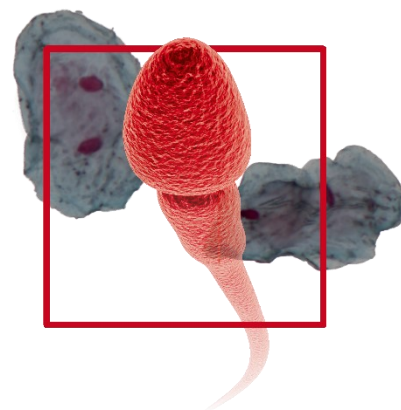


MetaSystems White Paper

CUSTOMIZATION PACKAGE SPERM DETECTION

MetaSystems – Innovative Solutions for Automated Microscope-based Imaging

Sperm cells are a crucial piece of evidence for solving sexual crimes and are usually detected by microscopy. Manual detection of sperm cells on a slide, however, can be a tedious and complex task. Automation of microscopy can be a possible way to efficiently overcome this challenge. Using deep learning algorithms implemented in the Metafer platform software, MetaSystems has put together a workflow that brings the benefits of artificial intelligence to the field of forensic microscopy.



Highlights

- Automated slide scanning can replace the lengthy and tedious manual search.
- Circa 15 to 20 minutes scanning time per slide with suitable slide preparation and hardware.
- Brightfield and fluorescence illumination for different staining types.
- Easy user review of spermatozoa with the convenient display of gallery images.
- Unattended overnight acquisition of images.
- Storage of all object coordinates of detected sperm cells and quick relocation on the slide.
- Efficient transfer of object coordinates to compatible laser microdissection systems.
- Standardized templates for report creation.
- Sophisticated case and image management.
- Integration to a Laboratory Information Management System (LIMS).
- Software add-on available for GLP compliance.

Automation Is Key to Reduce Backlogs

The labor-intensive and time-consuming search for sperm cells in forensic samples often represents a bottleneck in solving cases of alleged sexual assault. The outcome is an increasing backlog in many crime laboratories. A prominent example is the rape kit backlog in the USA. Sexual assault evidence kits, also informally called rape kits, are investigated in case of an alleged sexual assault. The materials of the rape kits are examined for the presence of spermatozoa and a DNA analysis is performed. The male DNA profiles are used to identify perpetrators and hold them accountable. The U.S. Government Accountability Office published a report in 2019, which

found that the number of backlogged DNA analysis requests rose from about 91,000 to about 169,000 untested samples from 2011 to 2017 (GAO-19-216 *1). Scott Berkowitz, CEO and founder of the Rape, Abuse, and Incest National Network (RAINN), was cited as follows in an article of The Washington Post: "I think the labs are doing a spectacular job, but they're drinking from a fire hose." (*2). To overcome this critical situation, the U.S. Department of Justice has released a publication on National Best Practices for Sexual Assault Kits (NCJ 250384 *3). One of the considerations listed in this publication to improve the situation is the incorporation of robotics and automation.

Automation of microscopy has the potential to play a key role to keep up with increasing sample amounts. MetaSystems has more than 35 years of experience in automated slide imaging for medicine and life sciences. With the Customization Package Sperm Detection, we can customize a slide scanning workflow based on the Metafer software to detect spermatozoa on microscope slides. We support crime laboratories in adapting the automation technology to the microscopic examination of rape kits or vaginal swab smears.

For microscope-based detection of spermatozoa in forensic samples, we can configure a scanning system operated by our Metafer software with the two illumination modes brightfield and fluorescence. Thus, the system could support different staining techniques, i.e., Christmas Tree staining (Nuclear Fast Red/Picroindigocarmine), Baecchi

stain (Acid Fuchsin and Methylene Blue), H&E (Hematoxylin/Eosin), and commercial fluorescent staining kits. This allows you to process slides with different staining types on the same scanning system.

Automated Detection of Sperm Fluorescent Markers with Machine Learning

To detect spermatozoa stained with a fluorescent staining kit, e.g., Sperm HY-LITER™ (Independent Forensics *4), we designed a machine learning approach. Developers configured an algorithm based on color, size, shape, and more features to detect sperm cells with a fully motorized microscope operated by our Metafer software.

In a study using mock sexual assault samples, human spermatozoa from vaginal swabs diluted 1:500 and mixed with blood, urine, and yeast were compared under manual observation and with a scanning system operated by the Metafer software. Spermatozoa counts agreed for 19 of 24 slides. Counts of three slides differed by only one spermatozoon. One slide had a difference of two spermatozoa and one slide had a difference of three spermatozoa (Moors and Frégeau, 2011 *5). The study concluded that for the used mock sexual assault specimens the automated detection of human spermatozoa was reliable and reproducible using the adapted Metafer software and the scanning system it controlled.

Deep Learning Advances Brightfield Techniques for Sperm Detection

Staining types examined in brightfield, such as Christmas Tree and Baecchi stain, are highly popular with our customers. Therefore, we have implemented one of the latest advancements of artificial intelligence: deep learning. While the principles of deep learning are decades-old, the recent availability of big data and computation power has pushed deep learning to a breakthrough. Deep learning is already in our everyday life, and you use it to unlock your phone with your face or to translate the menu in a foreign country's restaurant. Deep learning also pushes the frontiers in medicine and life sciences.

MetaSystems uses Deep Neural Networks (DNNs) to solve difficult image processing tasks. Finding spermatozoa in forensic specimens is one such challenge. DNNs learn from example images that are labeled by experts. During training, a DNN self-optimizes its predictions by comparing the predicted image label to the actual label given by the expert ("ground-truth"). This supervised learning strategy also allows to continuously measure the training progress of the DNN. After completing the training, the DNN is tested on a set of previously unseen images that was set aside before the training (around 5 % of data). In the internal validation study, our fully trained DNN correctly classified 99 % (937 out of 946) of images showing spermatozoa stained with Christmas

Tree staining. Usually, police and crime labs validate the adaptations made in the Metafer software and the scanning system controlled by it on their own and do not make validation data available for the public. However, we are happy to get you in touch with our existing customers in the forensic field.

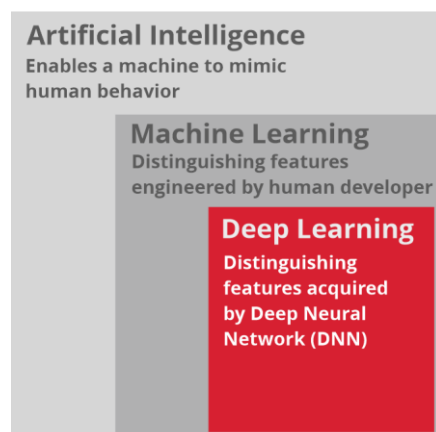


Figure 1: Deep learning is a subfield of artificial intelligence. A Deep Neural Network (DNN) optimizes its predictions by comparing the predicted image label to the actual label given by the expert.

The Customization Package can be configured for forensic specimens stained with Christmas Tree (Nuclear Fast Red/Picroindigocarmine), Baecchi (Acid Fuchsin/Methylene Blue) or H&E (Hematoxylin/Eosin) stain in brightfield illumination. An existing customer laboratory was able to scan a slide in 15 to 20 minutes. The Metafer software stores object coordinates of detected sperm cells and allows for easy relocation of cells on the slide. A suitable graphics card is required for DNN-based calculations.

Slide Capacity Is Scalable to Specific Demands

Systems operated with our Metafer software can be configured to meet the requirements of laboratories of different sizes. Various add-ons are available for small, medium, and large laboratories. If capacity requires 24/7 microscopy operation with the ability to prioritize urgent slides, an automated slide feeder can be added to the scanning system. This allows for unattended slide scanning overnight or on weekends. With a scalable capacity from 8 up to 800 slides being automatically scanned, we support our customers in high-throughput applications.

Forensic Starch Particle Detection

One way to prove that a condom was used in a sexual assault is to detect starch particles using light microscopy. Most latex condoms are coated with a thin layer of corn starch to prevent the latex sticking to itself, which makes the condom easier to unroll. When polarized light is used, the starch granules show the typical “Maltese cross” birefringence pattern when examined under the microscope.

Our colleagues are currently working on the incorporation of artificial intelligence to support the detection of starch granules in an automated microscope solution, which could be a promising addition to the DNN-supported sperm detection in forensic samples that we can already customize.

Sources

*1 GAO-19-216; United States Government Accountability Office, Report to Congressional Requestors, Title: DNA Evidence DOJ Should Improve Performance Measurement and Properly Design Controls for Nationwide Grant Program; March 2019.

*2 The Washington Post, 03/23/2019, <https://www.washingtonpost.com/crime-law/2019/03/23/nationwide-dna-testing-backlog-has-nearly-doubled-despite-billion-federal-funding/>

*3 NCJ 250384. The National Institute of Justice is the research, development and evaluation agency of the U.S. Department of Justice. Title: National Best Practices for Sexual Assault Kits: A Multidisciplinary Approach.

*4 Sperm HY-LITER™ (Independent Forensics, Illinois, USA).

*5 A. De Moors, C. Frégeau, Forensic Science International: Genetics Supplement Series 3 (2011) e35-e36.

About MetaSystems

For more than 35 years, MetaSystems has been developing and producing innovative solutions for automated microscopy-based imaging for the healthcare and biotechnology sectors. Our headquarters are located in the southwest of Germany in the Rhine-Neckar metropolitan region near Heidelberg.

We are a global company with an international team working in Germany and in our subsidiaries in North and South America, Europe, India, and China. Our customers can be found in institutes, hospitals, and universities in over 100 countries around the world.

We continuously develop our products in close connection with our users, thus combining innovation with tradition. Our modern approaches include an advanced workflow management that grows with your requirements and

the use of artificial intelligence. In many segments, this has enabled us to achieve an international top position on the market.

Want to Know More?

MetaSystems offers innovative solutions and customizations for automated microscopy imaging for numerous applications with brightfield and fluorescence illumination.

Would you like to know more? Please contact us at info@metasystems-international.com.

MetaSystems software provides, among other functions, features to assist users with image processing. These include, but are not limited to, the use of machine and deep learning algorithms for pattern recognition. The output generated in this process should be regarded as preliminary suggestions and, in any case, mandatorily requires review and assessment by trained experts.

MetaSystems offers **Customization Packages** for application workflows that have been successfully implemented for customer labs using standard Metafer platform functionality. It is expected that they can be implemented for other customer labs using similar workflows and slide preparation procedures. If a Customization Package is purchased, MetaSystems product specialists will – based on their experience from other similar application cases - support the customer lab in adapting the Metafer software configuration to their needs. The performance of the solution will depend on the quality of the customer slides and the expertise of the users, MetaSystems cannot specify or guarantee any performance parameters. The validation of the solution for clinical use is the sole responsibility of the customer lab.

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