1 Ben's Questions:

1. Has your group considered the MLSpike paper (Official Title: Accurate spike estimation from noisy calcium signals for ultrafast three-dimensional imaging of large neuronal populations in vivo)? My plan is to apply this to the data John shared with us, as it seems to be state of the art.

Within our processing of calcium imaging data, we are able to extract deltaF/F signals (calcium transients) using the CaImAn platform (Paper: CaImAn an open source tool for scalable calcium imaging data analysis). Based on these deltaF/F signals extracted, the CaImAn tool also implements a deconvolution process that predicts spikes from deltaF/F signals. Therefore, we obtain both delta F/F and deconvolved activity (i.e., "spikes"). As mentioned by Alfredo, we would like to stick with delta F/F.

2. Are you most interested in recovering states/firing-rates from the calcium data, or are you also interested in more accurate spike train reconstruction? (If only the states are of interest, I thought of directly inferring the states from the raw data).

We are interested in recovering states from calcium data (delta F/F).

3. Has anything changed regarding Calcium Imaging technology since the publishing of MLSpike in 2016? (higher yield, better time-scale, etc?). I am trying to narrow down an area I can improve.

Experimentally, there has been improvements in the calcium sensors (i.e, faster on/off kinetics, higher dynamic range, SNR, longer wavelength indications.), optics and microscopes and ability in recording across cortical columns (deeper into the brain for subcortical structures) using multiphoton microscopy.

2 Marija´s Questions:

1. Are the calcium data and the spike data obtained from the same or similar kind of experiments?

   If you are referring to the spikes in the data I uploaded, yes, both data come from same session of recording. If you are referring to other spike data provided previously, they are from a similar kind of experiment, however the duration of behavior periods may be slightly different.

2. Does the HMM identify the state based on the distribution of the neuron activities? (see Fig.1 in Mazzucato et al. 2015). I am asking because I am wondering if there is a way to identify the states using the (group) firing rates?

I will direct this question to Liam and Alfredo…sorry!

3. Is there any knowledge about the minimum or maximum length a state can last? I want to account

for that when considering changing the time bins.

I will direct this question to Liam and Alfredo …sorry!

3 Xiaokun's Questions:

1. For now, how do you extract the spikes for the calcium imaging data?

We use the CaImAn platform (Paper: CaImAn an open source tool for scalable calcium imaging data analysis) to extract both deltaF/F signals extracted and spikes. As mentioned by Alfredo, there are many methods in extracting spikes from calcium data. However, CaImAn uses the Online Active Set method to Infer Spikes (OASIS) which relies on sparse non-negative deconvolution. I am not an expert in the OASIS algorithm so I will point you to the CaImAN paper and original OASIS paper: Fast online deconvolution of calcium imaging data.