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Application of Computer Vision Methods in Automatic Analysis of Embryo Development

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***Abstract*—In vitro fertilization (IVF) is a process by which an egg is fertilized by sperm outside the body. This is very difficult procedure, and in the end of it, some of embryos should be selected to implant to the uterus of woman. The applied image processing methods are represented in this article, which detect and measure the embryos early development. The results of embryos detection is represented in this article also.**

Keywords—In vitro fertilization, computer vision, edge detection

I. INTRODUCTION

There are a lot of people with fertility problems in the world. Infertility is a disease that results in the abnormal functioning of the male or female reproductive system. According statistics given by the World Health organizations such as American Society for Reproductive Medicine (ASRM), and the American College of Obstetricians and Gynecologists (ACOG), there is 15% infertility of the reproductive age population with over 25% of couples. The infertility is recognize as a trouble of getting pregnant or sustaining a pregnancy. Therefore, there is an early growing need for assisted pregnancy treatment (2006 – 2010 National Survey of Family Growth) [1]. This is the reason, why in vitro fertilization (IVF) becomes the more and more popular research object for the researchers of different fields. Every year there are proposed new techniques, which helps to increase not only the statistics of IVF success, but emotional satisfaction level of individual couple. The success of IVF procedures resulting to a pregnancy is ~30% per single transfer. For that reason more than one embryo is transferred, which increase the risk of multiple pregnancies and consecutive complications and health problems [2].

In order to increase the pregnancy rate researchers have focused on image analysis features that improve embryo vitality evaluation as well as the selection of single embryo for implantation [6] and reducing the risk of multiple gestations.

In vitro fertilization - a procedure which aims to get the embryo to adapt the methods of "oocyte" fertilized sperm outside the human body. At the end of this procedure there are several embryos. There is a problem to choose the best embryo to be transferred to the uterus. Proper embryo selection is investigated a variety of techniques by different researches [5,7]. There are already established embryo scoring criterions, based on single image observation; unfortunately such a way of analysis disturbs the culture and is observer dependent [6]. In the fig. 1 there is shown, the embryonic stages of cell development (A- line). The main aim of the research involve of design of automated image analysis and embryo evaluation algorithm that would assist embryologist during most important embryo selection task.

The newest way is a time-lapse microscopy, which continuously monitors the development of the embryo without disturbing the culture conditions. This is an automatic image capturing method, when the computer finds and determines fetal position. Recently several devices were proposed for continuous monitoring of early embryo maturity by time-lapse technique [7]. Embryo development in real environment, looks like showed in fig. 1. Timeline (Fig. 1A) highlights the critical times between stages that predict successful development of human embryo. Molecular events (Fig. 1B) and time-laps images of human embryo. The automated computer tracking by Wang et al [8] is presented in (Fig. 1C). Fig. 1D shows the vital features that evaluates the success of development from the first and second mitotic division as well as synchronicall appearance of the third and fourth blastomers.

There are a lot of different biological, morphological and morphokinetical features, whose can describe the embryo development stage. It is really difficult, to make a decision about the quality of embryo from a single picture or set of pictures. For computer vision or machine vision specialist it is also hard challenge because the early embryonic growth is a progressive and a dynamic process [7] and some fragments may appear and disappear by missleading the embryo selection. One of the feature, by which user can make a decision, is the early nucleus fission time. Authors of [7] has shown that the embryos with too early cleavage time fail to implant. Therefore determination of cleavage moments is very important as well as some other physical markers such as the thickness of embryo coat, fragmentation level, or symmetry of nucleus. Authors of [9] has extended work of Wong et al [8] and proposed to build embryo development family tree by tracking cell division time and it correspondence to motherhood blastomers.

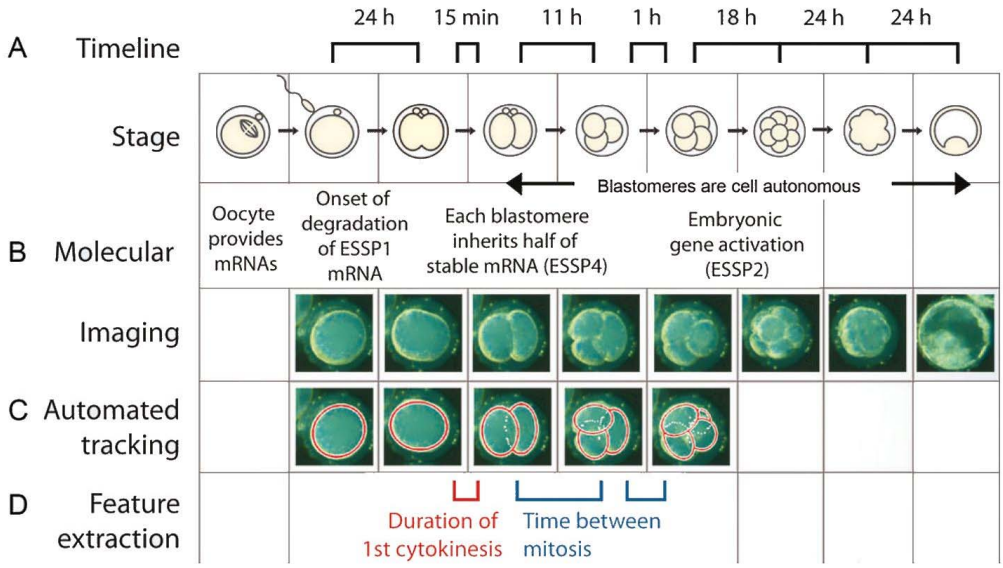


Figure 1. Images of human embryo development. Figure reproduced with permission from Wang et al. [8]

II. Computer Vision Methods

It is almost 25 years the time lapse and image analysis systems are used for assisted reproduction. At the beginning it was done only for documentation purposes by taking one image per hour. Recently, the proposed systems stores embryo images acquiring one per minute. Current commercial systems are tracking from 14 to 84 or more embryos at a time. So there are a lot of data to proceed. The automated time lapse systems, has to detect the embryo (position of the embryo), and track it during the embryo development. Most of techniques, just store the data and don't have any automatic algorithms for analysis. It means that "user" must to setup the device (to show the position in which embryo is located) and after "cycle" to proceed the data and select the "best" embryo manually. The automated computer vision and image analysis methods would improve the evaluation of embryo vitality as well as would reduce the value judgments of the user in best embryo selection.

The computer vision based methods which detects an early stage embryo cleavage can be grouped, basically, into two major groups, i.e., tracking-based and tracking-free (or brute force) methods. First group of methods applies computer vision algorithms which detects the contours of the embryo cells, measures an area of each individual cell and tracks them during whole development process. Tracking-free methods uses low level features extracted from time-lapse embryo images which corresponds certain cleavage stage of the embryo. The combination of low level images features forms certain recognizable patterns which are almost similar from stage to stage.

Tracking-based methods are based on an assumption that the embryo itself and cells from which consist the embryo have clear circular or elliptical shape. Therefore, the embryo detection task is simplified to detection to known or predictable number of ellipses in time-lapse image. Ellipse detection can be established using reduced quantization-free parameter space [10] or by analyzing of principal components [11]. Basically, three stable points are needed to fit an ellipse on the object contour [12-14]. Meanwhile the accuracy of ellipse detection highly depends on accurate detection of the object contour which is a difficult task in many cases dealing with embryo images. Methods such as active contours [15-16] level sets [17-18] and other [19] do not solve multiple detection of partly occluded objects.

Tracking-free methods uses feature extraction techniques, which can be grouped in four groups. First group is appearance-based approaches which incorporates well statistical methods such PCA, LDA, ICA and other. Feature-based approach computes Gabor features, Binary feature, Local binary patterns and others. Template-based approach uses certain image samples which are compared with a real time images. Part-based approaches computes local features of the object. Feature extraction techniques such as SIFT, SURF, FAST, ORB, BRIEF computes stable and discriminating features which are invariant to rotation and uneven illumination. All mentioned tracking-free methods highly depends on the training samples, from which features are extracted. The training sample should represent all possible variation of the traceable object.

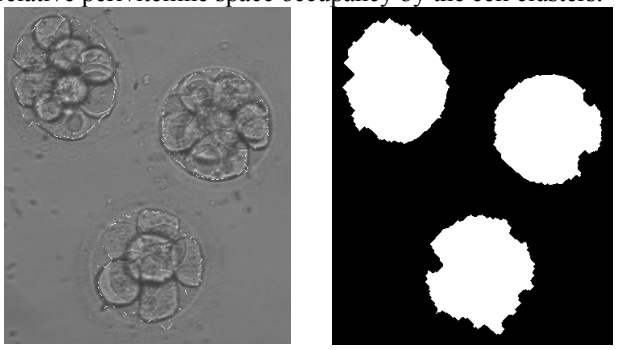
Image analysis by texture is used to segment non uniform content in the image. The texture analysis tries to identify the behavior and the variations of image pixels in regions. For embryo analysis it gives information about consistency, number of fractions and granularity.

For instance the entropy of an image is a measure of randomness in the image the *entropyfilt* function in MatLab gives such information depending on the neighbor's array. The local range of the image can be

found by a Matlab function called *rangefilt*. It uses the morphological functions to determine the maximum and minimum values in the specified areas. Local standard deviation of the image can be found by a MatLab function called *stdfilt*. It is also used to specific neighborhoods of various shapes such as disk, ball etc.

III. Analysis and Results

The purpose of these experiments is to investigate the ability of embryo identification on IVF Petri Dish. Al experiments were run within MatLab package environment. Photos for the analysis was taken from free available database [1], took by different techniques with various quality. Fig. 2. shows the results of applied classical background subtraction. The contours of blastomers within the individual embryo are shown in fig. 2b. As it is seen from fig. 2, the detection of embryos it is not hard task and by applying object tracking technique it is possible to follow the path of movement. From this figure it is possible to calculate the radius of embryo and relative perivitelline space occupancy by the cell clusters.



a) b)

Figure 2. The 3 ebryos (a) and boundaries of the cells (b)

Additionally, from fig. 2a it is possible to find the thickness of the pellucid zone. Usually, normal embryos are round or slightly elliptical objects; therefore by counting radial gray pixel variation from the center it is possible to detect the beginning and the end of embryo coat. The kurtosis and skewness of grey values shows the shell radius beginning and the end see Fig. 3.

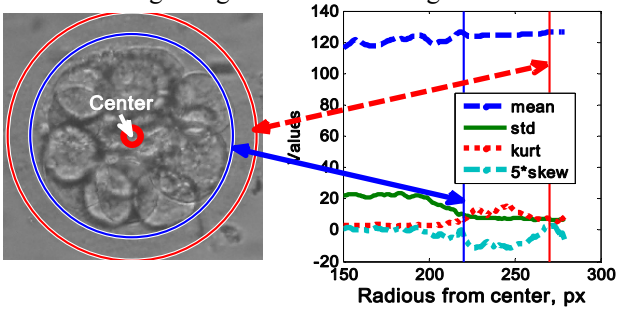
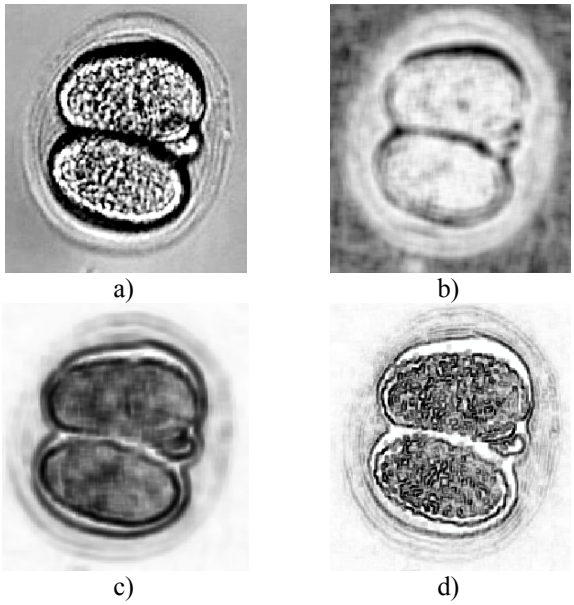


Figure 3. Detection of embryo pellucid zone

For counting cells, within the embryo, various "filt" type filters from MatLab were applied for cell's contours extraction. As it is seen from the Fig. 4 the stdfilt and rangefilt gives sharp contours representation of the cells.

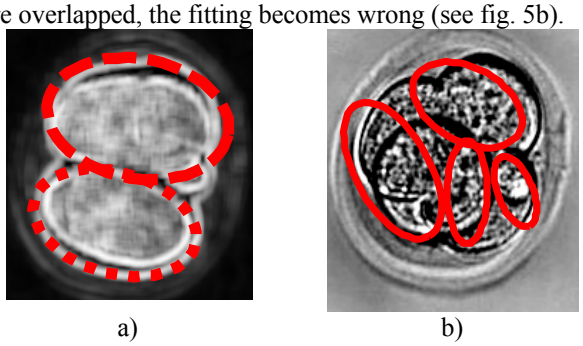


a) b)

c) d)

Figure 4. Embryo's cells (a- original picture) contours detection by: entropyfilt – b, stdfilt –c and rangefilt - d

Fitting the ellipse to the filtered image is not a trivial task. By adjusting parameters it is possible to obtain more or less proper fitting to 2 cells embryo, but, when the cells are overlapped, the fitting becomes wrong (see fig. 5b).



a) b)

Figure 5. Ellipse fitting to embryo's cells: a- 2 cels and b- 4 cells.

III. Conclusions

The embryo quality evaluation method based on image processing is presented in this work. The proposed method is dedicated for detection of the embryos as well as number of cells. It is very promising research and could be released in the real life. The results show that it is enough high detection rates, just if we have latest stages of embryo development. There are similar technologies which were presented by other researches, but those techniques are not widely applied. There are a lot of possibilities, to increase the detection accuracy of latest embryo development stages, because this is just a first phase of research.

References

[1] http://www.resolve.org/about/fast-facts-about-fertility.html/2015/02/10/09:00

[2] D. D. Neubourg and J. Gerris, "Single embryo transfer–state of the art," *Reproductive Biomedicine Online*, vol. 7, no. 6, 2003, pp. 615-622.

[3] T. F. Chan and L. A. Vese, "Active contours without edges," *IEEE Transactions on Image Processing*, vol. 10, issue 2, 2001, pp. 266-277.

[4] Y. Chen, D. Tseng, "Medical image segmentation based on Bayesian level set method," in *Proceedings of the Medical Images Information, Lecture Notes in Computer Science*, vol. 4987, 2007, pp. 25-34.

[5] I. Habibie, A. Bowolaksono, R. Rahmatullah, M. Nanda Kurniawan, "Automatic detection of embryo using particle swarm optimization based Hough transform," in *Proceedings of the International Symposium on Micro-NanoMechatronics and Human Science (MHS)*, 10-13 November 2013, pp. 1-6.

[6] J. Herrero, M. Meseguer, "Selection of high potential embryos using time-lapse imaging: the era of morphokinetics," *Fertil Steril*, vol. 99, 2013, pp. 1030-1034.

[7] M. Montag, J. Liebenthron and M. Köster, "Which morphological scoring system is relevant in human embryo development?," *Placenta*, vol. 32, issue 3, 2011, pp. 252-256.

[8] C. C. Wong, K. Loewke, N. Bossert, B. Behr, C. J. De Jonge, T. Baer, R. Reijo Pera, "Non-invasive imaging of human embryos before embryonic genome activation predicts development to the blastocyst stage," *Nature Biotechnology*, vol. 28, issue 10, 2010, pp. 1115-1121.

[9] M. Cicconet, M. Gutwein, K. C. Gunsalus, and D. Geiger, "Label free cell-tracking and division detection based on 2d images for timing analysis of early embryo development," *Computers in Biology and Medicine*, vol. 51, 2014, pp. 24-34.

[10] K. C. Chen, N. Bouguila, and D. Ziou, "Quantization-free parameter space reduction in ellipse detection," *Expert Systems with Application*, vol. 38, issue 6, 2011, pp. 7622-7632.

[11] H. Jiandong, "Ellipse detection based on principal component analysis," in *Proceedings of the International Conference on Computer Application and System Modeling*, 2010, pp. 258-261.

[12] J. K. Lee, B. A. Wood, and T. S. Newman, "Very fast ellipse detection using gpu-based rht," in *Proceedings of the 19th IEEE International Conference on Pattern Recognition ICPR'2008*, Tampa, USA, 8-10 December 2008, pp. 1-4.

[13] D. Prasad and M. Leung, "Clustering of ellipses based on their distinctiveness: An aid to ellipse detection algorithms," in *Proceedings of the 3rd IEEE International Conference on Computer Science and Information Technology (ICCSIT'2010)*, Chendu, China, 9-10 July 2010, vol. 8, pp. 292-297.

[14] T. Cooke, "A fast automatic ellipse detector," in *Proceedings of the International Conference on Digital Image Computing: Techniques and Applications (DICTA'2010)*, Sydney, Australia, 1-3 December 2010, pp. 575-580.

[15] D. E. Maroulis, M. A. Savelonas, D. K. Iakovidis, S. A. Karkanis and N. Dimitropoulos, "Variable background active contour model for computer-aided delineation of nodules in thyroid ultrasound images," *IEEE Transactions on Information Technology in Biomedicine*, vol. 11, issue 5, 2007, pp. 537-543.

[16] L. Ma and J. Yu, "An unconstrained hybrid active contour model for image segmentation," in *Proceedings of the 10th IEEE International Conference on Signal Processing (ICSP'2010)*, 2010, pp. 1098-1101.

[17] D. Cremers, "A multiphase levelset framework for variational motion segmentation," in *Proceedings of the International Conference on Scale Space Meth. Comput. Vis.*, June 2003, pp. 599-614.

[18] C. Li, C. Xu, K. Konwar, and M. D. Fox, "Fast distance preserving level set evolution for medical image segmentation," in *Proceedings of the 9th International Conference on Control Autom. Robot. Vis.*, 2006, pp. 1-7.

[19] J. Lie, M. Lysaker, X. C. Tai, "A binary level set model and some application to Munford-Shah image segmentation," *IEEE Transaction on Image Processing*, vol. 15, issue 5, 2006, pp. 1171-1181.