EEGs disclose significant brain activity correlated with synaptic fickleness

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We here study a network of synaptic relations mingling excitatory and inhibitory neuron nodes that displays oscillations quite similar to electroencephalogram (EEG) brain waves, and identify abrupt variations brought about by swift synaptic modulations. We thus conclude that corresponding changes in EEG series surely come from the slowdown of the activity in neuron populations due to synaptic restrictions. The latter happens to generate an imbalance between excitation and inhibition causing a quick explosive increase of excitatory activity, which turns out to be a (first-order) transition among dynamic mental phases. Besides, near this phase transition, our model system exhibits waves with a strong component in the so-called delta-theta domain that coexist with fast oscillations. These findings provide a simple explanation for the observed delta-gamma and theta-gamma modulation in actual brains, and open a serious and versatile path to understand deeply large amounts of apparently erratic, easily accessible brain data.

Today one successfully associates most brain activity with events in which large sets of neurons cooperate arbitrated by willful variations of their synaptic relations [1]. This broadcasts signals throughout, and EEG exploration on the cerebral cortex has thus become a relatively simple, convenient and inexpensive way of analyzing consequences of such an intriguing collaboration [2–5]. In fact, EEG studies deliver some overall image of the brain activity with good time accurateness that complements magnetic resonance analysis of better spatial resolution. Specifically, EEGs watch over frequencies and often distinguish δ, θ, α, β and γ “rhythms”—subsequently along the range 0.5 Hz to 35 Hz and more—, which are loosely associated to different states of consciousness such as say, deep sleep, anesthesia, coma, relax, and attention.

Truly, this is at present a main noninvasive tool to deepen on the brain operation under both normal and pathological conditions [6–9], and it is therefore convenient digging out on the interpretation of all of those waves details. Indeed, a number of prototypes have already addressed the origin and nature of observed brain oscillatory behavior, e.g. [2, 10–13]. Recently, following a hint [10] that α rhythms might come out from filtering of cooperative signs by interactions with noisy signals from different parts of the nervous system, it was explained the emergence of a wide spectrum of brain waves within a simple computational framework [11]. More specifically, this study has shown that a neural module can exhibit waves in a variety of frequency bands just by tuning the intensity of a noisy input signal. We interpret this result as suggesting that a unifying mechanism in some way occurs at some level of brain activity for a range of oscillations. In fact, existing literature by now has described [1] various well defined, let us say, dynamic phases, as well as transitions among them—typically, from states with a low and incoherent activity to others that show a high synchrony—where weak signals are processed efficiently in spite of much unrest around. One thus understands, for instance, that this ability is due to the very large susceptibility developed in the medium by a phase transition due to a mechanism occasionally termed as stochastic resonance [15].

The picture in previous theoretically-oriented EEG work, including [14], is mostly phenomenological and generally adopts a uniform and stationary description of the neuron relations efficiency, thus forgetting the actual possibility that synapses perform dynamically during the neuron cooperation processes [1, 16–15]. Nevertheless, synaptic relations surely vary with time while affecting essentially both the neuron network global behavior and the ensuing capacities to transmit information [1, 18–23]. For instance, a sort of sudden synaptic facilitation can allow for transient persistent activity after removal of a stimulus [22], which may be the basis for working memory. Moreover, It was reported that synaptic dynamics may induce in the human cortex bursting escorted of asynchronous activity [15], as well as instabilities prompting transitions among attractors, which allow for effective memory searching [23], in addition to a kind of ‘up-and-down states’ reported to occur in cortical neuron populations [24]. Aware of these and similar facts, we mathematically recast and generalize here both the more mesoscopic description in [2] and the algorithmic model in [14], perfecting them with detailed dynamic synapses and other realistic features. We thus show how certain levels of short-time ‘depression’ of the synaptic links induce transitions between states of synchronized excitatory-inhibitory neuron populations and global states of incoherent behavior. It follows that one may speak of kind of sharp phase transitions, clearly displaying metastability and hysteresis, that have been experimentally observed [25]. Furthermore, near such explosive variations, our model exhibits oscillations with a prominent component in the δ−θ band along with high frequency activity, namely, the δ−γ and θ−γ modulations already perceived in actual brain EEG recordings [26, 27], which have been associated with fluid intelligence [28]. Even more, we here associate such intriguing sharp variations with disruptions of the balance among excitation and inhibition produced by depression of ex-
citatory inputs into inhibitory neurons. This reduces the inhibitory activity thus prompting a sudden excitation increase that further reduces inhibition. Interestingly enough, a lack of the excitation-inhibition balance in the actual human brain could be crucial to understand the essentials of some recurrent neurological disorders such as epilepsy, autism and schizophrenia, e.g., \cite{20, 29}.

The simplest version of our model aims to capture the essentials of the cerebral cortex operation allowing for a network with excitatory (E) and inhibitory (I) neurons, the former occurring four times the latter. Furthermore, the amplitude of the corresponding postsynaptic responses follows the opposite ratio, i.e., the response evoked by any I is four times larger than that by any E. This is supposed to correspond to a realistic cortex balanced state \cite{31, 32}. We then represent a region of the cerebral cortical tissue with a large square of $N$ nodes with periodic boundary conditions and fulfilling such a balance, in which each I node influences a set of 12 neighboring E’s and it is influenced by 32 adjacent E’s. As in previous work \cite{10, 14}, we do not consider here E-E and I-I feedbacks. Besides, from the various familiar types of imaginable neuron dynamics, we refer to the celebrated integrate-and-fire case \cite{1, 33}. Namely, the cell membrane acts as a capacitor subject to several currents, which results in a potential $V$ for each neuron changing with time according to

$$
\tau \frac{dV}{dt} = -V + V^{\text{in}} + V^{\text{noise}}. \quad (1)
$$

Here, as in previous work \cite{10, 14}, the time constant $\tau$ is set equal to $\tau_1 (\tau_2)$ according the membrane cell voltage is above (below) certain resting potential, which we set to zero. The last two terms in (1) correspond to the voltage induced by the sum of all currents through the membrane, which we separate here in two main contributions. $V^{\text{in}}$ is the sum of inputs from adjacent neighbors that influence the given cell, while $V^{\text{noise}}$ accounts for any input from neurons in other regions of the brain. Assuming lack of correlations \cite{34}, we represent $V^{\text{noise}}$ as a Poisson signal characterized by a noise level parameter $\mu$.

It is now well established that, in human brains, synapses linking neurons may undergo variations in scales from milliseconds to minutes, in addition to more familiar long-term plastic effects. In fact, one observes short-term depression (STD), in which the synaptic efficacy decreases due to depletion of neurotransmitters inside the synaptic button after heavy presynaptic activity \cite{21}. In addition, there was reported kind of short-term facilitation characterized by an increase of the efficacy strength \cite{35, 37}, which results from a growth of the intracellular calcium concentration after the opening of the voltage gated calcium channels due to successive arrival of action potentials to the synaptic button. It seems that, in general, these two short-term mechanisms may compete \cite{1, 21} but, for simplicity, we just consider here synapses endowed of STD, and describe this by using the release probability $U$ and the fraction of neurotransmitters at time $t$ ready (to be released) after the arrival of an action potential $x_t$ \cite{20}. The ensuing image is that, each time a presynaptic spike occurs, a constant portion $U$ of the resources $x_t$ is released into the synaptic gap, and the remaining fraction $1 - x_t$ becomes available again at rate $1/\tau_{\text{rec}}$. Therefore,

$$
\frac{dx_t}{dt} = \frac{1 - x_t}{\tau_{\text{rec}}} - x_t \delta(t - t_{\text{sp}}), \quad (2)
$$

where the delta function makes that the second right-hand term only occurs for $t = t_{\text{sp}}$, the time at which a presynaptic input spike arrives. Assuming also the amplitude of the response proportional to the neurotransmitters fraction released after the input spike, the STD effect can be written, for E and I neurons respectively, as follows

$$
V_t^{\text{in}, d} = V_0 d U x_t \left[\Theta (t - t_{\text{sp}}) - \Theta (t - t_{\text{sp}} - t_{\text{max}})\right] \quad (3)
$$

$$
V_t^{\text{in}, h} = V_0 h U x_t \Theta (t - t_{\text{sp}}) e^{-\frac{(t - t_{\text{sp}})}{\tau_{\text{rec}}}} \quad (4)
$$

where $\Theta (X)$ is the Heaviside step function. The form of these inputs generated by E and I neurons are chosen so that the response generated on the postsynaptic neuron membrane matches data; see, for instance, \cite{14}. Thus, for simplicity, we model the excitatory synaptic input by a square pulse of width $t_{\text{max}}$ and maximal amplitude $V_0$, as described by Eq. (3), and the inhibitory input by a decaying exponential behavior with time constant $\tau_2$ and maximum amplitude $V_0 h$, as in Eq. (4). In addition, to account for synaptic strength variations that depend on presynaptic history, we multiply these input functions by a factor $U \cdot x_{\text{sp}}$, thus ensuring that the amplitude of the synaptic input is proportional to the amount of neurotransmitters released right after a presynaptic spike, which is an activity dependent factor through dynamics in Eq. (2). Note that there is no synaptic variability present when $U \cdot x_{\text{sp}} = \text{constant}$ occurring for $\tau_{\text{rec}} \to 0$. Furthermore, to prevent the membrane potential in (1) from reaching physiologically unrealistic levels, we impose upper and lower limits of $V_{\text{sat}} = 90mV$ and $V_{\text{min}} = -20mV$, respectively, around the resting membrane potential, $V_{\text{rest}} = 0$ as said. This is achieved by multiplying the different excitatory and inhibitory inputs by the terms $(V_{\text{sat}} - V)/V_{\text{sat}}$ and $(V_{\text{min}} - V)/V_{\text{min}}$, respectively.

Equations (1)-(4) fully describe the dynamics of the membrane potential in our basic model below a threshold for firing, which is in principle set $V_{th} = 6mV$ above
the resting membrane potential for both E and I neurons. Additionally, after generation of a spike at $t_f$, we assume an absolute refractory period ($t_a$) during which the neuron is unable to fire again, and a subsequent relative refractory in which the ability to produce new spikes is constrained. Therefore, we set

$$V_{th}(t) = \begin{cases} V_{sat} & t < t_f + t_a \\ 6 + (V_{sat} - 6) e^{-\kappa(t-t_f-t_a)/\tau} & t > t_f + t_a. \end{cases}$$

That is, the threshold is first set to $V_{sat}$ (during one hundred time steps, which gives $t_a = 4\, ms$) to impede any further spike generation during $t_a$. Then, it decays exponentially to its resting value of $6mV$ with a time constant $\kappa^{-1} = 0.5\, ms$ that mimics the existence of a relative refractory period.

Using this clear-cut and supposedly realistic model, we numerically analyzed how synaptic STD affects eventually emergent waves by carefully monitoring the network dynamics for adiabatically increasing values of the noise parameter $\mu$. Figure 1 illustrates the resulting average membrane potential of the E population versus $\mu$, which clearly illustrates the mentioned sharp transitions. That is, in the absence of STD (top panel in each column), waves do not vary essentially with the external noise amplitude within $\mu \in (0.5, 100)$, as already reported in [34]. This regime corresponds to the simplest and most familiar brain waves. However, when STD is on —namely, the synaptic efficacies vary with the system activity so that parameter $\tau_{rec}$ is large enough— an ‘explosive’ transition may show up as $\mu$ increases. This occurs at lower $\tau_{rec}$, the lower the maximal excitatory postsynaptic amplitude $V_{0}^{d}$ is. It is said ‘explosive’ in the sense that the transition shows hysteresis, from well-defined synchronized behavior to a state of high excitation and low coherence, as we vary $\mu$ adiabatically forward (purple line) and backward (green line). Ona may also name this a first-order phase transition by simple analogy with thermodynamics, though with the warning that the present setting is a nonequilibrium one [35].

The resulting phase diagram in the $(\mu, \tau_{rec})$ space is illustrated in figure 2. The solid quasi-vertical line, for $\mu < 0.5$, describes a (continuous or second-order) phase transition between a near silent phase A, with asynchronous sporadic spikes at low rate (corresponding to the asynchronous down state actually observed in the brain), and an oscillatory phase B, where brain waves emerge with increasing frequency as $\mu$ increases (see figure 1). As $\tau_{rec}$ increases in the system, figure 2 indicates that the brain waves disappear at a (first-order) transition (dashed line), where a new phase D of waves with high excitation and low coherence emerges. This sharp transition becomes smooth above a say ‘tricritical point’ (1.4, 268) (short quasi-vertical solid line on top). The small region C shows metastability as revealed by hysteresis. Note that when $\mu$ is large this region C narrows as noise level increases. In addition, region B contains (red and blue) areas in which brain waves sharply emerge with high values of the firing rates (>100 Hz) for E and I neurons.

Trying to deep on the nature of the sharp transition, we monitored (figure 3) the change with depression of both the mean firing rate and the mean amplitude of the oscillations in E and I neuron populations when it occurs (for $\mu = 3$). This shows that, as STD increases, E neurons induce the I ones to slowly decaying their firing rates as approaching the transition point, where they become silent. A feedback induced by this decay of the I activity makes the E’s to increase their firing activity until reaching (at the transition point) its maximum possible, then remaining firing at the maximum possible frequency. This induces important facts on the ensuing oscillations: the amplitude of the inhibitory component of the waves jumps to zero at the transition point, and the amplitude of the excitatory component decays to a very low value below $V_{th}$.

Also interesting is how the nature of the emerging waves changes with STD. For a relatively low noise, e.g. $\mu = 0.8$, the network’s response remains nearly unchanged, while the amplitude of the oscillations decays until no well-defined oscillatory behavior is observed as STD is increased (figure 4, case $\mu = 1$). Note that this transi-
For low noise (region A), there are random sporadic excitatory firing events unable to depolarize the I neurons. Region B shows well-defined rhythms ranging from $\alpha$ to $\gamma$ bands, while a higher depression induces ceasing of the inhibitory activity and a consequent absence of synchronicity and coherence in region D. Metastability as in figure 1 characterizes the region C. Red and blue colored areas in B indicate emerging waves with high values of the firing rates (>100 Hz) for E and I neurons, respectively. Dashed lines illustrate first-order phase transitions, while continuous lines denote second-order transitions.

Figure 3. Left: Average firing rate for E and I neurons as the level of STD is increased until the explosive transition occurs for an external depolarizing noise $\mu = 3$. Right: Corresponding average amplitude of the oscillations. This illustrates that the transition occurs because of a cease of firing of I’s due to the negative feedback of highly depressed I’s over E’s, which then start to fire at the transition point at the higher frequency, thus depressing even more the I’s until impeding their firing.

Figure 4. Emergence of “$\alpha$ rhythms” (around 10Hz) in the model for noise levels $\mu = 0.6, 0.8$ and 1.0, respectively, from left to right. Although the power of the main frequency of the waves decays as STD increases, this illustrates how these waves details are not dramatically affected by synaptic depression and the $\alpha$ band regime remains until $\tau_{\text{rec}} \approx 260$ ms, where the waves disappear (note that this transition becomes explosive for $\mu \gtrsim 1$ as shown in figure 5).

Figure 5. Left: Power spectra of the system response as a function of the recovery time $\tau_{\text{rec}}$ for $\mu = 3$. Right: time series of the emergent oscillations for particular levels of synaptic depression, namely, $\tau_{\text{rec}} = 0, 145, 230$ and 265 ms, respectively, from top to bottom. The associated power spectra for each of these series are highlighted (with the same color) in the surface plot of the left panel.

Concerning the effect of the E/I balance on emergent behavior, it interests how it affects the incidence of $\delta/\theta$ modulations around the transition, and how the appearance of this is affected by the level of synaptic depression. Figure 6 illustrates some effects of the ratio between the E and I synaptic efficacies. We observe that, when $V_d^I/V_h^I$ decreases and the inhibitory synapses become relatively more influential, the low frequency $\delta/\theta$ component becomes more significant for os-
oscillatory behavior (see Figure 6, top-right and bottom-left panels) while, when this ratio increases, the low frequency band components (δ and θ) tend to disappear (Figure 6, top-left and bottom-right panels). Additionally, an increase of $V_θ^d/V_θ^0$, which implies more excitation, makes the oscillations frequency more susceptible to changes on synaptic depression (see Figure 6, top-left and bottom-right panels), while a stronger inhibition tends to maintain the frequency of the emergent waves nearly unchanged against depression increases (Figure 6, top-right and bottom-left panels).

Summing up, we present in this Letter a very simple model that, recasting previous EEG related work, has two significant features. One is that it provides a well-defined set-up to undertake a systematic interpretation of apparently erratic brain EEG data. These are easily accessible today and, as we have foreseen here, happens to carry important information concerning the brains activity. Furthermore, this model is convenient to admit complements that one might suspect to be relevant in these scenarios such as, for instance, other synaptic mechanisms, complex synaptic networks and more realistic node neurons. In addition, and perhaps even more transcendent within this context, the framework presented here precisely illustrates how the concept of a (nonequilibrium) phase transition $\delta$ may be essential for an accurate description of the brain properties.

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