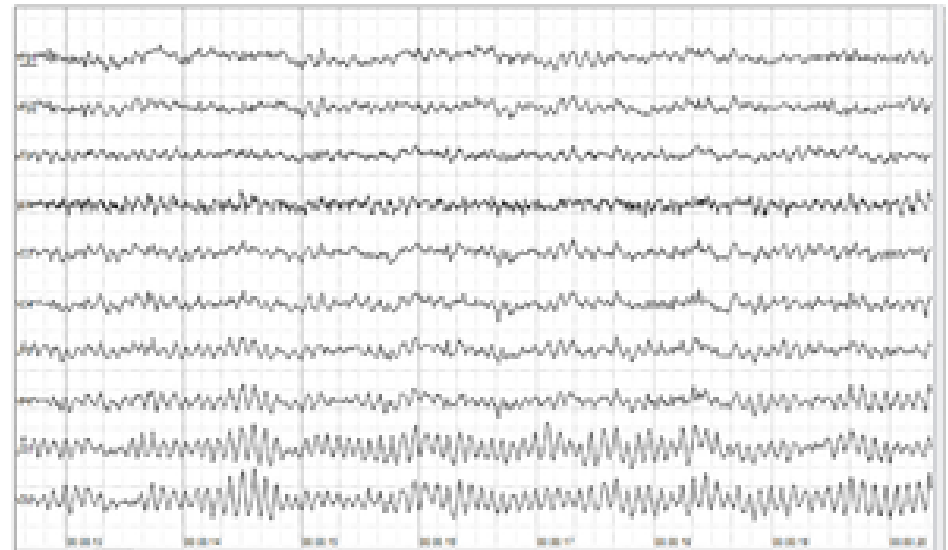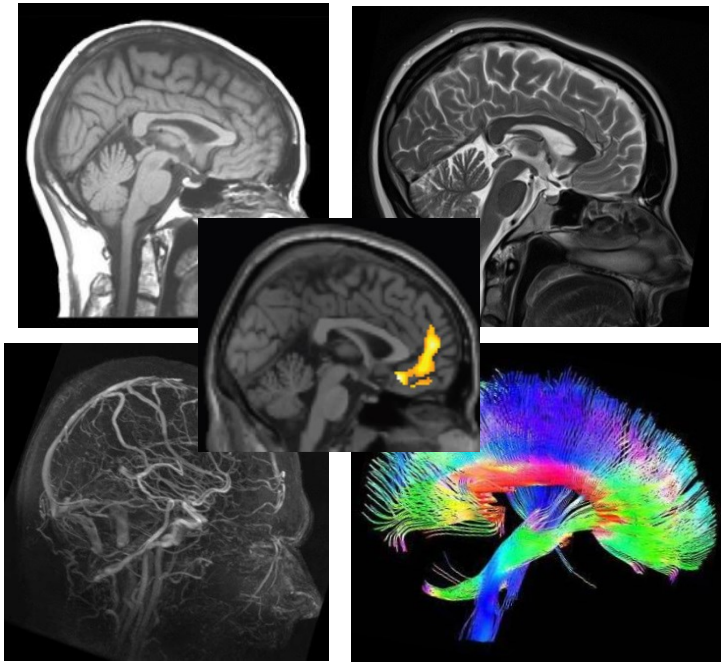
Confusion between Science and Engineering
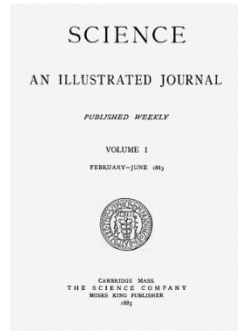
- Good engineering (signal processing) ≠ Good science!

- What is the distinction? Theory ladenness (i.e. prepared mind) in observation.

Norwood Hanson
(a.k.a. 'flying professor')
Patterns of Discovery (1958)

The real voyage of discovery consists not in seeking new landscapes, but in having new eyes.

Marcel Proust

Why Most Published Research Findings Are False

PLoS Medicine (2005)

John P. A. Ioannidis

- When the studies conducted in a field are smaller
- When effect sizes are smaller
- When there is a greater number and lesser preselection of tested relationships
- Where there is greater flexibility in designs, definitions, outcomes, and analytical modes [if one tries to compensate the lack of ground truth with signal processing… lots of colorful figures with no meaning!]
- When there is greater financial and other interest and prejudice
- When more teams are involved in a scientific field in chase of statistical significance [i.e. p-hacking]

EEG as adolesc-i-ence

- EEG is immature in both science and engineering.

- Excitement in engineering (new algorithm etc) is often confused with excitement in science.

- There are vast open possibilities—which can benefit from progress in signal processing.

Part 2 summary

Via synapse

Dipolar EEG source

From thalamus
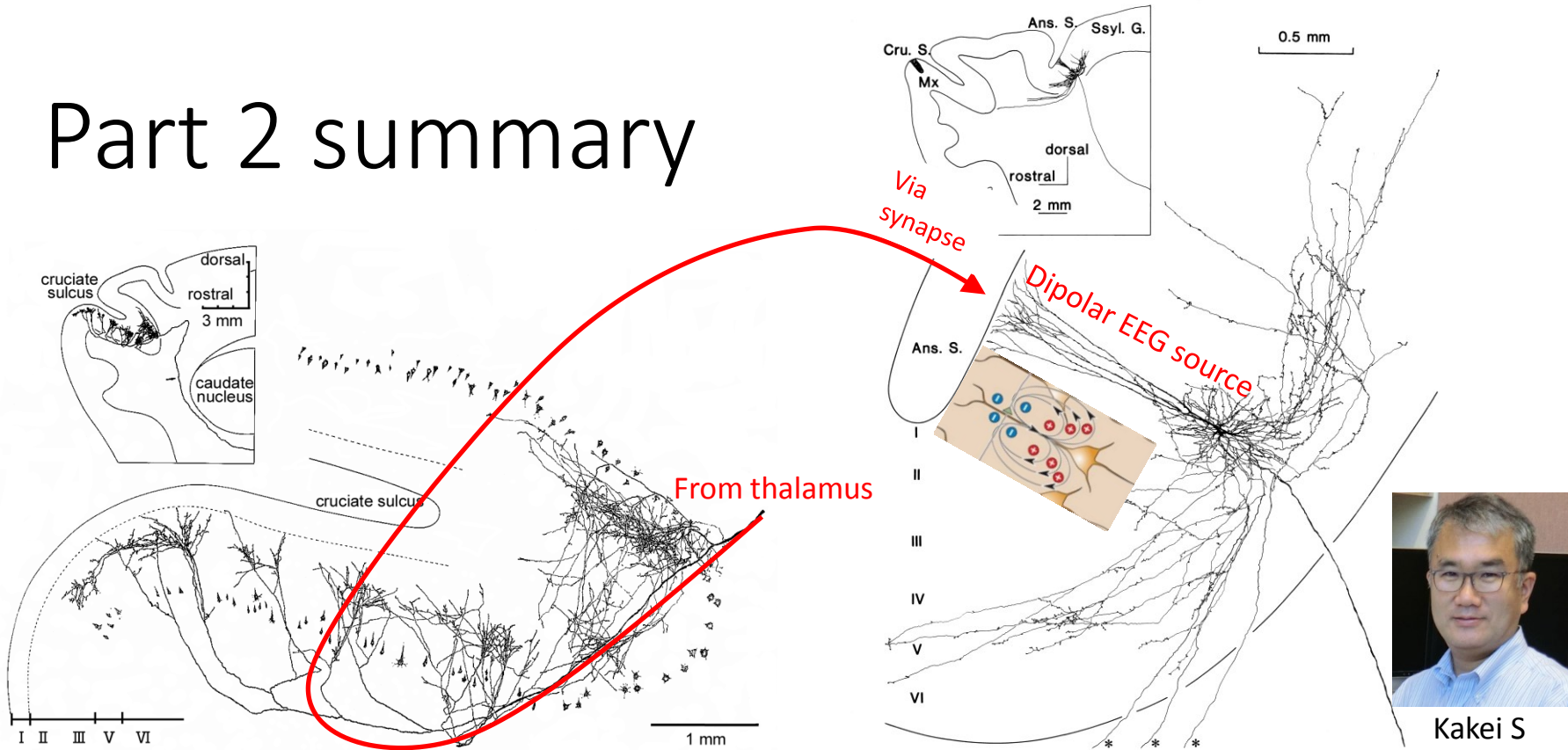
Thalamo-cortical axon (brings inputs)

Pyramidal neuron (forms dipolar EEG source)

Kakei S

- EEG has never been an X-ray of a brain because of no ground truth.

- There are analyses that produces sexy figures, but are we closer to the ground truth in doing so?

Figures courtesy of Shinji Kakei and Yoshikazu Shinoda

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Interlude

Part 3

- Future of EEG—Makoto's pessimism
- Present of EEG—Vacation of ground truth and adolesc-i-ence
- Past of EEG—Popperian defense in a *cul-de-sac*
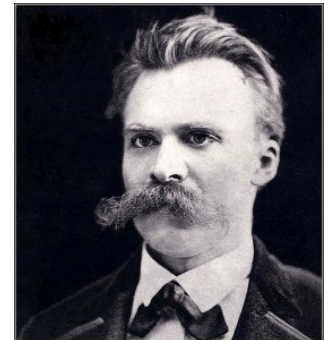
He goes back like every one who is about to make a great spring.
Friedrich Nietzsche

One-page history* of EEG and ERP

- Cayton (1875) reported animal ECoG.

- Berger (1929) and Adrian (1934) reported human scalp EEG.

- Davis (1939) is the first ERP paper. Davis mentored Galambos.

- Galambos and Sheatz (1962) is the first computer-averaged ERP paper.

- Galambos mentored Hillyard. Hillyard mentored many smart researchers. Among these mentees, Luck wrote the ERP handbook which is a good authority today.

UK

Germany

UK

Harvard (East Coast)

*a history seen by a Japanese post-doc at UCSD in 2017

Harvard-UC
(West Coast)

UC

UC

$38.95

31

What is science?
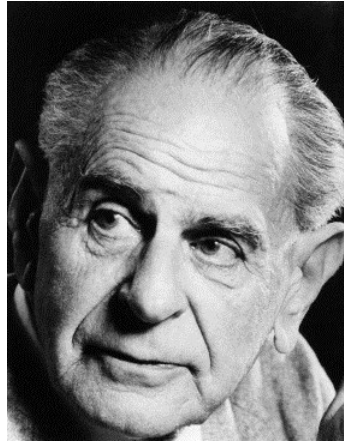
Karl Popper

- Make a *hypothesis,* design an experiment, and see if the result supports/not supports the hypothesis..

- If a theory is not falsifiable... it's NOT science!

- Probably it is useful as a defensive definition to reject pseudo sciences.

(Image from *Wikipedia*)

One-bit information generator

Hypothesis

Question

Experiment

Hypothesis supported

Hypothesis not supported

1   0
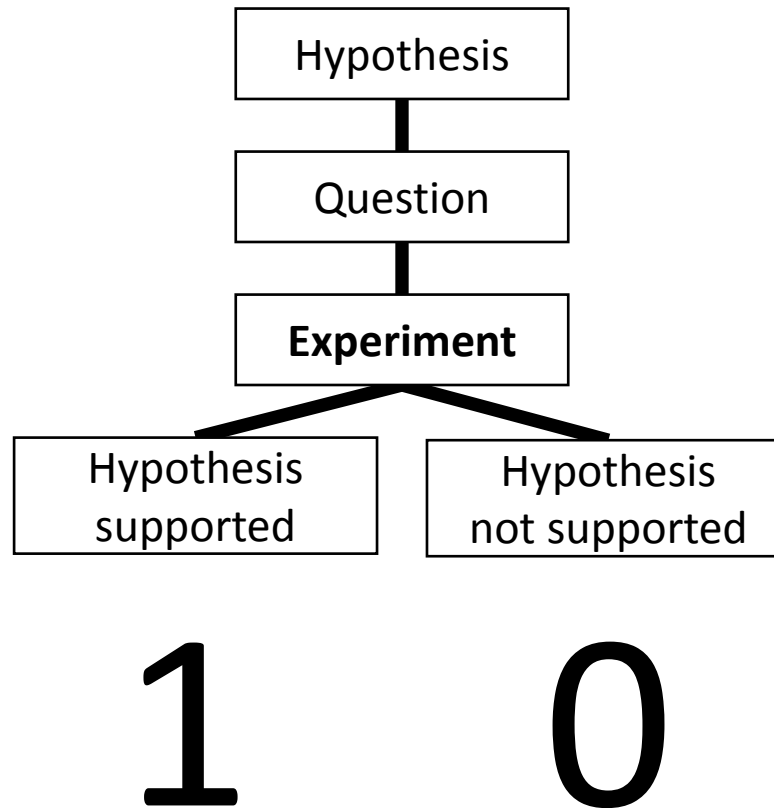
Popperian defense

- It's a claim that ANY measure is *equally* useful for the one-bit information generator!
  - Behavioral measure (Reaction time, response accuracy)
  - Electrophysiology (EEG, ECoG, LFP, single-unit recording)
  - BOLD signal (fMRI, fNIRS)
  - Chemical measure (PET, MR Spectroscopy)

One aspect of science as an intellectual game

Give me Fz, Cz, Pz data, and I can publish a *Science* paper!

http://www.thefamouspeople.com/profiles/images/karl-popper-3.jpg
Note Popper did not say these words.

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Evolutionary *cul-de-sac*

...they often pay up to a 20% premium for a home on such a street, according to one study [1].

- The ERP approach has been a great success since 70's, made lots of *Nature* and *Science* publications.

- The ERP paradigm is made so well that people can still publish papers using the same framework.

[1] http://www.npr.org/templates/story/story.php?storyId=5455743
https://thumbs.dreamstime.com/t/cul-de-sac-aerial-suburb-24550109.jpg
https://upload.wikimedia.org/wikipedia/commons/thumb/6/60/Culdesac.jpg/220px-Culdesac.jpg
https://www.sciencedaily.com/images/2012/06/120628130647_1_900x600.jpg

A rage outside the *cul-de-sac*

Harvard (East Coast)

Harvard-UC
(West Coast)

UC

UC
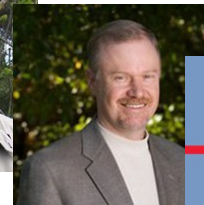
UC
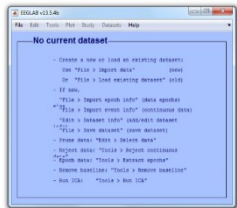
No. 1 used in the field
(Hanke and Halchenko, 2011)
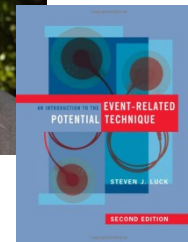
EEG authority at $38.95

- Galambos had another (and the last) mentee Makeig.
- Makeig was fluent in math (and music).
  - Wavelet transform on EEG in 1993.
  - Independent Component Analysis (ICA) in 1996.
- He started free, open-source library EEGLAB.

Traditional view of ERP

Visual Perception

Semantic processing/
motor execusion

Object
identification

Visual perception
Memory retrieval
Decision making
Motor execusion
Action monitoring
etc...

Piano?

No
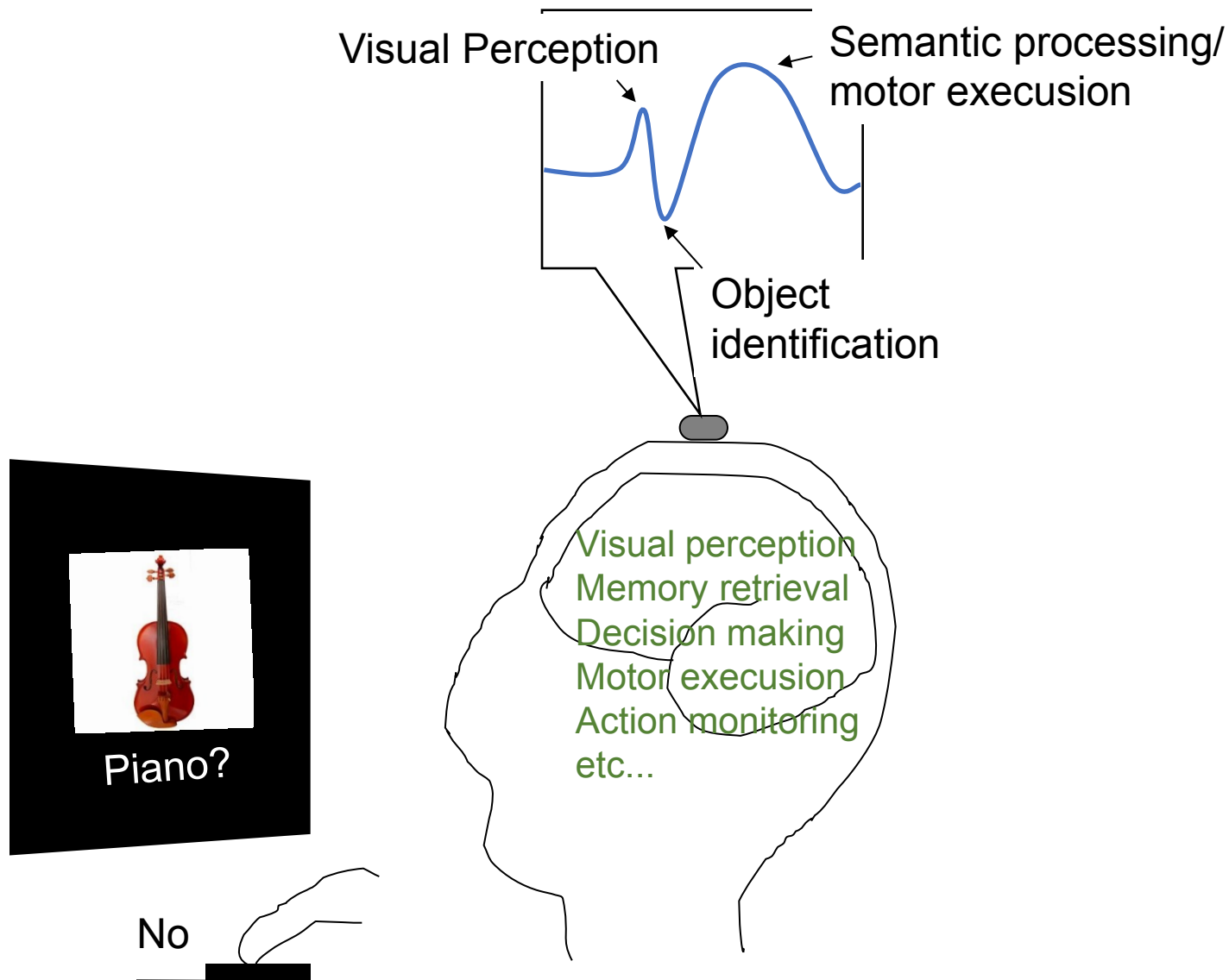
Seeing scalp-recorded signal from EEG sources
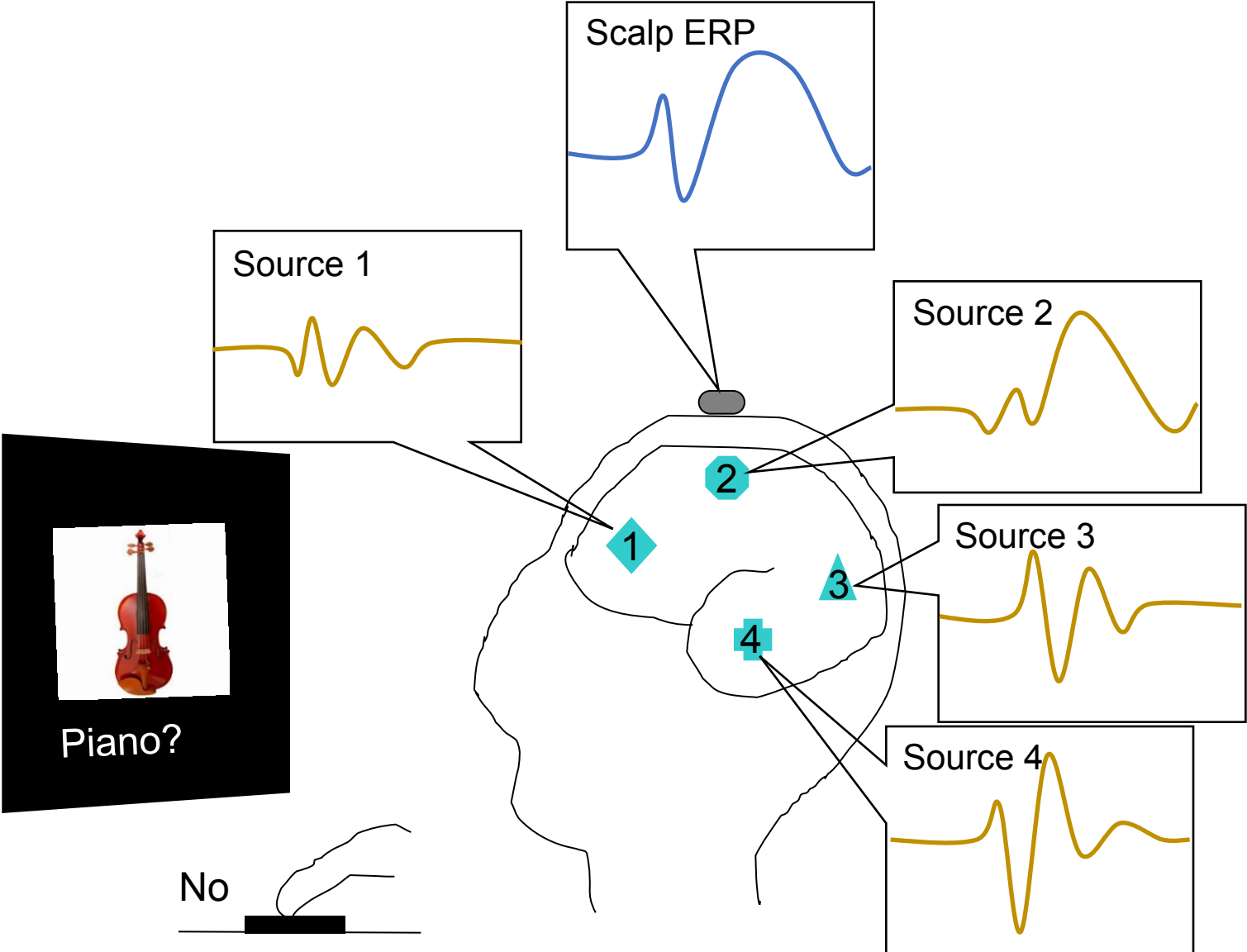
Mixing process during a cocktail party
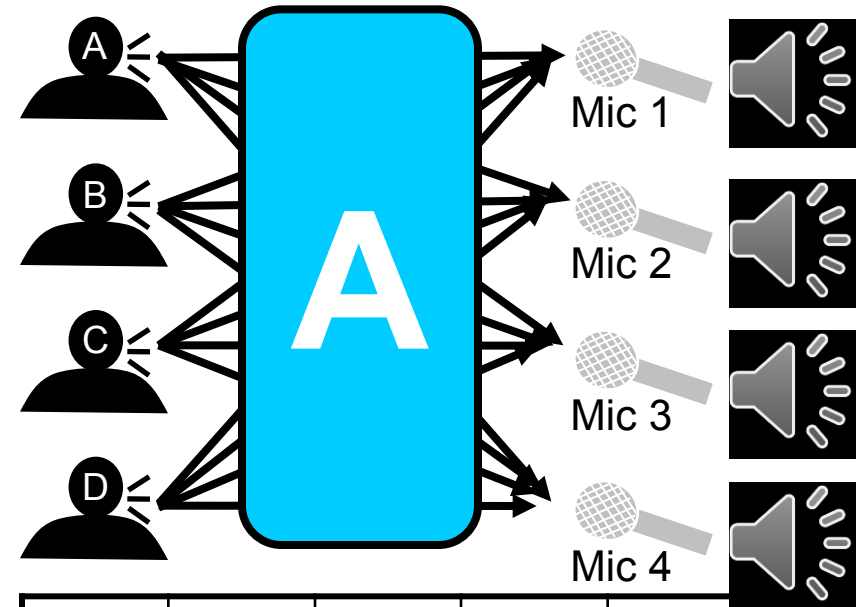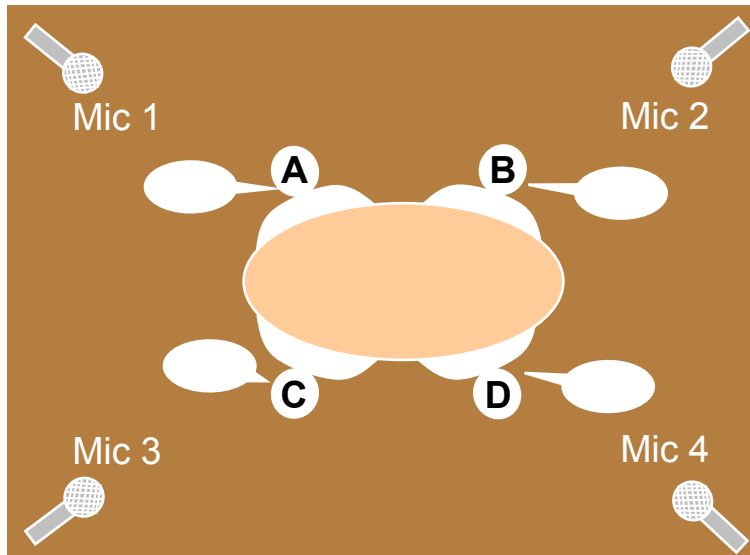
	Mic1	Mic2	Mic3	Mic4
A	20	21	25	34
B	17	23	31	29
C	27	30	25	18
D	31	28	16	25

Unmixing process using ICA
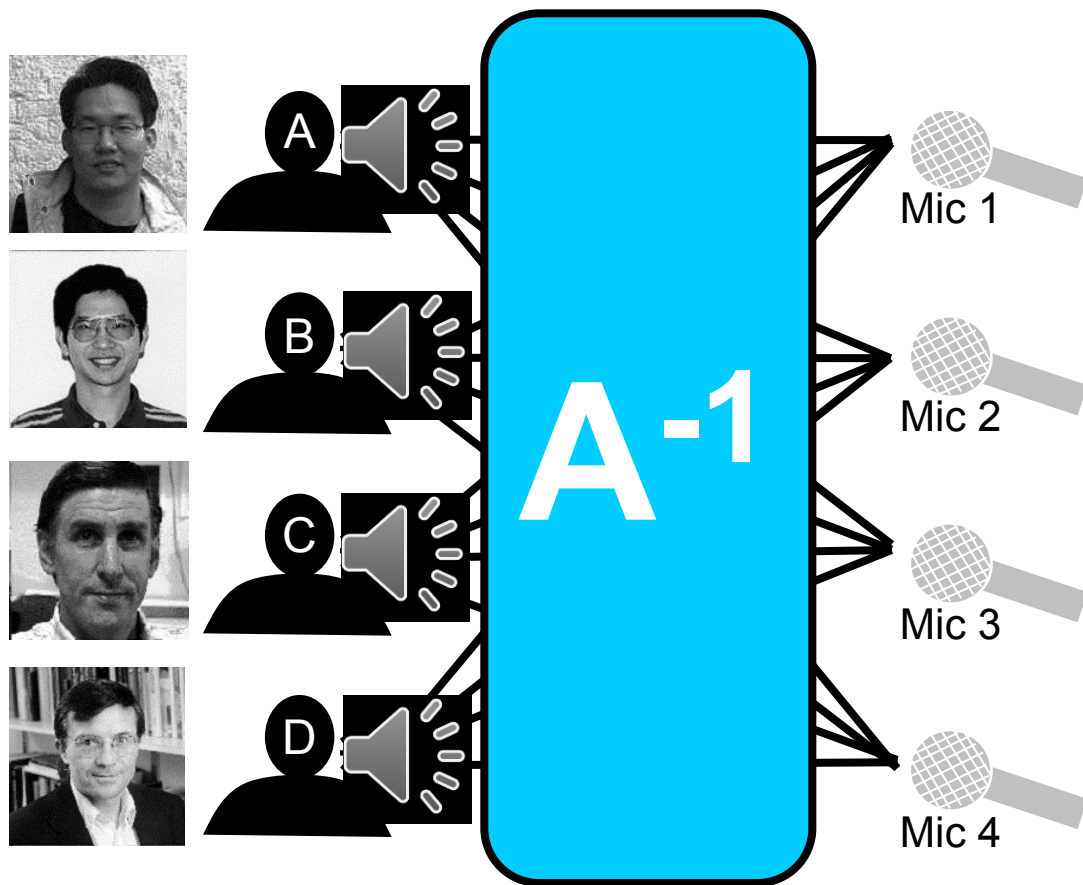
	Mic1	Mic2	Mic3	Mic4
A	0.9	-0.9	0.7	-0.6
B	-1.1	1.1	-0.8	0.8
C	0.5	-0.5	0.4	-0.4
D	-0.2	0.2	-0.2	0.2

(Photos and voices from ICA slide show presentation & demo in powerpoint by Makeig, 1999)

How to compute A^{-1}

PDF is close to Gaussian
due to $\sum$ (Central Limit Theorem)

Mixing

Unmixing
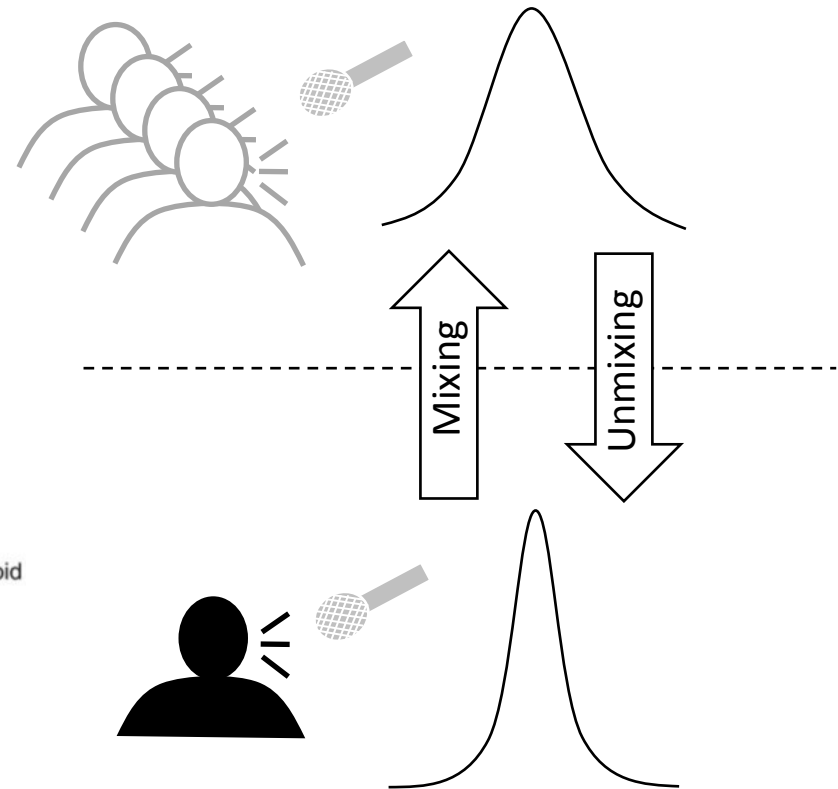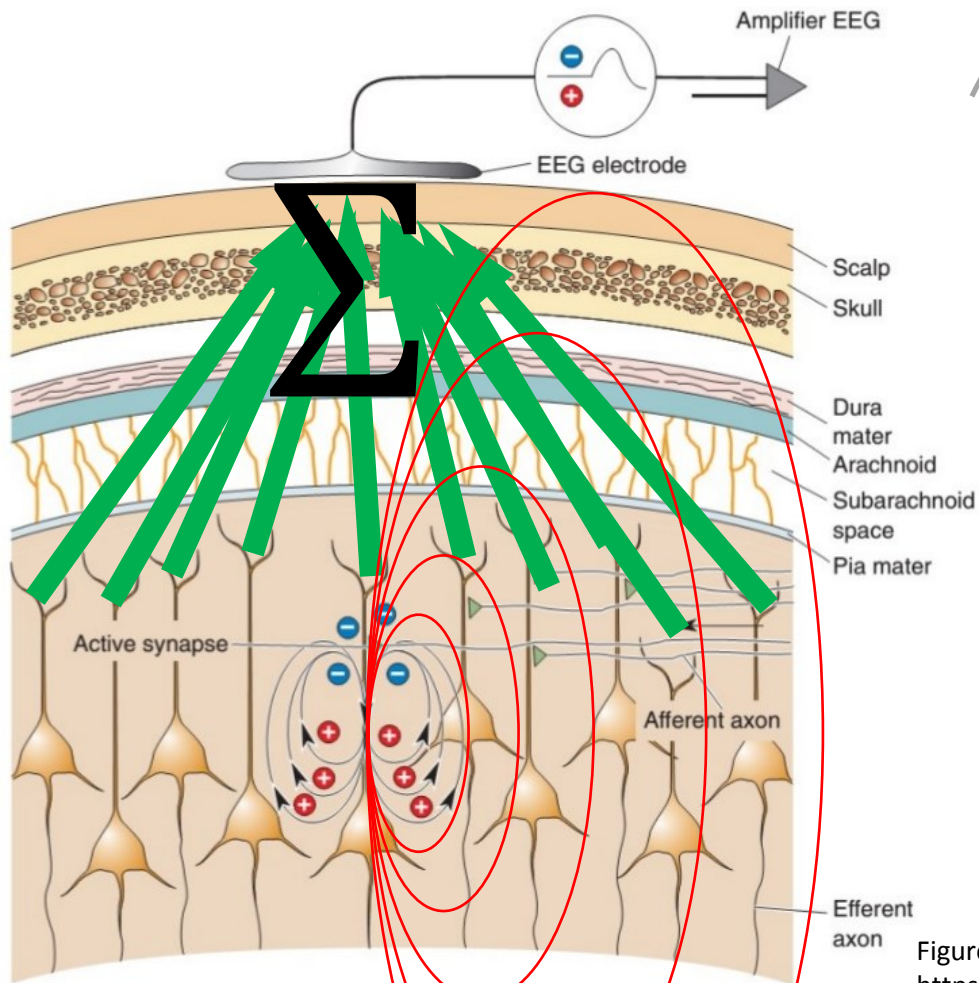
PDF is close to super-Gaussian
(sparsity of neural activity)

Amplifier EEG

EEG electrode

Scalp
Skull
Dura mater
Arachnoid
Subarachnoid space
Pia mater

Active synapse

Afferent axon

Efferent axon

$\sum$

Gaussian PDF == Dependent (i.e. Mixed)

Still Gaussian == Still a mixture!

Figures by Gaël Varoquaux
http://gael-varoquaux.info/science/ica_vs_pca.html

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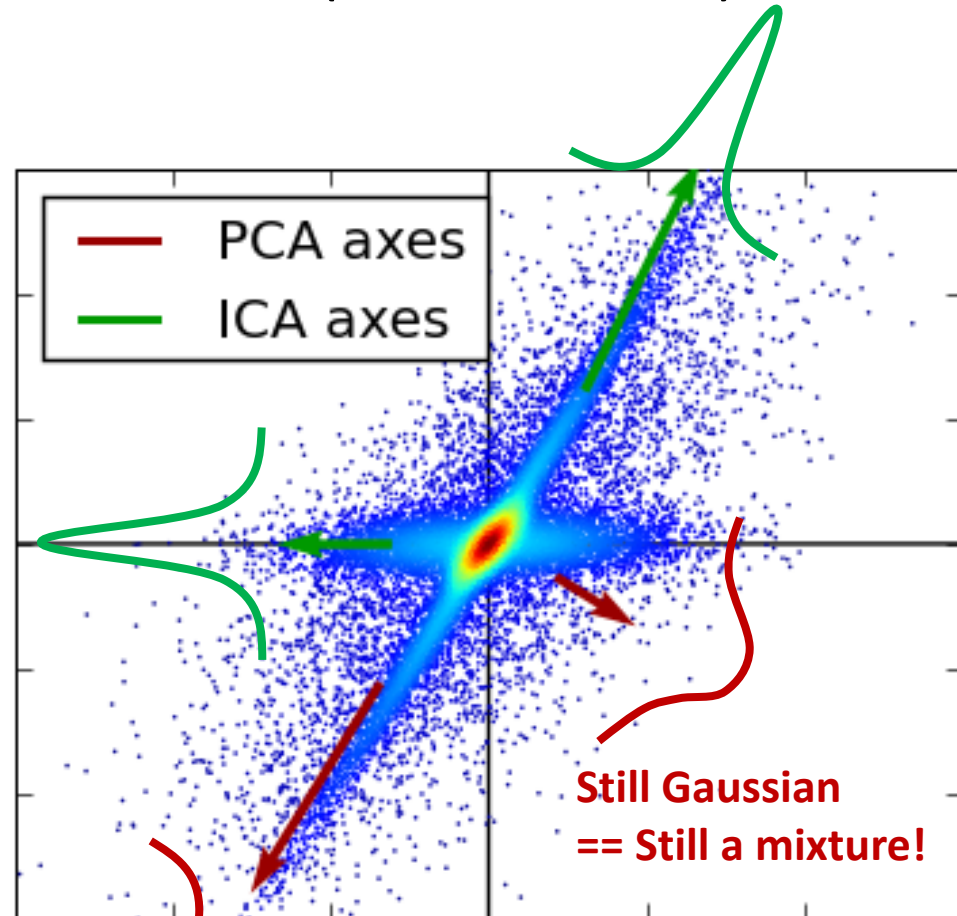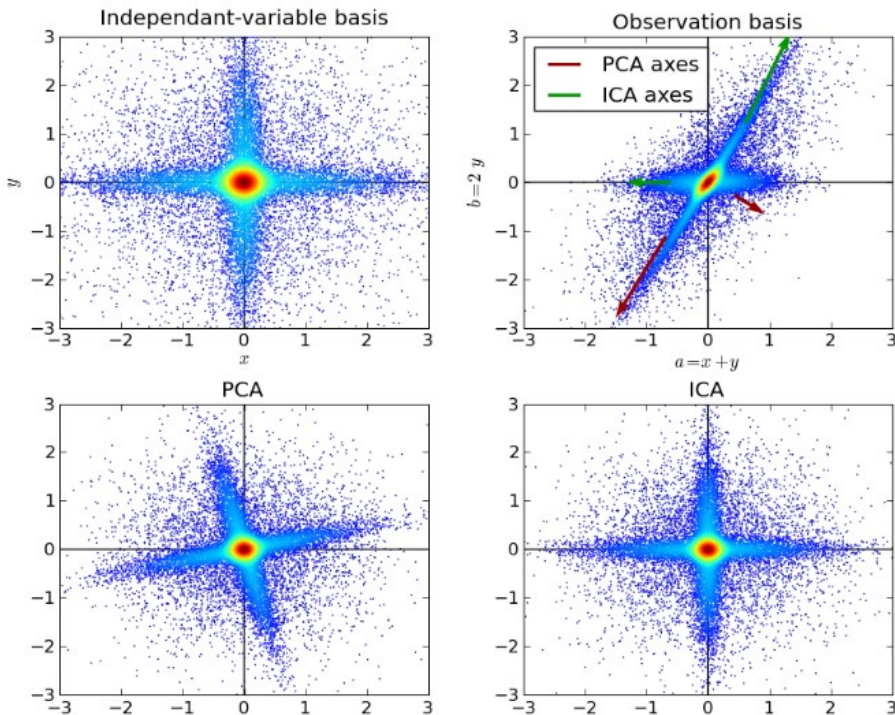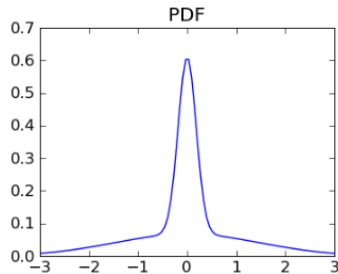
Independence-Dipolarity identity
(I-D identity, IDID)

Scalp-channel signal PDF

ch1   ch2   ch3
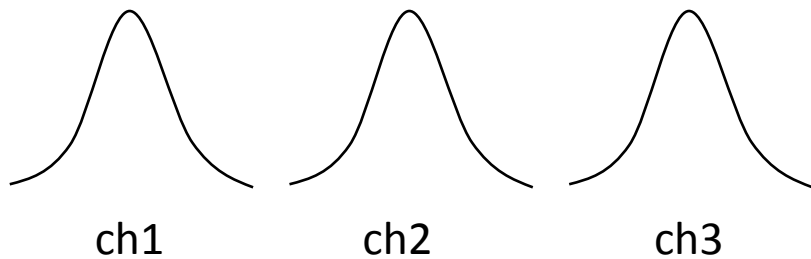
Independent Component PDF

IC1   IC2   IC3
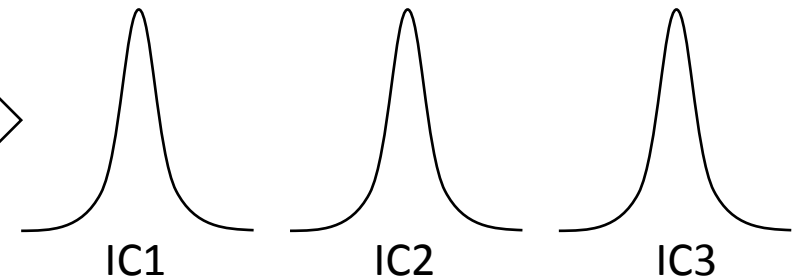
Temporally maximally independent
--> Tautological, due change.

'It's a non-trivial nature of the *I-D identity* that a spatial solution emerges from a temporal solution. Solving a temporal problem solves a spatial problem.'

Hirokazu Tanaka

Independent Component Scalp amplitude distribution
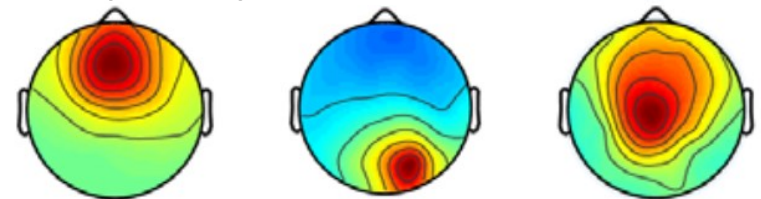
They are unexpectedly highly *dipolar*.
--> Unintended change!

What does it mean to be 'dipolar'?

Reversal Depth (i.e. dipole is here)
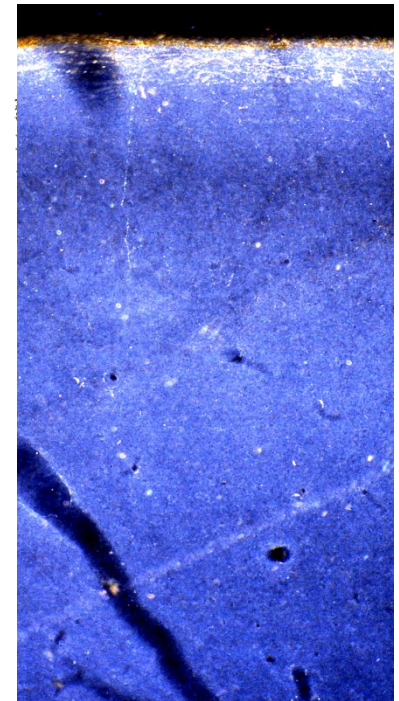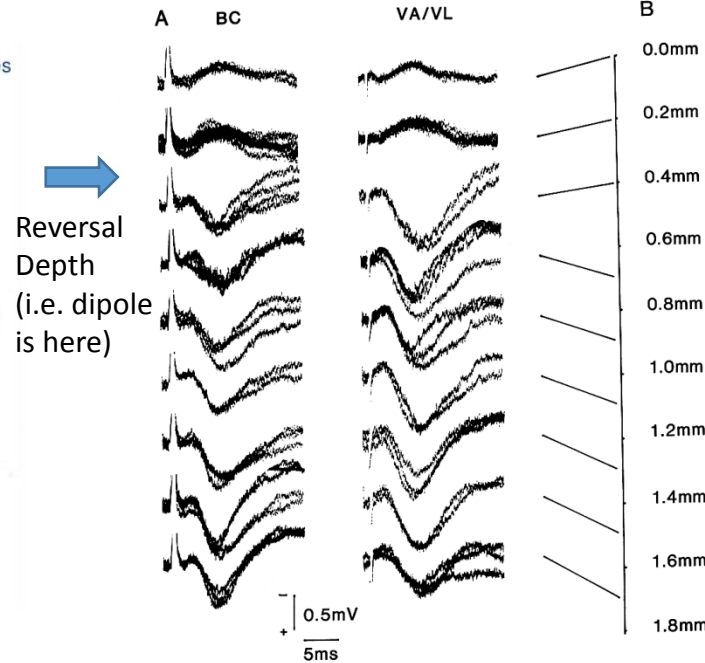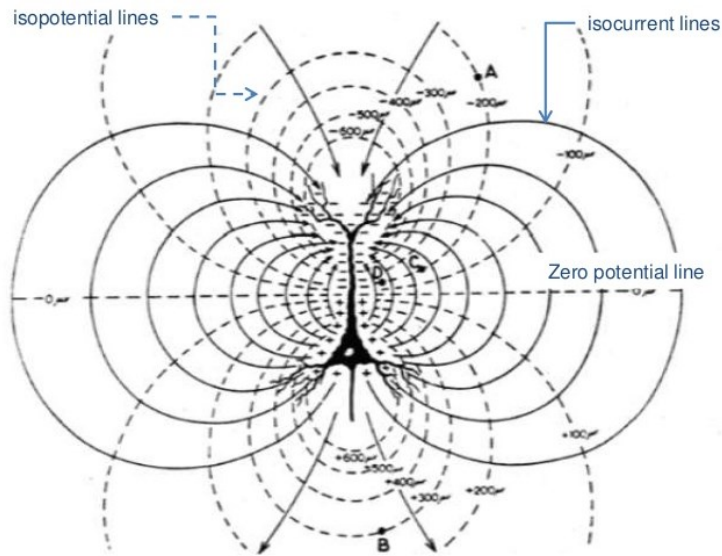
- Dipole is a biophysically valid distribution pattern of extracellular field potentials.
- Hence 'dipolarity' means 'neuro-originness'.

Figures courtesy of Shinji Kakei and Yoshikazu Shinoda

Independence-Dipolarity correlation

Independence Delorme et al. (2012)
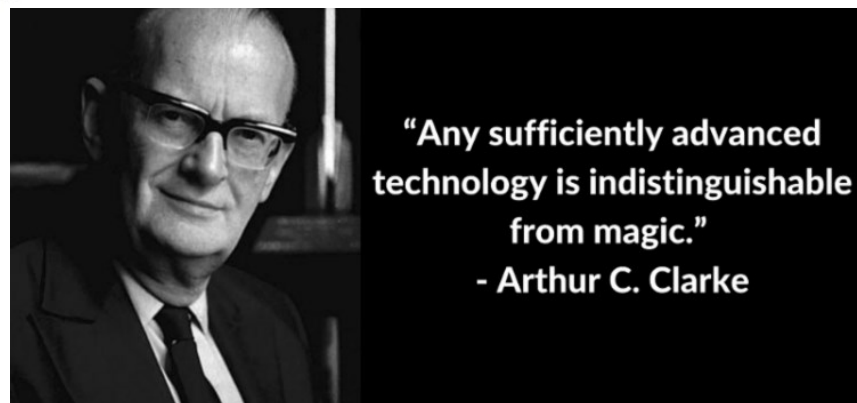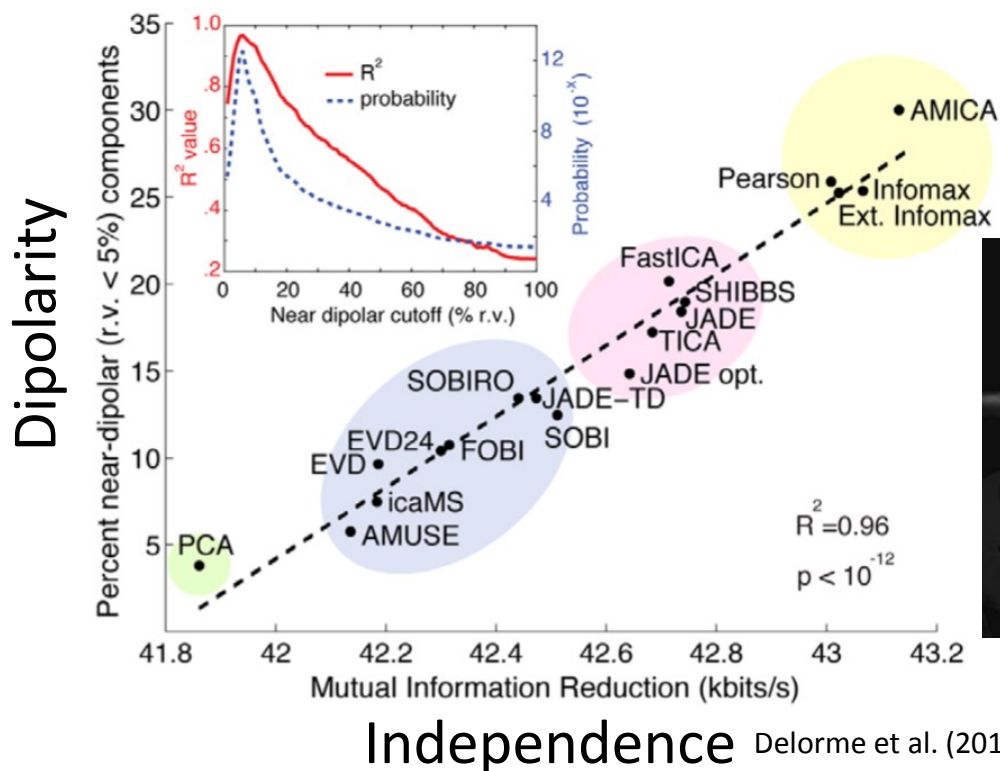
- Transforming channel data into temporally independent signals (magically) recovers *effective sources* of EEG.
- ICA relates to the ground truth?

http://ludwigiplaw.com/wp-content/uploads/2016/09/arthur_clarke.png

What does *I-D Identity* mean?

- Dipolarity indicates biophysical validity (Nunez). But dipolarity is only a sufficient condition of independence (e.g., sphering).

- Independence is not the only necessary condition for Blind Source Separation (e.g., SOBI).

- What does it mean?? Open questions.

Akaysha Tang

What makes ICA special among other signal processings?

	ICA's assumptions	Biophysical facts of EEG
Mixing Process	Linear	[Probably linear]
Mixing Speed	Instantaneous	Near the speed of light
Source PDF	Non-Gaussian	Super Gaussian
Definition of the 'source'	Temporally independent of each other	Unknown: empirical and analogical evidence by electrophysiology
Source spatial stationarity	Stationary	Non-stationary (traveling waves)
Source temporal stationarity	Stationary	Non-stationary (task-dependent)

EEG electrode

Active synapse

Afferent axon
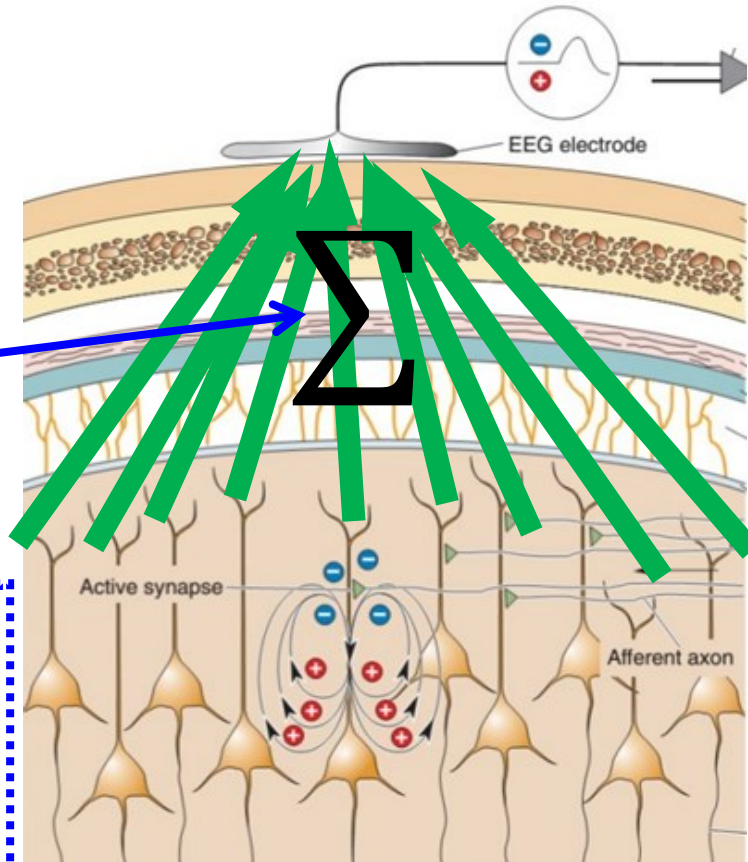
Benign/acceptable violations
(e.g. Using ERP paradigm helps to increase stationarity)

I-D identity indirectly proves it.

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An empirical evidence of physiological validity of ICA

- IC ERPs showed better correlations to neuropsych test scores in schizophrenia patients.

Table 3

Amplitude correlations. Summary of associations among scalp electrode Fz and source-resolved ERP amplitudes with clinical, neurocognitive and functional variables in schizophrenia patients. Correlations shown in bold exceed two-tailed Bonferroni significance level adjustments (Fz: $\alpha = 0.05/30 = 0.002$, $r^2 > 0.22$; source-resolved ERPs: $\alpha = 0.05/180 = 0.0003$; $r^2 > 0.28$). Number of significant correlations: Fz: uncorrected = 2, Bonferroni = 0; source resolved ERPs: uncorrected = 30, Bonferroni = 14.
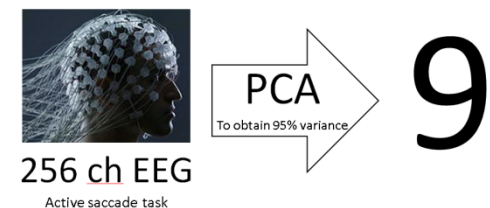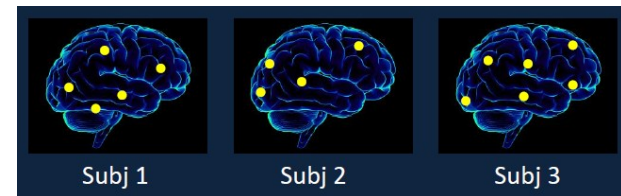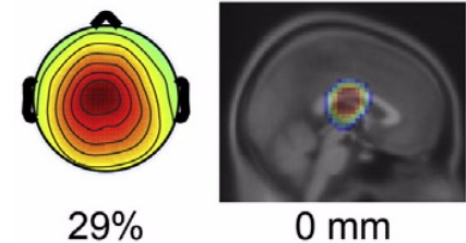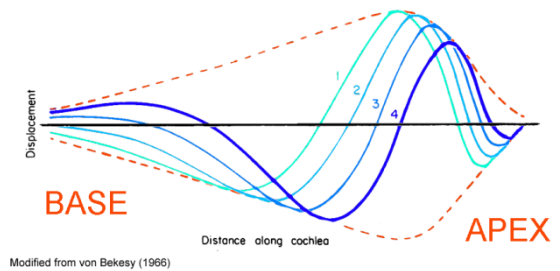
Channel ERP

	ERP	r^2
Scalp electrode (Fz)		
Verbal IQ (WRAT)	P3a	0.11
Functional capacity (UPSA)	RON	0.12

IC ERP

	ERP	r^2
R Superior temporal		
Working memory (LNS reorder)	RON	0.15
Verbal IQ (WRAT)	RON	0.15
Immediate verbal memory (CVLT)	**RON**	**0.28**
Delayed verbal memory (CVLT)	RON	0.26
Functional capacity (UPSA)	**MMN**	**0.48**
Functional capacity (UPSA)	RON	0.26
R inferior frontal		
Negative symptoms (SANS)	**RON**	**0.36**
Psychosocial functioning (SOF)	RON	0.24
Auditory attention (LNS forward)	**MMN**	**0.38**
Working memory (LNS reorder)	**MMN**	**0.30**
Verbal IQ (WRAT)	**MMN**	**0.46**
Ventral mid-cingulate		
Positive symptoms (SAPS)	**RON**	**0.29**
Negative symptoms (SANS)	**P3a**	**0.36**
Immediate verbal memory (CVLT)	**RON**	**0.41**
Delayed verbal memory (CVLT)	RON	0.24
Verbal IQ (WRAT)	**RON**	**0.29**
Executive functioning (WCST)	RON	0.24
Anterior cingulate		
Functional status (GAF)	MMN	0.18
Functional status (GAF)	RON	0.17
Immediate verbal memory (CVLT)	RON	0.25
Delayed verbal memory (CVLT)	RON	0.17
Medial Oribitofrontal		
Positive symptoms (SAPS)	**P3a**	**0.40**
Negative symptoms (SANS)	**P3a**	**0.54**
Psychosocial functioning (SOF)	**P3a**	**0.37**
Functional capacity (UPSA)	**P3a**	**0.32**
Dorsal mid-cingulate		
Verbal IQ (WRAT)	P3a	0.15
Executive functioning (WCST)	MMN	0.18

(Rissling et al., 2014)

Current limitations of ICA as EEG generative model

BASE

APEX

Displacement

Distance along cochlea

Modified from von Bekesy (1966)

- Traveling waves in ECoG

- Too-deep dipoles—the effective sources derived from ICA may not be limited to single dipoles (see the next slide).

29%   0 mm

- Inconsistent individual results

Subj 1   Subj 2   Subj 3

- Low 'true degrees of freedom'—only 10-20 good ICs (this is probably the nature of scalp EEG.)

256 ch EEG
Active saccade task

PCA
To obtain 95% variance

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ICA model is NOT the ground truth itself—hence 'effective' sources.

http://www.d.umn.edu/~jfitzake/Lectures/DMED/InnerEar/CochlearPhysiology/PlacePrinciple.html

Modular organization of thalamocortical projection

They form synchronous dipolar oscillators!

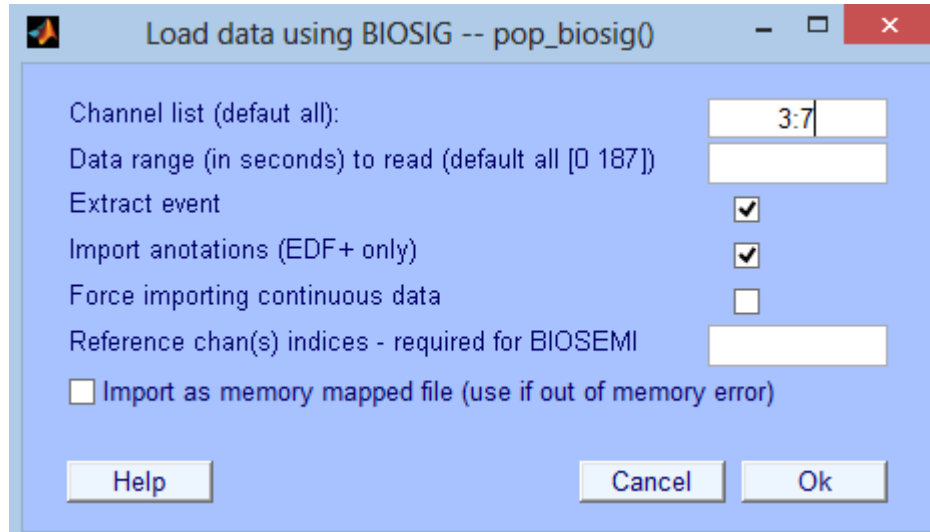Figures courtesy of Shinji Kakei and Yoshikazu Shinoda
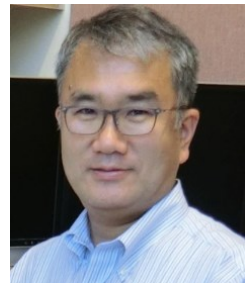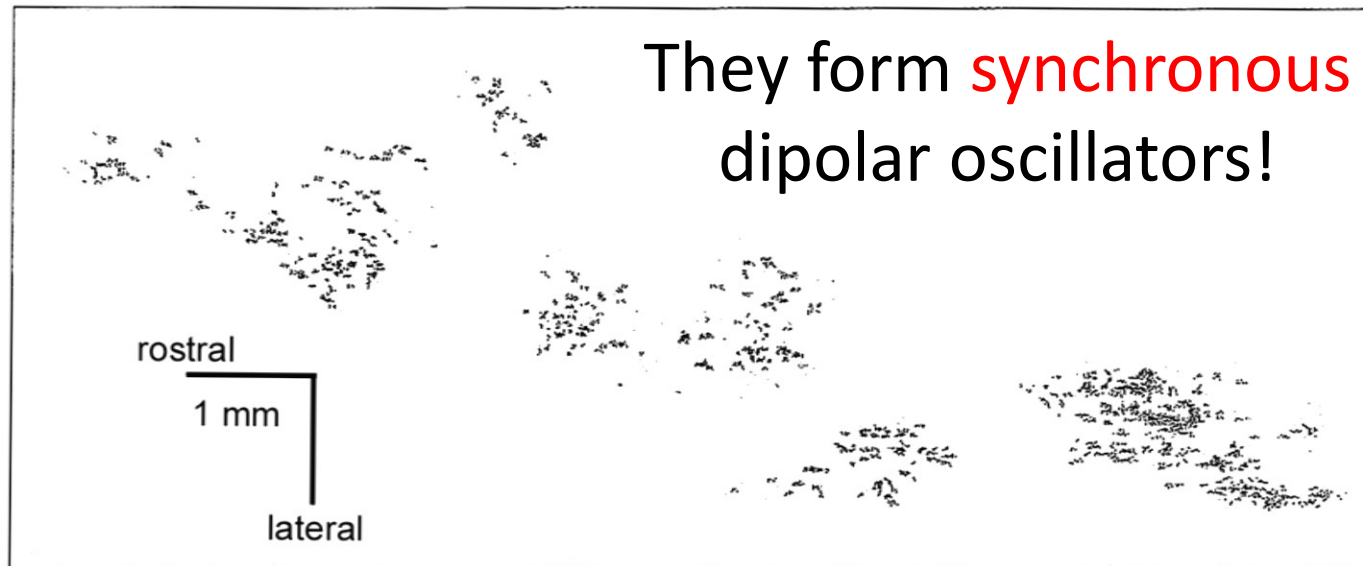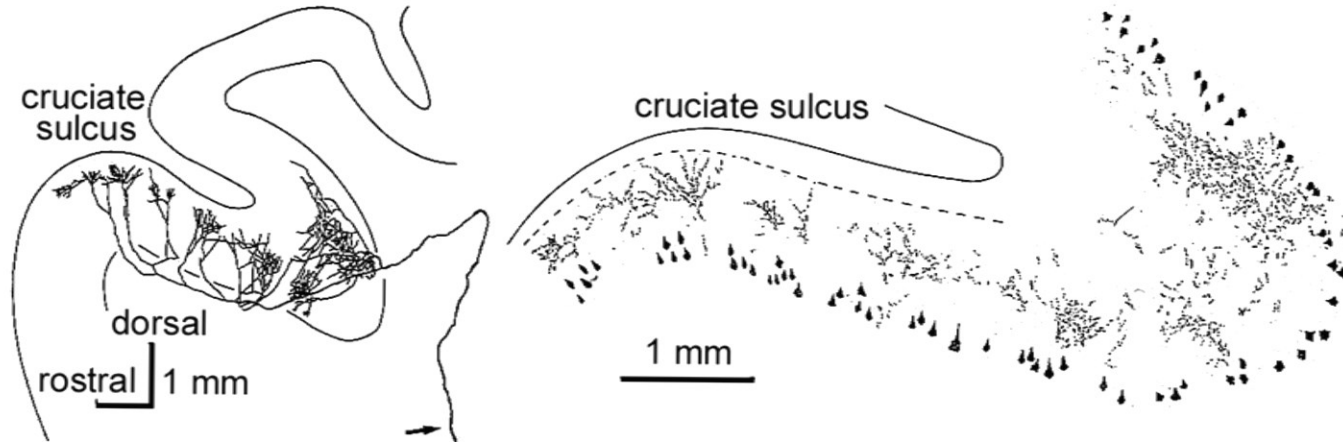
Part 3 Summary

- EEG has been serving to box models as a *one-bit information generator*.

- ERP paradigm, while successful, remains in an evolutionary *cul-de-sac* with *Popperian defense.*

- *I-D identity* means that transforming data to be temporally independent also achieves dipolarity.

- ICA can be seen as a process of non-Gaussianity maximization.
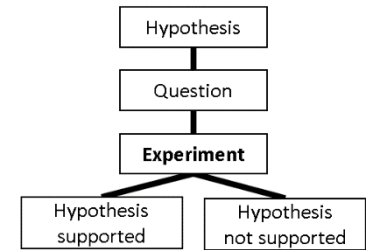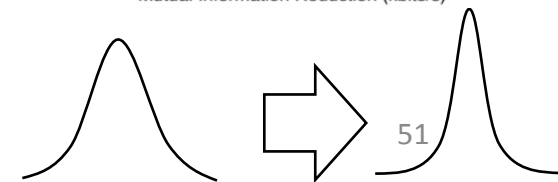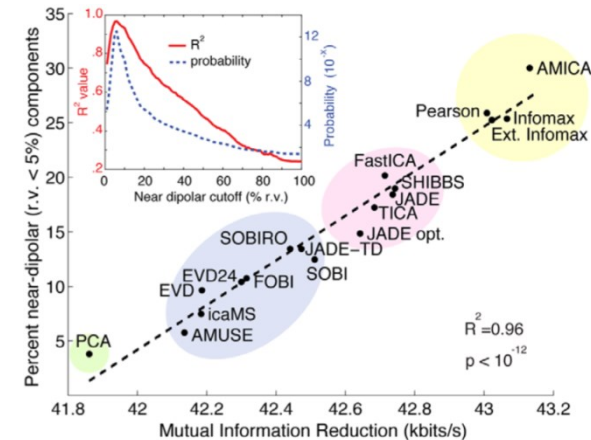
Outroduction

- EEGLAB delivers to the world the color of the sky in La Jolla—[0.67 0.77 1] in Matlab RGB triplet.

http://1.bp.blogspot.com/-DU43sOmydiU/U0TqKp8Q3-I/AAAAAAAAKqQ/xYzAlck37oI/s1600/Title+Pic+Temp.jpg

Grand summary and Conclusion

- *Makoto's pessimism* (the low degrees of freedom in EEG) is worth checking for the sake of future BCI.

- Proof is necessary to claim that in performing science the new dogma (i.e., engineering of EEG) does better job than the old dogma (i.e., box-model with one-bit information generator).

- Two possible scenarios—1) scientists explicitly ask the ground truth of EEG and underpin it, or 2) engineers bindly find algorithm that addresses the ground truth (without knowing).

- What do we do? I see a solution… Do you?
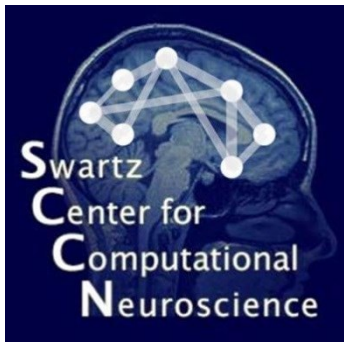
Thank you!

Hirokazu Tanaka and Nisou Miyakoshi
at Poway park, July 4 2014.