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9-612-002

REV: SEPTEMBER 9, 2011

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Digital microscopy is making me crazy!

I was working on a Zeiss confocal microscope, a very expensive microscope. I was taking images, and the next day I had a talk for a lab meeting. I captured the images, and then I wanted to prepare the material for the lab meeting. I said to myself. "No problem, I have the installation disk for the software, I can take it and go to my own computer." My desk computer was running on a more modern operating system, Windows 7, which the software from Carl Zeiss doesn't support. So I was getting a bit crazy already. I went back with my portable hard drive where I stored all of my data, and went back to the instrument where I acquired it, because I wanted to do the analysis quickly. But of course somebody else was using the instrument, which meant I couldn't get on there. Finally I went home where I have a Macintosh computer. And there of course the software was not running there as well, the Zeiss software. So in the end I downloaded ImageJ. It was cumbersome; I had to import the Zeiss images, using the import filter for it. I said to myself, I will do my analysis using it, then I can present it tomorrow. But it is making me crazy that Zeiss is not supporting me as a scientist in the way I actually need to work!"

— e-mail from Dr. Hellen Ishikawa, Ludwig-Maximilian-University Munich

Dr. Richard Ankerhold from Carl Zeiss MicroImaging read the e-mail from Ishikawa. He recognized that the software problem that was making Ishikawa crazy was a temporary issue. It was inevitable that whenever Microsoft released a new operating system that had significant changes in it from its predecessor, it took some time for companies like Carl Zeiss to update their applications to run in the new environment. He understood that part. But why was it sufficient for her to use ImageJ, a public domain image processing program that came from the National Institutes of Health? After all, it wasn't nearly as powerful or feature rich as the Zeiss software that came integrated with the confocal microscope. But could it be that ImageJ was good enough?

Ishikawa's lab also provided a window into the "rat race for high-end innovations" in microscopy, as Ankerhold described it. To be a lead supplier, a company had to be quick to spot the emerging needs and usage trends. The demands on the capabilities of the microscope systems often tested the limits of physics, yet these systems had to perform reliably in the hands of biologists who might not appreciate the subtleties or temperamental nature of leading edge instruments. The competition was tough: Leica, Olympus and Nikon were all world class, capable competitors on the high-end. Often scientists who were "lead users"[1] developed new techniques and then would start companies as well, and these entrepreneurial offshoots injected an unpredictable level of competition as high-end customers tolerated the generally not quite complete product in the name of being at the forefront of new techniques.

[1] Eric von Hippel at MIT coined this term to describe consumers of a product who will face needs that will become general in the market, but months or years ahead of the bulk of the market.

The question in Ankerhold's mind today focused on Carl Zeiss's broader software strategy. The company had pursued a modular strategy for its products to enable customers to tailor solutions to their advanced research problems. Its software was also modular to an extent, with a data acquisition module and a processing module. One challenge was the widely varied and constantly changing needs on the processing side for advanced research scientists, which made it difficult for Carl Zeiss to keep up and always offer what was hot at the moment. Yet in the mid-range and lower tiers of the market, and especially for clinical and industrial applications, customers wanted simple and reliable workflow solutions. This argued for integrated suites. For Richard, Ishikawa was a valuable source of market research on one segment of the market.

Carl Zeiss and digital microscopy solutions

Carl Zeiss MicroImaging was a business unit focused on advanced microscopy for the biological and medical sciences, clinical applications, and materials science and industrial sectors. Historically Carl Zeiss was one of the leaders in high-end optical microscopy. It built a variety of platforms from general purpose to specialized, and it was renowned for its precision and superior optical performance. The company offered a wide range of microscopes and microscope systems for some of the most demanding users.

Until the advent of photographic film, the predominant way of recording a microscope image of a specimen was hand drawing on paper while viewing through the eyepiece. Film made the recording of images straightforward, though obtaining the correct exposure and the long processing times were challenges. The advent of analog video cameras enabled an early form of electronic image acquisition, with "frame grabbers" producing digitized images. Much as high resolution solid state image sensors transformed film-based photography to digital, the arrival of the new technology vastly expanded what scientists could do with microscope images. Digital sensors like the charge coupled devices (CCDs) used in digital cameras enabled measurement of the flux of light coming from different points in a cell or tissue, and as instrumentation improved, researchers started to use digital microscopy as a tool for quantitative measurements. The tool started to be used for assays and screening of samples.

Digital microscopy meant a lot more data for the user. Not only were images captured at multiple magnifications, but basic experimental data and parameters from the data acquisition system would be saved. This auxiliary information, often called metadata, was usually stored somewhere in the image files, and each manufacturer utilized their own formats. As new data acquisition systems, imaging technologies, and new experimental techniques were developed, the data formats evolved and things got more complex for users.

Segmenting the market

While microscopy was truly a general purpose technology that had applicability in a broad range of fields, Carl Zeiss categorized its customers into two main groups: biomedical sciences, which included a dominant group of users in histology, pathology, neurosciences, cell biology and pharmacology, and an industrial segment, which was concentrated in quality inspection and material sciences. Biomedical research was composed of many disciplines. While most scientists in the field thought of themselves as pursuing a narrow discipline (cell biologists, neurobiologists, developmental biologists, etc.), in practice they often used similar model systems (single cell cultures, drosophila, zebrafish, mice, rats, etc.), similar imaging methods (multi-channel fluorescence, time-lapse, 3D image stacks, etc.), similar tools to stain their samples (fluorescently labeled antibodies

directed against proteins of interest, genetic labels like green-fluorescent-protein), and similar ways of visualizing or analyzing their results (co-localization, correlation, etc.). Thus even though scientists saw themselves in different disciplines, they often purchased the same microscopes systems with different software modules, accessories or configurations.

Biomedical research science principal investigators (PIs) often had extensive equipment within their own research groups. More specialized and expensive instruments were usually shared in multiuser core imaging facilities, a common practice with high-end scientific instruments. Some of the differentiating features of the two customer categories are listed in **Exhibit 1**.

Contained within the biomedical segment was a clinical sub segment in which microscopy users were principally concerned with the repetitive examination of specimens. Users here were generally medical lab technicians or trained scientists in pathology, histology, pharmacology or similar and related fields. Ankerhold explained the evolution of techniques, "It is very different types of work, what we see is some movement … you see certain research methods or applications become standard, particularly when they are coming from cancer research. Then it takes some years, sometimes even decades to move over first into clinically oriented research. And then it goes to the routine."

The industrial category was quite different. Users typically fell into a range of activities ranging from basic research in materials science to R&D, to quality assurance/quality control (QA/QC) and in-line process control. Use cases for a sampling of users can be found in **Exhibit 2**. Benno Radt, Advanced Development manager at Carl Zeiss MicroImaging commented on the evolution to a separate business unit for industrial applications:

> There is this whole world of material microscopy and we, Carl Zeiss had to address it to break out of biomedical research and to build a second pillar for our business. Every three or four years there was something that came up, so finally we said … we will split it … we have two business units, one is focusing on the biomedical or biosciences research, biosciences in general and the other one is industrial, where materials microscopy is the big part. Some results are shared, like R&D results are shared.

Modular systems to serve diverse needs

Because microscopy was such a general purpose technology, manufacturers like Carl Zeiss modularized their systems early on, defining internal component interfaces to externalize that would enable the easy interchange of parts and customization by users. Thus by specifying the dimensions of the eyepiece holder for example, users could select from a variety of different eyepieces that matched individual needs.

Modularization also decoupled the development of the system components, turning individual platforms into product families. The Zeiss Axio Lab system (see **Exhibit 3**) was a good example. It offered a plethora of different binocular viewing heads, base platforms, and special purpose attachments. **Exhibits 4a – 2e** illustrate the flexibility and configurability of the system. It offered a variety of different digital camera adapters (see top section of **Exhibit 4d**) so that users could attach their own compact digital camera, high end digital cameras, or Zeiss manufactured digital imaging systems. Company engineers could continue to develop new attachments and accessories for years to come, serving an installed base of users. The approach was generally limited to modularity within system families. One could not connect a Zeiss confocal microscope module to a microscope in the Zeiss Axio Lab series, for example.

The approach exemplified by the Axio Lab system enabled Carl Zeiss to offer the same system to biomedical as well as industrial customers. It would tailor specific software for each, as well as developing unique sales literature, applications briefs and selling approaches.

Software: data acquisition and analysis

As was the case for almost all modern scientific instruments that incorporated digital technology, software was a critical enabler. For the Axio Lab, Carl Zeiss offered the AxioVision program. Software functionality could be broadly grouped into several categories: data acquisition/instrument control, and image processing and analysis.

Instrument control included triggering the camera, but it also could encompass automatically adjusting the exposure, gain, white balance, or other parameters to optimize the resolution or utility of the recorded image. Images were stored in a Zeiss proprietary file format called ZVI that was tailored to the needs of scientific microscopy. Digital images were processed and saved in an uncompressed lossless format. Additional experimental data, like the objective (magnification) that was used, or the exact time points images were captured during the course of a multi-day experiment were stored in the file header. The user could also include comments, processing steps or measurement data.

Instrument control functions allowed the user to move any motorized parts of the microscope, to perform interactive measurement and automatic measurement of sample parameters such as dimensions or geometries. Some user groups were much more receptive to automation than others, as Ankerhold explained:

> We saw automation takes hold in pathology, which has a very nicely defined workflow. It is really nicely defined. It is not the same as in research where everybody thinks they are an individual and has to differentiate himself from others. We saw as well how biology is changing from purely qualitative studies where you have images and perhaps you measure something in the images, towards taking lots of images or even a time series of a sample, and then doing statistics on them. And from these statistics, you can move from more of a qualitative approach towards a quantitative approach.

It was important that data acquisition and instrument control were tightly integrated. This was because many experiments such as time-lapse acquisition or collection of a "z-stack," a collection of images at different depths in a sample, employed a sequential series of instrument control actions such as triggering a camera at regular time intervals or stepping a sample position on a microscope stage. The exact parameters would be recorded along with the corresponding images in sequence and stored for analysis. Ankerhold elaborated:

> In biology, in particular when it comes to quantitative approaches … it is all about images, that differ slightly from each other, that are not 100% identical. You need to categorize them by image analysis, sometimes quite complex image analysis. So you do this screening, that is the first thing … There is a standard way of acquiring the images. And secondly you run statistics and image analysis to find out whether there are categories that are similar in some respect, whether there are correlations between certain features. And this is something which takes place massively now in microscopy. It leads to the fact that users want more and more automated workflows.

AxioVision provided a large suite of data analysis functions. Users could perform many image enhancements or adjustments, scale or annotate images, measure intensity profiles, view multidimensional images in every dimension, or generate reports. They could align z-stack images, apply filtering functions and calculate many statistics. Users could use AxioVision in a standalone version, installed on a Windows PC. The program would read the ZVI files and users could do multiple analysis steps away from the instrument.

Is modular better? Or integrated?

The modular design of the Zeiss Axio system meant that sophisticated high-end users could customize configurations for specific research capabilities. Users would often select components from multiple manufacturers and integrate them into a custom workflow. This is often seen as the "job" of microscopy lab managers at some university microscopy centers. While Zeiss products held a strong number of the microscope platform positions in such laboratories, the software environment was quite heterogeneous and more often than not the facilities chose other software.

For certain types of high-end research problems, the MicroImaging unit sold packaged solutions that were assembled from its portfolio of products. **Exhibit 5** shows examples of a platform for live cell imaging and another for optical section applications, and **Exhibit 6** shows sample acquisition and application modules for biomedical and industrial customers. High end users in material science (on the industrial side) were actually not that different than for biological and medical, as Benno Radt observed:

> You have the material scientists who are operating in a mode more or less similar to the bioscience research guy … very operator driven, someone designing an experiment. Of course with different samples, different contrast settings, but the mindset is very similar. The scientists usually have those piled up hard drives. People want to use a whole variety of techniques. It's not only a single microscopist anymore, but often you have one principal scientist or investigator who has to make sure that the samples are investigated by different methods, contrasting methods. So you always have the problem that the performance isn't good enough or the technique is not just right, people have to use different instrumentation and somehow transfer files. Our users always want to have it more automated, like the way to actually get the data together and analyze it, even if it is from multiple sources - not only microscopy but also spectroscopy, elemental analysis, chemical analysis.

Some efforts at industry standardization for image data formats have emerged, generally driven by users. The Open Microscopy Environment (OME) was motivated by the desire to allow image data from any microscope to be stored, shared, and transformed without loss of any information on the experimental setting, imaging system, or processing software.[2] It included a data model implemented in a relational database to import, store, process, view and export data, and was designed to be compatible with traditional low-volume microscopy work all the way through high throughput image-based screening.

Clinical and QA/QC applications by their nature had a much higher need for automation, because of the repetitive nature of tasks. Integrated solutions seemed to make more sense in these circumstances. Many of these applications also did not demand the ultra-precision of Carl Zeiss's

[2] Ilya G Goldberg, Chris Allan, Jean-Marie Burel, Doug Creager, Andrea Falconi, Harry Hochheiser, Josiah Johnston, Jeff Mellen, Peter K Sorger and Jason R Swedlow, "The Open Microscopy Environment (OME) Data Model and XML file: open tools for informatics and quantitative analysis in biological imaging," *Genome Biology*, Vol. 6 (May 3, 2005), pp. R47:1 – 13.

hardware platforms. Rather there was a call for simplicity and robustness, especially in production environments. Radt elaborated:

> One trend I want to highlight is the usability, especially in the quality assurance and manufacturing, moving to the emerging markets with often less skilled users. And basically the massive demand to train a lot of different people because of the growing economies. The emphasis is really on usability, and basically shop floor hardened instruments, robust instruments. And that is different from the research needs, be it industrial or biosciences.

What will Ishikawa think?

Our scientist customers acquire a lot of images with our equipment, and then they need to analyze them. So there is acquisition software plus analysis software. It is one package in our case. And it comes with every instrument, on the control computer normally, it's bundled …You can export the files, and even set up a separate off-line computer. You could have our software there, but then you ran into the problem of how to get the data from the storage space to the other computer. Because our software is not the software that runs on a server. It is software that runs on the instrument.

— Richard Ankerhold

Hellen Ishikawa was the prototypical user. Like most users in the biomedical sciences, her principal output was in the form of scientific publications, presentations, and grant proposals. These users were highly mobile, and were part of a global research community. They wanted to show their work and their data, and as experiments and observations became more sophisticated, organizing and transporting the increasingly vast quantities of data was a growing challenge. Automation was required for the repetition of experiments, and this aggravated the challenge by making it easier to acquire even more data - resulting in vast amounts of image data to be handled - amounts way beyond the capacities of stand-alone PCs.

The other challenge was complexity. As the core microscopy facilities at numerous universities demonstrated, it took specialized expertise to set up such resources and train and support users of such advanced instruments. Ankerhold reflected:

> Multimodal, flexibly extendable microscopes with software that should serve every need and support all hardware components are often hard to learn. It is not an instrument where you have dedicated scientific questions and just do it on the right system and it is easy to use. No, you need to learn it first. There are pitfalls. Perhaps you go to an imaging facility, there you need to make an appointment, you have to follow the rules. You need to get training first, you need to wait in line. Finally you get access to expensive, high-end equipment with a technology that might even make your publication more impressive. You have technology experts that will help you. What would you do, if you have a dedicated scientific question – that is perhaps more standard and not so high-end? Would you still go the cumbersome way to that facility? What if you have an easy to use instrument that just serves your needs, is easy to use, fast to learn and works under your control, in your lab, in your workflow – just like the standard PCR, spectrometer or some dedicated purpose machine?

Making microscopes easy to use especially when dedicated to a single purpose could be very important. In such circumstances, automation (like in the world of digital consumer cameras) can be used to reduce complexity. Such instruments could be usable by someone who did not want to be a microcopy expert but rather wanted to concentrate on his or her biological or biomedical questions. It was also more of what the mid to lower tiers of the industrial market seemed to want. The scary thing

about such a system is that in many respects software would become a much bigger contributor to the overall system value than the hardware, the Zeiss microscopy platform. Did that mean that the hardware was getting commoditized? Certainly not at the high-end where performance demands continued apace, but what about the middle of the market and lower?

Ishikawa had demonstrated once again that Carl Zeiss also *de facto* had a modular software strategy. Users could export data to other software packages like ImageJ, and it was virtually impossible for Carl Zeiss to keep pace with all the innovations happening in the analysis software space. Reflecting on some of the application service provider models he had seen in other industries, he thought:

> I would say, listen, we take the machine that is the acquisition machine and control of the instrument. If they want they can also have the analysis on the machine, no problem, but one workflow would be to dump all the data on a server. Then you have several installations and other computers, or perhaps not even installations, you could have it as a thin client running over any web browser, where you actually access your data, you don't have to upload, you just leave it on the server because the servers can harness much more power for the analysis. So you just send jobs to that server, and you get the results. This way you would become independent of the operation system, you could use your Mac, you could use your iPad, you could be really mobile. You would not even have to bother so much about storage space, transport of your data, data backup and processing power. That would be my dream.

Ankerhold mused, "If our guys developed that it would be really cool, almost a bit visionary." Then he paused, "I wonder how we would make money?" He took another sip of coffee and then added, "I wonder what Hellen would say?"

Exhibit 1 Typical microscopy use cases in biomedical sciences category.

	Multi-user Core Imaging Facility	Individual Research Group, PIs
Job to be done	Provide imaging services (paid or unpaid) in support of surrounding research groups	Answer research questions using microscopy and imaging as a central or auxiliary tool
More specifically	As the head of a core imaging facility, I need to satisfy my clients with respect to: Functionality, availability, accessibility, convenience, and competency. Provide first-class service, always offering the functionality and technology needed for the problem at hand, and ensure that clients can efficiently use the instruments by providing training and maintaining uptime. Provide differentiation with respect to other university facilities by offering new technologies that are keeping up with the latest trends. Balance the interests of multiple clients with different applications across multiple systems.	The imaging system must fit into my research environment (research lab) and provide easy-to-use functionality even if users are not imaging experts. I need to answer scientific questions in my field, publish them in important and appropriate publications, market my results, and write grant proposals. On the one hand I need to differentiate my work from my competitors and always stay ahead of them through smart collaborations good people and appropriate technology to address my application needs. I need everything in my lab to run smoothly and efficiently.
Product / Offering	Ideally I would always have the right combination of functionality, up-to-date equipment, and high uptime. Administering the support and auxiliary functions including image data management and other services Ideally the core facility work would be easy so that I can focus on technological advances and differentiation as well as marketing the facility.	I need a system this all my particular application needs; I do not the things that I do not use. I need instruments that are easy-to-use and easy to learn.
Technical Support	I need high level technical support. I have some knowledge and capabilities and I need my suppliers to be peers.	If the system breaks, I needed to be repaired quickly I am not a technician.
Financing	I need to justify new equipment through a committee of users or their bosses. Usage, technology differentiation (reputation) or joint projects between groups are the main driver.	New investigators: I am just establishing a new research lab. I have one "big" chunk of money. I need to get working quickly and be prepared for the future. Established PIs: I am writing specific grant proposals aligned with my scientific questions based on my previous results and cool new ideas. I have clear limitations on investments. Purchases driven by my application needs (lead applications).

Source: Compiled from company interviews and information requests.

Exhibit 2 Typical microscopy use cases in industrial category.

	Basic Research	Research and Development	Quality Assurance/Quality Control Lab	In-line Process Control
Examples of problem to be solved	*Hypothetical structure of materials* Examine the outcome of a chemical reaction process, for example look for a self-assembling layer structure, the formation of particles, or examine different chemical phases in a final product.	*Particle analysis, Inclusion analysis, geological sample analysis* Classification and further analysis of particles, inclusions or other materials properties which appear as sample segments in an image or image stack.	*Production inspection and measurements* Inspection of a broad variety of parts in production. System is used for inspecting microscopic structures like coatings, electronics, solder connections, fabricated steps, boreholes or other structures.	*In-line process control* Inspection of silicon wafers, electronics, flat panel displays, parts of medical instrumentation. Machine must make determination of whether a part is within or outside of specification.
Sample preparation	Small structures on a support, for example a stack of layers on a silicon or glass slide, colloids which are dried on a support, or ground and polished surfaces of a novel material.	Particles on a filter, polished and etched metal (material) surface, native surface or volume.	The samples are a variety of fabricated parts like electronics, papers and textiles, plastic molded parts or packaging which are typically not prepared in a sophisticated way.	Specific to the production process. Machine has to be dedicated to this purpose. Need clear application understanding. System has to be customized to the industry and the customer.
Typical user	Skilled student who is supported by the principal investigator (PI) and a technical assistant who knows the instrument.	Materials analysis lab in industry, academia or service lab with trained technical assistants using the instrument and at least one principal investigator defining the workflow.	System is located either in a quality assurance lab or on the shop floor, being used for quality assurance. QA/QC lab technician typically performs the work. User is typically less educated with a broad variety of tasks without a special interest in microscopy. In smaller companies QA/QC lab is often used jointly for R&D purposes.	
Workflow	The sample is synthesized in a physical, chemical or biological production process. The samples are prepared before microscopy with a huge variety of methods. Samples are placed manually in the system. The imaging process is a highly interactive procedure in which the	Workflow typically has to be adapted for each series of experiments. Measurement performed repetitively in most cases. High scan speed for large area in combination with high resolution; customized feature extraction; statistics on data or extract “needle from a	A part is taken out of production and inspected or measured immediately. If the part cannot be taken out of production the microscope has to be moved to the inspection side. Users want to open predefined settings and run the inspection or measurement as easily as	Parts in a production line are automatically placed in the field of view. All settings have to be set automatically. The system makes a decision whether the part is within or out of spec. The parts that are out of spec are typically reviewed either at line or in a QA/QC lab in a review

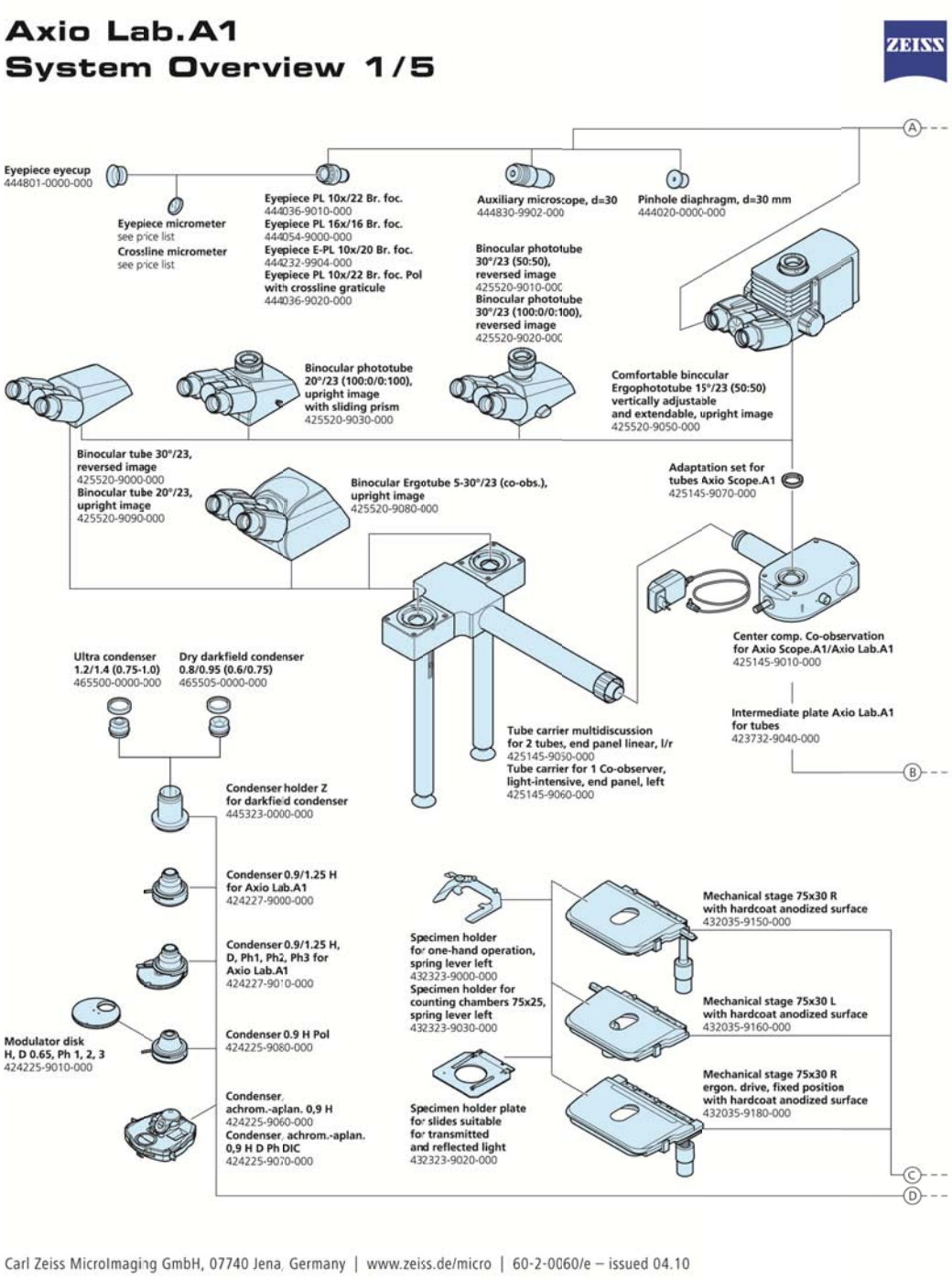
	operator and the scientist optimizes the instrument setting in order to see the desired material.	haystack." Samples are dissolved or brought into a gaseous phase and filtered afterwards; or Samples are cut, ground, polished and etched before microscopy. Samples placed manually or by a sample loader into the system. Once the experiment is defined the system should run with as little operator attention as possible (over-night runs). Results are screened by the operator and the PI. Often the results will be combined with those from other analytical techniques such as mass spectrometry, or elemental analysis.	possible. Users want to get the results in visual real time or ASAP, do not want to use additional instruments like bench top computers or other analysis machines to get the result. After a daily batch of measurements the user wants to store the data elsewhere like in a QA/QC software package.	process. Often the microscope mentioned in the QA/QC Lab case (next column to the left) is used for the review measurement.
Purchasing decision	Decision maker is often a department head or a purchasing department of a university who has to rely on the proposal of the PI. Often only one supplier can bid because the configuration can be highly specialized, so they are sole-sourced.	Decision maker is a lab-head who considers the needs/proposals of the PI and the users. Return on investment is an important prerequisite for the buying decision.	Decision maker is usually the head of QA/QC or the head of R&D and production. Fast ROI is important.	Buying decision typically part of the project plan, joint decision between the producer and the equipment manufacturer for the production line. The customer is often the equipment manufacturer.

Source: Compiled from company interviews and information requests.

Exhibit 3 Zeiss Axio Lab series, part of the Zeiss Axio family of microscopes

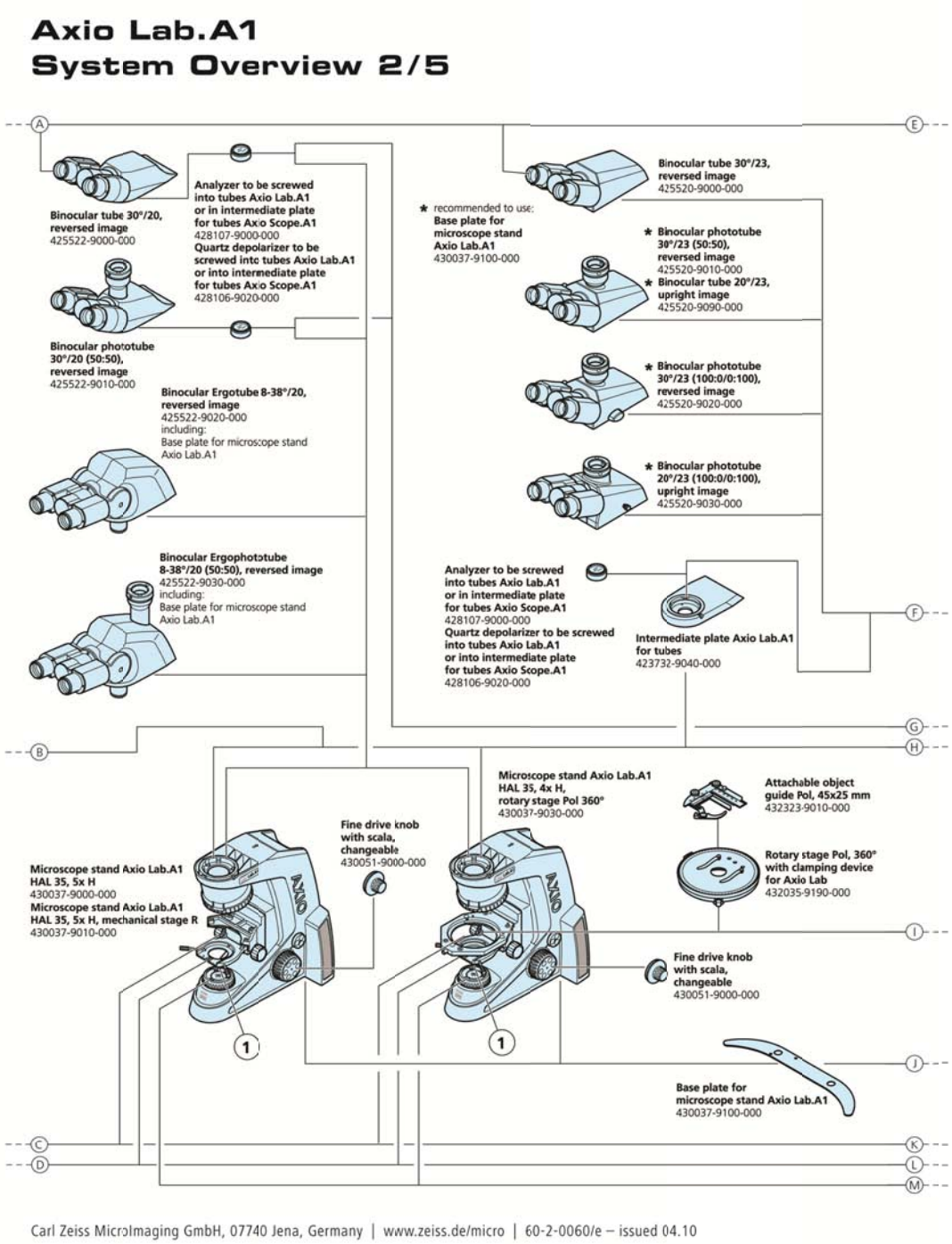
Source: Company photo, © 2011 Carl Zeiss AG, used with permission.

Exhibit 4a Modular architecture of the Zeiss Axio Lab series



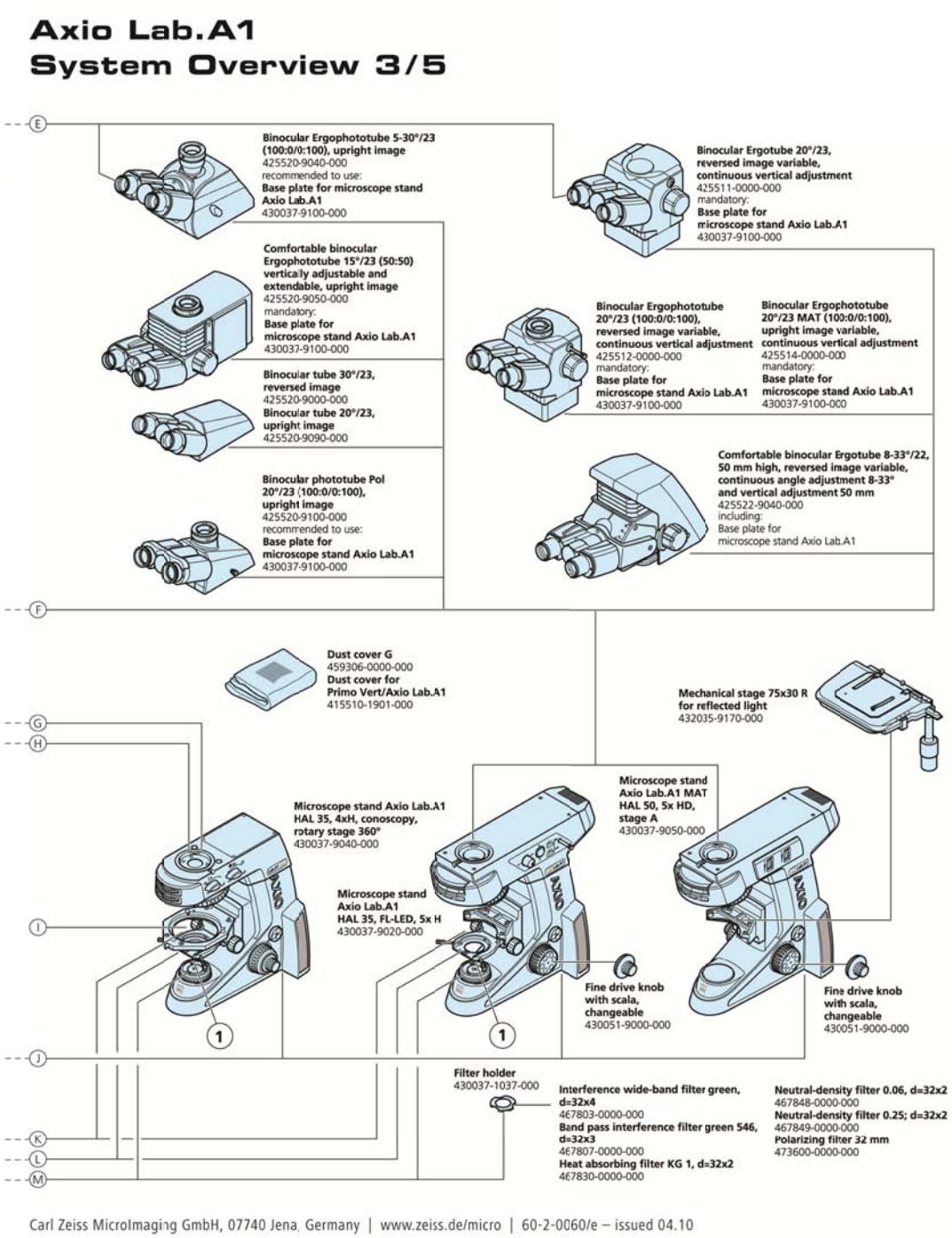
Source: Company brochure, © 2011 Carl Zeiss AG, used with permission.

Exhibit 4b Modular architecture of the Zeiss Axio Lab series



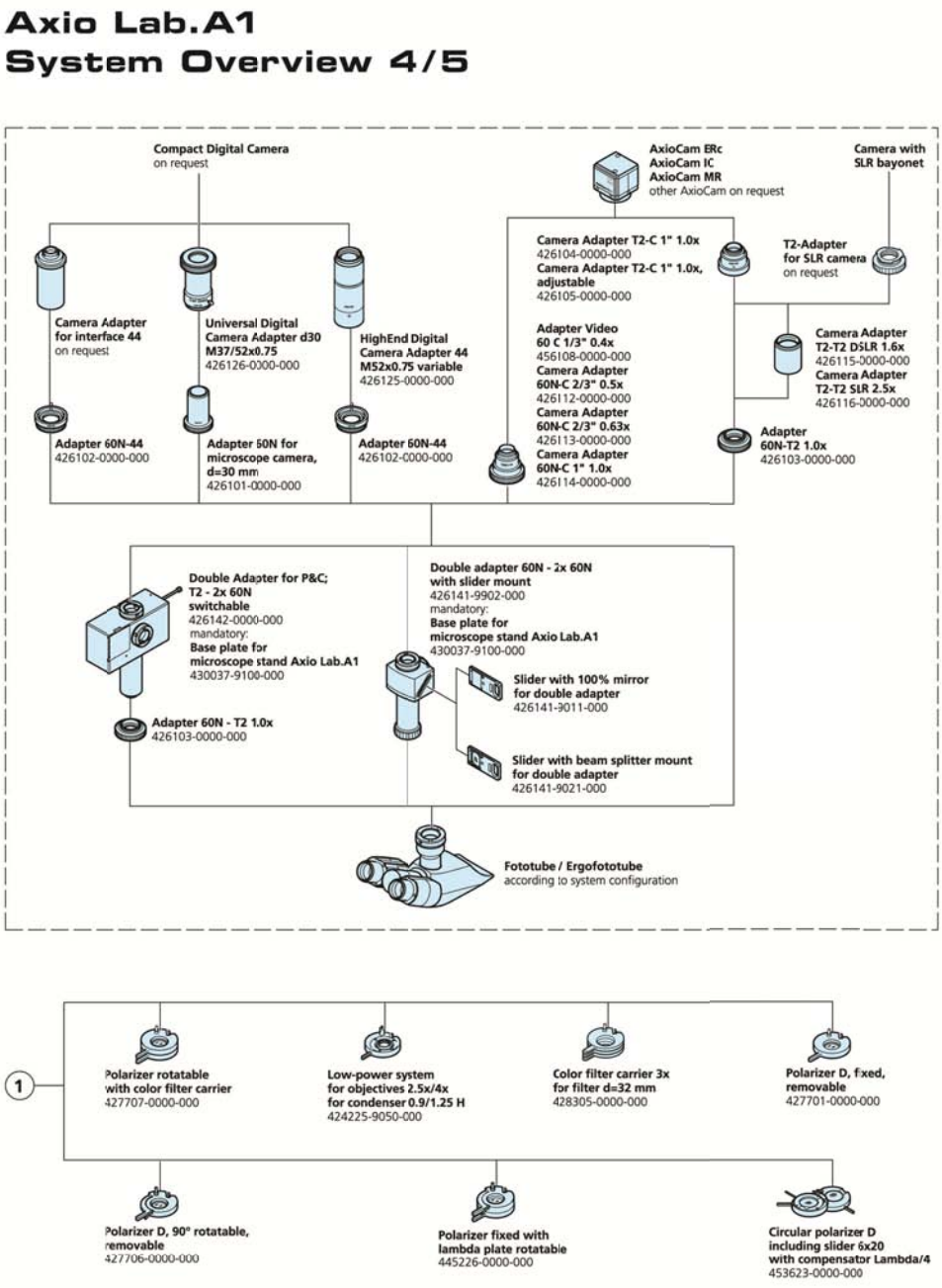
Source: Company brochure, © 2011 Carl Zeiss AG, used with permission.

Exhibit 4c Modular architecture of the Zeiss Axio Lab series



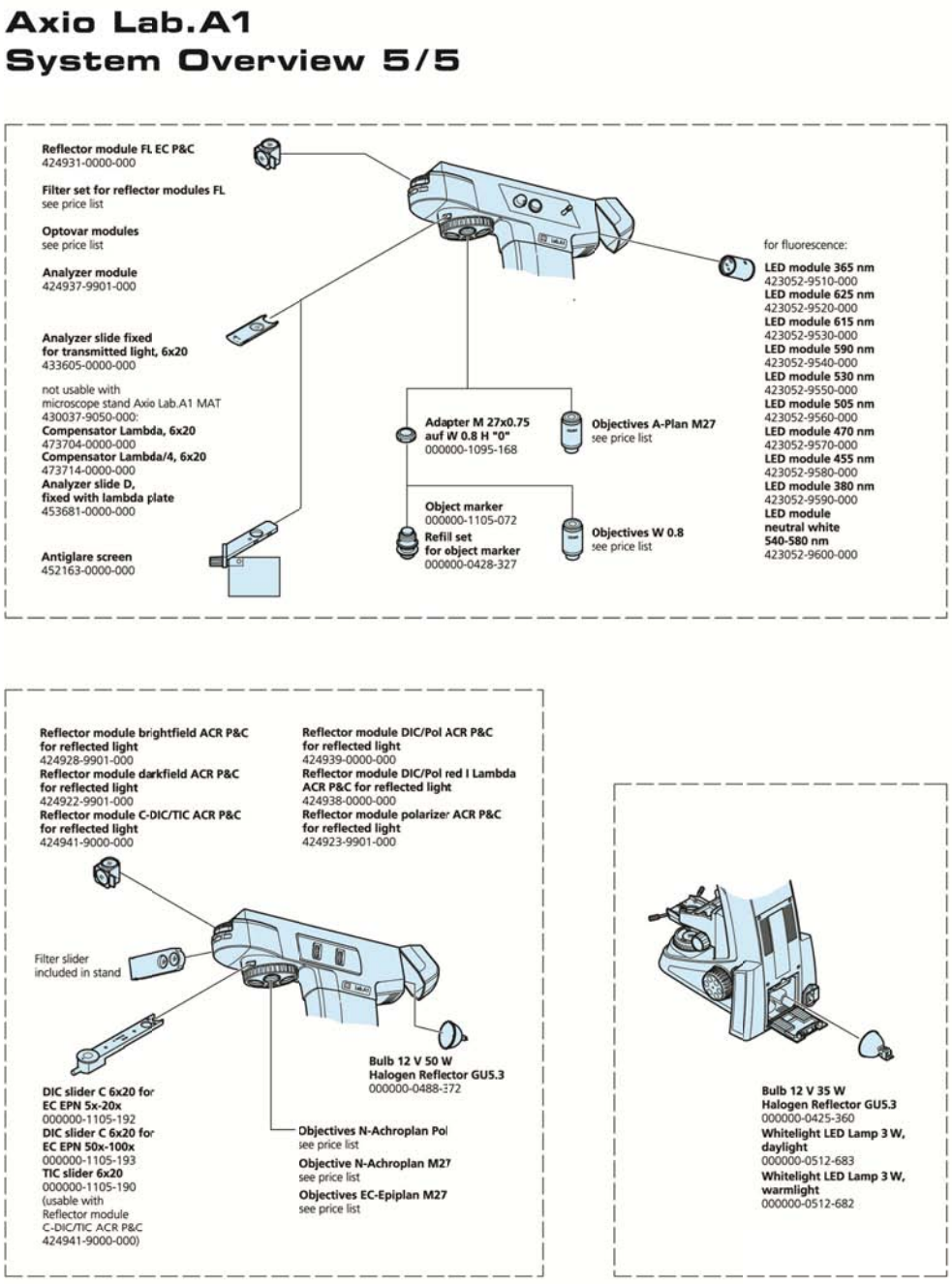
Source: Company brochure, © 2011 Carl Zeiss AG, used with permission.

Exhibit 4d Modular architecture of the Zeiss Axio Lab series



Source: Company brochure, © 2011 Carl Zeiss AG, used with permission.

Exhibit 4e Modular architecture of the Zeiss Axio Lab series



Source: Company brochure, © 2011 Carl Zeiss AG, used with permission.

Exhibit 5 Application specific high-end solutions built on the Zeiss Axio Imager or Zeiss Axio Observer

The Platform for Live Cell Imaging

Modern life science research calls for a powerful imaging system that can be used flexibly, is easy to operate, and is equipped with a whole host of functionalities. A convincing example of such a system is Cell Observer from Carl Zeiss.

Whilst offering the best components for the task, care has been taken to ensure seamless integration of all components. This allows imaging techniques from simple time lapse to complex heterogeneous experiments with the multidimensional Smart Experiments functionality. Reliable long-term imaging with computer-controlled incubation as well as high-speed imaging using streaming and precise trigger synchronization are all available within one single platform. This platform can be built upon when adding other techniques such as a Spinning Disk confocal unit or the ApoTome sectioning device.

Configuration

Microscopes
Inverted: Axio Observer

Excitation options
Various HBO or Xenon arc lamps, fast switchable Xenon lamp, Colibri LED light source

Hardware options
Fast piezo focusing, filter wheels, shutters, scanning stages, flexible incubation setups, high-resolution and sensitive CCD cameras, EM-CCD cameras for ultimate sensitivity, Dual Camera option for maximum speed and efficiency

Software
AxioVision, and options, e.g. Multidimensional Acquisition, Fast Acquisition, Physiology, 3D Deconvolution, Inside4D (rendering), 3D Measurements, Assaybuilder (high content analysis), Colocalization

Suddenly Everything Looks Different

ApoTome introduces optical sectioning capabilities to your widefield imaging system simply by inserting the ApoTome slider into the field stop position. Using structured illumination, out-of-focus blur is efficiently removed, resulting in brilliant optical sections of highest contrast and optimal resolution.

ApoTome achieves optical sectioning by using the principle of structured illumination microscopy. A grid pattern is projected into the focal plane, and an optical section is calculated online from three images with different grid positions. Thus, ApoTome maintains the ease of use of your widefield system but efficiently removes out-of-focus blur even in thicker samples, making ApoTome the system of choice for easy multicolor imaging of tissue sections.

Configuration

Microscopes
Upright: Axio Imager 2
Inverted: Axio Observer

Excitation options
HBO, HXP 120, or Colibri

Options
Different grids for optimal use of different objectives; Deconvolution of SIM images for optimal resolution

Software
AxioVision and options, e.g. Multidimensional Acquisition, 3D Deconvolution, Inside4D (rendering), 3D Measurements, Assaybuilder (high content analysis), Colocalization

Source: Company sales literature, © 2011 Carl Zeiss AG, used with permission.

Exhibit 6 AxioVision software for Carl Zeiss with sample acquisition and application modules for biomedical and industrial customers

Source: Company brochures, © 2011 Carl Zeiss AG, used with permission.