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DECENTRALIZED MOTION INFERENCE AND REGISTRATION OF NEUROPIXEL DATA

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ABSTRACT

Multi-electrode arrays such as "Neuropixels" probes enable the study of neuronal voltage signals at high temporal and single-cell spatial resolution. However, *in vivo* recordings from these devices often experience some shifting of the probe (due e.g. to animal movement), resulting in poorly localized voltage readings that in turn can corrupt estimates of neural activity. We introduce a new registration method to partially correct for this motion. In contrast to previous template-based registration methods, the proposed approach is *decentralized*, estimating shifts of the data recorded in multiple timebins with respect to one another, and then extracting a global registration estimate from the resulting estimated shift matrix. We find that the resulting decentralized registration is more robust and accurate than previous template-based approaches applied to both simulated and real data, but nonetheless some significant non-stationarity in the recovered neural activity remains that should be accounted for by downstream processing pipelines. Open source code is available at https://github.com/evarol/NeuropixelsRegistration.

***Index Terms*—** Microelectrode array, registration, decentralized algorithms, spike sorting, neuroscience

1. INTRODUCTION

Recent advances in multi-electrode array (MEA) technology enable the recording of neural activity throughout the brains of behaving animals, at single-cell spatial resolution and sub-millisecond temporal resolution, over timescales of hours or even days [3, 4, 5, 2]. During long recordings, it is inevitable that the probes will shift in position, due for example to subtle movements experienced by the brain during external movement of the animal. These shifts in turn translate into nonstationarities that can contaminate downstream analyses of the inferred neural activity. Therefore, inferring the amount of movement that is experienced by the MEA and correcting the voltage signal to account for this movement has been identified as a crucial step in the analysis of MEA data [6].

Since the MEA is equipped with a geometrical layout, one can think of the probe recording as a series of images of voltage readings, where each electrode acts as a pixel. Therefore, MEA motion correction can be cast as a video registration problem — but with several important caveats. First, the "videos" of voltage signals from active neurons are highly sparse relative to the sampling rate of voltage recordings; therefore salient landmarks that can be used to register one frame to another are absent in most of the recording. Second, when there is neural firing activity that can be used to anchor registration, the firing patterns may not be consistent over time, i.e., different subpopulations of neurons might be observable at different time intervals, creating a lack of correspondences for registration. Further, the signal to noise ratio of voltage recordings is not as high as those observed in many medical imaging registration tasks or natural image videos, further making the motion estimation problem difficult. Lastly, unlike traditional grid-like pixel layouts, MEAs occasionally have scattered pixel positions. This makes the signal interpolation step after displacement estimation challenging due to irregular placement of signal recordings.

[2] recently introduced template-based registration methods for Neuropixels data (see also [7] for an earlier approach), building on approaches that are popular for registering other types of neural recordings [8, 9]. The basic idea here is to learn a "template" image and to estimate the optimal shift in each timebin to match the data to the estimated template image. This approach works well when the observed neural activity is stable enough to form a single coherent template image across the full dataset, but fails if different neural populations are active during different temporal segments of the recording (implying that a single template will not fully capture the activity prevalent in each timebin).

Here we introduce a more robust *decentralized* registration approach. Instead of assuming the existence of a single template image, we estimate relative displacements with respect to every pair of frames, and then extract a global displacement estimate from the resulting matrix of pairwise local displacements. We show that one does not need to execute every pair of registration problems, as subsampling can be utilized to reliably estimate global displacement due to the low-rank nature of the estimated displacement matrix. The resulting decentralized registration framework significantly improves displacement estimation in several challenging experimental datasets.

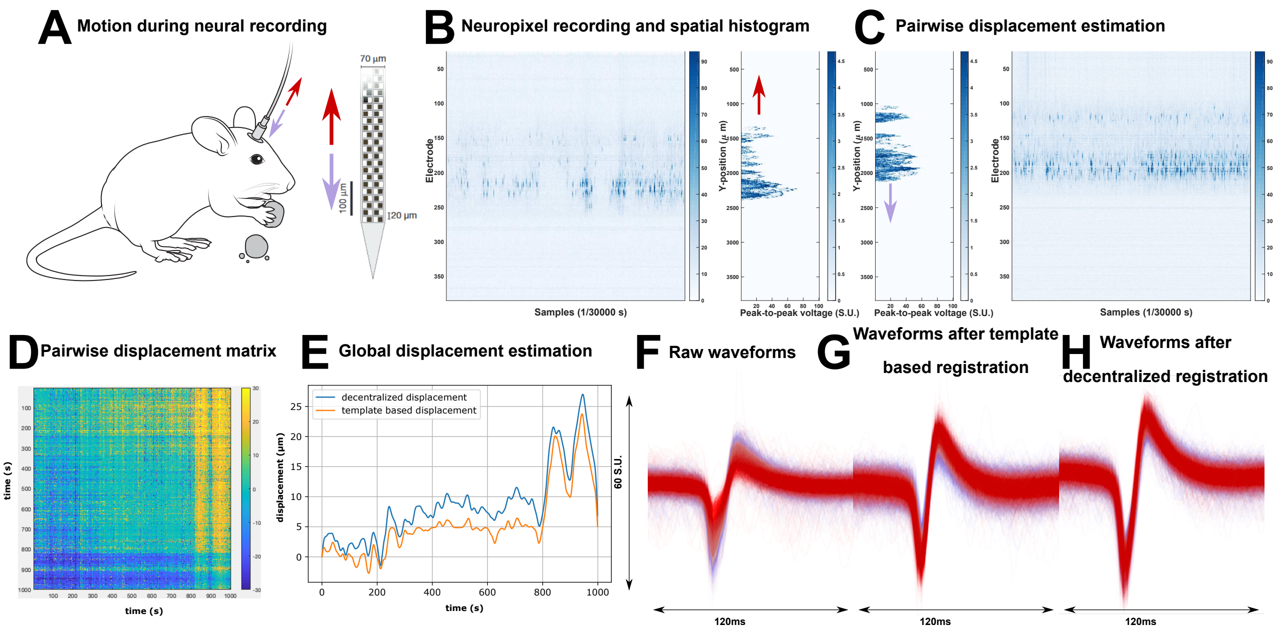

Fig. 1. In vivo electrophysiological recordings are subject to motion artifacts (**A**; mouse figure reproduced from [1]). To estimate the amount of motion, each time chunk of data (1 second) is represented using spatial histograms (**B**). The spatial histograms across all time chunks are pairwise registered to each other (**C**). Using pairwise displacement estimates (**D**), global positioning is inferred (**E**); dataset from https://github.com/flatironinstitute/neuropixels-data-sep-2020/blob/master/doc/cortexlab1.md. Global displacement is used to register the time chunks to a motion corrected space. The action potential superpositions prior to motion correction exhibit highly variable signal amplitudes due to motion (**F**; color indicates time within the trial, so we see that early spike shapes differ significantly from later spikes). Motion effects are reduced after registration, and the decentralized motion estimates yield a higher signal-to-noise ratio yield (**H**) compared to the template based registration approach in [2] (**G**).

2. METHODS

The proposed registration framework involves several steps, illustrated schematically in figure 1. First, the data is band-pass filtered (200Hz-3000hz) and normalized by median absolute deviation (MAD) to account for electrode specific noise levels. Then, following [2], the recording is broken into one-second time chunks, within which spatial histograms are extracted to represent the signal support (Fig.1-B). Spatial histograms capture the counts of events within each time chunk in bins that represent depth position along the electrode and signal amplitude[1]. All pairs of such histograms are registered to one another to estimate a decentralized displacement matrix which is then used to estimate global positioning (Fig.1-C,D,E). Given the global positioning, the electrode data in each time chunk is interpolated using Gaussian process regression (again, see [2] for details) to represent its values by undoing the observed displacement, yielding a registered, motion corrected recording (Fig.1-G). In the following sections, we describe the decentralized displacement estimation technique in further detail.

[1] Other featurizations of the data are possible and could be swapped in here in a modular fashion; the registration method described here only requires a distance function between the featurized data in different time bins. Good featurizations will be as invariant as possible to changes in firing rates between different time bins.

2.1. Decentralized displacement estimation

If we have collected T spatial histograms, each capturing the counts of signal events of particular spatial location and amplitude in non-overlapping segments of recording time, we can treat each of these histograms as a two-dimensional image and utilize existing subpixel registration algorithms [11] to infer the vertical displacement that maximizes the correlation between two histograms. Computing all such pairs of displacements, we can form a pairwise displacement matrix $\boldsymbol{D} \in \mathbb{R}^{T \times T}$. If subsampling is employed, i.e. only a subset of all pairs of displacements are estimated, we can denote the pairs of samples by which displacement is estimated by a subsampling bookkeeping matrix $\boldsymbol{S} \in \{0,1\}^{T \times T}$. Given $\boldsymbol{D}$ and $\boldsymbol{S}$, we can estimate the global positioning of time samples since the joint displacement information is a realization of a low-rank matrix (assuming sufficient rigidity) [12, 13]. We can decompose the low-rank system using the following objective:

$$\min_{\boldsymbol{p}} \|\boldsymbol{S} \odot (\boldsymbol{D} - (\mathbf{1}\boldsymbol{p}^T - \boldsymbol{p}\mathbf{1}^T))\|_F^2 \quad (1)$$

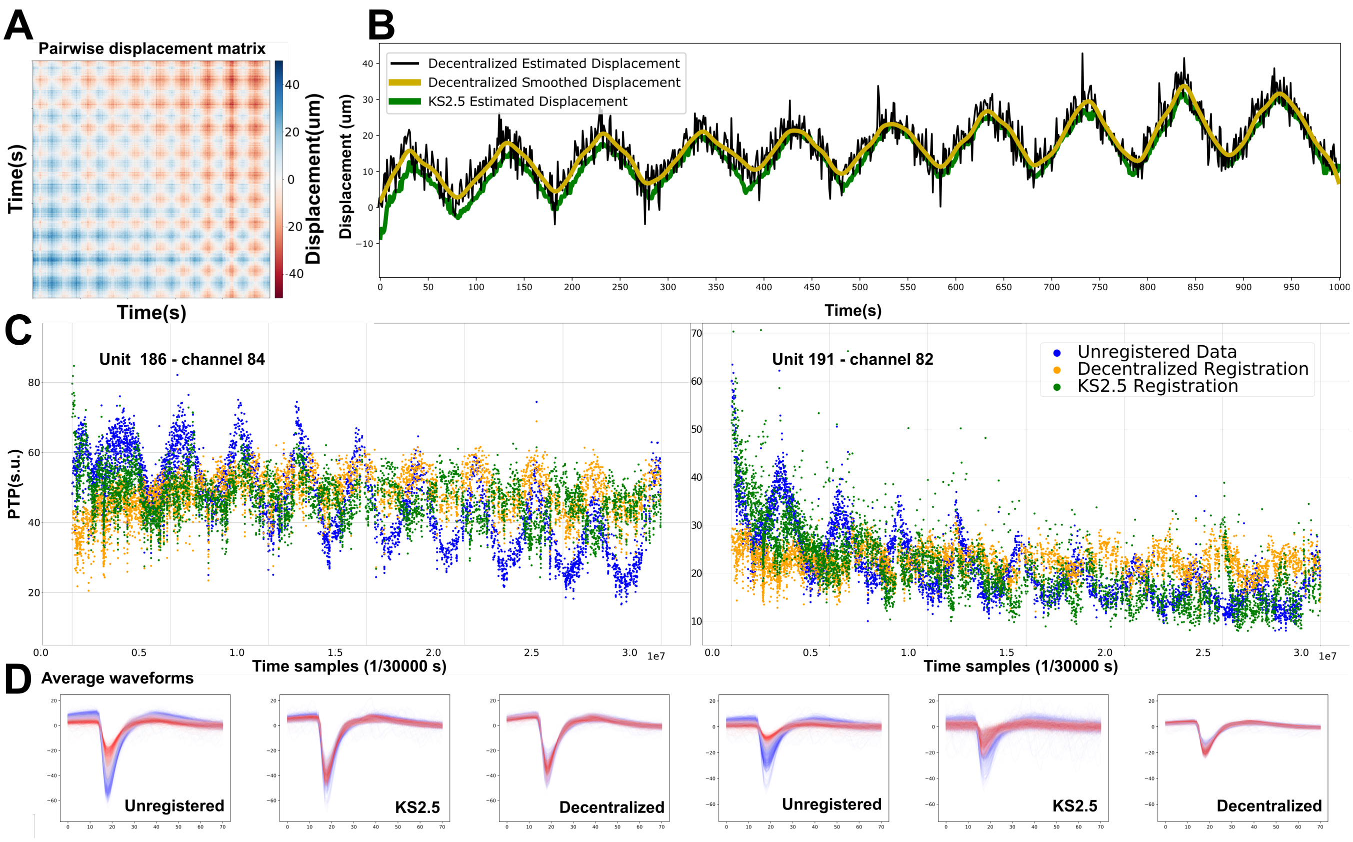

Fig. 2. Effect of registration on real data. (**A**) Pairwise displacement matrix that is used to robustly estimate global displacement, shown in (**B**) (black and yellow traces). The Kilosort2.5 [10] template-based estimate (green) is slightly different. (**C**) shows the peak-to-peak amplitude over time of all spiking events detected by Kilosort2 [10] on two channels, indexed by 163 and 194, in unregistered data (blue), after template based registration (green), and decentralized registration (yellow). The peak-to-peak variability is the lowest after decentralized registration — but notice that even in the best case there remains some motion-induced variability in the spike heights. (**D**) shows the units' action potential waveforms over time on each channel, in unregistered data and after template based registration and decentralized registration. Blue indicates that the waveform was early in the recording and red late in the recording. In both cases, the decentralized registration minimizes the motion-induced variability of the recovered spike shape.

which can be solved in closed form:

$$\boldsymbol{p} = \left(\mathrm{diag}(\mathrm{vec}(\boldsymbol{S}))\left(\boldsymbol{I} \otimes \boldsymbol{1} - \boldsymbol{1} \otimes \boldsymbol{I}\right)\right)^{\dagger} \mathrm{diag}(\mathrm{vec}(\boldsymbol{S}))\mathrm{vec}(\boldsymbol{D}) \tag{2}$$

Here $\otimes$ denotes the Kronecker tensor product, $\dagger$ denotes the Moore-Penrose pseudoinverse, $\mathrm{vec}(\cdot)$ denotes the matrix vectorization operation, $\mathrm{diag}(\cdot)$ denotes the diagonal matrix with input elements, and the entries of $\boldsymbol{p} \in \mathbb{R}^T$ reflect the relative displacements of the T spatial-histogram representations of the data (see Fig. 1D or 2A for examples).

Subsampling allows us to reduce the number of pairwise comparisons from $O(T^2)$ to $O(T\log(T)/\epsilon^2)$ while incurring an error of $(1 \pm \epsilon)$ relative to the full-sampled displacement estimate, due to the boundedness of displacement errors and Hoeffding's inequality [14, 15].

In addition to subsampling, the $\boldsymbol{S}$ matrix can further encode registration faults between the ith and jth samples i.e. displacement estimates that have incurred a loss greater than a particular variance threshold. By setting $\boldsymbol{S}_{i,j} = 0$ for all such cases, the displacement solution derived from (2) can result in improved registration performance in challenging datasets with low firing rates and large displacements.

In contrast, in template based registration, the positioning of each time point is estimated directly by inferring the displacement to a template, which is an average of all the spatial histogram representations. The main difference between decentralized registration and template based registration is that in decentralized registration, each time chunk of data is registered to each other, rather to a "central" template. Template-based registration is prone to displacement errors whenever a particular time chunk does not resemble the template.

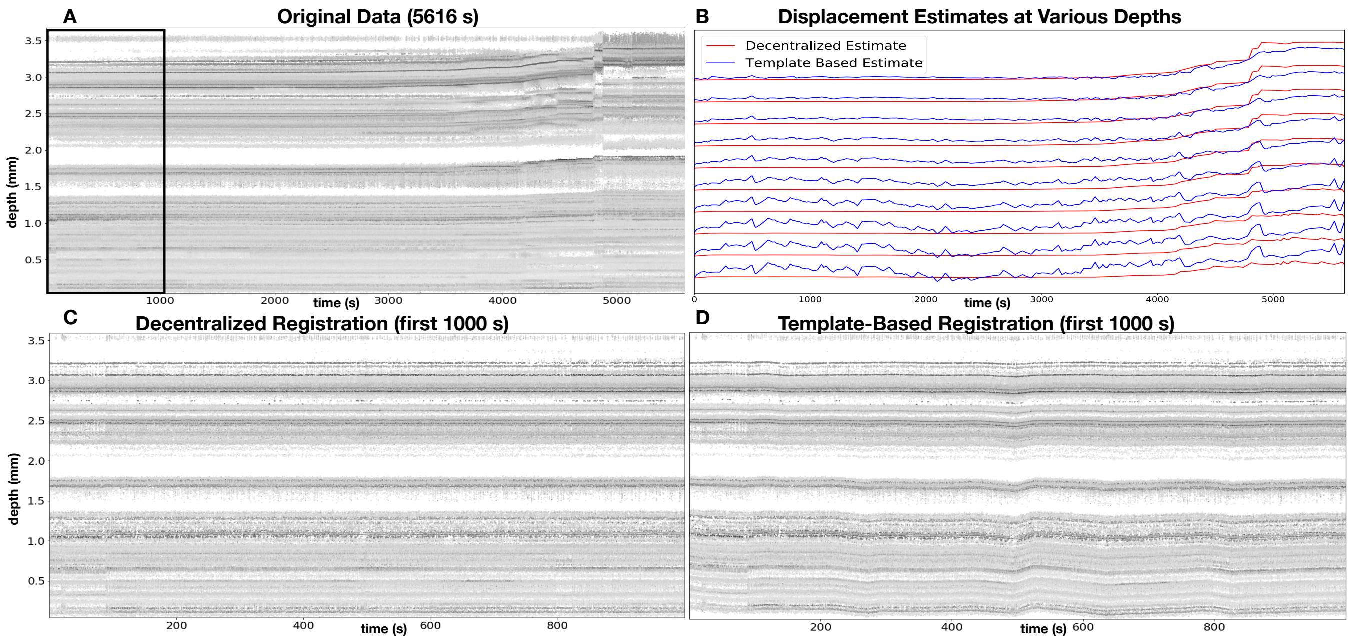

Fig. 3. Displacement estimation in a dataset with substantial non-rigid drift (data available through https://github.com/evarol/NeuropixelsRegistration). (**A**) shows the original spike depths and amplitudes (indicated by grayscale; darker ticks correspond to bigger spikes) over time in this recording. (**B**) shows displacement estimates by non-rigid template-based (blue) and decentralized (red) methods at 10 different depths. The decentralized estimates visually track the data from panel **A** accurately, while template based estimates remain very noisy (even after significant smoothing), as the estimated template is corrupted by the large shift at the end of the recording. (**C**) shows the spike depths and amplitudes of the first 1000 seconds (indicated by the black box in panel **A**) after decentralized registration, which is robust to the changes in firing patterns, while template based registration (**D**) induces significant noise and apparent motion in the recovered signal.

2.2. Non-rigid estimation

As noted in [2], the displacement along the probe may be non-constant, due most likely to differences in the rigidity of brain regions at different depths. (See Fig. 3 for an example.) To estimate a different displacement at each depth, we perform displacement estimation at K equally spaced depths. Instead of using a hard window to select these different subsets of data (as in [2]), we found that a more robust approach was to utilize soft windowing, where for each K selected depth, we upweight the data using a Gaussian window before estimating the optimal shift. Finally, again following [2], we apply Gaussian process regression to interpolate the registered data, given the spatiotemporal displacement field estimated above.

3. RESULTS

We explored the impact of registration on real data using a Neuropixels2.0 recording of 1000 seconds in which the experimenters purposely induced "artificial" drift, and compared our method to the state-of-the-art Kilosort2.5 registration [2]. Over the course of the experiment, the neurons move with respect to the MEA, and their spikes' detected amplitudes and shapes change over time. We spike-sorted the data using Kilosort2 [10] and manually curated the output to recover clean, interpretable neural units. The difference between Kilosort2.5 (green) and our decentralized approach (black and yellow, after smoothing) displacement estimates is shown in (Fig.2B). After registration, the peak-to-peak amplitude (Fig. 2C) and shapes of the units' waveforms (Fig.2D) become more stable over time. Decentralized registration leads to a better correction than Kilosort2.5 registration in the examples shown here, though importantly, even in the best case, there are some visible remaining motion-induced "wobbles" in the spike heights, which would need to be tracked by downstream spike sorting processing.

Next we chose a more challenging Neuropixels1.0 dataset, recorded in a mouse during the behavioral task described in [16]. This dataset displays an atypically large and non-rigid drift (Fig. 3A), leading to a failure in the template-based registration approach implemented in Kilosort2.5 [2] (panel D). The assumption of a single fixed template across the full temporal length of the experiment does not hold here, leading to noisy and inaccurate registration results. In contrast, the decentralized registration is more robust, leading to qualitative improvements in registration accuracy (panels B and C).

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