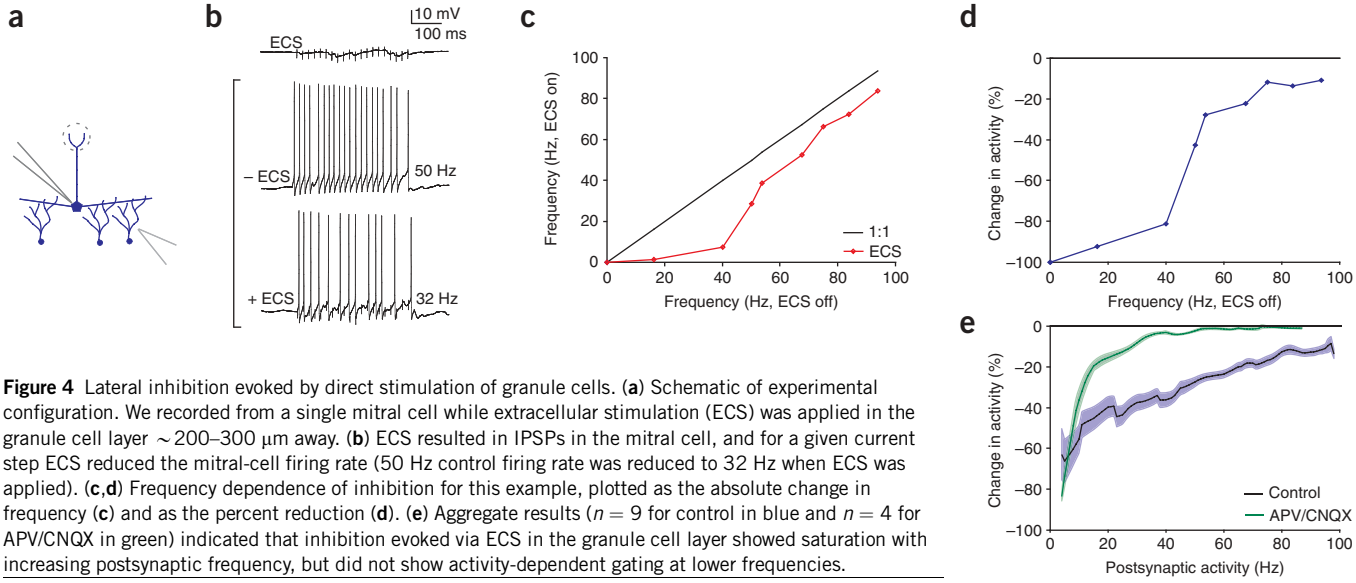

Figure 4 Lateral inhibition evoked by direct stimulation of granule cells. (**a**) Schematic of experimental configuration. We recorded from a single mitral cell while extracellular stimulation (ECS) was applied in the granule cell layer ~200–300 μm away. (**b**) ECS resulted in IPSPs in the mitral cell, and for a given current step ECS reduced the mitral-cell firing rate (50 Hz control firing rate was reduced to 32 Hz when ECS was applied). (**c**,**d**) Frequency dependence of inhibition for this example, plotted as the absolute change in frequency (**c**) and as the percent reduction (**d**). (**e**) Aggregate results ($n = 9$ for control in blue and $n = 4$ for APV/CNQX in green) indicated that inhibition evoked via ECS in the granule cell layer showed saturation with increasing postsynaptic frequency, but did not show activity-dependent gating at lower frequencies.

experiments (compare **Figs. 2d** and **6a**), and that the connectivity in the model was all-to-all, and thus had no spatial structure. Using this model, we tested whether such circuits would be sufficient to enhance contrast between similar stimuli and to decorrelate activity across populations of mitral cells responding to similar odors, similar to what has been observed *in vivo*[3]. The firing rate at which the strength of lateral inhibition was maximal was chosen to be approximately the mean activity in the network. Olfactory receptor–neuron activity was simulated by randomly assigning activity values to 60 points in a 25 × 25 array and convolving the map with a circular Gaussian function (s.d. of two pixels). After processing by activity-dependent lateral inhibition, the output of the network (analogous to mitral cell activity) showed increased contrast as compared with the initial input (**Fig. 6b**). In some examples, we tested whether spatial patterning was important by randomizing the positions of all pixels before running the simulation and then unrandomizing after the network had reached steady state (see **Supplementary Fig. 3** online). This randomization had no effect on the processing of the model, as would be expected given the all-to-all connectivity in the model.

We next examined the effect of dynamic lateral inhibition on simulated patterns of olfactory receptor–neuron inputs with varying degrees of similarity. We generated 16 input maps with varying degrees of correlation (**Fig. 6c**, see Methods). If activity-dependent lateral inhibition functions to increase the discriminability of similar odors, we should observe a decrease in correlation between initially similar responses, similar to that observed *in vivo*[3]. As predicted, applying this activity-dependent lateral inhibition to each map decreased the correlation between initially similar patterns of simulated odor-evoked activity. This change was evident in the cross-correlation matrices (compare left and right panels in **Fig. 6c**) and by computing the average level of pair-wise correlations of input and output (**Fig. 6d**,**e**). Models in which the strength of inhibition was independent of postsynaptic activity did not generate substantial levels of decorrelation, even when the overall level of inhibition reduced activity to a greater degree (**Fig. 6d**,**e**). This observation held whether the inhibition was modeled as subtractive or divisive, indicating that the activity dependence of lateral inhibition is critical for mediating decorrelation in networks

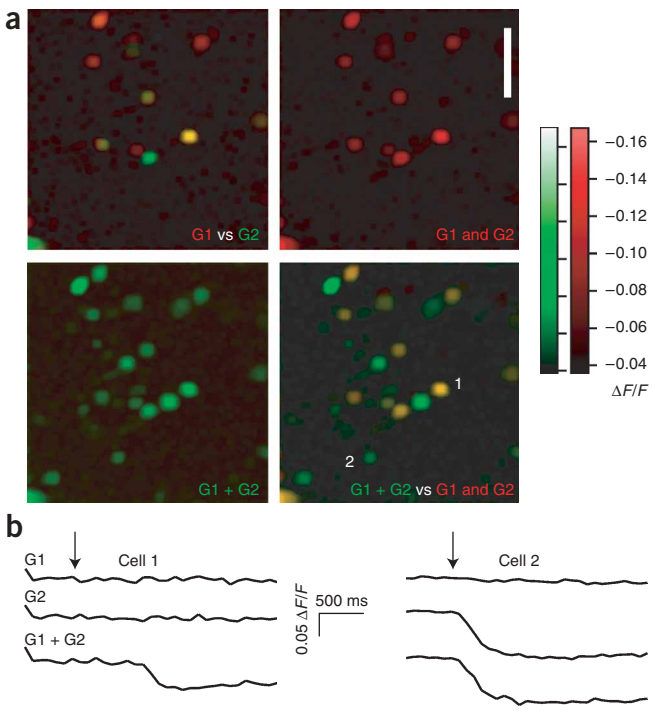

Figure 5 Overlapping and cooperative activation of granule cells following mitral cell stimulation. (**a**) Imaging of bulk-loaded calcium indicator (fura-2) from a population of granule cell–layer neurons. Images show calcium-induced changes in fluorescence ($\Delta F/F$) from populations of granule cells (images show minimum values for a given pixel across ten trials). The top left image shows the population of granule cells that were activated by stimulation of one glomerulus (G1, red) and a second glomerulus (G2, green). Yellow cells were activated by stimulation of either glomerulus. Top right, merged image in the red channel (G1 and G2). Bottom left, the population of granule cells evoked by simultaneous stimulation of both glomeruli (G1 + G2). Bottom right, the overlay of images from top right and bottom left. This overlay shows the population of granule cells that were activated only by simultaneous stimulation (in green). (**b**) Calcium transients from two cells shown in the images in **a**. Cells are labeled 1 and 2 in lower right panel of **a**. Arrows indicate time of stimulation.