

EE367 : Computational Imaging and Displays - Project Proposal

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3D Deconvolution in Light Sheet Fluorescence Microscopy

Abstract

3D deconvolution of microscopy images is very important for being able to clearly view the features in the biological specimen at least achieving optimal performance if not diffraction limited resolution. There are various algorithms and techniques for 3D deconvolution. However, the size of the problem makes some of the well known methods consume a lot of time which means that real-time 3D volume viewing is not possible. In this project, I hope to introduce and implement techniques that can perform the deconvolution in reasonable time for single-view images.

1. Introduction

Light Sheet Fluorescence Microscopy (LSFM) is a relatively new technique and has gained a lot of research interest owing to its optical sectioning capabilities, good resolution and faster acquisition rates. It was the Nature Methods : Method of the year 2014^[1]. However, the LSFM optical setup is also more complicated than conventional confocal microscopes. This also implies that the aberrations are more serious and hence deconvolution becomes very important to deblur the captured images. There are 3 main categories for 3D deconvolution for LSFM -- iterative, non-iterative and blind deconvolution. Inputs can be either multiple views^[2] of the same specimen where in focus components in one view can be leveraged to deconvolve other views which are not affected and achieve faster convergence. However, in this project we will consider only single view due to the design of the optical setup. The effective blur and noise in the system can be modeled by understanding the 3D spatially varying Point Spread Function (PSF) of the system. The image formation is modeled as a convolution of the ground truth with the PSF and the goal of deconvolution is to undo this transformation. PSF of a system can be theoretically calculated using optical simulations, Fourier optics and ray tracing or experimentally measured by using beads of a known geometry beforehand. Typical non-iterative techniques used are Wiener deconvolution and inverse filtering. Iterative techniques like Richardson-Lucy (RL) and Alternating Direction Method of Multipliers with Total Variation prior (ADMM-TV)^[3]. Both these techniques are based on statistical learning and require us to have a good guess of the PSF of the system which may otherwise not result in convergence. Maximum Likelihood Estimate (MLE), Bayesian statistics or specific priors are employed in such iterative techniques. On the contrary, blind deconvolution techniques which are computationally more expensive do not need to know the PSF of the system accurately and both the PSF and deconvolved images are iteratively computed at each step. The RL algorithm can be modified slightly to work in a blind setting. Recently, there have been tremendous developments in using deep learning for super-resolution, deblurring, 3D reconstruction and deconvolution^[4,5]. One such approach has been proposed that exploits the difference/anisotropy in axial and lateral resolution and learns by looking through different layers (lateral and axial) to develop the image formation model to yield the deconvolved image. It will not be wrong to call such a technique auto-deconvolution and is similar to blind deconvolution but it makes use of itself to perform the deconvolution.

2. Description

The schematic below shows the optical setup of our light-sheet microscope. We employ structured illumination to limit the out of focus contribution which will help us to image deeper into the tissue.

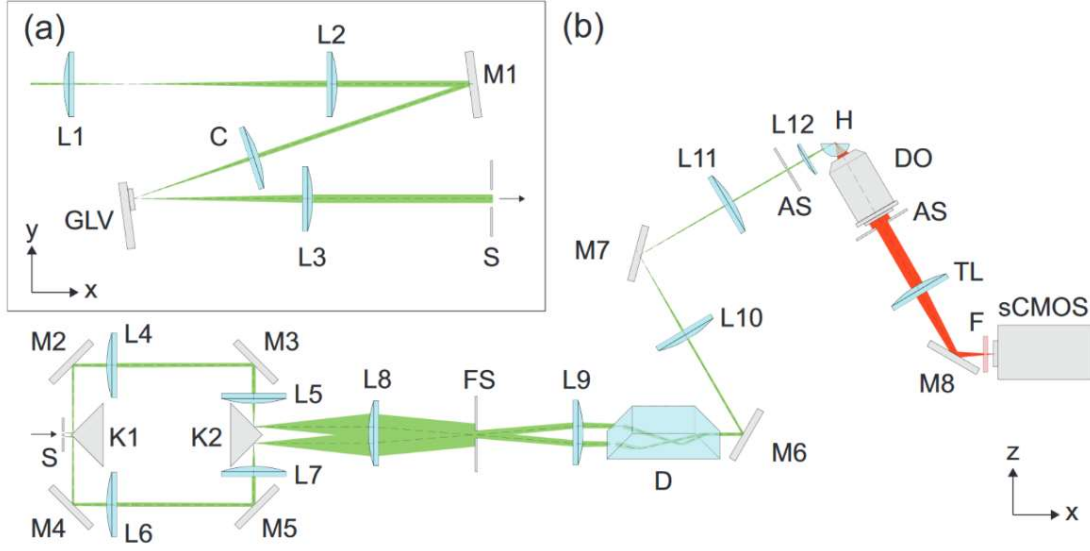


Fig. 1. Schematic of the Light Sheet Fluorescence Microscope with structured illumination

Since the optical setup is very complex, it is very difficult to theoretically model or simulate the PSF. We have instead chose to perform bead registration using fluorescent beads that have a diameter smaller than the diffraction limit to calculate the PSF accurately.

3. Proposal

The idea is to implement various techniques and see which algorithm performs better in terms of performance (quality) and speed (time efficiency).

To state the problem more formally, we can model the image formation as

$$\mathbf{Ax} = \mathbf{b}$$

where $\mathbf{b}$ is the captured stack, $\mathbf{x}$ is the sample volume that is being imaged, and $\mathbf{A}$ is the circulant matrix that represents convolution in 3 dimensions. However, it is important to note that when these operations are carried out in the iterative updates, the matrix $\mathbf{A}$ is never created or calculated explicitly: all operations are done in the Fourier domain using the OTF (magnitude of the Fourier transform of the PSF) and the Fourier transform of the stack.

Based on time required to get the bead registration for PSF measurement and actual specimen data, I wish to implement the following methods:

a. 3D Richardson Lucy Deconvolution (with or without Total Variation (TV) prior)

Richardson Lucy deconvolution for 3D is computationally expensive and hence the code should be made efficient enough. The idea is to use open source libraries based on NVIDIA CUDA ann OpenCL which help us leverage GPU and CPU compute effectively. The value of λ will be 0 if there is no TV prior.. The iterative updates for the 3D case are the same as in the 2D case. The iterative update is as follows:

$$\mathbf{x}^{(q+1)} = \frac{\mathbf{A}^T \left(\frac{\mathbf{b}}{\mathbf{A}\mathbf{x}} \right)}{\mathbf{A}^T \mathbf{1} - \lambda \left(\frac{\mathbf{D}_{\mathbf{x}\mathbf{x}}}{|\mathbf{D}_{\mathbf{x}\mathbf{x}}|} + \frac{\mathbf{D}_{\mathbf{y}\mathbf{x}}}{|\mathbf{D}_{\mathbf{y}\mathbf{x}}|} + \frac{\mathbf{D}_{\mathbf{z}\mathbf{x}}}{|\mathbf{D}_{\mathbf{z}\mathbf{x}}|} \right)} \mathbf{x}^{(q)}$$

b. Alternating Direction Method of Multipliers with Total Variation (ADMM-TV)

RL deconvolution is usually slow and takes many iterations to converge to a solution. ADMM form can speed up the process as well as increase likelihood that the algorithm converges to the true solution. ADMM formulation is very flexible in that it can incorporate various terms that can include PSF, noise (Poisson, Gaussian), distortion and other effects. With the help of proximal operators, one can iteratively solve for these and output the deconvolved image. ADMM^[6] is a very powerful formulation that solves problems of the form:

$$\begin{aligned} & \text{minimize} && f(x) + g(z) \\ & \text{subject to} && Ax + Bz = c \end{aligned}$$

where $\mathbf{x} \in \mathbf{R}^n$ and $\mathbf{z} \in \mathbf{R}^m$, where $\mathbf{A} \in \mathbf{R}^{p \times n}$, $\mathbf{B} \in \mathbf{R}^{p \times m}$, and $\mathbf{c} \in \mathbf{R}^p$. The augmented Lagrangian is

$$L_\rho(x, z, y) = f(x) + g(z) + y^T (Ax + Bz - c) + (\rho/2) \|Ax + Bz - c\|_2^2.$$

and can be solved iteratively by the following updates:

$$\begin{aligned} x^{k+1} &:= \underset{x}{\operatorname{argmin}} L_\rho(x, z^k, y^k) \\ z^{k+1} &:= \underset{z}{\operatorname{argmin}} L_\rho(x^{k+1}, z, y^k) \\ y^{k+1} &:= y^k + \rho(Ax^{k+1} + Bz^{k+1} - c) \end{aligned}$$

c. Isotropic reconstruction and deconvolution using Deep Learning

Major focus of this project is to see how Deep learning (Convolutional Neural Networks (**CNNs**)) can be used to model and learn the image formation model. The following cartoon shows the basic idea of how neural networks can be used for deconvolution ^[4,5].

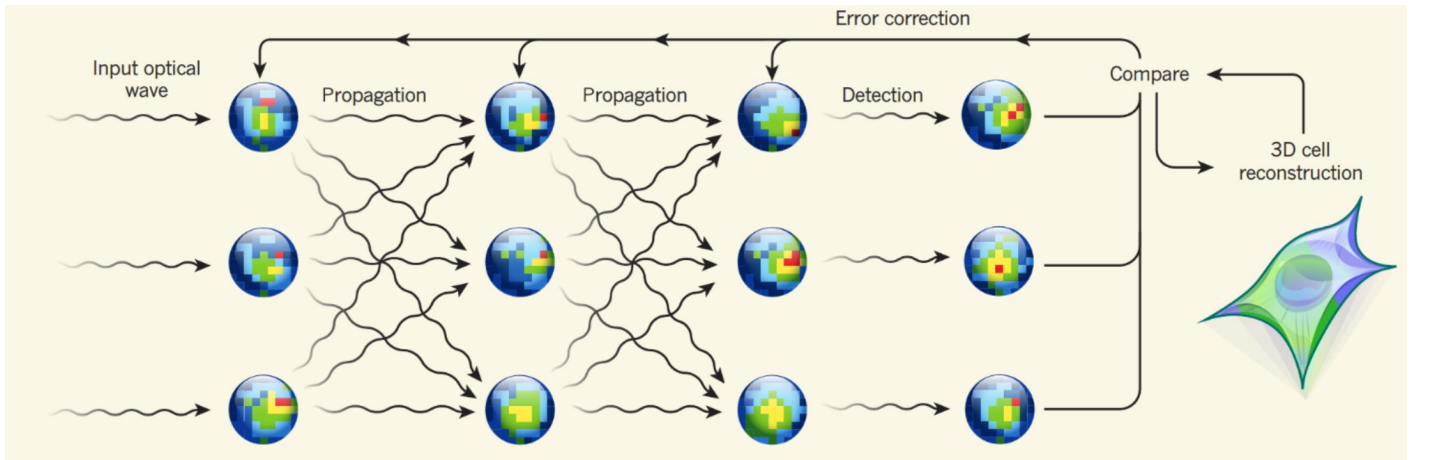


Fig. 1. Using machine learning for deconvolution. Image taken from Ref. 4

This approach can also be thought of as content-aware image restoration. Basically, this part of the project would be to try and implement the methods stated in Ref. 5 for deconvolution. In that paper, the authors use two architectures which can be explained as:

$C_{n,w,h}$: Convolutional layer with n filters of size (w, h)

$M_{p,q}$: Max pooling layer with a subsample factor of (p, q)

$U_{p,q}$: Upsampling layer with a subsample factor of (p, q)

Isonet-1 : $C_{64,9,9} - C_{32,5,5} - C_{1,5,5} - C_{1,1,1}$

Here, the first layer extracts features and maps the output non-linearly to resulting image estimate.

Isonet-2 : $C_{16,7,7} - M_{2,2} - C_{32,7,7} - M_{2,2} - C_{64,7,7} - U_{2,2} - C_{32,7,7} - U_{2,2} - C_{16,7,7} - C_{1,1,1}$

Here, the contractive part learns sparse representations of the input and skip connections that are sensitive to image details and the network then learns the residual to the input.

As no ground truth for the true signal is available, we make use of the resolution anisotropy between lateral and axial slices and aim to restore lateral resolution along the axial direction by appropriately defining a loss function.

4. Timelines

1. Get the bead registration and obtain the 3D PSF. (02/13/2018 - 02/20/2018)
2. Collect tissue images with the LSFM setup. (02/15/2018 - 02/20/2018)
3. Write code for methods 1 (RL) and 2 (ADMM). (02/13/2018 - 02/25/2018)
4. Write code for method 3 (Deep Learning). (02/20/2018 - 02/26/2018)
5. Analyze results and make final report. (02/26/2018 - 03/09/2018)

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