High performance computing and neuropsychiatry

Włodzisław Duch

Neurocognitive Laboratory,
Center of Modern Interdisciplinary Technologies,
Dept. of Informatics, Faculty of Physics, Astronomy & Informatics,
Nicolaus Copernicus University

Google: W. Duch

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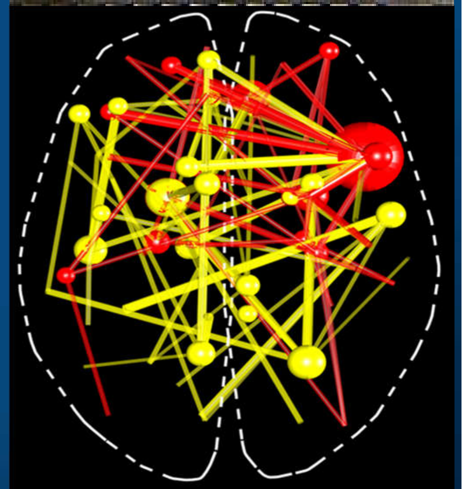
On the threshold of a dream … (50 y!)

Some ideas on how to optimize and repair human brains?



Duch W. (2012) Mind-Brain Relations, Geometric Perspective and Neurophenomenology, American Phil. Assoc. Newsletter 12(1), 1-7.
Duch, W. (2019) Mind as a shadow of neurodynamics. Physics of Life Reviews

Global Brain Initiatives
or why is this so important?

Costs of brain diseases

European Brain Council (EBC) reports (2010; 2014).
Consensus Statement on European Brain Research (2015) includes a chapter on Computational Neuroscience, data repositories and analytics.

179 million, or 1/3 of all European citizens, had at least one brain disorder.
45% of the total annual health budget of Europe!

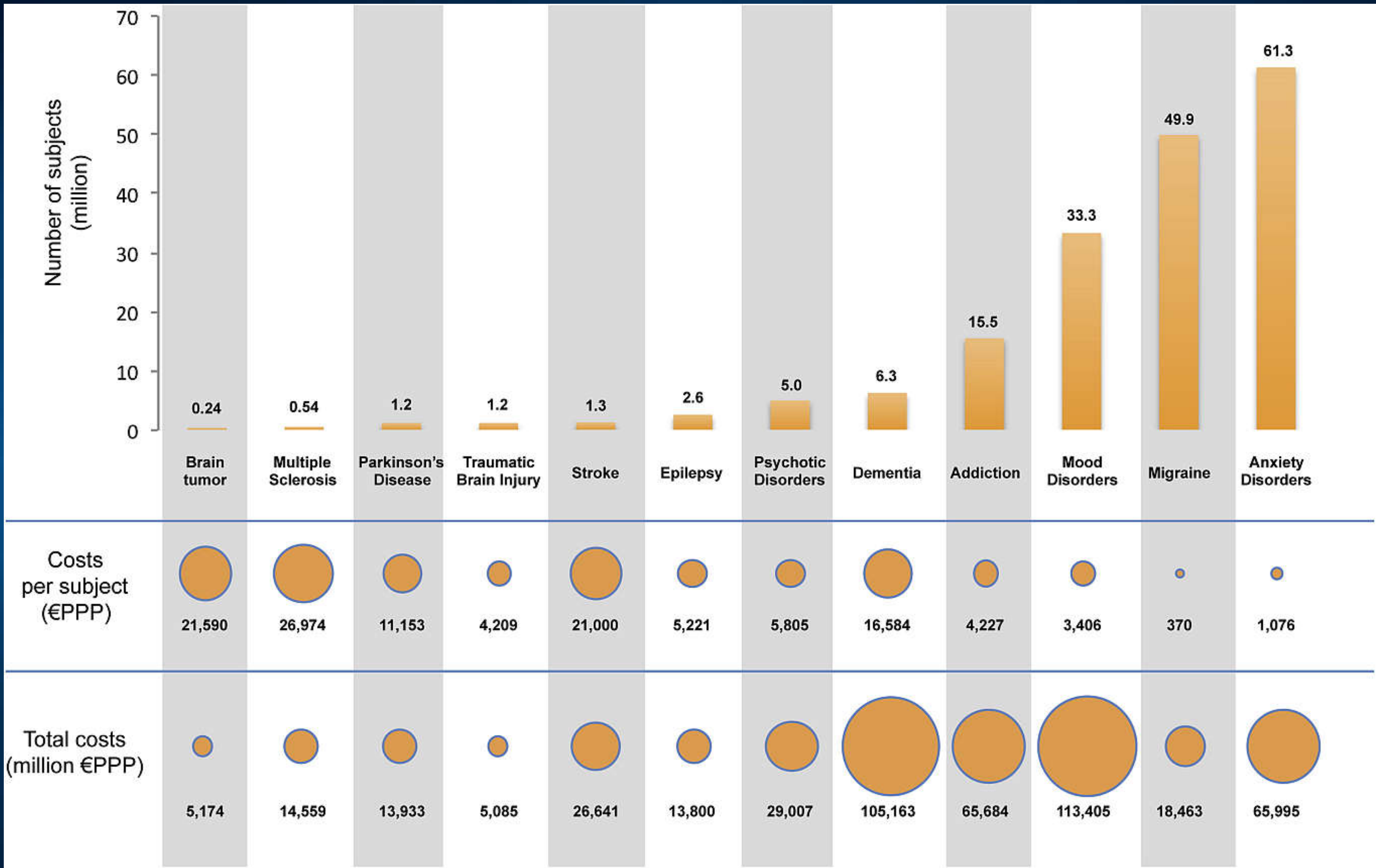
Total cost of brain disorders in EU estimated in 2010: 798 billion €/year,
average direct health care costs represent 37%,
direct nonmedical costs 23%, and indirect costs 40%.

China: >20% of population (~250 mln) suffering from some mental disorder.

Total costs of disorders of the brain in Poland, 2010 estimates.

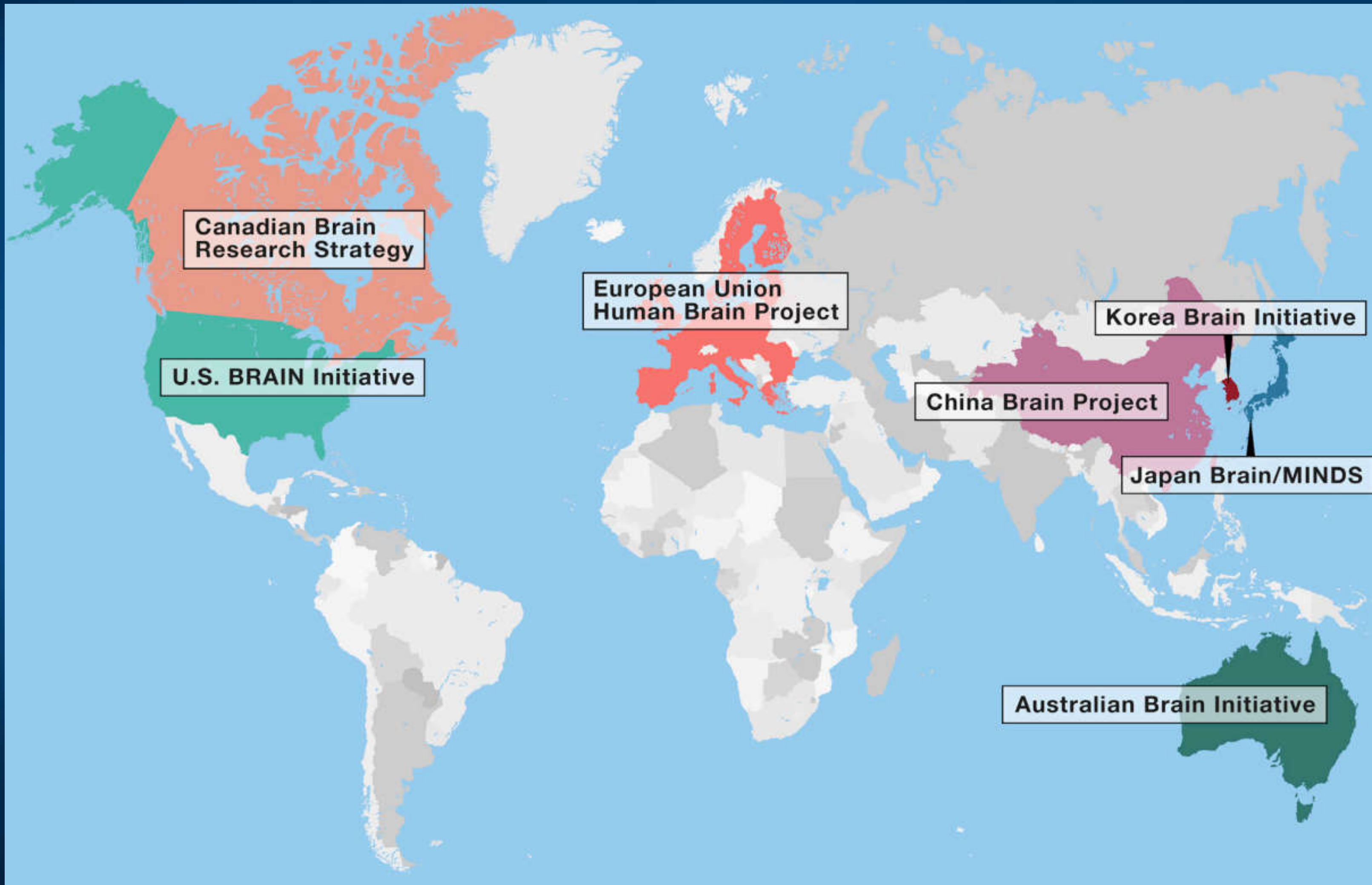
Addiction	Anxiety	Dementia	Epilepsy	Headache	Mood	Psychotic	Stroke	x1000
1 201	5 261	358	298	12 025	2 499	371	503	# people
2 501	2 882	2 480	745	1 559	4 489	3 723	2 187	mln €

Gustavsson et al. (2011). Cost of disorders of the brain in Europe 2010. *European Neuropsychopharmacology*, *21*(10), 718–779.

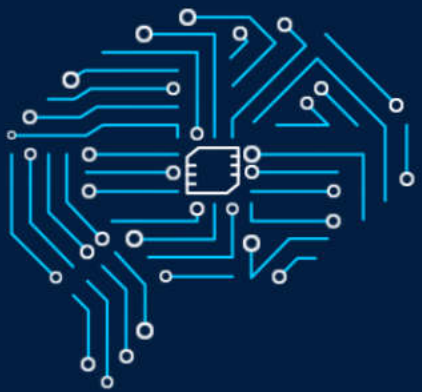


Number of subjects (million)
70
60
50
40
30
20
10
0
0.24
0.54
1.2
1.2
1.3
2.6
5.0
6.3
15.5
33.3
49.9
61.3
Brain tumor
Multiple Sclerosis
Parkinson's Disease
Traumatic Brain Injury
Stroke
Epilepsy
Psychotic Disorders
Dementia
Addiction
Mood Disorders
Migraine
Anxiety Disorders
Costs per subject (€PPP)
21,590
26,974
11,153
4,209
21,000
5,221
5,805
16,584
4,227
3,406
370
1,076
Total costs (million €PPP)
5,174
14,559
13,933
5,085
26,641
13,800
29,007
105,163
65,684
113,405
18,463
65,995

International Brain Initiatives



BRAIN INITIATIVE



Advance Neurotechnologies

Accelerate the development and application of new neurotechnologies.

Support multi-disciplinary teams and stimulate research to rapidly enhance current neuroscience technologies and catalyze innovative scientific breakthroughs.

Human Brain Project, EU Flagship, and Obama BRAIN Initiative (2013):
Brain **R**esearch through **A**dvancing **I**nnovative **N**eurotechnologies.

"Develop new technologies to explore how the brain's cells and circuits interact at the speed of thought, ultimately uncovering the complex links between brain function and behavior. Explore how the brain records, processes, uses, stores, and retrieves vast quantities of information. Help bring safe and effective products to patients and consumers."

Since 2013 numerous exciting developments in neurotechnology and our understanding of the brain have been made by scientists across the globe.

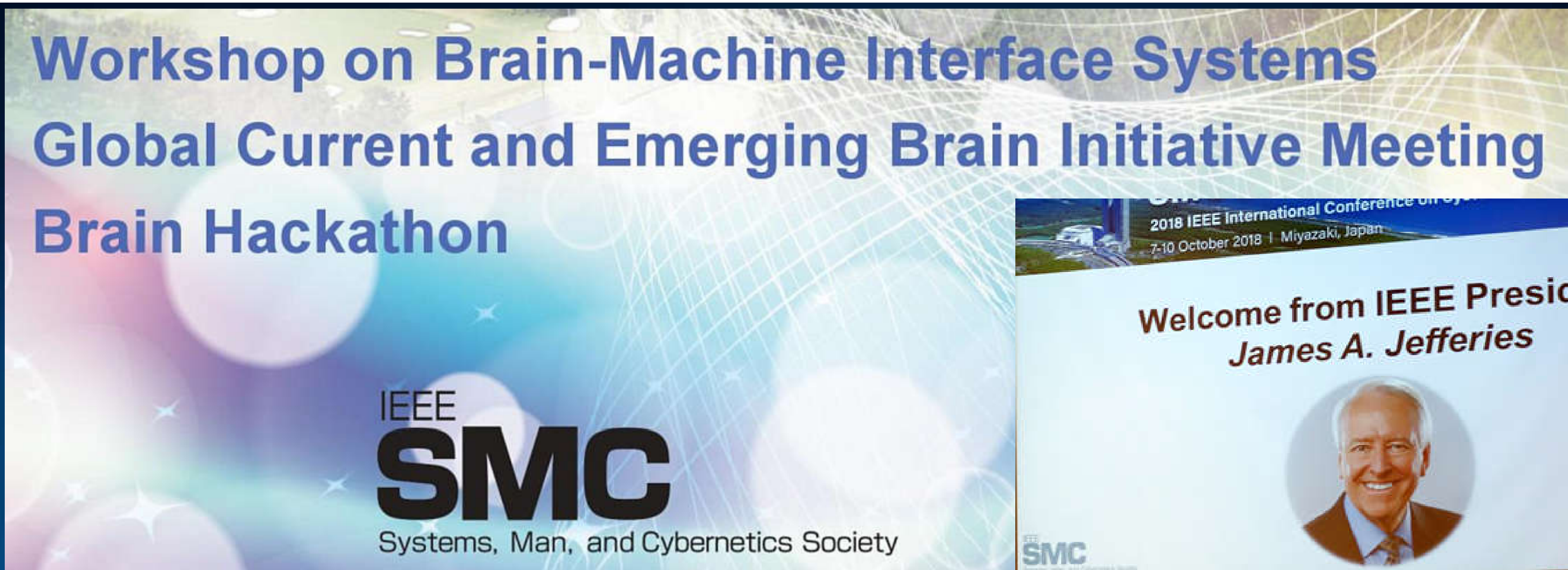
The mission of IEEE Brain is to facilitate cross-disciplinary collaboration and coordination to advance research, standardization and development of technologies in neuroscience to help improve the human condition.

20 IEEE Societies are involved, including:

IEEE Computational Intelligence Society; Computer Society; Consumer Electronics Society; Digital Senses Initiative; Robotics and Automation Society; Sensors Council; Signal Processing Society; Society on Social Implications of Technology; **Systems, Man, and Cybernetics Society**, International Neuroethics Society, and a few other societies.

Most these societies are also involved in artificial intelligence.

Satya Nadella (CEO, Microsoft): to celebrate National Disability Employment Awareness Month, I'm sharing examples of how technology can be applied to empower the more than one billion people with disabilities around the world.



Part of the Brain-Machines Interface Workshop and SMC2018 (M. Smiths, UC Berkeley). The IEEE SMC Society and the IEEE President, James Jefferies, are proud to invite you on to a special meeting of **Global Current and Emerging Brain Initiative leaders** and representatives from other groups working on large-scale multi-year brain projects from Australia, Canada, China, Europe (HBP), Japan, Korea, New Zealand, **Poland**, Russia, and US (NSF and NIH), with representatives from the **IEEE Brain Initiative**, International Neuroethics Society, industry, and other stakeholders.

IEEE welcomes collaborative discussions with all stakeholders to better align and integrate IEEE with other existing brain efforts.

EU steps in

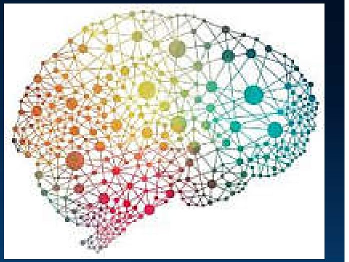
April 2018: Communication from the Commission to the European Parliament, the European Council, the Council, the European Economic and Social Committee & the Committee of Regions on Artificial Intelligence for Europe.

“Like the steam engine or electricity in the past, AI is transforming our world, our society and our industry. … The economic impact of the automation of knowledge work, robots and self-driving vehicles could reach between EUR 6.5 and EUR 12 trillion annually by 2025.”

By the end of 2018 EU private investments ~3 G€, USA 12-18 G€.
EU as a whole … at least 20 G€ by the end of 2020, then aim for > 20 G€/y.

- Digital Transformation 2021-27 includes:
  supercomputing (2.7 G€)+ AI (2.5 G€) + cybersecurity (2.0 G€) + advanced digital skills/use (700 M€).
- EurAI CLAIR (~2000 wspierających), 7.09 sympozjum.
  ELLIS, European Lab for Learning & Intelligent Systems
- **Coordinated Plan on Artificial Intelligence** 12/2018
  4 EU AI centers @ 12 M€ in 2019, including medical applications and NLP.

Neuroscience => AI



Hassabis, D., Kumaran, D., Summerfield, C., Botvinick, M. (2017). Neuroscience-Inspired Artificial Intelligence. *Neuron*, *95*(2), 245–258.

Affiliations: **Google DeepMind**, Gatsby Computational Neuroscience, Institute of Cognitive Neuroscience, Uni. College London, Uni. of Oxford.

Artificial neural networks – simple inspirations, but led to many applications.

Bengio, Y. (2017). The **Consciousness Prior**. *ArXiv:1709.08568.*

Amoset al. (2018). **Learning Awareness Models**. *ArXiv:1804.06318*.

AI Systems inspired by Neural Models of Behavior:

(A) **Visual attention**, foveal locations for multiresolution ‘‘retinal’’ representation, prediction of next location to attend to.

(B) **Complementary learning systems** and episodic control: fast learning hippocampal system and parametric slow-learning neocortical system.

(C) Models of **working memory** and the Neural Turing Machine.

(D) Neurobiological models of **synaptic consolidation** and the elastic weight consolidation (EWC) algorithm.

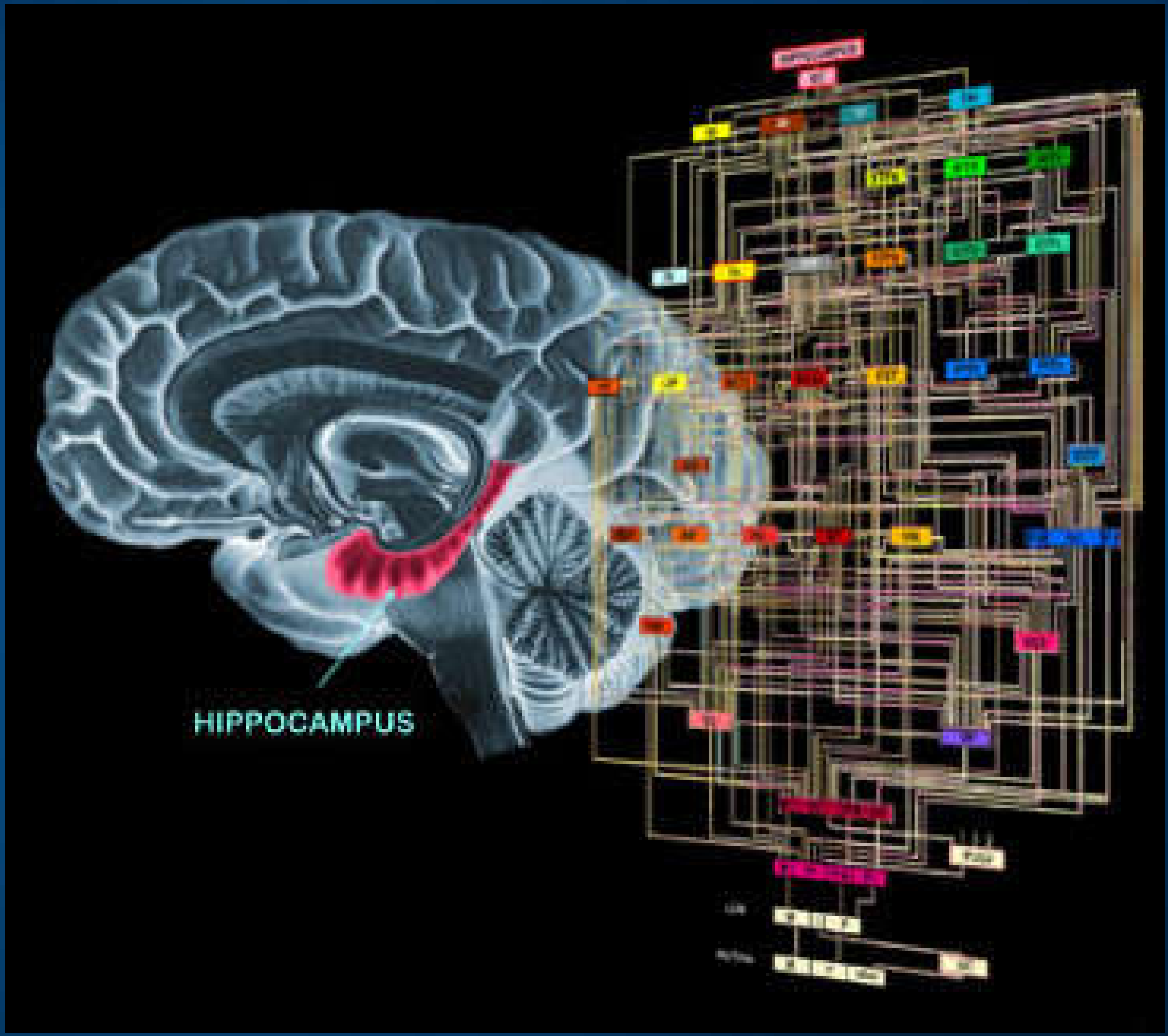
BICA, Brain-Inspired Cognitive Architecture

Understanding the brain from engineering perspective means to build a model of the brain showing similar functions.

Cognitive informatics, Neurocognitive Informatics.

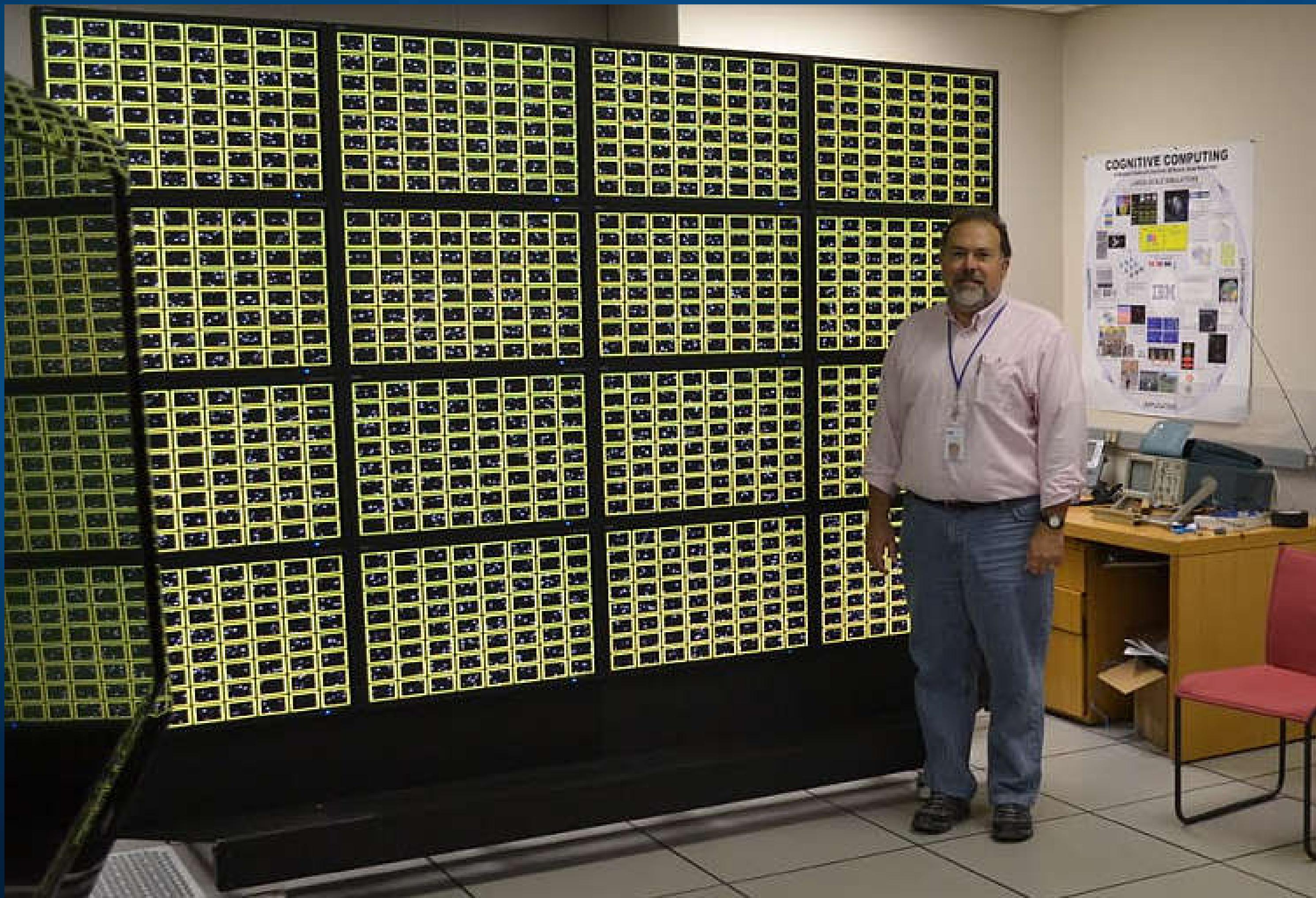
BICA = Brain Inspired Cognitive Architecture.

Review: Duch, Oentaryo, Pasquier, Cognitive architectures: where do we go from here? 2008



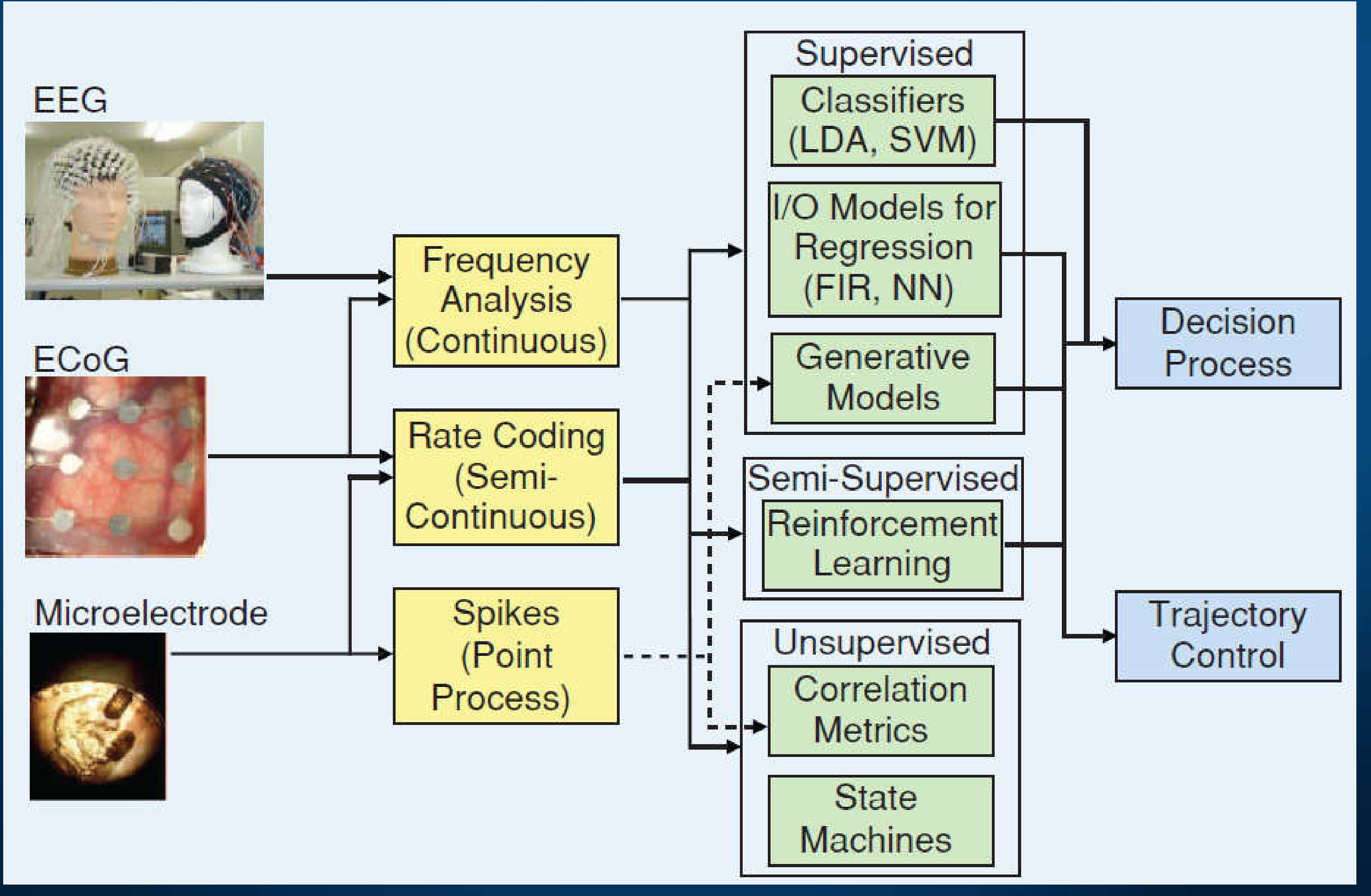
Neuromorphic wall

1024 TN neuromorphic chips, or 1B neurons and 256B synapses!
Complexity ~ horse brain, 1/4 gorilla, 1/6 chimpanzee.

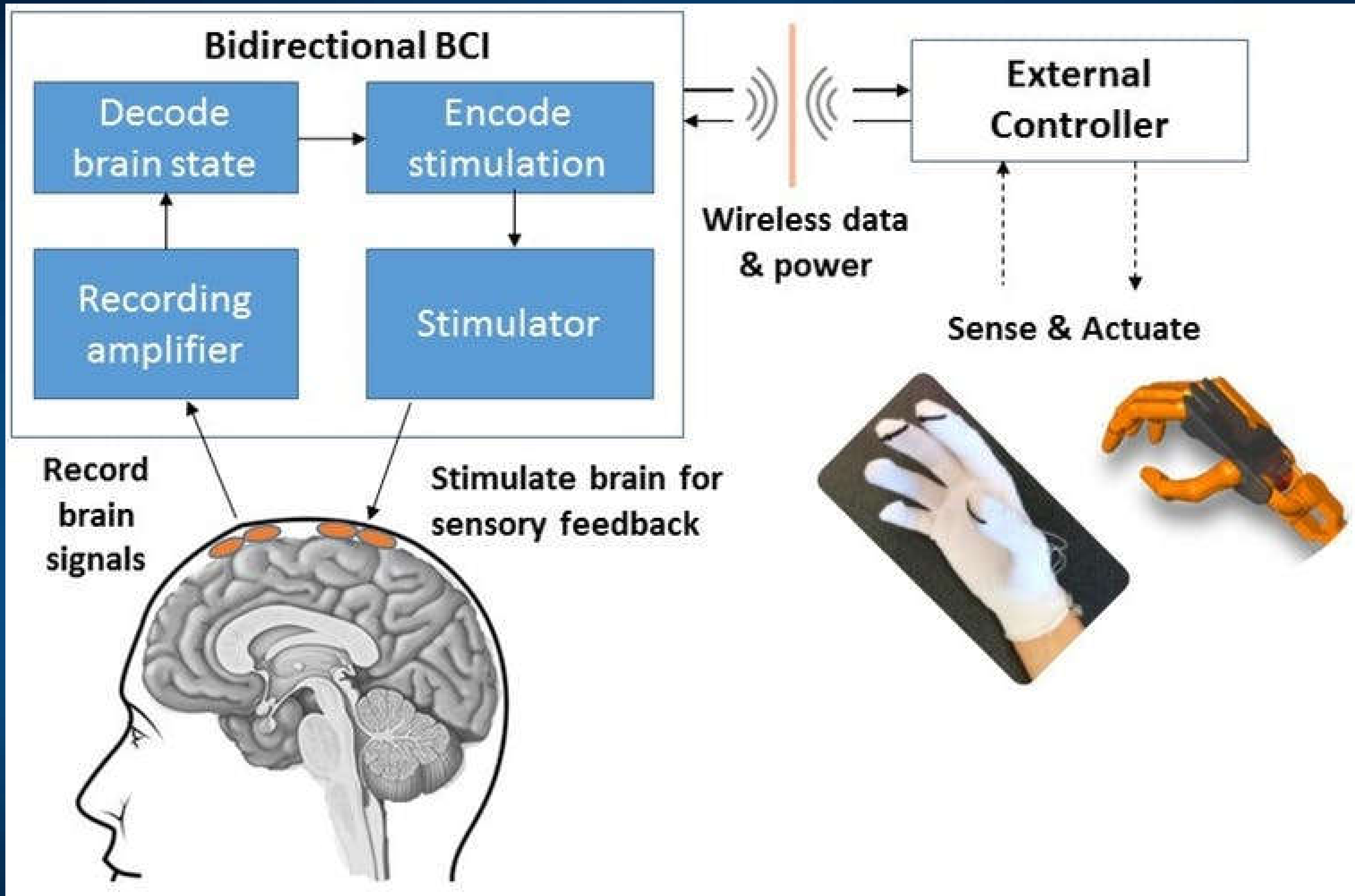


BCI: wire your brain …

Non-invasive, partially invasive and invasive signals carry progressively more information, but are also harder to implement. EEG is still the king!

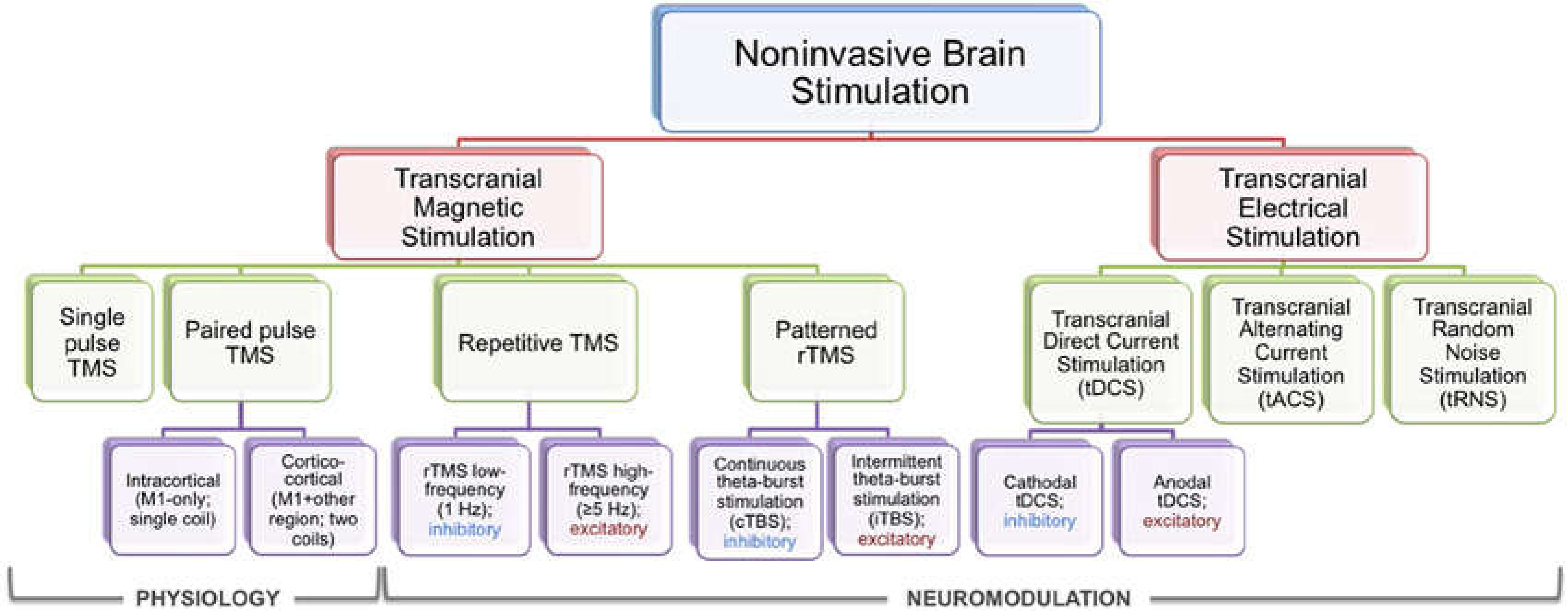


Brain-Computer-Brain Interfaces



Closed loop system with brain reading and stimulation for self-regulation. Sensory signals may com from Virtual Reality.

Brain stimulation



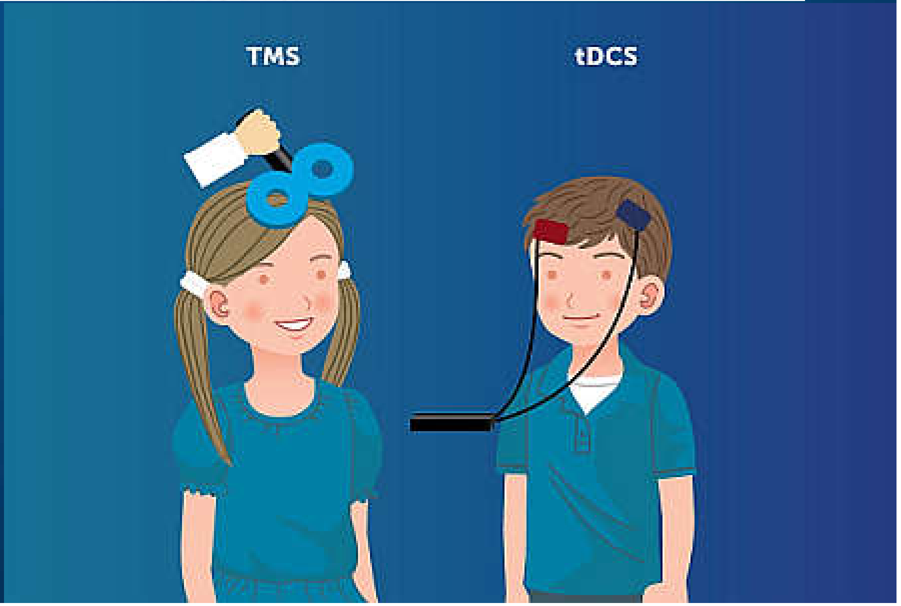
ECT – Electroconvulsive Therapy

VNS – Vagus Nerve Stimulation

Ultrasound, laser … stimulation.

Complex techniques, but portable phones are also complex.

Attention? Just activate your cortex, no effort is needed!



HD EEG/DCS?

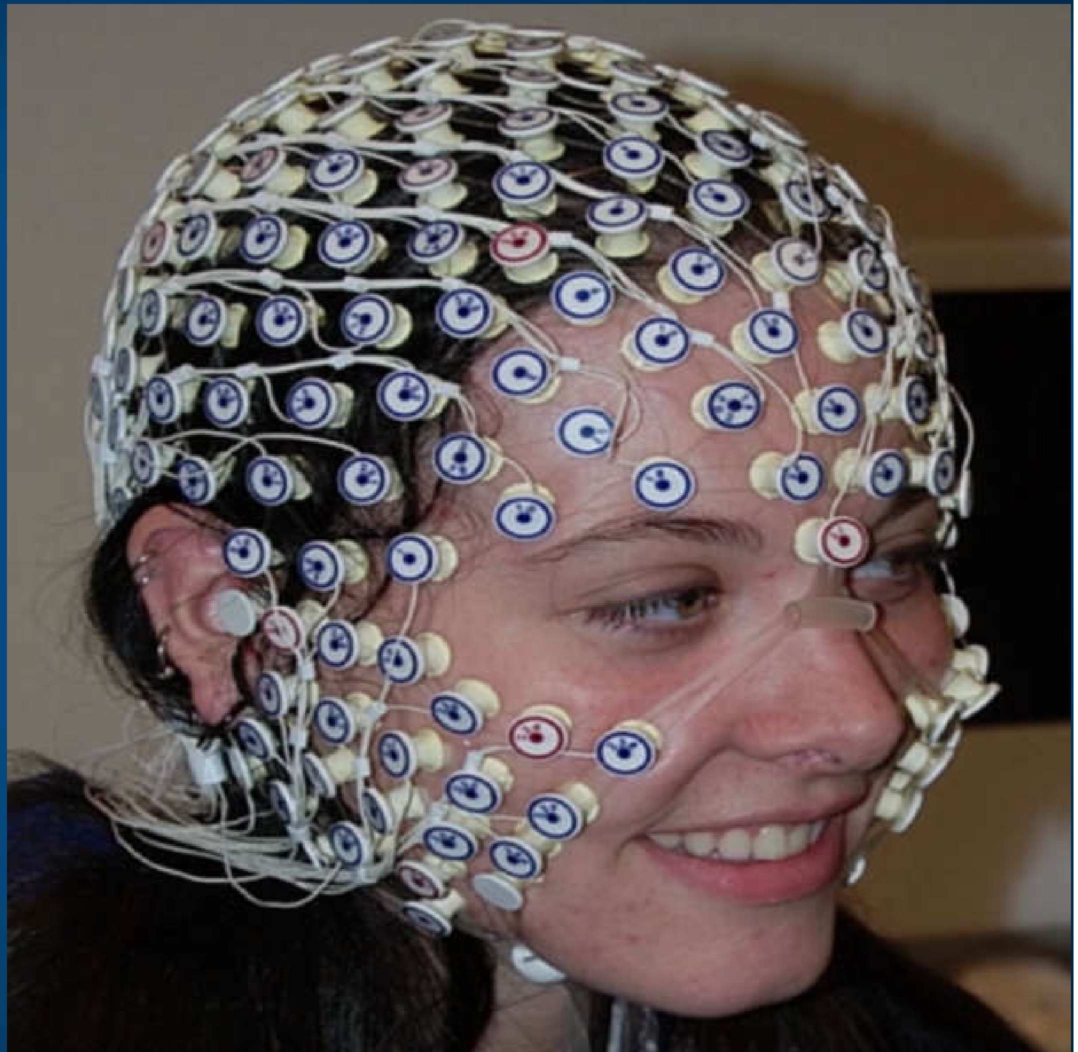
EEG electrodes + DCS.

Reading brain states
=> transforming to common space
=> duplicating in other brains

Applications:

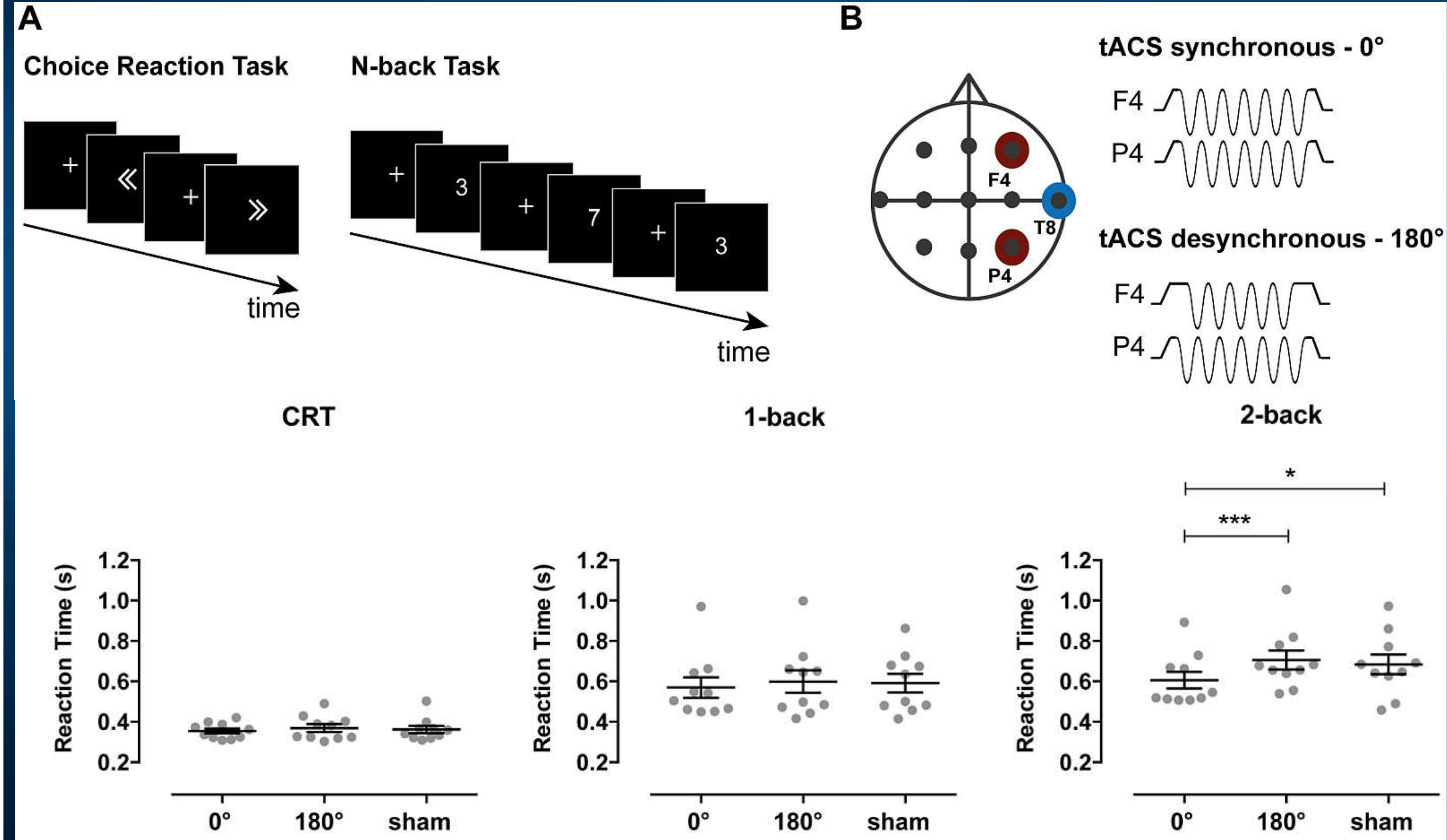
depression, neuro-plasticity, pain, psychosomatic disorders, teaching!

Multielectrode DCS stimulation with 256 electrodes induces changes in the brain increasing neuroplasticity.



Synchronize PFC/PC

Violante, I.R. et al. Externally induced frontoparietal synchronization modulates network dynamics and enhances working memory performance. ELife, 6 (2017).

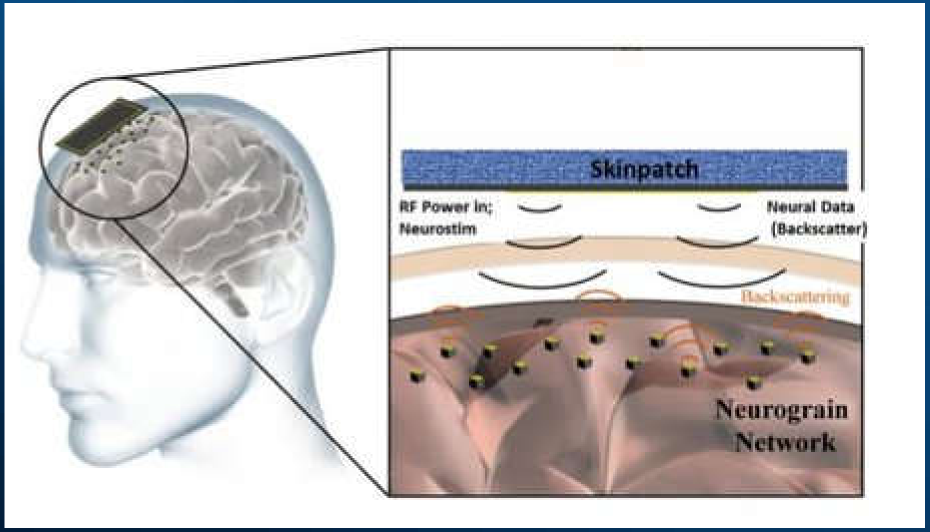


Million nanowires in your brain?

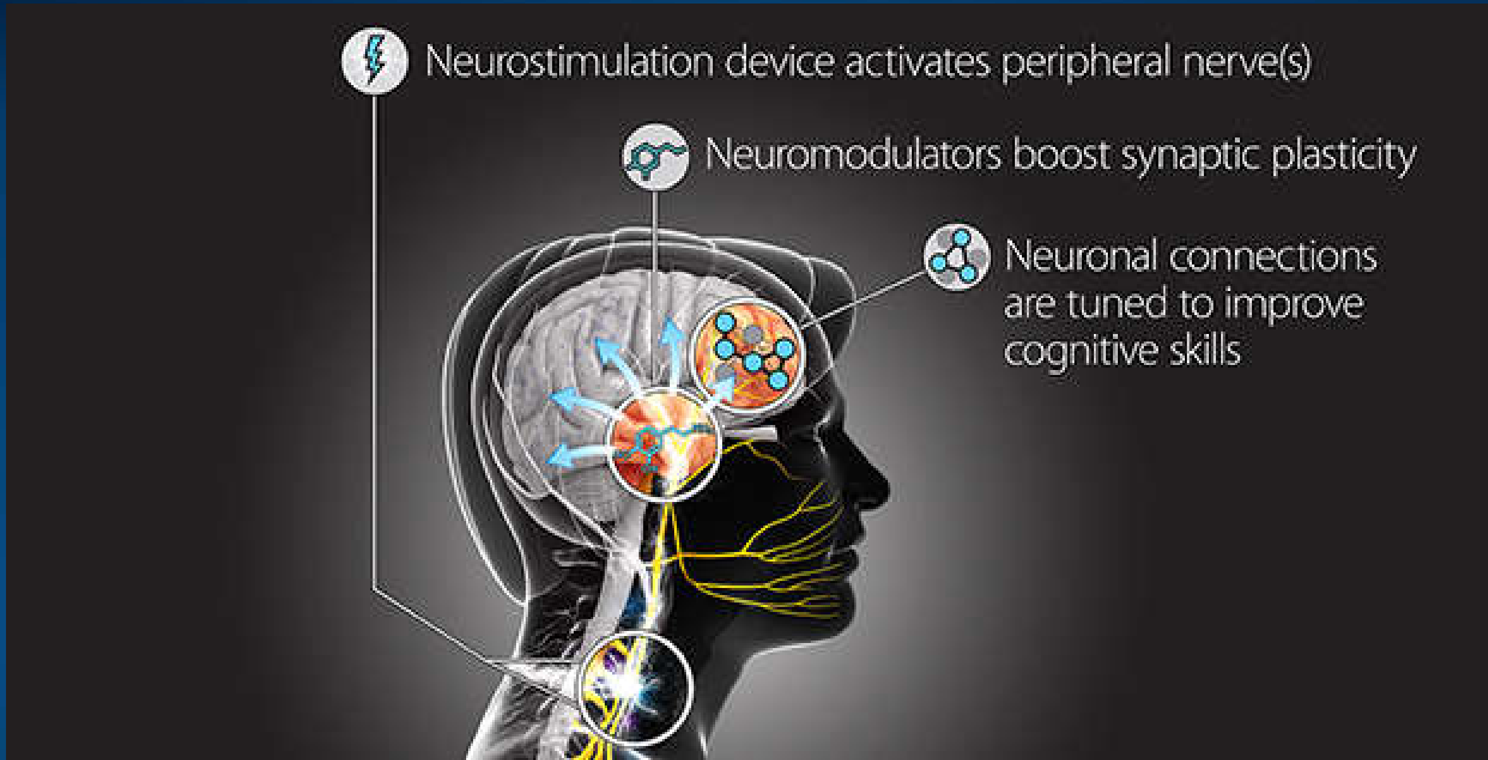
DARPA (2016): **Neural Engineering System Design (NESD)**
Interface that reads impulses of 10^6 neurons, injecting currents to 10^5 neurons, and reading/activating 10^3 neurons.

DARPA Electrical Prescriptions (ElectRx) project enables "artificial modulation of peripheral nerves to restore healthy patterns of signaling in these neural circuits. ElectRx devices and therapeutic systems under development are entering into clinical studies."

Neural lace i neural dust project for cortex stimulation.



Targeted Neuroplasticity Training

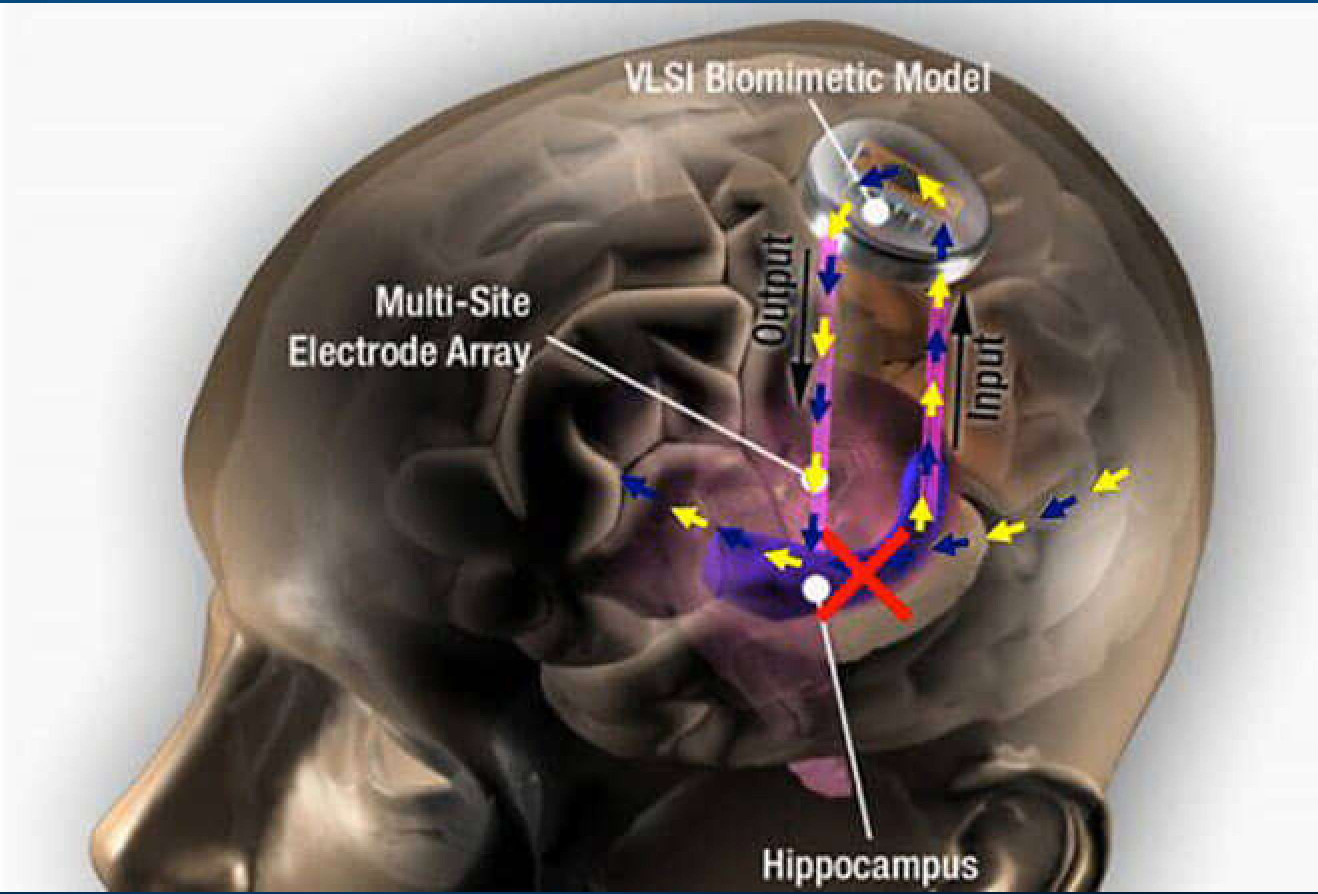


DARPA (2017): Enhance learning of a wide range of cognitive skills, with a goal of reducing the cost and duration of the Defense Department's extensive training regimen, while improving outcomes. TNT could accelerate learning and reduce the time needed to train foreign language specialists, intelligence analysts, cryptographers, and others.

Memory implants

Ted Berger (USC, Kernel): hippocampal neural prosthetics facilitate human memory encoding and recall using the patient's own hippocampal spatiotemporal neural codes. Tests on rats, monkeys and on people gave memory improvements on about 35% (J. Neural Engineering 15, 2018).

DARPA: Restoring Active Memory (RAM), new closed-loop, non-invasive systems that leverage the role of neural "replay" in the formation and recall of memory to help individuals better remember specific episodic events and learned skills.



Brain networks

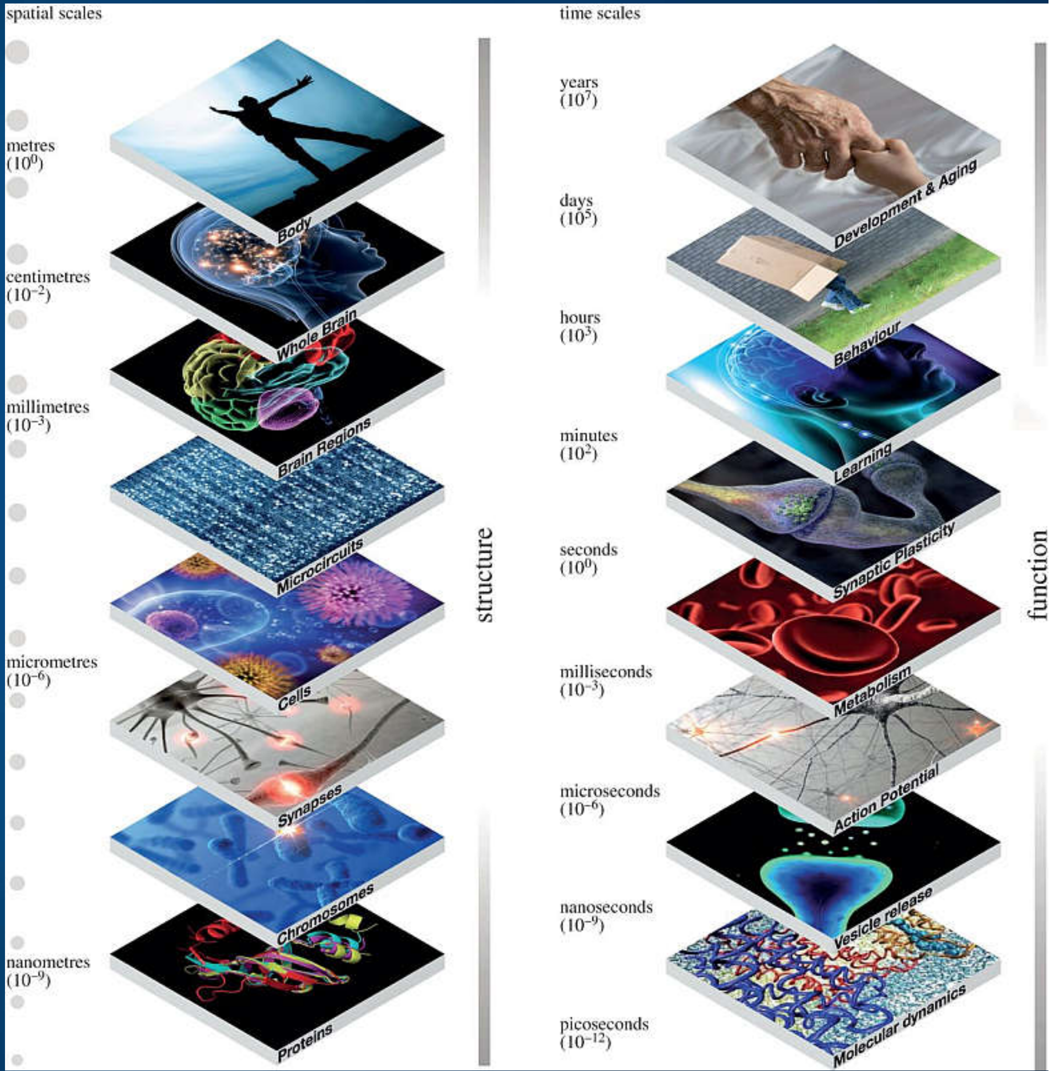
Neuropsychiatric phenomics

2008: The [Consortium for Neuropsychiatric Phenomics]

"… categories, based upon presenting signs and symptoms, may not capture fundamental underlying mechanisms of dysfunction" (Insel et al., 2010).

New approach: [RDOC NIMH].

Description of organisms at different levels will help to answer different types of questions.
Network level is in the middle and can be connected to the mental level via computational models.



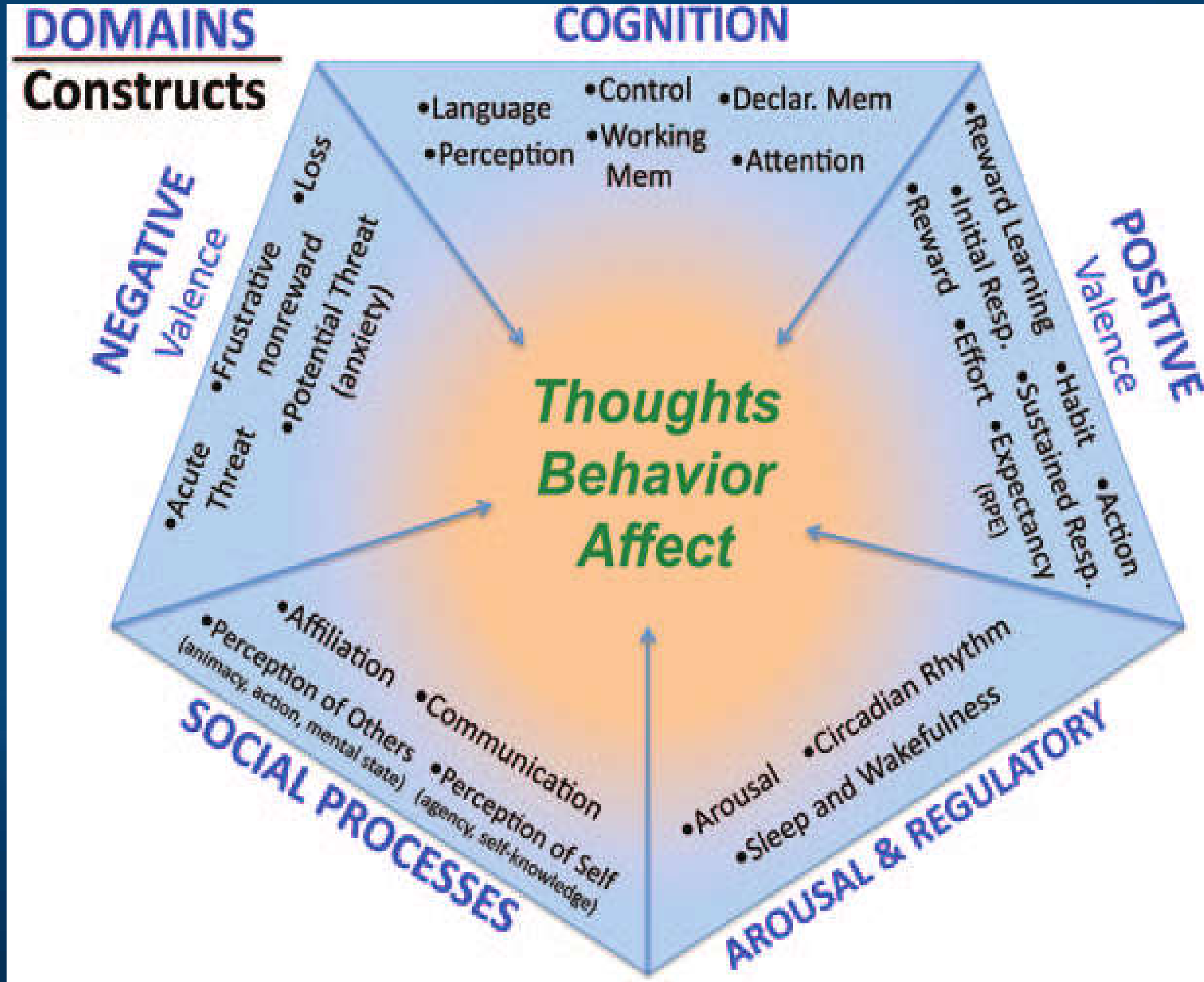
RDoC
Research Domain Criteria Initiative

NIMH RDoC Matrix for deregulation of 6 large brain systems.

Psychological constructs are necessary to talk about mental states.

Sensorimotor systems added in Jan. 2019 as sixth brain system.

How are they related to physical processes?



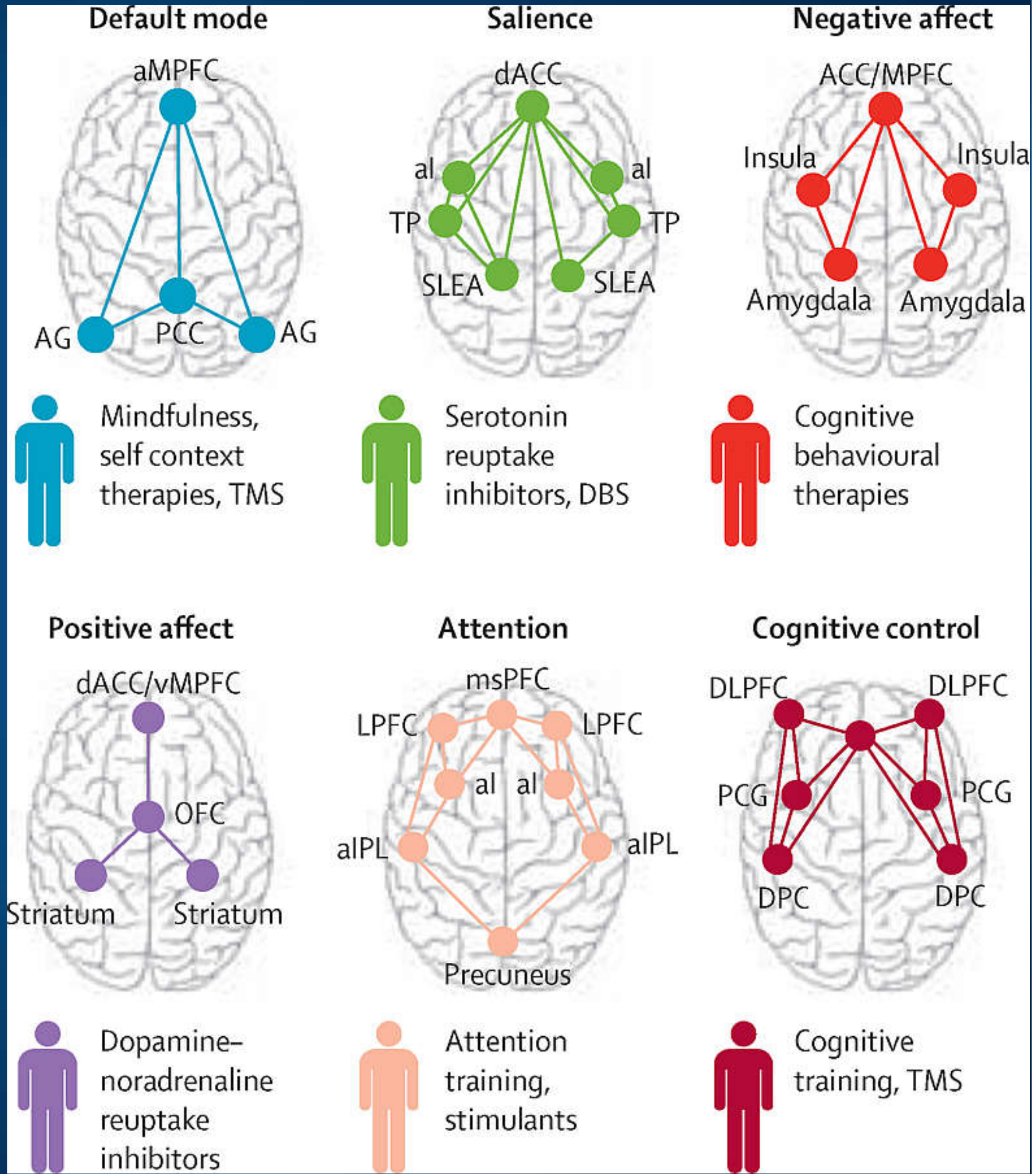
Multi-level phenomics

Research Domain Criteria (RDoC) matrix is based on **multi-level neuropsychiatric phenomics** describing large brain systems deregulation, but links to behavior should be analyzed at the network level, where specialized functions are implemented. **In AI:**

M. Minsky, Society of mind (1986)

Decompose brain network dynamics into meaningful components of activity related to various brain functions.

Include influence of genes, molecules, cells, **circuits**, physiology, behavior, self-reports on network functions.



RDoC Matrix for „cognitive domain”

Construct/Subconstruct		Genes XXX	Molecules	Cells	Circuits	Physiology	Behavior	Self-Report	Paradigms
Attention		Elements	Elements	Elements	Elements	Elements	Elements		Elements
Perception	Visual Perception	Elements	Elements	Elements	Elements	Elements	Elements	Elements	Elements
	Auditory Perception	Elements	Elements	Elements	Elements	Elements	Elements	Elements	Elements
	Olfactory/Somatosensory/Multimodal/Perception								Elements
Declarative Memory		Elements	Elements	Elements	Elements	Elements	Elements	Elements	Elements
Language		Elements			Elements	Elements	Elements	Elements	Elements
Cognitive Control	Goal Selection; Updating, Representation, and Maintenance ⇒ Focus 1 of 2 ⇒ Goal Selection				Elements			Elements	Elements
	Goal Selection; Updating, Representation, and Maintenance ⇒ Focus 2 of 2 ⇒ Updating, Representation, and Maintenance	Elements	Elements	Elements	Elements	Elements	Elements	Elements	Elements
	Response Selection; Inhibition/Suppression ⇒ Focus 1 of 2 ⇒ Response Selection	Elements	Elements	Elements	Elements	Elements	Elements	Elements	Elements
	Response Selection; Inhibition/Suppression ⇒ Focus 2 of 2 ⇒ Inhibition/Suppression	Elements	Elements	Elements	Elements	Elements	Elements	Elements	Elements
	Performance Monitoring	Elements	Elements		Elements	Elements	Elements	Elements	Elements
Working Memory	Active Maintenance	Elements	Elements	Elements	Elements	Elements			Elements
	Flexible Updating	Elements	Elements	Elements	Elements	Elements			Elements
	Limited Capacity	Elements	Elements		Elements	Elements			Elements
	Interference Control	Elements	Elements	Elements	Elements	Elements			Elements

Simulations of brain networks

Model of reading & dyslexia

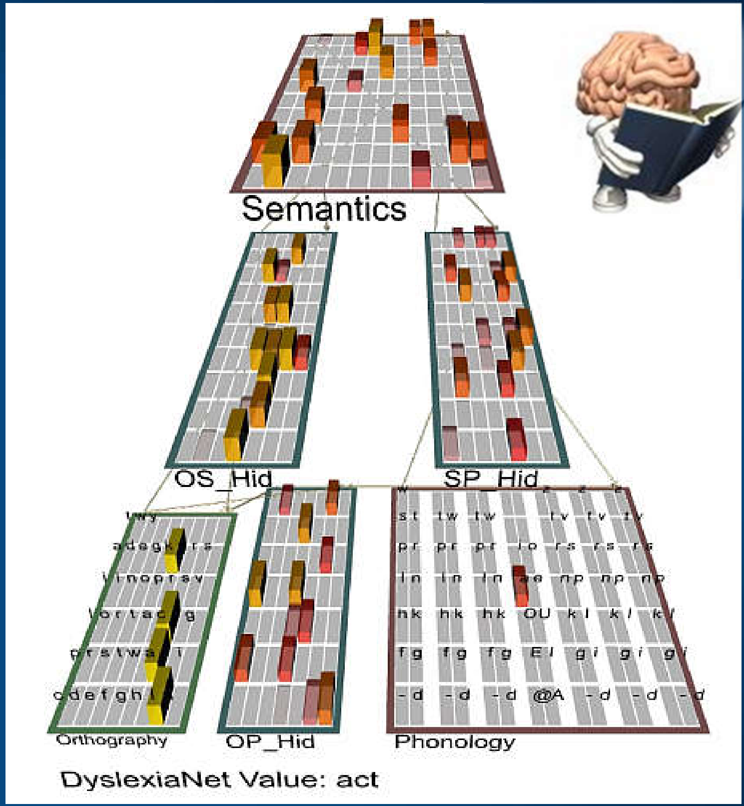
Emergent neural simulator:

Aisa, B., Mingus, B., and O'Reilly, R. The emergent neural modeling system. Neural Networks, 21, 1045, 2008.

3-layer model of reading:

orthography, phonology, semantics, or distribution of activity over **140 microfeatures** defining concepts.

In the brain: microfeature=subnetwork.
Hidden layers OS/OP/SP_Hid in between.



Learning: mapping one of the 3 layers to the other two.

Fluctuations around final configuration = attractors representing concepts.

How to see properties of their basins, their relations?
Model in **Genesis**: more detailed neuron description.

Computational Models

Models at various level of detail.

- Minimal model includes neurons with 3 types of ion channels.

Models of attention:

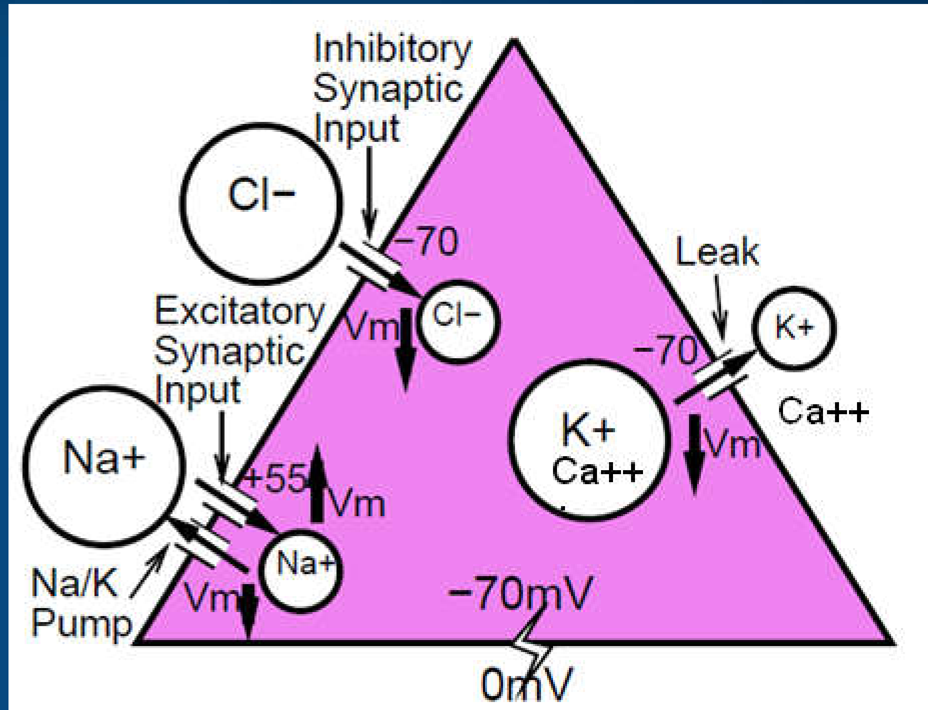
- Posner spatial attention;
- attention shift between visual objects.

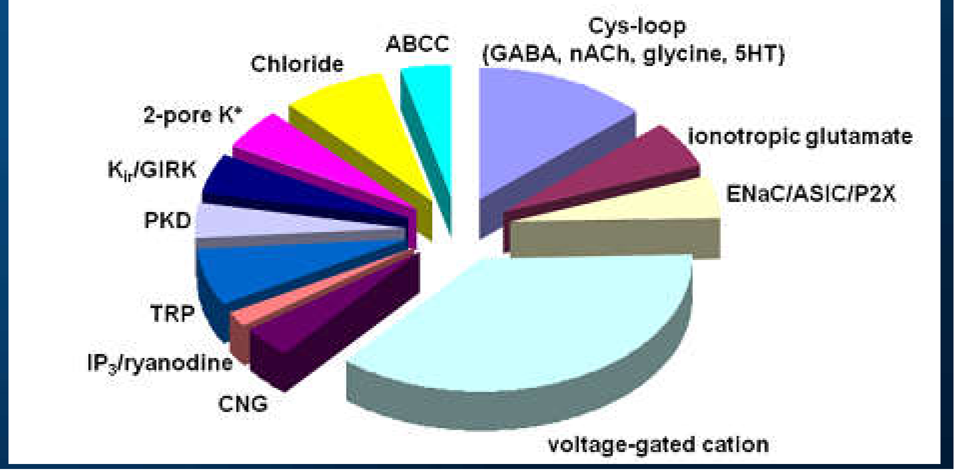
Models of word associations:

- sequence of spontaneous thoughts.

Models of motor control.

Critical: control of the increase in intracellular calcium, which builds up slowly as a function of activation. Initial focus on the leak channels, 2-pore K^+, looking for genes/proteins.



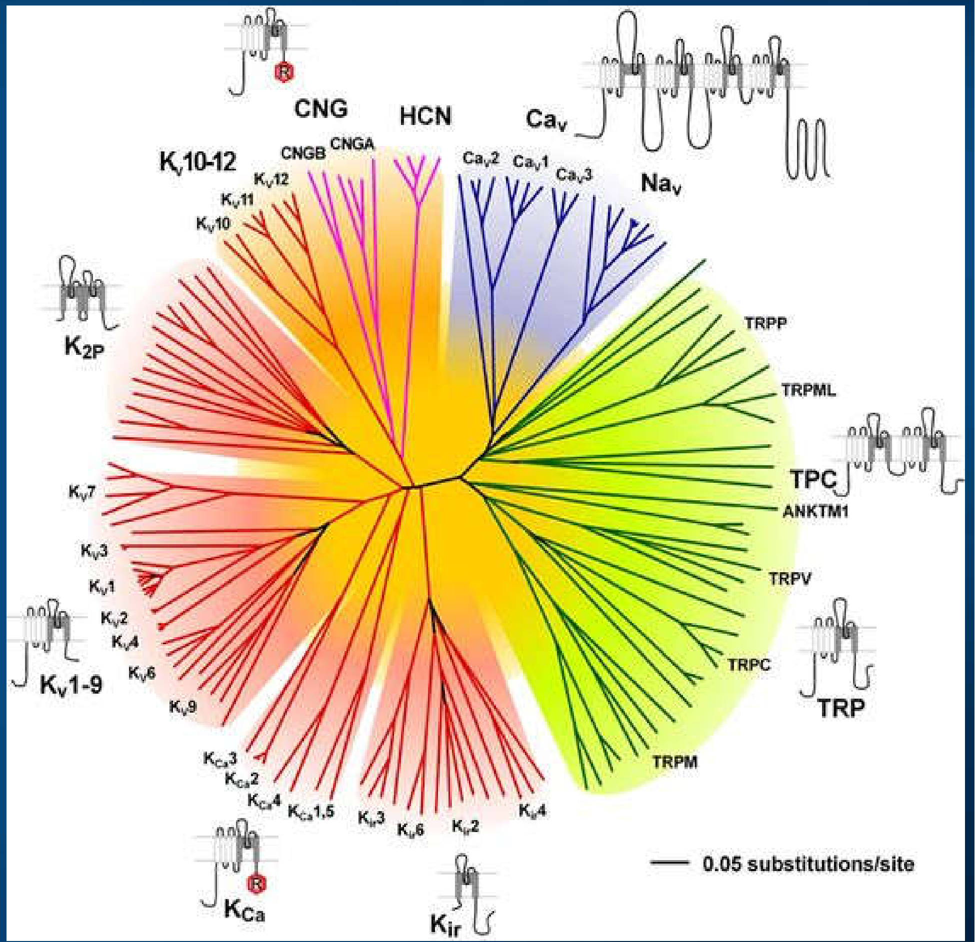


Ion channels

Hundreds of ion channels
have been identified in neurons …

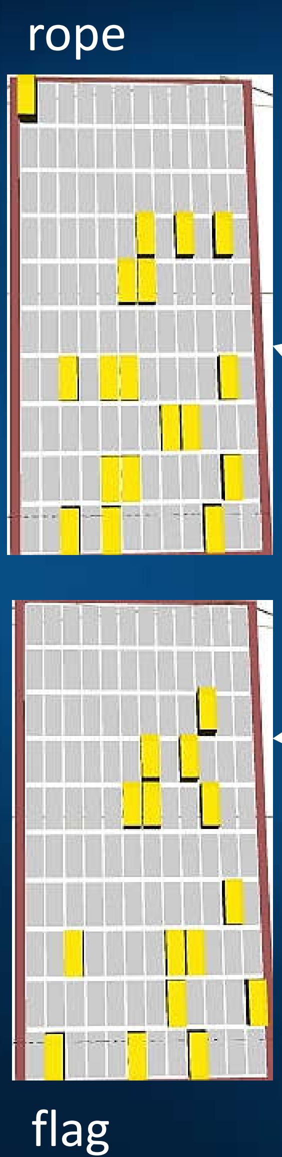
Major challenge for computational neurosciences:

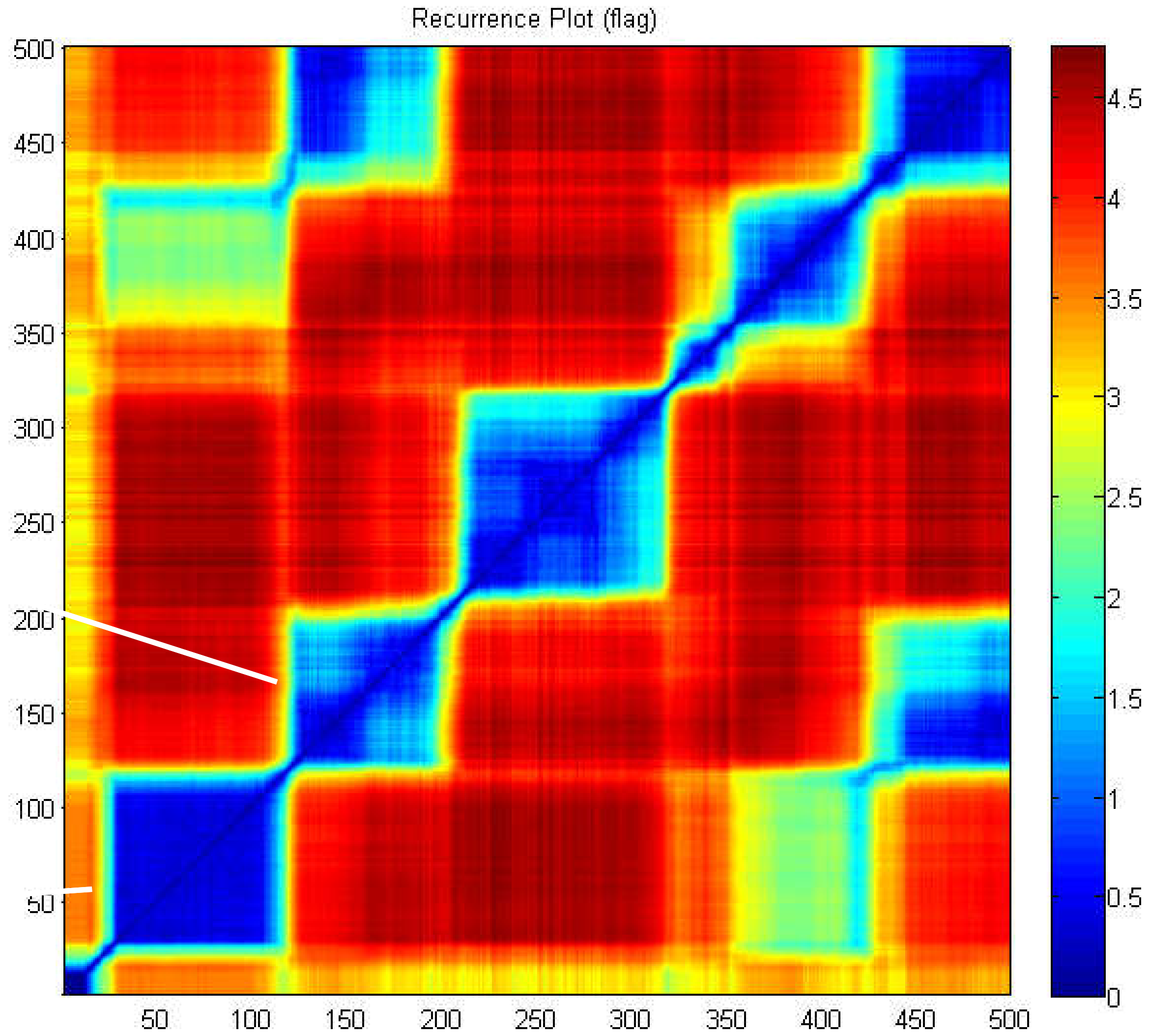
what happens with the nervous system when some of them are dysfunctional?



Plan for action: 8-fold way.

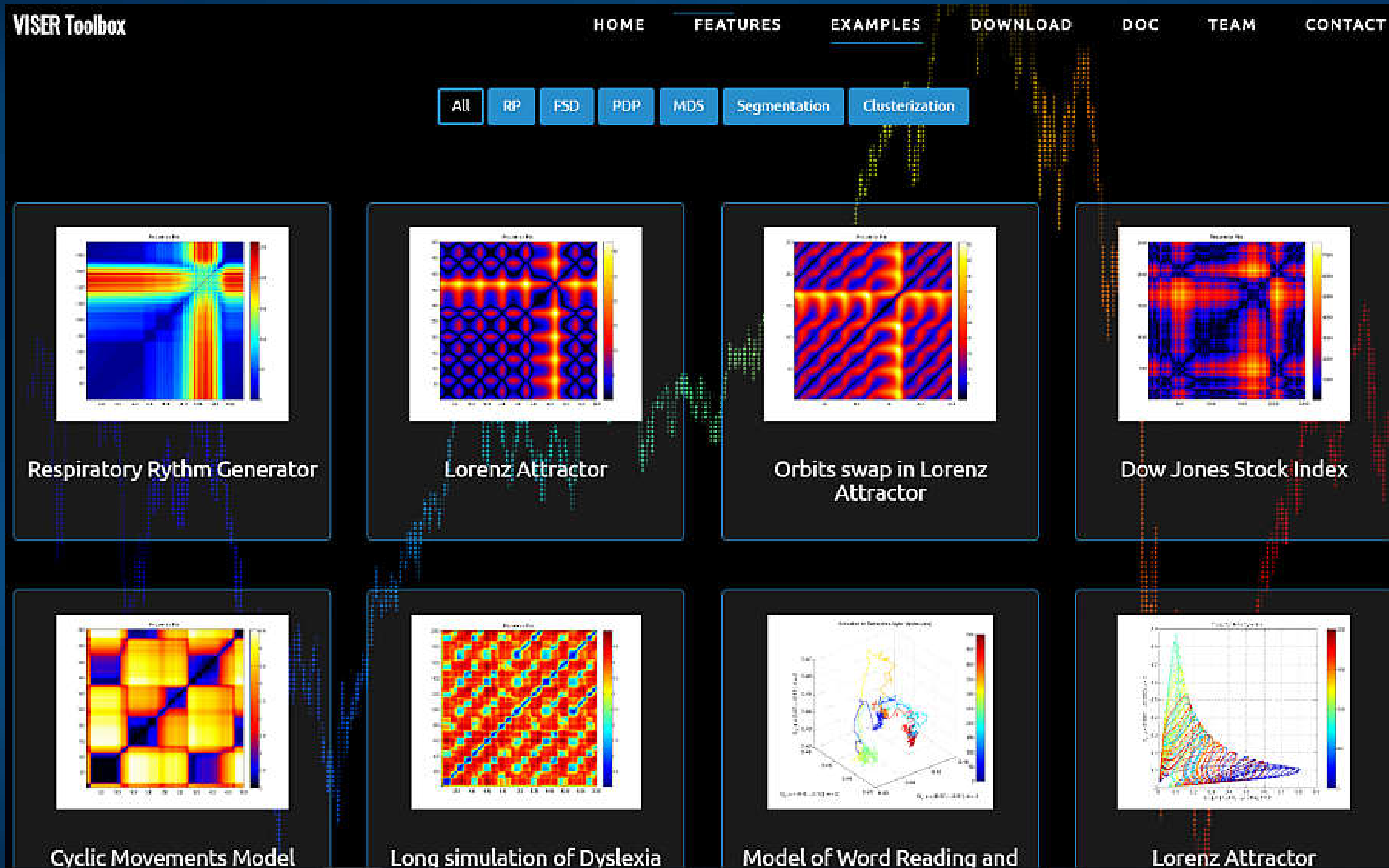
1. Focus on neurodynamics. Include ion channels and other biophysical parameters for neurons/networks in your models.
2. Create simulation of normal functions, ex: attention shifts.
3. Catalogue all possible changes in biophysical parameters that lead to specific deregulation of normal behavior, ex: all types of ion channels.
4. Look for dysfunctional proteins related to biophysical parameters, ex: those proteins that build ion channels.
5. Use gene expression atlases to find correlations of proteins with mutations. Explain diversity of mutations and weak disease signals.
6. Predict changes in real brain signals: EEG/MEG, neuroimaging, intracranial …
7. Analyze existing neuroimaging data, functional and anatomical. Perform new experiments to verify proposed mechanisms leading to dysfunctions.
8. Propose close-loop therapies. Psychosomatic pain is a good target.





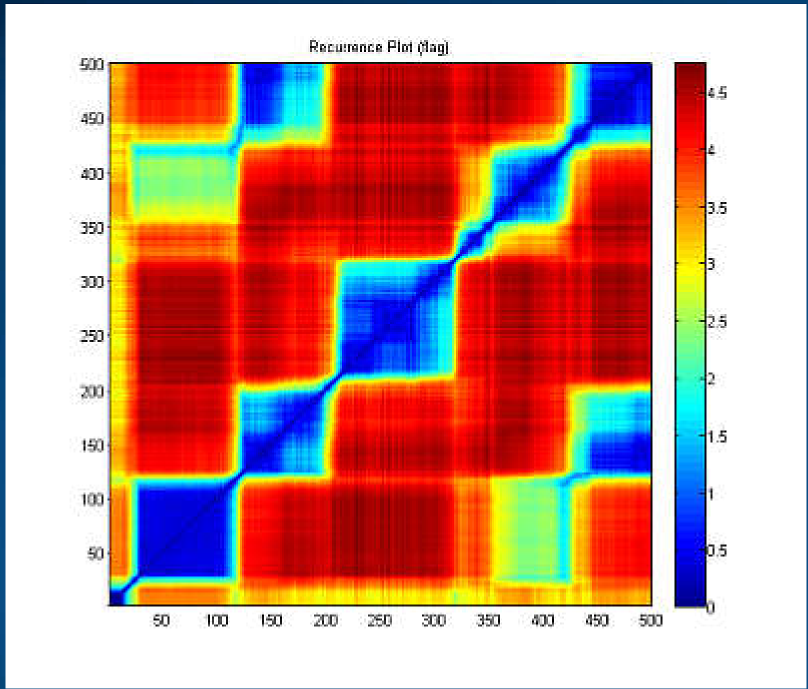
Transitions to new patterns that share some active units (microfeatures) shown in recurrence plots.

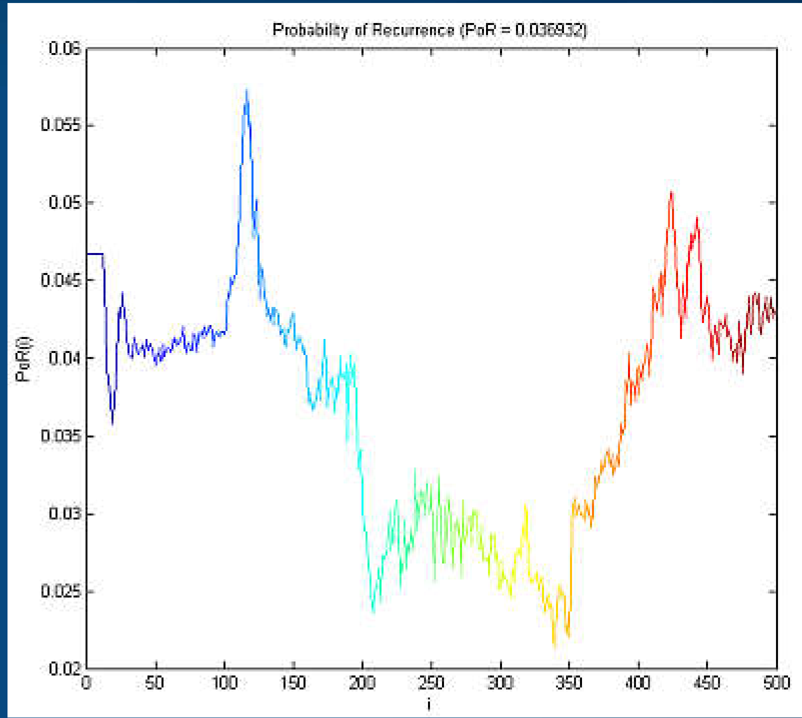
Viser toolbox



Nasz Viser toolbox (Dobosz, Duch) do wizualizacji szeregów czasowych w wielu wymiarach różnymi technikami.

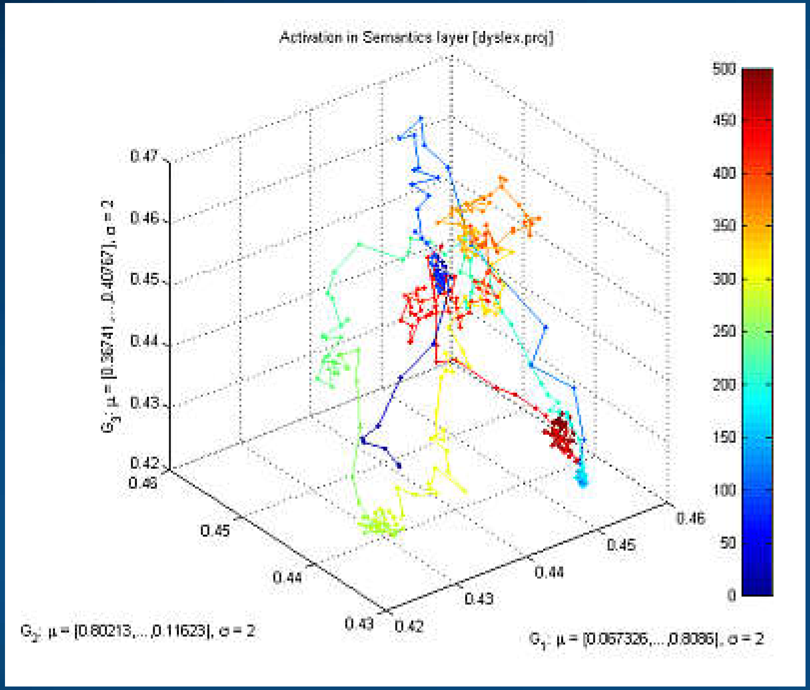
Probability of recurrence

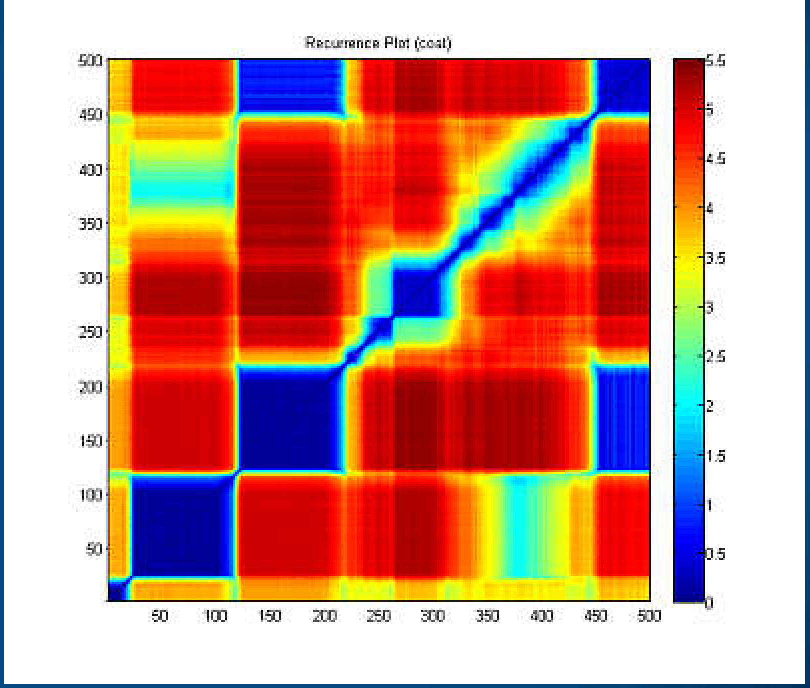




Probability of recurrence may be computed from recurrence plots, allowing for evaluation how strongly some basins of attractors capture neurodynamics.

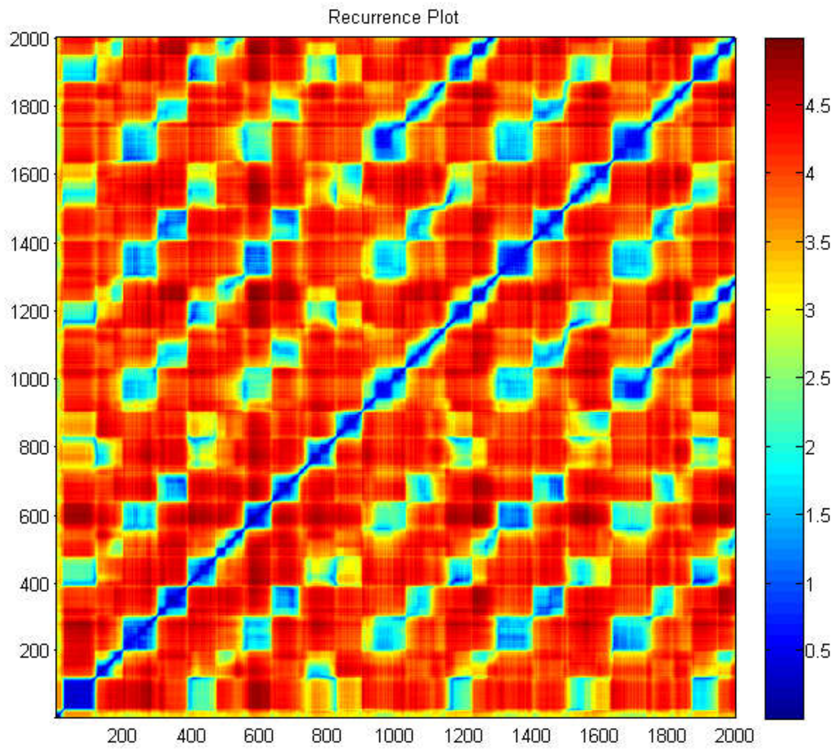
Fast transitions

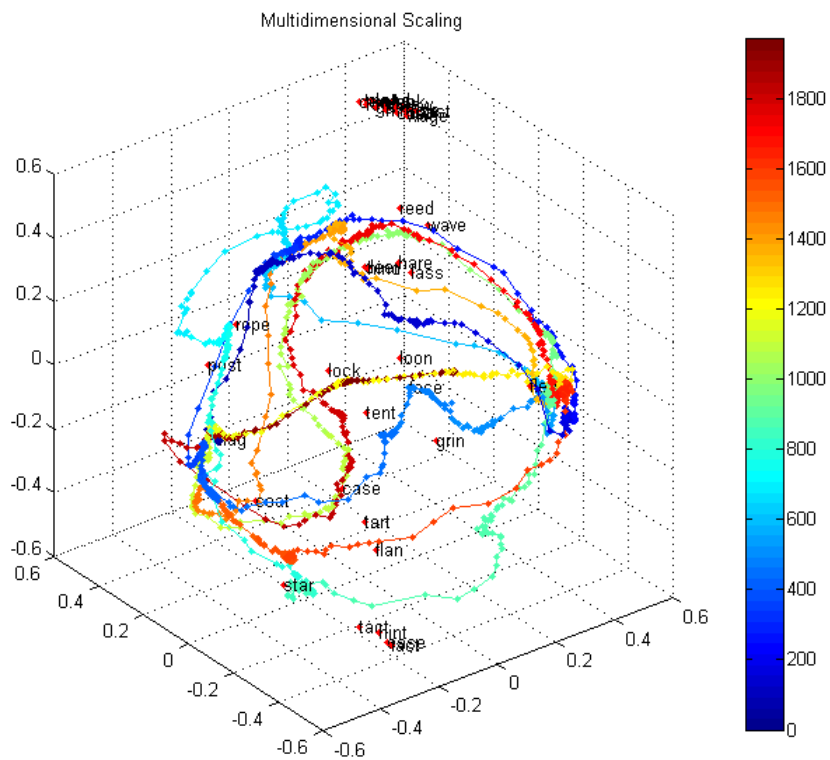




Attention is focused only for a brief time and than moved to the next attractor basin, some basins are visited for such a short time that no action may follow, corresponding to the feeling of confusion and not being conscious of fleeting thoughts.

Trajectory visualization

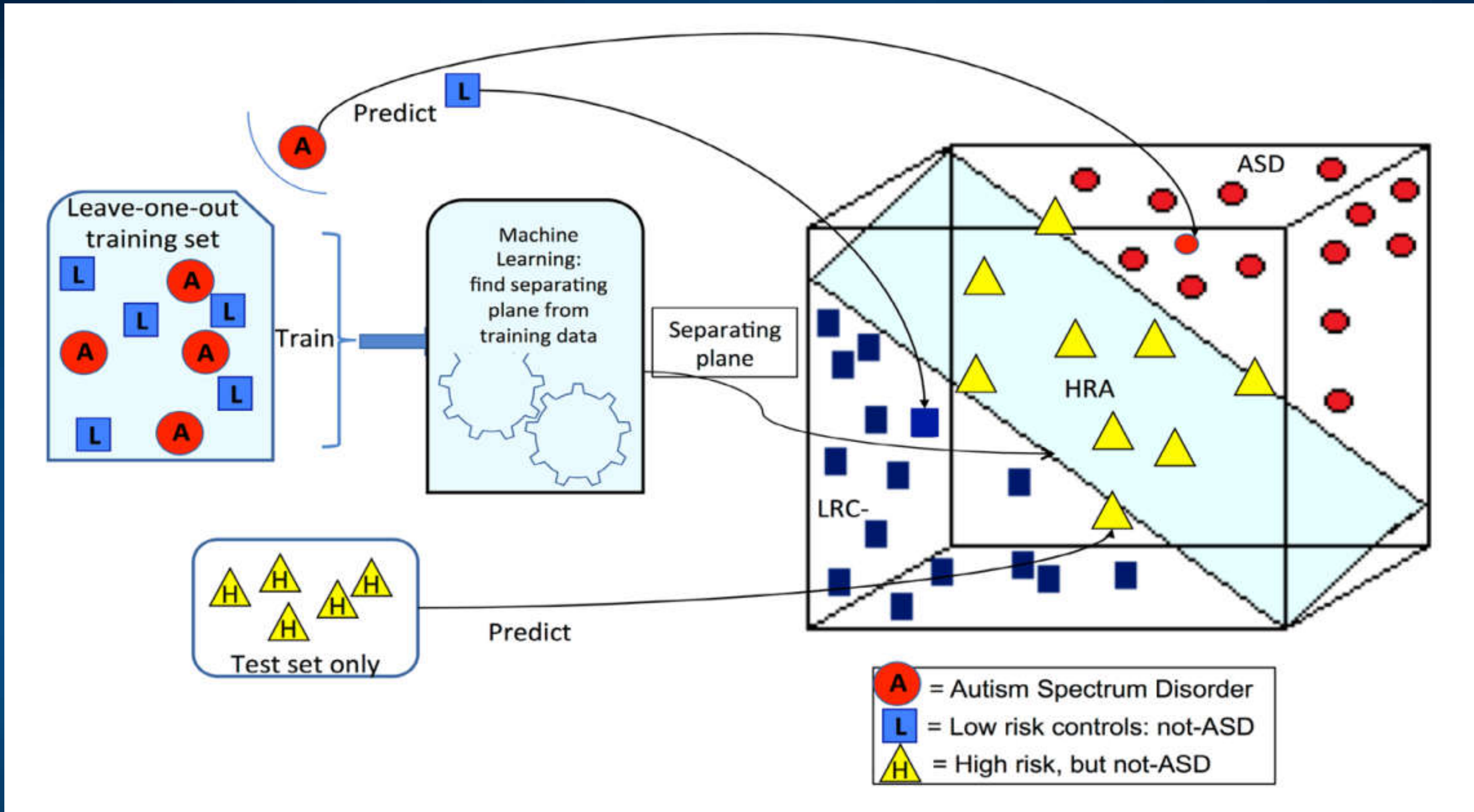




Recurrence plots and MDS/FSD/SNE visualization of trajectories of the brain activity. Here data from 140-dim semantic layer activity during spontaneous associations in the 40-words microdomain, starting with the word “flag”.

Our toolbox: http://fizyka.umk.pl/~kdobosz/visertoolbox/

ASD EEG SVM Classification



Wavelet decomposition, Recurrent Quantification Analysis, feature ranking and machine learning. Nonlinear features are critical to achieve good results, and their correlated with ASD depends on age.

EEG early ASD detection

Bosl, W. J., Tager-Flusberg, H., & Nelson, C. A. (2018). EEG Analytics for Early Detection of Autism Spectrum Disorder: A data-driven approach. Scientific Reports, 8(1), 6828.

EEG of 3 to 36-month old babies, 19 electrodes selected from 64 or 128.

Daubechies (DB4) wavelets transform EEG signal into 6 bands.

7 features from Recurrence Quantitative Analysis (RQA): RP entropy, recurrence rate, laminarity, repetition, max/mean line length, trapping time.

In addition sample entropy and Detrended Fluctuation Analysis was used.

Nonlinear features were computed from EEG signals and used as input to statistical learning methods. Prediction of the clinical diagnostic outcome of ASD or not ASD was highly accurate.

SVM classification with 9 features gave high specificity and sensitivity, exceeding 95% at some ages. Prediction using only EEG data taken as early as 3 months of age was strongly correlated with the actual measured scores.

EEG non-linear features

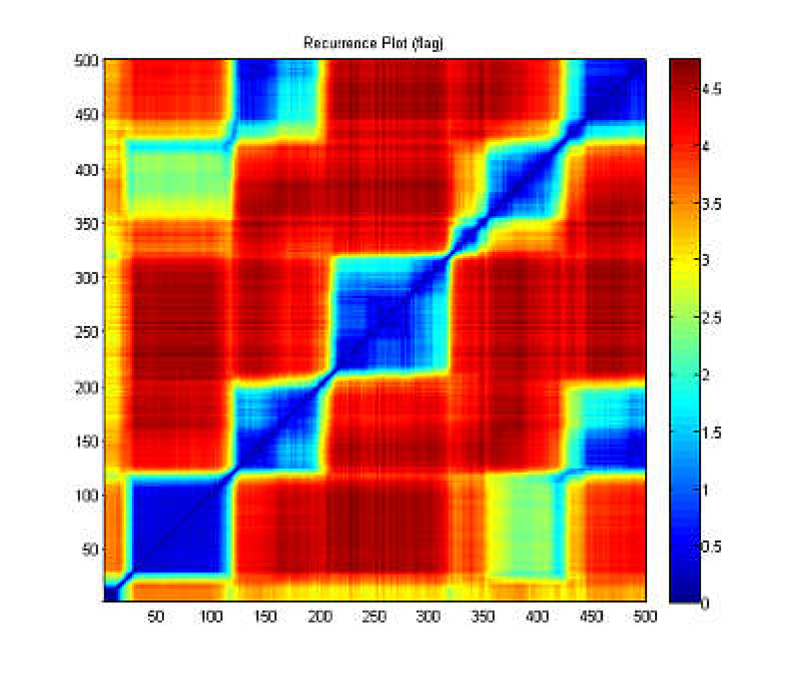
Features: not only structure, but also dynamics.

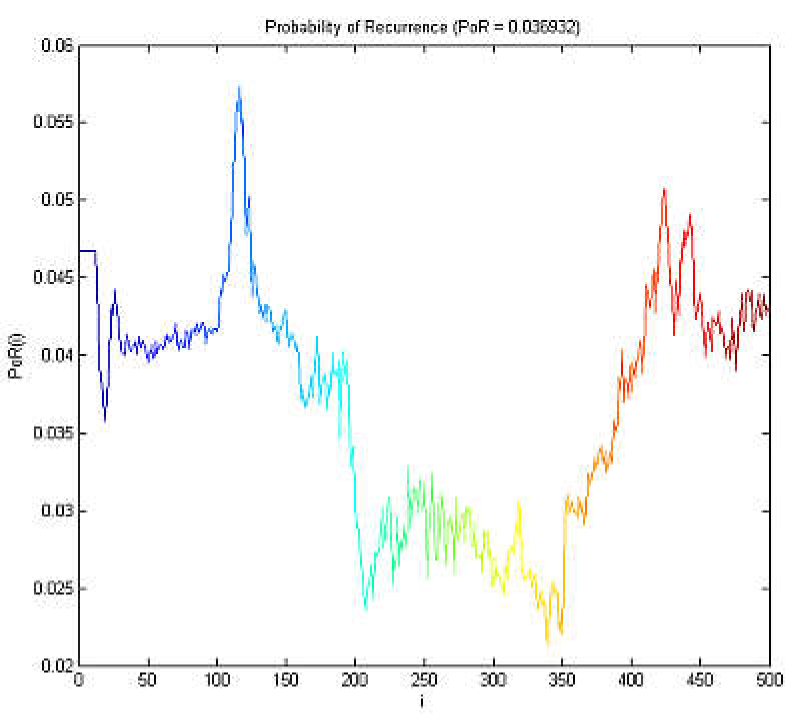
Nonlinear invariant measures of a time series and their physical interpretation, recurrence quantification analysis (RQA).

For example:

1. Sample Entropy (SampE)
2. Entropy derived from recurrence plot (L_entr).
3. Recurrence rate (RR), probability of recurrence.
4. Determinism (DET), repeating patterns in the system.
5. Laminarity (LAM), frequency of transitions between states.
6. Trapping time (TT), time in a given state.

Probability of recurrence





Probability of recurrence may be computed from recurrence plots, or from clusterization of trajectory points, allowing for evaluation how strongly some basins of attractors capture neurodynamics.

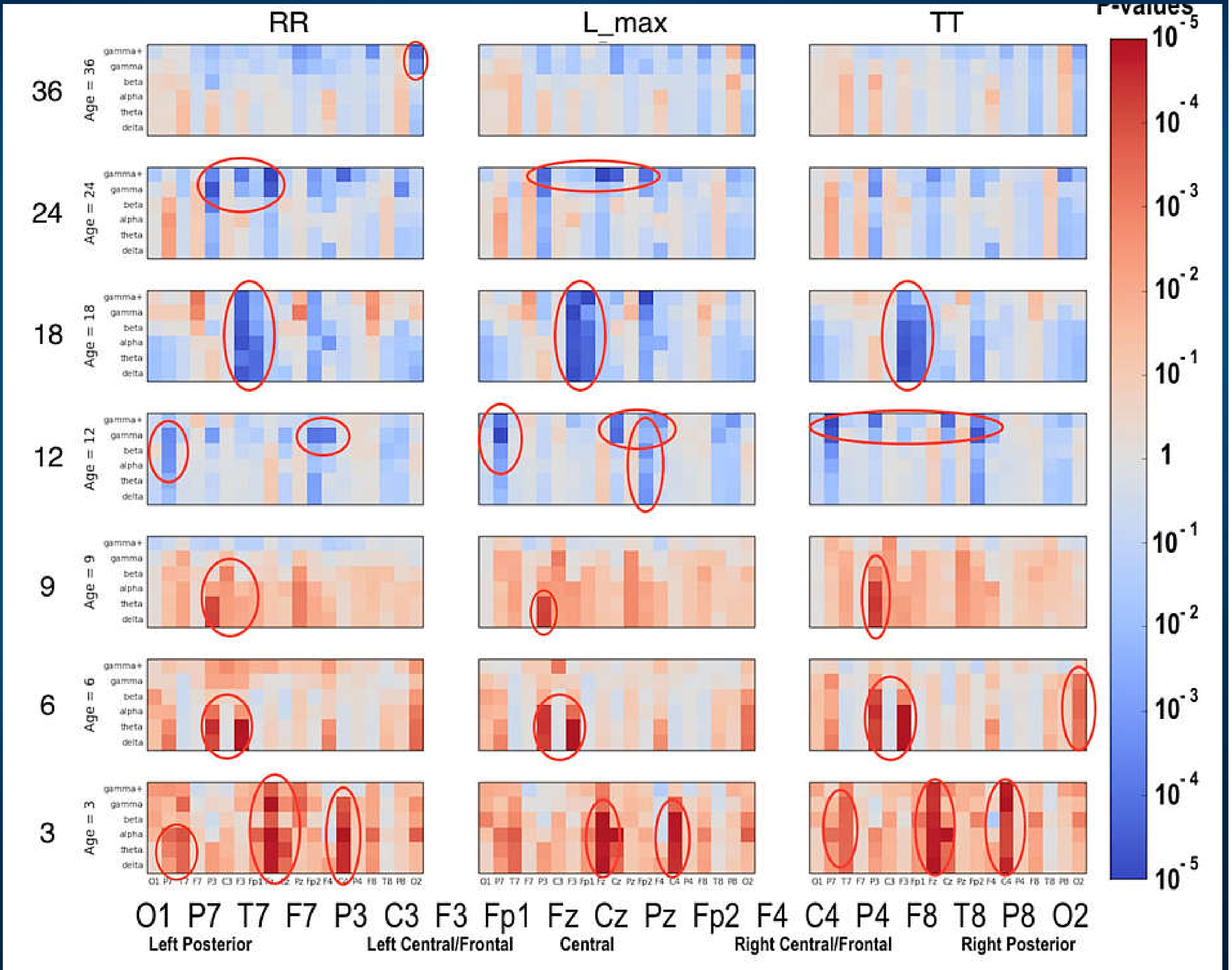
Our Viser Toolbox is used for all visualizations

ASD vs Low Risk Healthy

RR = recurrence rate

L_max = max line length, related to Lyapunov exponent

TT = trapping time

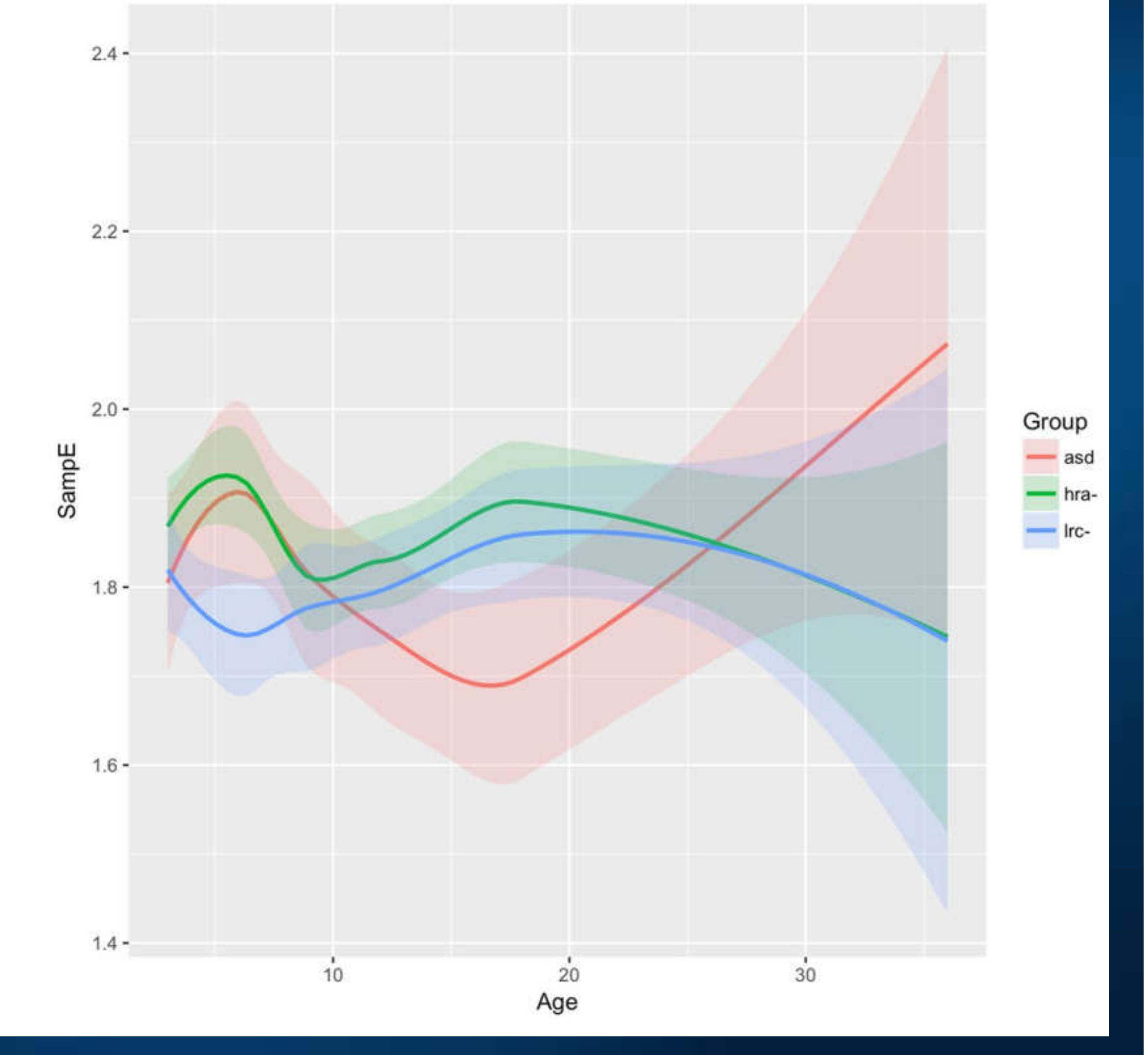


ASD EEG SVM Classification

Developmental trajectories for SampE in the left temporal region (T7 sensor) in higher frequencies (beta+gamma) for ASD, LRC-, and HRA-

LRC low risk controls

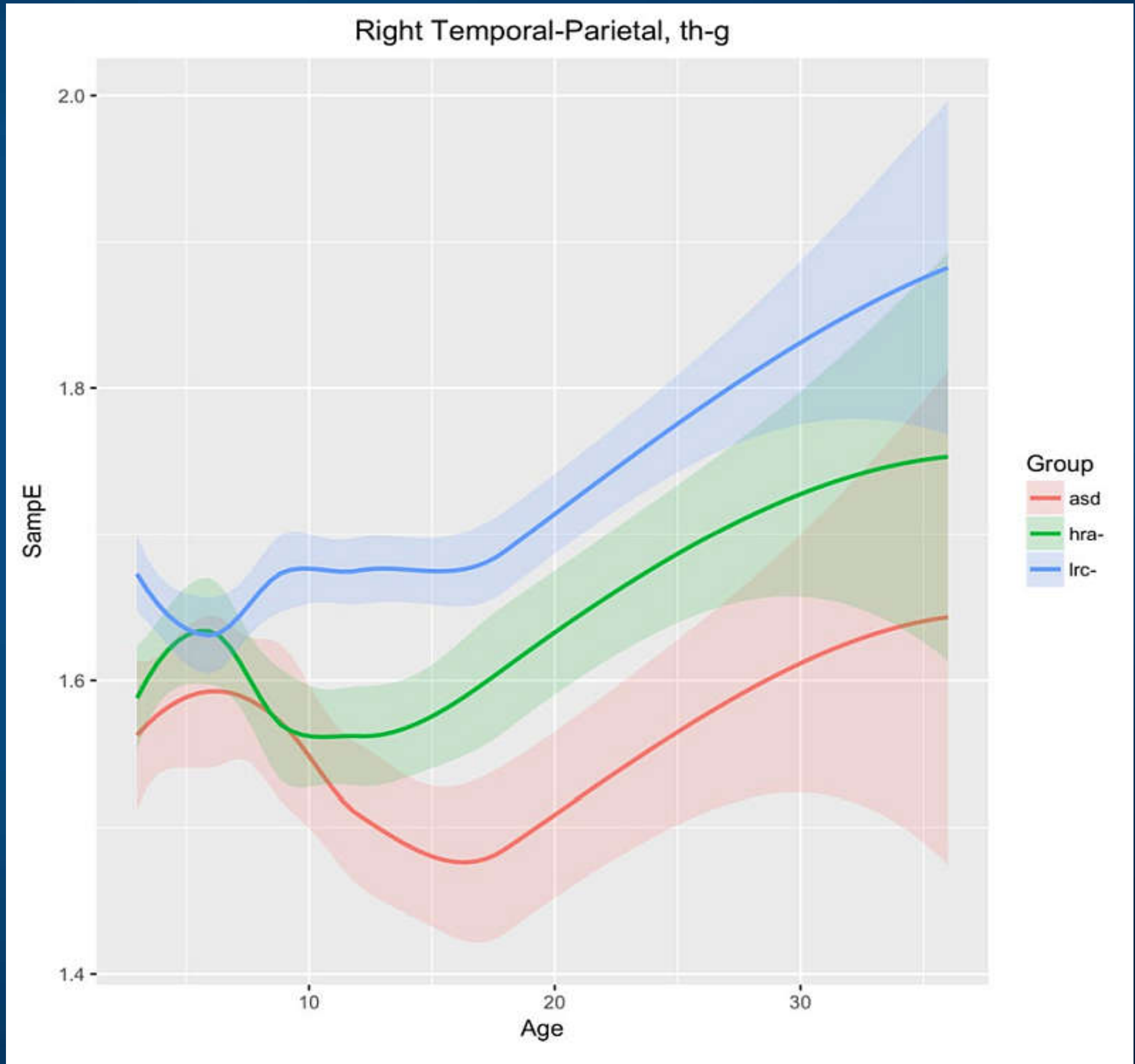
HRA high risk for ASD - no ASD



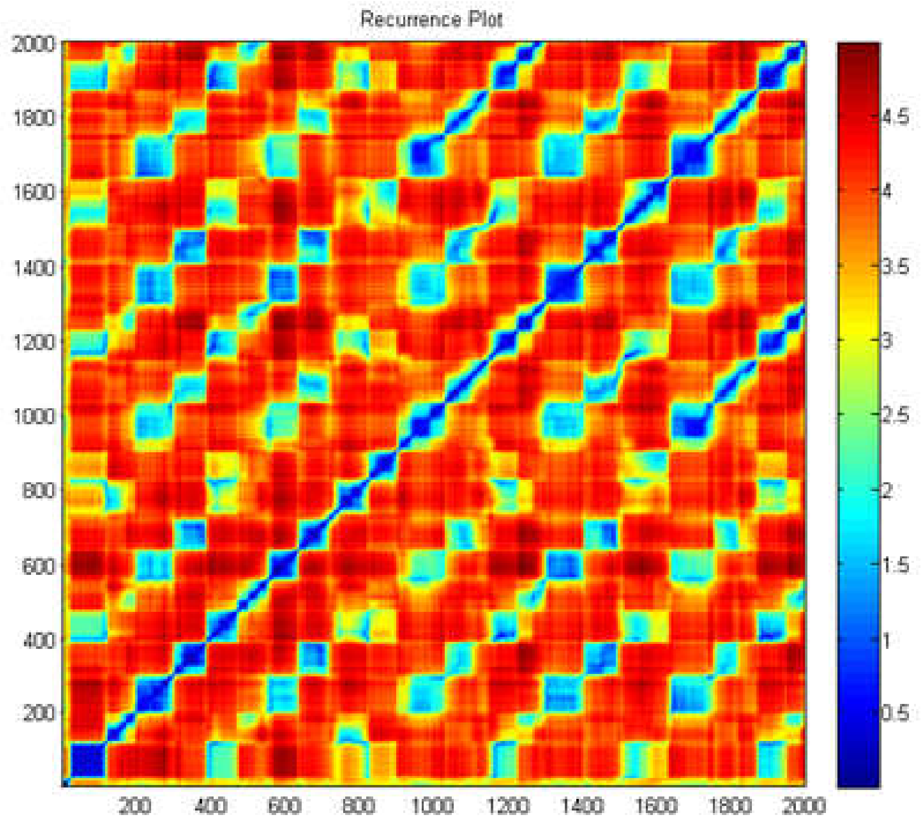
ASD EEG SVM Classification

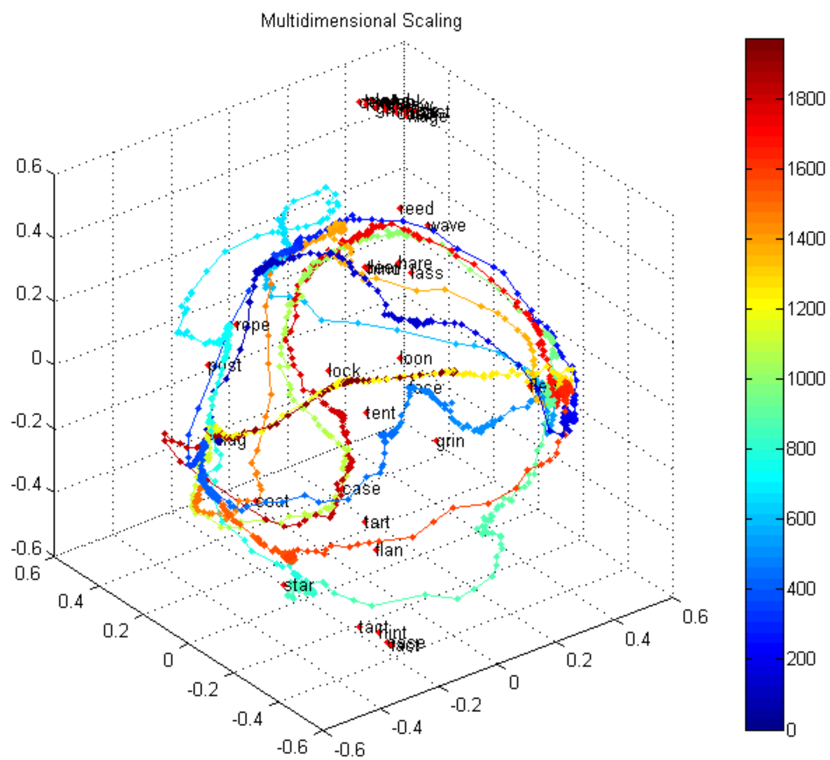
Developmental trajectories for SampE in the right temporal-parietal region

(T8 +P4+P8 sensors) in frequencies theta through gamma for ASD, LRC-, and HRA-.



Trajectory visualization



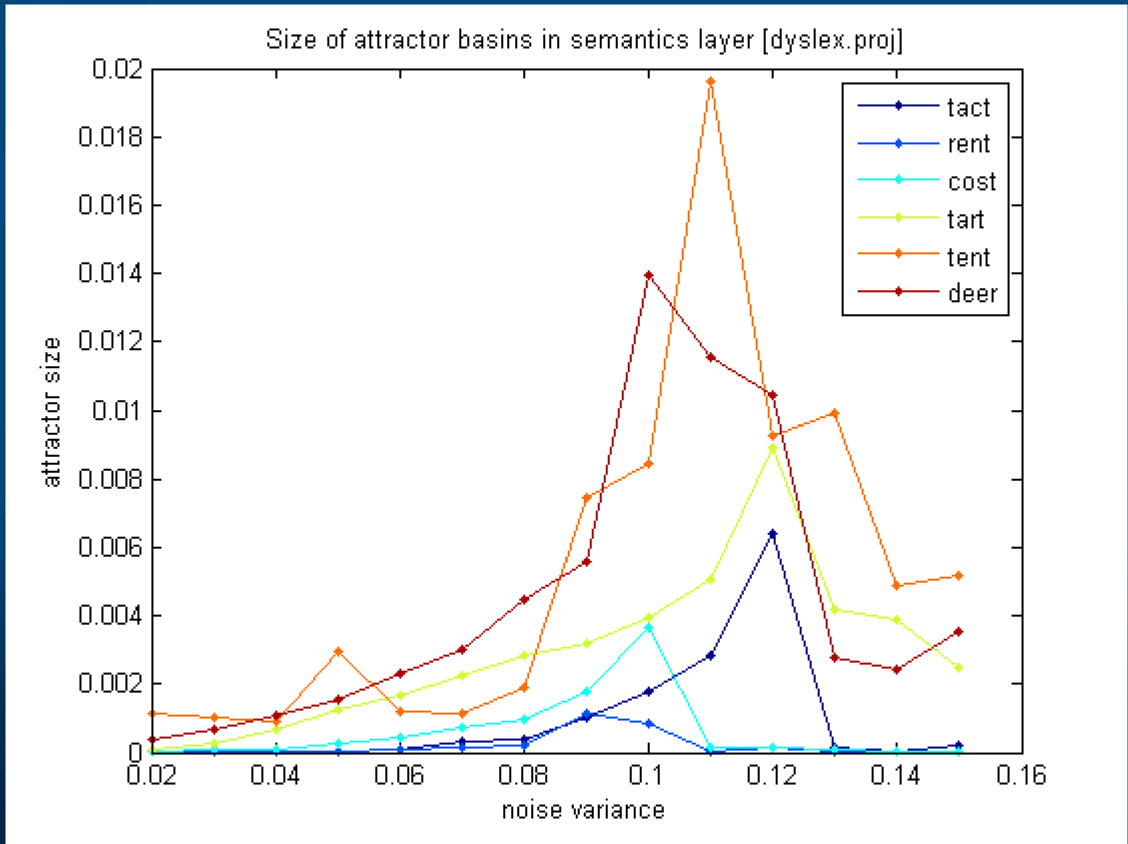


Trajectories may be visualized either using recurrence plots that shows relative changes of the trajectory or some form of visualization showing absolute positions of points on trajectories (MDS/FSD/SNE). Visualization shows transitions between microstates, or attractor states.

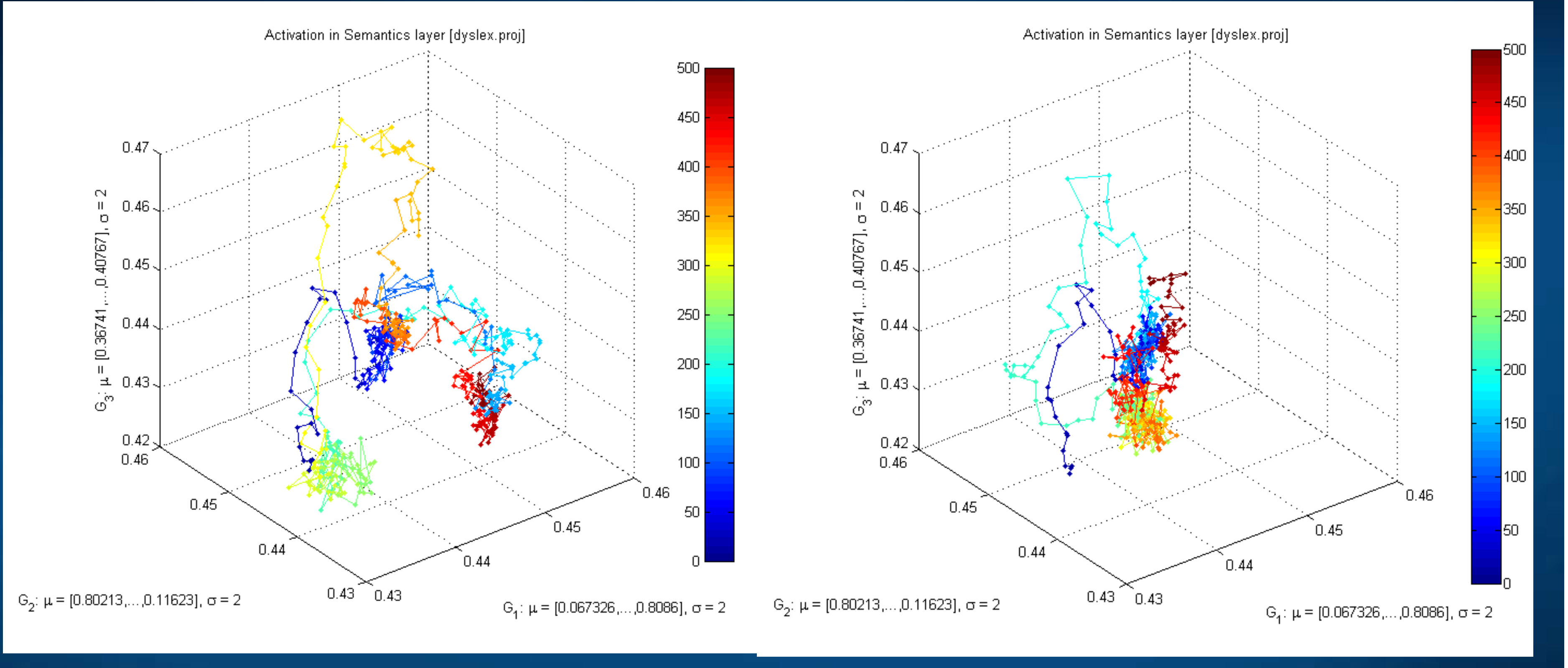
Depth of attractor basins

Variance around the center of a cluster grows with synaptic noise; for narrow and deep attractors it will grow slowly, but for wide basins it will grow fast.

Jumping out of the attractor basin reduces the variance due to inhibition of desynchronized neurons.



Typical Development vs. Autism

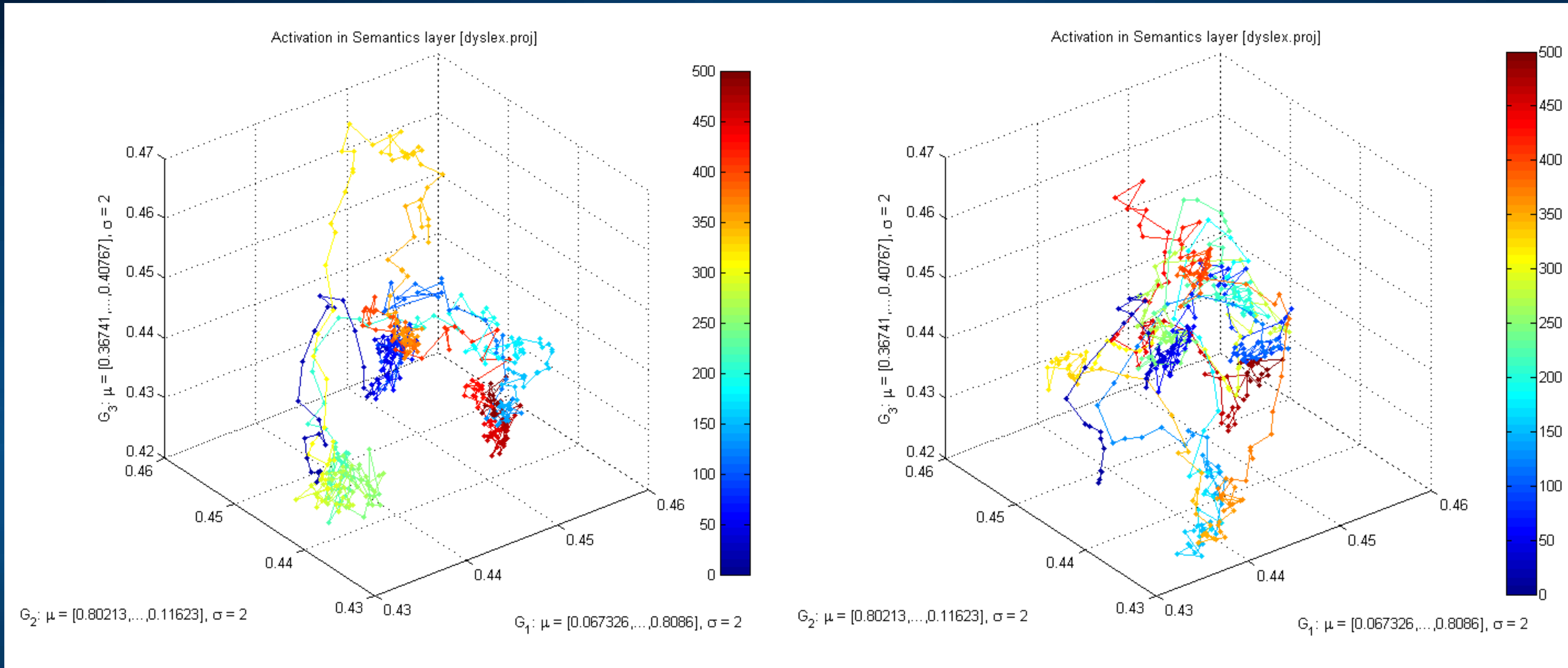


All plots for the flag word, different values of b_inc_dt parameter in the accommodation mechanism. b_inc_dt = 0.01 & b_inc_dt = 0.005

b_inc_dt = time constant for increases in intracellular calcium building up slowly as a function of activation, controls voltage-dependent leak channels.

http://kdobosz.wikidot.com/dyslexia-accommodation-parameters

Typical Development vs ADHD

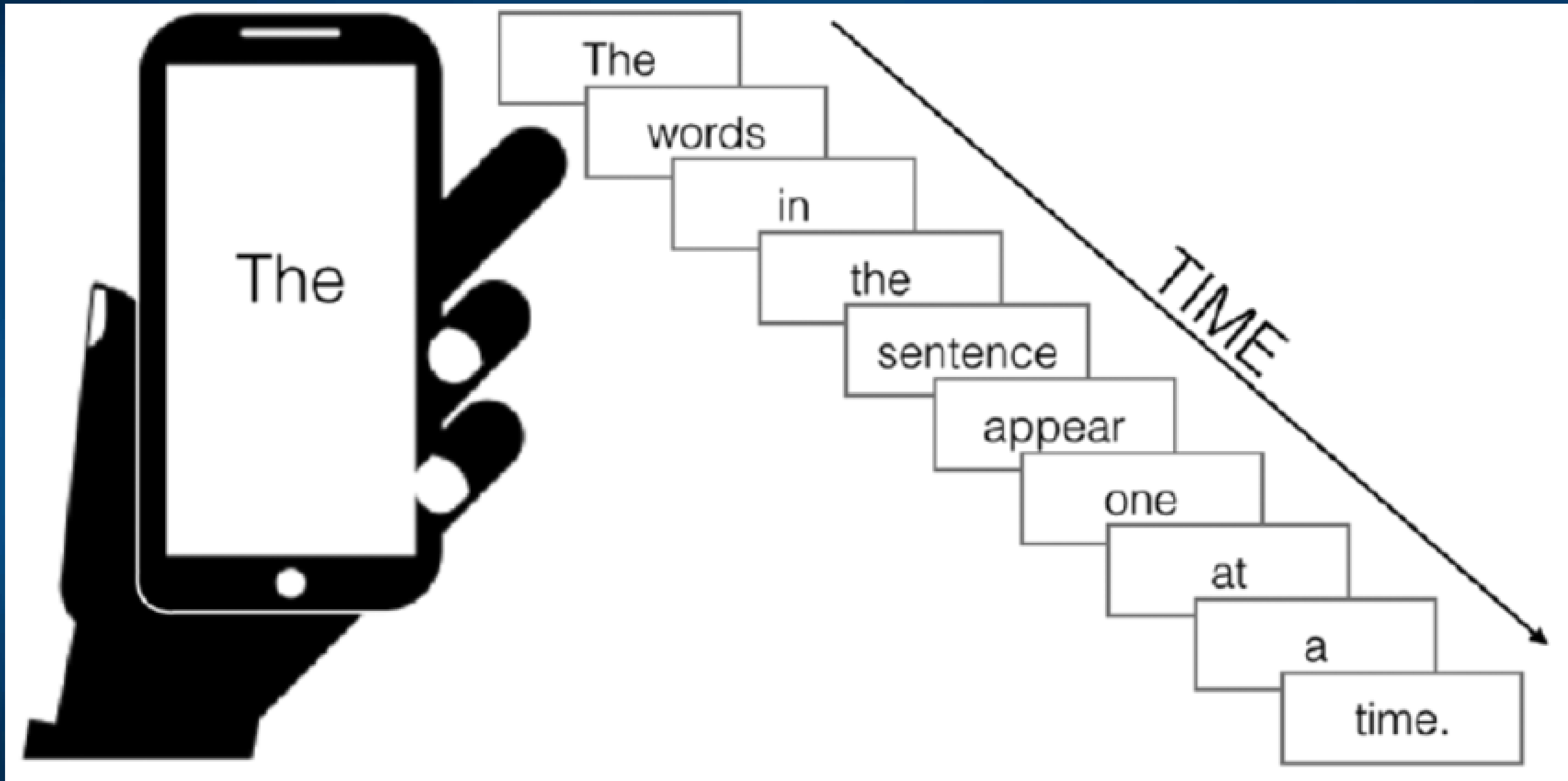


All plots for the flag word, different values of b_inc_dt parameter in the accommodation mechanism. b_inc_dt = 0.01 & b_inc_dt = 0.02.

b_inc_dt = time constant for increases in intracellular calcium which builds up slowly as a function of activation.

http://kdobosz.wikidot.com/dyslexia-accommodation-parameters

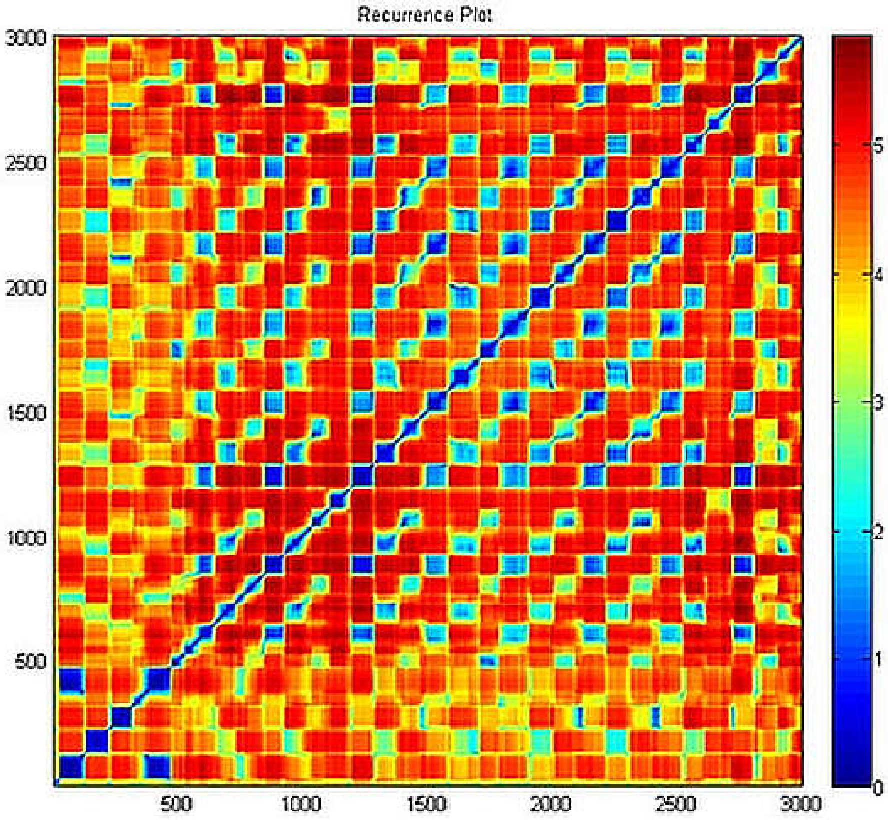
Rapid Serial Visual Presentation

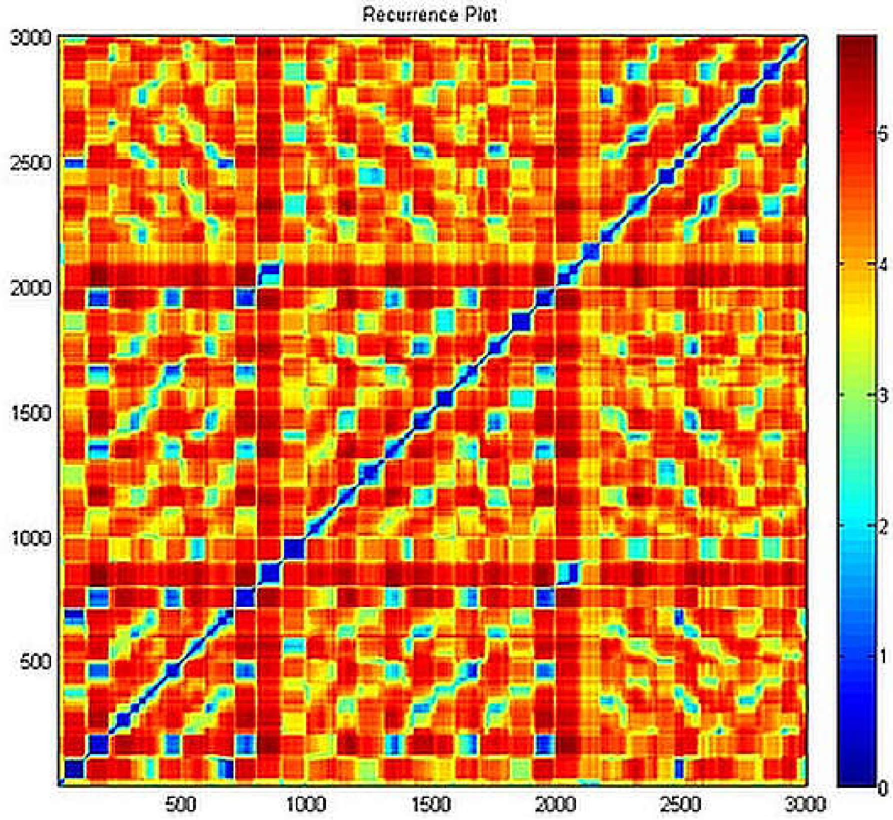


Any RSVP applications for fast reading.

Simulation: showing series of words, looking for attention/associations.
star => flea => tent => lock => tart => hind

RSVP: typical brain

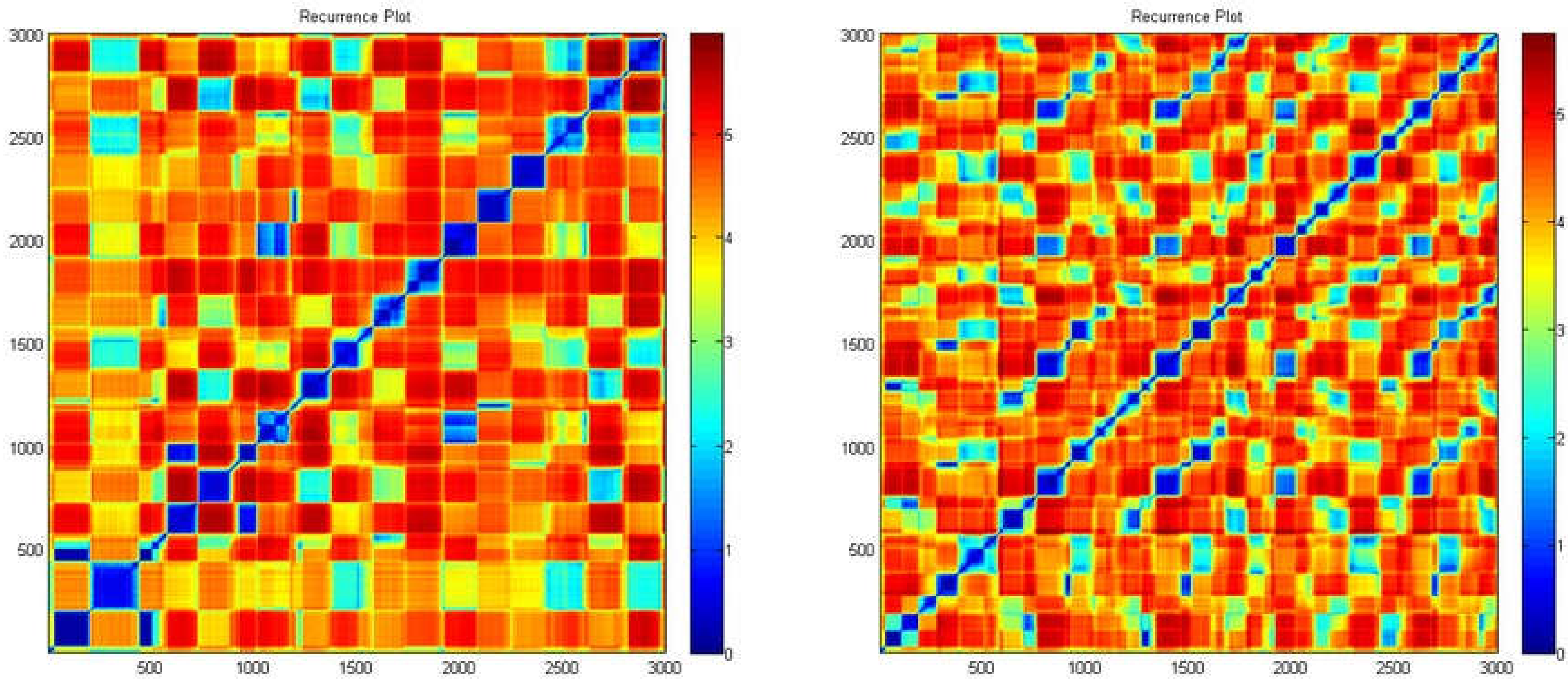




Normal speed
associations, context=>understanding
Some shallow microstates, no associations

too fast, speed 5x
microstates get blurred,
few associations

RSVP simulations: HFA

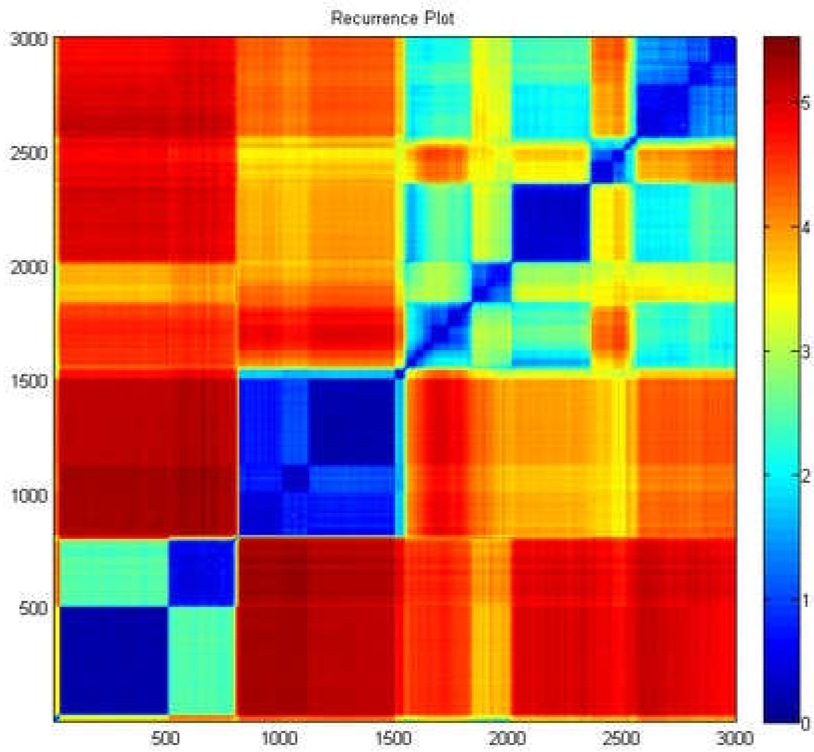


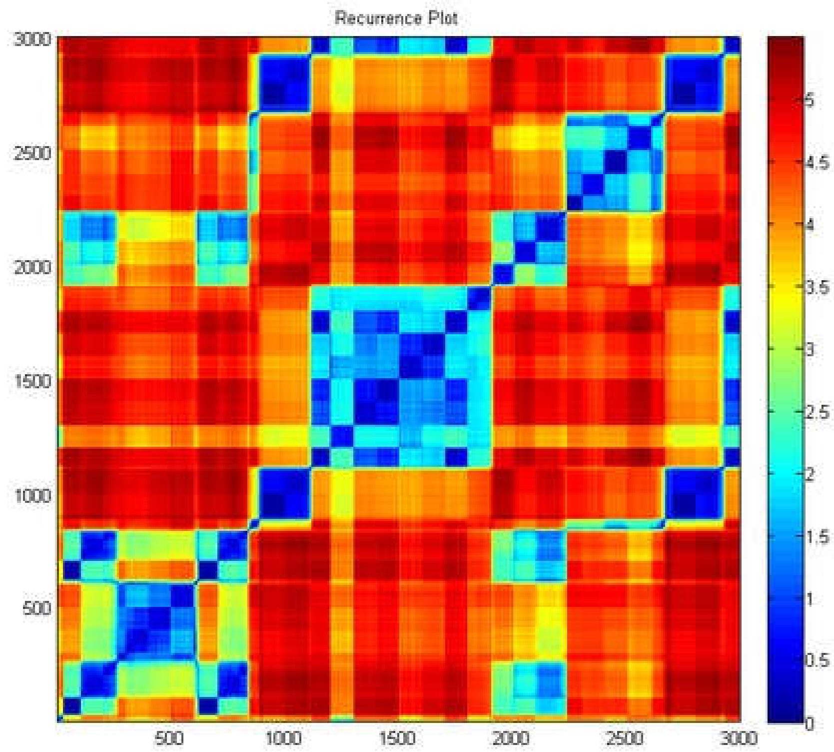
High functioning ASD case (HFA):

normal presentation
long dwelling times

fast presentation
enforced quick resynchronization
more internal stimuli.

RSVP simulations in deep autism





Normal speed
skipping some words,
no associations

fast presentation
more internal states
some associations arise

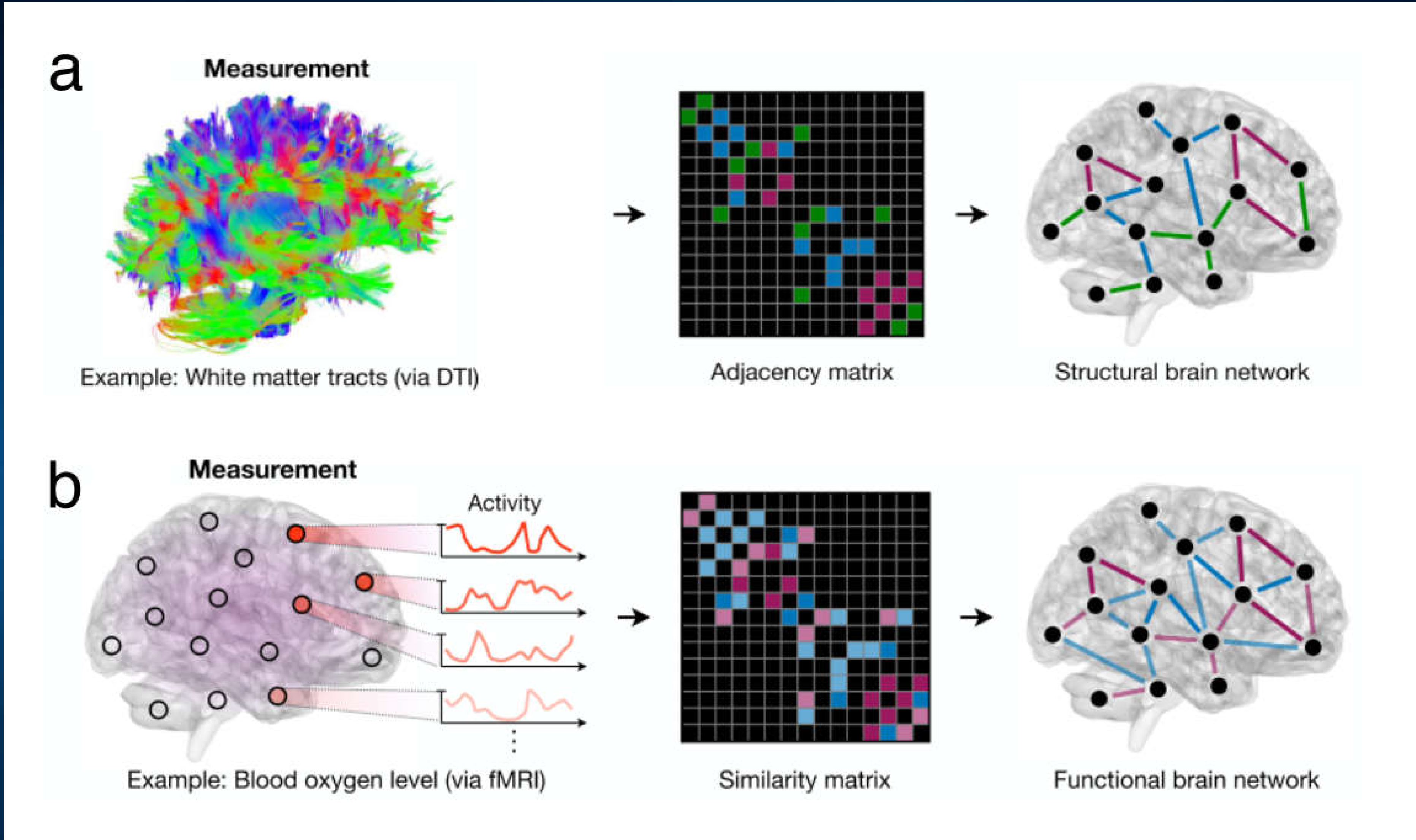
Brain Data

Possible form of Brain Fingerprints

fMRI: BFP is based on **V(X,t)** voxel intensity of fMRI BOLD signal changes, contrasted between task and reference activity or resting state.
EEG: spatial, spatio-temporal, ERP maps/shapes, coherence, various phase synchronization indices.

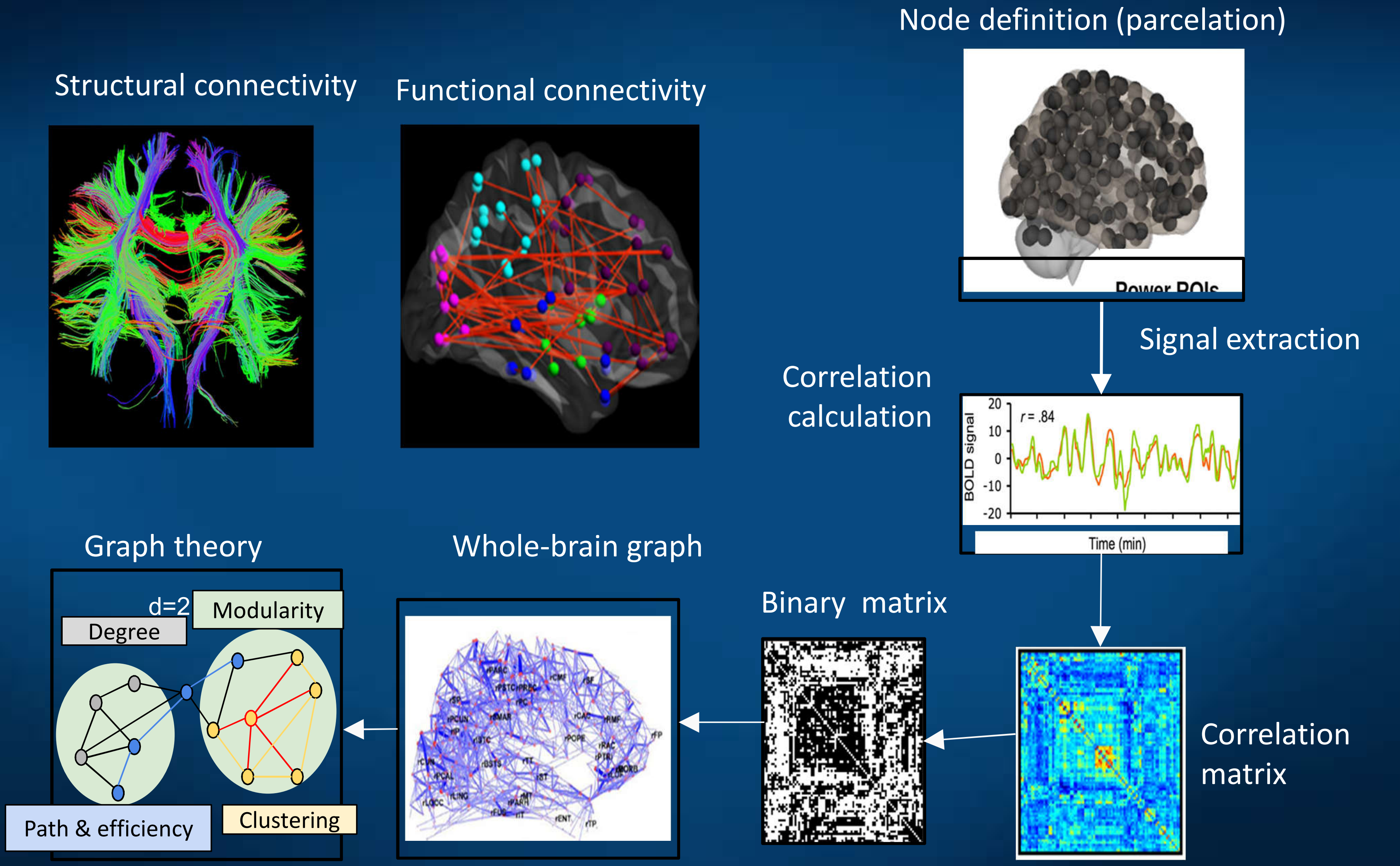
1. **Spatial/Power**: direct localization/reconstruction of sources.
2. **EEG microstates**, sequences & transitions, dynamics in ROI space.
3. **Spatial/Synch**: changes in functional graph network structure.
4. **Frequency/Power**: ERS/ERD smoothed patterns E(X,t,f).
5. **ERP global power maps**: spatio-temporal averaged energy distributions.
6. **EEG decomposition into components:** ICA, CCA, tensor, RP ...
7. Model-based: **The Virtual Brain**, integrating EEG/neuroimaging data.
8. Spectral fingerprinting (MEG, EEG), power distributions.

Neuroplastic changes of connectomes and functional connections as results of training for optimization of brain processes.



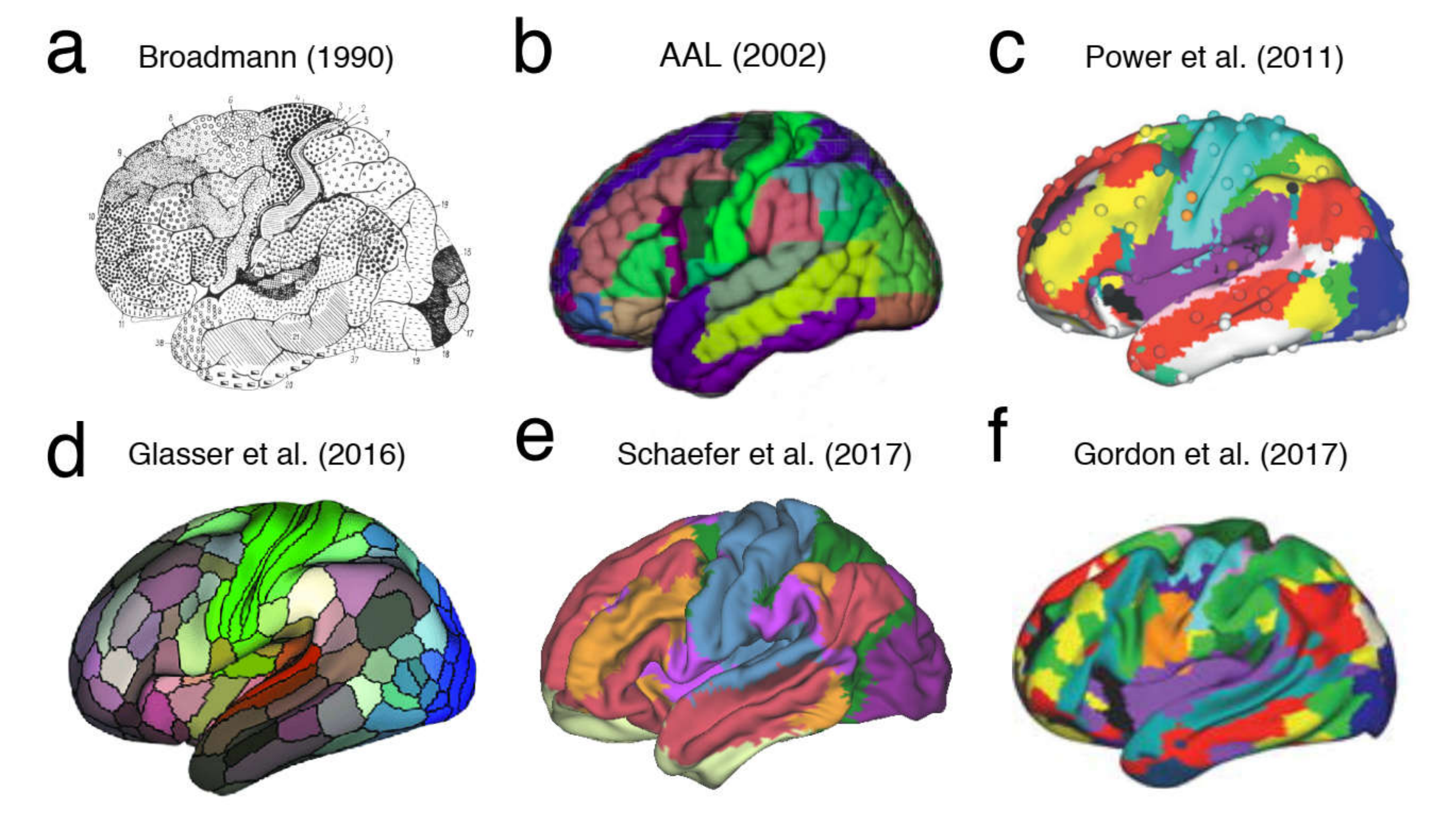
Lynn and Bassett (2018) The physics of brain network structure, function, and control. arXiv:1809.06441.

Human connectome and MRI/fMRI

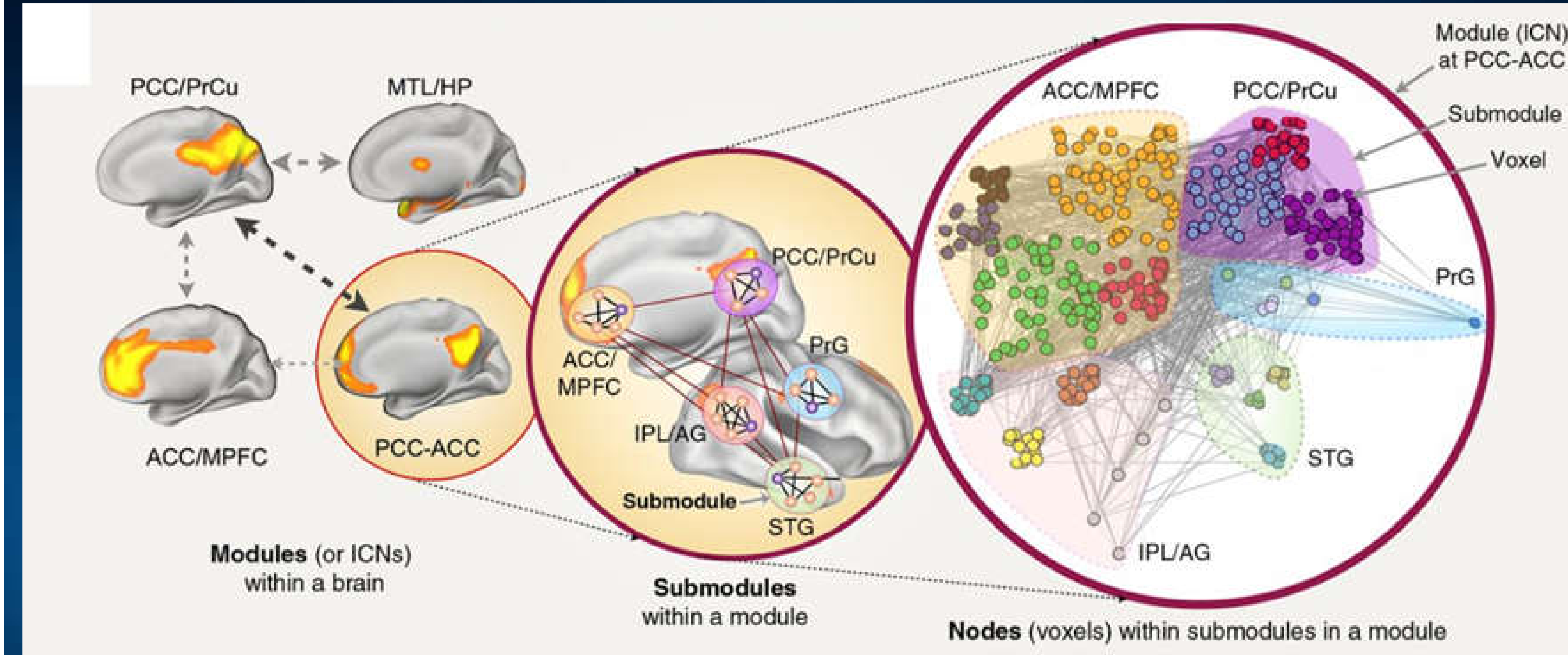


Many toolboxes available for such analysis.

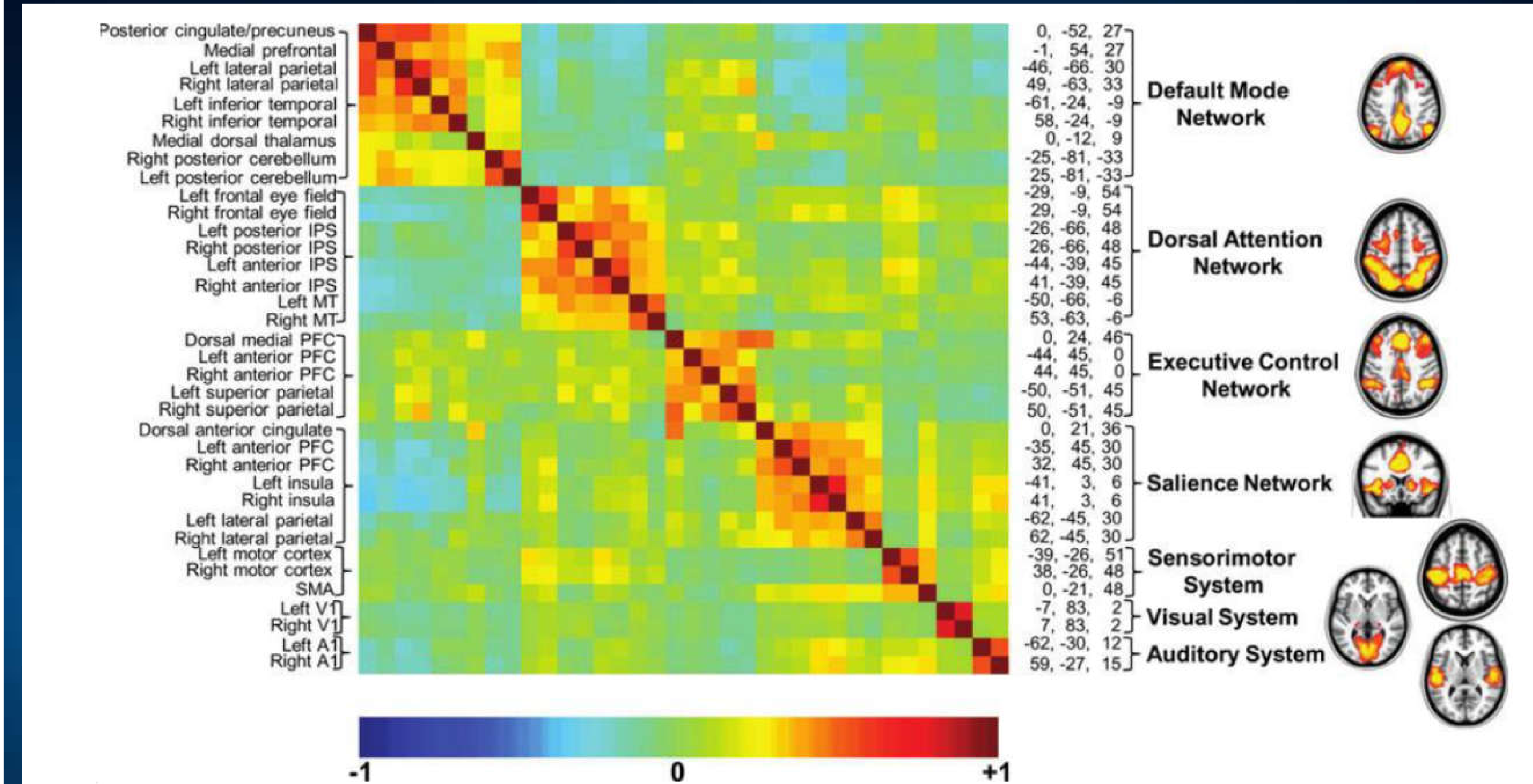
Bullmore & Sporns (2009)



(**a**) Broadmann areas - cytoarchitectonic, (**b**) Automated Anatomical Labelling (AAL) - macroanatomy, (**c**) Power parcellation, meta-analysis of fMRI studies, (**d**) Glasser, multi-modal approach, (**e**) Schaefer - functional connectivity, (**f**) Gordon et al. - functional connectivity. K .Finc, PhD thesis (2019)

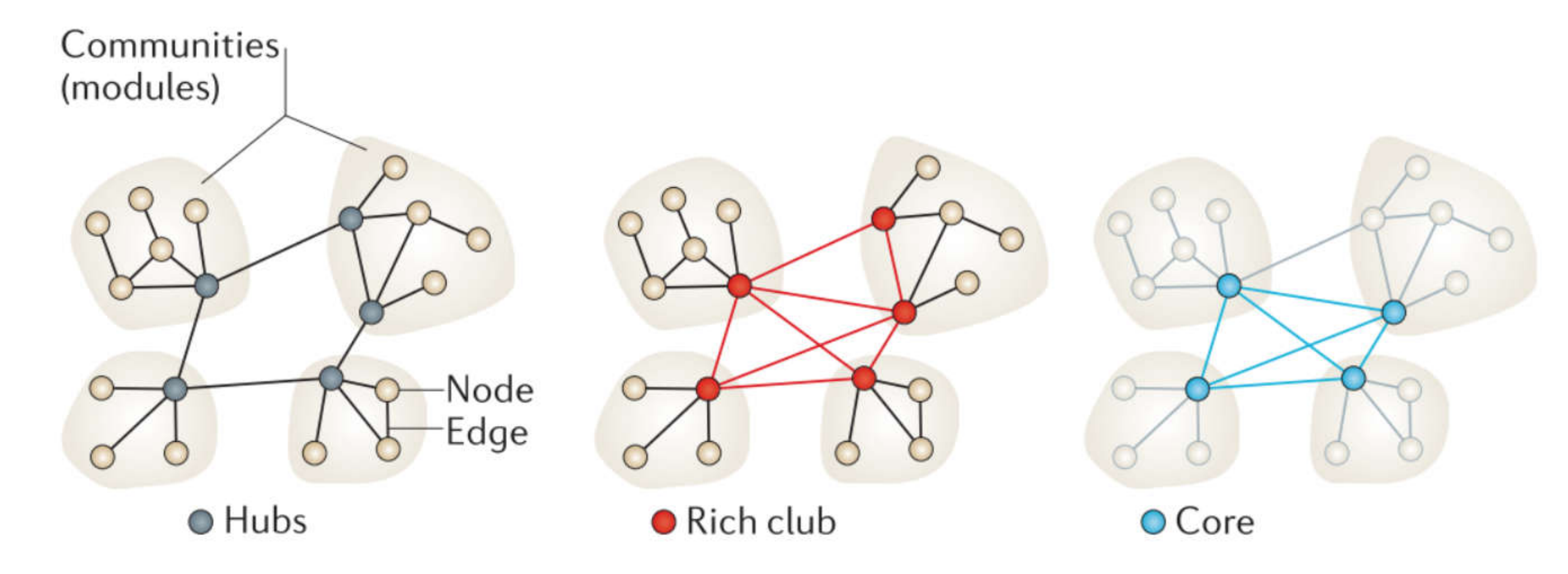


Hierarchical, modular Russian doll-like organization of the human brain networks. From Park and Friston (2013). Structural and functional brain networks: from connections to cognition. Science, 342(6158):1238411



Correlation matrix representing resting-state functional connectivity between selected brain regions Shows stronger connectivity for 7 large-scale brain networks: default mode (DM), dorsal attention (DAT), executive control network (FPN, CON), salience (SAL), sensorimotor (SOM), visual (VSN), auditory (ASN). Switching DMN ⇔ Salience ⇔ FPN

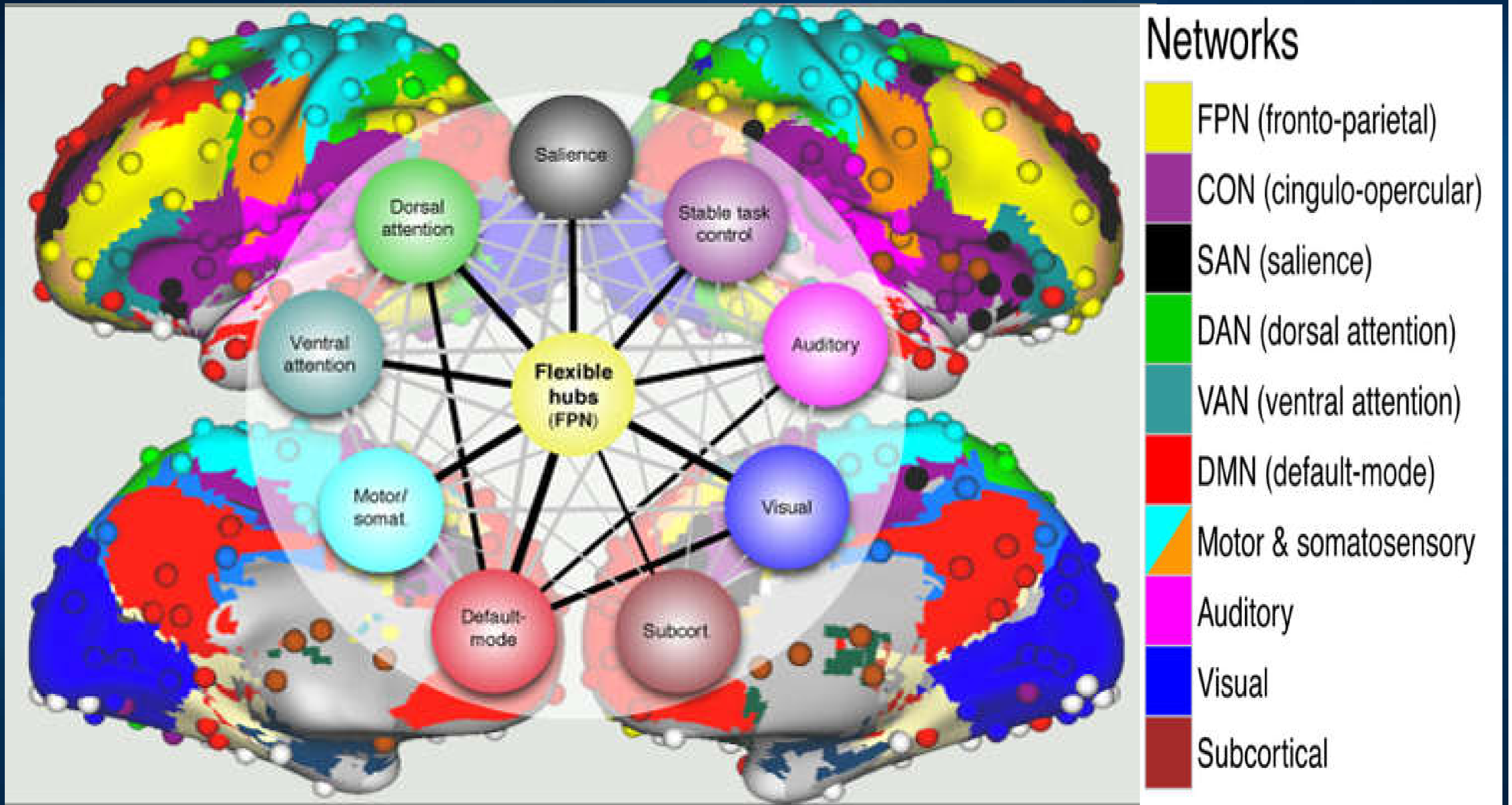
Network Neuroscience



Network neuroscience is focused on identifying network structures. Hubs, rich club and core of the network. Hubs connect modules via long-distance connections. Hubs are also often densely interconnected forming so called ’rich club’ or integrated core.

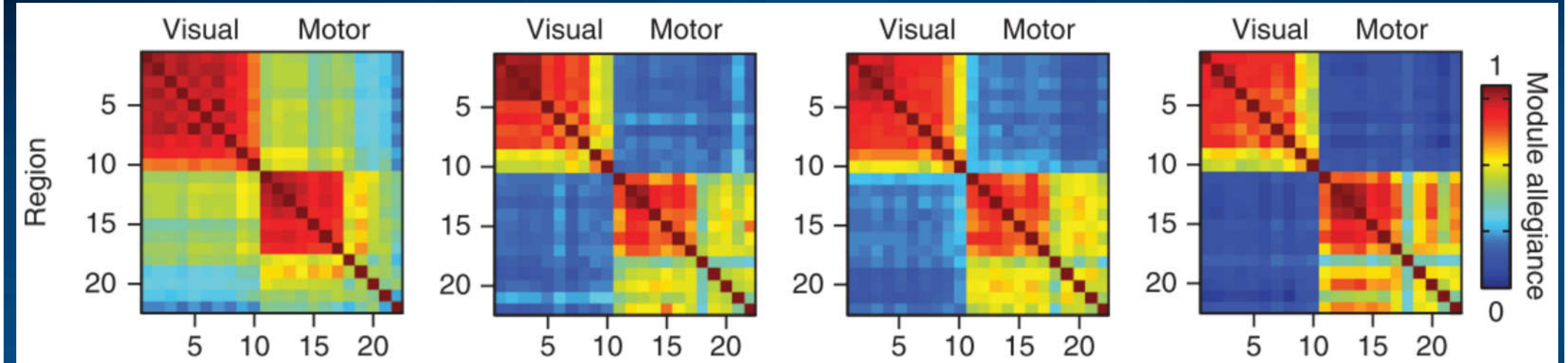
Bullmore and Sporns (2012) The economy of brain network organization. Nature Reviews Neuroscience, 13(5):336.

Neurocognitive Basis of Cognitive Control



Large scale canonical networks. Central role of fronto-parietal (FPN) flexible hubs in cognitive control and adaptive implementation of task demands (black lines=correlations significantly above network average). Cole et al. (2013).

Start Early training Middle Late



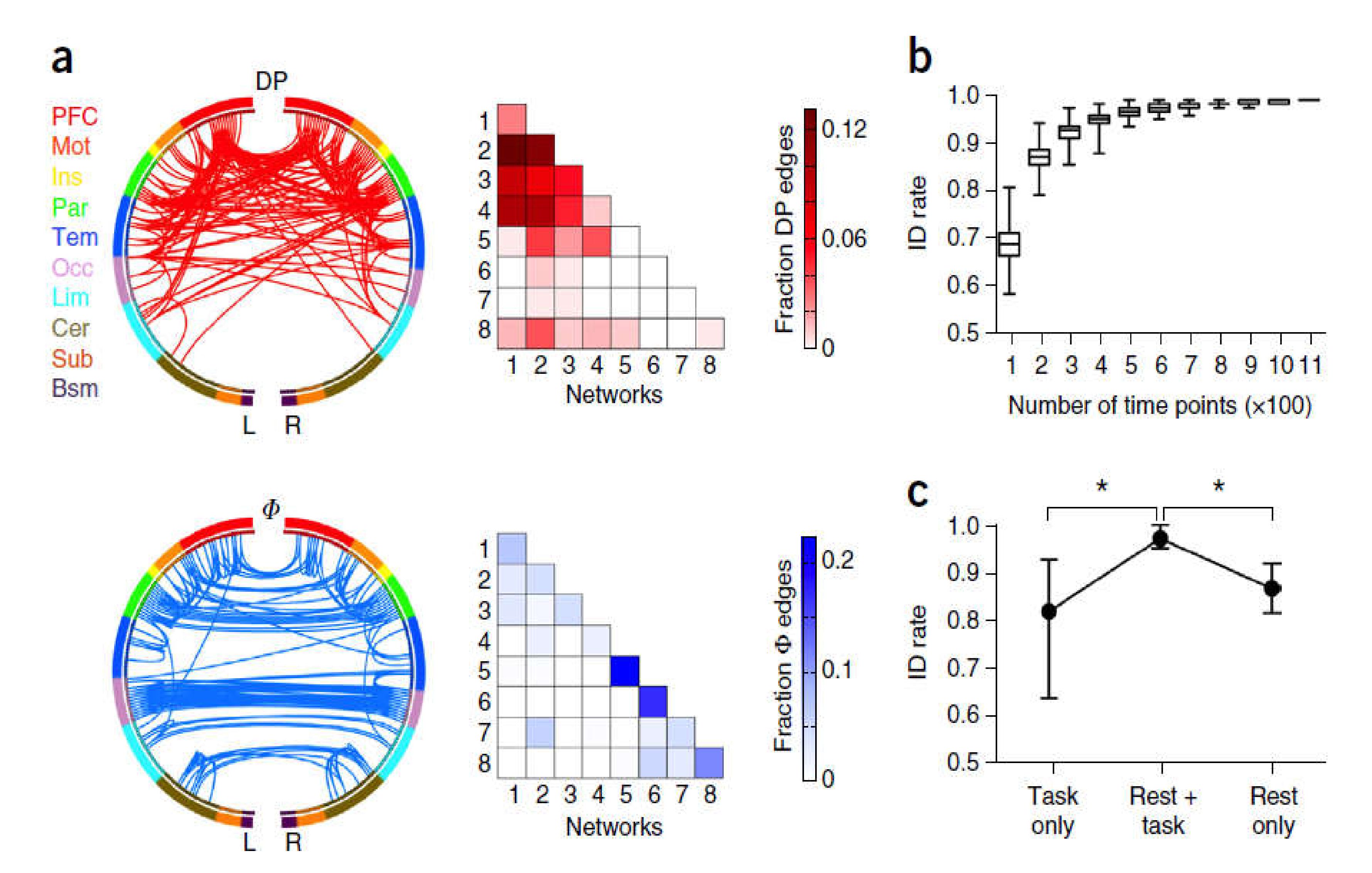
Sequence learning task: reproduce motion sequences represented on the screen as a visual stimuli. Automatization increases modularity, distinct subnetworks, reducing interference between different processes.

6-week motor sequence training resulted in autonomy of visual and motor areas.

Bassett et al. (2015) Learning-induced autonomy of sensorimotor systems. Nature Neuroscience, 18(5):744.

Reddy et al. (2018). Brain state flexibility accompanies motor-skill acquisition. NeuroImage, 171:135–147.

Finn et al. (2015), **Functional connectome fingerprinting**: identifying individuals using patterns of brain connectivity. Nature Neuroscience. Top: highly unique; Bottom: highly consistent connections.



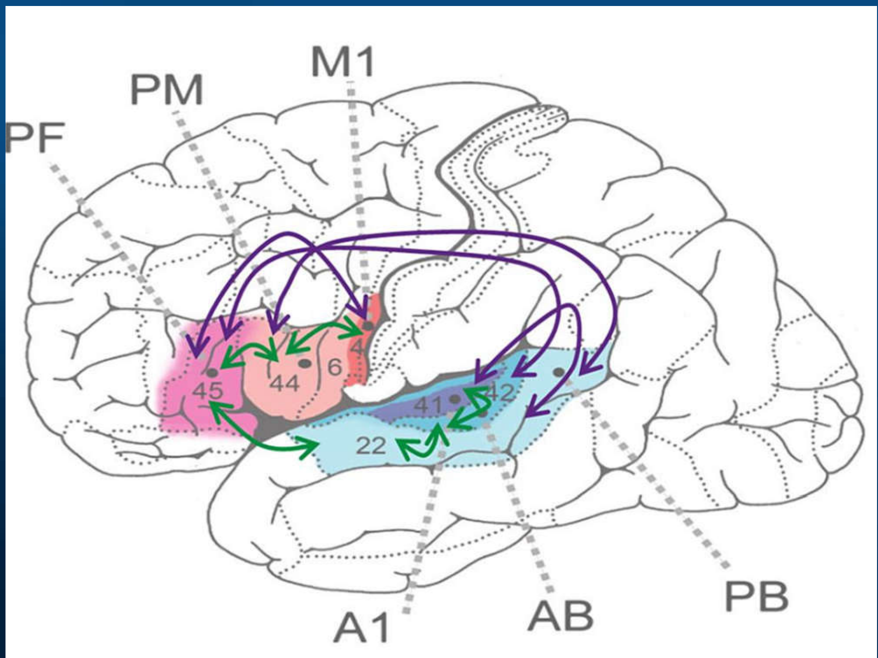
Fluid nature

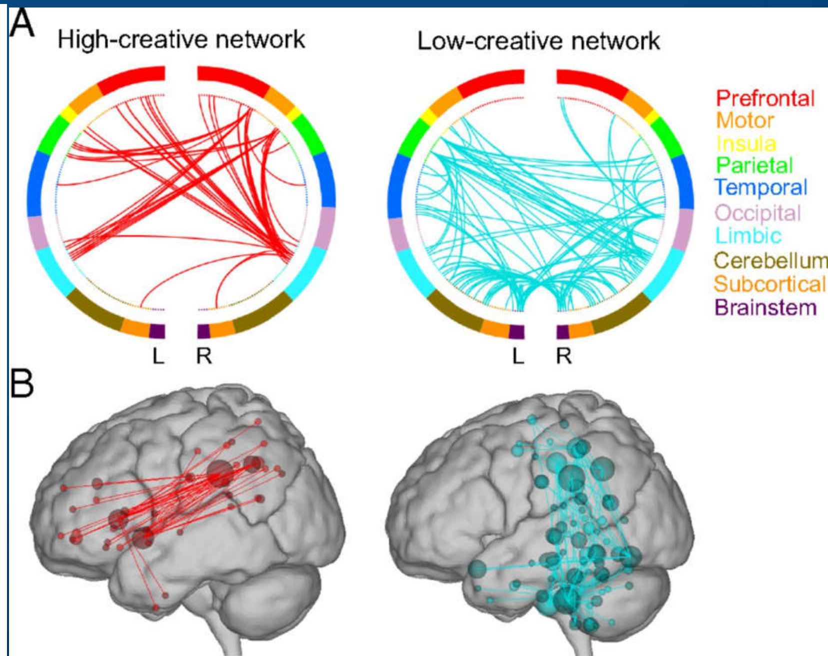
BABY Connectome Project
a UNC / UMN collaboration

Development of brain in infancy: first learning how to move, sensorimotor activity organizes brain network processes, rather consistent.

The Developing Human Connectome Project: create a dynamic map of human brain connectivity from 20 to 44 weeks post-conceptional age, which will link together imaging, clinical, behavioral, and genetic information.

Pointing, gestures, pre-linguistic (our BabyLab).



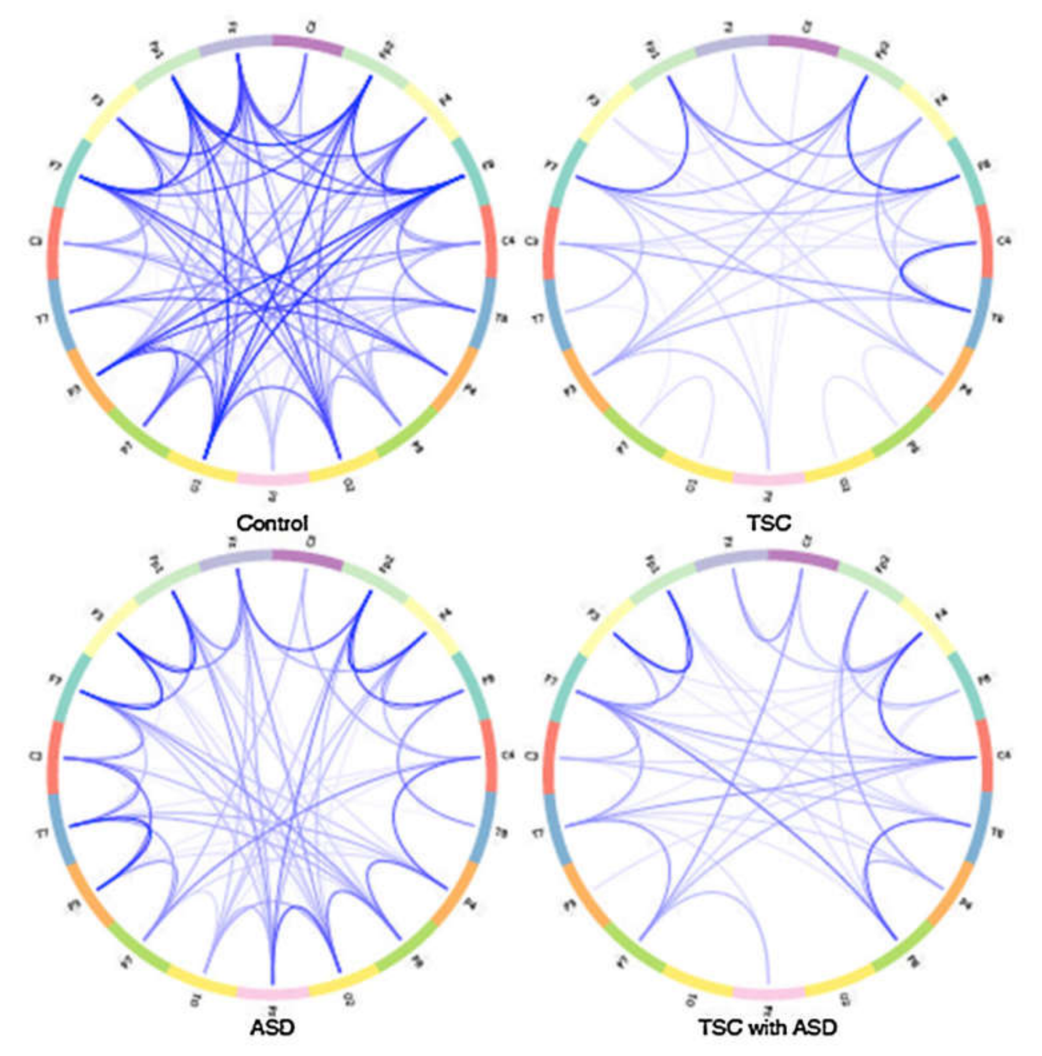


ASD: pathological FC

Comparison of connections for patients with ASD (autism spectrum), TSC (Tuberous Sclerosis), and ASD+TSC.

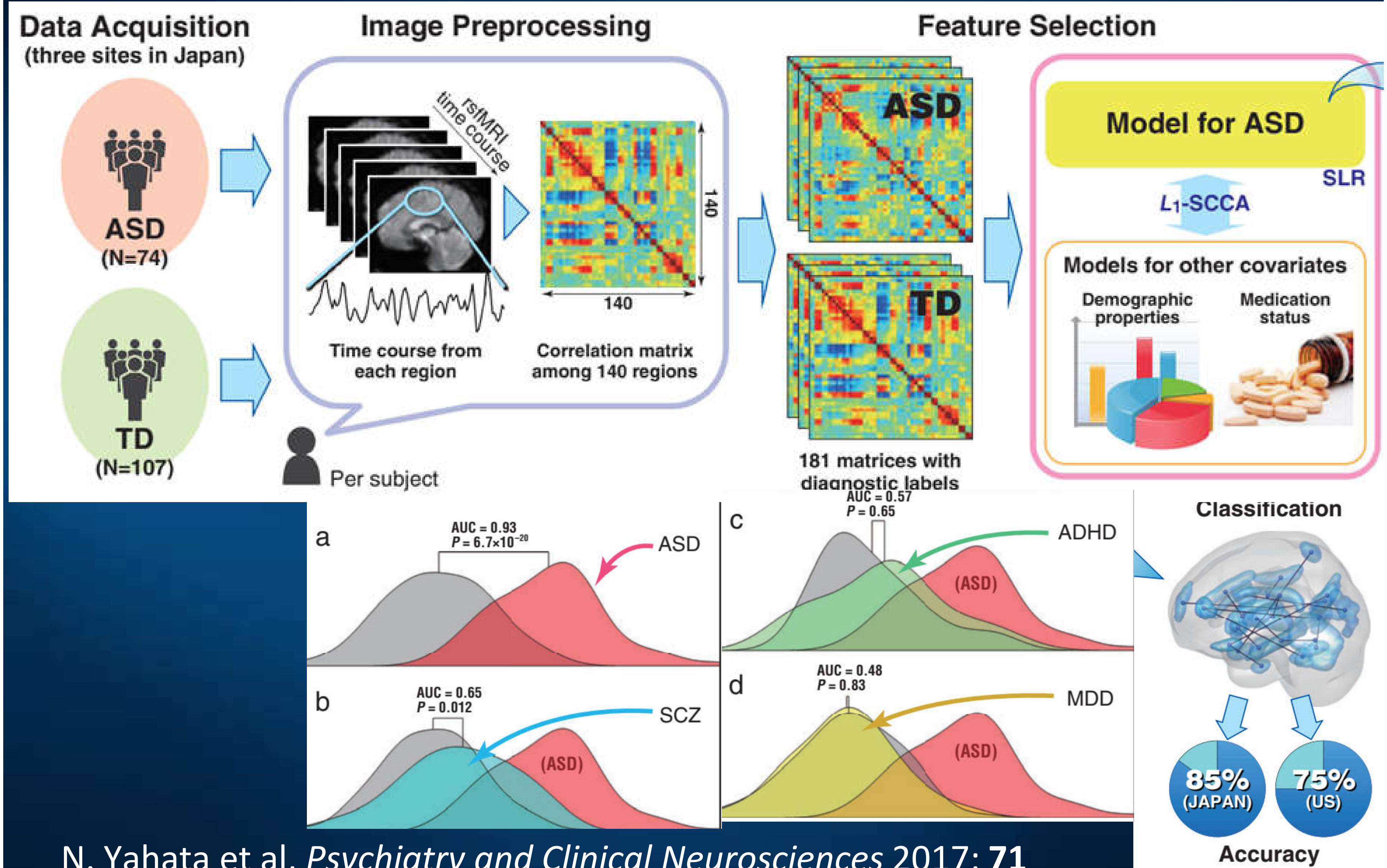
Coherence between electrodes. Weak or missing connections between distant regions prevent ASD/TSC patients from solving more demanding cognitive tasks.

Network analysis becomes very useful for diagnosis of changes due to the disease and learning; **correct your networks**!



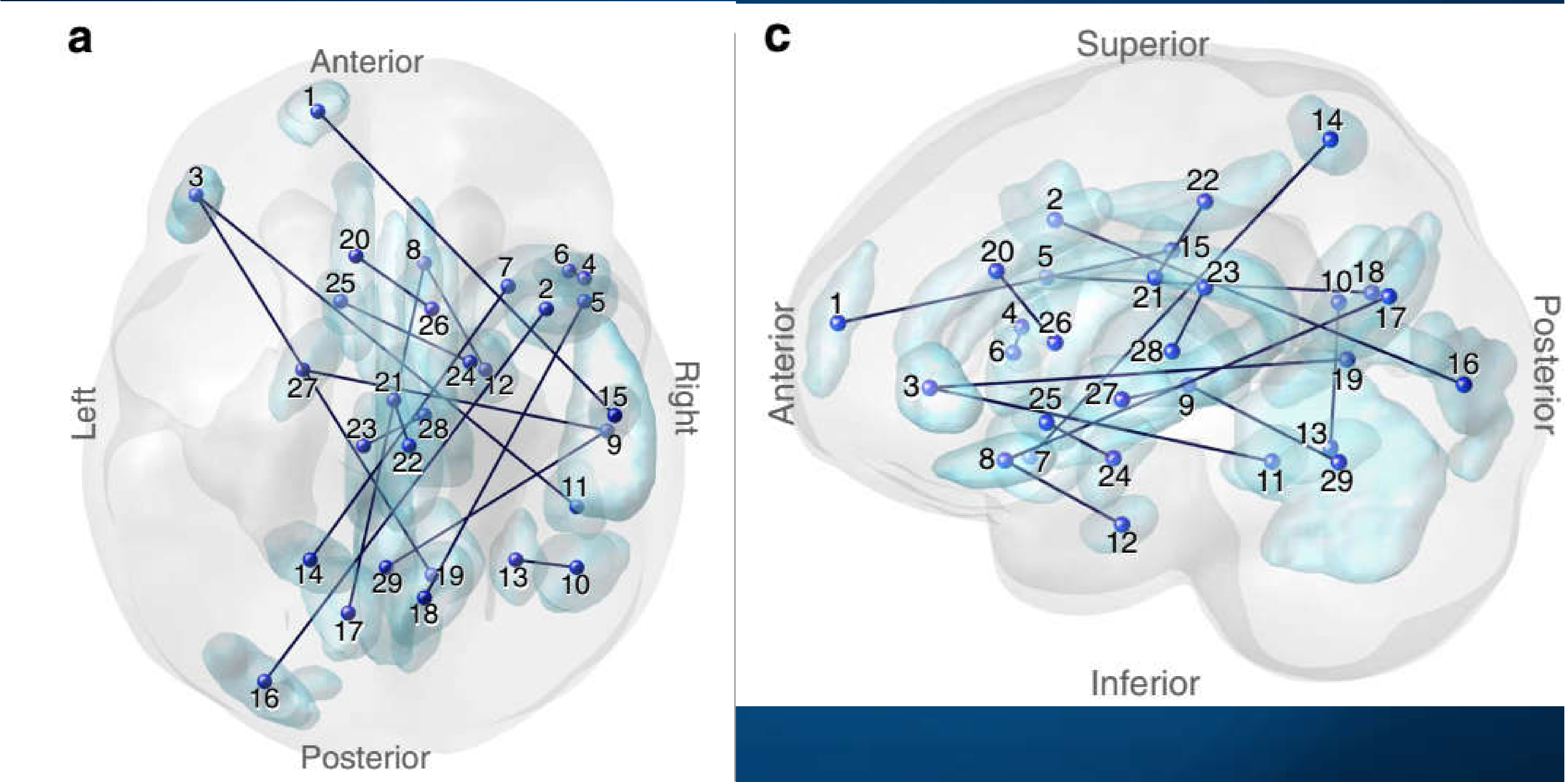
J.F. Glazebrook, R. Wallace, Pathologies in functional connectivity, feedback control and robustness. Cogn Process (2015) 16:1–16

Biomarkers from neuroimaging



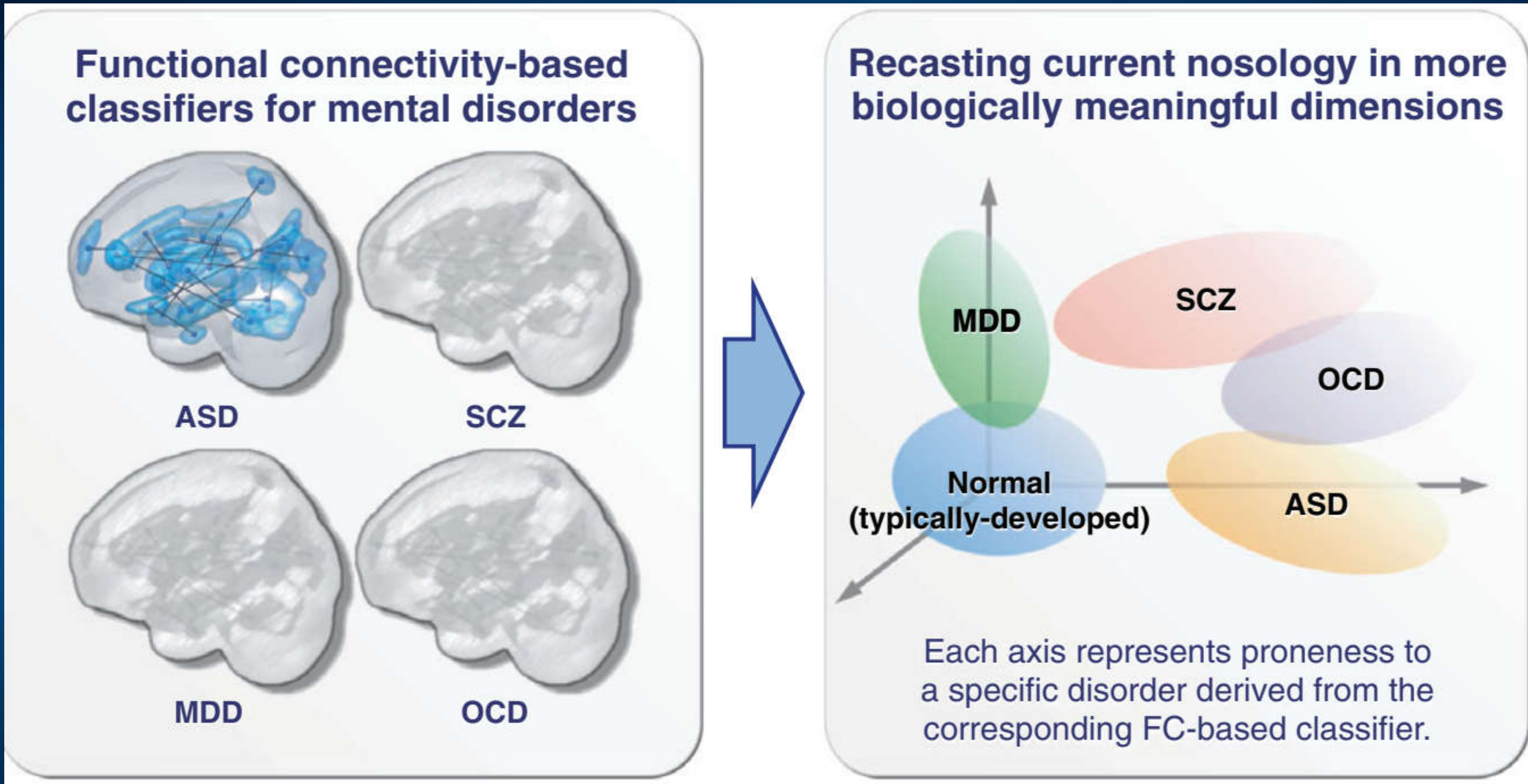
N. Yahata et al, *Psychiatry and Clinical Neurosciences* 2017: **71**

Selected connections



N. Yahata et al (2016): 29 selected regions (ROI) and 16 connections are sufficient to recognize ASD with 85% accuracy in 74 Japanese adult patients vs. 107 people in control group; without re-training accuracy was 75% on US patients.

Biomarkers of mental disorders



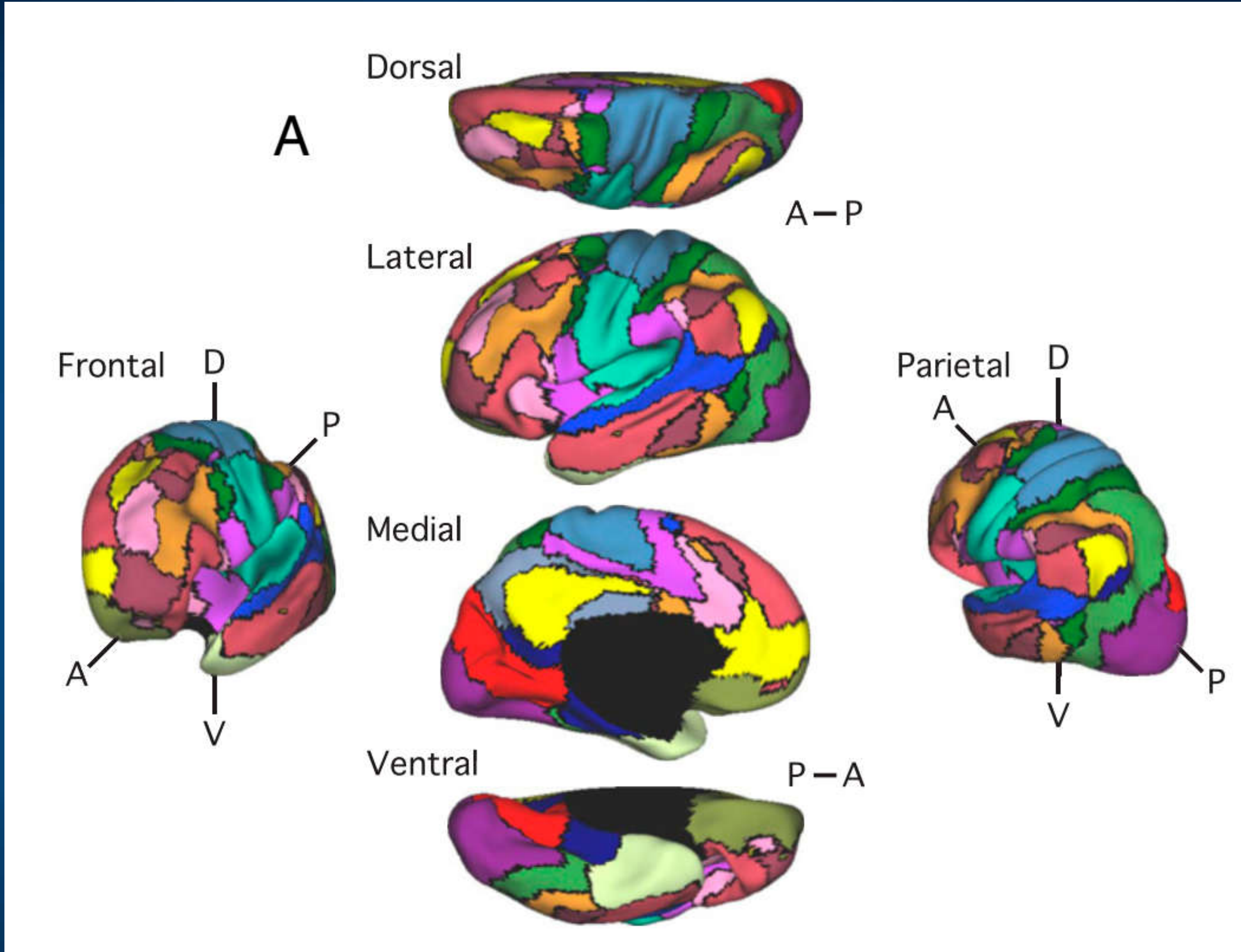
MDD, deep depression, SCZ, schizophrenia, OCD, obsessive-compulsive disorder, ASD autism spectrum disorder. fMRI biomarkers allow for objective diagnosis. N. Yahata et al, *Psychiatry & Clinical Neurosciences* 2017; **71**: 215–237

Intrinsic connectivity

Networks of functionally coupled regions.

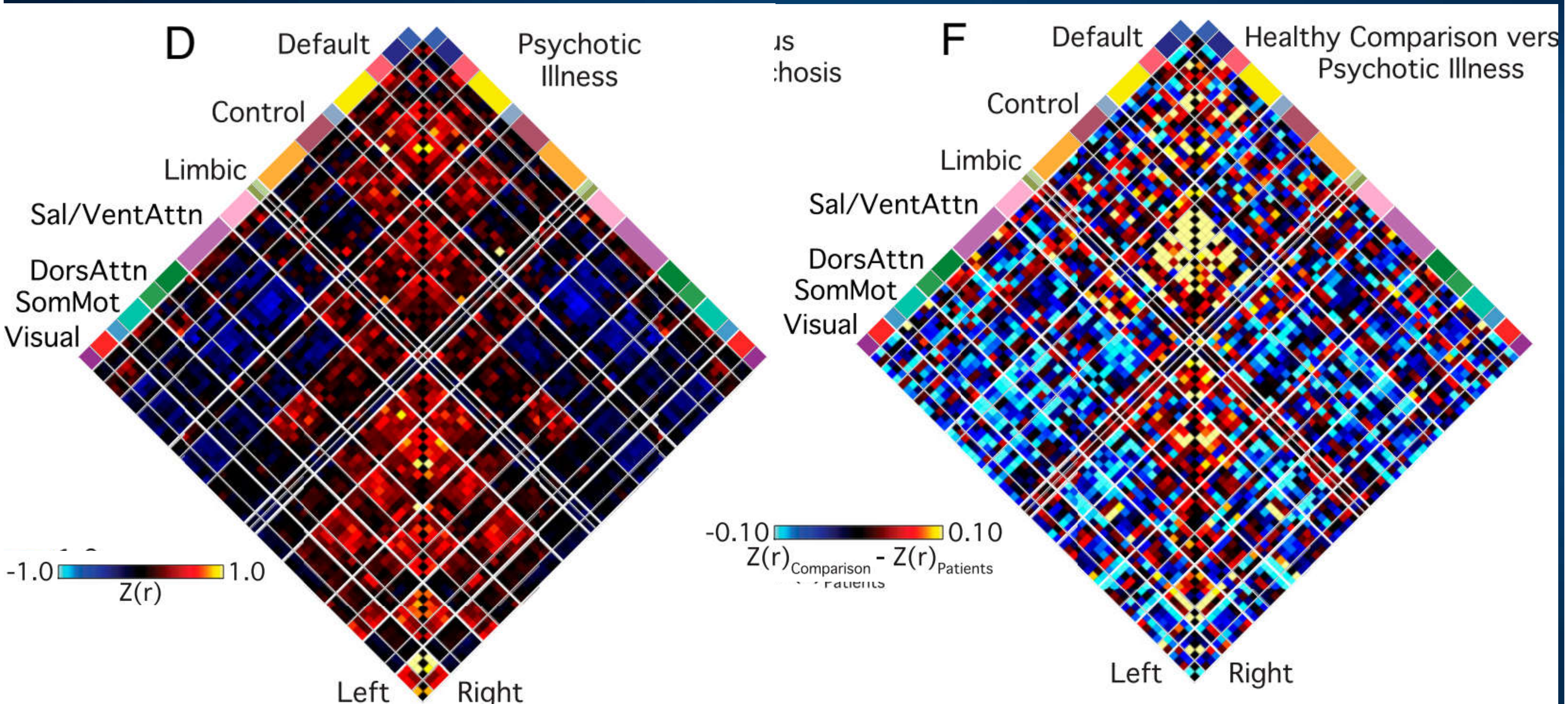
Clustering results for 1000 young adults.

18,715 spatial locations are characterized by functional coupling to the 1,175 ROI vertices (FreeSurfer).



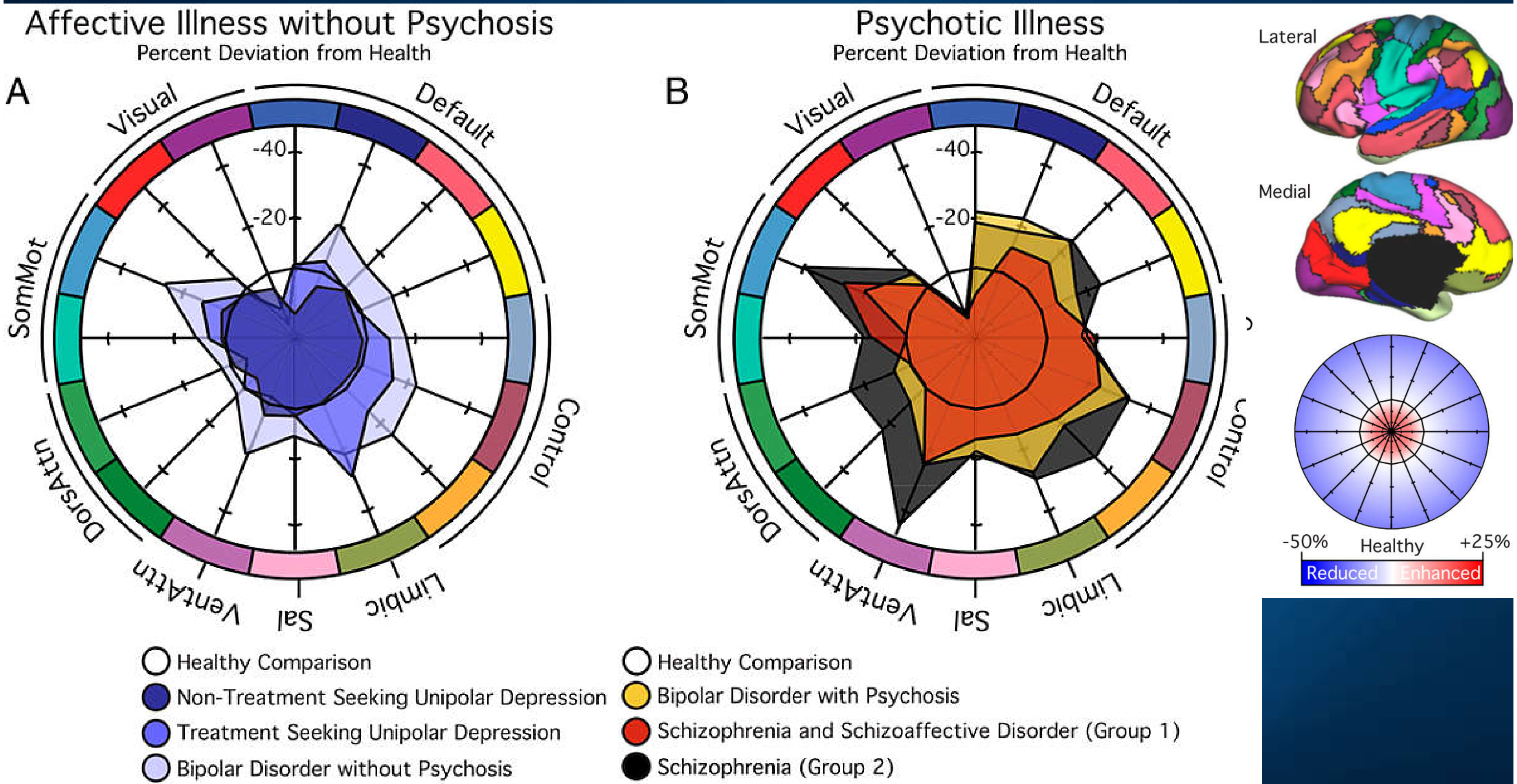
17-network intrinsic functional connectivity regions, from BTT Yeo et al. (2011). Colors = same network regions, similar correlation profiles.

Connectivity in patients vs healthy



Baker et al, Functional connectomics of affective and psychotic pathology. PNAS 116, 9050 (2019) Regions from the 17-network intrinsic functional connectivity solution by BTT Yeo et al. (2011)

Connectivity in patients vs healthy



Regions determined based on the 17-network solution from Yeo et al.
Control (health) = circle, % deviation shown.

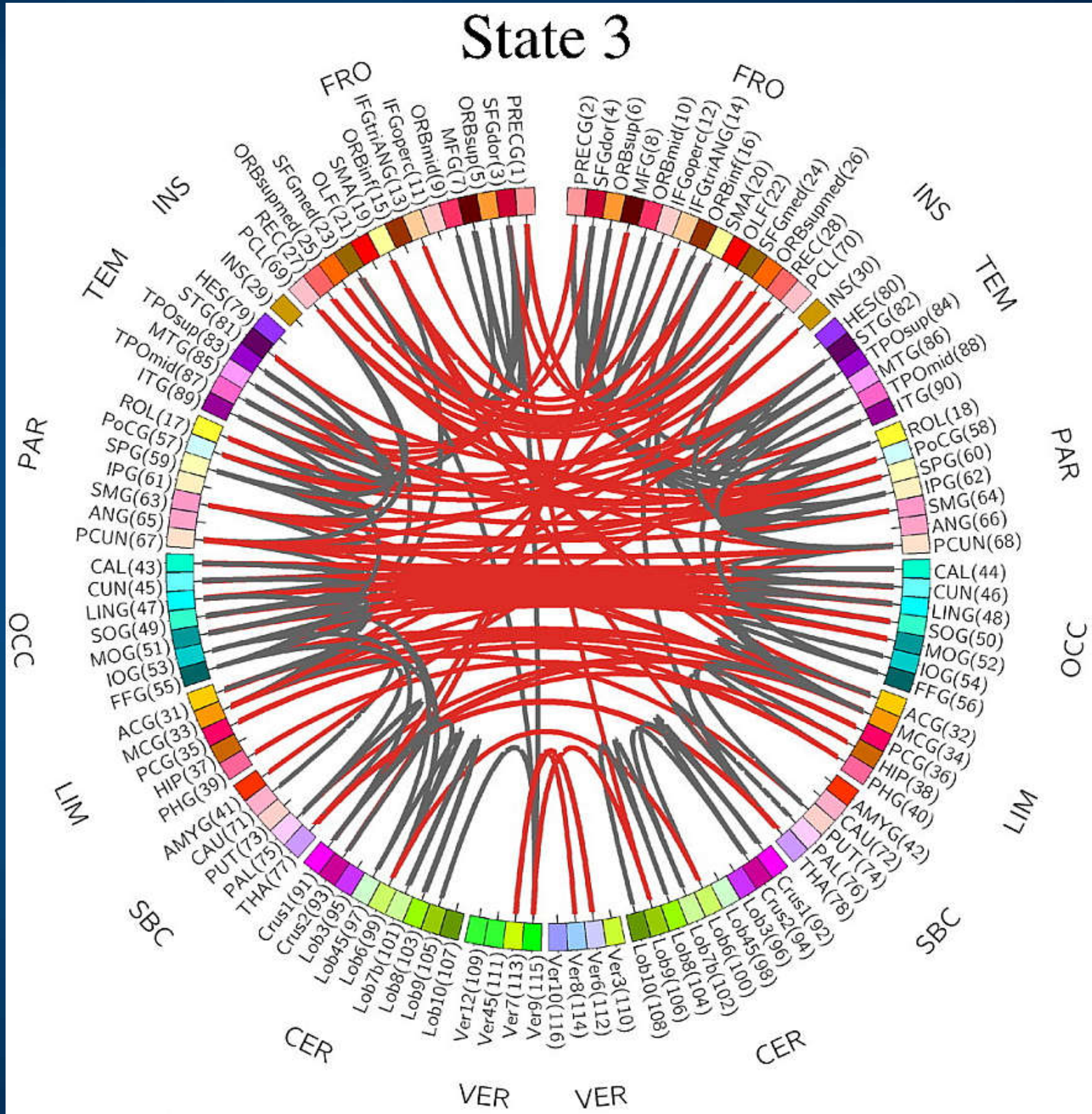
Negative connections in MCI patients

MCI patients (ADNI2), positive and negative functional connections in one of the 5 states of the Deep Auto-Encoder (DAE) + HMM models derived from the rs-fMRI time series.

Connections |W|>0.65.

Accuracy 72.6% with a sensitivity of 70.6% and a specificity of 75%.

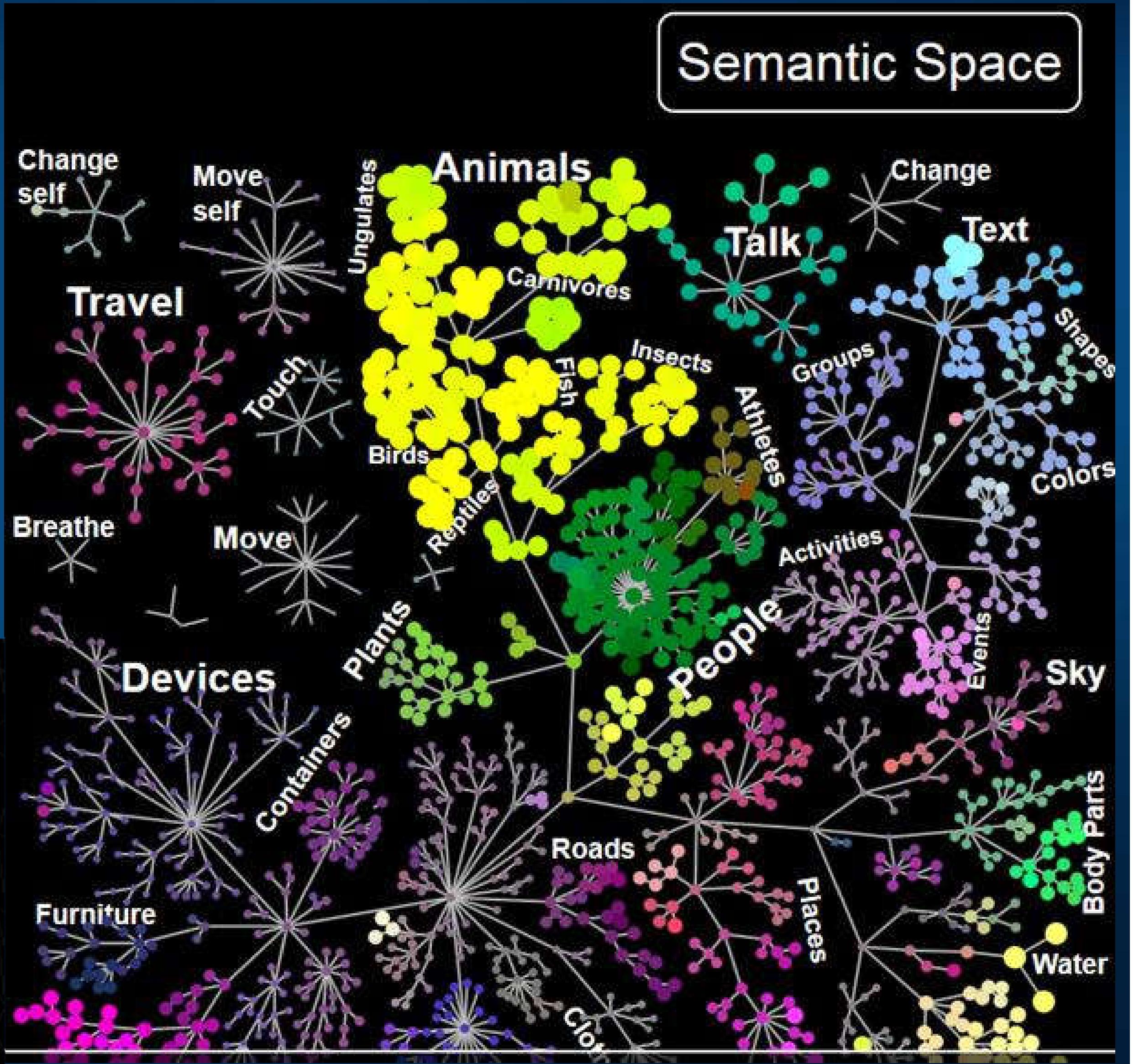
Suk et al. Neuroimage (2016)

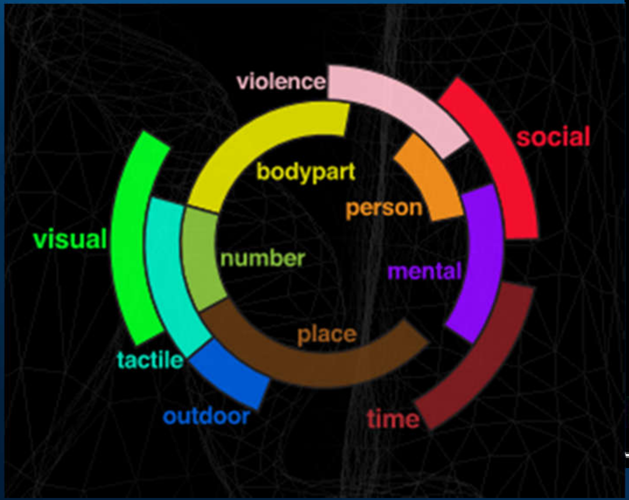


Decoding mental states

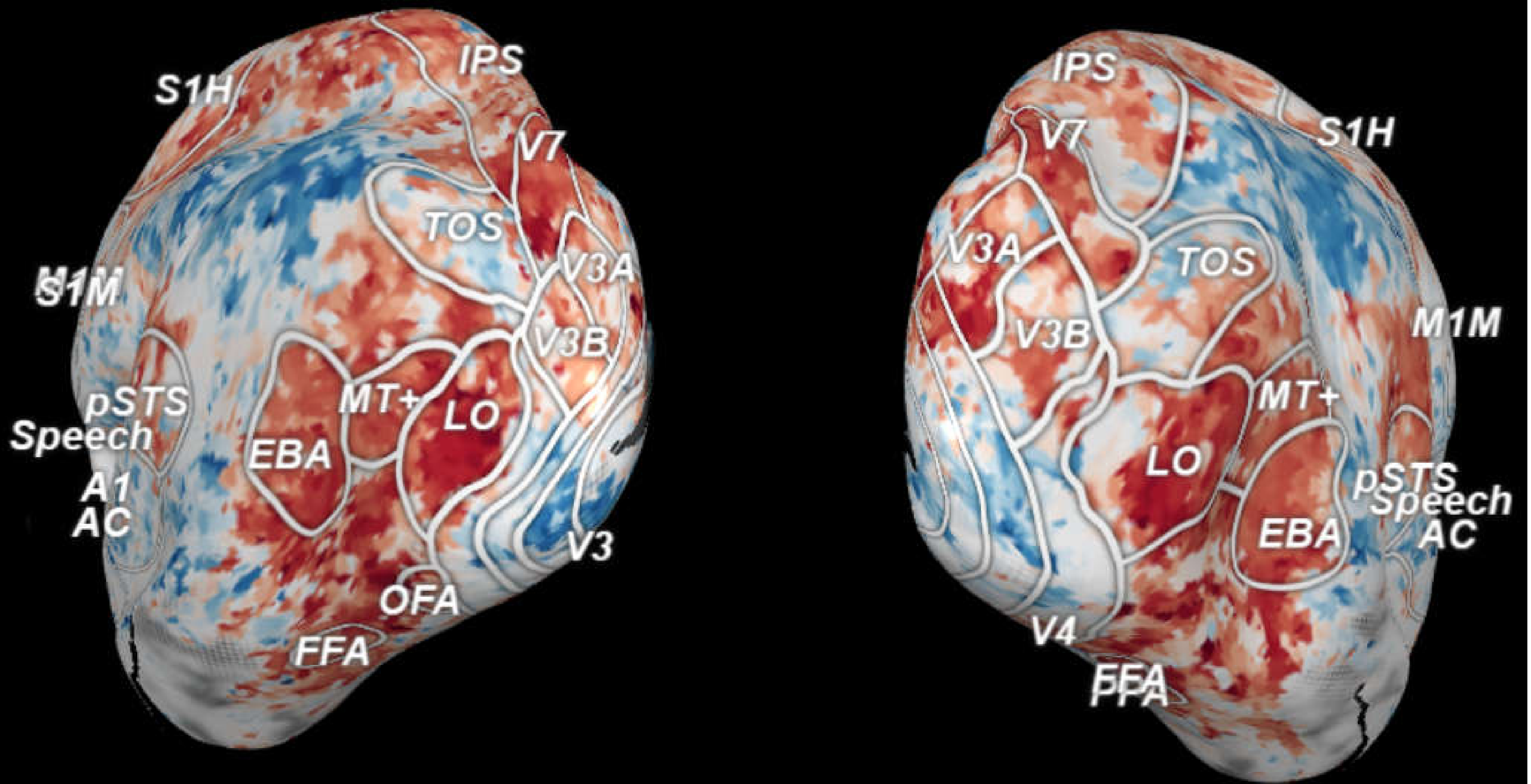
Semantic neuronal space

Words in the semantic space are grouped by their similarity.
Words activate specific ROIs, similar words create similar maps of brain activity.
Video or audio stimuli, fMRI 60.000 voxel).
[Gallant lab, Berkeley]().

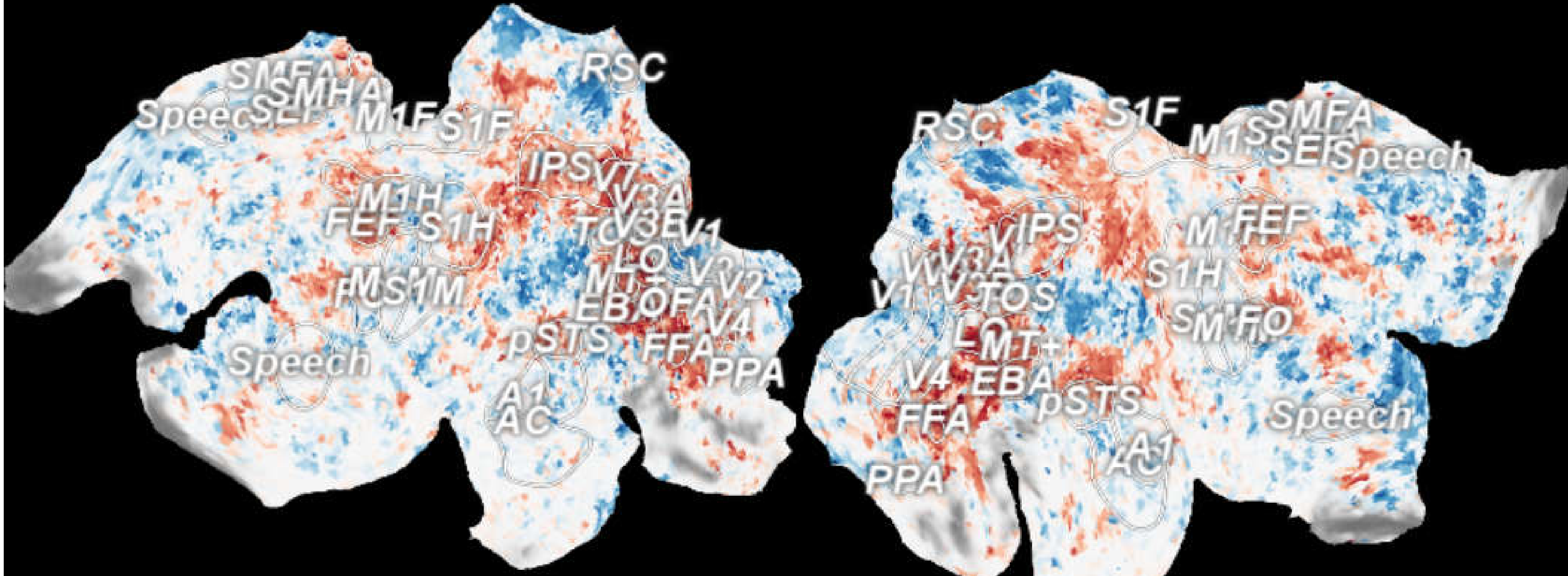




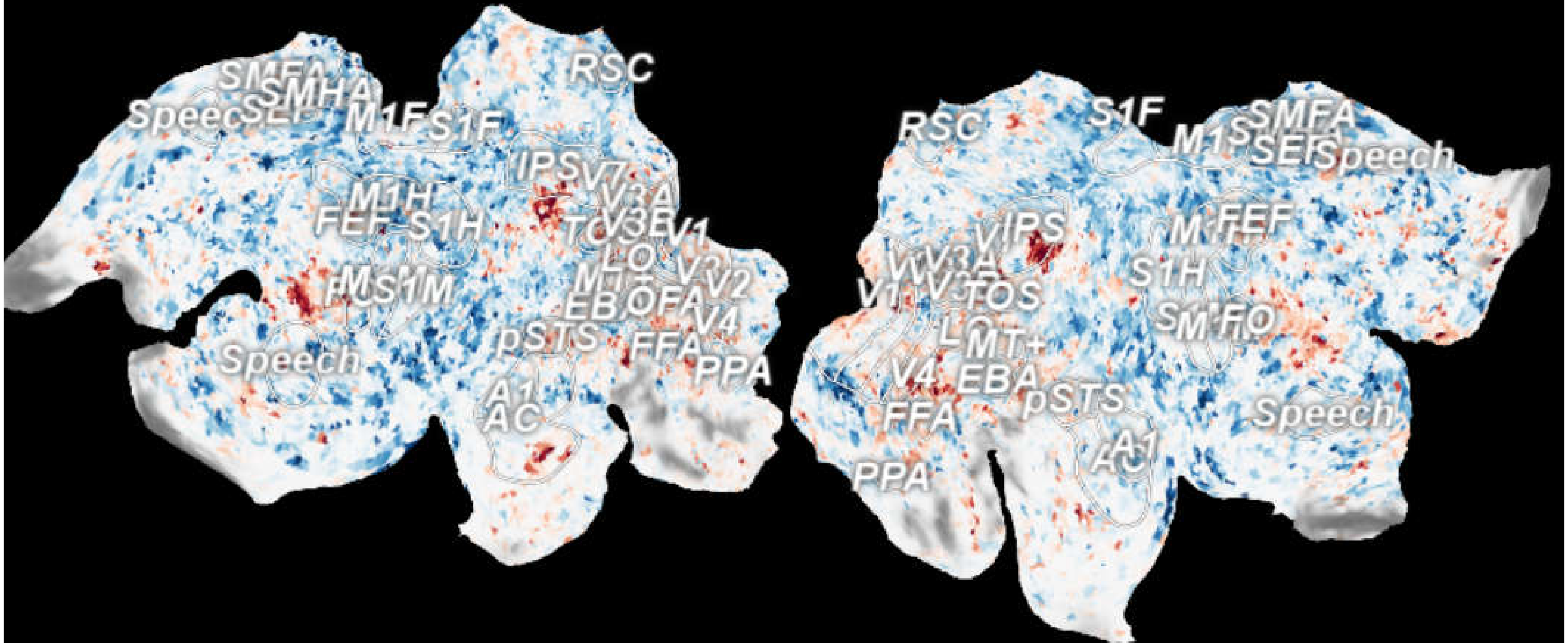
Category zebra: Passive Viewing



Category zebra: Passive Viewing



Category traffic light: Passive Viewing



65 attributes related to neural processes;

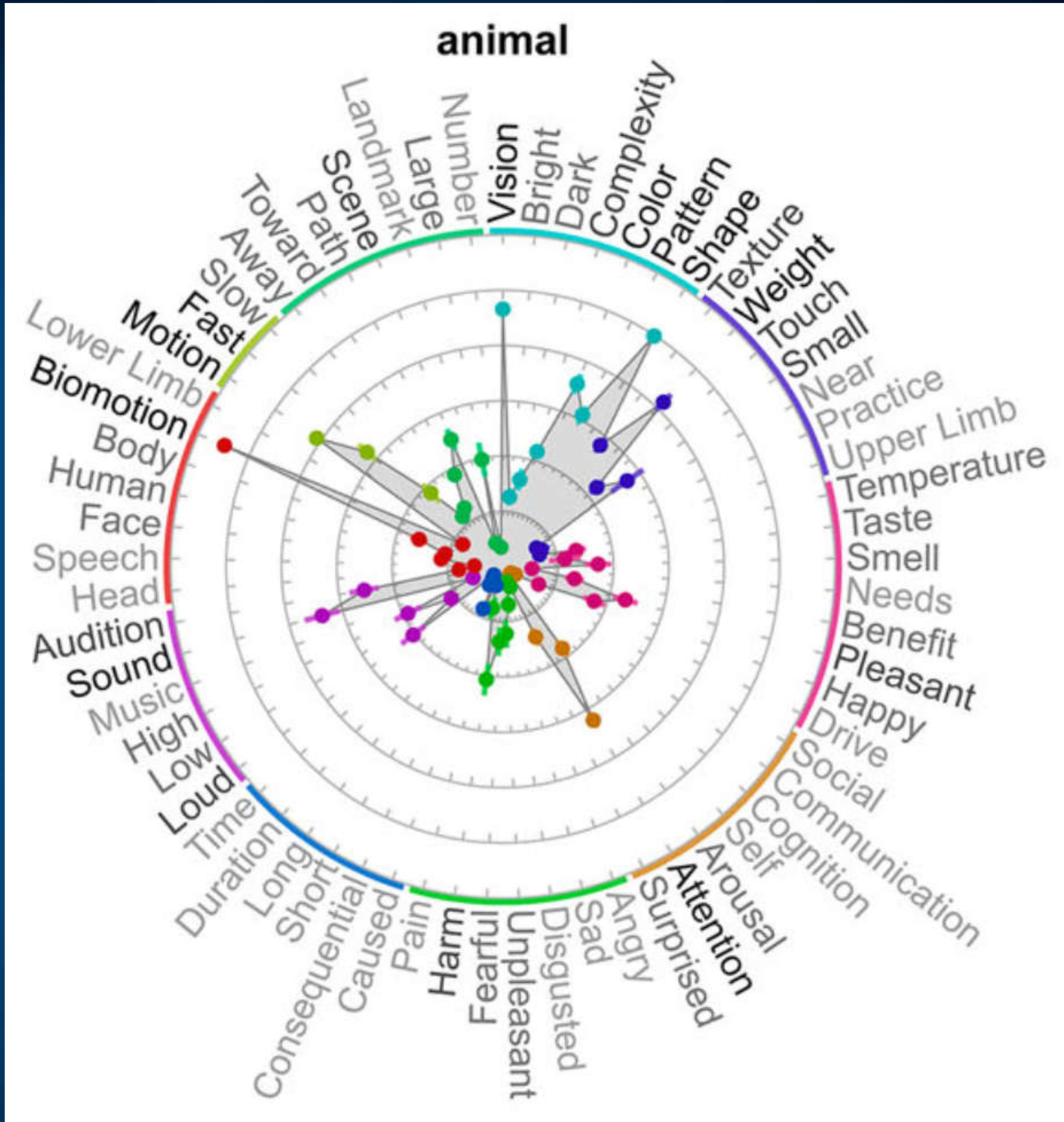
Colors on circle: general domains.

J.R. Binder et al

Toward a Brain-Based Componential Semantic Representation, 2016

More than just visual objects!

Decompose brain signals for a given concept into components coding these attributes.



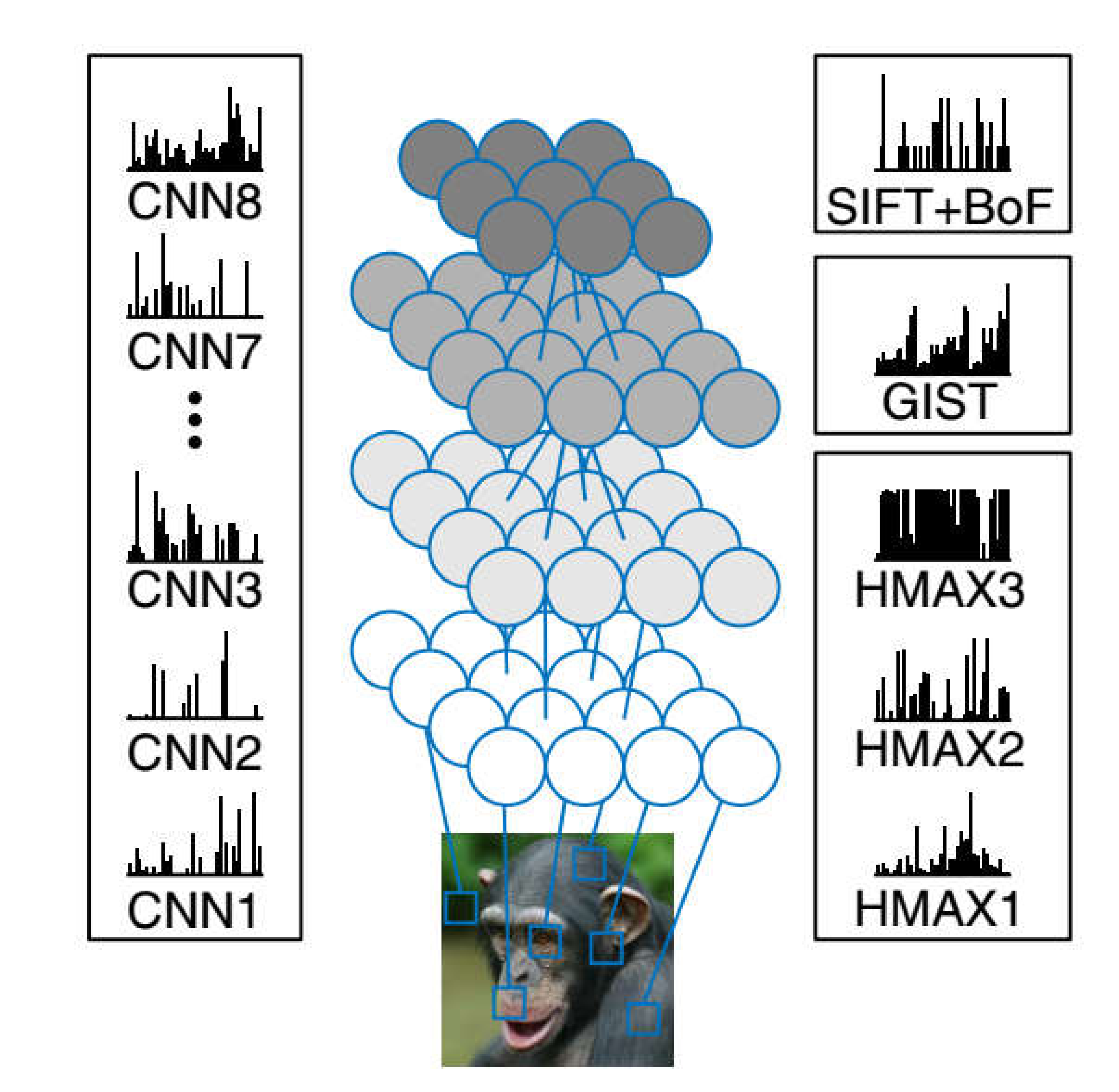
Mental images from brain activity

Can we convert activity of the brain into the mental images that we are conscious of?

Try to estimate features at different layers.

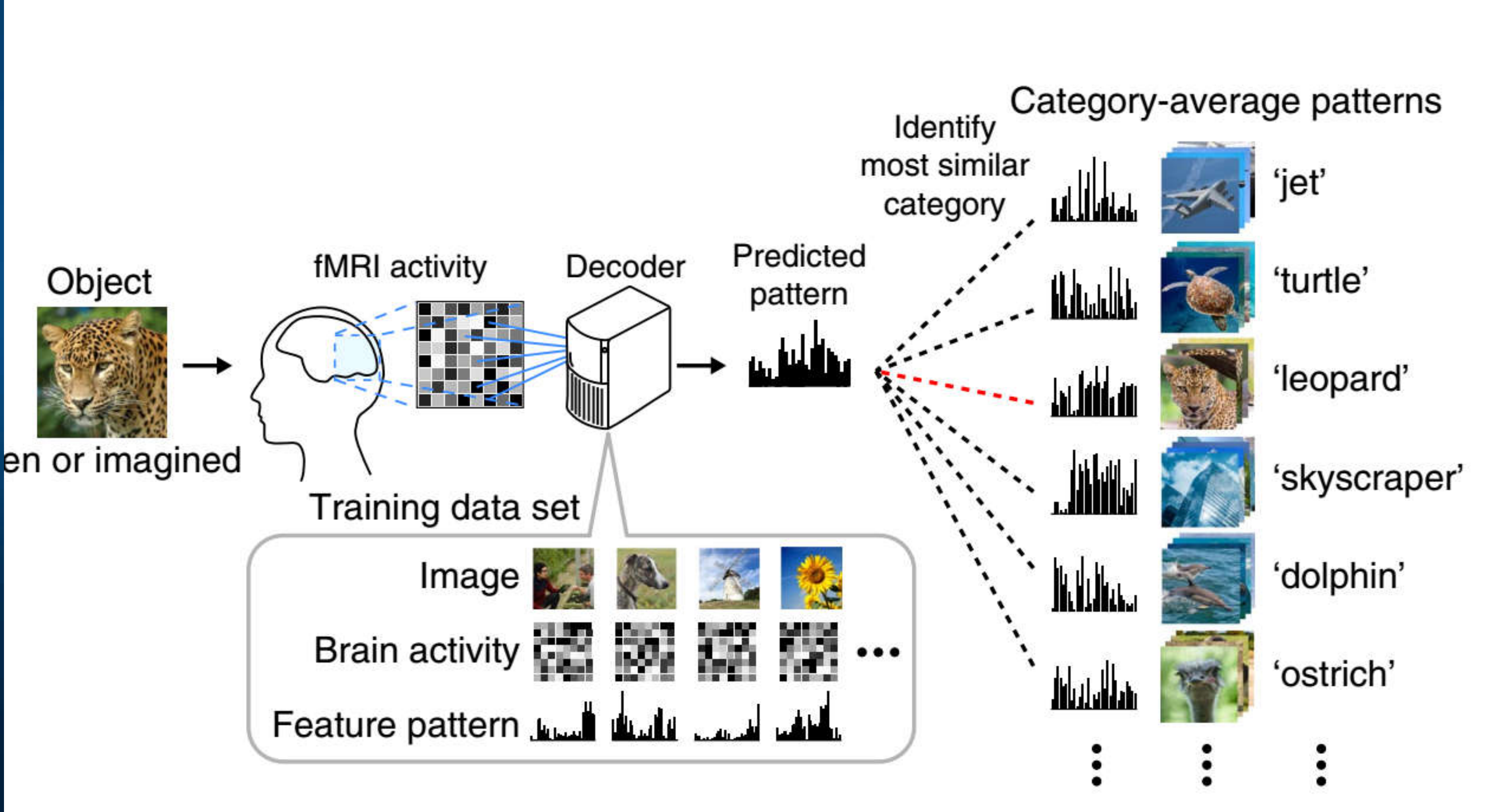
8-layer convolution network, ~60 mln parameters, feature vectors from randomly selected 1000 units in each layer to simplify calculations.

Output: 1000 images.

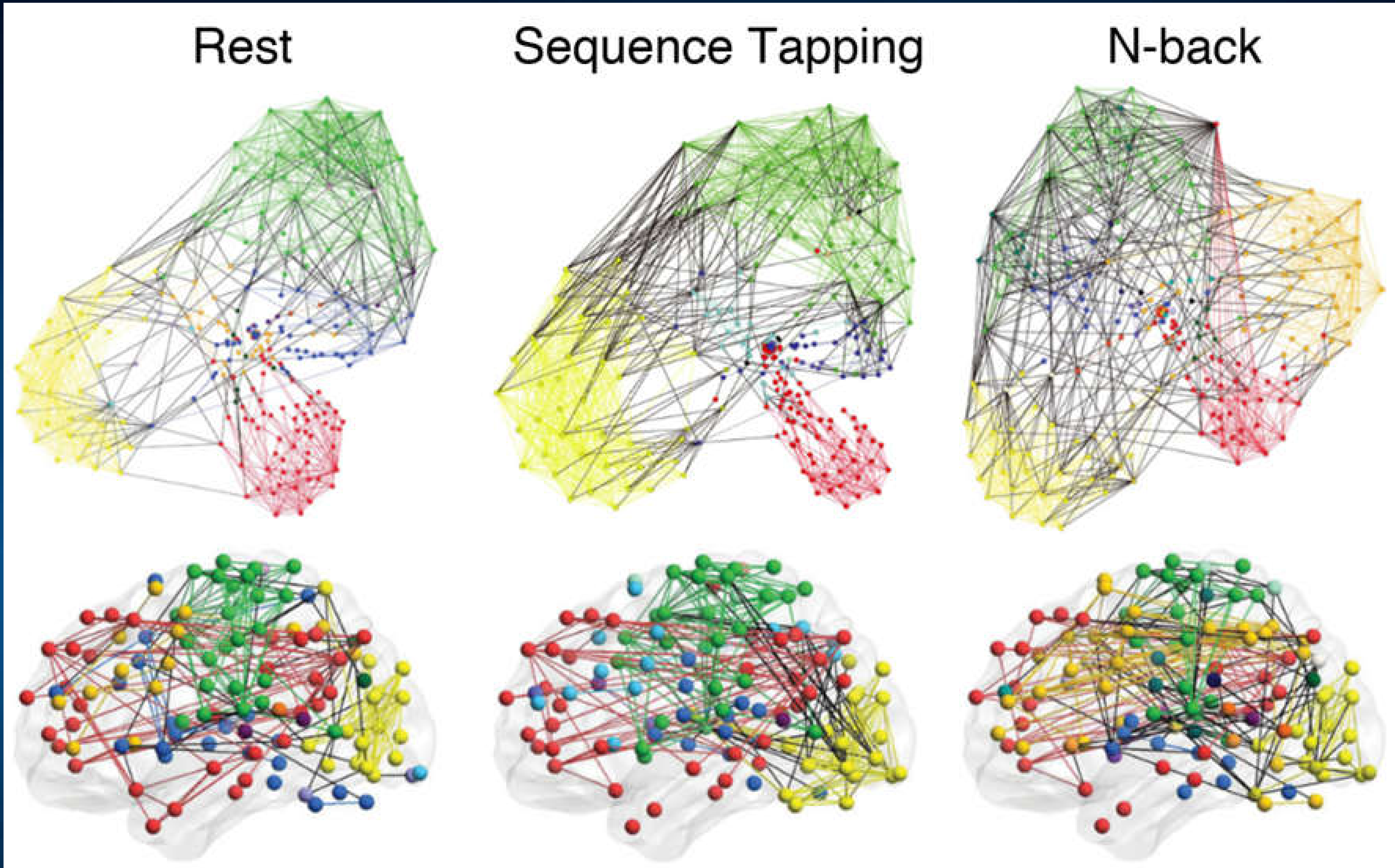


Brain activity ⇔ Mental image

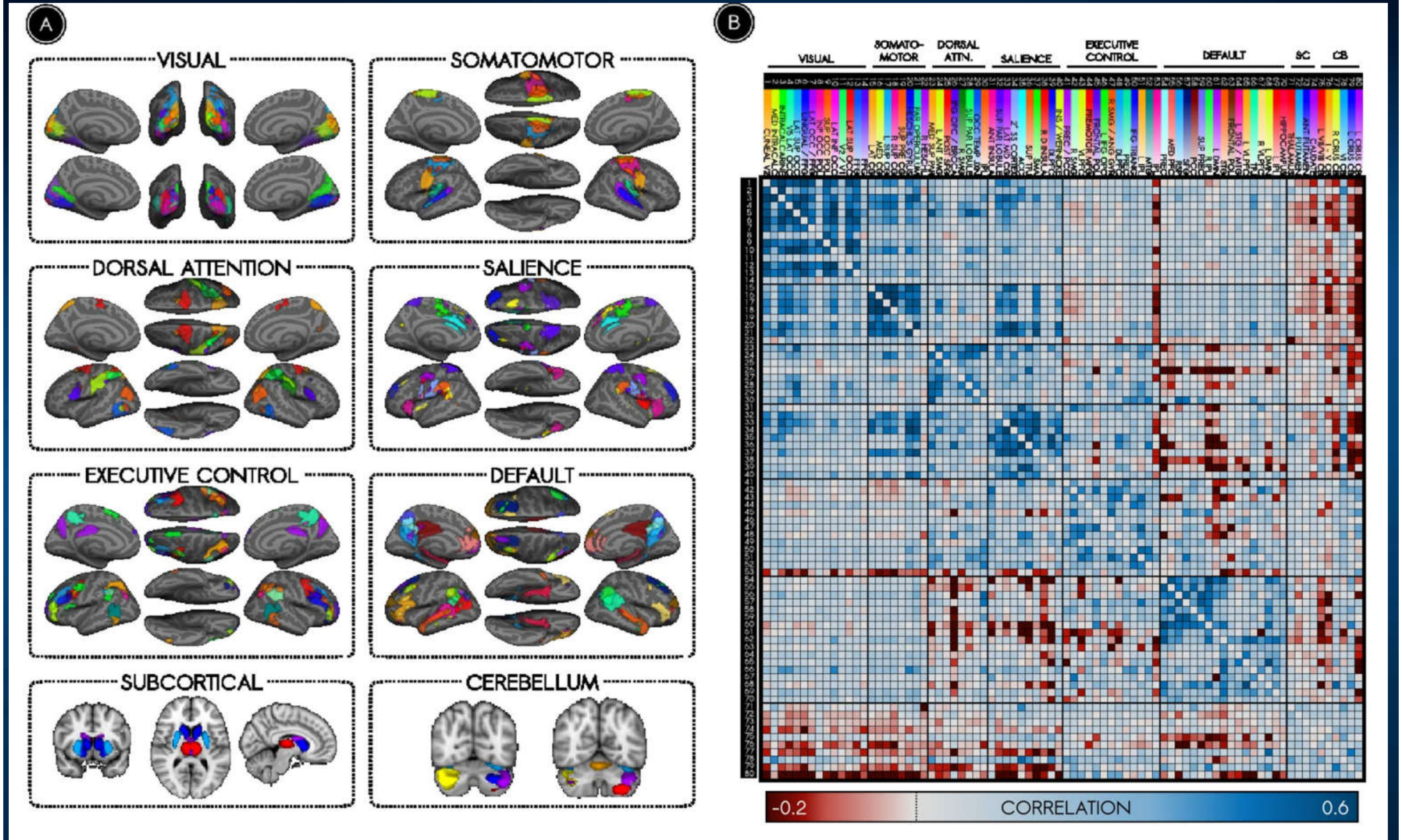
fMRI activity can be correlated with deep CNN network features;
using these features closest image from large database is selected.
Horikawa, Kamitani, Generic decoding of seen and imagined objects using hierarchical visual features. Nature Comm. 2017.



Neurodynamics

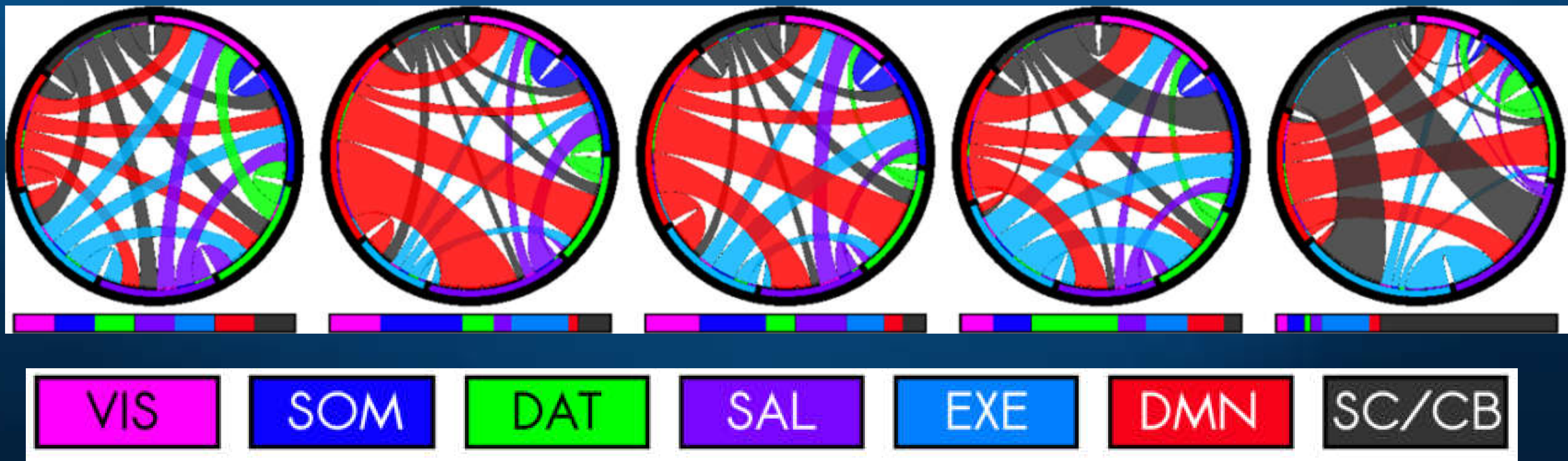


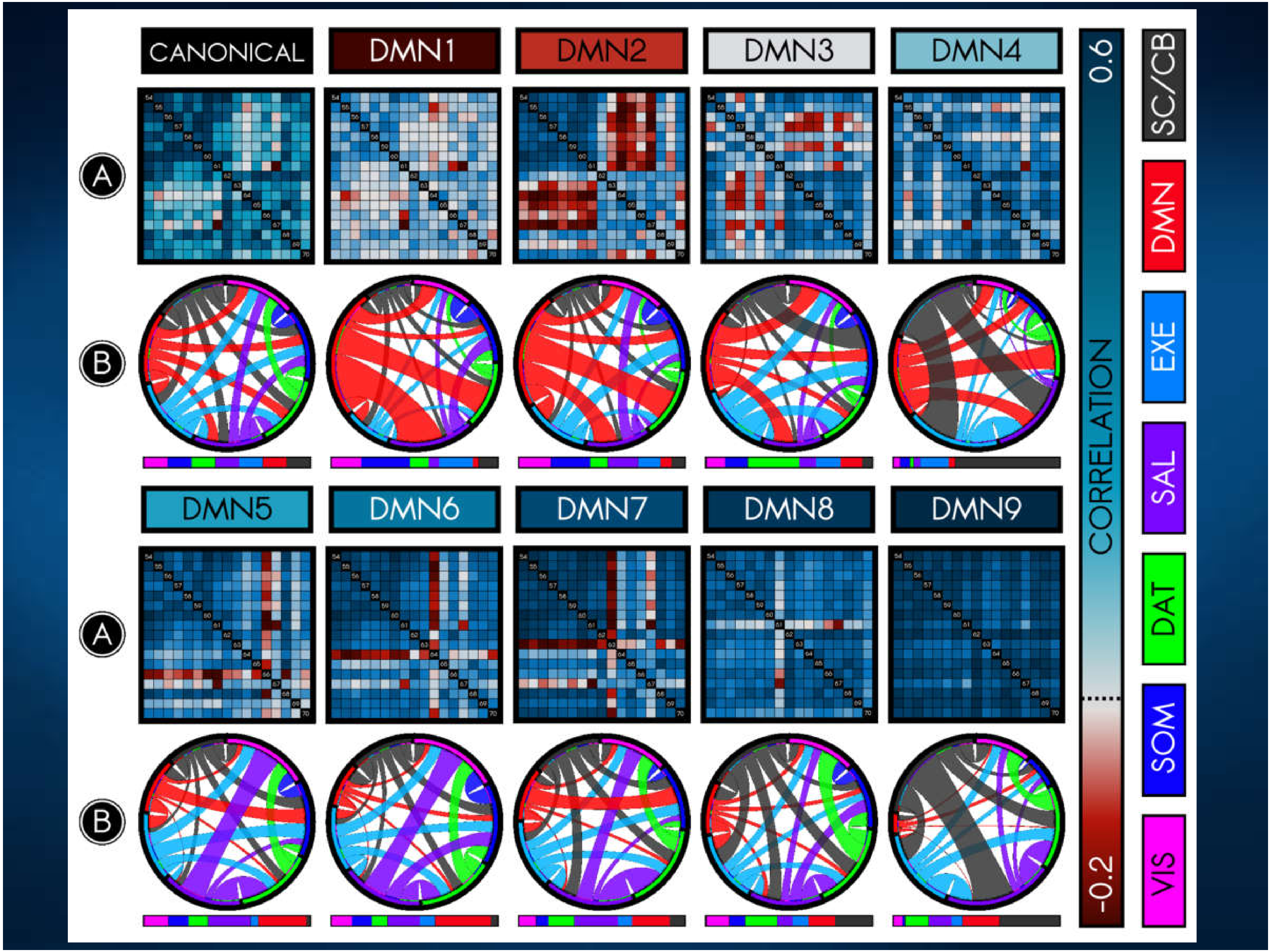
Color edges = within-module connections, black edges = between-module connections. Cohen and D'Esposito (2016). The segregation and integration of distinct brain networks and their relationship to cognition. J. of Neurosci, 36(48):12083–12094



Ciric et.al. (2017). Contextual connectivity: A framework for understanding the intrinsic dynamic architecture of large-scale functional brain networks. *Scientific Reports* 7, 6537

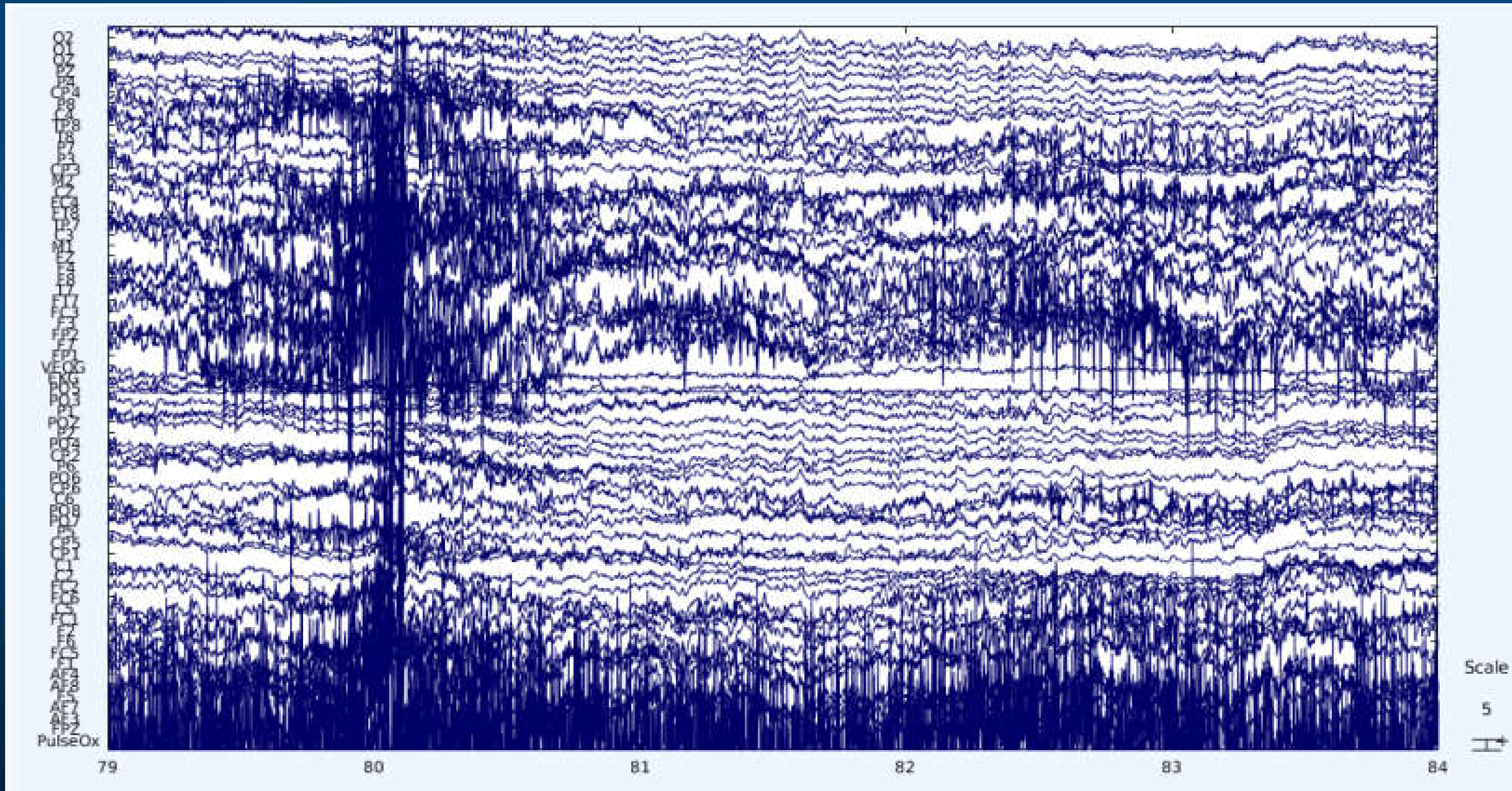
DMN time-averaged baseline.
Between-network allegiances (prob. that nodes are in the same community). Rim colors = canonical networks, rim length = greater allegiance to other networks, size of connections = strength of between-network allegiances.
DMN1: weak within-network allegiance strong to DAT, SAL, and VIS.




CANONICAL
DMN1
DMN2
DMN3
DMN4
DMN5
DMN6
DMN7
DMN8
DMN9
A
B
A
B
0.6
CORRELATION
-0.2
SC/CB
DMN
EXE
SAL
DAT
SOM
VIS

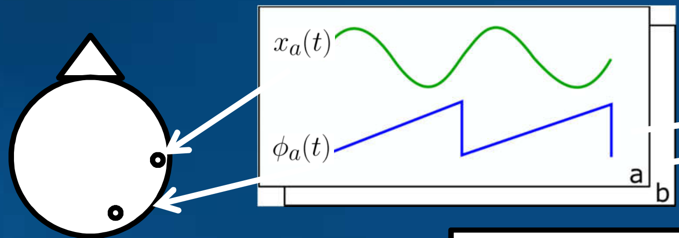
EEG

Removal of artefacts is only partially automatic, it involves a lot of manual work. Usually only a subset of electrodes is selected.



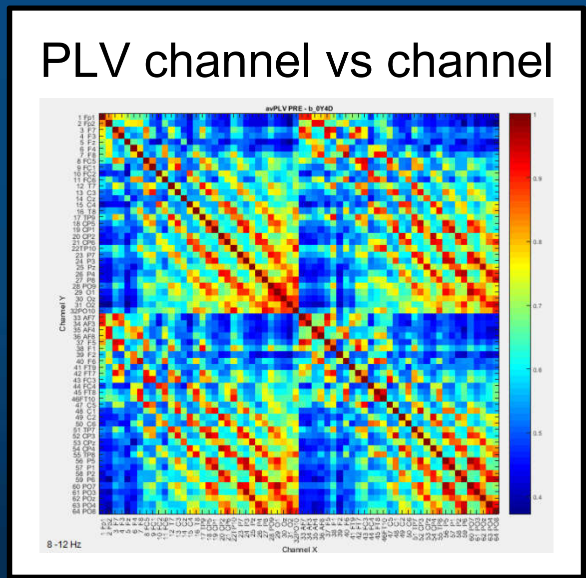
Functional connectivity changes

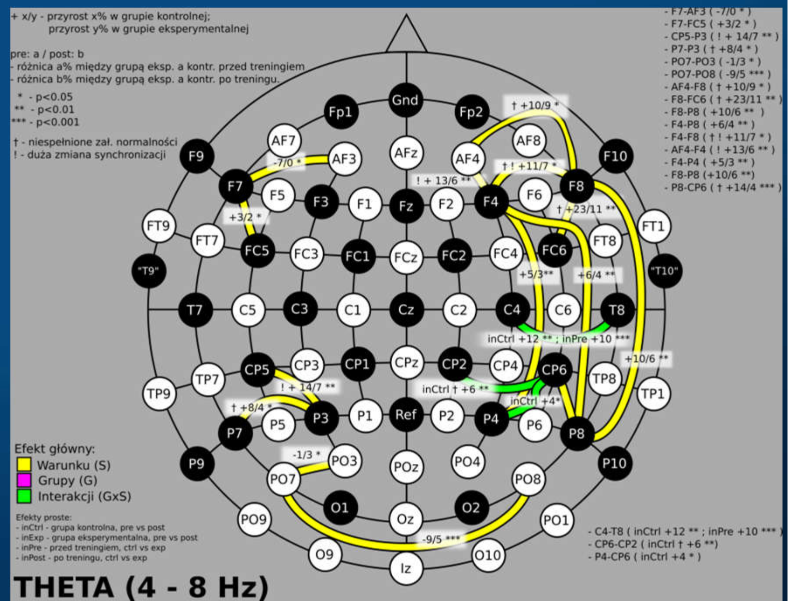
Influence of brain games on functional connectivity: **Phase Locking Value** (Burgess, 2013; Lachaux 1999), phase differences between signals measured at each electrode. PLV => synchronization maps, info flow.



$$\Phi(t) = \phi_a(t) - \phi_b(t)$$

$$PLV(a,b) = \frac{1}{T}\left|\sum_{t}^{T} e^{i\Phi(t)}\right|$$



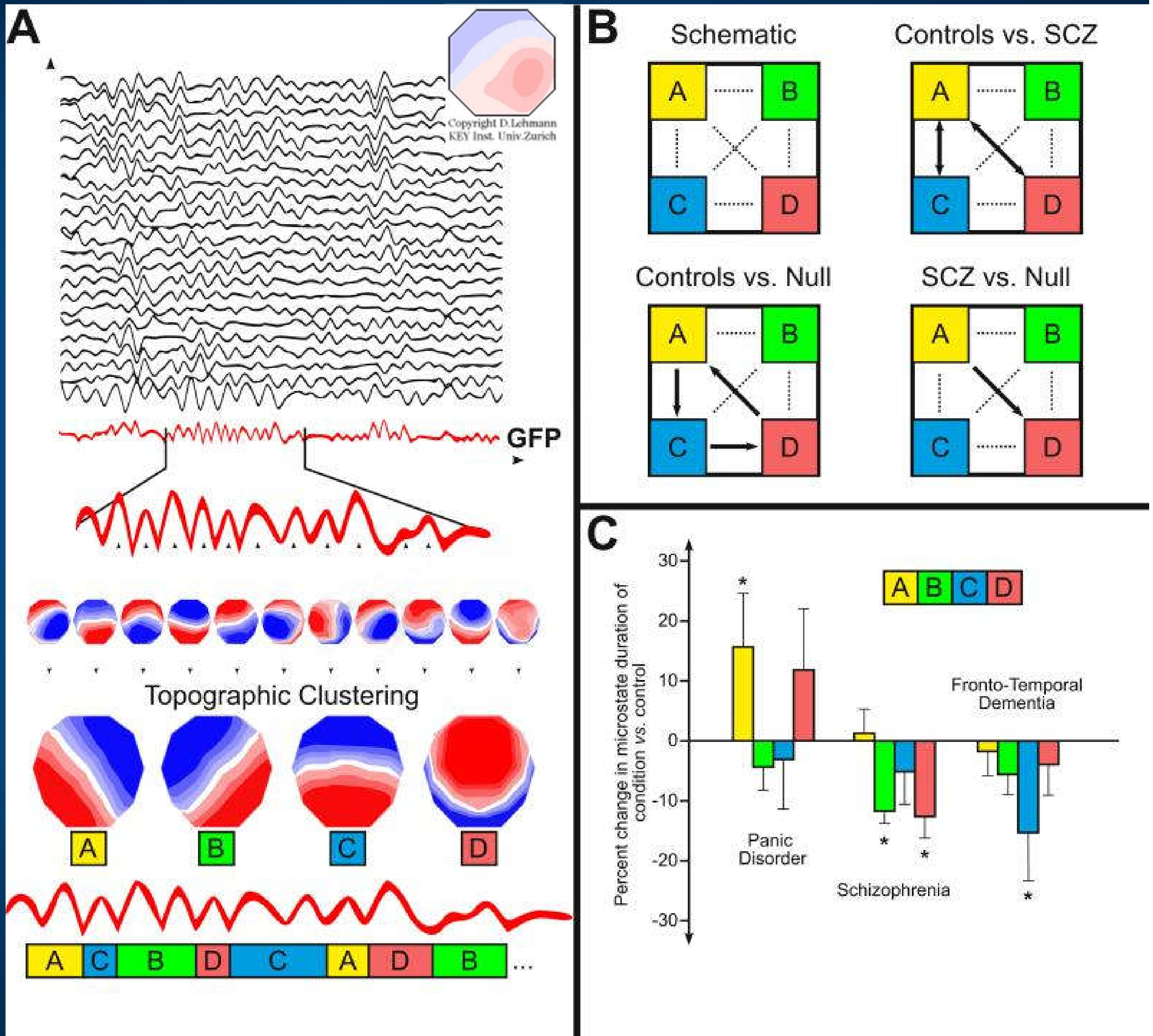


Microstates

Lehmann et al.
EEG microstate duration and syntax in acute, medication-naïve, first-episode schizophrenia.
Psychiatry Research Neuroimaging, 2005

Khanna et al.
Microstates in Resting-State EEG.
Neuroscience and Biobehavioral Reviews, 2015

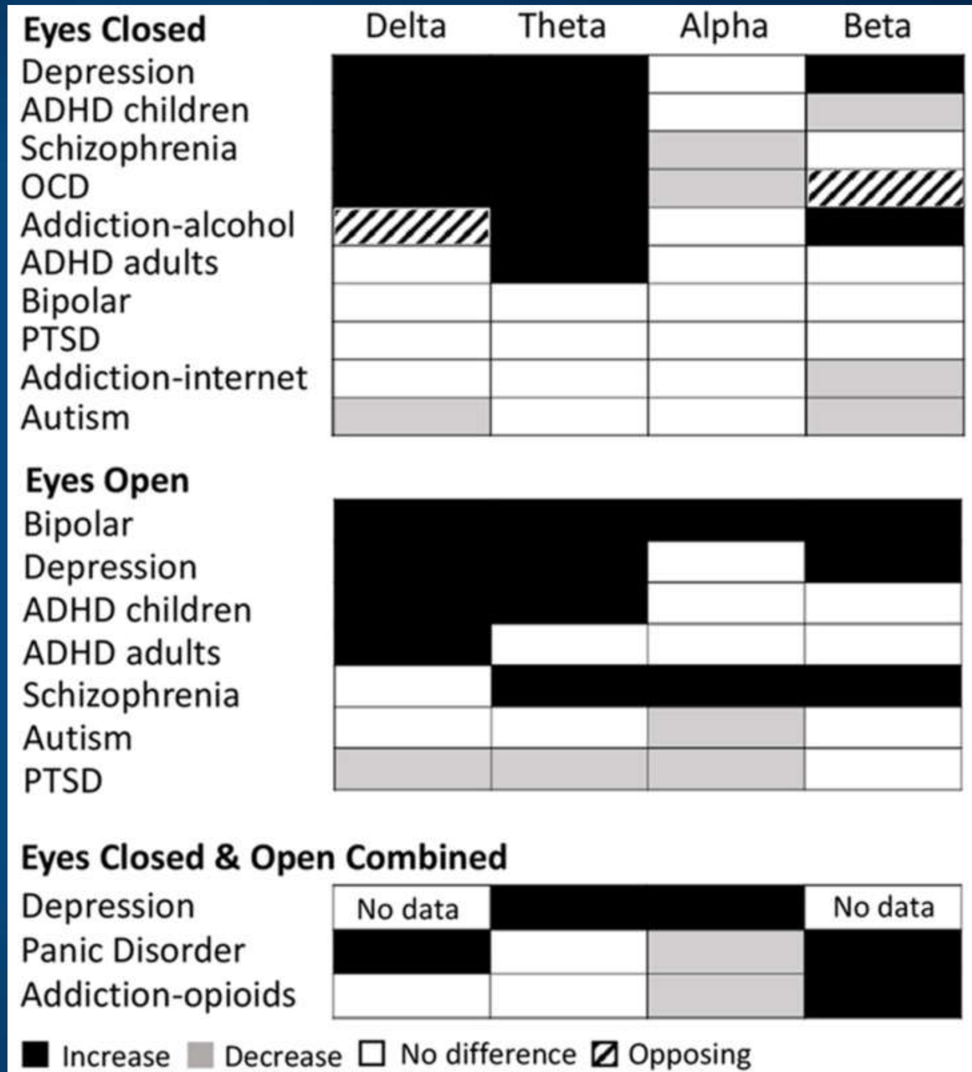
4-7 states 60-150 ms
Symbolic dynamics.



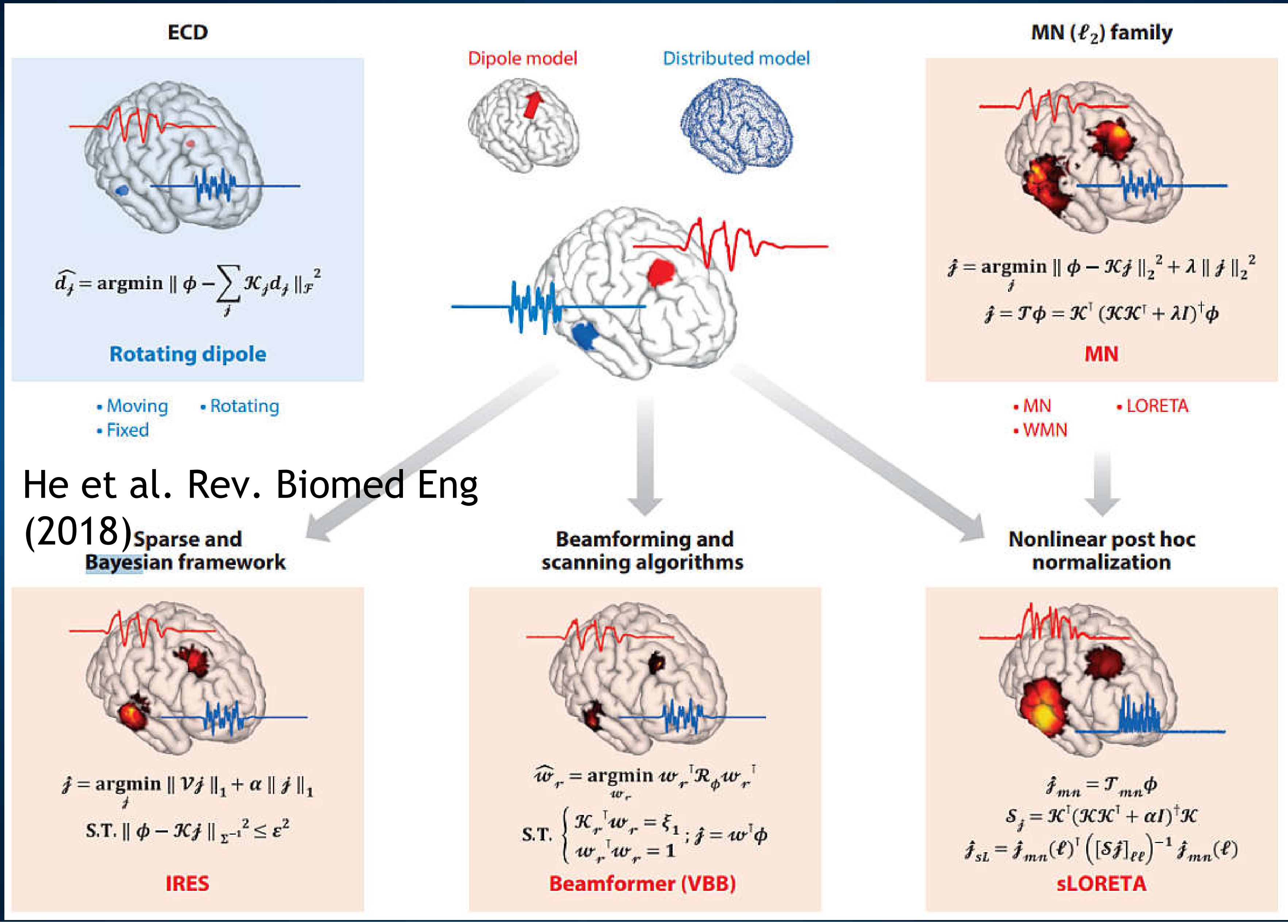
EEG bands and brain disorders

Differences in absolute power for each disorder (relative to control) for eyes closed condition (top), eyes open (middle) and eyes open and closed combined (bottom). White boxes indicate no change, black indicates an increase, and gray indicates a decrease. Hashed boxes - opposing results (contradictory).

Newson & Thiagarajan (2019). EEG Frequency Bands in Psychiatric Disorders: A Review of Resting State Studies. Frontiers in Human Neuroscience, 12. https://doi.org/10.3389/fnhum.2018.00521

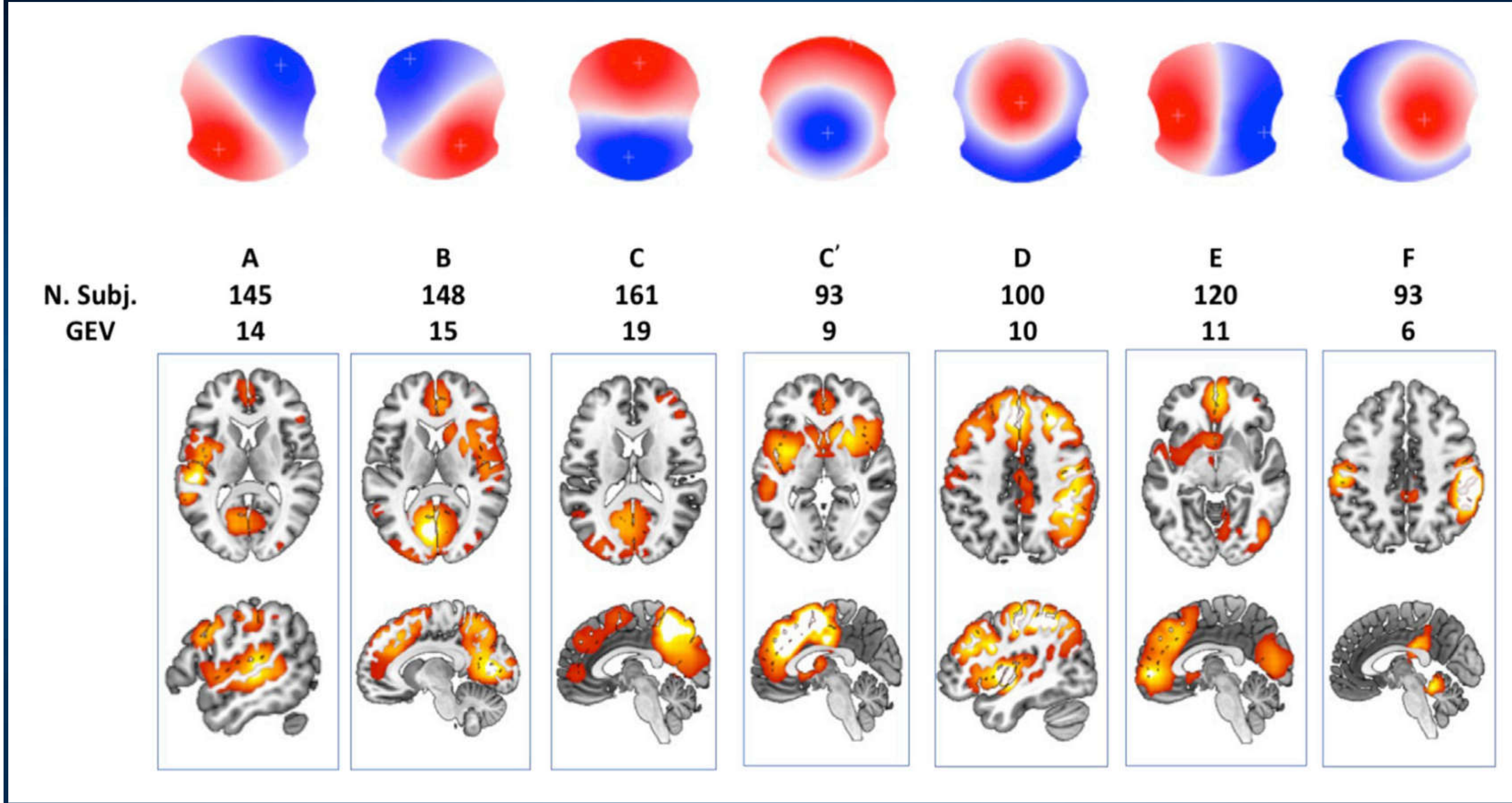


EEG localization and reconstruction



He et al. Rev. Biomed Eng (2018)

Microstates sources



Michel, C. M., & Koenig, T. (2018). EEG microstates as a tool for studying the temporal dynamics of whole-brain neuronal networks: A review. *NeuroImage*, *180*, 577–593. https://doi.org/10.1016/j.neuroimage.2017.11.062

Checkerboard reversal, 5 microstates

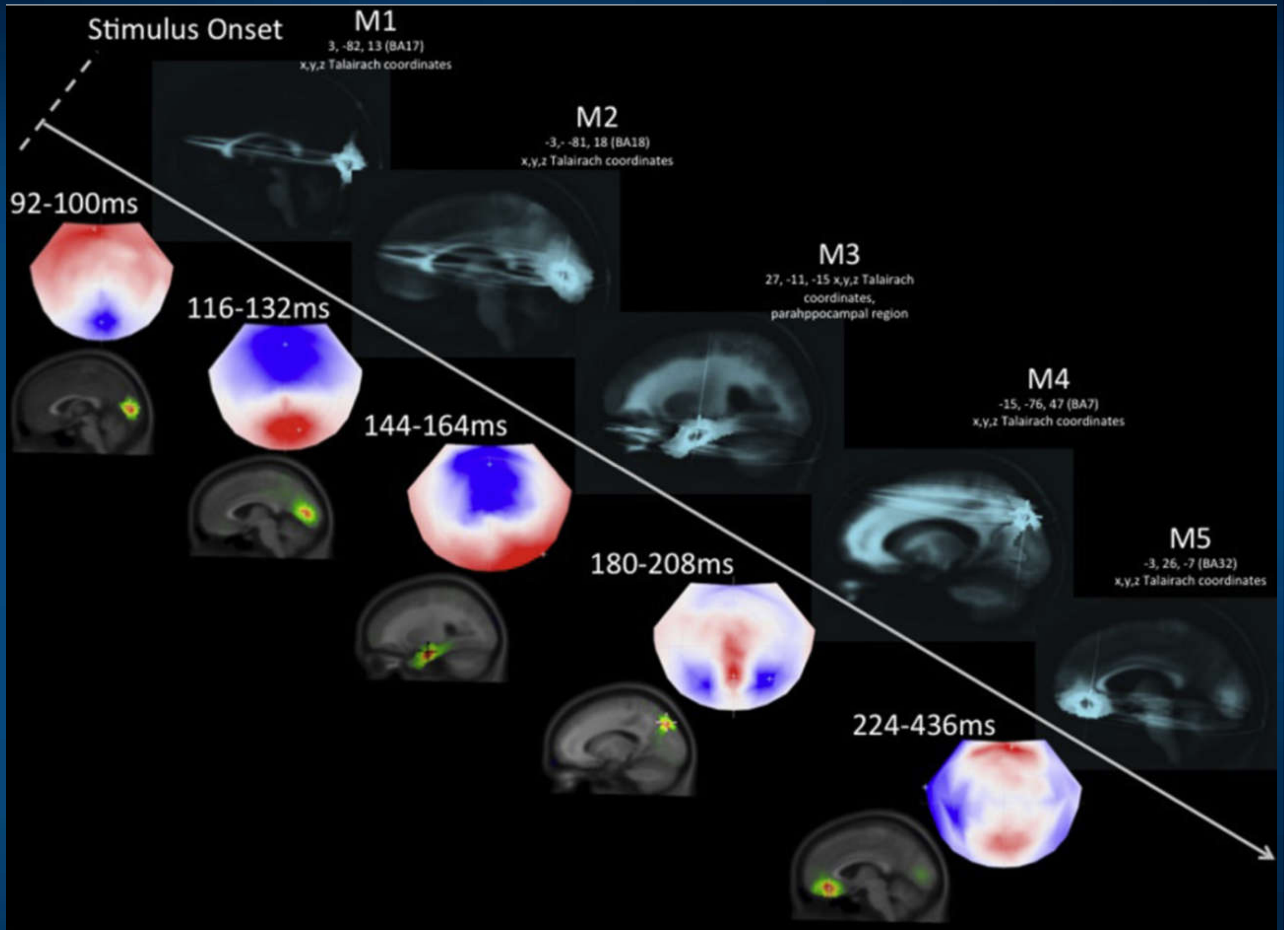
M1 => V1

M2 => V2

M3=>Para-
hippocampal

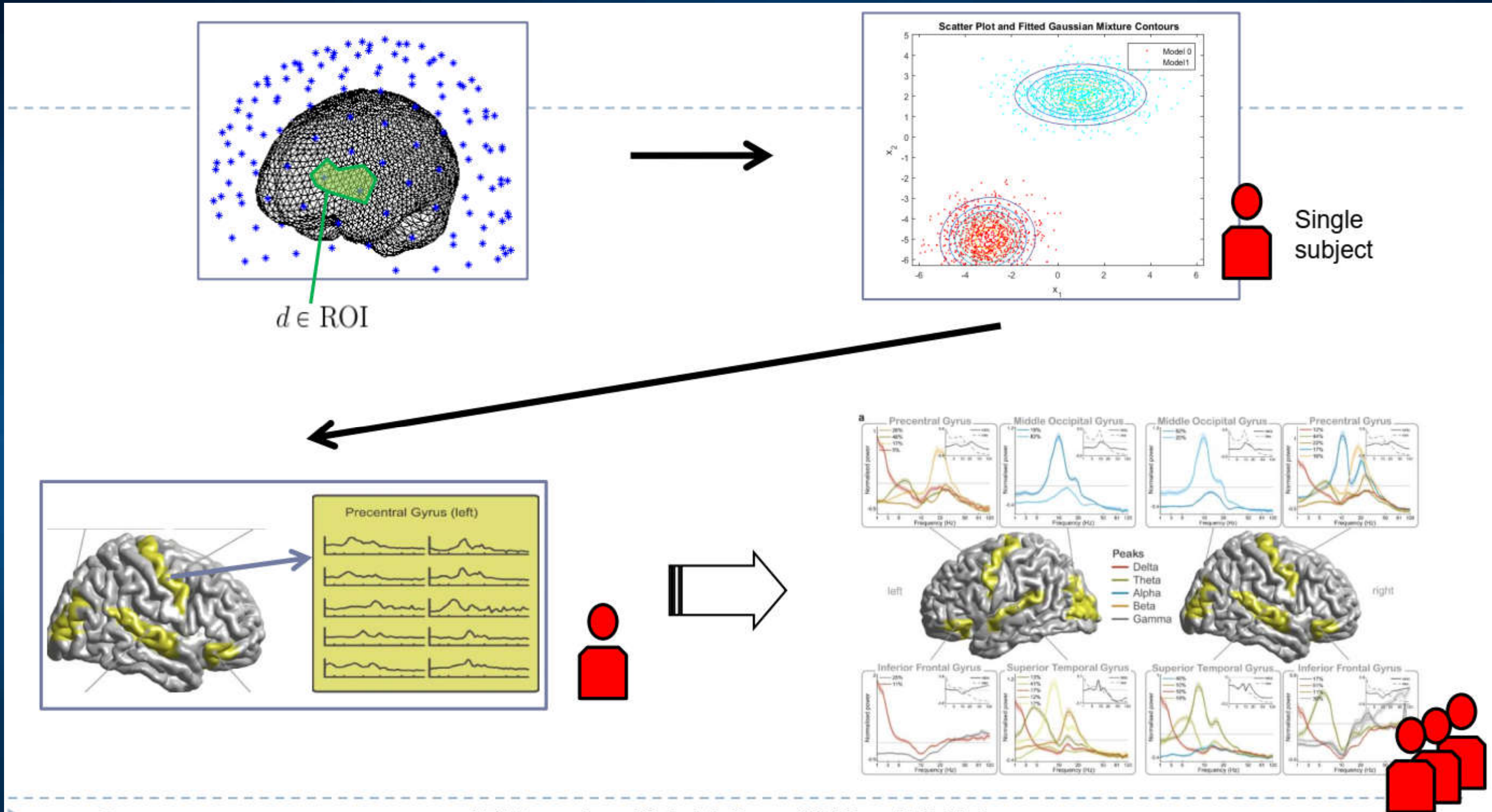
M4=>BA7, left
PC, precuneus

M5=>dACC



Cacioppo, S., Weiss, R. M., Runesha, H. B., & Cacioppo, J. T. (2014). Dynamic spatiotemporal brain analyses using high performance electrical neuroimaging: Theoretical framework and validation. *J. of Neuroscience Methods*, *238*, 11–34.

Spectral fingerprints

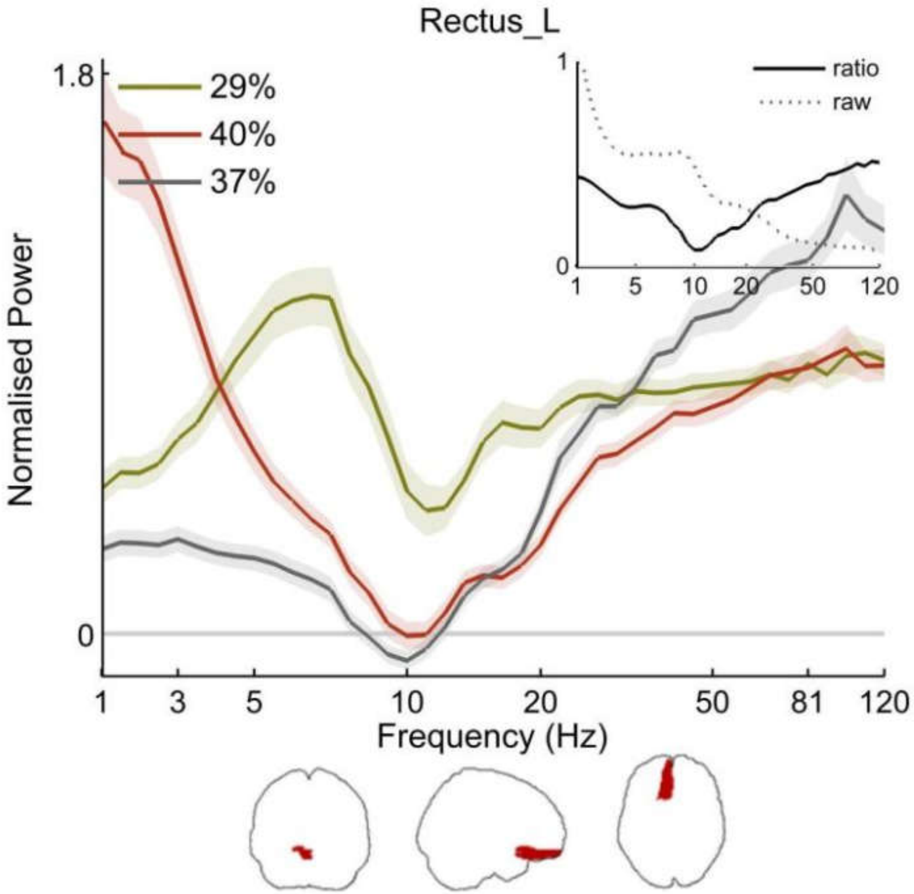


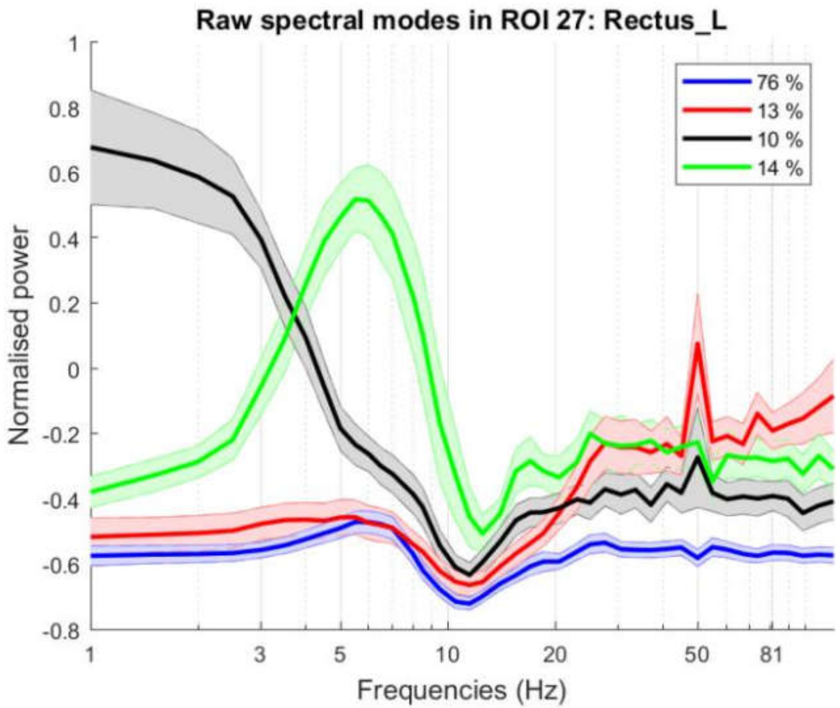
5

* Pictures from Keitel & Gross 2016 and Fieldtrip beamforming tutorial

A. Keitel i J. Gross, „Individual human brain areas can be identified from their characteristic spectral activation fingerprints”, *PLoS Biol* 14(6), e1002498, 2016

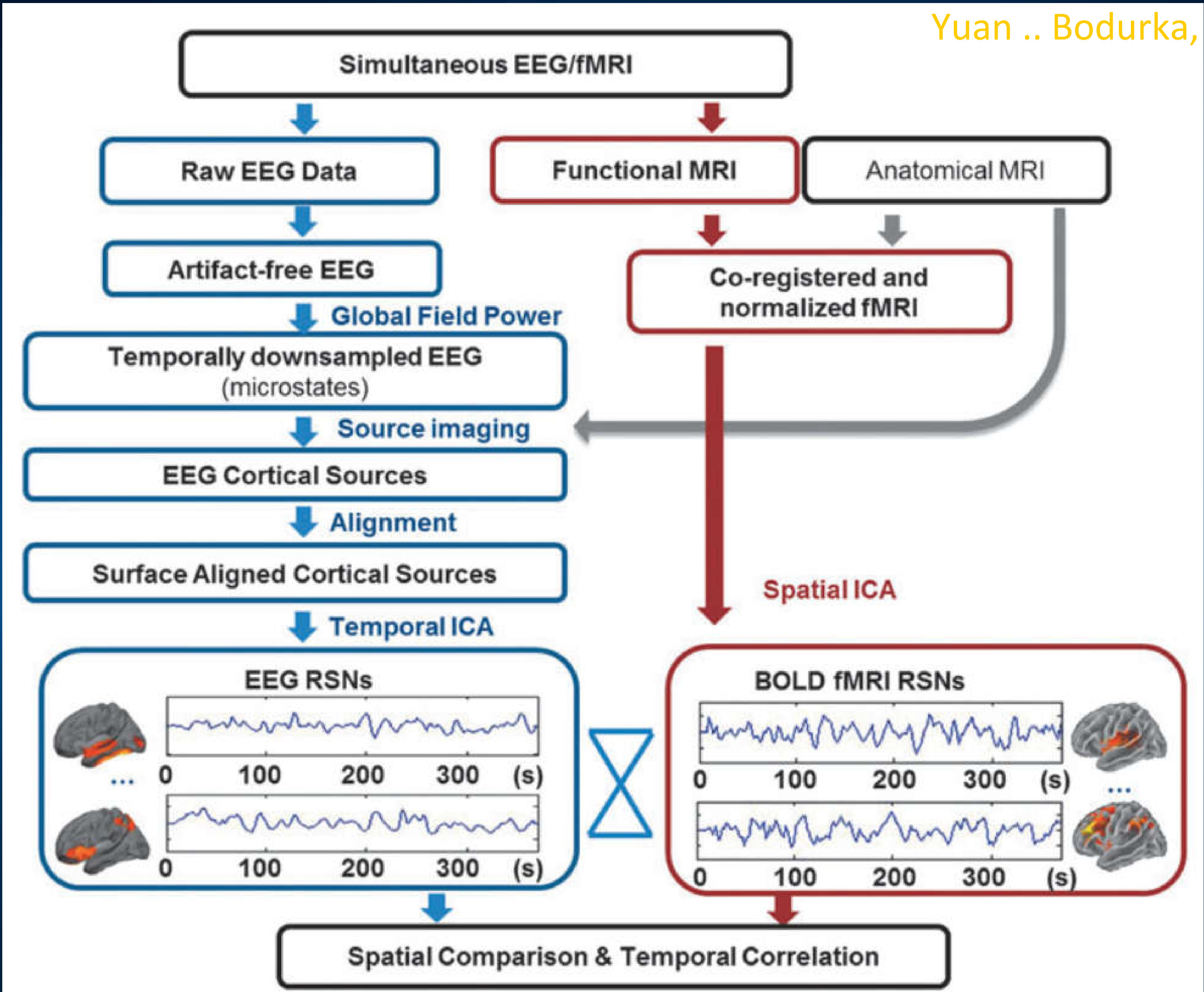
Spectral fingerprints



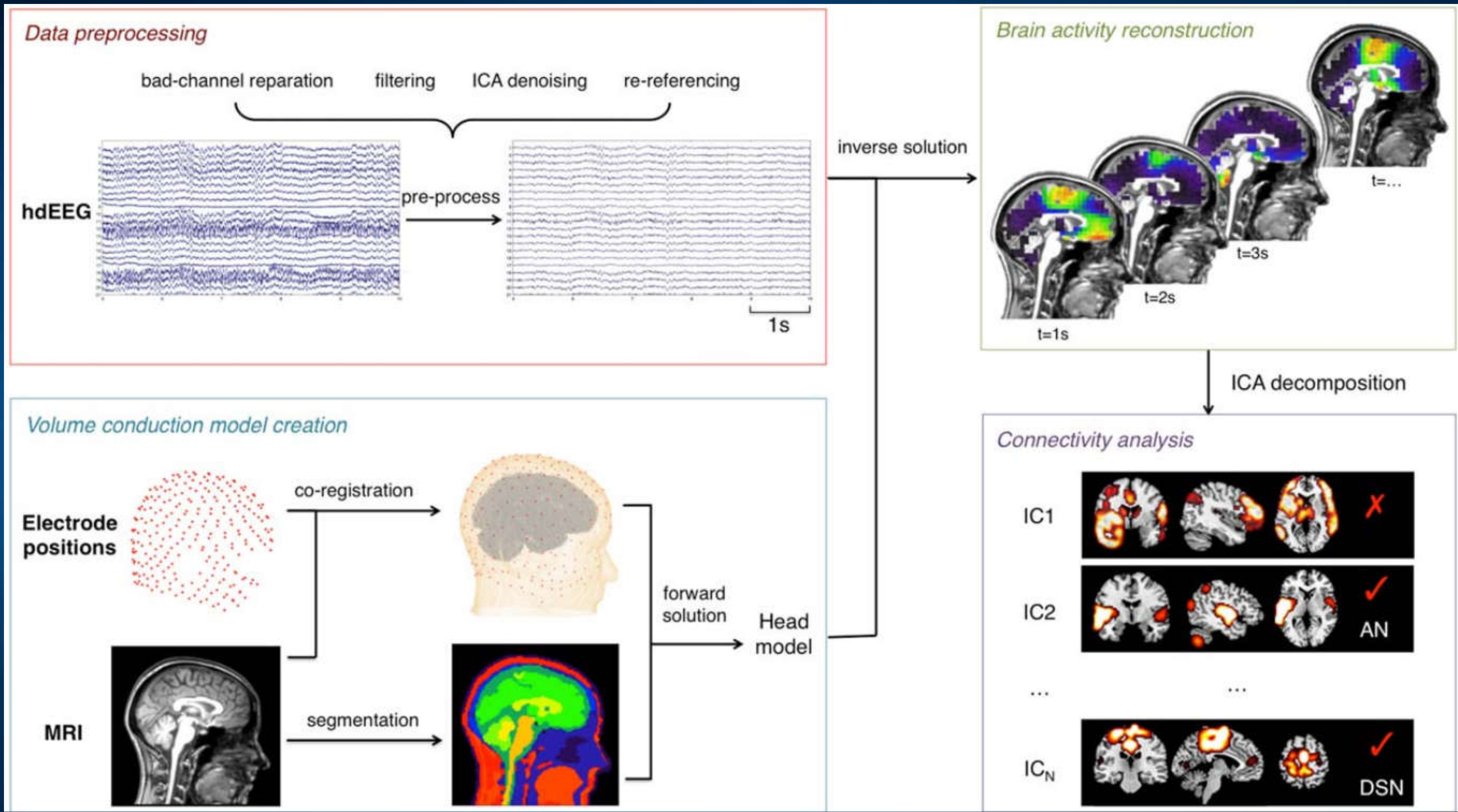


A. Keitel i J. Gross, „Individual human brain areas can be identified from their characteristic spectral activation fingerprints", *PLoS Biol* 14, e1002498, 2016

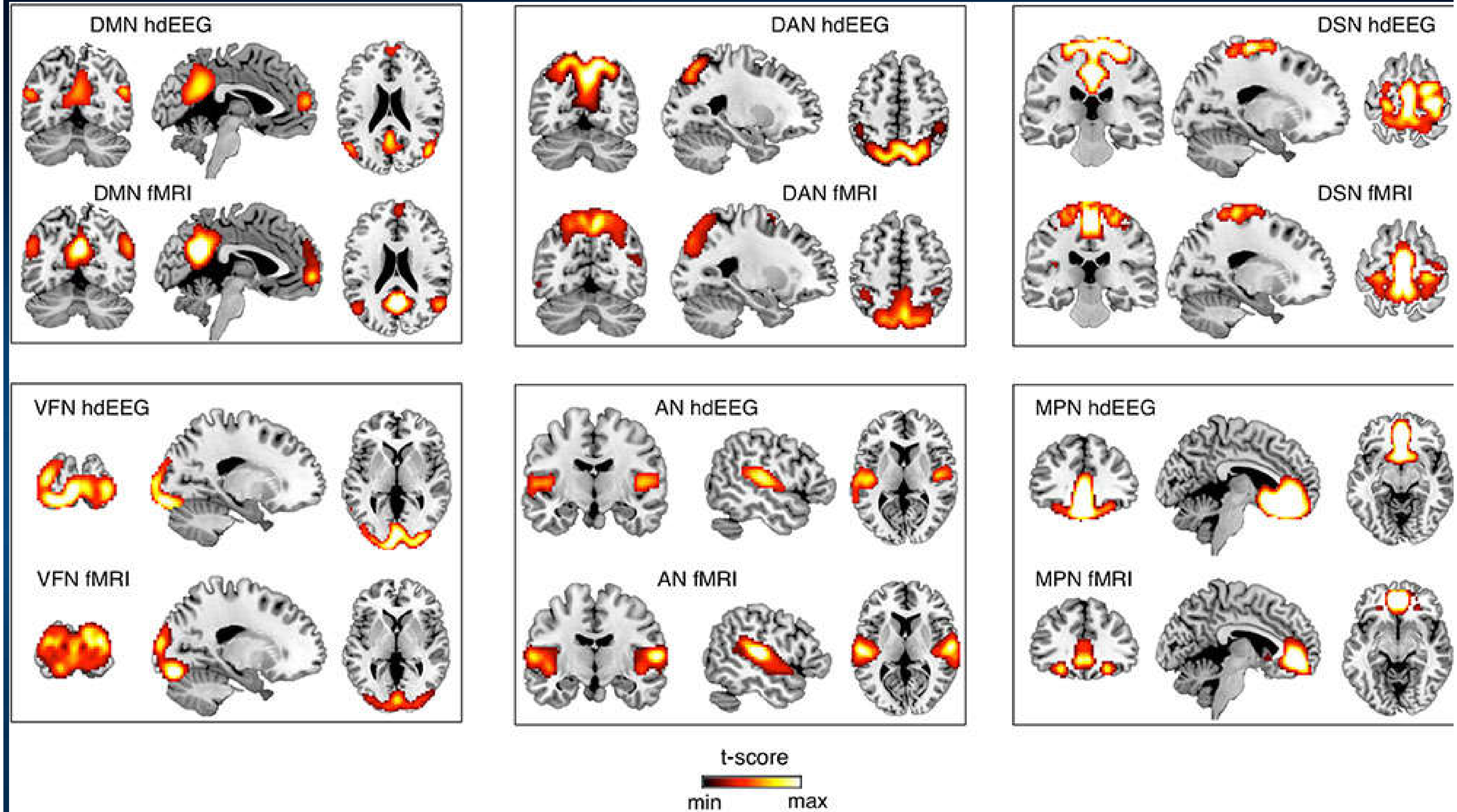
Yuan .. Bodurka, 2015



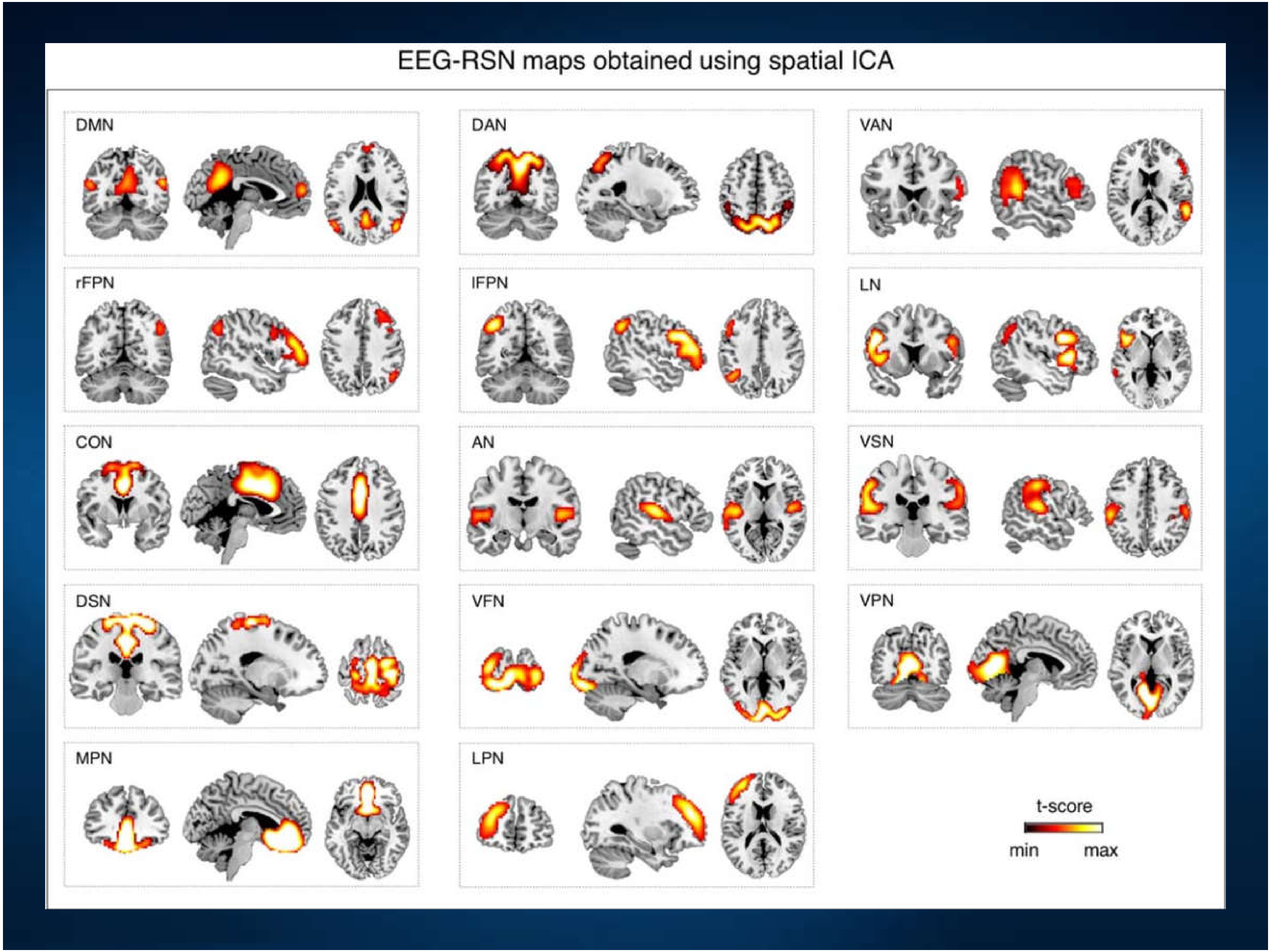
14 networks from BOLD-EEG



Liu et al. Detecting large-scale networks in the human brain. HBM (2017; 2018).

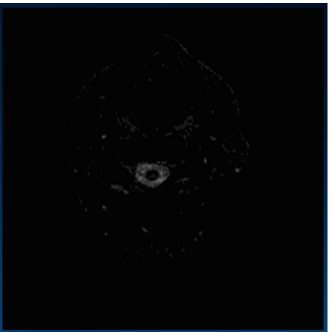


sICA on 10-min fMRI data (N = 24, threshold: $p < 0.01$, TFCE corrected). DMN, default mode network; DAN, dorsal attention network; DSN, dorsal somatomotor network; VFN, visual foveal network; AN, auditory network; MPN, medial prefrontal network.


EEG-RSN maps obtained using spatial ICA
DMN
DAN
VAN
rFPN
lFPN
LN
CON
AN
VSN
DSN
VFN
VPN
MPN
LPN
t-score
min
max

Plan for action - lessons from ASD

1. Focus on neurodynamics. Include ion channels and other biophysical parameters for neurons/networks.
2. Create simulation of normal functions, ex: attention shifts.
3. Catalogue all possible changes in biophysical parameters that lead to specific deregulation of normal behavior, ex: all types of ion channels.
4. Look for dysfunctional proteins related to biophysical parameters, ex: those proteins that build ion channels.
5. Use gene expression atlases to find correlations of proteins with mutations. Explain diversity of mutations and weak disease signals.
6. Predict changes in real brain signals: EEG/MEG, neuroimaging, intracranial …
7. Analyze existing neuroimaging data, functional and anatomical. Perform new experiments to verify proposed mechanisms leading to dysfunctions.
8. Propose close-loop therapies. Psychosomatic pain is a good target.



Perspectives

- Many brain states are now linked to specific mental states, and can be transformed into signals that we can understand: motor intentions, plans, images, inner voices …
- Some large-scale functional networks have reasonable (although still not perfect) interpretation, for example sensory networks, dorsal and ventral attention networks, executive control, motor networks.
- Individual differences and many psychological functions are directly linked to connectome and functional networks, including multistable properties.
- AI/ML draws inspirations from brain research, but also neural network models and learning algorithms (CNN, recurrence networks, reinforcement learning) help to interpret information processing in the brain.
- Many neurocognitive technologies are coming, helping to diagnose, repair and optimize brain processes.

In search of the sources of brain's cognitive activity

Project „Symfonia”, 2016-21

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Maureen Clerc, *Inria*
Carole Goble, *University of Manchester*
William Grisham, *UCLA*
Michael Hawrylycz, *Allen Institute for Brain Science*
Henry Kennedy, *INSERM*
Naomi Penfold, *ASAPbio*
Ariel Rokem, *University of Washington*
Frances Skinner, *University of Toronto*
Pedro Valdes-Sosa, *Cuban Neuroscience Center, University of Electronic Science and Technology China*
Kirstie Whitaker, *University of Cambridge*
Alexander Woodward, *RIKEN CBS*
Jaroslaw Zygierewicz, *University of Warsaw*

Session themes

- Global brain projects: infrastructure interoperability and sustainability
- Data management and workflows in neuroscience
- Future of academic publishing
- Comparative and predictive connectomics
- Brain Computer Interface (BCI)
- Neuroinformatics challenges in behavioral studies
- Building open science communities

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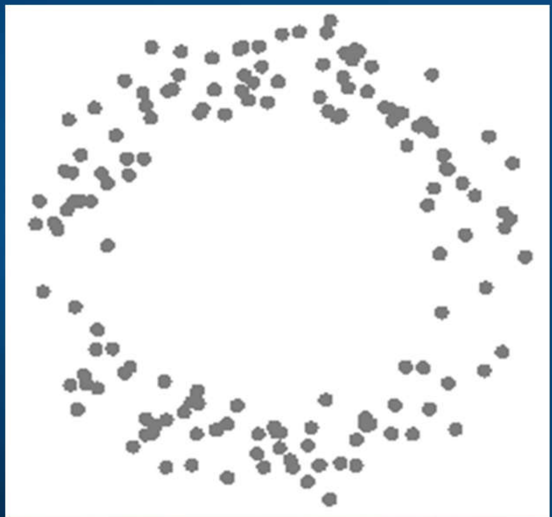
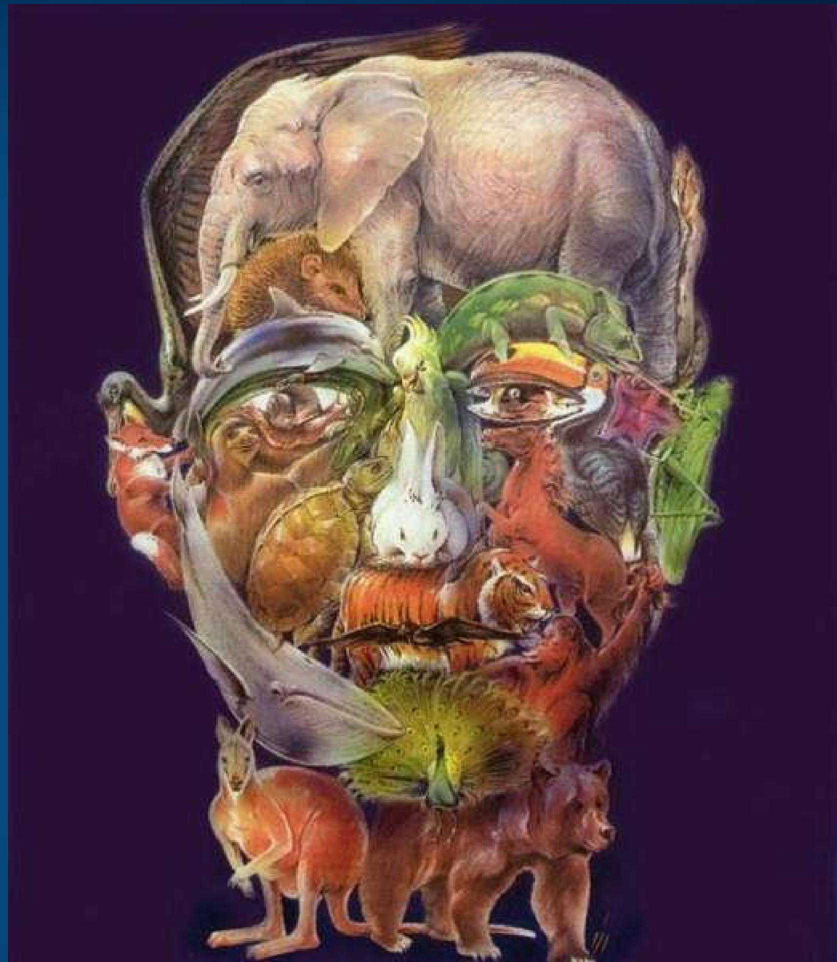
Thank you for synchronization of your neurons





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