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Simulating place field dynamics using spike timing-dependent plasticity

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Abstract

Spatial firing fields (place fields) of rat hippocampal cells undergo changes when the rat runs stereotyped routes. Previously, Mehta et al. [Experience-dependent asymmetric shape of hippocampal receptive fields, Neuron 25 (2000) 700–715] indicated that spike timing-dependent plasticity (STDP) might explain the observed shift of the place field center of mass and the development of skewness. In this study, by using simulations of spiking neurons with STDP, we demonstrate that STDP may cause a shift and negative skewness in the synaptic weights vector; however, we explain why these changes do not necessarily result in negative skewness of place fields. We further explore the parameters and additional mechanisms that favor the development of skewness.

Keywords: Place cell; Hippocampus model; Backward shift; Skewness; STDP

1. Introduction

Firing rates of cells in the rat hippocampus correlate with the location of the animal [14]; such cells are called place cells, and their response regions are called place fields (Fig. 1A). Place fields are not static. They can become asymmetric (skewed) and their center of mass (COM) shifts backwards with experience when the rat runs stereotyped routes [4,6,11,12]. These experience-dependent changes could be involved in encoding sequences of locations in learned routes and might be important for navigation and sequence prediction [2,7,9].

Mehta et al. [12] presented a feed-forward, rate-based model that simulated the backward COM shift and the development of negative skewness observed in CA1 place fields. The learning rule used by Mehta et al. [12] was a rate-based rule motivated by STDP [1,8,10]. Although Lee et al. [6] replicated the backward shift of the place field COM in both CA1 and CA3, the development of robust negative skewness was seen only in CA3, not in CA1. To understand this discrepancy, the present study explored conditions under which place fields become negatively skewed. Additionally, we wished to determine whether the STDP mechanisms employed by Mehta et al. [12] in a rate-based model would produce stable place fields in stochastic simulations with a spiking neuron model and whether such a stochastic model could explain the heterogeneous COM shifts exhibited by different individual place cells.

2. Methods

2.1. Model scheme

A feed-forward model was constructed with 1000 input cells (the input layer) and one output cell receiving weighted inputs from the input layer (Fig. 1B). All of the input cells had identical, non-plastic, Gaussian place fields and the centers of these place fields were evenly distributed along a circular track with a circumference of 2 m. Unless otherwise indicated, the width (full-width at half-maximum) of the input place fields was set at 0.3 m, which was derived from empirical data [6,11,12] and had been used in the previous model by Mehta et al. [12]. The place field's magnitude at a given location determined the probability that the respective input cell would generate a spike. For the stochastic model, every input cell had a probability of generating a spike at every time step. We also simulated a deterministic analog of the model in which input cells did not actually fire spikes, but instead the probability was used as a 'fractional spike'. This 'fractional spike'

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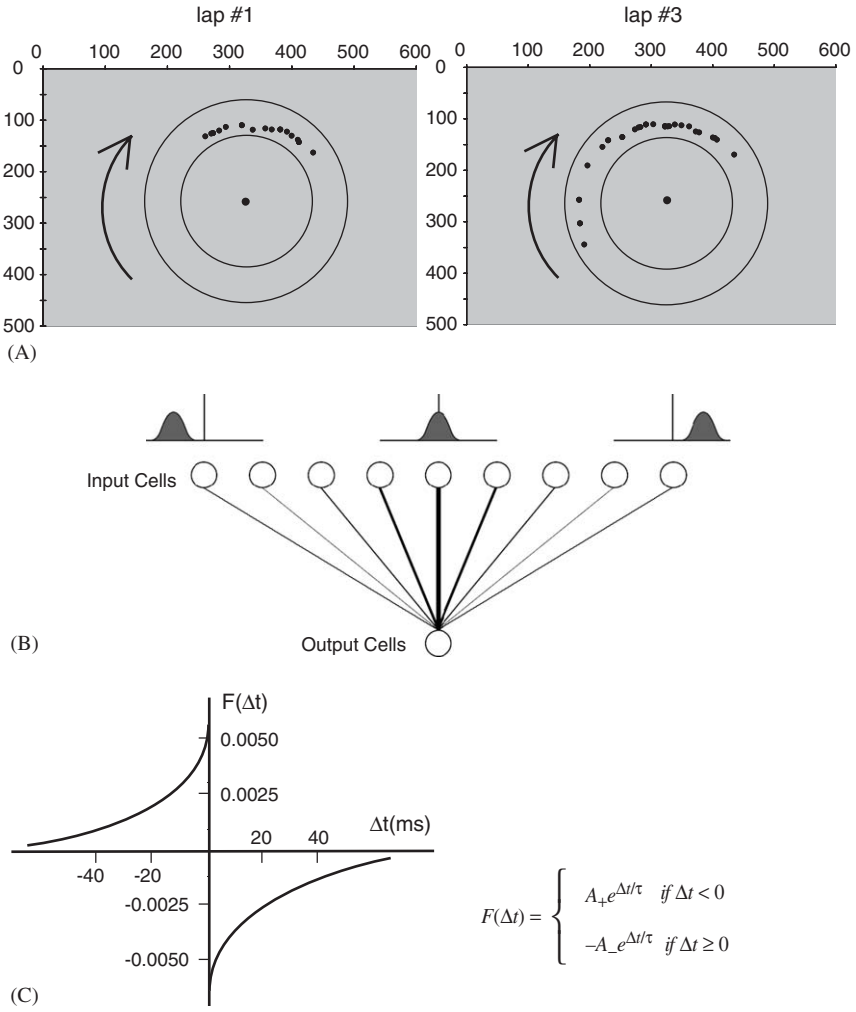

Fig. 1. Place field dynamics and the STDP model. (A) The firing pattern of a place cell recorded from a rat running clockwise on a circular track. The dots on the circular track are the positions where the place cell generated a spike. Left: firing on the first lap is almost symmetric. Right: on the third lap, low-frequency firing starts to appear earlier on the track, causing the place field to become negatively skewed and the COM to shift earlier (backwards). (B) A feed-forward model consists of 1000 presynaptic cells (only 9 cells illustrated here) and a single postsynaptic output cell. The output cell receives weighted inputs from every input cell. The centers of the place fields of the input neurons are evenly distributed along a circular track (2 m circumference). The lines between the input layer and output cell represent synaptic connections, and the thickness of the lines indicates synaptic strength or synaptic weights. (C) The STDP modification function. F is the change of peak conductance or maximal synaptic strength due to a single pre- and postsynaptic event. Δt is the time of the presynaptic spike minus the time of the postsynaptic spike. When $\Delta t < 0$, the presynaptic spike leads the postsynaptic spike and the synapse is potentiated. When $\Delta t \geqslant 0$, the presynaptic spike lags or equals the postsynaptic spike and the synapse is depressed. A_+ and A_- determine the maximal amounts of modification, which occur when Δt is close to 0.

contributed input to the postsynaptic cell and was used as a weighting number for plasticity events.

2.2. Stochastic input

The probability that an input cell will fire a spike is

$$P_{\mathrm{sp}}(x_i|x_0) = \alpha \mathrm{e}^{-(x_i - x_0)^2/2\sigma^2},$$

where α is a scaling factor that controls the firing rate of input cells, x_0 is the center of the place field, x_i is the current position of the rat, and σ determines the width of the place field (full-width at half-height $= 2.355\sigma$). Total synaptic input to the postsynaptic cell is generated randomly by

$$I_{\mathrm{s}} = \sum_i w_i \theta(P_{\mathrm{sp}}(x_i|x_0) - random(i)),$$

where w_i is the synaptic weight from input cell i, $random(i)$ is a random number between 0 and 1 generated independently for each input, θ is the heaviside function which has the value 0 if its argument is less than 0 and 1 if its argument is larger than 0.

2.3. Deterministic input

An input cell fires a fractional spike at every time step. The size of the spike is

$$S(x_i|x_0) = \alpha \mathrm{e}^{-(x_i - x_0)^2/2\sigma^2},$$

where α is a scaling factor that controls the firing rate of input cells, x_i is the current position, x_0 is the place field center, and σ determines the width of the place field. Total synaptic input to the postsynaptic cell is

$$I_s = \sum_i w_i S(x_i|x_0),$$

where w_i is the synaptic weight from input cell i.

2.4. Leaky integrate and fire output neuron

For both deterministic and stochastic models, the output cell is a leaky integrate and fire neuron that receives weighted inputs from all of the 1000 input cells and generates individual whole spikes:

$$dV/dt = (V - E_l)/\tau_l + \beta I_s,$$

where V is the membrane potential, E_l is the leak current equilibrium potential (−60 mV), τ_l is the time constant for this leak current (25 ms; [15]), I_s is the synaptic input current, and β is a scaling factor that controls the total synaptic input level to ensure that the peak firing rate of the output cell is in the right frequency range of 10–100 Hz found in the experiments [6, 12].

2.5. STDP learning

The synaptic weight vector between the input cells and the output cell is initially Gaussian, as is the output place field. The synaptic weights are plastic and subject to an additive STDP learning rule (Fig. 2):

$$F(\Delta t) = \begin{cases} A_+ e^{\Delta t/\tau} & \text{if } \Delta t < 0, \\ -A_- e^{\Delta t/\tau} & \text{if } \Delta t \geqslant 0, \end{cases}$$

where A_+ is the maximal amount of LTP modification (0.005; except in Fig. 4B) and A_- is the maximal amount of LTD modification (0.00525; except in Fig. 4B), Δt is the time difference between the presynaptic spike and the postsynaptic spike, τ is the time constant (20 ms) for determining the actual amount of LTP or LTD based on Δt. All parameters here (A_+, A_-, τ) are after Song et al. [15] and the synaptic weights are updated as in Song et al. [15]. For the deterministic model, each postsynaptic spike generates an STDP event for all incoming synapses, but these STDP events are weighted by the 'fractional spike': the probability of having a presynaptic spike at this synapse.

3. Results

3.1. STDP alone causes backward COM shift but insignificant skewness in place fields

To investigate place field plasticity due to STDP, we set up a one layer network (Fig. 1B) similar to a previous model [12]. In both the deterministic and stochastic models, the COM of synaptic weights and the COM of the output firing rates (or the output place field) shifted backwards with increasing laps (Fig. 2). In addition, there was a growth of total synaptic weights and, consistent with experimental results [11], a growth of total firing rates.

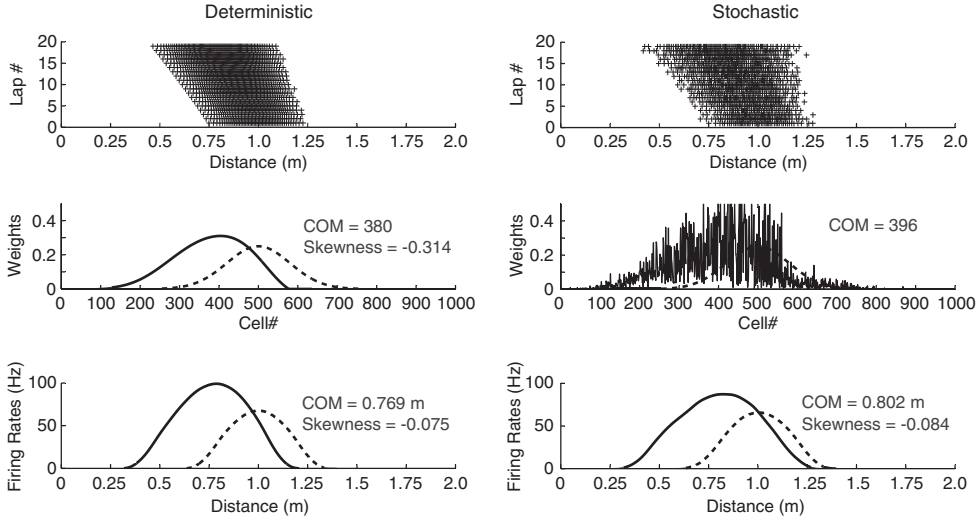

Fig. 2. Both deterministic and stochastic STDP models show backward COM shift but little skewness of the place field after learning. Top panels: raster plots showing spikes generated by the output cell in each lap. Middle panel: the synaptic weights are originally Gaussian (dashed line) but become skewed after 20 laps (solid line) in both the deterministic and stochastic models. Bottom panel: the initial place field of the output cell (dashed line) had its peak firing at position 1.0 m. After 20 laps, the place field shifted backward and the peak firing shifted to about 0.75 m (solid line). The inset numbers show the COM and skewness after 20 laps. The skewness for the weights in the stochastic model is not given here because sensitivity to noise in the two ends of the linearized track makes it an unreliable indicator of the actual shape of the curve.

However, while the synaptic weight vector was significantly skewed after 20 laps (skewness = −0.314 for the deterministic model), the place fields were not obviously skewed at the end of the simulation (skewness = −0.075 for the deterministic model; skewness = −0.084 for the stochastic model). Therefore, STDP caused a significant skewness of the synaptic weight vector onto the output neuron but did not cause an appreciable change in the skewness of the place field, similar to the CA1 place fields reported by Lee et al. [6].

3.2. A 'convolution effect' greatly reduces skewness when the input width is broad

To understand the discrepancy between the skewness of the synaptic weight vector and the skewness of the output firing rates, it is necessary to understand how synaptic weights between the input layer and the output cell are translated into output firing rates. In the model, the total synaptic inputs (I_s over time or distance) to the output cell is the convolution of the input place field (a fixed Gaussian distribution) and the synaptic weights. The total synaptic inputs, through the leaky integrate and fire model, determines the outputs over time and hence the shape of the output place field.

In a simplified mathematical model, we use arbitrary input functions and synaptic weights to demonstrate the effect of convolution on skewness (Fig. 3). The width of the input place field is varied from 0.72 to 0.072 m while the synaptic weights maintain the same shape and skewness (−0.7886). The output firing rate is approximated by convolving the synaptic weight vector with the input place fields, and passing this through a threshold-linear function. When the input Gaussian is broad (width = 0.72 m), convolution of the input place field and the synaptic weights results in little skewness (−0.0548). The outputs, which correspond to the total synaptic inputs above the threshold of 40% peak synaptic input, show even less skewness (−0.0125). When the input field is narrow (width = 0.072 m), however, convolution of the input place field and the synaptic weights results in a skewness (−0.7334) similar to that of the synaptic weights. The outputs have an intermediate level of skewness (−0.3204). When the input field has an intermediate width (width = 0.3 m), which is the width used in most of our other simulations, the total synaptic inputs to the neuron and the outputs are skewed (−0.3286 and −0.0929), but less so than the synaptic weights. For comparison, the results from the deterministic model fed with the same skewed synaptic weights are also shown (Fig. 3, fourth row, dashed lines). The threshold of 40% in the simplified model was chosen because it gave the outputs that matched the outputs from the full deterministic model best. However, no matter what threshold is chosen, the trend observed here should still hold.

Throughout the study we assume that the input place field is a symmetric Gaussian. What if the input place field is also skewed or becomes skewed with experience? The simplified model indicates that the output can be significantly more skewed if the input is skewed in the same direction as the weights while the width remains the same (Fig. 3 right column). Therefore, skewed weights translate to skewed outputs only when the width of the input place field is relatively narrow or the input place field is also skewed in the same direction. When the width of the input place field is broader than the width of the synaptic weights, the skewness is diminished when it is passed from synaptic weights to output.

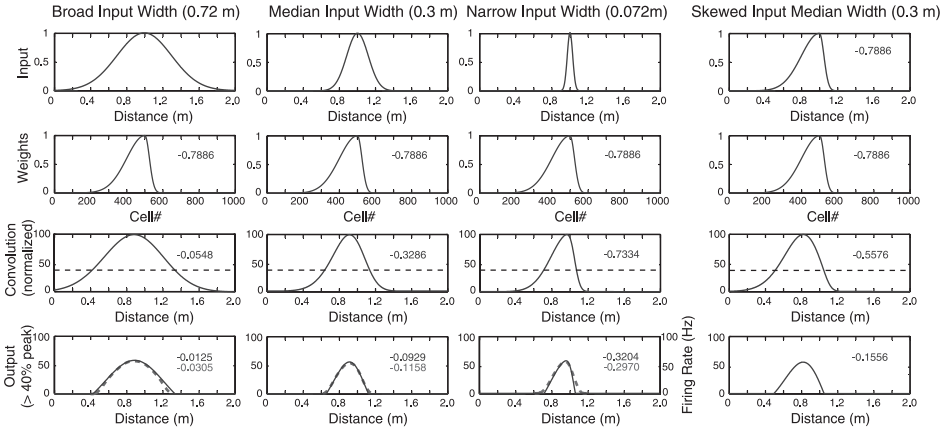

Fig. 3. Relationship of skewness of synaptic weights and skewness of output place fields demonstrated by the simplified convolution model. First row: input fields with broad, medium, and narrow Gaussian widths (first 3 columns) and skewed medium widths (right column). Second row: same skewed synaptic weights used in all four simulations. Third row: convolution of the input place filed and the synaptic weights. The peak value in each convolution is normalized to 100. A threshold of 40% peak value is shown in dashed lines. Fourth row: convolutions above the 40% threshold (solid line) and outputs from the deterministic model fed with same synaptic weights (dashed line). The inset numbers are the skewness of the output place fields from the convolution model (upper) and the deterministic model (lower).

3.3. Broad input width is necessary for heterogeneous COM shift of place fields

Experimental results showed variability in both the magnitude and the direction (backward or forward) of the COM shift among different individual cells, although on average the COM of place fields always shifted backwards (Fig. 4A). To test this heterogeneity in our stochastic model, we repeated the simulation many times using the same parameter settings and plot the results in one graph (Fig. 4B). With the median input width (0.3 m; left panel), backward COM shifts were observed in all instances, although the degree of COM shifts varied somewhat. However, no forward COM shift was observed even after the learning rate was increased to 8 times the standard learning rate. Forward COM shifts were only observed when the input width was set to a larger value (0.72 m; right panel). However, the variance as well as the total amount of COM shifts was still less than that found in the experiments. Learning rates higher than 8 times the standard learning rates made the stochastic model unstable. These results lead to the experimental prediction that COM-shift variability may systematically vary along the septotemporal axis of the hippocampus, with the broader place fields of the temporal (ventral) hippocampus showing more variability than the more specific place fields of the septal (dorsal) hippocampus [5]. Similarly, manipulations that systematically alter place field size (e.g., [13]) may also systematically affect the variability of the COM shift.

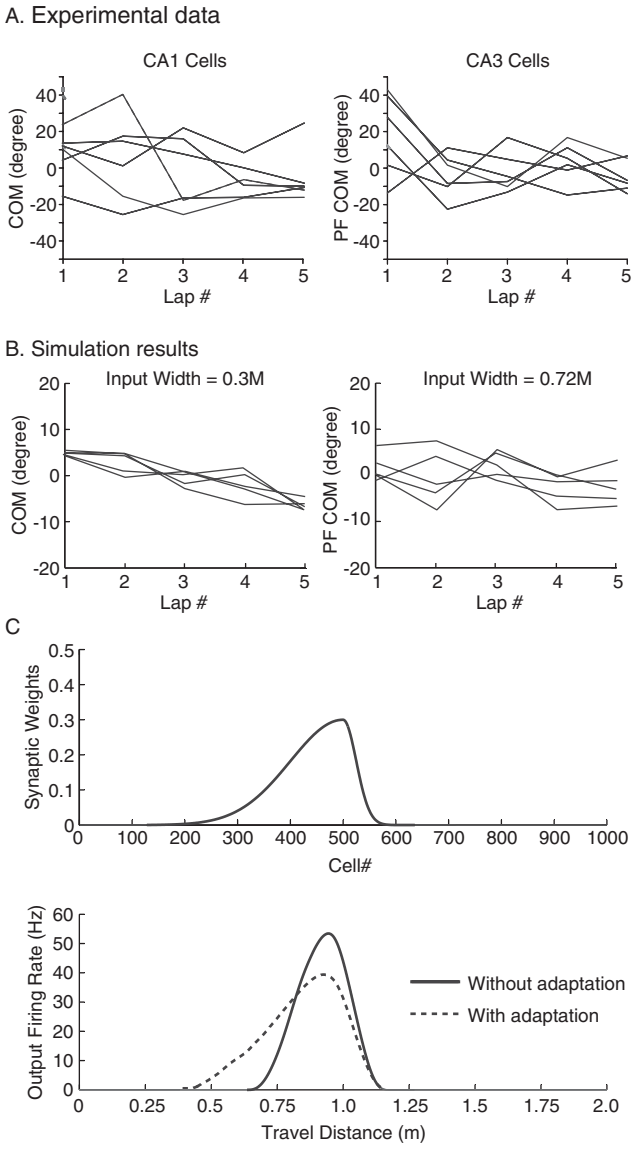

Fig. 4. Influence of input width and firing rate adaptation on the place field dynamics. (A) Experimental recordings from different individual CA1 and CA3 cells showing heterogeneity of the COM shift. (B) 5 stochastic simulations each for medium and broad input place fields, indicating that a broad input place field is necessary for heterogeneity of COM shift. (C) Provided with the same skewed synaptic weights (upper panel), outputs (bottom panel) from the adapting model (dashed line) show much more skewness than output from the non-adapting model (solid line).

3.4. Firing rate adaptation helps to pass on skewness from synaptic weights to output

In Mehta et al.'s [12] experiment and model of CA1 place fields, both synaptic weights and the firing rates (the place field) became significantly skewed after learning. However, Mehta et al.'s model included firing rate adaptation, which could enhance skewness (see also [16]). We performed simulations (Fig. 4C) in which firing rate adaptation was added to the deterministic model ([3], Eqs. (5.13) and (5.14)). Because adaptation greatly reduced firing rates, the total synaptic input was scaled up several fold to achieve similar firing rates as in the non-adapting model. The output of the adapting model was more skewed than the output of the non-adapting model fed with the same skewed synaptic weights. Adaptation enhanced skewness because the greater total synaptic input allowed the adapting model to start firing earlier, which "uncovered" the left-hand tail region of the synaptic weights. Firing on the right-hand side was much less affected because the skewed synaptic weights had a much shorter right-hand tail and the output cell already adapted at that point. Adaptation itself does not necessarily generate negative skewness (it sometimes generates positive skewness on a non-skewed weight distribution). However, the increase in total synaptic inputs that was necessary to obtain reasonable firing rates, together with adaptation, help uncover the skewed firing rates from a skewed synaptic weight distribution.

4. Discussion

This study was motivated by inconsistent results of skewness changes and COM shifts observed in experimental data. Significant negative skewness in CA1 place

cells was found in one experiment [12] but was less robust in other, similar experiments [6,11]. While these experiments agreed that, on average, the COM of place fields shifts backwards [4,6,11,12], there was variability among individual place cells that could not be easily accounted for by stochastic firing. With this model, we investigated factors that influence development of skewness and COM shifts, which can provide clues to understand the variability of results under different experimental conditions or in different individual place cells.

Although it is possible to obtain a COM shift as well as negative skewness of the weight vectors in our simulations, skewness in synaptic weights may not result in similar skewness in the output firing rates because of the 'convolution effect'. The skewness of output place fields can depend on non-synaptic mechanisms such as input width, input skewness, and firing rate adaptation. This leads to two potential explanations for the discrepancy between Mehta et al.'s result and Lee et al.'s result. First, because the CA1 cells recorded in Mehta et al.'s experiment had a much higher in-field firing rate than the CA1 cells recorded in Lee et al.'s experiment (14.7 Hz vs. 3.4 Hz), it is conceivable that the former was firing in the adaptive state and therefore "uncovered" much of the skewness in the weight vector while the latter was not. Second, CA1 cells recorded in the two experiments might have come from different areas along the transverse axis of the hippocampus. Lee et al. [6] targeted the proximal part of CA1, which received inputs from CA3 with more broadly tuned place fields than previous reports on CA3. Because of the convolution effect, these broad inputs may have filtered out the skewed synaptic weight vector.

While the backward COM shift appears to be less affected by the factors mentioned above, stochastic simulations demonstrate that the degree of variability observed in the COM shift might be related to the width of inputs to the plastic place cells. Therefore, our model predicts a correlation between the variability in the COM shift and the width of the inputs to the place cell.

The shift in COM and the development of negative skewness are a consequence of the causality of the STDP rule, and are not accounted for by a rate-based, correlational rule. Although prior work has demonstrated that NMDA-receptor blockers abolish the backward shift [4], the current simulations show that a number of factors interact to determine the final shape of the output place field, even though the STDP learning causes the synaptic weight distributions to become negatively skewed under all conditions. Thus, caution must be exercised when inferring from observed changes in firing rates to possible underlying changes in the synaptic weights.

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