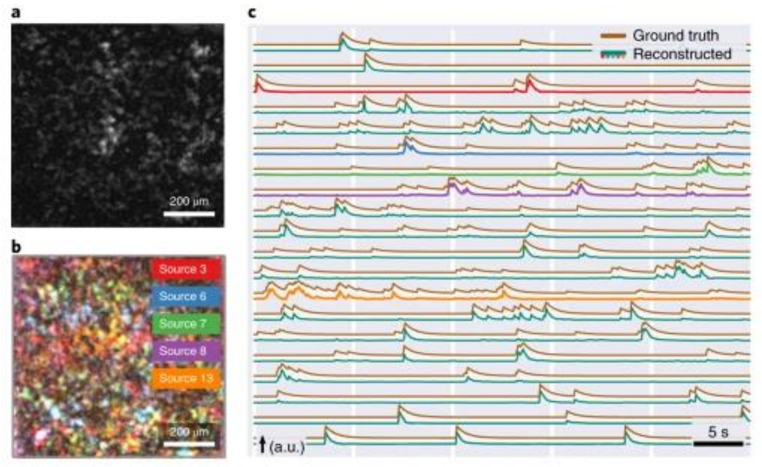
Non-negative Matirx Factorisation (NNMF) for Recovery of Time Traces from Overlapping Signals

EE367

Introduction and Objective

Recovery of signals from through highly scattering tissue (e.g. time varying signals such as fluorescent traces from biological tissue) is an important problem. A particular restricted case is when we are interested in simply extracting time traces of scattered signals without explicitly recovering their original (pre-scattered) footprint. This can be thought of as a blind source problem. A powerful approach is NNMF, used for separation of spatial and temporal footprints to allow for denoising by separating signal traces from background [2]. Recently this approach was used to recover the temporal variations of signal fluorescent markers under scattering tissue [1].

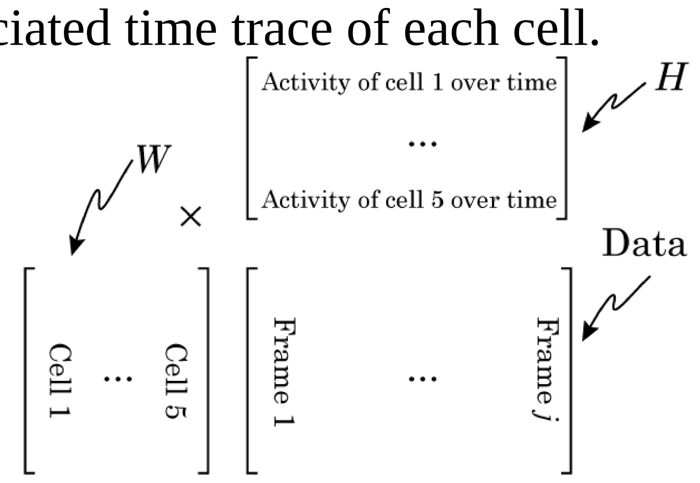


We will use simulated data to explore NNMF for extracting noise, overlapping time traces.

Non-Negative Matrix Factorisation

NNMF is a form of unsupervised learning similar to PCA where the components of some dataset are extracted and ranked based on their variance [3]. The highest ranked components describe the most characteristic components of the data based on the way the components were extracted.

We illustrate below how a vectorized video dataset can be factorized into a matrix of weights representing a spatial component, e.g. for each "cell" and a temporally varying component, for the associated time trace of each cell.



NNMF specifically extracts these components with the constraint that the components must be non-negative. Since many measurements are composed of purely positive values, this constraint makes sense to have for those measurements.

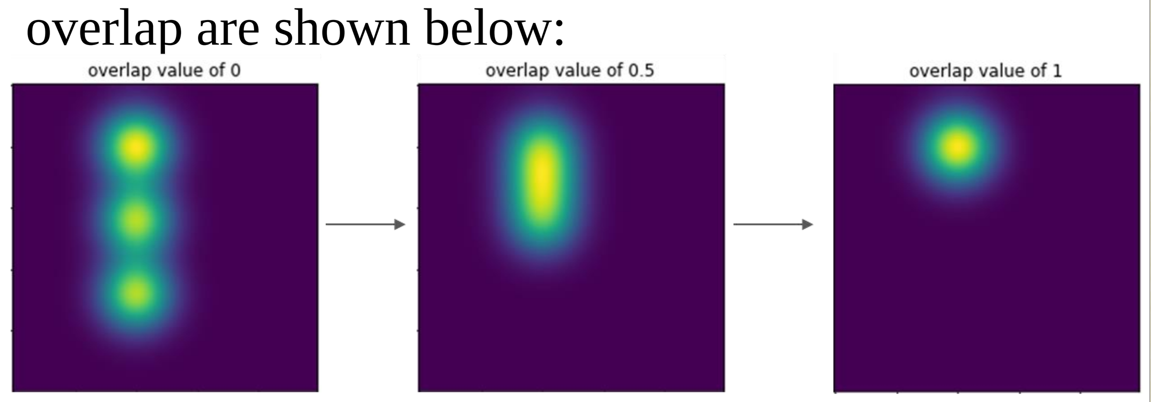
Methods

Creation of Simulated Data

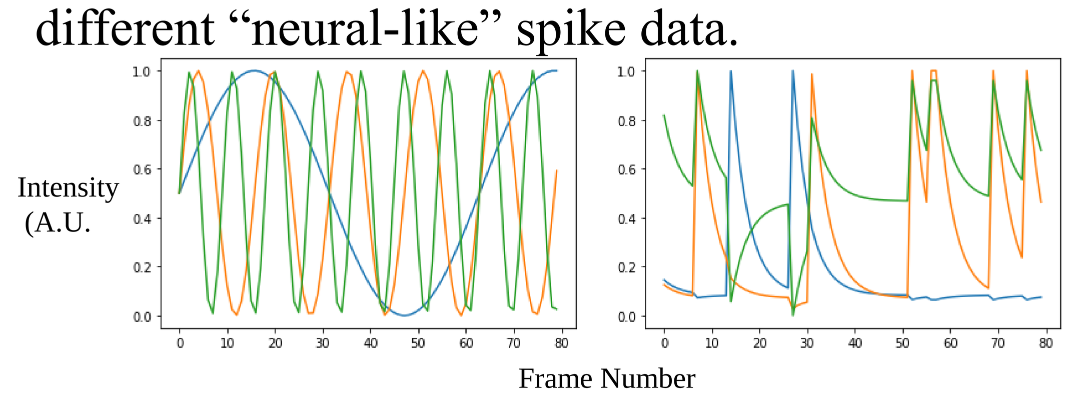
Create simulated "video" dataset by modelling the pattern of light from a single source region after scattering as a Gaussian spots, and then creating an image frame by superimposing many Gaussians with varying degrees of overlap. We then apply different time varying intensity traces to each of these Gaussians and apply noise. We implement the NNMF algorithm and benchmark its accuracy in recovering our original "ground truth" time intensity traces under various noise conditions.

Investigation Plan

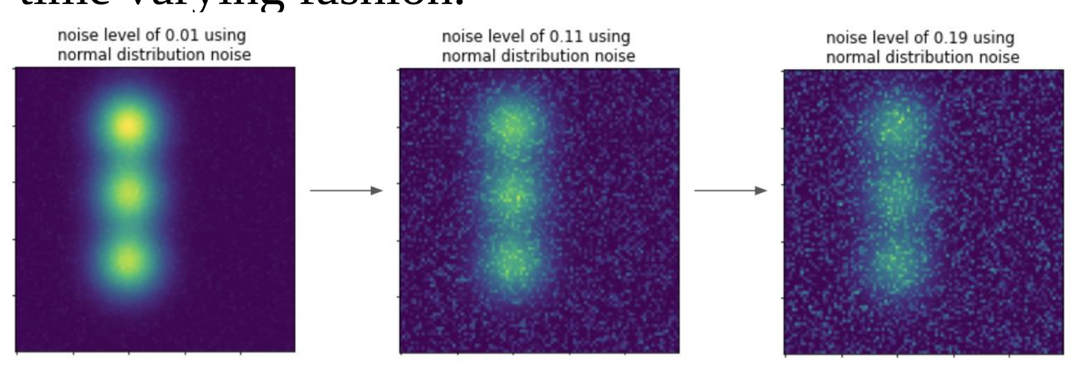
Example datasets with various degrees of spatial overlap are shown below:



We show below two types of overlaid time traces that applied to different Gaussians, one with sinusoidal modulation at different frequencies, and different "neural-like" spike data.



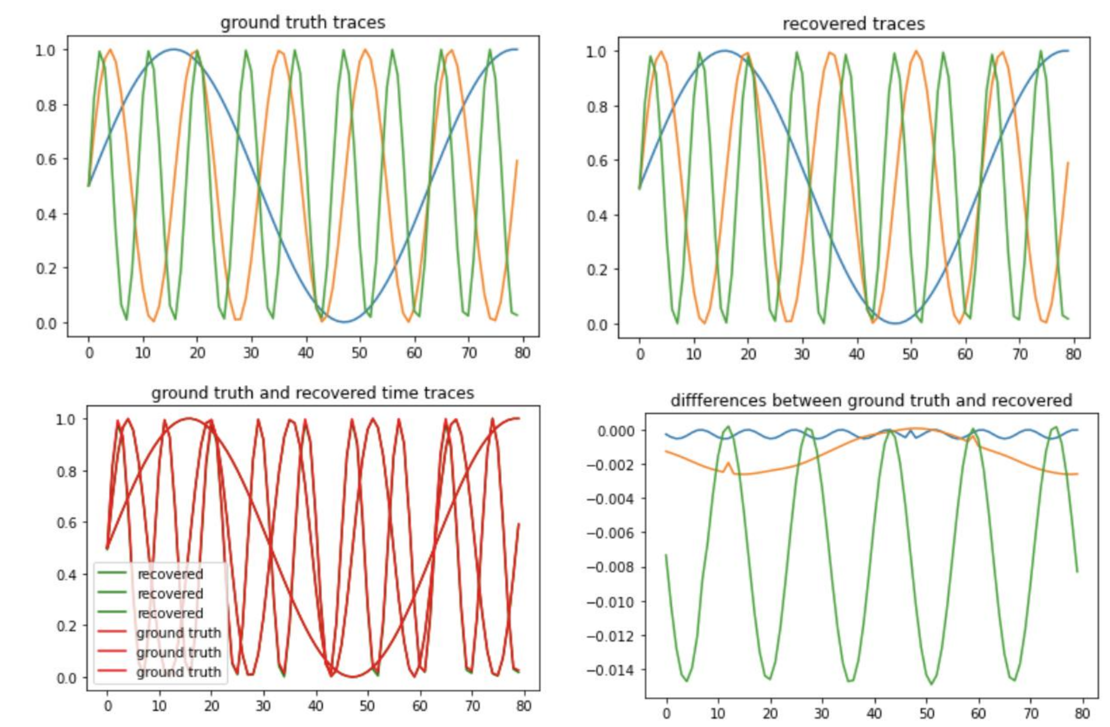
We also vary the noise level and apply different types of noise (uniform and normal) in a static and time varying fashion.



Results and Discussion

Recovery of randomly positioned sinusoidally modulated traces

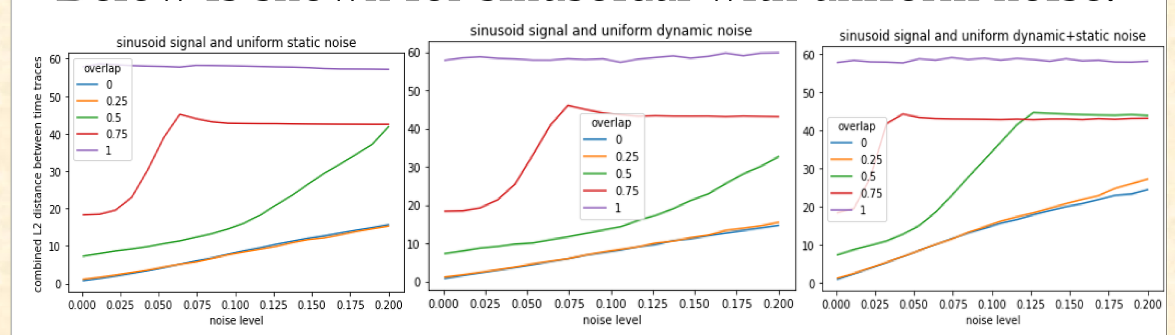
We first show that NNMF allows for recovery of ground truth traces with high fidelity from sinusoidal applied patterns, with Gaussian spots applied randomly and without overlap.



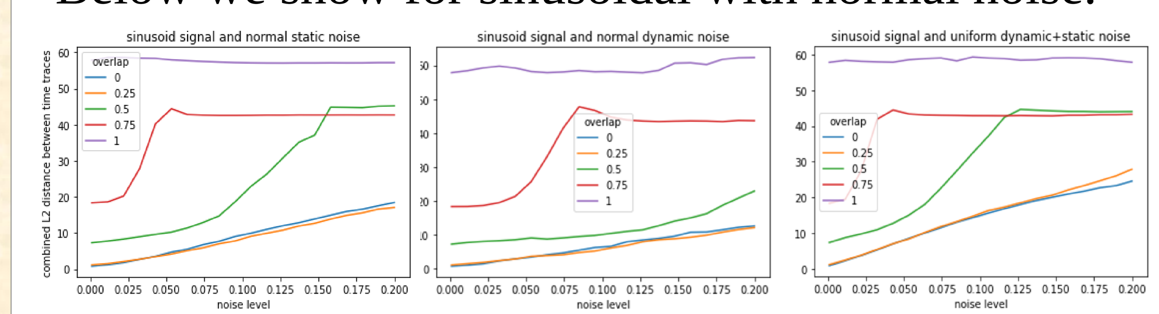
Recovery of modulated traces at various overlap degrees as a function of noise

We then investigate how the reconstruction fidelity varies as a function of noise for different noise types, with various degrees of overlap, again for sinusoidal signals. We quantify the reconstruction by taking the L2 norm of the difference between recovered traces and the ground truth.

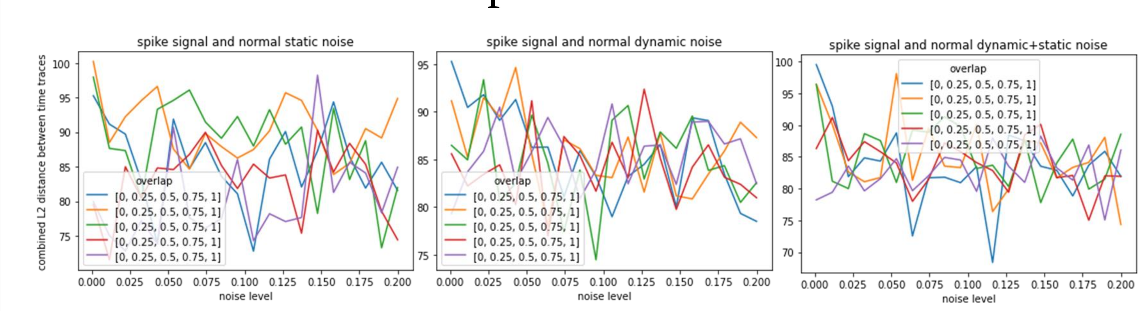
Below is shown for sinusoidal with uniform noise.



Below we show for sinusoidal with normal noise.



Below we show for spike data with normal noise.



Discussion and Conclusions

We see that NMF allows for recovery of ground truth traces with high fidelity from simple sinusoidally applied patterns without overlap.

When applied to sinusoidal time trace patterns, at low overlap, the signals can be recovered even in the presence of increasing noise, for all cases of static, dynamic and static and dynamic noise. Even at full overlap, the signals can be recovered at low noise conditions and the quality of the reconstructions decrease as noise increase, before hitting a plateau where they are too noisy to reconstruct. However, at full overlap, the reconstructions are poor even at low noise, indicating that the system cannot recover fully overlapping signals. However, for simple sinusoidal signals, it is highly promising that even "75%" overlapped signals can be recovered in some noise.

However, on the spike data, recovery is overall quite poor for all types of noise and overlap. This may indicate that the recovery is poor, and that more complex frequency content signals are harder to reconstruct. However it may also suggest that our "L2 norm" fidelity criterion is not accurate at representing how well the system gets the spike timing right.

NNMF is a valuable technique for recovery of time traces from noisy data. It's performance on complex trace data can be further investigated, along with the possible use of alternative algorithms such as constrained non negative matrix factorization to improve fidelity (CNMF) [2].

References

[1] Moretti, C., Gigan, S. Readout of fluorescence functional signals through highly scattering tissue. Nat. Photonics 14, 361–364 (2020). https://doi.org/10.1038/s41566-020-0612-2

[2] Pnevmatikakis EA, Soudry D, Gao Y, Machado TA, Merel J, Pfau D, Reardon T, Mu Y, Lacefield C, Yang W, Ahrens M, Bruno R, Jessell TM, Peterka DS, Yuste R, Paninski L. Simultaneous Denoising, Deconvolution, and Demixing of Calcium Imaging Data. Neuron. 2016 Jan 20;89(2):285-99. doi: 10.1016/j.neuron.2015.11.037. Epub 2016 Jan 7. PMID: 26774160; PMCID: PMC4881387.https://www.cell.com/neuron/pdfExtended/S0896-6273(15)01084-3

[3] Lee, D., Seung, H. Learning the parts of objects by non-negative matrix factorization. Nature 401, 788–791 (1999). https://doi.org/10.1038/44565