Unsupervised Deep Learning approach for image registration in Correlative Microscopy for the localization of Nanoparticles

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Background incl. aims
Various microscopic methods such as scanning tunneling microscopy, atomic force microscopy, electron microscopy, and confocal laser scanning microscopy are already present in the ongoing research scenario and provide a lot of information to researchers. Each of these microscopic methods provides different information about the local structure of the sample under investigation, depending on the interaction of the probe with the sample. In general, the information obtained from two different microscopy methods is complementary. Correlative Light- and Electron Microscopy (CLEM) is the potential tool for determining the localization and identification of biological images combining different fluorescence labelling image with an electron microscope image. Automated Multi-modal registration with reference to the prediction of landmarks is a very challenging problem. We demonstrate the image registration of correlative light and electron microscopy (CLEM) images with the precise localization of landmark positions using a training-free, unsupervised deep learning approach.

Methods
Microscopy imaging with Deep Learning (DL) have transformed the field of biological sciences and is expected to be capable of providing relevant features of images to perform complex analysis tasks. The imaging problems include image segmentation or classification [1], object detection and image resolution are experimentally performed using Deep Learning methods. Deep learning techniques such as deep neural networks (DNNs) have produced ground breaking performance for computer vision and image classification. Image registration is the very first and crucial step for intracellular studies. This is achieved by aligning two different images of the same object taken by different image sources [2]. Images with different modalities can provide additional and unique information about the localized structures [3] e.g. cells, tissues, proteins, etc. Till now, various methods are proposed and even implemented either based on neural networks or supervised approach but they all are manually driven, require lot of time and high accuracy for landmarks. So, we implement a DL based architecture to achieve the multi-modal image registration without using any landmark assumptions or modeling of the images.
Results

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CLEM technique is used to get information at different length scales. The electron microscopy provides high resolution with detailed information of the sample to the nano level and the fluorescence microscopy highlights the different regions of interest using fluorescent labels. We apply feature mapping is achieved through a deep neural network and we optimized the homography hyperparameters using different learning rates at each hidden layer of neural network and regularly optimize for the minimized neural estimation loss (MINE) and generates the transformation matrix. With the calculated transformation matrices, the fluorescence channel can then be overlaid on the EM image quite easily with pixel accuracy for CLEM output. The obtained CLEM micrograph can be viewed in the graphic figure.

Conclusions

We are presenting an unsupervised DL approach for registering CLEM datasets with automated unsupervised localized landmarks. The DNN was trained by using training free MINE network with matrix exponential. It is time efficient and can handle CLEM data up to an image size of 5120 x 5120 pixels (even RGB images) and, due to the generated transformation matrices, registration of multi-channel images are also possible. The bottleneck of our neural network depends on the estimation that how fast and accurately the network optimized itself. Our DNN identifies the required features as precisely as the manual landmark based methods and promises to provide better optimized results. For training DNN, we do not require any image dataset and it is optimized in approx. 5 hours and after that, it does not require any further optimization for linear image pairs. Thus, the computing time is reduced to a few seconds per image pair and therefore, it is possible to process a large number of image datasets in a very short time even without human supervision or training.

Graphic:

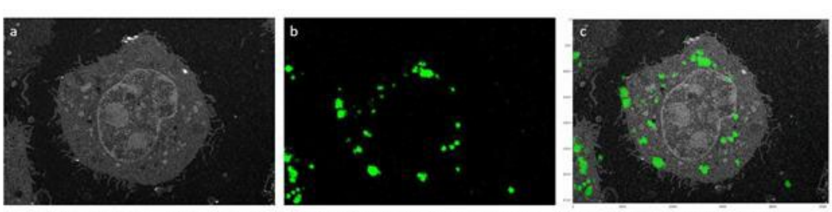

Fig. 1. Correlative Light-Electron Microscopy (CLEM) micrograph (a) represents electron microscopy image, (b) represents fluorescence microscopy image and (c) represents CLEM micrograph featuring nanoparticles (NPs).

Keywords:

Correlative microscopy, image registration, DNN

Reference:

1. G Balakrishnan et al., IEEE transactions on medical imaging 38(8) (2019), p. 1788
2. O Ronneberger, P Fischer and T Brox. in "International Conference on Medical image computing and computer-assisted intervention", (Springer, Cham)
3. A Nan et al., Medical Imaging with Deep Learning. PMLR (2020)