

Electronic Supplementary Material

Modulation of value-based decision making behavior by subregions of the rat prefrontal cortex

Jeroen P.H. Verharen^{1,2,3}, Hanneke E.M. den Ouden⁴, Roger A.H. Adan^{1,5}, Louk J.M.J. Vanderschuren^{2,5,*}

¹ Brain Center Rudolf Magnus, Department of Translational Neuroscience, University Medical Center Utrecht, 3584CG Utrecht, The Netherlands.

² Department of Animals in Science and Society, Division of Behavioural Neuroscience, Faculty of Veterinary Medicine, Utrecht University, 3584CM Utrecht, The Netherlands.

³ Helen Wills Neuroscience Institute, Department of Molecular and Cell Biology, University of California Berkeley, Berkeley, CA 94720, United States

⁴ Donders Institute for Brain, Cognition and Behaviour, Radboud University, 6525HR Nijmegen, The Netherlands.

⁵ These authors contributed equally.

* Corresponding author: l.j.m.j.vanderschuren@uu.nl, +31-30-2535239

Online Resource 1

Supplementary Statistics Table

Figure	Test used	<i>n</i>	p value	Test statistic	Effect size (Partial eta squared)	
1c Reversals	2-way repeated measures ANOVA	49 rats	Main drug effect p = 0.0006***	Main drug effect F(1, 44) = 13.63		
			Main group effect p = 0.0003***	Main group effect F(4, 44) = 6.469		
			Group * drug interaction p = 0.1252	Group * drug interaction F(4, 44) = 1.913		
		post-hoc Holm- Sidak ACC group (sal vs BM)	10 rats	p = 0.9931	t(44) = 0.009	Measurement 1 = 0.1615 Measurement 2 = 0.1380 Average = 0.0000
		post-hoc Holm- Sidak PrL group (sal vs BM)	12 rats	p = 0.1636	t(44) = 1.948	Measurement 1 = 0.0846 Measurement 2 = 0.4889 Average = 0.3676
		post-hoc Holm- Sidak IL group (sal vs BM)	9 rats	p = 0.0285 *	t(44) = 2.818	Measurement 1 = 0.3291 Measurement 2 = 0.1913 Average = 0.5022
		post-hoc Holm- Sidak mOFC group (sal vs BM)	9 rats	p = 0.8780	t(44) = 0.4559	Measurement 1 = 0.4254 Measurement 2 = 0.0705 Average = 0.0361
	post-hoc Holm- Sidak IOFC group (sal vs BM)	9 rats	p = 0.0215 *	t(44) = 3.007	Measurement 1 = 0.0954 Measurement 2 = 0.5068 Average = 0.3506	
1c Rewarded	2-way repeated measures ANOVA	49 rats	Main drug effect p < 0.0001 ****	Main drug effect F(1, 44) = 21.80		
			Main group effect p = 0.0174 *	Main group effect F(4, 44) = 3.362		
			Group * drug interaction p = 0.4666	Group * drug interaction F(4, 44) = 0.9099		
		post-hoc Holm- Sidak ACC group (sal vs BM)	10 rats	p = 0.3814	t(44) = 1.110	Measurement 1 = 0.6551 Measurement 2 = 0.0699 Average = 0.1992
	post-hoc Holm- Sidak PrL group (sal vs BM)	12 rats	p = 0.0414 *	t(44) = 2.672	Measurement 1 = 0.1703 Measurement 2 = 0.3810 Average = 0.4303	
	post-hoc Holm- Sidak IL group (sal vs BM)	9 rats	p = 0.3814	t(44) = 1.262	Measurement 1 = 0.0023 Measurement 2 = 0.0898 Average = 0.1157	

Figure	Test used	n	p value	Test statistic	Effect size (Partial eta squared)
	post-hoc Holm-Sidak mOFC group (sal vs BM)	9 rats	p = 0.0071**	t(44) = 3.402	Measurement 1 = 0.1153 Measurement 2 = 0.5617 Average = 0.6077
	post-hoc Holm-Sidak IOFC group (sal vs BM)	9 rats	p = 0.1367	t(44) = 2.036	Measurement 1 = 0.0573 Measurement 2 = 0.2831 Average = 0.2941
1c Trials complete d	2-way repeated measures ANOVA	49 rats	Main drug effect p = 0.3012 Main group effect p = 0.0026 Group * drug interaction p = 0.3942	Main drug effect F(1, 45) = 1.094 Main group effect F(4, 45) = 4.791 Group * drug interaction F(4, 45) = 1.046	
1c Response latency	2-way repeated measures ANOVA	49 rats	Main drug effect p = 0.7208 Main group effect p = 0.0709 Group * drug interaction p = 0.9479	Main drug effect F(1, 44) = 0.1294 Main group effect F(4, 44) = 2.328 Group * drug interaction F(4, 44) = 0.1793	
3 Reward learning	2-way repeated measures ANOVA	49 rats	Main drug effect p < 0.0001**** Main group effect p = 0.0002*** Group * drug interaction p = 0.5832	Main drug effect F(1, 44) = 20.40 Main group effect F(4, 44) = 7.020 Group * drug interaction F(4, 44) = 0.7195	
	post-hoc Holm-Sidak ACC group (sal vs BM)	10 rats	p = 0.3578	t(44) = 1.305	Measurement 1 = 0.1450 Measurement 2 = 0.1148 Average = 0.1672
	post-hoc Holm-Sidak PrL group (sal vs BM)	12 rats	p = 0.0111*	t(44) = 3.246	Measurement 1 = 0.1065 Measurement 2 = 0.6025 Average = 0.5714
	post-hoc Holm-Sidak IL group (sal vs BM)	9 rats	p = 0.3578	t(44) = 1.036	Measurement 1 = 0.0000 Measurement 2 = 0.2580 Average = 0.0923
	post-hoc Holm-Sidak mOFC group (sal vs BM)	9 rats	p = 0.1466	t(44) = 2.002	Measurement 1 = 0.1956 Measurement 2 = 0.1571 Average = 0.2475
	post-hoc Holm-Sidak IOFC group (sal vs BM)	9 rats	p = 0.0435*	t(44) = 2.653	Measurement 1 = 0.3670 Measurement 2 = 0.4936 Average = 0.5913

Figure	Test used	<i>n</i>	p value	Test statistic	Effect size (Partial eta squared)	
3 Punish- ment learning	2-way repeated measures ANOVA	49 rats	Main drug effect $p < 0.0001^{****}$	Main drug effect $F(1, 44) = 44.63$		
			Main group effect $p < 0.0001^{****}$	Main group effect $F(4, 44) = 8.281$		
			Group * drug interaction $p = 0.1345$	Group * drug interaction $F(4, 44) = 1.860$		
		post-hoc Holm- Sidak ACC group (sal vs BM)	10 rats	$p = 0.3798$	$t(44) = 0.8871$	Measurement 1 = 0.0251 Measurement 2 = 0.0486 Average = 0.0614
		post-hoc Holm- Sidak PrL group (sal vs BM)	12 rats	$p = 0.0007^{***}$	$t(44) = 4.179$	Measurement 1 = 0.4016 Measurement 2 = 0.5421 Average = 0.6335
		post-hoc Holm- Sidak IL group (sal vs BM)	9 rats	$p = 0.0011^{**}$	$t(44) = 3.945$	Measurement 1 = 0.2946 Measurement 2 = 0.4343 Average = 0.5327
		post-hoc Holm- Sidak mOFC group (sal vs BM)	9 rats	$p = 0.0497^*$	$t(44) = 2.318$	Measurement 1 = 0.6776 Measurement 2 = 0.2121 Average = 0.6304
	post-hoc Holm- Sidak IOFC group (sal vs BM)	9 rats	$p = 0.0019^{**}$	$t(44) = 3.382$	Measurement 1 = 0.4988 Measurement 2 = 0.6789 Average = 0.7280	
3 Stickiness	2-way repeated measures ANOVA	49 rats	Main drug effect $p = 0.0005^{***}$	Main drug effect $F(1, 44) = 14.07$		
			Main group effect $p = 0.2508$	Main group effect $F(4, 44) = 1.397$		
			Group * drug interaction $p = 0.0137^*$	Group * drug interaction $F(4, 44) = 3.540$		
		post-hoc Holm- Sidak ACC group (sal vs BM)	10 rats	$p = 0.9494$	$t(44) = 0.3050$	Measurement 1 = 0.0440 Measurement 2 = 0.0976 Average = 0.0261
		post-hoc Holm- Sidak PrL group (sal vs BM)	12 rats	$p = 0.9494$	$t(44) = 0.4848$	Measurement 1 = 0.0001 Measurement 2 = 0.1298 Average = 0.0174
		post-hoc Holm- Sidak IL group (sal vs BM)	9 rats	$p = 0.0010^{**}$	$t(44) = 4.046$	Measurement 1 = 0.3641 Measurement 2 = 0.2258 Average = 0.6792
		post-hoc Holm- Sidak mOFC group (sal vs BM)	9 rats	$p = 0.0115^*$	$t(44) = 3.157$	Measurement 1 = 0.6981 Measurement 2 = 0.0675 Average = 0.6443
	post-hoc Holm- Sidak IOFC group (sal vs BM)	9 rats	$p = 0.9494$	$t(44) = 0.1775$	Measurement 1 = 0.0040 Measurement 2 = 0.0113 Average = 0.0022	

Figure	Test used	<i>n</i>	p value	Test statistic	Effect size (Partial eta squared)
3 Explore/ exploit	2-way repeated measures ANOVA	49 rats	Main drug effect p = 0.8299 Main group effect p = 0.1193 Group * drug interaction p = 0.2838	Main drug effect F(1, 44) = 0.04671 Main group effect F(4, 44) = 1.948 Group * drug interaction F(4, 44) = 1.303	

Online Resource 2

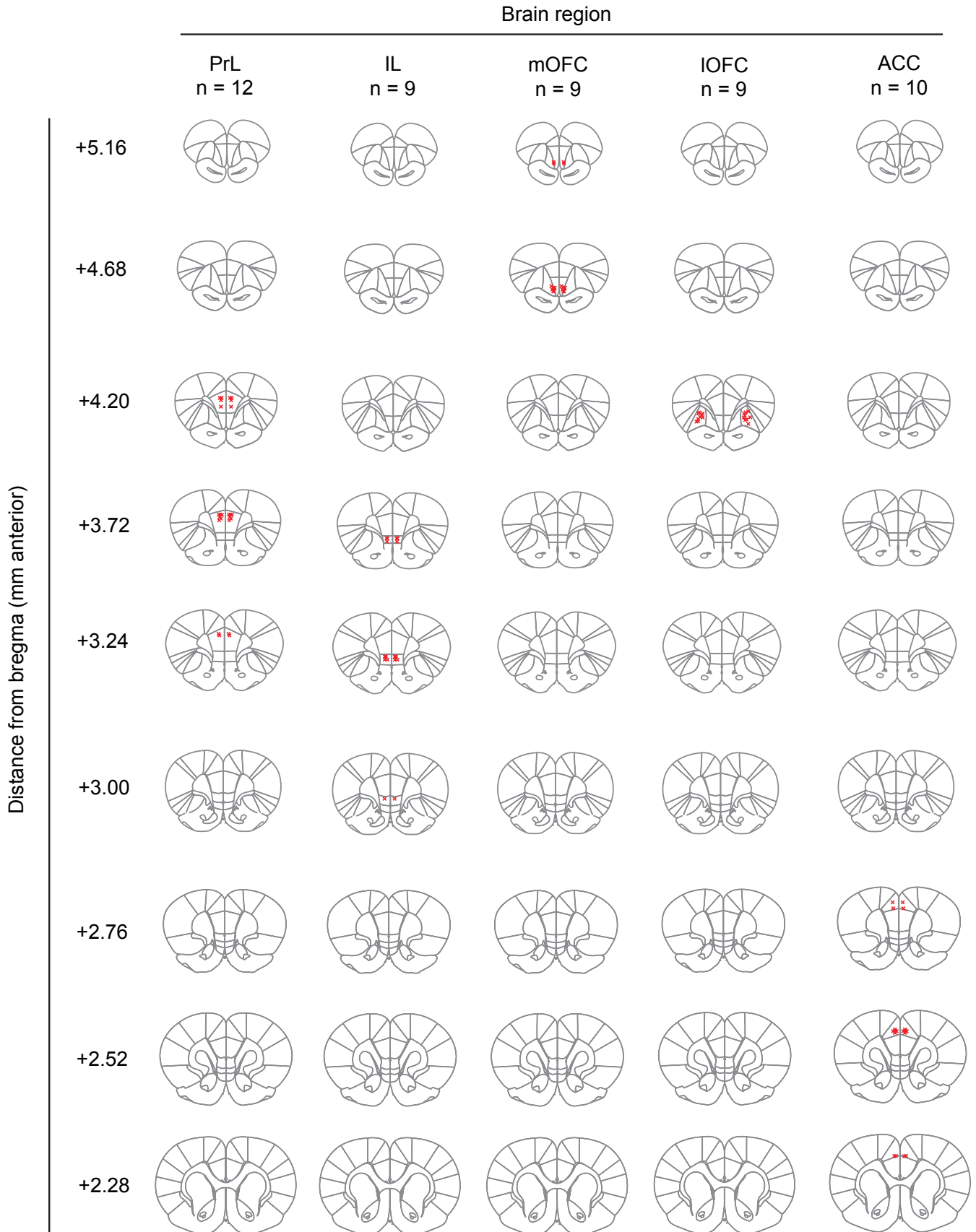
Table containing the equations of the different models

Model	Free parameters	Learning model	Observation equation
RW1	α, β	$Q_{s,t} = \begin{cases} Q_{s,t-1} + \alpha \cdot \text{RPE}_t & \text{for win trials} \\ Q_{s,t-1} + \alpha \cdot \text{RPE}_t & \text{for lose trials} \end{cases}$	$P_{\text{right},t} = \frac{\exp(\beta \cdot Q_{\text{right},t})}{\exp(\beta \cdot Q_{\text{left},t}) + \exp(\beta \cdot Q_{\text{right},t})}$
RW2	$\alpha^+, \alpha^-, \beta$	$Q_{s,t} = \begin{cases} Q_{s,t-1} + \alpha^+ \cdot \text{RPE}_t & \text{for win trials} \\ Q_{s,t-1} + \alpha^- \cdot \text{RPE}_t & \text{for lose trials} \end{cases}$	$P_{\text{right},t} = \frac{\exp(\beta \cdot Q_{\text{right},t})}{\exp(\beta \cdot Q_{\text{left},t}) + \exp(\beta \cdot Q_{\text{right},t})}$
RW3	$\alpha^+, \alpha^-, \beta, \pi$	$Q_{s,t} = \begin{cases} Q_{s,t-1} + \alpha^+ \cdot \text{RPE}_t & \text{for win trials} \\ Q_{s,t-1} + \alpha^- \cdot \text{RPE}_t & \text{for lose trials} \end{cases}$	$P_{\text{right},t} = \frac{\exp(\beta \cdot Q_{\text{right},t} + \pi \cdot \phi_{\text{right},t})}{\exp(\beta \cdot Q_{\text{left},t} + \pi \cdot \phi_{\text{left},t}) + \exp(\beta \cdot Q_{\text{right},t} + \pi \cdot \phi_{\text{right},t})}$
RW-PH	α, β, π, η	$Q_{s,t} = \begin{cases} Q_{s,t-1} + \alpha \cdot \gamma_t \cdot \text{RPE}_t & \text{for win trials} \\ Q_{s,t-1} + \alpha \cdot \gamma_t \cdot \text{RPE}_t & \text{for lose trials} \end{cases}$ with $\gamma_t = \eta \cdot \text{RPE}_t + (1 - \eta) \cdot \gamma_{t-1}$	$P_{\text{right},t} = \frac{\exp(\beta \cdot Q_{\text{right},t} + \pi \cdot \phi_{\text{right},t})}{\exp(\beta \cdot Q_{\text{left},t} + \pi \cdot \phi_{\text{left},t}) + \exp(\beta \cdot Q_{\text{right},t} + \pi \cdot \phi_{\text{right},t})}$

In this table, α = Rescorla-Wagner learning rate, β = choice stochasticity, π = stickiness factor, η = Pearce-Hall associability factor, $Q_{s,t}$ = value of nose poke s on trial t , $p_{s,t}$ = choice probability of nose poke s on trial t , ϕ = boolean that is 1 if nose poke s is chosen on the previous trial and 0 if unchosen on previous trial, RPE = reward prediction error, and γ_t = associability on trial t .

Online Resource 3

Infusion locations



Online Resource 4

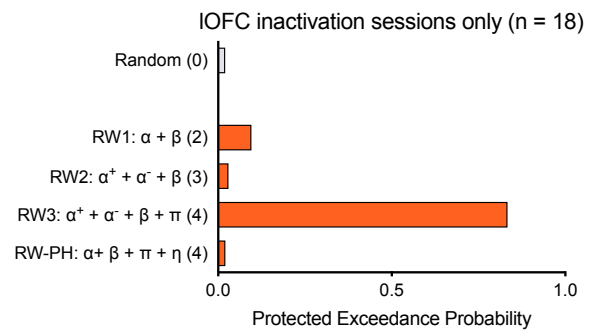
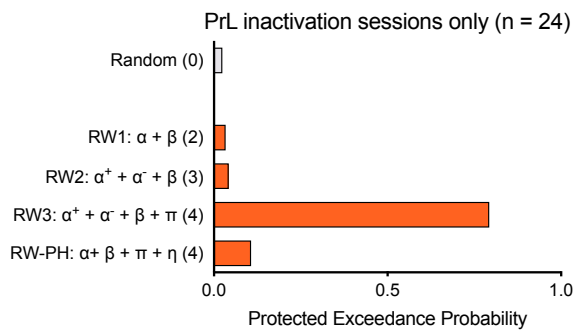
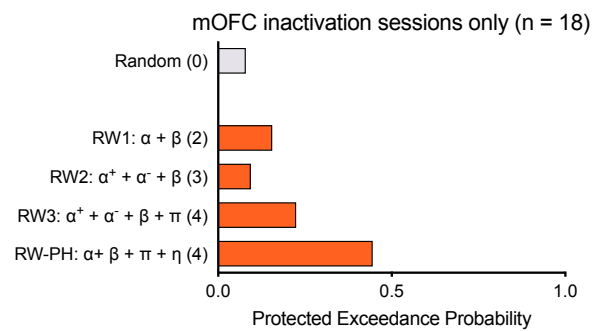
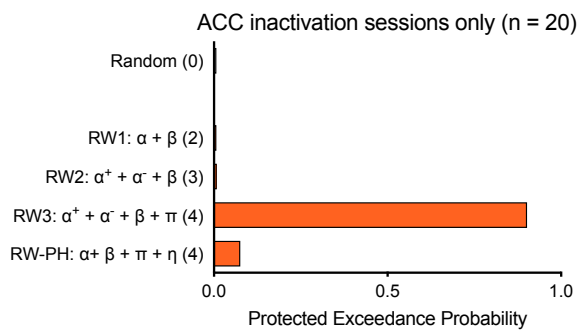
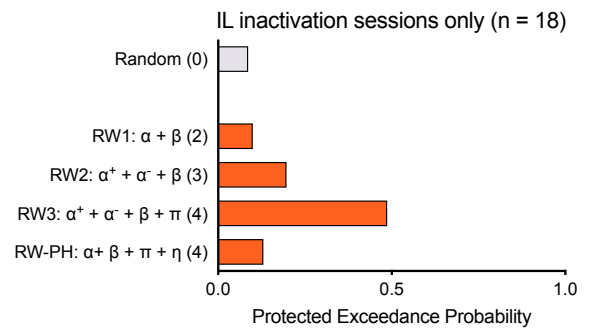
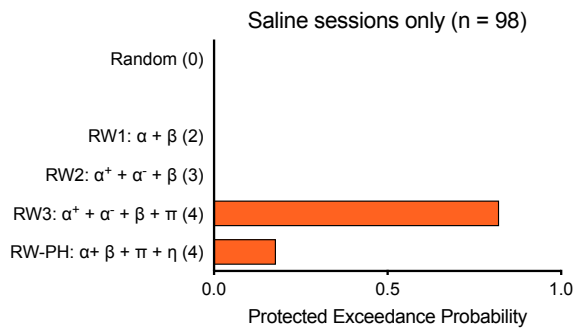
Model selection

	Model	Free parameters	Aggregate LL	$P_{\text{explained}}$	Aggregate AIC	Aggregate BIC	# of sessions best described by model	XP	PXP
1	Random	-	-32757	0.5000	65514	65514	0/196	0	0
2	Rescorla-Wagner 1	α, β	-28815	0.5435	58414	59761	40/196	0	0
3	Rescorla-Wagner 2	$\alpha+, \alpha-, \beta$	-28415	0.5481	58007	60026	25/196	0	0
4	Rescorla-Wagner 3	$\alpha+, \alpha-, \beta, \pi$	-27818	0.5551	57204	59897	74/196	0.9999	0.9999
5	Rescorla-Wagner-Pearce-Hall hybrid	α, β, π, η	-27973	0.5533	57513	60206	57/196	0.0001	0.0001

Abbreviations: LL, log-likelihood; $P_{\text{explained}}$, fraction of choices explained by the model on every single trial (total trials on average ≈ 241); AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion; XP, exceedance probability; PXP, protected exceedance probability.

Online Resource 5

Model selection per inactivation condition



Online Resource 6

Simulated data showing the number of reversals per 100 trials for different values of explore/exploit parameter β

