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Multiple objects detection in biological images using a marked point process framework

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ABSTRACT

The marked point process framework has been successfully developed in the field of image analysis to detect a configuration of predefined objects. The goal of this paper is to show how it can be particularly applied to biological imagery. We present a simple model that shows how some of the challenges specific to biological data are well addressed by the methodology. We further describe an extension to this first model to address other challenges due, for example, to the shape variability in biological material. We finally show results that illustrate the MPP framework using the "simcep" algorithm for simulating populations of cells.

Contents

1. Introduction

Detecting multiple instances of a given object from images is a major issue in computer vision as it often represents the first step towards image understanding and interpretation. For example, in remote sensing, the description of land cover (especially when dealing with high resolution images) relies on a previous detection of objects in the scene such as buildings, trees or roads. In computational biology this problem also appears frequently in order to evaluate, characterize or classify a population of biological objects such as cells, vesicles within cells or RNA/protein complexes [1,2]. A particular case can be the initialization of a tracking algorithm to study, for example, vesicles trajectories [3]. In addressing biological applications some specific issues have to be considered due to the variability of biological material within and between different classes of objects. For example, objects representing other biological material may be mixed with the actually targeted ones, thus the image cannot be simply modeled as a collection of objects of interest in a background. Besides, the size of these targeted objects is sometimes close to the voxel size, making the differentiation between objects and noise particularly complicated. In this paper,

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we present a methodological framework that provides tools to solve the different issues raised by multiple biological objects detection from microscopic images. We will particularly develop the following:

- Issue 1: How to address the intensity heterogeneity that prevents from considering a global threshold on the intensity in order to separate to objects from background ?
- Issue 2: How to deal with nuisance objects that do not belong to the targeted class of objects but cannot be considered as background neither ?
- Issue 3: How to deal with a high density of objects that generates clusters of possibly overlapping objects ?
- Issue 4: How to handle the shape variability between objects ?
- Issue 5: How to detect objects that consist of a few pixels ?
- Issue 6: How to deal with both 2D and 3D datasets ?

Throughout the literature that addresses this problem, we distinguish both global as well as local methods. Global methods usually consider a threshold to separate the background from pixels belonging to objects. Each n-connected group of pixels tagged as object is then analyzed. A watershed segmentation is then performed on the distance map inside each component to split it into individual objects. Each individual object is finally selected or rejected depending on its size and shape, considering for example a circularity parameter. This classical approach is usually the one proposed by common image analysis software such as Matlab, the particle analyzer of Fiji or Cell Profiler [4,5]. Nevertheless, issue 1 is not addressed within this approach. In consequence, in order to remove background variation, a high pass filter has to be previously applied. Issues 2,3 and 4 are partially solved if the objects of interest have more or less a circular shape and can be bounded by particular minimum and maximum sizes that discriminate them from nuisance objects. The shape of the detected object is arbitrarily defined by the watershed algorithm, so issue 4 is not addressed. Finally, issue 5 is not addressed in case of noisy data. In local approaches, a first step usually consists of seeds detection. A growing process then extends each seed to define an object using, for example an active contour or marker controlled watershed. This process allows the object shape recovery only if they are initially properly localized by the seeds. Therefore, the seeds detection is crucial. Some strategies to obtain these seeds include local maxima after a global threshold or a template matching process [6]. Issue 1 can be partially solved by considering a low threshold when seeds are defined by local maxima. Issue 2 is not addressed whereas clusters are split arbitrarily when two growing objects intersect.

In this paper we present the marked point process modeling (MPP) as a framework to solve the different issues described above. These models derived from the application of point processes to spatial statistics. They have proven their efficiency and robustness in various fields of computer vision in order to evaluate populations of, for example, trees, buildings, roads, people in a crowd or flamingos. A survey of marked point processes applied to image analysis can be found in [7]. Herein we focus on biological images and show how to derive specific models to accurately address the different issues mentioned above.

2. Method

2.1. Marked Point Process

Let us consider an object space $\mathcal{O} \subset \mathbb{R}^m$ that contains the geometrical description of the object of interest. For example if we consider the set of disks with radius bounded by r_{min} and r_{max}, then $\mathcal{O} = [r_{min}, r_{max}] \subset \mathbb{R}$.

We consider the configuration set Ω as the union of all the possible finite sets of objects lying in a subspace $\mathcal{S}$ of $\mathbb{R}^m$ defined by the support of the image:

$$\Omega = \bigcup_{i=0}^{\infty} \Omega_i, \tag{1}$$

where

$$\Omega_i = \{\omega_1, \ldots, \omega_i\} \in (\mathcal{S} \times \mathcal{O})^i \tag{2}$$

is the set of configurations containing exactly i objects, $\omega_i = (p_i, m_i), p_i \in \mathcal{S}$ is the center of the object and $m_i \in \mathcal{O}$ are the marks. We define a marked point process [8] by athe Gibbs density as follows:

$$\forall \omega \in \Omega, d\pi(\omega) = \frac{1}{Z} \exp\left[-U(\omega)\right] d\pi_0(\omega), \tag{3}$$

where π_0 is the measure of the Poisson process and $U(\omega)$ is the energy function that evaluates each configuration of objects. The lower the energy function value the more probable is the particular object configuration. In the context of image analysis, the energy function embeds a data term, $U_D(\Omega|I)$, that evaluates the consistency of any object with respect to the data I as well as a prior, $U_P(\Omega)$, that reflects constraints on the objects geometry and repartition in the image plane.

Let us consider a first example, shown in Fig. 1, where the image $\{I(s), s \in L\}$ on the lattice L consists of circular cells on a dark background. We first define a data term that measures the contrast between a candidate object and its neighborhood as follows:

$$P(I|\Omega = \{\omega_1, \ldots, \omega_i, \ldots, \omega_n\}) = \exp -U_D(\Omega|I) \text{ with} \tag{4}$$
$$U_D(\Omega|I) = \sum_{i=1}^{n} u_d(\omega_i),$$

where $u_d(\omega_i)$ is a contrast term we defined as:

$$u_d(\omega_i) = \begin{cases} 1 - \frac{d(\omega_i)}{d_0} & \text{if } d(\omega_i) < d_0 \\ exp\left(\frac{d_0 - d(\omega_i)}{3d_0}\right) - 1 & \text{otherwise.} \end{cases} \tag{5}$$

In Eq. (5), $d(\omega_i)$ is a distance between pixels in the object ω_i and pixels in the external boundary $\partial\omega_i$ (see Fig. 2). For example the Bhattacharyya distance is defined by:

$$d(\omega) = \frac{1}{4} \frac{(\mu_o - \mu_b)^2}{\sigma_o^2 + \sigma_b^2} + \frac{1}{2} \log\left[\frac{\sigma_o^2 + \sigma_b^2}{2\sigma_o\sigma_b}\right], \tag{6}$$

where μ_o (resp. μ_b) and σ_o^2 (resp. σ_b^2) are the mean and variance of pixels in ω (resp. $\partial\omega$.

In order to prevent object overlap as much as possible, we add the following prior:

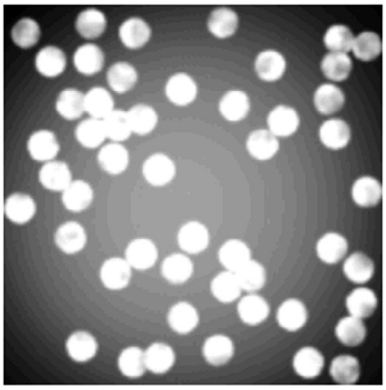

Fig. 1. Example of an image containing a collection of objects on a background.