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Core Processes in Intelligent Robotic Lab Assistants: Flexible Liquid Handling

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Abstract— **Laboratory automation is a suitable solution to establish higher reproducibility with less manual work and thus higher quality standards in life sciences. To date, mobile robots are capable of performing autonomous pick-and-place tasks in the laboratory, and specialized pipetting machines can be used for sequenced liquid handling. However, the complex and creative process of developing new research protocols requires flexible robotic systems that can perform tasks such as pipetting in more versatile ways. In addition, the correct technique, according to ISO standards, has a great influence on precision and accuracy and therefore on reproducibility. This paper introduces our Intelligent Robotic Lab Assistants in the framework of our holistic, human-like, but standardized paradigm for collaborative lab automation, AI.Laboratory. Our system demonstrates mastery of pipetting following ISO 8655 as a force-sensitive robotic manipulation skill, which is a key component of our taxonomy of cell culture skills and the first steps toward true intelligent robotic laboratory assistants. This intelligent robotic pipetting skill is a versatile tool for general handling of µL-liquids, using only standard laboratory equipment that can be flexibly positioned in the robot's workspace. To demonstrate its pipetting performance, flexible handling of small volumes from 10 µL to 1000 µL was experimentally validated to the ISO 8655 standard, demonstrating superhuman performance that outperformed laymen, human experts, and other commercial and non-commercial robotic pipetting systems.**

I. INTRODUCTION

Standardization is a major challenge in life sciences, especially when it comes to methods or experiments involving cell cultures. Since the first successful cultivation of cells in 1907 [1], process control of cell cultures has changed considerably. By providing optimal conditions for cells, such as highly optimized cell media, controlled temperature and CO_2 gassing, primary or immortalized cell lines proliferate and can be used in many applications, where they often even replace animal experiments. The fight against impurities and contaminants, as well as the dynamic behavior of the cells themselves, have increased the complexity of cell research processes and thus the demands on researchers, making each step of the process increasingly cumbersome, chaotic, dynamic, and sometimes unpredictable [2]. The awareness of quality problems in life science experiments has moved more and more into the focus of the research community and some are already calling it a reproducibility crisis [3]. To overcome these quality problems, the Good Laboratory Practice (GLP) has been in place since 1972 [4] which for cell research is supplemented by the recently updated Good Cell Culture Practice (GCCP) [5]. In addition, on the laboratory equipment side ISO standards guide the reproducibility by definitions for e.g. piston-operated volumetric apparatus in ISO 8655-1 [6]. Although all these regulations

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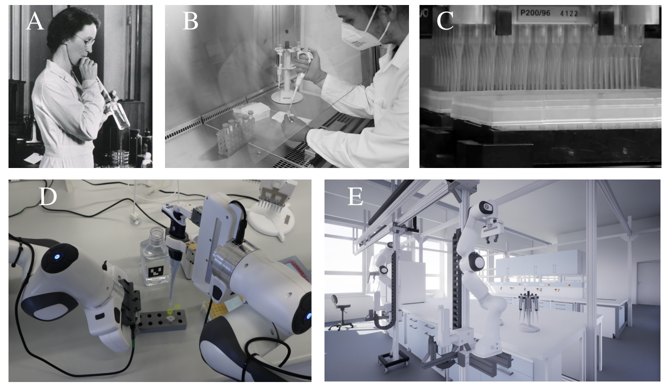

Fig. 1. History of pipetting: A) Cell culture methods of the time 1938 (NIH Image Gallery from Bethesda, Maryland, USA, copy right free via Wikimedia), B) Cell culture methods nowadays, C) Automation approach with Beckman Coulter BioMek FX (NIAID, Bethesda, Maryland, USA, copyright free via Wikimedia), D) Our approach: Intelligent Robotic Lab Assistants and E) its digital Twin.

are well defined their implementation is not always easy in everyday laboratory work. The required unbroken chain of custody for all materials and samples used, is a good example for their difficult implementation. These problems can be solved either by more manpower and even more precise physical work or by digitization and automation. However, the complex and creative process of developing new research protocols requires not only standardization but also a certain degree of process flexibility, e.g., in adjusting process parameters or complete workflows such as the spontaneous use of other labware without the need for time-consuming re-implementation and process optimization. Rigid and unintelligent industry-standard automation is not the solution; rather, intelligent, collaborative robot automation is required to enable an efficient symbiosis between human and machine.

In this paper, we therefore propose our Intelligent Robotic Lab Assistants master pipetting as a force-sensitive robotic manipulation skill following the ISO 8655 standard. The robotic system represents the core elements of our AI.Laboratory concept and it is shown that it is able to perform pipetting precise and flexible to non-standard and non-fixed flasks using common lab equipment. From our point of view, this system is the next step in the evolutionary chain of pipetting as shown in Fig. 1, and represents the first stages on the way to true intelligent robotic laboratory assistants. This work is outlined as follows. Section II defines general domain requirements for intelligent collaborative automation of cell culture processes and compares existing systems with ours under these aspects. In addition, our solution concept AI.Laboratory is presented and compared. Furthermore, the process requirements for flexible liquid handling in the µL-range are defined and evaluated if and how they are fulfilled by the existing systems and ours. The subsequent Section III details our system design and architecture. To validate our

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TABLE I
DOMAIN REQUIREMENTS FULFILLED BY DIFFERENT SYSTEMS.

Domain requirement	[7]	[8], [9]	[10]–[12]	[13]	[14]	Our system
Safety measures in physical HRI		(✓)	(✓)		(✓)	✓
Process monitoring for quality control & reproducibility				✓	✓	✓
Seamless integratability in common laboratory infrastructure and workflows			✓			✓
Ability to work in spatially confined, sterile environments		✓		✓		✓
Remote control for emergency or error correction					(✓)	✓
Scalability up to a decentralized network of systems			✓			✓

system and its pipetting performance, our experiment setup, protocol, and results are presented and discussed in Section IV. Section V concludes our work.

II. PROBLEM STATEMENT AND CONTRIBUTION

A. Related Work

The first fully automated laboratory following the total laboratory automation (TLA) approach was opened by Dr. Masahide Sasaki in Japan in the early 1980s [7]. He developed a complex conveyor and robotic system connecting existing analytical instruments to transfer clinical samples among them, similar to an industry production line. A more general approach was taken in [8] with the Life Science Assistant (LiSA). LiSA connects the equipment with its mobile base and a selective compliant assembly robot arm (SCARA) that performs pick-and-place tasks. Due to the possible human-robot interaction (HRI), the authors were the first tackling the topic of human safety in a robot operated laboratory. Similar to this, [9] proposes a mobile platform with a 6-degrees-of-freedom (6-DoF) robotic arm for pick-and-place tasks. They outsourced the pipetting task to an Andrew+ (Andrew Alliance S.A., Switzerland), performing basic vertical liquid handling in the µL-range. In contrast, [15] presents a fixed two-arm industrial robot with a hip joint that allows the robot to rotate toward surrounding laboratory equipment to perform automated chromatography-mass spectrometry analyses. To ensure human safety, the entire system is housed in a cage. Follow-up publications present and validate dual-arm pipetting with conventional pipettes and modified electric pipettes [10], [16]. In 2017, the same robotic dual-arm system, specialized for laboratory automation, was re-introduced to the scientific community by its manufacturer to conceptualize its potential use in a cloud-based biology-as-a-service approach [11]. The authors in [12] chose a similar approach to [15] by using a two-armed robot for pipetting tasks with 8-channel common pipettes to perform quantitative SARS-CoV-2 serological assays. Following the TLA approach, the StemCellDiscovery system in [13] is an automated robotic laboratory for cell cultivation enclosed in a clean room cabinet and totally separated from the human operator. They use a 6-DoF industrial robot arm mounted on a linear axis to perform pick-and-place tasks, while a Microlab STAR (Hamilton Company, Reno, NV, USA) handles liquid handling. With the "mobile robotic chemist" [14] from 2020, a less closed TLA approach from material chemistry automation was introduced. Similar to [7], they operate specially modified instruments that have been permanently mounted at specific locations. The two liquid delivery systems they use are peristaltic pump systems for delivering volumes in the milliliter range. To operate all instruments, a mobile manipulator is used. A self-optimizing experiment scheduler controls the pick-and-place tasks between instruments, while humans are no longer involved in the entire process. The initial setup of the experiment is an exception, which is sill done by the human in a none collaborative manner.

B. Domain Requirements

The TLA approach enables high reproducibility, fast processing and direct result acquisition with lower personnel and operating costs, due to a high degree of process automation. However, from the experimenter's point of view, it quickly becomes clear that a laboratory robot should empower the experimenter to engage in creative development processes and not hinder him by binding him to a rigid automation protocol. Needed is an intelligent laboratory robot as a helper and tool in the laboratory for e.g. dangerous, difficult, or repetitive tasks, while the experimenter contributes domain knowledge and scientific questions. From this viewpoint, specific domain requirements for intelligent robotic laboratory automation have been identified, which are shown in Table I and discussed in the following subsections. Similar approaches are lumped together under one column.

1) Safety measures in physical HRI: So far, safety in physical HRI is a rarely treated topic in the context of robotic laboratory automation. The existing safe laboratory robots use enclosures [12], [16] or strong velocity restrictions up to standstills if humans get too close to the robot [8], [14]. Although these methods ensure *human safety in terms of physical injuries*, they do not allow any HRI and the *human safety with respect to hazardous substances* as well as the *safety of the robot and thus also that of the experiment* are totally untreated.

2) Process monitoring for quality control & reproducibility: There are again few systems addressing this requirement to some extent. The current implementations are limited to either logs of each cell product, material and disposable item used in the process [13] or simple CCTV camera surveillance of the laboratory and a human "decision maker" watching the stream [14]. Though these methods allow monitoring of some processes in their system, the methods and the level of detail of the recorded data may not be sufficient for some processes. For example, tracking a pipette tip only with cameras becomes difficult due to limited resolution, interference such as reflections and occlusions.

3) Seamless integratability in common laboratory infrastructure and workflows: The high degree of variation in laboratory tasks and the rapid development cycle of new techniques and technologies are often based on standard operating procedures (SOPs) and tools that are common in every laboratory. In order to cope with this demand, robot integratability into existing laboratories is a key requirement. Cautious approaches to this are described in [16], [9], and [12]. They modified common pipettes for their robots, but neither publication describes whether or how the modified tools could still be used by humans. An additional factor for integrability is a certain degree of compactness, mobility, and task flexibility to even navigate in labs designed for humans and to cope in shared workspaces.

TABLE II
PROCESS REQUIREMENTS OF PIPETTING FULFILLED BY DIFFERENT SYSTEMS (C=COMMERCIAL LIQUID HANDLER).

Process requirements: Pipetting	[9](c)	[11], [16]	[12]	[13](c)	Our System
Controlled pipette tip pickup and removal to prevent leaking pipette tips*	✓			✓	✓
Holding the pipette vertically during aspiration*	✓	✓	✓	✓	✓
Appropriate immersion depth of the pipette tip*				✓	✓
Sufficient pre-wetting the pipette tip*	✓			✓	✓
Dispensing against vessel wall*					✓
Stripping the pipette tip on the vessel wall after dispensing*					✓
Pipetting equipment identification and detection	✓				✓
Aspirating from/Dispensing into various non-standard container		✓			✓
Can flexibly perform pipetting operations at different locations		✓			✓

4) Ability to work in spatially confined, sterile environments: Cell cultivation requires sterility. Existing publications ensure this by placing its entire system in a clean room chamber [13] or take advantage of the ability to house its commercial liquid handling system in a biosafety workbench [9]. This leads to large and demanding maintenance and cleaning procedures and fully blocked laboratory instruments. Therefore, human-like sterile working in spatially confined environments is required.

5) Remote control for emergency or error correction: Many lab routines involve handling hazardous substances as well as cell culture protocols that require 24/7 supervision. Robotic laboratory automation is perfectly suitable for such tasks, even though error situations can occur, as shown in [14]. Therefore, an emergency remote control must be available. As the only laboratory robot system [14] has provided this by allowing the reset/restart of the workflow remotely if deemed safe to do so. A fully transparent telepresence interface to a human operator covering real-time visualization, remote control, and full telemanipulation, however, is not mentioned although it would be reasonable.

6) Scalability up to a decentralized network of systems: In order to accelerate future life science research through high-throughput and work parallelization, scalability is our last domain requirement. TLA systems can only be up-scaled with large effort and high costs due to their complexity, while general purpose systems are well suited for this. Nevertheless, to the best of the authors' knowledge, [11] is still the only one to even consider up-scaling to a fleet of connected robots to create a cloud biology service.

C. Solution Paradigm - AI.Laboratory

To meet the aforementioned domain requirements, we present our overall solution paradigm AI.Laboratory; see Fig. 2. This concept is inspired by Industry 4.0 [17] and the AI.Factory[1]. By combining a multitude of our Intelligent Robotic Laboratory Assistants, we aim to create a networked, flexible and powerful tool for life science researchers capable of generating standardized and reproducible high-throughput data. Through the structure in Fig. 2 high-level user commands can be translated into one robotic process chain which is scheduled between the laboratory instruments and Intelligent Robotic Lab Assistants. Those in turn plan and execute every single robot action or motion to ultimately control and understand experimental process. To use the system as a tool, a symbiosis of human and machine must be accomplished, where both work with an aligned and safe physical interaction paradigm. This is to be accomplished by a broad standardized robotic skill set building a versatile laboratory skill taxonomy. The Intelligent Robotic Lab

[1]https://www.mirmi.tum.de/mirmi/research/work/kifabrik/, last opened Jul. 28, 2022

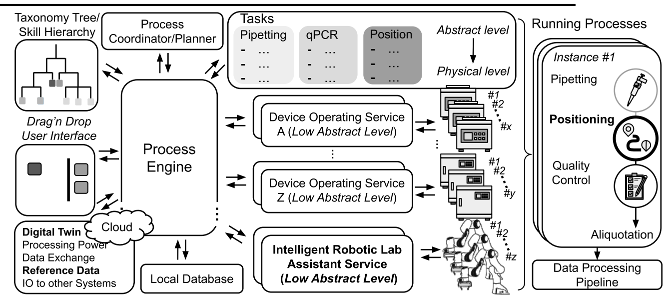

Fig. 2. AI.Laboratory - System Overview.

Assistants as the core element of the AI.Laboratory are presented and evaluated on the pipetting task in this paper. The special process requirements for this are shown in Table II and handled in the next section. Here, similar approaches are lumped together under one column and [7] and [8] are excluded because, to the best of the author's knowledge, no information is available about the liquid handling systems. Also [14] is excluded from this table as its liquid handling system was not designed for pipetting tasks in µL range.

D. Process Requirements: Pipetting

A part of the process requirements are recommendations stated in ISO 8655-6 [18], which are marked with an asterisk in Table II. The other parts are connected directly to the domain requirements.

1) Controlled pipette tip pickup and removal to prevent leaking pipette tips: According to ISO 8655-2 [19], leaky pipette tips are one of the main sources of errors in pipetting. To the best of the authors' knowledge, only Andrew+ [9] , with a spring retainer for the tip box that applies the proper force when picked up, and the Microlab STAR in [13] with its active metal coupling system have solved this problem, which are system-specific solutions. Other systems such as [16] use position control without force feedback, which does not ensure tightness.

2) Holding the pipette vertically during aspiration: This requirement is met by all systems. Most systems solve this requirement by design, as they are vertical pipetting machines, or by complex motion planning such as [16] and [12].

3) Appropriate immersion depth of the pipette tip: Non-compliance with the correct immersion depth and vertical position of the pipette tip may lead to joint measurment error of up to 1 % [18]. Nevertheless, only the Microlab STAR in [13] takes care of this actively with a capacitive or pressure signal detection to measure the liquid level online and adjust to it. This measurement technique is strongly dependent on the physical and chemical properties of the liquid. In [16], the operations are restricted to static immersion depth coupled with their used vessel types and known fluid levels.

4) Sufficient pre-wetting the pipette tip: Not pre-wetting the pipette tip can result in measurement errors of up to

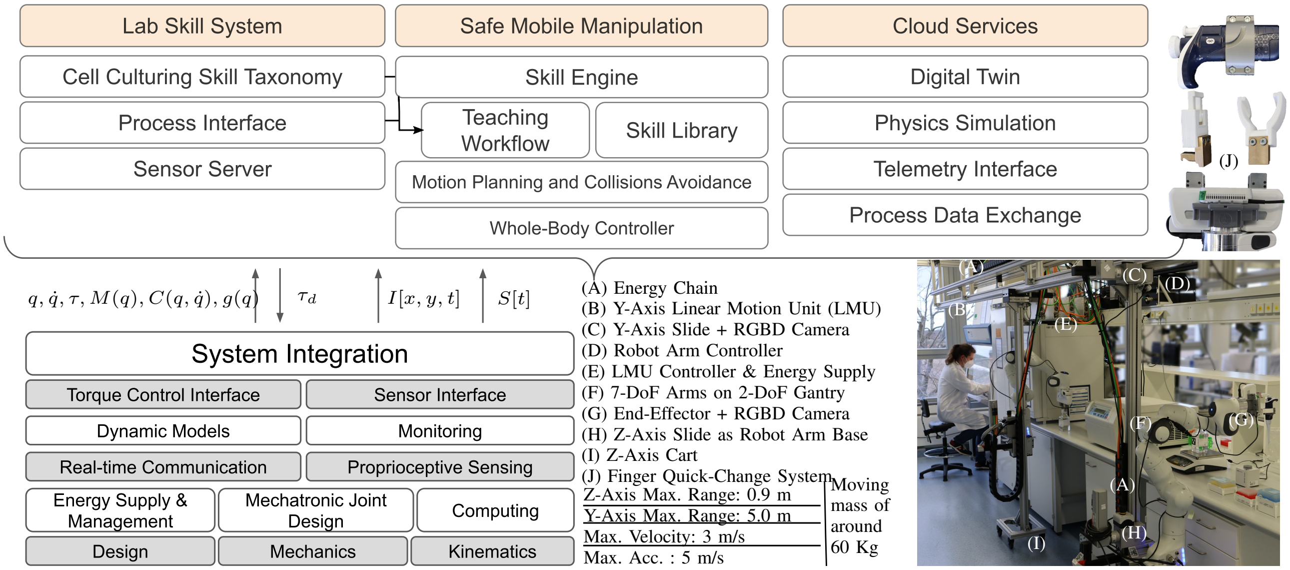

Fig. 3. Intelligent Robotic Lab Assistants architecture. Each Intelligent Robot Lab Assistant is controlled via a torque interface τ_d. The telemetry data such as joint torques τ, positions and velocities q, $\dot{q}$ as well as model parameters of the inertia matrix $M(q)$, the Coriolis matrix $C(q, \dot{q})$ and its gravity vector $g(q)$ of each 9-DoF system are transmitted to various software services via an EtherCAT real-time interface. The video image $I[x, y, t]$ of a large number of cameras and other sensor data $S[t]$ are sent to the sensor server with low latency and further to the other software services.

$2\,\%$ [19]. The Microlab STAR used in [13] and [9]'s system Andrew+ have this feature built in while the other systems do not mention its implementation in their publication.

5) Dispensing against vessel wall and stripping the pipette tip on the vessel wall after dispensing: Vertical pipetting machines cannot meet these process requirements because of their construction. However, neither [16] nor [12] mention this feature. Measurement deviations from the nominal volume of up to $3\,\%$ may occur [18].

6) Pipetting equipment identification and detection: Device identification and recognition, as a domain-related process requirement, enables flexible handling of dynamically changing experimental setups, which may occur frequently in shared human-robot workspaces. Solely [9]'s Andrew+ system has this feature to some degree. The disposables are arranged in boxes whose exact position is determined by scanning its front panel. While this method ensures some flexibility, it is limited by the size of its front desk and can not be rearranged while operation.

7) Aspirating from and dispensing into various non-standard containers: Only [16] show to some degree that their system is capable of pipetting into non-standard vessels. However, their system remains tied to stationary vessel carriers.

8) Can flexibly perform pipetting operations at different locations: To promote shared workspaces and workflow integration, the flexibility to perform pipetting operations in multiple locations, such as directly into an analyzer or sterile in a safety cabinet, is an important requirement. Some approaches use mobile manipulators such as [9] and [14] to add some aspect of flexible integration to their process flows. However, it appears that mobile manipulators at this stage of technology are only capable of performing pick-and-place tasks in the laboratory, requiring a large space to maneuver while also lacking sufficient pose repeatability ($\leq 0.1\,\mathrm{mm}$). With further technological development of mobile manipulators, such as torque control with real-time interfaces in $1\,\mathrm{kHz}$ ranges for safe human-robot interactions, better repeatability of platform position, and stability in terms of vibration reduction for accurate dynamic motions and smaller mechanical structures, this technology is a promising solution for flexible integration into a laboratory environment. A different approach is taken by [11], [16]'s system using a hip joint to spherically extend its working range, which is still quite limited and not sufficient from our perspective.

E. Technical Solution

As the core component of the AI.Laboratory concept, the Intelligent Robotic Lab Assistants are our technical solution to all the above mentioned drawbacks of current robot pipetting approaches. The pipetting process requirements are explicitly addressed in Section III-C.2 and III-B.3, which are embedded in our skill system and mechatronic design. The full system overview is presented in Fig. 3, which is divided into its mechatronic platform and three main pillars: 1) Lab Skill System, 2) Safe Mobile Manipulation, and 3) Cloud Services. To address the enormous complexity and diversity of tasks associated with the use of general laboratory equipment, we present our Lab Skill System as the first pillar of our approach in Section III-A. It is built on a continuously growing taxonomic arrangement of lab skills. Many of the latter are related to the use of a biosafety cabinet to maintain sterile conditions while cell culture processes. To cope with spatially limited working areas, such as biosafety cabinets, and to obtain a sufficiently large working area while maintaining low moving mass and low vibration, we built a horizontally and vertically moving platform that forms a y-z gantry system. The robot manipulator used is the FE robot arm (Franka Emika GmbH, Germany). This mechatronic design is presented and discussed in Section III-B. As second pillar of the Intelligent Robotic Lab Assistants, we propose a safety concept for safe mobile manipulation including *human safety in terms of physical injury*, *human safety in terms of hazardous materials*, and *safety of the robot and, hence, of the experiment* by applying safety measures in design, control, planning, and prediction in Section III-C.1. The third pillar Cloud Services is handled in Section III-D and enables together with the process interface and sensor server from Section III-A, process control and monitoring as well as remote control of our system.

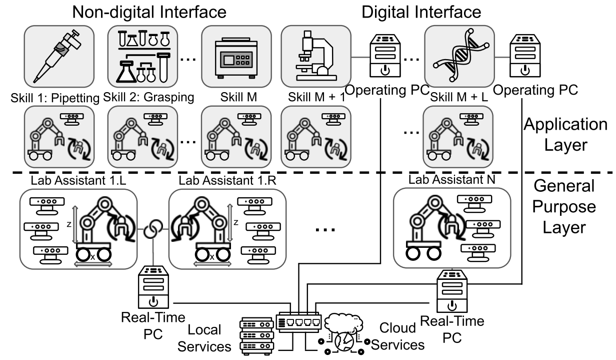

Fig. 4. Lab Skill System for Intelligent Robotic Lab Assistants.

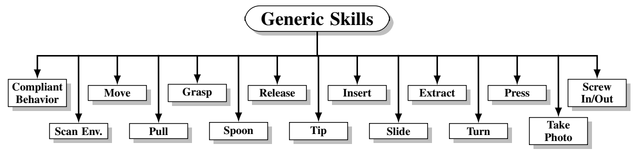

Fig. 5. Low-Level Robotic Manipulation Skills.

III. SYSTEM DESIGN AND ARCHITECTURE

A. Design Philosophy - Lab Skill System

The design philosophy of our system focuses on managing the complexity, diversity, and sheer scale of cell culture tasks. For this purpose, we have developed the Lab Skill System shown in Fig. 4, which is based on a minimal set of low-level force-sensitive manipulation skills (see Fig. 5). Comparing our approach with existing systems like [15]'s motion elements, our focus is on force-sensitive manipulation than non-reactive motion, and thus can capture more modalities of robotic tasks and their complexity. How these lower-level skills are formalized in terms of robot actions is explained in an earlier work [20] for the skill of insertion, which deals with the well-known peg-in-hole problem. These elementary building blocks are arranged and parameterized appropriately for each skill and, if available, connected to the application programming interface (API) of the specific laboratory instrument by using the SiLA communication protocols [21]. On this foundation, we develop our basic and cell-specific laboratory skills, which form our taxonomy of cell culture skills described in Fig. 6. Each skill in the taxonomy is associated with applications/tasks and thus the corresponding tools and robot fingers to use the tool. This, in the grand scheme of things, forms the Application Layer. As an indispensable element, we use a passive Finger Quick-Exchange System for the robotic fingers in our approach so that our Intelligent Robotic Lab Assistants can flexibly and quickly use the various tools required for the respective skill. More details about the Finger Quick-Exchange System are described in Section III-B.2. Together with the robotic system, the sensor and other software services, this forms the General Purpose Layer of our Lab Skill System.

1) Process Interface: The process interface of our system represents the cockpit for the human experimenter and runs as a decentralized local app. Here, all systems can be controlled with real-time telemetry plus low-latency camera feeds and other sensor data. Based on our skill concept, complex processes consisting of parameterized skills or completely new skills can be developed and shared.

2) Local Sensor Services: The sensor server is the heart of our exteroceptive monitoring, operating on local hardware. It has built-in plug-and-play camera service via USB for various brands such as Intel Real-Sense (Intel Corporation,

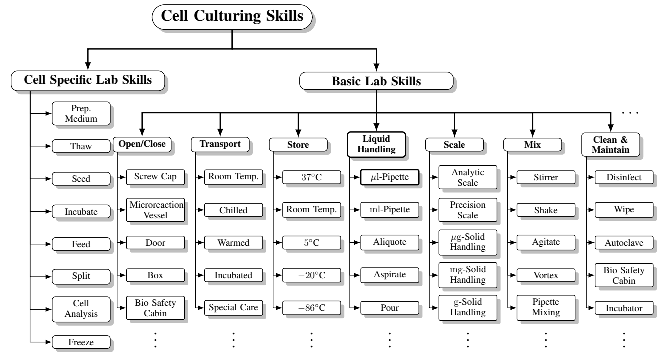

Fig. 6. Excerpt of our Cell Culturing Skill Taxonomy.

USA) or Luxonis OAK-D (Luxonis, USA) and many more or simple User Datagram Protocol (UDP)-based video streaming from any other camera with streaming capability. This includes low-latency camera streaming from the server, camera calibration services and additional integrated sensor readouts like inertial measurement unit (IMU) or depth measurement data. The framework also provides a simple software pipeline to integrate further sensors such as environmental sensors or additional tracking systems. The core service of the sensor server is the integrated computer vision framework with squared fiducial marker (ArUco [22]) for object identification and pose detection or low-latency marker-less human pose estimation. All data from this service is sent with a direct interface to the robotic systems and the process interface.

B. Mechatronic Platform

1) Modular Multi-Arm Gantry Robot: The main mechatronic system of our two Intelligent Robotic Lab Assistants consists of one robot arm each with 7-DoF, a pose repeatability of $< \pm 0.1\,\mathrm{mm}$ (following ISO 9283), and maximal payload of $3\,\mathrm{kg}$ (manufacturer data). Furthermore, it has link-side torque sensing in each joint, providing torque control and fast collision detection for safe operation. The robot base is mounted on a pedestal at the z-axis of the respective y-z gantry system forming a 9-DoF robotic systems. Each robotic system has a Finger Quick-Exchange System mounted at the end effector along with a high-resolution RGBD camera. Further RGBD cameras are mounted at the top of each z-axis pointing towards the workspace and two OAK-D cameras at the side wall of the corridor pointing towards the complete gantry system. The two 9-DoF robot systems share a y-axis and are mounted mirror-inverted so that the bars of the z-axis face each other, allowing manipulations with two arms if required. The y-z gantry system uses two servo motors each with its own control and power supply unit (item Industrietechnik GmbH, Germany). The z-axis of the gantry system is equipped a holding brake to save energy during long manipulation tasks. The y-axis, on the other hand, is a free-running axis that, thanks to its upper suspension and a carriage system at the base, can be moved easily and with low friction for robot teaching purposes or in possible clamping situations. The carriage system is additionally designed to reduce vibrations to enable robust robotic manipulation tasks. The gantry system has position and velocity sensing with a capacitive incremental encoder system and torque estimation over current measurements. Each linear motion unit has a pose repeatability of $0.1\,\mathrm{mm}$ according to the manufacturer. The entire system is embedded in a self-developed C++ multi-robot operating system running Ubuntu 20.04 with a Linux real-time kernel (5.14.0-rt16) on an Intel NUC

9 Extreme Kit-BXNUC9i9QNX (Intel Corporation, USA) PC. Full-body $1\,\mathrm{kHz}$ real-time position, velocity, and torque control is provided utilizing libfranka API and an EtherCAT communication pipeline. A robot operating system (ROS) interface is also integrated for non-real-time communication.

2) Finger Quick-Exchange System: For our Intelligent Robotic Lab Assistants there is no simple gripper solution that allows the handling of all objects or tools relevant to the tasks in question. To enable a rapid switching of grippers suitable for different tasks, we use a Finger Quick-Exchange System with our robot arm. The two parts of the system function like a guided latch bolt and strike system, where the bolt is the robot-mounted part and the strike is tool-mounted. Fig. 3 (J) shows the former with the latch bolt inside the guiding hole and the latter with a fitting pin together with the latch strike at its end. The robot couples the two parts by simply sliding the pin into the hole, while the bolt-strike system locks it in place. To uncouple both parts, the force sensitivity of the robot is exploited. It presses the unlock mechanism against a fixture, which releases the pin, and the finger slides back into the magazine.

3) Pipetting Finger System: The pipetting fingers shown in Fig. 3 (J) have the task of gripping, holding and simultaneously pressing the pipetting button to enable one-handed pipetting. This pipetting finger system consists of two different finger shapes that mimic the human hand when using the pipette. The upper finger controls the electric plunger system of the pipette by pressing a push button at its top. It also serves as a safety lock to prevent losing the gripped pipette by gently clamping it. With this finger, the robot has complete control over the pipetting process and can stop it if necessary, while the pipette can be configured via a Bluetooth protocol. The finger is designed to be compliant through a spring-magnet mechanism to allow rapid change of pipettes while attached to the end effector of the robot. The lower finger is the gripping system for pipettes and functions similarly to the key-lock principle. The lock is a cuff with quarter-circle grooves that is clamped around the pipette. The cuff is designed to be as small as possible and without sharp edges to still allow normal use of the pipette by a human operator. The key is the counterpart to the cuff with matching sliding rails. This system provides mechanical constraints for the gripped pipette in the x-y-z direction and holds it firmly on the key. Gripping or releasing the pipette on the pipette carousel is only possible with a rotary motion around the tool center point (TCP) and with the gripper fully open.

C. Safe Mobile Manipulation - Pipetting

1) Safety Features: A self and object collision avoidance system that controls the posture of the robot arm is embedded in the system. It is realized by a simplified representation of the robotic links, the linear axis, and other obstacles using cylinders and spheres, following the principle of [23]. Close distances between these bodies result in repulsive forces and push the corresponding parts of the robot away. In this way, object and self-collisions can be avoided and robot safety is ensured, which in turn improves the robustness and thus the safety of the experiment process. To comply with the robotic safety standards for HRI [24] the power and force limiting Safe Motion Unit (SMU) [25] is embedded in the control loop. It correlates the maximum safe robot velocity with the moving mass and the shape and direction of the potential collision surface, and ensures human safety in collisions by scaling down the planned velocity if necessary. Nevertheless, the efficiency of the robot remains high because our system has a relatively low mass compared to other mobile robots, and the Intelligent Robotic Lab Assistant decides when to turn off the SMU based on the current position of the human provided by our sensor services. Additional safe torque off modules for the linear axis and a compliant control of the whole system further improve safety and human comfort in HRI. However, potentially the greatest danger to humans in laboratory environments comes from hazardous materials handled by robotic systems working in tandem with humans. To the author's knowledge, this very specific area of robot safety has not been addressed in any standard or publication to date. Therefore, we require the Intelligent Robotic Lab Assistants to have full knowledge of the hazards that the reagents may pose to humans or itself. Based on this, safety strategies must be planned prior to hazardous material handling. Options include acoustic and visual warning signals, immediate interruption of the process, or active blocking of the hazardous area with the robot arm as soon as a human enters the robot's work area.

2) Pipetting Skill: The pipetting skill can be divided into three phases and six individual skill elements.

a) Preparation Phase: This phase involves the selection of the pipette planned in the protocol and the pickup of the pipette tip belonging to the pipette. It is important to identify and recognize the positions of the objects involved, such as the pipette carousel and the pipette tip box, beforehand using ArUco markers. With the help of the measured position and orientation of the carousel, the necessary rotation for a specific pipette can be calculated. This calculation is based on the distribution of the pipettes on the carousel. Each pipette can be assigned an angle to a previously defined position to which the pipette is to be rotated. After the pipette alignment process, the pipette is picked up using a force controlled manipulation strategy. Before the pipette tip pickup, its filling state must be checked so the latter does not happen in an empty slot. An edge detection algorithm is used to match the fill state with the pipette tip positions in the database. The numerically nearest and existing tip is selected. Depending on the pipette, the correct force limits for tightly sealing the tip with the pipette are retrieved from a database determined by previous experiments.

b) Process Phase: In this phase, the liquid to be pipetted is aspirated and then dispensed into the target vessel. As already mentioned in the process requirements, the entry angle and the immersion depth during aspiration are crucial for the accuracy of the process. To estimate the liquid level, the weight of the container of the source liquid is measured during pipetting. With the help of the empty weight data and geometry of the container stored in the database, the liquid level can be estimated. This information is used to ensure an immersion depth of at least $2\,\mathrm{mm}$ when aspirating the liquid. Similar to the pipette box, the position of the target well is referenced in the database via its marker on the labware. After each tip change, prewetting is performed by a tenfold aspiration and dispensing loop in the source liquid container before the actual pipetting process begins. During dispensing, it is important to dispense against the vessel wall in a force-controlled manner and to wipe the tip along the wall after the process is complete in order to also dispense hanging droplets from the tip.

c) Post Process Phase: The used pipette tip is discarded and the pipette is put back on the pipette carousel. To

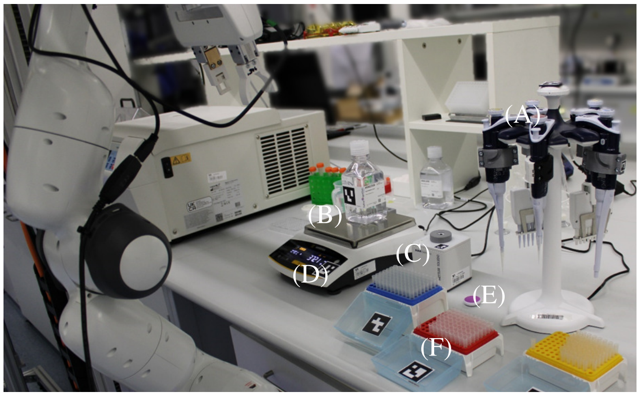

Fig. 7. Experimental setup: (A) electrical Bluetooth pipettes on power carousel, (B) bidistilled water, (C) SmartCheck pipette check device, (D) precision scale, (E) environment sensor, (F) pipette tip boxes.

TABLE III
MEASUREMENT RESULTS WITH ENV. CONDITIONS: $\theta_a = 21.1\,°\mathrm{C}, p_a = 952.2\,\mathrm{hPa}$ AND $h_a = 37.4\,\%$

Model	V_s/µL	System	n	$\overline{V}$/µL	e_s/µL	η_s/%	s_r/µL	CV/%
P10M	10	Robot	36	9.85	-0.15	1.5	0.12	1.2
		Human	3×36	9.87	-0.13	1.3	0.28	2.8
P200M	50	Robot	36	50.04	0.04	0.07	0.12	0.23
		Human	3×36	49.6	-0.4	0.7	0.4	0.8
	100	Robot	36	99.3	-0.7	0.7	0.3	0.3
		Human	3×36	99.1	-0.9	0.9	0.8	0.8
	200	Robot	36	199.2	-0.8	0.4	0.4	0.2
		Human	3×36	198.1	-1.9	1.0	2.3	1.1
P1200M	100	Robot	36	99.9	-0.1	0.1	0.4	0.4
		Human	3×36	99.7	-0.3	0.3	1.2	1.2
	300	Robot	36	299.1	-0.9	0.3	0.6	0.2
		Human	3×36	295.6	-4.4	1.5	4.8	1.6
	1000	Robot	36	997.1	-2.9	0.3	1.3	0.1
		Human	3×36	981	-19	1.9	10.8	1.1

dispose a used pipette tip, the pipette is guided into the waste container and its tip removal button is pressed with the appropriate force against a rod hanging above the waste container. The pipette is stored in the same way as it is picked up in reverse order.

D. Cloud Services

The heart of our cloud services is our digital twin. This is a virtual scale replica of our Intelligent Robotic Lab Assistants embedded in the lab infrastructure. The digital twin is implemented as an Unreal Engine 5 (UE5) server with high-resolution meshes and materials. Its physical backbone is a self-developed Mujoco plugin for UE5 for online multi-body dynamics simulation. In addition, the digital twin has a low-latency UDP-based connection to the telemetry data of our systems to merge with its physical counterpart. With these cloud services, immersive telepresence, transparent process monitoring, and a data recording system to detect system failures are possible. In the further course of this research we will use this infrastructure for process optimization with optimal trajectory planning prior to process execution and online collision avoidance in dynamically changing environmental conditions.

IV. EXPERIMENTAL RESULTS

In the following sections we define our setup, the procedures, and validation methods of our pipetting experiment.

A. Setup and Procedures

The pipetting equipment used consists of three electrical Bluetooth pipettes with maximum volumes of $10\,\mu\mathrm{L}$, $200\,\mu\mathrm{L}$ and $1200\,\mu\mathrm{L}$ PIPETMAN M P10M/P200M/P1200M BT Connected (Gilson, USA). They are stored and charged in a PIPETMAN M Power (Gilson, USA) carousel (A) and controlled via the Pipette Pilot software (Gilson, USA) in standard pipetting mode with the aspiration/dispensation speed of 6 (maximum). Pipette tips are picked up from the tip boxes (F) DIAMOND DL10ST, D200ST and D1200ST, respectively. All process materials were randomly placed in the workspace of the robots before the experiment. If a tool cannot be reached by the robot arm in a suitable way, the linear motion system is used to make this possible. Bidistilled water (B) is transferred to a SmartCheck (Mettler Toledo, Switzerland) analytical scale (C) including an evaporation trap. Temperature, relative humidity and air pressure are measured using a Tempo disc (Blue Maestro, United Kingdom) sensor beacon (E).

B. Quality Control of Robot Performance

We follow the ISO 8655-6 gravimetric reference test method [18] to determine the volumes pipetted with our robotic system and thus measure pipetting quality. The measurement protocol consists of repetitions of transferring different volumes: For the P10M pipette it is $10\,\mu\mathrm{L}$; for P200M it is $50\,\mu\mathrm{L}$, $100\,\mu\mathrm{L}$ and $200\,\mu\mathrm{L}$; and for P1200M it is $100\,\mu\mathrm{L}$, $300\,\mu\mathrm{L}$ and $1000\,\mu\mathrm{L}$. To compare the pipetting performance of robotic system and humans we proceed according to ISO 8655-6 [18]: For each pipetting configuration we calculate the mean volume pipetted $\overline{V}$, its systematic error e_s and its repeatability standard deviation s_r. From the latter two we determine the resulting systematic error in percent η_s (trueness) and the coefficient of variance CV also known as random error or precision.

C. Results

The measurement results for the 7 different pipetting configurations are summarized in Table III. For each configuration, $n = 36$ pipetting procedures were carried out with the robotic system. For comparison, we provide the average values of three non-expert humans that each carried out 36 measurements for the same configurations. We performed more than the recommended 10 measurements to include the possible symptoms of fatigue of the non-expert person. Fig. 8 shows the comparison of the coefficient of variance CV (top) and the systematic error in percent (bottom) between the original values[2] given by the manufacturer of the pipette we used ($n = 10$), the system of Fleischer et al. [10] ($n = 10$), the industrial pipetting system Microlab Star ($n = 10$) (Hamilton[3], USA), the values from a pipetting study with human experts [26] ($n = 10$), and our results. It should be mentioned that the pipetting study with human experts only provided CV-values and that [10] only gives values of $20\,\mu\mathrm{L}$ (shaded) instead of $10\,\mu\mathrm{L}$ and Gilson only gives values of $1200\,\mu\mathrm{L}$ (checkered) instead of $1000\,\mu\mathrm{L}$, which is not an ideal comparison, but only gives a direction here. As can be seen, the Intelligent Robotic Lab Assistant provides more accurate results for all measurements except the plain Gilson pipette values and a minor disadvantage to [10] of the CV at $1000\,\mu\mathrm{L}$. The excellent performance of the robot is due to the pipetting protocol (cf. Section II-D), which the robot can easily follow, but given the small deficits compared to a

[2] https://de.gilson.com/pub/media/docs/2022_LT380069-11%20Pipette%20Specs%20Chart_web.pdf, last opened Jul. 28, 2022

[3] https://assets-robotics.hamiltoncompany.com/TN-1405-02_CO-RE-96-Probe-Head-pipetting-specs_V2.pdf?v=1537460631, last opened Jul. 28, 2022

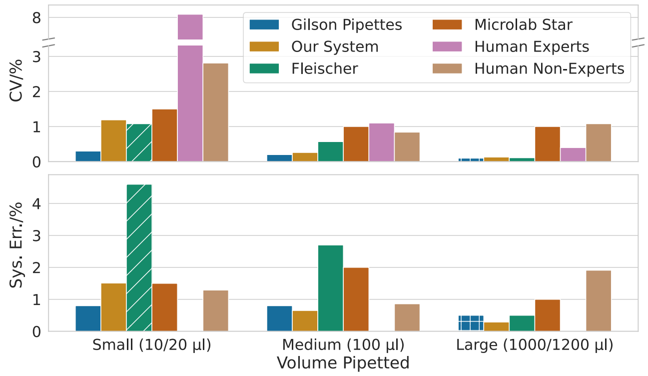

Fig. 8. Comparison of coefficient of variation and the systematic error for different systems and pipetting volumes (shaded: 20 µL, checkered: 1200 µL).

simple Gilson pipette, one can also see that this process can be further optimized.

V. CONCLUSIONS

This paper defines domain requirements for intelligent collaborative automation of cell culture processes and outlines our solution paradigm AI.Laboratory. As the technological platform for this paradigm, we introduce our Intelligent Robotic Lab Assistants. Our unique mechatronic design and extensive software infrastructure, including our Lab Skill System, real-time whole-body control interface, safety features, and cloud services, such as our digital twin system, are presented and discussed. Since we focus on the pipetting task as the first validation application of our system, we first defined process requirements following the pipetting standard ISO 8655 and build our robotic process accordingly. With our experimental results we have shown that our system is able to meet the process requirements by pipetting µL-liquids precisely and flexibly into non-standard and non-fixed vessels using only common laboratory equipment. In follow-up studies, we plan to conduct further experiments to validate the robustness and throughput of our pipetting process in normal but also in more complex pipetting tasks, e.g. pipetting directly into an analyzer, pipetting into microfluidic devices, or general sterile pipetting in a safety cabinet. In addition, further research will include detailed experimental validation of the domain requirements we have defined for our system as we expand the implementation of our robotic lab skills framework for other applications in the laboratory.

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