Modelling synaptic lifetime distributions with Kesten processes

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Introduction

The wiring of cortical circuits is highly dynamic. Spine sizes fluctuate even in the absence of neural activity and there is constant synaptic turnover [1]. In models of cortical circuits, two major mechanisms are typically considered to drive the efficacies of synaptic connections: Spike-timing dependent plasticity (STDP) is often assumed to strengthen or weaken synaptic connections in an additive manner, independent of the current weight. Synaptic normalization, on the other hand, acts multiplicatively on synapses by scaling their efficacies by a varying factor that might depend on the availability of synaptic resources [2] (see Fig. 1).

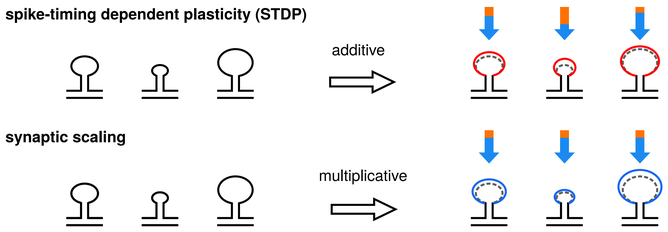

Figure 1: Spike-timing dependent plasticity changes synaptic efficacies additively, while synaptic normalization acts multiplicatively on the synaptic weights.

To model fluctuations of synaptic spine sizes over time, a stochastic process called Kesten process has been suggested [3, 4]. In this process, a random variable X_n at time step n is updated by scaling it with a random multiplicative factor a_n and then adding a random increment b_n according to

$$X_{n+1} = a_n X_n + b_n. \tag{1}$$

This stochastic model has been successfully used to describe the distribution of synaptic spine sizes measured in experiments. Here we extend the Kesten process by including the explicit creation and elimination of spines. Simulation and analysis of the model reveals that the distribution of lifetimes approximately follow a power law, as has been recently identified in experiments in the rat neocortex [1].

Model

We consider a Kesten process X_n that models spine size dynamics. A given spine size X_n at time step n is updated as $X_{n+1} = a_n X_n + b_n$ as in (1). Here, both a_n and b_n are drawn randomly at each time step from a normal distribution, $a_n \sim \mathcal{N}(\mu_a, \sigma_a^2)$ and $b_n \sim \mathcal{N}(\mu_b, \sigma_b^2)$. To model synapse growth and pruning processes, we consider a population of N synapses. Each synapse has a random time T_{init}, uniformly distributed in $[0, T_{\text{max}}]$, at which it is initialized with size X_0. The synaptic spine size X_t then evolves according to (1).

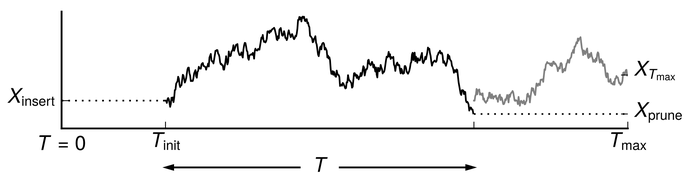

Figure 2: Adapted Kesten simulation model allows the tracking of lifetimes and size distributions

The lifetime of a synapse is the number of time steps from T_{init} until for the first time $X_t < X_{\text{prune}}$, where X_{prune} is a fixed parameter smaller than X_0 for the population. In this event the synapse gets pruned and a new synapse with size X_0 is inserted into the network (Fig. 2). In the case that X_t doesn't fall below X_{prune} until T_{max}, the lifetime is recorded as $T = T_{\text{max}} - T_{\text{init}}$. At the end of the simulation the sizes $X_{T_{\text{max}}}$ are recorded for all N synapses.

Results

We simulated $N = 5 \times 10^5$ synapses evolving as Kesten processes and recorded lifetime and weight distributions. First, we systemically tested the effect of the distribution parameters on lifetime and weight distributions. We found that within parameter ranges as for example used in the Kesten model of Statman et al. [4], the variance of the multiplicative component σ_a^2 has negligible effect on lifetime and weight distributions. This allowed us to further reduce the Kesten model in complexity and allowed us to consider an autoregressive AR(1) process of the form

$$X_{n+1} = a X_n + b_n, \tag{2}$$

where $a \in (0, 1)$ and $b_n \sim \mathcal{N}(\mu_b, \sigma_b^2)$ instead. The mean of the multiplicative component μ_a does affect both weight and lifetime distributions significantly and we found that biologically realistic distributions arise when μ_a is close to 1, as for example in [4] ($\mu_a \approx 0.99$). Indeed, in match with experimental data [1, 5] and predictions from network simulations [6] we found that for unbiased additive change ($\mu_b = 0$), a power law-like distribution of synaptic lifetimes emerges (Fig. 3A), while the distribution of spine sizes $X_{T_{\text{max}}}$ resembles a lognormal distribution.

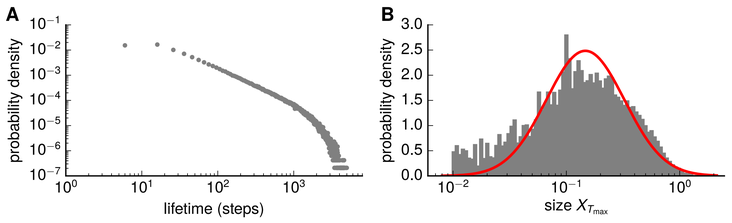

Figure 3: Dynamical properties of network connectivity modelled by AR(1) process as in (2). **A** Lifetime distribution of synapses created at time step T_{init} uniformly distributed in $[0, T_{\text{max}}]$. **B** Distribution of spine sizes $X_{T_{\text{max}}}$ at time step $X_{T_{\text{max}}}$ (grey) and lognormal fit (red). Parameters for both: $a = 0.9987$, $\mu_b = 0$, $\sigma_b^2 = 0.22$, $X_{\text{insert}} = 0.1$, $X_{\text{prune}} = 0.01$.

We found the variance σ_b^2 of the additive component to have little effect on both the lifetime and spine size distributions. Interestingly however, the bias in the additive change affects both distributions significantly. A bias towards increases in size ($\mu_b > 0$) moves the tail of the lifetime distribution towards higher lifetimes (Fig. 4A) and shifts the mean of the spine size distribution towards higher values (Fig. 4B).

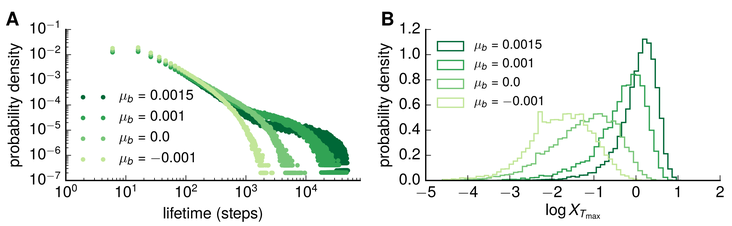

Figure 4: The bias of additive change in size strongly affects both lifetime and weight distributions.

Network simulations

What parameters of a cortical circuit could match μ_b in the stochastic model and thus similarly shape the lifetime and weight distributions of synapses? To test this we simulated a detailed network model similar to [7]. In the model we simulated $N_e = 400$ excitatory and $N_i = 80$ inhibitory leaky integrate-and-fire neurons with membrane noise over $T = 1000$ s. Synapses are conductance based and network connections within the excitatory population are inserted randomly over time at a low weight and eliminated if the weight falls below a global threshold. Spike-timing dependent plasticity and slow multiplicative synaptic normalization drive the synapse dynamics. We found that a parameter D, defined as integral of the STDP window for potentiation and divided by the integral of the STDP window for depression,

$$D = \frac{A_{\text{LTP}}\,\tau_{\text{LTP}}}{-A_{\text{LTD}}\,\tau_{\text{LTD}}}, \tag{3}$$

where A_{LTP}, A_{LTD} are the amplitudes and τ_{LTP}, τ_{LTD} the time constants for STDP windows for potentiation and depression, shows a similar shaping of lifetime distributions in the network model (Fig. 5A). We see however qualitatively different behaviour in the dynamics of the synaptic weight distributions (Fig. 5B).

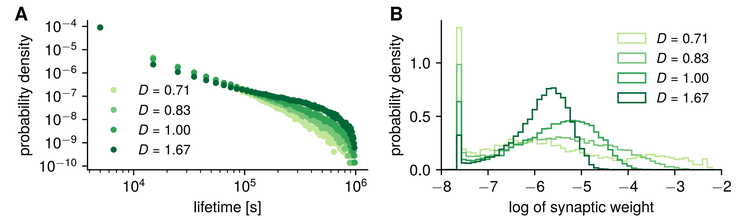

Figure 5: In detailed network simulations the synaptic lifetime and weight distributions are shaped by the overall ratio D between synaptic potentiation and depression.

Interestingly, we find that a large number of other network parameters, such as membrane noise, do not affect the synaptic lifetimes. This points towards a fundamental relationship between the additive weight dynamics and the lifetimes of synapses.

Key points

- For analysis of synaptic lifetime and spine size distributions, the Kesten process model can be reduced to simpler autoregressive AR(1) process
- Lifetime distributions in the model approximately follow a power law, while the distribution of spine sizes is lognormal-like, matching experimental findings
- In both stochastic model and network simulations the bias in the additive changes in synaptic weight systematically shapes the lifetime and weight distributions

References

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