Correcting Drifted FIB-SEM Images using a Model-Based Registration Approach

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Abstract
In many common 3D scanning methods used for imaging biological material, the scanning method itself may at each imaged section induce drift from the previous section causing a misalignment in the slice direction. Drift can have a variety of causes such as charge gradients in the material and physical movement of the material. Correcting this drift is crucial to any subsequent work on the images since the drift skews distance measures. Since any statistics or shape analysis is deeply dependent on the accuracy of such distance measures, this is likely to have significant consequences for the biological conclusions which one may present.

Misalignment Affects Vesicle Shape
Drift is usually too subtle, happening at sub-pixel scales, to accurately notice by looking at consecutive images in the image plane, but upon creating an image across image sections reveal some of the most noticeable misalignments. In these areas, a noticeable stretching of synaptic vesicles can be seen (See below image for example). Vesicles are small numerous objects found near neuron active zones.

(Left) A look inside a section of a FIB-SEM dataset with significant drift present. (Right-Top) Example of a stretched vesicle when viewing the image across multiple sections. (Right-Bottom) Example of the stretched vesicle when viewing the image in a single section, i.e., in the image plane.

The shape of vesicles is determined primarily by the local environment and more specifically primarily dominated by surface tension. We can thus assume that optimally, in the non-drifted state, the vesicles should be spherical. We leverage this property by translating the images to enforce this sphericality. The shape variation of vesicles can for the purpose of this work, be modeled in the variation the ellipsoid allows.

Vesicle to Ellipsoid Pipeline
We propose two ways to acquire ellipsoid parameter estimates from the vesicles (Top) Manually annotating boundary points of vesicles, and fit the ellipsoid by minimizing the SSD to an ellipsoid using the distance normal to the ellipsoid. (Bottom) Classify the vesicles using your favorite classifier, cluster the inner points using K-Means clustering and then use cluster centers as prior for a 3D Active Contour Model to get the ellipsoid parameters.

Estimating the drift per vesicle
Given an ellipsoid estimate of one vesicle in the standard algebraic representation

\[
x^T \begin{bmatrix} A & D & E \\ D & B & F \\ E & F & C \end{bmatrix} x = 1 \ .
\]

The drift is usually simply a translation of each slice, and if we assume the drift is constant across each vesicle, this corresponds to a shear transformation on the vesicle. Enforcing spherical shape as a function of the slice direction, we get the, per ellipsoid, drift parameters

\[
S_x = \frac{DE - BE}{AB - D^2} \ , \quad S_y = \frac{DE - AF}{AB - D^2} .
\]

To get an estimate for the drift per section, we average the drift parameters for each ellipsoid present in that section. The resulting estimate is thus slightly smoothed if drift varies heavily.

Datasets

**FIB-SEM Dataset**
- 1065 × 1536 × 2948 voxels
- Emulates membranes
- Emulates vesicles
- CA1 Hippocampus brain region of healthy adult mouse

**Synthetic Dataset**
- 200 × 300 × 300 voxels
- Emulates vesicles
- Emulates membranes

Experiments & Results

**FIB-SEM Dataset**
- Section-by-section drift estimate on a synthetic dataset with known drift.
- Experiment with standard registration methods using Cross-Correlation and Locally Orderless image registration was similarly ineffective at finding the correct drift.

**Synthetic Dataset**
- State of the art image registration methods fail to find the correct drift.
- Estimating drift using an ellipsoid model is both feasible and highly accurate in areas across sections with near constant drift.
- A more accurate result may be possible by estimating fitting the ellipsoids only across pair-wise sections.

Conclusion

- State of the art image registration methods fail to find the correct drift.
- Estimating drift using an ellipsoid model is both feasible and highly accurate in areas across sections with near constant drift.
- A more accurate result may be possible by estimating fitting the ellipsoids only across pair-wise sections.

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