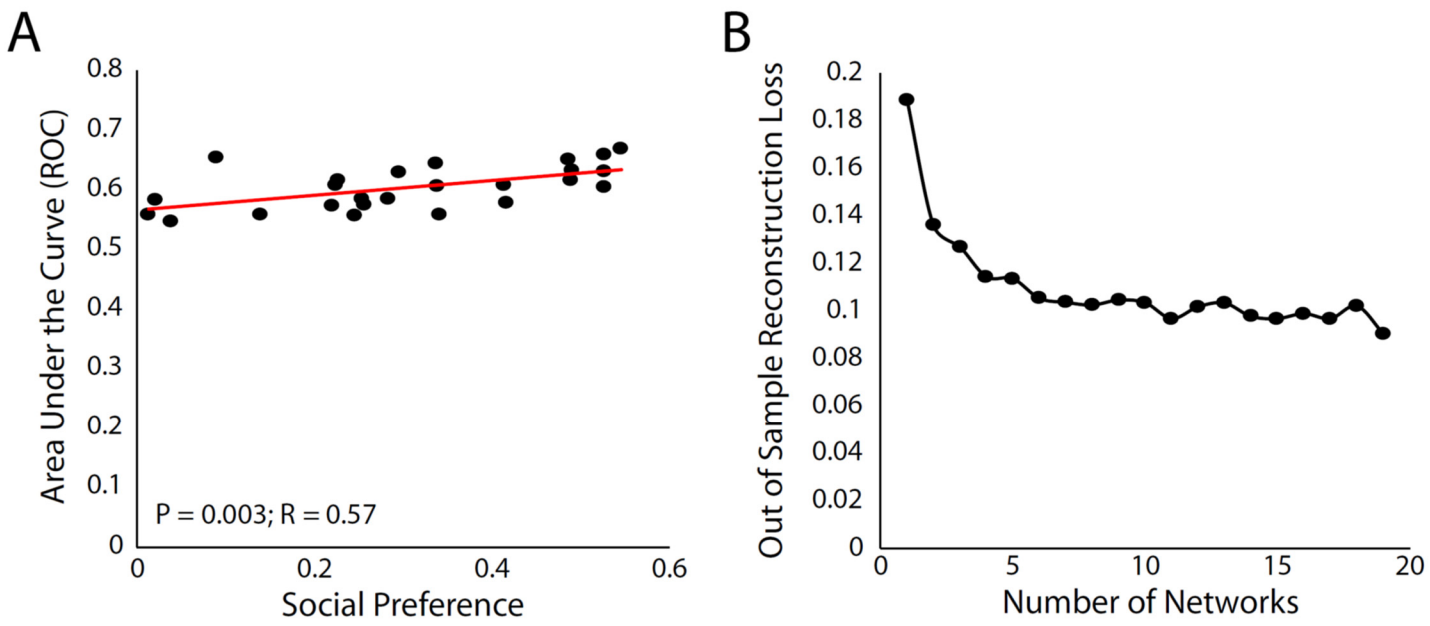
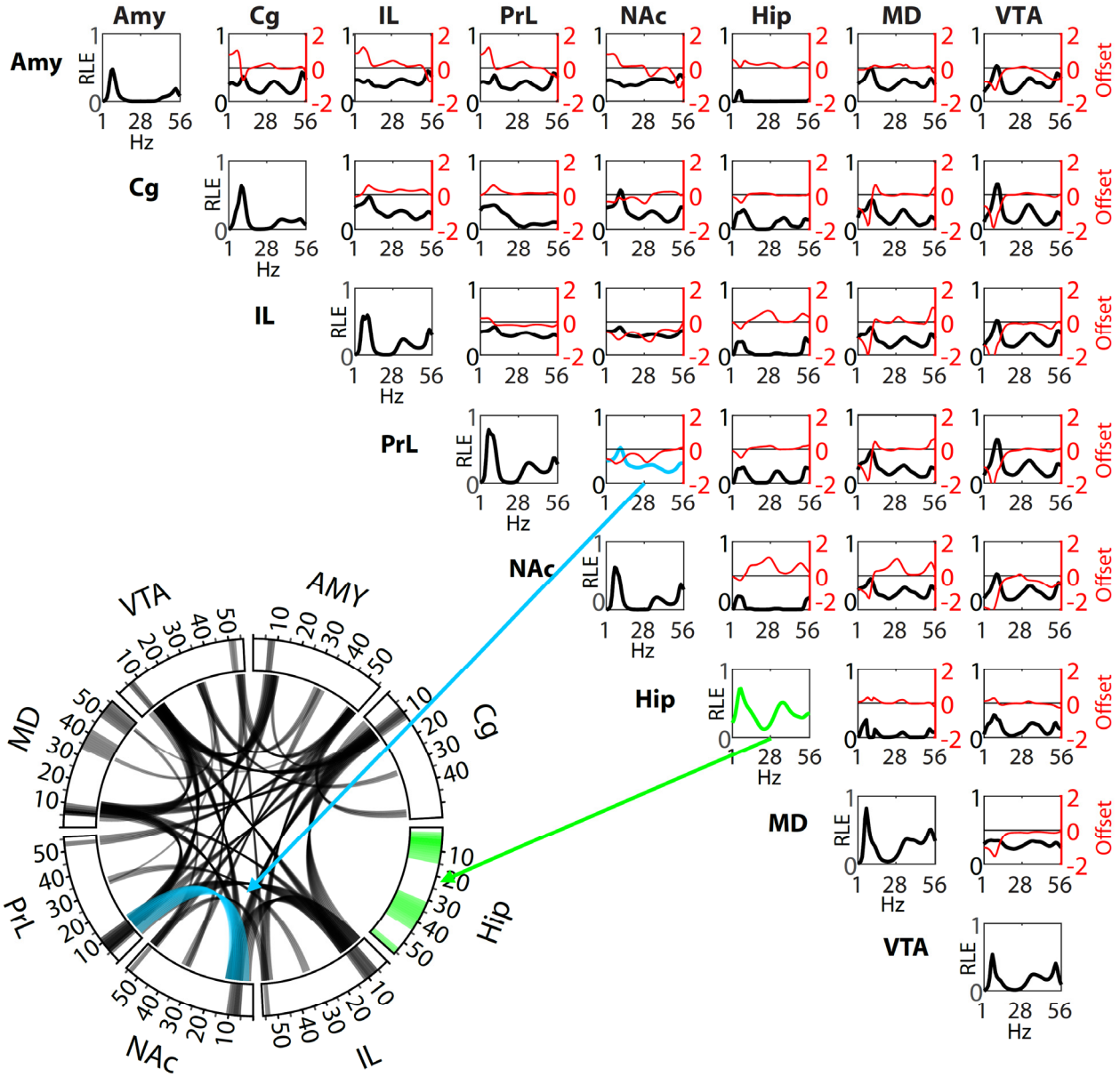
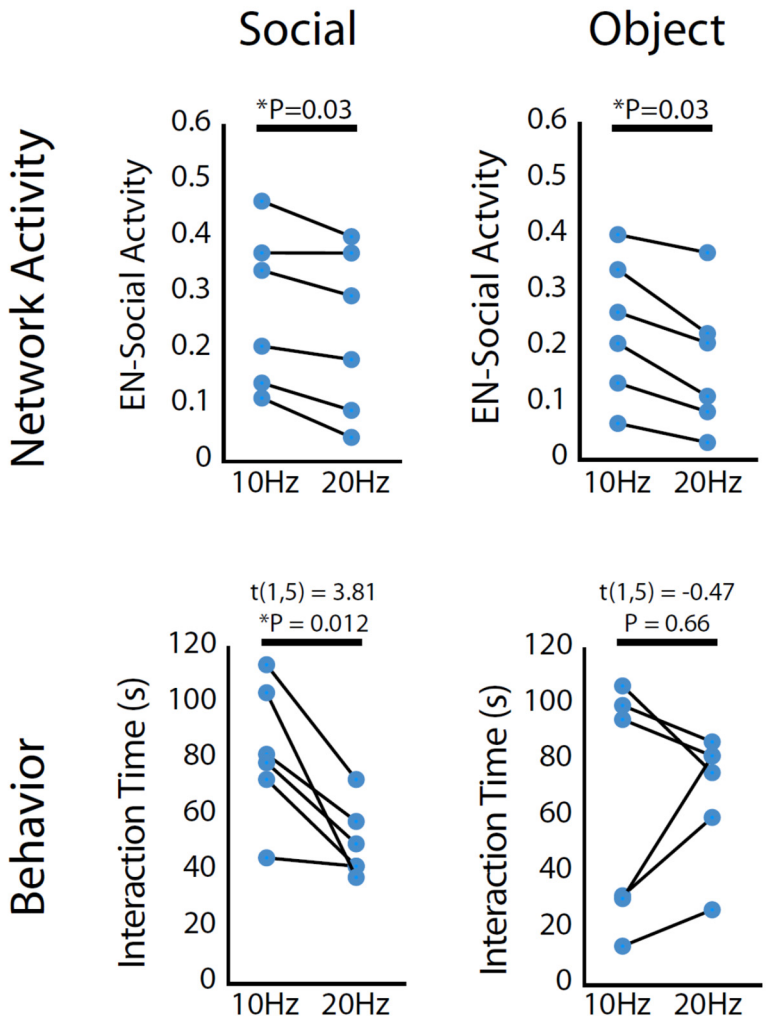
Supplemental Figures



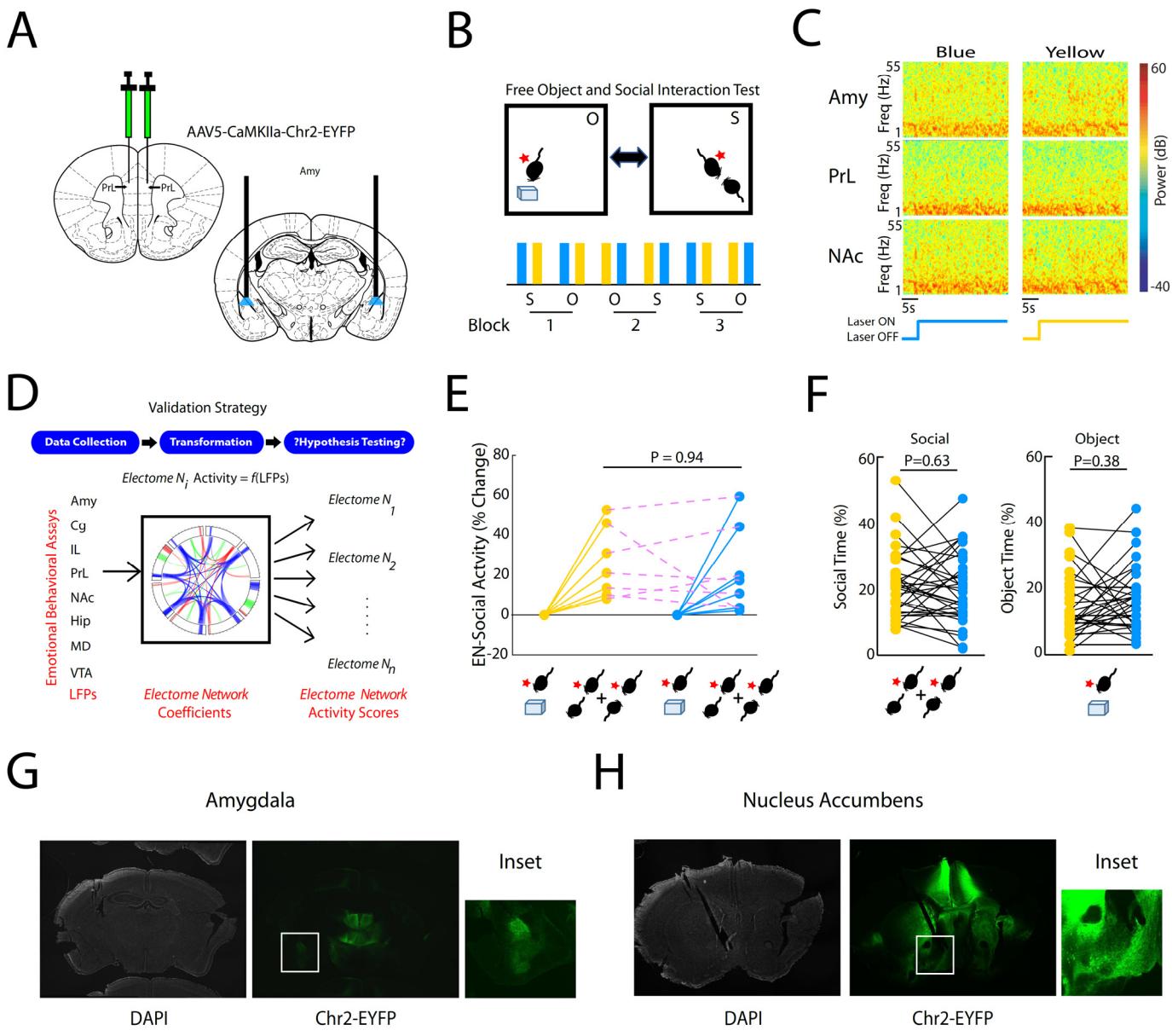
Supplemental Figure S1: Selection of model features, related to Fig. 1. A) We initially trained an unsupervised PCA model using power and synchrony measures across the implanted areas for each animal. We used 70% of the social and object timepoints for model training, and the remaining 30% of the data was used for hold-out testing. Since the area under the curve of the receiver operating characteristic for each animal was correlated with their social preference, we weighed individual mice within our subsequent dCSFA-NMF Electome model based on this behavioral measure. Thus, in addition to encoding the difference between social and object interactions, this approach also encouraged dCSFA-NMF to learn a network that also jointly encoded social preference. **B)** We calculated the out-of-subject reconstruction loss using the initial dCSFA-NMF model vs. the numbers of trained networks. Gains in the reconstruction loss diminished with >6 networks.



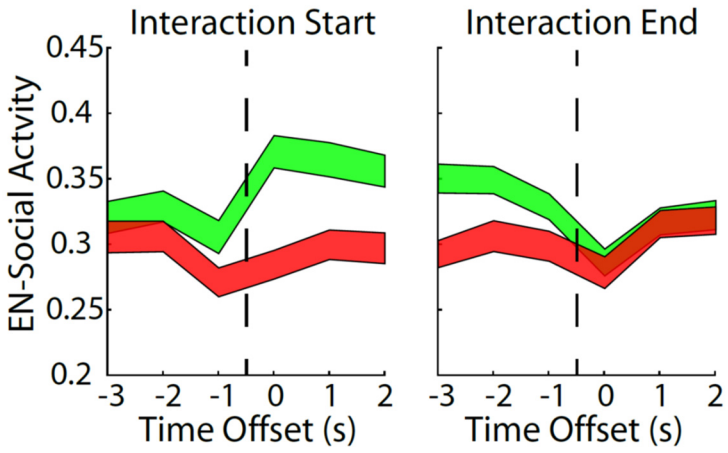
Supplemental Figure S2: Power and synchrony measures that define the Social-*Electome* Network, related to Fig. 2 and 4. Brain areas are shown to the top and the left identifying power and synchrony density functions for *Electome Factor* 1. Amplitude values (shown in black) reflect the relative LFP spectral energy (RLE) observed at each frequency, where the *Electome Factor* is normalized to the total energy observed across the 6 networks. The offset between the two non-normalized granger synchrony functions for each brain area pair (A→B and B→A) are also shown in red (i.e. directionality; axis scale to the right). Positive spectral offsets correspond to frequencies at which the area listed along the top leads the area listed on the left. Negative spectral offsets correspond to the frequencies at which the area listed on the left leads the area listed on the top. The circular plot depicts the frequencies for power (outer rim) and synchrony (curved lines connecting two regions) above an amplitude threshold of 0.33. As a representative example, the power measures for ventral hippocampus (Hip) are highlighted in bright green in both the circular and correlation plots; synchrony between prelimbic cortex (PrL) and nucleus accumbens (NAc) are highlighted in cyan.



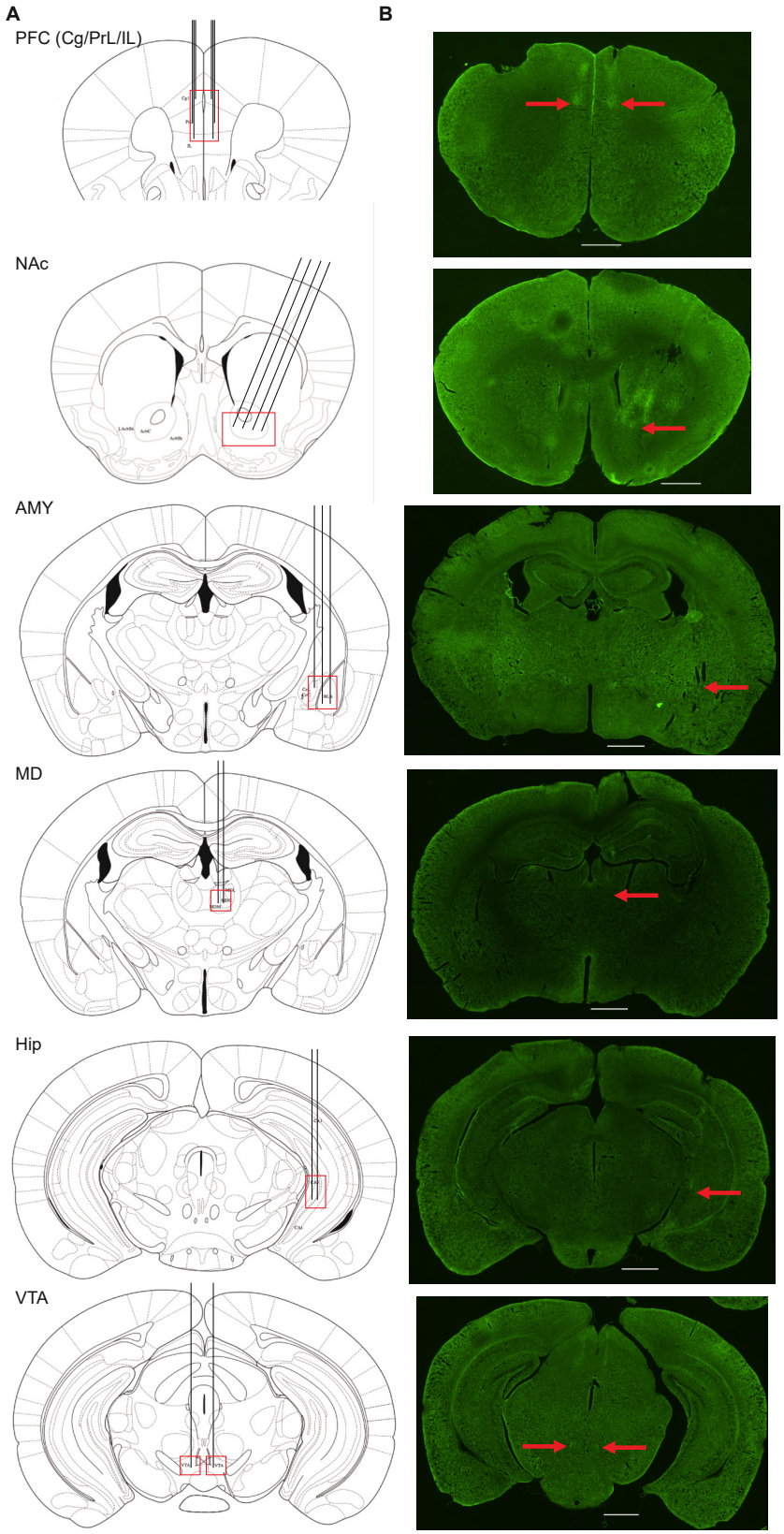
Supplemental Figure S3: Frequency specific effects of prefrontal cortex to nucleus accumbens circuit element casual activation, related to Fig. 7. Network activity observed during social and object interactions in response to 10Hz vs. 20Hz PrL→NAc Stimulation (top). Behavior observed during social and object interactions in response to 10Hz vs. 20Hz PrL→NAc Stimulation (bottom).



Supplemental Figure S4: Causal activation of the prefrontal cortex to amygdala circuit element does not enhance *EN-Social* activity, related to Fig. 7. A) Targeting strategy used to activate Prelimbic cortex terminals in amygdala. **B)** Experimental paradigm for FOSIT. **C)** Power spectral plots show representative spectral patterns from a mouse during blue (left) and yellow (right) light stimulation trials included in analysis. **D)** Strategy used for *EN-Social* validation. **E)** *EN-Social* activity during blue light stimulation. Network activity was pooled across periods of social interaction by the subject mice and compared between the blue and yellow light stimulation periods. **F)** Social (left; P>0.05) and object interaction time (right; P>0.05) during blue and yellow light stimulation.



Supplemental Figure S5: Event-related activity of *EN-Social*, related to Fig. 1 and 2. As part of our strategy outlined in Fig. 5A, twenty-eight new healthy mice were implanted with recording electrodes, and neural data was acquired during the social preference test (10 sessions). We then projected LFP data into the Social-*Electome* network model learned from the initial training animals. Note that the same behaviorally relevant network dynamics are observed in these hold-out mice (compare to Fig. 2B). Data shown as mean±s.e.m.



Supplemental Figure S6: Electrode targeting strategy and histological confirmation, related to Fig. 1 and 2. A) Electrode bundles were centered within the red boxes shown for each target brain area. **B)** Representative histological images are shown with red arrows highlighting electrode tracks.

Supplemental Table S1: Extended Author Contributions, related to STAR Methods

Stephen D. Mague	Jointly conceived two-chamber social interaction experiment; jointly built electrodes; jointly performed electrode implantations in C57BL/6J mice for two-chamber social interaction experiment with KD; jointly performed electrode implantations for sucrose drinking and elevated plus maze experiments with CB; jointly analyzed behavioral data for two-chamber social interaction experiments and performed neurophysiological data processing for all experiments presented in the paper with CB, EA, NN, and KKW; jointly conceived FOSIT experiment with KD and AT; jointly conceived and performed optogenetic stimulation experiments with KD and KKW; jointly performed histological confirmations for all experiments with LJD, GET, EA, NN CB, and KKW; jointly supervised all data collection and wrote the paper with DEC and KD.
Austin Talbot	Developed and implemented the CSFA-NMF machine learning analyses utilized for all neurophysiological analysis in the paper including the model discovery and projections of new neurophysiological data into the initial model space; edited the paper.
Cameron Blount	Built electrodes for C57BL/6J mice two-chamber social interaction test, FOSIT, EPM and ANK2 experiments. Jointly implanted mice for EPM experiment; jointly collected data for C57BL/6J mice two-chamber social interaction test experiment with LJD and NN; Collected data for FOSIT in C57BL/6J mice; jointly collected data for ANK2 experiments with KKW and ALB; jointly analyzed behavioral data for two-chamber social interaction experiments and performed neurophysiological data processing for all experiments presented in the paper with SDM, EA, NN, and KKW; jointly performed histological confirmations for all experiments with LJD, SDM, GET, EA, NN, and KKW.
Kathryn K. Walder-Christensen	Jointly collected data for ANK2 experiments with CB and ALB; jointly conceived and performed optogenetic stimulation experiments with KD and SDM; jointly performed histological confirmations for all experiments with LJD, SDM, GET, EA, NN, and CB; edited the paper.
Lara J. Duffney	Jointly collected data from C57BL/6J mice for two-chamber social preference experiment with CB and NN; jointly performed histological confirmations for all experiments with EA, GET, NN, CB, and KKW; jointly conceived of two-chamber social preference experiment for C57BL/6J mice with KD.

Elise Adamson	*Jointly performed behavioral and neurophysiological data processing for two chamber experiments in* C57BL/6J *with* SDM, *CB,* NN, and KKW; Conceived, collected data, and performed neurophysiological data processing for sucrose drinking experiment; jointly performed histological confirmations for all experiments with LJD, SDM, GET, NN, CB, and KKW; edited the paper.
Alexandra L. Bey	Performed all behavioral analysis for FOSIT experiment; jointly collected data for ANK2 experiments with KKW and CB; edited the paper.
Nkemdilim Ndubuizu	Jointly collected data from C57BL/6J mice for two-chamber social preference experiment with CB and LJD; jointly analyzed behavioral data for two-chamber social interaction experiments and performed neurophysiological data processing for all experiments presented in the paper with CB, EA, SDM, and KKW; jointly performed histological confirmations for all experiments with LJD, SDM, GET, EA, CB, and KKW.
Gwenaëlle E. Thomas	Jointly performed histological confirmations for all experiments with SDM, LJD, EA, NN CB, and KKW; edited the paper.
Dalton Hughes	Conceived, collected data, and performed neurophysiological data processing for elevated plus maze experiment.
Yael Grossman	Jointly collected data and performed neurophysiological data processing for chronic social defeat stress experiment with RH.
Rainbo Hultman	Jointly collected data and performed neurophysiological data processing for chronic social defeat stress experiment with YG.
Saurabh Sinha	Analyzed LFP data from ANK2 mice for seizure activity.
Alexandra M. Fink	Contributed to preprocessing of data for Spike-*Electome Factor* analysis.
Neil M. Gallagher	Implemented granger features for data processing; jointly contributed to data preprocessing for elevated plus maze and sucrose consumption tasks.
Rachel L. Fisher	Jointly built electrodes for ANK2 experiments; Built all optoelectrodes for optogenetics studies; Contributed to histological confirmations ANK2 experiments.
Yong-hui Jiang	Jointly supervised LD with KD.

David E. Carlson	Supervised development of all aspects of CSFA-NMF machine learning analyses and data processing methodology; wrote the paper with SDM and KD.
Kafui Dzirasa	Jointly conceived of experiments with LJD, AT, KKW, DH, EA, SDM, DEC; jointly performed surgical implantations for all experiments with SDM and CB; jointly performed optogenetic experiments with SDM and KKW; jointly analyzed neurophysiological data with AT; supervised all behavioral and neurophysiological experiments with SDM; wrote the paper with SDM and DEC.