Fraunhofer
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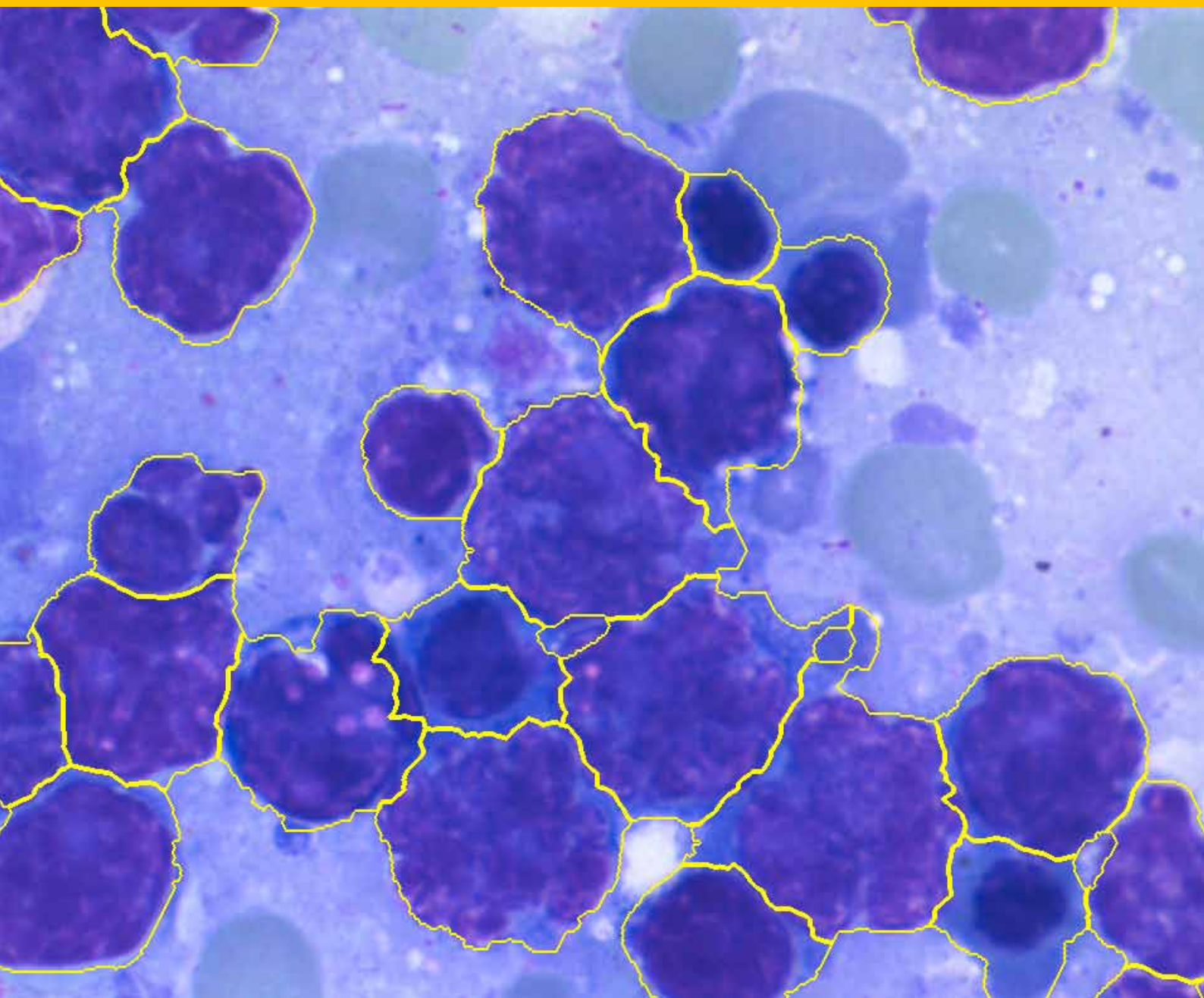
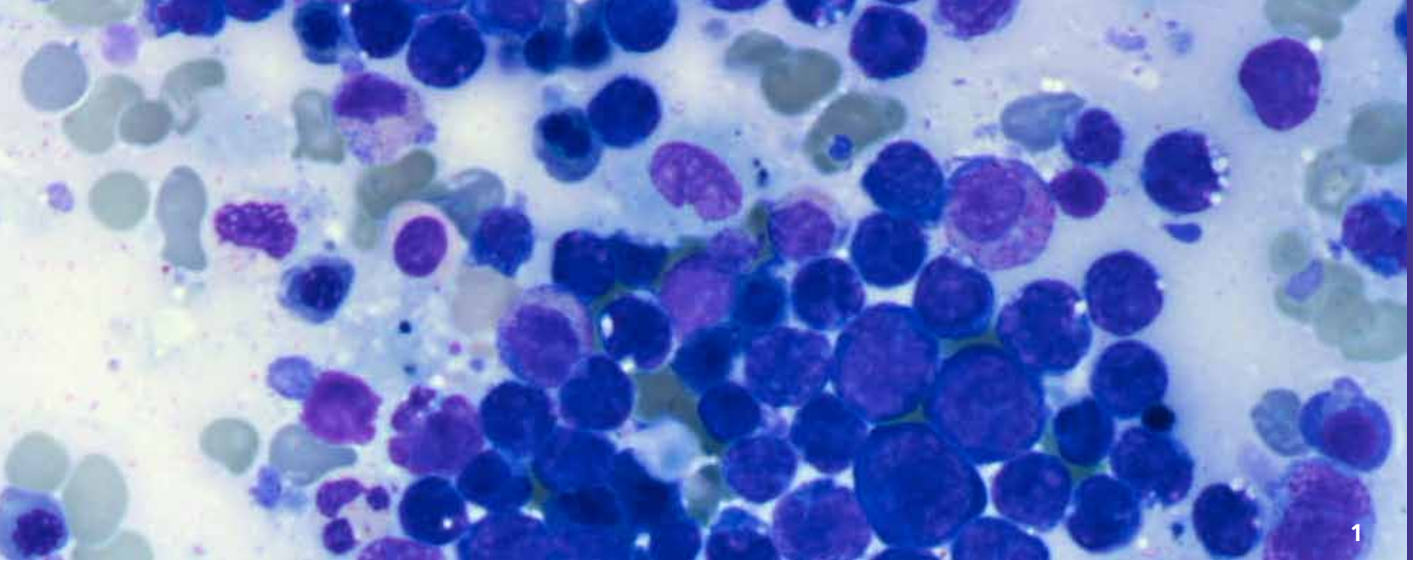
FRAUNHOFER INSTITUTE FOR INTEGRATED CIRCUITS IIS

MICROSCOPY

SOFTWARE AND SYSTEMS FOR HEMATOLOGY





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HEMATOLOGY

Examination and assessment of peripheral blood and bone marrow represents an essential source of information in connection with medical diagnostics of numerous disease patterns such as inflammations, allergies, bacterial infections or various types of blood diseases such as anemias and leukemias. For such purpose, a sample of venous blood is taken and examined by flow cytometry. However, depending on the disease pattern, visual control of the smear under a microscope is required in many cases. For example, assessment of malignant lymphomas and leukemias requires extensive examination of prepared bone marrow specimens.

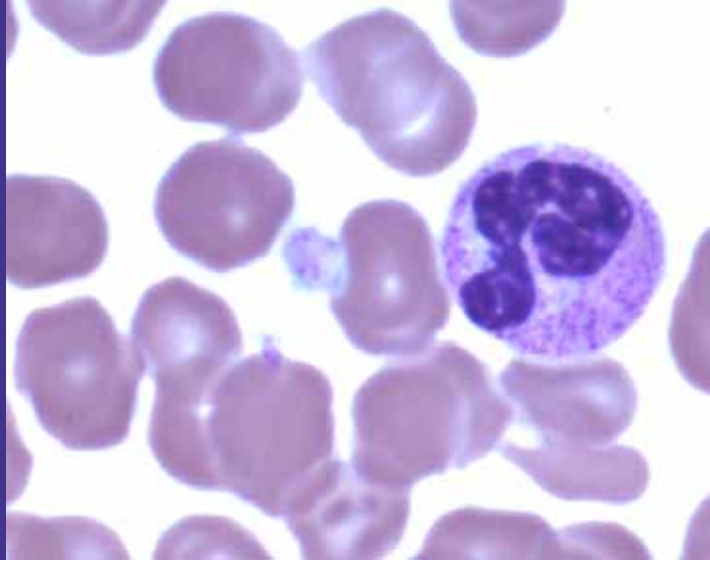
Due to increasing centralization, higher quality requirements and cost pressure in the health care system, laboratories are forced to continuously increasing automation. In the special field of computer-assisted microscopy (CAM) for hematology the Department of Image Processing and Medical Engineering of the Fraunhofer IIS offers corresponding solutions from algorithms for image processing to completely integrated systems.

DIFFERENTIAL BLOOD COUNT – HemaCAM®

The differential white blood cell count represents an important component of hematology. The HemaCAM® system allows for automated analysis of blood smears, and supports classification of cells. HemaCAM® reduces labor time, increases quality of diagnosis, and contributes to the creation of a rapid and objective differential blood cell count, also in case of suspicious blood samples.

It is composed of a high-power microscope with a motorized stage that can be transversally and vertically moved by a computer. An insertable frame allows for simultaneous placement of up to eight slides per round. The table can be used to move the slides between objective lens and light source, and enables fully automated recording. The HemaCAM® software can be intuitively operated via a graphical user interface and controls all functions of the microscope and finally presents the results of the analysis.

The HemaCAM® system is certified as in-vitro diagnostic device in accordance with the Medical Devices Act and is distributed all over Europe by our industrial partner Horn Imaging GmbH since October 2010. The correspondingly required specifications, documents and the risk management up to design and performance of the legally required performance evaluation study were performed by the Fraunhofer IIS Medical Engineering Test and Demonstration Center METEAN. HemaCAM® is subject to continuous further development and can also be customized.



BONE MARROW

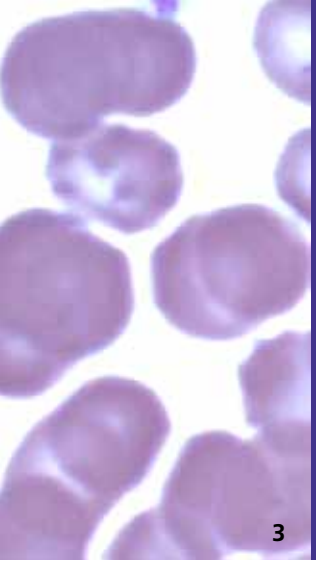
Cytological examination of the bone marrow includes sampling and microscope-based examination of bone marrow cells from the vertebral body. The most important indicators for this are deviations of the differential blood count, clarification of causes with anemias, exclusion of bone marrow involvement with malignant lymphomas (malignant diseases of lymph nodes, palatine tonsils, spleen and bone marrow) and suspected leukemia (blood cancer).

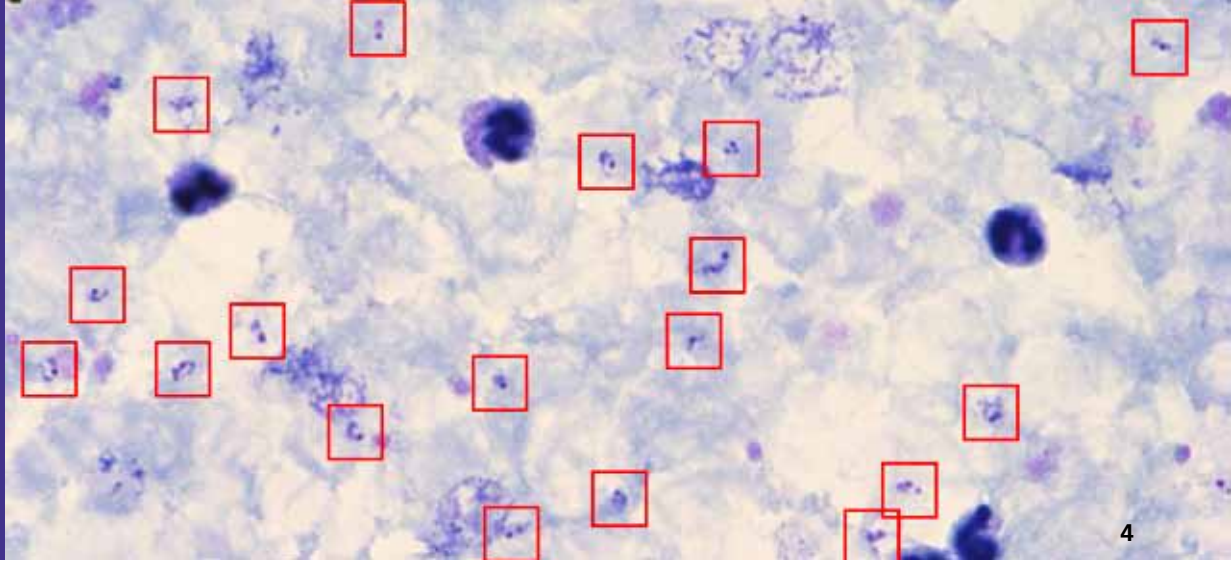
Leukemias are diseases of the blood-forming system and are characterized by increased formation of white blood cells (leukocytes) and their precursors. The increased count of leukocytes eliminates normal blood formation in the bone marrow and can be verified in the peripheral blood, where the normal blood components are reduced. Thus, morphological assessment of blood stem cells represents the basis for making a diagnostic decision, and often it is also a decision guidance for further medical diagnostics and therapy.
Fraunhofer IIS develops methods and systems for analysis of prepared bone marrow specimens. Such prepared specimens are digitized with an automated microscope and then analyzed on a high-performance computer. Evaluation regions are defined for the recorded image data, and the correspondingly present cells are automatically segmented and separated from the surrounding cells. The various maturation stages of the blood cells can be characterized, classified and statistically evaluated by using a number of characteristics describing cell morphology. Such evaluation is decisive for further diagnostics and therapy.

MALARIA

Malaria is a highly infectious disease with extensive occurrence in tropical and subtropical regions. It is caused by a parasite of the Plasmodium species and transmitted by the Anopheles mosquito. According to WHO data, approx. 243 million malaria cases occurred globally in 2008. Microscopy-based examination of stained blood smears on the basis of the thin and particularly also the thick blood smear represents the gold standard for diagnosis. As even a small number of pathogens may result in infection, sampling of such a prepared specimen represents a very time-consuming and exhausting process.

Fraunhofer IIS develops systems for automatic digitalization and evaluation to support analysis of prepared malaria specimens. For this, a multitude of views on the smears is captured by the camera and automatically examined for presence of plasmodia. This is initially performed with the thick blood smear. In case of determination of an infection with plasmodia, the type of the malaria pathogen can be identified on the thin blood smear. Robust detection algorithms allow for high sensitivity and minimize false-positives, i. e. indication of malaria infection although there is no malaria infection actually present.





DIGITALIZATION

Automated microscopes can be used to efficiently and rapidly digitize prepared specimens so that they are flexibly, globally and above all age-resistantly conserved and made available. Such so-called ‚virtual slides' can be easily displayed and navigated on the monitor by using PC-based or Internet-based systems.

We develop software platforms and basis technologies for various applications that are required for efficient and safe digitalization of slides and enable detailed visualization of samples on the PC or via the Internet. A semi-automatic universal scanning platform enables digitalization, visualization and annotation of various prepared specimens. Correspondingly, a multitude of biological samples such as blood, bone marrow, cerebrospinal fluid or histological sections can be digitized. Individually configurable profiles allow for adjustment of scanning parameters to the respective task. In a first step a lens with low magnification is used to create a slide overview. Based on this overview regions manually selected by the user can be digitized with any possible higher magnifications (e.g. 5x, 10x, 20x, 40x, 100x). This results in the so-called ‚virtual slide' that consists of the overview scan and the high-resolution views included into the same coordinate system. This enables almost stepless zooming of the samples as well as smooth and artifact-free navigation through the whole digitized slide.

Fields of application include image documentation of prepared specimens at the hematological laboratory, digitalization for scientific purposes, presentations and conferences as well as training and education. Adjustment and extension for specific purposes is possible at any time.

QUALIFICATION

Learning of the morphologic differentiation of cells by microscopy requires years of experience. Such ability must be continuously perfected by viewing and studying of numerous microscopic images in atlases as well as selected prepared specimens. Currently, the demographic development results in increase of the demand for preparation, communication and standardized testing of corresponding knowledge. The digitized specimens can be presented as so-called ‚virtual slides' on the monitor, thus allowing for easy navigation and viewing - just like you are using a microscope. This may improve education and training of specialists.
The technologies developed at Fraunhofer IIS such as stitching of large-area micrograph panoramas enable rapid and ergonomic access to correspondingly processed digital prepared specimens. Textual and graphical annotations can be supplemented and displayed. Such meta information also allow for easy comparison to a qualified expert's opinion, correspondingly making the individual training success quantifiable. Adaption to further fields of application is easily possible.

1 Smeared bone marrow aspirate according to Pappenheim staining.

2 Computer-assisted creation of differential blood counts by using HemaCAM®.

3 Segmented neutrophil in peripheral blood.

4 Automatic detection of plasmodia (malaria pathogens).

Title:
Automatically segmented blood cells in prepared bone marrow specimen.

OUR OFFER

The Department of Image Processing and Medical Engineering develops realizable technical solutions for medical technology, laboratory diagnostics and biomedicine. Industry and service providers of any size benefit from contract research. We offer know-how to small and medium-sized companies without own R&D department and may serve as an ‚extended workbench'.

We are pleased to offer our services – from feasibility studies for your specific problem and customized evaluation of large amounts of image data to research and development projects. Besides adaption and licensing of available algorithms and methods into existing systems, we also implement the whole control software and user interface upon request.
We provide support with technical documentation, performance of risk management as well as planning and performance of clinical studies and performance assessment studies in accordance with the applicable directives (DIN EN14971, 93/42/EEC, 98/79/EC) and the legal requirements as per Medical Devices Act, particularly via the Fraunhofer IIS Medical Engineering Test and Demonstration Center (METEAN), which is located in and connected to the University Clinics of Erlangen.

- **TECHNOLOGY AND MARKET STUDIES**
- **FEASIBILITY STUDIES AND DEVELOPMENT OF CONCEPTS**
- **DEVELOPMENT OF ALGORITHMS AND SYSTEMS**
- **RESEARCH AND DEVELOPMENT SERVICES**
- **CUSTOMER-SPECIFIC EVALUATION OF IMAGE DATA**
- **TECHNICAL DOCUMENTATION AND RISK MANAGEMENT**
- **PLANNING AND PERFORMANCE OF CLINICAL STUDIES**

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