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Editorial

System Concepts for Robots in Life Science Applications

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For a long time, robot-based automation solutions have found their way into industrial production and manufacturing. The field of industrial robots developed rapidly over the past few decades. The goals of automation using robots are to increase productivity, to reduce production costs and to improve product quality. In addition, people should be relieved of repetitive and ergonomically unhealthy activities or even protected from situations that are dangerous to humans. Although all of these goals and motivations can also be applied to life sciences laboratories, the level of automation in this area has so far been low. Applications in the pharmaceutical industry, especially in the area of drug development, are an exception. Drug discovery and development have been major drivers of developments in laboratory automation since the 1990s. Classic analytical or chemical laboratories (e.g., in quality control, food analysis or environmental monitoring), on the other hand, have so far been largely characterized by manual processes. Analytical measurement systems already have a high degree of automation. On the other hand, sample preparation procedures required prior to chemical-analytical measurement are usually only partially automated. Fully automated solutions are rare and are more likely to be found in large laboratories (such as medical diagnostics laboratories). Smaller laboratories and academic institutions only have a low degree of automation, which is due in particular to the high investment costs, the complex programming of the systems, and the frequently changing sample and application types.

The increasing financial pressure, increasing number of samples due to official requirements or epidemic/pandemic situations, as well as a further increasing shortage of skilled workers also increase the need for automation of laboratory processes for classic laboratories in the life sciences. The choice of suitable automation solutions depends on the type of laboratory, the type and number of samples to be processed, and the structure of the underlying sample preparation processes.

By definition, robots are "reprogrammable, multifunctional manipulators designed to move material, parts, tools or specialized devices through variable programmed motions for the performance of a variety of tasks" [1]. They consist of different joints and arm links that, together, form a kinematic chain. Depending on the number of joints, different degrees of freedom are possible. Robots are available in different configurations. Linear robots (also called Cartesian robots) only have translational joints and consist of several interconnected linear drive systems (TTT). They have three degrees of freedom and a positioning accuracy that remains constant over the entire work area. They are used extensively in laboratory automation, especially in liquid handling systems. Cylindrical robots have one rotary and two translational joints (RTT). They are characterized by a relatively large range (depending on the length of the translational axis) as well as a high rotational speed and have 3–4 degrees of freedom. A typical representative is the Zymate (Zymark, Hopkinton, MA, USA), which was one of the first robots in the field of laboratory automation. A configuration with two rotary and one translational joint (RRT) is called a horizontal articulated arm robot. These robots can move very quickly and have a cylindrical design. They are also known as SCARA (Selective Compliance Assembly Robot) robots. Typical representatives with four DOFs are the Epson Spider and the systems of the SCARA-T

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series (Epson, Meerbusch, Germany). Vertical swivel arm robots (articulated robots) only have rotary joints, enable complex paths to be traveled and are extremely flexible. They have six degrees of freedom and are widely used in laboratory automation. Which robotic configuration is used depends heavily on the particular application. The most important parameters include the accuracy required at the operating point, the maximum possible payload, the cycle time for the processes, and the range and the required number of degrees of freedom. Since the amount of programming, complexity and susceptibility to errors as well as the costs increase with an increasing number of degrees of freedom, robots used should have only the required degrees of freedom.

To carry out special activities such as gripping, suitable end effectors are required, which are installed at the end of the robot arm. They have to be adapted to the respective requirements. If, for example, vessels of very different sizes and masses are to be transported in a system, it may be necessary to change the grippers in the process sequence.

Robots have long been used in many industrial applications. Classic industrial robots are characterized by high payloads that are not required in normal everyday laboratory work. They are usually associated with high costs and, due to the speed and resulting forces, require safety devices such as enclosures or light curtains. This requires additional space and makes it difficult to access automation systems. A new class of robots has increasingly been developed in recent years; cobots (collaborative robots) are lightweight robots that do not work separately from humans but rather work together with humans [2]. The name "cobot" is a bit misleading, as there are rarely cases of real collaboration between humans and robots in laboratory operations. Coexistence is more common; here, humans and robots do not have a common working space but work in close proximity without a protective space. Cooperation is achieved when humans and robots share the work space but work at different times.

Due to a lighter construction, a construction without corners and edges, as well as lower operating speeds, collisions between humans and robots lead to fewer injuries compared with industrial robots. In addition, they have additional safety precautions that can, among other things, detect approaching people and then stop the systems from operating. Some systems also have touch-sensitive surfaces that can even detect slight collisions. Current versions of the ISO 10218 Part 1/2 and ISO/TS 15066 standards also define the safety requirements for collaborative robots [3–5]. The payload of cobots is usually limited and is typically in the range of up to 10 kg. The speed is lowered to a max of 250 mm/s compared with industrial robots. Thus, safety precautions such as enclosures and light barriers are not required. In addition, the compact structure and size requires less space.

Cobots are offered by numerous manufacturers worldwide. The most important players in this market segment include ABB (Zurich, Switzerland), Denso (Kariya, Japan), Doosan Robotics (Suwon, Korea), Fanuc (Oshino, Japan), Franka Emika (Munich, Germany), Kassow Robots (Kastrup, Denmark), Kuka (Augsburg, Germany), Neura Robotics (Metzingen, Germany), Omron (Kyoto, Japan), Stäubli (Pfäffikon, Switzerland) and Universal Robots (Odense, Denmark).

Stationary robots are permanently installed and can only work in a geometrically limited work area. The size and shape of the work area depend on the respective robot type. Mobile robots, on the other hand, move in a (theoretically) unlimited workspace that can be characterized by changing environmental conditions. In contrast to stationary robotics, the working and collision areas of a mobile robot are not precisely defined. The work space can be very large; it is also subject to constant changes. The term "mobile robot" describes a robot that can move freely in an unrestricted space. Various mobile robot systems are currently available on the market including the KMR iiwa (Kuka, Augsburg, Germany), the humanoid platforms Talos and REEM-C, as well as wheel-driven platforms with different levels of equipment (PAL Robotics, Barcelona, Spain) or the proAnt platform (ASTI Mobile Robotics GmbH, Berlin, Germany). Other providers are Omron Industrial

Automation (Kyoto, Japan), Fetch Robotics (San Jose, CA, USA), Neobotix (Heilbronn, Germany), Robotnik (Barcelona, Spain) and DrRobot (Richmond Hill, ON, Canada).

Different system concepts are conceivable for the use of robots in life science applications. The decision to use a particular system depends on a large number of factors. The most important factor is the type of processes to be automated. A precise analysis of the individual sub-steps of an overall process is required here. If only simple liquid handling steps and no special requirements regarding the process conditions are required, classical liquid handling systems in microtiter plate formats can be used. Feeding the samples onto microtiter plates is not possible for all applications. In medical-diagnostic applications in particular, it is necessary to handle individual samples in order to avoid mix-ups and contamination of the patient samples. Another important factor to consider for automation is the amount of sample to be processed. The vessel sizes as well as the volumes to be handled in the process vary depending on the amount of sample. This has a direct impact on the space requirements of an automation system. Another crucial question is the flexibility of the automation solution. Proprietary solutions that are designed and implemented for a desired application are usually inexpensive and highly effective in processing. The lack of flexibility with respect to the application or the process sequences has a disadvantageous effect. This results either in high costs for the reconfiguration of the system or the decision to shut down the system. In the life sciences sector, in contrast to classic industrial applications, this is usually not useful due to the frequently changing application requirements. Flexible systems that can be used for different processes are more cost-intensive than proprietary solutions. In particular, higher costs for the control software must be taken into account here, since a high degree of flexibility is required. If components of the automation systems are also to be used for other applications (e.g., use of a high-performance mass spectrometer both in an automated environment and in manual mode), higher-level workflow management systems are also required. Further influencing factors include the situation within the room and the financial resources available for the implementation of the automation project. These are often limited, especially in SME laboratories. In addition, the existing spatial capacities must be considered for life science laboratories; funding for the construction of completely new buildings is rarely available.

Liquid handling systems are among the classic robotic solutions used in life science laboratories. They consist of Cartesian robots, which generally realize the liquid transfer between different vessels. The uniform format of the microtiter plate provides the possibility of automating the process steps as well as parallel processing of the samples. This form of sample processing has established and proven itself particularly in the field of drug development. Simple liquid handling systems can be expanded to workstations with additional modules. These often include not only heaters and shakers but also incubators, centrifuges or optical readers. The systems are equipped with additional grippers for transporting the samples. Numerous specialized workstations are available for specific applications.

If the systems are also used for processing individual samples, the samples should preferably be arranged in microtiter plate format. Depending on the vessel size, 2 to 96 samples can be provided for the systems in the MTP footprint. Systems with a limited number of dispensing channels are usually used for processing individual samples. Dosing heads with a flexible distance between the individual dispensing channels are particularly suitable for optimal adaptation to the vessel sizes.

For more complex applications, automation systems can be designed and implemented with a central robot. Depending on the application, robots with four or more degrees of freedom are preferably used. The central robot is surrounded by a number of other automation devices. In this concept, the robot only has a central transport function. Suitable grippers are required to transport the samples in microtiter plate or single sample format. The intelligence required for processing the samples lies in the integrated subsystems (liquid handler, heater, shaker, sealer, peeler, reader, etc.). This may also require the development of suitable automated systems, e.g., for opening and closing vessels or the filtration of larger sample quantities. Complex robot systems with a central robot were used for the determination of enantiomeric excesses [6], the determination of mercury in wood samples [7], the determination of elemental compositions of incrustations in clogged biliary endoprostheses [8] and arthrosis research [9].

In the aforementioned variant of a complex robot-based system, the robot only serves as a system integrator but is not involved in the direct manipulation of the samples. The special systems required such as liquid handler, capper, heater, shaker, etc. are often very expensive. In addition, the processes cannot generally be automated 1:1, i.e., changes in the process flows are required in the course of automation. Particularly, in highly regulated areas, this leads to the need for costly and time-consuming re-validations. One possibility for avoiding this and to work with classic laboratory devices that are used in manual operation is the use of dual-arm robots. Due to the high number of degrees of freedom, they can execute process steps and sequences similar to humans. These robots are also central robots in an automation system and realize the transport of samples and labware between different stations. In addition, they can carry out individual process steps such as opening and closing vessels, pipetting, filtering, etc. In complex systems, they also enable the transfer of prepared samples to analytical systems and the operation of manual systems such as ultrasonic baths or similar, which cannot be controlled externally via electrical signals. With this system concept, the use of almost all devices and systems available in the laboratory is possible. However, it is often necessary to design special grippers or adapters. In addition, automated subsystems can of course also be integrated. Dual-arm robot-based systems were used for the analysis of epidermal models [10], the determination of enantiomeric excesses [11] or the determination of cholesterol in biliary endoprosthesis [12].

In concepts with central robots, the number of usable devices depends on the range of the robot. To extend the range, the robots can be mounted on a rail and thus receive a further degree of freedom. This principle was for example used for the ORCA robots (Beckman Coulter, Indianapolis, IN, USA).

The current development in the field of robotics is increasingly leading to more cost-effective systems, so that the costs associated with highly complex systems can be greatly reduced. This also enables completely new system concepts for the automation of life sciences laboratories. It is thus possible to combine different subsystems with one robot. This creates small, locally limited automation stations. Classical devices and systems from the manual laboratory can be used in this approach. The spatial requirements are also low due to the size of the robots used. In connection with mobile robots, the complete automation of life science laboratories is achieved.

Since existing, inexpensive devices are used, the costs of this automation approach are manageable. However, they increase with the number of stations equipped to the robot, which currently still leads to reservations. The high flexibility with regard to the expandability of the overall system is advantageous. New stations can be added, and old stations can be removed or modified. This is a great advantage especially for research laboratories and laboratories with changing task profiles. In connection with mobile robots, the complete automation of life science laboratories is achieved.

The connection of different partially or fully automated as well as fully manual stations is usually still carried out today by human staff. This is associated with a high ergonomic burden for laboratory staff. In addition, manual transport reduces human creative activities. The throughputs in the system are limited and depend on working hours, the number of available staff and their involvement in other activities. Mobile robots can be used to take over transport tasks. In connection with the use of these helpers, numerous questions have to be solved. This includes the position determination and navigation of the mobile robots. Different methods can be used here. Another important point is the transfer of samples and labware between the mobile robot and the target stations. High levels of precision are required here for optimal, fully automatic operation.

Mobile robots move in a common space with humans. Suitable safety precautions are therefore required to prevent the machines from colliding with or affecting people. Different sensory principles can be applied here. In addition to shock sensors that can detect collisions, contactless distance determination can be carried out using infrared or ultrasound-based methods. A precise image of the surroundings of the mobile robot is possible using camera-based methods. In addition to collision detection/avoidance, intelligent systems should also enable the use of suitable algorithms to react to such events and to develop alternative routes. Another point is direct human–robot communication, which in the simplest case can take place via displays or touch displays on the mobile systems. In addition, speech- [13] and gesture-based methods are also being developed [14].

The use of mobile robots in laboratories is still in its infancy and is currently only beginning to development. In the future, further innovative developments are to be expected in this area in particular. The basic usability of a KMR iiwa for automation in a synthesis laboratory was demonstrated by Burger et al. [15]. Extensive investigations into the usability of mobile robots in the laboratory were carried out by Liu et al. [16]. Abdulla et al. described a procedure for multi-floor navigation [17]. Processes based on human–robot interaction could be used successfully for collision avoidance [18], and Neubert et al. reported on the integration of mobile robots into complex workflow management systems [19].

This Special Issue on "Robotics in Life Science Applications" aims to consolidate recent developments and applications of robot-based systems for classical laboratory application. The published papers focused on the development of suitable robotic technologies including robots, navigation, and grasping and placing processes. Another focus is on the application of robotic systems in life science applications.

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References

1. *ANSI/RIA R15.06-1999*; National Robot Safety Standard. Robotics Industries Association: Ann Arbor, MI, USA, 1999.
2. Colgate, J.E.; Peshjin, M.A. Cobots. U.S. Patent 5,952,796, 14 September 1999.
3. *ISO/DIS 10218-1.2:2021*; Robotics—Safety Requirements—Part 1: Industrial Robots. International Organization for Standardization: Geneva, Switzerland, 2021.
4. *ISO 10218-2:2011*; Robots and Robotic Devices—Safety Requirements for Industrial Robots—Part 2: Robot Systems and Integration. International Organization for Standardization: Geneva, Switzerland, 2011.
5. *DIN ISO/TS 15066:2017-04*; DIN SPEC 5306:2017-04 Roboter und Robotikgeräte—Kollaborierende Roboter (ISO/TS 15066:2016). International Organization for Standardization: Geneva, Switzerland, 2017.
6. Fleischer, H.; Thurow, K. *Automation Solutions for Analytical Measurements*; Wiley-VCH: Weinheim, Germany, 2018; pp. 73–89.
7. Vorberg, E.; Fleischer, H. A Highly Flexible, Automated System providing Reliable Sample Preparation in Element-und Structure-Specific Measurements. *J. Lab. Autom.* **2016**, *21*, 671–681. [CrossRef] [PubMed]
8. Fleischer, H.; Ramani, K.; Blitti, K.; Roddelkopf, T.; Warkentin, M.; Behrend, D.; Thurow, K. Flexible Automation System for Determination of Elemental Composition of Incrustations in Clogged Biliary Endoprosteses Using ICP-MS. *SLAS Technol.* **2018**, *23*, 83–96. [CrossRef] [PubMed]
9. Fleischer, R.; Roddelkopf, T. Semi-Automated Determination of Heavy Metals in Autopsy Tissue Using Robot-assisted Sample Preparation and ICP-MS. *Molecules* **2021**, *26*, 3820. [CrossRef] [PubMed]
10. Schmidt, F.F.; Schwarz, T. Applicability of a Dual-Arm Robotic System for Automated Downstream Analysis of Epidermal Models. *Appl. In Vitro Toxicol.* **2016**, *2*, 118–125. [CrossRef]
11. Chu, X.; Klos, M.; Thurow, K. Efficient application of dual-arm robots in analytical measurements using motion frames. In Proceedings of the 2018 IEEE International Instrumentation and Measurement Technology Conference (I2MTC), Houston, TX, USA, 14–17 May 2018.
12. Fleischer, H.; Drews, R.R. Application of a Dual-Arm Robot in Complex Sample Preparation and Measurement Processes. *J. Lab. Autom.* **2016**, *21*, 671–681. [CrossRef] [PubMed]
13. Deuerlein, C.; Langer, M.; Seßner, J.; Heß, P.; Franke, J. Human-robot-interaction using cloud-based speech recognition systems. *Procedia CIRP* **2021**, *97*, 130–135. [CrossRef]
14. Nuzzi, C.; Pasinetti, S.; Pagani, R.; Ghidini, S.; Beschi, M.; Coffetti, G.; Sansoni, G. MEGURU: A gesture-based robot program biulder for Meta-Collaborative workstaions. *Robot. Comput. Integr. Manuf.* **2021**, *68*, 102085. [CrossRef]
15. Burger, B.; Maffettone, P.M.; Gusev, V.V.; Aitchison, C.M.; Bai, Y.; Wang, X.; Li, X.; Alston, B.M.; Li, B.; Clowes, R.; et al. A mobile robotic chemist. *Nature* **2020**, *583*, 237–241. [CrossRef] [PubMed]

16. Liu, H.; Stoll, N.; Junginger, S.; Thurow, K. Mobile Robot for Life Science Automation. *J. Adv. Rob. Syst.* **2013**, *10*, 288. [CrossRef]
17. Abdulla, A.A.; Liu, H.; Stoll, N.; Thurow, K. A New Robust Method for Mobile Robot Multifloor Navigation in Distributed Life Science Laboratories. *J. Control Sci. Eng.* **2016**, *2016*, 3589395. [CrossRef]
18. Ghandour, M.; Liu, H.; Stoll, N.; Thurow, K. A hybrid collision avoidance system for indoor mobile robots based on human-robot interaction. In Proceedings of the 2016 17th International Conference on Mechatronics—Mechatronika (ME), Prague, Czech Republic, 7–9 December 2016.
19. Neubert, S.; Gu, X.; Göde, B.; Roddelkopf, T.; Fleischer, H.; Stoll, N.; Thurow, K. Workflow management system for the integration of mobile robots in future labs of life sciences. *Chem. Ing. Tech.* **2019**, *91*, 294–304. [CrossRef]