MetaSystems White Paper

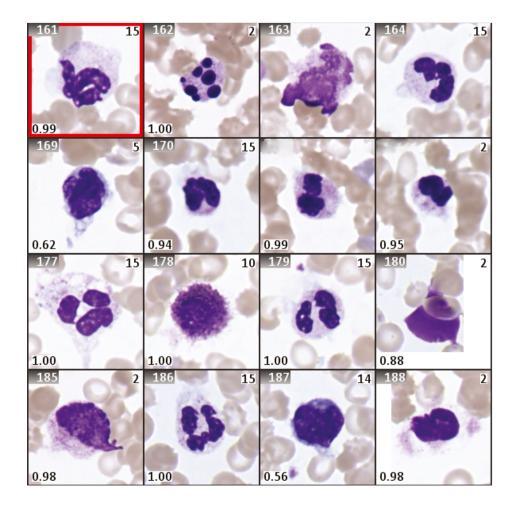
Customization Package Extended Blood Cell Detection

Differential blood counts are essential for hematological testing, but manual microscopy is labor-intensive, and flow cytometry lacks the ability to detect subtle morphological changes. To bridge this gap, MetaSystems has adapted an Al-supported workflow that automates the acquisition of slides and pre-catagorizes detected blood cells. The solution includes a real-time image gallery and a dedicated RapidScore keyboard for quick validation and re-classification. This helps our users with an efficient, flexible, and dynamic cell classification.



You May Benefit From:

- Automated image captures of peripheral blood smears without user intervention.
- Deep Neural Networks (DNNs) to assist in detecting and classifying blood cells.
- Real-time image gallery for convenient display of single cell classes or all detected objects.
- Fast expert review using the dedicated RapidScore keyboard.
- Effortless uptake of additional cell classes during expert review.
- One-click relocation of found objects using the gallery object relocation function.





Customization Meets Intelligence

Accurate blood cell differential counts are essential for diagnosing hematological disorders. However, many laboratories still face a dilemma: Manual microscopy offers high sensitivity but is time-consuming and depends heavily on the operator's expertise. On the other hand, flow cytometry provides speed and standardization but often misses subtle morphological changes that can be highly relevant. This situation creates a gap, especially in cases that require both visual precision and high throughput.

MetaSystems addresses to bridge this gap with a specialized workflow built on microscopy automation, artificial intelligence, and seamless integration into lab-specific procedures - the Customization Package Extended Blood Cell Detection. Developed in close collaboration with laboratory experts, the customization package builds on the Metafer Platform Software and supports flexible adaptations to individual laboratory requirements for the evaluation of peripheral blood smears.

Workflow in Practice

Deep learning is revolutionizing image processing in medicine and life sciences. At MetaSystems, we trained Deep Neural Networks (DNNs) to support complex classification tasks in hematology. Unlike traditional algorithms, DNNs learn to recognize relevant features directly from expert-labeled image data. Within the workflow, the DNN technology is seamlessly integrated into several key steps of the slide scanning process.

During the pre-scan, the system automatically identifies suitable regions on the slide that contain the relevant parts of the blood smear. It then detects and selects individual cells within these regions for subsequent high-resolution imaging. Scan times vary depending on the sample area and chosen parameters. Our application specialists help fine-tune these settings to ensure the optimal balance between speed and image quality. Finally, a DNN pre-classifies 16 relevant categories, including nucleated RBCs, granulocytes, monocytes, lymphocytes, and platelets.

These DNN-generated classifications provide a starting point and are subject to expert review. Professional users validate or correct DNN-generated results using the dedicated RapidScore keyboard. This intuitive device enables rapid verification and re-classification. Additional cell classes can be included effortlessly during the review process.

The software enables reliable cell relocation with a single click, even after de-staining the slide. This is especially important in critical cases and when subsequent analyses, such as FISH, are required.

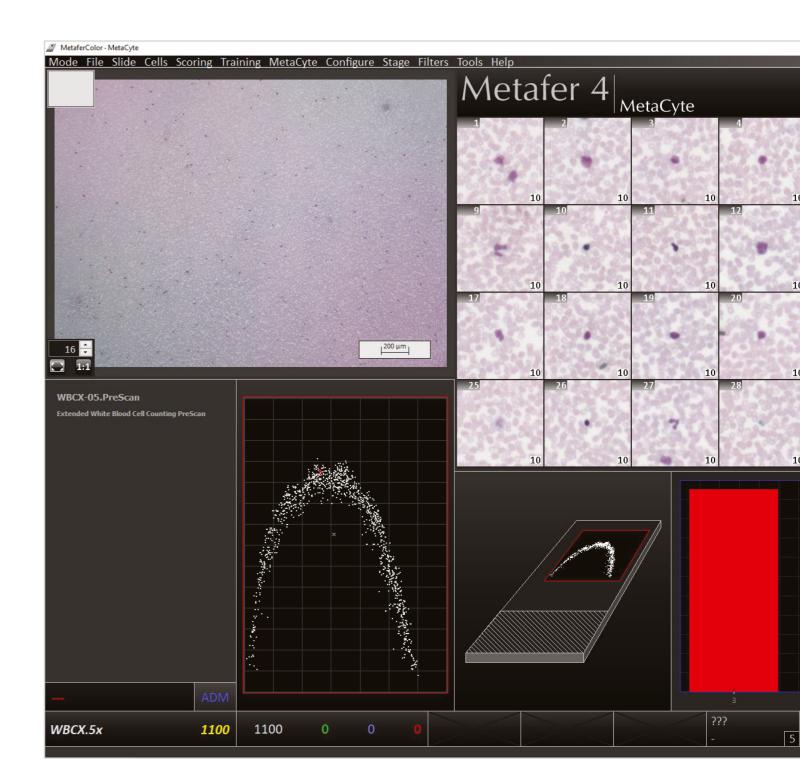
Systems operated with our Metafer software can be configured to meet the requirements of laboratories of different sizes. If capacity requires 24/7 microscopy operation, an automated slide feeder can be added to the scanning system. With a scalable capacity from 8 up to 800 slides being automatically scanned, we support our customers in high-throughput applications.

This partial software screenshot illustrates the automated output of a low-magnification pre-scan obtained from a peripheral blood smear.

Leveraging DNN technology, the software identifies suitable areas on the slide for subsequent high-resolution imaging.

Users can view the selected Fields of View (FOVs), access a gallery of individual objects centered within each frame, and navigate a virtual slide displaying the precise positions of all detected objects.







This software screenshot shows the result of a high-magnification main scan of a peripheral blood smear.

The Metafer-operated scanning system acquires high-resolution images of each object detected during the pre-scan and a DNN assigns them to cell categories.

These DNN-generated suggestions must be confirmed or corrected by an expert. For this purpose, individual objects can be inspected in detail by browsing the image gallery.



DNN TRAINING AND VALIDATION

How It Works: Deep Neural Networks Explained

Deep learning is a specialized branch of artificial intelligence (AI) that enables algorithms to autonomously learn from large datasets. At the core of this approach are Deep Neural Networks (DNNs) – complex statistical models loosely inspired by the structure of the human brain. These networks consist of multiple computational layers, each one extracting increasingly abstract features from the input images. In practical terms, the early layers of a DNN might detect simple visual elements like shapes or colors, while deeper layers combine these elements into meaningful representations, such as "looks like a lymphocyte" or "resembles a monocyte."

To enable the network to recognize relevant patterns, it must be trained on large sets of pre-classified example images. During training, the DNN adjusts its internal parameters iteratively, comparing its predictions to the actual, correct output (so-called ground-truth). Through this process, called back-propagation, the model gradually

improves its accuracy until it is able to generalize to new, previously unseen image data.

Training Data: The Foundation

Since the training images are the only source of knowledge, they must not only be correctly pre-classified by professionals, but also show the objects-of-interest in all relevant variations. Thereby, the DNN learns robust features for image differentiation. In hematology, this means the network must be exposed to expertly annotated microscopy images that capture the full range of morphological variations seen in practice.

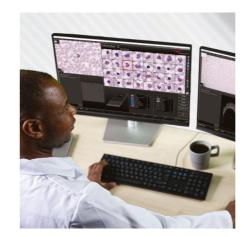
Training a DNN is a computationally intensive process that can take anywhere from several days to weeks. As we use established standard methodologies for the supervised development of Al models, static DNNs are generated that are not modifiable during routine use. While training data shapes the learning process of a DNN, validation data is essential to objectively assess its performance.

Validated Performance

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 input data).

In this publication, we provide the performance data from the internal validation of the DNN (as of June 2025), which categorizes the high-resolution images into 16 groups. The performance values for the individual classes are shown in the adjacent table. This shows that, with the exception of three classes (Promyelocytes, Band Granulocytes, and Plasma Cells), the DNN can assign the images in the validation data set highly reliably to the class determined by experts.

For the mentioned three classes with performance values around 70%, two factors seem to play a role: First, these cell classes occur less frequently in the input data set. Second, they share high visual similarity to other classes. If a higher performance is desired for these classes, additional sample images must be provided for further training.





Validation of DNN-generated results is mandatory in clinical environments. With the proposed MetaSystems workflow, validation can be easily performed on screen, even on seperate workstations.

The RapidScore keyboard allows swift confirmation or correction of DNN-generated pre-classifications with just one keystroke.

For the performance evaluation of the trained DNNs, we use independent test data, which is an established standard methodology for the supervised development of AI models.

The table presents the performance data from the internal validation of the DNN (as of June 2025), which classifies high-resolution images into 16 distinct categories.

In practice, these automatically generated suggestions must be confirmed or re-classified by experts.

Class Name	Perfor- mance %
Artifacts	90
Nucleated RBCs	95
Myeloblasts	93
Promyelocytes	71
Myelocytes	94
Meta-Myelocytes	85
Band Granulocytes	71
Segmented Granulocytes	99
Basophil Granulocytes	94
Eosinophil Granulocytes	95
Monocytes	95
Lymphocytes	93
Atypical Lymphocytes	81
Plasma cells	73
Smudge cells	94
Platelets	98



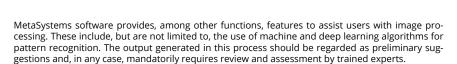
About MetaSystems

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 achieve an international top position.

an advanced workflow management and the use of artificial intelligence. In many segments, this has enabled us to



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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