2 Activity dependent model for neuronal avalanches

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Cortical networks exhibit diverse patterns of spontaneous neural activity, including oscillations, synchrony and waves. The spontaneous activity often in addition exhibits slow alternations between high activity periods, or bursts, followed by essentially quiet periods. Bursts can last from a few to several hundreds of milliseconds and, if analysed at a finer temporal scale, show a complex structure in terms of neuronal avalanches. As discussed in previous chapters, neuronal avalanches exhibit dynamics similar to self-organized criticality (SOC), see Bak (1996); Jensen (1998); Maslov et al. (1994); Davidsen and Paczuski (2002). Avalanches have been observed in organotypic cultures from coronal slices of rat cortex (Beggs and Plenz, 2003), where neuronal avalanches are stable for many hours (Beggs and Plenz, 2004). The size and duration of neuronal avalanches follow power law distributions with very stable exponents, typical features of a system in a critical state, where large fluctuations are present and system responses do not have a characteristic size. The same critical dynamics has been measured also in vivo in rat cortical layers during early post-natal development (Gireesh and Plenz, 2008), in the cortex of awake adult rhesus monkeys (Petermann et al., 2009), as well as in dissociated neurons from rat hippocampus (Mazzoni et al., 2007; Pasquale et al., 2008) or leech ganglia (Mazzoni et al., 2007). The term SOC usually refers to a mechanism of slow energy accumulation and fast energy redistribution driving the system toward a critical state, where the distribution of avalanche sizes is a power law obtained without fine tuning of a particular system or model parameter. The simplicity of the mechanism at the basis of SOC suggests that many physical and biological phenomena characterized by power laws in the size distribution, might represent natural realizations of SOC. For instance, SOC has been proposed to model earthquakes (Bak and Tang, 1989; Sornette and Sornette, 1989), the evolution of biological systems (Bak and Sneppen, 1993), solar flare occurrence (Lu and Hamilton, 1991), fluctuations in confined plasma (Politzer, 2000), snow avalanches (Faillettaz et al., 2004), and rainfall (Peters et al., 2002).

While the sizes and durations of avalanches have been intensively studied in neuronal systems, the quiet periods between neuronal avalanches are much less understood. In vitro preparations, such quiescent periods are often called down-states and can last up to several seconds, in contrast to periods of avalanche activity, which gen-
erally are shorter in duration. The quiet periods measured between bursts can last up to several seconds. The emergence of these down-states can be attributed to a variety of mechanisms: a decrease in the neurotransmitter released by each synapse, either due to the exhaustion of available synaptic vesicles or to the increase of a factor inhibiting the release (Staley et al., 1998) such as the nucleoside adenosine (Thompson et al., 1992), the blockage of receptor channels by the presence, for instance, of external magnesium (Maeda et al., 1995), or else spike adaptation (Sanchez-Vives et al., 2000). A down-state is therefore characterized by a disfacilitation, i.e. reduction of synaptic activity, indicative of a large number of neurons on their long-lasting return to their resting membrane potentials (Timofeev et al., 2001). It was shown analytically and numerically, and discussed in previous chapters, that self-organized critical behaviour characterizes up-states, whereas down-states are subcritical (Millman et al., 2010).

Here we discuss a neural network model based on SOC ideas that take into account synaptic plasticity. Synaptic plasticity is one of the most astonishing properties of the brain, occurring mostly during development and learning (Albright et al., 2000; Hensch, 2004; Abbott et al., 2000), it is defined as the ability to modify the structural and functional properties of synapses in response to past activity in the network. Such modifications in the strength of synapses are thought to underlie memory and learning. Among the postulated mechanisms of synaptic plasticity, the activity dependent Hebbian plasticity constitutes the most developed and influential model of how information is stored in neural circuits (Hebb, 1949; Tsien, 2000; Cooper, 2005). In order to get real insights into the relation between macroscopic network dynamics and the microscopic, i.e. cellular, interactions inside a neural network, it is necessary to identify the basic ingredients of brain activity that could be responsible for characteristic scale-free behaviour as such observed for neuronal avalanches. These insights are the basis for any further understanding of the diverse additional features, such as the interpretation by practitioners of EEG time series for diagnosis or the understanding of learning behaviour. Therefore, the formulation of a neuronal network model that yields the correct scaling behaviour for spontaneous activity is of crucial importance for any further progress in the understanding of the living brain.

2.1 The model

In order to formulate a new model to study neuronal activity, we incorporated (De Arcangelis et al., 2006b; Pellegrini et al., 2007) into a SOC framework three important neuronal ingredients, namely action potential firing after the neuronal intracellular membrane potential reaches a threshold, the refractory period of a neuron after firing an action potential, and activity-dependent synaptic plasticity. We consider a lattice of \( N \) sites where each site represents the cell body of a neuron and each bond a synaptic connection to a neighboring neuron. Each neuron is characterized by its intracellular membrane potential \( v_i \). The number of connections from one neuron to other neurons are established by assigning to each neuron \( i \) a random out-going
Figure 2.1 Three excitatory (red) neurons and one inhibitory (blue) neuron embedded in a larger network (grey neurons). Synaptic connections for the four neurons, indicated by arrows, can be excitatory (red) or inhibitory (blue). The connectivity degrees are:

- $k_{out_1} = k_{out_3} = k_{out_4} = 3$
- $k_{out_2} = 5$
- $k_{in_1} = k_{in_3} = k_{in_4} = 1$
- $k_{in_2} = 2$

connectivity degree, $k_{out_i}$. The distribution of the number of out-connections is chosen in agreement with the experimentally determined properties of the functional network connectivity (Eguiluz et al., 2005) in human adults. Functional magnetic resonance imaging has indeed shown that this network has universal scale free properties, namely it exhibits a scaling behaviour $n(k_{out}) \propto k_{out}^{-2}$, independent of the different tasks performed by the subject. We adopt this distribution for the number of pre-synaptic terminals of each neuron, over the range of possible values between 2 and 100. Two neurons are then connected with a distance dependent probability, $p(r) \propto e^{-r/r_0}$, where $r$ is their euclidian distance (Roerig and Chen, 2002) and $r_0$ a typical edge length. Once the network of output connections is established, we identify the resulting degree of in-connections, $k_{in_j}$, for each neuron $j$. An example of a small network is shown in Fig 2.1. To each synaptic connection we then assign an initial random strength $g_{ij}$, where $g_{ij} \neq g_{ji}$. Moreover, synapses can have an excitatory or inhibitory character: Some neurons are chosen to be inhibitory, i.e., all their outgoing synapses are inhibitory, to amount a total fraction $p_{in}$ of inhibitory synapses in the network.

Whenever at time $t$ the value of the potential in neuron $i$ is above a certain threshold $v_i \geq v_{max}$, approximately equal to $−55mV$ for real cortical neurons, the neuron fires, i.e. generates action potentials which arrive to each of the $k_{out_i}$ pre-synaptic buttons and lead to a total production of neurotransmitter proportional to $v_i$, whose value can be larger than $v_{max}$. This choice implies that the neurotransmitter production depends on the integrated stimulation received by the neuron, as it happens for real neurons where the production is controlled by the frequency of the action potential. As a consequence, the total charge that could enter into the connected neurons is proportional to $v_i k_{out_i}$. This charge is distributed among the post-synaptic neurons proportionally to the strength of the connection $g_{ij}$, which is implemented by the normalization $\sum_k g_{ik}(t)$, the total strength of all synapses outgoing from neuron $i$ to the $k$ post-synaptic neurons. The temporal evolution of the membrane voltage is
Figure 2.2 Two neuronal avalanches in the scale-free network. 250 neurons are connected by directed bonds (direction indicated by the arrow at one edge), representing the synapses. The size of each neuron is proportional to the number of in-connections, namely the number of dendrites. The two different avalanches are characterized by pink and blue colours. Connections and neurons not involved in the avalanche propagation are shown in grey.

Therefore

\[ v_j(t+1) = v_j(t) \pm \frac{v_i(t)k_{out_i}}{k_{in_j}} \sum_k g_{ij}(t) \]  

(2.1)

where \( k_{in_j} \) is the in-degree of neuron \( j \). This factor implies that the received charge is distributed over the surface of the soma of the post-synaptic neuron, proportional to the number of in-going terminals \( k_{in_j} \). Moreover, this normalization preserves the controlled functioning of the firing cascades in networks where highly connected neurons are present, as in scale free networks. The plus or minus sign in Eq.(2.1) is for excitatory or inhibitory synapses, respectively. After firing, a neuron is set to zero resting membrane potential and remains in a refractory state for \( t_{ref} = 1 \) time steps, during which it is unable to receive or transmit any charge. We wish to stress that the unit time step in Eq.(2.1) does not correspond to a real time scale, it is simply the time unit for charge propagation from one neuron to its neighbors. The synaptic strengths have initially equal value, whereas the neuron potentials are uniformly distributed random numbers between \( v_{max} - 1 \) and \( v_{max} \). Moreover, a small random fraction (10%) of neurons is chosen to be boundary sites, with a potential fixed to zero, playing the role of sinks for the charge. An external stimulus is imposed at a random site and, if the potential reaches the firing threshold, the neuron fires and an cascade of firing neurons can evolve in the network.
2.1.1 Plastic adaptation

As soon as a neuron is at or above threshold $v_{\text{max}}$ at a given time $t$, it fires according to Eq. (1). Then the strength of all the synapses connecting to active neurons are increased in the following way

$$g_{ij}(t + 1) = g_{ij}(t) + \alpha(v_j(t + 1) - v_j(t))/v_{\text{max}}$$

(2.2)

where $\alpha$ is a dimensionless parameter. Conversely, the strength of all inactive synapses is reduced by the average strength increase per connection,

$$\Delta g = \sum_{ij,t} \delta g_{ij}(t)/N_b$$

(2.3)

where $N_b$ is the number of connections active in the previous avalanche. This normalization implements a sort of homeostatic regulation of plastic adaptation: The more active connections are strengthen on average, the more inactive ones are weakened. The adaptation of synaptic strength is therefore tuned by a single parameter, $\alpha$, which represents the ensemble of all possible physiological factors influencing synaptic plasticity. The quantity $\Delta g$ depends on $\alpha$ and on the response of the network to a given stimulus. In this way our neuronal network "memorizes" the most used paths of discharge by increasing their synaptic strengths, whereas less used synapses atrophy. Once the strength of a synaptic connection is below an assigned small value $\sigma_t$, we remove it, i.e. set it equal to zero, which corresponds to what is known as synaptic pruning. These mechanisms correspond to a Hebbian form of activity dependent plasticity, where the conjunction of activity at the presynaptic and postsynaptic neuron modulates the efficiency of the synapse (Cooper, 2005). To insure the stable functioning of neural circuits, both strengthening and weakening of Hebbian synapses are necessary to avoid instabilities due to positive feedback (Desai, 2003). However, different from short-term plasticity, such as short-term facilitation or short-term depression, in our model, the change of synaptic strength does not depend on the frequency of synapse activation (Albright et al., 2000; Paulsen and Sejnowski, 2000; Braunewell et al., 2001). It should be also considered that, in the living brain, many synapses exhibiting plasticity are chemical synapses with functional properties different from electrical synapses. For instance, Hebbian plasticity at excitatory synapses is classically mediated by postsynaptic calcium dependent mechanisms (Bi and Poo, 2001). In our approach the excitability of the postsynaptic neuron is simply modulated by the value of the intracellular membrane potential of the presynaptic neuron.

2.2 Neuronal avalanches in spontaneous activity

We applied the plasticity rules of equations 2.2-2.3 during a series of $N_p$ stimuli to adapt the strengths of synapses. In fact, the more the system is actively strengthening
used synapses, the more unused synapses will weaken. This plastic adaptation proceeds until only few connections are pruned in response to the stimuli. The system at this stage constitutes the first approximation to a trained brain, on which measurements are performed. These consist of a new sequence of stimuli, by increasing the intracellular membrane potential of a randomly selected neuron until it fires an action potential. We monitor the propagation of neuronal activity as a function of time.

After each stimulus, we measure the size distribution of the neuronal cascades (see Fig 2.2). The cascade size is defined either as the total number of firing neurons, or the sum of their intracellular membrane potential fluctuations during a cascade. This distribution exhibits a power law behaviour, with an exponent equal to $1.5 \pm 0.1$ (see Fig. 2.3). This power law identifies the cascading activity as neuronal avalanches. The avalanche activity is quite stable with respect to various parameters. The power law is also robust for densities of inhibitory synapses up to 10%, whereas it is lost for higher densities. Moreover, the distribution of avalanche durations, defined as the time period from the first spike to the last spike within an avalanche, is also a power law with an exponent close to $-2.0$ (see Fig 2.3). Both these values show excellent agreement with experimental data (Beggs and Plenz, 2003). Extensive simulations have verified that the critical behaviour of avalanche distributions does not depend on parameter values or network properties (regular, small-world, Apollonian networks) (de Arcangelis and Herrmann, 2012). Moreover, these scaling properties do not depend on system size, indicating that the network is in a critical state and self-regulates, by adjusting synaptic strengths, thereby producing the observed scale-invariant behaviour.

It is interesting to notice that recently the statistics of neuronal cascades has been measured in anaesthetized rats treated with a GABA inhibitor to induce epileptic behaviour (Osorio et al., 2010). Under these conditions, the size distribution shows the presence of large events with a characteristic size in an almost periodic regime. This periodicity therefore induces a shoulder in the waiting time distribution, i.e. the time between the beginning of two successive avalanches. Different is the case for slices of rat cortex which do not undergo any pharmacological treatment (Beggs and Plenz, 2003; Stewart and Plenz, 2006; Lombardi et al., 2012b), where spontaneous activity is critical, i.e. the size distribution is a power law over several orders of magnitude and no characteristic size or periodicity is detected.

### 2.2.1 Power spectra

In order to compare with medical data, we calculate the power spectrum of the time series for neuronal activity, i.e. the square of the amplitude of the Fourier transform as function of frequency. The average power spectrum (see Fig 2.4) exhibits a power law behaviour with exponent $0.8 \pm 0.1$ over more than three orders of magnitude. This is the same value as the exponent found generically for medical EEG power spectra (Freeman et al., 2000; Novikov et al., 1997). We also show in Fig 2.4 the magnetoelectroencephalography obtained from channel 17 in the left hemisphere of
Figure 2.3 The distributions of avalanche size (circles), duration (squares) and the total potential variation during one avalanche (triangles) for 100 configurations of scale-free network with $N = 16000$ neurons ($\alpha = 0.6, N_p = 10000, p_{in} = 0.05$). The dashed line has a slope -1.5, whereas the dot-dashed line has a slope -2.1. The continuous line represents the experimental distribution of avalanche sizes in rat cortex slices. Experimental data are shifted for better comparison, no quantitative comparison is made between the size of experimental avalanches and the potential variation for numerical data.

We have checked that the value of the exponent is stable against changes of the parameters $\alpha$, $v_{max}$ and $N_p$, and also for random initial bond conductances. For $\alpha = 0$ the frequency range of validity of the power law decreases by more than an order of magnitude. Fig 2.4 also shows the power spectrum for a small world network with 1% rewired connections and a different set of parameters $\alpha$, $N_p$, $v_{max}$. The spectrum has some deviations from the power law at small frequencies and tends to the same universal scaling behaviour at larger frequencies over two orders of magnitude. The same behaviour is found for a larger fraction of rewired connections. We have also studied the power spectrum for a range of value of $p_{in}$, the probability of inhibitory synapses. For a density up to 10% of inhibitory synapses the same power law behaviour is recovered within error bars. For increasing density, the scaling behaviour is progressively lost and the spectrum develops a complex multi-peak structure. These results suggest that the balance between excitatory and inhibitory synapses plays a crucial role for the overall behaviour of the network, similarly to what can occur in some severe neurological and psychiatric disorders (Rubenstein and Merzenich, 2003; Powell et al., 2003).

The scaling behaviour of the power spectrum can be interpreted in terms of a stochastic process determined by multiple random inputs (Hausdorff and Peng, 1996). In fact, the output signal resulting from different and uncorrelated superim-
Figure 2.4 Power spectra for experimental data and numerical data ($L = 1000$, $\alpha = 0.03$, $N_p = 10$, $v_{\text{max}} = 6$) for the square lattice (middle line) and the small world lattice (bottom line, $L = 1000$, $\alpha = 0.05$, $N_p = 1000$, $v_{\text{max}} = 8$) with 1% rewired connections. The experimental data (top line) are from ref. [Novikov et al., 1997] and frequency is in Hz. The numerical data are averaged over 10000 stimuli in 10 different network configurations. The dashed line has a slope 0.8.

posed processes is characterized by a power spectrum with power law behaviour and a crossover to white noise at low frequencies. The crossover frequency is related to the inverse of the longest characteristic time among the superimposed processes. The value of the scaling exponent depends on the ratio of the relative effect of a process of given frequency on the output with respect to other processes. $1/f$ noise corresponds to a superposition of processes of different frequency having all the same relative effect on the output signal. In our case the scaling exponent is smaller than unity, suggesting that processes with high characteristic frequency are more relevant than processes with low frequency in the superposition (Hausdorff and Peng, 1996).

2.3 Learning

Next we study the learning performance of this neuronal network when it is in a critical state [De Arcangelis and Herrmann, 2010]. In order to start activity, we identify input neurons at which the rule to be learned is applied and the output neuron at which the response is monitored. These neurons are randomly selected under the condition that they are not located at a boundary and they are separated in the network by a distance $k_d$. Here, $k_d$ represents the chemical distance between two neurons, namely the number of connections in the shortest path between them, which differs from the euclidian distance. $k_d$ can be thought of the number of hidden layers
in a perceptron. We test the ability of the network to learn different rules: AND, OR, XOR, and a random rule RAN, which associates to all possible combinations of binary states at three inputs a random binary output. More precisely, the AND, OR and XOR rules are made of three input-output relations, whereas the RAN rule with three input sites implies a sequence of seven input-output relations. A single learning step requires the application of the entire sequence of states at the input neurons, and then monitoring the state of the output neuron. For each rule, the binary value 1 is identified by the firing of the output neuron, i.e., when the intracellular membrane potential of the output neuron reaches a value greater or equal to $v_{\text{max}}$ at some time during the activity. Conversely, the binary state 0 at the output neuron corresponds to the state of a neuron which has been depolarized by excitatory input but failed to reach firing threshold of the membrane potential during the entire avalanche. Once the input sites are stimulated, their activity may bring to threshold other neurons and therefore lead to avalanches of firings. We impose no restriction on the number of firing neurons and let the avalanche evolve to its end according to Eq. (2.1). If, at the end of the avalanche, the activity did not reach the output neuron, we consider that the state of the system was unable to respond to the given stimulus, and as a consequence to learn. We therefore increase uniformly the intracellular membrane potential of all neurons by units of a small quantity, $\beta = 0.01$, until the activity in the network has reached the output neuron, after which we compare the state of the output neuron with the desired output.

Plastic adaptation is applied to the system according to a non-uniform negative feedback algorithm. Namely, if the output neuron is in the correct state according to the rule, we keep the value of synaptic strengths. Conversely, if the response is incorrect, we modify the strengths of those synapses involved in the activity propagation by $\pm \alpha / d_k$, where $d_k$ is the chemical distance of the presynaptic neuron from the output neuron. The sign of the adjustment depends on the nature of the incorrect response: If the output neuron fails to be in a firing state, we strengthen all active synapses by a small additive quantity proportional to $\alpha$. Conversely, synaptic strengths are weakened if the neuron fired when it was supposed to be silent. This adaptation rule thus provides feedback in response to the incorrect answer. The feedback is applied locally to the corresponding output neuron as well as propagating backwards towards the input sites triggered locally at the output site. The biological realization of such a feedback mechanism can be thought of as a binary error signal that is locally applied at the output site and diffuses towards the input site.

Next, we analyse the performance of the system to learn different input-output rules. Fig 2.5 shows the fraction of configurations learning the XOR rule versus the number of learning steps for different values of the plastic adaptation strength $\alpha$. We notice that the larger the value of $\alpha$, the sooner the system starts to learn the rule, however the final percentage of learning configurations is lower. The final rate of success increases as the strength of plastic adaptation decreases. This result is due to the highly non-linear dynamics of the model, where firing activity is an all or none event controlled by the threshold. The result that all rules give a higher percentage of success for weaker plastic adaptation, is in agreement with recent experimental findings on visual perceptual learning, where better performances are measured when
minimal changes in the functional network occur as a result of learning (Lewis et al., 2009).

We characterize the learning ability of a system for different rules by the average learning time, i.e. the average number of times a rule must be applied to obtain the right answer, and the asymptotic percentage of learning configurations. This is determined as the percentage of learning configurations at the end of the teaching routine, namely after $10^6$ applications of the rule. The average learning time scales as $\tau \propto 1/\alpha$ for all rules, independent of parameter values. The asymptotic percentage of success increases by decreasing $\alpha$ as a very slow power law, $\propto \alpha^{-0.03} \pm 0.01$, where the exponent is the average value over different rules. We check this scaling behaviour by appropriately rescaling the axes in Fig. 2.5. The curves corresponding to different $\alpha$ values indeed all collapse onto a unique scaling function. Similar collapse is observed for the OR, AND and RAN rules and for different parameters $k_d$ and $p_{in}$. The dynamics of the learning process shows therefore universal properties, independent of the details of the system or the specific task assigned.

Finally we explicitly analyse the dependence of the learning performance and its scaling behaviour for different model parameters. The learning behaviour is sensitive to the number of neurons involved in the propagation of the signal, and therefore depends on the distance between input and output neurons and the level of connectivity in the system. We investigate the effect of the parameters $k_d$ and $k_{min}$ on the performance of the system. Systems with larger $k_{min}$ have a larger average number of synapses per neuron, producing a more branched network. The presence of several alternative paths facilitates information transmission from the inputs to the output site. However, the participation of more branched synaptic paths in the learning process may delay the time the system first gives the right answer. As expected the performance of the system improves as the minimum out-connectivity degree increases, with the asymptotic percentage of success scaling as $\sim k_{min}^{0.4}$. On the other hand, also the chemical distance between the input and output sites plays a very im-
important role, as the number of hidden layers in a perceptron. Indeed, as $k_d$ becomes larger, the length of each branch in a path involved in the learning process increases. As a consequence, the system needs a higher number of tests to first give the right answer and a lower fraction of configurations learns the rule after the same number of steps. The percentage of learning configurations, as expected, decreases as $\sim k_d^{-0.3}$ and similar behaviour is detected for all rules. Finally, as the system size increases, the number of highly connected neurons becomes larger. A well connected system provides better performances, therefore we could expect that the size dependence reflects the same effect. The learning performance indeed improves with system size, since, for the same out degree distribution, the overall level of connectivity improves for larger systems.

2.4 Temporal organization of neuronal avalanches

Here we focus on the overall temporal organization of neuronal avalanches both in organotypic cultures and neuronal networks simulations. Each avalanche is characterized by its size $s_i$, and its start and end times, $t_i^s$ and $t_i^f$. The properties of temporal occurrence are analysed by evaluating the distribution of waiting times $\Delta t_i = t_{i+1}^s - t_i^f$. This is a fundamental property of stochastic processes, widely investigated for natural phenomena (De Arcangelis et al., 2006a) and used to discriminate between a simple Poisson and a correlated stochastic process. Indeed, in the first case the distribution is an exponential, whereas it exhibits a more complex behaviour with power law regime if long-range correlations are present. For a wide variety of phenomena, earthquakes, solar flares, rock fracture, etc., this distribution always shows a monotonic behaviour. In some of the current book chapter and in an article by Ribeiro et al. (2010) this distribution has been analysed for freely behaving and anaesthetized rats. The distributions show consistently a decreasing behaviour. Universal scaling features are observed when waiting times are rescaled by the average occurrence rate for freely behaving rats, whereas curves for anaesthetized rats do not collapse onto a unique function.

In Fig 2.6 we show the waiting time distribution for different cultures of rat cortex slices (Lombardi et al. 2012b). The curves exhibit a complex non-monotonic behaviour with common features: an initial power law regime and a local minimum followed by a more or less pronounced maximum. This behaviour is not usually observed in natural phenomena and suggests that the timing of avalanches in organotypic cultures is not governed by a pure Poisson process. In order to investigate the origin of this behaviour, we simulate avalanche activity by our model, considering that the system slowly alternates between up-states and down-states (Lombardi et al. 2012b). The basic idea is, that after a large avalanche, activated neurons become hyperpolarized and the system goes into a down-state where the neuronal stimulation has a small random amplitude. Conversely, after a small avalanche, active neurons remain depolarized and the system is in an up-state, where stimulation depends on the previous avalanche activity. In order to implement these mechanisms in the nu-
Figure 2.6 The distribution of waiting times for seven different slices of rat cortex exhibits a non-monotonic behavior, undetected in any other stochastic process. All curves show an initial power law regime between 10 and about 200ms, characterized by exponent values between 2 and 2.3. For $\Delta t > 200\text{ms}$ curves can become quite different with the common characteristics of a local minimum located at $200\text{ms} < \Delta t_{\text{min}} < 1\text{s}$, followed by a more or less pronounced maximum at $\Delta t \simeq 1 - 2\text{s}$.

Numerical procedure, we fix a threshold value, $s_{\Delta v}^{\text{min}}$, for the avalanche size measured in terms of the sum of depolarizations of all active neurons, $s_{\Delta v} = \sum \delta v_i$. More precisely, if the last avalanche is larger than a threshold, $s_{\Delta v} > s_{\Delta v}^{\text{min}}$, the system transitions into a down-state and neurons that were active in the last avalanche become hyperpolarized proportional to their previous activity, namely we reset

$$v_i = v_i - h\delta v_i$$

(2.4)

where $h > 0$. This rule introduces a short range memory at the level of a single neuron and models the local inhibition experienced by a neuron, due to spike adaptation, adenosine accumulation, synaptic vesicle depletion, etc. Conversely, if the avalanche just ended had a size $s_{\Delta v} \leq s_{\Delta v}^{\text{min}}$, the system either will remain in an up-state, or will transition into an up-state. All neurons that fired in the previous avalanche are set to the depolarized value

$$v_i = v_{\text{max}}(1 - s_{\Delta v}/s_{\Delta v}^{\text{min}})$$

(2.5)

The neuron’s intracellular potential depends on the response of the whole network via $s_{\Delta v}$, in agreement with experimental measurements that the neuronal membrane potential remains close to the firing threshold during an up-state. $s_{\Delta v}^{\text{min}}$ controls the extension of the up-state and therefore the level of excitability of the system. The high activity in the up-state must be sustained by collective effects in the network, otherwise the depolarized potentials would soon decay to zero, and therefore the random stimulation in the up-state has an amplitude that depends on past activity. Eqs.
Figure 2.7 Distribution of durations of down-states (a) and up-states (b) for 100 configurations of a network of $N = 64000$ neurons with $p_{in} = 0.05$, $\alpha = 0.9$, $s_{\Delta v}^{min} = 160$, $d_d = 0.15$ and $c_d = -0.65$. Data are averaged over the number of configurations.

(3) and (4) represent the simplest implementation of the neuron up- and down-state. Each equation depends on a single parameter, $h$ and $s_{\Delta v}^{min}$, which introduce a memory effect at the level of single neuron activity and the entire system, respectively. In order to reproduce the behavior observed experimentally, the parameters $s_{\Delta v}^{min}$ and $h$ are controlled separately. However, our simulations show that the ratio $R = h/s_{\Delta v}^{min}$ is the only relevant quantity controlling the temporal organization of avalanches.

Following the above procedure, the system indeed transitions between up- and down-states, though with different temporal durations, respectively (see Fig 2.7). The distribution of up-state durations is consistent with an exponential decay in agreement with previous numerical results [Millman et al., 2010]. Conversely, the down-states exhibit a sharply peaked distribution with a most probable value at about 200 numerical time units. Avalanches are characterized by power law distributions for the size and the temporal duration with exponents in good agreement with experimental results.

Next we measure the waiting time distribution between successive avalanches. In the analysis of the temporal signal we consider avalanches involving at least two neurons, whereas single spikes are considered background noise. We measure the waiting time as the time delay between the end of an avalanche and the beginning of the successive one. We notice that long waiting times generally occur after large avalanches, corresponding to down-states, whereas short ones are detected during up-states (see Fig 2.8). The scatter plot of the waiting time as a function of the previous avalanche shows that experimental data are quite scattered. In order to evidence a scaling behaviour, we evaluate the expectation value of the waiting time as function of the cumulated activity over a temporal bin. These data exhibit a scaling behaviour that is fully reproduced by numerical data. The good agreement between experimental and numerical results confirms the validity of our approach.
The numerical waiting time distributions (see Fig 2.9) exhibit the non-monotonic behaviour of the experimental curves, where the position of the minimum is controlled by the value of $s_{\Delta v}^{min}$ and the power law regime scales with the same exponent $\sim -2$ as experimental data. The agreement between the numerical and the experimental distributions is confirmed by the Kolmogorov-Smirnov test at a $p = 0.05$ significance level. Both distributions pass the statistical test with $p = 0.99$ (left panel) and $p = 0.68$ (right panel). The different contribution from the two states is reflected in the activity temporal scale (inset of Fig 2.9). The up-state generates strongly clustered avalanches, yielding the power law regime of the waiting time distribution, whose extension depends on $s_{\Delta v}^{min}$. Large $\Delta t$ between avalanches generated in the up-state are observed with a very small probability, which increases with decreasing $h$. Conversely, the waiting time distribution evaluated in the down-state has a bell-shaped behaviour centered at large waiting times which depends on $h$, i.e. for a larger disfacilitation of the network the probability to observe intermediate waiting times decreases in favour of long $\Delta t$. The presence of the minimum and the height of the relative maximum are sample dependent (Fig 2.7) and for each sample simulations are able to reproduce the different behaviours by choosing the appropriate parameter values. However, the agreement between numerical and experimental data depends uniquely on the ratio $R = h/s_{\Delta v}^{min} \simeq 10^{-4}$, expressing the subtle balance between excitation and inhibition. For different samples, optimal agreement is realized for the same value of the ratio $R$. For instance, enhancing the excitatory mechanism, by increasing the threshold value $s_{\Delta v}^{min}$, clearly produces a major shift in the data (Lombardi et al., 2012b). Increasing the inhibitory mechanism, by tuning the hyperpolarization constant parameter $h$, generates the opposite effect, recover-
ing the good agreement with experimental data. It is interesting to notice that the avalanche size and duration distributions exhibit the experimental scaling behaviour for the set of parameters expressing the balance between the excitatory and inhibitory components.

The abrupt transition between the up- and down-state, controlled by a threshold mechanism, produces the minimum observed experimentally. However, this mechanism alone is not sufficient to reproduce the non monotonic behaviour. Indeed, simulations of up-states and down-states only in terms of different drives, without the dependence of the single neuron state on up- and down-states, provide a monotonic behaviour (Lombardi et al., 2012b). The initial power law regime is followed by a plateau and a final exponential decay. The power law regime is still observed in this case, since this is mainly controlled by the drive in the up-state which introduces correlations between successive avalanches. Therefore, the introduction of inhibitory mechanisms following activity, i.e. the hyperpolarizing currents in the down-state and the neuron disfacilitation, are crucial ingredients to fully reproduce the dynamics of the transition between the different activity states.

2.5 Conclusions

Several experimental evidences suggest that the brain behaves as a system acting at a critical point. This statement implies that the collective behaviour of the network is more complex than the functioning of the single components. Moreover, the
emergence of self-organized neuronal activity, with the absence of a characteristic scale in the response, unveils similarities with other natural phenomena exhibiting scale-free behaviour, such as earthquakes or solar flares. For a wide class of these phenomena, self-organized criticality has indeed become a successful interpretive scheme. However, it is important to stress that the observation of a scale-free response is not a sufficient indication for temporal correlations among events. For instance, the waiting time distribution for the original sand pile model is a simple exponential (Jensen, 1998), since avalanches are temporally uncorrelated. Several natural stochastic phenomena, characterized by temporal correlations and clustering, provide similar non-exponential distributions, all with a monotonic functional behaviour.

Our model inspired by self-organized criticality is able to capture the scaling behaviour of avalanches in spontaneous activity and to reproduce the underlying power law behaviour measured by EEG in human patients. Besides reproducing neuronal activity, the network is able to learn Boolean rules via plastic modification of synaptic strengths. The implemented learning dynamics is a cooperative mechanism where all neurons contribute to select the right answer and negative feedback is provided in a non-uniform way. Despite the complexity of the model and the high number of degrees of freedom involved at each step of the iteration, the system can learn successfully even complex rules. In fact, since the system acts in a critical state, the response to a given input can be highly flexible, adapting more easily to different inputs. The analysis of the dependence of the performance of the system on the average connectivity confirms that learning is a truly collective process, where a high number of neurons may be involved and the system learns more efficiently if more branched paths are possible. The role of the plastic adaptation strength, considered as a constant parameter in most studies, provides a striking new result: The neuronal network has a “universal” learning dynamics, even complex rules can be learned provided that the plastic adaptation is sufficiently slow.

Moreover, the temporal organization of avalanches exhibits a complex non-monotonic behaviour of the waiting time distribution: Avalanches are temporally correlated in the up-state, whereas down-states are long term recovery periods where memory of past activity is erased. The model suggests that the crucial feature of this temporal evolution is the different single neuron behaviour in the two phases. This result provides new insights into the mechanisms necessary to introduce complex temporal correlations within the framework of self-organized criticality. The good agreement with experimental data indicates that the transition from an up-state to a down-state has a high degree of synchronization. Moreover it confirms that alternation between up and down-states is the expression of an homeostatic regulation which, during periods of high activity, is activated to control the excitability of the system, driving it into the down-state, and avoiding pathological behaviour. Network mechanisms in the up-state, where neurons mutually sustain the activity, act as a form of short-term memory. This is the crucial effect giving rise to the initial power law regime in the waiting time distribution, a clear sign of temporal correlations between avalanches occurring close in time in the up-state. Conversely, in the down-state, the system slowly goes back to the active state, with no memory of past
activity.

These collective effects must be supported by the single neuron behaviour, which toggles between two preferential states, a depolarized one in the up-state and a hyperpolarized one in the down-state. The model suggests that the depolarized neuron state is a network effect: the avalanche activity itself determines how close to the firing threshold a neuron stays in the up-state. Conversely, the hyperpolarized state is a form of temporal auto-correlation in the neuron state: the higher the neuron response during the previous avalanche the lower is its membrane potential. The hyperpolarizing currents act as a form of memory of past activity for the single neuron. The critical state of the system is therefore the one that realizes the correct balance between excitation and inhibition via self-regulating mechanisms. This balance ensures the scale free behaviour of avalanche activity and bursts of correlated avalanches in the up-state.