UNIVERSITÄT BERN

Faculty of Medicine VetSuisse Faculty Faculty of Science

Microscopy Imaging Center

Annual Report 2015 Microscopy Imaging Center (MIC) University of Bern

Ϊ,



MIC Images as title page (Abadier M, et al., Eur J Immunol 45: 1043-1058, 2015)

Résumé

The **M**icroscopy Imaging Center (MIC) is the center of excellence for high-end microscopy in life sciences and beyond at the University of Bern. It associates scientists and their institutions involved in microscopy.

The MIC organizes central access to numerous high-end microscopes and imaging systems for all university members. It is the platform for scientific communication in the field of microscopy and imaging in the life sciences.

Founded in 2005, the MIC permanently increased its activities and is well recognized for its coordinative function in microscopy and imaging. In 2015, the MIC has still the official performance mandate from the University's leadership established in 2012.

Updated information about the MIC is available under www.mic.unibe.ch

MIC Activities according to the performance mandate

- Operating, maintaining and providing access to high-end microscopy equipment
- Microscopy services like sample preparation, data handling, stereology
- Know-how platform for high-end microscopy
- Coordinating access and use of shared equipment
- · Performance and utilization reporting of equipment
- Coordination of microscopy investment and related application support
- Teaching in cutting-edge microscopy (lectures, practical modules)
- Quality management in microscopy
- Publicity of microscopy activities at the University of Bern (e.g. yearly MIC symposium

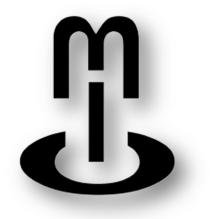
MIC Organization

The steering panel of the MIC is its **Commission**, where decisions are taken. Involvement of the **MIC-Commission members** is voluntary. The **MIC Coordinator** (Dr. Stefan Tschanz) is the primary contact person and executive of the MIC. The **MIC Board** (chair: Prof. Britta Engelhardt, Medical Faculty, Prof. Volker Heussler, Faculty of Science, Prof. Michael Stoffel, VetSuisse Faculty) represent the MIC within each of the Faculties and to University leadership. In 2015, the MIC was able to implement the position of a core light microscopy manager (Dr. Yury Belyaev).

Participating Faculties:	3
Participating institutions:	12
MIC-Commission members:	25 (+1)

MIC Equipment

Shared microscopes	46	
Mesoscopes (various techniques)	3	
Light Microscopes (various techniques)	32	
Electron Microscopes (various techniques)	8	
Further imaging instruments (Atomic Force / Micro-CT)	3	



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30.04.2014

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The MIC story

Microscopy encompasses today a huge diversity of techniques which allow imaging of structures from molecules to full organisms in 2D, 3D and 4D. It is the essential tool in modern life and natural sciences linking functional information with structures.

The Microscopy Imaging Center at the University of Bern (MIC) is *THE* platform for high-end microscopy and provides easy access to an impressive portfolio of leading-edge imaging techniques. Most of the tasks in modern microscopy can be solved with equipment *and* knowhow provided by MIC affiliates. It is widely acknowledged as facility for knowledge exchange as well as a valuable teaching resource for high-end microscopy at the University of Bern.

The range of high-end microscopes accessible through the MIC allows scientists at the University of Bern to stay competitive at an international level.

All MIC associated institutes (from the three participating faculties and the Adolf Merkle Institute in Fribourg) forming the core of the MIC, provide at least one representative. Together these representatives constitute the MIC Commission. The majority of equipment accessible through the MIC is located in these member institutes. However, every scientist of the University of Bern as well as from other research institutions may benefit from all the services offered by the MIC.

The MIC is defined as a support organization according to the principle of **decentralized equipment location** and **central coordination**. This ensures to have at every microscope a supporting team that is really experienced and focused to the provided technology. This compensates by far some disadvantages of the decentralized location.

During the quarterly meetings of the MIC Commission, all relevant steering decisions related to high-end microscopy are defined. The rates for shared microscope usage were fixed for all participating institutions.

All relevant investments in the field of microscopy were evaluated by the MIC Commission, helping to boost innovation and avoid redundant purchases. The optimal structured investment planning of the MIC was so well appreciated that in Summer 2015 an almost complete funding of microscopy equipment prioritized by the MIC was made possible by the University leadership.

The MIC Commission meetings are valued discussion events. Here, the experts in microscopy techniques keep us up-to-date of the latest knowledge and techniques.

The MIC's goal is to continuously increase expertise in cutting-edge microscopic techniques among young and advanced scientists at the University of Bern. This year's MIC symposium focused on the hot topic of Host-Pathogen interaction with lectures from local and international experts in the field. The symposium was once again a big success unifying researches and particularly microscopists from all over Switzerland.

The "Cutting Edge Microscopy" lecture series, part of the unique teaching program provided by the MIC, was attended by 43 Students. The "MIC modules" providing in-depth training for dedicated microscopy techniques were followed by dozens of students.

The working concept of the MIC as an inter-faculty competence center is seen as promising and successful pilot for other University core facilities. Therefore, as in 2014 the University's Leadership supported the MIC to the sum of CHF 120'000. This was used for basic operation of the MIC. Among others the MIC administrative tools (see below) were refined and the administrative processes further simplified. Part of the budget was also made available for teaching costs.

The success of the MIC is crucially depending on the voluntary time effort provided by every MIC member allowing shared usage of microscopes. The downside of this success, however, is that labor to run the MIC has started to impair the scientific work of those researches maintaining the microscopes. This point was also acknowledged by the University leadership. They were convinced of our concept of a MIC based "Core Light Microscopy Manager" and committed to finance 50% of the salary costs. After careful evaluation of candidates, the physicist Dr. Yury Belyaev started this function in November 2015.

The MIC has proven its function as the center of excellence in high end

microscopy with outstanding facilities and expertise among the community of scientists at the University of Bern as well as across Swiss and international microscopy experts.

Organization of the MIC

The Microscopy Imaging Center unites scientists and institutions involved in high-end microscopy. The MIC is based on shared use of microscopy equipment and collaborative work of the participating institutions. The high quality of the MIC services critically relies on voluntary efforts of the MIC members and institutes.

Every institution using and providing high-end microscopy may join the MIC commission, preferably by defining a representative experienced in microscopy.

Institutions from the Faculty of Medicine, the Faculty of Natural Sciences, the VetSuisse Faculty at the University of Bern and the Adolphe Merkle Institute of the University of Fribourg are involved in the MIC organization.

The directive panel of the MIC is the **MIC-Commission**, which consists of 25 delegates (MIC-members) from all participating institutions. The steering panel of the MIC is the **MIC-Board** which consists of the chair person (Prof. Britta Engelhardt, also a representative from the Medical Faculty), the MIC coordinator (Dr. Stefan Tschanz) and one representative from each of the participating faculties (Prof. Volker Heussler - Faculty of Science, Prof. Michael Stoffel, VetSuisse Faculty) [Fig. 1].

Open trades, such as evaluation requests for new equipment are communicated to the MIC coordinator. Together with the MIC-Board, topics are pre-evaluated and prepared for the MIC-Commission meetings where the Commission decides by voting. The participants from the University of Fribourg do not vote for items specifically related to the University of Bern

The MIC-Commission meets four times a year. Every meeting is concluded with a comprehensive protocol that acts as directive for the MIC (accessible for members on the web).

MIC support is organized on several levels (see Fig. 1): General requests are collected by the MICcoordinator and are dispatched to dedicated contact person (see also contact page on <u>http://www.mic.unibe.ch</u> or Table 1). Light microscopy support is specifically provided by the core light microscopy manager. Specific contact persons can also be contacted directly.

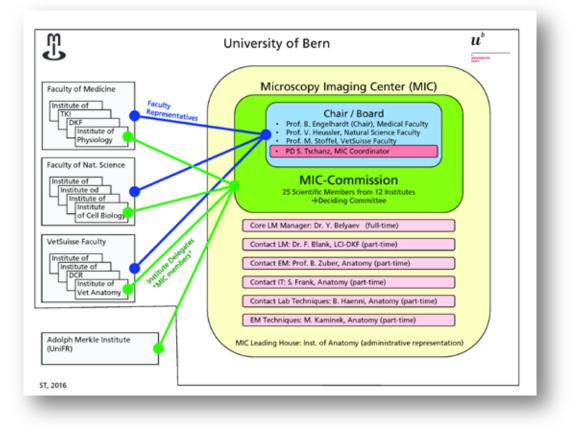


Fig. 1: Organigram of the MIC

Faculty	Institute	Delegates (MIC-members) (state Dec. 2015)
Medicine	Anatomy	PD Dr. Edik Babiychuk Dr. Yury Belyaev (core light microscopy manager) Beat Haenni (core technician) PD Dr. Stefan Tschanz (coordinator, contact stereology) Prof. Dr. Benoît Zuber (contact electron microscopy)
	ARTORG Center	Prof. Dr. Olivier Guenat
	Biochemistry and Molecular Medicine	Prof. Dr. Dimitrios Fotiadis Prof. Dr. Roch-Philippe Charles
	DKF / Pneumology	Dr. Fabian Blank (contact light microscopy) (head of Live Cell Imaging facility,-DCR)
	DKF	Prof. Dr. Robert Rieben
	Pathology	Dr. Ilaria Marinoni
	Pharmacology	Prof. Dr. Shida Yousefi
	Physiology	Prof. Dr. Thomas Nevian Prof. Dr. Ernst Niggli
	Theodor-Kocher Institute	Prof. Dr. Britta Engelhardt (chair , board) PD Dr. Ruth Lyck Prof. Dr. Jens Stein
Science	Applied Physics	Prof. Dr. Martin Frenz
	Cell Biology	Prof. Dr. Volker Heussler (board) Prof. Dr. Peter Meister
	Plant Science	Dr. Sarah Robinson
VetSuisse	Division of Veterinary Anatomy	Prof. Dr. Michael Stoffel (board) Prof. Dr. Sven Rottenberg (new)
University of Fribourg	Adolphe Merkle Institute	Prof. Dr. Barbara Rothen-Rutishauser Dr. Dimitri Vanhecke (contact image processing)

Table 1: Participating Institutions and Members of the MIC

MIC Coordinator

The MIC coordinator, Stefan Tschanz (30% part time position dedicated to the MIC), is the primary contact person and manager for all MIC matters. He is the addressee for support requests regarding administrative, teaching, funding and other issues. If support can't be provided directly, he mediates the appropriate contacts. The contact person for **light microscopy** is the new core light microscopy manager Dr. Yury Belyaev and the head of the Live Cell Imaging facility at DCR Dr. Fabian Blank, for **electron microscopy** Prof. Benoît Zuber, Institute of Anatomy, for **image processing** Dr. Dimitri Vanhecke (Adolphe Merkle Institute; University of Fribourg) and Dr. Belyaev and for microscopy lab issues Beat Haenni, Institute of Anatomy (see MIC web site).

The coordinator organizes the MIC-Commission meetings four times a year, manages all teaching administration and organizes the international MIC meeting once a year. His administrative tasks comprise all forms of reporting including equipment usage and financial statistics. He is responsible for the internet presence of the MIC (web site and equipment manager) and is also the main contact person for data and image handling issues. He helps scientists to prepare successful grant applications for microscopy investments.

Stefan Tschanz has been the MIC coordinator for the past five years.

MIC Core Light Microscopy Manager

Since November 2015 the MIC has a dedicated core light microscopy manager. The physicist Dr. Yury Belyaev substantially amplifies the support in light microscopy with his full time position.

The effort of MIC members providing access to high-end microscopes tended to impair their own scientific work, however a sign of the good operation of the MIC. In 2013 the idea arose to implement a dedicated MIC based core manager position for light microscopy. We could convince the University board of this concept and got a commitment for half of its funding.

After a careful evaluation of 13 international candidates, Dr. Yury Belyaev, physicist with a long standing experience in microscopy and formerly facility manager at the EMBL Heidelberg (D) was selected and started his position in November 2015.

His functional specification involves the following points:

- Device administration and responsibility
- Device maintenance (includes competence for the operation budget)
- Device configuration and safeguarding of device availability
- Unified contact to microscope manufacturers
- Guiding local "Super-Users"
- Introduction of new users and 2nd level user support
- Maintaining continuity and cross-linking of device-specific know-how

He operates in those MIC institutions that requested his support and therefore also funded the remaining 50% of his salary in a shared manner.

Located at the Institute of Anatomy, next to the coordinator S. Tschanz - who is his supervisor and collaborator - he visits the involved institutions on a regular basis as well as on demand.

Already after some months Dr. Belyaev is the central contact person of the MIC for technical support and his expert knowledge is highly appreciated among all microscopy users. Furthermore he intensifies the contact to other national and international microscopy facilities as well as to microscopy companies benefiting from his existing professional network.

Leading house: Institute of Anatomy

The Institute of Anatomy functions as "leading house" for the MIC, in order to have a specific contact point and address for financial transactions. Most of the MIC core staff (coordinator, web master, core lab technician, core microscopy technician) are members of the Institute of Anatomy but are partly paid out of the budget of the MIC (see "Financial support by the University Leadership"). Due to its extensive experience in microscopy techniques and a large portfolio of equipment, the Institute of Anatomy is well suited for this task.

Performance Mandate ("Leistungsauftrag")

The MIC has an official mandate from the University Leadership defining its responsibilities as a center of excellence for microscopy. The mandate is associated with an annual financial support of CHF 120'000 to cover basic operating costs incurred by the MIC, i.e. administrative costs (labor and consumables), development of specific IT tools (website, reservation system) and some smaller maintenance work.

The University Leadership, represented by the Rector, Prof. Martin Täuber, defined the following objectives in 2012:

The MIC shall be the central access point for high-end microscopy in life sciences for the entire University of Bern. It provides for the coordination of users. In addition, the MIC evaluates and coordinates investments in life science high-end microscopy for the participating faculties.

- Qualified setup of high-end microscopy
- High quality image analysis
- · Optimal use and coordination of existing resources
- Teaching programs in the field of microscopy
- · Quality management by standardizing processes
- Increasing the success of funding applications
- · Standardizing microscopy fees
- Public relations for distinct placing of the MIC as a center of excellence in microscopy
- Promotion of knowledge transfer within the University of Bern and to the outside

(Translated from the original "Leistungsauftrag", 24.01.2012)

Based on a successful evaluation of the performance mandate, the MIC will continue to have this commitment by the University leadership for another year.

The MIC was defined as pilot organization to demonstrate the feasibility of shared competence centers at the University of Bern (Prof. Christian Leumann, current Vice Rector Research and future Rector of the University of Bern). The success of the MIC confirmed the concept of such interfaculty centers.

Financial support by the University Leadership

The performance mandate given by University Leadership is associated with an annual financial fund of CHF 120'000 used for basic operation of the MIC.

The MIC-Board and Commission together with the University Board decided to use a substantial part of this money for compensating salary costs of persons located at the Institute of Anatomy, as the leading house.

In 2015 the MIC commission decided to renounce from funding maintenance costs or small repairs. Instead, the money is dedicated expenses of central MIC importance, such as maintenance of MICBook reservation application, acquisition of tools for the core light microscopy manager (microscope calibration tools, IT infrastructure), for teaching costs and for meeting charges (MIC-Day, MIC-Retreat, MIC-Day). For the latter, a substantial part is covered by sponsoring of the major microscopy companies.

The remaining reserves will be kept as reserve for repair emergencies. The MIC commission will also decide on a potential usage for common imaging software licenses (Imaris, Arivis etc.).

		Comment
Financial Support University Leadership 2015	CHF 120'000.00	
Salary costs	CHF 104'270.40	MIC Commission decision
MIC Cash Reserve	CHF 15'729.60	
Cash expenses		
Maintenance		
Maintenance Server MICBOOK (N. Fankhauser)	CHF 500.00	(paid in 2016)
Teaching costs		
TKI, Bern, Dr. G. Enzmann	CHF 1000.00	
DKF-LCI, Dr. F. Blank	CHF 1000.00	
Core light microscopy manager		
IT infrastructure	CHF 1'918.60	
Microscopy calibration tools	CHF 2'188.24	
Huygens Software	CHF 1'977.04	recalled
Administration / Travel	CHF 1'252.70	
Sum cash expenses:	CHF 9836.58	
Reserves	CHF 5893.02	

Table 2: University Funding Report

Table 3: Salary policy MIC

Function	Part	Salary class	Salary Points
Coordinator	30%	23	43.20
Core Lab Technician	15%	16	12.60
IT / Web master	10%	16	8.40
Administration	10%	13	7.20
EM Technician	10%	15	8.40
	75%		SP: 79.80
Total salary cost per year			104'270.40 CHF
MIC cash reserve, guaranteed by the Anatomy			15'729.60 CHF

MIC Revenues and Expenses

The MIC central financial assessment that is organized in collaboration with the central Finance Department of the University allows to list all microscopy-related charges and incomes of MIC associated Institutes. The assignment of transactions is easy but voluntary. Some costs may not be listed in the following overview (see Table 4).

While initial investment for expensive high-end microscopy systems is mainly covered by research grants, maintenance and repair costs have to be funded by the institutes where the microscopes are located. Some incomes are generated by fee-based usage of the systems. However, maintaining the microscopes does stress regular financial resources of the institutes.

The straightforward and comprehensive work-flow of the **MIC financial reporting** tool is easily applicable. Most of the MIC member institutes submit their financial transactions via this process. The assignment is done by just labeling transactions with the so-called "Projekt-Abrechnungs-Objekt" (PAO).

Financial turnover that was assessed by the MIC financial reporting in 2015:

Revenues (pooled):	Usage fees (+ 27% compared to 2014)	111'771.27	
	Total revenues	CHF 111'771.27	
Expenses: (pooled):	Repair, updates, extensions, service contracts.		CHF 273'490.69
Remaining g	ap , financed through Institute fu	Inds	CHF -161'719.42

Table 4: Revenues and Expenses

This table does not claim to be complete. Some items may be missing and the correct categorization in retrospect is irresolvable.

Visibility of the MIC

Information on the MIC can be found online at http://www.mic.unibe.ch.

Our website provides easy access to all relevant information related to high-end microscopy.

In 2015 the site, which was one of the first following the APP – Layout of the new corporate design of the University of Bern was completely reorganized, matching the needs of the users and following a problem-based workflow.

The intranet functionality was further expanded to fully automated listing of equipment and teaching purposes, the latter closely related to the KSL. The announcement of trainings, teaching and symposia is fully automated and database driven. It consists of an easy to use registration function for participants and allows a new participation statistics.

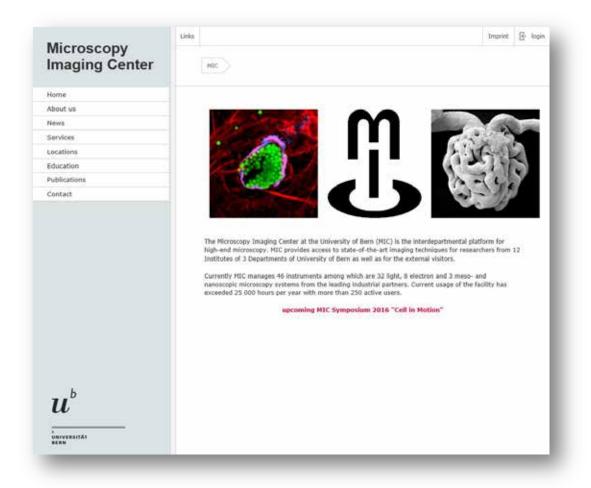


Fig. 2: Print Screen of the MIC Website with a new base structure, according to the Corporate Design of the University of Bern (WEB-APP layout)

In the fourth successive year, the most relevant search portal "Google" displays the URL of the MIC in the first position when "microscopy bern" is entered in the international (google.com) or national (google.ch) search: (<u>http://www.google.com/search?q=microscopy+bern</u>). In other search engines it ranked on top positions. The MIC is also present on the Swiss Bio Imaging network of microscopy core facilities (<u>http://www.swissbioimaging.org</u>).

MIC Symposium

This year's whole day MIC symposium was again attended by almost 100 microscopy enthusiasts from Bern and beyond.

The topic was "Visualizing pathogen host interactions".

3 international and 3 local experts gave us a fascinating insight into the possibilities of modern imaging and microscopy in this hot-topic of bio-medical research.

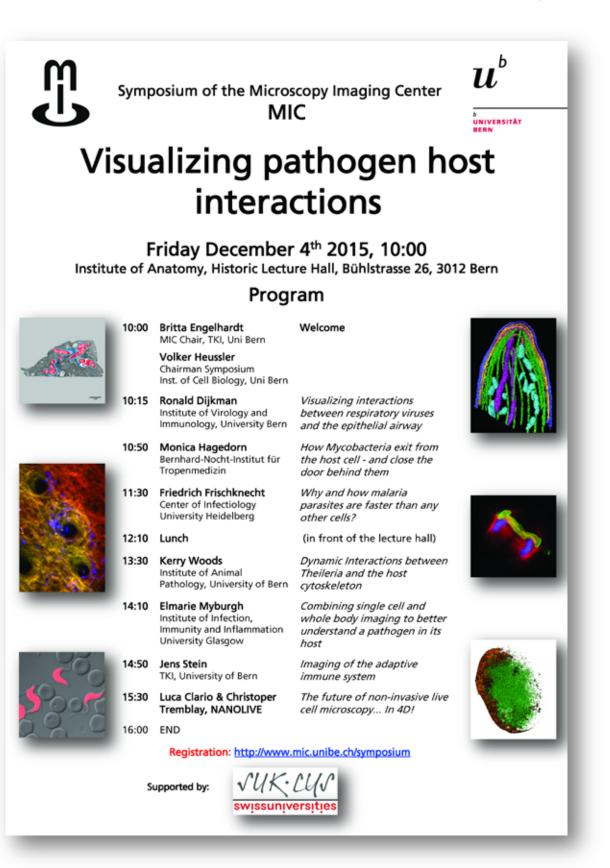


Fig. 3: Flyer of the MIC Symposium 2015

Microscopy Equipment and Services

The key function of the MIC is to provide access to high-end microscopes for all scientists at the University of Bern and other institutions. Consequently, the equipment inventory of the MIC is a key performance indicator for the efficacy of the MIC.

More and more data handling (image processing, image reconstruction, data analysis etc.) becomes a substantial if not dominant part of microscopy. Also with respect to expenses microscopy related IT can become extensive and may overcharge the budget of single research groups or institutes.

The MIC therefore increases its effort in coordinating IT infrastructure and imaging software as well as knowledge in the field of imaging. These steps are done in close contact with the central IT department in order to provide centralized solutions for all MIC affiliates and University members.

MIC equipment portfolio

In 2015 the net number of available microscopy systems in the MIC has not increased.

However four systems could be replaced by new microscopes and two were upgraded with significant functional increase providing newest imaging capabilities.

Microscopic	Technique (Portfolio 2015)	#	
Mesoscopy	Light / Laser sheet	2	
Mesoscopy	Optical Projection	1	3
	Fluorescence (Widefield)	10	
by	Confocal Laser Scanning Microscopy (2 replaced)	16	
osco	Spinning Disk System	1	
Micr	Super Resolution System	1	
Light Microscopy	High Content Analysis	1	
Li	Slide Scanner	1	
	other LM (Reflected Light, Stereo microscope)	2	32
nc Vqo	TEM (incl. one Tomography TEM) (<i>1 replaced</i>)	5	
Electron Microscopy	Serial Block Face SEM	1	
Mic	SEM	2	8
Other	Atomic Force Microscope	2	
Other	Micro CT (X ray) (<i>1 replaced</i>)	1	3
	(4 replacements in 2015)	Sum	46

Table 5: Available MIC equipment

Technique	System name	Institute	Extension	New 2015
Mesoscopy	LaVision BioTec Ultramicroscope System	Physiology	Laser Sheet	
	Selective Plane Illumination Microscope	ТКІ	Laser Sheet	
	Bioptonics Optical Projection Tomography scanner	ткі	Optical Projection	
Stereo- Microscope	Leica MZ16 Stereoscope	ТКІ		
Wide-field	Intravital microscope IVM-500	ТКІ	Live,	
	Zeiss M2	Anatomy	Automatic stage	
Reflective Light	Keyence VHX-600	Vet. Anatomy		
Fluorescence	General Electric INCell Analyzer 2000	Vet. Anatomy	High Content Analysis	
	Leica DMI4000 B fluorescence system	DCR		
	Nikon Biostation CT	DCR	Live, Long-term live	
	Nikon Eclipse E600	ТКІ		
	Nikon Eclipse TE-2000-4	Pathology	Live	
	Nikon Optiphot 2	Anatomy		
	3DHISTECH Slide Scanner, Zeiss based	IBMM	Automatic scanning	
	Zeiss Axiolmager with Apotome	Vet. Anatomy		
	Zeiss AxioObserver with Apotome	ТКІ	Live	
	Zeiss Axiovert 35 with transmission detector	Pharmacology		
CLSM	Customized Two-Photon Microscope (Built: T. Nevian)	Physiology	Multi-Photon, Live	
	LaVision Biotec TrimScope Two-Photon microscope	ТКІ	Live, Multi-Photon	
	Leica TCS SP2	Cell Biology		
	Leica TCS SP2 MP	Physiology		
	Leica TCS SP5	Plant Sciences	Live	
	Nikon Eclipse Ti-E, A1R MP	Applied Physics		
	Nikon TE2000E	IBMM		
	Olympus Fluoview 1200	Physiology		Х
	Olympus FV 1000	DCR vet		
	VisiTech VtEye confocal with point-scanner	Physiology		
	Zeiss LSM 5 Duo live	Anatomy	Live	
	Zeiss LSM 5 exciter	Pharmacology	Live	
	Zeiss LSM 510	Pharmacology		
	Zeiss LSM 880 (NEW, replacement)	Anatomy	AiryScan	Х
	Zeiss LSM710 (NEW AiryScan module)	DCR	Live, AiryScan	Х
Super Resolution	Leica SP8 X STED (NEW 3D STED module)	Cell Biology	Live, 3D STED	Х
Spinning Disk	iMIC TIII Photonics / FEI	Cell Biology		
Scanning EM	Zeiss DSM 982	Vet. Anatomy	STEM	
Ū	Philips XL 30 FEG	Anatomy		
SBF SEM	FEI Quanta 250 FEG, with Gatan 3View	Anatomy	3D	
Transmission EM	FEI Tecnai F20	Anatomy	Tomography	
	FEI Morgagni	Anatomy		
	FEI Tecnai Spirit (NEW, replacement)	Anatomy		Х
	Philips CM 12 (ana)	Anatomy		
	Philips CM 12 (vet)	Vet. Anatomy		
Atomic Force	Veeco Bioscope II, AFM add-on for Zeiss	Applied	brightfield and AF	
Atomic Force	Axiovert 200	Physics	brightneid dild / l	
	Nanoscope II	IBMM		
X-Ray	SkyScan MICRO Computer Tomography System (NEW, replacement)	Anatomy	µ Tomography	X
	System (NEW, replacement)			

Table 6: Detailed list of MIC equipment

Usage modes of MIC equipment

Most of the high-end systems available at the MIC are subject to usage fees.

The MIC-Commission has defined compulsory rates for each category of devices. The rates are published on the MIC website (<u>http://www.mic.unibe.ch/rates.php</u>). Hourly rates and 200 hour packages for heavy usage are offered. The package fee is calculated on the basis of about 15% of a one-hour fee. Packages are effective within one calendar year. Several instruments can be booked with an operator, charged at a higher rate. For long-term and over-night usage instrument administrators can offer special rates.

Usage of some instruments as part of a scientific collaboration with a major contribution of the local experts may be free of charge.

For usage of MIC equipment by non-university clients, especially from the industry higher rates are applied, in most cases twice the university rate.

Some institutions offer microscopy as a full service from sample preparation to microscopic image acquisition. The individual rates including work costs of the lab technician and operator are combined as an all-inclusive rate.

Utilization statistics of MIC equipment

The degree of utilization of microscopes is a benchmark for the appropriate sharing of the MIC equipment. It allows us to assess the efficiency of microscopy systems and to determine further requirements. By means of the booking system MICBOOK, which manages all the equipment's bookings centrally (see below), the MIC staff has easy access to detailed reports.

A statistical analysis of utilization of MIC microscopes in 2015 is presented here. During this period 231 scientists worked on MIC systems.

In 2015 roughly 30'000h were booked which represents increase of +7% in 2015.

¹/₄ of the microscopes showed full-time degree of utilization, some with a day and night occupation. The mean degree of utilization was 50% what clearly indicates that the microscopes are used on a regular base. Taking into account starting time and specimen preparation this is a very high degree of usage.

Teaching

The teaching activity provided by the MIC includes a lecture series on high-end microscopy and several practical modules focusing on particular imaging techniques.

Teaching is performed by experts in the fields coming from all participating institutions.

Cutting Edge Microscopy Lectures Series

This lecture series comprises two hour lessons throughout the entire fall semester covering all relevant high-end microscopy topics (see Table 7).

The Cutting Edge lectures series is a unique approach of the University of Bern. To our knowledge, no other university presents microscopy in such comprehensive way across faculties.

The lectures on 18 topics are given by 15 experts in their respective fields. In 2015 the new topic "Serial Block Face microscopy" was added.

All topics of the lectures are coordinated and discussed between all contributing lecturers. The unique microscopy "demo parcours" deserves particular mention. All the students get a hands-on demonstration of six high end microscopes located at the Bühlplatz area.

A written exam evaluating the learning success has to be accomplished at the end of the course. The students get 3 ECTS points and are admitted to the advanced practical MIC modules.

Since the start of the Cutting Edge lecture series in 2010 (40 students), its reputation has steadily increased. In 2015, 50 students from several Master and PhD programs registered for the series. The exam was successfully passed by 80% of the candidates.

The formal evaluation of the lecture series by 27 of the 50 students, conducted in collaboration with the evaluation office of the University of Bern (evaSys), indicated a good perception and ranking with respect to quality, scope and relevance.

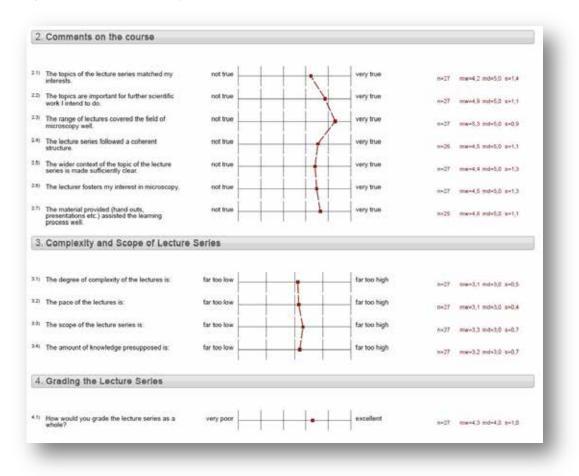


Fig. 4: EvaSys evaluation of the Cutting Edge lectures

Table 7: Cutting Edge Program 2015



Lecture series "Cutting Edge Microscopy" HS2015

Microscopy Imaging Center (MIC)

Every Friday, 8:15-10:00, Locations:

KSL ID: 9256

Institute of Anatomy, Bühlstrasse 26, Room A224

EXAM: 8:30 - 11:00 Lecture Room G. Wokerstrasse 5 Nr 3 on ->

Date	Subject	Lecturer
18.09.2015	2h Introduction to Cutting Edge Microscopy (including practical	Tschanz S. (Anatomy)
	part in the Histology room of the Institute of Anatomy)	
25.09.2015	Group A:	
	- 1h Physical basics of LM imaging, part 1	Frenz M. (IAP)
	- 1h Microscopy Demos	Various teachers
	Group B:	
	- 2h Microscopy Demos	Various teachers
02.10.2015	Group A:	
	- 2h Microscopy Demos	Various teachers
	Group B:	
	- 1h Physical basics of LM imaging, part 1	Frenz M. (IAP)
	- 1h Microscopy Demos	Various teachers
09.10.2015	1h Physical basics of light optical imaging, part 2	Frenz M. (IAP)
	1h Fluorescence Microscopy	Blank F. (DKF, MU50)
16.10.2015	Specific applications:	
	1h Laser scanning microscopy	Rothen-Rutishauser B.
		(AMI)
	1h CLSM specific applications (FRET, FRAP, Spectral unmixing)	Yousefi S. (PKI)
	& digital image restoration (huygen and Imaris software)	
23.10.2015	1h Calcium-imaging with confocal microscopy	Niggli E. (Physio)
	1h Super resolution imaging	Nevian T. (Physio)
30.10.2015	1h Intravital microscopy	Enzmann G. (TKI)
	1h Multiphoton-intravital microscopy	Moalli F. (TKI)
06.11.2015	1h Live cell imaging: The time factor	Lyck R. (TKI)
	1h 3D imaging by structured illumination	Lyck R. (TKI)
13.11.2015	1h Optical projection tomography	Stein J. (TKI)
	1h Atomic Force Microscopy in Biology	Fotiadis D. (IBMM)
20.11.2015	2h Transmission Electron Microscopy	Vanhecke D. (AMI)
27.11.2015	2h Scanning Electron Microscopy	Stoffel M. (Vet. Anatomy)
04.12.2015	MIC-Symposium	
11.12.2015	1h Cryoelectron Microscopy	Zuber B. (Anatomy)
	1h Serial Block Face SEM	Zuber B. (Anatomy)
18.12.2015	2h Stereology	Tschanz S. (Anatomy)
15.01.2016	2h Written exam. Presence 8:30, in front of the Lecture Hall G.	Tschanz S. (Anatomy)

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MIC modules

Eleven different practical microscopy modules were offered by the MIC (see Table 8). Many of them were almost fully booked. All modules dealing with microscopes were undertaken on state of the art devices provided by the MIC.

Table 8: MIC Modules 2015

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Microscopy Imaging Center (MIC)

Lectures and practical modules 2015/2016

Name of the module	Type of module	Semester/Duration	Lecturer	ECTS
Cutting Edge Microscopy (see special time table)	Lecture series	HS - 2h per week		3
Basic module - Histologic/microscopic methods	Practical	HS - 1h lecture + 3 half-day practicals	Christa Rhiner (Cell Biology)	3
Microscopy Applications for Immunological Research	Lecture and Practical	HS - 3 days	Marcus Theien (IRB, Bellinzona)	1.5
Conventional fluorescence microscopy, laser scanning microscopy and digital image processing	Practical	FS - 2 days (March-Møy)	Blank Fabian (LCI DKF)	1
3D image acquisition by grid projection	Practical	FS - 1 day	Ruth Lyck (TKI)	0.5
In vitro Live Cell Imaging	Practical	FS - 2 days	Ruth Lyck (TKI)	1
Transmission electron microscopy	Practical	FS - 1 days	Benoît Zuber (Anatomy)	0.5
Stereology Workshop	Practical	FS - 5 days	Stefan Tschanz (Anatomy)	2.5
Scanning electron microscopy	Practical	FS - 2 days	Michael Stoffel (Vetsuisse)	1
Multiphoton Intravital Microscopy	Practical	FS - 1 days	Jens Stein (TKI)	0.5
Intravital Microscopy	Practical	FS - 2 days	Gaby Enzmann (TKI)	1
Optical Projection Tomography (OPT)	Practical	FS - 1 days	Jens Stein (TKI)	0.5
Immunchistochemistry, immunofluorescence and microscopy in paraffin embedded sections	Practical	HS, 5 days (November)	Fabian Blank (LCI DKF)	2.5

Торіс	Teacher	Institute	Participants
Basic module - Histologic/microscopic Lecture and Practical	Christa Rhiner	Cell biology	14
Intravital Microscopy	Gaby Enzmann	ТКІ	1
Microscopy Applications for Immunological Research	Markus Thelen	IRB Bellinzona	10
Multiphoton Intravital Microscopy	Jens Stein	ТКІ	6
Immunohistochemistry, immunofluorescence and microscopy in paraffin embedded sections	Fabian Blank	DCR LCI	5
Practical course in fluorescent staining, fluorescence microscopy, confocal microscopy and image analysis	Fabian Blank	DCR LCI	14
Scanning electron microscopy	Michael Stoffel	Vet. Anatomy	4
Stereology Workshop	Stefan Tschanz	Anatomy	20
Transmission EM practical	Benoît Zuber	Anatomy	3

Table 9: Module attendance 2015

Image Processing

The series of training in image processing started in 2014 was continued in 2015 with the focus BITPLANE Imaris.

Two workshops were offered; a first introducing Imaris and a second providing advanced knowledge and training. The workshops were presented by teachers from BITPLANE and the hands-on trainings done in IT-poolrooms of the central IT department.

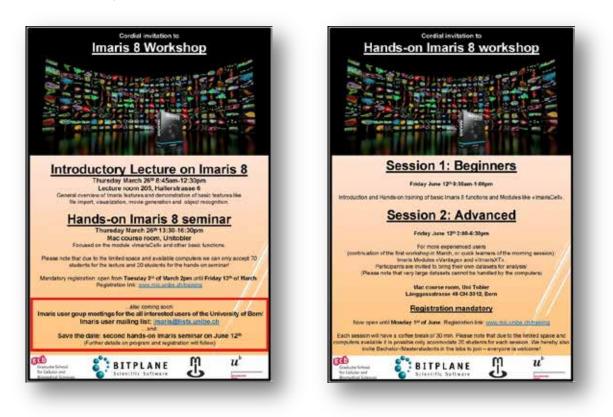


Fig. 5: Imaris Workshops

Grant application support

A key task of the MIC is coordination, evaluation and possible support of funding proposals in the field of microscopy.

Funding from Faculty resource committees and University sources in the field of Microscopy is only accessible if the respective projects are evaluated by the MIC commission. It seems that the Swiss National Science Fund also appreciates the advises of the MIC: R'Equip proposals for microscopy equipment should always be accompanied by a MIC evaluation.

The extraordinary costs of high-end microscopes and imaging systems require a coordinated and concerted investment strategy that unites many research groups and avoids redundancies. Such a strategy lowers the costs and exploits the valuable resources with higher efficiency.

It is essential to focus on those technologies which match the needs of the research community best and which allow for highest scientific level *and* an optimal degree of utilization.

The MIC, with all its members and member institutes, has a privileged position enabling it to survey the current situation of the University as a whole and to help to improve the chances of grant applications.

A concise work-flow detailing the interactions between the Resource Committee of the Medical faculty, the applicants and the MIC has been established together with the Resource Committee (see Fig. 6). This process streamlines the communication between all the participants.

Based on this model, the other participating Faculties (Science and VetSuisse) adopt similar guidelines.

Two R'Equip proposals (Multiphoton system, Prof. Jens Stein, TKI and DeltaVision System, Prof. Sven Rottenberg, Vet. Pathology) were unfortunately not funded by the Swiss National Foundation. However the GE DeltaVision fluorescence System of Prof. Rottenberg could be realized by other sources partially initiated by the MIC.

Support to successful applications

In 2015, the MIC supported the following microscopy investments at the University of Bern:

•	Prof. Ch. Müller, Institute of Pathology,	
	"EVOS Invers-Fluoreszenzmikroskop",	CHF 56'594
•	Prof. J. F. Dufour, Hepatology / DKF	
	"Microscope & MetaMorph Software", widefield fluorescence	CHF 40'000
•	Prof. H. U. Simon, Pharmacology and Prof. A. Perren, Pathology	
	"Confocal laser scanning microscope" ZEISS CLSM 700	CHF 199'000

In Summer 2015 the University granted extra funding to the faculties. Due to a concise and wellstructured investment planning of the MIC providing a comprehensive priority list a substantial part of the funds were assigned to the MIC. Several projects could be realized:

	Institut für Physiologie (med) [Ernst Niggli]	Konfokalmikroskop OLYMPUS Fluoview 1200 in dediziertem experimentellem Setting	CHF177'207.00
•	Institut für Anatomie (med) [Benoît Zuber]	Routine Transmissions Elektronenmikroskop, FEI Tecnai Spirit	CHF 485'599.50
•	Institut für Anatomie (med) [Edik Babiychuk]	Standard Konfokal Mikroskop ZEISS LSM 880	CHF 640'599.50
•	Departement Klinische Forschung, LCI (med) [Fabian Blank]	Airyscan Upgrade für existierendes ZEISS LSM710 Mikroskop, inklusive Z-Piezo insert	CHF 191'594.00
·	Institut für Zellbiologie (phil.nat.) [Volker Heussler, Pierre Meister]	Upgrade 2D -> 3D STED für bestehendes LEICA SP8 Superresolution Mikroskop	CHF 355'000.00
	CHF 1'850'000.00		

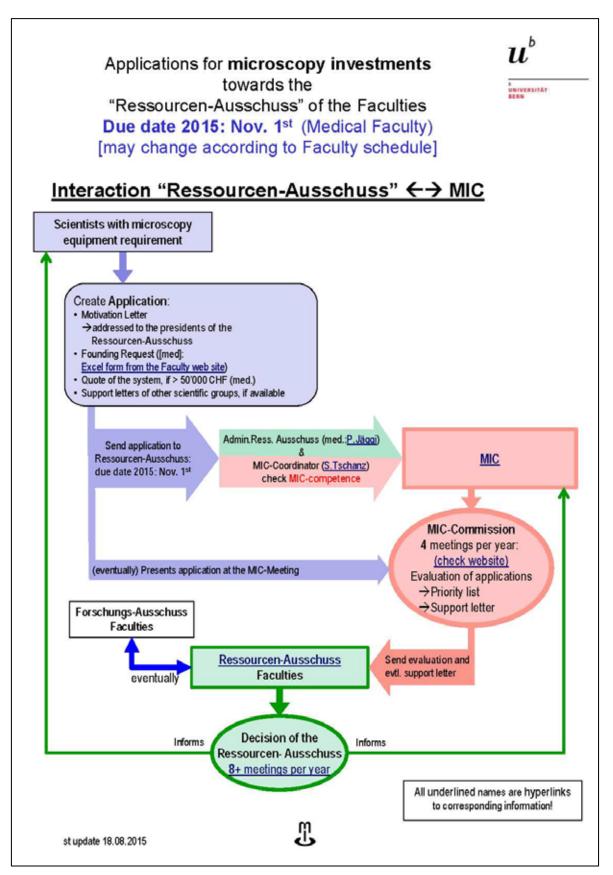


Fig. 6: Funding support work-flow

Publications resulting from work at the MIC in 2015

Users of MIC equipment and services are prompted to mention the MIC as provider of support in the acknowledgements of publications. List of MIC-associated publications (1-40)

- 1. Abadier M, Haghayegh Jahromi N, Cardoso Alves L, Boscacci R, Vestweber D, Barnum S, Deutsch U, Engelhardt B, and Lyck R. Cell surface levels of endothelial ICAM-1 influence the transcellular or paracellular T-cell diapedesis across the blood-brain barrier. *Eur J Immunol* 45: 1043-1058, 2015.
- 2. Ahrens HE, Petersen B, Herrmann D, Lucas-Hahn A, Hassel P, Ziegler M, Kues WA, Baulain U, Baars W, Schwinzer R, Denner J, Rataj D, Werwitzke S, Tiede A, Bongoni AK, Garimella PS, Despont A, Rieben R, and Niemann H. siRNA mediated knockdown of tissue factor expression in pigs for xenotransplantation. *Am J Transplant* 15: 1407-1414, 2015.
- 3. Bichsel CA, Hall SR, Schmid RA, Guenat OT, and Geiser T. Primary Human Lung Pericytes Support and Stabilize In Vitro Perfusable Microvessels. *Tissue Eng Part A* 21: 2166-2176, 2015.
- 4. Bongoni AK, Kiermeir D, Denoyelle J, Jenni H, Burlak C, Seebach JD, Vogelin E, Constantinescu MA, and Rieben R. Porcine extrahepatic vascular endothelial asialoglycoprotein receptor 1 mediates xenogeneic platelet phagocytosis in vitro and in human-to-pig ex vivo xenoperfusion. *Transplantation* 99: 693-701, 2015.
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- 6. Burda PC, Roelli MA, Schaffner M, Khan SM, Janse CJ, and Heussler VT. A Plasmodium phospholipase is involved in disruption of the liver stage parasitophorous vacuole membrane. *PLoS Pathog* 11: e1004760, 2015.
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- 8. Dai C, Basilico P, Cremona TP, Collins P, Moser B, Benarafa C, and Wolf M. CXCL14 displays antimicrobial activity against respiratory tract bacteria and contributes to clearance of Streptococcus pneumoniae pulmonary infection. *J Immunol* 194: 5980-5989, 2015.
- 9. Digigow RG, Vanhecke D, Rothen-Rutishauser B, Clift MJD, and Petri-Fink A. Uptake and Intracellular Fate of Peptide Surface-Functionalized Silica Hybrid Magnetic Nanoparticles In Vitro. *Part Part Syst Char* 32: 188-196, 2015.
- 10. Gantenbein B, Gadhari N, Chan SC, Kohl S, and Ahmad SS. Mesenchymal stem cells and collagen patches for anterior cruciate ligament repair. *World J Stem Cells* 7: 521-534, 2015.
- 11. Guggisberg S, Benneker LM, Keel MJ, and Gantenbein B. Mechanical Loading Promoted Discogenic Differentiation of Human Mesenchymal Stem Cells Incorporated in 3D-PEG Scaffolds with rhGDF5 and RGD. *Int J Stem Cell Res Ther* 2: 2015.
- 12. Henke D, Rupp S, Gaschen V, Stoffel MH, Frey J, Vandevelde M, and Oevermann A. Listeria monocytogenes spreads within the brain by actin-based intra-axonal migration. *Infect Immun* 83: 2409-2419, 2015.
- 13. Hurrell BP, Schuster S, Grun E, Coutaz M, Williams RA, Held W, Malissen B, Malissen M, Yousefi S, Simon HU, Muller AJ, and Tacchini-Cottier F. Rapid Sequestration of Leishmania mexicana by Neutrophils Contributes to the Development of Chronic Lesion. *PLoS Pathog* 11: e1004929, 2015.
- 14. Levayer R, Hauert B, and Moreno E. Cell mixing induced by myc is required for competitive tissue invasion and destruction. *Nature* 524: 476-480, 2015.
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subcapsular macrophages leading to widespread deposition on follicular dendritic cells. *Front Immunol* 6: 114, 2015.

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- 23. Rozman S, Yousefi S, Oberson K, Kaufmann T, Benarafa C, and Simon HU. The generation of neutrophils in the bone marrow is controlled by autophagy. *Cell Death Differ* 22: 445-456, 2015.
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