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# Accelerated gradient-based methods for phase estimation in differential-interference-contrast microscopy

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In the last forty years, differential-interference-contrast (DIC) microscopy has gained popularity in biomedical research as an effective optical microscopy technique used to observe unstained transparent specimens under a transmitted-light configuration. The DIC image formation is caused by the interference of two orthogonally polarized beams, which are laterally split of a few tenths of a micrometer by a Wollaston prism, phase shifted when passing through different materials across the specimen and then successively recombined by a sliding prism. The resulting image has a three dimensional, high contrast appearance, which can be enhanced by adjusting the sliding prism along the direction of the split in order to introduce a uniform phase difference between the two beams. From the mathematical viewpoint, the DIC image acquisition is described by the following

nonlinear model [1, 5]

$$o_{k,\lambda} = \left| h_{k,\lambda} * e^{-i\frac{\phi}{\lambda}} \right|^2 + \eta_k, \quad (1)$$

where  $\phi \in \mathbb{R}^n$  is the true phase function,  $k$  is the rotation index and  $\lambda$  is the value of the RGB wavelength in micrometers,  $o_{k,\lambda} \in \mathbb{R}^n$  and  $h_{k,\lambda} \in \mathbb{C}^n$  are respectively the observed image and the DIC Point-Spread-Function at the  $k$ -th rotation of the specimen and illumination wavelength  $\lambda$ ,  $*$  is the convolution operator,  $|\cdot|^2$  is the component-wise square modulus and  $\eta_k$  is the realization of a Gaussian random variable with zero mean and variance  $\sigma^2$ . Following the rotational-diversity model proposed in [5] and furtherly extended in [1], one is interested in retrieving the specimen's phase function from a set of DIC intensity images acquired at different rotations of the specimen. Since this problem is highly ill-posed, one must look for a solution of the following regularized minimization problem

$$\min_{\phi \in \mathbb{R}^n} J_{LS}(\phi; o) + J_R(\phi), \quad (2)$$

where  $J_{LS}$  is a least-squares term measuring the distance between the observed image  $o_{k,\lambda}$  and the predicted image and  $J_R$  is the regularization term.

When a differentiable regularizer, such as a Tikhonov penalty term, is considered, one can address (2) by means of a nonlinear conjugate gradient method [5], which is particularly suited for least squares problems. However, the computation of the line search parameter at each iteration may require several evaluations of both the function and its gradient in order to ensure convergence [4], which significantly increases computational time when such evaluations are expensive, as is the case of the DIC functional. Furthermore, a conjugate gradient method can not handle the presence of a non differentiable regularizer, such as the total variational functional.

To overcome these limits, we propose to address the problem of phase estimation in DIC microscopy by means of a recently proposed proximal-gradient method [2]. The key features of this approach are the use of an Armijo-like rule to determine the step size along the descent direction and the possibility of adopting a variable metric to compute the proximal point. Since providing an efficient scaling matrix for the DIC problem is a quite difficult task, the acceleration of the method relies uniquely on a clever adaptive choice of the stepsize at each iteration [3]. The method is shown to be efficient both when the total variational functional and a smooth approximation of it is used. In the latter case, the method shows also significant improvements in terms of efficiency and stability with respect to widely used conjugate gradient methods.

## References

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