- *"Everything rests by changing"*

Heraclitus, (535-475 BCE)

So, Where are we exactly?

Single-Trial Variability
in Early Visual Neuromagnetic Responses :
An Explorative Study based on the Regional Activation
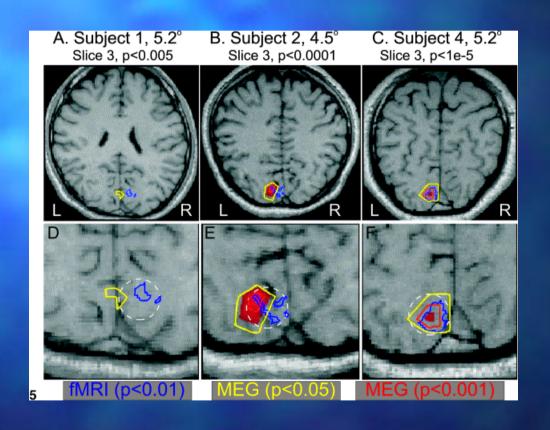## Contributing to the N70m peak

🖐 *is **N70m peak** a reproducible response at the single-trial level ?*

🖐 *is "signal + noise" a valid model ?*

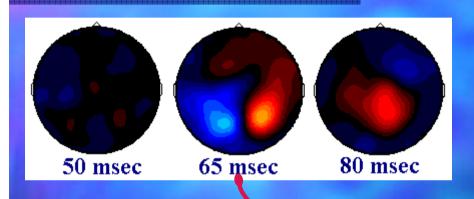🖐 *is **ensemble averaging** an appropriate response-recovery technique ?*

Objectives

❶ to exploit the **temporal resolution** of MEG signal
to precisely **characterize the nature** of response variability

❷ to identify the dominant sources
contributing to the variability observed in the MEG signal

❸ to associate the variability seen in the multichannel signal
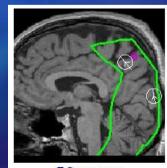with the activity in early visual areas

[F. Moradi et al., NeuroImage, 2003]

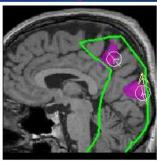# " Consistent and precise localization of brain activity in human primary visual cortex by MEG and fMRI "

**From
the multichannel MEG signal
to
tomographic estimates of brain activity**

50 msec   65 msec   80 msec
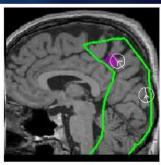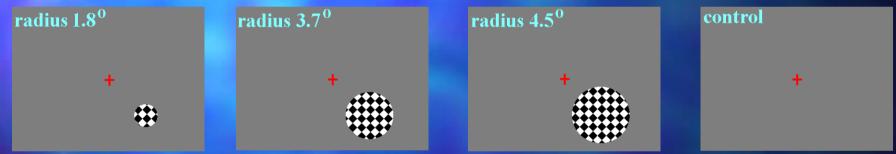
50 msec   65 msec   80 msec
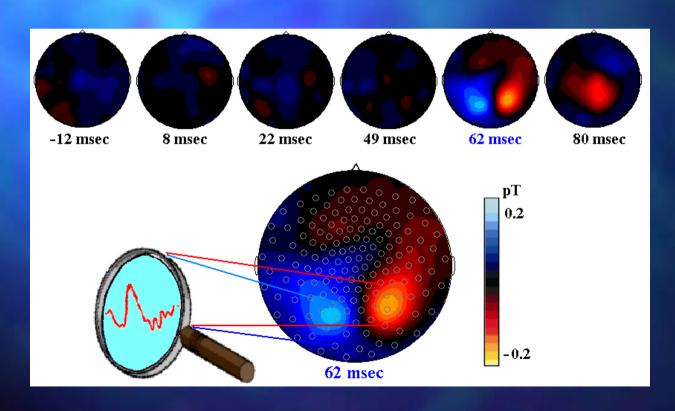
MEG signal recording and preprocessing

- 2 subjects from the "fMRI & MEG"-study participated

- 3 different runs of pattern reversal stimulation (1.43 Hz) & 1 subject baseline run were recorded

radius 1.8°   radius 3.7°   radius 4.5°   control

- for each run, 240 trials were recorded, with 625 Hz s.f. using the 151-channel whole-head Omega biomagnetometer.

- 3rd gradient formation, band-pass filter : 1-120 Hz, powerline removal, cardiac artifact elimination.

- trials were extracted : -100 to 200 msec and those without eye related activity were selected.

Methods

① **Design of the spatial filter used to extract the temporal patterns conveying the regional response dynamics**

single trials

1

2

3

N-2

N-1

N

average

0

1pT

0.1 sec

x y

pT

0.2

y 0

-0.2

0 0.2 0.4 pT

x

2

3

1

y

0.2

0

-0.2

-0.2 0 0.2 x

y

0.2

0

-0.2

-0.2 0 0.2 x
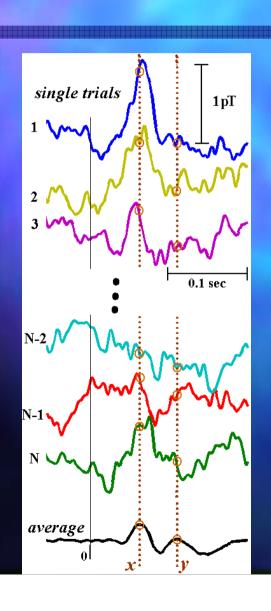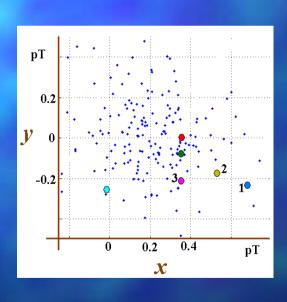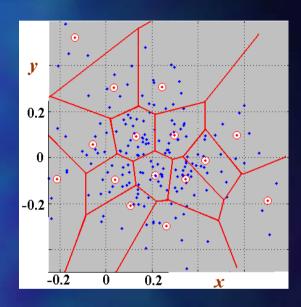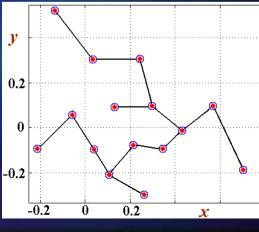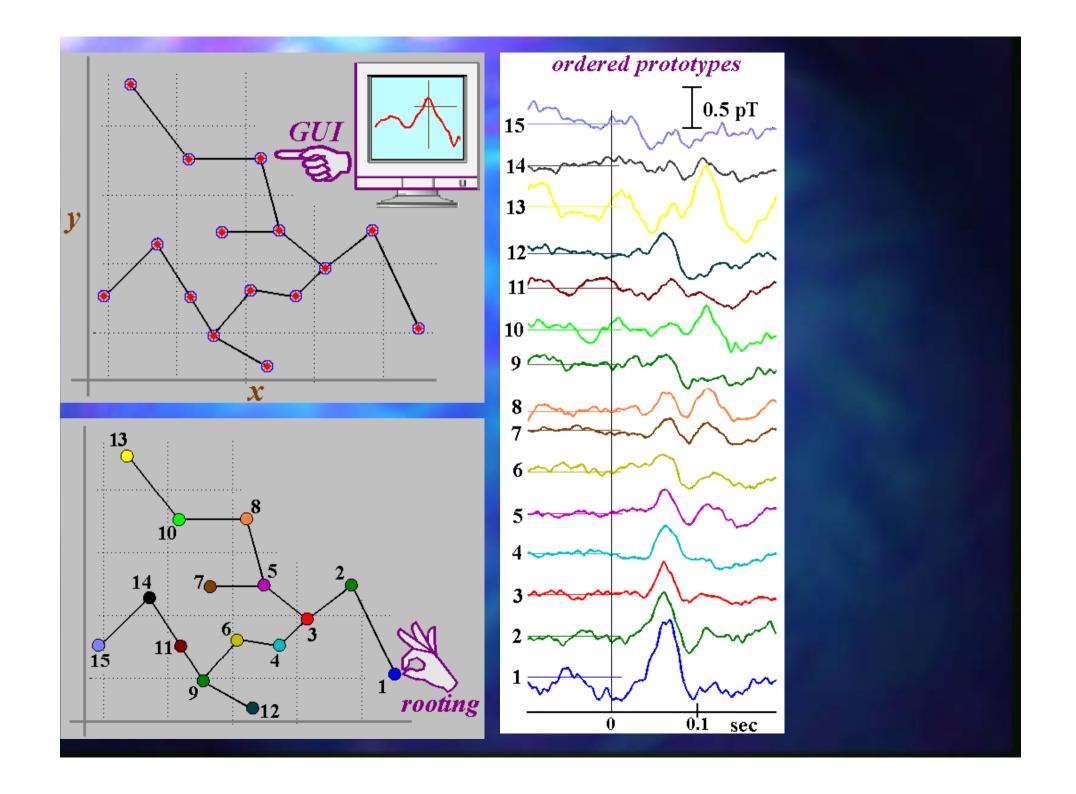
③ within-group analysis of regional response dynamics
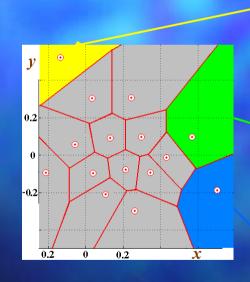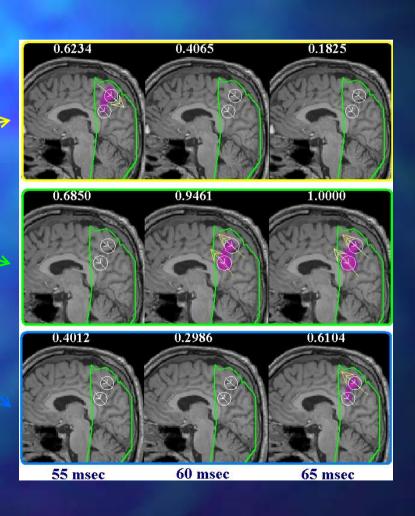
④ *within-group analysis of multichannel single-trial signals*

multichannel prototypes

0 msec   20 msec   40 msec   60 msec   80 msec   100 msec

⑤ *within-group analysis*
of single-trial MFT-solutions
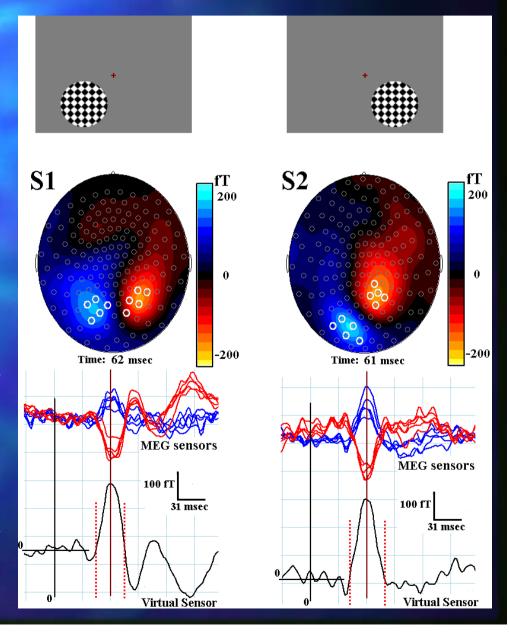
Results

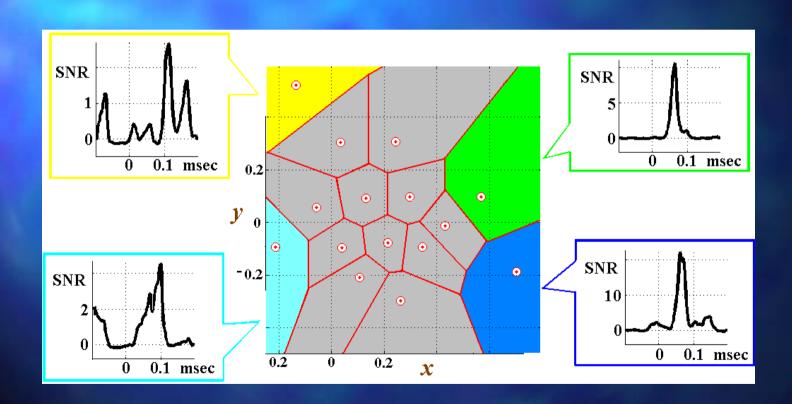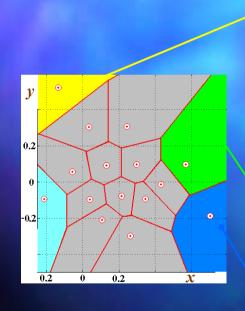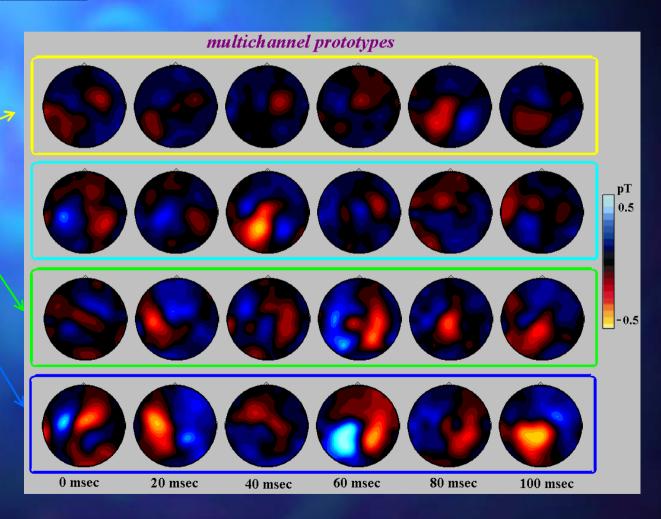The Virtual Sensor design from the averaged MEG signal (4.5°-run)
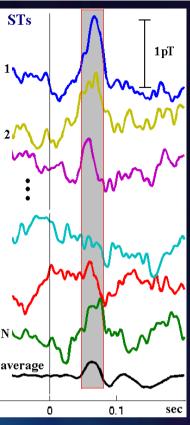
Feature extraction based on the N70m latency-range
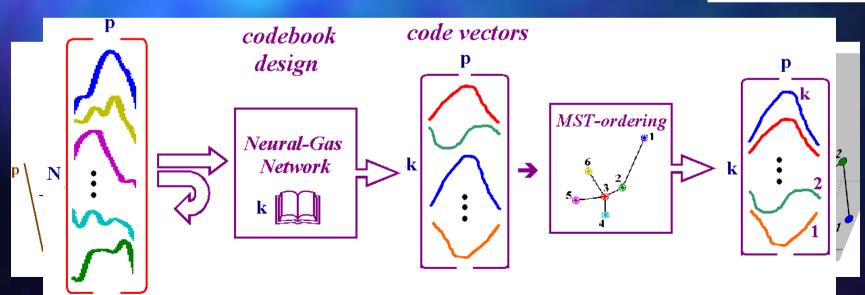
the brain waves captured by the Virtual Sensor
mainly reflect the dynamic behavior of the generators
responsible for the formation of the averaged N70m-peak
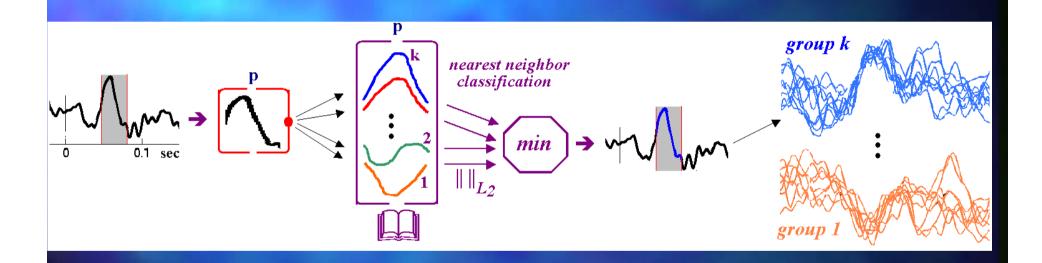
Based on the single-trial snapshots of regional brain activity
corresponding to the N70m-related latency-range
the response variability was described
using a Vector-Quantization scheme.

➔ The design of the encoder

➔ The application of the encoder

The design of the encoder (from the 4.5^o run, k=10)

STs

1pT

average

codebook design

code vectors

Neural-Gas Network

MST-ordering
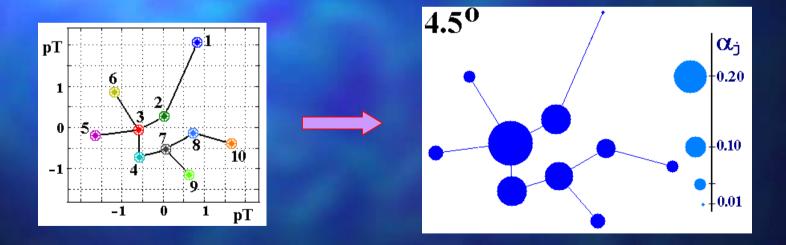
The application of the encoder (to all runs)
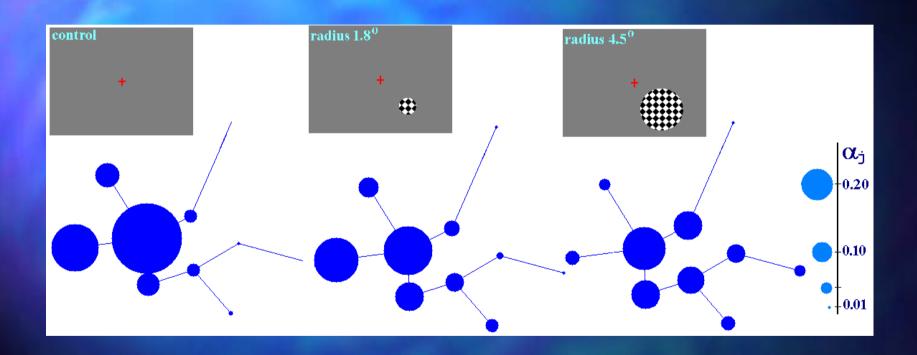
Visualizing the VQ results
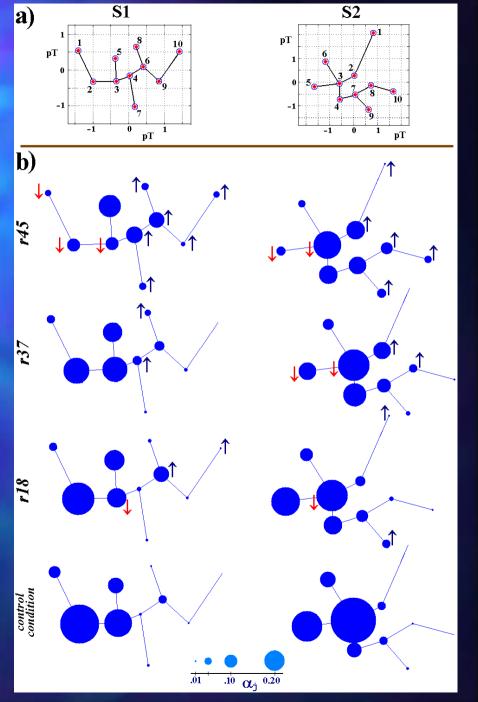
i. By computing a 2D representation of the designed codebook and
ii. depicting graphically the distribution of N70m snapshots in the k=10 groups
with the node size

The codebook could be kept fixed across the different runs
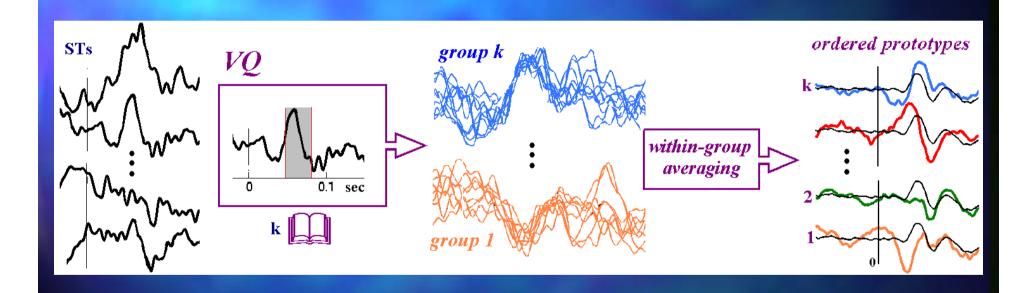
The Voronoi-regions were populated in a stimulus-size-dependent manner
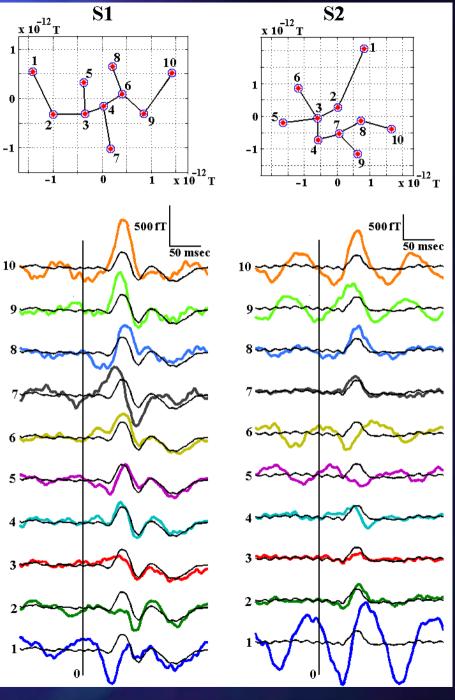
By within-group averaging,
prototypes of regional brain activity were formed.
The computed prototypes of evoked response were compared with each other
and contrasted with the ensemble average

a rich dynamic behavior
of the N70m generators
was revealed

The 2D-sketch
of the codebook
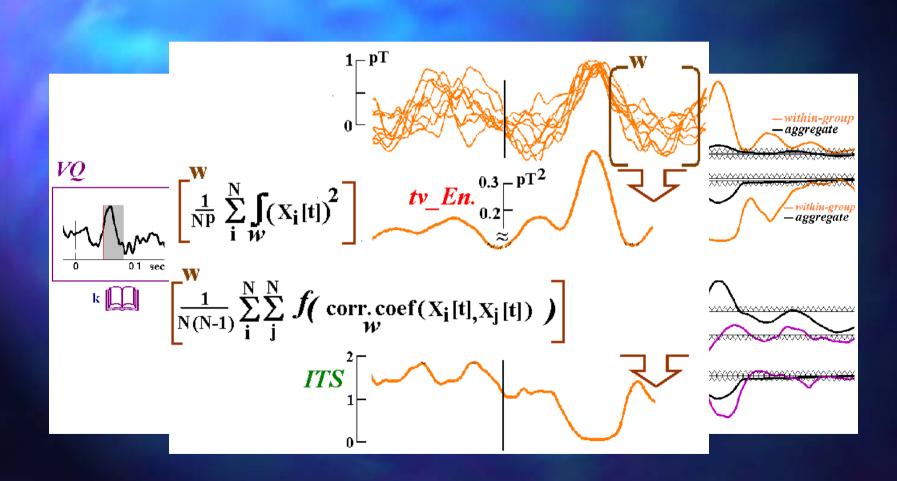
transient response
vs.
oscillatory activity
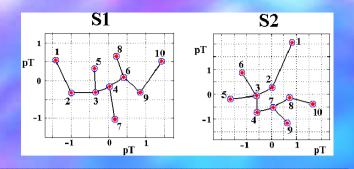
Distinct response modes ?
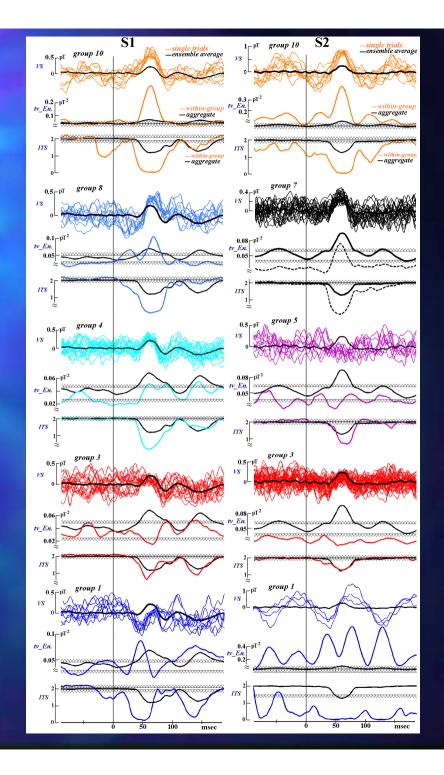
The ordered prototypes
of regional brain activity

Using two signal descriptors :
    the *time-varying energy* & *the inter-trial synchronization*
expressing *amplitude-modulation* and *phase-modulation* accordingly,
we provided a within-group characterization of the evoked response

A highly adaptive system is stimulated

Within a run the response mode changes :
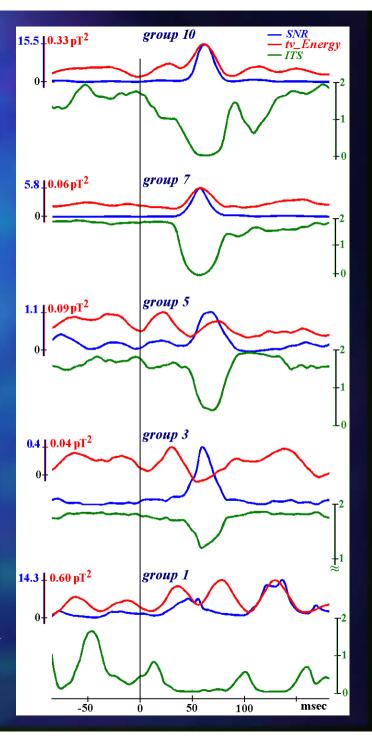
from

stimulus-locked *increase in the energy*   (10)

to
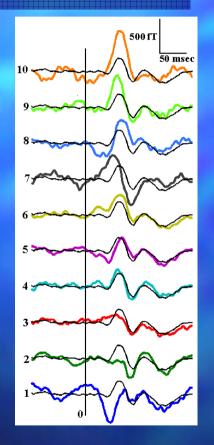
phase-resetting of the ongoing regional activity (5)
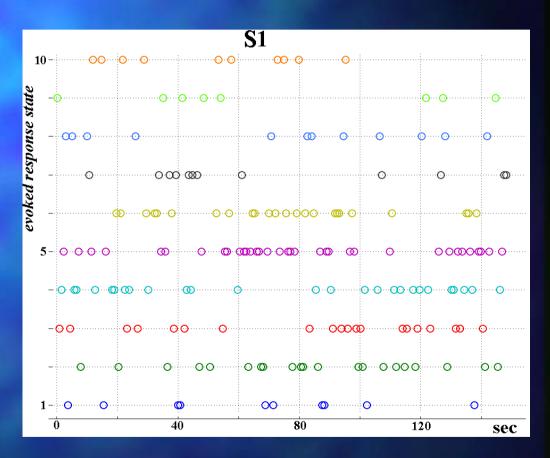
….. And stimulus-induced *desynchronization*

… or *Enhancement* of the ongoing rhythmic activity

Trial-to-trial non-stationarity

is the transition between successive responses a stochastic process ?

A ***Markovian Analysis***
of evoked response succession

The ***Transition Matrix*** was computed for each run
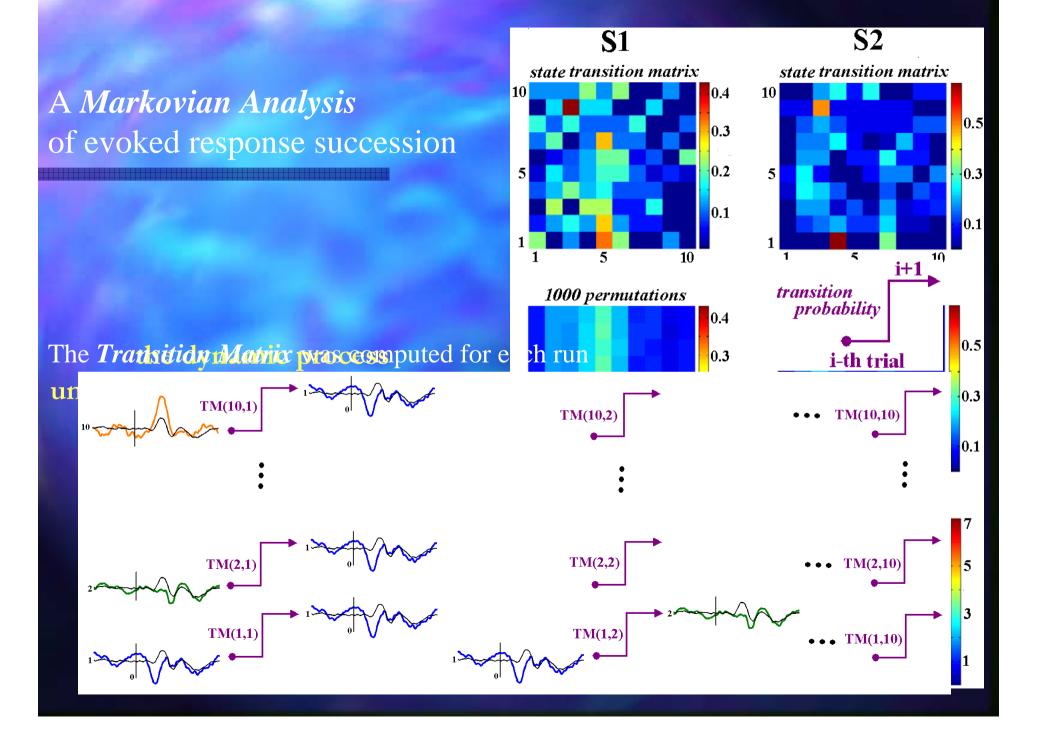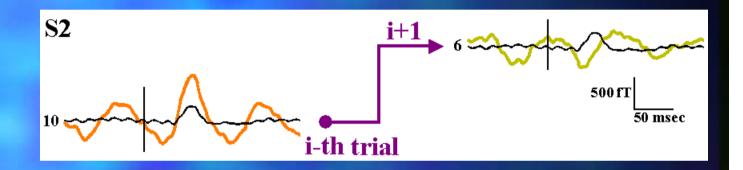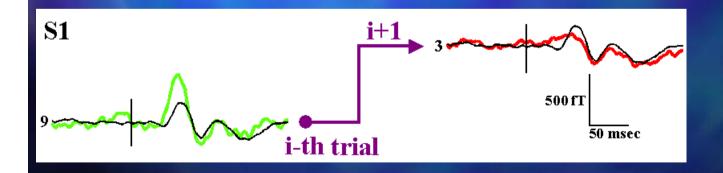
The transition from
a high-responsiveness state
to a low-responsiveness state
was the most important "law"
governing the sequence of responses
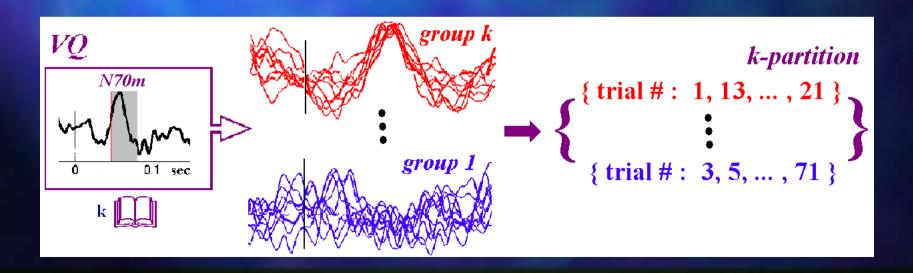
which are the generators of N70m-response variability ?

We applied the *k-partition* to the corresponding single-trial estimates
of current source density produced by tomographic analysis *(MFT)*
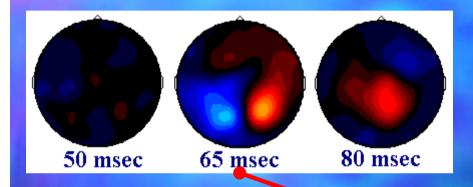
and
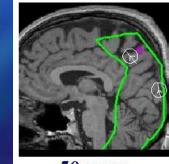
we computed spatiotemporal prototypes of localized brain activity

(MFT-based prototypes)
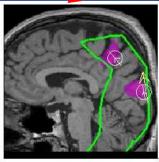
The k-partition was the "thread"
connecting the MEG-signal
with the tomographic estimates

50 msec 65 msec 80 msec

k-partition

{ trial # : 1, 13, ... , 21 }

{ trial # : 3, 5, ... , 71 }
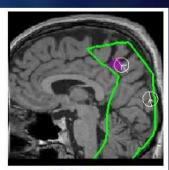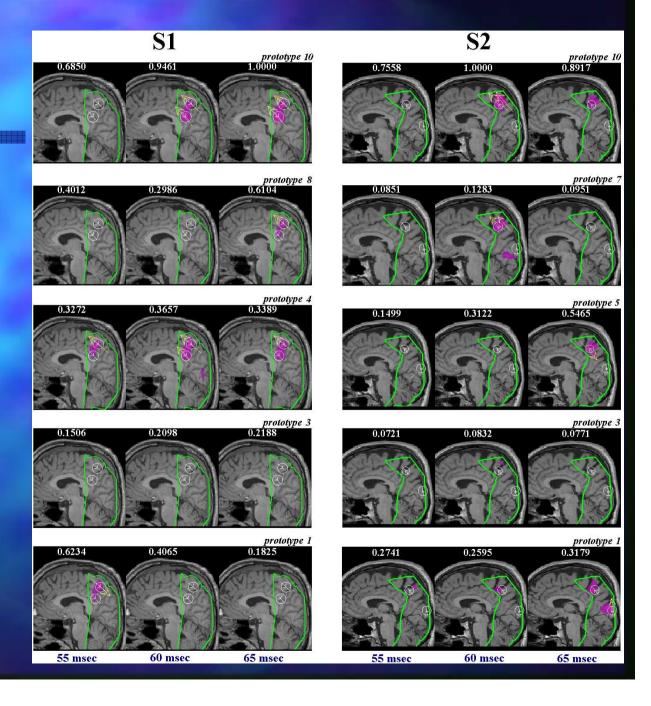
50 msec 65 msec 80 msec
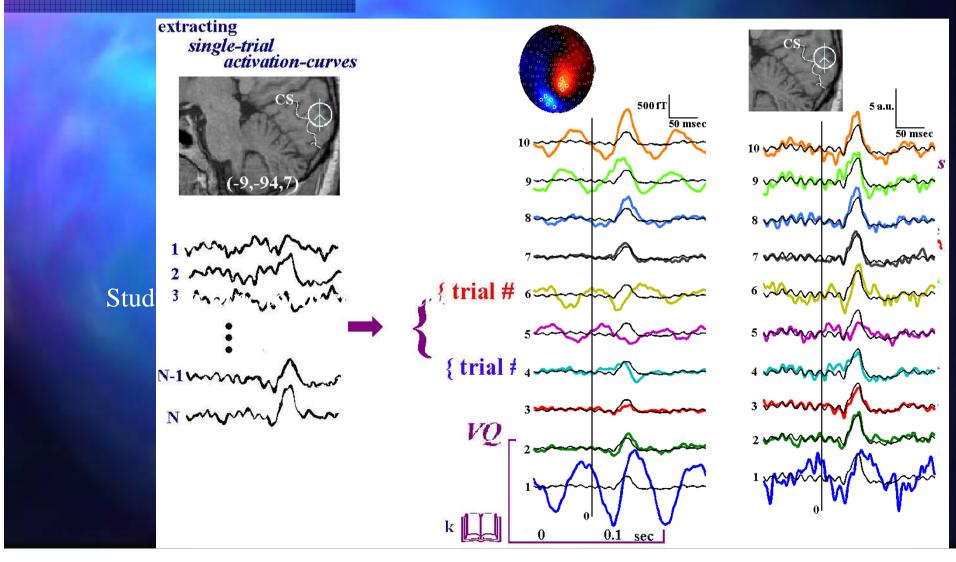
By visual exploration of MFT-based prototypes :

- Polymodal parietal areas (BA5 & BA7) contribute mostly to the N70m-related brain waves
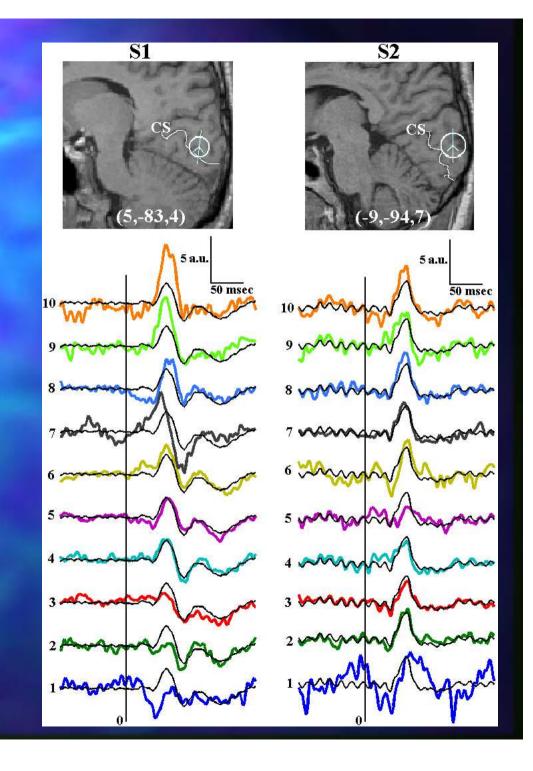
- V1 contribution is considerably weaker
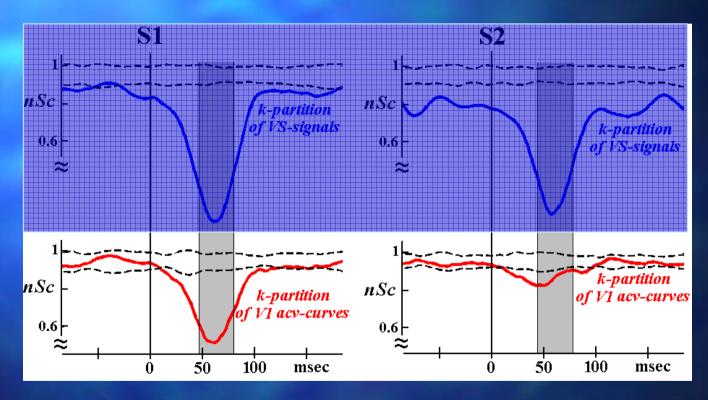
Is there any relationship between N70m-response variability and activity in early visual areas ?

- *structural similarity*
between the set of VS-patterns
and the set of ROI acv-curves
was detected

This structural similarity
was quantified using a functional
from *partitional-clustering*

**The k-partition constitutes
a valid description of single-trial variability,
in the post-stimulus period, for the acv-curves**

averaged signal
vs.
single-trial signals
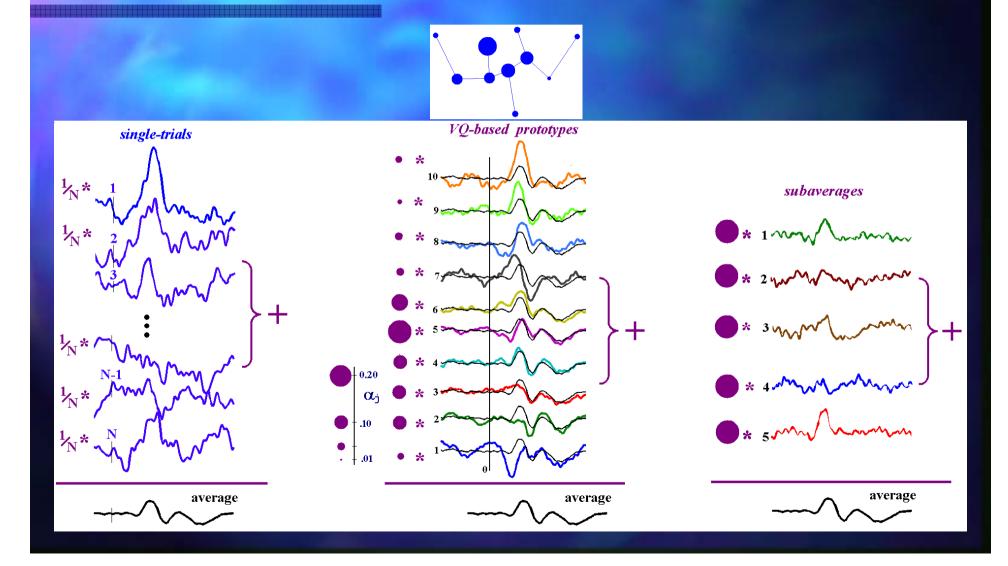
- **Bridging the gab, by means of subaveraging**

- **The average can be modeled as weighted average of the VQ-based prototypes**

$$\overline{x}(t) = \frac{1}{N} \sum_{i}^{N} x_i(t) = \sum_{j}^{k} \alpha_j \ y_j(t)$$

$$y_j(t) = \frac{\sum_{i}^{N} u_{ij} \ x_i(t)}{N_j} \ , \quad \alpha_j = \frac{N_j}{N} \ , \quad N_j = \Sigma_{i=1}^{N} u_{ij}$$

$$\overline{x}(t) = \frac{1}{N} \sum_{i}^{N} x_i(t) = \sum_{j}^{k} \alpha_j \ y_j(t)$$

single-trials

VQ-based prototypes

subaverages

$\frac{1}{N} *$ 1

$\frac{1}{N} *$ 2

3

$\frac{1}{N} *$

N-1

$\frac{1}{N} *$

$\frac{1}{N} *$ N

+

10

9

8

7

6

5

4

3

2

1

α_j

0.20

.10

.01

0

+

* 1

* 2

* 3

* 4

* 5

+

average

average

average
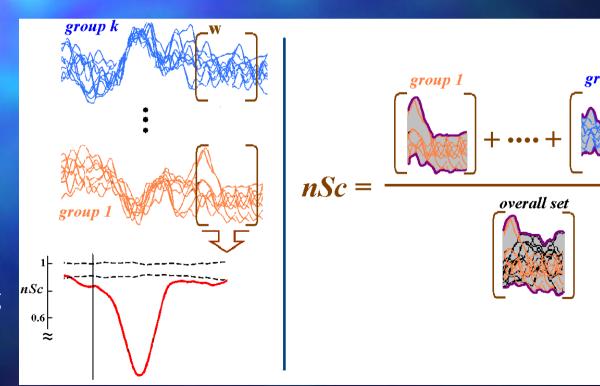
This kind of modeling is informative
for describing the variability in a set of responses
 <u>only</u> if the formed subaverages are different from each other

$\Leftrightarrow$

if the groups of single-trials
are forming compact, well-separated clusters

Normalized scattering

random partition $\rightarrow$ 1

VQ   k 📖

N70m

0   0.1   sec

k-partition

$$\left\{ \begin{array}{c} \{\text{ trial \# : } 1, 13, ..., 21 \} \\ \vdots \\ \{\text{ trial \# : } 3, 5, ..., 71 \} \end{array} \right\}$$
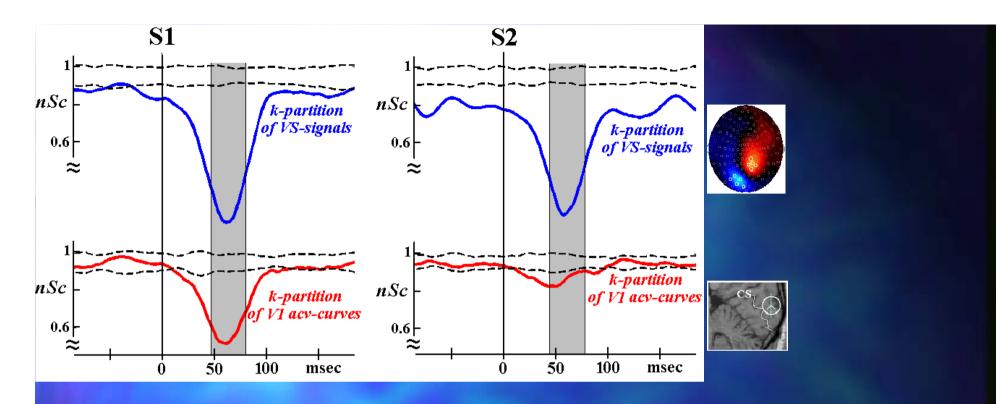
The k-partition
which had been computed from the N70m-snapshots
was applied to the regional and local responses.

The induced-grouping was validated, using the nSC-index,
for both the set of responses.

We can consider the computed nSc-curve
as the "autocorrelation" function of the N70m-variability
for the Virtual-Sensor signals

&

as the "transfer function" showing how/if the N70m-variability
manifests itself in the set of V1-ROI signals.
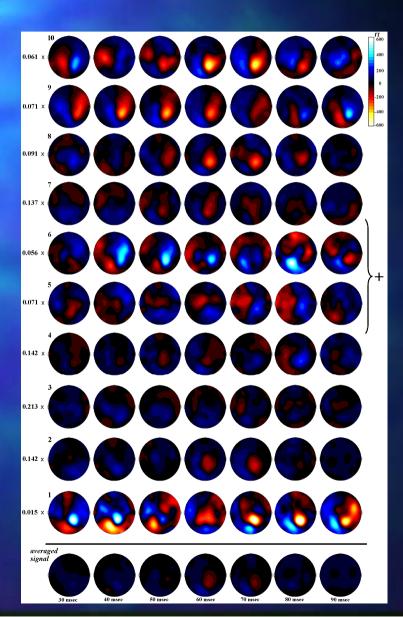
For the VS-signals (i.e. regional brain activity),
the k-partition is a valid description well-before the stimulus-onset.

The ongoing activity before the stimulus-onset
is functionally coupled with the subsequent regional response
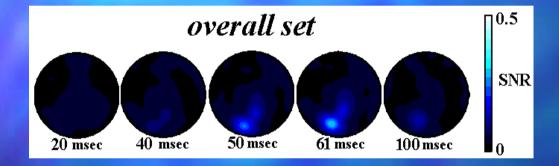
For the V1-ROI signals (i.e. local brain activity)
the k-partition is a valid description
for a confined latency-range in the post-stimulus period.
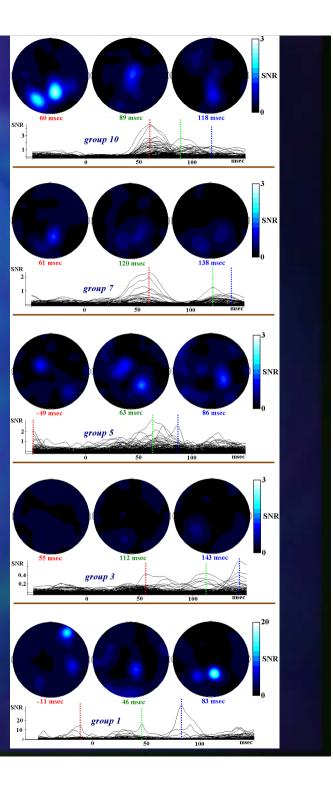
There is a strong coupling of the responses
in early visual areas to the regional dynamics.

**Distinct response dynamics
are fused into one single timecourse
by ensemble-averaging**
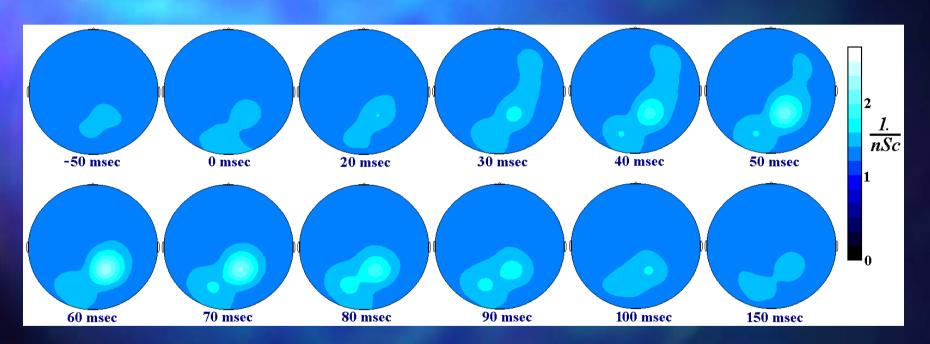
There is a loss of information;
which can be restored
by VQ-based grouping

overall set

20 msec   40 msec   50 msec   61 msec   100 msec

Directed / Supervised Data Mining

Validation of the k-partition for the multichannel MEG signal

Concluding
Remarks

The broad spectrum of N70m responses

was described by means of principal modes
which summarized the variability in the MEG signal

and further used for exploring the source of that variability
based on estimates of reconstructed brain activity

Our results revealed complex nonlinear interactions

between the sensory input and the ongoing activity
resulting to a *state-dependent response*

with a wide range of characteristic time scales

At the level of single-trial activity,

the *polymorphic response* to a simple stimulus
is generated by a coupling of polymodal areas

and cooperative activity in striate and extrastriate areas

Discussion

[Kisley & Gerstein, J. Neurosci., 1999]:

The response in rat auditory cortex is modulated by the preceding ongoing activity.
 "The observed variability was attributed to rapid transitions
between different levels of thalamocortical excitability"

[Fries et al, Nat. Neurosci., 2001]:

Stimulus-induced covariation of distinct brain areas (in cats).
"Coherent oscillations mediate the functional coupling between brain areas"

[Hupe et al, J.Neurophysiol., 2001]:

Feedback connections act on the early part of the responses in monkey visual cortex.
➔   "Temporally compact" visual cortex

[Lutz et al., PNAS, 2002]:

The human EEG response is modulated by background activity.
"Variability is controlled by subject's cognitive "context"
<u>and</u> characteristic patterns of synchrony between brain areas"

✉ is "signal + noise" a valid model ?

✉ is ensemble averaging
an appropriate response-recovery technique ?

due to **Trial-to-Trial Non-Stationarity :**

Unless there is a predominant mode,
the computed average
is a mirage of the response generation process
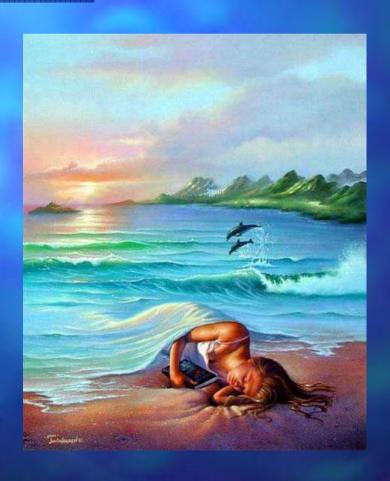where different dynamics have been collapsed.

✍ *are there systematics behind the seemingly random single-trial fluctuations*

✍ *can we decipher the Brain-Waves ?*

- Ordered code-book.

" The concepts I understand are great,
but I believe that the concepts I can't understand are great too.
However, the reader needs to be an excellent swimmer
like those from Dilos, so not to be drown from this (code) book ".

- Socrates

With many thanks .....

to a lot of people ....