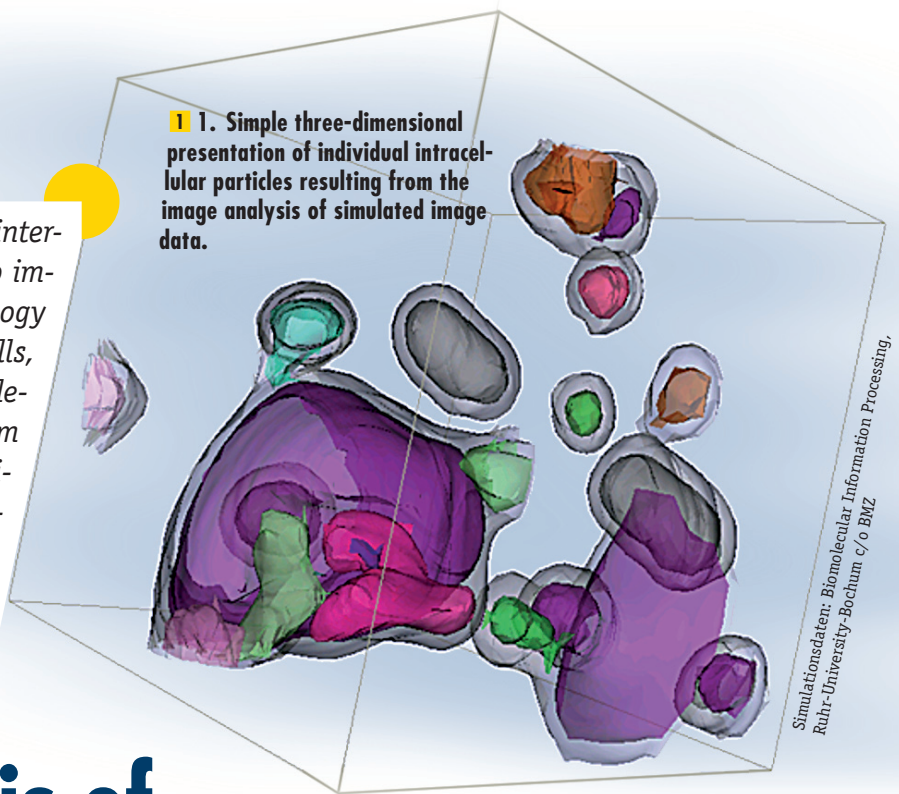


Image data must be analyzed and interpreted reliably and reproducibly to improve the understanding of morphology and functions of cell organelles, cells, organs or organisms. Definiens has developed a new image analysis platform based on its computer language Cognition Network Language, which analyzes the image data automatically and context-based.

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1 Simple three-dimensional presentation of individual intracellular particles resulting from the image analysis of simulated image data.



Simulationsdaten: Biomolekular Information Processing, Ruhr-University-Bochum c/o BMZ

# Analysis of multi-dimensional image data

It is impossible to imagine biological and medical examinations without imaging instruments. In particular, image data are often the primary source of information in research and development of new cell assays, biomarkers as well as new drugs. New image analysis tools, for example, in optical microscopy, generate extensive image data within an ever shorter period of time that must then be evaluated precisely and reliably. The automatic, computerized analysis and interpretation of data is gaining increasingly in importance. Within this process the quantification of image contents helps the collection and understanding of morphology, processes,

conditions and functions inside cell organelle, cells, tissue, organs and organisms.

A prerequisite for the reliable and reproducible interpretation of image contents is the image analysis, which includes the calculation of a tabular or pictured description of the underlying image. There are a number of different procedures and algorithms [1] available for the segmentation of image data as well as for the classification of objects.

## Computer versus person

The information calculated by computers has to date been based almost exclusively on the detection of conspicuous

single elements. Existing context information, such as relevant objects in images of other section planes – or in relation to confocal microscopic imagery in the same section – can be taken into consideration to a lesser extent for technical reasons. Hence these systems are still far-off from the cognitive-diagnostic skills of a human expert in their efficiency.

The majority of these systems are based on pixel-based algorithms, procedures and applications. Object and context-based algorithms and procedures for image analysis, on the other hand, have only been developed intensively in recent years. Both pixel-based and object-based image analyzing procedures have benefits and drawbacks. A combination of the two approaches would be ideal both in relation to quality and to the speed of the image analysis.

## Image analysis solutions

The Definiens Cognition Network Technology® represents a significant step in the direction of automatic perception of image data. The goal of this technology is to develop reproducible image analysis solutions, drawing on the expertise of specialists, which can analyze a large volume of images with complex contents fully automatically, in great detail and in respect of quantity as well as quality. The techno-

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2 Image analysis of optical cross-sections of breast biopsies by the Definiens Developer – three-dimensional view of the nuclei

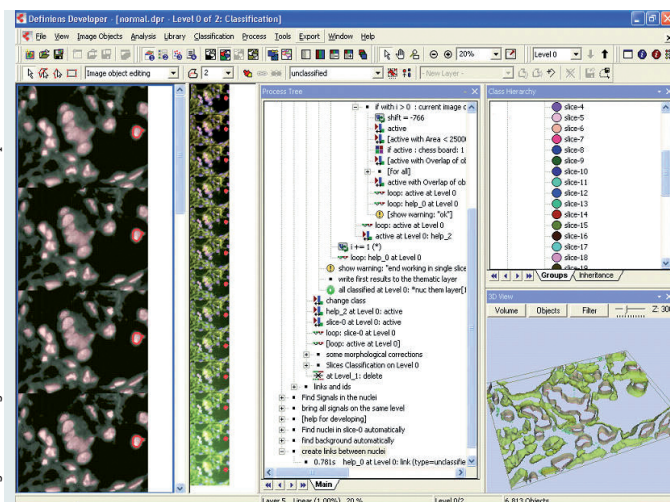


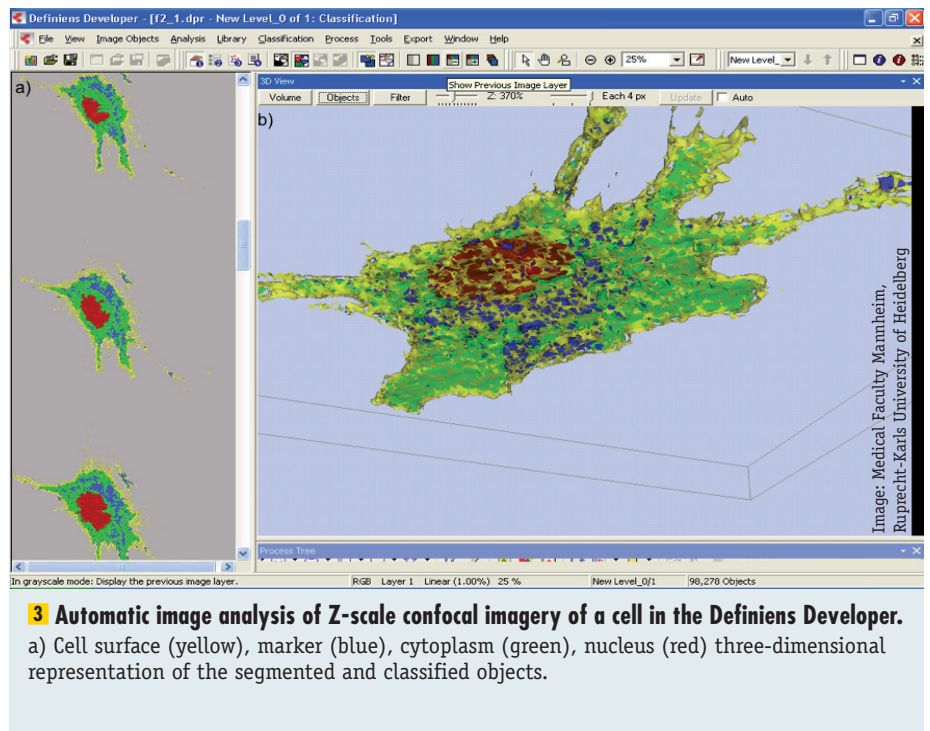
Image: Pathologisches Institut Luzerner Kantonspital

logy is based on the concept of imaging elementary mechanisms of human perception in an image analyzing procedure. As opposed to automatic image analyzing procedures, human beings possess two particular skills, which can not be attained to any extent by machines. These are: drawing context-related conclusions as well as being able to incorporate complex expertise into these conclusions. Human beings are able to process a significantly higher degree of complexity than computers are currently able to process. The challenge consists of entering complex knowledge into a system in a – for the human mind - natural way and formulating a simple context-driven analysis so that the input knowledge will find feasible application.

The new image analyzing procedure is based on the concept of information processing with the Cognition Network Language (CNL). The basic idea consists of the stepwise development of an object network in the course of an automated perception of image data. The new computer language CNL helps to formulate this procedure naturally. Special links permit the setting up of object hierarchies and the allocation of objects to object classes. The combination of pixel and object-based algorithms is also possible and consequently allows the processing to be accelerated. Every developed image analyzed solution can be saved as a rule and applied for other data sets [2, 3].

For example, pixels are represented as objects at the level of the smallest image unit. At the next hierarchical level, pixel objects can be integrated to form larger units e.g. nuclei, cell organelles or cytoplasm. These objects organize themselves at the next hierarchical level to form objects, which build respective individual cells. If required, this procedure can be enhanced further in that diverse united cell structures are combined to form organs, organs to organisms and organisms to species.

If the required data do not exist in an image, the contents of several images can be linked together and metadata, e.g., information originating from texts and tables can be consulted or integrated. This permits the analysis of multidimensional image data, e.g., three-dimensional imagery of cells or united cell structures. Findings from the modeling and simulation of biological processes, which, for example, represent cell particles and their development in alphanumeric format, could be converted to three-dimensional images and analyzed as image data.




### 3 Automatic image analysis of Z-scale confocal imagery of a cell in the Definiens Developer.

a) Cell surface (yellow), marker (blue), cytoplasm (green), nucleus (red) three-dimensional representation of the segmented and classified objects.

### Wide application spectrum

The image analysis software from Definiens is widely used in biology, medicine and pharmaceutical research. The unique selling proposition of the software is the opportunity to analyze a wide spectrum of image modalities. These include electronic microscopy, microscopy in high-throughput and high-content workflows for image-based assays in biology, research and development of new drugs and biomarkers as well as pathology and radiology. One example shows the analysis of optic cross-sections obtained from the microscopy of breast biopsies (see fig. 2). Cell nuclei or united cell structures are extracted as “single” objects and analyzed and quantified morphologically, volumetrically and in relation to individual objects or in united structures of adjacent objects. From three-dimensional data sets originating from cytological confocal microscopy, individual cell organelle, cells and groups of cells can be prepared with the aid of the image analysis software representations (see fig. 3)

A further example is demonstrated by the image analytical result originating from the analysis of simulated image data (see fig. 3). The simulations define the development and behavior of particles and vesicles during intracellular processes. The alphanumeric data resulting from the simulation is transformed into image data and analyzed with the aid of the Definiens Developer. This application is currently

being enhanced for the analysis of sequences of three-dimensionally simulated image data. The goal is to process the findings of experiments, simulations and metadata on one common platform and consequently to transform information from one domain to the other. In this way, for example confocal image data can be appropriately analyzed and then used as an input for the modulation. Reciprocally, simulation findings can be used to improve experiments following analysis. 

### Literature:

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