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Joint Optimization of Spatial Registration and Histogram Compensation for Microscopic Images

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Abstract— **An iterative registration algorithm, the Lucas-Kanade algorithm, is combined with the histogram transformation to jointly optimize the spatial registration and the histogram compensation. Based on a simple regression model, a nonparametric estimator, the empirical conditional mean, is used for the histogram transformation function. The proposed algorithm provides a good performance in registering microscopic images that have different exposure or histogram properties, and can easily adopt other histogram compensation schemes and variations of the Lucas-Kanade algorithms due to its implicit flexibility. Joint registration with a third-order polynomial warp and compensation is conducted for microscopic images that have different magnifications.**

Keywords— **Histogram compensation, Lucas-Kanade algorithm, Registration.**

I. Introduction

Research on the registration of images has been significantly conducted in various fields, such as computer vision and medical/biological imaging. Superposing the multiple captured images into a single image can increase the dynamic range of the pixel levels and improve the signal-to-noise ratio if all images are properly aligned and exposed. Furthermore, aligning differently magnified images is of importance in constructing a 3D structure from serial section images. A serial section image of the transmission electron microscopy (TEM) is shown in Fig. 1. Using the serial section images of low-magnification, we reconstructed a 3D structure of trichomonas. Note that the shape of flagella (AF) can be more accurately described from the high-magnification image. However, the global position of AF should be tracked from the low-magnification images (see the arrows). Hence, we need an alignment between low and high-magnification images.

In the formation of images, the exposure settings and even the histogram of image are appropriately adjusted to obtain a good image depending on the object with illumination. Furthermore, during the process of film developing, each image can have different histogram properties even for the same exposure settings. When we align differently exposed images, we may use a feature-based technique, which is less sensitive to the exposure difference. However, to reduce the effect of the different exposure on the registration, we should compensate the exposure difference during registration. To perform the exposure compensation, two images should contain the same scene and be aligned with respect to the overlapped scene [1]. For an accurate registration, contradictively, the images should have the same exposure. Therefore, devising a joint optimization technique for the registration and the exposure, or the *histogram compensation* in a broad sense, is required.

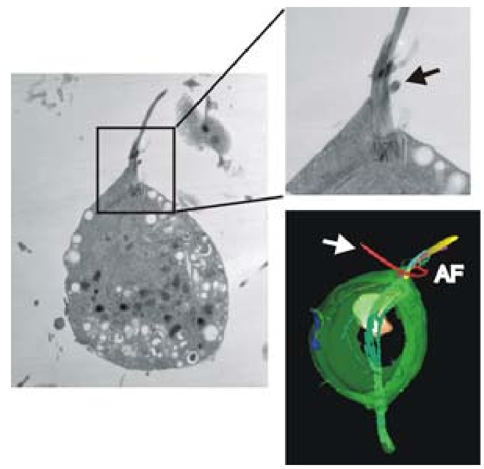

Fig. 1. 3D reconstruction of trichomonas from serial section TEM images with different magnifications (AF: anterior flagella).

Mann [5] and Candocia [1] conducted joint registration with the comparametric exposure compensation. In [1], a continuous piecewise-linear function fitting was performed on the comparagram in order to obtain a comparametric function for the exposure compensation, and the 8-parameter perspective warp is used for the registration. To solve a joint optimization problem, a closed form linear equation including both piecewise-linear function and the warp is derived. In this paper, an iterative algorithm, which is based on the Lucas-Kanade algorithm [3], is proposed to jointly optimize the spatial registration and the histogram compensation. The proposed approach has a separable optimization phases of registration and compensation based on the *coordinate descent method* [4, p. 227]. Hence, in terms of the flexibility in implementation, the proposed method is more advantageous than those of Mann and Candocia. In the proposed algorithm, the histogram compensation is conducted by using the his-

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togram transformation function (HTF). Based on the *simple regression model*, a nonparametric estimator, the empirical conditional mean (ECM), and parametric estimators, such as the polynomial functions (POL), are designed for HTF. For warping the microscopic images, a third-order polynomial approximation with 20 parameters is employed in this paper.

II. Histogram Compensation

In this section, a histogram compensation problem is considered based on the simple regression model using a pair of images that have the same scene.

A. Simple Regression Model and Nonparametric Estimators

Let $\mathbf{x} = (x, y) \in \mathbb{R}^2$ denote vectors containing the pixel coordinates. Let $U(\mathbf{x})$ and $V(\mathbf{x})$ denote a reference and an input images, respectively. Suppose that each image has m pixels and the images take values from a finite set $\mathcal{V} := \{v_i\} \subset \mathbb{R}$, of which size is n. Thus, n could be 256 as an example. Based on a simple regression model, consider a map η as $v \mapsto \eta(v)$, where $v \in \mathcal{V}$ and $\eta(v) \in \mathbb{R}$. We then define an average of squared error between two images, U and a compensated image $\eta(V)$:

$$\delta(\eta) := \frac{1}{m} \sum_{\mathbf{x}} [U(\mathbf{x}) - \eta(V(\mathbf{x}))]^2. \quad (1)$$

Here, the sum is performed over all of the pixels $\mathbf{x}$ in $V(\mathbf{x})$. We call η an HTF for the histogram compensation. An optimal η is given by the regression function between U and V. An inductive method to find the regression function is based on minimizing $\delta(\eta)$ with respect to η. An empirical optimum η^o that achieves the empirical minimum, $\min_\eta \delta(\eta) = \delta(\eta^o)$, is given by a nonparametric estimator defined as

$$\eta^o(v) := \sum_{\mathbf{x}} I_{\{V(\mathbf{x})\}}(v) \cdot U(\mathbf{x}) / \sum_{\mathbf{x}} I_{\{V(\mathbf{x})\}}(v), \quad (2)$$

if $\sum_{\mathbf{x}} I_{\{V(\mathbf{x})\}}(v) \neq 0$, and $\eta^o(v) := 0$ otherwise, for $v \in \mathcal{V}$. Here, for a set $S \subset \mathbb{R}$, $I_S(v) = 1$ if $v \in S$, and $I_S(v) = 0$ otherwise. We call this estimator ECM. To generalize or smooth the ECM curve for relatively small sample size cases, the Nadaraya-Watson estimator with the *Epanechnikov* kernel can be employed [7].

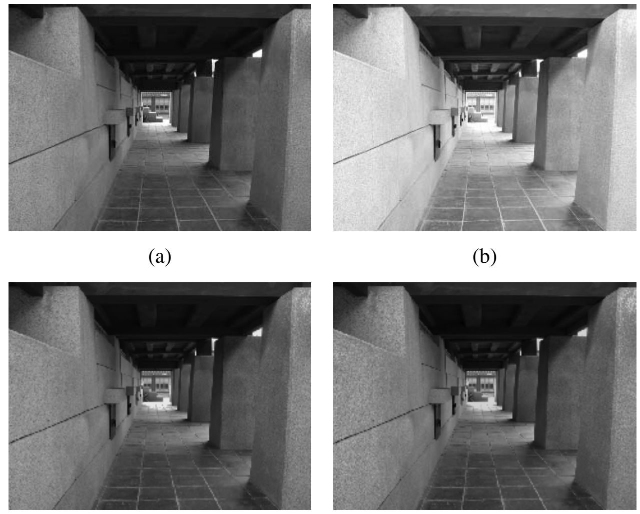
B. Parametric Estimators

In the aspect of generalization, designing parametric estimators is sometimes advantageous than the nonparametric case of ECM. To design a parametric estimator for HTF, we consider a global p-th order POL:

$$\eta_{\mathrm{POL}}(v) := a_0 + \cdots + a_{p-1} v^{p-1} + a_p v^p,$$

where $p = 1, 2, \ldots$, and $a_0, \ldots, a_p \in \mathbb{R}$ are the polynomial coefficients. Note that the polynomial is an approximation of ECM, and a special case of $p = 1$ is the *affine function*, which is used in the affine correction [6, Proposition III.3]. A continuous piecewise-linear (PWL) function fitting [2, p. 117] can be used.

In Fig. 2, an example of histogram (exposure) compensation for differently exposed images with ECM and POL



(a) (b) (c) (d)

Fig. 2. Histogram compensation for differently exposed images. (a) Reference image (1/80sec, f8). (b) Input image (1/30sec, f8, 36.93dB, HDE=36.92dB). (c) Compensated by ECM (9.83dB). (d) Compensated by POL (5th-order, 11.32dB, HDE=5.95dB).

is shown. The errors of (1) are shown in decibel. The error curves of ECM, POL, and PWL are compared in Fig. 3(a). The ECM error provides the minimum bound from its definition, and the POL curve shows a fast convergence with respect to the order. However, the PWL curve shows high errors even for large numbers of segments N. The estimators of ECM and POL in Fig. 2 are illustrated in Fig. 3(b) with PWL. Here, POL and PWL have similar designing complexity ($p + 1 = N - 1$ with $p = 5$). The shape of POL is very similar to that of ECM. However, the PWL curve shows a knot-placing problem at the right part of the curve.

C. Histogram Discrepancy Error

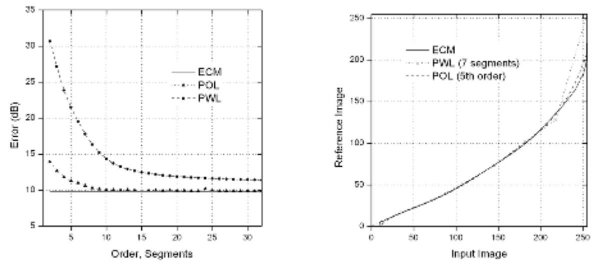
We now define an error that represents a degree of histogram difference between images. δ of (1) can be expanded with a function of η^o as $\delta(\eta) = \delta(\eta^o) + \rho_m(\eta)$, where $\rho_m(\eta) := m^{-1} \sum_{i=1}^{n} m_i [\eta^o(v_i) - \eta(v_i)]^2$ and $m_i := \sum_{\ell=1}^{m} I_{\{V_\ell\}}(v_i)$. Let us say that the histograms of images are 'identical' if an ECM η^o between images satisfies $\eta^o = \bar{\eta}(v) := v$ for $v \in \mathcal{V}$. We now define the *histogram discrepancy error* (HDE) as

$$\text{HDE:} \quad \rho_m(\bar{\eta}) = \delta(\bar{\eta}) - \delta(\eta^o) = \frac{1}{m} \sum_{i=1}^{n} m_i [\eta^o(v_i) - v_i]^2,$$

which represents an averaged error between ECM and $\bar{\eta}$. Note that HDE is equal to the error improvement through ECM η^o. Hence, if HDE is not zero, then we can reduce the compensation error $\delta(\eta)$ to $\delta(\eta^o)$. However, if HDE is zero, then we cannot reduce δ using any HTF, which implies the 'identical' histograms of two images.

III. Joint Optimization of Registration and Compensation

In this section, a joint optimization algorithm is proposed. For registering images, we employ the Lucas-Kanade



(a) (b)

Fig. 3. Histogram compensation. (a) Compensation error with respect to p and N. (b) Estimators for HTF.

algorithm [3], which is a Gauss-Newton gradient descent optimization scheme [4].

A. Spatial Transformations

Let $\mathcal{W}_t(\mathbf{x};\mathbf{p}) \in \mathbb{R}^2$ denote a warp for given $\mathbf{x}$, where $\mathbf{p} = (p_1, \ldots, p_t) \in \mathbb{R}^t$ is a vector of t parameters. The warp $\mathcal{W}_t$ takes the pixel $\mathbf{x}$ in the coordinate frame of the template image $T(\mathbf{x})$ and maps it to the sub-pixel location $\mathcal{W}_t$ in the coordinate frame of the image U. Here, the template image T is a part of V and has m_0 ($\le m$) pixels. For microscopic images, we may consider the affine warp $\mathcal{W}_6$, which includes the 2D translation and rotation operations, and the focal length. The perspective warp $\mathcal{W}_8$, which is composed of 8 parameters, is not appropriate for microscopic applications. Furthermore, a second-order polynomial approximation $\mathcal{W}_{12}$ of a warp shows a similar result of the first-order case, $\mathcal{W}_6$. However, we found that a *third-order polynomial approximation* $\mathcal{W}_{20}$, which includes the second-order *polynomial radial distortion model*, shows a good performance. The third-order approximation is given by

$$\mathcal{W}_{20}(\mathbf{x};\mathbf{p}) = \begin{pmatrix} p_1 + p_2 x + p_3 y + p_4 x^2 + p_5 xy + p_6 y^2 \\ \quad + p_7 x^3 + p_8 x^2 y + p_9 xy^2 + p_{10} y^3, \\ p_{11} + p_{12} x + p_{13} y + p_{14} x^2 + p_{15} xy + p_{16} y^2 \\ \quad + p_{17} x^3 + p_{18} x^2 y + p_{19} xy^2 + p_{20} y^3 \end{pmatrix}.$$

In the proposed joint algorithm, these 20 parameters will be estimated along with HTF for the histogram compensation in an iterative manner.

B. Joint Optimization Algorithm

In order to jointly optimize the spatial registration and the histogram compensation, we now propose a histogram-compensating Lucas-Kanade algorithm, which iteratively decreases the following overall compensation-registration error:

$$\delta(\eta, \mathbf{p}) := \frac{1}{m_0} \sum_{\mathbf{x}} \left[U(\mathcal{W}_t(\mathbf{x};\mathbf{p})) - \eta(T(\mathbf{x})) \right]^2, \quad (3)$$

with parameters η and $\mathbf{p}$ based on the coordinate descent method. Each iteration of the proposed algorithm is composed of the following two separable optimization phases:

- Histogram compensation: $\min_\eta \delta(\eta, \mathbf{p})$,
- Spatial registration: $\min_{\Delta\mathbf{p}} \delta(\eta, \mathbf{p} + \Delta\mathbf{p})$,

and an update $\mathbf{p} \leftarrow \mathbf{p} + \Delta\mathbf{p}$. The first phase is searching an optimal HTF, e.g., the ECM η^o of (2). The second phase is then searching an optimal increment of $\Delta\mathbf{p}$. Consequently the compensation-registration error of (3) decreases to a limit. In order to minimize $\delta(\eta, \mathbf{p} + \Delta\mathbf{p})$, we use a first-order Taylor expansion of $\delta(\eta, \mathbf{p} + \Delta\mathbf{p})$ [3] as

$$\frac{1}{m_0} \sum_{\mathbf{x}} \left[U(\mathcal{W}_t(\mathbf{x};\mathbf{p})) + \nabla U \frac{\partial \mathcal{W}_t}{\partial \mathbf{p}} \Delta\mathbf{p} - \eta(T(\mathbf{x})) \right]^2. \quad (4)$$

Using (4), A closed form of $\Delta\mathbf{p}$ that approximately achieves $\min_{\Delta\mathbf{p}} \delta(\eta, \mathbf{p} + \Delta\mathbf{p})$ is derived in [3]. The proposed algorithm is now summarized as follows:

Histogram-Compensating Lucas-Kanade Algorithm:

0) Set a template T with an initial warp with $\mathbf{p}$.
1) Warp U with $\mathcal{W}_t(\mathbf{x};\mathbf{p})$ to compute $U(\mathcal{W}_t(\mathbf{x};\mathbf{p}))$.
2) Compute η^o from (2) using T and U as the input and reference images, respectively, and obtain $\eta^o(T(\mathbf{x}))$.
3) Compute an optimal increment $\Delta\mathbf{p}$.
4) If $\|\Delta\mathbf{p}\| < \epsilon$, then stop with η^o and $\mathbf{p}$. Otherwise, $\mathbf{p} \leftarrow \mathbf{p} + \Delta\mathbf{p}$ and goto Step 1).

A panorama image is then constructed by mosaicking $U(\mathcal{W}_t(\mathbf{x};\mathbf{p}))$ and $\eta^o(V(\mathbf{x}))$. Since the estimator η^o for HTF is designed using only the template T, generalization of the estimators should be deliberated as shown in Section II-B. We can also successfully compensate U instead of V using the obtained $\mathbf{p}$.

Suppose that η^o and $\mathbf{p}^o$ satisfy $\delta(\eta^o, \mathbf{p}^o) = \min_{\eta,\mathbf{p}} \delta(\eta, \mathbf{p})$ for a given $\mathcal{W}_t$. The HDE for the joint optimization case is then given by

$$\text{HDE:} \quad \rho_m(\bar{\eta}) = \delta(\bar{\eta}, \mathbf{p}^o) - \min_{\eta,\mathbf{p}} \delta(\eta, \mathbf{p}).$$

If the proposed algorithm achieves $\mathbf{p}^o$, then we can calculate HDE to see the histogram difference.

IV. Numerical Results

We now show numerical results on the proposed joint optimization algorithm. Figs. 4(a) and (b) are pancreas TEM images, which have different magnifications, respectively. To align the images, the low-magnification image is enlarged by employing an interpolation technique as in Fig. 4(c). Here, Figs. 4(b) and (c) are for V and U in (3). A registration result by the Lucas-Kanade algorithm of $\mathcal{W}_{20}$ without the histogram compensation is shown in Fig. 4(d). We can notice the histogram (brightness) difference. Fig. 5(a) is a histogram compensated image based on ECM by using Fig. 4(d). As shown in a part image of Fig. 5(c), we can notice a serious misregistration (see the arrow) even though we reduce the histogram difference. However, we can notice a good registration result from the proposed joint algorithm as shown in Figs. 5(b) and (d). Here, HDE $\approx$ 12.89dB assuming an optimal $\mathbf{p}^o$ from the proposed joint algorithm.

The compensation-registration error with respect to the iteration is shown in Fig. 6. The registration without histogram compensation ('Lucas-Kanade') shows a large error as 14.18dB. Even though the error is significantly reduced to

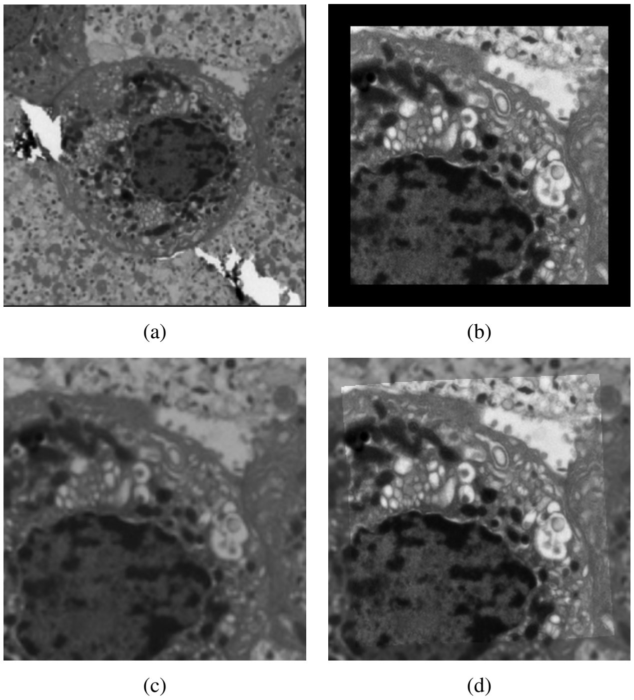


Fig. 4. TEM images of pancreas and registration. (a) Low-magnification of $5800\times$. (b) High-magnification of $13500\times$. (c) Interpolated low-magnification image. (d) Registered by Lucas-Kanade ($\mathcal{W}_{20}$) without histogram compensation (14.18dB).

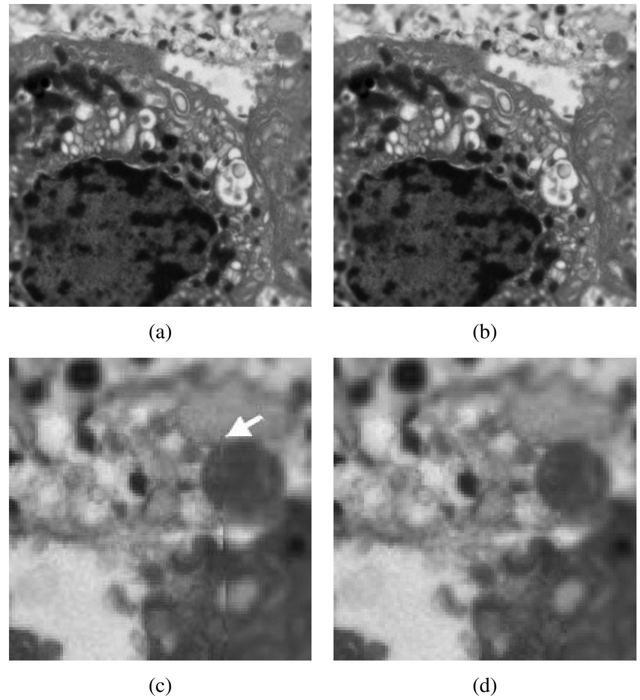


Fig. 5. Registration results. (a) Histogram compensation with ECM after Lucas-Kanade (9.35dB). (b) Proposed algorithm with ECM (8.43dB, HDE $\approx$ 12.89dB). (c) and (d) are magnified parts of (a) and (b), respectively.

9.35dB by separately compensating the histogram ('Lucas-Kanade + ECM'), the error curve is not monotonically decreased. The proposed algorithm with ECM shows a fast decreasing error curve and further reduces the error to 8.43dB. We can also obtain similar curves for the POL and PWL cases.

In Table I, the improvement of registration from the proposed joint algorithm is observed for different microscopic image pairs that have different histograms, i.e., HDEs. We can notice that the images that have larger HDEs show more improvements through the proposed algorithm.

TABLE I

COMPENSATION-REGISTRATION ERRORS AND HDES IN DECIBEL

Image pairs	A	B	C	D	E
Lucas-Kanade + ECM	9.35	6.37	7.59	5.28	4.87
Proposed/ECM	7.95	5.85	7.12	5.14	4.81
Improvement	1.40	0.52	0.47	0.14	0.06
HDE $\approx$	10.71	10.97	9.42	-0.49	-2.94

V. CONCLUSION

In this paper, we conducted a joint optimization of the spatial registration and the histogram compensation in an iterative manner. For TEM images, the Lucas-Kanade algorithm with a third-order polynomial warp and ECM for estimating HTF are employed. The proposed algorithm shows a better registration result compared to a separated registration/compensation scheme. The proposed algorithm has an advantage over the joint approaches of Mann [5] and

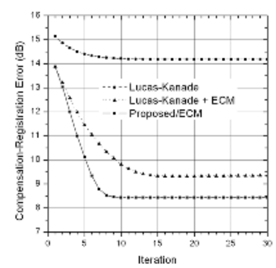


Fig. 6. Compensation-registration errors with respect to the iteration.

Candocia [1] especially in terms of flexibility. For example, we can easily adopt other estimators for HTF, such as POL and PWL. Furthermore, we can easily test various warps depending on applications, and even employ several different updating rules for the Lucas-Kanade phase.

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