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FLEXIBLE DUAL-ARM ROBOT IN AUTOMATED SAMPLE PREPARATION AND MEASUREMENT PROCESS

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ABSTRACT

The degree of automation in the area of analytical measurements is still low—in contrast to well-automated bioscreening and high-throughput screening applications. Typical analytical measurement processes are very complex and involve transportation, sample preparation including direct manipulation and operation of laboratory devices as well as measurement and data evaluation. A wide variety of vessels and containers is used for chemicals and samples; the processes are often changing and have to be modified frequently. The demand for flexible and adaptable automation solutions is high. Flexibility includes the use of multiple instruments— conventional manual instruments and automation equipment— and an easy system change to a wide variety of applications. Dual-arm robotic systems captivate by their human like structure and the possibility to perform processes in the same way as human laboratory assistants. Especially in highly regulated areas, this property may be a big advantage since existing manual standard procedures can still be used. A dualarm robotic system is presented for fully automated sample preparation and measurement. A new concept for robot motion planning and process generation is introduced to increase the system performance—processing times and flexibility. The motion planning approaches were practically compared by performing a sample preparation process with subsequent determination of the enantiomeric excess of amino acids. The results show a reduction of the processing time of 30.3% with measurement results close to the manual procedure.

I.INTRODUCTION

Laboratory automation is developing rapidly, with parallelly advancing technology stimulating the field. Several robotic systems are commercially available in recent times, which have introduced greater efficiency, standardization, accuracy, safety and quality to laboratory processes. Singlearm robots have been used extensively for life science applications e.g., in bioscreening and drug development. However, dual-arm robots now find their place in laboratory automation and are an emerging trend. They can not only perform transportation, but can also be used for direct manipulation tasks. Dual-arm robots are well suited for laboratory sample preparation procedures using standard equipment and devices, which plays an important role, especially in highly regulated areas. In contrast to classic bioscreening applications, a complex sample preparation is usually performed prior to analytical measurements including extraction, concentration, derivatization, dilution, filtration, shaking, heating or cooling. Toxic and harmful chemicals, reagents and organic solvents are often used. The procedures differ greatly depending on the sample type, the components to be analyzed and the measurement technique. Typical applications include environmental monitoring, drug development, food and beverage control, medical applications, material sciences, and industrial quality control [8]. Dual-arm robots are a promising approach to solve the challenges in automation in the field of analytical measurements. In general, the use of multipurpose dual-arm robots is on the rise in laboratory applications. Dualarm robots have several advantages, including the ability to perform tasks similar to a human operator due to the multiple jointed arms. The two robot arms can be independently operated, in cooperation or synchronously, what enables a wide and flexible motion range [9, 10]. The processing of biochemical specimens typically involves extensive manual work. An initial single arm system was further improved by the implementation of two synchronously operated robotic arms to demonstrate the screening of samples for enzymatic activity [11, 12]. Humanlike dual-arm robots are typically used in assembly applications [13-15]. There is an increasing trend for applying these robots in laboratory processes. A dual-arm robot of the SDA series (Yaskawa, Kitakyūshū, Japan) was integrated into an automation system for preparing anti-cancer dosages [16]. Another system based on the SDA10 dual-arm robot was developed for automated downstream analysis of epidermal models [17]. All of these application examples have a limited flexibility within a pre-defined application and processing area. In contrast, analytical measurements require highly flexible automation systems with a usability for different applications. Therefore, the robotic process generation and motion planning have to be designed independent of a special application to reach a maximum of flexibility.

II.LITERATURE REVIEW

T. Chapman, "Lab automation and robotics: Automation on the move," Nature, vol. 421, no. 6923, pp. 661, 663, 665-666, 2003.

Since clinical laboratories began using robotics in the early 1980s to manage their thousands of samples a day, automated systems have become commonplace. By rapidly and tirelessly performing processes that would have been done manually — from sample storage and retrieval to running customized assays — modern automated systems can greatly increase the throughput of a laboratory, free up researchers from repetitive tasks, and monitor and manage the raw data produced.

Automation is now increasingly common in agricultural, food and environmental analytical labs, but it is the demands of the pharmaceutical industry for high-throughput screening of potential drug candidates (see *Nature* **418**, 453–459; 200210.1038/418453b) that is most influential in driving the technology forward. Researchers now have whole genomes of potential drug targets at their disposal for testing against an array of drug candidates, and high-throughput automation is rapidly becoming a necessity.

"Automation is used in a broad range of approaches in pharmaceuticals, from early combinatorial creation to high-throughput screening," says Robin Felder, director of the Medical Automation Research Center at

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the University of Virginia in Charlottesville and president of the Association for Laboratory Automation. “The skills of creating a new drug start with synthesizing novel molecules — it used to be one scientist, one molecule, one week. Now, one molecular chemist can turn out 100 good compounds a week.”

Many pharmaceutical and biotechnology companies would be unable to function without high levels of automation. A typical end-user is Cyprotex, based in Macclesfield, UK, which aims to improve the efficiency of drug discovery by using industrial-scale testing and proprietary software to predict how drug candidates will act in the body. The assays that could rule out an otherwise promising drug candidate are for absorption, distribution, metabolism and excretion. To avoid a bottleneck in the drug-discovery process, these assays have to be carried out as rapidly as the drug candidates are identified. “We have automated the assays, which are currently running at 100–200 compounds a week in major pharmaceutical companies, to where we can run 2,000–5,000 compounds a week,” says David Leahy, founder and chief scientific officer at Cyprotex. “We think there's a potential for running, if we pick one assay, say 750,000 compounds a year.”

But this level of automation brought technical challenges. Specialist consultancy The Automation Partnership (TAP) in Royston, UK, worked with Cyprotex to adapt TAP's proprietary BasePlate liquid-handling robots to Cyprotex's particular requirements. Cyprotex also automated many of its analytical instruments to run standardized tests on compounds coming through the high-throughput process.

Cyprotex is now in a position to extend its automated systems to carry out a wider range of important assays. “We think automation gives us a screening capacity that is at least an order of magnitude higher than a typical pharmaceutical company, at a unit cost that is possibly 20-fold less,” says Leahy.

Benchtop automated liquid handling and sample-dispensing systems are now routine in most life-science laboratories. Such systems will become even more ubiquitous with the introduction of a new wave of lower-cost modular devices with much the same functionality as the systems used by big-pharma labs. “The pharma labs have the deepest pockets, but a new generation of automated systems is becoming available that's more the 'Volkswagen' of the market,” says Felder.

Xiril, a young Swiss company founded in Hombrechtikon by a team of specialists in robotic liquid-handling, has a range of pipetting robots that costs about 20–30% less than comparable systems. The Xiril robots are primarily aimed at low-to-medium-throughput operations, particularly for processes that have not yet been automated.

“We believe we can fill a market for liquid-handling processes that are often done manually, even in labs that are highly automated,” says the firm's chief executive Heinz Abplanalp. Xiril has also developed automated systems for magnetic-bead separation.

At the more expensive end of the liquid-handling market, the trend is towards increasing miniaturization. Given the high cost of many reagents used in biomedical experimentation, considerable savings can be made simply by using less. Allegro Technologies, a Dublin-based company spun out of Trinity College, has the proprietary technology to dispense droplets up to 1,000 times smaller than those from standard equipment. The company claims that this could reduce the cost of some experiments sixfold.

Allegro's latest range of pipetting systems uses electromagnetically controlled valves to deliver droplets of 20 microlitres down to 20 nanolitres in volume. The firm has licensed its technology to US instrument manufacturers Gilson of Middleton, Wisconsin, and Beckman Coulter in Fullerton, California, and has also put the pipettes into its own robotic system.

Being able to manipulate tiny volumes of liquid means that entire lab processes can be miniaturized. Using technology developed for the semiconductor industry, chips a few centimetres square can be etched with microscopic channels in which routine preparation procedures and assays can be carried out.

III.EXISTING SYSTEM

In general, robots can be integrated into automation systems in two ways: they can be applied only as transport systems, or the robotic components can directly perform manipulation tasks. For many years, the latter option has been established in the field of industrial automation. The transfer and execution of a manual process using a robotic component is the main task of an industrial automation system. The human arm and hand should be replaced and the human abilities reproduced by using a technical system. Examples can be found in the automotive industry, precision engineering, food processing, heavy mechanical and electromechanical engineering, and medicine

IV.PROPOSED SYSTEM

In contrast to classic bioscreening applications, a complex sample preparation is usually performed prior to analytical measurements including extraction, concentration, derivatization, dilution, filtration, shaking, heating or cooling. Toxic and harmful chemicals, reagents and organic solvents are often used. The procedures differ greatly depending on the sample type, the components to be analyzed and the measurement technique. Typical applications include environmental monitoring, drug development, food and beverage control, medical applications, material sciences, and industrial quality control [8]. Dual-arm robots are a promising approach to solve the challenges in automation in the field of analytical measurements. In general, the use of multipurpose dual-arm robots is on the rise in laboratory applications. Dualarm robots have several advantages, including the ability to perform tasks similar to a human operator due to the multiple jointed arms. The two robot arms can be independently operated, in cooperation or synchronously, what enables a wide and flexible motion range.

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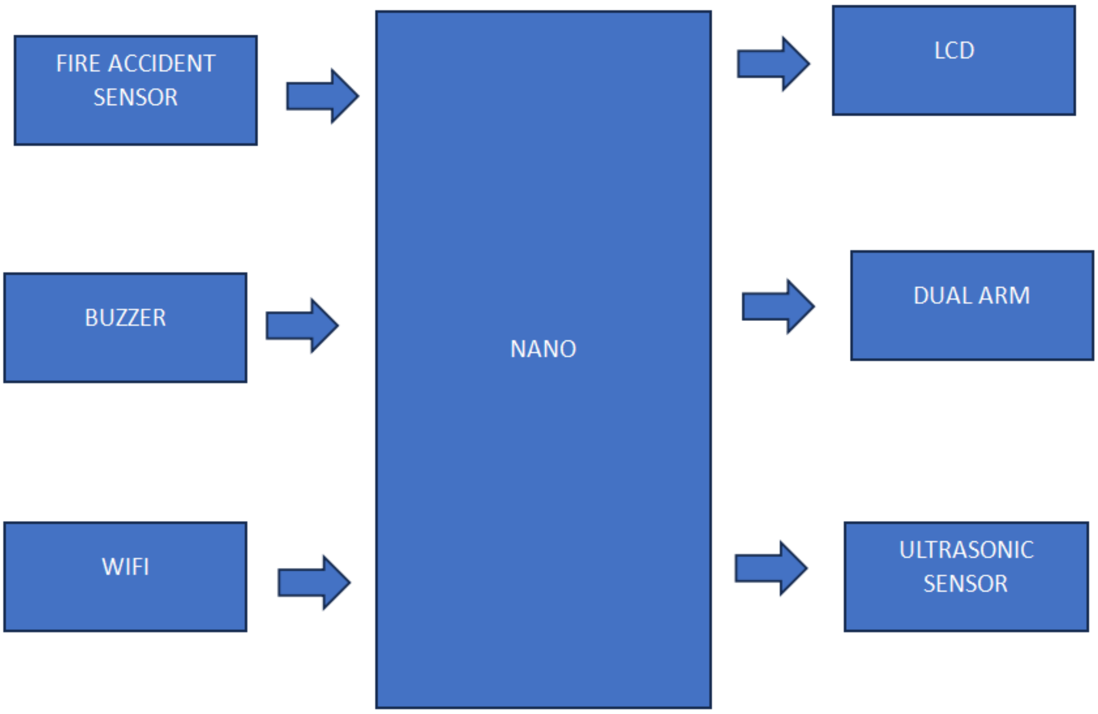
Block diagram



V.CONCLUSION

The dual-arm robot system was successfully improved to decrease processing times and to increase the flexibility for integrating multiple applications using the Motion Planning Approach II in RS-2. The advanced robot system was tested with the measurement process for the determination of the enantiomeric excess of the amino acid proline. The pipetting and transportation times could be reduced by approx. 30%. Multiple sample preparation processes can be flexibly planned and carried out with the advanced Motion Planning Approach II. The system is flexible enough that additional new processes, instruments and labware can be integrated without extensive changes to the existing software system. The dualarm robotic system enables creating fast, robust and flexible automated sample preparation processes in analytical laboratories.

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