1. *About panels E and F of Fig. 2 - from your response it appears that Chn #1 in panel E is not necessarily the same as Chn #1 in panel F....and so on.  Just making sure.*

Panel E and F represent inter-peak intervals and location of maximum peak recorded in all Chns (n=16), respectively. Each point represents mean and SD in each Chn. Panel E is the time-intervals between peaks of feedback currents during reverberations i.e. consistent inverse observed frequency in power spectrum. All 16 Chns showed similar inter-event interval (Panel E), it indicates the principal neurons are recruited at regular intervals (4 ms). Panel F shows when did the amplitude reached maximum in each Chn. It shows recruited principal neurons synchronized their feedback within ≈ 20 ms from the initial spike in all chns (panel F), regardless of the slice they are sampled from. This is one of the reasons we thought the circuits may have a modular organization to show consistent temporal characteristics in all slices.

1. *We would like a clean trace of a typical current clamp trace from panel 2-H, so that we can estimate elevation in membrane potential, # of spikes, ISI, etc.  -*TEXT or MATLAB formats will work for us.

Included MATLAB file of CC traces of evoked reverberations.

1. *About our question related to spont rates - would you happen to have the information for the in vivo case, since our network model will be based on the in vivo case (but can do in vitro also if needed).*

BLA principal neurons rarely spike even in *in vivo.* Recordings from interneurons are sparse. *In vitro,* interneurons hardly spiked spontaneously outside SWs. For this model, I think it is reasonable to keep spontaneous firing as nil for all neurons.

*You mention that simultaneous inputs from two Pyrs should be sufficient to drive a Chn to threshold. In the case of a Chn cell, input from one Pyr is sufficient per the data in your document, but wanted to be sure. For instance, are there cases where a Chn spike did not evoke a Pyr spike, i.e., no feedback to the Chn at all?  Is that also true for a PV cell, i.e., input from one Pyr is sufficient to drive it over threshold?*

Both Chns and other interneurons receive strong monosynaptic inputs from principal neurons. We observed single spike in a principal neuron could drive interneurons (including Chn) to threshold. But for the model, we could keep 2 principal neurons as a minimal requirement to drive other interneurons.

Yes, Chn evoked excitation of principal neurons show failures (i.e. no feedback). We do not know the factors that determine GABAergic excitation at the AIS. Our preliminary investigations suggest dynamic regulation of AIS excitability (i.e. current threshold to initiate a spike) by activity of Kv and Nav. Sub-threshold currents mediated by Kv7 channels and persistent sodium currents by Nav1.6 might determine the AIS excitability. We are looking into these mechanisms.

1. *You mention that each Chn could synapse on to 50 -100 pyramidal neurons. What fraction of the Pyrs reciprocate the connections?  Maybe the Pyrs close to the Chn (with XX um) reciprocate the connections? We will need that value/guess to constrain our network model.  Also, how many connections does a Chn receive from PV neurons?*

In our sample, we had about 40% reciprocal connections (9/22 Chn – Pri pairs). Our samples are usually within 50 µm radius from the Chn. But axons of Chn extend to 200 -300 µm in the BLA.

I do not have an estimate for PV synapses on Chns. I would think at least 2 PV neurons may converge on a Chn. Somatic GABA synapses are not always inhibitory and can facilitate spike initiation if they occur within specific time-windows (Allan T. Gulledge and Greg J. Stuart. Excitatory Actions of GABA in the Cortex. Neuron, Vol. 37, 299–309). It is possible PV inputs to Chn may initially facilitate spike initiation but as the inhibition increase it may silence Chns.

*6. This is about the AIS part of the model, something that we are not very familiar with:  We were trying to interpret the following statement on the very last section of your document, 'Proposed subcellular mechanism:......."*

*- "The axonal spiking activity without somatic AP facilitates high frequency glutamatergic activity observed in SW reverberations".  Does this perhaps mean that is there is somatic AP, this will reduce the # of AIS spikes, by perhaps pulling charge away from AIS, etc.? Would be good if you can shed light on this.*

*In vitro* and *in vivo,* spikelet (truncated APs with small amplitude) have been observed in principal neurons recorded with sharp electrodes. They tend occur during oscillatory activity in the network such as gamma band or SWs. The source of spikelet initiation and what drives them remains unclear. Here is a recent paper that looked into possible mechanisms using modelling:

Martina Michalikova, Michiel W. H. Remme, Richard Kempter.  *Spikelets in Pyramidal Neurons: Action Potentials Initiated in the Axon Initial Segment That Do Not Activate the Soma.* PLoS Comput Biol13(1):e1005237.

<http://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1005237>

Our evidence indicate Chn excite at the AIS, we think this might initiate a spikelet (an axonal spike) without somato-dendritic component. Axons possess electrical properties to fire at high frequency (small geometry, high density of ion channels, etc) compared to soma, and somato-axonal segregation could possibly an energetically favourable way to operate under such network activity. Experimental evidence for this mechanism is still lacking. I am currently working on these experiments.

*7. Also, under 'Expected Outcomes' - we are able to show using the Hu et al. model that only AIS spikes are seen at the resting potential. We did not understand the second item: "Increase in intrinsic excitability at the AIS of principal neurons......"  We were able to show it using the conductance densities in Hu et al. We were just curious how you increased excitability of Nav channels....just for our own information. About decreasing excitability of Kv7, maybe blockers were used.*

*We were able to demonstrate item 3 also using the parameters from Hu et al.*

Yes, we did some experiments using Kv7 blockers and they consistently increased amplitude of Chn evoked feedback, possibly through recruitment of more principal neurons and also increased success rate of reverberations. But this needs to be interpreted with caution since Kv7 blockers also enhance neurotransmitter release.

We also noted stimulation of cortical/ thalamic inputs to the BLA increased success rate and amplitude of chn evoked and spontaneous reverberations. It indicates external synaptic inputs could facilitate synchronized activity in the BLA. A possible explanation for this could be increase in excitability in the BLA after stimulation, possibly through increase in sub threshold Nav currents. But this is a speculation and requires direct measurements with experiments.