Supplementary Material: Striatal neuropeptides enhance selection and rejection of sequential actions

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The following is a complete technical description of both the spiking striatal microcircuit model (including phenomenological neuropeptide models) and the basal ganglia–thalamocortical loop model, as per the format suggested by Nordlie et al. (2009).

Table S1. Striatal microcircuit: Summary

Striatal microcircuit: Model summary	
Populations	Three: D1 MSNs, D2 MSNs, and FSIs
Topology	—
Connectivity	GABAergic: All-to-all, pruned according to probability profile Neuropeptide: GABAergic, pruned according to probability profile To basal ganglia–thalamocortical loop: Fixed channel–convergent
Neuron model	Modified Izhikevich point neurons with reset condition and fixed voltage threshold
Channel models	—
Synapse model	Conductance-based single–exponential with dopamine and neuropeptide modifiers
Plasticity	—
Input	Independent Poisson spike sources representing sensory cortex project to each neuron MCtx output from BG–thalamocortical loop
Measurements	Raster log of spikes and converted rate output

Table S2. Striatal microcircuit: Populations

Striatal microcircuit: Populations			
Name	**Type**	**Size**	**Organisation**
D1 MSNs (d1)	Modified Izhikevich	3000	Six action channels $c_1 \ldots c_6$
D2 MSNs (d2)	Modified Izhikevich	3000	of 500 sequential neurons
FSIs (fs)	Modified nonlinear Izhikevich	60	—

Table S3. Striatal microcircuit: Connectivity

Striatal microcircuit: Connectivity	
Connection	**Algorithm**
MSN $\rightarrow$ MSN (GABA)	For d1 $\rightarrow$ d1, d1 $\rightarrow$ d2, d2 $\rightarrow$ d1, d2 $\rightarrow$ d2: 1. Create all–to–all connections 2. Assign each connection value $R \sim U([0,1])$ 3. Connection probability $P = \frac{\text{Number of afferent connections}^*}{\text{Number of target neurons}}$ 4. Remove connections where $R \leq P$
MSN $\rightarrow$ MSN (SP)	For d1 $\rightarrow$ d1, d1 $\rightarrow$ d2: Diffuse: All GABA connections co-release SP Pruned: All GABA connections except $\text{d1}_1 \rightarrow \text{d1}_6$, $\text{d1}_1 \rightarrow \text{d2}_6$ co-release SP Unidirectional: Only GABA connections $\text{d1}_c \rightarrow \text{d1}_{c+1}$, $\text{d1}_c \rightarrow \text{d2}_{c+1}$ where $c < 4$ co-release SP
MSN $\rightarrow$ MSN (ENK)	For d2 $\rightarrow$ d1, d2 $\rightarrow$ d2: All GABA connections co-release enkephalin
FSI $\rightarrow$ MSN	For fs $\rightarrow$ d1, fs $\rightarrow$ d2: As MSN $\rightarrow$ MSN (GABA)
FSI $\rightarrow$ FSI (GABA)	For fs $\rightarrow$ fs: As MSN $\rightarrow$ MSN (GABA)
FSI $\rightarrow$ FSI (GAP)	For fs $\rightarrow$ fs: As MSN $\rightarrow$ MSN (GABA) except: 1. Begin with all fs $\rightarrow$ fs synapse connections

*Values for expected number of afferent connections taken from Table 5, Humphries et al. (2010)

Table S4. Striatal microcircuit: Neuron models

Striatal microcircuit: Neuron models		
Name	**Dynamics**	**Modifications**
D1 MSN	$C\dot{v} = k(v - v_r)(v - v_t) - u + I$ $\dot{u} = a\left[b(v - v_r) - u\right]$ $I = I_{\text{ampa}} + I_{\text{gaba}} + B(v)I_{\text{nmda}}$	$v_r \leftarrow v_r(1 + K\phi_1)$ $d \leftarrow d(1 - L\phi_1)$
D2 MSN	Reset: if $v > v_{\text{peak}}$ then $v \leftarrow c, u \leftarrow u + d$	$k \leftarrow k(1 - \alpha\phi_2)$
FSI	$C\dot{v} = k(v - v_r)(v - v_t) - u + I$ $\dot{u} = \begin{cases} -au & \text{if } v < v_b \\ -a\left[b(v - v_b)^3 - u\right] & \text{if } v \geq v_b \end{cases}$ $I = I_{\text{ampa}} + I_{\text{gaba}}$ Reset: if $v > v_{\text{peak}}$ then $v \leftarrow c, u \leftarrow u + d$	$v_r \leftarrow v_r(1 - \eta\phi 1)$
Rate–to–spike	Each timestep, emit spike if $y_i^{\text{mc}} r_{\text{max}} \tau_{\text{bg}} > P$	$P \sim U([0,1])$

Table S5. Striatal microcircuit: Synaptic models

Striatal microcircuit: Synaptic models	
Type	**Dynamics**
Synapse	$I_z = \bar{g}_z h_z (E - v)$ $\dot{h}_z = \frac{-h_z}{\tau_z}$, and $h_z(t) \leftarrow h_z(t) + \left[1 - \frac{h_z(t)}{N_z}\right] S_z(t)$ Where z is AMPA, GABA or NMDA and $S_z(t)$ is the number of presynaptic spikes arriving at receptors for z at time t $B(v) = \frac{1}{1 + \frac{[\mathrm{Mg}^{2+}]_0}{3.57} \exp(-0.062v)}$
Neuropeptide	$A_p(t) = \sum_i S_p \left[\exp\left(\frac{-(t-t_i)}{\tau_f^p}\right) - \exp\left(\frac{-(t-t_i)}{\tau_r^p}\right)\right]$ $N_p(t) = \beta_p \left[1 - \exp\left(-\frac{A_p(t)}{\lambda_p}\right)^{b_p}\right]$ Where p is SP or enkephalin and S_p is the number of spikes causing a release of neuropeptide p
Gap junction	$\tau \dot{v}_{ij}^* = (v_i - v_{ij}^*) + (v_j - v_{ij}^*)$
Name	**Modifications**
D1 MSN	$I_{\text{nmda}} = I_{\text{nmda}}(1 + \beta_1 \phi_1)$
D2 MSN	$I_{\text{ampa}} = I_{\text{ampa}}(1 - \beta_2 \phi_2)$
D1 & D2 MSN	$I_z = I_z \left[1 + N_{\text{sp}}(t - \tau_d^{\text{sp}})\right] \left[1 - N_{\text{enk}}(t - \tau_d^{\text{enk}})\right]$ Where z is AMPA or NMDA
FSI	$I_{\text{gaba}} = I_{\text{gaba}}(1 - \epsilon_2 \phi_2)$

Table S6. Striatal microcircuit: Inputs

Striatal microcircuit: Inputs			
Input	**Targets**		
	D1 MSN	D2 MSN	FSI
Sensory cortex (sc)	$\mathrm{sc}_c^i \rightarrow \mathrm{d1}_c^i, 1 \leq i \leq 500$	$\mathrm{sc}_c^i \rightarrow \mathrm{d2}_c^i, 1 \leq i \leq 500$	$\mathrm{sc}_c^i \rightarrow \mathrm{fs}^i, 1 \leq i \leq 60$
MCtx (mc)	$\mathrm{mc}_c \rightarrow \mathrm{d1}_c^i, 1 \leq i \leq 500$	$\mathrm{mc}_c \rightarrow \mathrm{d2}_c^i, 1 \leq i \leq 500$	$\mathrm{mc}_c \rightarrow \mathrm{fs}^i, 1 \leq i \leq 60$

Table S7. Striatal microcircuit: MSN properties

Striatal microcircuit: MSN properties		
Param.	**Value**	**Source**
a	0.01	Mahon et al. (2000)
b	-20	Izhikevich (2007)
c	-55mV	
k	1	
v_r	-80mV	
v_{peak}	40mV	
C	15.2pF	Humphries et al. (2009)
d	91	
K	0.0289	
L	0.331	
v_t	-29.7mV	
α	0.032	

Table S8. Striatal microcircuit: FSI properties

Striatal microcircuit: FSI properties		
Param.	**Value**	**Source**
a	0.2	Izhikevich (2007)
b	0.025	
d	0	
k	1	
v_{peak}	25mV	
v_b	-55mV	
C	80pF	Tateno et al. (2004)
c	-60mV	
v_r	-70mV	
v_t	-50mV	
ϵ	0.625	Fitted to Gorelova et al. (2002)
η	0.1	Fitted to Bracci et al. (2002)

Table S9. Striatal microcircuit: Synapse properties

Striatal microcircuit: Synapse properties		
Parameter	**Value**	**Source**
$E_{\text{ampa}}, E_{\text{nmda}}$	0mV	Moyer et al. (2007)
E_{gaba}	-60mV	
τ_{ampa}	6ms	
τ_{nmda}	160ms	
τ_{gaba}	4ms	
τ_{bg}	0.1ms	Tuning (see text)
$\tau_{\text{fs-gap}}$	5ms	Fitted to Galarreta and Hestrin (1999)
$[\text{MG}^{2+}]_0$	1mM	Jahr and Stevens (1990)
g_{ampa} Ctx–MSN	0.4nS	Tomkins et al. (2014)
g_{ampa} Ctx–FSI	1nS	Fits linear rise in EPSC data from Gittis et al. (2010)
g_{nmda}	0.2nS	Fixed by maintaining the 2:1 AMPA:NMDA ratio from Moyer et al. (2007)
g_{gaba} MSN–MSN	0.75nS	Koos et al. (2004)
g_{gaba} FSI–MSN	3.75nS	Tomkins et al. (2014)
g_{gaba} FSI–FSI	1.1nS	Gittis et al. (2010)
$g_{\text{fs-gap}}$	5ns	Fitted to Galarreta and Hestrin (1999)
β_1	0.5	Tomkins et al. (2014)
β_2	0.3	
ϕ_1, ϕ_2	0.3	
$N_{\text{ampa}}, N_{\text{gaba}}$	2000	Tuning (see text)
N_{nmda}	600	
r_{max}	2000	

Table S10. Striatal microcircuit: Neuropeptide properties

Striatal microcircuit: Neuropeptide properties		
Parameter	**Value**	**Source**
β_{sp}	0.47	Blomeley and Bracci (2008)
τ_r^{sp}	10ms	Tuning (see text)
τ_f^{sp}	200ms	
τ_d^{sp}	40ms	
λ_{sp}	5.5	
b_{sp}	2.5	
β_{enk}	0.3	Blomeley and Bracci (2011)
τ_r^{enk}	15ms	Tuning (see text)
τ_f^{enk}	300ms	
τ_d^{enk}	400ms	
λ_{enk}	4.5	
b_{enk}	1	

Table S11. Basal ganglia–thalamocortical loop: Summary

Basal ganglia loop: Model summary	
Populations	Five: MCtx, STN, GPe, GPi/SNr, VLT
Topology	—
Connectivity	Within BG loop: One–to–one and all–to–all To striatal microcircuit: Fixed channel–divergent
Neuron model	Leaky integrator
Channel models	—
Synapse model	—
Plasticity	—
Input	Rate–converted Poisson spike sources representing sensory cortex project to MCtx and STN Rate–converted spiking MSN output from striatal microcircuit projects to GPe and GPi/SNr
Measurements	Activity rate output

Table S12. Basal ganglia–thalamocortical loop: Populations

Name	**Type**	**Size**	**Organisation**
MCtx (mc) STN (stn) GPe (gp) GPi/SNr (snr) VLT (vlt)	Leaky integrator	6	Six action channels $c_1 \dots c_6$ of 1 neuron each

Table S13. Basal ganglia–thalamocortical loop: Connectivity

Connection	**Type**
MCtx $\rightarrow$ VLT MCtx $\rightarrow$ STN	One–to–one
STN $\rightarrow$ GPe STN $\rightarrow$ GPi/SNr	All–to–all
GPe $\rightarrow$ STN GPe $\rightarrow$ GPi/SNr GPi/SNr $\rightarrow$ VLT VLT $\rightarrow$ MCtx	One–to–one

Table S14. Basal ganglia–thalamocortical loop: Neuron models

Basal ganglia loop: Neuron models	
Activation	$\dot{a} = k(a - u) + u$
Output	$y(t) = F(a(t), \theta) = \begin{cases} 0 & \text{if } a(t) \leq \theta \\ a(t) - \theta & \text{if } \theta < a(t) < 1 - \theta \\ 1 & \text{if } a(t) \geq 1 - \theta \end{cases}$
Spike–to–rate	$r_i^s(t) = \sum_i S_s \left[\exp\left(\frac{-(t - t_i)}{\tau_f}\right) - \exp\left(\frac{-(t - t_i)}{\tau_r}\right) \right]$ $y_i^s(t) = 1 - \exp\left(-\frac{r_s(t)}{\lambda_s}\right)^{b_s}$ Where s is d1, d2 or sc and S_s is the number of spikes arriving from population s
Name	**Dynamics**
MCtx	$u_i^{\text{mc}} = w_{\text{mc}} y_i^{\text{sc}} + w_{\text{vlt}} y_i^{\text{vlt}}$ $y_i^{\text{mc}} = F\left(a_i^{\text{mc}}, 0\right)$
STN	$u_i^{\text{stn}} = w_{\text{stn}} y_i^{\text{sc}} + w_{\text{stn}} y_i^{\text{mc}} + w_{\text{gp}} y_i^{\text{gp}}$ $y_i^{\text{stn}} = F\left(a_i^{\text{stn}}, -0.25\right)$
GPe	$u_i^{\text{gp}} = w_{\text{gp}} \sum_j^n y_j^{\text{stn}} - y_i^{\text{d2}}$ $y_i^{\text{gp}} = F\left(a_i^{\text{gp}}, -0.2\right)$
GPi/SNr	$u_i^{\text{snr}} = w_{\text{snr}} \sum_j^n y_j^{\text{stn}} - y_i^{\text{d1}} - w_{\text{gp}} y_i^{\text{gp}}$ $y_i^{\text{snr}} = F\left(a_i^{\text{snr}}, -0.2\right)$
VLT	$u_i^{\text{vlt}} = w_{\text{mc}} y_i^{\text{mc}} + w_{\text{snr}} y_i^{\text{snr}}$ $y_i^{\text{vlt}} = F\left(a_i^{\text{vlt}}, 0\right)$

Table S15. Basal ganglia–thalamocortical loop: Inputs

Basal ganglia loop: Inputs		
Input	**Targets**	
	STN	MCtx
Sensory cortex (sc)	$\text{sc}_c^i \rightarrow \text{stn}_c, 1 \leq i \leq 500$	$\text{sc}_c^i \rightarrow \text{mc}_c, 1 \leq i \leq 500$
	GPi/SNr	GPe
D1 / D2 MSNs (d1 / d2)	$\text{d1}_c^i \rightarrow \text{snr}_c, 1 \leq i \leq 500$	$\text{d2}_c^i \rightarrow \text{gp}_c, 1 \leq i \leq 500$

Table S16. Basal ganglia–thalamocortical loop: Weights and properties

Basal ganglia loop: Weights and properties		
Parameter	**Value**	**Source**
$w_{\text{sc–d1}}$	0.5	Humphries and Gurney (2002)
$w_{\text{sc–d2}}$	0.5	
$w_{\text{sc–stn}}$	0.5	
$w_{\text{sc–mc}}$	0.5	Tuning (see text)
$w_{\text{mc–d1}}$	0.5	Humphries and Gurney (2002)
$w_{\text{mc–d2}}$	0.5	
$w_{\text{mc–stn}}$	0.5	
$w_{\text{mc–vlt}}$	1	
$w_{\text{vlt–mc}}$	1.05	Tuning (see text)
$w_{\text{d1–snr}}$	-1	Humphries and Gurney (2002)
$w_{\text{d2–gp}}$	-1	
$w_{\text{stn–snr}}$	0.8	
$w_{\text{stn–gp}}$	0.8	
$w_{\text{gp–stn}}$	-1	
$w_{\text{gp–snr}}$	-0.4	
$w_{\text{snr–vlt}}$	-1	
k	0.9608	
τ_r	9ms	Tuning (See text)
τ_f	10ms	
$\lambda_{\text{d1}}, \lambda_{\text{d2}}$	15	
λ_{sc}	850	
$b_{\text{d1}}, b_{\text{d2}}$	1	
b_{sc}	1.5	

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