A Bayesian Approach for Joint Cell Tracking and Segmentation in Microscopy Videos

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1 Introduction

We have used an our novel joint segmentation and tracking algorithm which is an expansion of our method described in [1]. We ran our method on three data sets, namely Fluo-C2DL-MSC, Fluo-N2DH-GOWT1 and Fluo-N2DH-SIM+. The parameters set for each data set is presented in Table 1.

2 Method

2.1 Problem Formulation

Let $\mathcal{C} = \left\{C^{(1)}, ..., C^{(K)}\right\}$ denote K cells in a time lapse microscopy sequence, containing $\mathcal{T}$ frames. Let $I_t : \Omega \rightarrow \mathbb{R}^+$ be the t-th frame, in that sequence, where Ω defines the 2D image domain of I_t, and $t = 1, ..., \mathcal{T}$. We assume that each I_t is a gray-level image of $\mathcal{K}_t$ cells which form a subset of $\mathcal{C}$. Our objective is twofold and consists of both cell segmentation and frame-to-frame cell association defined as follows:

Segmentation: For every frame I_t, find a function $f_t \colon \Omega \rightarrow L_t$, (where L_t is a subset of $\mathcal{K}_t + 1$ integers in $[0, \ldots, K]$) that assigns a label $l_t \in L_t$ to each pixel $\mathbf{x} = [x, y] \in \Omega$. The function f_t partitions the t-th frame into $\mathcal{K}_t + 1$ regions, where each segment $\mathit{\Gamma}_t^{(k)} = \{\mathbf{x} \in \Omega | f_t(\mathbf{x}) = l_t = k, \}$ forms a connected component of pixels, in frame I_t, that belongs to either a specific cell in $\mathcal{C}$ or to the background, i.e. $\mathit{\Gamma}_t^{(0)}$.

Association: For every frame I_t find an injective function $h_t : L_{t-1} \rightarrow L_t$ that corresponds cell segments in frame $t-1$ and frame t. As we will show in the following, the segmentation and association steps are merged and $\mathit{\Gamma}_t^{(k)}, k \geq 1$ defines the segmentation of cell $C^{(k)}$ in frame t.

2.2 Time series analysis

For every cell $C^{(k)}$ there exist a number of properties that describe its state at a given time t. Let $\xi_t^{(k)}$ denote the hidden state vector that holds the true, unknown, state of the cell. In the following discussion the superscript (k) is removed for clarity. In our case the state vector holds the following features:

$$\xi_t = [c_{x_t}, c_{y_t}, v_{x_t}, v_{y_t}, \epsilon_t]^T = \left[\mathbf{c}_t^T, \mathbf{v}_t^T, \epsilon_t\right]^T \tag{1}$$

where $\mathbf{c}_t = [c_{x_t}, c_{y_t}]^T$ denote the COM of the cell at time t and $\mathbf{v}_t = [v_{x_t}, v_{y_t}]^T$ denote the COM velocities. The variable ϵ_t is the shape uncertainty variable, which will be explained in 2.3. We assume that the state

vector approximately follows a linear time step evolution as follows: $\xi_t = \mathrm{A}\xi_{t-1} + w_{t-1}$, where $\mathrm{A} \in \mathbb{R}^{5\times5}$ is the state transition model, and $w_t \in \mathbb{R}^5$ is the process noise drawn i.i.d from $\mathcal{N}(\mathbf{0}, \mathrm{Q}_t)$. In our case: $A_{i,i} = 1, i = 1\dots5$; $A_{1,3} = A_{2,4} = 1$. Since the true state is hidden, the observed state is $\zeta_t = \xi_t + r_t$, where $r_t \in \mathbb{R}^5$ is the measurement noise drawn i.i.d from $\mathcal{N}(\mathbf{0}, \mathrm{R}_t)$. The process and measurement noise covariance matrices $\mathrm{Q}_t, \mathrm{R}_t$ are assumed to be known.

In order to predict the state of a cell at t we utilize the Kalman Filter [3]. The predicted (a priori) state vector estimation and error covariance matrix at t given measurements up to time $t-1$ are: $\hat{\xi}_{t|t-1} = \mathrm{A}\hat{\xi}_{t-1|t-1}; \quad \Sigma_{t|t-1} = \mathrm{A}\Sigma_{t-1|t-1}\mathrm{A}^T + \mathrm{Q}_t^T$

The a posteriori state estimate and error covariance matrix at time t given measurements up to and including time t are: $\hat{\xi}_{t|t} = \mathrm{A}\hat{\xi}_{t|t-1} + G_t\left(\zeta_t - \hat{\xi}_{t|t-1}\right);\ \Sigma = (\mathrm{I} - G_t)\,\Sigma_{t|t-1}$

where the Kalman Gain matrix is given as: $\mathrm{G}_t = \Sigma_{t|t-1}\left(\Sigma_{t|t-1} + \mathrm{R}_t\right)^{-1}$.

2.3 Dynamic Shape model

The estimated segmentation of a cell $C^{(k)}$ in frame t, i.e. $\hat{\Gamma}_{t|t-1}^{(k)}$ is obtained by a translation of the cell segmentation in frame $t-1$:

$\hat{\Gamma}_{t|t-1}^{(k)} = \left\{\mathbf{x}|\left(\mathbf{x} - \hat{\mathbf{v}}_{t|t-1}^{(k)}\right) \in \Gamma_{t-1}^{(k)}\right\}$, where, $\hat{\mathbf{v}}_{t|t-1}^{(k)} \cdot 1$, is the estimated cell displacement. The respective signed distance function (SDF) $\hat{\phi}_{t|t-1}^{(k)} : \Omega \to \mathbb{R}$ is constructed as follows:

$$\hat{\phi}_{t|t-1}^{(k)}(\mathbf{x}) = \begin{cases} \min_{\mathbf{x}' \in \partial\hat{\Gamma}_{t|t-1}^{(k)}} d_E(\mathbf{x}, \mathbf{x}') & \mathbf{x} \in \hat{\Gamma}_{t|t-1}^{(k)} \\ -\min_{\mathbf{x}' \in \partial\hat{\Gamma}_{t|t-1}^{(k)}} d_E(\mathbf{x}, \mathbf{x}') & \mathbf{x} \notin \hat{\Gamma}_{t|t-1}^{(k)} \end{cases} \tag{2}$$

where $d_E(\cdot,\cdot)$ denotes the Euclidian distance and $\partial\hat{\Gamma}_{t|t-1}$ denotes the estimated segmentation boundary. We define the probability that a pixel $\mathbf{x}$ belongs to the domain of cell k by a logistic regression function (LRF):

$$\hat{\Phi}_{t|t-1}^{(k)}(\mathbf{x}) = P\left(\mathbf{x} \in \Gamma_t^{(k)}\right) \triangleq \left(1 + \exp\left\{-\frac{\hat{\phi}_{t|t-1}^{(k)}(\mathbf{x})}{\hat{\epsilon}_{t|t-1}^{(k)}}\right\}\right)^{-1} \tag{3}$$

where, $\hat{\epsilon}_{t|t-1}^{(k)}$ is the estimation of $\epsilon_t^{(k)} \triangleq d_H\left(\partial\Gamma_{t-1}^{(k)}, \partial\Gamma_t^{(k)}\right) \cdot \frac{\sqrt{3}\pi}{2}$ which denotes the calculated boundary uncertainty. The LRF slope is determined by $\epsilon_t^{(k)}$. We set $\epsilon_t^{(k)}$ such that the standard deviation of the probability density function (PDF) corresponding to $P\left(\mathbf{x} \in \Gamma_t^{(k)}\right)$ is equal to the Hausdorff distance between the aligned cell boundaries i.e. $d_H\left(\partial\Gamma_{t-1}^{(k)}, \partial\Gamma_t^{(k)}\right)$. Note, that large temporal fluctuations in a cell boundary, increase d_H, which in turn smooth the LRF slope and increase the shape uncertainty. Eq.3 defines our dynamic shape model.

2.4 MAP Segmentation and Association

We now present the flow of the proposed segmentation algorithm given the state vector estimation $\hat{\xi}_{t|t-1}$ and cell segmentation of the previous frame. Consider the image I_t with $\mathbf{c}_t^{(k)}$. We model the PDFs of the foreground and background intensities, $f_{FG}(\cdot)$ and $f_{BG}(\cdot)$ respectively by a mixture of Gaussians. The intensity based probability of being a cell or background is defined as follows:

$$P_t^{(BG)}(\mathbf{x}) = \frac{\alpha f_{BG}(I_t(\mathbf{x}))}{\alpha f_{BG}(I_t(\mathbf{x})) + (1-\alpha) f_{FG}(I_t(\mathbf{x}))};\ P_t^{(FG)}(\mathbf{x}) = 1 - P_t^{(BG)}(\mathbf{x}) \tag{4}$$

where $0 < \alpha < 1$ is a predetermined weight.

For each cell segment, in frame t, we construct a DSM, $\hat{\Phi}_{t|t-1}^{(k)}$, as explained in 2.3. We use the FM algorithm [2] to find the shortest path from each pixel $\mathbf{x}$ to the estimated COM of a cell k s.t. a speed image $\hat{S}_{t|t-1}^{(k)} : \Omega \to [0,1]$. The FM distance, $d_{FM}\left(\mathbf{x}, \hat{\mathbf{c}}_{t|t-1}^{(\mathbf{k})} | \hat{S}_{t|t-1}^{(k)}\right)$, is the minimal geodesic distance from $\mathbf{x}$ to $\hat{\mathbf{c}}_{t|t-1}^{(\mathbf{k})}$. In other words, the value of $\hat{S}_{t|t-1}^{(k)}(\mathbf{x})$ is the speed of a pixel $\mathbf{x}$ along the shortest path to $\hat{\mathbf{c}}_{t|t-1}^{(\mathbf{k})}$. For each pixel $\mathbf{x}$ in frame t we define its speed $\hat{S}_{t|t-1}^{(k)}(\mathbf{x})$ as the product of three terms: 1. The intensity based probability of belonging to the foreground (Eq.4). 2. The spatial prior of being part of a specific cell i.e. the DSM (Eq.3). 3. The "traversability" which is inverse proportional to the image edges in frame I_t and defined by $g(\nabla_{\mathbf{x}} I_t) = \left(1 + \frac{|\nabla_{\mathbf{x}} I_t|}{\|\nabla_{\mathbf{x}} I_t\|_2}\right)^{-2}$:

$$\hat{S}_{t|t-1}^{(k)} = P_t^{(FG)} \cdot \hat{\Phi}_{t|t-1}^{(k)} \cdot g(\nabla_{\mathbf{x}} I_t) \tag{5}$$

The absolute value of the spatial gradient, i.e. $|\nabla_{\mathbf{x}} I_t|$, can be interpreted as "speed bumps" which make the "FM journey" more difficult across edges.

The posterior probability that $\mathbf{x}$ belongs to C_k is inverse proportional[1] to the difference between its geodesic and Euclidean distances to $\hat{\mathbf{c}}_{t|t-1}^{(\mathbf{k})}$ (Fig.

$$P_t^{(k)}(\mathbf{x}) \propto \left(d_{FM}\left(\mathbf{x}, \hat{\mathbf{c}}_{t|t-1}^{(k)} | \hat{S}_{t|t-1}^{(k)},\right) - d_E\left(\mathbf{x}, \hat{\mathbf{c}}_{t|t-1}^{(k)}\right) + 1\right)^{-1} \tag{6}$$

The final segmentation is given as the MAP of (6):

$\Gamma_t^{(k)} = \left\{\mathbf{x} | \arg\max_{k' \in L_t} P_t^{(k')}(\mathbf{x}) = k\right\}$. In fact, we see that cell association is inherent to the defined segmentation problem, since each cell is segmented using its estimated properties from the previous frame. We disregarded cells with sizes smaller or larger than predefined thresholds T_{min} and T_{max} respectively. A mitosis was defined when a given cell was split into more than one connected component.

3 Parameters:

[1] $P_t^{(k)}(\mathbf{x})$ is normalized such that $\sum_{k'} P_t^{(k')}(\mathbf{x}) = 1$

Data Set	Seq	α	T_{min}	T_{max}	PatchSize	GMM
Fluo-C2DL-MSC	01	0.9	1000	50000	800	TRUE
	02	0.75	2500	250000	inf	TRUE
Fluo-N2DH-GOWT1	01	0.1	1000	100000	150	TRUE
	02	0.5	1000	100000	150	TRUE
Fluo-N2DH-SIM+	01	0.15	500	50000	150	FALSE
	02	0.8	300	30000	150	FALSE

Table 1. Parameters Table

References

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