A ROBUST ACTIVE CONTOUR APPROACH FOR STUDYING CELL DEFORMATION FROM NOISY IMAGES

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ABSTRACT

This work presents a generalized formulation of the Snake model defining new terms for the internal and the external energy functionals. These modifications conjugate features of the object contour as well as the inside of the shape. The obtained model is significantly more accurate spatially on the image plane and temporally on the frame sequence. In particular, the application to single cell analysis is in focus: In this context, we show how to cast the specific problem into the extended framework we propose. Shape descriptors and suitable metrics are then derived from the curve representation. The boundary identification produced through the classic formulation shows a poor and imprecise segmentation and leads to misleading metrics. The new model instead represents the boundary and the derived shape parameters in a way more consistent with the visual perception of shape evolution and deformation.

Key Words: *deformable models, snake, shape analysis, stem cells.*

1 INTRODUCTION

In the past few decades, the fast advances in computer science have revolutionized our ability of obtaining and analyzing medical and biological data, with impact on a wide range of applications in research and therapy. Computer vision has become a strong ally for the biomedical researcher and clinical operator, becoming a supporting technology for the medical staff [1]. In particular, researchers in the fields of stem cell research express the necessity of methodologies and procedures to quantify cell and tissue modifications after specific stimuli or along the natural growth. Even if the skills of biomedical staff in reading and interpreting the analysis data are beyond reach for nonmedical researcher, considering a set of medical or biological images, it is easy to note that, roughly speaking, the level of "noise" heavily affects the interpretation of the represented data: These images often exhibit poor contrast, non-uniform background illumination, resulting in boundaries that are not sufficiently sharp to be segmented. Very few works address this problem [2], and the majority focus on image enhancement or derive enhancement [3] to highlight edges. In some contexts these solutions show their insufficiency, missing a key point of the problem, namely the possibility of getting information not relying on edges.

In this perspective we propose a Snake framework that contributes with an improved yet agile new formulation. The model is able to cope with high level of noise, corrupted images, and to embed a model of the object of interest. The approach, close in spirit to the work in [4], combines synergically a number of ingredients, resorting to classical computer vision techniques, a priori biomedical information, mathematical modeling and bio-inspired modeling.

2 GENERALIZED SNAKE MODEL

In the context described in the Introduction it is of paramount importance to formulate a model accurate in the dynamic representation of the deformation and able to yield accurate shape metrics. The purpose of this section is thus to present a Generalized Active Contour framework and show how to specialize it to the analysis of single cell shape (object *A* in the following).

To begin with, we introduce Snakes as parametric models obtained as an energy minimizing curves. In the original formulation by Kass and coworkers [5], an acceptable solution C is characterized by an energy functional:

$$\mathcal{E}(C) = \mathcal{S}(C) + \mathcal{P}(C) = \int_{\partial A} \alpha(s) \left| \frac{\partial C}{\partial s} \right|^2 + \beta(s) \left| \frac{\partial^2 C}{\partial s^2} \right|^2 \mathrm{d}s + \int_{\partial A} \mathcal{F}\left[I(C(s)) \right] \mathrm{d}s \tag{1}$$

where the two terms $\mathcal{S}(C)$ and $\mathcal{P}(C)$ are respectively the *internal energy*, computed directly on the geometric model of the curve, and the *external energy*, a term accounting for the image *I* according to a transformation $\mathcal{F}(I) : \mathbb{R}^2 \to \mathbb{R}$.

The Generalized Active Contour we propose takes the form

$$\mathcal{S}(A, C) = \mathcal{S}\left(\left| \frac{\partial C}{\partial s} \right|, \left| \frac{\partial^2 C}{\partial s^2} \right|, \mathcal{S}_i(A, C) \right) \qquad \mathcal{P}(A, C) = \mathcal{P}(I(A), \mathcal{P}_j(A, C)) \tag{2}$$

where the extended energy functionals show a suitable combination of $\mathcal{S}_i$ and $\mathcal{P}_j$ terms. Each term tackles a specific aspect of *A* such as metrics of the shape, color or texture properties, or time evolution.

The rationale behind this approach is in the following statement [6]: *A plane shape $A \in \mathbb{R}^2$ has a 1-dimensional side given by features of its boundary $C = \partial A$; and a 2-dimensional side given by its interior. No successful theory of shape description can ignore one or the other.* In this sense, we extend the energy functional terms by integrating any other relevant aspect such as the geometric model, physical properties and even non video data. Generalized Active Contours provides a standard and manageable framework to do this. Hereafter, we specialize the discussion to suit the cell application, providing directions to build the terms $\mathcal{S}_i$ and $\mathcal{P}_j$ using linear probability density. This section gives a brief mathematical explanation, more examples and a more theoretical discussion are reserved for the full paper. As a general guideline, given a metric τ for *A* (computed on *A*, ∂A or outside *A*) a probability density $\Phi(\tau)$ can be derived via a learning phase, analytically, or inferred empirically. It is then possible to define an energy term $E_i(A, C)$, both for $\mathcal{S}_i$ and $\mathcal{P}_i$, as a function of $\Phi(\tau)$, whose minima correspond to high probability behaviors. The Energy term drives the Snakes towards a configuration compatible with $\Phi(\tau)$, still allowing some degree of freedom in the same way the probability density does.

Cells evolve in time undergoing a continuous change in shape appearance by protruding appendages that adhere to the culture surface (1*D*-side of the shape). In this sense, the smoothness imposed in the Snake's standard formulation counteracts this behavior: Conversely a curvature term allowing the boundary curvature κ to assume negative values enforces a spiky appearance. A simple energy term capturing this feature can use a piecewise linear probability density with maximum curvature value τ_{max}:

$$\mathcal{S}_{spike}(C) = -2 \frac{\tau_{max} - \tau_{spike}(C)}{\tau_{max}} \qquad \text{where} \quad \tau_{spike}(C) = \int_{\partial A} \kappa(s) \mathrm{d}s \quad \text{and} \quad \kappa(s) = \frac{\partial^2 C(s)}{\partial s^2}. \tag{3}$$

Similarly, the presence of a rest shape for the cell can also be exploited:

$$\max_{\tau} \left(\Phi(\tau) - \Phi(\tau_{rest}) \right)^2 \qquad \text{where} \quad \tau_{rest} \text{ is measured w.r.t. the rest shape.} \tag{4}$$

Cells viewed from a microscope often show a bright halo, due to the scattering properties of the living material enhanced by the thinness of the cells at the border. These optical phenomena are common in

back-lit organic materials. This information is related to the inside cell texture (f_W defined in A) and neighborhood features (f_b defined in ΔA). The related contributions (2D shape descriptors) are:

$$\tau_W(C) \;=\; \int_A [I_W(\omega) - f_W(\omega)]^2 \, d\omega \qquad f_W(\omega) = \text{inner texture prototype} \qquad (5)$$

$$\tau_b(C) \;=\; \int_{\Delta A} [I_b(\omega) - f_b(\omega)]^2 \, d\omega \qquad f_b(\omega) = \text{neighborhood prototype} \qquad (6)$$

This kind of measures maps directly into energy terms and drives the snake towards a suitable interior and a suitable neighbor background, a-priori defined (details here omitted). Hence, for the specific cell application, the Active Contour is based on the following global functionals, whose terms are linearly combined:

$$S(A,C) = S\left(\left| \frac{\partial C}{\partial s} \right|, \left| \frac{\partial^2 C}{\partial s^2} \right|, \kappa(C), \Phi(A), A_{rest} \right) \qquad \mathcal{P}(A,C) = \mathcal{P}(I(A), f_W(A), f_b(A)) \qquad (7)$$

We present in Fig. 1 the results of the application of the proposed model in some frames from a video sequence of a cell deformation. The standard Active Contour formulation is not able to correctly detect the cell shape: Errors accumulate over frames and end up with a general failure of the tracking algorithm. Nonetheless, even in the first frames of the sequence, the Active Contour fails in capturing all the fine details, such as protein spikes and ridges, yielding erroneous statistics.
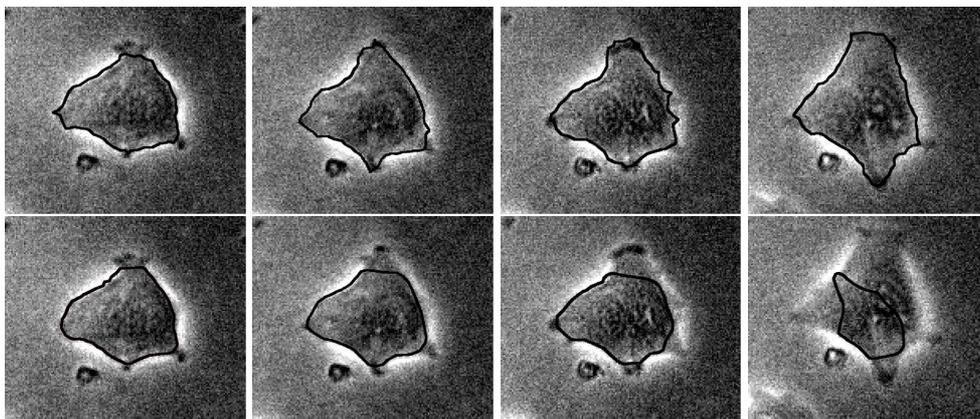

Figure 1: Cell dynamic detection. The first row is obtained using the proposed Snake model, while the second row is produced with the original formulation.

3   THE MEASURE OF SHAPE

The measure of shape mainly serves two purposes: on the one side there is a *control purpose*, namely the translation of the distance between two objects in the shape space, on the other there is a *classification purpose*, aiming at learning the shape representation. Several approaches can be exploited, among which we recall a statistical shape analysis approach based on landmarks and a functional approach relying on curve representations. The latter naturally exploits the accurate reconstruction of the shape provided by the Active contour: Given a planar shape $A \subset \mathbb{R}^2$ a simple way to derive a measurement $f(A) \in \mathbb{R}^n$ is to refer to linear filters: $f(A) = \int \psi(A) dA$, with $\psi(\bullet)$ suitable base functions. A polynomial set of functions ($\psi(x,y) = x^p y^q$) in the filter formulation produces the order $(p+q)$ curve moments $m_{p,q}(C)$. Although the moment description captures various levels of the shape distribution, single moments (especially the high order ones) link poorly to perceivable principal deformation, thus failing in supporting the perception with actual measurements. To provide a complete set of shape descriptor

able to describe the continuous evolution while keeping consistency with the perception, we instead introduce the concept of *sphericity* as a scaled ratio between shape area $\Phi(A)$ and perimeter $\Lambda(A)$, refer to the definition of *ellipticity* and *ellipticity variance* given in [7], and to the classical definition of total and average *curvature* κ_{tot} and κ_{avg}. We also complete the set of shape parameters by defining two additional quantities *spikeness* Σ and *boundary activity* Γ, which we consider strongly coupled with the visual activity of the cells:

$$\Sigma(\mathcal{C}) = \oint_{\mathcal{C}} \left| \frac{\partial^2 \mathcal{C}(s)}{\partial s^2} - \kappa_{avg}(\mathcal{C}) \right| ds \qquad \Gamma(\mathcal{C}) = \left(\Lambda(\mathcal{C}) - \frac{1}{n} \cdot \sum_{j=t-n}^{t-1} \Lambda(\mathcal{C}_j) \right)^2 \qquad (8)$$

where $\mathcal{C}_j$ refers to the shape $\mathcal{C}$ at time step j and n controls the temporal averaging. The computation of these quantities benefits from the underlying proposed Snake model, in that it is more accurate and conveys more information about the dynamics of the shape and the deformation process (Fig. 2).
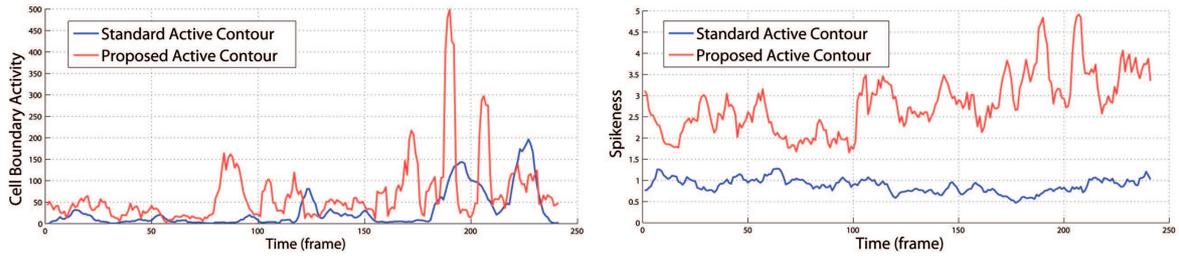

Figure 2: Shape metrics. Evolution of spikeness and boundary activity, according to the proposed and original snake model.

4 CONCLUSIONS

The development of the proposed Active Contour model is an element in a framework of study of wider perspective, where the measurement of the shape and its deformation is a central issue. In this regard, this model presents appealing properties of robustness and accuracy in the detection, validated with several cells in different experimental conditions. For the sake's of brevity, insights and many technical details have been omitted, and also references to the more general picture of the whole shape problem.

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