Cover Image: Inspired by the inclusion geometry model from the article “Numerical analysis of the factorization method for EIT with a piecewise constant uncertain background” H Haddar and G Migliorati 2013 Inverse Problems 29 065009.
TGV-based flow estimation for 4D leukocyte transmigration

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Abstract: The aim of this paper is to track transmigrating leukocytes via TGV flow estimation. Recent results have shown the advantages of the nonlinear and higher order terms of TGV regularizers, especially in static models for denoising and medical reconstruction. We present TGV-based models for flow estimation with the goal to get an exact recovery of simple intracellular and extracellular flows, as well as its implication on realistic tracking situations for transmigration through barriers. To study and quantify different pathways of transmigrating leukocytes, we use large scale 4D fluorescence live microscopy data in vivo.

Keywords: TGV, Optical Flow, Tracking, Leukocytes, Transmigration.

1 Introduction

In the past few years, mathematical reconstruction and analysis of 4D data received great attention. In a medical context, its meaning for the recognition and control of a huge variety of diseases is outstanding. An example for the influence of such data analysis is the movement of leukocytes. These cells are part of the immune system and are largely involved in defeating infectious diseases. Leukocyte transmigration denotes the process where leukocytes leave the circulatory system through endothelial cells and move towards a damaged tissue. Nowadays, the process of capturing leukocytes to the endothelial layer is well understood. However, many aspects of the mechanisms of the transmigration are still unexplored like the fact that leukocytes use two different pathways for transmigration. These pathways are referred to as transcellular and paracellular. A leukocyte taking the transcellular pathway moves straight through the body of an endothelial cell. During this process, it forms a hole into the endothelial cell, which gets closed after the leukocyte has left. If a leukocyte takes the paracellular pathway, it moves through junctions of endothelial cells. In this case, the hole is not built into an endothelial cell but into the contact between the cells. Little is known about the mechanical constraints or the kinetic differences of leukocytes preferring one of the pathways. The usage of 4D data allows us to get detailed insight into these processes. We use 4D (3D + time) in vivo data of a fluorescence microscope that shows the leukocytes as well as the endothelial cell contacts. Figure 1 shows a time step of a data set where the leukocytes are colored in green and the endothelial cell contacts are colored in red.

We analyze the behavior of the leukocytes to detect differences between the two pathways concerning e.g. movement, velocity and shape. In this way, we try to get more information about the advantages and disadvantages of the single pathways and aim at discovering the reasons for a preference in specific situations. Since we are especially interested in intracellular movement, we use L1 optical flow models with a total generalized variation (TGV) regularizer. By using a TGV prior it is possible to detect smooth transitions within flow fields. These transitions approximate realistic intracellular flows better than the piecewise constant parts and discontinuities that are detected by TV models (staircasing effect). Moreover, the TGV regularizer is still able to keep sharp discontinuities at flow boundaries related to the contour of leukocytes.
2 Higher-order regularization for optical flow

The performance of flow estimation is based on the assumption of brightness constancy. If we regard the brightness \( f \) of two consecutive images at a distinct place \((x, y)\) and time \(t\), we assume

\[
\frac{\partial f}{\partial t} + \frac{\partial f}{\partial x} \frac{dx}{dt} + \frac{\partial f}{\partial y} \frac{dy}{dt} = 0 .
\]

We are searching for a vector field \( u(x, y) = (u_1(x, y), u_2(x, y)) \) that satisfies (1), i.e. we want to solve the inverse problem

\[
K u = g ,
\]

with \( K = \nabla \cdot u \) and \( g = -f_t \).

To approximate a solution, we use a variational model

\[
\min_u J(u) = \min_u \{ \lambda D(u, f) + R(u) \}
\]

with a positive regularization parameter \( \lambda \), a data fidelity term \( D \) and a regularization term \( R \). We use an L1 norm for the data term. Thus, from (2) we get

\[
D(u, f) = \int_\Omega |f_t + (\nabla f)^T \cdot u| .
\]

A variety of former studies (e.g. [1]) consider total variation (TV) as a regularizer for the optical flow model, i.e.

\[
R(u) = \sup_{p \in C^2_0(\Omega; \text{Sym}^2(\mathbb{R}^n)), \|p\|_\infty \leq 1} \int_\Omega u \text{div} p .
\]

Recently, other imaging topics showed that higher order regularization can have significant advantages for specific applications [2, 3]. For the case of denoising, Benning et al. [4] show that the TGV regularizer is able to reconstruct smooth transitions as well as sharp edges. This specialty is a consequence of the combination of first and second order derivatives in the TGV functional. A TGV regularizer, where \( \beta \) weights first versus second order components, has the following form:

\[
R(u) = \sup_{p \in C^2_0(\Omega; \text{Sym}^2(\mathbb{R}^n)), \|p\|_\infty \leq \beta, \|\nabla p\|_\infty \leq 1} \int_\Omega u \text{div}^2 p dx .
\]

3 Optimization and numerical realization

We adapt the idea of higher order regularization to perform flow estimation for transmigrating leukocytes. A primal realization of the TGV functional is given by

\[
R(u) = \min_{u, v} \int_\Omega \alpha_1 |\nabla u - v| + \alpha_0 |\nabla v| .
\]
Obviously, ignoring one term results in a primal realization of the TV functional. To take advantage of this characteristic, we split the functional into a TV equivalent part and a remaining part. Therefore, we introduce Lagrange multipliers \( p \) and \( q \) and obtain a saddle point formulation for the overall objective functional \( J \):

\[
\min_{u \in \mathbb{R}^{2 \times N}, \nu \in \mathbb{R}^{2 \times N}} \max_{p \in P, q \in Q} \left\{ \alpha_1 (\nabla u - \nu, p) + \alpha_0 (\nabla v, q) + \lambda D(u, f) \right\},
\]

where the model parameters \( \alpha_1 \) and \( \alpha_0 \) are related to \( \beta \), and the convex sets \( P \) and \( Q \) are given by \( P = \{ p \in \mathbb{R}^{2 \times N}, \| p \|_\infty \leq 1 \} \) and \( Q = \{ q \in \mathbb{R}^{2 \times N}, \| q \|_\infty \leq 1 \} \). To solve this equation, we use a primal-dual algorithm, which is mainly based on an algorithm of Ranftl et al. [5], who use TGV for a stereo matching problem:

\[
p_{n+1} = \mathcal{P}_P \left( p_n + \tau_p \alpha_1 (\nabla \tilde{u}_n - \tilde{v}_n) \right) \tag{3}
\]

\[
q_{n+1} = \mathcal{P}_Q \left( q_n + \tau_q \alpha_0 (\nabla \tilde{v}_n) \right) \tag{4}
\]

\[
u_{n+1} = (I + \tau_u \partial D)^{-1} \left( u_n + \tau_u \alpha_1 \nabla \cdot (p_{n+1}) \right) \tag{5}
\]

\[
v_{n+1} = v_n + \tau_v (\alpha_0 \nabla \cdot q_{n+1} + \alpha_1 p_{n+1}) \tag{6}
\]

\[
\tilde{u}_{n+1} = 2u_{n+1} - u_n \tag{7}
\]

\[
\tilde{v}_{n+1} = 2v_{n+1} - v_n \tag{8}
\]

with stability parameters \( \tau_p, \tau_q, \tau_u, \text{and} \ \tau_v \). (3) minimizes the first order dual variable, (4) minimizes the second order dual variable. (5) minimizes the primal variables. (6) combines the first and the second order derivatives. (7) and (8) serve as relaxations. By ignoring (4),(5) and (8), and setting \( \tilde{v} = 0 \) in (3), this algorithm reduces to the L1-TV algorithm of Chambolle and Pock [6]. The operators \( \mathcal{P}_P \) and \( \mathcal{P}_Q \) project the variables onto the sets \( P \) and \( Q \):

\[
(P_P(\hat{\nu}))_{i,j} = \frac{\hat{p}_{i,j}}{\max\{1, \| \hat{p}_{i,j} \| \}}, \quad (P_Q(\hat{\nu}))_{i,j} = \frac{\hat{q}_{i,j}}{\max\{1, \| \hat{q}_{i,j} \| \}}.
\]

The resolvent operator in (5) evaluated at \( \hat{u} = u_n + \tau_u \nabla \cdot (p_{n+1}) \) is explicitly given by

\[
(I + \tau_u \partial D)^{-1}(\hat{u}) = \hat{u} + \begin{cases} 
\tau_u \lambda \nabla f & \text{if} \quad f_t + (\nabla f)^T \cdot \hat{u} < -\tau_u \lambda |\nabla f|^2 \\
-\tau_u \lambda \nabla f & \text{if} \quad f_t + (\nabla f)^T \cdot \hat{u} > \tau_u \lambda |\nabla f|^2 \\
-(f_t + (\nabla f)^T \cdot \hat{u}) \frac{\nabla f}{|\nabla f|^2} & \text{if} \quad |f_t + (\nabla f)^T \cdot \hat{u}| \leq \tau_u \lambda |\nabla f|^2.
\end{cases}
\]

### 4 Numerical results

To depict the differences between TV and TGV regularization for optical flow, we compare the results for both methods with the ground truth result of a 2D synthetic dataset from the IPOL database [7]. Figure 2 clearly shows the typical staircasing effect for TV regularization. In contrast, the regularization with TGV is able to approximate smooth transitions instead of piecewise constant parts. Additionally, the borders of the sphere are still visible in the TGV results. Table 1 verifies that the TGV regularizer reaches improved results compared to the TV regularizer for the chosen synthetic dataset. Both the average endpoint error and the average angular error are smaller for TGV.

Figure 3 shows the result of 3D flow estimation with TGV regularization for experimental leukocyte data. Since the cells are moving fast, we incorporated multiscale steps in the TGV algorithm. Otherwise, the large distances would prohibit a continuous flow inside a cell. To receive a better relation between regularization and resolution of the images, we adapted the regularization parameter in each multiscale step. The higher the resolution of the images the less we regularize. This avoids an enlargement of the influence of small fragments, especially in regions with only little flow. To utilize the whole 3D space of the data, we extended the dimension of the introduced algorithm. Similar to the synthetic data, the TGV approximation also achieves smooth transitions for the intracellular flows, while keeping the sharp edges at the borders of the moving areas. Moreover, the intracellular effect of transmigration becomes obvious through opposed directions of the vector field at the region of the barrier.
Figure 2. Vector field and color coding results for synthetic flows from [7]. The grey horizontal lines in the color coding results specify the position that was chosen for the 1D plots.

Table 1. Average endpoint error (EPE) and average angular error (AAE) of flow estimations for $\lambda = 15$.

<table>
<thead>
<tr>
<th></th>
<th>EPE</th>
<th>AAE</th>
</tr>
</thead>
<tbody>
<tr>
<td>TV</td>
<td>0.1491 pixels</td>
<td>1.3647°</td>
</tr>
<tr>
<td>TGV</td>
<td>0.0916 pixels</td>
<td>1.3512°</td>
</tr>
</tbody>
</table>

5 Conclusion

Applying TGV to optical flow leads to results, which bear similar characteristics as TGV denoising results. It is possible to approximate smooth transitions in situations where flow estimation with TV offers piecewise constant parts. Furthermore, the TGV regularizer keeps discontinuities at flow boundaries similar to TV. Both characteristics are important to gain information about the intracellular dynamics of migrating leukocytes. Cells are not expected to have strong edges in intracellular flow. However, cell contours are often related to the boundary of the real cell flow. Thus, TGV seems to be an adequate regularizer for analyzing leukocyte behavior.
The algorithm used in this paper can easily be improved by applying Bregman iterations to overcome a loss of contrast in the flow components, see [8] for further details. Another possible adaption is to improve the step sizes by line search. However, in this paper we focused on pointing out the results of applying TGV to a molecular cell biology problem.

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References


Figure 3. 3D flow estimation with experimental data of transmigrating leukocytes.