A NEW VARIATIONAL METHOD TO DETECT POINTS IN BIOLOGICAL IMAGES

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ABSTRACT

We propose a new variational method to isolate points in biological images. As points are fine structures they are difficult to detect by derivative operators computed in the noisy image. In this paper we propose to compute a vector field from the observed intensity so that its divergence explodes at points. As the image could contains spots but also noise and curves where the divergence also blows up, we propose to capture spots by introducing suitable energy whose minimizers are given by the points we want to detect. In order to provide numerical experiments we approximate this energy by means of a sequence of more treatable functionals by a Γ-convergence approach. Results are shown on synthetic and biological images.

***Index Terms*—** biological images, points detection, Γ-convergence

1. INTRODUCTION

In biological images, detection of points is an important issue. For instance in a membrane affected by some virus, a point can represent an immune cell which biologists wish to count. Another example is provided by target proteins in subcellular structures like organelles and vesicles. In all these applications, isolating points from the other structures like curves could be of vital importance. For more details on this subject we refer to [18] and the references therein.

In this work we propose a new model for point detection, where a point is considered as a singularity in the image given in term of a proper differential operator defined on a vector field. We provide a new variational formulation for detection of such singularities in noisy images as biological ones.

2. THE VARIATIONAL METHOD

In the variational model $\Omega \subset \mathbb{R}^2$ is an open set (the image domain), and $I : \Omega \to \mathbb{R}$ is the initial image. In order to predetect the point of the image, we use a vector field U_0 linked to the initial image I, which can be singular on points. Such a vector field can be provided by the gradient ∇f of the weak solution f of the classical Dirichlet problem.

$$\begin{cases} -\Delta f = I & \text{on } \Omega \\ f = 0 & \text{on } \partial\Omega. \end{cases} \tag{1}$$

Indeed it is possible to show that in a neighborood of a singular point of I the divergence of ∇f is equal to ∞. This feature makes the divergence operator the appropriate one to detect points.

From a practical point of view, working with vector field U_0 rather than I allows us to handle with a first order differential operator and permits us to formulate the minimization problem in a common functional framework.

Unfortunately the singular set of $U_0 = -\nabla f$ could contains several structures, that we want to remove from the original image like for instance curves or points generated by some noise. Hence, we have to clear away all the structures we are not interested in, by building up, starting from the initial data U_0, a new vector field U whose singularities are given by the points of the image I we want to isolate. Thus, from one hand we have to force the concentration set of the divergence measure of U_0 to contain only the points we want to catch, and on the other hand we have to regularize the initial data U_0 outside the points of singularities. To this end, we propose to minimize an energy involving a competition between a divergence term and the Hausdorff measure $\mathcal{H}^0$, which simply counts the number of points. More precisely the energy is the following

$$J(U, P) = \int_{\Omega\setminus P} |\mathrm{div}U|^2 + \lambda \int_{\Omega} |U - U_0|^p + \mathcal{H}^0(P), \tag{2}$$

where P denotes the set of points we want to detect and the exponent p is strictly less than 2. The restriction on p is due to the fact that, in general, the initial vector field U_0 belongs to the space $L^p(\Omega; \mathbb{R}^2)$ for any $p < 2$ (see [17]).

Like in the classical Mumford-Shah (see [15] and also [1, 5] for a general survey on free discontinuity problems) functional for the detection of contours, the first integral is a regularization term, the second one is a data term and the last one counts the singularities in the image.

It is worth noticing that this approach allows to remove curves in the image which usually is a difficult task in the literature. Indeed to achieve this goal, one should find a differential operator singular on nothing else but points. Such an operator exists (see [4]) but its

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discrete version recognized a curve in the image as a sequence of a points (see for instance [2]). On the contrary, our energy, thanks to presence of the measure $\mathcal{H}^0(P)$ which counts the number of points, strongly penalizes the presence of curve in the image, giving an infinite value for curves.

In order to provide computer examples, we must approximate the functional (2) by means of a sequence of more convenient functionals from the point of view of the numerical minimization. The approximation, we suggest in this paper, is based on the so called Γ-convergence, the notion of variational convergence introduced by De Giorgi (see [10, 11]). This theory is designed to approximate a variational problem by a sequence of different variational problems with more regularity. The most important feature of the Γ-convergence relies on the fact that it implies the convergence of minimizers of the approximating functionals to those of the limiting functional. For a general survey on the Γ-convergence we refer, among others, to [5, 8].

More in details, the energy we are interested in, is given by (2). In view of the discretization the main difficulty is represented by the counting measure $\mathcal{H}^0(P)$ which has to be substituted by proper integral term for the minimization. If we deal with a length measure, like for instance in the countour detecting problem, such an operation could be done in a useful way (see [13, 14]). The crucial idea is then to replace the term $\mathcal{H}^0(P)$ of the functional (2) by a more, variationally speaking, handy, functional involving a smooth domain whose perimeter is given by the length measure $\mathcal{H}^1$. Following some suggestions from the paper of Braides and March (see [6, 7]) such a functional is given by:

$$G_{\beta_\varepsilon}(D) = \frac{1}{4\pi}\int_{\partial D}\big(\frac{1}{\beta_\varepsilon} + \beta_\varepsilon \kappa^2(x)\big)d\mathcal{H}^1(x); \tag{3}$$

where D is a set of discs set containing the points of the set P, κ is the curvature of its boundary, the constant $\frac{1}{4\pi}$ is a normalization factor, and β_ε infinitesimal as $\varepsilon \to 0$. Roughly speaking the minimum of each functional is achieved on the union of balls of small radius, so that when $\beta_\varepsilon \to 0$ the functional shrink to the atomic measure $\mathcal{H}^0(P)$. Now we use the Modica-Mortola's approach (see [14]) to compute the length measure $\mathcal{H}^1$. This measure can be computed using a regularizing sequence depending on a regular scalar function w taking values into $[0,1]$:

$$\mu_\varepsilon(w,\nabla w)dx = \big(\varepsilon|\nabla w|^2 + \frac{V(w)}{\varepsilon}\big)dx, \tag{4}$$

where $V(w) = w^2(1-w)^2$ is a double well functional. It is shown in [13, 14] that when $\varepsilon \to 0$ the solution w_ε which minimizes (4) tends to a boolean function taking values in $\{0,1\}$, and such that the length of the interface between level sets 0 and 1 is minimal. Then (4) approximate the length measure $d\mathcal{H}^1$. So it gives an approximation of the first term of the integral in (3). The last step is to approximate the second term of the integral in (3), that is the curvature term κ. Such an approximation is based on a celebrated conjecture due to De Giorgi (see [9]) recently proven in [16]. This argument states that we can replace the term κ by the term $2\varepsilon\Delta w - \frac{V'(w)}{\varepsilon}$. So that we can formally write the complete approximating functional:

$$\begin{aligned}\Phi_\varepsilon(U,w): &= \int_\Omega w^2|\mathrm{div}(U)|^2dx + \frac{1}{4\pi}\int_\Omega \beta_\varepsilon(2\varepsilon\Delta w \\ &- \frac{V'(w)}{\varepsilon})^2dx \\ &+ \frac{1}{\beta_\varepsilon}\int_\Omega \mu_\varepsilon(w,\nabla w)dx \\ &+ \lambda\int_\Omega |U-U_0|^p dx,\end{aligned} \tag{5}$$

The first variation of this functional leads to the following gradient flow system

$$\begin{aligned}\frac{\partial U}{\partial t} &= 2\nabla(w^2\mathrm{div}U) - 2\lambda p(\frac{U-U_0}{|U-U_0|^{2-p}}) \\ \frac{\partial w}{\partial t} &= -4\frac{\Delta h}{\beta_\varepsilon} + \beta_\varepsilon h \\ &+ \frac{2}{\varepsilon^2}\frac{1}{\beta_\varepsilon}V''(w)h - 2w|\mathrm{div}U|^2\end{aligned} \tag{6}$$

where h is given by the equation

$$h = 2\varepsilon\Delta w - \frac{1}{\varepsilon}V'(w).$$

From one hand if $(U_\varepsilon, w_\varepsilon)$ is a minimizing sequence of Φ_ε, then w_ε must be very close to the values 1 when ε goes to 0, since the double well potential is positive except for $w_\varepsilon = 0, 1$ and w must be equal to 1 on the $\partial\Omega$. On the other hand, near the points where the divergence is very big, w_ε must be close to 0. When $\varepsilon \to 0$, β_ε goes to 0 as well, so that the singular set D is given by an union of balls of a small radius β_ε. Therefore, while the functions U_ε approximate a minimizer U of the original functional, the level set $\{w_\varepsilon = 0\}$ approximate the set P.

3. DETECTION

In our model the image contains an atomic measure. Thus, in order to find an initial vector field which copies the singularities of the initial image, we use the gradient of the solution of the Dirichlet problem (1). In this way we obtain a vector field whose divergence is singular on a proper set which contains the points we want to detect. In general this set could contain other structures. For instance if the initial image is a measure concentrated both on points and on curves, the divergence of $-\nabla f$ is singular on points and on curves at the same time. Besides if there is some noise in the image, it could be not clear how to differentiate the singular points due to the noise, from those we want to catch. As a consequence, by solving the problem (1), we get just a predetection, which has to be refined. To this purpose we search for a minimizer of the energy $\Phi_\varepsilon(U,w)$ via solving equations (6) with initial data U_0 given by $-\nabla f$. So we obtain a vector field U whose divergence is relevant only on the set P and a function w whose zeros give the set P.

4. DISCRETIZATION

The image is an $N \times N$ vector. We endowed the space R^{2N} with the standard scalar product and standard norm. Let $I \in \mathbb{R}^{2N}$. Then the gradient ∇I is an element of the space $\mathbb{R}^{2N} \times \mathbb{R}^{2N}$ given by: $(\nabla I)_{i,j} = ((\nabla I)^1_{i,j}, (\nabla I)^2_{i,j})$ where

$$(\nabla I)^1_{i,j} = \begin{cases} I_{i+1,j} - I_{i,j} & \text{if } i < N \\ 0 & \text{if } i = N, \end{cases}$$

$$(\nabla I)^2_{i,j} = \begin{cases} I_{i,j+1} - I_{i,j} & \text{if } j < N \\ 0 & \text{if } j = 0. \end{cases}$$

The discrete version of the divergence operator is simply defined as the adjoint operator of the gradient: $\mathrm{div} = -\nabla^*$. Then we can define the discrete version of the Laplacian operator as $\Delta I = \mathrm{div}(\nabla I)$.

4.1. Discretization in time

We simply replace $\frac{\partial U}{\partial t}$ and $\frac{\partial w}{\partial t}$ by $\frac{U^{n+1}_{i,j} - U^n_{i,j}}{\delta t}$ and $\frac{w^{n+1}_{i,j} - w^n_{i,j}}{\delta t}$ respectively. Then we write the system (6) in the form (for simplicity we omit the dependance on ε)

$$\begin{cases} U_1^{n+1} = & \delta t \Phi_{U_1}(U_n, w_n) \\ U_2^{n+1} = & \delta t \Phi_{U_2}(U_n, w_n) \\ w^{n+1} = & \delta t \Phi_w(U_n, w_n). \end{cases}$$

We initialize our algorithm with $U(0) = \nabla f$, where f is the solution of the problem (1). To initialize our algorithm, we need of an initial guess on w. So we choose $w(0) = 1$.

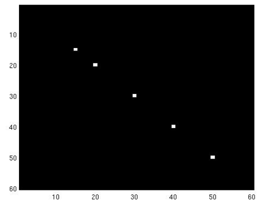
5. EXAMPLES

5.1. Parameter settings

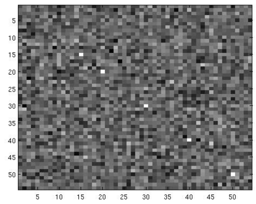
Before running our algorithm, all the parameters have to be fixed. The most important are ε and β_ε , which govern the set D approximating points we want to detect. Those parameters are related by the condition $\lim_{\varepsilon \to 0} \frac{\varepsilon}{\beta_\varepsilon} = 0$. Furthermore, since the mesh grid size is 1 and β_ε gives the radius of a ball centered in the singular point we want to detect, from a discrete point of view the smallest value we can take is $\frac{\sqrt{2}}{2}$. Then we use the values 0.2 for ε, 0.7 for β_ε. Concerning the parameter λ we mainly used the small value $\lambda = 0.1$, in order to force the algorithm to regularize as much as possible the initial data U_0. Since we deal with small values of ε, in order to have some stability, we must take a small discretization time step, Practically we mainly used the value $\delta t = 1 \times 10^{-6}$. Concerning the stop criterion we iterate the algorithm until max $\left\{ \frac{|U_1^{n+1} - U_2^n|}{|U_1^n|}, \frac{|U_2^{n+1} - U_2^n|}{|U_2^n|}, \frac{|w^{n+1} - w^n|}{|w^n|} \right\} \le 0.001$. Finally we set $p = 1, 5$.

5.2. Results

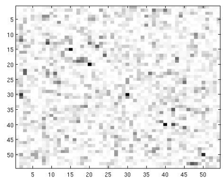
Our task is to catch the finest structure present in the image: the so called spots, that is the bright points. After the minimization process we obtain a function w who takes values close to 0 on the points of the image and close to 1 otherwise. This makes possible, by fixing a threshold value $\alpha = 0.5$, the detection of the spot. Then the points are simply given by the level-set $\{w_\varepsilon \le 0.5\}$. We test our algorithm on synthetic images first. The figure 1 shows how resistant to the noise our model is. In (a) we display a synthetic image with intensity 1 on five points and 0 otherwise. In (b) we add a significant gaussian noise to the initial image, the $PSNR$ is 5.5Db. In (c) we show the function w before fixing the threshold value α. Finally in (d) ,by choosing $\alpha = 0.5$, we retrieve the five points of the initial image in (a). We point out that a simple tresholding cannot be easily applied, since it would be much more difficult to fix a threshold value starting from the image, while our method allows to choose the threshold value in an easier way (see [12] for more details).



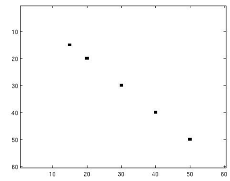
(a) Original image



(b) Noisy image



(c) the function w

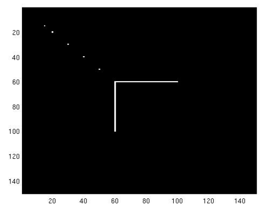


(d) the set $\{w \le 0.5\}$

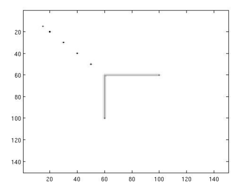
Fig. 1. *Synthetic noisy image PSNR 5.5Db: we test our algorithm on noisy images. When the parameters ε and β_ε are small as much as possible the detection is accomplished .*

In figure 2 we test our algorithm on curves and points at the same time. The result is that, as desired, our algorithm is capable of eliminating the curve from the initial image. We stress that this goal is not achieved by classical detecting-points methods (see for instance [2] on this subject). According to the continuous setting when ε takes values close to 0 the approximating energy (5) behaves similarly to the limit energy (2), so that the presence of the curve is penalized in the minimization process. Then the set $\{w_\varepsilon \cong 0\}$ contains nothing else but points. Finally in figure 3 and 4 we deal with biological images of spots. Our task is catching the finest structure present in the image. In figures 3 and 4 the isolated points are detected, while the branches of the cellule are not.

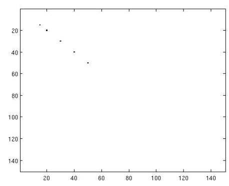
In every numerical examples, the parameters are all fixed as specified in the previous section.



(a) Original image

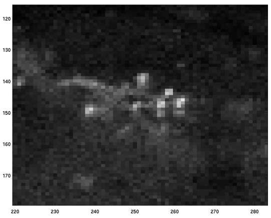


(b) the function w

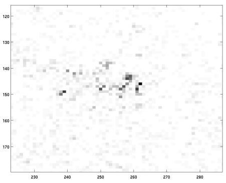


(c) the set $\{w \le 0.5\}$

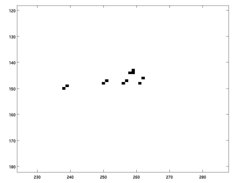
Fig. 2. *Synthetic image: curve and points are present in the initial image. As expected our method is capable of removing the curve from the image.*



(a) Original image

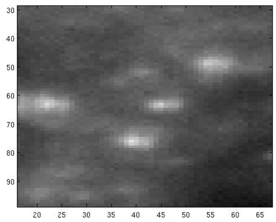


(b) the function w

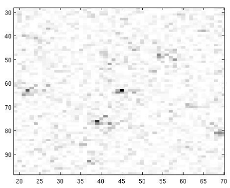


(c) the set $\{w \leq 0.5\}$

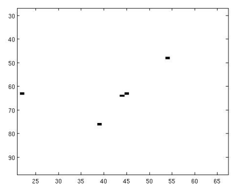
Fig. 3. (a) The original image of biological cell.(b) The function w takes values close to 0 on points.(c) By fixing a threshold value α we are capable of isolating the spots from the filament in the image.



(a) Original image



(b) the function w



(c) the set $\{w \leq 0.5\}$

Fig. 4. (a) The original image of biological cell with spots.(b) Even in this case the funcion w takes values close to 0 near the points we want to detect.(c) By fixing a threshold value α we isolate the spots in the image.

6. CONCLUSION

In this work, a new variational method for spot detection in biological images has been proposed and tested. We emphasize that, according to our knolewdge, our method it is the first method which makes possible isolating the spots from a filament in the observed image. Moreover it also permits in a noisy image to fix in a noisy image a threshold value in a simple and direct way.

Finally we believe that a suitable generalization of this method for the detection of spots and even filaments in 3-D biological images can be provided. This is a subject of our current investigation

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