Potential Use of Smartphone as a Tool to Capture Embryo Digital Images from Stereomicroscope and to Evaluate Them by an Artificial Neural Network

Diego de Souza Ciniciato[1,*], Maria Beatriz Takahashi[1,*], Marcelo Fábio Gouveia Nogueira[2] and José Celso Rocha[1]

[1]*Laboratório de Matemática Aplicada, School of Sciences and Languages, Universidade Estadual Paulista (Unesp), Av. Dom Antonio 2100, Assis, Brazil*

[2]*Laboratório de Micromanipulação Embrionária, School of Sciences and Languages, Unesp, Av. Dom Antonio 2100, Assis, Brazil*

[*]*Both authors contributed equally to the study*

Keywords: Smartphone, Embryo Classification, Artificial Neural Network-based Software, Graphic User Interface.

Abstract: An online graphical user interface connected to a server was developed aiming to facilitate access to professionals worldwide that face problems with bovine blastocysts classification. The blastocysts assessment is carried on using images taken from an inverted microscope, which usually requires more expensive devices such as digital camera and computer software. Smartphone camera quality and tasks processing are getting better with technology advances. Therefore, a smartphone can be attached to the eyepiece lens to provide Real-Time evaluation, and thus reducing costs when comparing to computers, cameras, and software that are commonly used for this purpose.

1 INTRODUCTION

Brazilian cattle production has an important contribution to the economy and social aspects of this country. With approximately 215 million livestock units and leader in meat exportations since 2004, Brazil is also the leader in *in vitro* production of bovine embryos worldwide (Ministério do Planejamento, Desenvolvimento e Gestão - Instituto Brasileiro de Geografia e Estatística IBGE, 2016). This production has utmost importance for international and national improvement in cattle genetics and productivity. The production of cattle embryos for commercial purposes follows the steps: they are produced *in vitro* and transferred to synchronized receptors when they reach the blastocyst stage (Hyttel *et al.*, 2010). To help to identify the quality embryos, which is associated with the success of pregnancy, the International Embryo Technology Society (IETS) recommends an embryo classification system. This system is based on morphological evaluation and establishes three quality grades: excellent or good, "1"; fair, "2"; or poor, "3" (Bó and Mapletoft, 2013).

However, this classification is directly affected by the embryologist's accuracy and experience to evaluate the embryo variables related to the development and pregnancy potential (Lindner and Wright, 1983; Bó and Mapletoft, 2013). The reason for this interference is that the morphological analysis does not measure any objective variables to determine the embryo classification. Moreover, the analysis by the human vision is based on a comparison between objects or images. In this regard, human vision has difficulties at judging color or brightness of shapes and features, which requires measuring scales or relative size, angle and positions of several objects to identify their characteristics (Russ, 2016). Thus the analysis by an embryologist is subjective and has low reproducibility (Bényei *et al.*, 2006). Indeed, the same embryo can be classified with different degrees of quality by different embryologists (inter-evaluator error) or even by the same embryologist at different moments (intra-evaluator error), especially in cases when the quality grade is borderline (Farin *et al.*, 1995). Together with inexperience, the tiredness and the mood of the evaluator could contribute to the major

Ciniciato D., Takahashi M., Gouveia Nogueira M. and Rocha J.
Potential Use of Smartphone as a Tool to Capture Embryo Digital Images from Stereomicroscope and to Evaluate Them by an Artificial Neural Network.
DOI: 10.5220/0006518501850189
In *Proceedings of the International Conference on Computer-Human Interaction Research and Applications (CHIRA 2017)*, pages 185-189
ISBN: 978-989-758-267-7

causes of the subjective and low reproducibility of this standard system of embryo assessment.

Therefore, several methods have been or are being developed to provide an optional evaluation for embryo classification that does not have external effects. Some of them includes a semi-automatized image segmentation process with the use of artificial intelligence (AI) for human embryos (Gonzalez, 2004), an automatic segmentation procedure of bovine embryos without AI (Melo *et al.*, 2014), a semi-automatized grading method of human blastocyst using a support vector machine (Santos Filho *et al.*, 2012), embryo metabolism analysis, cellular respiration measurements, the use of zona pellucida birefringence, microRNA profile determination, analysis based on logistic regression and evaluation by time-lapse video (reviewed by Rocha *et al.*, 2016). However, none of these methods are totally effective, and, despite being subjective and old, the visual morphological analysis is still widely used (Lindner and Wright, 1983; Farin *et al.*, 1995; Richardson *et al.*, 2015).

Recently, there have been attempts at creating a method based on digital image processing to determine the viability of human embryos by detecting blastomeres (Singh *et al.*, 2014; Tian *et al.*, 2014) or trophectoderm (Singh *et al.*, 2015). Additionally, using processing and digital image analysis in the quality evaluation of mouse blastocysts, a previous study used an artificial neural network technique with significant success (Matos, Rocha and Nogueira, 2014). However, as far as we can determine from the studied literature, a classification method using digital image processing has not been applied to bovine blastocysts.

In this context, a method based on artificial neural network (ANN) combined with genetic algorithm (GA) was developed to train an ANN to classify bovine blastocyst images based on the IETS standards (Rocha *et al*., 2017). In this study, a 482 bovine blastocysts images dataset were used to train some ANNs, from which the best obtained 76.4% of accuracy. The input set was the variables extracted from image processing and the output was the mode from grading of three experienced embryologists. The use of three evaluations avoids the bias of using a single evaluation as the standard for the ANN training. The Kappa index of the inter-evaluator agreement was 0.571 (482 images, $P<0.001$), and the three ANNs obtained 0.616 for the same dataset (482 images, $P<0.001$). This represents that the ANN technique was more consistent than the embryologists' evaluation. Moreover, the intra-evaluator agreement was 0.28, 0.41 and 0.47 (48 images, $P<0.001$), and when compared to the ANNs, there were 100% agreement (Kappa index of 1.0), which supports the robustness and low subjectivity of an ANN.

The present position paper is a continuation in a deeper way of the previous work (Rocha *et al*., 2017), aiming the development of a Graphical User Interface due to users that could not be familiar with the programming environment and do not use/have an inverted microscope. In addition, embryologists from around the world can access the technique online, without downloading or install the software. Furthermore, we describe the application of smartphone adapters for stereomicroscope ocular lens to classify embryos in Real-Time.

2 METHODOLOGY

A server for image processing and classification of bovine blastocysts was developed aiming to democratize the technology available in our research group. The access to the server is by the link below: http://blasto3q.com. The image processing and evaluation are carried out by the algorithm Blasto3Q, which is described in (Matos, Nogueira and Rocha, 2012, 2014). The users can access this computational tool by a multiplatform application available on the same server. The application has a friendly and intuitive interface for users, and it has additional functionalities comparing to the desktop version, such as the evaluation of multiple images in parallel. Due to the high processing cost for each image, we choose to centralize this operation on the server. If this action were carried on in the smartphone, the execution time should increase considerably, which is not desired by users. Therefore, the smartphone just captures the blastocyst images and receive the results from classification.

On the server-side, there is a MATLAB® application (version R2017a) that works in service mode, which executes several scanning of databases to search non-processed requisitions. Each service runs one process at a time, however, it can process several instances, and thus the processing of different requests will be performed in parallel and simultaneously.

For a greater user experience, an intuitive user interface was developed to general users, which runs on the client-side. This interface communicates by requests to the server. Each new processing request is initialized by the desired image uploaded into the server. This request is added to the database in the

end of the requests queue and it will be processed according to its rank. The process is finished with the output that the users want.

Therefore, there is an extremely light and fast application that can perform in devices compatible with HTML5 (more modern navigators). Nowadays a large part of devices provides this markup language, and an advantage is that it is possible to use the application in different operating systems (for example, both Android and iOS can execute the application). The user can access this software wherever they are, if they have an internet connection. The results are processed in few seconds.

Figure 1: Graphical User Interface evaluating bovine blastocyst as grade 2 ("fair") since the highest vector was the yellow that is related to the fair degree.

In Figure 1, there is an example of the application interface describing an *in vitro* produced bovine embryo image taken from a smartphone juxtaposed to an eyepiece of the stereomicroscope. For this purpose, we used a Samsung S6 coupled to a macro lens (Figure 2) to allow the proximity of the smartphone lens with the eyepiece. With this apparatus, the image of the embryo on the eyepiece could be captured by the smartphone lens and using the zoom of the phone to fill the screen with the image. Moreover, we used the maximum of magnification of the stereomicroscope (*i.e.*, 60 x, Leica M80).

3 DISCUSSIONS

The smartphone development allowed the creation of new technologies and applications. Nowadays the daily tasks made by a computer and a smartphone are very similar, as we can access websites and software on both devices. The smartphones have advantages due to easy portability, and they are lighter and cheaper than computers. Moreover, the recent improvement of new generation smartphones' cameras allowed taking images with higher quality than previous generations.

Figure 2: Illustrative image of the macro lens attached to the lens of the smartphone (left) and the macro lens alone with its clipper (right).

In this context, the application of cheaper and robust technology in research laboratories is required to reduce costs. The image records using microscopy in any laboratory usually requires desktop computers and expensive digital cameras and software to analyze them. Also, expensive inverted microscopes are often required to obtain those images with a high quality when recording mammalian oocytes and embryos. The development of an application that is functional in any device (smartphone or other devices, such as desktop and tablet) to evaluate images of blastocysts from microscopy allows Real-time assessment, reduce costs, and solve a subjective issue in blastocysts classification.

Several adapters were developed to attach the smartphones to the eyepieces of a microscope, which provide better ergonomic, simple and fast ways to take pictures of the sample, as in anatomic pathology analysis using mobile devices (Lehman and Gibson, 2013; Roy *et al.*, 2014) and diagnostic of diseases using deep learning (Quinn *et al.*, 2016) both attached to conventional light microscope. In this way, besides the macro lens attached to the smartphone lens, an adapter to a better stabilization

and focal plane quality could useful. Also, the standardization of the blastocysts images by image processing steps keeps the features from the blastocysts, which allows the software interprets it properly.

The improvement of this technology processing can be achieved by cloud computing, which is a model related to applications called 'Software as a service'. The basis for this model is to run on distant computers linked by a cloud that is owned and operated by others and that connect to users' computers via a web browser. The advantages of this method are the access to applications and data from different computers that are connected to the cloud, less risk of missing data and dynamically scalable (Armbrust *et al.*, 2010).

4 CONCLUSIONS

The bovine blastocyst classification by Artificial Neural Network available as a graphical user interface provides a robust method to embryologists that are not familiar with programming languages. Also, the smartphone adapters for microscope eyepiece should provide better ergonomic and a Real-Time assessment of bovine embryos.

ACKNOWLEDGEMENTS

The authors' research is supported by grants # 2012/50533-2, 2013/05083-1, 2006/06491-2, 2011/06179-7, 2012/20110-2 and 2016/19004-4 from São Paulo Research Foundation (FAPESP). We also thank Agência UNESP de Inovação (AUIN) for processing the national and international patents of the invention.

REFERENCES

Armbrust, M. *et al.* (2010) 'A view of cloud computing', *Communications of the ACM*, 53(4), p. 50. doi: 10.1145/1721654.1721672.

Bényei, B. *et al.* (2006) 'The effect of internal and external factors on bovine embryo transfer results in a tropical environment', *Animal reproduction science*, 93(3–4), pp. 268–279.

Bó, G. and Mapletoft, R. (2013) 'Evaluation and classification of bovine embryos', *Animal Reproduction*, 54(935), pp. 344–348.

Farin, P. W. *et al.* (1995) 'Agreement among evaluators of bovine embryos produced in vivo or in vitro', *Theriogenology*, (95), pp. 339–349.

Gonzalez, R. (2004) *Digital Image processing using Matlab*. Upper Saddle River New Jersey: Pearson Prentice Hall.

Hyttel, P. *et al.* (2010) *Essentials of domestic animal embryology*. Saunders/Elsevier.

Lehman, J. S. and Gibson, L. E. (2013) 'Smart teledermatopathology: a feasibility study of novel, high-value, portable, widely accessible and intuitive telepathology methods using handheld electronic devices', pp. 513–518. doi: 10.1111/cup.12108.

Lindner, G. and Wright, R. W. J. (1983) 'Bovine embryo morphology and evaluation', *Theriogenology*, 20(313), pp. 407–416.

Matos, F. D., Nogueira, M. F. G. and Rocha, J. C. (2012) 'Método para determinação da viabilidade e qualidade de embriões'. Brazil.

Matos, F. D., Nogueira, M. F. G. and Rocha, J. C. (2014) 'Method for determining embryo viability and quality'. Brazil.

Matos, F. D., Rocha, J. C. and Nogueira, M. F. G. (2014) 'A method using artificial neural networks to morphologically assess mouse blastocyst quality', *Journal of Animal Science and Technology*, 56.

Melo, D. H. *et al.* (2014) 'Algorithms for automatic segmentation of bovine embryos produced in vitro', *Journal of Physics: Conference Series 490*, pp. 1–4.

Ministério do Planejamento, Desenvolvimento e Gestão - Instituto Brasileiro de Geografia e Estatística IBGE. Produção da pecuária municipal 2015. IBGE 43, 1-47 (2016). e-Book (bulletin) <http://biblioteca.ibge.gov.br/visualizacao/periodicos/84/ppm_2015_v43_br.pdf>.

Quinn, J. A. *et al.* (2016) 'Deep Convolutional Neural Networks for Microscopy-Based Point of Care Diagnostics', in *Proceedings of International Conference on Machine Learning for Health Care*.

Richardson, A. *et al.* (2015) 'A clinically useful simplified blastocyst grading system', *Reproductive BioMedicine Online*, 31, pp. 523–530.

Rocha, J. C. *et al.* (2016) 'Methods for assessing the quality of mammalian embryos: How far we are from the gold standard?', *JBRA Assisted Reproduction*, 20(3), pp. 150–158.

Rocha, J. C. *et al.* (2017) 'A method based on artificial intelligence to fully automatize the evaluation of bovine blastocyst images', *Scientific Reports*, 7(Article number: 7659).

Roy, S. *et al.* (2014) 'Smartphone adapters for digital photomicrography', *J Pathol Inform*, (October). doi: 10.4103/2153-3539.137728.

Russ, J. C. (2016) *The Image Processing Handbook*. Seventh. CRC press.

Santos Filho, E. *et al.* (2012) 'A method for semi-automatic grading of human blastocyst microscope images', *Human Reproduction*, 27, pp. 2641–2648.

Singh, A. *et al.* (2014) 'Automatic blastomere detection in day 1 to day 2 human embryo images using partitioned graphs and ellipsoids', *IEEE International Conference on Image Processing (ICIP)*, pp. 917–921.

Singh, A. *et al.* (2015) 'Automatic segmentation of trophectoderm in microscopic images of human blastocysts', *IEEE Transactions on Biomedical Engineering*, 62(1), pp. 382–393.

Tian, Y. *et al.* (2014) 'Automatic Blastomere Recognition from a Single Embryo Image', *Computational and Mathematical Methods in Medicine*, 2014.