Motivation

Histopathology: the microscopic observation of biological tissues, became the gold standard in the diagnosis and prognosis of a number of common and critical pathologies such as breast cancer.

The analysis of breast cancer surgical slides in order to rate the malignancy of breast tumours is a highly technical and tedious task.

In most of the major pathology departments, the pathologist follows a protocol called the Nottingham Grading System (NGS) in which the analysis of size, shape and appearance of cell nuclei is required (nuclear pleomorphism).

The observation of cell nuclei is thus a major aspect of most histopathological studies.

Challenge: accurate detection and extraction of nuclei which can also overlap

Contribution:

- an application of the Marked Point Processes (MPP) based model developed for multiple complex-shaped object extraction from images
- a comparative study with two state-of-the-art algorithms: the Gradient in Polar Space (GiPS) model and a level set based model proposed by K. Mosaliganti et al.

Methods

Marked Point Process based model (MPP)

1. Configuration of circles is sampled from Lebesgue-Poisson distribution
2. The circles are then adapted to the image using the gradient descent of the ‘object’ energy producing a configuration of objects representing nuclei in the image
3. Every object is kept in the current configuration or removed from it with a probability depending on the difference of the total energy without or with this object
4. The optimal configuration of objects in image is found if all the objects added and only them are removed, otherwise the process is repeated

Gradient in Polar Space model (GiPS)

1. Nuclei detection:
   - application of a Gamma-correction to enhance the input image and of a thresholding to generate a binary image
   - separation the joint or overlapping nuclei using dilution and erosion morphological operators
   - nuclei centers of mass search by applying a distance transform on the eroded image
2. Nuclei extraction:
   - segments the image into patches containing the nuclei
   - a polar transform of the coordinate system is then performed on every patch with the center of mass of the nucleus as the origin
   - a median filter is applied for noise removal, and a biquadratic filtering is used to produce a gradient image from which nuclei boundaries are delineated

K. Mosaliganti’s Level Set based model (KMLS)

1. Separation (roughly) of the foreground (nuclei) from the background using a thresholding and a convex shape of nuclear intensity with a Gaussian kernel applied to the input image
2. A level set segmentation for refining the nuclei boundaries
3. The overlapping or joint nuclei separation using a Voronoi diagram of nuclei

Conclusion

The MPP model proved a promising solution for the extraction of cell nuclei from breast cancer slide images able to overperform the two other state-of-the-art methods

Results

Typical extraction results for the 3 methods on the same area of an image

<table>
<thead>
<tr>
<th>Method</th>
<th>Nb. of detected nuclei</th>
<th>Nb. of constructed pairs</th>
<th>Global detection score (F-measure)</th>
<th>Global extraction score (average Jaccard index)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPP</td>
<td>204</td>
<td>827</td>
<td>0.7058</td>
<td>0.5489</td>
</tr>
<tr>
<td>KMLS</td>
<td>1078</td>
<td>942</td>
<td>0.6674</td>
<td>0.6292</td>
</tr>
<tr>
<td>GiPS</td>
<td>25</td>
<td>290</td>
<td>0.6317</td>
<td>0.5800</td>
</tr>
</tbody>
</table>

For each method: number of nuclei detected, number of ‘candidate-reference’ pairs constructed, global detection score (F-measure) = 2 * |Precision * Recall| / (Precision + Recall) and global extraction score (average Jaccard index) = |A ∩ B| / |A ∪ B|, A and B being surfaces of a candidate nuclei and its reference respectively.

Distribution of the pairwise extraction accuracy scores (individual Jaccard indices) for each of the 3 methods.

Perspectives:

- parameter estimation (circle initialization, image modeling) via machine learning, which were calibrated experimentally
- the stability of the extraction: define multiple classes of objects in order to better capture the variety in terms of size, shape, and texture of nuclei, which is possible because of the generality of the MPP model with arbitrarily-shaped objects involved

References:

