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Final Report: An Integrated System for Automating Artificial Metalloenzyme Evolution

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6. AUTHORS
Jared C. Lewis

5d. PROJECT NUMBER

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5801 South Ellis Avenue
Chicago, IL 60637 -5418

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The views, opinions and/or findings contained in this report are those of the author(s) and should not contrued as an official Department of the Army position, policy or decision, unless so designated by other documentation.

14. ABSTRACT
Controlling the selectivity of chemical reactions and conducting these reactions in biological systems, where they could have a transformative impact on manipulating living systems, stand as key challenges in synthetic chemistry. Artificial metalloenzymes (ArMs) could achieve these goals by combining the reactivity of synthetic metal catalysts and the adaptability and efficiency of enzymes. As part of a research program funded in part by the ARO (62247-LS), we have made several exciting advances in ArM research, including the first demonstration of ArM evolution. As we have developed new techniques to enable these advances, further progress has become limited by

15. SUBJECT TERMS
directed evolution, laboratory automation, artificial metalloenzyme

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a. REPORT	b. ABSTRACT	c. THIS PAGE			Jared Lewis
UU	UU	UU	UU		19b. TELEPHONE NUMBER 773-702-3546

Report Title

Final Report: An Integrated System for Automating Artificial Metalloenzyme Evolution

ABSTRACT

Controlling the selectivity of chemical reactions and conducting these reactions in biological systems, where they could have a transformative impact on manipulating living systems, stand as key challenges in synthetic chemistry. Artificial metalloenzymes (ArMs) could achieve these goals by combining the reactivity of synthetic metal catalysts and the adaptability and efficiency of enzymes. As part of a research program funded in part by the ARO (62247-LS), we have made several exciting advances in ArM research, including the first demonstration of ArM evolution. As we have developed new techniques to enable these advances, further progress has become limited by the low throughput of the instrumentation available in my laboratory for protein evolution. This not only slows the progress of our proposed research but also saddles students, the creative engines of research, with tedious and repetitious tasks that keep them from tackling higher level problems. This award funded the design and installation of a system for automating most tasks involved with ArM engineering. As expected, this system is widely used by my group and has facilitated and standardized our ArM evolution efforts.

Enter List of papers submitted or published that acknowledge ARO support from the start of the project to the date of this printing. List the papers, including journal references, in the following categories:

(a) Papers published in peer-reviewed journals (N/A for none)

Received		Paper
01/13/2017	1	Hao Yang, Alan M. Swartz, Poonam Srivastava, Hyun June Park, Ken Ellis-Guardiola, David M. Upp, Gihoon Lee, Ketaki Belsare, Yifan Gu, Chen Zhang, Raymond E. Moellering, and Jared C. Lewis. Evolving Artificial Metalloenzyme Selectivity via Random and Combinatorial Mutagenesis, submitted, ( ): . doi:
01/13/2017	4	David M. Upp, and Jared C. Lewis. Selective C-H Bond Functionalization Using Repurposed or Artificial Metalloenzymes, Current Opinion in Chemical Biology, ( ): . doi:
01/13/2017	3	Fabian Schwizer, Yasunori Okamoto, Tillmann Heinisch, Yifan Gu, Michela M. Pellioni, Vincent Lebrun, Raphael Reuter, Valentin Köhler, Jared C. Lewis, Thomas R. Ward. Endowing Organometallic Catalysts with a Genetic Memory: Artificial Metalloenzymes, Chemical Reviews, ( ): . doi:
01/13/2017	6	Poonam Srivastava, Hao Yang, Ken Ellis-Guardiola, Jared C. Lewis. Engineering a dirhodium artificial metalloenzyme for selective olefin cyclopropanation, Nature Communications, ( ): . doi:
TOTAL:	**4**	

Number of Papers published in peer-reviewed journals:

(b) Papers published in non-peer-reviewed journals (N/A for none)

Received	Paper

TOTAL:

Number of Papers published in non peer-reviewed journals:

(c) Presentations

2016
University of Minnesota, 11/17, 2016
Scripps Research Institute, 11/4, 2016
Scripps Institute of Oceanography, 11/3, 2016
Tufts University, 10/18, 2016
University of Wisconsin, 10/11
University of Rochester, 10/7
University of Michigan, 9/20
Aachen-Osaka Catalysis Symposium (Aachen, Germany), 8/5
Organic Reactions and Processes GRC, 7/17-7/21
Biocatalysis GRC, 7/10-7/15
Abbvie, 6/17
Princeton University, 5/3
University of Pennsylvania, 5/2
Stanford University, 4/13
Gilead Sciences, 4/12
Loyola University Chicago, 3/24
UC Berkeley, 2/9
UCSF, 2/8
Emory University, 1/27
UC Irvine, 1/14
Caltech, 1/13

2015
Biocatalysis and Cooperative Catalysis sessions, Pacifichem, Honolulu, HI, 12/18 and 12/19
Yale University, 10/29
University of Illinois, Urbana/Champaign, 10/26
The Role of the Outer Coordination Sphere on the Activity of Enzymes and Molecular Catalysts Symposium, ACS National Meeting, Boston, MA, 8/16
Chicago Organic Symposium, 7/11
C-H Functionalization Symposium, Canadian Chemistry Conference, 6/15
Hope College, 4/17
Calvin College, 4/16
ACS Chemical Biology Lectureship Symposium, ACS National Meeting, Denver, CO, 3/24
Metals in Biology GRC, Stiefel Lecture, 1/28

Number of Presentations: 32.00

Non Peer-Reviewed Conference Proceeding publications (other than abstracts):

Received Paper

TOTAL:

Number of Non Peer-Reviewed Conference Proceeding publications (other than abstracts):

Peer-Reviewed Conference Proceeding publications (other than abstracts):

Received Paper

TOTAL:

Number of Peer-Reviewed Conference Proceeding publications (other than abstracts):

(d) Manuscripts

Received Paper

TOTAL:

Number of Manuscripts:

Books

Received Book

TOTAL:

Received	Book Chapter

TOTAL:

Patents Submitted

Patents Awarded

Awards

2016 Dreyfus Teacher-Scholar Award
2015 Ed Stiefel Young Investigator Award (given by the Metals in Biology GRC)
2014 NSF CAREER Award

Graduate Students

NAME	PERCENT_SUPPORTED
FTE Equivalent:	
Total Number:	

Names of Post Doctorates

NAME	PERCENT_SUPPORTED
FTE Equivalent:	
Total Number:	

Names of Faculty Supported

NAME	PERCENT_SUPPORTED
FTE Equivalent:	
Total Number:	

Names of Under Graduate students supported

NAME	PERCENT_SUPPORTED
FTE Equivalent:	
Total Number:	

Student Metrics

This section only applies to graduating undergraduates supported by this agreement in this reporting period

The number of undergraduates funded by this agreement who graduated during this period: 0.00

The number of undergraduates funded by this agreement who graduated during this period with a degree in science, mathematics, engineering, or technology fields:..... 0.00

The number of undergraduates funded by your agreement who graduated during this period and will continue to pursue a graduate or Ph.D. degree in science, mathematics, engineering, or technology fields:..... 0.00

Number of graduating undergraduates who achieved a 3.5 GPA to 4.0 (4.0 max scale):..... 0.00

Number of graduating undergraduates funded by a DoD funded Center of Excellence grant for Education, Research and Engineering:..... 0.00

The number of undergraduates funded by your agreement who graduated during this period and intend to work for the Department of Defense 0.00

The number of undergraduates funded by your agreement who graduated during this period and will receive scholarships or fellowships for further studies in science, mathematics, engineering or technology fields: 0.00

Names of Personnel receiving masters degrees

NAME

Total Number:

Names of personnel receiving PHDs

NAME

Total Number:

Names of other research staff

NAME PERCENT_SUPPORTED

FTE Equivalent:
Total Number:

Sub Contractors (DD882)

Inventions (DD882)

Scientific Progress

The original proposal outlined a system that had been designed in collaboration with ThermoFisher to automate operations associated with ArM evolution. We required that the proposed design integrate instrumentation existing in our laboratory and allow use of all instruments individually for low throughput experiments. In addition, the design and software interface needed to be simple enough so that students, rather than a trained technician, could readily learn and operate the system. ThermoFisher's extensive experience with such systems, and the ease of use of their Momentum software, more than accommodated these requirements. Designs and quotes for similar systems from Hudson Robotics and BioSero were also obtained, but these were inferior to the ThermoFisher system in terms of cost, robotic arm capability, and software simplicity. Following extensive discussions with all three companies, we moved forward with the ThermoFisher system.

Further design discussions with Thermo led to a finalized system that incorporated most of the originally proposed instrumentation organized in a layout more appropriate for the space available in my laboratory. The final design did not include the originally proposed PCR thermocycler because its cost exceeded the maximum DURIP award amount from all vendors. On the other hand, the design did include space, specific deck mounts, and hardware for the thermocycler and an automated incubator/shaker (originally proposed as an "add-on") so that these instruments can be readily incorporated at a later date. Multiple site visits by Thermo software engineers were required to design Momentum software drivers for all of our existing instruments (covered by the original quote; a major benefit of the Thermo bid). A full description of the final system is provided as a supplementary file on the ARO extranet. Following this lengthy design process, system installation and training was finished on April 29, 2016.

The system went into immediate use for its proposed purposed of facilitating the evolution of dirhodium artificial metalloenzymes for selective carbene insertion reactions. The originally proposed colony picking and reaction setup/assay modules within the system greatly facilitated both of these aspects of directed evolution. Moreover, the system was used to develop modified evolution protocols involving automated 96-well filter plate purification steps, multiple transfers from 24-to-96 well plates, and a variety of other operations. Students rapidly learned the momentum software to run the instruments in an automated fashion, and they are able to take instruments offline for simple low throughput operations as originally proposed. This system was used extensively to complete the work in a manuscript describing the first use of random mutagenesis for artificial metalloenzyme evolution (currently submitted for publication and uploaded to the ARO extranet). In short, the system meets all of the originally proposed goals, functions as promised by ThermoFisher, and will continue to facilitate our ARO-funded research on artificial metalloenzymes for years to come.

Technology Transfer

ThermoFisher SCIENTIFIC

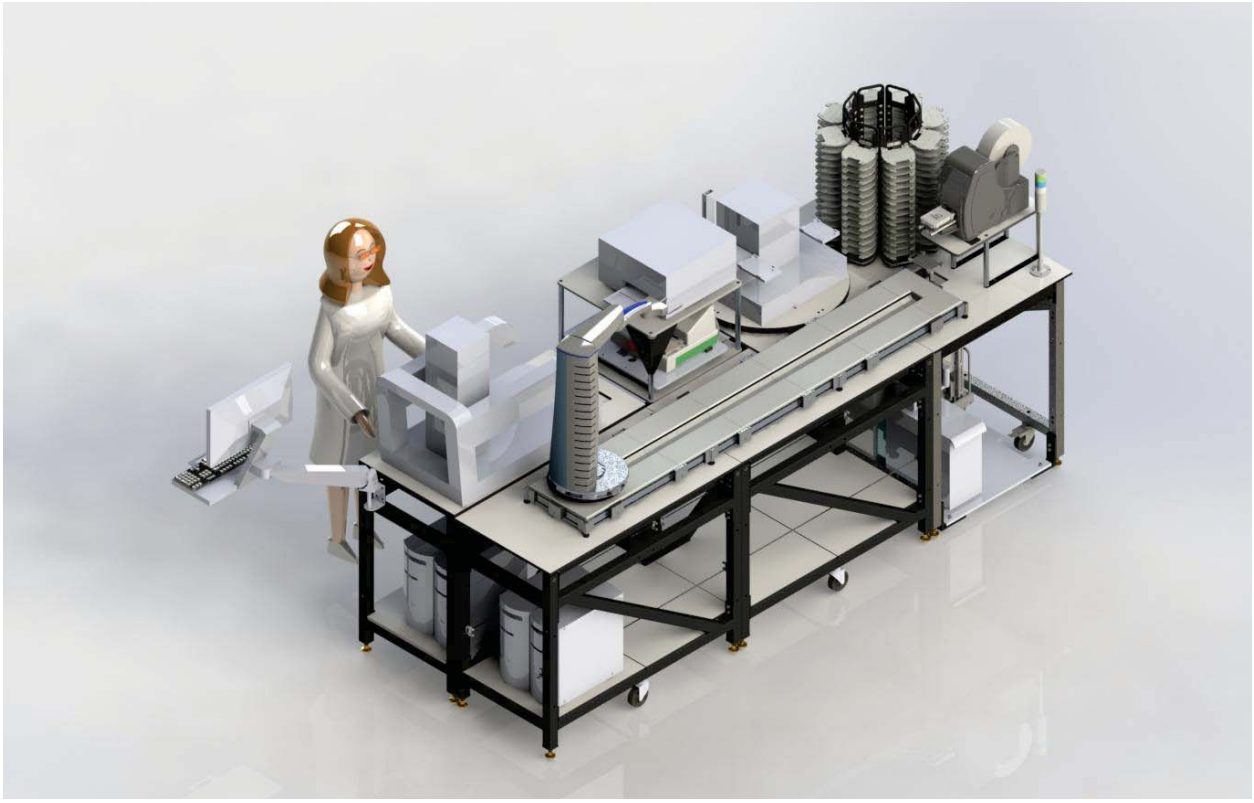
The world leader in serving science

THE UNIVERSITY OF CHICAGO

LOR0260-15

University of Chicago

Spinnaker Workstation Statement of Work



Version: 1.0

March 1, 2016

Created by: Soheal Sayed

soheal.sayed-rahman@thermofisher.com

Table of Contents

List of Tables

Revision History

Revision	Author	Date	Comments
1.0	Soheal Sayed	02-22-2016	- Initial Revision

Legal Notices

Customer-initiated changes to the approved version of this specification may require, at Thermo CRS Ltd's discretion, engineering change orders, additional costs, and changes in the delivery schedule. These changes include, but are not limited to:

- Changes to the system's hardware and software
- Changes to the terms and conditions of the order
- Changes in containers or lids handled by the system
- Changes in the assays the system automates
- Changes in the assumptions upon which the specification is based

Third-party equipment supplied by Thermo CRS Ltd or the customer will be certified by an accredited institution such as, but not limited to, CE, CSA, UL, or TÜV. If the equipment is not so certified, an engineering change order and additional cost may be required, as determined by Thermo CRS Ltd.

If reagent storage is specified in this document and provided by Thermo CRS Ltd, the following disclaimer applies: "The plastic resin information provided herein is provided by the container manufacturer and is reprinted with their permission. It should only be used as a guide when selecting lab ware. Test lab ware for 72 hours under expected or proposed conditions of use, BEFORE putting the lab ware into service on this system. Test with care to avoid injury or property damage. Thermo CRS Ltd does not warrant (neither expressed nor implied) that the information in this section (or table) is accurate or complete, or that any material is suitable for any purpose."

This specification is subject to Thermo CRS Ltd's standard terms and conditions of sale.

For More Information

For more information about this specification, contact Soheal Sayed at soheal.sayed-rahman@thermofisher.com or by telephone at +1 (289) 313-1887 or at +1 (905) 407-4813.

For more information about Thermo Fisher Scientific and its products and services, open your Web browser to http://www.thermofisher.com

Introduction

University of Chicago requires Thermo CRS Ltd to provide a new automation platform that will support their researches. The system has been assigned project number LOR0260-15.The automation platform will run under Thermo Scientifics' Momentum™ automation software to control the workflow and all devices in the system. Components will be integrated & tested at Thermo CRS Ltd facility. The platform will be shipped & installed by Thermo CRS Ltd at University of Chicago in Illinois, USA where the automation system will complete installation and testing. This document further details the requirements & defines the roles and responsibilities for both Thermo CRS Ltd & University of Chicago for the design, implementation & testing of this project.

Order Documents

The current order is based on the following documents:

Table 1 Order Documents

Document	Document ID	Version
Vendor Quotation(s)	SQ0260	N/A
Customer Purchase Order	DR9606956	N/A
Statement of Work	LOR0260-15 University of Chicago Workstation	1.0

Scope of Order

The scope of this order is defined through the documentation noted in the Table 1 above in conjunction with this specification. Changes or additions to the components or works listed in these documents will require a change order to complete and may result in delays and/or schedule changes to the order. Changes to the scope of order can result in a price change and need to be mutually agreed upon between University of Chicago & Thermo CRS Ltd. Scope Changes (Change Orders) shall be defined and invoiced separately under their own order number. Changes shall not delay the execution of the already agreed upon order.

Project Stakeholders

Project stakeholders are those that will have a major role in the definition, implementation & approval of the system and are listed in the tables below.

University of Chicago

Table 2 University of Chicago Stakeholders

Name	Position	Telephone	E-mail
Jared Lewis	Assistant Professor (Chemistry)	(773) 702-3546	jaredlewis@uchicago.edu

Thermo CRS Ltd

Table 3 Thermo CRS Ltd Stakeholders

Name	Position	Telephone	E-mail
Soheal Sayed	Project Lead, Systems Integration	+1(289) 313-1887	soheal.sayed-rahman@thermofisher.com
Nathan Obeid	Manager, Operations & Systems Integration	+1 (289) 313-1819	nathan.obeid@thermofisher.com

University of Chicago's Spinnaker Workstation

The following section contains information regarding the automation system & the party responsible for supplying components that will make up the University of Chicago Spinnaker Workstation.

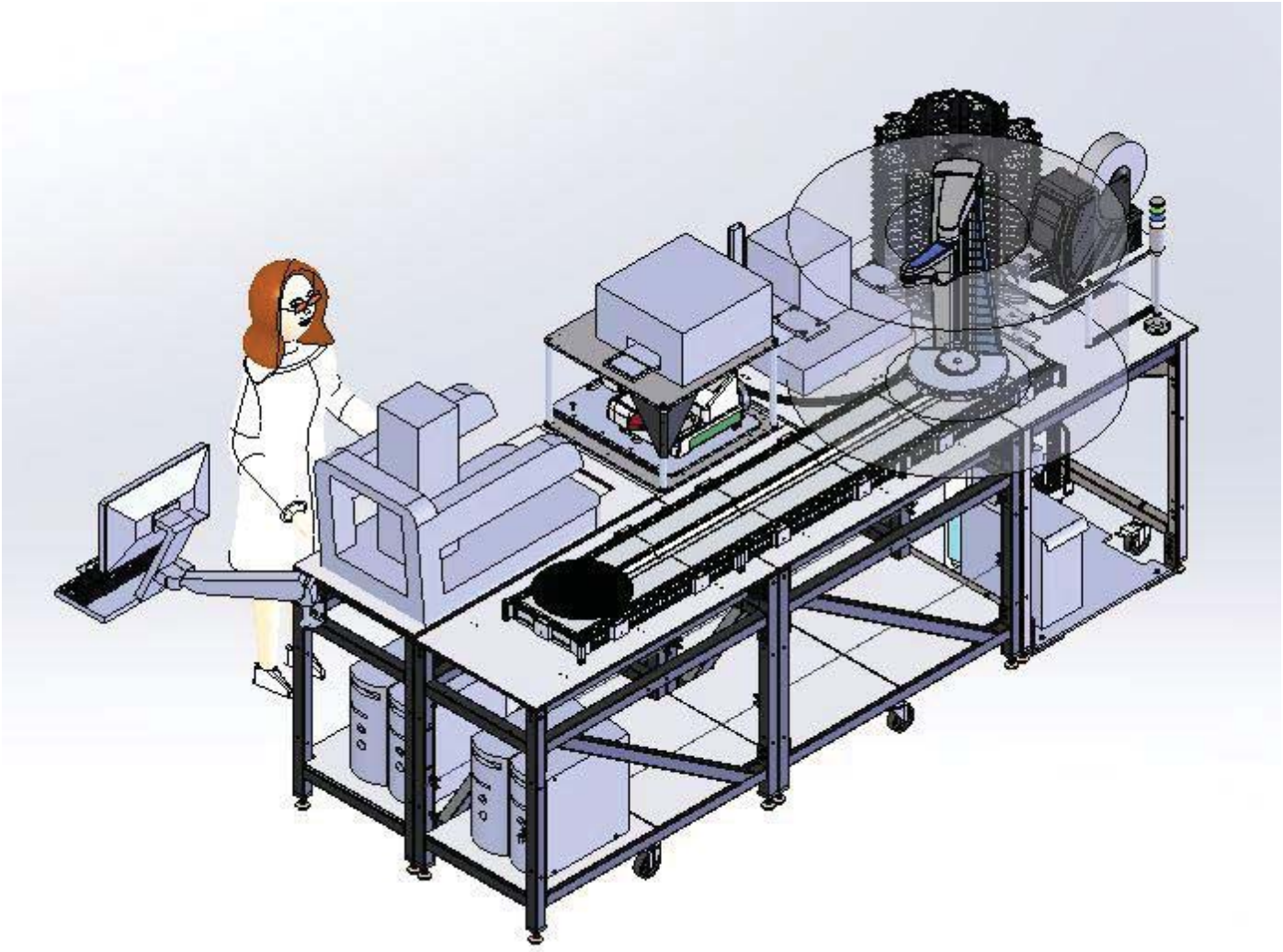


Figure 1-1 : Isometric View (Track Side)

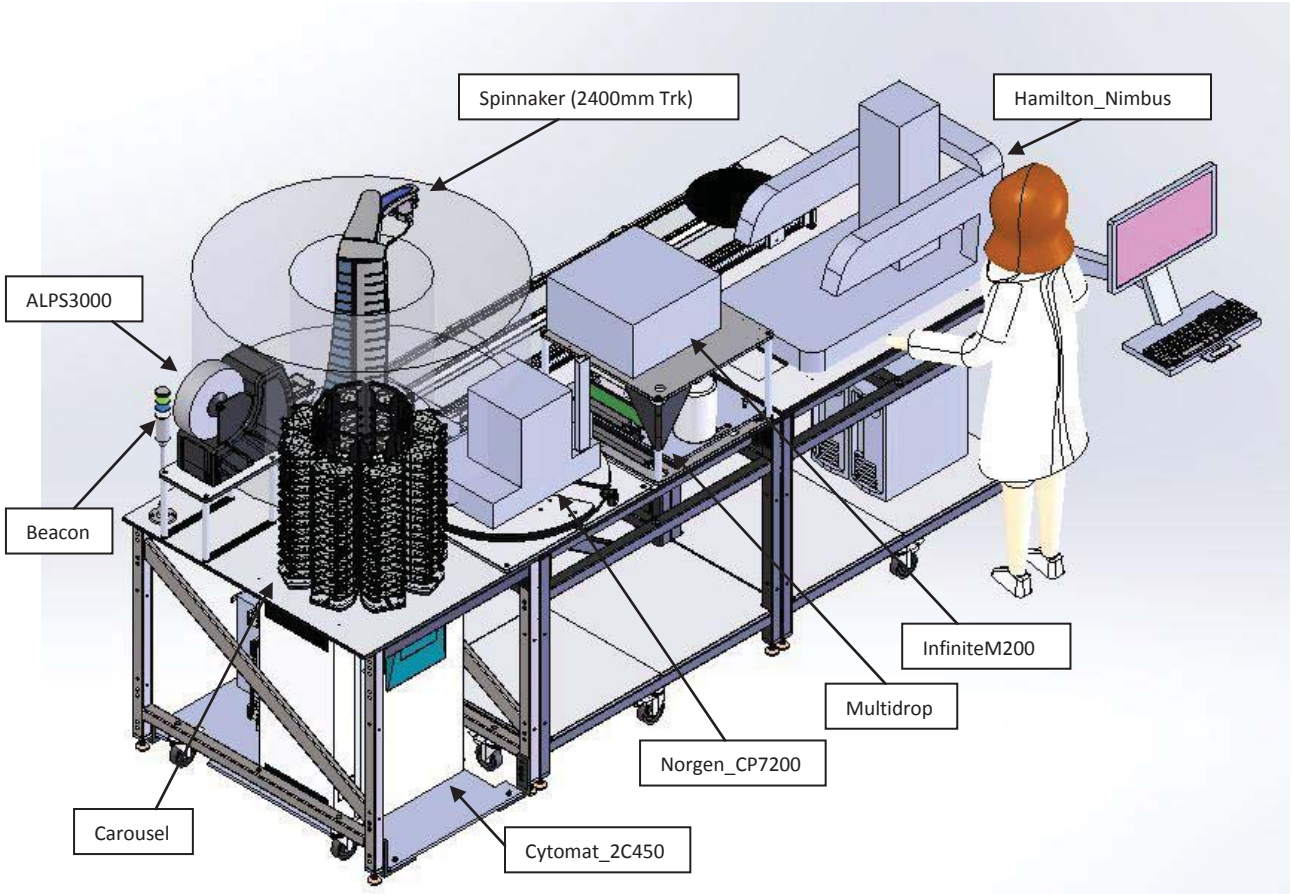


Figure 1-2 : Isometric View (User Side)

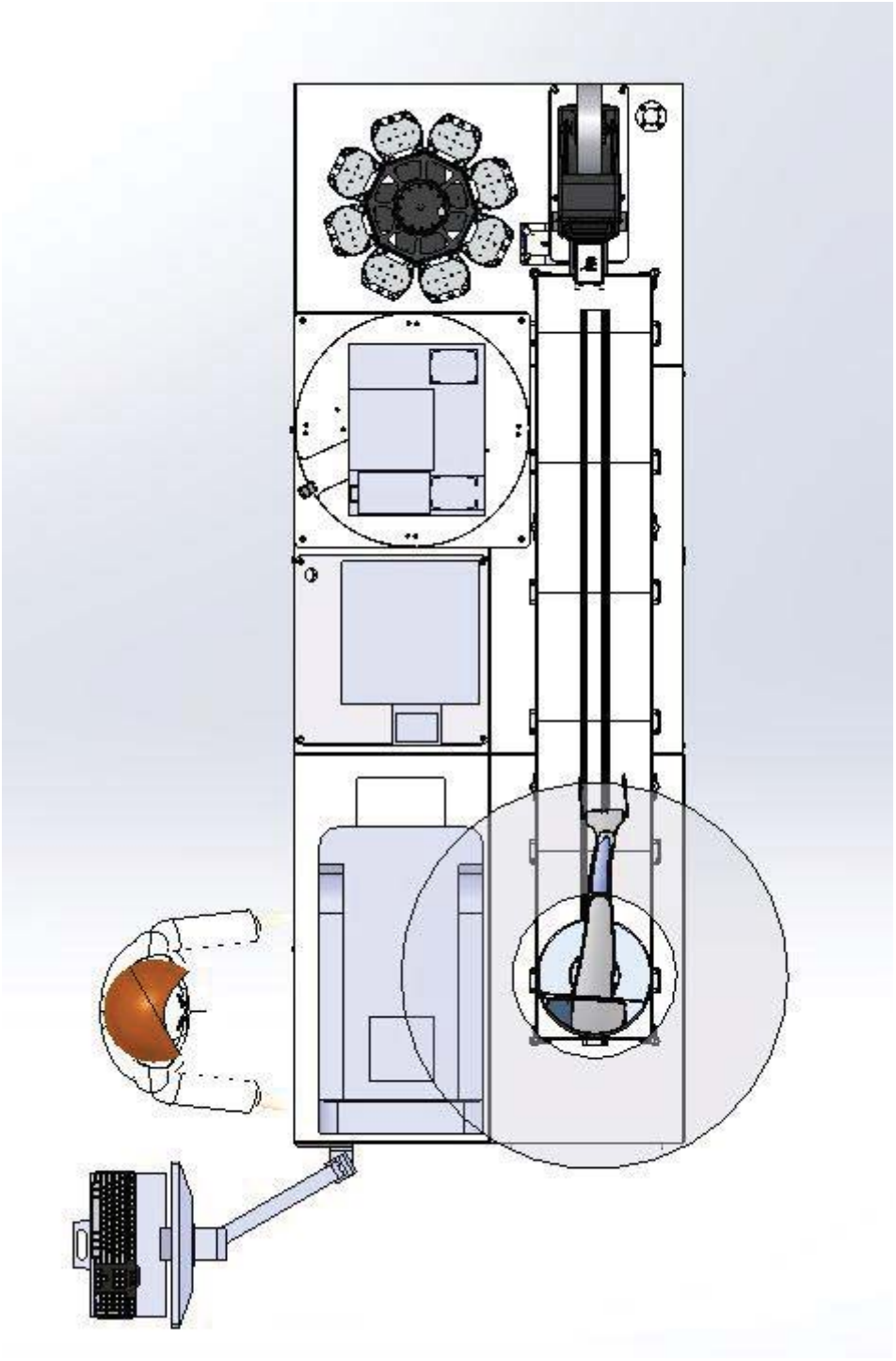


Figure 1-3 : Top View

System Components

Thermo Supplied Components

Table 4 Thermo Supplied Hardware

Component	Manufacturer	Part Number(s)	Quantity
ORS Track, 2400mm Long Track (Above Table)	Thermo Scientific	F01852	1
T3 Carsl, 8P Base Mount - ORS	Thermo Scientific	F01963	1
4-Port DVI KVM Kit w/Cables	Thermo Scientific	S02146	1
Pneumatic Base Kit	Thermo Scientific	K00104	1
Intgrtn Kit, Multidrop Combi	Thermo Scientific	KLI021	1
Intgrtn Kit, TecanInfiniteM200	Thermo Scientific	KLI123	1
Intgrtn Kit, Abgene ALPS 3000	Thermo Scientific	KLI042	1
Receptor & Table Top - 1200mm	Thermo Scientific	F01881	1
Ergotron Stylview Combo Arm	Thermo Scientific	R10337	1
Ergotron Arm Support	Thermo Scientific	T02489	1
SPK, Stand Alone Mover	Thermo Scientific	F01981	1
SPK, 2 Dual Random Access Htls	Thermo Scientific	F01989	5
Dell Automation PC w/4xSerial	Thermo Scientific	F01826	1
Intgrtn Kit, General Locator	Thermo Scientific	KLI128	2
Moxa Uport 1410 USB to 4 port	Thermo Scientific	R09537	1
Rackmount Kit, Receptor	Thermo Scientific	K00091	1
Beacon for Momentum Systems V3	Thermo Scientific	P00136	1
GPSYS IO Box, F5 Art. Robot	Thermo Scientific	F01791	1
Proflex 3x32 Well PCR System ***(Not intended for Automation)***	Thermo Scientific	IN00135	1
Custom Components			
Mezzanine Assy, Cantilever	Thermo Scientific	CI01056	1
Welded Frame Receptor,Custom		CI01060	1
Welded Frame Receptor,1200		CI01061	1
Table Cube,1200mm-2C450 Ubench		CI01057	1
Turntable Assy, Norgren Picker		CI01058	1

Table 5 Thermo Supplied Software & Service

Component	Manufacturer	Part Number(s)	Quantity
Momentum, Single Mover License (*Momentum Version 4.0.2*)	Thermo Scientific	MSI0001	1
Momentum™ Concurrent Interface	Thermo Scientific	MSI0003	6 (3 in SPK Bundle & 3 in ORB0073)
Additional Instrument Integration	Thermo Scientific	ORB0073	3
Momentum,Norgen Syst. (***Driver Development***)	Thermo Scientific	MSI0004	1

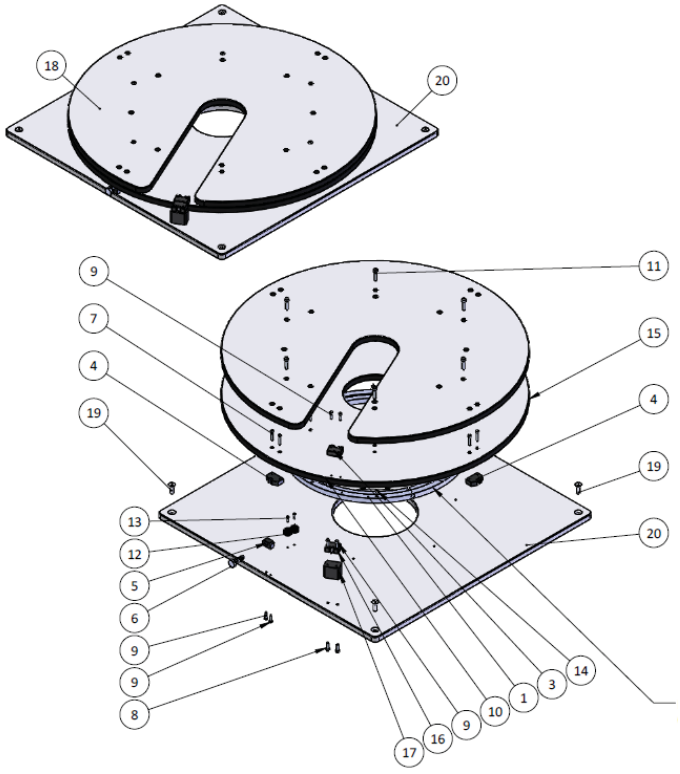


Figure 2-1 : Colony Picker Turntable

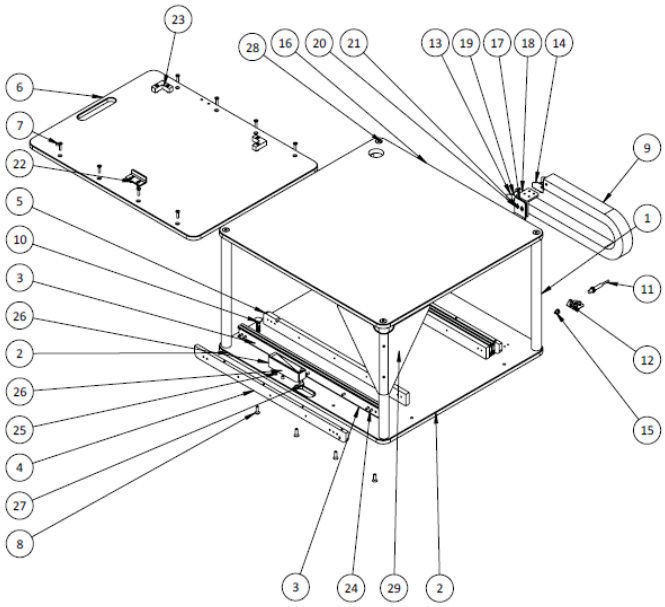


Figure 2-2 : Mezzanine with Sliding Platform

Customer Supplied Components

Table 6 Customer Supplied Instruments (+ Accompanying Software)

Component	Manufacturer	Part Number(s)	Quantity
ALPS3000 Sealer	Thermo Scientific	-	1
Infinite M200 Reader	Tecan Group	-	1
CP7200 Colony Picker	Norgren/Wagner	-	1
Multidrop Combi	Thermo Scientific	-	1
Nimbus-96 Liquid Handler	Hamilton Robotics	-	1

Note:- 6 Momentum device interface are for 5 above mentioned instruments and the additional interface is used for the Plate Carousel.

Additional Information:

- System designed to accommodate future expansion/addition of an under-bench Thermo Scientific Cytomat 2C450 Incubator with lift station without modification of existing platform.
- Spinnaker Carousel on system will be modified to have 6 Deepwell Hotels and 2 Standard Mictroter Storage. [Total Deepwell Storage : 6 Hotels x 8 DW/ea = 48 DW Blocks][Total Standard Storage: 2 Hotels x 15 Plate/ea = 30 Standard Plates]
- System equipped with a safety beacon that displays different color set-ups to imply status of the system – beacon also has a buzzer in cases of an error.
- Sliding shelf (TFS Combi) as well as the turntable (Norgren CP7200) will be equipped with sensors that will be monitored by the automation system. In the event that either of these were moved from the automation position (manual use, service, etc) and not returned – Momentum will halt movement to the instrument, thus avoiding a crash. Air pressure delivered to the system will also be monitored and in the event that air pressure drops, an error will be displayed to the user.
- Waste cut-out has been implemented into the table which has the Nimbus-96 instrument to allow for the disposal of tips – Cutout elongated to serve as a waste for the robot to use as well for plates/lids.

Momentum™ Controller & Networking

This section details the configuration, setup & customer responsibilities for the Momentum™ controller & that will operate the automated system. Momentum™ is built on a .NET platform and is currently compatible with the Windows® 7 Professional 32-bit or 64-bit US English OS. Although Momentum™ is compatible with these versions of Windows, 3rd party vendor software may not be. It is the customer's responsibility to ensure that when supplying or requesting equipment that will run on the Momentum™ controller that they verify the OS listed will be compatible with the vendor software. Any issues that arise from incompatibilities of vendor or 3rd party software becomes the sole responsibility of the customer and will be a chargeable service should Thermo CRS Ltd have to troubleshoot or correct.

Table 7 Local Network Configuration

Computer Name	IP Address
Momentum PC	10.0.0.10
Hamilton Nimbus PC	10.0.0.11
Tecan Infite M200 PC	10.0.0.12
Norgren CP7200 PC	10.0.0.13

- All PC's will be connected to a network hub to form the local system network. The Momentum PC supplied will have 2x Ethernet ports to be connected to the University of Chicago network if desired for file storage. If any of the other PC's are meant to be used on the University of Chicago network as well, it would be up to University of Chicago to ensure that PCs are supplied with 2 network ports (PCIe Network Card Added, USB-LAN adapter)

Software Configuration

Installation of additional software after shipment from Thermo CRS Ltd & issues that arise from that installation becomes the sole responsibility of the customer and will be a chargeable service should Thermo CRS Ltd have to troubleshoot or correct.

Table 8 Standard Controller Specifications

Item	Detail
Manufacturer/Model	Dell Optiplex 3010 Mini-tower
Processor	Intel® Core™ i5 3470 (3.20GHz,6M)
Memory	8GB DDR3 Non-ECC SDRAM,1333MHz, (1DIMM)
Hard Drive	1TB SATA 3.0Gb/s and 16MB DataBurst Cache™
Operating System	Genuine Windows® 7 Professional 32-bit or 64-bit English
Hardware	5 x DB9 Serial Ports, 2 x NIC

Networking

Due to the nature of integrated systems & the various IT requirements that differ from customer to customer, networking & integrating a system into a customer's network can prove difficult without internal IT support that understands the requirements and makes the necessary arrangements to implement them. Therefore, should a customer require the PC be on their network it is required that the customer provides a dedicated IT contact throughout the life of a project, from specification to implementation, in order to limit any delays in the system integration. The system/IT support contact for the University of Chicago Spinnaker Workstation is listed in the table below.

Table 9 University of Chicago IT Contact

Name	Position	Telephone	E-mail
Jared Lewis	Assistant Professor (Chemistry)	(773) 702-3546	jaredlewis@uchicago.edu

Remote Access

As part of the Service and Support of the system a remote windows session can be set up to allow Thermo CRS Ltd to access the system remotely to better assist the customer with troubleshooting. Cisco WebEx™ is the preferred software for remotely assisting customers and the client will be setup by Thermo CRS Ltd prior to installation at the customer's site. The customer will be responsible for ensuring the proper connections & settings to allow remote connectivity are in place in order to receive remote support for their system.

Important Note: *Any Networking or additional software requirements from University of Chicago must be submitted to Thermo CRS Ltd for review & approval into this specification. If no requirements are submitted prior to the completion and approval of this specification, the Momentum™ Controller & system PC's will be set-up onsite in a networking environment suitable for Thermo CRS Ltd to integrate and run the system. Any network or IT changes & subsequent work that may arise from these changes after the approval of this specification will be a chargeable service.*

Consumables

The system will be setup, and tested with customer supplied labware that is of standard SBS format plates, and tip boxes. Configuration of labware will be done during the configuration and testing of the system. The customer will be trained to configure more labware if desired in the future.

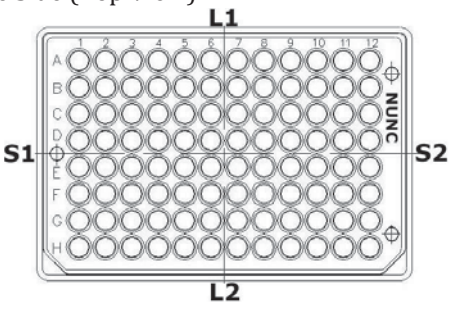
Important Note: *A mover requires a minimum of 3.5mm (h) x 45mm (w) flat surface on labware to ensure gripper reliability for picking & placing into instrument nests. The customer should ensure that all provided labware, labware combinations (i.e. Plates/Lids) & instruments provide this minimum clearance in the instrument nest.*

Barcodes

The system barcode reader can read the code types listed in the following table. The barcode labels to be used on the associated containers in the workstation are detailed in the table below.

Plate Diagram

Barcode Side (Top View)



Barcode Location (Side View)

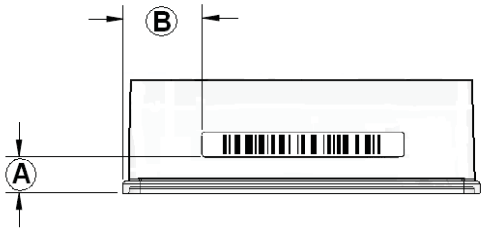


Table 10 Consumable Barcode Details

Plate	Barcode Type	Barcode Side	Label Size (mm)	Barcode Location
Source Plates	☒ Code 128 ☐ Code 39 ☐ Interleaved 2/5 ☐ Code Codabar	☒ Short Side S1 (A1) ☐ Short Side S2 ☒ Long Side L1 ☐ Long Side L2	mm(H) x mm(W)	If desired this option can be implemented by introducing barcoded plates

In the case of a read failure an error message will be displayed with the option of entering the barcode manually if the intervene option was chosen or a 'NOCODE' string including a date_time stamp will be assigned to the plate. In unattended mode the "NOCODE" string will automatically be assigned without user error message.

The Spinnaker built-in barcode reader reads a barcode. Momentum receives that barcode data, associates that data with the identity of the container (identified uniquely with container name, iteration number, batch name, and other information), and stores the data. That barcode data is available for standard Momentum uses such as log entries, for process uses that are user-defined such as making decisions or forming names when creating extra files or folders, and for devices, if the device supports it.

System Safety

Safety & Security

University of Chicago is responsible for the following tasks:

- Complying with appropriate health and safety regulations for use of the system or its components.
- Ensuring operators are adequately trained to operate the system safely.
- Ensuring that adequate measures are taken to protect personnel from potentially hazardous materials.

Emergency Stops

The Spinnaker system handles emergency stopping of the system with the following:

- Emergency stop button, when triggered, will immediately halt all robot movement. The E-Stop button(s) on the Spinnaker Workstation is located on a remote E-stop pendant. Triggering an E-Stop will immediately cut power to the robot arm only.

The software will suspend on the detection of an e-stop condition raised by the e-stop. All instruments in process will finish their operations. All robots & attached peripherals E-Stopped will require a physical reset of the E-Stop chain in order to be active again.

Air Filter Regulator unit

The Automated system includes an Air filter regulator unit that controls the air supply on the entire system. To turn the system Air pressure ON, Rotate the air Regulator valve clockwise until it reads "SUP".

- ALPS3000 sealer detects low pressure and error is returned back to Momentum. Air regulator on system (directly from source air) will also be monitored by the I/O box in the event that an instrument on the system does not have such functionality.

Documentation

General documentation of the system and components will be delivered with the system. The documentation will be in electronic format, except those from third parties that are only available in printed form. Additional documentation can be made available on a per request basis and at an additional cost.

The following documentation will be delivered with the system:

- General instructions on how to use the automation software
- Reference material on the driver interface between the automation software and each instrument (When Available)
- Basic information on any Thermo CRS Ltd or third-party components
- Specification Document

Training

Integration Demonstration & Familiarization

After the system is installed Thermo CRS Ltd will provide a basic overview/familiarization of the system and software. This session includes: powering on/off of all system components, proper startup and shutdown procedures and general robot use knowledge. A brief tutorial covering the teaching of robot locations, a simple introduction to Momentum™ including Processes, Experiments & how to start and stop a Momentum™ run. This overview should take approximately 4 hours at its maximum. Thermo CRS Ltd, in consultation with the customer may decide to demonstrate the system to the user during parts of the installation or provide a complete overview at the end of the installation. This Integration Demonstration & Familiarization is intended as a brief introduction to the Momentum™ software components & the physical system and is not intended to replace the in-depth Momentum™ training courses that are available for purchase.

Warranties

Warranties on customer-supplied components and materials will be neither assumed nor managed by Thermo CRS Ltd.

Facilities

Thermo CRS Ltd's Site

Initial integration and testing of the system (if applicable) will take place at the following vendor's site:

Thermo CRS Ltd
5250 Mainway
Burlington ON
L7L 5Z1
Canada

University of Chicago' Site

Final integration and testing of the system will take place at the following customer site:

University of Chicago
5735 S. Ellis Ave.
SCL 317
Chicago, IL
60637
USA

Utilities & Environment

The system is estimated to require the following utilities for installation:

Table 11 Utilities & Environment Details

Item	Detail
Compressed Air	Clean, dry & oil free air supply at minimum pressure of 100 PSI (6.9 bar) supplied at the system with a 6mm air line or a quick disconnect fitting
 Electricity	NEMA 5-20R_T, 120VAC, 1 phase – Total of 4 circuits are needed for system (Please see attached power distribution worksheet)
Ethernet	Local subnet with either static or dynamic IP addresses, 2 connections are required
Environment	Ambient Temperature: 15 – 25 °C Humidity: 40 – 80 percent, non-condensing Atmosphere: no excessive airborne contaminants that require special design precautions. Space: • Unoccupied space, 1 m wide around 3 sides of the table, unless absolutely impossible. • Floor will be level. • Floor will be capable of supporting a min. 2500kg.

Onsite Integration

The Thermo CRS Ltd Integration team will be onsite for approximately 10-15 business days to build, teach & test the robotic system. The final 2 days of this time requires University of Chicago's involvement for performance of test runs, final approval and Integration Demonstration & Familiarization. Prior to the system being installed at the customer's site and Thermo personnel coming onsite, arrangements should be made for the Thermo CRS Ltd installation team to provide the following:

- General facility information & safety training (If required)
- Emergency contact information & access to the work area including badges/key-fobs or other means of access throughout the installation.
- Required utilities are installed and active in the installation area.
- Installation area that is clean & free of debris with all Customer supplied instruments & components in the installation area. Should the installation area be an active lab or working area and/or existing instruments are being used for integration, decontamination will be completed and the decontamination form(s) provided to the Thermo CRS Ltd representative on arrival.
- A suitable amount of labware to operate the system and perform testing.
- Resources and equipment for lifting system components in excess of 25kg onto the lab system.
- Shop-Vac or Vacuum for work area cleanup during installation.

If Thermo CRS Ltd is delayed due to unfulfilled customer responsibilities onsite and is required to extend their stay past the quoted time this will be dependent on the integrators overall schedule, and will be chargeable to the customer at a standard daily rate (per person) for the length of the delay.

Customer Responsibilities

This section describes the typical items in which the customer is responsible for during the integration and installation of the automation system.

Components Integrated at University of Chicago

The customer will arrange for the availability of all customer-supplied components and materials at the customer's site or from third-party vendors, as necessary for components requiring integration into the system for final installation verification. This includes ensuring that all protocols/scripts/macro required in running of the system protocols listed in this document are created and validated about 2 weeks prior to the acceptance Testing start date.

Components Integrated at University of Chicago

The customer will arrange and pay for the shipment of customer-supplied components and materials to the customer's site. Confirmation of delivery & setup of customer-supplied components and materials to the customer's site will be made prior to the arrival of Thermo CRS Ltd for the installation.

Customer supplied instruments are required to be setup and ready for integration prior to the start of installation efforts by Thermo CRS Ltd onsite. This includes ensuring that all protocols/scripts/macro's required in running of the system protocols listed in this document are created and validated. The customer will arrange and pay for the setup, testing & movement of customer-supplied components onto the lab system for onsite integration & SAT, should the instrument require such steps to be integrated. If used/existing instruments are being used for integration, decontamination should be completed and the decontamination form(s) provided prior to onsite work commencing.

Receiving Shipped Components

After the system is shipped from Thermo CRS Ltd, the system will be received by the customer. The customer will inspect for damage but not unpack the system packages.

The customer will be responsible for the coordination and cost of transporting all packages from the receiving dock to the location of installation. This includes ensuring that the packages can be transported from the shipping dock to the location of installation. The path from the receiving dock to the location of installation should be able to accommodate a typical crate size of 915mm (height) x 915mm (width) x 915mm (depth). It is the customer's responsibility to ensure that the transportation & path to the installation site is suitable prior to installation in order to avoid delays to the system installation.

Installation Completion Criteria

The system installation is considered complete once it functionally satisfy's the following three categories. No other testing or requirements will be introduced to consider the system complete.

*Thermo CRS Ltd is **not** responsible for writing of the instrument's "protocols", and/or "templates" that are called upon in running of Momentum™. All tests will be run dry or with water if requested. No biological and/or chemical substances will be used during the installation.*

Setup

- New platform will be setup as per agreed layout and hardware components will be integrated.
- Momentum™ & peripheral software will be installed and configured for the specified system components and labware.
- Mover paths & instrument nest positions will be taught and configured.
- Custom hardware verified to have the fit & functionality as designed.

Validation

- *General functionality Demonstration* brings the system up to a running state and then shut down to demonstrate that all components (Software & Hardware) in the workstation are functioning and can communicate as part of a complete system.
- System Error Recovery & Safety Demonstration shows the ability of the system to be stopped in an emergency situation, recovered, and returned to normal operation. This will be demonstrated by activating the mover's stop button, removing labware from the system during operation & recovering from the introduced errors.

Basic Training

- Overview of the system hardware & peripherals.
- Introduction to the Workstation core software & their basic functionality.
- Overview of running the *Basic Instrument test* method/protocol(s) including:
    - Setting up for a run (loading labware, preparing devices & ensuring platform is clear)
    - Executing and Monitoring a run
    - Completing a run (Removal of labware & shutting down the system)

These three categories will be verified & documented using the attached Installation Checklist and finalized by the signatures of Thermo CRS Ltd & the end customer once completed.

Statement of Work Approvals

University of Chicago

Name	Title	Date	Signature
Jared Lewis	Assistant Professor (Chemistry)		Digitally signed by Jared C. Lewis DN: cn=Jared C. Lewis, o=University of Chicago, ou=Department of Chemsitry, email=jaredlewis@uchicago.edu, c=US Date: 2016.03.07 13:11:10 -06'00'

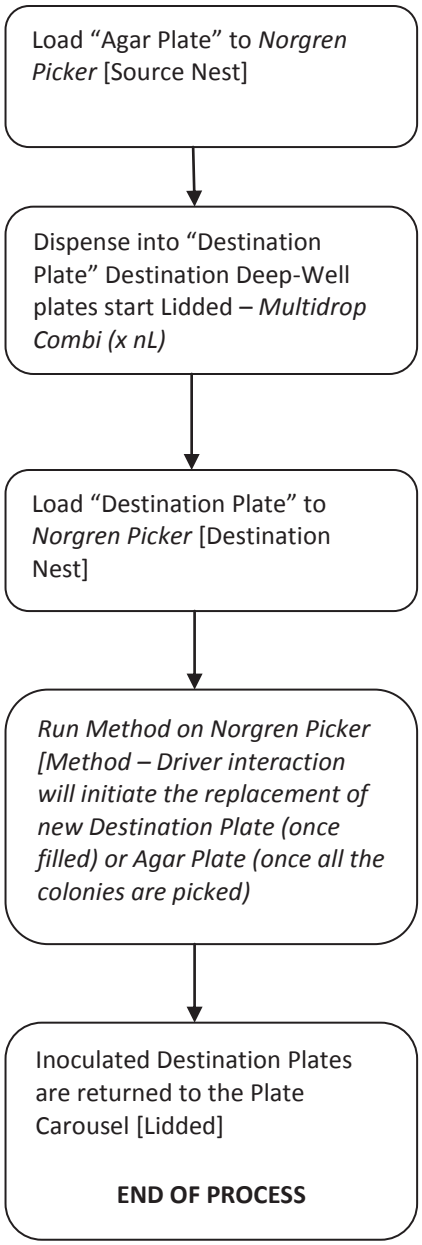
Thermo CRS Ltd

Name	Title	Date	Signature
Soheal Sayed	Project Manager	02/22/2015	

Test Method:-

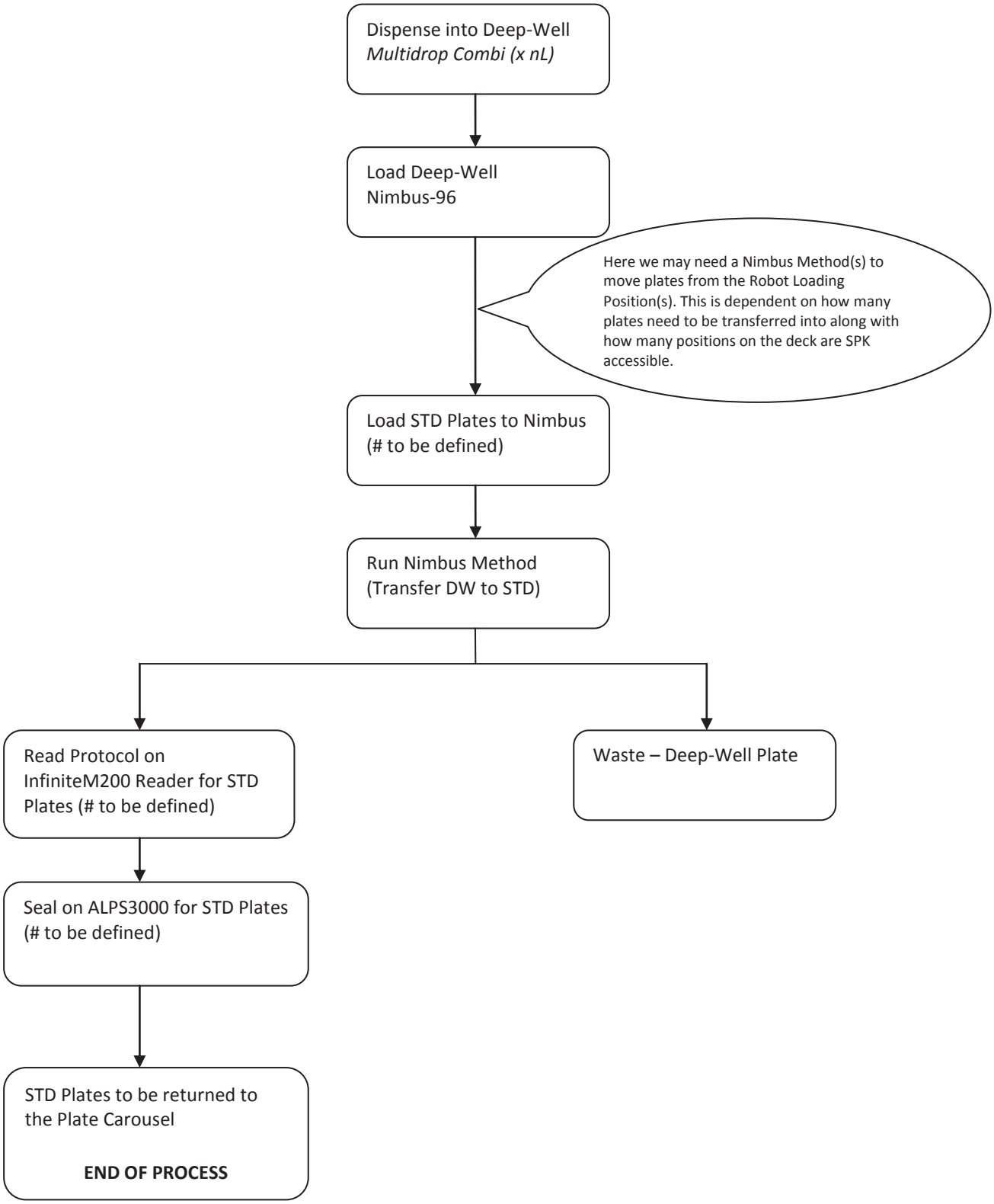
Method 1 : Colony Picking

1) User to load desired quantity of Agar Plates (Source) and Deepwell Culture Plates (Anticipated Qty) into Plate Carousel



Method 2: Liquid Handling/Assay

User will load DW-blocks and Standard plates into the Plate Carousel



Installation Completion Checklist

Items		Completed	
	Name	**Yes**	**No**
	System platform setup as per agreed layout & new platform components installed	☐	☐
Setup	Instruments unpacked (if required) and/or moved to new location & positions fixed with locators relative to associated mover	☐	☐
Setup	Momentum™ Controller configured with Momentum™, peripheral software & mover controllers	☐	☐
Setup	Defined labware is validated & configured in Momentum™ software	☐	☐
Setup	All Mover paths & instrument nest positions have been taught and configured in MoverTeach	☐	☐
Validation	General Functionality Demonstration (System Communications & start up)	☐	☐
Validation	System Error Recovery & Safety Demonstration	☐	☐
Basic Training	Using Mover Teach software to define & teach nest location(s)	☐	☐
Basic Training	Configuring & running the Basic System process using Momentum™ software	☐	☐

The system has successfully fulfilled all the items in the checklist and has completed the Installation stage.

Thermo CRS Ltd.	
Signature	
Name	
Title	
Date	

University of Chicago	
Signature	
Name	
Title	
Date	

Power Distribution

LOR0260 University of Chicago Power Distribution					
DEVICE	**CCT1**	**CCT2**	**CCT3**	**CCT4**	**BTU/HR**
PC Monitor	1				55
DELL PC	2	2			3294
THERMO CAROUSEL			1		275
ABGENE 3000 SEALER			1		1098
Cytomat® 2 C450 INCUBATOR			1		1922
LAUDA RE207/B CHILLER UNIT FOR CYTOMAT 6001				1	3843
SPINNAKER w/ BENCHTRACK	1				275
TECAN INFINITE M200		1			357
Hamilton Nimbus96	1				1098
THERMO MULTIDROP (COMBI)		1			96
Norgren CP720 Colony Picker		1			824
TOTAL	1288.0	1224.8	1380.0	1610.0	
% Capacity	75%	71%	80%	93%	
Total System BTU/Hr:					13135
# of Plugs:	5	5	3	1	14
Rated Amps Per Circuit:	14.2	12.1	15.7	16.8	
Average Amps Per Circuit:	11.2	10.7	12.0	14.0	

Guarding Waiver

ThermoFisher SCIENTIFIC

The world leader in serving science

RELEASE, HOLD HARMLESS AND INDEMNIFICATION AGREEMENT

Thermo CRS Ltd., a Thermo Fisher Scientific company, ("Thermo") strongly urges all of its customers to purchase Spinnaker Workstations with the Thermo recommended safety shielding. Failure to purchase and use the safety shielding while operating the Spinnaker could result in serious personal injury and property damage. For this reason, Thermo strongly suggests that you also purchase the safety shielding in conjunction with your purchase of a Spinnaker Workstation.

If you elect to purchase the Spinnaker Workstation without the recommended safety shielding, Thermo requires that you sign this Release, Hold Harmless and Indemnification Agreement, under which you agree to release, hold harmless and indemnify Thermo from and against any and all claims and liability arising out of injuries and damage resulting from the use of the Spinnaker Workstation which could have been prevented with the Thermo recommended safety shielding.

Release, Hold Harmless and Indemnification: University of Chicago, including its affiliates, officers, directors, employees, shareholders, agents, representatives, successors and assigns (collectively "We") have been repeatedly and comprehensively informed by Thermo that use of the *Spinnaker Workstation* without the Thermo recommended safety shielding can result in serious personal injury and/or property damage, and We clearly understand the risks involved in using the Spinnaker without the safety shielding, including without limitation the risk of serious bodily injury and/or property damage. Nevertheless, We have decided despite such recommendation not to purchase the Thermo recommended safety shielding, and We agree to assume all such risks. It is understood that We, University of Chicago, will provide the appropriate safety and guarding solution(s) for the *Spinnaker Workstation* system We have purchased from Thermo.

THEREFORE, WE HEREBY NOW AND FOREVER RELEASE, HOLD HARMLESS AND DISCHARGE THERMO, ITS AFFILIATES, SUCCESSORS, ASSIGNS, EMPLOYEES, OFFICERS, DIRECTORS, SHAREHOLDERS, AGENTS AND REPRESENTATIVES (THE "INDEMNIFIED PARTIES") FROM AND AGAINST ALL ACTIONS, CLAIMS, DAMAGES, LIABILITIES, LOSSES, COSTS AND EXPENSES, KNOWN OR UNKNOWN, FORSEEN OR UNFORSEEN, RESULTING FROM, RELATED TO, IN CONNECTION WITH OR ARISING FROM USE OF THE SPINNAKER WORKSTATION WITHOUT THE RECOMMENDED SAFETY SHIELDING (THE "DAMAGES") AND SHALL INDEMNIFY AND DEFEND WITH COMPETENT AND EXPERIENCED COUNSEL THE INDEMNIFIED PARTIES FROM AND AGAINST ANY AND ALL DAMAGES IN CONNECTION WITH THE USE OF THE SPINNAKER WORKSTATION WITHOUT THE RECOMMENDED SAFETY SHIELDING, INCLUDING WITH OUT LIMITATION ANY AND ALL DAMAGES ARISING FROM, RELATED TO, OR IN CONNECTION WITH USE BY OUR EMPLOYEES, AGENTS, REPRESENTATIVES, CONTRACTORS AND CUSTOMERS OF THE SPINNAKER WORKSTATION WITHOUT THE RECOMMENDED SAFETY SHIELDING.

Severability and Choice of Law: We agree that this Agreement and any dispute or claim hereunder shall be governed for all purposes by the laws of the Commonwealth of Massachusetts, USA, notwithstanding its conflicts of laws provisions. We further expressly agree that this Agreement is intended to be as broad and inclusive as is permitted by Massachusetts law and that if any portion thereof is held invalid, it is agreed that the balance shall, notwithstanding, continue in full legal force and effect.

Acknowledgment and Understanding: We fully understand the recommendations made to us by Thermo in relation to the recommended safety shielding and the consequences of its non-use, and We fully understand and agree to the release, hold harmless, indemnification, and other provisions contained in this Agreement.

Laboratory Automation
Scientific Instruments

Thermo CRS Ltd.
5344 John Lucas Drive

Burlington, ON
L7L 6A6

(905) 332-2000
(905) 332-1114 fax

www.thermofisher.com

ThermoFisher SCIENTIFIC

We have read this Agreement, fully understand its terms, and **understand that We are giving up substantial rights, including our rights to sue and to other legal remedies.** We acknowledge that We are signing this Agreement freely and voluntarily, and **intend our signature to be a complete and unconditional release of all liability.**

This Agreement shall be binding upon our successors, assigns, transferees, employees, officers, directors, agents and representatives.

Accepted and Agreed:

By: Digitally signed by Jared C. Lewis DN: cn=Jared C. Lewis, o=University of Chicago, ou=Department of Chemsitry, email=jaredlewis@uchicago.edu, c=US Date: 2016.02.25 12:10:40 -06'00'

(Must have signing authority within Customer's Organization)

Print Name: Jared Lewis

Title: Assistant Professor

Company Name: University of Chicago

Date: 2/26/2016

Decontamination Notice

ThermoFisher SCIENTIFIC

Thermo CRS Ltd.
Laboratory Automation
5250 Mainway
Burlington, ON, L7L 5Z1 Canada

Phone: 905-335-2255
Toll Free (North America): 800-365-7587
Website: www.thermo.com

Decontamination Notice

To protect Thermo Fisher Scientific personnel involved with the handling of any items, we require that this document be completed and signed. The signer is legally responsible for the accuracy of the information below and must be a signing officer of the company or an individual who can bind the company. Note that **instruments will not be handled or worked on by Thermo Fisher Scientific unless** either the Hazardous Materials Waiver section on the Return of Merchandize Authorization form is signed, or a copy of this form is completed, signed, and provided to the Thermo personnel who is about to handle the equipment mentioned onsite at the time of the onsite activities.

System or Item Description	Serial Number

List the hazardous material(s) that were in contact with the above components and the decontamination method used to remove or decontaminate each material:

Hazardous Material	Decontamination Method

The undersigned confirms that the above items, which are being returned, have been appropriately decontaminated as per the above methods prior to being shipped:

Name (print):	Title (print legibly):
Company:	Department:
Address:	Province/State:
Country:	Postal Code:
Signature:	Date: