

MECOS-C2: Robust cytomorphological measurements and their automation

In spite of 40 year history of computer cytomorphometry its practical usage is much less than was expected. Originated difficulties can be separated into principal (morphological parameters of a given biospecimen type are not enough informative, may be a new specimen preparation techniques will be more successful), and technical, which can be overcome just now using appropriate image analysis technologies and algorithms.

Technical difficulties are produced by immanent properties of biospecimens - their own great variability and presence of a lot of uncontrolled exposures, which change morphology. Rules, which cytopathologist uses for cell sorting, are difficult for formalization. Only a few parameters such as optical density, nucleus and cytoplasm square are evident. But already nucleus contour has no simple quantitative description. Initial not fitted to given specimen morphological features are not stable (vary significantly from the same type cell to cell inside of a given specimen and additionally between different specimens). For example cell colors vary following to a variety of coloring conditions and individual specimen properties. Texture features depend of optics and focus quality. Cell square depends of a smear thickness and so on. Simultaneous usage of many such features doesn't increase stability of quantitative cell type morphology description.

Extremely high variability of cell images defined descriptions of cell types in quality terms with their subjective advantages for visual analysis and disadvantages for automation.

Cell sample morphology of a specimen under indicated condition is to be considered as unsteady random process realization formed under group of uncontrolled external parameters (pathology, lab conditions, human factor and many others). Literature known numerous attempts to apply usual threshold statistics of stationary process on the base of initial morphology features couldn't produce effective cell morphology description.

At that time the problem of cell morphology description has been solved comparatively successfully in robotic microscopy systems for a set of concrete automated cytological analyses. Robotic system MECOS-C2 uses enough universal algorithm which can be applied to many cytological analyses allowing to consider it as common method of attack.

MECOS-C2 uses among others the following methods.

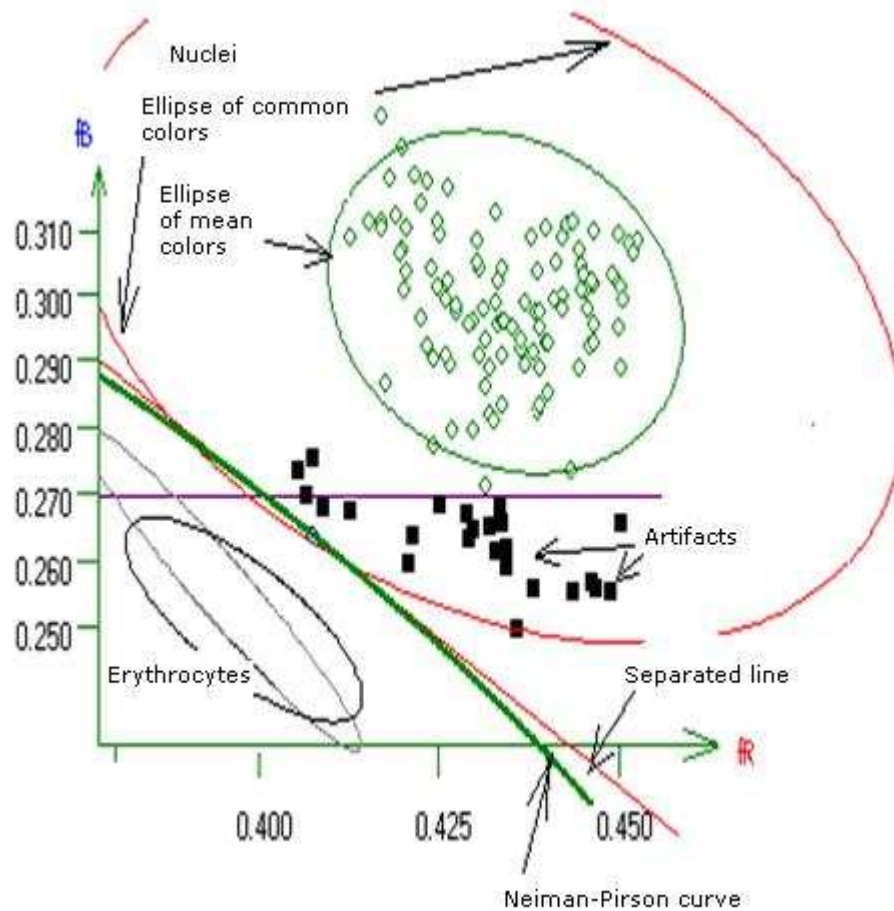
Normalizations are applied systematically, that is measurements only relative distinctions are made (local optical density, normalization of cell colors by colors of main subpopulation, nucleus square by local smear thickness and so on). Robust adaptable to a given specimen algorithms are applied practically without a priori threshold parameters used. The adaptation is realized by analysis of inherent specimen cell population structure.

The adaptation to a given specimen includes the following steps.

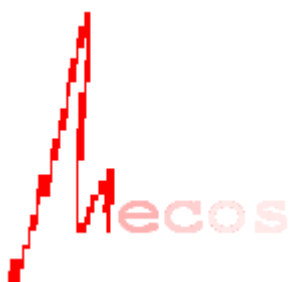
1. Tasks of image segmentation and objects sorting to homogeneous groups are solved by methods of clustering without teacher.
2. Amount of clusters made is evaluated by specially fitted statistics criteria.
3. Mechanism of hypotheses statement and their following testing is used. The hypotheses are concerning to quantity of regions in image, quantity of object types in specimen, boundaries between groups locations. Hypotheses are formed on the data analysis.
4. Sorting may be realized after clustering using homogeneous groups preliminary separated.
5. Boundaries between regions of any object type in features space depend on relative positions of all objects previously sorted.
6. As object sample gathering is automated a volume of a sample is statistically adequate to sample objects variability.

Above automated analysis is possible not only for natural specimens under microscope but also for virtual slides produced by other laboratories with representative specimen sample forming.

The MECOS-C2 algorithms under consideration are available for usage in different tasks of quantitative cytology. It must be mentioned that potency of cytomorphometry application depends on not only correct features choice and population structure analysis but also on automation of these processes.



MECOS-C2. Example of object population clustering in task of leukocyte detection. Leukocyte nuclei separation from erythrocytes and artifacts in plane of relative colors.



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