Supplement to:

Deep brain stimulation alleviates parkinsonian bradykinesia by regularizing pallidal activity

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The main manuscript details simulations with the version of a computational model of the basal ganglia thalamic circuit (Terman et al., 2002; Rubin and Terman, 2004) described here. The XPP implementation will be provided upon request.

Briefly, sixteen point neurons in each of the four regions – subthalamic nucleus (STN), globus pallidus externus (GPe), globus pallidus internus (GPi) and pallidal receiving thalamic cells (TC) – comprise the model. Each neuron is represented by ordinary differential equations (ODEs) describing the membrane potential and ionic channel conductance gates as described below. All parameter values are listed in Tables 1-4.

Basal Ganglia Neurons. Neurons in basal ganglia (i.e. STN, GPe and GPi) were described by five ODEs.

$$c_m \frac{dV}{dt} = I_{app} - I_{Na} - I_K - I_{Ca} - I_T - I_{ahp} - I_L - I_{syn} \qquad \frac{dc}{dt} = -\epsilon(I_{Ca} + I_T + k_{Ca} c)$$

$$\frac{dn}{dt} = \frac{\phi_n}{\tau_n}(n_\infty - n) \qquad \frac{dh}{dt} = \frac{\phi_h}{\tau_h}(h_\infty - h) \qquad \frac{dr}{dt} = \frac{\phi_r}{\tau_r}(r_\infty - r)$$

Applied (I_{app}) and synaptic (I_{syn}) currents are discussed in the main text, *NEURONAL INPUTS.* Ionic currents were:

$$I_{Na} = G_{Na} m_\infty^3 h (V - V_{Na}) \qquad I_K = G_K n^4 (V - V_K) \qquad I_{Ca} = G_{Ca} s_\infty^2 (V - V_{Ca})$$

$$I_T = G_T a_\infty^3 b_r (V - V_{Ca}) \qquad I_{ahp} = G_{ahp} \frac{c}{c + k_{ahp}} (V - V_K) \qquad I_L = G_L (V - V_L)$$

Gating steady states and time constants were $x_\infty = \left(1 + e^{(V-\theta_x)/\sigma_x}\right)^{-1}$ and $\tau_x = \tau_{x0} + \tau_{x1} / \left(1 + e^{(V-\psi_x)/\xi_x}\right)$. For pallidal neurons $b_r = r$, while for STN neurons $b_r = \left(\left(1 - e^{-14.29r}\right) / \left(1.028 + e^{-14.29r}\right)\right)^2$.

Thalamic Neurons. Thalamic cells were described by three ODEs:

$$c_m \frac{dV}{dt} = I_{smc} - I_{Na} - I_K - I_T - I_L - I_{syn} \qquad \frac{dh}{dt} = \frac{1}{\tau_h}(h_\infty - h) \qquad \frac{dr}{dt} = \frac{1}{\tau_r}(r_\infty - r)$$

where the current from sensory motor cortex (I_{smc}) was a time varying input signal. The ionic currents were:

$$I_{Na} = G_{Na} m_\infty^3 h (V - V_{Na}) \qquad I_K = G_K n^4 (V - V_K)$$

$$I_T = G_T p_\infty^2 r (V - V_{Ca}) \qquad I_L = G_L (V - V_L)$$

where the steady state gating variables were described by $x_\infty = \left(1 + e^{(V-\theta_x)/\sigma_x}\right)^{-1}$, with time constants $\tau_h = \left(.128 e^{(V+46)/-18} + \frac{4}{1 + e^{(V+23)/-5}}\right)^{-1}$ and $\tau_r = 28 + e^{(V+25)/-10.5}$. The potassium activation gate was defined in terms of the sodium inactivation gate: $n = ¾ (1-h)$.

References

Rubin JE, Terman D. High frequency stimulation of the subthalamic nucleus eliminates pathological thalamic rhythmicity in a computational model. *J Comput Neurosci* 16: 211-235, 2004.

Terman D, Rubin JE, Yew AC, Wilson CJ. Activity patterns in a model for the subthalamopallidal network of the basal ganglia. *J. Neurosci* 22: 2963-2976, 2002.

Tables

Table 1. Current Parameters

		STN	GPe	GPi	TC
c_m	pF/μm^2	1	1	1	1
V_L	mV	-60	-55	-55	-70
V_{Na}	mV	55	55	55	50
V_K	mV	-80	-80	-80	-90
V_{Ca}	mV	140	120	120	0
G_L	nS/μm^2	2.25	0.10	0.10	0.05
G_{Na}	nS/μm^2	37.5	120	120	3
G_K	nS/μm^2	45	30	30	5
G_T	nS/μm^2	0.5	0.5	0.5	5
G_{Ca}	nS/μm^2	0.50	0.15	0.15	
G_{ahp}	nS/μm^2	9	30	30	
ε	μm^2/zC	37.5	100	100	
k_{Ca}	pA/μm^2	22.5	15	15	
k_{ahp}	Ø	15	30	30	

Table 2a. Advanced Gate Parameters

	θ	σ	φ	τ_0	τ_1	ψ	ξ
	mV	mV	Ø	ms	ms	mV	mV
STN							
h	-39	3.1	0.75	1.0	500	-57	3.0
n	-32	-8.0	0.75	1.0	100	-80	26
r	-67	2.0	0.50	7.1	17.5	68	2.2
GPe & GPi							
h	-58	12	.05	.05	.27	-40	12
n	-50	-14	.10	.05	.27	-40	12
r	-70	2	1	30	0	0	1

Table 2b. Simple Gate Parameters

	θ	σ
	mV	mV
STN		
m	-30	-15
s	-39	-8.0
a	-63	-7.8

	θ	σ
	mV	mV
GPe & GPi		
m	-37	-10
s	-35	-2
a	-57	-2

	θ	σ
	mV	mV
TC		
h	-41	4.0
r	-84	4.0
m	-37	-7.0
p	-60	-6.2

Table 3. Synaptic Parameters

synapses from		STN	GPe	GPi
Vsyn	mV	0	-85	-85
G_{syn}	nS/μm^2	0.15	0.50	0.04
α	ms^{-1}	3	2	2
β	ms^{-1}	0.01	0.04	0.04
θ_z	mV	-9	-37	-37
σ_z	mV	-8	-2	-2

Table 4. Tonic Applied Currents

		STN	GPe		GPi	
			CTRL	w/PD	CTRL	w/PD
I_{app}	pA/μm^2	25	20±2	5±2	21	12