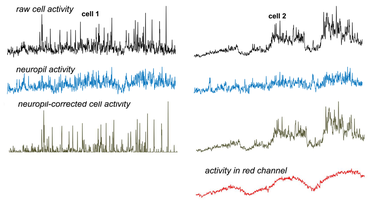
Drift correction for electrophysiology and two-photon calcium imaging

Marius Pachitariu*, Carsen Stringer*, Nick Steinmetz, Matteo Carandini, and Kenneth D Harris

hhmi janelia Research Campus | UCL

Problem: Drift is bad for science. Can we understand drift, and fix it?



Understanding "drift"

Slow drift can be non-rigid

Fast drift is mostly rigid (phew!)

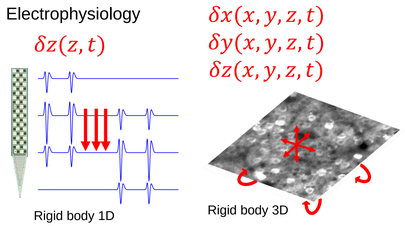
	Electrophysiology	Two-photon
	Tissue relaxation after probe insertion, hemodynamics etc.	Temperature changes, hemodynamics, inflammation etc.
	Behaviorally induced Up and down jitter, bigger than in 2p	**Behaviorally induced** Mostly translation, but also rotational

Engineering a fix for drift:

We design **generative models** that capture the effect of drift on the raw recorded data.

We use these models to **infer the drift**, given the data.

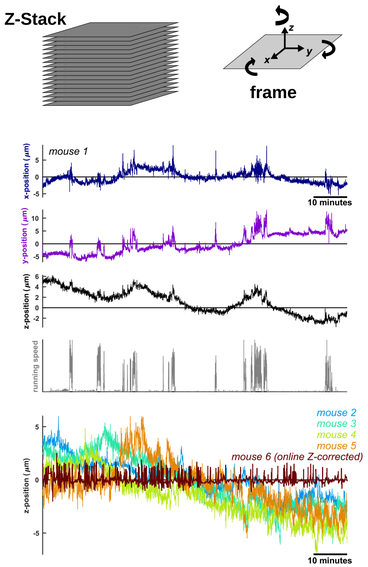
Enforcing **rigidity on fast timescales** allows us to estimate drift from noisy data.

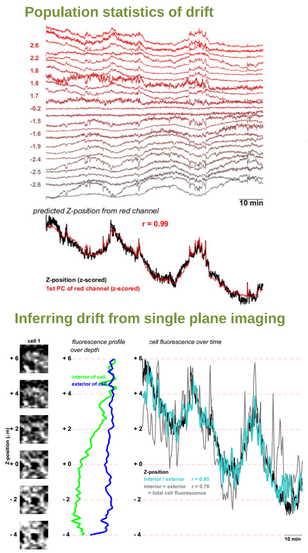


To do list:

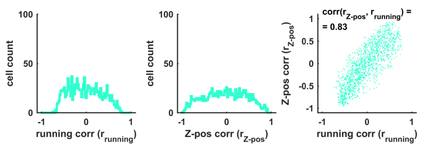
- once we know the drift, can we devise fast & accurate **interpolation** methods to re-align data?
  we think so
- is the **sampling** of Neuropixels dense enough?
  probably
- do you need to align 2p imaging data **online**?
  yes & we have code

Signatures of drift in 2p imaging

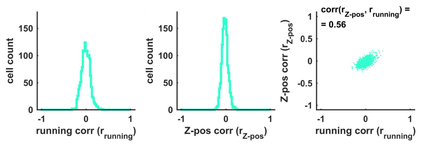




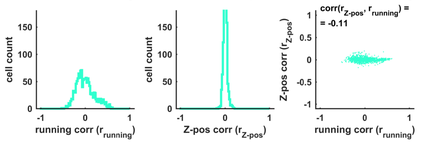
Cells' correlation with running might be explained by their correlation with z position



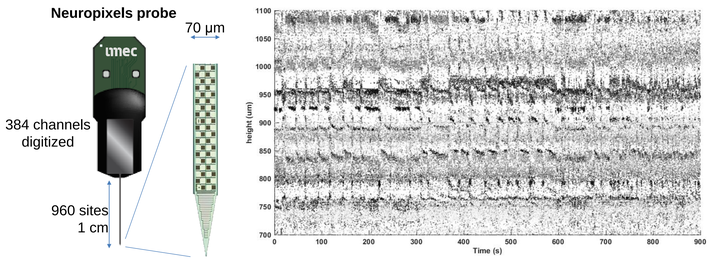
Running baseline-subtraction aggressively removes correlations



Correction based on Z-position is more effective



Signatures of drift in electrophysiology



Jun, Steinmetz et al, *Nature* 2017

Each dot is a spike.
Darker dots are larger amplitudes.

Estimation of drift through generative models

Generative model for spike sorting: *Kilosort*

recorded voltage

$$V(z,t) = \sum_k A_{\sigma(k)}(z, t - t_k) \cdot x(k) + noise$$

cluster assignment; electrode / depth; spike template; amplitude

Waveform model: $A_j = U_j * V_j^T$

Drift in the spatial mask: $U^t_{\sigma(k)}(z, 1:3) = U_{\sigma(k)}(z - \Delta z(z,t), 1:3)$

Δz changes slowly over space and time:

minimize $\|d_z(z_1, t_1) - d_z(z_2, t_2)\|^2$, where $t_1 \approx t_2,\ z_1 \approx z_2$

Two-photon generative model: *rigid 3D translation*

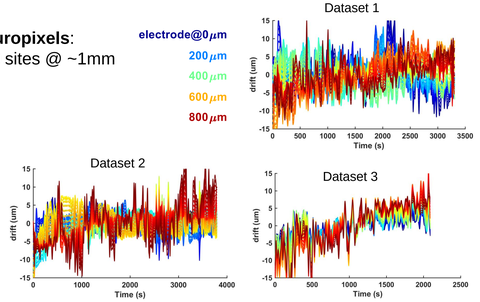
recorded frame; pre-recorded Z-stack; unknowns

$$\text{Image}(x,y,t) = Z\big(x + \Delta x(t), y + \Delta y(t), \Delta z(t)\big) + noise$$

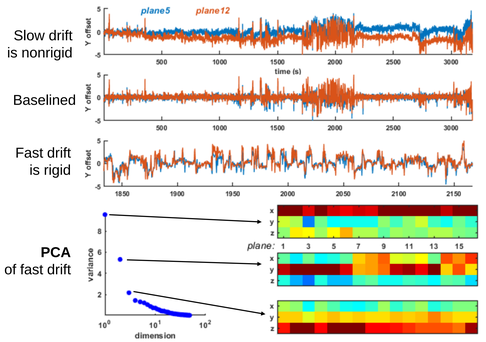
- we ignore activity dependence
- we additionally whiten and low-pass the frames and z-stack

Spatiotemporal statistics of drift

Neuropixels: 120 sites @ ~1mm

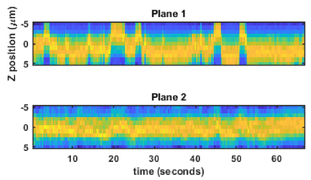


Two-photon mesoscope



Rigid, rotational motion is well-approximated by a linear model

Rotational motion exists:

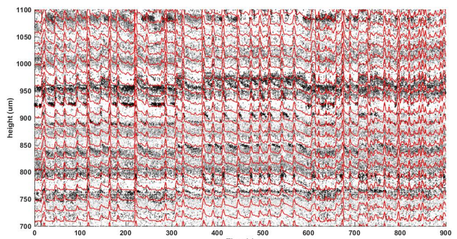


$$I(x,y,z,t) = Z(x',y',z')$$
$$x' = x + \Delta x + \delta x \quad \text{(translation; effect of rotation)}$$
$$\begin{bmatrix}\delta x\\ \delta y\\ \delta z\end{bmatrix} = R\begin{bmatrix}x\\ y\\ z\end{bmatrix},\quad R \approx \begin{bmatrix}1 & \alpha & \beta\\ -\alpha & 1 & \gamma\\ -\beta & -\gamma & 1\end{bmatrix}$$

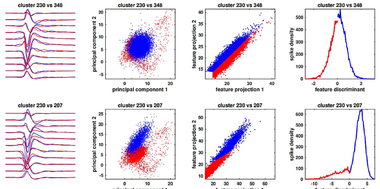
Linear approximation follows from:

$$\mathrm{R} = R_\alpha R_\beta R_\gamma,\ R_\alpha = \begin{bmatrix}\cos(\alpha) & \sin(\alpha) & 0\\ -\sin(\alpha) & \cos(\alpha) & 0\\ 0 & 0 & 1\end{bmatrix} \approx \begin{bmatrix}1 & \alpha & 0\\ -\alpha & 1 & 0\\ 0 & 0 & 1\end{bmatrix}$$

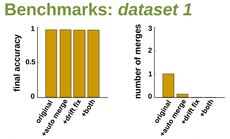
Drift correction helps with spike sorting



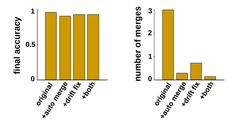
Automatic merges after drift correction



Benchmarks: *dataset 1*



Benchmarks: *dataset 2*



See Suite2p and Kilosort for code
https://github.com/cortex-lab/KiloSort
https://github.com/cortex-lab/Suite2P

Acknowledgments

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