

A novel room concept for shared resource laboratories

Christian Kukat¹  | Eckhard Neumann² | Eugenio Fava³ | Hans Fried⁴ 

¹FACS & Imaging Core Facility, Max Planck Institute for Biology of Ageing, Cologne, Germany

²Department for Technical Infrastructure, German Center for Neurodegenerative Diseases (DZNE), Bonn, Germany

³Core Research Facilities and Services, German Center for Neurodegenerative Diseases (DZNE), Bonn, Germany

⁴Core Research Facilities and Services, Light Microscope Facility, German Center for Neurodegenerative Diseases (DZNE), Bonn, Germany

Correspondence

Hans Fried, Core Research Facilities and Services, Light Microscope Facility, German Center for Neurodegenerative Diseases (DZNE), D-53127 Bonn, Germany.
Email: hans.fried@dzne.de

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Abstract

Shared resource laboratories/core facilities (SRLs) are centralized platforms that house and provide access to complex and expensive research equipment. Due to the highly complex nature of the instrumentation they support, SRLs have special environmental requirements for their laboratory space. Here, we describe the planning and establishment of a large light microscopy SRL, with a special focus on room layout, custom-designed air conditioning and vibration, which can also be adapted to proteomics, genomics, and flow or mass cytometry SRLs.

KEYWORDS

core facility, light microscope facility, room layout, shared resource laboratory, SRL, temperature, vibration

1 | INTRODUCTION

Complex and expensive research equipment is often housed in centralized platforms, known as core facilities or shared resource laboratories (SRLs; [1]). Dedicated staff maintain the equipment and facilitate user access. Due to the highly complex nature of the instrumentation, SRLs have special environmental requirements for the laboratory space they occupy. These challenges are very similar, no matter if the SRL provides services for light or electron microscopy, medical imaging, proteomics, genomics, metabolomics, or mass or flow cytometry. The main categories of the challenges are room layout, dust, lighting, noise, electricity, gas supply, temperature, humidity, and vibration [2–5].

The demand for electricity, control of room light, and gas supply differs in SRLs from standard laboratories. In SRLs, electric equipment may be bulky and the equipment turnover is usually more frequent than in standard laboratories. Thus, the number and the position of standard sockets and three-phase current sockets need to be planned.

Similarly, supply valves for gases such as pressurized air, oxygen, nitrogen or carbon dioxide must be conveniently accessible during operation. In some SRLs, ambient light must be controllable from full darkness to normal light conditions. The ability to control room lighting independently in different areas of a room may be required. In recent years, tightly-controlled temperature and minimal floor vibration have become more critical for using sensitive instruments often found in SRLs. For example, many new instruments on the market have ever-growing specifications for resolution and imaging speed where temperature fluctuations and floor vibration drastically compromise the achievable resolution and image quality.

Although general considerations and requirements for the laboratory space of SRLs have been discussed previously [4–9], the effectiveness of different strategies has not been well documented and remains only anecdotally reported. In particular, high-end microscope room temperature stability requirements have been increasing but data on air conditioning performance in an SRL has not been shown. In this publication, we describe in detail one concept for a large light

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microscopy SRL at the German Center for Neurodegenerative Diseases (DZNE) in Bonn, Germany and provide measurement results for its environmental performance. The SRL was built with three design goals: (1) elimination of vibration where possible and isolation of unavoidable vibration; (2) moving heat-producing or vibrating devices away from sensitive instruments and into adjacent rooms, and (3) development of a custom-designed feedback-controlled air-conditioning system. We provide data on room temperature fluctuations under different operation conditions. This data will be helpful for planning sensitive experiments and designing new SRLs. In addition, we give examples of how our main concerns can be addressed where pre-existing standard laboratory space is converted into an SRL.

2 | METHODS AND RESULTS

2.1 | Room layout

It is crucial for the planning of an SRL to estimate the expected size in terms of equipment, user numbers, and personnel [4]. We built our light microscopy SRL to accommodate 25–35 complex microscopes; some in their own small rooms and some in large combined microscope rooms (Figure 1 and Supplementary Figure 1). All microscope rooms can be reached via an entrance room with automatically closing fire-protection doors and equipped with clean room lab coats, lockers, and a hand-washing sink. Doors between entrance rooms and microscope rooms serve no fire-/fume-protection function, and can therefore be lighter and induce less vibration when closing the doors. Clean room lab coats and sticky door mats are used to minimize dust import.

Small rooms (<20 m²) allow better control over room illumination and ambient noise, but do not accommodate large and bulky instruments. In addition, they make maintaining stable room temperature more complicated (see below). Large rooms (>>20 m²) are more flexible because they can accommodate several instruments, and as a result have the additional feature that SRL users can communicate with each other while working. However, based on the experience made during the SARS-CoV-2 pandemic it is important to note that, unlike large rooms, single instrument rooms allow users to work according to social distancing policies without additional structural or individual effort [10, 11]. Further important considerations include how to optimize for common workflows, providing space for system testing, teaching, instrument demonstrations, possibility for wet lab work, furniture, and storage capacity. How to optimize these aspects has been described in detail elsewhere [5, 6, 12].

An obvious way to reduce temperature fluctuations in instrument rooms is to place heat-producing accessory devices outside of the room [4, 8]. We designed utility corridors with storage space and heavy-duty shelves for vibration- and heat-producing devices, including chillers, multiphoton pump lasers, and power supplies. These devices remain connected to their microscopes via openings in the walls (Figure 2). Cable openings are 30 × 20 cm (width × height). Larger windows (75 × 80 cm width × height) with vertically-closing

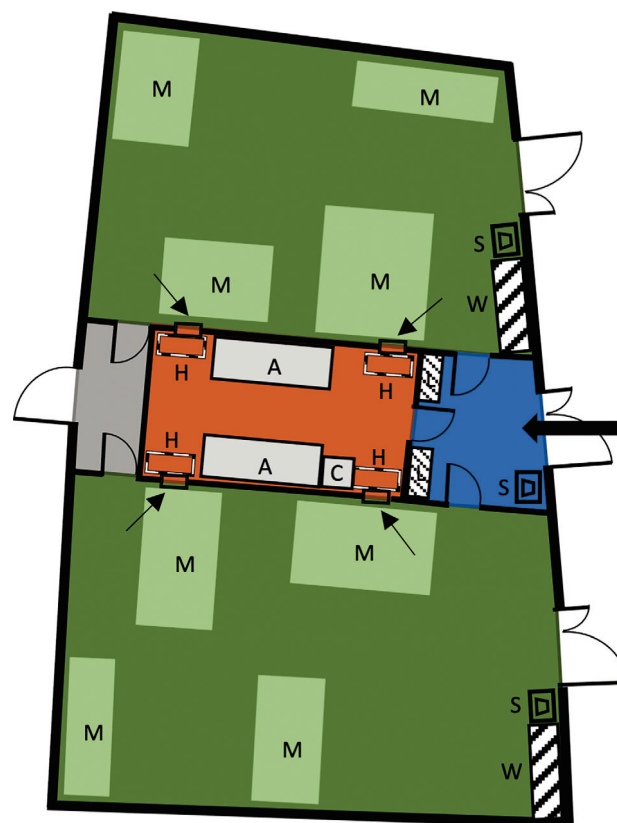


FIGURE 1 Room layouts for Shared resource laboratories. Two microscope rooms (dark green, 55 and 70 m²) with microscope setups (light green), an entrance room (blue), a utility corridor (orange), and a flight path (gray). A, air handling unit of the forced air-cooling device; C, cooling cabinet; H, heavy-duty shelf; L, lockers and lab coats; S, sink; W, wet lab bench. Bold arrow indicates main entrance to the facility area and small arrows indicate window and cable openings connecting a microscope setup with the adjacent heavy-duty shelf in the utility corridor. [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com/doi/10.1002/cyto.a.24795)]

slides were also necessary, because multiphoton pump lasers are connected to their microscopes with cables and light guides that cannot be removed, therefore they had to be transported through the wall into the utility corridor still attached to the microscope. Both the window slides and cable openings are brush-sealed. Heat-producing devices in utility corridors are cooled by close control air conditioners (RC group IT cooling, next evo cw s u, 8 or 12 kW). In one utility corridor, we installed two close control air conditioners for nine multiphoton pump lasers, 10 chillers, and several power supplies, with a combined total nominal heat production of more than 20 kW/h (Figure 2 and Supplementary Figure 1b). This arrangement also reduces vibration (see below) and noise, which is advantageous for two reasons. First, sound is a vibration which can affect microscope performance; for example, Zeiss LSM980 room requirements specify noise levels below 55 dB. Second, noise significantly alters animal behavior, so it benefits both behavioral animal or intravital microscopy experiments and also SRL user comfort. Use of utility corridors reduced noise levels in the microscope rooms to 45 ± 3 dB.

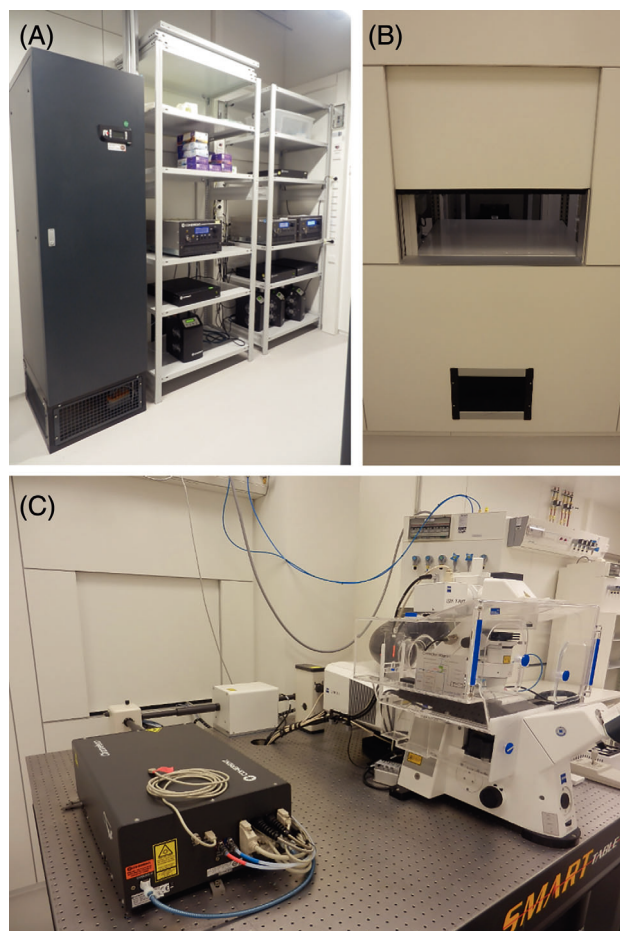


FIGURE 2 Utility corridors with heavy-duty shelves are connected via windows and cable openings with microscope rooms. (A) Cooling cabinet and two heavy-duty shelves with multiphoton pump lasers and chillers in a utility corridor. (B) Window and cable opening in the wall viewed from the microscope room. Vertically opening slide is half closed. (C) Multiphoton microscope installed adjacent to window and cable opening. Vertically opening slide is completely closed. [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com)]

2.2 | Temperature

Even 1 to 2°C temperature changes during microscope operation can result in a dramatic performance drop [13, 14]. The manufacturer-recommended room requirements for many high-end microscopes specify temperature fluctuations during operation of no more than 1°C (Leica TCS SP8 STED: 1°C, DeltaVision OMX Flex: 1°C/h, Zeiss LSM980: 0.5°C/h, Zeiss Elyra7: 0.5°C, Nikon N-STORM: 0.5°C). Maintaining stable room temperatures within such a narrow range is a major challenge and cannot be achieved with standard room air conditioning.

Our custom-designed air conditioning solution (Ingenieurgesellschaft Feldmeier mbH) uses large-area forced-air cooling (System ETA by Howatherm Klimatechnik GmbH) with high air volume turn-over rates. The conditioned air blown into the room features a small temperature difference to the set temperature (22°C).

Up to 48 air exchanges per hour (up to 7100 m³/h) are needed to achieve temperature stability during maximum microscope usage. To prevent drafts, large forced-air outlets, in the form of a textile-based ductwork distribution system, and grid-covered extraction points between each textile-based ductwork are used (Figure 3). The grid covers have a mesh size of 0.5 mm to prevent possible escape of *Drosophila* fruit flies, a model organism used at our SRL. Our two large microscope rooms (55 and 70 m², Figure 1) each have their own air-cooling system. Three smaller rooms (<25 m², Supplementary Figure 1A, B) share a single air-cooling system in series. The temperature and volume flow rate of the input air is generated in the air handling unit feedback-controlled based on the measured room temperature (Figure 4). Control response characteristics (graphs in Figure 4) must be carefully adjusted to achieve fast response time without introducing strong overshooting resonating temperature changes. A detailed description of the air conditioning design and its feedback regulation is in the supplements.

We installed thermometers (W&T, Web-Thermometer Pt100 #57715) in three different places in the microscope rooms: (1) at the wall, where a thermostat provides feedback to the air handling unit; (2) in the air extraction ducts in the ceiling, a convenient way to measure average room temperature since the air from all extraction sites mixes before reaching this location; and (3) next to the microscopes themselves. During various microscope usage conditions, the extraction duct thermometer and the wall thermometer showed no major differences (ΔT of $0.2^\circ\text{C} \pm 0.1^\circ\text{C}$, averaged over 1430 h), demonstrating that the wall thermometer alone could reliably be used for regulating the air-conditioning (Supplementary Figure 2). However, in two cases we had to change the position of the wall thermometer (or the placement of the nearby microscope) to protect the thermometers from local temperature fluctuations. In addition, we observed that the extraction duct temperature and the wall temperature differed more in a large room with four different microscope setups: When only the microscopes located far from the wall thermometer or only microscopes close to the wall thermometer were used, differences were on average $0.3^\circ\text{C} \pm 0.3^\circ\text{C}$ with a maximum of 1.1°C reached only once in the 1430 h measurement interval and for few minutes (Supplementary Figure 2). In our final configuration, the wall thermometers are placed a few centimeters away from the wall, approx. 1.5 m above the floor, and at least 1 m away from any heat producing device or door. The wall thermometers are used for feedback regulation of air-conditioning (Figure 4).

Next, we compared actual room temperature, as measured at the wall thermometers to set temperature (in our case 22°C) during microscope usage. We found that, most of the time, room temperature differed from set temperature by less than 0.5°C. The large room showed less variation from the set temperature (data from Figure 5C, D: $0.04^\circ\text{C} \pm 0.07^\circ\text{C}$, maximum 0.8°C) than the small rooms (data from Figure 5E: $0.3^\circ\text{C} \pm 0.2^\circ\text{C}$, maximum 0.9°C).

For best microscope performance, keeping stable room temperature over time is more important than maintaining any particular room temperature. Thus, we analyzed temperature changes (ΔT) in 1 h

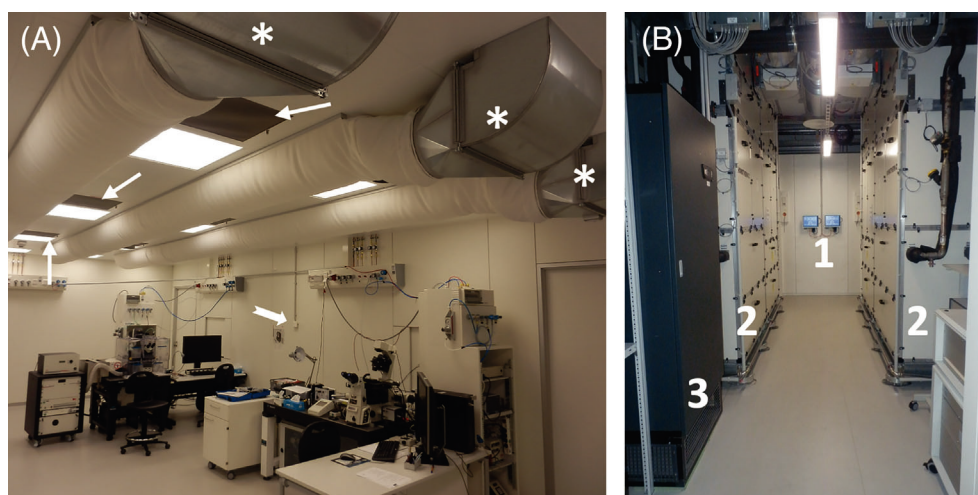


FIGURE 3 The forced air-colling air-condition system. (A) Microscope room with textile-based ductwork distribution systems for conditioned air supply into the microscope rooms (asterisk) and room air extraction openings covered with a Drosophila tight grid (thin arrows). There are six more extraction openings in the room which are not visible in the image. Thermometer for controlling the temperature (bold arrow). (B) Utility corridor behind the wall seen in panel (a) with control panels (1) for the forced air-cooling devices (2) and a cooling cabinet (3) to regulate temperature in the utility corridor. [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com/doi/10.1002/cyto.a.24795)]

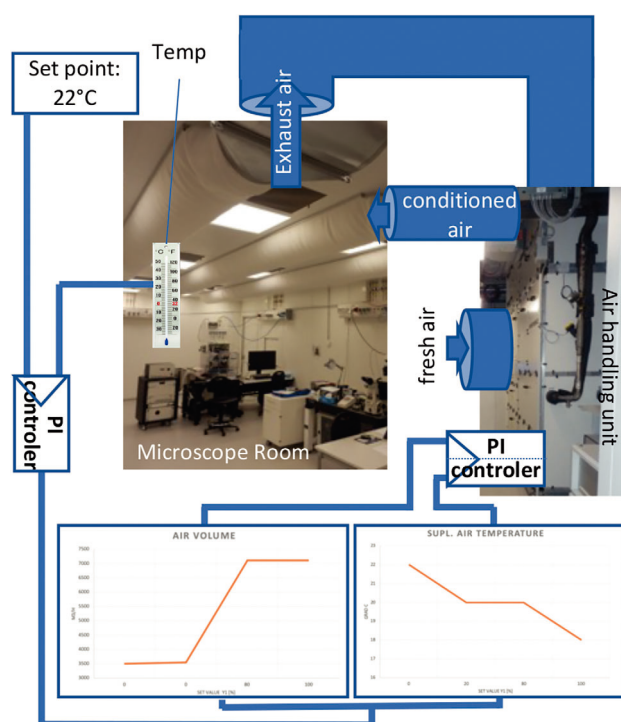


FIGURE 4 Feedback loop of the air conditioning system. Conditioned air from the air handling unit is blown via the textile-based ductworks into the microscope rooms. The air in the microscope rooms is extracted via extraction openings in the ceiling and pumped back into the air handling unit. When the temperature in the microscope rooms changes, proportional-integral (PI) controllers regulate the air volume and air temperature of the air handling unit to maintain the temperature at the setpoint of 22°C. Air volume and temperature is generated in the air handling unit according to a given room temperature as shown in the graphs. Constantly, 8-fold room air volume per hour of fresh air is mixed with the extracted air from the microscope rooms. [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com/doi/10.1002/cyto.a.24795)]

and 12 h at the wall thermometers of the small rooms and large room shown in Figure 5 during a one-week time period. The average delta T after 1 h was $0.1^{\circ}\text{C} \pm 0.1^{\circ}\text{C}$ with a maximum of 0.9°C (no difference between large and small rooms). The average temperature fluctuation after 12 h was $0.1^{\circ}\text{C} \pm 0.1^{\circ}\text{C}$ with a maximum of 0.8°C for large rooms and $0.3^{\circ}\text{C} \pm 0.2^{\circ}\text{C}$ with a maximum of 1.4°C for small rooms.

Finally, we investigated local temperature changes next to the microscopes in use. Rather large local temperature changes during usage of laboratory equipment have been reported previously [2]. Thermometers were placed at a distance of 20–50 cm to the heat producing device closest to the microscope objective (e.g., cooling fins of cameras or scan heads). The location of microscopes and thermometers is shown in Figure 5A, B. In all rooms and at all tested microscopes, we observed surprisingly small temperature differences between the microscope thermometers and the wall thermometers. Weeks with heavy usage of the microscopes are shown in Figure 5D, E. The temperature difference remained below 0.5°C (average of $0.2^{\circ}\text{C} \pm 0.1^{\circ}\text{C}$) while microscopes were in use, most of the time. Only on few days, at some microscopes in the large room, temperature differences reached 0.8 – 1.5°C .

Our results demonstrate that the goal to implement an air-conditioning to regulate the room temperature within $\pm 1^{\circ}\text{C}$ was reached. In most cases we could even reach the more stringent temperature stability of $\pm 0.5^{\circ}\text{C}/\text{h}$. With our air-conditioning concept and microscope usage conditions large rooms can be kept at a much more stable room temperature than small rooms.

After several years of usage, with about 200 users per year, the air-conditioning system is still working with unchanged performance. Neither the ductwork nor the grid cover for air extraction has accumulated dust. Only in the light microscope room section in the animal facility, where we observe more dust than in our standard laboratories, did the grid covers require cleaning after 3 years.

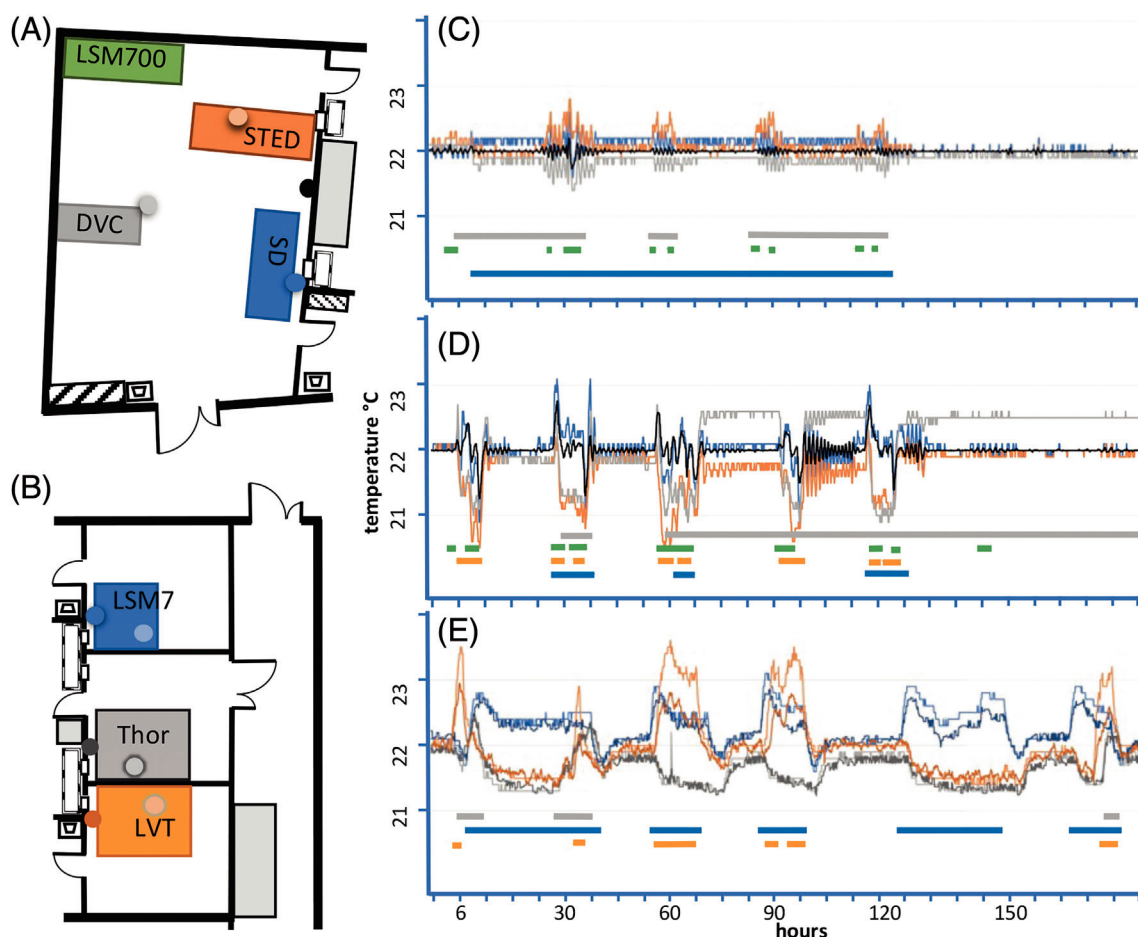


FIGURE 5 Temperature trends of three representative weeks in four different microscope rooms. (A) Position of microscopes (Leica STED, orange rectangle (STED); Zeiss LSM700, green rectangle (LSM700); Delta Vision Core, gray rectangle (DVC); Andor Spinning Disk, blue rectangle (SD)), wall thermometer (black circle), and thermometers at microscopes (orange, gray, and blue circles). (C) and (D) Temperature trend of 2 weeks in the room shown in (A). Temperature trends and microscope usage (bars) are color coded with colors indicated in (A). (B) Position of microscopes (Zeiss LSM7MP, blue rectangle (LSM7); Thorlabs resonant 2P setup, gray rectangle (Thor); LaVision Trim Scope II, orange rectangle (LVT)), wall thermometers (dark blue circle, black circle, and dark orange circle), and thermometers at microscopes (light blue circle, gray circle, and light orange circle) in three rooms. (E) Temperature trend in the room shown in (B). Temperature trends and microscope usage (bars) are color coded with colors indicated in (B). [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com/doi/10.1002/cyto.a.24795)]

2.3 | Vibration

Minute movements of the floor or walls can lead to artifacts in light microscope images, significantly reducing the overall achievable resolution. Leica Microsystems and Zeiss specify that the floor on which high-end microscopes are located should not vibrate more than $12.5 \mu\text{m/s}$. Usage of specialized anti-vibration tables dampens floor vibrations above 4 Hz, but at frequencies below 3 Hz table efficiency drops considerably (see compliance and transmissibility curves of various vendors like Newport, Thorlabs, or OPTA GmbH). In addition, even minute floor vibrations can intensify at 1–2 Hz, which is the natural frequency of the isolator of anti-vibration tables (see transmissibility curves of various vendors like Newport, Thorlabs, or OPTA GmbH).

Anything touching the microscope table can introduce vibrations, including heating and cooling devices, external light sources for fluorescence illumination, camera ventilation, or air compressors for anti-vibration tables. We took those components off the microscope

tables and moved them to custom-designed 19-inch racks (Waldner Group, Germany) equipped with six individual power circuits (four power sockets each) and gas valves (oxygen, carbon dioxide, nitrogen, carbogen, and pressurized air) shown in Figure 6A–D. The 19-inch racks are connected to room electrical outlets and gas supply and can be equipped with a variety of commercially available inlays. For example, pull-out inlays allow positioning microscope components above the microscope table without touching it.

In our SRL, close control air conditioners and air handling units of the forced air-cooling devices are sources of vibration. To reduce the impact of these vibrations, close control air conditioners rest on anti-vibration mats and the air handling units of the forced air-cooling devices have anti-vibration spring feet (Figure 6E, F). To test their efficacy, we outsourced floor vibration measurements (Kötter Consulting Engineers). Floor vibrations were measured under all possible air conditioning modes and at multiple sites in each room. Results indicate that floor vibrations remain below the manufacturer-recommended

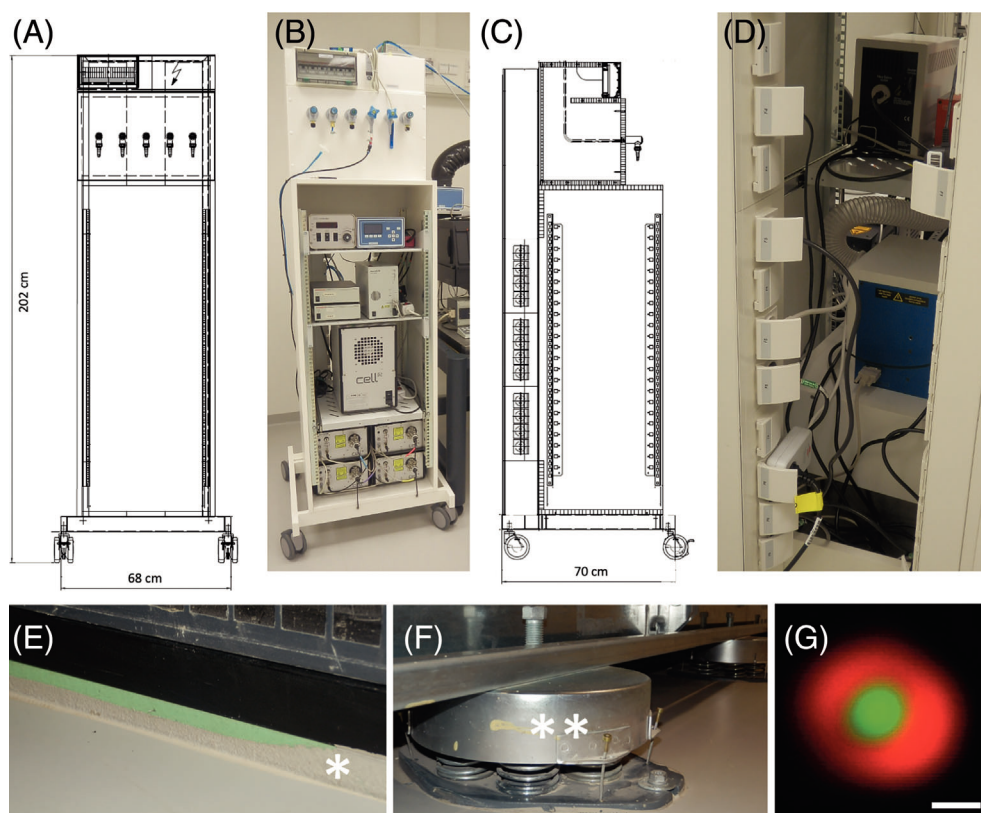


FIGURE 6 Custom designed 19" racks and anti-vibration devices. (A) Technical drawing of the instrument rack in front view. (B) Instrument rack with gas valves for all common gases and fuses for six electrical circuits for convenient access in the front. Supply of all gases and high voltage power is on top of the instrument racks. (C) Technical drawing of the instrument rack in side view. (D) Six individual electric circuits with four sockets each in the back. (E) Cooling cabinets on anti-vibration mats (asterisk). (F) The air handling units of the forced air-cooling devices on spring feet anti vibration sockets (double asterisk). (G) Image taken on a STED microscope (Leica STED) done with highest zoom settings (zoom 40 \times) showing reflection on a gold bead from the excitation laser spot (647 nm, in green) and depletion donut (775 nm, in red). The image demonstrates that vibrations are below the detection limit. Note that the anti-vibration table was not inflated. [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com/doi/10.1002/cyto.a.24795)]

threshold of 12.5 $\mu\text{m/s}$ (Supplementary Figure 3) under all air conditioner operating settings. The mean effective (RMS) vibration velocity of microscope room floors was $3.8 \pm 2.2 \mu\text{m/s}$ without air-conditioning and $5.9 \pm 2.5 \mu\text{m/s}$ with maximal air-conditioning. In all microscope rooms the vertical vibration axis showed the largest effective vibration velocity (Supplementary Figure 3).

Due to our different efforts to minimize vibration at the microscopes, we achieved a remarkable low level of vibration. This could be proven for example on our stimulated emission depletion (STED) super-resolution microscope. Images taken on the STED microscope show no vibration artifacts. Even if highest zoom settings are applied and the antivibration table has not yet been inflated, no vibration artifacts are visible in images of reflection on a gold bead (Figure 6G).

2.4 | What can be done if an existing laboratory is converted to an SRL?

Most of the topics discussed above can also be addressed in existing laboratories. Sometimes, major refurbishment is needed to meet the minimum requirements for SRL environmental conditions.

In a light microscope facility two issues require most attention—temperature and vibration. To minimize vibration, spring sockets, anti-vibration mats, and anti-vibration tables may be installed later on as well. The 19-inch rack solution described above may be used if vibration of devices associated with the microscope causes artifacts. Slamming doors can cause vibration in walls, which creates air vibrations and can shake shelves and benchtops built into the wall; a door closer which prevents slamming and will be beneficial for microscope and cell sorter labs.

To maintain stable room temperature, it is advisable to pay attention to the air condition system and its feedback regulation. Often, feedback regulation or position of the thermostat sensor, as described above, can be optimized. In addition, in many laboratory buildings, drywall can be modified rather easily to create windows and cable openings so that heat-producing devices can be placed in neighboring spaces. Local heat extraction devices can be built and connected to the air ventilation system of the building (Supplementary Figure 4). Some devices such as laser racks often have already an outlet, which can be connected to the air extraction. We have seen this solution in many different SRLs, but it is not always as effective as expected. It is recommended to have not a

tight connection, but rather leave some opening between the rack and the tubing to prevent overheating in the rack in case of a ventilation failure.

In a room with heavy heat load, air-conditioning can be retrofitted or upgraded. It is advisable to select an air conditioner with greater capacity than theoretically needed. An example from another SRL (in the Max Planck Institute for Biology of Ageing, Cologne, Germany) is one small pre-existing lab space with only 2 kW cooling capacity that was equipped with two high-end flow cytometry cell sorters. During operation, the temperature was constantly rising (Supplementary Figure 5). On average, the room temperature differed from set temperature about 1°C ($0.9^{\circ}\text{C} \pm 1.1^{\circ}\text{C}$, data from Supplementary Figure 5). Maximal difference from set temperature was 4°C . As an initial temperature stabilization measure, a mobile cooling device with 3.2 kW cooling capacity was added, but the cooling capacity was still insufficient. The retrofitting of forced-air cooling with a capacity of 7 kW enabled us to remove the mobile cooling device and maintain the temperature range required for the instruments (Supplementary Figure 5). On average, the room temperature differed from set temperature by less than 0.2°C ($0.1^{\circ}\text{C} \pm 0.2^{\circ}\text{C}$, data from Supplementary Figure 5). Maximal difference from set temperature was 0.6°C . The downside of this solution is a pronounced cold draft which negatively affects working conditions of the lab workers. The blown in air temperature measured at the outlet of the cooling device was approx. 14°C . In addition, cold draft is a common source of movement artifacts at high-end microscopes. In the above-described situation, the fully enclosed flow cytometry sorters operated in this room did not show any negative impact.

3 | DISCUSSION

Our data demonstrates that sophisticated air conditioning concepts are available to achieve the high level of temperature stability required for high-end equipment in SRLs. Often, standard laboratory air-condition concepts are insufficient and need to be upgraded or retrofitted if high temperature stability is required. In such a scenario, the common practice of separating large rooms with curtains to avoid light pollution needs to be carefully planned. If the curtains affect the airflow within the room, particularly if the curtains separate the supply and exhaust air, maintaining the highest temperature stability in all sections of the room becomes much more difficult, if not impossible. In our experience, light pollution can be avoided with black, light-tight incubation chambers or small curtain solutions around the microscope stage. If the highest temperature stability specified in the room requirements of the most demanding commercial microscope setups have to be met, a concept needs to be developed during the planning phase of a new building. One instrumentation per room controlled by one forced-air cooling system should provide the most stable solution. However, this requires a considerable amount of space and budget. The two solutions we described (multiple microscope setups per room controlled by one forced air-cooling system or one microscope setup per room with three neighboring rooms controlled

by one forced-air cooling system) provide a reasonable compromise with acceptable performance. Even with a good concept a temperature stability of 0.5°C during 1 h or 12 h may need additional strategies such as local heat extraction and limitation of further usage in the room during sensitive experiments. Furthermore, the positions of the temperature sensors in the room have a significant impact on the results of the measurements especially if a precision well below 1°C has been specified for acceptable performance. We propose that the SRL community should make an effort to develop and agree upon measurement protocols with the instrument vendors. Only such protocols will enable us to generate a common understanding if a laboratory environment allows for the best performance of a high-end instrument.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

ORCID

Christian Kukat  <https://orcid.org/0000-0003-1508-0229>

Hans Fried  <https://orcid.org/0000-0001-7557-1199>

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SUPPORTING INFORMATION

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