Morphological texture study of the chromatin in lymphoid cells

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Abstract

This paper deals with an application of mathematical morphology to quantitative cytology: the analysis of chromatin (nuclear texture) in lymphocytes. In particular, we are interested in two approaches: a nucleus classification, based on the level of chromatin density and a segmentation of the nucleus, which can be used to study the spatial organisation of the nucleus structure. The proposed algorithms have been tested with a selection of images from our image base.

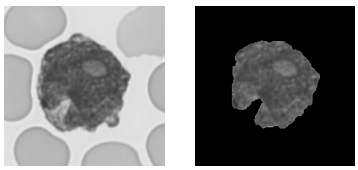
Keywords: mathematical morphology, texture analysis, quantitative cytology, chromatin density.

1 Introduction

Diagnosis on lymphoproliferative disorders (leukaemia) uses the lymphocyte morphology as the principle basis for the identification of lymphoid cancer. Nuclear chromatin distribution (also known as chromatin density), an important feature used in nuclear sorting, can be quantified with textural analysis [1] [2]. In the present work, we describe two applications of the mathematical morphology in order to analyse the nuclear texture of lymphocytes.

For all the results that are presented below, we suppose that the lymphocyte, fig. 1(a), has been correctly segmented and the nucleus is isolated, fig. 1(b). The algorithm used in order to segment is the *watershed with markers* (the details concerning its implementation may be found in [3]).

The second section provides a background reminder on granulometries and then, describes the method, a morphological analysis of the chromatin density level, used in order to classify nuclei. Section 3 presents the nucleus inner segmentation using a morphological algorithm. Finally, the conclusions are summarised in section 4.



(a) (b)

Figure 1: (a) A lymphocyte (stained with May-Grünwald Giemsa). (b) Isolated nucleus.

2 Granulometries and texture classification

A selection of four nuclei of different texture (each one from a different pathology) is shown in fig. 2. The technique used in order to classify them works with the luminance component, and with isotropic ganulometries. The structuring element is an octagon of size n.

2.1 Definition of granulometry

Matheron introduced the notion of granulometry and the extension to grey tone functions was made by Serra [4]. A granulometry is the study of the size distributions of the objects of an image. Formally, a *granulometry* can be defined as a decreasing family of *openings* $\Gamma = (\gamma_\lambda)_{\lambda \geq 0}$:

$$\forall \lambda \geq 0, \forall \mu \geq 0, \gamma_\lambda \gamma_\mu = \gamma_\mu \gamma_\lambda = \gamma_{\max(\lambda,\mu)}$$

Moreover, granulometries by *closings* (or *anti-granulometry*) can also be defined as families of increasing closings. Performing the granulometric analysis of an image I with Γ is equivalent to mapping each opening of size n with a measure $m(\gamma_\lambda(I))$ of the opened image $\gamma_\lambda(I)$. This measure is typically the volume in the greyscale case. The granulometric curve, or *pattern spectrum* of I with respect to Γ, denoted $PS_{\gamma(I)}$ is defined as the following (normalised) mapping:

$$\forall n \geq 0, PS_{\gamma(I)}(n) = \frac{m(\gamma_n(I)) - m(\gamma_{n-1}(I))}{m(I)}$$

The pattern spectrum $PS_{\gamma(I)}$ maps each size n to some measure of the bright image structures with this size. By duality, the concept of pattern spectra extends to anti-granulometry by closings, and is used to characterize the size of dark image structures. We can also use a *pseudo-granulometry* curve (an *anti-pseudo-granulometry*) obtained by replacing the opening (closing) by *erosion* (*dilation*). Texture classification and feature extraction by granulometries has many applications in the medical

and industrial sector [5] [6]. In the present work, the four granulometric curves have been used, particularly, the structuring element (octagon in square grid) increases $n + 2$.

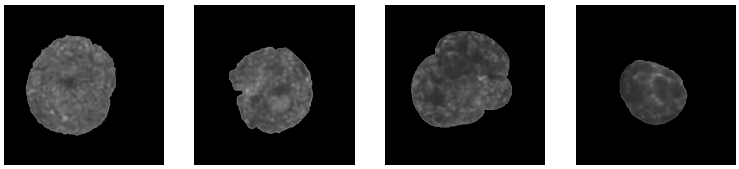
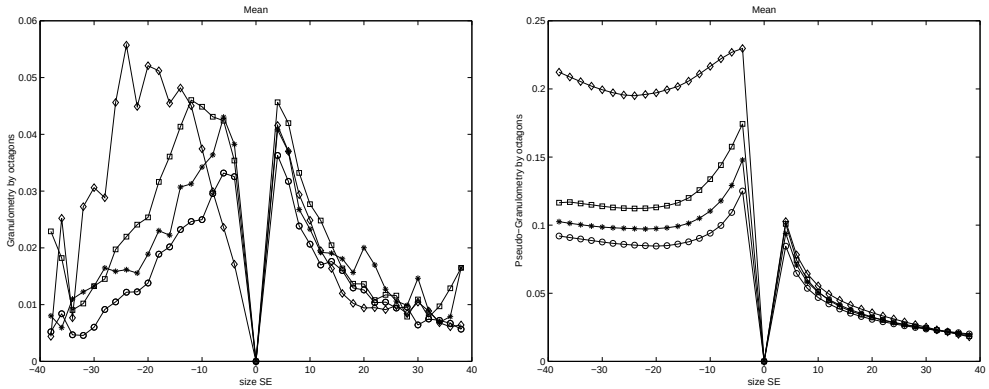


Figure 2: Selection of nuclei with different chromatin texture: from the least dense (left) to the densest (right).

2.2 Results

In fig 3 the results obtained are described. For each one of the four classes (four pathologies), to be studied, we have taken a selection of five nuclei. The shown curves correspond to the mean granulometries obtained for each case. It is easy to see that the combined use of the information given by the four curves allows us the immediate classification. On the other hand, the use of several nuclei of the same type is justified because we are sorting cellular populations.



(a) (b)

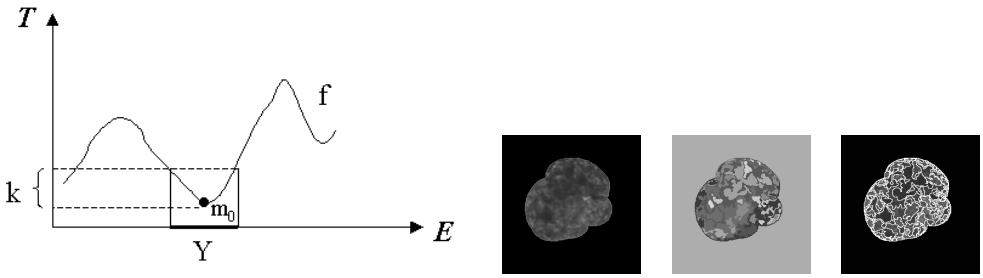
Figure 3: (a) The closing (negative side of the graphic) and opening (positive) curves by octagons. (b) The dilation (negative) and erosion (positive) curves by octagons.

3 A morphological approach to the study of chromatin organization

The image data inside the nucleus are relatively unstructured, characterised by random patterns. But, the nuclear texture may present, in certain pathologies or clinical phases, organised patterns (nucleolus, inclusions, etc). Below, we will present a possible approach based on the *jump connection segmentation*, introduced by Serra [7] and the Salembier's technique [8] of *region growing in partition lattices*, in order to try to split the nucleus into regions having perceptual properties that can be parameterized.

3.1 Jump connection

The *jump connection* of size k from the minima is defined as a connection composed of all connected sets around each minimum, and where the value of f is less than k above the minimum (the variation of f is $\leq k$ and jumps from one zone to another), fig. 4(a). Similarly, one can start from the maxima, or take the intersection of both connections. Fig. 4(b) shows the result of this segmentation of range $k = 5$ (maxima and minima simultaneously), which is oversegmented. Note also that before segmenting, we have simplified the image using a *leveling*, a filter introduced by Meyer [9] that extends the flat zones.



(a) (b)

Figure 4: (a)Jump connection: Y is the connected component of f from m_0 of range k. (b)Nucleus segmentation: original (left), jump connection of range 5 (center), frontiers superimposed on original image (right).

3.2 Region merging

There are several possible alternatives to be followed in order to reduce the over-segmentation and to obtain a more optimal result. Of course, the first approach is to take a higher k, however, in this case, the selection of k is sensible enough, and for high values of k the result is not satisfactory. The segmentation will be further refined by the classical *region growing algorithm*, based on merging initial regions (initial partition) according to a similarity measure between them. Efficient implementation of the merging process uses a *hierarchical queue* and a *Region Adjacency Graph* structure [8]. In our approach, the result of the jump connection is considered as the *finest partition* (initial partition). For the region merging process, each region is defined by its *median* (more robust that the mean) and the merging criterion is the *contrast* h between neighbouring regions (note that the iteration of the contrast operator is idempotent). Fig. 5 shows the result of the global approach ($k = 5$, $h = 10$). Starting from this final partition, each region can be characterised (feature extraction), looking for to define a chromatin organisation descriptor.

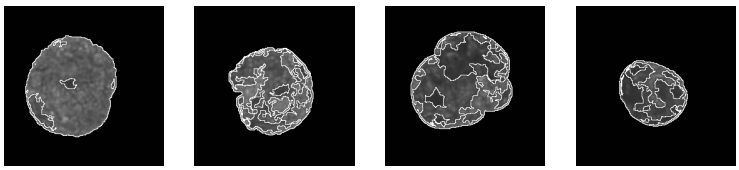


Figure 5: Results of segmenting the nuclei.

4 Conclusions

We have presented the ability of granulometries to characterise the texture in the context of quantitative cytology. The simplicity and the robustness of these algorithms allows us their systematic use as part of a global descriptor of the lymphocytes. A comparative study with other techniques, such as Fourier transform and statistical description, has shown that in order to obtain similar results, the computational load is lower in our approach than using these others. Concerning the other approach, at present, we are performing distinct studies using our image base in order to test the choice of parameters and looking for an optimal characterisation of the obtained regions. Note that their implementation is already efficient. In conclusion, we could say that the presented methods are complementary and applicable to different study scales on cytology.

Acknowledgments

The authors would like to thank Prof. Georges Flandrin of Hôpital Necker-Enfants Malades, Paris, France, for providing the image base and for discussion about nuclear texture perception.

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