Introduction

- In vivo recordings in the behaving monkey show that prefrontal (PFC) cortical cells maintain an elevated state of firing during the delay period associated with working memory tasks (Goldman-Rakic, 1990). This firing depends on a specific level of dopamine (DA) in the PFC (Williams and Goldman-Rakic, 1995). The level of dopamine in the PFC is related to the specific properties of the item that is remembered (Constantinidis et al., 2001).

- The effects of dopamine on cortical neurons in vivo are controversial, but it is clear that DA decreases excitability of layer V pyramidal neurons and many simulated synapses to prefrontal neurons (Lisman et al., 1998) and recurrent drive through NMDA receptors (Lisman et al., 1998) and recurrent inhibition (Wang, 2001; Scheler and Fellous, 2001).

- We use a hybrid network made of a real rat prefrontal neuron and many simulated synapses to show that the dopamine modulation of the membrane of the real neuron coupled to the simulated modulation of synaptic transmission allows for in-vivo-like sustained firing.

Methods

- In vivo: Layer V pyramidal cells in 2-3 weeks old Sprague-Dawley rats. Whole cell patch technique at 35°C. All drugs are bath applied. We use dopamine with ascorbic acid (<0.01%), DNQX (10 μM), APV (50 μM), Bicuculline (20 μM) (Fellous et al., 2001).

- Background conductance noise: 2 Ornstein-Uhlenbeck (OU) processes with time constants 2.7 ms (AMPAR), and 10.7 ms (GABAA) (Destexhe et al., 2001).

- Feedback conductance: Alpha function. NMDA depends on voltage (Jahr and Stevens, 1990).

- We use the reactive clamp technique to input conductance in feedback mode.

- Reactive Clamp

- NMDA alone

- AMPA alone

- GABA alone

- NMDA and AMPA

- NMDA and GABA

- AMPA and GABA

- Background synaptic noise (extra-columnary) 0.5mV (time constant: 0.5 ms)

- Background synaptic noise (extra-columnary) 1mV (time constant: 1 ms)

- Background synaptic noise (extra-columnary) 2mV (time constant: 2 ms)

1. DA decreases excitability

2. DA increases the NMDA response

3. Reactive Clamp

4. Recreating in vivo conditions

5. DA increases the signal-to-noise ratio in a simulated working memory task

6. The standard deviation of the background noise sets the gain. Emergence of multi-stability

7. Sustained activity in DA is robust to perturbations

Conclusions

- Dopamine (40 μM) decreases the excitability of rat prefrontal cortex cells in layer V and increases NMDA currents.

- Reactive clamp coupled to a stochastic model of extra-columnar background noise recreates in vivo membrane fluctuations, spontaneous spiking with high CV, and low input resistance.

- Under simulated in-vivo-like conditions, DA enables the sustained firing of prefrontal cells in response to a ‘cue’. Dopamine increases the signal-to-noise ratio.

- The standard deviation of the extra-columnar inputs sets the gain of PFC cells and regulates their firing rate during the delay period.

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