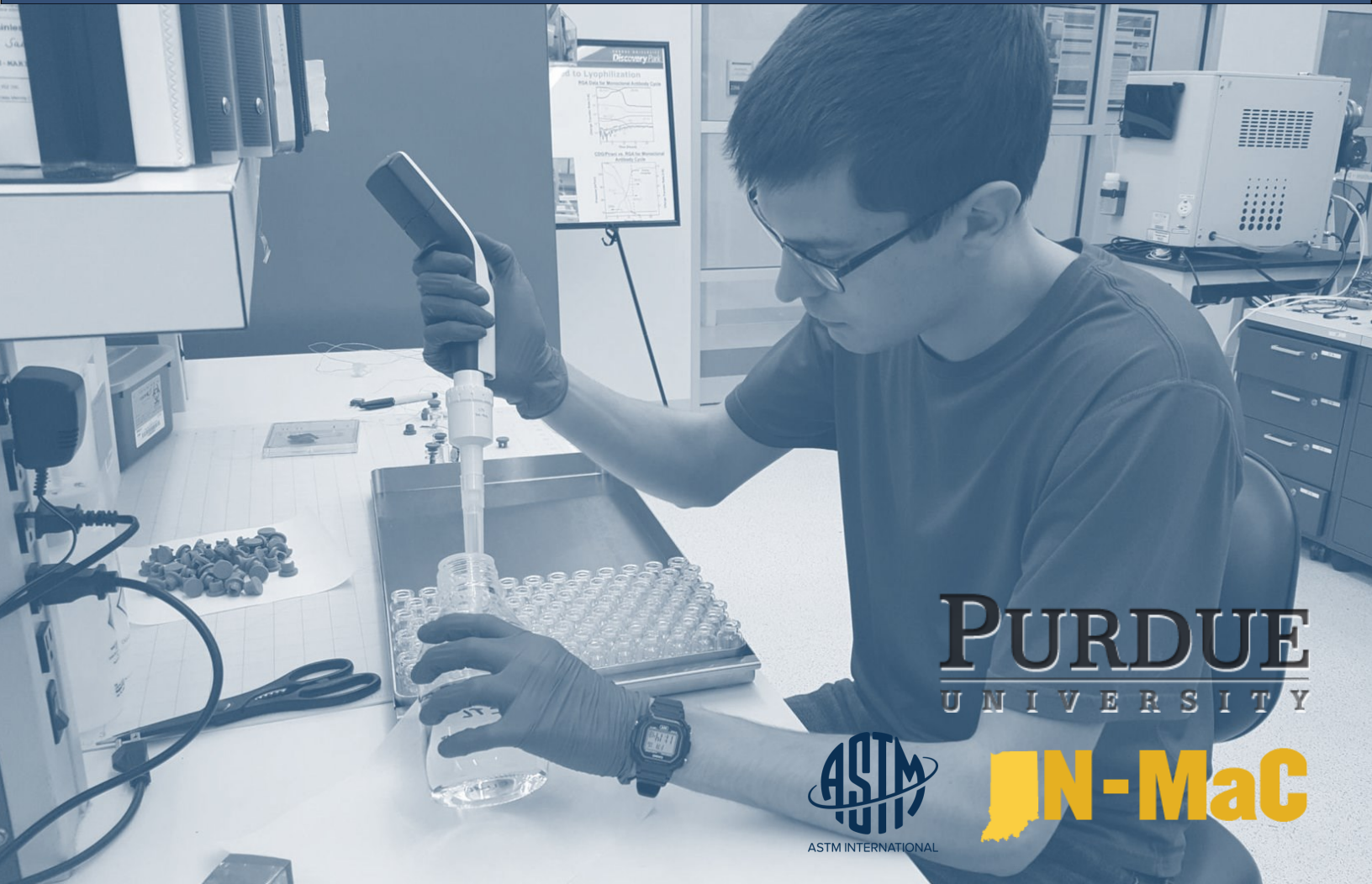


LYO
hub.org

Advanced Lyophilization
Technology Consortium

ANNUAL REPORT

2018



PURDUE
UNIVERSITY

ASTM
ASTM INTERNATIONAL

IN-MaC

Table of Contents

Directors' Message	3
LyoHUB Membership	4
Affiliations	5
Awards/Grants	6
Meetings	6
Special Presentations	7
Industry Visits/Conferences	8
Special Projects	9
LyoHUB Lyophilization Technology Roadmap.....	10
Best Practices	11
LyoLaunchPad	11
Demonstration Facility.....	12
Education/Training	14
LyoHUB in the News.....	15
Contacts	15

DIRECTOR'S MESSAGE



Greetings from LyoHUB!

This has been a year of growth, accomplishment and increasing impact for LyoHUB. We welcomed **three new member companies** in 2017, expanding our expertise in lyophilization process modeling software and pharmaceuticals. Another major pharmaceutical company joined in April 2018, bringing the current number of members to **16**. We completed, published and celebrated our **lyophilization technology roadmap** in 2017, the culmination of a two-year effort. We thank Steve Shade for leading the roadmap process and all of the 100+ contributors! The roadmap will guide the journey of advancing lyophilization through small steps in the right direction and, hopefully, some giant leaps.

Throughout the year, we offered **workshops and training** on lyophilization technologies, and disseminated new ideas through webinars. We're intent on advancing lyophilization through **research**; we've received a selection notice from the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL) to develop atmospheric spray freeze-drying. Our Demonstration Facility completed nearly 180 lyophilization runs in 2017, and we worked toward our first LyoHUB-sponsored, pre-competitive collaborative research projects. In **outreach and engagement**, we hosted 30 industry visits to our facility, made seven on-site visits to various companies and gave presentations at various regional, national and international conferences. We also hosted our first LyoHUB visiting scholar. In response to member priorities, we're committed to disseminating **best practices** in lyophilization and enhancing our **regulatory interface**. We're pleased to report that our first best practices paper published in early 2017 has already been widely disseminated with over 3,800 downloads. LyoHUB also joined the American Society for Testing and Materials (ASTM) last year, providing a route to convert best practices papers into consensus standards and led the effort to establish the **ASTM E55.05 Subcommittee on Lyophilization**. All this activity put us in the news, too: LyoHUB was featured in more than a dozen news articles in 2017.

A big "thank you" to our member companies, their scientists and engineers, our LyoLaunchPad participants, Purdue University, the University of Connecticut, and our students and postdocs for helping make 2017 a success for LyoHUB. We are especially grateful to Jen Gray for her central role in keeping everyone connected and making the hub move smoothly. We look forward to continuing to work with all of you to advance lyophilization technology in 2018, and in the years to come.

With best wishes,

Alina Alexeenko and Liz Topp
Co-Directors

MEMBERSHIP

LyoHUB industry membership expanded in 2017 from 12 companies to 15 with the addition of *Siemens PLM Software*, *Fresenius Kabi* and *Bristol-Myers Squibb*, and from 15 members to 16 in 2018 with *Abbott* joining!



Freeze Drying Solutions

Member Since 2014



Member Since 2014



Member Since 2015



Member Since 2015



Member Since 2015



Member Since 2016



Member Since 2016



Member Since 2016



Member Since 2016



Member Since 2016



Member Since 2016



Member Since 2016



Member Since 2017



Member Since 2017



Member Since 2017



Member Since 2018

AFFILIATIONS



In 2017, LyoHUB became an official Purdue University Center and joined IN-MaC as a SME focused industrial consortium <http://www.purdue.edu/in-mac>

IN-MaC utilizes integrated partnerships among industry, academia, and government to address education, workforce, new technology adoption, and research for future competitiveness. It strives to transfer technology, research and information to industry quickly in order to remain competitive.



LyoHUB became a member of the American Society for Testing and Materials (ASTM) International <https://www.astm.org/> in 2017 and led the initiative to establish the E55.05 Committee on Lyophilization

E55.05 Lyophilization subcommittee of E55 committee: The scope of this sub-committee is to develop, disseminate and educate standard practices and guides relevant to lyophilization of parenterals and other pharmaceutical and biological products. The work of the subcommittee will cover all aspects of process and equipment design, operation and qualification, quality assessment, process understanding and control. <https://www.astm.org/COMMITTEE/E55.htm>

Committee E55 on Manufacture of Pharmaceutical and Biopharmaceutical Products

Staff Manager: [Travis Murdock](#) 610-832-9826

Subcommittees and Standards

Standards under the jurisdiction of E55

Each main committee in ASTM International is composed of subcommittees that address specific segments within the general subject area covered by the technical committee. Click on the subcommittee links below to see the title of existing standards for each subcommittee. Then, click on the resulting titles to see the standard's scope, referenced documents, and more.

- [E55.01](#) Process Understanding and PAT System Management, Implementation and Practice
- [E55.03](#) General Pharmaceutical Standards
- [E55.04](#) General Biopharmaceutical Standards
- [E55.05](#) Lyophilization

E55.05 INAUGURAL CHAIRS



Dr. Arnab Ganguly
Chair
IMA Life



Dr. Jim Searles
Vice-Chair
Pfizer

AWARDS/GRANTS



MAX85

In March 2018, a proposal submitted by Drs. Alexeenko, Topp and Zhou to NIIMBL received a selection letter. The 18 month, \$1.6 million project, "NIIMBL PC-1 RFP: The Atmospheric Spray Freeze Drying Project", will be led by Purdue University in collaboration with LyoHUB member Roche Genentech, as well as Aerosol Therapeutics, Merck & Co. and Janis Research Company. "This project further develops Atmospheric Spray Freeze Drying as a new, disruptive technology to dry solutions of heat sensitive pharmaceutical products. By employing advanced sensor technologies, heat and mass transfer modeling and biomolecule stability studies, the project will 1) advance the second-generation laboratory-scale ASFD equipment to a third generation pilot machine over 18 months with a target increase in capacity of x20; and 2) document preservation of model biomolecules with ASFD and compare ASFD powders to the traditional lyophilization/ freeze-drying and spray drying methods. This Project will validate ASFD advantages over current freeze-drying quantitatively to prepare for commercialization via testing for product quality, yield, and activity." The work on this project will be completed in the LyoHUB demonstration facility. This disruptive technologies proposal applies directly to the equipment priorities which emerged during the LyoHUB roadmapping process.

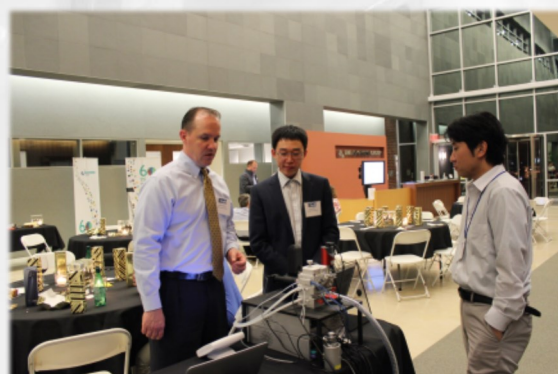


MEETINGS

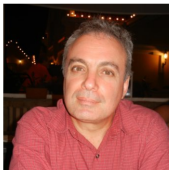


The LyoHUB 2017 Annual Meeting was held at the McCrone Group's building in Westmont, Illinois on Wednesday, April 12, 2017.

A tour of their lovely facility and interesting microscope museum were featured.



SPECIAL PRESENTATIONS



Dr. Ali Afnan
 President, Step Change Pharma, Inc.

Senior Staff Fellow at FDA from 2003-2010
 Senior member of core PAT Policy team and co-author of PAT Guidance; member of team drafting and finalizing Process Validation Guidance.
 Science and Policy advisor to the director of the Office of Pharmaceutical Science responsible for development and implementation of policies related to review of New, Generics and Biotechnology products; development and establishment of FDA Guidances; FDA representative to industry, trade associations.
 Collaborating with consensus standards organizations, and establishing technical committee E55 in ASTM.

"Consensus Standards 101" Webinar for LyoHUB Members

July 20, 2017

Potential Lyo-Hub Collaborative Project?

Vial "Fogging": Causes and Cures

Steve Nail
 October, 2017

December 21, 2017

Potential Lyo-Hub Collaborative Project?

Is There a Default "Stopper-of-Choice" for Freeze-Dried Drug Products?

Steve Nail
 October, 2017

November 16, 2017

ASTM INTERNATIONAL
 Helping our world work better

Technical Committee E55 Manufacture of Pharmaceutical and Biopharmaceutical Products

Travis Murdock
 Manager, Technical Committee Operations
 E55 Staff Manager

www.astm.org

January 25, 2018

Lyophilization in Microgravity

Presentation by
 Jeremy Hinds, Eli Lilly & Company

March 22, 2018

Centro de Química Estrutural
 Instituto Superior Técnico
 Universidade de Lisboa
 Portugal

New Tools for Prediction of Stability of Freeze Dried Products - A Cold Perspective

Miguel A. Rodrigues
 Centro de Química Estrutural
 Instituto Superior Técnico
 University of Lisbon
 Lisboa, Portugal
 miguelrodrigues@tecnico.ulisboa.pt

Co-founder of Smartfreez
 www.smartfreez.com

February 22, 2018

INDUSTRY VISITS/ CONFERENCES



MAX85

LyoHUB/BPOG Joint Session: September 13, 2017 in Cambridge



Industry Visits to LyoHUB:

- Aerosol Therapeutics, April 2017
- Freund Vector, April 2017
- NIIMBL, May 2017
- Massachusetts Institute of Technology, June 2017
- Abbott Laboratories, July 2017
- Genentech, July 2017
- Eli Lilly, July 2017
- AbbVie, July 2017
- Fresenius Kabi, July 2017
- Vitacyte, July 2017
- Singota, July 2017
- IMA Life, July 2017
- Northwestern University, July 2017
- SP Scientific, July 2017
- McCrone Group, July 2017
- Siemens PLM, July 2017
- Metler Toledo, July 2017
- AbbVie, August 2017
- University of Connecticut, July 2017
- Baxter, July 2017
- Vivolac Cultures Corporation, July 2017
- IMA Life, August 2017
- Texas A&M University, September 2017
- Greene Tweed, October 2017
- IN-MaC, October 2017
- Cook Pharmica, October 2017
- Daiichi-Sankyo, October 2017
- Taylor University, October 2017
- Nipro PharmaPackaging, November 2017

Industry Visits to LyoHUB (Continued):

- Pfizer, December 2017
- CASIS, February 2018
- Commissioning Agents, February 2018
- Fresenius Kabi, February 2018
- AbbVie, February 2018
- Global Pharmaceutical Manufacturing Leadership Forum (GPMLF) , March 2018
- AbbVie, March 2018
- Baxter, March 2018
- Eli Lilly, March 2018
- Pancopia, March 2018

Conference Presentations or Posters:

- AAPS, May 2017
- ISL-FD Cuba, September 2017
- ISL-FD East Coast, September 2017
- IN-MaC Manufacturing Forum, October 2017
- CPPR Meeting, October 2017
- PepTalk 2018, January 2018
- Peck Symposium, March 2018

LyoHUB Visits to Companies:

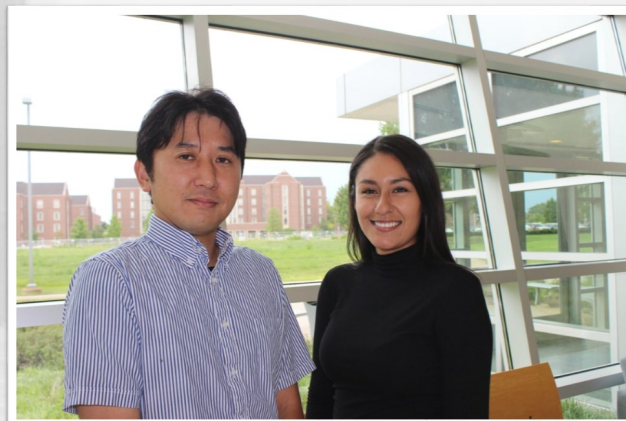
- AbbVie, May 2017
- Genentech, May 2017
- Pfizer, September 2017
- Vitacyte, November 2017
- Fresenius Kabi, November 2017
- AbbVie, January 2018
- Allergan, January 2018

SPECIAL PROJECTS



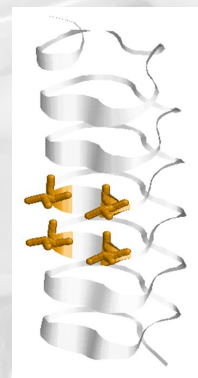
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LyoHUB welcomed Dr. Tatsuhiko Kodama, a 1-year visiting scholar from Daiichi-Sankyo Co. (Japan), and sponsored Yasmeen Solano, a summer visiting student from Cal State Los Angeles who collaborated on a LyoHUB-sponsored project, “**Effects of Antifreeze Protein on the Crystallization of Common Lyoprotectants in Freeze-dried Solids**”. *Industry Mentor: Dr. Evgenyi Shalaev, Allergan, Faculty Mentor: Dr. Xin Wen, Cal State LA*



Background: Antifreeze Proteins (AFPs)

- Found in fish and insects for extreme cold weather protection.
- Lower freezing temperature of body liquids by a non-colligative way without affecting the melting point.
- AFPs control ice crystallization through specific binding to ice crystals and inhibiting the growth of the ice. As a result, a gap is created between the freezing and melting temperatures, a phenomenon known as thermal hysteresis.
- AFPs can also control the crystallization of other industrial important compounds, such as trehalose and mannitol.
- Potential industrial use.



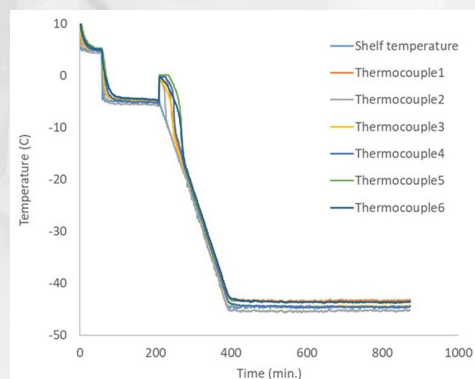
Dr. Kodama also conducted other research such as the project below:

Effect of Ice Fog-Controlled Ice Nucleation on Solution Weight

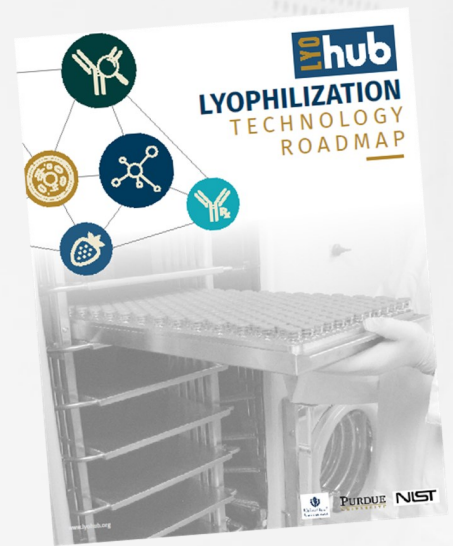
- Ice fog method provides control of ice nucleation temperature, improving uniformity in cake resistance across a vial batch, higher sublimation rates and elegant cake.
- Question: does ice fog add any weight to the product in vials?
- Purpose: Investigate the weight changes for solution in glass vials with and without ice fog nucleation.

Full report is on the LyoHUB website

Typical product temperature profile during freezing process with controlled nucleation



LYOHUB LYOPHILIZATION TECHNOLOGY ROADMAP



The NIST-sponsored Lyophilization Technology Roadmap was published and distributed in September 2017. Since September 12, it has been downloaded 691 times. It is available to all on the LyoHUB website at

<https://pharmahub.org/groups/lyo/roadmap>



Dr. Michael Pikal provided remarks at the Roadmap launch.



Please join us as we
CELEBRATE the
**LyoHUB Lyophilization
Technology Roadmap!!**

What: Reception to celebrate and distribute the roadmap!
When: Tuesday, September 12, 2017
Time: Immediately following the ISL-FD meeting, approx. 5:30 PM
Where: Pfizer (610 Main St, Kendall Square, Cambridge, MA)

If you are planning to attend and are NOT attending the ISL-FD meeting, please let Jen Gray know (if you haven't already) at gray160@purdue.edu

We hope to see you on Tuesday, September 12th!
THANK YOU, roadmap contributors!



Dr. Alina Alexeenko introduces the Roadmap



Dr. Stacy Springs provided remarks at the Roadmap launch from perspective of NIIMBL.



There was great media interest, resulting in coverage such as this Inside Indiana Business Video:

<http://www.insideindianabusiness.com/Clip/13726100/lyohub-trying-to-advance-freeze-drying#.WcADDbYtDWk.twitter>

BEST PRACTICES



LyoHUB published our first lyophilization best practices paper, **“Recommended Best Practices in Instrumentation Process Monitoring in Pharmaceutical Freeze Drying”**. It is available with open access and has received over 3,800 downloads since February 2017:

<http://link.springer.com/article/10.1208/s12249-017-0733-1>



Best Practices Papers in Progress:

Scale Up and Tech Transfer

Led by *Serguei Tchessalov and Bakul Bhatnagar (Pfizer)*

Equipment Qualification

Led by *Arnab Ganguly (IMA Life)*



MILLROCK TECHNOLOGY
INNOVATIVE BY DESIGN
millrocktech.com

Recommended Best Practices in Freeze Dry Metrology WEBINAR, Presented by Dr. Steven Nail, Baxter Pharmaceuticals
Mar 30, 2018 2:00 PM in Eastern Time (US and Canada)

As part of a LyoHub initiative, a consortium of experts, lead by Dr. Steven Nail, has developed information on best practices in monitoring of product status during pharmaceutical freeze drying. This webinar will cover the main recommendations of this group for both laboratory and production freeze dryers. Included will be topics such as the difference between thermocouples and resistance temperature detectors.....

LYOLAUNCHPAD



New LyoLaunchPad projects:

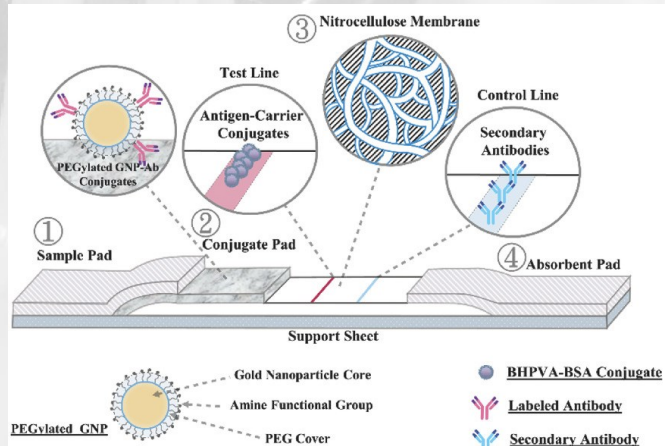
Corvidia Project: Preparation of lyophilized formulation for an amphipathic peptide

Dr. Miko Cakmak, Purdue Materials & Mechanical Engineering: Freeze drying of tough multiple-network hydrogels



Published Paper—LyoLaunchPad Project

Aminolated and Thiolated PEG-Covered Gold Nanoparticles with High Stability and Antiaggregation for Lateral Flow Detection of Bisphenol A



Lin-Kai Lin, Aytakin Uzunoglu, Lia A. Stanciu
First Published: 27 December 2017
<https://doi.org/10.1002/sml.201702828>

DEMONSTRATION FACILITY

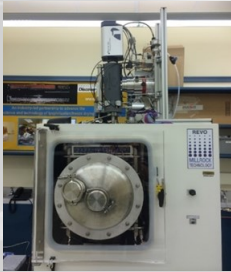
In February 2016, LyoHUB opened the **Lyophilization Technology Demonstration Facility** located in the Birck Nanotechnology Center at Purdue Discovery Park. The facility, where collaboration on breakthrough technologies can be advanced with a goal of accelerating adoption and decreasing time to market, is equipped and supported by LyoHUB's industry members. The facility also offers various hands-on training opportunities for academic and industry users. Full equipment listings and capabilities can be found on the LyoHUB website at <https://pharmahub.org/groups/lyo/demofacility>



LyoHUB demo facility is located in Birck Nanotechnology Center, Room 2261.



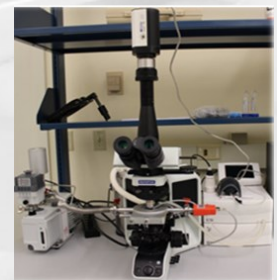
REVO lyophilizer with controlled nucleation and in-situ mass spectrometer.



LYOSTAR™ 3 Freeze-Dryer with controlled nucleation and mass flow meter



Development Freeze-Dryer/ Lyophilizer MICROFD



McCrone Freeze-Drying Microscope

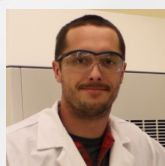
Tools available on Website:

- LyoCalculator <https://pharmahub.org/resources/lyocalculator>
- Lyo Chamber Pressure Variation Calculator <https://pharmahub.org/resources/pressurevar>
- LyoHUB Best Practice Paper, Recommended Best Practices for Process Monitoring in Pharmaceutical Freeze Drying <http://link.springer.com/article/10.1208/s12249-017-0733-1>
- LyoHUB Lyophilization Technology Roadmap https://pharmahub.org/groups/lyo/lyohub_roadmapping
- Presentations, such as "Developing Transferable Freeze Drying Protocols using Accuflux® and a MicroFD®" <https://pharmahub.org/groups/lyo/tools>

CONTACTS



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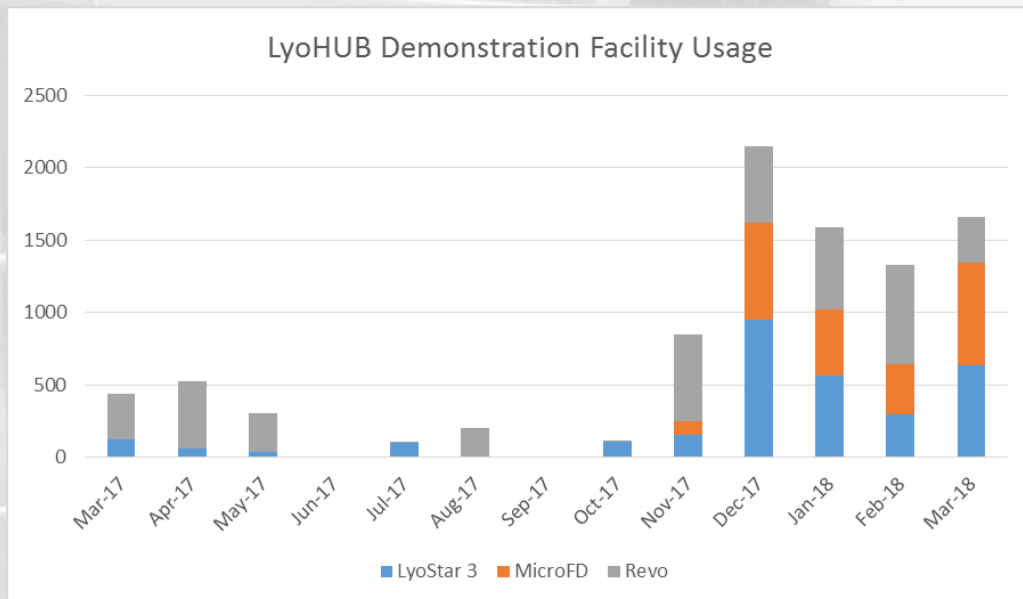


Drew Strongrich
Super User
astrongr@purdue.edu



Karthik Chandrababu
Super User
balakrk@purdue.edu

DEMONSTRATION FACILITY



Total Number of Lyophilization Runs:
 (2/26/16-3/26/17): **87**
 (3/1/17-3/30/18): **178**

Average Time for Lyophilization Run (in hours):
 (2/26/16-3/26/17): **33.25**
 (3/1/17-3/30/18): **51.83**

Total Lyo Run Time:
 (2/26/16-3/26/17) **2,971.37 hours**
 (3/1/17-3/30/18) **9,227.17 hours**

New Projects in the LyoHUB Demonstration Facility:

- Wireless pressure sensor characterization (Purdue AAE)/National Science Foundation (NSF) project
 - ◊ Real-time in-situ ambient gas pressure and temperature monitoring for enhanced process control and sublimation rate quantification.
- RGA analysis of drying performance in co-solvent formulations/Center for Pharmaceutical Processing Research (CPPR) and Baxter project
 - ◊ Quantification of the relative extraction rates between water and a co-solvent under various process conditions. Results are directly correlated with dried cake properties (both amorphous and crystalline).
- Lyophilization of Anammox bacteria mix (Pancopia/NASA)
 - ◊ Optimization of freeze-drying formulation and process for biological wastewater treatment at the space station



Alina Alexeenko (Purdue), Bill Cumbie (Pancopia), Karthik Chandrababu and Drew Strongrich (Purdue)

New Users Trained on Lyophilization Equipment from March 2017-2018

Name	Affiliation	Name	Affiliation
Tatsuhiro Kodama	LyoHUB/Visiting Scientist from Daiichi-Sankyo	Andrew Karaki	Medicinal Chemistry & Molecular Pharmacology, Purdue
Rishabh Tukra	IPPH/Topp lab	Rajashekar Kammari	IPPH/Topp lab
Monika Lavan	IPPH/Knipp lab	Mohamed AbouGhaly	IPPH/Topp lab
Arjun Kalra	IPPH/Li lab	Yasmeen Solano	LyoHUB Summer Intern from California State, LA
Harshil Renawala	IPPH/Topp lab	Lia Bersin	IPPH/Topp lab
Iris Cho	IPPH/Topp lab	Tong Zhu	AAE/Alexeenko lab
Maie Taha	IPPH/Yeo lab	Gayathri Shivkumar	AAE/Alexeenko lab
Sugandha Saboo	IPPH/Taylor lab	Sharad Mangal	IPPH/Zhou lab
Dana Moseson	IPPH/Taylor lab	Nivedita Shetty	IPPH/Zhou lab

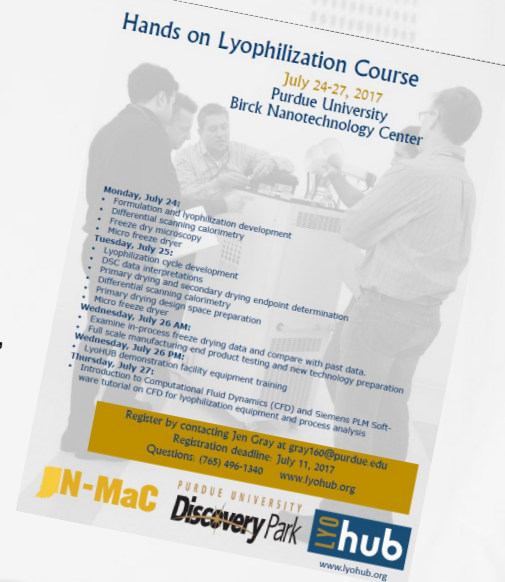
EDUCATION & TRAINING

LYO101 Hands-on 2.5-day course July 2017 for Purdue students/postdocs taught by Baxter Biopharma team (Greg Sacha, Lindsay Wegiel, Steve Nail) using equipment in LyoHUB demo facility

1.5-day workshop on new technologies and modeling tools for Purdue and industry users

Participants:

- **15 students and postdocs** - sold out in 1 hour
- **20 industry participants:** Eli Lilly (3), Genentech, Vitacyte (3), Vivolac, IMA Life, Singota, Fresenius Kabi (2), AbbVie (2), SP Scientific, Baxter (3), Pfizer (2), NW Peptides
- **2 Equipment demos:** McCrone and Metler Toledo
- **Software demo:** Siemens StarCCM



LYO101: Formulation and Process Development for Lyophilization taught by industry experts offered to Purdue students and staff and filled to capacity within minutes of registration opening.

Fundamentals of Freeze Drying, A Short Course offered at Allergan in January 2018

The course objective is to expand your knowledge base and improve your critical thinking skills in the science and technology of freeze drying. Special emphasis is given to the primary drying phase of the freeze drying process. The focal point of the course is for participants to use a Lyo-Calculator Excel spreadsheet to construct a graphical design space and identify optimum primary drying process conditions.

Steve Nail, Baxter Global Science and Technology

Introduction

1. Advantages and limitations of freeze drying
2. Product quality attributes
3. Process overview

The Freezing Process

1. Supercooling and ice nucleation
2. Characterization of freezing behavior
3. Establishment of upper product temperature limit during primary drying

Primary Drying

1. Heat transfer considerations
2. Mass transfer considerations

Understanding equipment capability

1. Factors that could limit equipment performance
2. Sonic velocity and "choked" flow
3. Measuring equipment capability

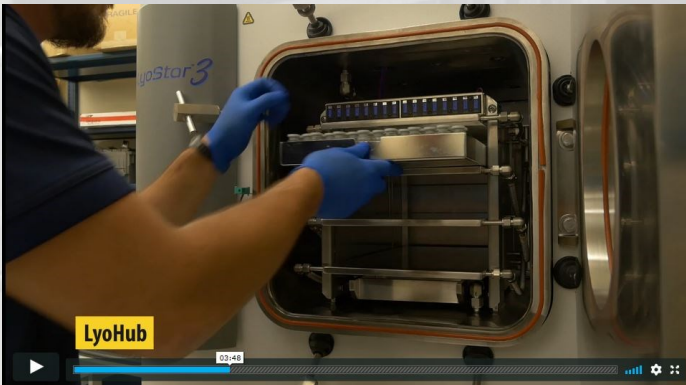
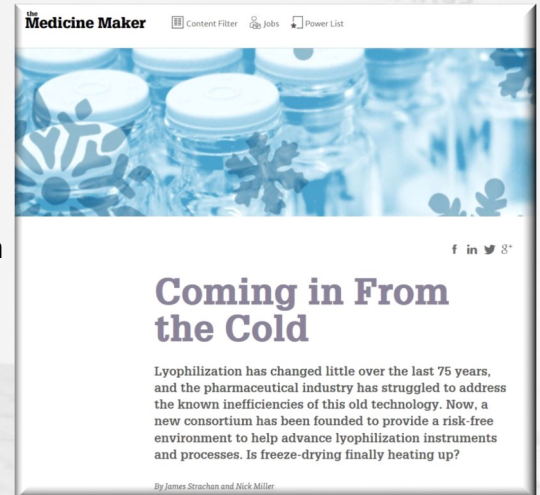
Brief description of secondary drying

Putting it all together – constructing a graphical design space



LYOHUB IN THE NEWS

- December 4, 2017 **Medicine Maker** “Coming in From the Cold”
- October 26, 2017 **IN-MaC website** featured in video
- September 14, 2017 **Inside Indiana Business** “LyoHUB tries to advance lyophilization”
- September 11, 2017 **Purdue News** “Key process to be modernized in production of lifesaving drugs, food preservation”
- September 11, 2017 **Phys.org** “Key process to be modernized in production of lifesaving drugs, food preservation”
- September 12, 2017 **Quality Assurance Magazine** “Purdue University Tackles Modernization of Lyophilization for Food and Drugs”
- January 18, 2019 **PhamTech.com** “Experts Partner to Optimize Lyophilization”
- January 18, 2018 **BioSpace** “Purdue Research Hub to Transform Freeze-Drying Process Used to Make Lifesaving Drugs, Preserve Food”
- January 18, 2018 **Pharmaceutical Manufacturing** “Purdue Research Hub looks to make Lyophilization Obsolete”
- January 18, 2018 **WGFA Radio** “Purdue research hub to transform freeze-drying process used to make Lifesaving Drugs, Preserve Food”



- January 18, 2018 **The Exponent** “Purdue research hub to transform freeze-drying process used to make Lifesaving Drugs, Preserve Food”
- January 19, 2018: **Purdue News** "Purdue research hub to transform freeze drying process used to make lifesaving drugs, preserve food"
- January 29, 2018 **AgFuse** “Purdue research hub to transform freeze drying process used to make lifesaving drugs, preserve food”
- February 19, 2018 **Purdue Exponent** "Purdue-based consortium works on improving freeze-drying technology"

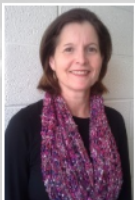
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Annual Member Meeting, April 2017, Chicago



www.LyoHUB.org



<https://twitter.com/lyohub>