

Architecture for a Combined Mobile Robot and Human Operator Transportation Solution for the Hierarchical Life Science Automation

S. Neubert¹, T. Roddelkopf², X. Gu², B. Göde¹, S. Junginger¹, N. Stoll¹ and K. Thurow²

¹*Institute of Automation, University of Rostock, Friedrich-Barnewitz-Str. 8, 18119 Rostock, Germany*

²*Center for Life Science Automation (celisca) Friedrich-Barnewitz-Str. 8, 18119 Rostock, Germany*

Keywords: Life Science Automation, Laboratory Execution System, Mobile Robot Integration, Dynamical Scheduling, Human Machine Interaction.

Abstract: Modern laboratories for life sciences often include several different integrated automation systems to increase throughput and quality, to reduce efforts for human operators and to reduce the costs of processes. Typically, the planning and monitoring of methods are prepared and executed directly on local computers of the automation systems. Moreover, a manual replenishing of resources and a manual transfer of samples and labware between interacting automation systems are required in order to ensure end-to-end operations in a 24/7 mode.

This work describes the architecture and the pilot solution of a hierarchical workflow management system (HWMS), which integrates distributed automation systems by combined use of mobile robots and human operators as transportation units. With a graphical process design tool a material flow-oriented diagram can be created, which describes the correlations of distributed subsystems in a complex workflow. The HWMS schedules the workflows and controls the execution autonomously dependent on the planned process diagrams. Two front-end components located on the process control layer simplify the integration and support the control of the required subsystems. With smart device communications human operators can be integrated in the workflow for transportation and assistance tasks as a necessary alternative to the robots.

1 INTRODUCTION

The 24/7 operation and the integration of automated workstations are basic requirements in life science processes to increase the throughput and the processing quality and to reduce the effort of monotonous processing steps and the risk of potentially hazardous setups for laboratory assistants (Patel et al., 2014; Lam et al. 2012).

A further reason to invest into automation in life science laboratories is cost reduction (Cork and Sugawara, 2002). However, currently only single devices, automated workstations (e.g. liquid handlers including peripheral devices) and integrated automation systems (workstations, which include one or more local transportation robots) are commonly found in life science automation, as for example seen in (Andersen et al., 2012; Liu et al., 2010; Sutherland et al., 2014). Especially larger systems consisting of distributed automated devices, workstations and integrated automation systems – here called *automation systems* – often provide

unresolved challenges regarding their complete automation. The obvious reason is the non-existent sample transportation control between the automation systems and a required higher level control system (complex automation system) for the synchronization of all sub processes.

For preparation matters such as manual supply of resources or a manual transport, especially in systems with frequently changing tasks, the assistance of a human operator is still essential. A continuous progress of several running life-science processes requires an appropriate involvement of the operators. The operators must always be informed about all necessary manual steps required to keep the process chain running.

This article describes a development to increase the level of automation in life sciences by setting up a hierarchical control solution combined with mobile robots and mobile devices in the instrument layer. In modern laboratory automation systems, these components enable higher system integration and a higher degree of effectiveness by reducing the

waiting time between distributed sub processes. An additional effect is the transition from automation as part of a manual chain to manual steps as an integral part of full automation in life science processes. This transition is necessary due to the fact that non-continuous interaction between human and machine processes builds a bottleneck in the workflow, especially when processes are executed parallel by robots and involved humans. Thus, the interconnection of robot- and human-controlled sub processes needs to be managed for a continuous effective workflow.

Personal digital equipment, such as smartphones and tablet PCs, are often used in laboratories to support the human operators. They allow to access, e.g. laboratory information management systems (LIMS) or electronic laboratory notebooks (ELN) (Göde et al., 2007) or to use the wide range of mobile device applications to calculate, to monitor or to analyze data (de Souza, 2010). Mobile device interfaces can also be found in special devices such as the Optima XPN centrifuge of Beckman Coulter, which can be monitored and controlled via an iOS app (Muenz, 2012). Concerning more complex applications smartphones and tablet PCs are a comparatively new trend in life science laboratories.

2 ARCHITECTURE

The architecture of the developed systems follows the typical automation structure of laboratory automation as shown in fig. 1. The highest level in this architecture is the **hierarchical workflow management system (HWMS)**. It is located in the workflow control layer of the structured automation. The name HWMS results from its position and dependency to the complex hierarchical structured sub-architecture below and it is classified as a specialized manufacturing execution system (MES), a so called laboratory execution system (LES). In section III the HWMS is described in detail.

In the process control layer a general differentiation is made between transportation and automation systems' tasks, which is correspondingly based on the two subsystems at the front end as follows:

- The **transportation and assistance control system (TACS)** permits the adaption and distribution of transportation and assistance orders from the HWMS and ensures their routing to the transportation resources (pool of mobile robots or alternative human operators).

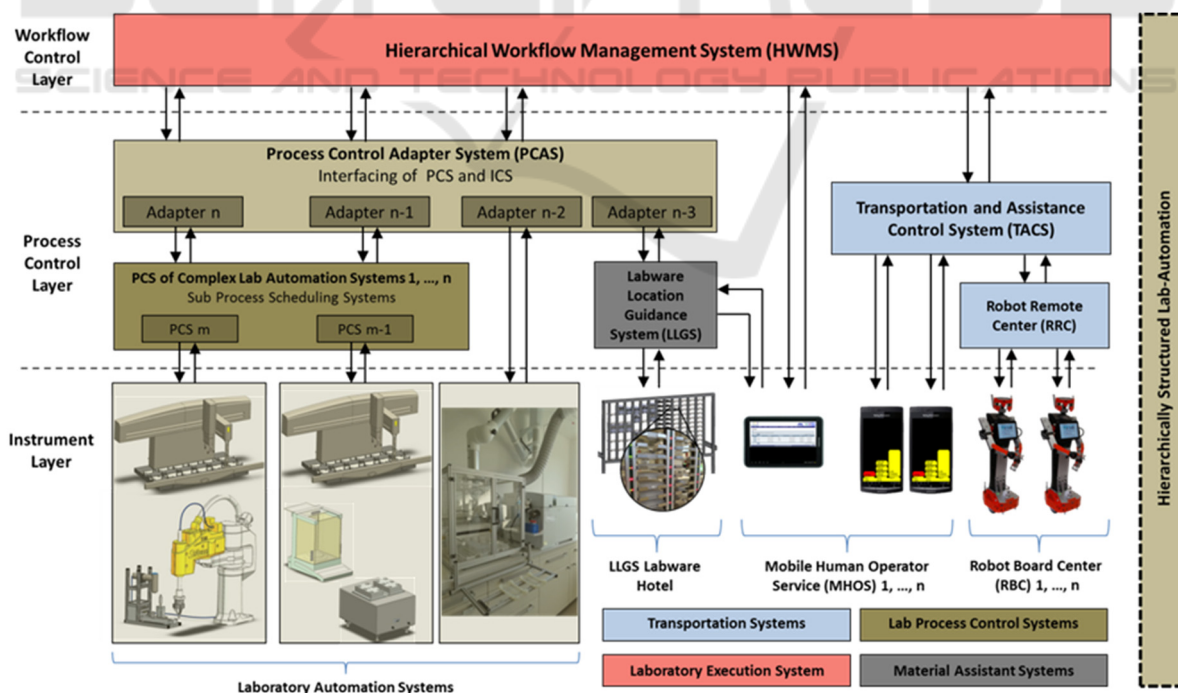


Figure. 1: Architecture of the total system in the hierarchical structured laboratory automation.

- The **process control adapter system (PCAS)** consists of several instances, which interact individually between the HWMS and the more or less integrated automation systems, controlled by process control systems (PCS) / scheduling systems or vendor specific instrument control systems (ICS).

Both systems adapt, execute and control the required sub processes dependent on the orders of the HWMS and return process-status information. The systems are integrated by web-services-oriented interfaces, which allow decoupled accesses from the superordinated control systems. To relieve the HWMS those systems have a sufficient application-oriented intelligence to make own decisions for the handling of sub processes

Dependent on the specificity of the order, the TACS is able to dynamically schedule the transportation and assistance orders for a planned process between the available transport resources. An internal list containing performance information of all different transport resources allows an automated selection of the best fitting mobile robot or human operator. Each transportation resource only receives one order at the same time, whilst the orders can be more complex. For example, this can be a labware transportation order of 20 different objects (identified by barcode) or a list of assistance orders to prepare and / or to monitor an automation system (especially for human operators).

The group of transport resources is differentiated into the following two options:

- The **robot board center (RBC)** executes the transportation of labware via mobile robots (H20 Robot – Dr Robot Inc.). This unit includes the navigation, the *pick and place* process, door control procedures and the active collision avoidance. The RBC requires the superordinate robot remote center (RRC) in the process control layer as central control instance for all mobile robots. It has the responsibility for path planning, central status information collection and decision making regarding the most qualified robot, which is selected by available power status and the optimal current start position (Liu et al., 2012 & 2012 & 2013).
- The **mobile human operator service (MHOS)** partly functions as a manual backup to the RBC. However, by integration of human operators, such as laboratory assistants, MHOS is additionally able to provide orders for manual or special tasks that cannot be performed by automated systems. The MHOS is based on

mobile devices such as smartphones and tablet PCs, which communicate directly with the TACS.

The PCAS allows the connection to the involved PCS to initiate runs of the automation systems for complex laboratory tasks, including sample preparation, dosage, analytical measurements, or evaluation processes. General used PCS are complex scheduling software systems such as SAMI® EX, VWorks®, Microlab® VENUS or Clarity (Delaney et al., 2013). Parallel to the automation systems with PCS properties, single devices are required, which can be integrated via the specified manufacturer software (ICS) located in the instruments layer. Therefore, the PCAS allows the direct access to the instrument layer of the structured laboratory automation and enables a higher integration flexibility for the resource variety of the workflow control layer.

A labware location guidance service (LLGS), triggered by the PCAS, organizes the control of special indicator systems to simplify human-machine interactions. This refers for example to complex labware storage hotels (400 positions) with dynamic visual information that indicates the status of every position slot to the human operator in current and future processes of an automation line.

3 HIERARCHICAL WORKFLOW MANAGEMENT SYSTEM

LES, like the HWMS, encapsulate complex automation processes and ensure a stronger decoupling of potentially superordinated control systems (as e.g. the Business Process Management System - BPMS) and the required automation environment. Therefore, the HWMS includes the complete adaption of the heterogeneous automation systems' environments and simplifies the integration of more real-time sensitive sub processes for the end-to-end process automation (Neubert et al., 2016).

The developed HWMS includes a relational recursive database, which manages workflow process definitions, workflow instances, locations, labware, automation systems, mobile devices and mobile robots. A web-portal allows the users and system administrators to manage these environmental parameters, which is most frequently required for the definition of new labware and for printing the appropriate barcodes. Based on these parameters an

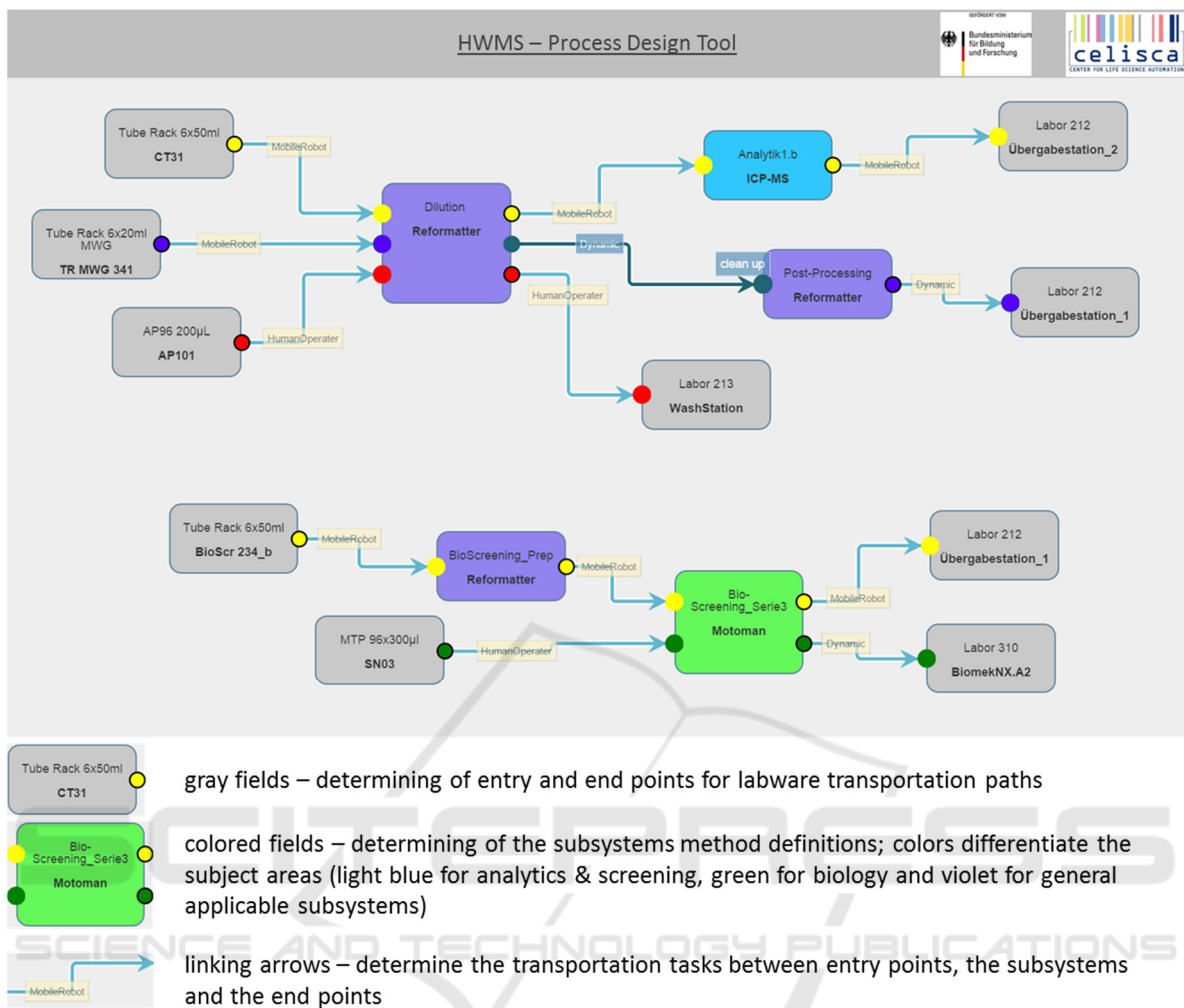


Figure 2: Material flow-oriented process model.

integrated graphical process design tool allows the definition of an abstracted material flow diagram to chain distributed heterogeneous PCS and ICS by embedding all intersystem transport tasks in laboratories (see fig. 2). Therefore, the user defines the entry point for the labware into the workflow, combines the required subsystems and determines the already prepared methods of the PCS and ICS in the process design tool. In practice these methods are normally created for general procedures; thus it can be used for different applications and combinations. During the definition of the process diagram the HWMS supports interactions with the subsystems to receive planning-relevant information (e.g. scheduling results of the PCS, labware start positions of sub processes, status information) and to implement them in the background into the technical and the material-flow-oriented process model as e.g. the number of the required labware path inputs and

outputs for a subsystems method execution (see fig. 2). These labware paths allow to follow the involved labware groups, which are defined by their function in the process. In contrast to the labware path input positions, which are defined in the start conditions of a PCS-method, the output positions are not always available during the planning phase. The reasons for that are process-dependent logical decisions in the PCS-method, which influence the distribution of the labware on the final transfer position (labware path output position). The HWMS requests these output positions from the PCS during the runtime, directly after finishing the subprocess, to receive the actual positions of all paths.

The transportation tasks in the process model will be integrated implicitly by the graphical linking of the subsystems labware path inputs and outputs. Process-model options allow e.g. the definition of


```

<?xml version="1.0"?>
<Mobile-Commands ID="253" Type="Command" Client="Mobile_14">
  <Transport CommandName="Transport">
    <Source Lab="Labor 2.13" LabBC="Lab_2_13" Dev="manually preparation" DevBC="Dev_1" Pos="Pos1" PosBC="Pos_1"/>
    <Destination Lab="Labor 2.11" LabBC="Lab_2_11" Dev="reformatter" DevBC="Dev_3" Pos="Pos1" PosBC="Pos_1"/>
    <Rack BC="R4-F3">
      <PosData Pos="1">
        <LWData Name="MTP96" BC=""/>
      </PosData>
      <PosData Pos="2">
        <LWData Name="MTP96" BC="CB6-A12"/>
        <LWData Name="MTP96" BC="CB6-A17"/>
        <LWData Name="MTP96" BC="CB6-A24"/>
      </PosData>
      <PosData Pos="3">
        <Container BC="C3-F6" PosMax="B3">
          <ConPos Pos="A1">
            <LWData Name="Falcon Tub" BC="FT-143"/>
          </ConPos>
          <ConPos Pos="B2">
            <LWData Name="Falcon Tub" BC="FT-121"/>
          </ConPos>
        </Container>
      </PosData>
    </Rack>
  </Transport>
</Mobile-Commands>

```

Figure 3: Communication protocol on the basis of xml.

the kind of transporter (mobile robot or human operator). In the technical process model the executability of the transporter decision will be validated and corrected if necessary. Alternatively this decision can also be passed to the TACS, if both kinds of transporters can execute the specific task. The end point determines the final position for the labware after the competition of the workflow. The complexity and the required usability of the process diagram demand a specified notation as applied, which can be very complex when using standards from higher level control systems as e.g. BPMN 2.0 (Business Process Model and Notification) (OMG, 2011).

For the execution of the planned process workflow, the material flow diagram has to be translated in a processible format, separated in logical sub processes (primary divided into transport and automation system processes) and scheduled together with all workflows to be performed. For the latter a scheduler in the process controller is used, which works with a genetic algorithm. It generates an optimized execution order of the sub processes in consideration of the limited numbers of resources (e.g. applicable integrated automation systems or transport units) and assigned priorities (Gu et al., 2016).

Depending on the scheduling results the process controller verifies the subsystems and triggers the required subprocesses to execute arranged methods or tasks (e.g. labware transport, pipetting process by a liquid handler) on them, after starting the execution by the user. The execution will be assumed by the structured subsystems on the

subordinated process-control and instrument-control layer.

Due to the fact that the conditions of the environment can change, for example by newly started workflows, which have to be implemented in the total workflow, by changings in the number of available transportation units (robots have to charge or can be broken, human operators have a limited working time or have to fulfil other tasks) or by unforeseeable delays, which can occur especially during the transportation processes, a dynamic scheduling is required (Schäfer, 2004). It is realized by a rescheduling of the total workflow during the execution and is triggered by the detection of such changings (delay measurements or notifications about the available number of transportation units).

4 INTERACTION AND COMMUNICATION

The HWMS is a web-based telematics platform, which is primarily integrated by the laboratory's computing environment. It provides the interfaces to structured automation systems and considers the usability of process definition and execution for a wide range of life science laboratories. Thus, the data transfer between the HWMS and the process control layer's front-end systems is based on web-services, which allow a simple and flexible integration of all web-service providing subsystems. The HWMS uses this to send process instructions and to request the status of the front-end subsystems to correlate the information and to initiate required

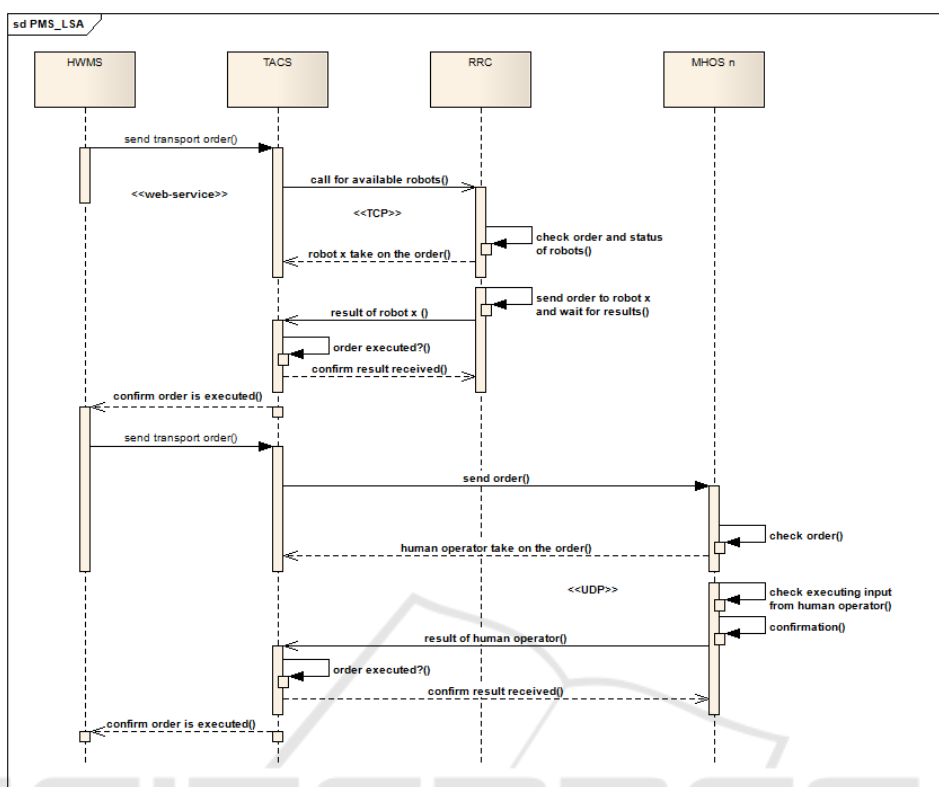


Figure 4: UML Sequence diagram of the communication process between HWMS and the transportation control system.

processes in the subordinated architecture, following the scheduling result.

In case of the PCAS, every PCS or ICS has a preceded individual service instance, which uses available service-oriented communication or framework interfaces to access the automation systems for workflow control. During the execution of a sub process, the PCAS observes the running process and offers status and error information on request to the HWMS to inform the requesting user and to resume the process chain.

Main function of the TACS is the distribution of transportation orders for robots and human operators. The TACS works centralized and provides, in analogy to the PCAS, a web-service for the communication to the HWMS. Depending on the availability of the operators, the restrictions of the user for the process and the reliability of the different operators for the current order, the TACS decides whether a robot or the human operator is more qualified or can finish the order faster. Furthermore, the TACS distributes assistance orders such as sample preparation, restocking resources at a workstation, prepare a laboratory automation system for other processes or check their status after

execution faults. Currently these kinds of orders can only be done by human operators.

The communication between the TACS and the transportation resources (RRC or MHOS) is realized by using a flexible XML-based message protocol transmitted via TCP or UDP, dependent on the unit's type. For the mobile robots, the RRC represents the remote station to the TACS, which uses TCP-communication and forwards the orders to the requested robot (Liu et al., 2012). On the other hand, the TACS integrates the separated MHOS units based on several mobile devices via the UDP protocol. The properties of UDP allow the TACS to communicate with an almost unlimited number of MHOSs without a continuous connection to the single devices. It is less dependent on possible connection interruptions, which may occur when human operators leave the local wireless network.

Both kinds of transport resources work with a highly structured XML-message protocol, which contains all relevant information, such as the places of source and destination and the list of labware including the barcode. In fig. 3 a transportation order is shown, which is based on a general transportation rack with three positions in the ANSI/SBS footprint

dimensions for microtiter plates. On these positions combinations of microtiter plates and adapting racks for different kinds of tubes, also in stack format, are possible.

For every message dispatched by the TACS a confirmation concerning the correctly received command is expected. This implies completeness, correct decompression and readability of the message. After having finished the order, the executive transport resources will send a confirming reply back to the TACS. In fig. 4 the communication cycle between HWMS, TACS and both kinds of transportation resources are visualized in a sequence diagram.

5 MOBILE HUMAN OPERATOR SERVICE

As an alternative to the transportation by the mobile robots, which is described more precisely in (Liu et al., 2012 & 2012 & 2013), human operators are still required for particular processing steps or for limitations of robot pools and for special transportation orders in life science processes. To include a group of human operators into the automated process, every single operator needs a separate mobile interface to be flexible and to receive orders from the TACS. Therefore, Android-based mobile devices are used, which are available in different formats. In general, mobile devices combine a flexible I/O-interface with high connectivity and other functionalities, such as integrated cameras.

Via an Android-based laboratory application (LApp), the human operators are logging-in themselves to the TACS. Thus, they are registered as being available to receive transportation and assistance orders, dependent of the operator's individual role. All orders are listed and can be selected by the operator to see more details and further handling. A graphical overview of the transportation order allows seeing the expected positioning of the labware for the process on the destination side. In case of preparing an automation system, this has a determined arrangement of the labware dependent on the current method. These arrangements can consist of up to three stacks, each with up to ten single microtiter plates or other labware (see Fig. 5). The arrangement needs to be maintained to avoid mistakes and to prevent the workstation from re-sort processes, especially if the space is limited.



Figure 5: Screenshot of the mobile device list and graphical user interface with the required transport arrangement of the labware.

To reduce the effort for the human operator, the mobile device camera is used to identify the labware's barcode and to allocate a labware to a position in the arrangement, when the position is allowed to be edited. This can appear when a workstation is equipped with empty labware of the same type. In this case, the MHOS initializes the start position for the sample tracking across the overall process.

Furthermore, the HWMS and even the integrated stock management are available via the mobile device's web browser. In this case, the human operator can register, re-sort or find goods in the stock management, which can be distributed all over the institution. Label printers also enable the printing of self-defined barcodes to identify new labware. All these functionalities are also obtainable via stationary computers.

6 CONCLUSION

This paper describes an architecture to combine distributed conventional hybrid and heterogeneous automation systems with mobile robots and human operators (integrated by mobile devices) to solve the demands of automated transportations between

them. Thus, the automation level in life science laboratories can be increased and the human operators can also be integrated in required assistance tasks in runtime.

The HWMS allows the handling of master data and stock management, which is the basis for planning life science processes over several automation systems. By an integrated process design tool the end user can plan workflows including these automation systems by a material-flow-oriented process model. The resulting models can be executed parallel by means of a dynamic scheduler (based on genetic algorithm) to optimize the use of the required resources (e.g. automation systems, mobile robots, human operators) in the complex workflow. Variable transfer positions between the automation systems are also tolerated by the HWMS. By using mobile robots, HWMS accomplishes an important requirement of life science automation as a complex *process connector* between distributed automation systems in a building.

The TACS and the PCAS build the front end of the process-control layer and share the control over the automation systems as well as the mobile robots and mobile devices. Both systems distribute and adapt the orders for the corresponding automation subsystems, whereby the TACS is able to conduct dynamic transportation-unit allocations for each intersystem transport process. For the communication between the TACS and the subsystems, a uniform XML-message-protocol via TCP and UDP is used. The PCAS consists of individual services on the local computers of the heterogeneous automation systems to implement the whole performance range of the systems.

Especially the MHOS unit, available on smart phone or tablet PC, integrates laboratory assistants increasingly in the running workflow. The requirements of the system, which cannot be performed by mobile robots, will be directly submitted via transportation or assistance orders to human operators.

In summary, the presented workflow management system located on the workflow control layer is able to speed up the laboratory work in general, to reduce the effort for human operators and to combine human and machine in an automated or semi-automated process albeit this puts the observation function for the human operators more in the center stage. Thus, the automated system receives the control role concerning time management, while the focus of the human operators

is on manual preparation steps and on observing the process as a whole.

Although humans currently transport faster than the robots, used in this solution, the process-integrated robot operators have the advantage of being able to react immediately to a command, to manage dangerous transportation orders and to operate 24/7. Thus, although the advantages of human and robot operators differ, they are both useful depending on the respective requirements and a parallel availability of both operators cover processes around-the-clock and high priority or special transportation orders, too.

ACKNOWLEDGEMENTS

The authors thank the Ministry for Economic Affairs, Construction and Tourism of Mecklenburg-West Pomerania (Germany, FKZ: V-630-S-105-2010/352, V-630-F-105-2010/353) and the Federal Ministry of Education and Research (FKZ: 03Z1KN11, 03A1KI1) for the financial support of this project. This work has been supported by the European Union.

REFERENCES

- Patel, S. N., Prajapati, K. R., Sen, D. J., 2014. Automation by Laboratory Robotics in Pharmaceutical Research Industry: A latest venture in innovative idea. In: *World Journal of Pharmacy and Pharmaceutical Science (WJPPS)*, vol.3 (2), pp. 2098–2105.
- Lam, C. W., Jacob, E., 2012. Implementing a laboratory automation system: experience of a large clinical laboratory. In: *J Lab Autom*, vol.17 (1), pp. 16–23.
- Cork, D. G., Sugawara, T., 2002. *Laboratory automation in the chemical industry*. New York: Marcel Dekker.
- Andersen, D., Rasmussen, B., Linnet, K., 2012. Validation of a fully automated robotic setup for preparation of whole blood samples for LC-MS toxicology analysis. In: *J Anal Toxicol*, vol. 36 (4), pp. 280–287.
- Liu, L., Zhang, R., Pajak, L., 2010. Automation of Human IgG, Glucose, Lactate, and Oxygen Assays on Biomek NXP Span-8 Automation Workstation and PARADIGM Detection Platform. In: *Journal of the Association for Laboratory Automation*, vol. 15 (5), pp. 414–418.
- Sutherland, J. D., Tu, N. P., Nemcek, T. A., Searle, P. A., Hochlowski, J. E., Djuric, S. W., Pan, J. Y., 2014. An Automated Synthesis-Purification-Sample-Management Platform for the Accelerated Generation of Pharmaceutical Candidates. In: *Journal of Laboratory Automation*, vol. 19 (2), pp. 176–182.

- Göde, B., Holzmüller-Laue, S., Rimane, K., Chow, M.-Y., Stoll, N., 2007. Laboratory Information Management Systems – An Approach as an Integration Platform within Flexible Laboratory Automation for Application in Life Sciences. In: *Proc. of the 3rd Annual IEEE CASE*, Scottsdale, AZ, USA, Sept 22-25, pp. 841–845.
- de Souza, N. (ed), 2010. The scientist and the smartphone. In: *NatMet*, vol. 7 (2), p. 87.
- Muenz, R., 2012. The right choice of centrifuges. In: *Lab Manager*, p. 51.
- Liu, H., Stoll, N., Junginger, S., Thurow, K., 2012. A common wireless remote control system for mobile robots in laboratory. In: *Proc. of the IEEE I2MTC Conference 2012*, pp. 688-693.
- Liu, H., Stoll, N., Junginger, S., Thurow, K., 2013. An Application of Charging Management for Mobile Robot Transportation in Laboratory Environments. In: *Proc. of the IEEE I2MTC Conference 2013*, pp. 435-439.
- Liu, H., Stoll, N., Junginger, S., Thurow, K., 2012. A Floyd-Dijkstra Hybrid Application for Mobile Robot Path Planning in Life Science Automation. In: *Proc. of the 8th IEEE International CASE 2012*, Seoul, Korea, pp. 279-284.
- Delaney, N. F., Echenique, J. I. R., Marx, C. J., 2013. Clarity: an open-source manager for laboratory automation. In: *J Lab Autom*, vol.18 (2), pp. 171–177.
- Neubert, S., Göde, B., Gu, X., Stoll, N., Thurow, K., 2016. Potential of Laboratory Execution Systems (LEs) to Simplify the Application of Business Process Management Systems (BPMSs) in Laboratory Automation. In: *JALA*, Online First, December 2016.
- OMG. Business Process Model and Notation (BPMN) Version 2.0. 2011. <http://www.omg.org/spec/BPMN/2.0>
- Gu, X., Neubert, S., Stoll, N., Thurow, K., 2016 Intelligent Scheduling Method for Life Science Automation Systems. In: *Proc. IEEE International Conference on Multisensor Fusion and Integration 2016*, pp. 156-161.
- Schäfer, R., 2004. Concepts for dynamic scheduling in the laboratory. In: *JALA*, vol.9 (6), pp. 382–397.