

Supplementary Data 1: Results of CPB test on MERFISH U2OS data at $d=4\mu$. We detected 304 gene pairs at CPB FPR < 2% (CPB p-value < $1e-4$). Table also contains colocalized cells i.e. cells in which the gene pair was detected proximal pair (PP p-value < $1e-3$). The primary category denotes the category with the highest number of proximal pairs across all cells (Methods).

Supplementary Data 2: Results of CPB test for top 304 pairs on MERFISH U2OS data at $d=1\mu$ (FPR < 20%, CPB p-value < 0.015). Top 304 pairs were chosen to match the size of d-colocalized pairs at $d=4\mu$.

Supplementary Data 3: Results of overlap of the set of d-colocalized gene pairs with co-expressed gene pairs. Co-expressed gene pairs are identified based on Pearson correlation of whole-cell transcript counts, and the top 304 pairs are taken to match the size of the d-colocalization map.

Supplementary Data 4: Results of overlap of the set of d-colocalized gene pairs with gene pairs having RRI score > 35.

Supplementary Data 5: Results of top 108 gene pairs from CPB test (FPR = 0%, CPB p-value < $1e-10$) on Seqfish NIH/3T3 cell line at $d=2\mu$.

Supplementary Data 6: Results of differential colocalization (both category 1 and category 2) on MERFISH mouse brain hypothalamus data. p_{uncond} denotes the p-value of hypergeometric test on the set of colocalized pairs and set of cells of one type. One vs all test was performed on each cell type independently. A threshold of $5e-6$ was used for p_{uncond} (Bonferroni corrected p-value = 0.05). p_{cond_g1} and p_{cond_g2} denotes the conditional p-value denoting if the cell type specificity arises simply because one of the genes in the pair is expressed specifically in that cell type (Methods). Furthermore, a hypergeometric test is performed on the set of colocalized cells and cells with higher gene expression. p-value obtained from such test was used in ranking to obtain gene markers (top 10 genes). min_rank1 denotes the minimum rank of either of the gene.

Supplementary Data 7: Results of differential colocalization of category 2 gene pairs on MERFISH mouse brain hypothalamus data.

Supplementary Data 8: Results of differential colocalization of category 2 gene pairs on aggression vs naïve mouse hypothalamus data (Methods).

Supplementary Data 9: Results of differential colocalization of category 2 gene pairs on three regions of mouse brain Xenium data (Methods).

Supplementary Data 10: Results of spatial modulation on mouse brain data (LLR>17). *i_s_ct_specific* is 1 if there is significant overlap between the set of colocalized cells and cells of any type.