Data analysis methods in the neuroscience

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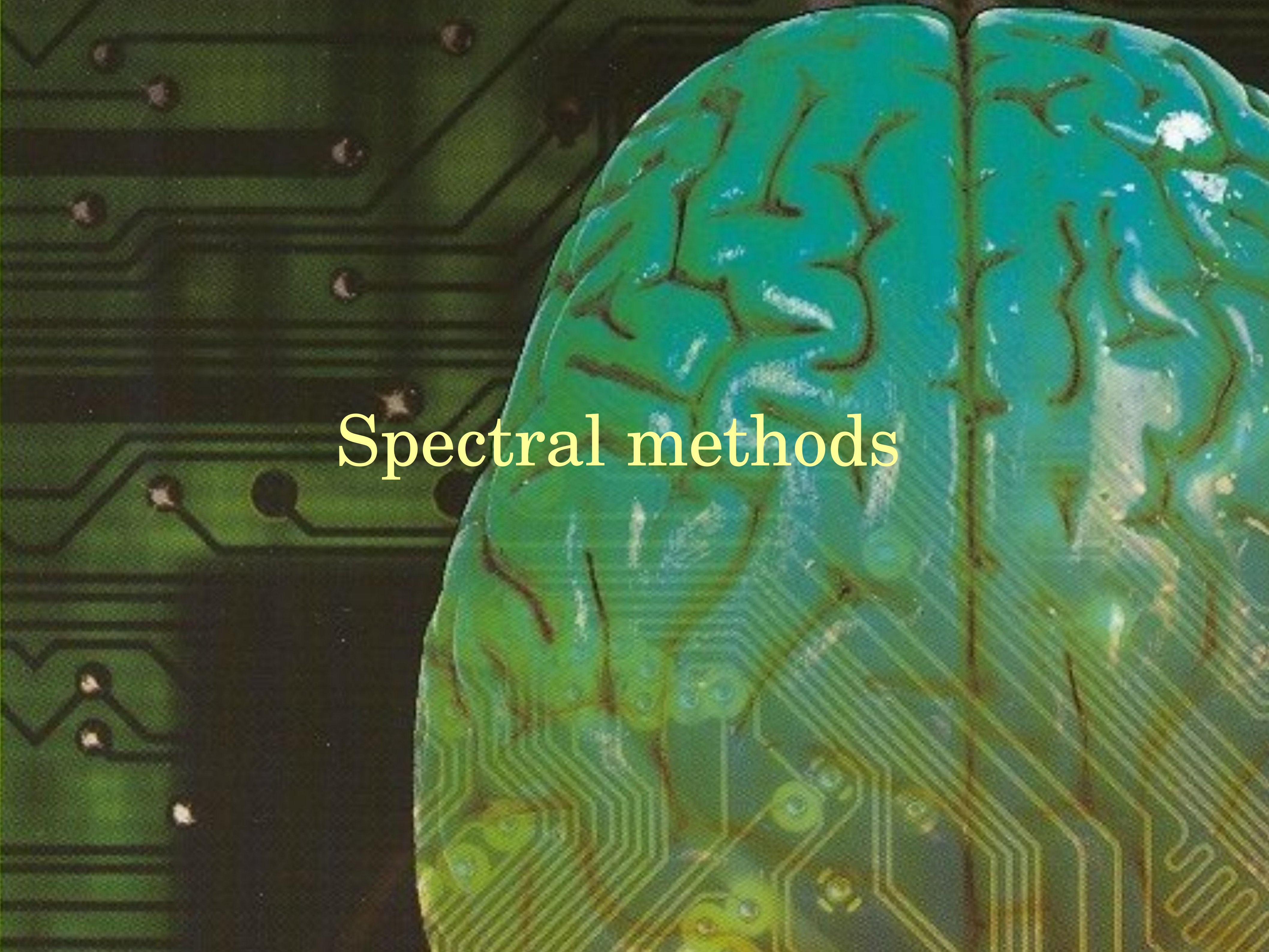


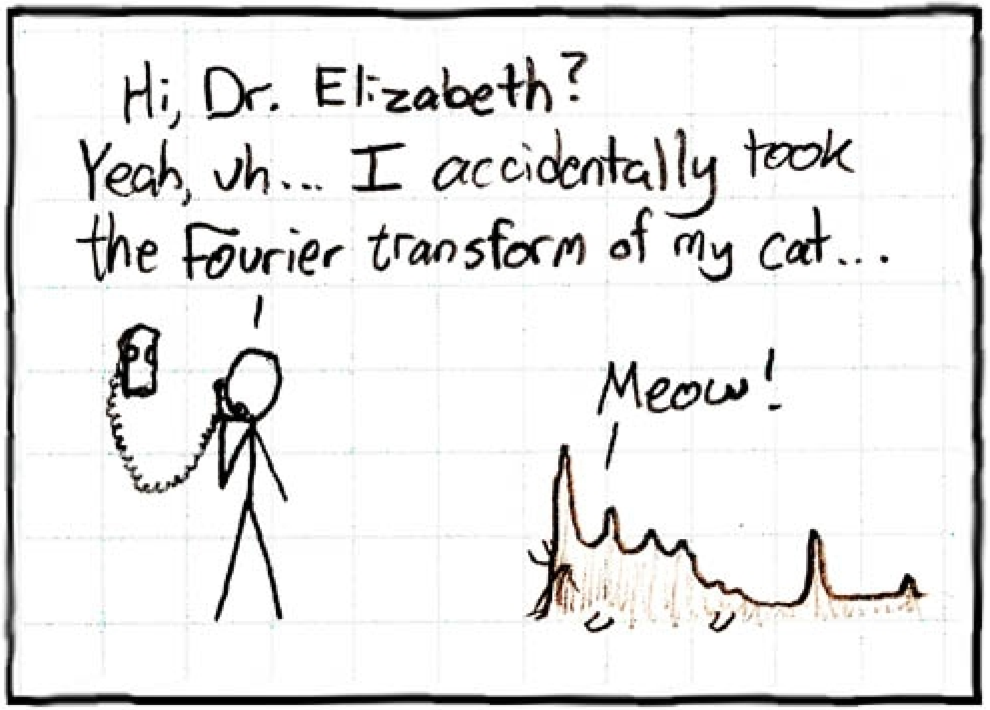
Spectral methods

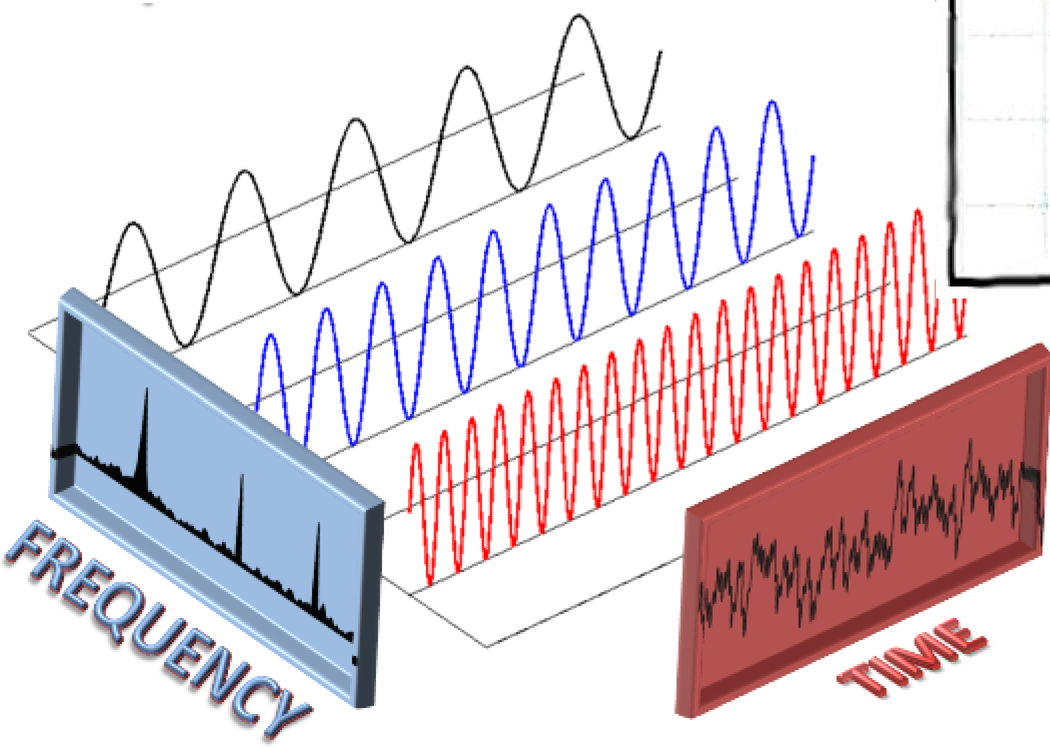

Methods applicable to one time
series

The Fourier transformation

$$g(t) = a_0 + \sum_{m=1}^{\infty} a_m \cos\left(\frac{2\pi mt}{T}\right) + \sum_{n=1}^{\infty} b_n \sin\left(\frac{2\pi nt}{T}\right)$$

$$= \sum_{m=0}^{\infty} a_m \cos\left(\frac{2\pi mt}{T}\right) + \sum_{n=1}^{\infty} b_n \sin\left(\frac{2\pi nt}{T}\right)$$





The Fourier transformation

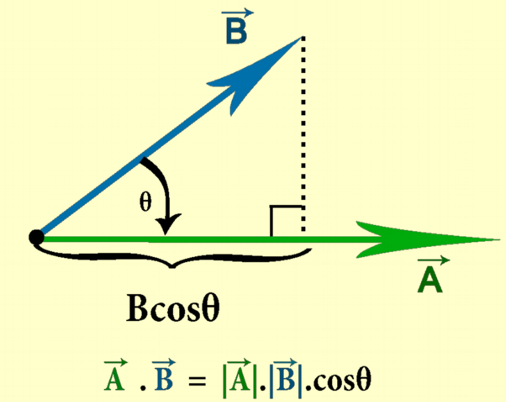
$$\bar{A}\cdot\bar{B} = AB\cos\theta = (A\cos\theta)B = A(B\cos\theta)$$

$$i\cdot i = j\cdot j = k\cdot k = 1; \quad i\cdot j = j\cdot k = k\cdot i = 0;$$

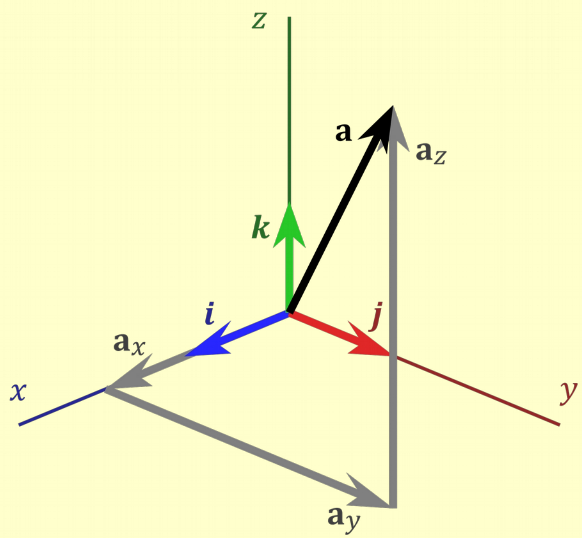
$$\bar{A}\cdot\bar{B} = (A_x i + A_y j + A_z k)\cdot(B_x i + B_y j + B_z k)$$

$$= A_x B_x + A_x B_x + A_x B_x$$

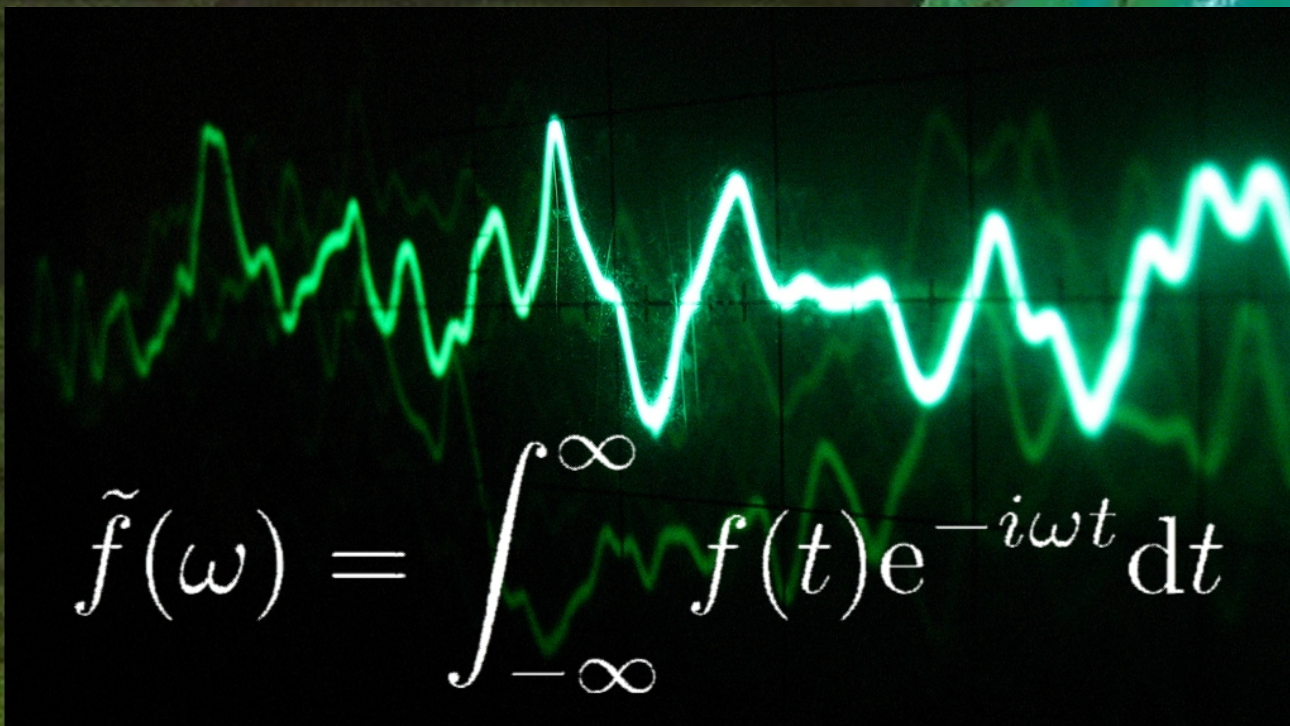
$$\bar{A}\cdot\bar{B} = AB(\hat{e}_A\cdot\hat{e}_B) = AB(1)(1)\cos\theta = AB\cos\theta$$

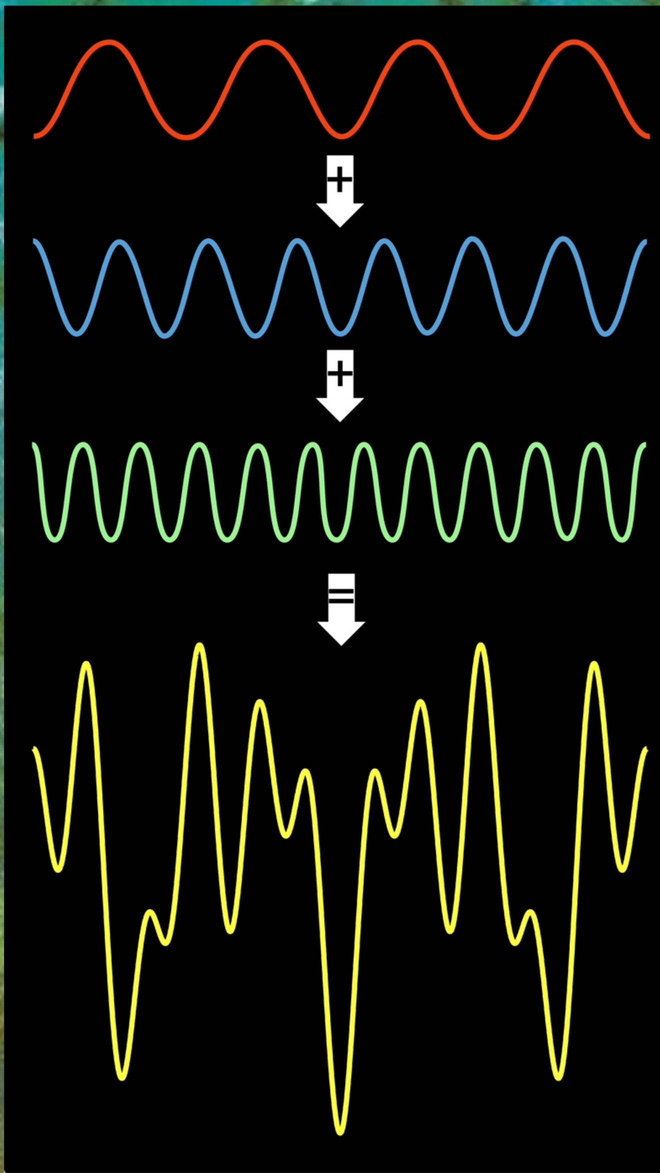


Coordinates: projection (dot product) onto the orthogonal unit vectors (base) of the coordinate system



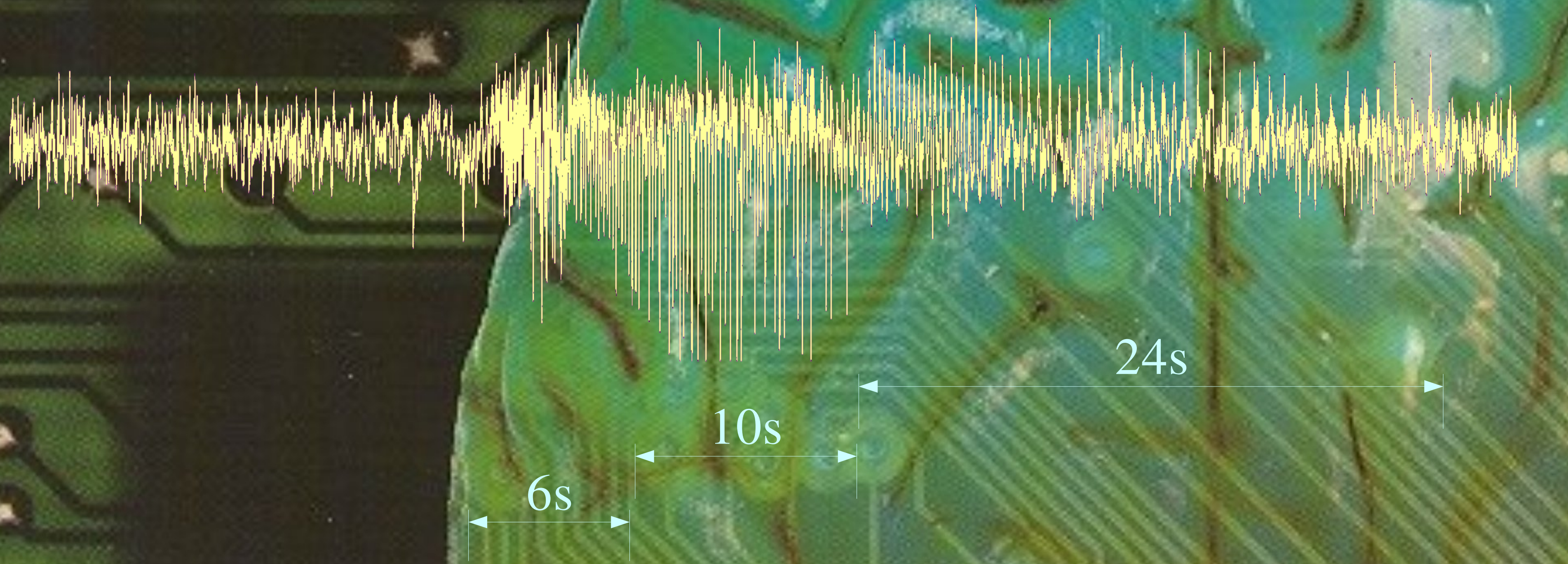
The Fourier transformation





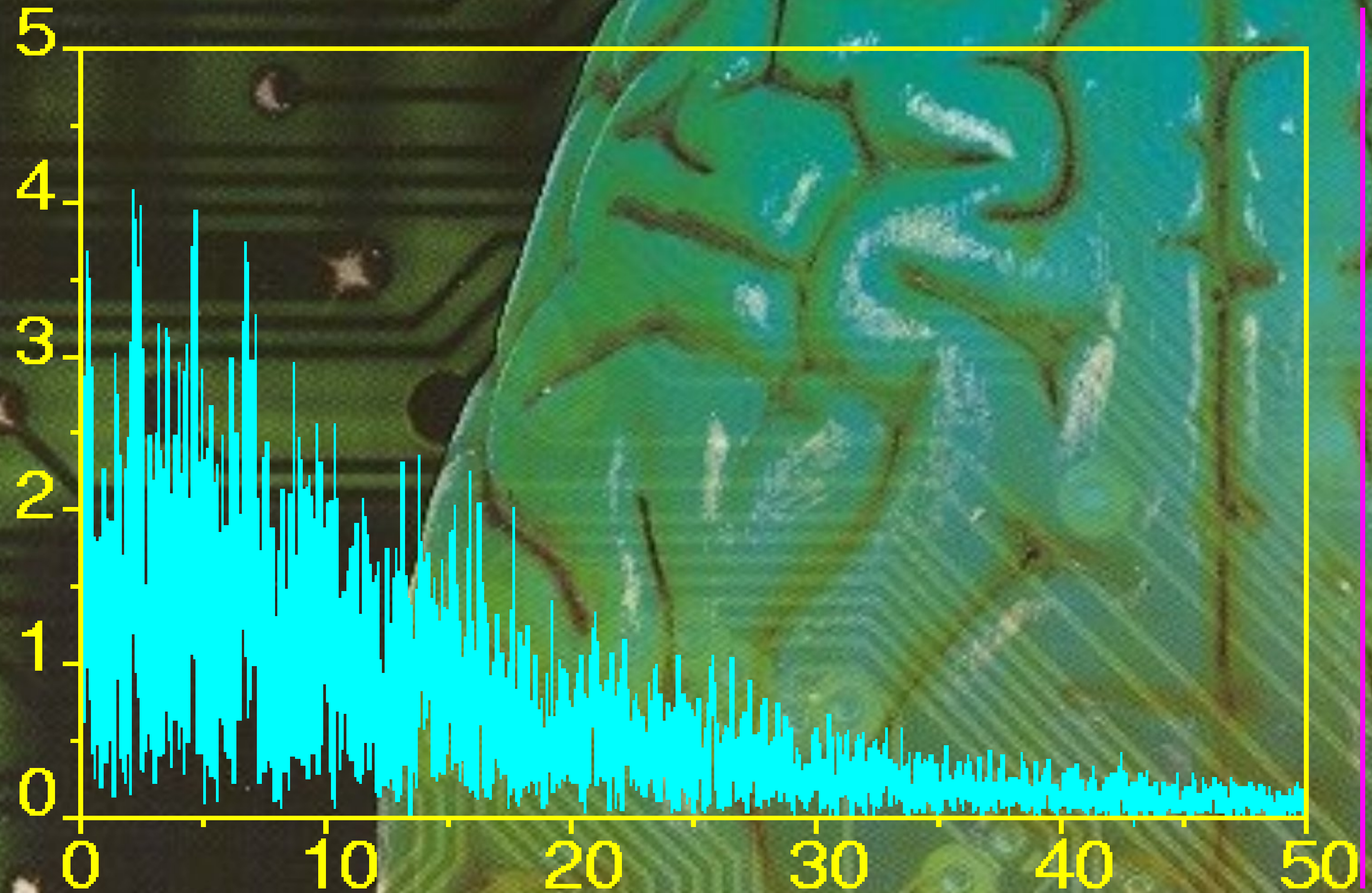
Example: Slow dynamics of the epileptic seizure

An experimental epilepsy model: Generalized epilepsy evoked by local application of 4-Aminopyridin, ECoG:



Three phases of the seizure can be distinguished, based on amplitudes, frequencies and waveforms.

The Fourier spectrum



Frequency (Hz)

The Fourier spectrum

What about the frequency axis? How do we know, which spectrum element conrresponds to which frequency?

We need the sampling frequency: F, measured in Hertz.
The length of the Fourier spectrum is equal to the length of the original data set: N samples
The total length of the recording in sec is T=N/F

The N-th spectrum line corresponds to the sampling frequency: F
Note: the spectrum is meaningfull only until F/2, the Nyquist frequency.
F/2 is the maximal frequency which could be mesured by F sampling frequency.

Thus the frequency step, or the unit of the frequency axis is F/N=1/T

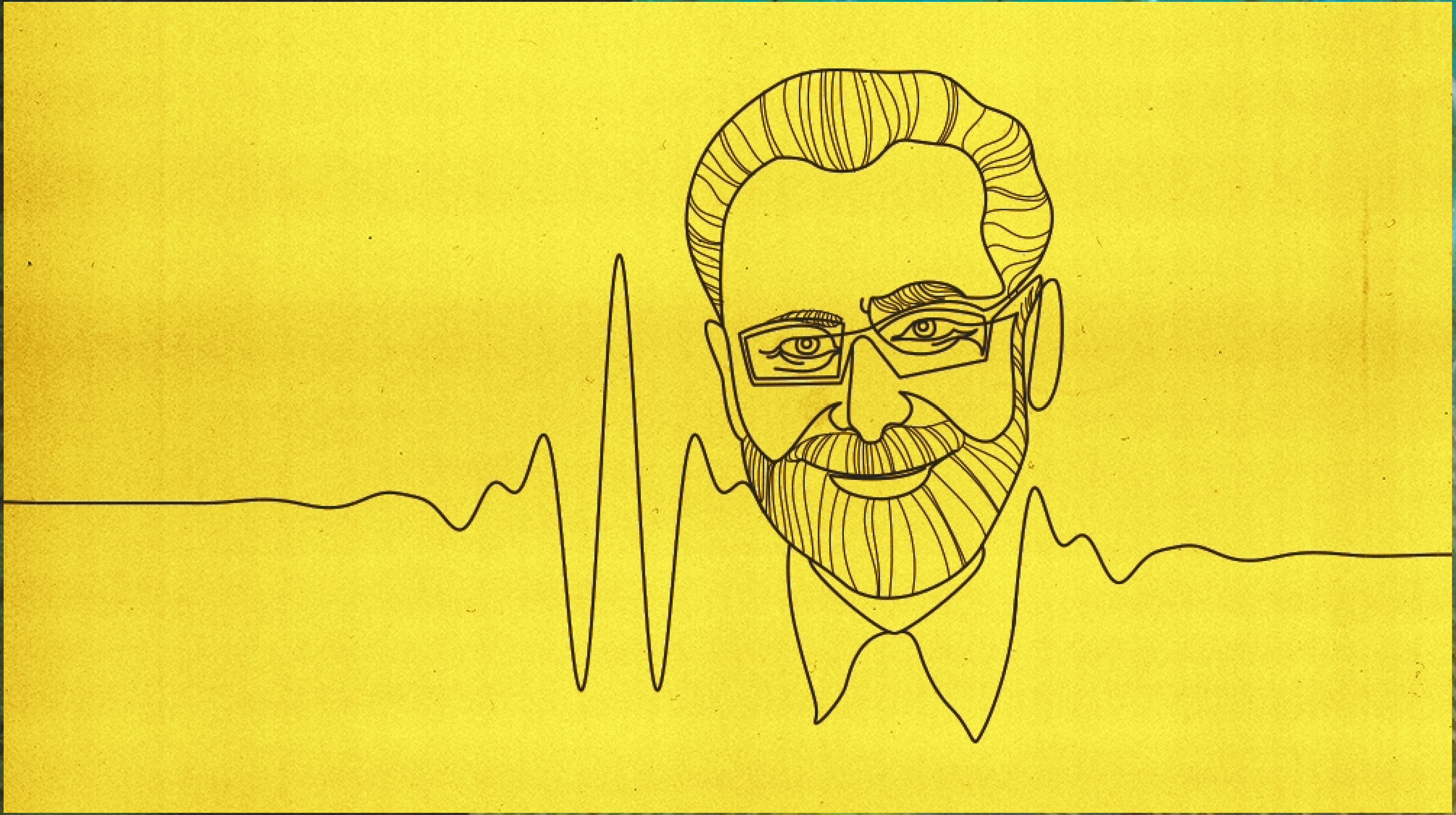
The Fourier spectrum

Fine details:

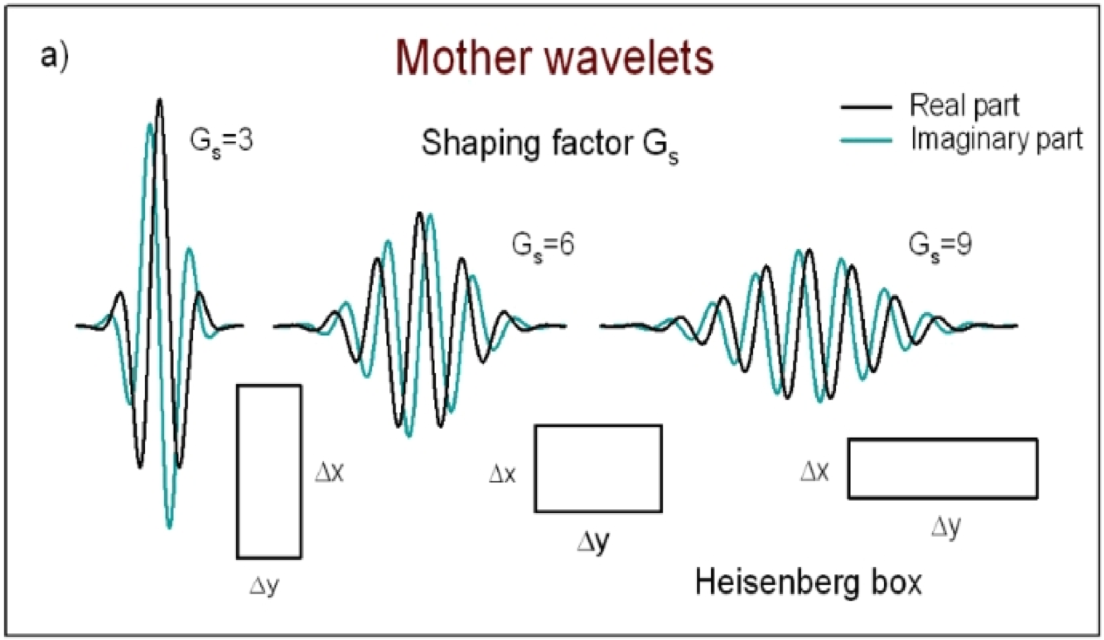
- The results of the FFT algorithm is a vector of complex numbers of length N.
- Real part corresponds to the cosine, the imaginary part for the sine functions. From their ratio, a phase can be calculated for all frequencies.
- The square of the absolute value is the power spectrum.
- The first element of the spectrum is the 0 frequency, the offset constant or mean of the data series. It breaks the symmetry, as it only appears at the lower end of the spectrum.
- The real part of the rest N-1 element is symmetrical, the imaginary part is antisymmetrical.
- The frequencies above N/2 are also called negative frequencies, and can be drawn from -F/2 to 0.
- For data series consist of even samples, the Nyquist frequency (F/2) appears only onece in the middle of the spectrum, while for odd samples if appears twice.

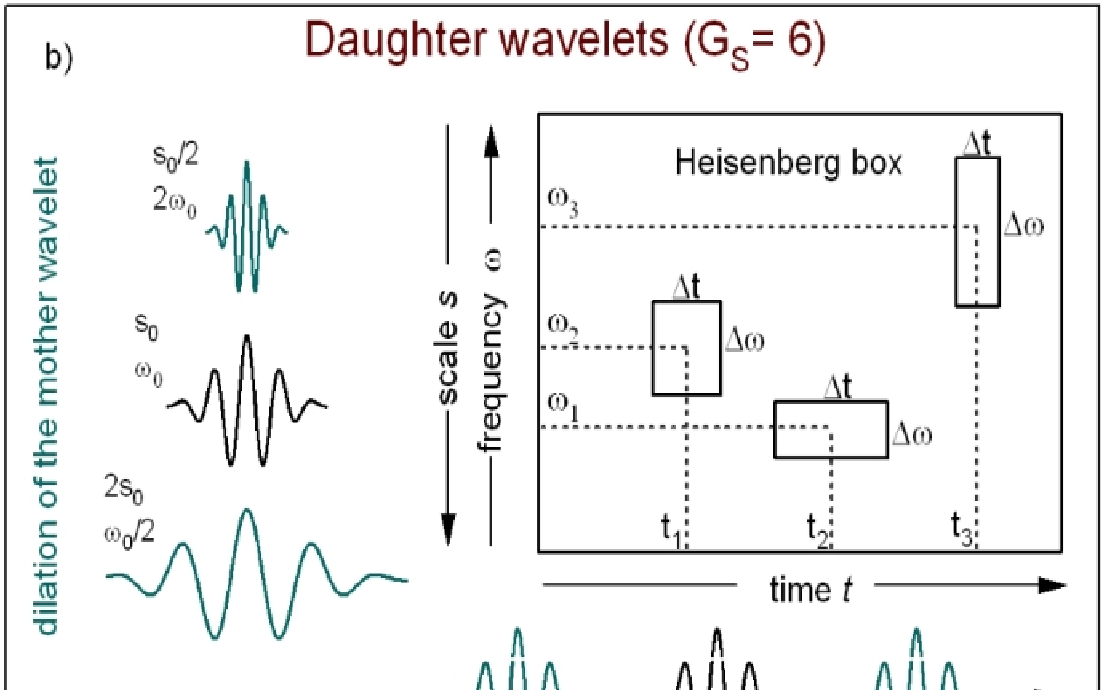
Wavelet-transformation

Ywes Meyer Abel-prize 2017



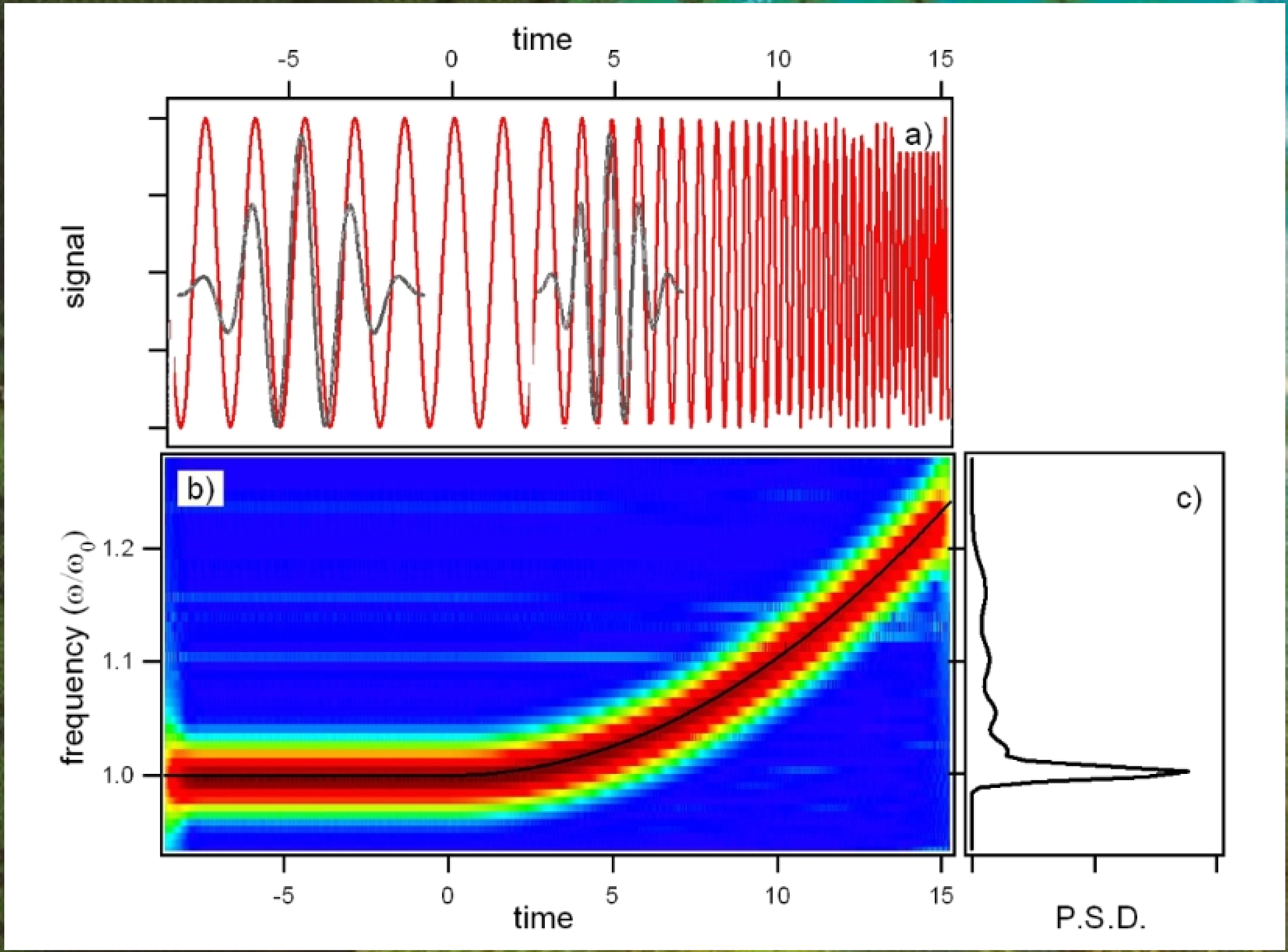
Wavelet-transformation



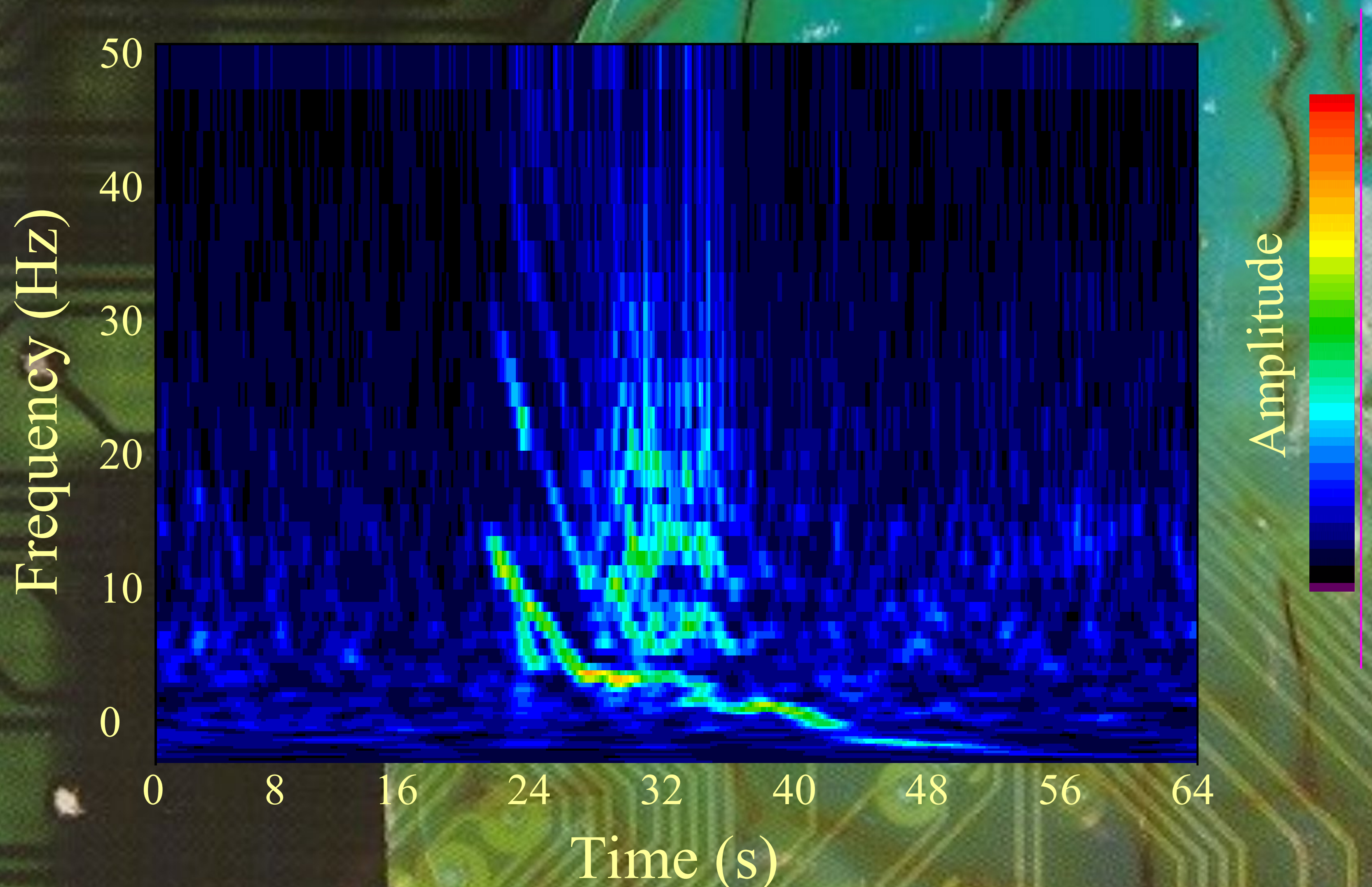


$$\Phi_{s,d}(t) = \frac{1}{\sqrt{s}}\Phi\left(\frac{t-d}{s}\right)$$

Wavelet-transformation

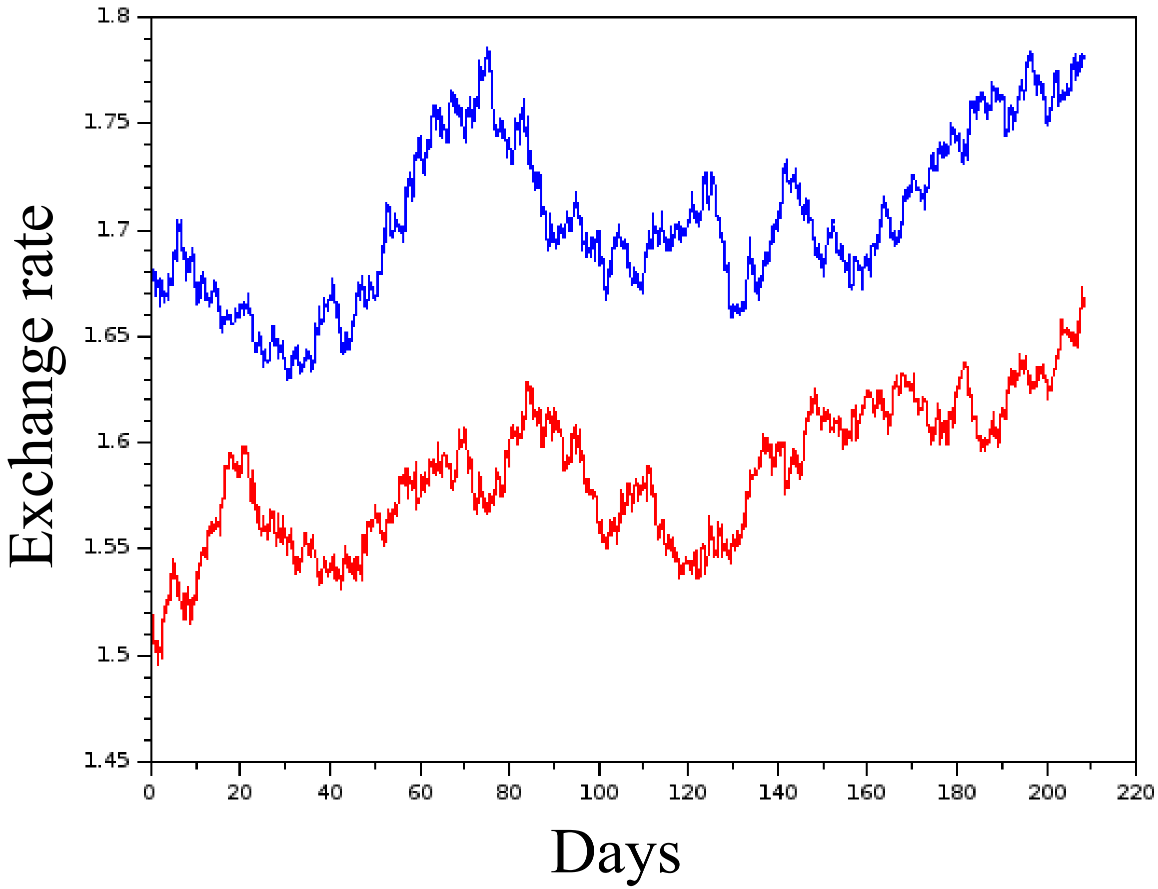


Wavelet-transformation of the ECoG

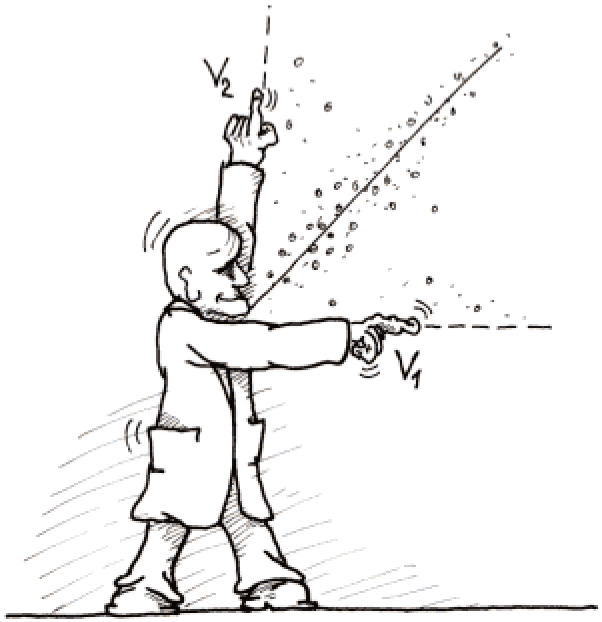


How to find connection between data series?

The traditional method: Correlation
(more precisely, the linear correlation coefficient)



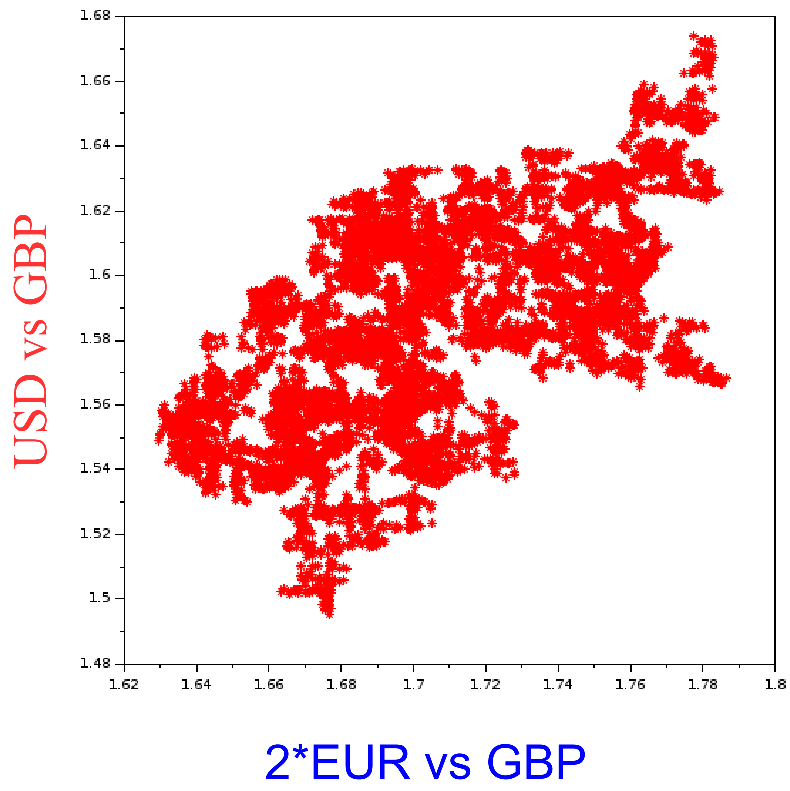
USD vs GBP
2*EUR vs GBP



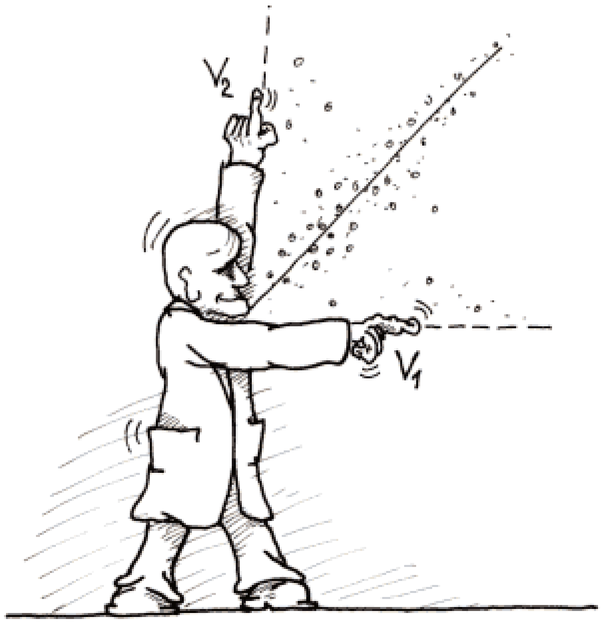
How to find connection between data series?

The traditional method: Correlation
(more precisely, the linear correlation coefficient)

$$r_{xy} = \frac{\sum_{i=1}^{n}(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_{i=1}^{n}(x_i - \bar{x})^2 \sum_{i=1}^{n}(y_i - \bar{y})^2}}$$

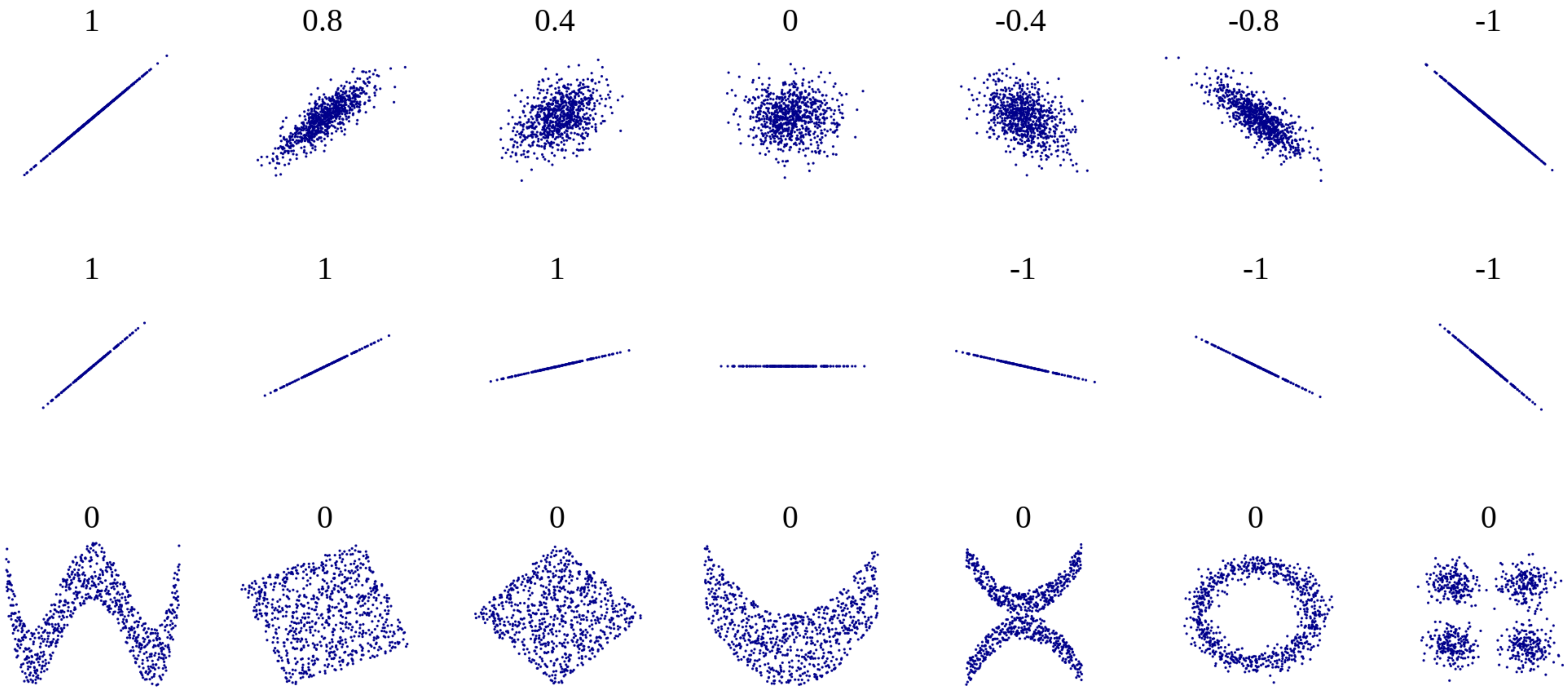


R=0.6

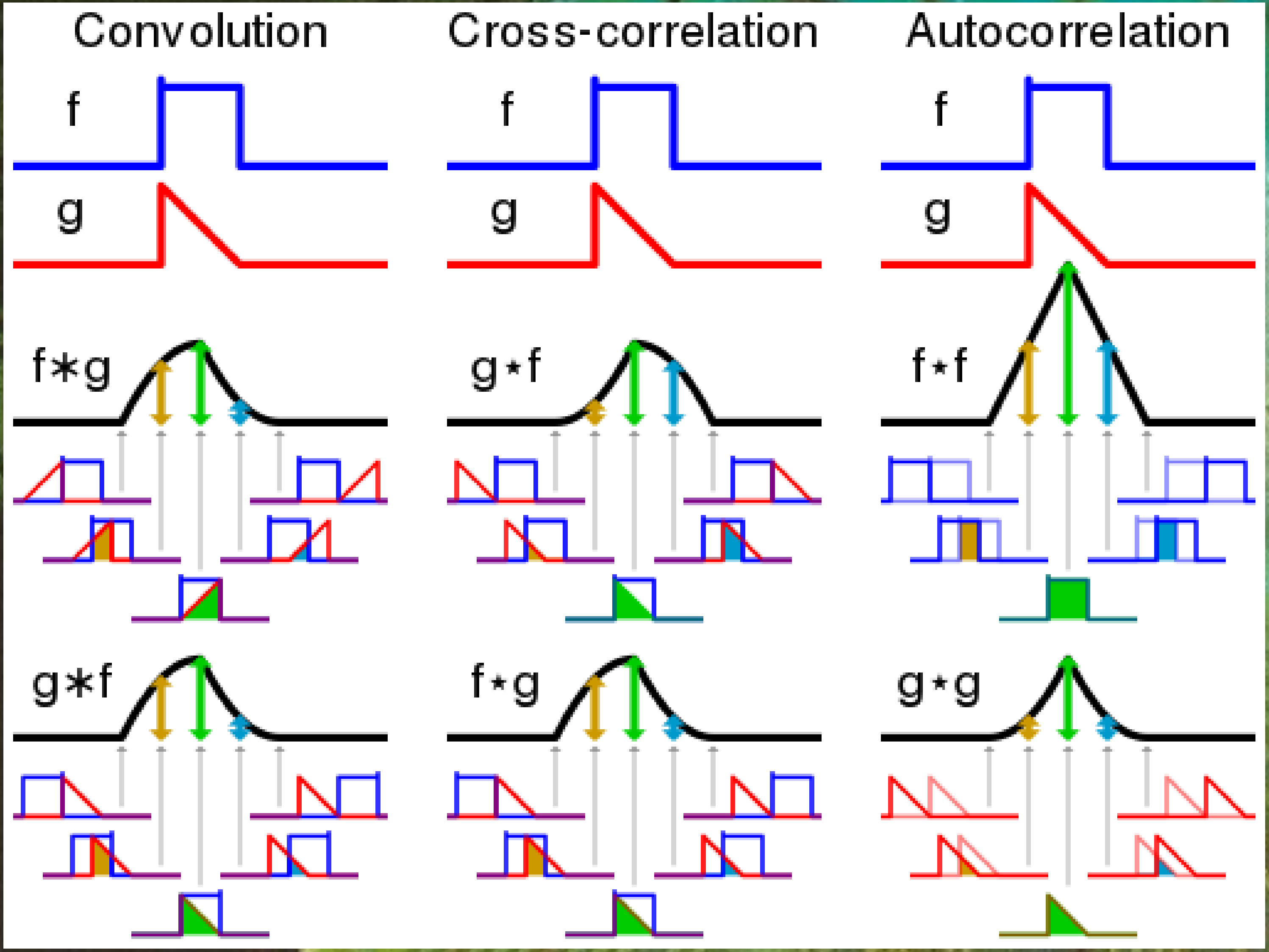


What does the correlation tells us?

Problem 1: it is possible, that there is a clear connection between the two time series, but the correlation is 0 because of the non-linear form of connection.



Convolution, cross- and auto- correlation



Innovative Methodology

J Neurophysiol 92: 600–608, 2004;
10.1152/jn.01170.2003.

Characterization of Neocortical Principal Cells and Interneurons by Network Interactions and Extracellular Features

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Center for Molecular and Behavioral Neuroscience, Rutgers, The State University of New Jersey, Newark, New Jersey 07102

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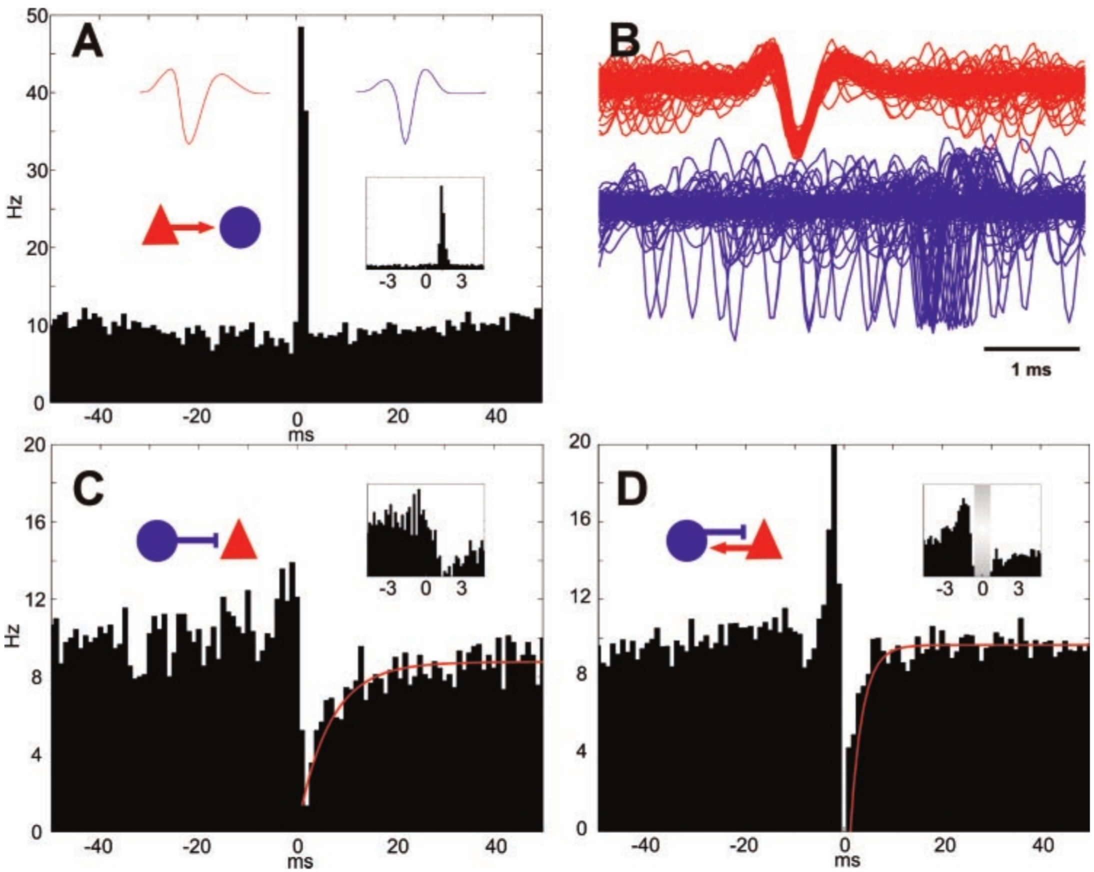

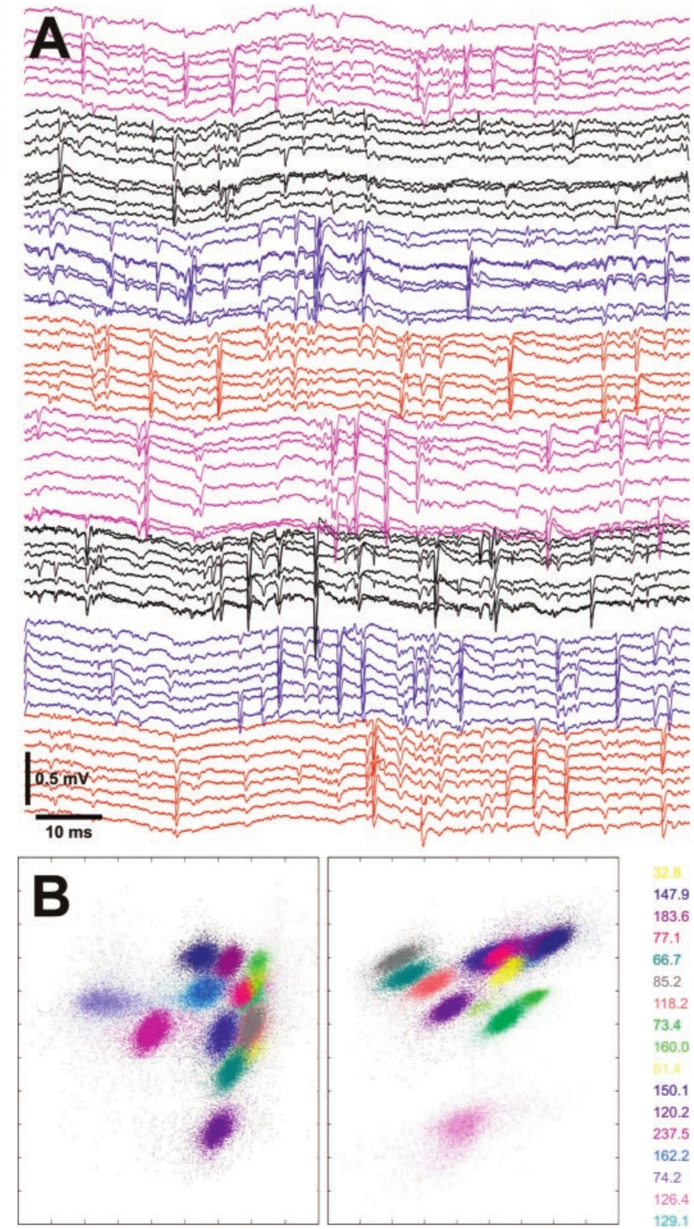

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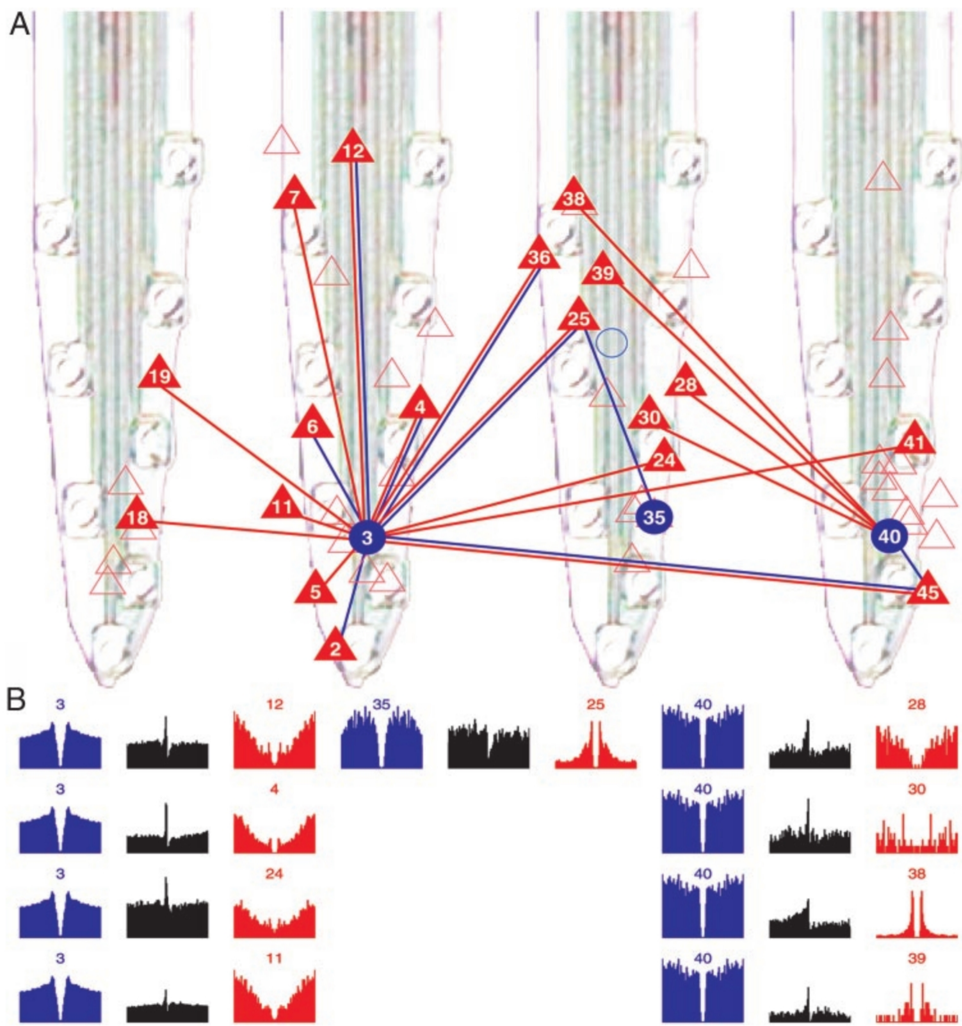
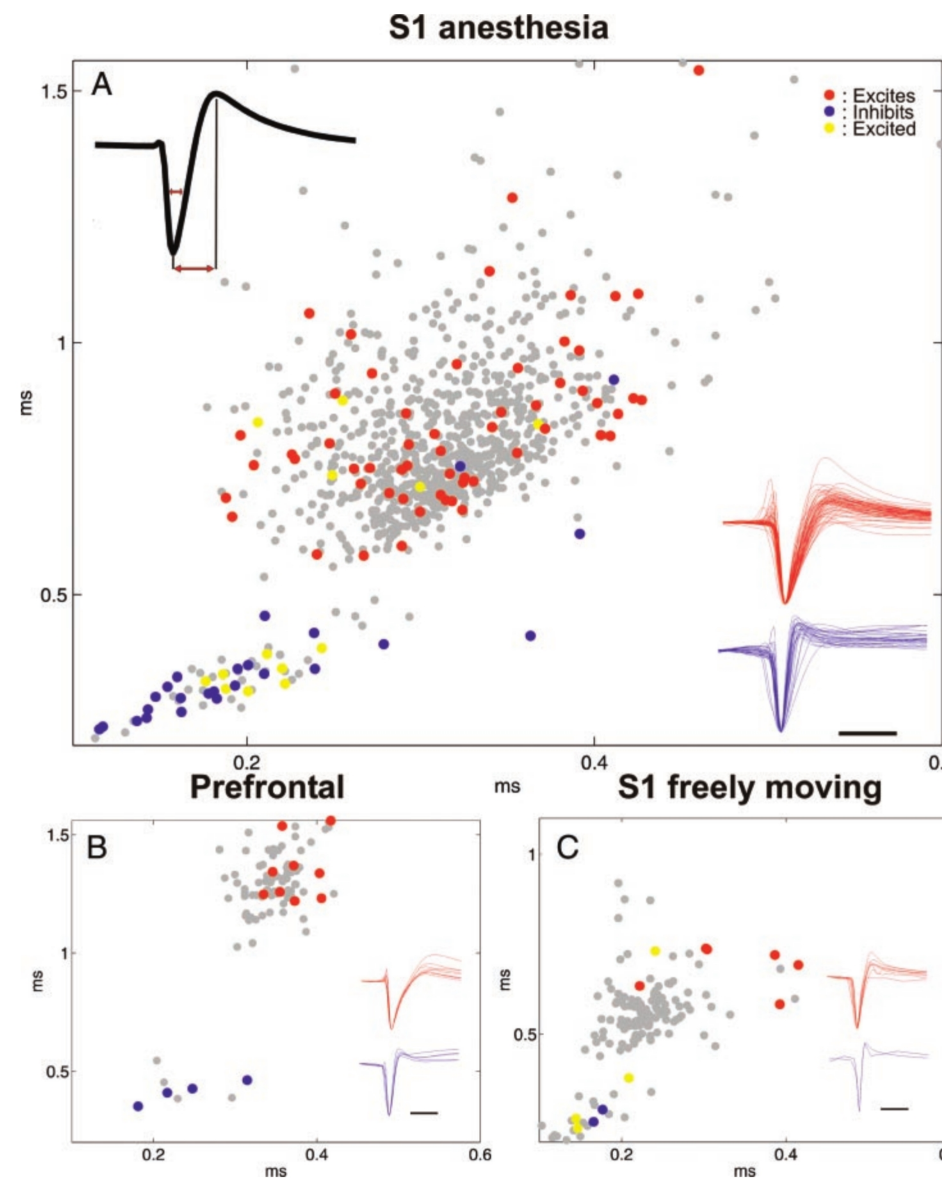
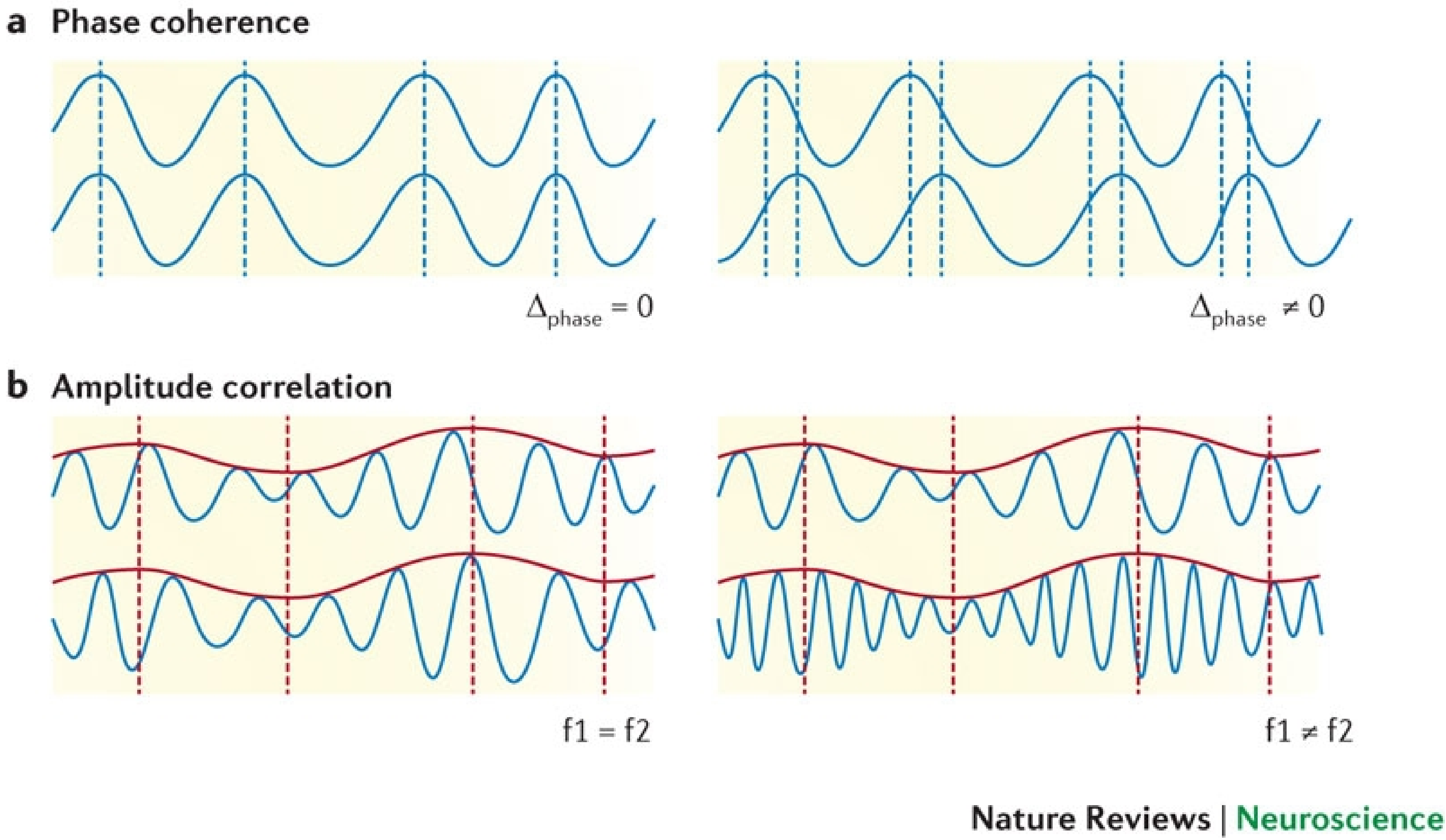




Coherence


a Phase coherence
$\Delta_{phase} = 0$
$\Delta_{phase} \neq 0$
b Amplitude correlation
f1 = f2
f1 ≠ f2
Nature Reviews | Neuroscience

Correlation vs. Coherence

The linear correlation coefficient

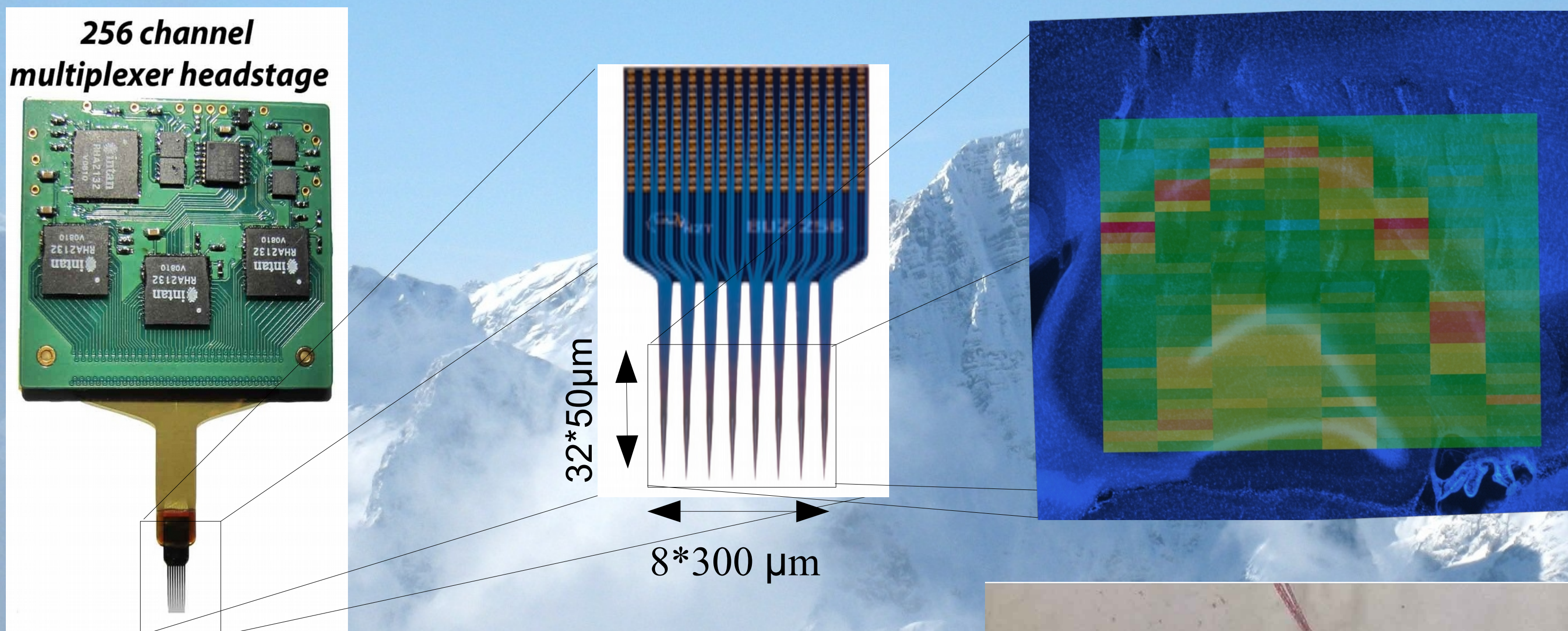
$$r_{xy} = \frac{\sum_{i=1}^{n}(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_{i=1}^{n}(x_i - \bar{x})^2 \sum_{i=1}^{n}(y_i - \bar{y})^2}}$$

Coherence spectrum

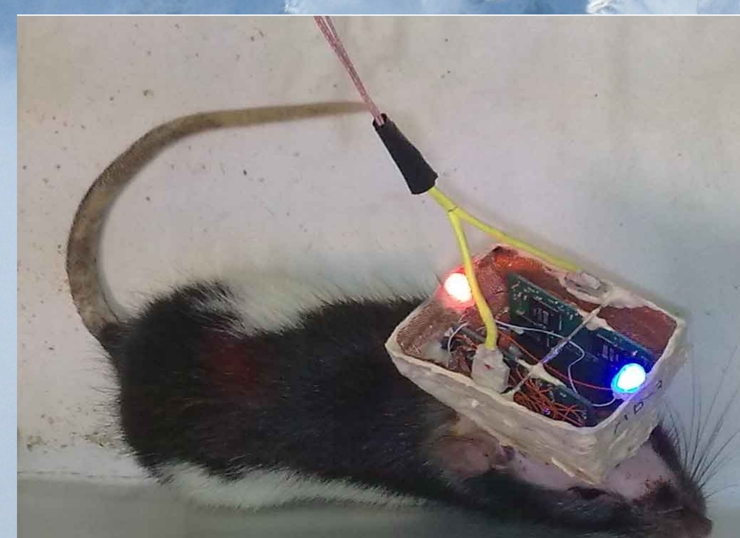
$$Coh(f) = \frac{\left|\sum_{i=1}^{N} F_1(f) \cdot F_2^*(f)\right|^2}{\sum_{i=1}^{N}\left|F_1(f)\right|^2 \cdot \sum_{i=1}^{N}\left|F_1(f)\right|^2}$$

Micro-electro imaging

2 dimensional, 256 channel electrode system



Made possible parallel monitoring of the many subareas of the hippocampus and cc. 100 sorted and identified neurons.

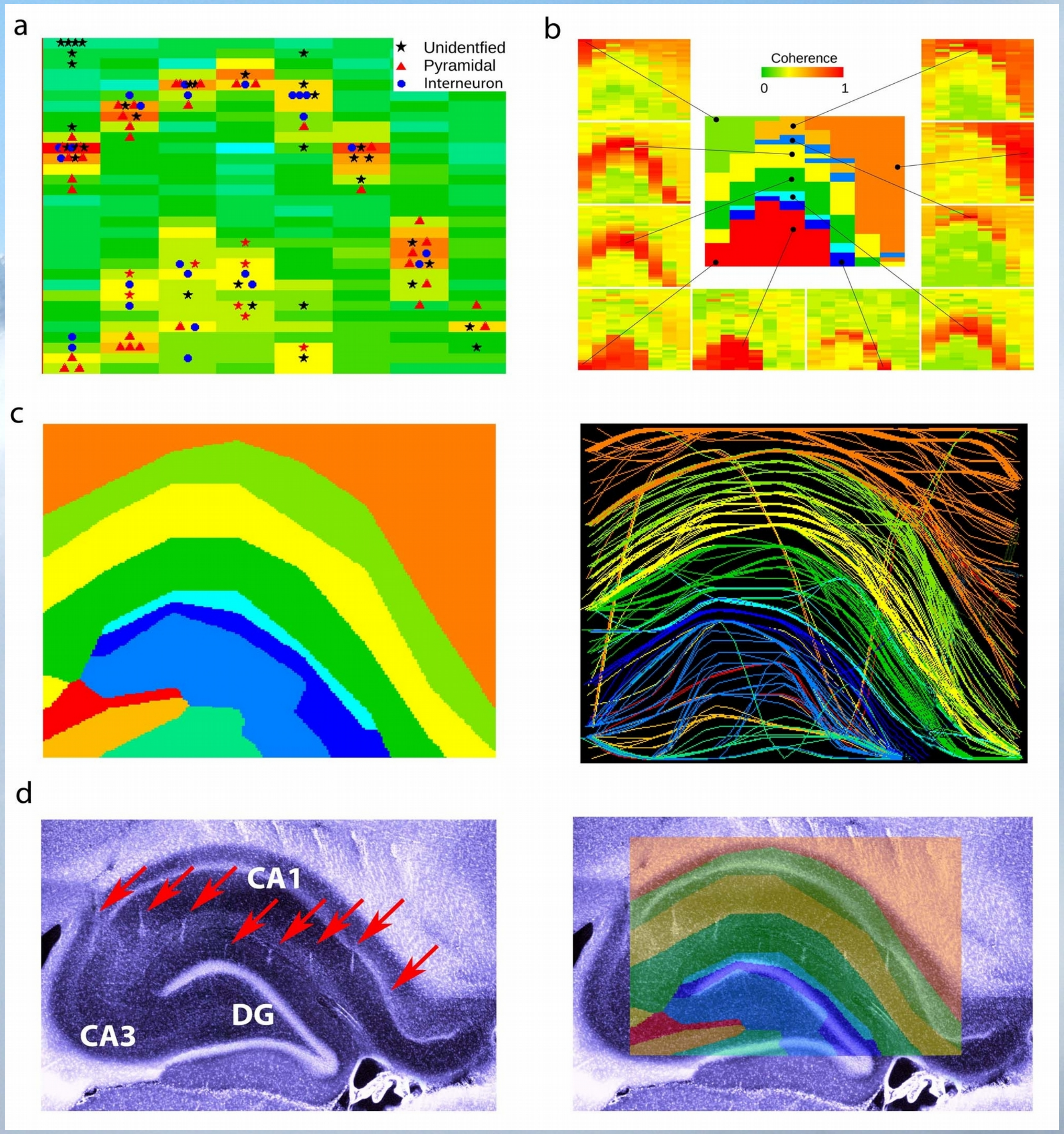


Micro-electro imaging

Micro-electro anatomy

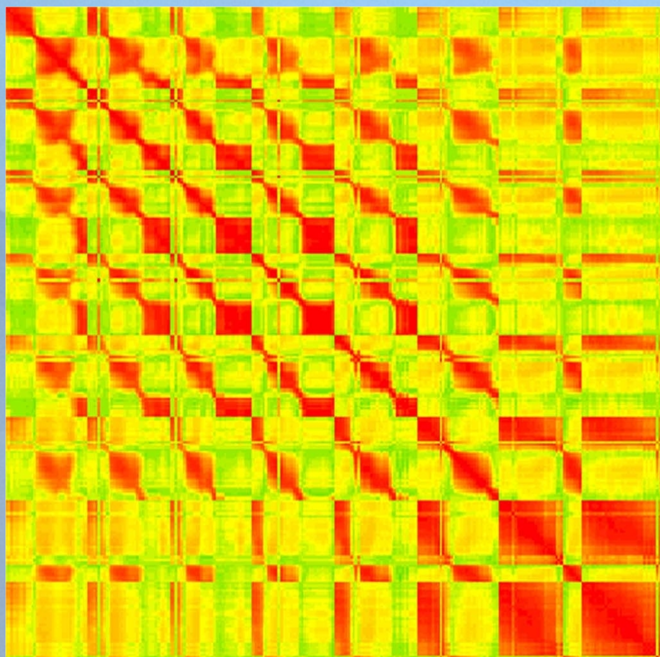
The high frequency power map show the somatic layers, which corresponds to the positions of the sorted individual neuros. The fusion of this high frequency power map with the result of the coherence clustering resulted a detailed layering map of the hippocampus. This electro-anatomical map corresponded well to the tissue histology.

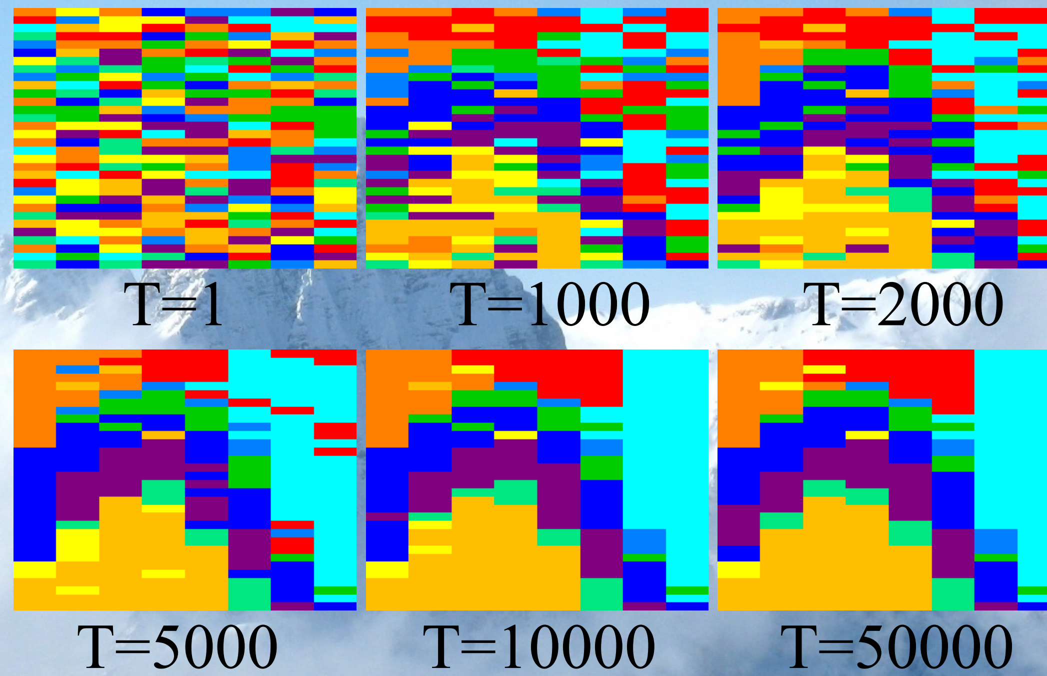
Berényi et al. J Neurophysiology 2014



Micro-electro imaging

Micro-electro anatomy

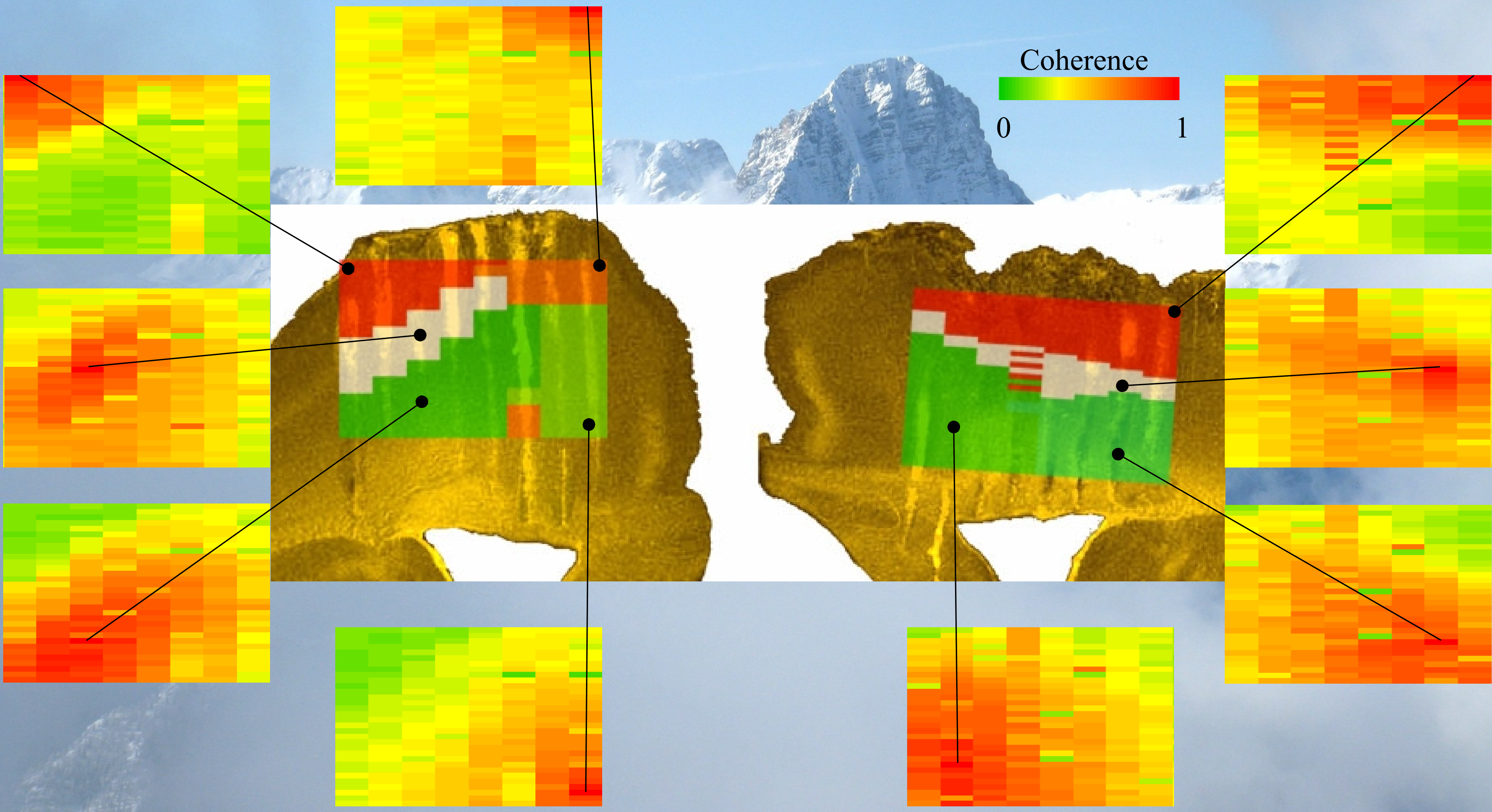




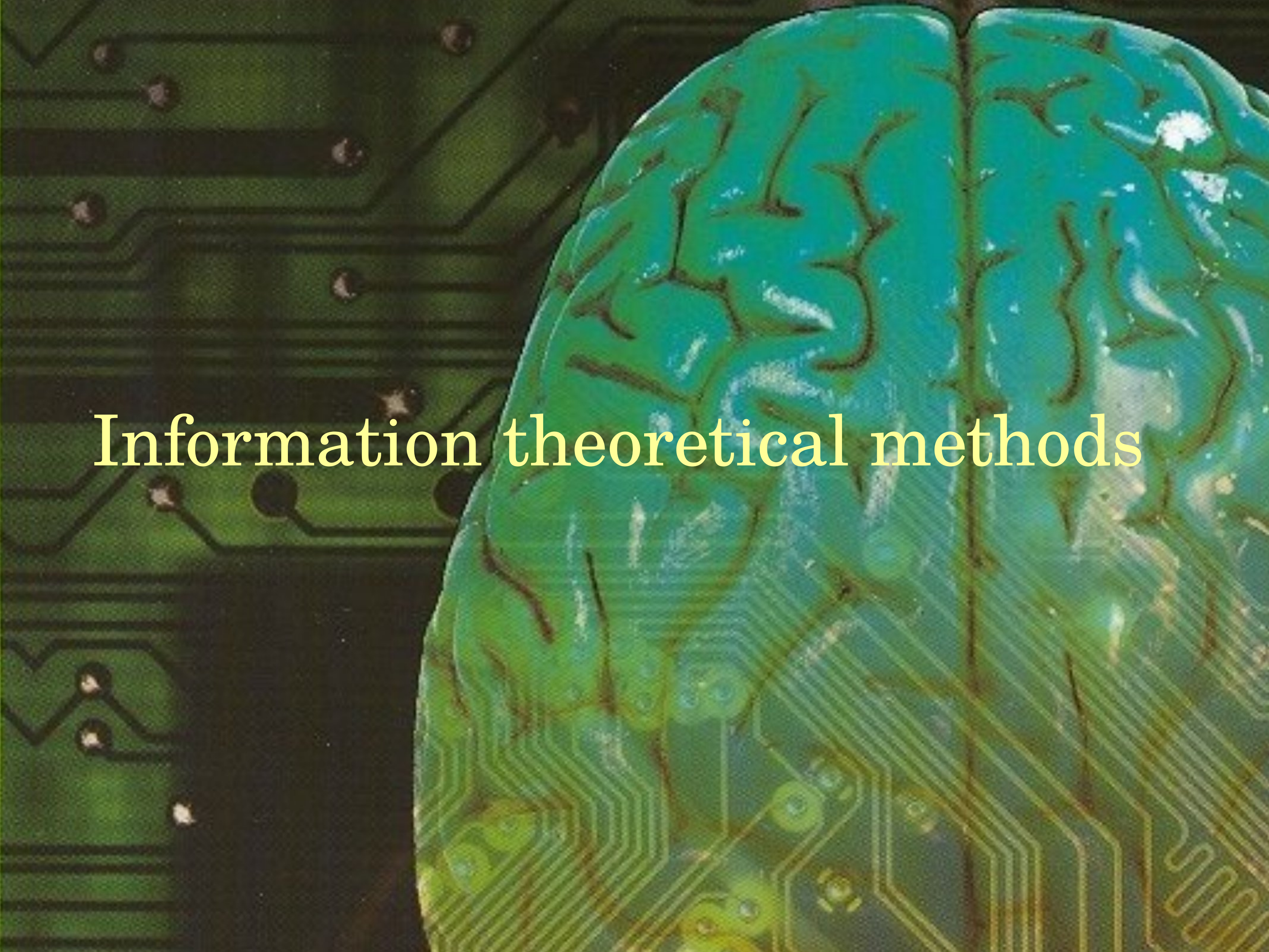
Layer structure of the hippocampus are revealed under the assumption, that the channels in the same layer receive similar synaptic inputs, but with different temporal delays. Thus coherence and the coherence based clustering could reveal the anatomical layers.

Micro-electro imaging

Micro-electro anatomy:
512 channel electrode system in the neocortex



Information theoretical methods



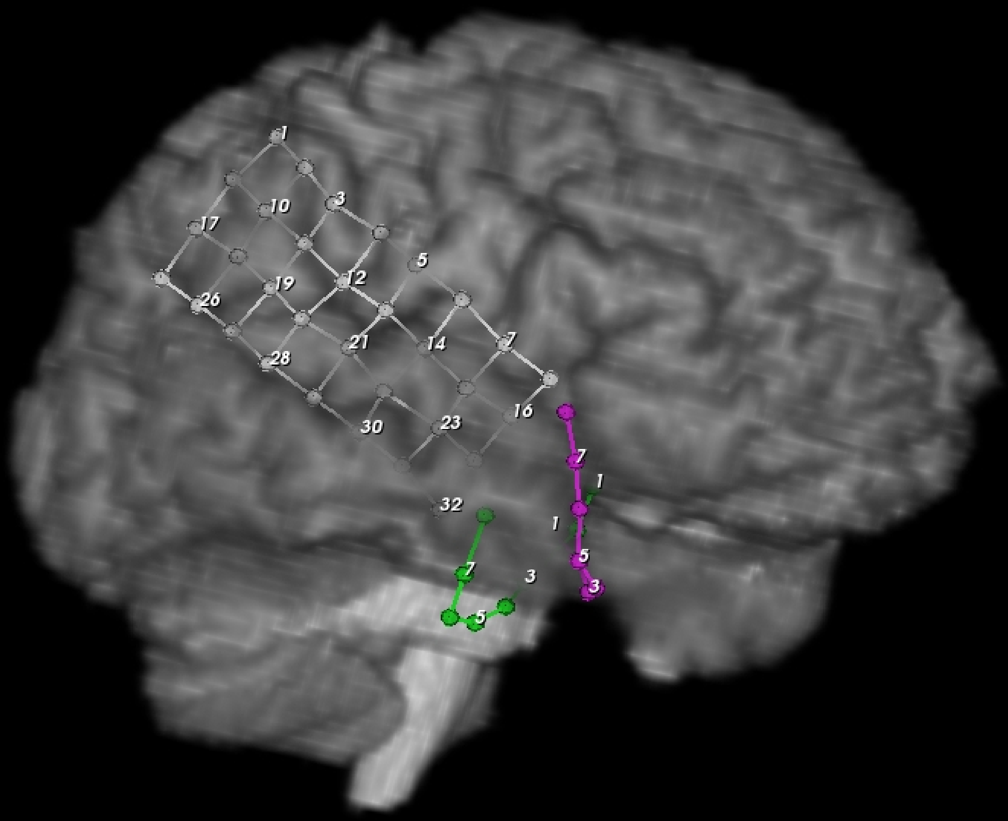
Information theoretical measures

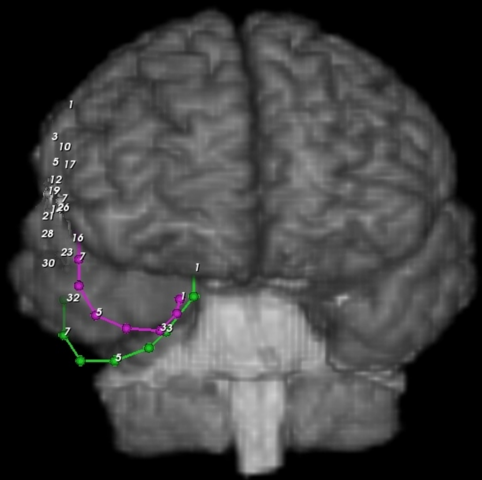
Entropy:

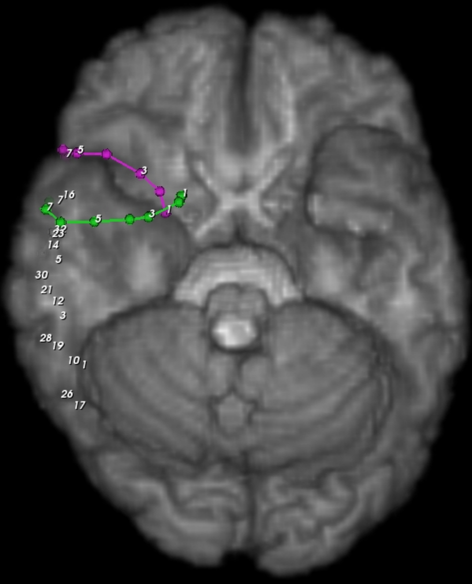
$$H(X) = -\sum_x p_x \log(p_x)$$

- Entropy is a measure of disorder and informaition content
- P_x is the probability of state x
- Depending on the state space, there are different entropies
- Spectral entropy, approximate entropy...

MRI with implanted subdural grid electrodes



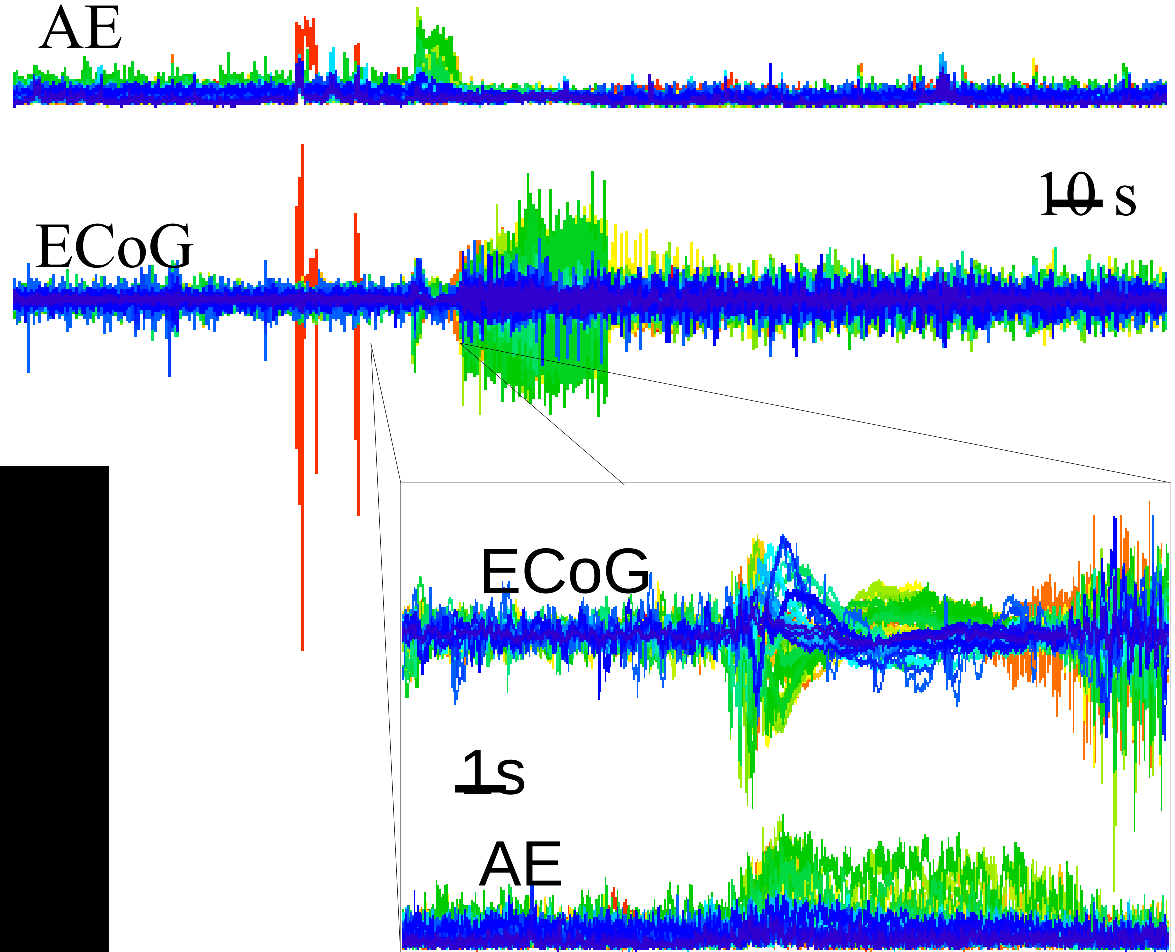


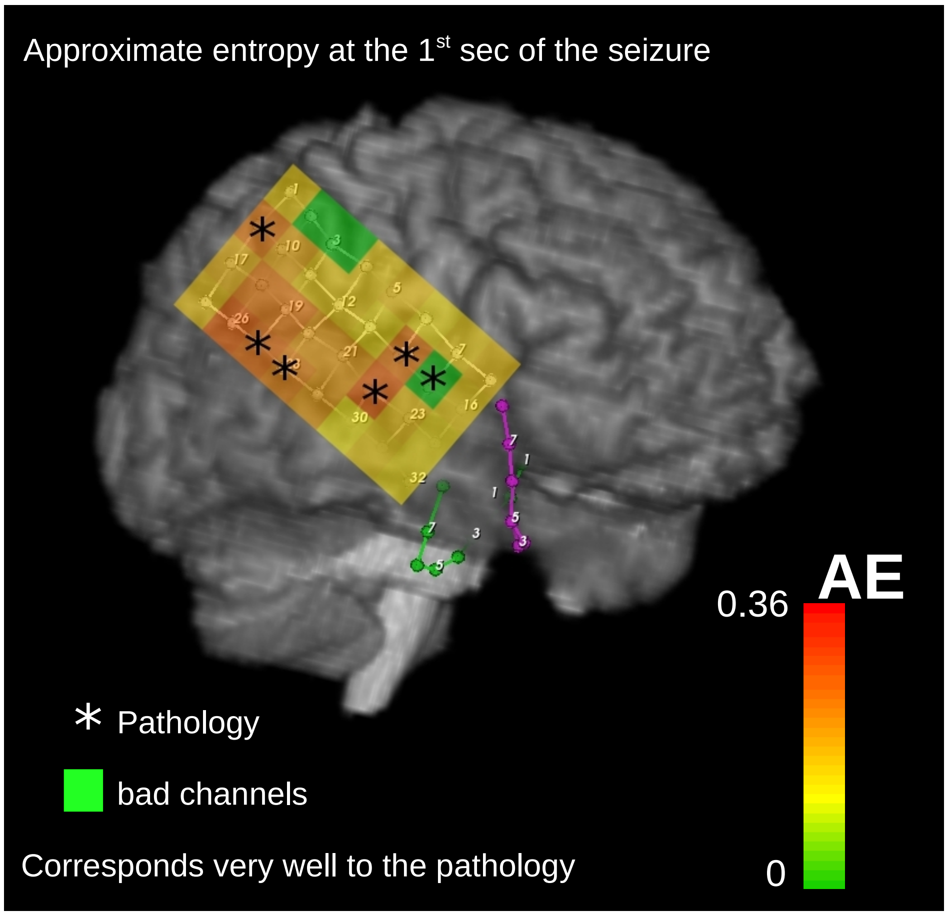


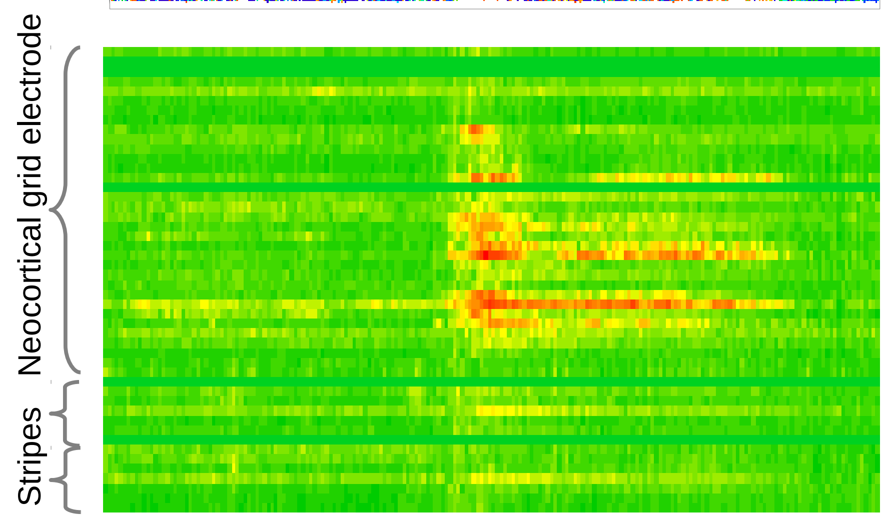
4*8 channels in the grid plus 2*8 channels
In two strip electrodes, 1024 Hz sampling

Entropy of the ECoG during seizure initialization

The Approximate Entropy (AE) is significantly increased solely during the initial, low amplitude phase of the seizure, then AE is decreased below the baseline during the high amplitude phase of the seizure. The positions of the increased AE values during the first sec of the seizure corresponds very well to the seizure onset zone,







Publisher on two conference posters: Hungarian Neuroscience Meeting 2015 and the Hungarian Neurosurgery Conference 2014

Information theoretical measures

Mutual information

$$I(X;Y) = H(X) + H(Y) - H(X,Y)$$

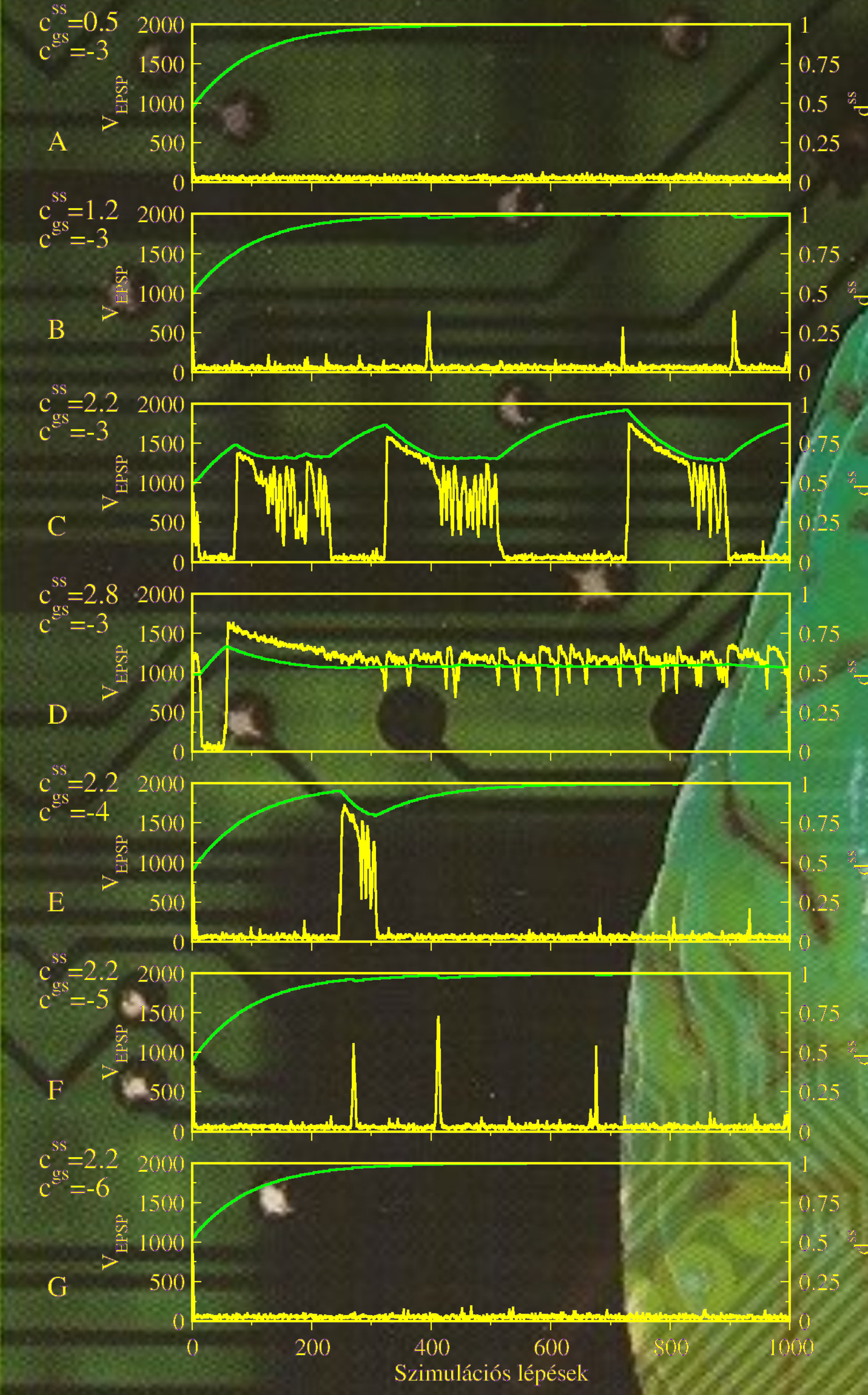
$$H(X) = -\sum_x p_x \log(p_x)$$

Phase-space reconstruction

The reconstructed pseudo-attractor in the state space, constructed from the data and its derivatives ($a(t)$, $a^1(t)$, $a^2(t)$ ...) is topologically equivalent to the systems real attractor in its original state space, according to the Whitney theorem.

Derivation increases noise, so the ($a(t)$, $a(t+dt)$, $a(t+2dt)$ ... delayed coordinates, return maps are used in stead: Takens'-theorem.

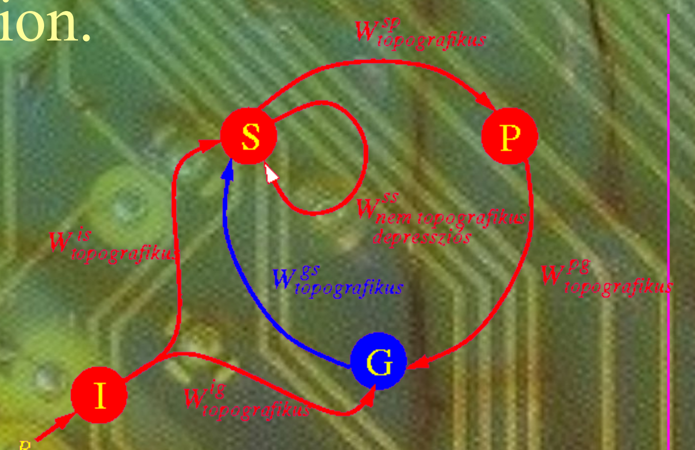
A simple epilepsy model



The change in the relative strength of the recurrent excitation and in inhibition results in:

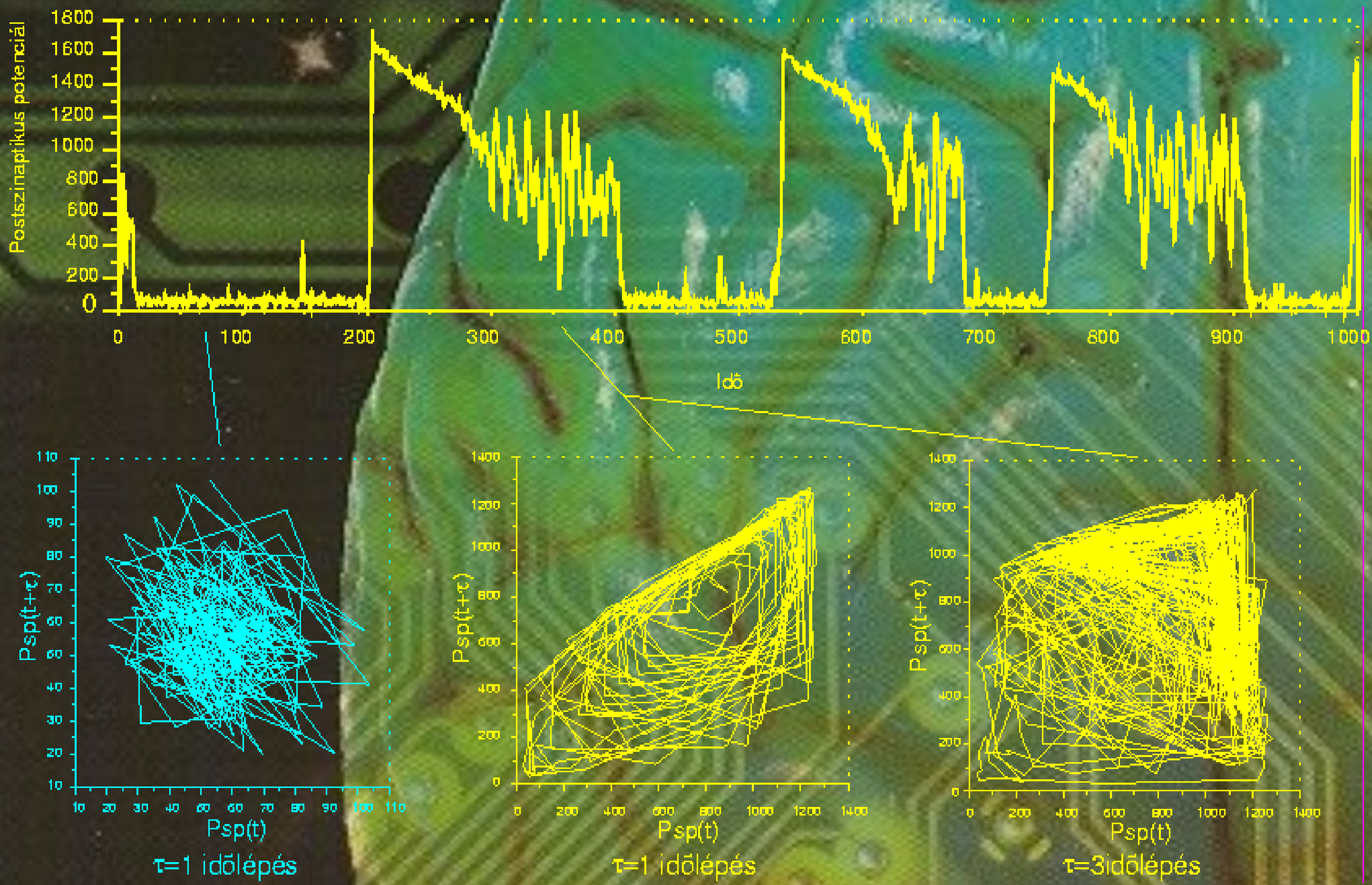
- spikes
- seizures with complex dynamics
- status epilepticus

The seizures can be eliminated by increasing the strength of the inhibition.

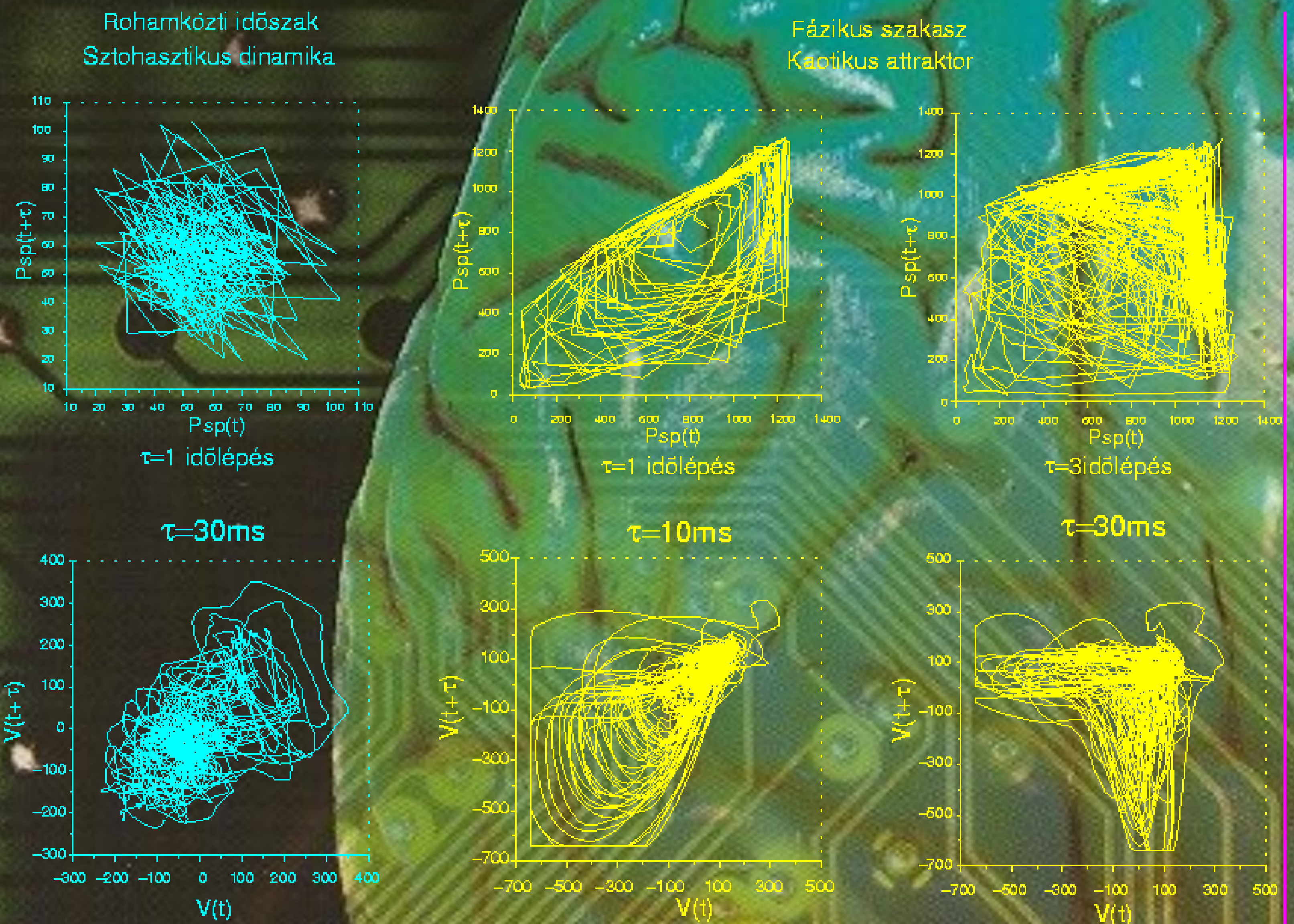


Reconstructed attractors from the simulated time series and their changes

The synaptic depression decreases the activation and drives the system into the regime of the irregular (chaotic) oscillation



Comparison of the reconstructed attractors from the simulation and the epileptic ECoG



Phase space reconstruction

What to do with the reconstructed attractors?

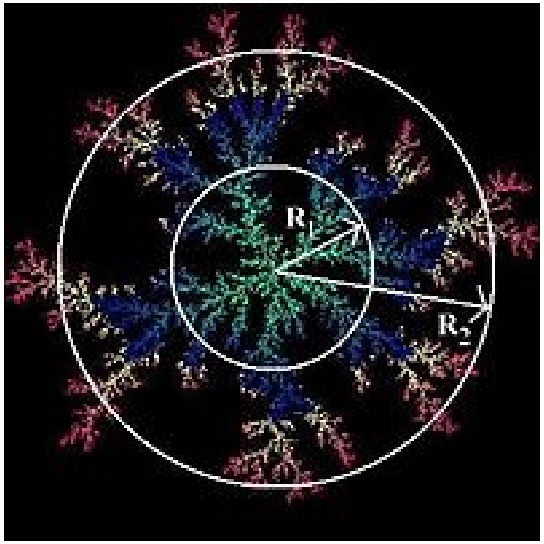
It is not easy to determine the type (topology) of the attractor, based on the noisy measurements.

It is possible to measure its dimension, for example: L2-dimension. $N=L^d$ where N is the number points in a sphere with radius L.

It is possible to measure the average Ljapunov-exponent, meaning the average instability of the paths.

What else?

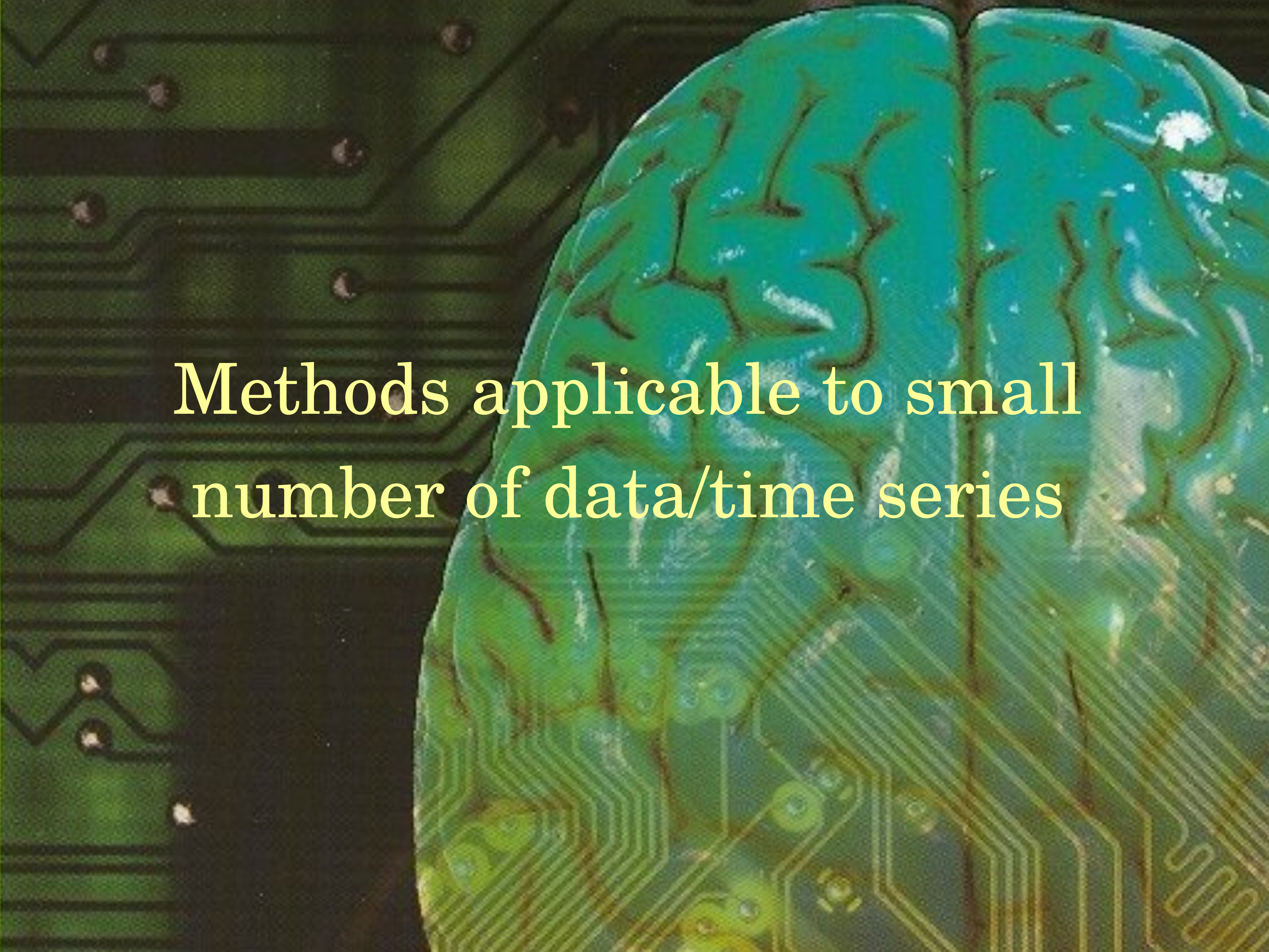
How to measure the dimension of the manifold?



$$N(r) = N_0 \cdot r^D$$

$$D = \frac{Ln\left(\frac{N_i}{N_{i+1}}\right)}{Ln\left(\frac{r_i}{r_{i+1}}\right)}$$

Let's take two radii and count the number of points within the spheres: the exponent of the increase with respect to the radius gives us the dimension.

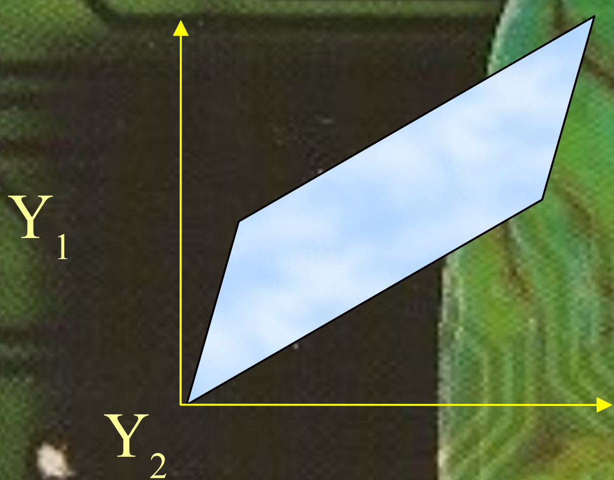


Methods applicable to small number of data/time series

The cocktail-party problem and the principal component analysis (PCA)

$$Y_i(t) = \sum W_{ij} X_j(t)$$

Let's search for the directions correspond to maximal variance



Principal component analysis

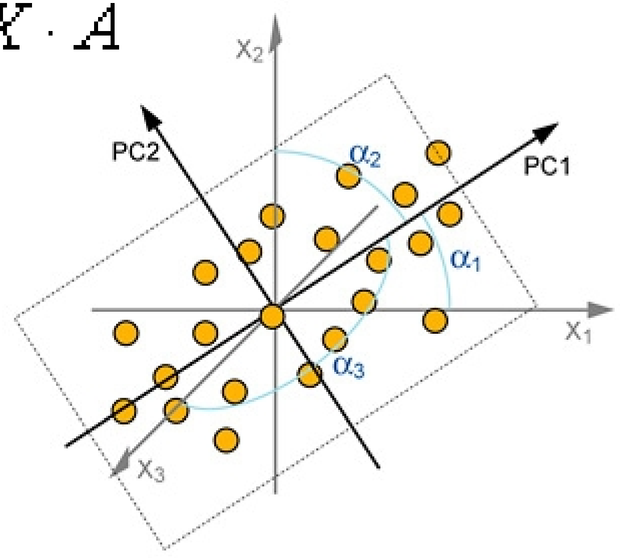
$$\overline{x_n} = \frac{1}{K}\sum_{k=1}^{K} x_{kn}$$

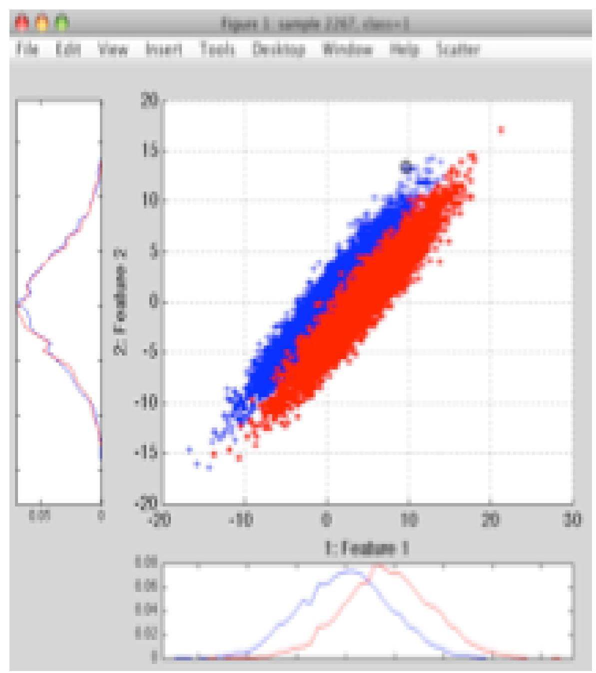
$$\sigma_n = \sqrt{\frac{1}{K-1}\sum_{k=1}^{K}(x_{kn} - \overline{x}_n)^2}$$

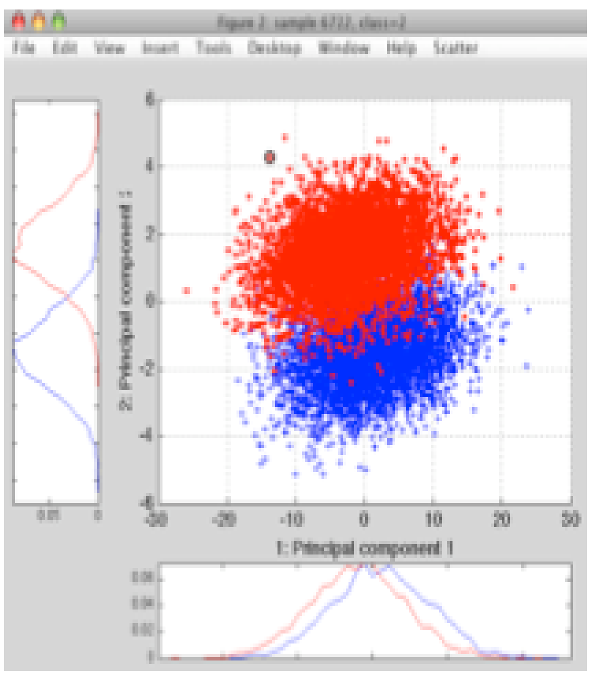
$$S = \left(covar[y_i, y_j]_{i,j=1}^{N}\right) \approx \left(\frac{1}{K-1}\sum_{k=1}^{K} y_{ki} y_{kj}\right)_{i,j=1}^{N} = \frac{1}{K-1} Y^T \cdot Y$$

$$S \cdot X' = \lambda \cdot X'$$

$$Z = X \cdot A$$







Principal component network, derivation of Oja's rule:

$$w_i(n+1) = w_i(n) + \eta y(\mathbf{x}(n)) x_i(n)$$

$$w_i(n+1) = \frac{w_i(n) + \eta y(\mathbf{x}(n)) x_i(n)}{\left(\sum_{j=1}^{m} [w_j(n) + \eta y(\mathbf{x}(n)) x_j(n)]^p\right)^{1/p}}$$

$$w_i(n+1) = \frac{w_i(n)}{(\sum_j w_j^p)^{1/p}} + \eta \left(\frac{y(n) x_i(n)}{(\sum_j w_j^p)^{1/p}} - \frac{w_i(n) \sum_j y(n) x_j(n) w_j(n)}{(\sum_j w_j^p)^{1+1/p}} \right) + O(\eta^2)$$

$$y(\mathbf{x}(n)) = \sum_{j=1}^{m} x_j(n) w_j(n)$$

$$\|\mathbf{w}\| = (\sum_{j=1}^{m} w_j^p)^{1/p} = 1$$

$$w_i(n+1) = w_i(n) + \eta y(n)(x_i(n) - w_i(n) y(n))$$

The cocktail-party problem and the independent component analysis (ICA)

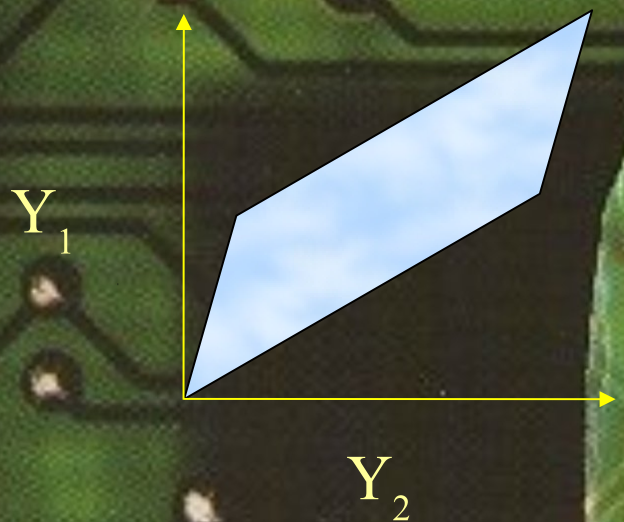
$$Y_i(t) = \sum W_{ij} X_j(t)$$

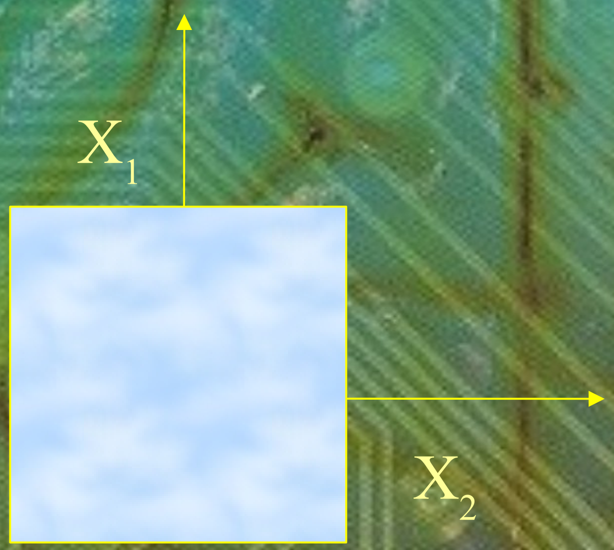
Let's search for the most independent directions! The basic idea is the central limit theorem: Linear combination of two independent variables is closer to the Gaussian distribution than the original. Thus, let's search for the least Gaussian sources. How to measure the “non-Gaussianity”? Eq: Skewness, entropy...

The cocktail-party problem and the independent component analysis (ICA)

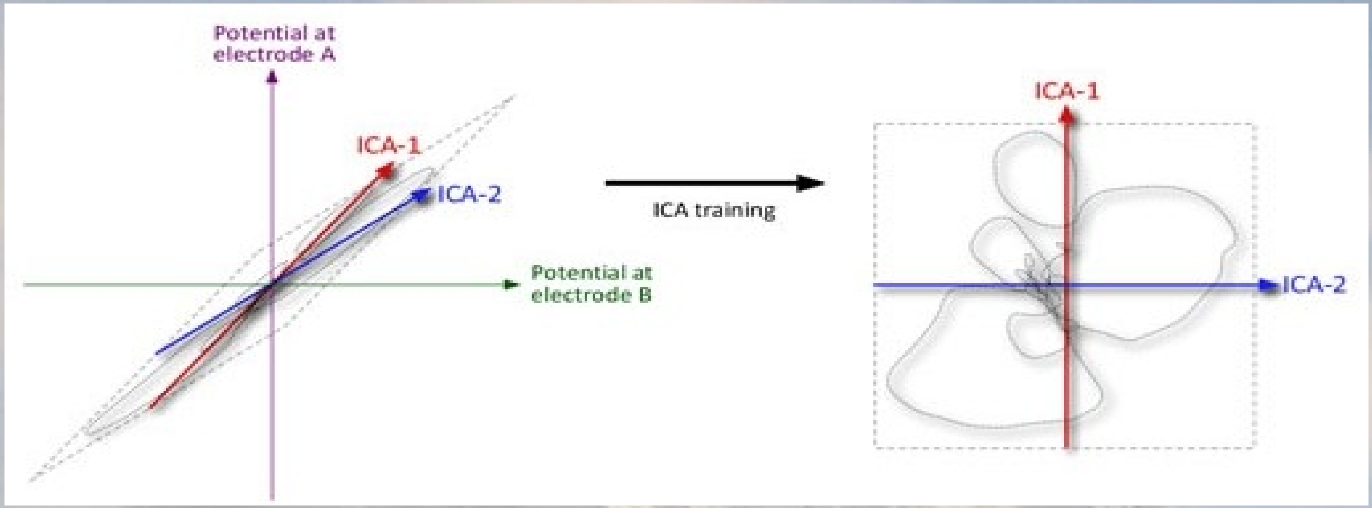
$$Y_i(t) = \sum W_{ij} X_j(t)$$

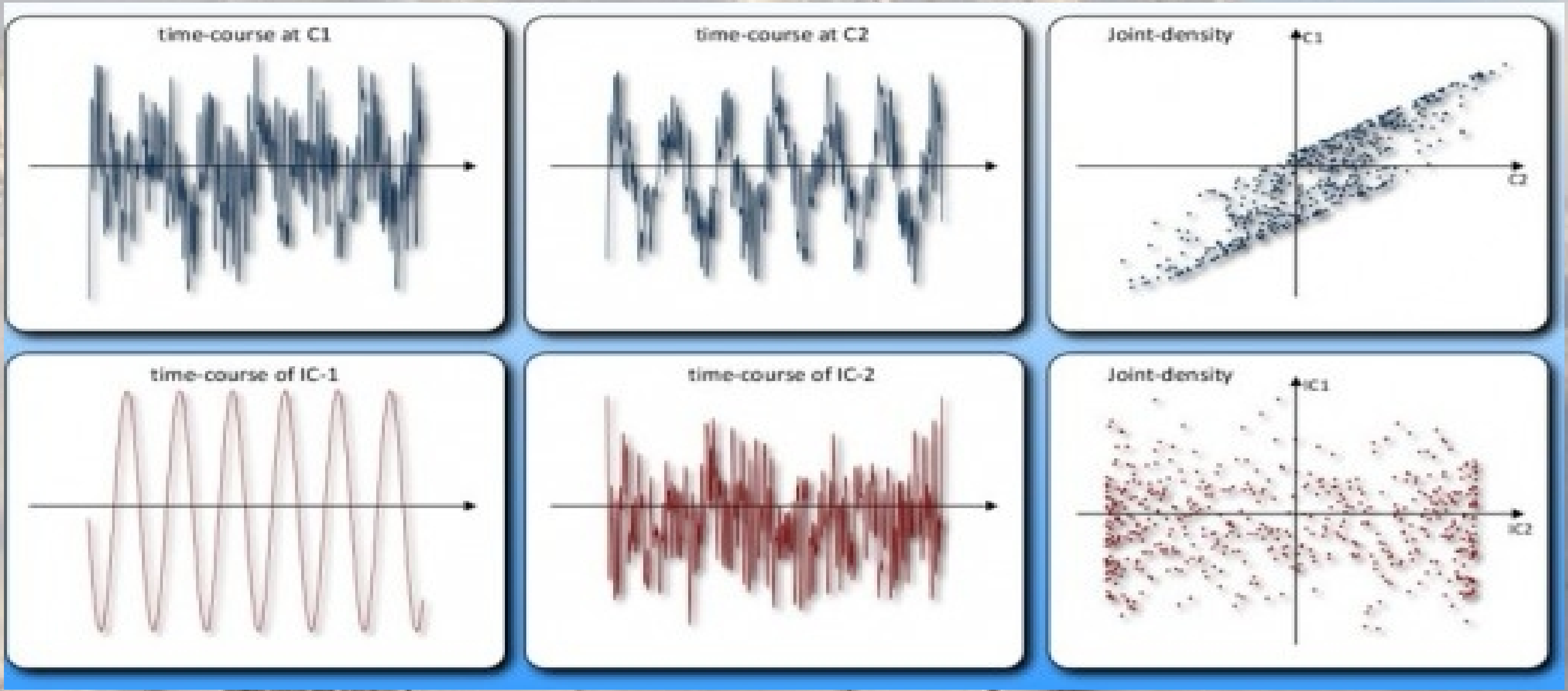
The most independent directions:



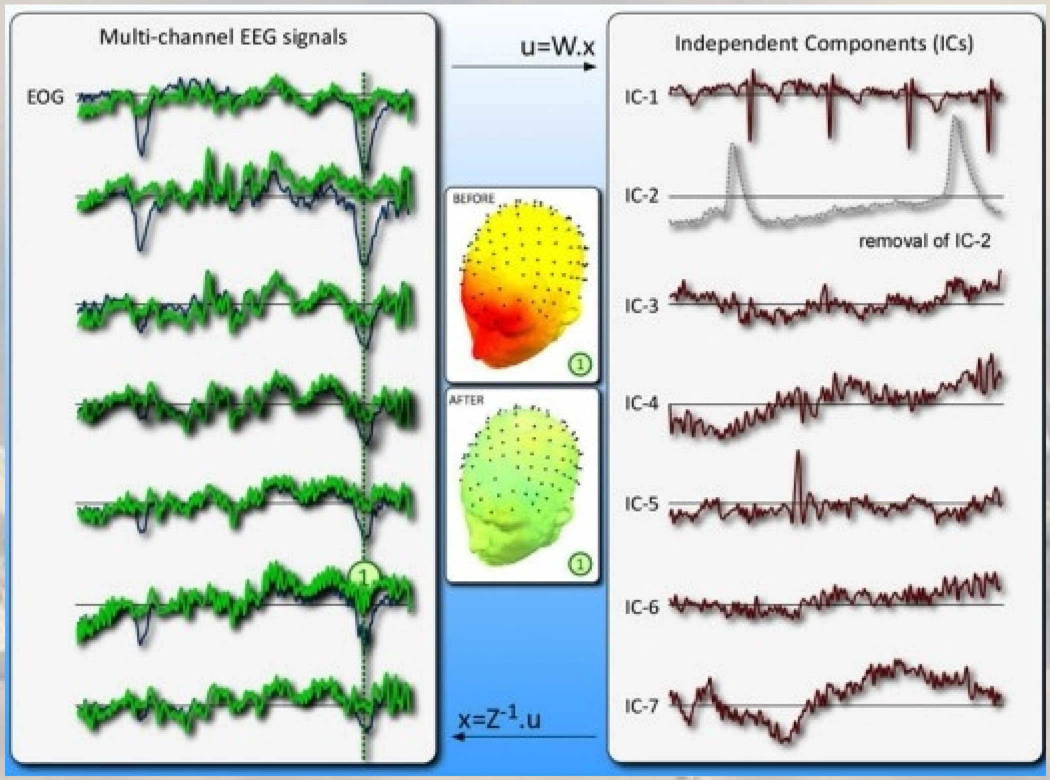


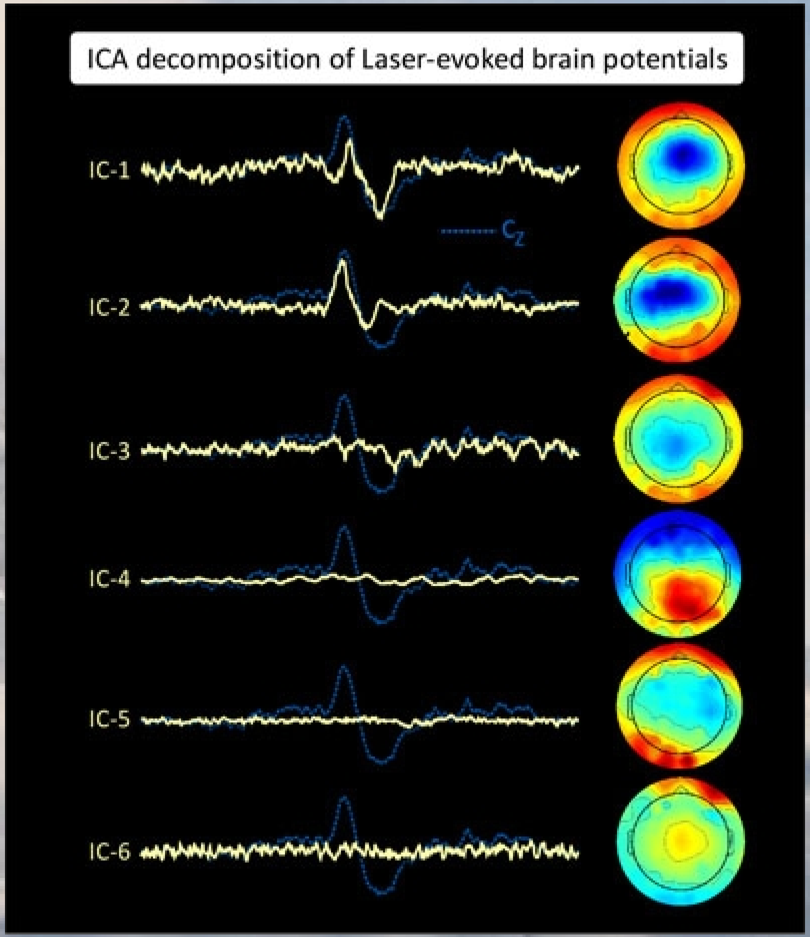
Independent component analysis (ICA)





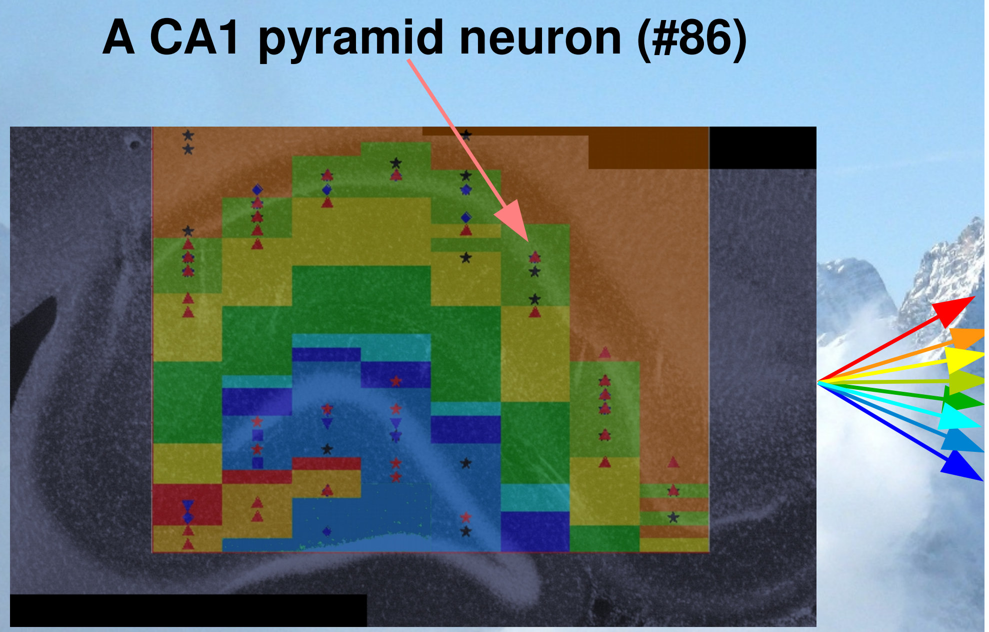
Independent component analysis (ICA)

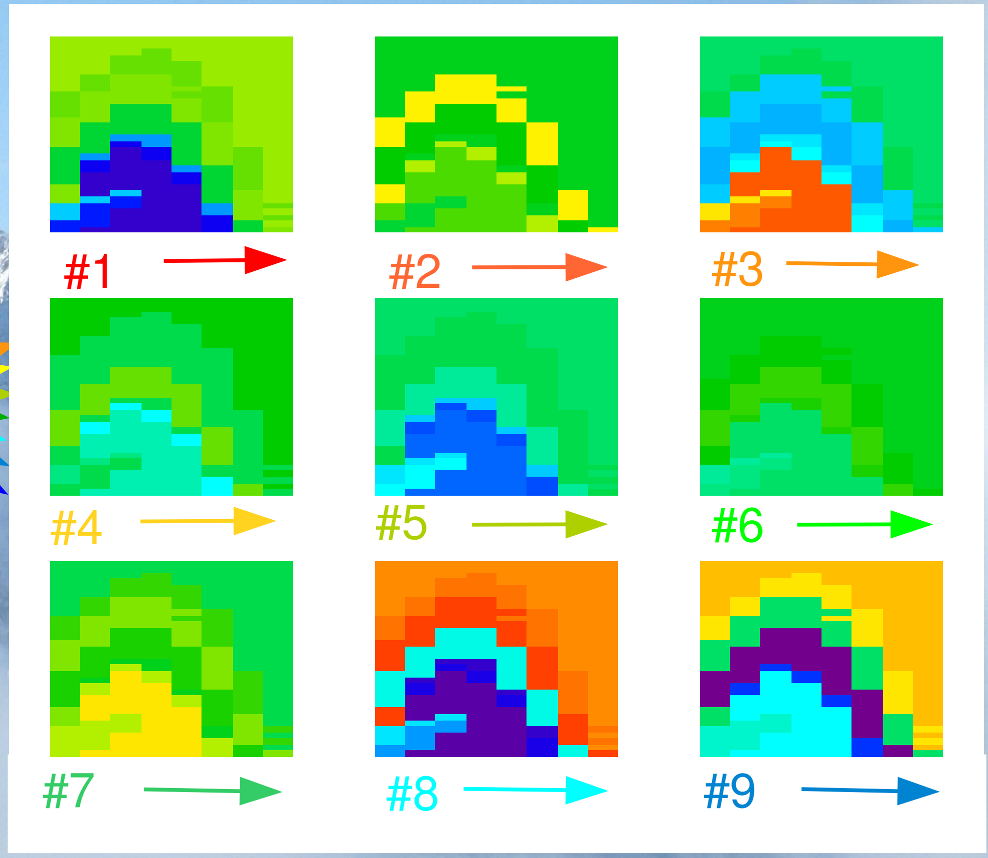




Micro-electro imaging

Inputs of a neurons from different layers

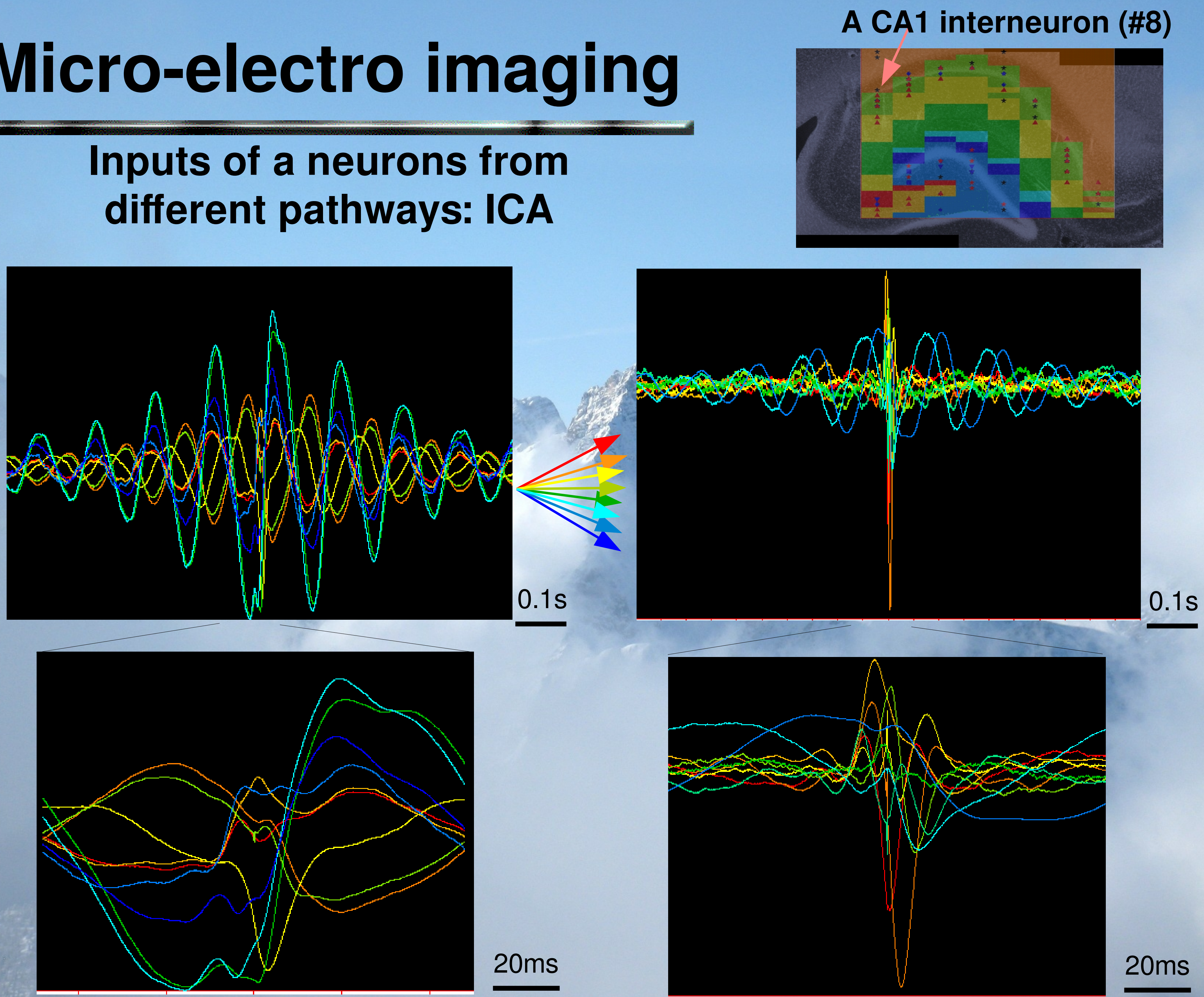




The spike triggered average EC potential patterns have been decomposed into 9 different independent components by ICA. Some of them clearly corresponds to the signals of specific pathways and mechanisms: component #2 corresponds to Schaffer collateral, #8 and #9 together correspond to the Theta.

Micro-electro imaging

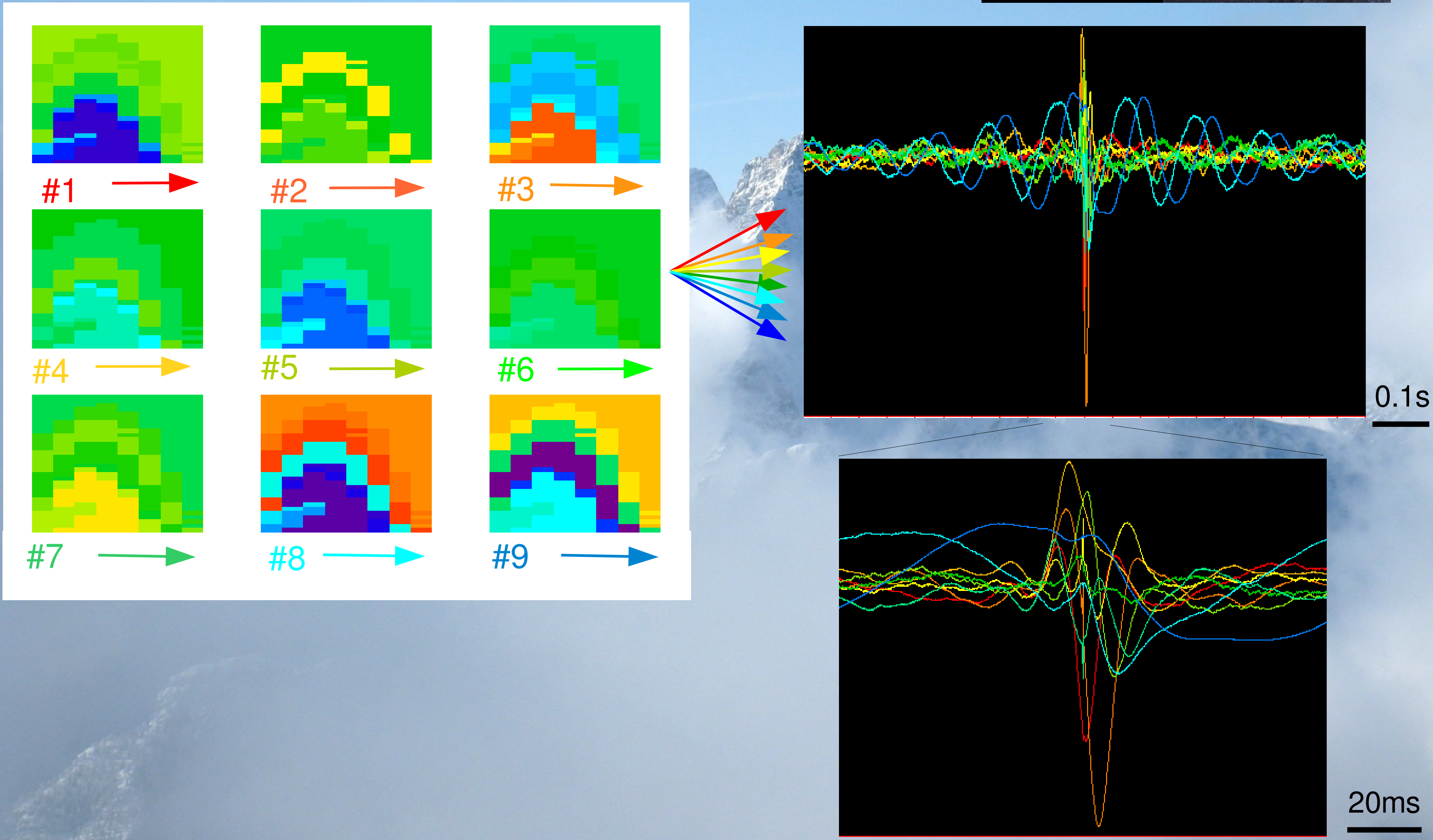
Inputs of a neurons from different pathways: ICA



Micro-electro imaging

Inputs of a neurons from different pathways: ICA

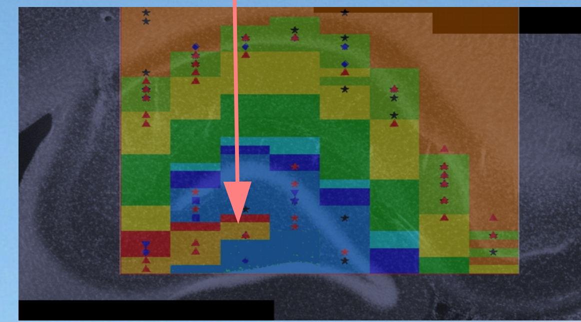
A CA1 interneuron (#8)

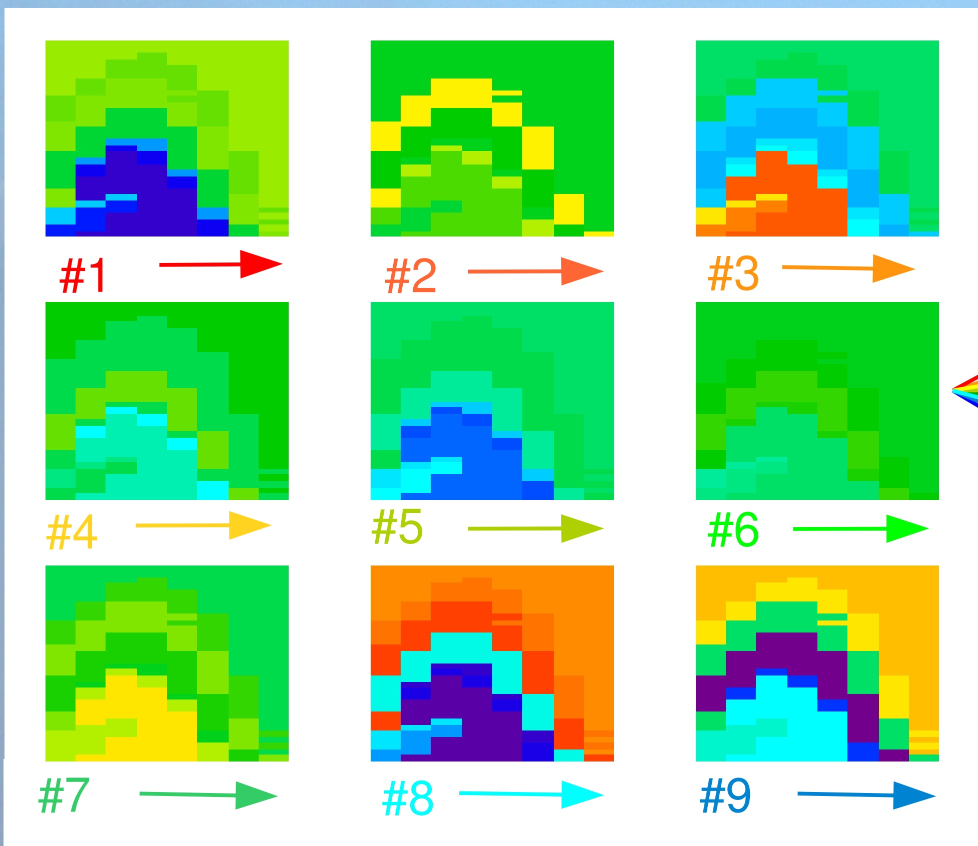


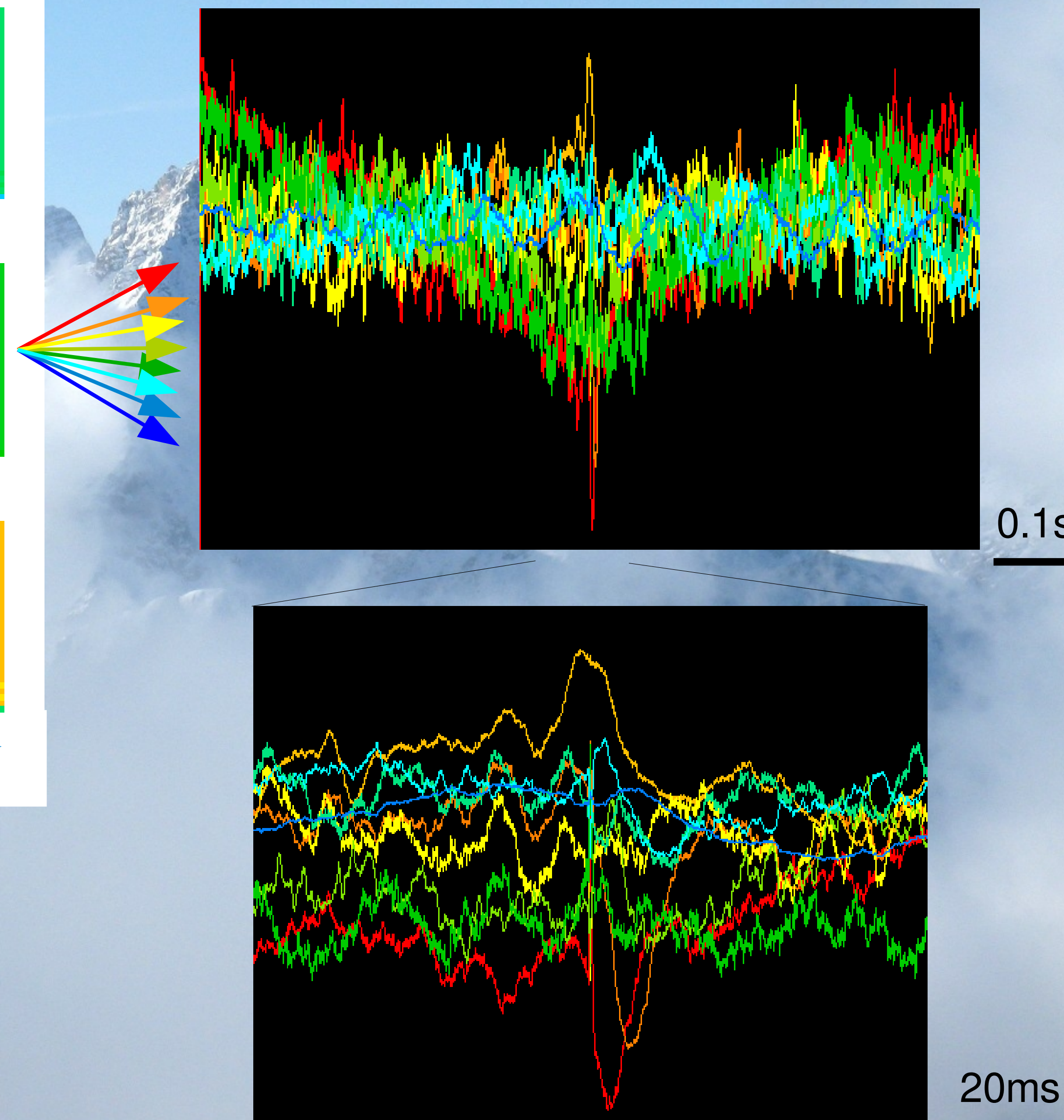
Micro-electro imaging

Inputs of a neurons from different pathways: ICA

A CA3 pyramid neuron (#56)

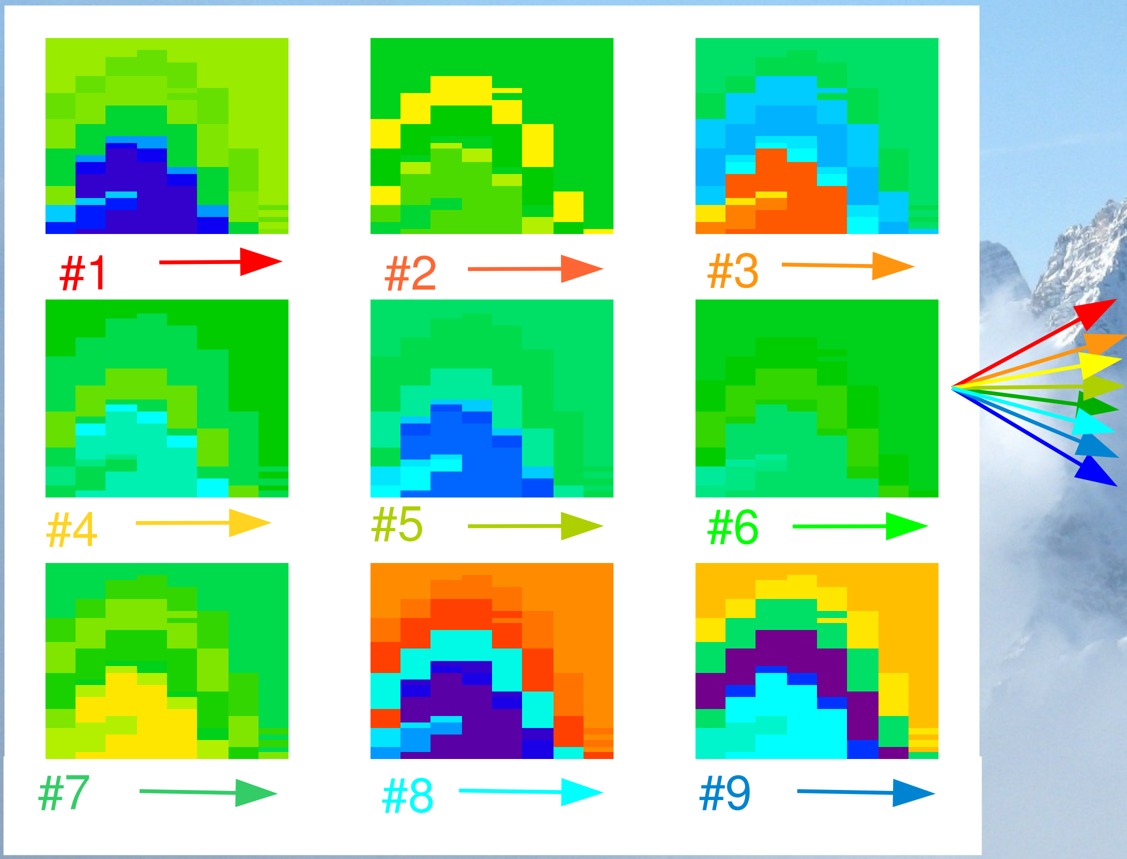


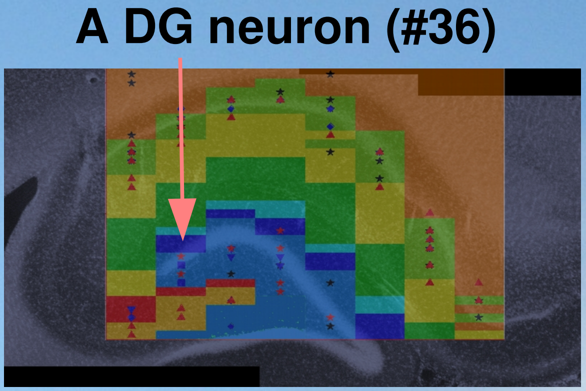


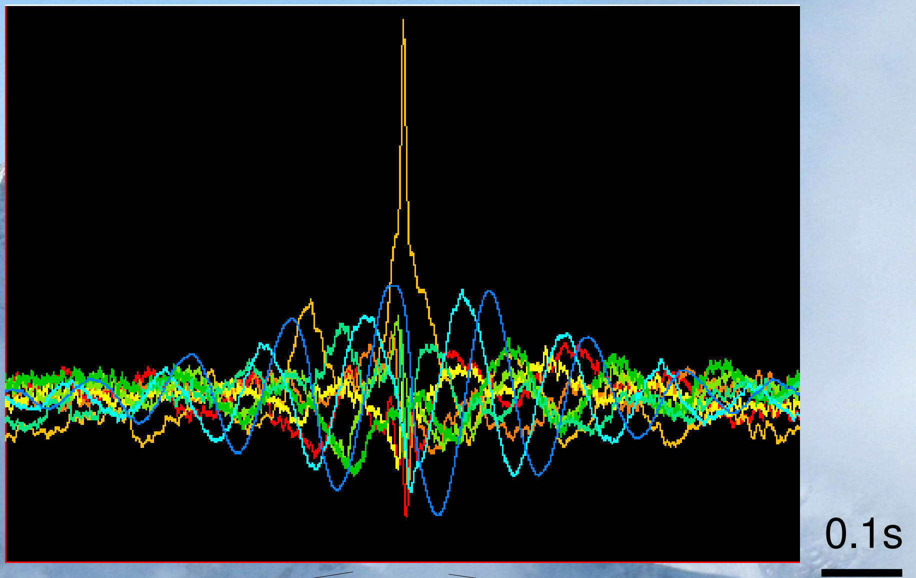


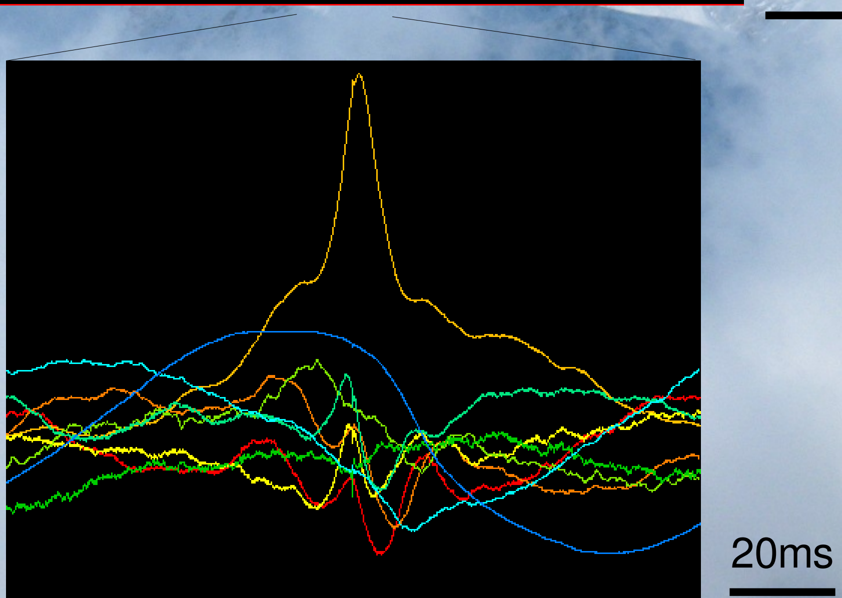
Micro-electro imaging

Inputs of a neurons from different pathways: ICA



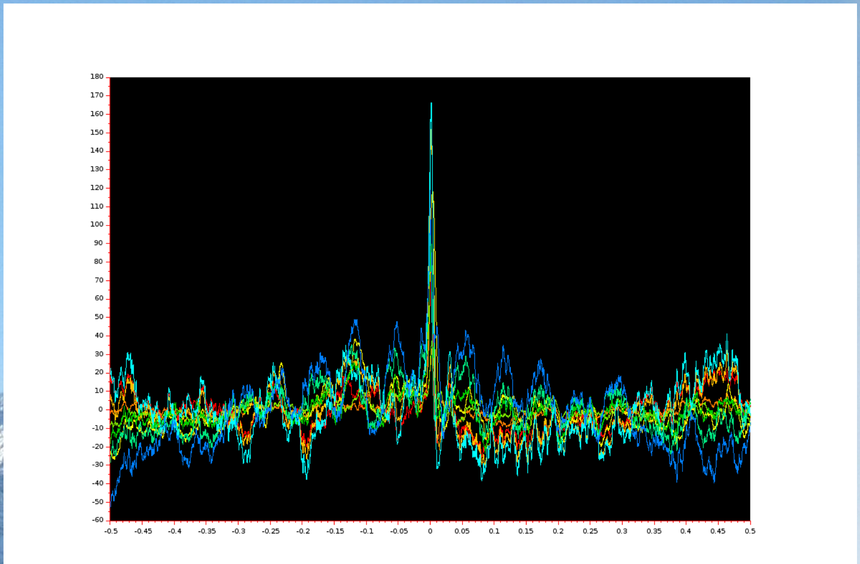




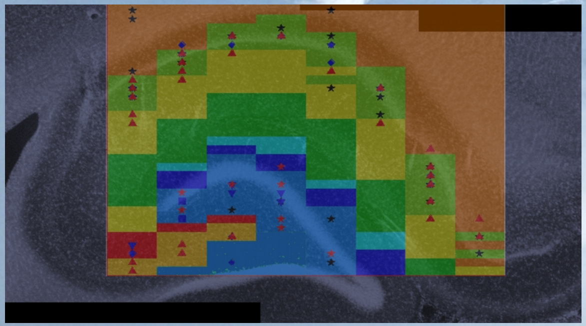


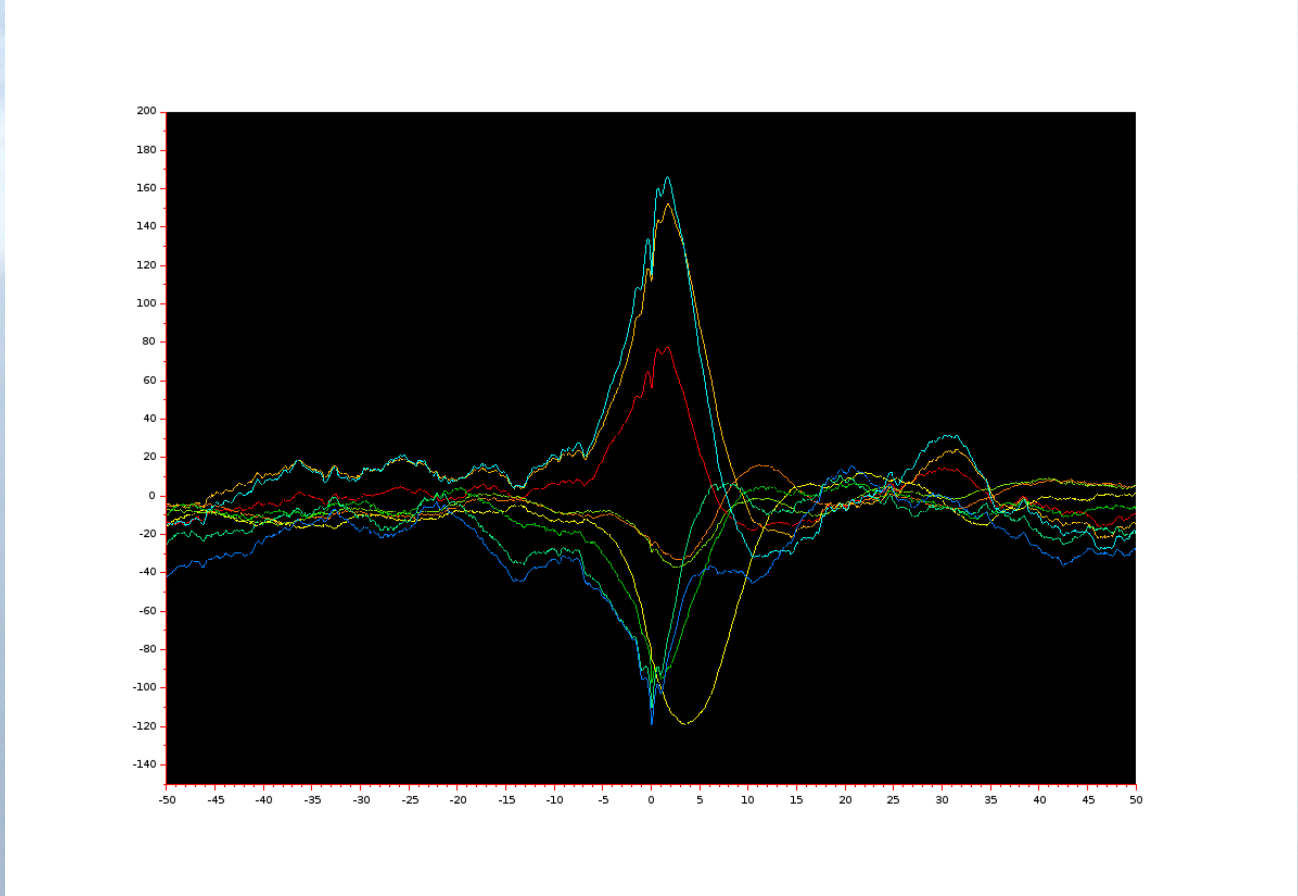
Micro-electro imaging

Cell type specific potentials
Reconstructed without theta



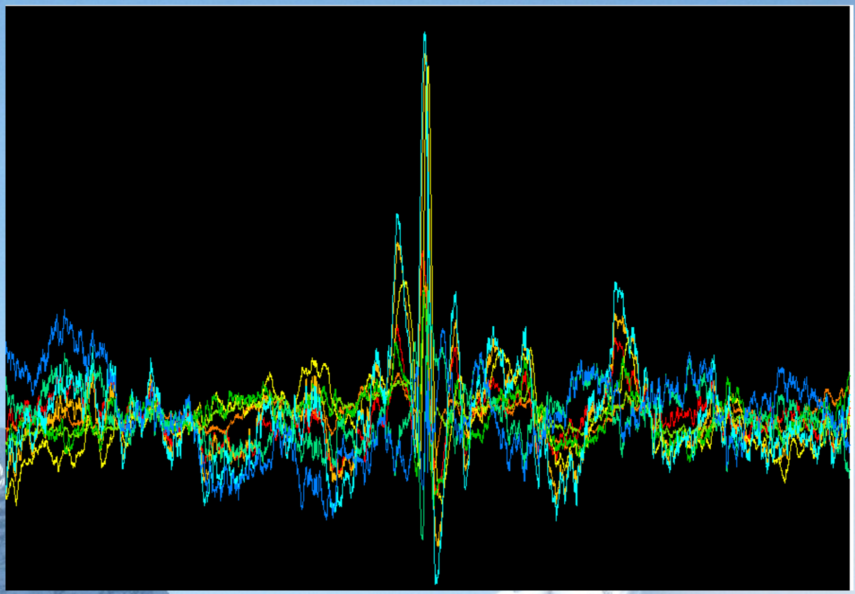
DG granular neurons (n=8)



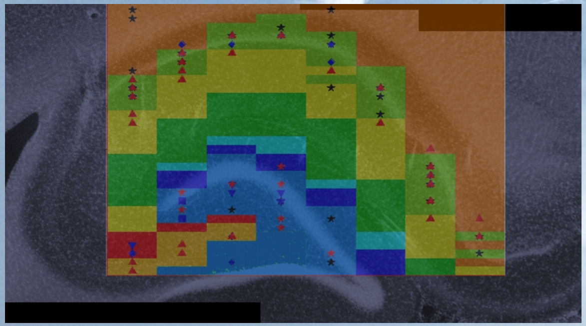


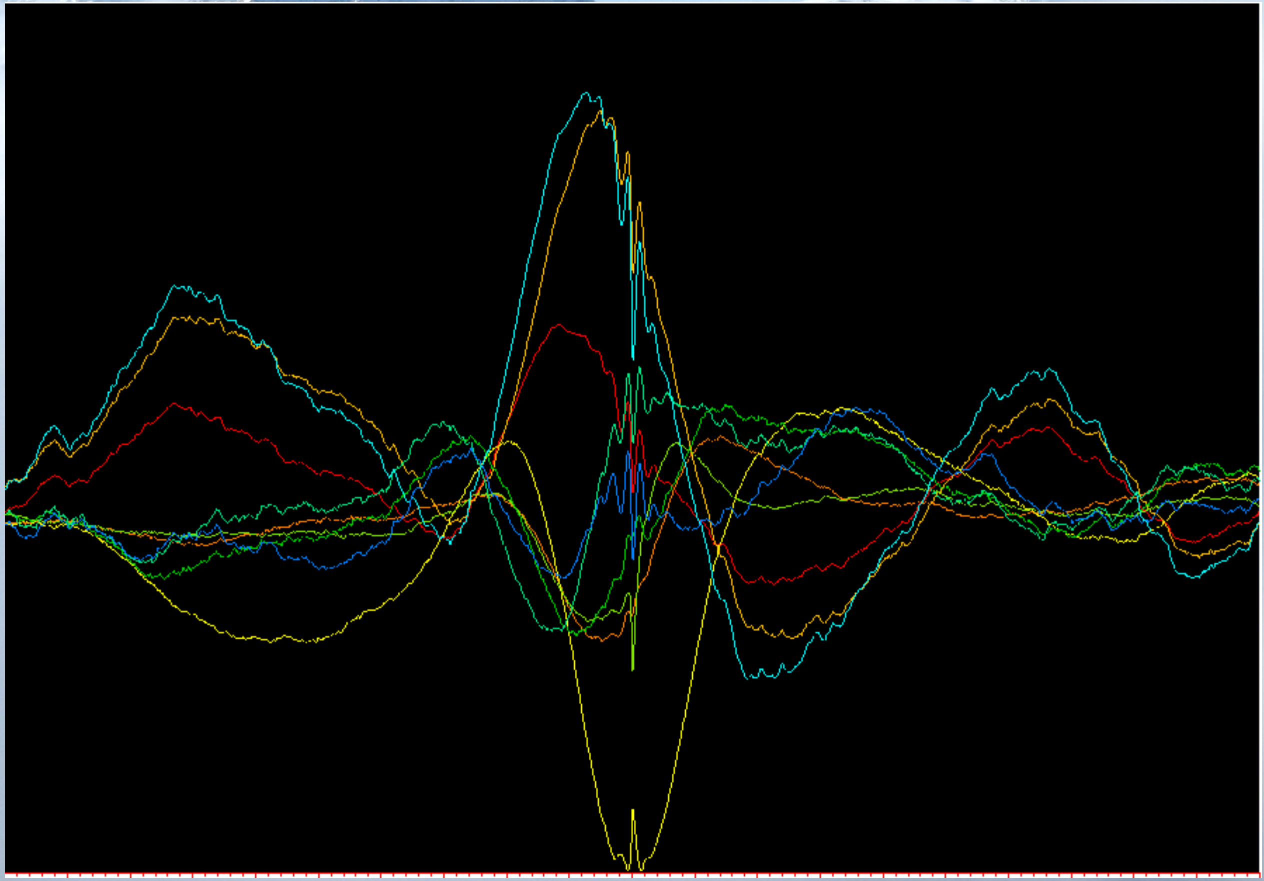
Micro-electro imaging

Cell type specific potentials
Reconstructed without theta



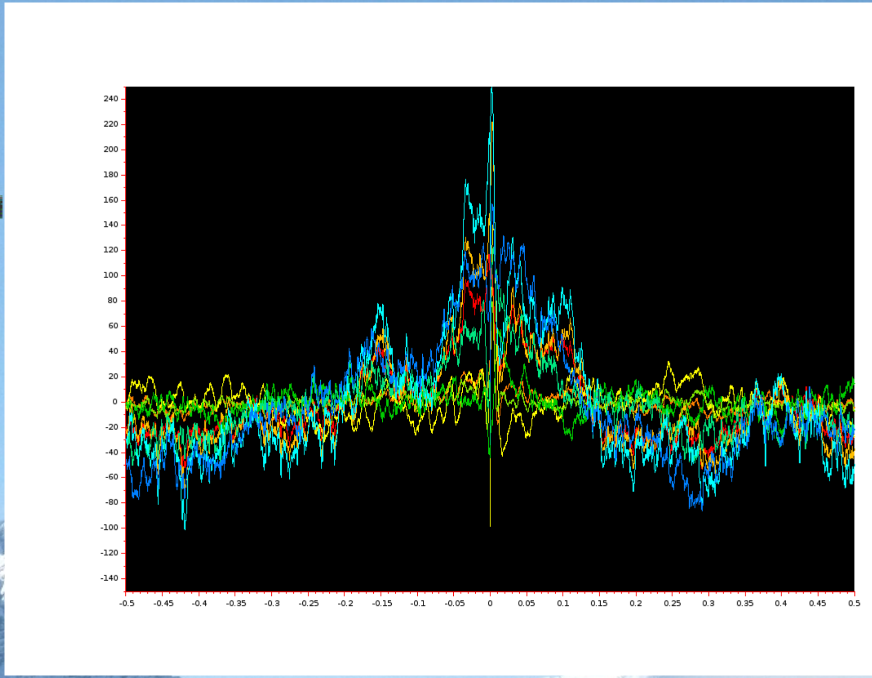
CA1 pyramidal neurons (n=29)



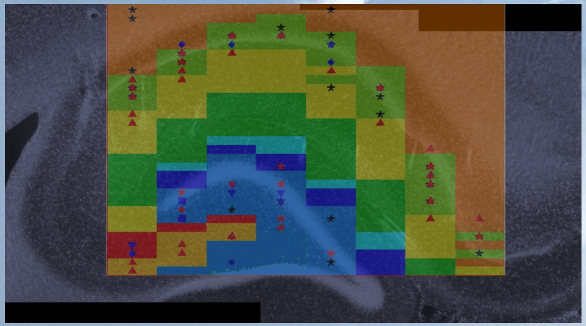


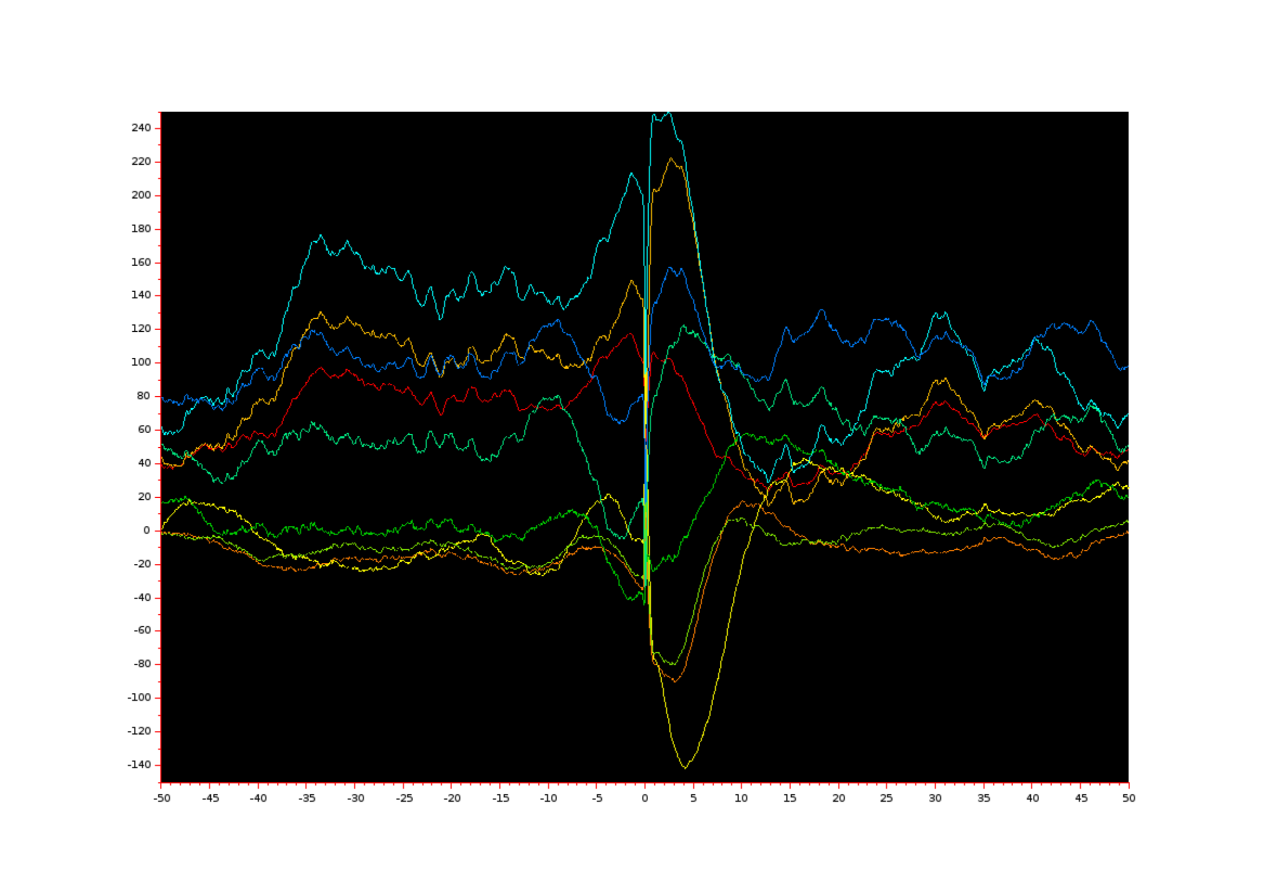
Micro-electro imaging

Cell type specific potentials
Reconstructed without theta



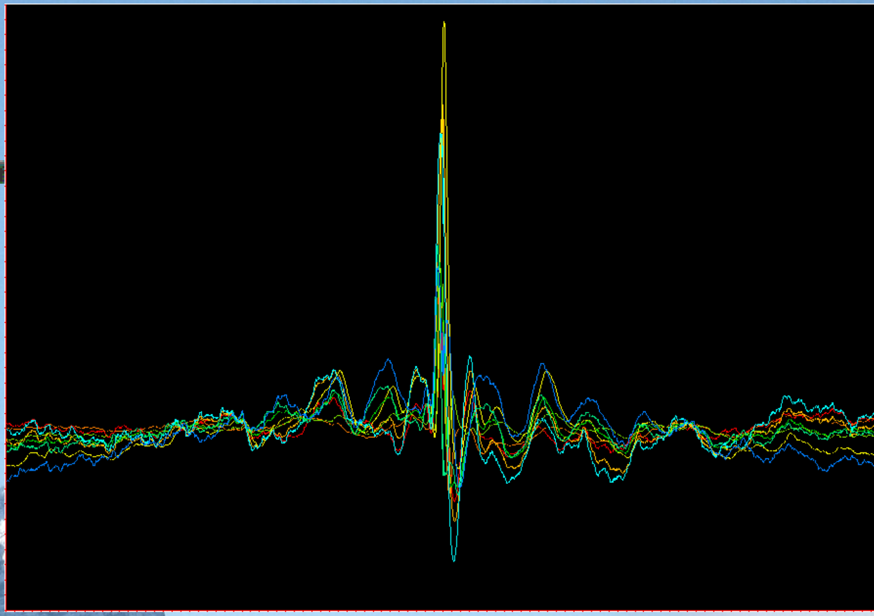
CA3 pyramidal neurons (n=8)



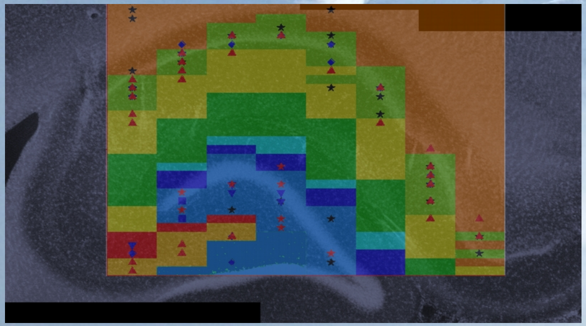


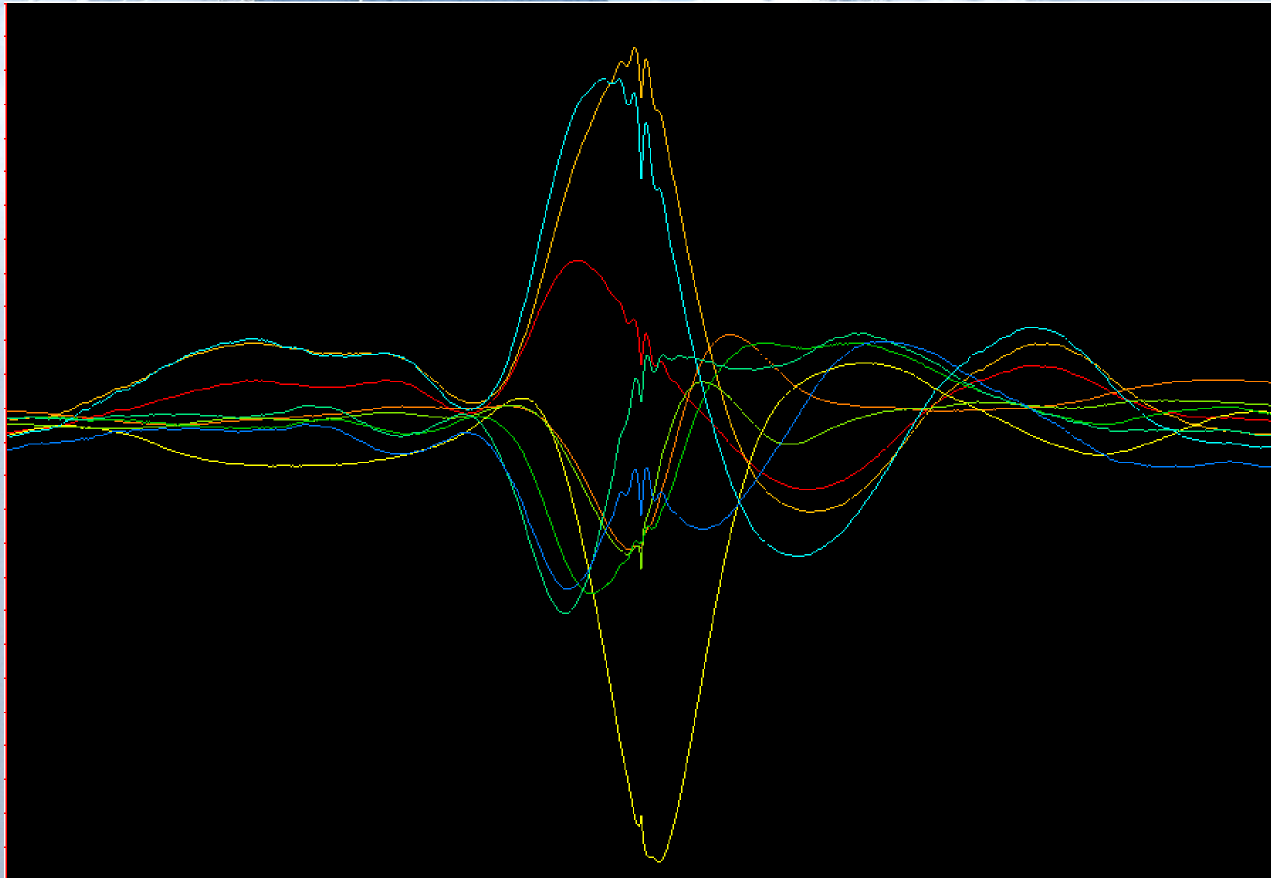
Micro-electro imaging

Cell type specific potentials Reconstructed without theta



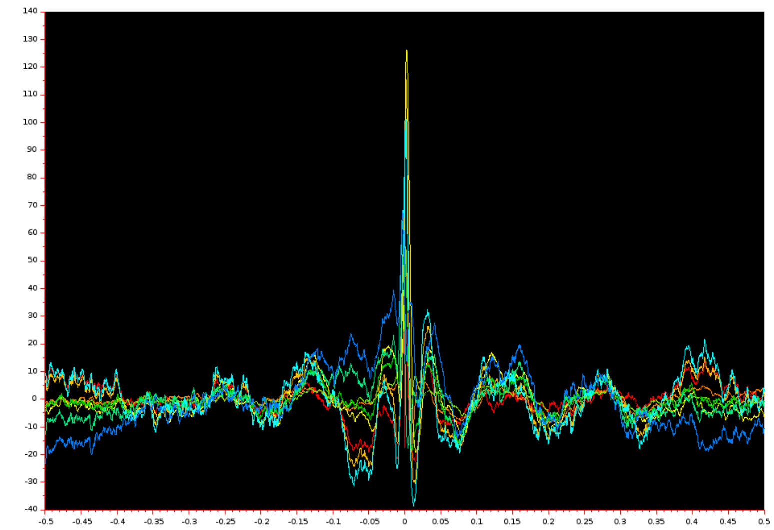
CA1 PV neurons (n=16)



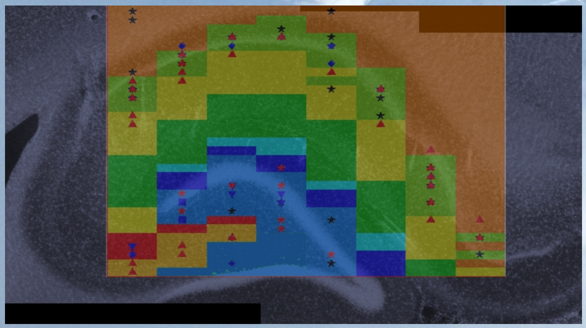


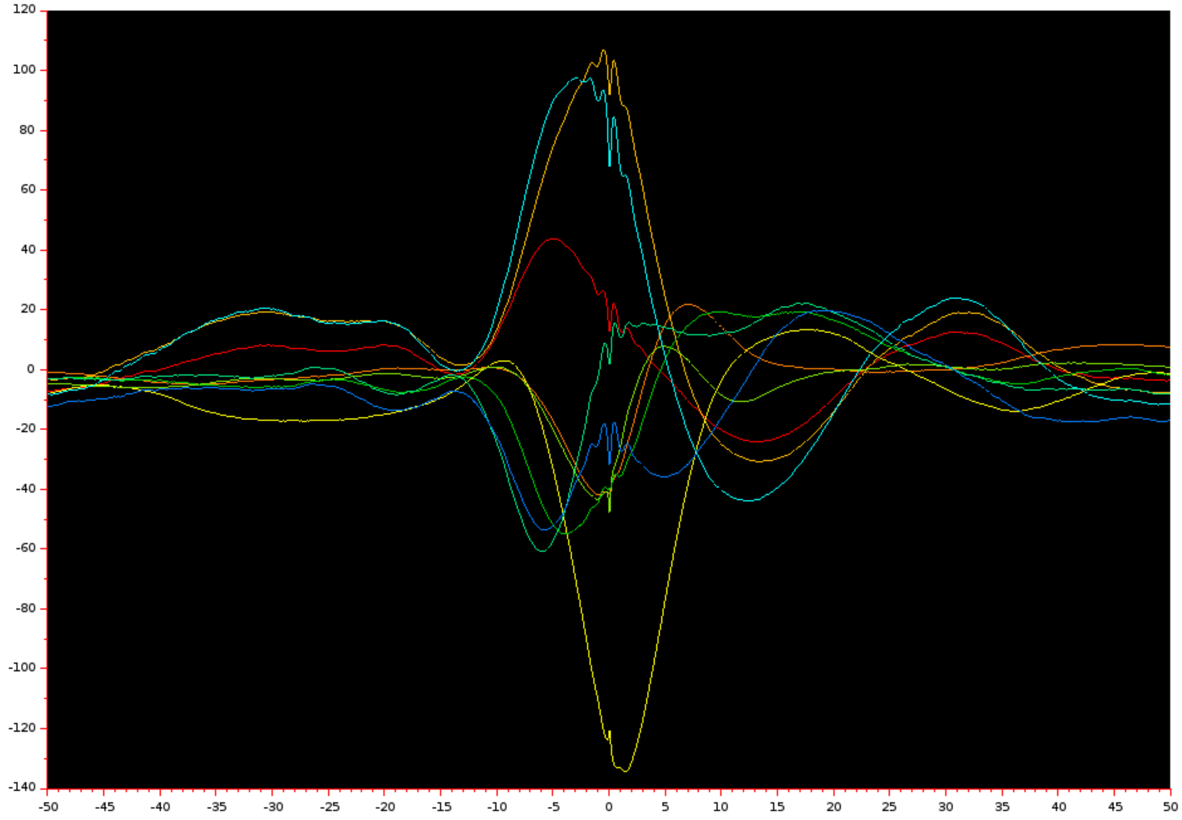
Micro-electro imaging

Cell type specific potentials Reconstructed without theta

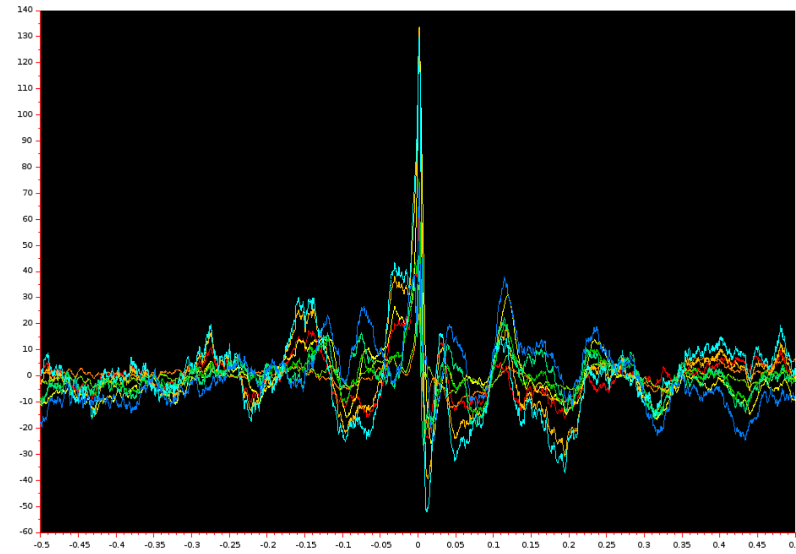


CA3 PV neurons (n=2)



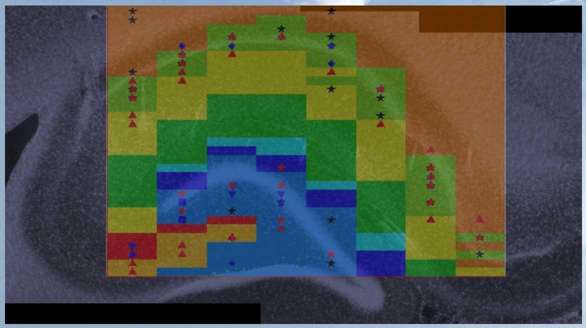


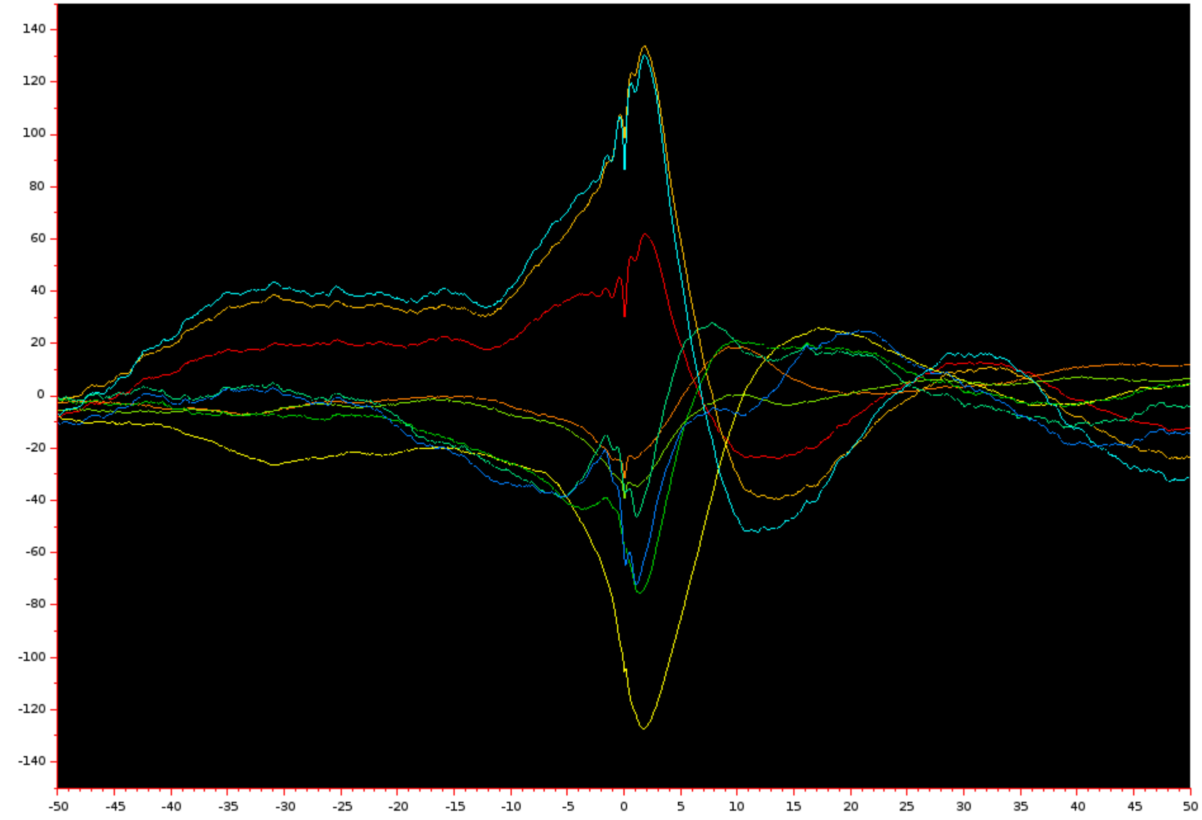
Micro-electro imaging



Cell type specific potentials Reconstructed without theta

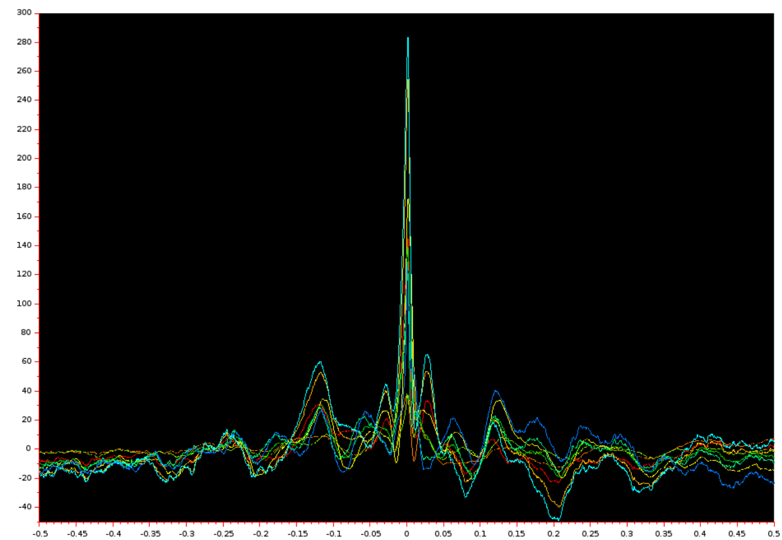
DG (CA3?) PV neurons (n=2)



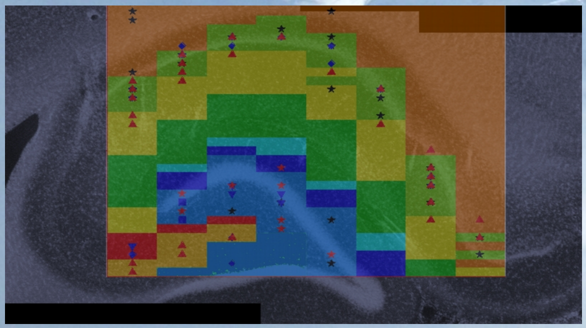


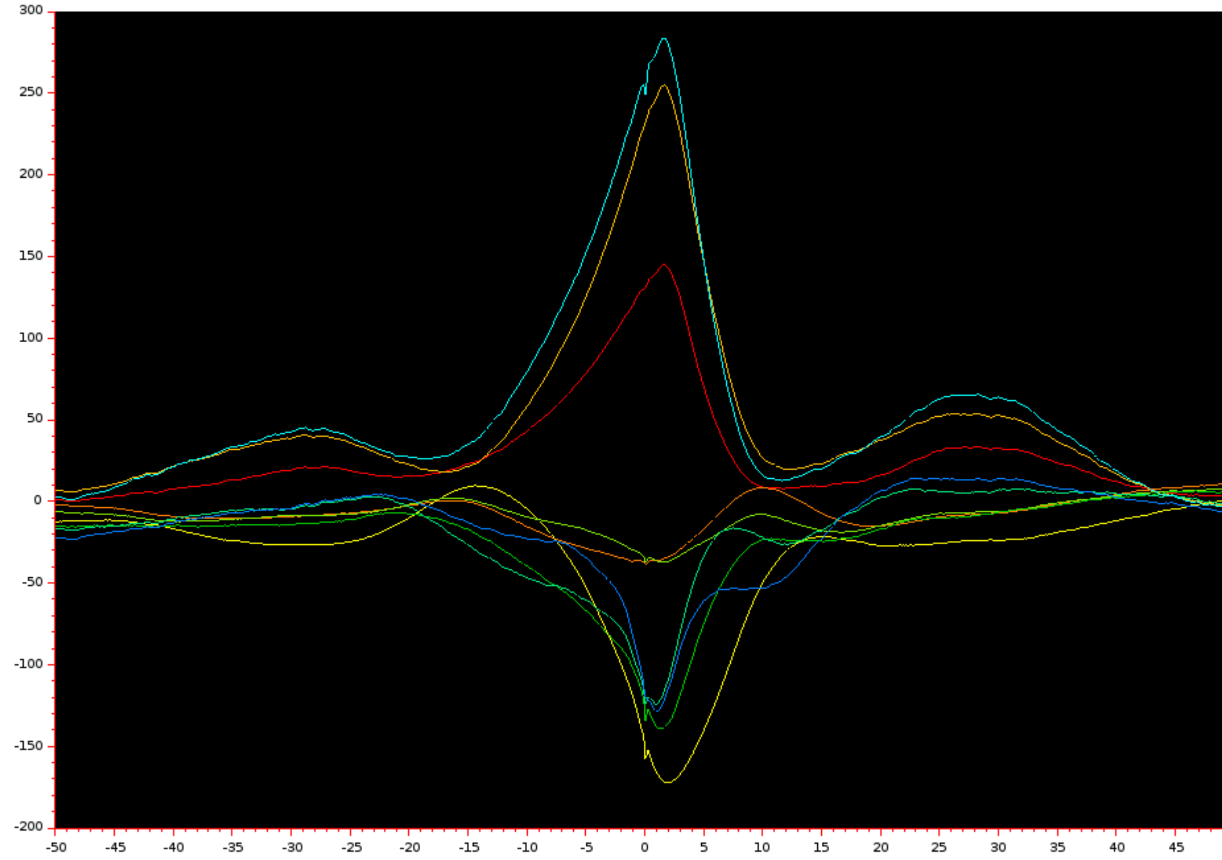
Micro-electro imaging

Cell type specific potentials Reconstructed without theta



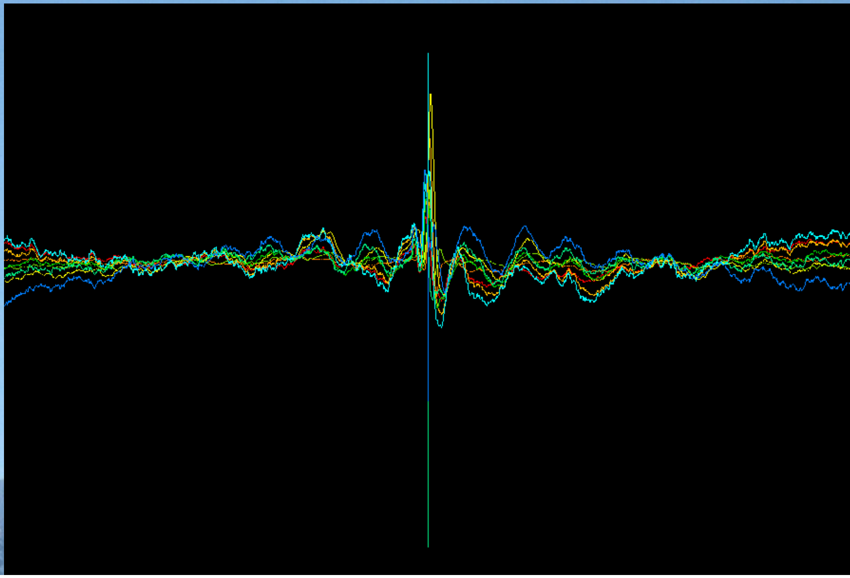
DG AxoAx neurons (n=4)



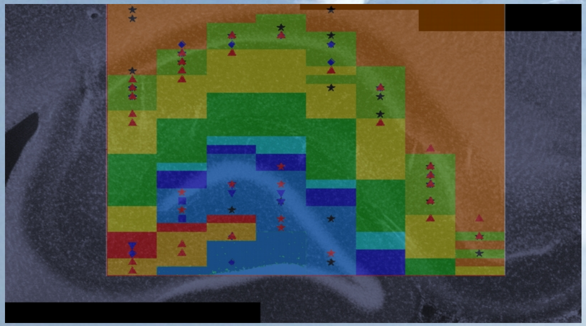


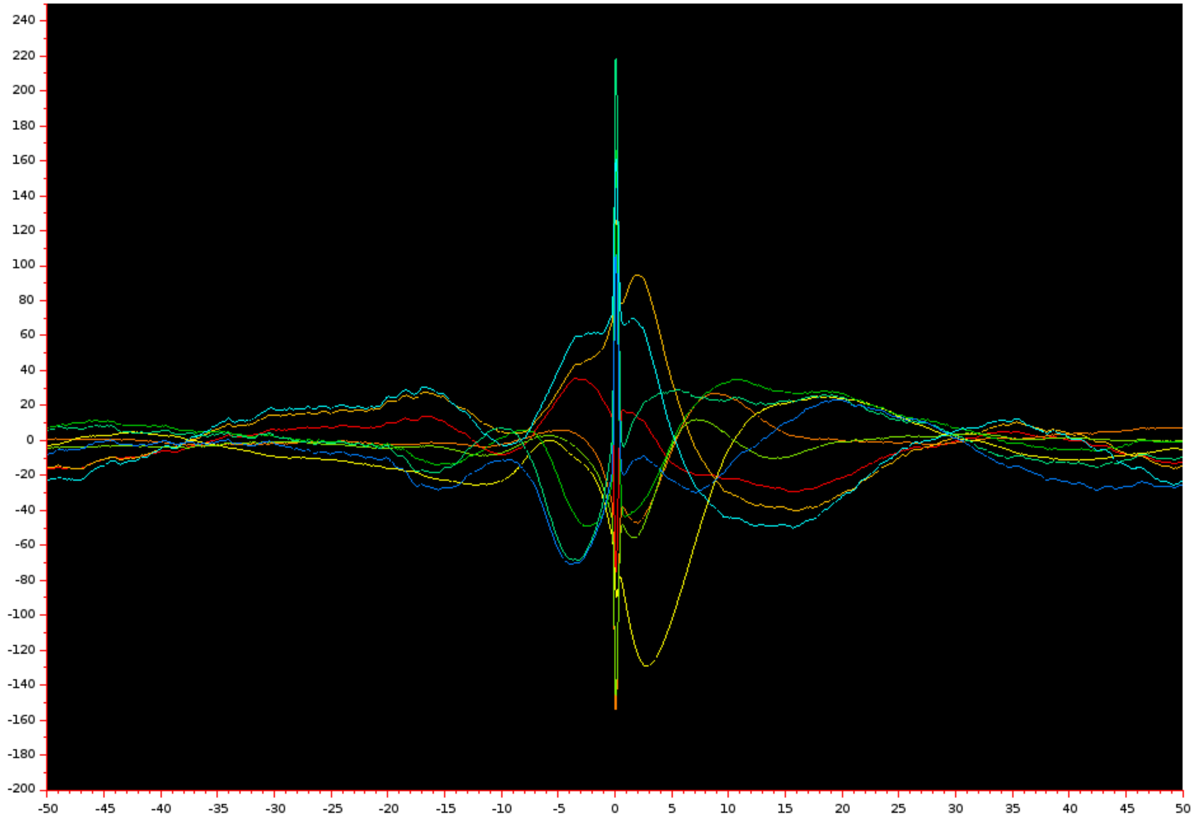
Micro-electro imaging

Cell type specific potentials Reconstructed without theta



CA3 AxoAx neurons (n=1)





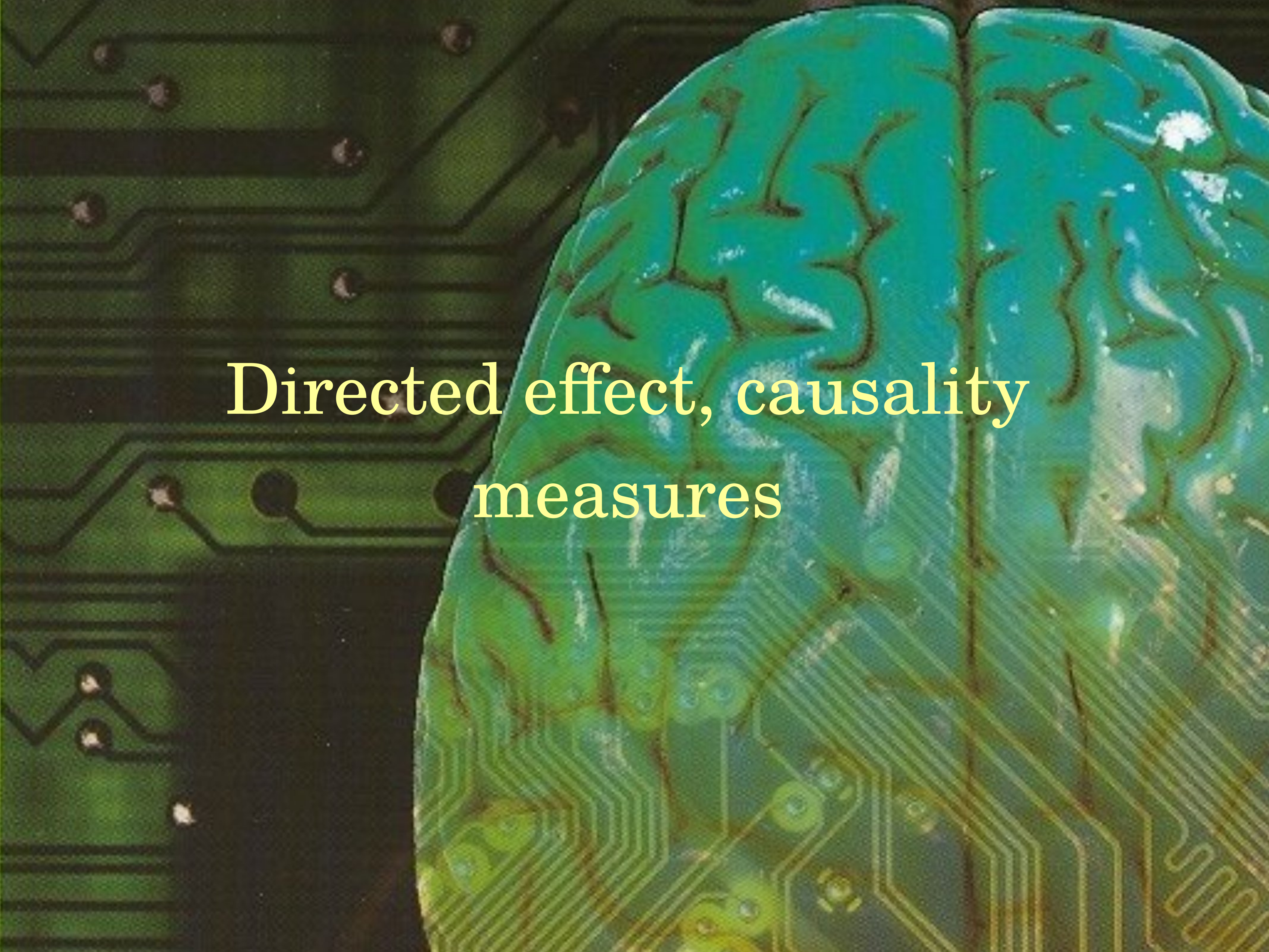
ARMA and ARIMA model fitting

$$X(t) = \sum A_i X(t-i)$$

$$X(t) = \sum A_i X(t-i) + \sum B_j X'(t-j)$$

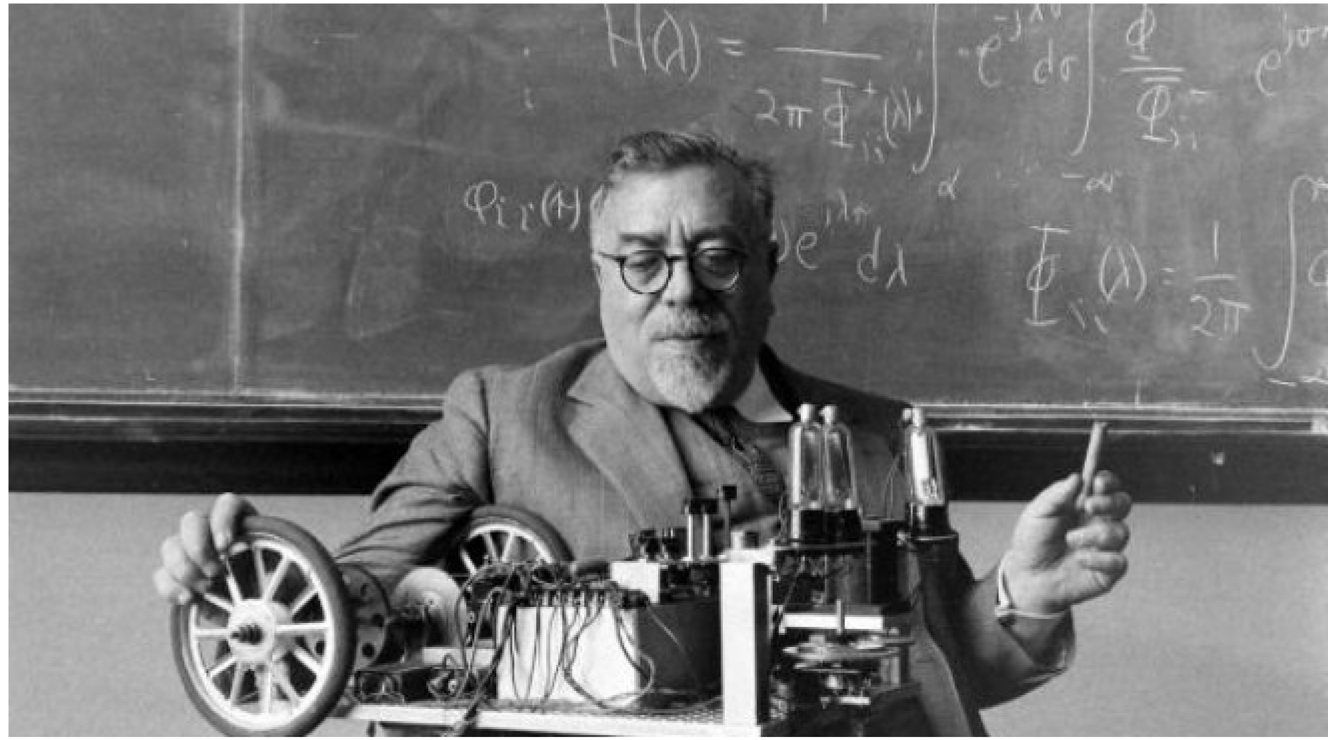
Partial autocorrelation

Directed effect, causality measures

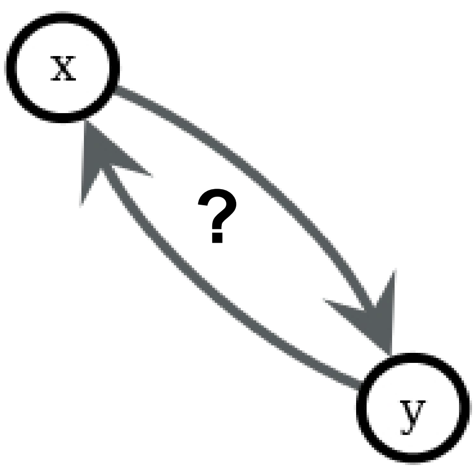


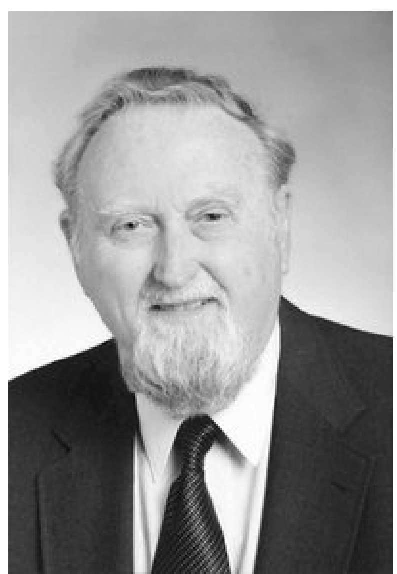
Granger-causality

The original idea came from Norbert Winer



x → ***y***, if the inclusion of past ***x*** values improves the prediction quality on ***y***





Clive Granger
Publication 1969

Nobel price in
Economic Sciences 2003

Causality measures

Granger-causality

$$X(t) = \sum_{i}^{p} a_1(j)\, X(t-j) + \epsilon_1(t)$$

$$Y(t) = \sum_{i}^{p} d_1(j)\, Y(t-j) + \eta_1(t)$$

$$X(t) = \sum_{j}^{p} a_2(j)\, X(t-j) + \sum_{j}^{p} b_2(j)\, Y(t-j) + \epsilon_2(t)$$

$$Y(t) = \sum_{j}^{p} c_2(j)\, X(t-j) + \sum_{j}^{p} d_2(j)\, Y(t-j) + \eta_2(t)$$

Causality measures

Granger-causality

$$\Sigma_1 = Var(\epsilon_1(t)) \qquad \Sigma_2 = Var(\epsilon_2(t))$$

$$\Gamma_1 = Var(\eta_1(t)) \qquad \Gamma_2 = Var(\eta_2(t))$$

$$F_{Y \rightarrow X} = \log(\Sigma_1) - \log(\Sigma_2)$$

$$F_{X \rightarrow Y} = \log(\Gamma_1) - \log(\Gamma_2)$$

$$F_{YX} = \log(\Sigma_2 \Gamma_2) - \log(\Sigma_2^2 - cov^2(\epsilon_2(t)\eta_2(t)))$$

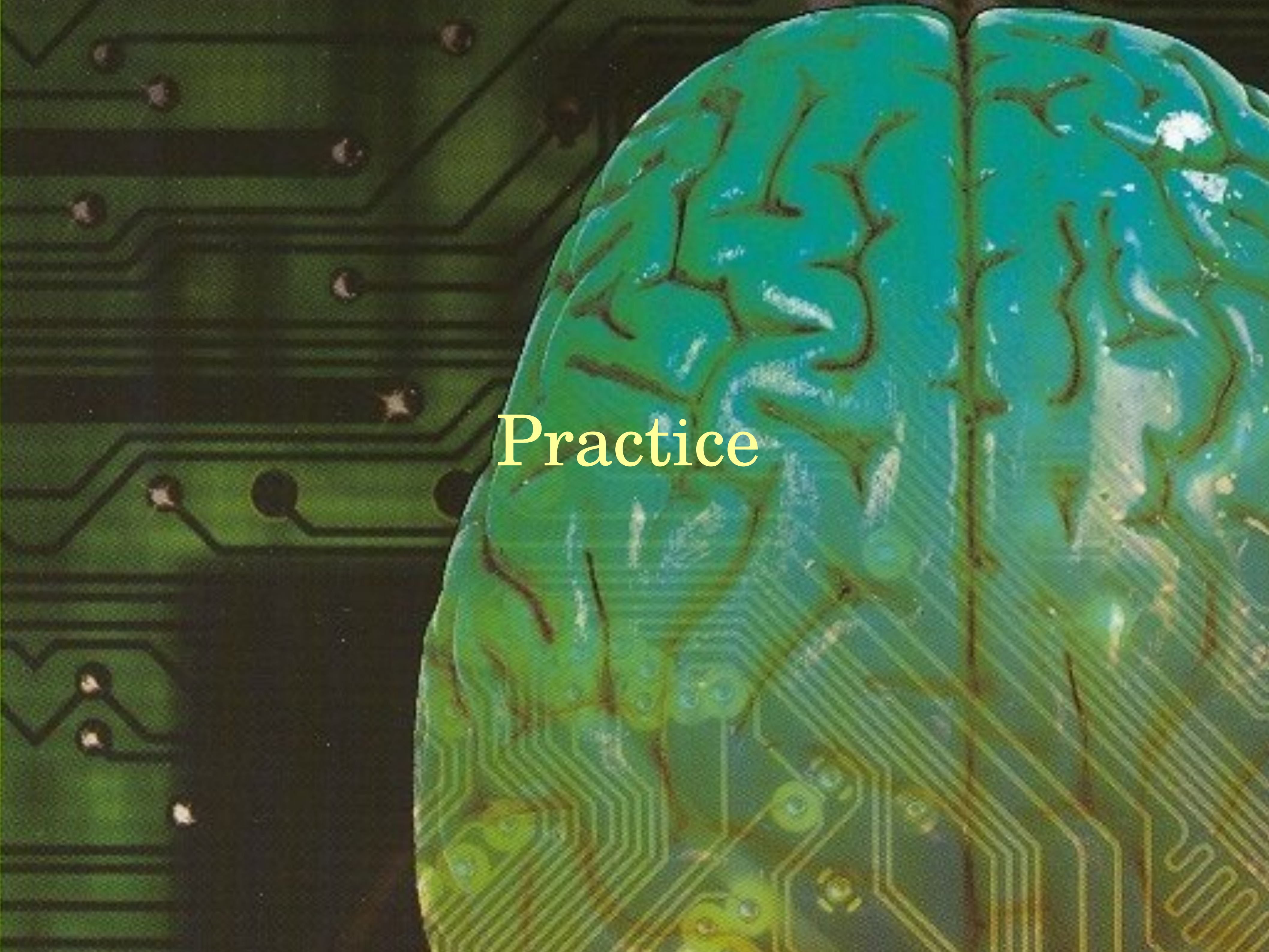
Problems with the Granger-causality

Model dependency can be ameliorated by using nonlinear extensions, kernel solutions or model free transfer entropy method.

But,

The problem implied by self-predictability and uncertain outcome for bidirectional coupling is inherent in the basic principle:
In case of circular coupling, the information contained by the second data series is already available in the system's own past.

Practice



Practice

```
stacksize(2e8)
getd ~/TANIT/SummerSchool15/PRACTICE
loadmatfile('~/TANIT/SummerSchool15/PRACTICE/Seizure1.mat');
st=1e3;
chn=43;
cm1=CorrFor(adat,1,5e3);
stn=floor(size(adat,1)/st);
scm=zeros(stn,chn);
cmm=zeros(stn*chn,chn);
for k=1:stn
l1=(k-1)*st+1;
l2=k*st;
[cm]=CorrFor(adat,l1,l2);
cmm((k-1)*chn+1:k*chn,:)=cm;
scm(k,:)=mean(cm,'r');
end

socol(24);
tplot(scm);
```