X-ray2EM: Uncertainty-Aware Cross-Modality Image Reconstruction from X-ray to Electron Microscopy in Connectomics

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Abstract

Comprehensive, synapse-resolution imaging of the brain will be crucial for understanding neuronal computations and function. In connectomics, this has been the sole purview of volume electron microscopy (EM), which entails an excruciatingly difficult process because it requires cutting tissue into many thin, fragile slices that then need to be imaged, aligned, and reconstructed. Unlike EM, hard X-ray imaging is compatible with thick tissues, eliminating the need for thin sectioning, and delivering fast acquisition, intrinsic alignment, and isotropic resolution. Unfortunately, current state-of-the-art X-ray microscopy provides much lower resolution, to the extent that segmenting membranes is very challenging. We propose an uncertainty-aware 3D reconstruction model that translates X-ray images to EM-like images with enhanced membrane segmentation quality, showing its potential for developing simpler, faster, and more accurate X-ray based connectomics pipelines.

Main Contributions

- The first utilization of deep learning techniques to translate between the X-ray and EM modalities in connectomics.
- Our model demonstrates state-of-the-art reconstruction quality with 3D consistency and further improves the membrane segmentation performance.
- Our model also provides interpretable uncertainty maps during 3D reconstruction.

Methods

Uncertainty-Aware Cross-Modality Image Reconstruction Model. The 3D generator $G$ processes an image $x$ from the X-ray image domain $X$ to look similar to an image $y$ from the EM image domain $Y$ and outputs a corresponding uncertainty map. The 3D discriminator $D_Y$ learns to distinguish between a real EM image $y$ and a reconstructed output $G(x)$. The fixed pre-trained segmentation network $F_S$ measures the distance between the predicted membrane probability map $F_S(G(x))$ from the ground truth EM and the predicted membrane probability map $F_S(G(x))$ from the EM-like reconstruction. The model is optimized with a weighted combination (Eq. 1) of an adversarial loss (Eq. 2), a negative log-likelihood (NLL) (Eq. 3), and a segmentation-consistency loss (Eq. 4).

\begin{equation}
    L(G, D_Y, X, Y) = \psi_{GAN}(G, D_Y, X, Y) + \psi_{NLL}(G, X, Y) + \psi_{seg}(G, X, Y)
\end{equation}

\begin{equation}
    \psi_{GAN}(G, D_Y, X, Y) = \mathbb{E}_{y \sim p_{data}(y)}[-\log D_Y(y)] + \mathbb{E}_{x \sim p_{data}(x)}[\log(1 - D_Y(G(x)))]
\end{equation}

\begin{equation}
    \psi_{NLL}(G, X, Y) = \frac{1}{N} \sum_{i=1}^{N} \left| Y_i - G(x_i) \right|^2 + \frac{1}{2} \log(2\pi\sigma^2)
\end{equation}

\begin{equation}
    \psi_{seg}(G, X, Y) = \left| F_S(G(x)) - F_S(y) \right|
\end{equation}

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EM Reconstruction Results

<table>
<thead>
<tr>
<th>Method</th>
<th>PSNR</th>
<th>SSIM</th>
<th>DSC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full 2D</td>
<td>14.070</td>
<td>0.140</td>
<td>0.129</td>
</tr>
<tr>
<td>Full 3D</td>
<td>14.703</td>
<td>0.143</td>
<td>0.130</td>
</tr>
<tr>
<td>Full 3D w/ $L_1$</td>
<td>14.707</td>
<td>0.153</td>
<td>0.132</td>
</tr>
<tr>
<td>Full 3D + Seg</td>
<td>14.774</td>
<td>0.150</td>
<td>0.134</td>
</tr>
<tr>
<td>Ground Truth EM</td>
<td>14.738</td>
<td>0.149</td>
<td>0.132</td>
</tr>
</tbody>
</table>

Quantitative Evaluation on Reconstruction Quality. PSNR: peak signal-to-noise ratio; SSIM: structural similarity index measure; DSC: dice score; Best: best score; Underlined: second best score.

<table>
<thead>
<tr>
<th>Method</th>
<th>Jaccard</th>
<th>Dice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full 2D</td>
<td>0.613</td>
<td>0.656</td>
</tr>
<tr>
<td>Full 3D</td>
<td>0.599</td>
<td>0.590</td>
</tr>
<tr>
<td>Full 3D + Seg</td>
<td>0.600</td>
<td>0.602</td>
</tr>
</tbody>
</table>

Quantitative Evaluation on Membrane Segmentation. Jaccard score; Dice score; Best: best score; Underlined: second best score.

Uncertainty Estimation Results. Visualization of uncertainty estimation. Reconstruction & Uncertainty: Gaussian output distribution (mean & variance) generated by the models. Error: $L_1$ norm between the reconstruction and the ground truth EM.