Cellular tissue detection in microscopic images

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1 Problem statement

We are given one-channel intensity image of a cellular tissue from a microscope (Fig. 1). The problem is to find pixels of membranes, which are represented by bands of high brightness between cells.

2 Local approach

Our current approach is the following:

1 Find nodes. We define node as a junction of membranes.

2 Compute the most probable membrane trajectories between all pairs of nodes and estimate their likelihood based on image data.

3 Threshold the detected membranes on estimated likelihood.

On the first step we use Harris corner detector. It finds all ground truth nodes in addition to 50% wrong detections. Note that most of false positive detections

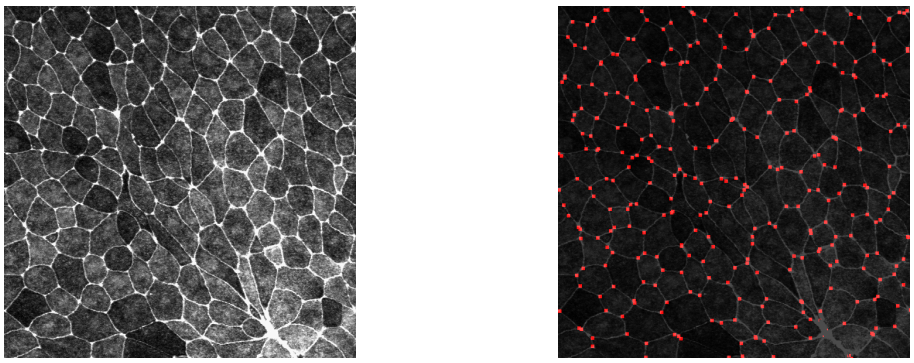

Figure 1: Left – source image. Right – found nodes.

belong to the interior of membranes. See Fig. 1 for examples of detected nodes.

On the second step we search for membranes containing pairs of nodes in form of continuous lines one pixel thick. We consider only the nodes with Euclidean distance less then certain threshold. Then we find a path that maximizes the sum of intensities of pixels between two nodes using dynamic programming. Whenever there is a ground truth membrane that connects a pair of nodes, the method detects it correctly. The problem is we don't know if there is a membrane for a certain pair of nodes. We address it on the next step.

On the third step we threshold the mean value of intensity of the detected membrane to make the decision if it represents some actual membrane in the image. Let m be the set of membrane points. We consider membrane m correct iff

$$\frac{1}{|m|}\sum_{p\in m} I_p > C$$

where C is a parameter of our method.

The described method detects membranes with 95% recall and 43% precision. Note that on the first step we find the nodes with recall more than 95%, so there are a lot of wrong nodes, which leads to more false positive membrane detections.

We found all the membranes and all the nodes along with some trash, and now we need to separate trash from correct candidates. The method is essentially local, because it treats neighbouring candidate membranes independently. Cells, bounded by the membranes must satisfy a requirements of a cell model, in terms of features like area, convexity, number of the membranes, etc.

3 Global optimization approach

In order to increase precision we are going to leverage prior information on the number of membranes incident to a node.

Let $Q = \{q_1, q_2, \ldots, q_s\}$ be the set of s candidate nodes found at the first step, $M = \{m_1, m_2, \ldots, m_n\}$ be the set of n candidate membranes $m_i = \{p_{i_1}, p_{i_2}, \ldots, p_{i_k}\}$ computed at the second step.

We introduce the hidden variables $T = \{t_1, \ldots, t_s\}, t_j \in \{0, 1\}$ which are the set of indicators corresponding to the nodes, and $X = \{x_1, \ldots, x_n\}, x_i \in \{0, 1\}$ which are the set of indicators corresponding to the membranes. Indicator should be 1 iff the candidate membrane/node really persists in the image.

We propose to optimize the following functional:

$$E(X,T) = \sum_{j=1}^{s}\psi_j(t_j) + \sum_{i=1}^{n}\phi_i(x_i) +$$
$$+\sum_{j=1}^{s}\sum_{l=1}^{k(j)}\xi_{jl}(t_j, x_{j_l}) + \sum_{j=1}^{s} h_j(x_{j_1}, \ldots, x_{j_{k(j)}}) \to \min_{X,T}$$

where $k(j)$ is the number of candidate membranes intersected at the j-th candidate node, and $j_1, \ldots, j_{k(j)}$ are the indeces of those membranes. This expression could be thought of as a graphical model (Fig. 2).

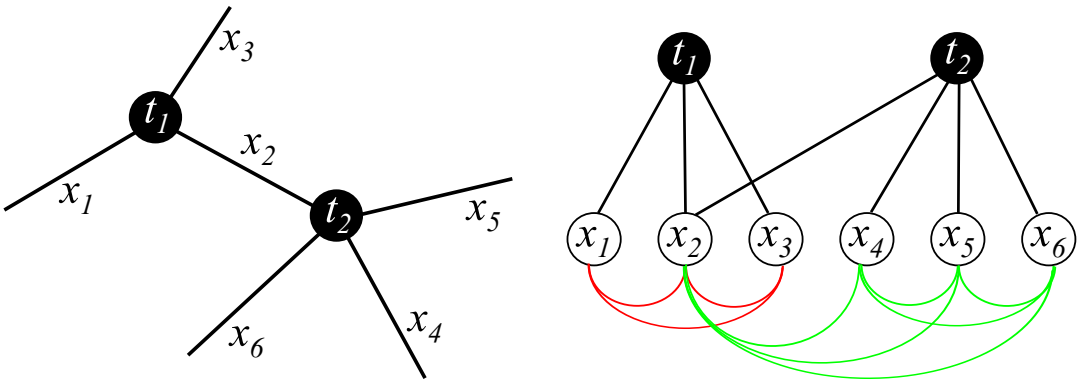

Figure 2: Representation of graphical model.
Left — the structure of cellular tissue. Vertices of the graph are nodes, edges — membranes. Each edge corresponds to a variable from the set X, each node — to a variable from T. **Right** — graphical model. Each membrane is connected to its end nodes and a group of membranes which share a node forms a higher order clique. Black color — pairwise terms, red and green — higher order terms.

The terms in the formulation have the following meaning: $\psi_j(t)$ considers brightness of the pixels that correspond to the j-th node or Harris detector output, $\phi_i(x)$ penalizes i-th membrane with small mean intensity:

$$\phi_i(x) = \begin{cases} \log\left(\frac{1}{|m_i|}\sum_{p\in m_i} I_p\right), & x = 1 \\ const, & x = 0 \end{cases}$$

ξ_{jl} forbids membranes without nodes on their ends:

$$\xi_{jl} = \begin{cases} +\infty, & \text{if } t_j < x_{j_l} \\ const, & \text{otherwise} \end{cases},$$

$h_j(t, x, \ldots)$ considers a number of membranes intersected at the j-th node:

$$h_j(x_{j_1}, \ldots, x_{j_k}) = -\log f\left(\sum_{l=1}^{k} x_{j_l}\right).$$

Function $f(x)$ is an empirical distribution of the number of membranes intersected at one node. We calculate it using statistics from manually marked images (see Fig. 3).

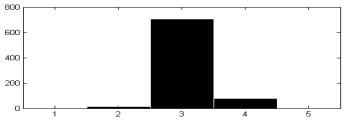

Figure 3: Histogram of the number of membranes intersected at one node. We have marked one of images manually to calculate it.