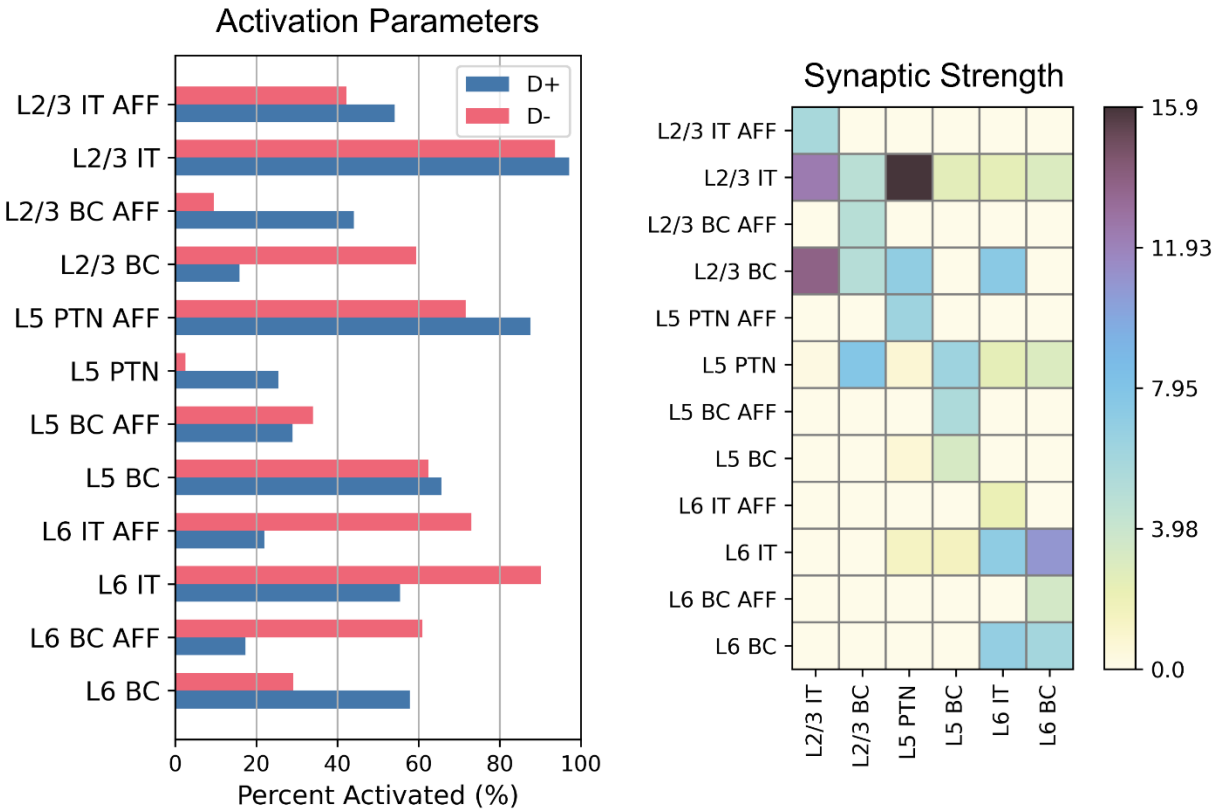


1 S1 APPENDIX

2 Fig A



3

4 **Fig A. Activation and synaptic weight scalar parameters for the unified model.**

5 *Activation parameters control the proportion of a cell population that generates an action potential in*

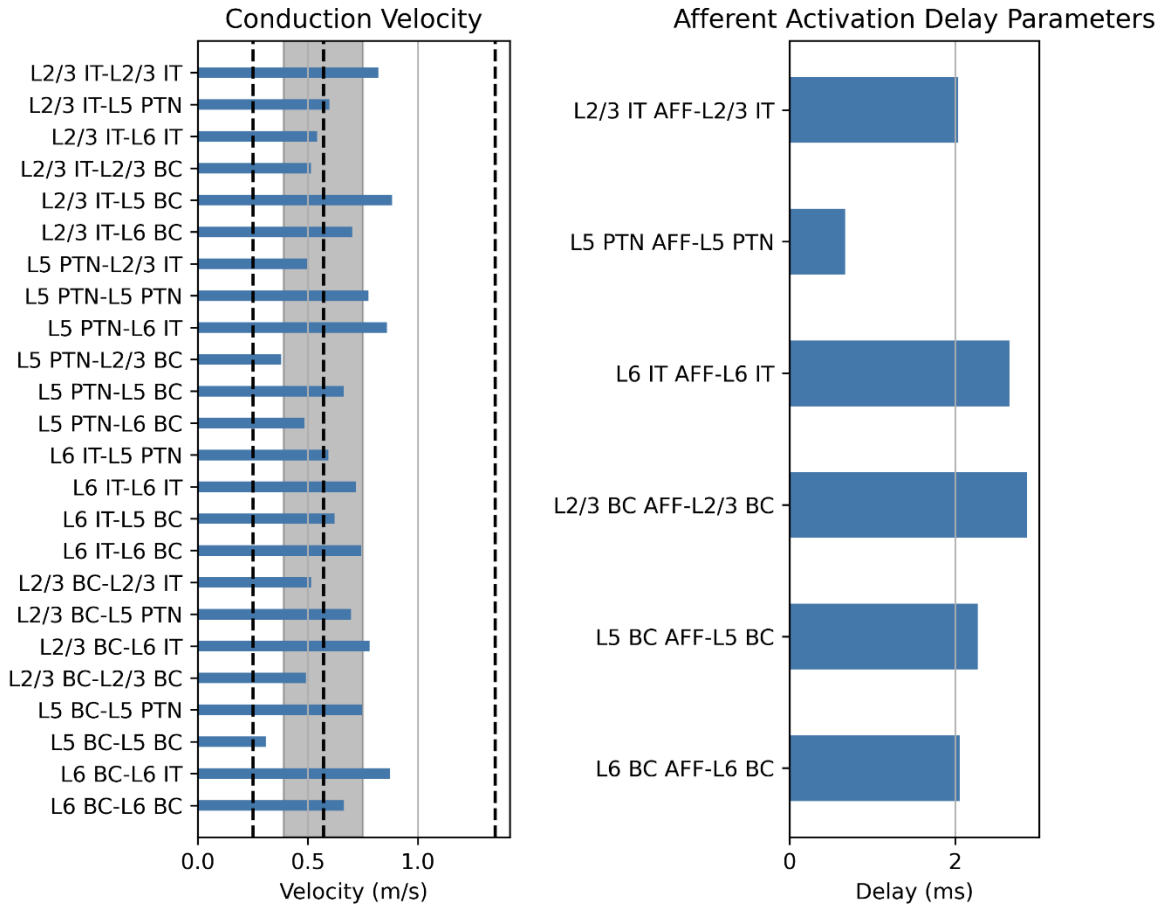
6 *response to the TMS stimulus. Synaptic strengths of the unified model are on the right. Presynaptic*

7 *neurons are arranged on the y-axis, and their maximal synaptic conductance on their postsynaptic*

8 *targets along the x-axis are coded according to the color bar. IT: Intratelencephalic neuron. PTN:*

9 *Pyramidal tract neuron. BC: Basket cell. AFF: Afferent.*

10 Fig B



11

12 **Fig B. Conduction velocities and afferent activation delays for the unified model.**

13 *IT: Intratelencephalic neuron. PTN: Pyramidal tract neuron. BC: Basket cell. AFF: Afferent.*

14

15

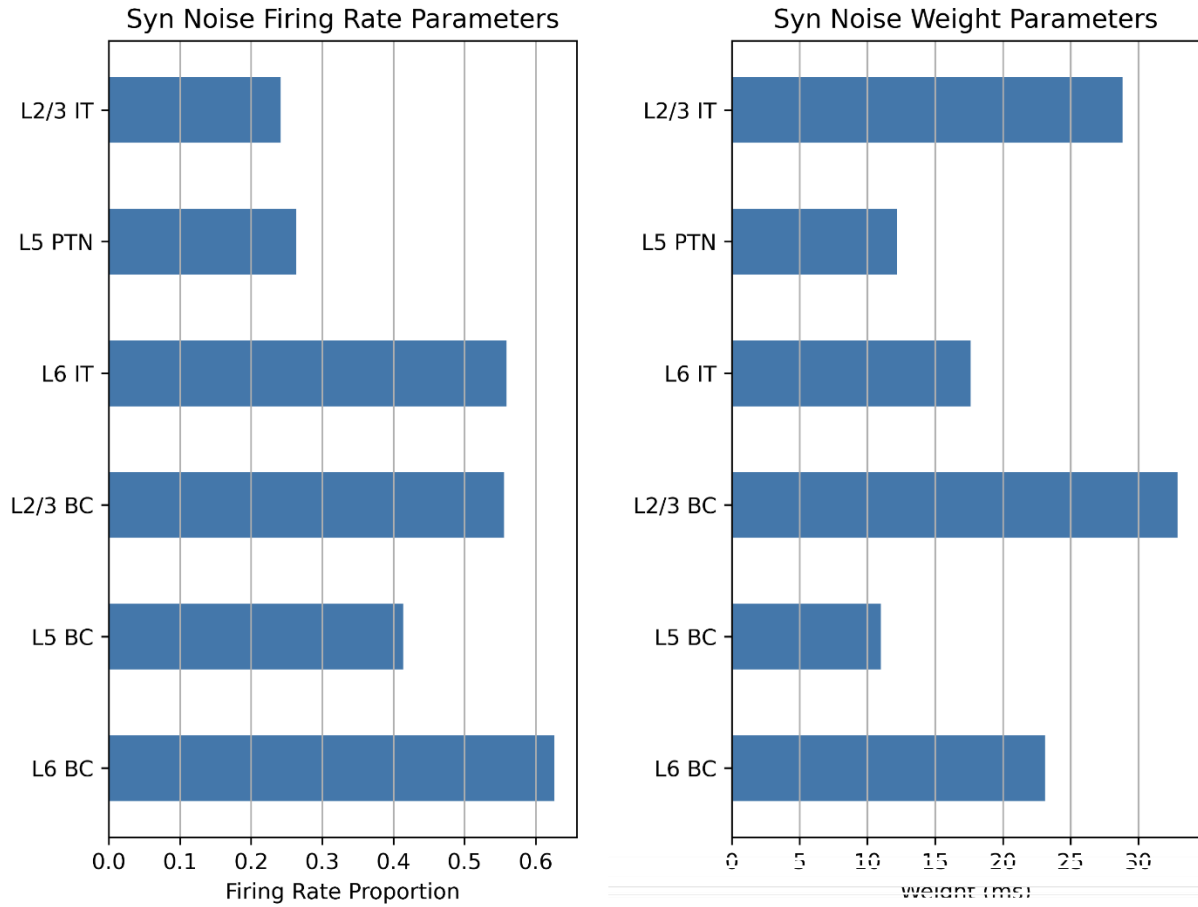
16

17

18

19 Fig C

20



21

22 **Fig C. Synaptic noise firing rates and synaptic noise weights for the unified model.**

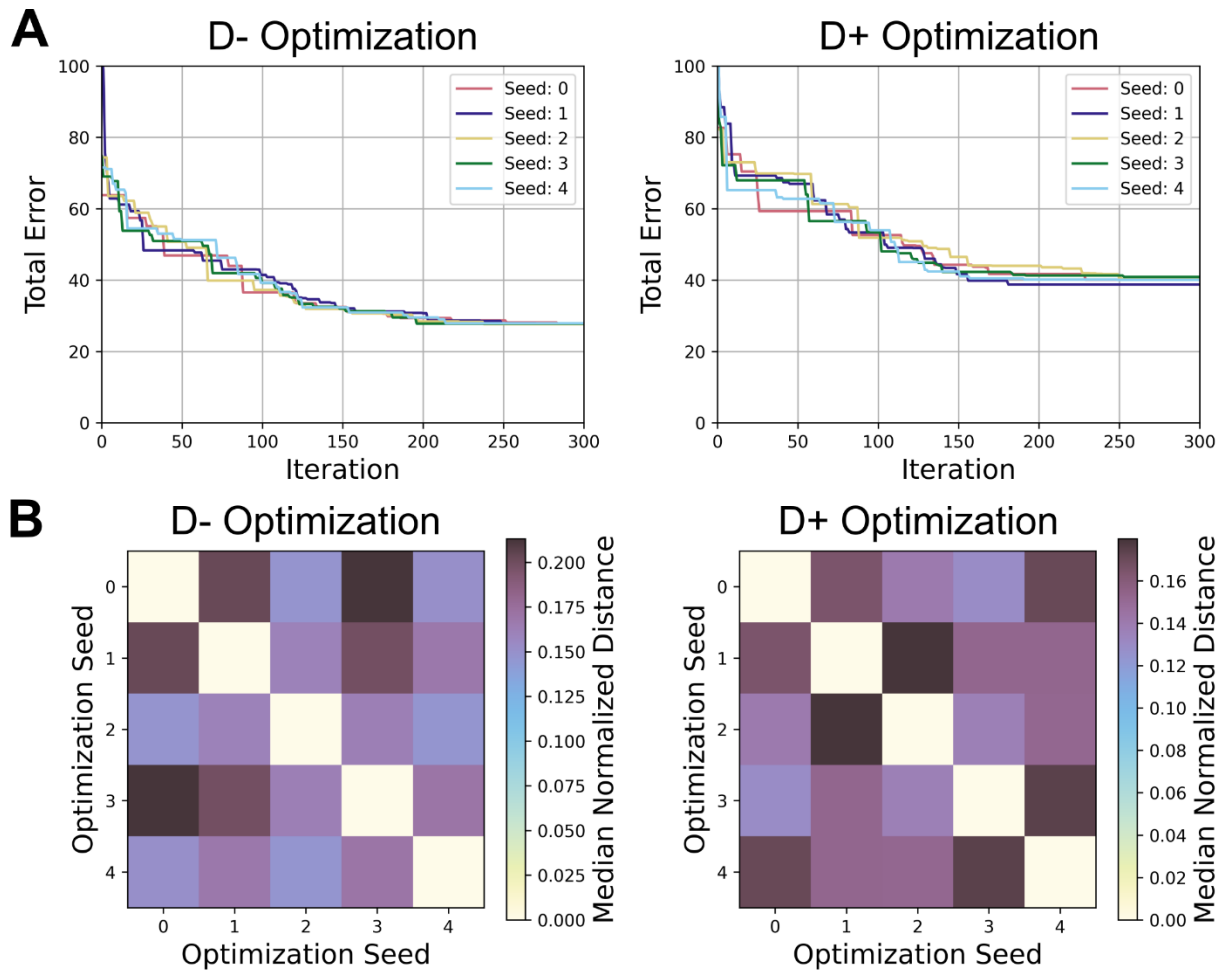
23 *IT: Intratelencephalic neuron. PTN: Pyramidal tract neuron. BC: Basket cell. AFF: Afferent.*

24

25

26

27

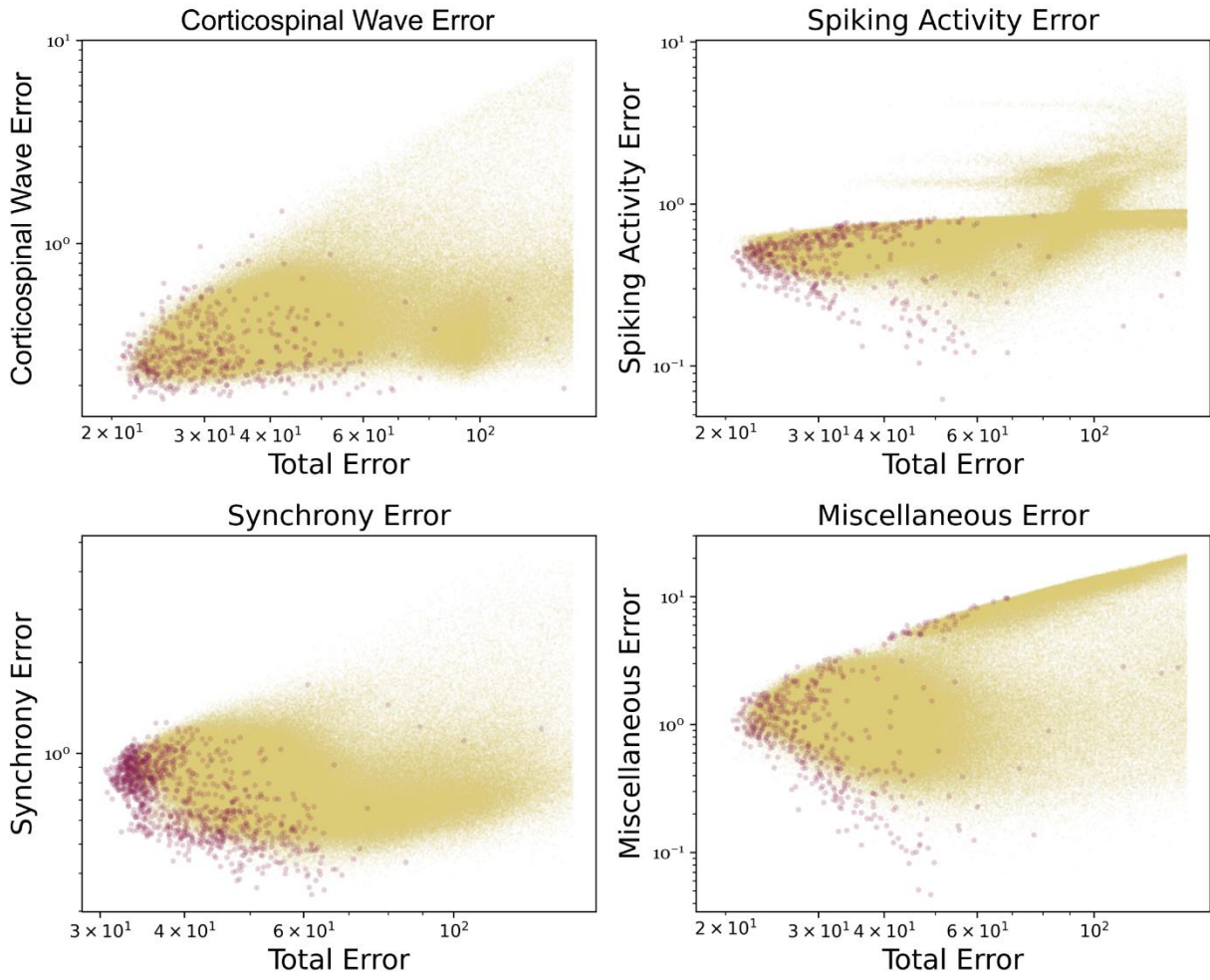


29

30 **Fig D. Characterizations of convergence from optimization.**

31 *A) The cumulative lowest total error is plotted as a function of optimization iteration. Four evolution*
 32 *seeds were run for each responder type (D+ and D-). All seeds converged to errors of similar magnitude.*

33 *B) The normalized distances of the parameters of the best solutions for each optimization run. The*
 34 *Euclidean distance of the best solutions was normalized by the maximum possible distance given the*
 35 *bounds of the explored parameter space. The diagonals of the matrix are zero because they represent*
 36 *the distance between a solution and itself. The overall normalized distances were 15.5 to 17.2% for D+*
 37 *and D-, respectively.*



39

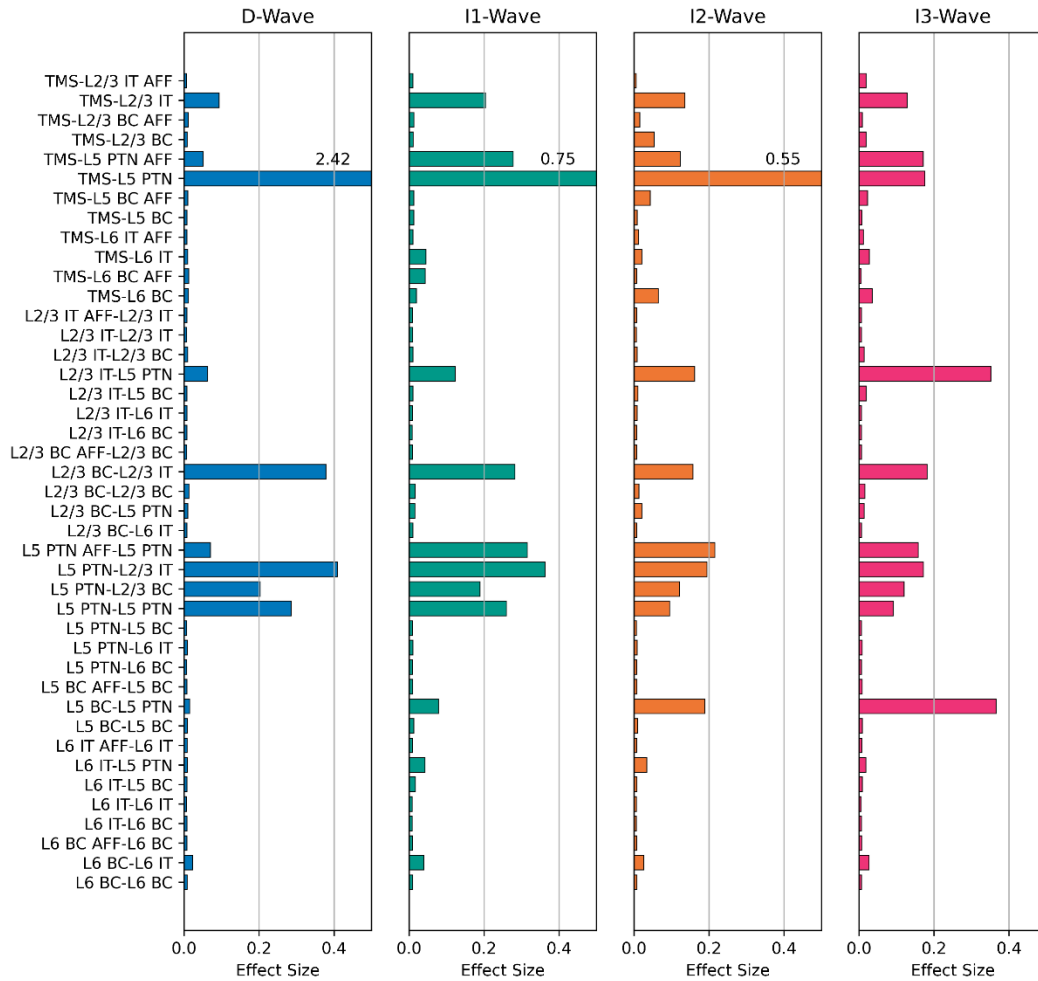
40 **Fig E. Visualization of reduced pareto front.**

41 *Objectives were grouped into categories, and their combined error was plotted against the total error.*

42 *Red dots indicate particles that were pareto dominant, and yellow particles indicate the remaining*

43 *particles. The correlation between the category error and the total error is a representation of the pareto*

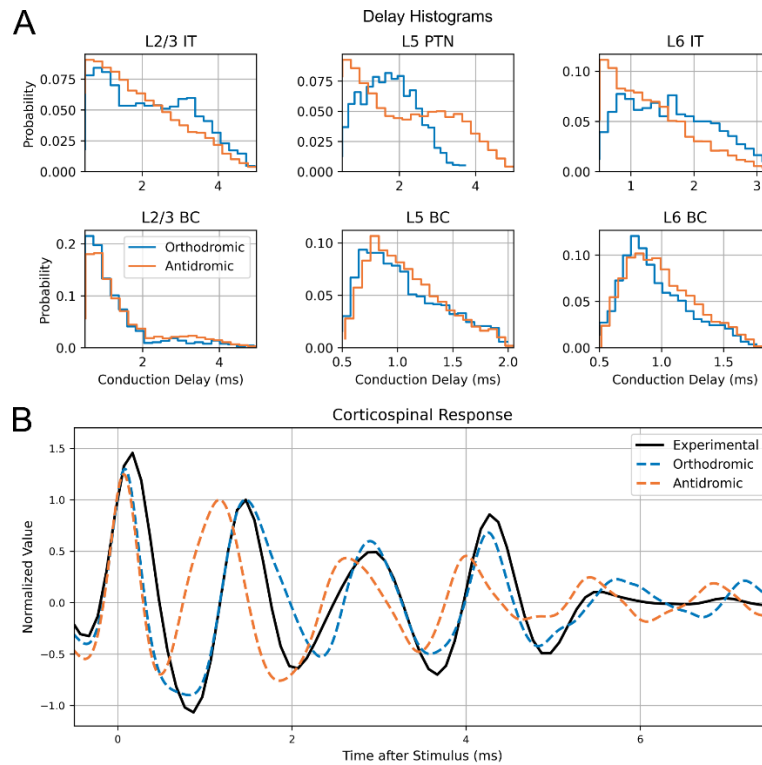
44 *front and how the category error changes as total error is minimized.*



46

47 **Fig F. Effect sizes for all parameters and all waves.**

48 *Effect size was calculated as the integrals of the absolute values of the partial derivatives of the*
 49 *polynomial fits to the TVAT surfaces. Effect sizes were not normalized, and the x-axis maximum was*
 50 *chosen to allow visualization of the smaller effect sizes. Effect sizes that are greater than the x-axis*
 51 *maximum have their values listed above their corresponding bars. Y-axis labels are shared across*
 52 *subplots. IT: Intratelencephalic neuron. PTN: Pyramidal tract neuron. BC: Basket cell. AFF: Afferent.*



54

55 **Fig G. Conduction delay histograms resulting from orthodromic and antidromic propagation of action**
 56 **potentials.**

57 Orthodromic propagation used the cell body as the initiation point to compute conduction delays.

58 Antidromic propagation randomly selected a single presynaptic terminal to be activated. The activation

59 then propagated antidromically to activate all other terminals connected to the same axon. A) The

60 resulting conduction delay histograms across all neurons of each cell type are plotted. B) The

61 corticospinal response of the optimized model with each activation type is shown. Orthodromic and

62 antidromic activation result in similar histograms except for L5 PTN and L6 IT with the orthodromic-

63 based delays exhibiting a later peak compared to antidromic-based delay. The effect on the corticospinal

64 response in the model is that the I-waves are similarly proportionally delayed and is consistent with the

65 longer latencies in the L5 PTN conduction delay histogram.

66 Table A

67 **Table A. List of Optimized Synaptic Weight Parameters**

Synaptic Weight Parameters

| | |
|--|--|
| L2/3 IT to L2/3 IT (AMPA/NMDAR) | L2/3 BC to L5 PTN (GABA _B R) |
| L2/3 IT to L5 PTN (AMPA/NMDAR) | L2/3 BC to L6 IT (GABA _A R) |
| L2/3 IT to L6 IT (AMPA/NMDAR) | L2/3 BC to L6 IT (GABA _B R) |
| L2/3 IT to L2/3 BC (AMPA/NMDAR) | L2/3 BC to L2/3 BC (GABA _A R) |
| L2/3 IT to L5 BC (AMPA/NMDAR) | L2/3 BC to L2/3 BC (GABA _B R) |
| L2/3 IT to L6 BC (AMPA/NMDAR) | L5 BC to L5 PTN (GABA _A R) |
| L5 PTN to L2/3 IT (AMPA/NMDAR) | L5 BC to L5 PTN (GABA _B R) |
| L5 PTN to L5 PTN (AMPA/NMDAR) | L5 BC to L5 BC (GABA _A R) |
| L5 PTN to L6 IT (AMPA/NMDAR) | L5 BC to L5 BC (GABA _B R) |
| L5 PTN to L2/3 BC (AMPA/NMDAR) | L6 BC to L6 IT (GABA _A R) |
| L5 PTN to L5 BC (AMPA/NMDAR) | L6 BC to L6 IT (GABA _B R) |
| L5 PTN to L6 BC (AMPA/NMDAR) | L6 BC to L6 BC (GABA _A R) |
| L6 IT to L5 PTN (AMPA/NMDAR) | L6 BC to L6 BC (GABA _B R) |
| L6 IT to L6 IT (AMPA/NMDAR) | L2/3 IT AFF to L2/3 IT (AMPA/NMDAR) |
| L6 IT to L5 BC (AMPA/NMDAR) | L2/3 BC AFF to L2/3 BC (AMPA/NMDAR) |
| L6 IT to L6 BC (AMPA/NMDAR) | L5 PTN AFF to L5 PTN (AMPA/NMDAR) |
| L2/3 BC to L2/3 IT (GABA _A R) | L5 BC AFF to L5 BC (AMPA/NMDAR) |
| L2/3 BC to L2/3 IT (GABA _B R) | L6 IT AFF to L6 IT (AMPA/NMDAR) |
| L2/3 BC to L5 PTN (GABA _A R) | L6 BC AFF to L6 BC (AMPA/NMDAR) |

68

69 *IT: Intratelencephalic neuron. PTN: Pyramidal tract neuron. BC: Basket cell. AFF: Afferent.*

70

71

72

73 Table B

74 **Table B. List of Optimized Delay, Activation, and Noise Parameters**

Parameters

| | |
|---|---|
| Conduction velocity scalar L2/3 IT to L2/3 IT | Activation propagation delay stdev. L2/3 IT AFF |
| Conduction velocity scalar L2/3 IT to L5 PTN | Activation propagation delay stdev. L2/3 BC AFF |
| Conduction velocity scalar L2/3 IT to L6 IT | Activation propagation delay stdev. L5 PTN AFF |
| Conduction velocity scalar L2/3 IT to L2/3 BC | Activation propagation delay stdev. L5 BC AFF |
| Conduction velocity scalar L2/3 IT to L5 BC | Activation propagation delay stdev. L6 IT AFF |
| Conduction velocity scalar L2/3 IT to L6 BC | Activation propagation delay stdev. L6 BC AFF |
| Conduction velocity scalar L5 PTN to L2/3 IT | Proportion activated L2/3 IT |
| Conduction velocity scalar L5 PTN to L5 PTN | Proportion activated L2/3 BC |
| Conduction velocity scalar L5 PTN to L6 IT | Proportion activated L5 PTN |
| Conduction velocity scalar L5 PTN to L2/3 BC | Proportion activated L5 BC |
| Conduction velocity scalar L5 PTN to L5 BC | Proportion activated L6 IT |
| Conduction velocity scalar L5 PTN to L6 BC | Proportion activated L6 BC |
| Conduction velocity scalar L6 IT to L5 PTN | Proportion activated L2/3 IT AFF |
| Conduction velocity scalar L6 IT to L6 IT | Proportion activated L2/3 BC AFF |
| Conduction velocity scalar L6 IT to L5 BC | Proportion activated L5 PTN AFF |
| Conduction velocity scalar L6 IT to L6 BC | Proportion activated L5 BC AFF |
| Conduction velocity scalar L2/3 BC to L2/3 IT | Proportion activated L6 IT AFF |
| Conduction velocity scalar L2/3 BC to L5 PTN | Proportion activated L6 BC AFF |
| Conduction velocity scalar L2/3 BC to L6 IT | Noise weight L2/3 IT |
| Conduction velocity scalar L2/3 BC to L2/3 BC | Noise weight L2/3 BC |
| Conduction velocity scalar L5 BC to L5 PTN | Noise weight L5 PTN |
| Conduction velocity scalar L5 BC to L5 BC | Noise weight L5 BC |
| Conduction velocity scalar L6 BC to L6 IT | Noise weight L6 IT |

| | |
|---|--------------------|
| Conduction velocity scalar L6 BC to L6 BC | Noise weight L6 BC |
| Activation propagation delay L2/3 IT AFF | Noise rate L2/3 IT |
| Activation propagation delay mean L2/3 BC AFF | Noise rate L2/3 BC |
| Activation propagation delay mean L5 PTN AFF | Noise rate L5 PTN |
| Activation propagation delay mean L5 BC AFF | Noise rate L5 BC |
| Activation propagation delay mean L6 IT AFF | Noise rate L6 IT |
| Activation propagation delay mean L6 BC AFF | Noise rate L6 BC |

75

76 *IT: Intratelencephalic neuron. PTN: Pyramidal tract neuron. BC: Basket cell. AFF: Afferent.*

77

78

79