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# Interacting neural ensembles in orbitofrontal cortex for social and feeding behaviour

Joshua H. Jennings<sup>1,6</sup>, Christina K. Kim<sup>2,6</sup>, James H. Marshel<sup>1,6</sup>, Misha Raffiee<sup>1</sup>, Li Ye<sup>3,4</sup>, Sean Quirin<sup>1</sup>, Sally Pak<sup>1</sup>, Charu Ramakrishnan<sup>1</sup> & Karl Deisseroth<sup>1,2,3,4,5\*</sup>

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<sup>1</sup>Department of Bioengineering, Stanford University, Stanford, CA, USA. <sup>2</sup>Neurosciences Program, Stanford University, Stanford, CA, USA. <sup>3</sup>Department of Psychiatry and Behavioral Sciences, Stanford University, Stanford, CA, USA. <sup>4</sup>Howard Hughes Medical Institute, Stanford, CA, USA. <sup>5</sup>CNC Program, Stanford University, Stanford, CA, USA. <sup>6</sup>These authors contributed equally: Joshua H. Jennings, Christina K. Kim, James H. Marshel. \*e-mail: [deissero@stanford.edu](mailto:deissero@stanford.edu)

### Supplementary Note 1.

To probe local subnetwork activation during stimulation of activity-defined cellular ensembles, we individually targeted members of each cell class (feeding or social) with optogenetic spiral stimulation in the absence of behavioral stimuli. We classified cell class by recording neural activity during subsequent feeding and social behavioral sessions, prior to the stimulation session (**Methods**).

During feeding-cell stimulation, we identified neurons that were either indirectly inhibited or excited (e.g. not directly targeted by 2-photon stimulation; **Extended Data Fig. 10a-c**). Many of these cells were characterized as non-social and non-feeding responsive (NSNF) during the previous behavioral imaging sessions, based on individual-cell statistics. However, when re-examined as a population grouped as those indirectly excited by optogenetic feeding cell stimulation, these were also found to be significantly excited during naturalistic caloric consumption. Likewise NSNF neurons that were inhibited by feeding cell stimulation were also inhibited during the baseline feeding session as well (**Extended Data Fig. 10d-f**;  $n = 97$  excited NSNF cells,  $n = 95$  inhibited NSNF cells from 9 mice; excited cells mean  $dF/F$  response =  $0.012 \pm 0.0042$  (s.e.m.), inhibited cells mean  $dF/F$  response =  $-0.014 \pm -0.0061$  (s.e.m.)), providing evidence that the network effects observed during precise feeding cell stimulation are also naturalistically recruited, and thus may bear physiological relevance to behavior.

Within the same animals, we also performed optogenetic stimulation of similar numbers of social cells, and again observed both indirectly excited and inhibited non-targeted cells (**Extended Data Fig. 10g-i**). We found that social cells in OFC exhibit a preferential potency for inhibiting the feeding subnetwork; selective stimulation of social cells inhibited a greater fraction of feeding neurons than did feeding cell stimulation (**Extended Data Fig. 10j**; social cell stim mean = 3 indirectly inhibited feeding cells  $\pm 1$  s.e.m., mean = 11 total indirectly inhibited cells  $\pm 4$  s.e.m.,  $n = 6$  mice; feeding cell stim mean = 0.8 indirectly inhibited feeding cells  $\pm 0.5$  s.e.m., mean = 12 total indirectly inhibited cells  $\pm 2$  s.e.m.,  $n = 9$  mice, Mann-Whitney  $U = 4.50$ ,  $P = 0.01$ ). This influence could be overcome, however; the magnitude of feeding cell inhibition from social cell stimulation was significantly greater during the first stimulation trial compared to subsequent trials (**Extended Data Fig. 10k-l**; 10 stim-targeted social cells per animal,  $n = 16$  indirectly inhibited

feeding cells from 6 mice;  $P = 0.04$ , Wilcoxon signed-rank test). Conversely, this property of decaying influence (seen for the social  $\rightarrow$  feeding subnetwork interaction) was not seen (rather, the opposite) in neuronal populations that did not exhibit significant responses to social stimuli (non-social responsive (NS) cells), as the magnitude of feeding cell inhibition during the first trial of NS cell stimulation was significantly less than subsequent trials (**Extended Data Fig. 10m-n**; 10 stim-targeted NS cells per mouse,  $n = 24$  indirectly inhibited feeding cells from 9 mice,  $P = 0.04$ , Wilcoxon signed-rank test).