

# Imaging centers spread across the globe – partnerships between cooperation and academia ((biotech highlight)) Ulrike Engel

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# Imaging centers spread across the globe - partnerships

# between cooperation and academia ((biotech highlight))

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Abbreviations: NIC, Nikon Imaging Center;

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#### ((NO Abstract, introduction starts here without heading))

In the last eight years, Nikon Imaging Centers have been set up as collaborations between University Institutes and the Nikon Cooperation on science campuses across the world. This article summarizes the philosophy of the partnership between cooperation and academia, and how the Nikon Imaging Centers operate as light microscopy facilities within the research communities they are part of.

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## 1, The Nikon Imaging Centers as collaboration between Nikon and Academia

There are currently 8 Nikon Imaging Centers world wide, three in the United States, two in Asia and three in Europe. The first Nikon Imaging Center (NIC) was opened in 2001 at Harvard Medical School (Boston, MA, USA). It was the idea of Marc Kirschner, who was head of the Cell Biology Department at that time. He and his colleagues in the department had already pioneered live microscopy for the quantitative understanding of cell and developmental questions. So the idea was not to bring microscopes to needy scientists, who have never seen a microscope equipped with a digital camera, but to use the synergy of scientific excellence and cutting edge equipment. This collaboration was a big success with the scientific community at Harvard Medical School and has encouraged the formation of more NICs. In the meantime, 7 more NICs were created all over the world based on this working formula. The NIC at the University of Heidelberg, Germany, opened in September 2005. Next came the Nikon Imaging Center at Hokkaido University (2005), Oxford University (2006), the University of California San Francisco (2006), the Singapore Bioimaging Consortium (2007), the Institut Curie in Paris (2007), and Northwestern University in Chicago (2008).

I have witnessed the early NIC at Harvard Medical School (NIC@HMS) as a post-doctoral fellow and I have planned and directed the NIC at the University of Heidelberg (NIC@HD)

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during the last 3 years. Based on my experience as both a user and staff of the NIC, I will try to outline the philosophy of the NICs and what they bring to the scientific community. In all cases, these centers are set up as a partnership between a University Institute and the Nikon Cooperation. The directors and staff of the facilities are hired by the University, and the centers are embedded in the scientific community door to door with research labs. The NICs are built on local initiative and serve the needs of the scientific community they operate in. The NIC@HD was initiated by Thomas Holstein at the Institute of Zoology and Jörg Kukulies from Nikon, Germany. After one and a half years in the Zoology Institute it is now located at the new Bioquant building. Like other light microscopy facilities, the NICs main mission is to make equipment accessible to a large number of scientists, and to provide guidance in using it. Currently, the NIC@HD is serving 240 active users from more then 90 research groups. The type and number of equipment is negotiated between the academic partner and the local Nikon branch. We started with 5 systems and then rapidly agreed to add more as the demands grew. After its first 3 years the NIC@HD now offers 9 imaging setups (see Table 1) and we have considerably diversified the range of possible applications. Visitors to the NICs are often impressed by the abundance of equipment and cannot help to wonder whether there is a catch somewhere as the equipment is loaned to the University free of charge. Are these centers just "outlets" of Nikon, where the University provides the sales location? Is the staff trying to talk users into buying equipment? This is not how the Nikon Imaging Centers operate. Nevertheless, it is clear that the local Nikon branches and Nikon Japan have endorsed the NICs in their global marketing strategy and it is important to them, that the NICs are showcases for Nikon's imaging products. They are set up prominently in research hot spots, where a large number of postdocs and future group leaders become familiar with Nikon systems. However, the "displayed" products are put to the acid test as users work on them more than <u>10</u> hours a day. The NICs operate within an environment where users have the choice: Heidelberg has an astounding number of advanced microscope

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systems at both the University and other research centers. An enormous advantage for the researchers at NICs is the support that is added to the instrumentation. The instruments are kept in top working condition and there is always somebody who knows how to operate their advanced functions. Frequently, this is not the case when instruments are acquired by individual groups.

The exchange of experience between facility users and the NIC staff also involves the product specialist of Nikon. This way, Nikon learns about new applications and imaging demands. The good relation with the Nikon specialists helps the facility to operate and maintain the highly sophisticated equipment. The relation between academic staff and Nikon employees is generally relaxed and frank. A main reason for this might be the agreement between University and Nikon that the NICs will not purchase microscopes from Nikon's main competitors. This way the Nikon specialists are not in the position where they have to "advertise" their products and thus they share a lot more information with the NIC staff. In turn, the NIC staff is trying to give critical feedback to improve setups. At the NIC@HD we have given a lot of input directly to programmers during the early development of the NIS-Elements software.

In addition to Nikon, other companies also contribute equipment to the NICs. These are often local alliances and differ from NIC to NIC. In the case of the NIC@HD, Hamamatsu Photonics is sponsoring cameras, the German company AHF Analysentechnik provides filters, the Dutch company Scientific Volume Imaging is bringing its worldwide renowned deconvolution package to the NIC@HD. Perkin Elmer also operates as a major contributor, as one of the two spinning disk systems on a Nikon inverted microscope is sponsored by them. And the second one? It was bought through a German Research program grant, as well as the LaVision Biotec 2-photon system on the Nikon fix stage microscope (Table 1). It is not uncommon, that sponsored and bought equipment is hosted in the NICs, as the foremost interest of the facility is to provide a comprehensive choice of equipment. For the grant

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holders it is attractive to put their instruments within an existing facility. The choice of what type of sponsored equipment should be part or the Imaging Center is made by the directors and steering committee of the NIC together with the companies who join the effort. Technically, the equipment is loaned and does not become property of the University. This works as a big advantage for the academic partner. Equipment is replaced when advanced models become available. In the last 3 years we have exchanged all the inverted microscopes from TE2000 to the new Ti series with automated xy-stages and hardware focus. The TIRF setup was completely motorized, and we added 3 entirely new systems. As the systems are loaned, planning is much more flexible. Often, new innovations make existing instruments completely unpopular to users and upgrading the instrument is sometimes not possible or extremely costly. NICs have the opportunity to test whether an instruments suits the needs of the scientific community and can otherwise negotiate for a replacement. Of course, there is a down side to the exchange of instrumentation as it contradicts the fundamental principle to "never change a running system". Installing a new system usually means a lot of trouble shooting and extra work for the staff and the new setup is sometimes met by initial skepticism on the user side. Even changing just the software on a single microscope station can mean that 50 users have to be retrained.

#### **<u>2</u>** The equipment

The dream for both users and staff would be to have one type of microscope that covers all applications, or at least have every setup driven by a single software package. Unfortunately, doing microscopy is more like traveling: you have to change the means of transport all the time. Let us assume you want to look at actin dynamics in a moving cell. The obvious choice for a 3D time lapse study is a spinning disk confocal microscope (Fig, 1 and Fig, 2A-D), yet \_ even finer details of the actin cortex can be imaged with total internal reflection fluorescence microscopy (TIRFM; Fig, 2E). Then again, fluorescence recovery after photobleaching

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(FRAP) experiments have to be done on a laser scanning confocal microscope, unless the spinning disk has a photo bleaching unit. If the cellular dynamics need to be monitored in tissue, this might require the use of a 2-photon microscope, which allows to generate fluorescence signals in deeper cell layers. Most of the systems at the NIC@HD (see Table 1) are confocal microscopes or systems that also generate optical sections like the TIRFM and the 2 photon setup. In cases where specimens are flat, wide field fluorescence microscopes with sensitive cameras provide a valuable alternative as they offer an excellent signal to noise ratio for weak fluorescence signals.

## <u>3</u> The software that drives the microscopes

Using different equipment also means that users will encounter different types of software. Even though we have endorsed the Nikon NIS-Elements software at the NIC@HD and work with Nikon microscopes only, we are currently using 3 additional software packages for image acquisition (Volocity from Improvision, ImSpector Software from LaVision Biotec, Formatted: Subscript

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Nikon Biostation software). The quality of the software is key to the overall performance of the system. Nowadays it is possible to perform microscopy without oculars (*e.g.* on the Nikon Biostation, see Table 1), but not without using software to drive the different hardware components and sensors. The automation of microscope components in combination with a smart software allow to store microscope settings and recall them with one mouse click. The facility staff can prefabricate imaging protocols and pass them on to users. This way, even researchers without profound knowledge of microscopy can perform complicated imaging routines, which were previously the privilege of the experts.

In addition to the microscope setups, the NICs provide additional extra computers for data evaluation, storage of data on servers, specialized software for data rendering and deconvolution. While the NIC@HD relies on commercial software in the facility, we also use and teach ImageJ for image analysis [2], simply because it is a non-proprietary software which is available to users in their labs, at home, and in their future career.

#### **<u>4</u>** Service to the scientific community

In many respects the NICs run like other light microscopy facilities. They provide equipment, training of researchers, maintenance of microscopes and the logistics that make it possible to share instrumentation among many people [3, 4]. Different from other core facilities, light microscopy facilities have quickly moved away from "full service" where staff would acquire images for researchers. Instead providing a working environment that allows researchers to perform cutting edge microscopy has been proven to be much more successful. This way, researchers become "users" empowered to generate and improve imaging results. The by far most time consuming task for the NIC staff is to train and advise users. In their very resourceful article on light microscopy facilities, the staff of the light microscopy facility at the Max Planck Institute for Cell Biology and Genetics, Dresden, devote a whole paragraph to users [4]. They state: "Users are what it is all about; they can be a blessing and a curse! Good

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users push staff for assistance with cutting-edge applications, provide valuable feedback about the state of equipment, and are key to recognizing new trends...Bad users are selfish monsters who expect the equipment to be in top working condition when they want to use it, but give no thought to the condition in which they leave it". Little needs to be added to this angled but apt characterization, though I should mention that all shades between good and bad exist. Also, in quantitative terms, the ratio between good and bad is something like 100:1. As a consequence, the staff gets used to good users very quickly and is then annoyed at the occasional black sheep.

In all the NICs, the researchers are trained individually, on their own samples. This is demanding for the staff, as they do not show (or show off with) beautiful samples they already know, but try to optimize settings together with the researchers. For this reason, most staff members are PhD qualified and often have a post-doctoral or other professional research experience. In order to optimize the imaging experiment, the staff must know the microscope, but also get a quick understanding of the sample. It is ridiculous to painfully enhance the sensitivity of the sensor, when it would have been very easy to increase the expression level of a GFP construct, or to improve the staining protocol. Experienced staff can save the users a lot of trouble not related to the microscope directly. They help in setting up live experiments, getting expression levels right, discriminating autofluorescence from real signal. This does not mean that for all imaging experiments, solutions are straightforward. There are live specimen, which are very dim and nevertheless very interesting. Also, an application may demand extremely quick acquisition and requires that the staff optimize the instrument for sensitivity, speed and resolution.

The projects at the NIC@HD range from simple morphological analysis to experiments where imaging is used as a read-out of physiological activity in the cell (<u>*e.g.*</u> Calcium Imaging, FRETsensor) and protein interaction (<u>*e.g.*</u> FRAP and fluorescent resonance energy transfer). To setup  $\alpha'$  successful experiment detailed knowledge about all imaging components is required [5] and as for

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every scientific experiment appropriate controls need to be incorporated. Otherwise, serious misinterpretation might occur, for example crosstalk between channels might be taken as colocalization of two markers. To see researchers jump to more demanding imaging techniques without an understanding of the <u>basics</u> has a disheartening effect on the staff of the imaging facilities [6]. It is their job to make researchers aware of pitfalls, but ultimately the interpretation of the results falls into the responsibility of the researchers. To promote and deepen the understanding of principles in microscopy and discuss advanced applications the NICs also provide courses on a regular basis, which are extremely popular with PhD students.

#### 5 Outlook

The research conducted at the NIC@HD over the last three and a half years has contributed to around Deleted: 50 50 peer-reviewed research papers. Given the delay between data acquisition and publication this is likely to rise steeply during the next years. The projects are very diverse and it is only possible to list a few examples (Table 1). Looking back on the last three years, we were able to exchange and improve setups, making new applications possible (fast FRAP experiments, simultaneous Deleted: photoactivation and acquisition). Other experiments have become much more productive (e.g. time- Deleted: e.g. lapse acquisition is now done with hardware focus and multi-point acquisition). To take part in the fast progress of light microscopy-based research, the NICs depend on the dedication of both Nikon and the University to continuously invest into the NICs. They relay on Nikon's sustained commitment to provide hardware and new innovations. As we are increasingly combining high content with high throughput imaging, we need high resolution microscopes which can perform fast and parallel acquisition without compromising on sensitivity. To evaluate the resulting experimental data, smart ways to handle and analyze the large data sets need to be developed by University IT specialists. It is Deleted: the task of the NIC staff to integrate knowledge and pass it on to users. Each of the NICs worldwide has its own focus of expertise, but systematic exchange of information amongst the NICs and other imaging centers is a largely untapped resource, and will help to develop solutions to common

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problems and foster the development of novel imaging solutions.

I would like to thank Nikolas Herold for image data shown in Fig. 2 and Günther Gerisch for providing Dictoystelium, labeled yeast and experimental support for data displayed in Fig. 1. Thanks go to Takeharu Nagai (NIC@HU), Jennifer Waters (NIC@HMS) and the Imaging Facilities Dresden, especially Britta Schroth-Diez for discussions on light microscopy facilities and to Georg Stöcklin for critical reading of the manuscript.

 The author has declared no conflict of interest.

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[1] Misgeld, T., Kerschensteiner, M., In vivo imaging of the diseased nervous system. Nat. Rev.

Neurosci. 2006, 7, 449-463.

[2] Rasband, W.S., ImageJ, U. S. National Institutes of Health, Bethesda, Maryland, USA,

http://rsb.info.nih.gov/ij/, 1997-2008.

[3] DeMaggio, S., Running and setting up a confocal microscope core facility. Methods Cell.

Biol. 2002, 70, 475-485.

[4] Anderson, K. I., Sanderson, J., Peychl, J., Design and Function of a Light-Microscopy

Facility, in: Shorte, S. L., Frischknecht, F. (Eds.), Imaging Cellular and Molecular Biological

Functions, Springer, Berlin Heidelberg 2007.

[5] Waters, J. C., Live-cell fluorescence imaging. Methods Cell. Biol. 2007, 81, 115-140.

[6] Pearson, H., The good, the bad and the ugly. *Nature* 2007, 447, 138-140.

[7] Hoebe, R. A., Van Oven, C. H., Gadella, T. W., Jr., Dhonukshe, P. B., et al., Controlled light-

exposure microscopy reduces photobleaching and phototoxicity in fluorescence live-cell imaging.

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59 60 Nat\_Biotechnol\_ 2007, 25, 249-253.
[8] Wang, Y., Janicki, P., Koster, I., Berger, C. D., et al., Xenopus Paraxial Protocadherin regulates morphogenesis by antagonizing Sprouty. *Genes Dev*\_ 2008, 22, 878-883.
[9] Adamczyk, P., Meier, S., Gross, T., Hobmayer, B., et al., Minicollagen-15, a novel minicollagen isolated from Hydra, forms tubule structures in nematocysts. J. Mol\_ Biol\_ 2008, 376, 1008-1020.

[10] Moers, A., Nurnberg, A., Goebbels, S., Wettschureck, N., Offermanns, S.,  $G\alpha 12/Ga\alpha 13$ deficiency causes localized overmigration of neurons in the developing cerebral and

cerebellar cortices. *Mol. Cell. Biol.* 2008, 28, 1480-1488.

[11] Renz, M., Betz, B., Niederacher, D., Bender, H. G., Langowski, J., Invasive breast cancer cells exhibit increased mobility of the actin-binding protein CapG. *Int. J. Cancer* 2008, *122*,

1476-1482.

[12] Jarve, A., Muller, J., Kim, I. H., Rohr, K., et al., Surveillance of siRNA integrity by

FRET imaging. Nucleic Acids Res. 2007, 35, e124.

[13] Gutscher, M., Pauleau, A. L., Marty, L., Brach, T., *et al.*, Real-time imaging of the intracellular glutathione redox potential. *Nat. Methods* 2008, *5*, 553-559.

[14] Appel, N., Zayas, M., Miller, S., Krijnse-Locker, J., et al., Essential role of domain III of

nonstructural protein 5A for hepatitis C virus infectious particle assembly. *PLoS Pathog*. 2008, *4*, e1000035.

[15] Clarke, M., Muller-Taubenberger, A., Anderson, K. I., Engel, U., Gerisch, G.,

Mechanically induced actin-mediated rocketing of phagosomes. *Mol. Biol. Cell* 2006, *17*, 4866-4875.

[16] Goulimari, P., Knieling, H., Engel, U., Grosse, R., LARG and mDia1 Link Ga12/13 to

Cell Polarity and Microtubule Dynamics. Mol. Biol. Cell 2008, 19, 30-40.

[17] Bacon, C., Endris, V., Rappold, G., Dynamic expression of the Slit-Robo GTPase activating protein genes during development of the murine nervous system. J. Comp. Neurol. 2009, 513, 224-236.

#### **Figures and Tables**

ļ		,1	Deleted: Figure 1¶
	Figure 1. Actin dynamics in the amoebae of <i>Dictyostelium discoideum</i> captured by spinning		Formatted: Font: Bold, Not Italic
ļ	disc confocal microscopy in 3D and time. Cells expressing a construct of an actin-binding		
	protein, GFP-LimE (green), show that actin accumulates at the cortex (c), around intracellular		
	vacuoles (v) and prominently builds up in filopodia (f) and endocytic cups. Actin		
	polymerization drives endocytosis (en) of solid particles like yeast (A) or allows for bulk		
	uptake of liquid (B), a process called macropinocytosis (mp). (A) Cell in the process of		
	engulfing a yeast (red, TRITC stained). (B-D) Dictyostelium cells undergoing spontaneous		
	shape changes, which have been reconstructed in space (36 z-slices) and time (as indicated).	1	Deleted. Huygens
	The z-stacks were deconvolved with a theoretical PSF using <u>Huygens</u> 3.0 to enhance	/	
1	localization accuracy. (B) Single optical slice through the middle of cells. (C) Maximum	1	<b>Deleted:</b> 10
	projection. (D) Angled projections (renderings) of different time points. Scale bars are $10 \mu m$ .		
ļ	Image: Ulrike Engel.		
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	<b>Figure 7</b> T cell line expressing GEP live act (green) to highlight actin dynamics. The cells		Deleted: #

Figure 2_T-cell line expressing GFP live-act (green) to highlight actin dynamics. The cells
settle on a substrate covered with modified HIV virus particles (red). (A-D) Live imaging on a
spinning disk confocal microscope (21 z-slices, 0.15_µm spacing, time as indicated). (A) 3D
view of the cell in a side projection (B) orthogonal maximum projection. (C) Optical xy-slice
and reconstructed xz- and yz-slices allow to determine the exact position of a virus particle
that has bound to the cell (white arrow head). (D) Insert detail (3_µm length) is magnified to

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show the movement of virus particle (white arrow head) with actin flow (time in seconds). (E) TIRFM of cell attaching to substrate. Only the actin cytoskeleton directly in contact with the substrate is visible and makes it possible to discern actin bundles at the cortex. Sale bars are 10\_µm. Images: N. Herold, University of Heidelberg.

Tabla 1	Equipment and Appli	cations at the NIC@HD		1	Deleted
	Equipment and Appli			_2''	
Number	Type of Instrument	Short Description	Applications		
setups					
2	Laser scanning	Special features in addition to	Fixed and live		
	confocal	standard LSCM:	morphology in 3D and 4		
	microscopes	Nikon A1R with galvano- and	channels [ <u><i>e.g.</i></u> 8, 9]		Deleted: e.g.
	(LSCM) with	resonant scanner allows for	Comparative		
	standard and	frame rates of 30 fps and for	immunocytochemistry,		
	spectral detectors:	photoactivation while	such as analysis of		
	Nikon C1Si and	acquiring images. Fast z-	knockout mice phenotypes		
	Nikon A1RSi on	acquisition with a piezo-based	[10]. FRAP experiments		
	Nikon Ti inverted	z-stepper. The C1 is equipped	[11]. Photactivation in		
	microscope with	with controlled-light exposure	hippocampal neurons.		
	automated xy-	microscopy, (CLEM [7]),	FRET [12] and FRET-		
	stage and hardware	which reduces phototoxicity. 7	based sensors [13] and		
	focus.	Laser lines cover the range of	other ratio imaging.		
		405- 640nm	In-vivo cell migration in		
		Plan Apo objectives with	cancer models.		
		chromatic correction from UV			

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		to red.		
2	Perkin Elmer	Yokagawa CSU22-based	Mostly subcellular	
	UltraView ERS	spinning disk confocal	structure at high spatial	
	spinning disk	microscope for real time	and temporal resolutions,	
	confocal	confocality equipped with xy-	such as	
	microscopes on	table and piezo-based z-	cytoskeletal dynamics in	
	Nikon Ti/Te2000	stepper.	neuronal outgrowth,	
	inverted	Laser lines cover the range of	actin dynamics during	
	microscope with	405 to 640 nm.	virus binding (Fig. 2A-E),	
	Prior automated	Images are mainly recorded	virus particle production	
	xy-stage H117.	with high numerical aperture	[16], actin dynamics (Fig.	Exemption Fo
		lenses (e.g. 100x Plan Apo	1) and	-
		VC) onto an EM-CCD.	organelle propulsion in	
		Special feature:	Dictyostelium [9]. Force	
		Photokinesis unit allows for	measurement in malaria	
		FRAP and Photoactivation	parasites.	
		experiments in region of	Live experiments in cells	
		interests.	and invertebrate animals	
			with genetically encoded	
			Ca <sup>2+</sup> and redox sensors	
			[13].	
			-4	
1	LaVision Biotec 2-	2-photon laser setup on fix-	Dynamic morphology or	-
	photon microscope	stage microscope equipped	physiological sensors (e.g.	Delatadi
	(TRIM scope) on	with dipping lenses for	$Ca^{2+}$ ) in thick specimen.	Deleted: e.g.

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	Nikon FN-1 fix	physiological microscopy. The	Acute brain slices, small	
	stage microscope.	Femto-second pulses range	embryos or in-vivo	
		from 700- <u>1150 nm and allow</u>	imaging in mice.	Deleted: 1150
		for excitation of blue to red		
		emitting dyes. The signal is		
		detected on descanned photo		
		multiplier tubes. A special		
		feature is the multi-beam		
		scanning and fast detection on		
		2 cameras.		
1	Nikon Total	Objective TIRF (with 60x or	Receptor clustering,	
	Internal Reflection	100x Plan 1.49) on inverted	focal adhesion dynamics,	
	Microscope	fully automated microscope	vesicle fusion, virus cell	
	(TIRFM) equipped	with hardware focus,	interaction (see Fig. 2E).	
	with Sutter fast	automated xy-stage and	Microtubule cell cortex	
	filter wheels for	sensitive cameras (Orca-AG or	interactions during	
	TIRF or epi	back-illuminated EM-CCD).	migration [6].	
	illumination multi-	TIRF illumination (488 and	Ca <sup>2+</sup> imaging in TIRF	<b>Deleted:</b> 561
	channel time lapse.	<u>561</u> nm lasers) and wide field	(Fluo-4) and	
		fluorescence can be combined.	epifluorescence mode	
			(Fura-2).	
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1	Nikon 90i	Fully automated upright	Immunofluorescence for	
	automated upright	fluorescence microscope	overview and high	
	microscope	equipped with fluorescence,	resolution.	

		differential interference	Automated acquisition of
		contrast and Plan Apo	large sections (stitching)
		objective series.	[17].
1	Nikon multi-zoom	Fluorescence and differential	In- situ hybridization and
	microscope AZ100	interference contrast on zoom	immunofluorescence of
		microscope for magnifications	whole mounts. Nerve
		5x-400x	outgrowth in organotypic
			slices.
1	Nikon Biostation	Environmentally enclosed	Long term imaging over
	•	timelapse microscope with	several days: cells cycle
		multi-fluorescence and multi-	studies, RNAi phenotypes,
		point acquisition.	malaria infection of liver
			cells.





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