Supplemental material for *Influence of phasic and tonic dopamine release on receptor activation*

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This file contains supplementary information regarding Dreyer et al (Dreyer et al., 2010).

1 Visualization of receptor occupancy after synchronized release

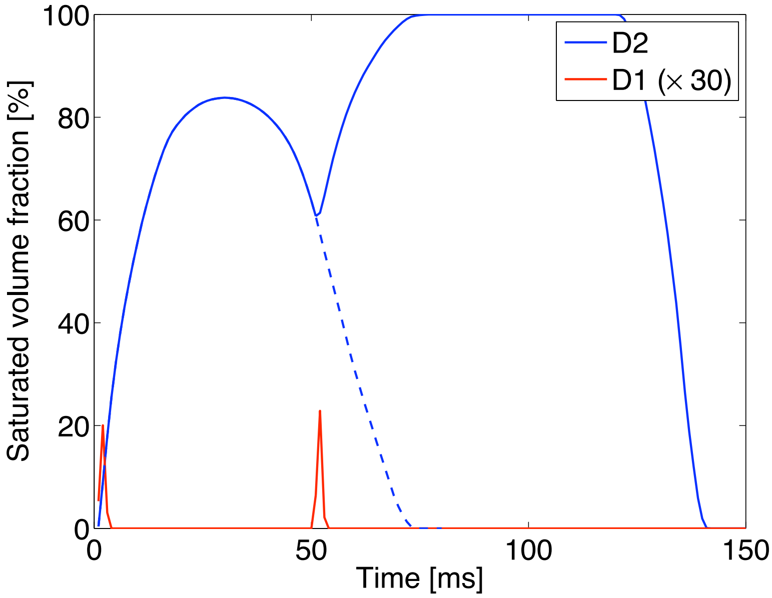

Figure S 1: Time evolution of 'saturated' volume (SV_i , volume fraction of simulation space where C ≥ EC_{50}^{i} where i = 1, 2 indicates the type of receptor) for D1 (red) and D2 receptors (blue). Note that SV_1 has been amplified 30 times to fit on the graph. Solid lines correspond to Movie S2, and dashed line to Movie S1. The release occurs at t = 0 ms and t = 50 ms.

We provide 2 animations of release from terminals. Here we used synchronized release from N_{ph} =20 neurons. There was no tonic activity (N_{to} = 0). In the animations the possible release sites from the 20 neurons are indicated as black dots. When a synchronized spike occurs 6% of these emit a full quantum of dopamine simultaneously. In the animations filled regions correspond to the regions of simulation space where D2 receptors are more than 50% occupied ('saturated'). When the filled region covers the entire simulation cube, the concentration of dopamine is higher than EC_{50}^{2} everywhere in simulation space. The red regions indicate where the local concentration of dopamine is high enough to occupy 50% of the D1 receptors. Movie S1 shows the time evolution of the saturated regions following a single synchronized release event. Movie S2 shows saturated regions during two synchronized releases.

The saturation volume for D1 and D2 receptors corresponding to the animations are shown in Figure S 1. We found SV_2 to reach 84% after the first synchronized spike. The release second synchronized spike was sufficient to maximize SV_2 to 100%. On the other hand, SV_1 was less than 1% during the first and second spike.

2 Ratio of occupancy of D2 and D1 receptors

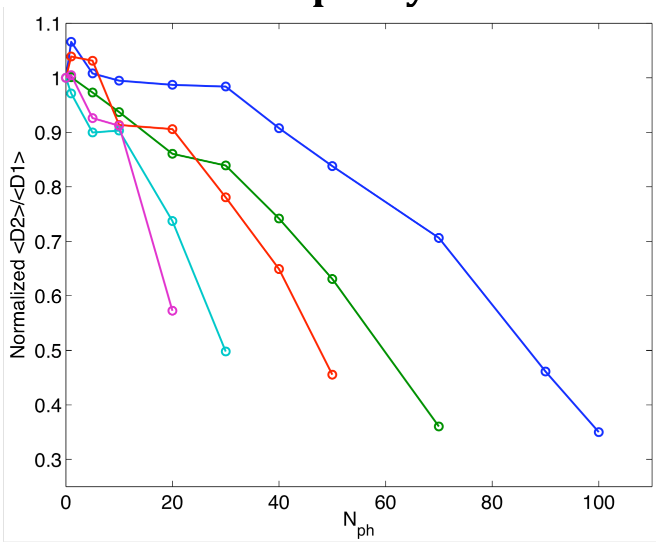

Figure S 2: Occupancy of D2 receptors from phasic firing patterns compared to tonic firing at same activity levels. Color indicates the total number of neurons in active population: blue, 100; green, 70; red, 50; cyan, 30; and purple, 20.

Figure S 2 illustrates the ratio between average occupancy of D2 and D1 receptors as function of N_{ph}. In the plot, the curves are normalized so that <D2>/<D1> by pure tonic activity is 1. Note that N_{ph} cannot exceed the total number of active neurons.

3 Comparison between Michaelis Menten uptake model and simulations

3.1 Predictions of tonic and phasic dopamine by Michaelis-Menten model

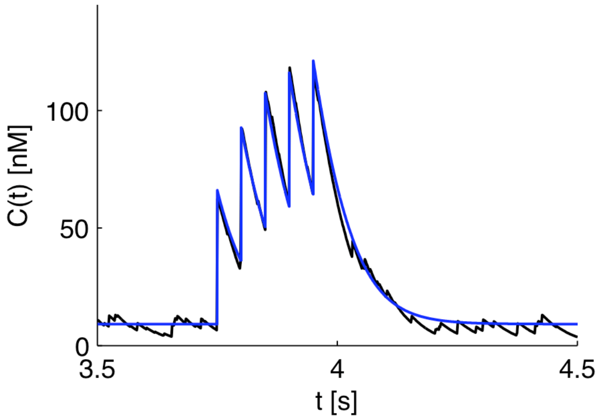

Figure S 3: Phasic and tonic dopamine levels can be predicted by simplified models. The plot shows a typical burst with background firing. The simulation parameters were N_{ph} =40 and N_{to} =60 with 4 Hz average firing rate of the non synchronized neurons. Black line is the volume averaged dopamine determined by the 3D simulation, blue line is the Michaelis Menten uptake model. We used 1 ms time step in the numerical integration, and used base line corrected values V' and K' as given by Eqns 13 and 14 in the manuscript.

We compared the output from the simplified Michaelis Menten model, based on phasic and tonic release, with the more elaborate simulation. The result is shown in Figure S 3. We found that tonic level is well described by Equation 7 of the manuscript. The amplitude of the synchronized release was found as $N_{ph}\Delta C$ where ΔC is given by Equation 5 of the manuscript. During the 5 synchronized spikes, the height of the dopamine transient corresponded well with simulation.

3.2 Average dopamine levels and receptor occupancies by Michaelis-Menten model

For the purpose of comparing the activation of receptors predicted by the Michaelis Menten uptake model with the simulation, we again vary the size of the population of neurons from 20 up to 100, N= 100, green N = 70, red = 50, cyan N= 30 and purple N=20) using the same firing patterns as in Figure 3 of the manuscript (Dreyer et al.). The baseline level was calculated using Equation 5,6 and 7 of the manuscript. The baseline-corrected uptake was determined using Equations 9 and 10.

The results are shown in Figure S 4. We find the main results from the simulation, average dopamine level and receptor activation, to be reproduced by the Michaelis Menten model.

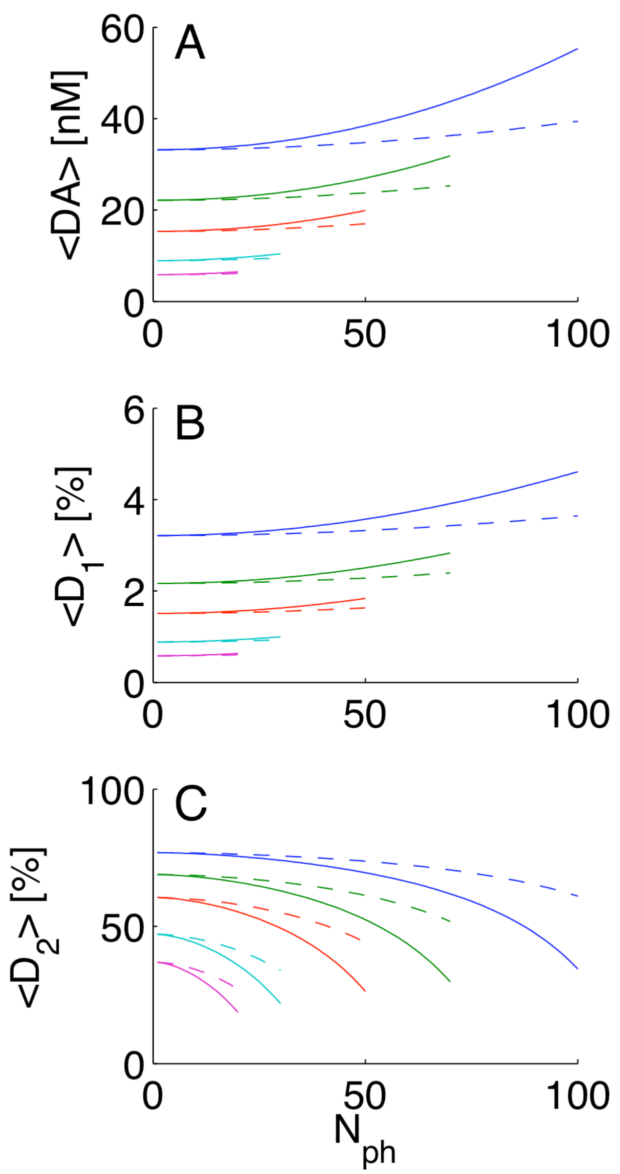

Figure S 4: Michaelis-Menten model predicts main output from simulations. The color code refers to the same values of $N = N_{ph} + N_{to}$ as in Figure 3 of the manuscript. Solid lines indicate the results from the Michaelis Menten model of bursts. Dashed lines indicate predictions of the same model but with regular firing pattern.

References

Dreyer JK, Herrik KF, Berg RW, Hounsgaard J (2010) Influence of phasic and tonic dopamine release on receptor activation. J Neurosci submitted.