STATISTICAL MEMORY OF MEG SIGNALS AT PHOTOSENSITIVE EPILEPSY

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Here we discuss the remarkable role of the statistical memory effects in the human brain functioning at photosensitive epilepsy (PSE). We have analyzed three independent statistical memory quantifiers for the magnetoencephalographic (MEG) signals. These quantifiers reflect the dynamical characteristics of neuromagnetic brain responses to a flickering stimulus of different color combinations. Results for a group of control subjects are contrasted with those from a patient with PSE. The emergence of the strong memory and the transition to a regular and robust regime of chaotic behavior of the signals in separate areas is characteristic for a patient with PSE versus a healthy brain.

The spatiotemporal characteristics of brain electromagnetic activity have received considerable interest, and many studies have been performed in order to understand the origin and the role, as well as the dynamics of neural activity [Malmivuo & Plonsey, 1995; Billock *et al.*, 2001; Wolf, 2005; Jiang *et al.*, 2003]. Measurements of the magnetoencephalogram (MEG) as well as the electroencephalogram (EEG) provide unique insights into the dynamic behavior of the human brain as they are able to follow changes in neural activity on a millisecond time-scale [Hämäläinen *et al.*, 1993]. The physical processes of the physiological activity of neurons can be registered with noninvasive

measurement techniques on the basis of EEG and MEG. These macroscopic electrophysiological techniques allow to trace the time evolution of neural population activation with millisecond temporal resolution. Neural electromagnetic responses are handled by the same physical processes that relate to electric and magnetic fields in other complex systems.

Here we describe that the statistical memory effects play an important role in the functioning of human brain. Particularly, it means that the appearance of strong memory effects (and respectively, large memory times scales) in the stochastic dynamics of neuromagnetic signals specifies the pathological or catastrophic breaking of dynamic states of the healthy human brain. As an example, we will show here that the occurrence of strong memory effects in the stochastic behavior of neuromagnetic responses of human brain recording by MEG is accomplished by the generation and the existence of PSE.

From the beginning, statistical quantifiers of memory in time series for physiological systems that has been studied in EEG and MEG signals, both of healthy subjects and patients (including epilepsy patients) are based on the detrended-fluctuation analysis (DFA) [Goldberger *et al.*, 2000]. On the other hand, one of the most powerful tools for the quantitative description of statistical memory effects of random processes in the physiological data is the use of Zwanzig–Mori's kinetic equations. By the use of arguments in [Mokshin *et al.*, 2005] one arrives at a chain of interrelated finite-difference kinetic equations for the discrete time correlation function (TCF) $a(t) \equiv M_0(t) = \langle \delta x(t) \delta x(0) \rangle / \langle \delta x^2(0) \rangle$ of the fluctuation $\delta x(t) = x(t) - \langle x(t) \rangle$. Here $x(t) = (x_1; x_2; \ldots; x_N)$ is a random discrete-time process, i.e. $x_j = x(t_j)$, $t_j{=}j\ \tau$ and τ is a discretization time-step, $j = 1, 2, \ldots, N$. This TCF is then related to memory functions (MF) of the higher orders $M_i(t)$, $i = 1, 2, \ldots$ through the set of interconnected equations. Here $M_i(t) = \langle W_i(t) W_i(0) \rangle / \langle W_i^2(0) \rangle$ is a memory function of ith order, $W_i(t)$ is the corresponding dynamic orthogonal variable. Discrete MF's $M_i(t)$ together with corresponding relaxation parameters quantify the diverse memory effects. The whole set of MF's quantifies all singularities of the memory effects for complex systems. For the discrete time series the whole set of MF's $M_i(t)$ and relaxation parameters can be calculated directly from the experimental data [Mokshin *et al.*, 2005].

Here we use the reasons in [Mokshin *et al.*, 2005] to study the role of memory effects in the dynamics of complex systems. The characterizing of memory is based on the use of a set of dimensionless statistical quantifiers which are capable to measure the strength of memory that is inherent to the complex dynamics. First similar measure of memory is the quantity $\varepsilon_i(\omega) = \{\mu_i(\omega)/\mu_{i+1}(\omega)\}^{1/2}$. Second measure is defined as $\delta_i(\omega) = |\tilde{M}_i'(\omega)/\tilde{M}_{i+1}'(\omega)|$. Here, $\mu_i(\omega) = |\tilde{M}_i(\omega)|^2$ is a power spectrum of the corresponding memory function $M_i(t)$, $\tilde{M}_i'(\omega) = d\tilde{M}_i(\omega)/d\omega$ whereas $\tilde{M}_i(\omega)$ is a Fourier transform of the MF $M_i(t)$. The measures $\varepsilon_i(\omega)$ are suitable for the quantification of the memory on a relative scale whereas the second set $\delta_i(\omega)$ proves to be useful for the quantifying of the amplification of the role of relative memory effects inherent to the different complexity levels. Both measures provide for a very informative approach as statistical criteria in the comparison of the relaxation scales and the memory time scales. In the cases $\{\varepsilon, \delta\} \gg 1$ one can observe a complex dynamics with the short-range temporal memory scales. At the limit $\{\varepsilon, \delta\} \to \infty$ these processes possess δ-like memory. When $\{\varepsilon, \delta\} > 1$ one can consider a situation with moderate (intermediate) memory strength. And the case with both ε, $\delta \sim 1$ matches up typically to more regular and robust processes with the features of strong memory.

Experimental data for PSE are MEG's signals recorded from the group of nine healthy human subjects and from the patient with PSE [Bhattacharaya *et al.*, 2004]. PSE is a common type of stimulus-induced epilepsy, defined as recurrent convulsions precipitated by visual stimuli, particularly a flickering light. The diagnosis of PSE involves finding paroxysmal spikes on an EEG in response to the intermittent light stimulation. To elucidate the color-dependency of PS in normal subjects, brain activities subjected to uniform chromatic flickers with whole-scalp MEG has been measured. All further details of MEG experiment including the numbers ($n = 1, 2, 3, \ldots, 61$) of sensors and subjects, scheme of experiments can be found in [Bhattacharaya *et al.*, 2004].

Now we can proceed to memory analysis of PSE experimental data. With our set of Figs. 1–7, we present the results of numerical calculations and the analysis of the data within the framework of the nonequilibrium statistical approach for stochastic processes in discrete complex systems [Mokshin *et al.*, 2005]. In Fig. 1, we depict the typical data

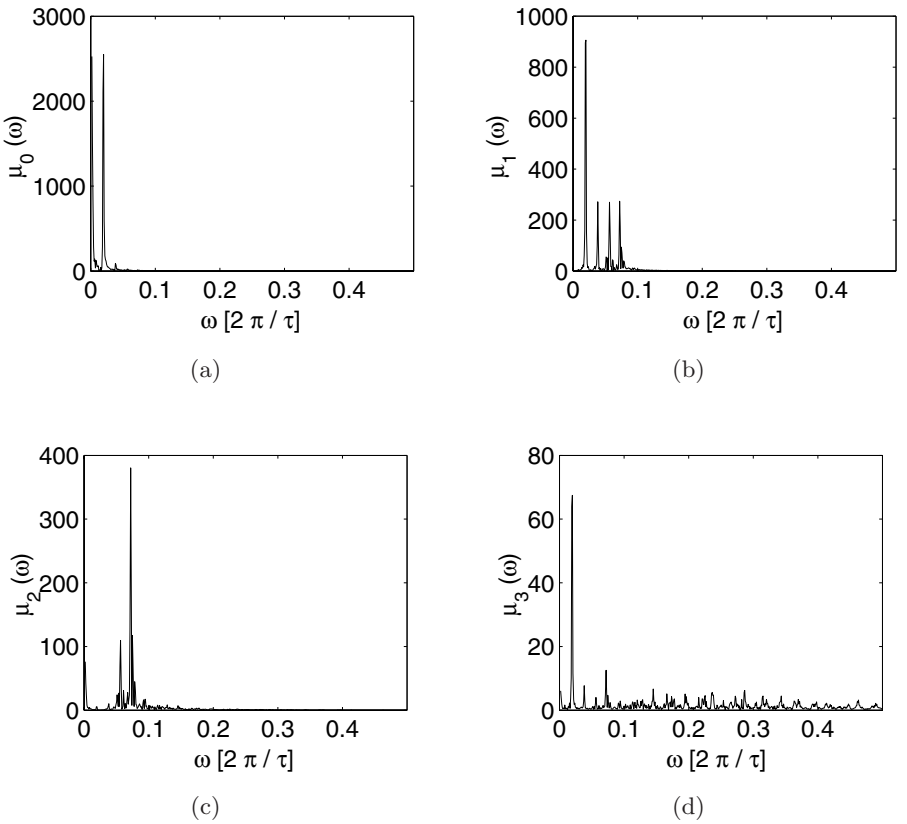


Fig. 1. Power spectra $\mu_i(\omega), i = 0, 1, 2$ and 3 for a healthy subject (No. 7), sensor No. 10 (an R/B combination of the light stimulus) for the set of four time correlation functions: (a) for the initial TCF $a(t)$; (b) for the first order MF $M_1(t)$; (c) for the second order MF $M_2(t)$; (d) for the third order MF $M_3(t)$.

for one concrete healthy subject (No. 7) in comparison with a PSE patient (Fig. 2) for a Red–Blue (RB) combination of the color stimulus. We see here the multifractal behavior of spectra for the healthy brain and the absence of similar behavior for the patient with PSE. The appearance of the sharp peak at the same frequency $\omega = 0.2$ f.u., 1 f.u. $= 2\pi/\tau$ is characteristic for all spectra for the patient with PSE. The observed distinction in the spectra is caused by the essential role of the statistical memory.

From the frequency dependence of the first informational measure of memory in Fig. 3 the role of the memory effects is more prominent. We see the fractal behavior of first memory measure $\varepsilon_1(\omega)$ for both (R/B and R/G) types of the light stimulus for the healthy brain. For the patient with PSE, similar fractals breakdown due to the origination of the strong memory effects. The difference in memory effects for the healthy brain versus that of patient with PSE is more sharp especially for the zones of the low and superlow frequencies where long-range correlations are incorporated: first zone for $0.7 \cdot 10^{-1}$ f.u. $< \omega < 0.5$ f.u., second zone for $2 \cdot 10^{-2}$ f.u. $< \omega < 0.7 \cdot 10^{-1}$ f.u. and third zone for $0 < \omega < 2 \cdot 10^{-2}$ f.u., 1 f.u. $= 2\pi/\tau, \tau = 0,02$ s.

The second measure of memory $\delta_i(\omega), i = 1, 2$ and 3 describes the memory effects in the largest scales: Fig. 4 for the healthy brain and Fig. 5 for the patient with PSE. The difference in the memory effects for healthy brain versus that of a patient is especially surprising at the point $\omega = 0$. Here this difference measures approximately 1000 times! A similar fact arises due to the long-range correlations in the human brain neuronal activity. The crucial role of the strong memory in the stochastic dynamics of neuromagnetic responses for the patient with PSE is essential.

To draw the conclusion on the role of the statistical memory effects we also show the averaged data for the whole group of nine healthy subjects versus the patient with PSE in Figs. 6 and 7. In Fig. 6, the topographic dependence of the second measure of memory $\delta_1(\omega = 0; n)$, n is a sensor number, for healthy brain versus that of a patient with PSE demonstrate the striking difference in the impact

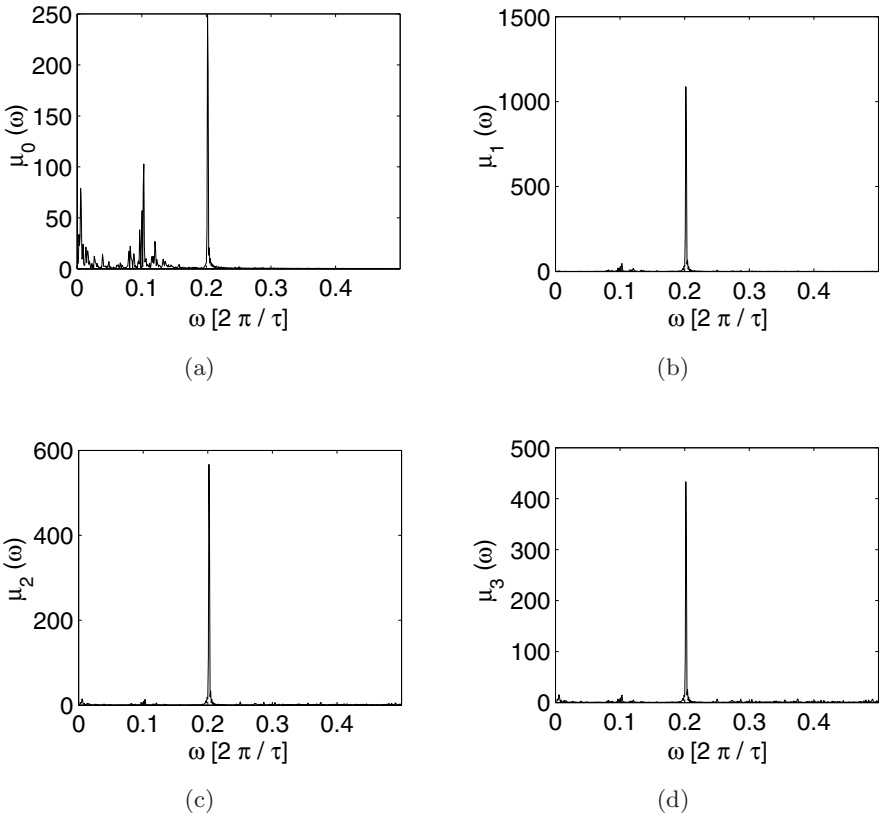


Fig. 2. Power spectra $\mu_i(\omega), i = 0, 1, 2$ and 3 for the patient with PSE, sensor No. 10 (an R/B combination of the light stimulus) for the set of four time correlation functions: (a) for the initial TCF $a(t)$; (b) for the first order MF $M_1(t)$; (c) for the second order MF $M_2(t)$; (d) for the third order MF $M_3(t)$. The sharp peak at same frequency $\omega = 0.2$ f.u. (1 f.u. $= 2\pi/\tau$) is characteristic for all spectra.

of strong memory effects especially for the sensors with No. 5, 23, 9, 11, 14 and 23. Here, we have used an R/B combination of the light stimulus and data are averaged for the whole group of the nine healthy subjects. For example, for sensor $n = 5$ the difference acquires approximately a valuation of 10^4 times!

To specify the role of the strong memory, we study further the spatial dependence in terms of a novel information measure, the index of memory, which is defined by:

$$\nu(n) = \frac{\delta_1^{\text{healthy}}(0; n)}{\delta_1^{\text{patient}}(0; n)}.$$

This third measure quantifies the sharp revision of memory effects in individual MEG sensors in the patient with PSE versus the healthy group. By means of $\nu(n)$ we can try to find the special zones (sensors) on the human cerebral cortex that are responsible for the mechanism of PSE. In Fig. 7 we have presented the topographic dependence on information measure $\nu(n)$ for the healthy brain (averaged on the whole group of nine subjects) in comparison with that of the patient with PSE. As shown in Fig. 7, the specific role of the individual zones on the human cerebral cortex with the sensors No. 10, 5, 23, 40 and 53 is proved. The sharp increase of the role of the memory effects in the stochastic behavior of the neuromagnetic signals is clearly visible for sensors with these numbers. The observed points of MEG sensors locate the regions of a protective mechanism against PSE in a human organism: in the frontal zone (sensor $n = 10$), right ($n = 5$) and left ($n = 23$) temporal zones, the left parietal ($n = 40$) and the occipital ($n = 53$) zones. The early activity in these sensors may reflect the protective mechanism that suppresses cortical hyperactivity due to chromatic flickering.

Earlier we showed [Bhattacharaya *et al.*, 2004] that brain responses against chromatic flickering in healthy subjects represent strong nonlinear structures whereas nonlinearity is dramatically reduced to minimal in patients. Here we report that the patient's brain show significantly stronger statistical memory effects than in healthy brains.

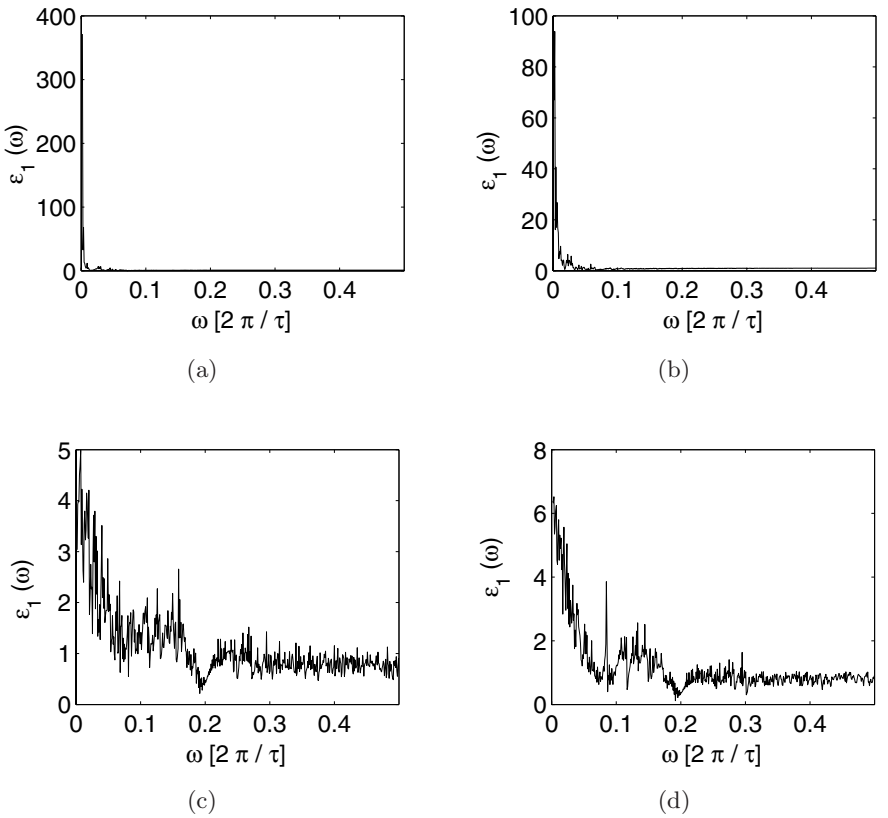


Fig. 3. The frequency dependence of the first point $\varepsilon_1(\omega)$ for sensor No. 10: for the healthy No. 7 (a and b) and for the patient with PSE (c and d) (for an R/B (a and c) and an R/G (b and d) combination of the light stimulus). The emergence of the weak memory with $\varepsilon_1(\omega) \gg 1$ for the healthy and strong memory with $\varepsilon_1(\omega) \sim 1$ for the patient with PSE is evident. This testifies the remarkable role of the memory in MEG signals at PSE.

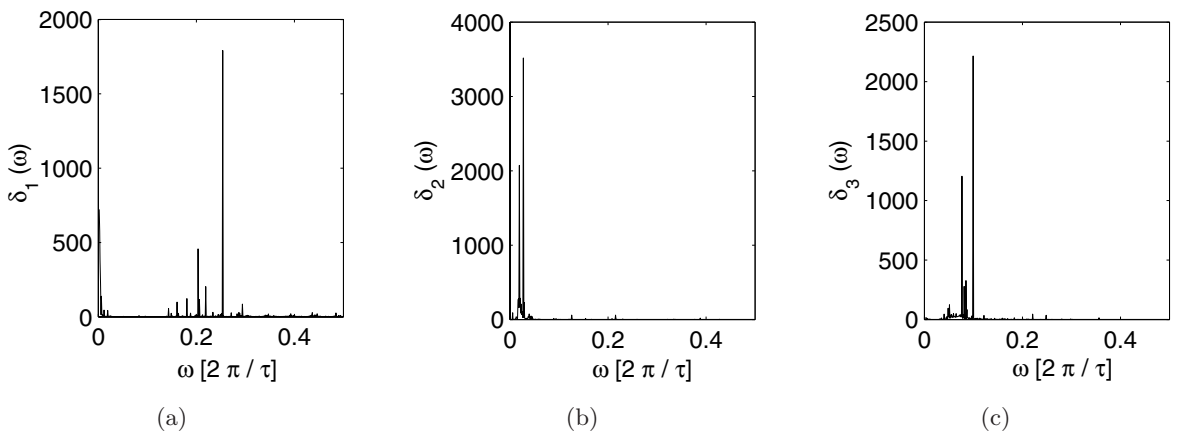
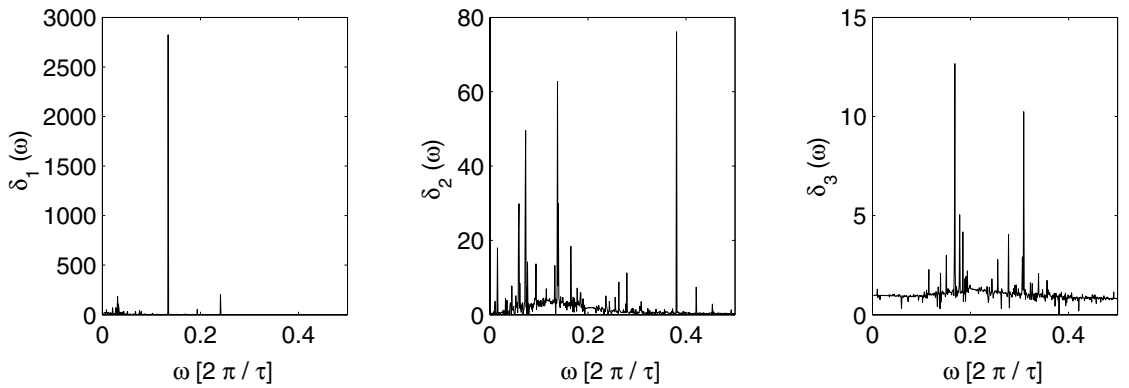


Fig. 4. The frequency dependence of the first three points of the second measure of memory $\delta_i(\omega)$, (a) $i = 1$, (b) $i = 2$, (c) $i = 3$ for the healthy No. 7, sensor No. 10 (an R/B combination of the light stimulus). One observes that the use of $\delta_i(\omega)$ amplifies the role memory multiply.



(a) (b) (c)

Fig. 5. The frequency dependence of the first three points of the second measure of memory $\delta_i(\omega)$, (a) $i = 1$, (b) $i = 2$, (c) $i = 3$ for the patient with PSE, sensor No. 10 (an R/B combination of the light stimulus). Use of $\delta_i(\omega)$ amplifies the role memory multiply.

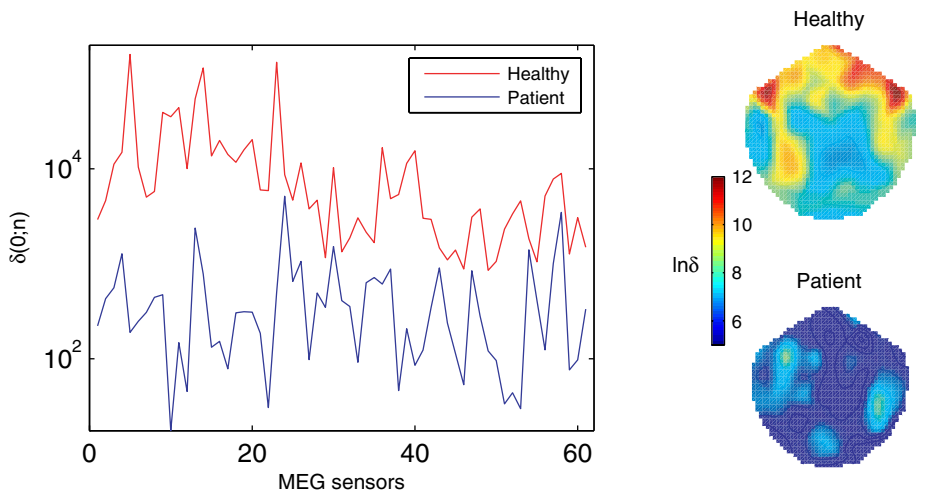


Fig. 6. The topographic dependence of the first point of the second measure of memory $\delta_1(\omega = 0; n)$ for the healthy brain on average in the whole group (upper line) versus that of a patient (lower line) for an R/B combination of the light stimulus. One observes that the singular weak memory effects for the healthy brain on average in sensors with Nos. 5, 23, 14, 11 and 9.

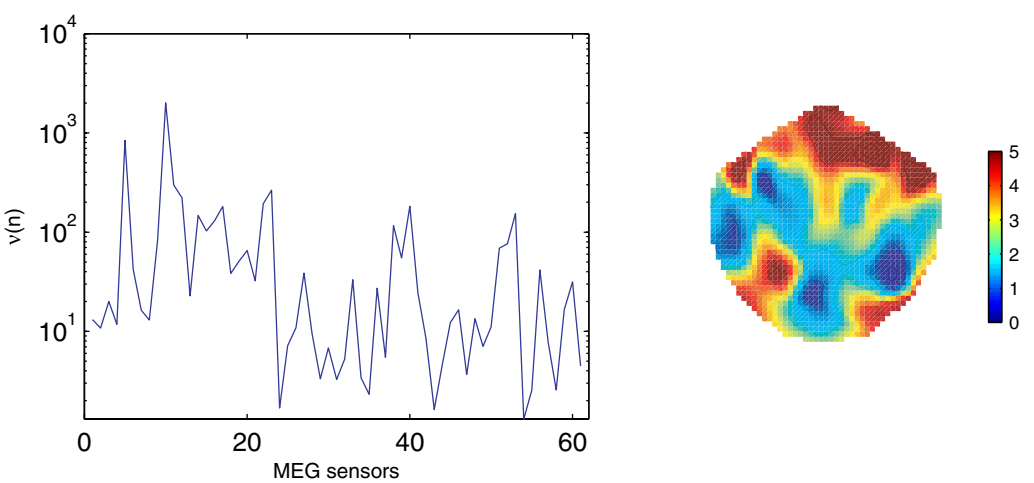


Fig. 7. The topographic dependence of the memory index $\nu(n) = \nu_1(n; 0)$ for the entire group of healthy brain on average versus patient for an R/B combination of the light stimulus. Strong memory in patient versus healthy brain appears clearly in sensors with Nos. 10, 5, 23, 40 and 53.

Acknowledgments

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References

Bhattacharya, J., Watanabe, K. & Shimojo, Sh. [2004] "Nonlinear dynamics of evoked neuromagnetic responses signifies potential defensive mechanisms against photosensitivity," *Int. J. Bifurcation and Chaos* **14**, 2701–2720.

Billock, V. A., de Guzman, G. C. & Kelso, J. A. S. [2001] "Fractal time and $1/f$ spectra in dynamic images and human vision," *Physica D* **148**, 136–146.

Goldberger, A. L., Amaral, L. A. N., Glass, L., Hausdorff, J. M., Ivanov, P. Ch., Mark, R. G., Mietus, J. E., Moody, G. B., Peng, C.-K. & Stanley, H. E. [2000] "PhysioBank, PhysioToolkit, and PhysioNet: Components of a new research resource for complex physiologic signals," *Circulation* **101**, e215–e220.

Hämäläinen, M., Hari, R., Ilmoniemi, P. J., Knuutila, J. & Lounasmaa, O. V. [1993] "Magnetoencephalography-theory, instrumentation, and applications to noninvasive studies of the working human brain," *Rev. Mod. Phys.* **65**, 413–497.

Jiang, T., Luo, A., Lia, X. & Kruggel, F. [2003] "A comparative study of global optimization approaches to MEG source localization," *Int. J. Comput. Math.* **80**, 305–324.

Malmivuo, J. & Plonsey, R. [1995] *Bioelectromagnetism, Principles and Applications of Bioelectric and Biomagnetic Fields* (Oxford University Press, NY–Oxford), pp. 1–471.

Mokshin, A., Yulmetyev, R. M. & Hanggi, P. [2005] "Simple measure of memory for dynamical processes described by a generalized Langevin equation," *Phys. Rev. Lett.* **95**, 200601–4.

Wolf, F. [2005] "Symmetry, multistability, and long-range interactions in brain development," *Phys. Rev. Lett.* **95**, 208701–4.