Cell Segmentation in Phase Contrast Microscopy by Constrained Optimization

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ABSTRACT

Utilization of automatic cell segmentation process is difficult to identify in a cell due to halo and shade-off distortions when observing the phase contrast microscopy images. Therefore, it is an important step to restore artifact-free images made ready for segmentation process. The main focus of this paper is to define a gradient projection algorithm to restore images based on the minimization problem of quadratic objective function with non-negative constraints. The proposed algorithm converges to a global minimum solution independent on initialization. The experimental result shows that the proposed algorithm can restore artifact-free images, which could produce high quality segmentation results using a simple thresholding method.

Keywords: Cell Segmentation, Constrained Optimization, Image Restoration, Inverse Problem, Phase Contrast Microscopy

INTRODUCTION

Phase contrast microscopy is a contrast-enhancing optical technique that can be utilized to produce high-contrast images of transparent specimens, such as living cells, microorganisms, thin tissue slices, lithographic patterns, fibers, latex dispersions, glass fragments, and subcellular particles (including nuclei and other organelles) that are not visible with simpler bright field microscope (Murphy, 2001). Phase contrast microscopy takes advantage of minute refractive index differences within cellular components and between unstained cells and their surrounding aqueous medium to produce contrast in these and similar transparent specimens (Hughes, 1958). However, shade-off and halo distortions could appear in phase images related to the geometrical and optical properties of phase contrast microscopy, creating difficulties in the phase segmentation process (Otaki, 2001; Piper, 2007). The shade-off effect
results in a degradation of contrast moving from
the center of the object toward its boundaries.
Phase images are usually surrounded by halos
obscuring details along the boundaries of the
specimen.

In the past decades, several attempts have
been made in phase contrast cell segmentation,
e.g., variance-based method (Bradhurst et al.,
2008), weak watershed transforms assembly
(Debeir et al., 2008), combination of watershed
and graph cut (Wiesmann et al., 2012), combina-
tion of hybrid watershed and region growing
(Orikawa & Tanaka, 2010), and deformable
model fitting methods proposed in (Ambuhl et
al., 2011; Seroussi et al., 2012). These methods
did not consider the image formation process of
microscopy images and treated them as natural
images. Rather than attempt to apply generic
segmentation methods on microscopy images,
Yin et al. proposed to model its image formation
process (Yin et al., 2012). Based on the linear
imaging model and input image properties, they
formulated a regularized quadratic cost function
and solved this problem by using non-negative
multiplicative updating (Sha et al., 2007). We
adopted their model and introduce our algorithm
to solve constrained quadratic programming
problem. We have chosen the gradient projec-
tion algorithm due to the simple constraints in
this restoration problem.

METHOD

Description of the Model

The linear model for microscope image is given
by the imaging equation:

\[ g(x, y) = h(x, y) * f(x, y) + C \]  \hspace{1cm} (1)

where \( h(x, y) \) represents the point spread
function (PSF), \( g(x, y) \) represents the recorded
image, \( f(x, y) \) represents the actual object, the
constant \( C \) corresponds to an image back-
ground and \( * \) indicates that 2D convolution.

The PSF for the phase contrast microscope
is:

\[ h(u, v) = \text{airy}(\sqrt{u^2 + v^2}) - \delta(u, v) \]

Let \( g(x, y) \) be the \( m \times n \) matrix, here
\( (x, y) \) take on only integer values. Then, the
matrix \( g(x, y) \) can be converted to a \( mn \times 1 \)
column vector by lexicographic ordering. Let this
column vector be \( g \):

\[
\begin{bmatrix}
g(1,1) \\
g(1,2) \\
\vdots \\
g(1,n) \\
\vdots \\
g(m,n)
\end{bmatrix}
\]

Then the linear model (1) can be expressed
using matrix notation:

\[ g = Hf + C \]  \hspace{1cm} (2)

where \( H \) is a block-Toeplitz matrix con-
structed from the PSF kernel, which is dis-
cretized as a \((2M + 1) \times (2M + 1)\) matrix. Each
row of \( H \) has only \((2M + 1) \times (2M + 1)\)
nonzero elements corresponding to the PSF
kernel, thus \( H \) is an \( mn \times mn \) symmetric sparse
matrix.

The first step to restore image \( f \) from
equation (2) is to remove non-uniform back-
ground. We refer to the (Wu et al., 2008) to
estimate background. The corrected image is
computed by subtracting the estimated back-
ground image from the recorded image. Thus,
new linear model is

\[ g = Hf \]  \hspace{1cm} (3)

Due to the ill-conditioned nature of the
image restoration problem, an attempt to solve
\( f \) from equation (3) by inverse transformation
can result in undesirable effect in the solution.
The Letter

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