MetaSystems White Paper

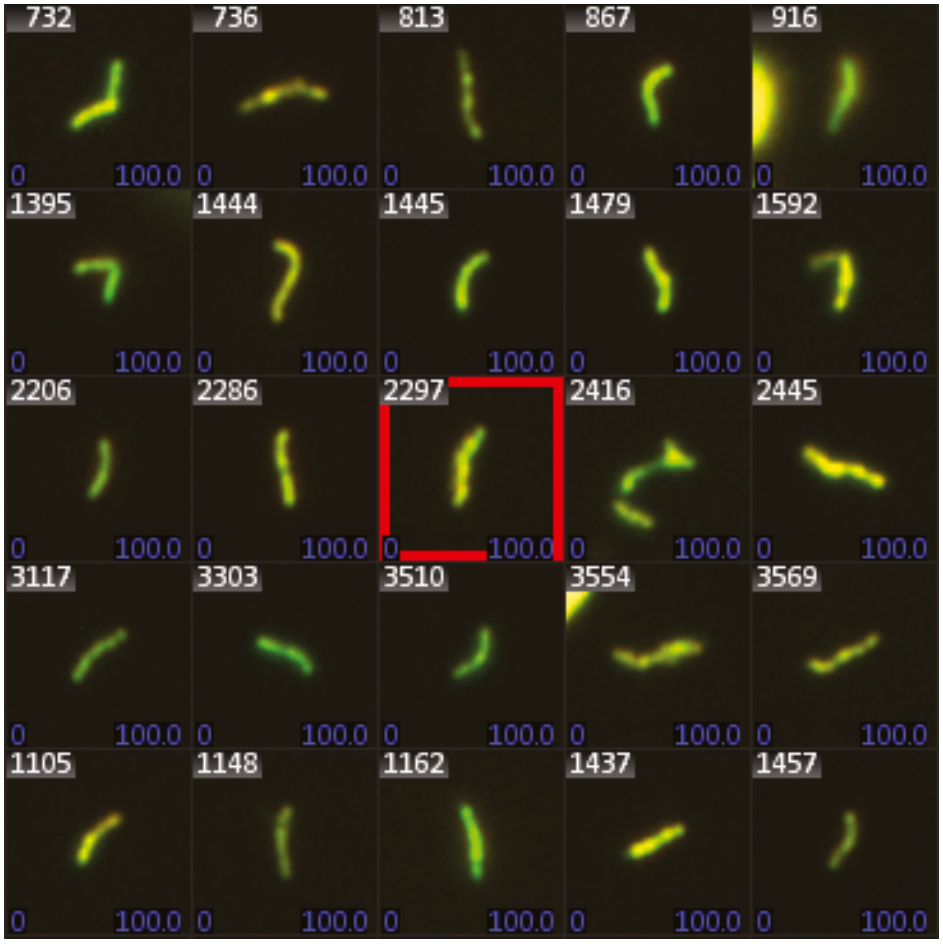
Customization Package Mycobacteria Detection

WHITE PAPER

Microscopy offers a rapid, cost-effective method for TB triage and plays a key role in monitoring treatment success by quantifying bacterial presence over time. However, manual screening is labor-intensive, time-consuming, and prone to operator-dependent variability. Recognizing these limitations, MetaSystems has customized a workflow for automated microscopy that integrates artificial intelligence, enabling efficient acquisition and evaluation of Auramine-stained slides.

You May Benefit From

- Automated image acquisition of Auramine-stained slides without user interaction.
- Deep Neural Networks (DNN) assisting in the pre-classification of Auramine-stained objects, e.g. mycobacteria.
- Real-time image gallery of detected objects for convenient on-screen assessment.
- Optional grading suggestions for expert review.
- Easy one-click re-location of found objects for closer examination, e.g. after Ziehl-Neelsen re-staining.
- Efficient management of cases and images with Neon.



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Customization Meets Intelligence

Tuberculosis (TB) remains one of the world's most pressing infectious diseases, with millions of new cases reported annually. Rapid and reliable detection of mycobacteria is critical not only for timely diagnosis but also for effective treatment monitoring.

Microscopy has long been a cornerstone of TB testing due to its cost-effectiveness and accessibility, particularly in high-burden regions. However, traditional manual screening of Auramine-stained slides is labor-intensive, time-consuming, and prone to operator-dependent variability.

To address these challenges, MetaSystems has collaborated closely with laboratory professionals to customize a workflow for automated slide scanning with the Metafer platform software, supported by Deep Neural Network (DNN) technology.

Automated image acquisition of large sample areas reduces operator workload, while standardized scanning protocols enhance reproducibility across users. The integrated DNNs detect and pre-qualify Auramine-stained objects in the images, and the software can optionally generate grading proposals that are subject to expert review. In addition, built-in data management ensures full traceability from image acquisition to reporting. The outcome is a laboratory process that merges the efficiency of automation with the expertise of trained professionals, allowing experts to retain full control of the final interpretation.

Automated Workflow for Auramine-Stained Slides

Imaging is performed with a 20x objective. A pre-scan is not required, and for most cases, single-plane scanning is sufficient. In situations with unusually thick or insufficiently diluted samples, additional focal planes may be added. Laboratories can define the number of camera fields individually, for example, the 300 Fields of View (FOVs) recommended by the World Health Organization (WHO). Processing time per slide varies depending on slide preparation, scanning settings, and sample area, but with guidance from our application specialists, imaging parameters can be tailored to individual laboratory needs.

For laboratories that complement Auramine staining with Ziehl-Neelsen staining, the system stores the precise XY coordinates of every detected object. This enables users to instantly re-locate objects of interest under the microscope after re-staining, ensuring consistent documentation and facilitating rapid confirmatory assessment.

Result Proposals and Expert Validation

Automatically detected objects are presented to users as proposals, which trained specialists can easily confirm, modify, or reject. This ensures that the responsibility remains with qualified professionals, while the DNN technology acts as a powerful assistant in reducing manual workload.

The software also supports the implementation of grading systems for the detected objects. Depending on laboratory requirements, results can be reported as absolute counts per area or graded according to pre-defined evaluation criteria. Individual grading parameters may be adapted in consultation with our application specialists, and further customization is available as an additional service.

Reports can be generated directly with the case and image management software called Neon, which is fully integrated into the Metafer platform software. Alternatively, results can be seamlessly transferred to a Laboratory Information System (LIS) for streamlined reporting and documentation within existing laboratory infrastructure.

One Platform – Multiple Applications

Microbiology laboratories typically process a wide variety of sample types, including respiratory specimens, swabs from different body regions, blood, and wound secretions. Consolidating these different applications on a single Metafer-operated scanning system makes digital microscopy not only technically versatile but also economically attractive, as it enables a faster return on investment.

In addition, a Metafer-operated scanning system can be configured as an automated "hybrid" platform, extending its use beyond microbiology and allowing laboratories to combine diverse techniques from different fields within one integrated system.

◀ *Advances in artificial intelligence now provide laboratories with new opportunities to increase efficiency, standardize processes, and improve reproducibility.*
Our Customization Packages are services to adapt and optimize an automated scanning system operated by the Metafer platform software.
The here presented Customization Package Mycobacteria Detection is adapted to streamline the processing of Auramine-stained slides by combining automated microscopy with Deep Neural Network (DNN) technology. This powerful approach keeps experts in full control of the final interpretation and transforms conventional microscopy into a versatile, scalable solution for modern microbiology laboratories.

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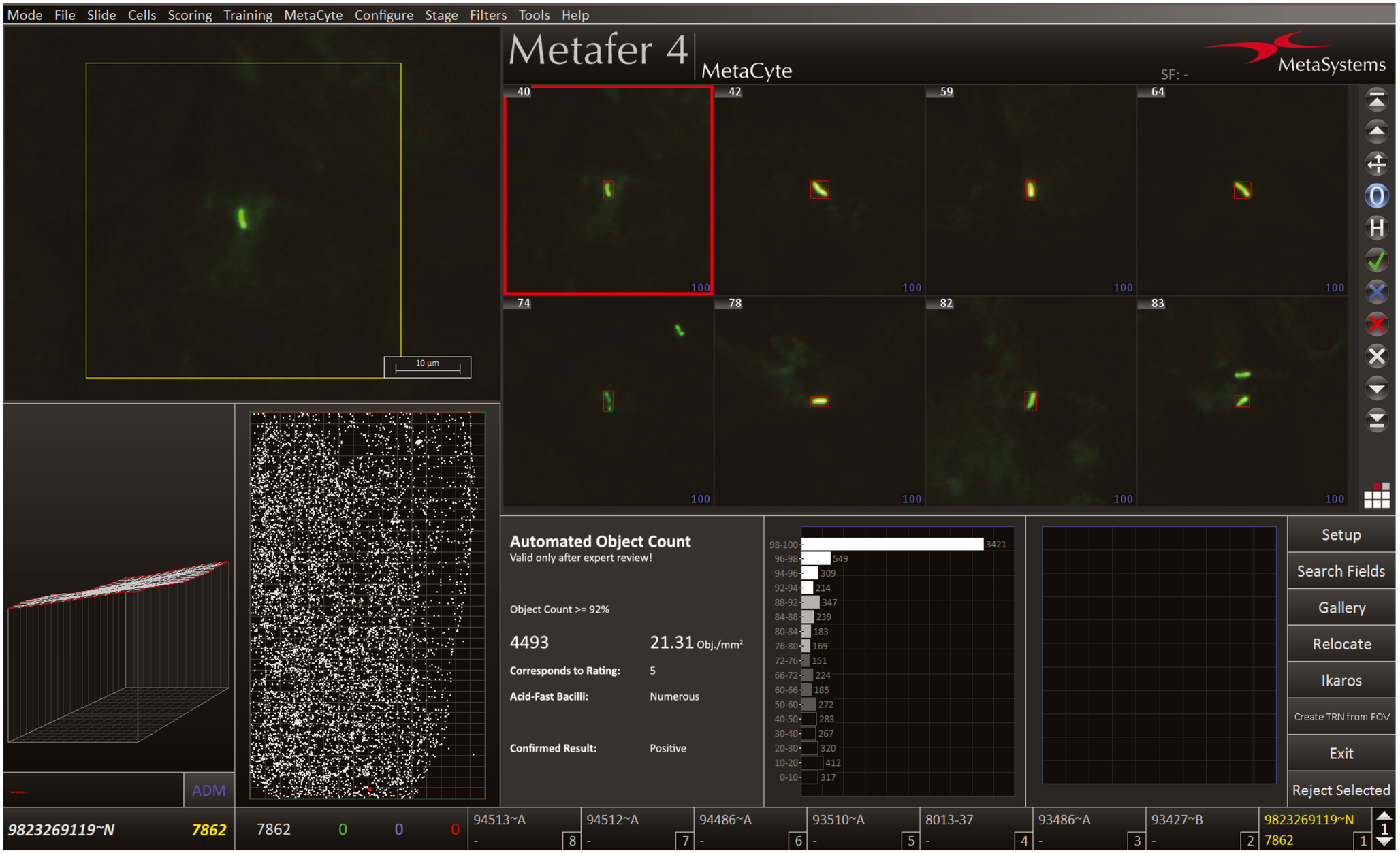


The adjacent software screenshot illustrates an exemplary scan acquired with a Metafer-operated scanning system. Leveraging Deep Neural Network (DNN) technology, the software detects and pre-qualifies Auramine-stained objects as either "bacteria" or "non-bacteria." These automated suggestions are then subject to expert confirmation or correction. For this purpose, individual objects can be reviewed in detail by browsing the image gallery.

Understanding Deep Neural Networks

Deep learning is a specialized field of artificial intelligence (AI) that allows algorithms to autonomously learn from large datasets. At the center of this approach are Deep Neural Networks (DNN) – highly complex statistical models loosely inspired by the structure and function of the human brain.

These networks consist of multiple computational layers, each of which extracts increasingly abstract features from the input images. For example, the early layers of a DNN might detect simple visual patterns such as edges, shapes, or colors. Deeper layers then combine these elements into more meaningful representations, such as "resembles a bacterium". This hierarchical feature extraction enables the network to distinguish mycobacteria from background structures or staining artifacts.

DNN Training

To enable the network for recognizing relevant patterns, it must be trained on large sets of expertly pre-classified microscopy images. During training, the DNN continuously adjusts its internal parameters by comparing its predictions with the actual, correct output (so-called ground truth). This iterative optimization process, known as backpropagation, gradually increases the accuracy of the model until it is capable of generalizing to new, previously unseen images.

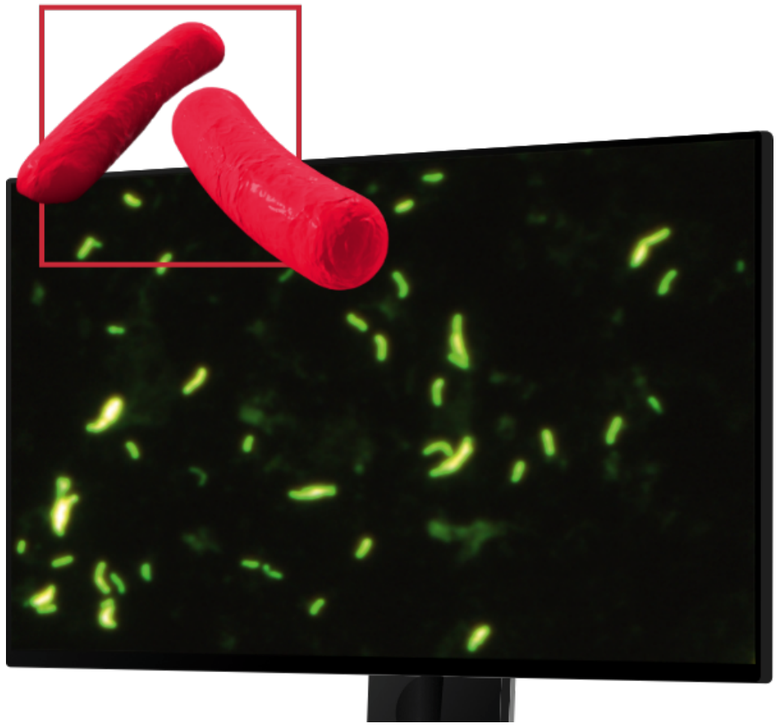
Because the training images form the sole foundation of the network's knowledge, they must not only be correctly annotated by trained specialists but also represent the full spectrum of relevant visual variations. For mycobacteria detection, this means the dataset must include examples of Auramine-stained bacteria across a wide range of intensities, morphologies, and slide preparations, as well as negative samples and potential look-alikes. In this way, the DNN learns to capture robust, generalizable features that can be applied reliably in routine laboratory work.

Training a DNN is a computationally intensive process that can take anywhere from several days to weeks. As we use established standard methodologies for the supervised development of AI models, static DNNs are generated that are not modifiable during routine use.

Performance Assessment

While the training data defines how the DNN learns, an independent validation dataset is essential to objectively measure its performance. After training, the model is tested on a reserved subset of images (approximately 5% of the total data) that it has never encountered before. This step provides an unbiased evaluation of how well the DNN can detect Auramine-stained mycobacteria under realistic conditions.

In this publication, we present performance data from the internal validation of the DNN (as of July 2025). In our assessment, the fully trained DNN correctly identified 92% of detected objects, demonstrating its accuracy and reliability for supporting Auramine-based mycobacteria detection. Ongoing development efforts aim to further enhance the network's performance.



SCIENTIFIC PUBLICATIONS

"With a national laboratory staff shortage and a local low mycobacterial infection rate, this instrument when combined with culture, can reliably triage-negative AFB-smear respiratory slides and identify positive slides requiring manual confirmation and semi-quantification."

Desruisseaux C, Broderick C, Lavergne V, Sy K, Garcia D, Barot G, Locher K, Porter C, Caza M, Charles MK. 2024. Retrospective validation of MetaSystems' deep-learning-based digital microscopy platform with assistance compared to manual fluorescence microscopy for detection of mycobacteria. J Clin Microbiol 62:e01069-23. https://doi.org/10.1128/jcm.01069-23.

"Assistance by the scanning and analysis system allowed for a higher sensitivity (40/56 positive slides detected) than manual microscopy (34/56 positive slides detected), while greatly reducing manual slide-analysis time from a recommended 5–15 min to around 10 s per slide on average."

Horvath L, Hänselmann S, Mannsperger H, Degenhardt S, Last K, Zimmermann S, Burckhardt I. 2020. Machine-assisted interpretation of auramine stains substantially increases throughput and sensitivity of microscopic tuberculosis diagnosis. Tuberculosis, Volume 125, 2020, 101993, ISSN 1472-9792. https://doi.org/10.1016/j.tube.2020.101993.

"We can show that using an automated scanning and analysis system for auramine-stained slides to assist diagnosis can improve sensitivity of detection and reduce manual slide-handling time."

Hwang Y, Park S, Kim J, Kim T, Ryoo S. 2021. Evaluation of Machine-Assisted Interpretation of Auramine Stains for Diagnosis of Pulmonary Tuberculosis. Proceedings of the Fall Conference of the Korean Society for Tuberculosis and Respiratory Diseases, 129(0), pp 665-666.

About MetaSystems

For almost 40 years, MetaSystems has been developing innovative solutions for automated microscopy-based imaging for the healthcare and biotechnology sectors. Our headquarters are located in the southwest of Germany 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 and the use of artificial intelligence. In many segments, this has enabled us to achieve an international top position.

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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