How to use PharmaHUB

www.PharmaHUB.org

A source for supplemental pharmaceutical course material

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2012 ASEE Summer School for Chemical Engineering Faculty

Orono, ME
July 2012

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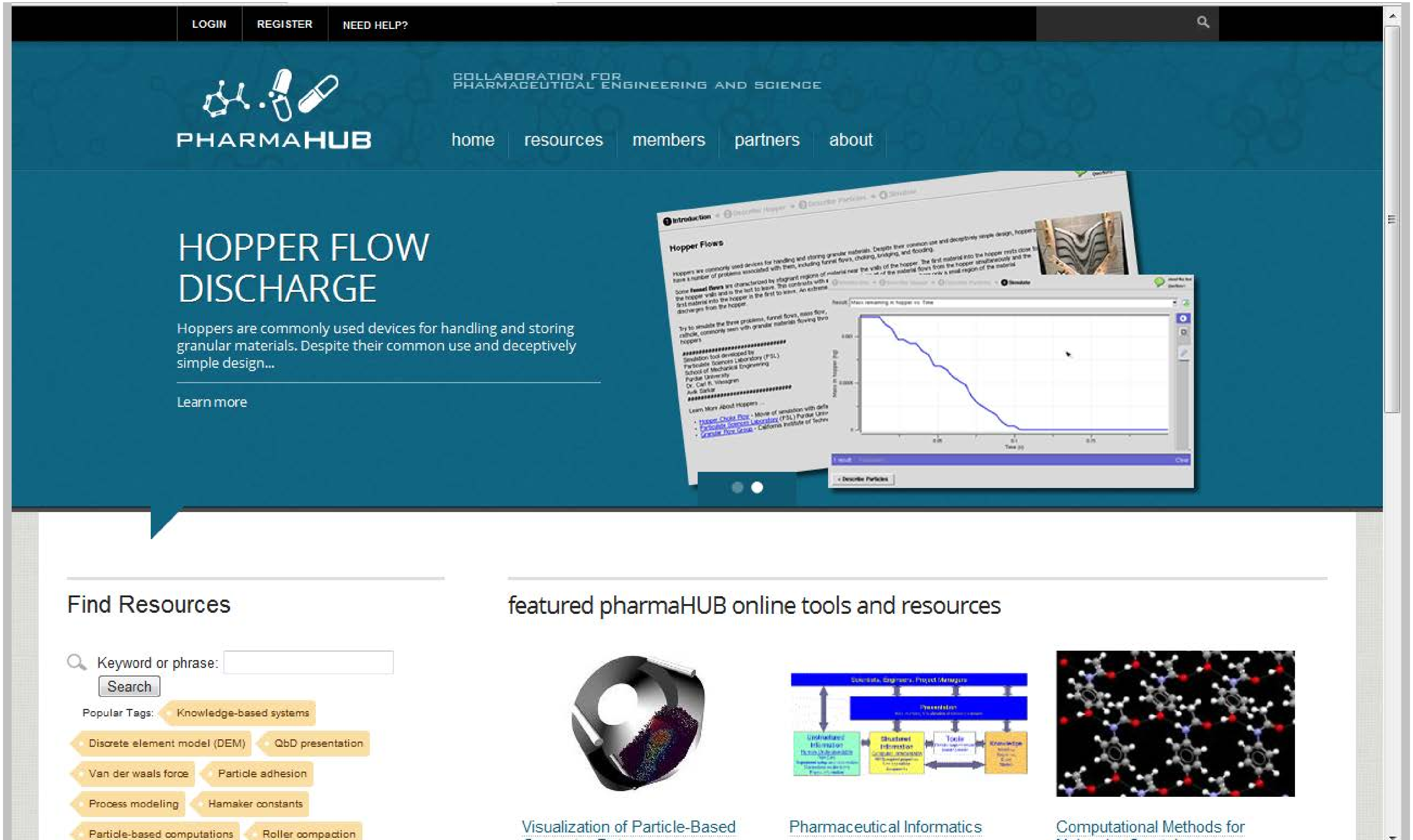
www.pharmahub.org



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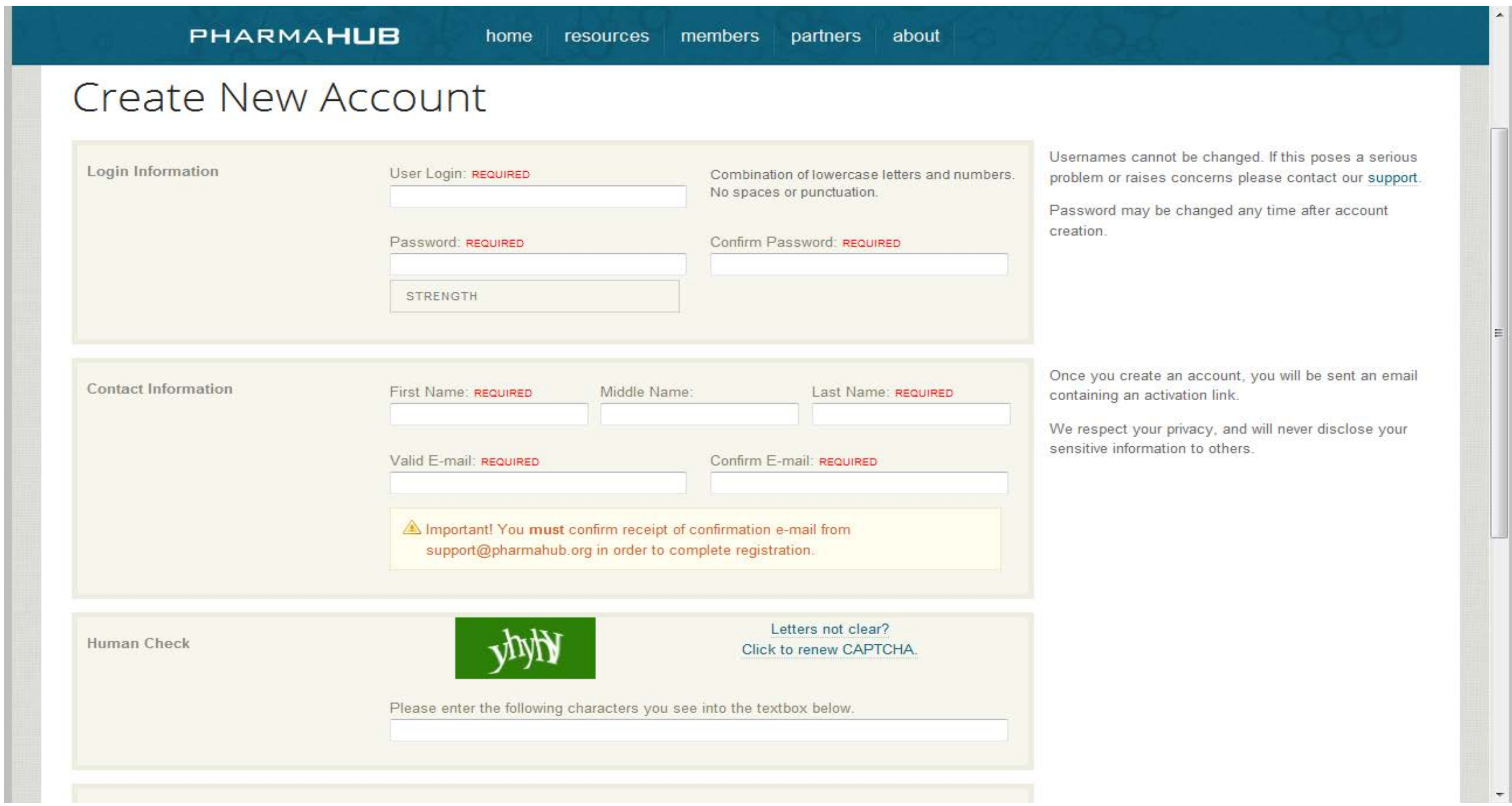
Register for an account

Registration on PharmaHUB is FREE!



- To access the materials available on PharmaHUB, move mouse over "Resources" in the main toolbar

- Here you can access all of the resources available on PharmaHUB

- Each of the links provides access to different resources

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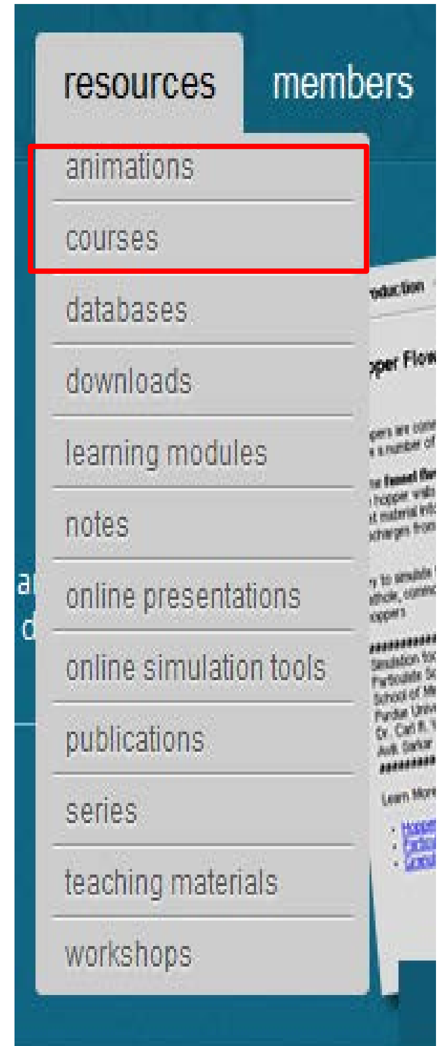
Resources

- Animations
  - Animations for visualizing particle motion
  - A video lecture on soft particle discrete element method of modeling

- Courses
  - Introduction to API process development
  - Graduate level computation methods for molecular crystals
  - An introduction to the discrete element method of modeling
  - Building statistical models and applying this to various experiments



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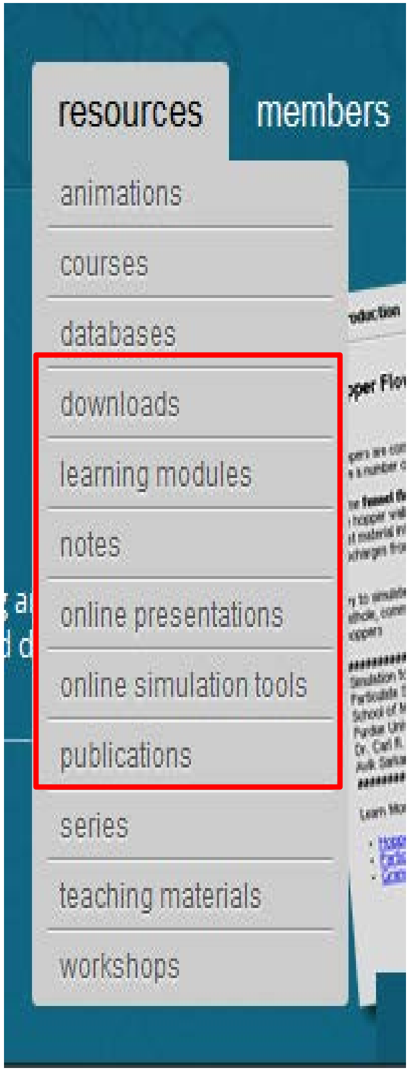
Resources

- Downloads
  - Web browser plug-in for uploading presentations
  - ParticleVis: software for visualizing particle motion
  - A tablet compaction scale-up program
  - ViewStruct: software for visualizing crystal structures
- Online Presentations
  - Presentations uploaded for a class or project
  - Some presentations can be viewed online with a presenter and are timed
  - Others can be downloaded as a Powerpoint or pdf
- Learning Modules
  - None available at this time
- Publications
  - Journal articles
  - Presentations
  - General information



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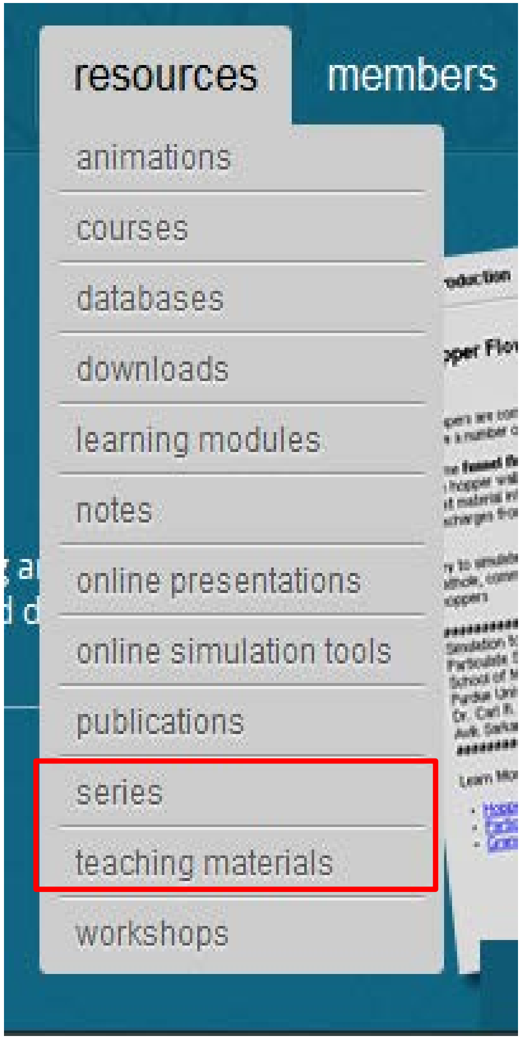
Resources

- Series
  - These series contain all resources on PharmaHUB related to specialized topics
  - Particle and thin film adhesion
  - Pharmaceutical informatics
  - Purdue ontology for pharmaceutical engineering
    - The body of pharmaceutical data generated by Purdue
  - Visualization of particle-based computer data

- Teaching Materials
  - Various teaching materials used in:
    - Courses
    - Series

- Workshops
  - None available at this time



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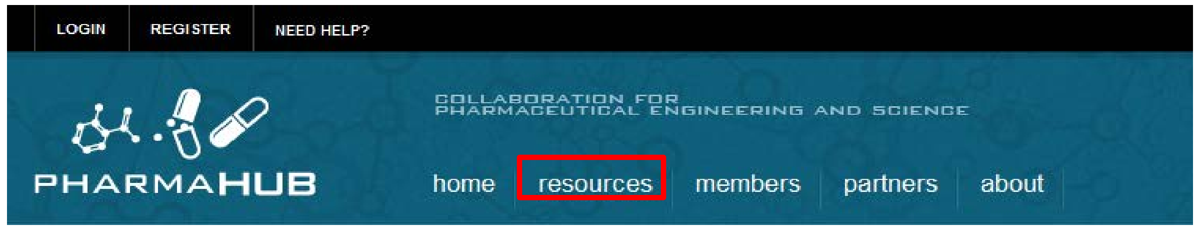
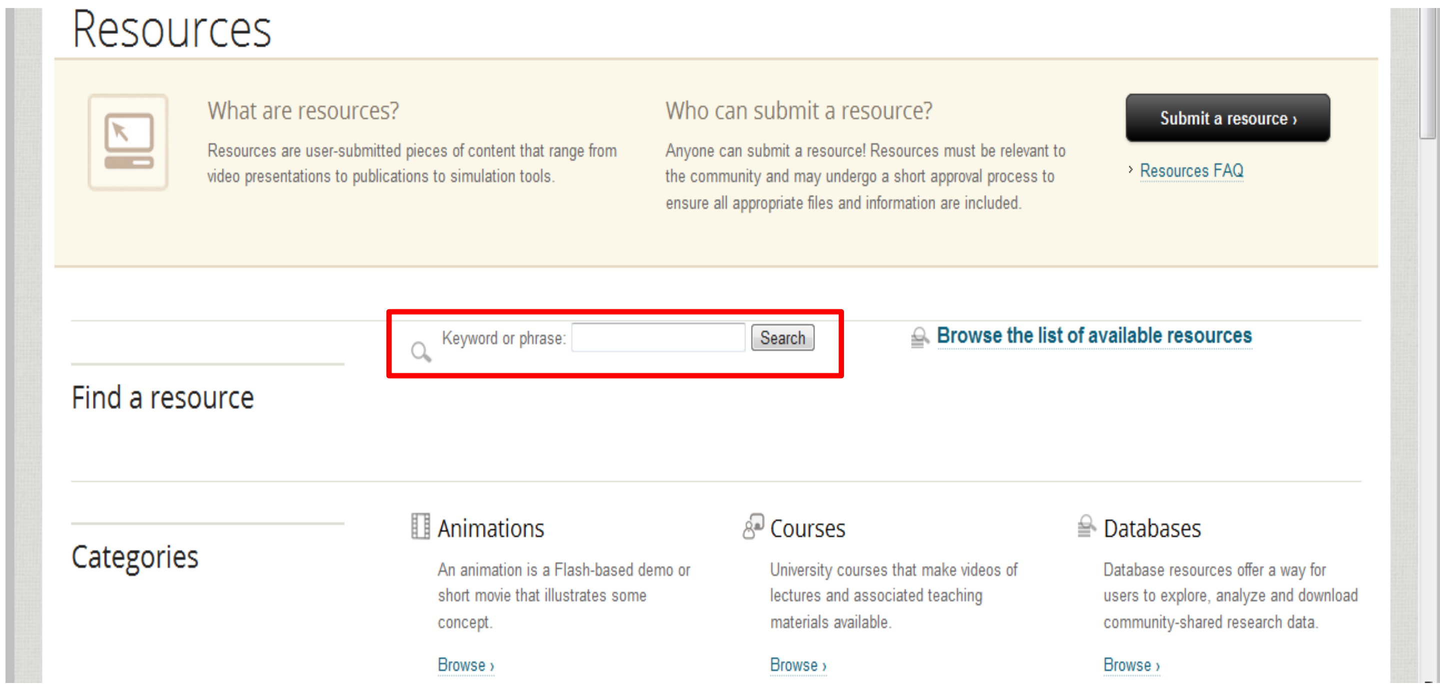
Accessing Resources

- Left click on "Resources"



- Search for resources or select from the different "Categories"



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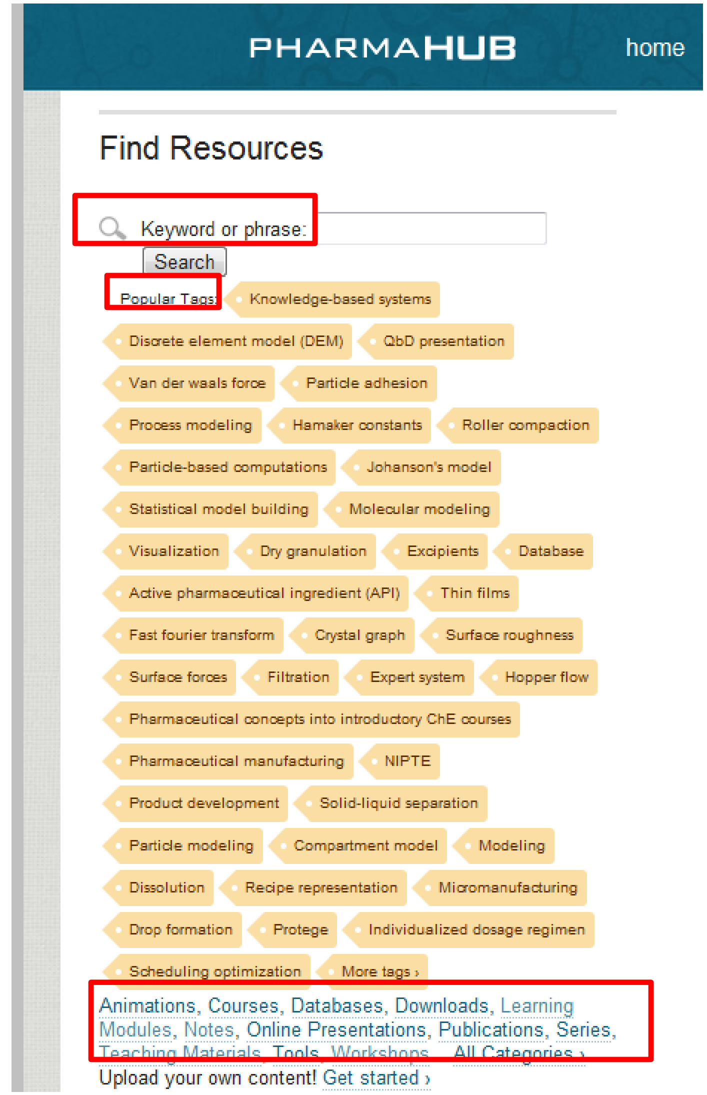
Another Way to Access Resources

- On home page, lower left hand corner has a small resource section
- Search for resources, select a topic in popular tags, or select a category



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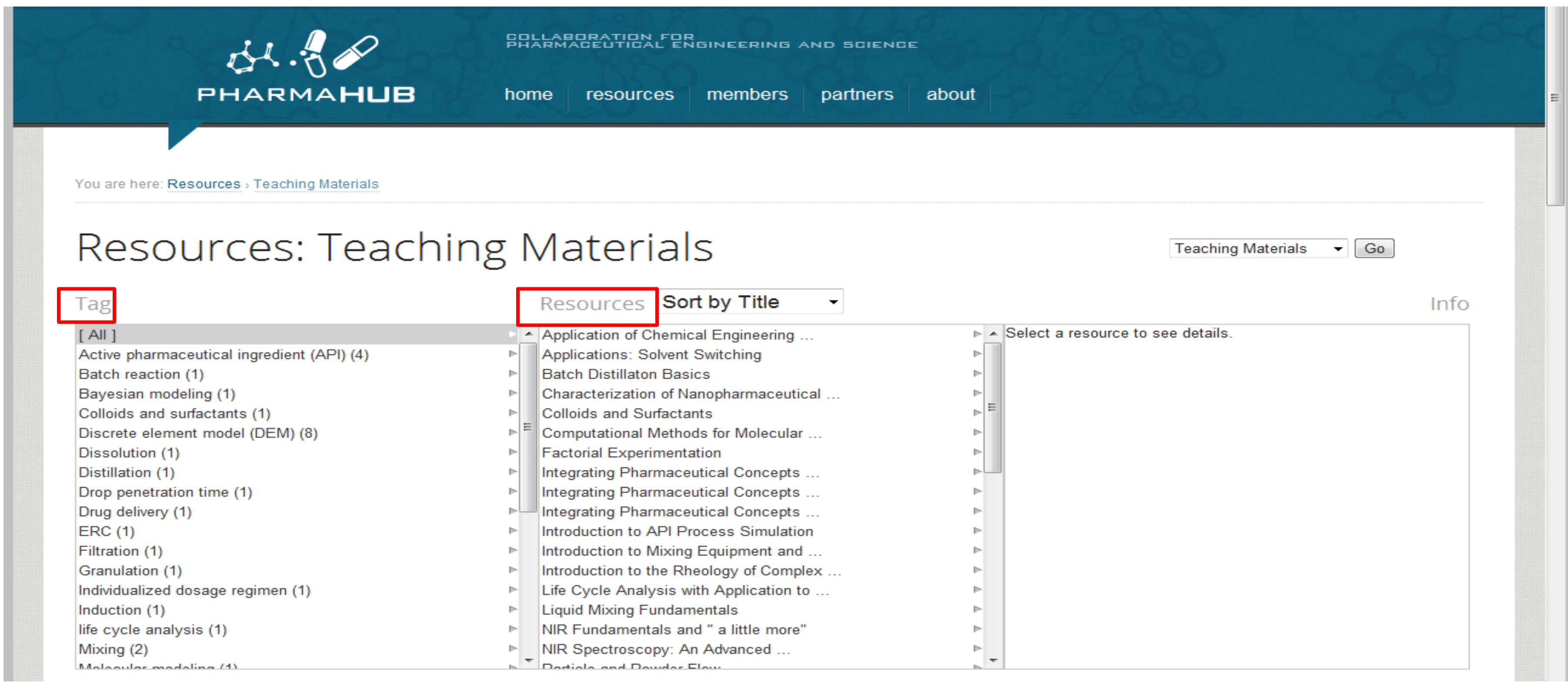
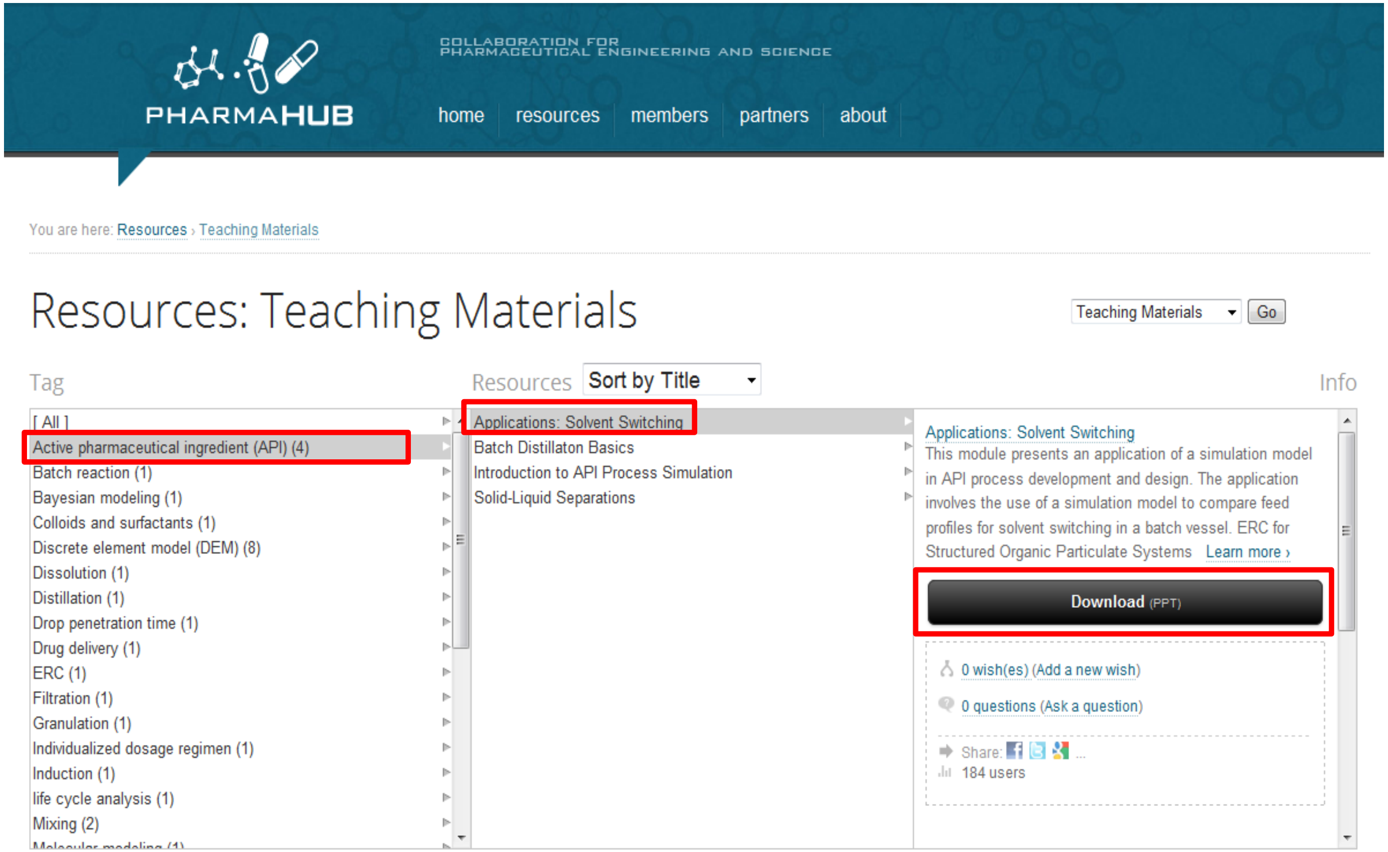
Another Way to Access Resources

- Items in the “Tag” box refer to various categories
- Items in the “Resources” box refer to different topics within each category



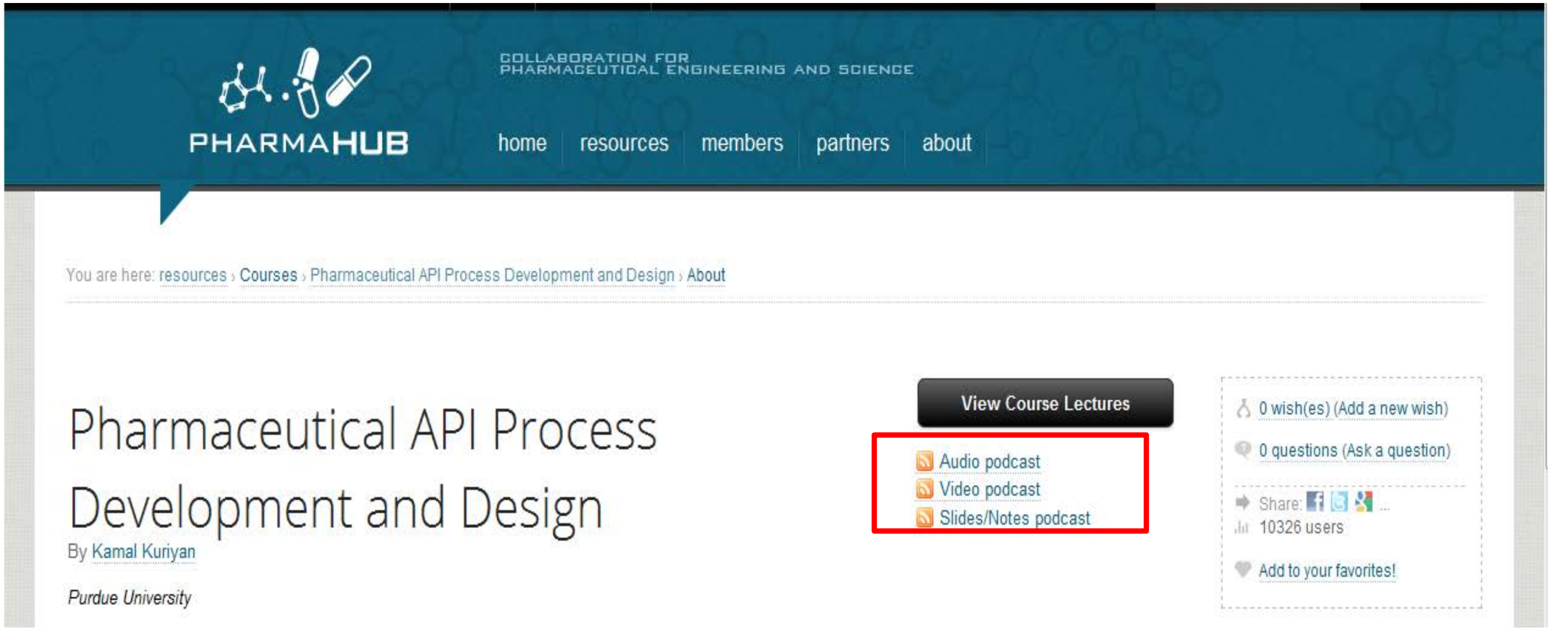
Another Way to Access Resources

- Select an item under "Tag"
- Select an item under "Resources"
- You will be able to access the material by clicking the "Download" link



Another Way to Access Resources

- Can access certain resources through podcasts
  - Video podcasts
  - Audio podcasts



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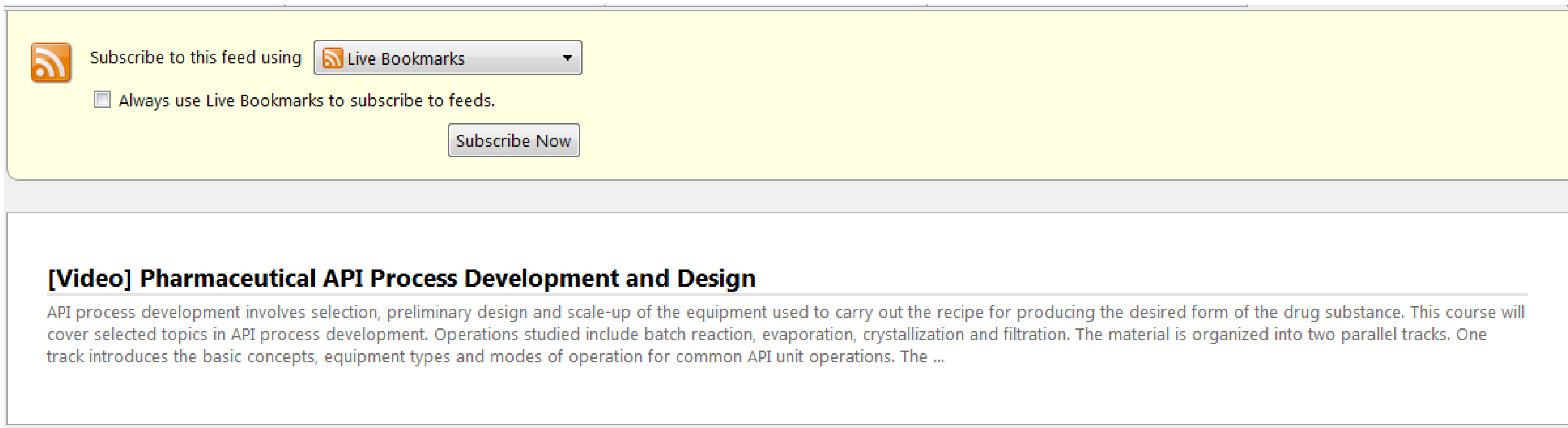
Another Way to Access Resources

- When selecting podcasts, must subscribe to content



- When subscribed, the you will be able to access content in the Bookmarks Toolbar

- All checked podcasts are empty at the moment

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Course Materials

- Mass & Energy Balances
- Fluid Transport
- Heat Transfer
- Thermodynamics
- Kinetics & Reaction Engineering
- Separations
- Process Design
- Introduction to Pharmaceutical Engineering
- Pharmaceutical Engineering Unit Operations
- Crystallization
- Particulate Processing

Course Materials

	Intro Chem Eng.	Fluid Transport	Unit Ops.	Seps.	Intro to Pharma	Heat Transfer	Crystallization	Advanced Topics	Design	Statistical Model Building	Kinetics and Reaction Engineering	Thermo
Integrating Pharmaceutical Concepts into Introductory Chemical Engineering Courses - Part I	✓											
Introduction to Mixing Equipment and Processes in Pharmaceutical Operations			✓		✓							
ERC-SOPS Educational Modules	✓	✓	✓		✓							
Introduction to API Process Simulation	✓				✓	✓					✓	
Pharmaceutical Bulk Drug Production	✓				✓				✓			
Solid-Liquid Separations				✓								
Batch Distillaton Basics	✓			✓								✓
Particle Processing and Modeling in the Pharmaceutical Industry			✓				✓	✓				
Review of Statistics	✓	✓	✓	✓	✓	✓				✓		

Note: Only representative Teaching Materials included

Mass & Energy Balances

- Integrating Pharmaceutical Concepts into ChE courses (Word document - Compendium of Problem Sets, Farrell, Savelski, Slater, Rowan University, 2010)
  - Location:
    - Search “Mass and Energy Balances”
  - 3 problem sets with numerous problems integrating pharmaceutical concepts into ChE curriculum
    - Unit conversions
    - Balances on reactive/non-reactive processes
    - Process variables
    - Overall mass and energy balances

C. Stewart Slater (2010), "Integrating Pharmaceutical Concepts into Introductory Chemical Engineering Courses - Part I," https://pharmahub.org/resources/360. (C. Stewart Slater – Rowan University)

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Mass & Energy Balances

F&R 4.3c TB1.16e (Powder blending calculations)

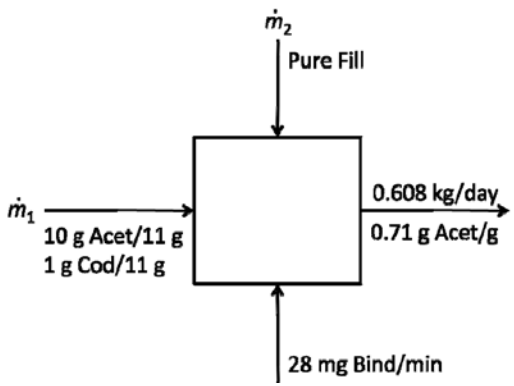
One of the unit operations in the pharmaceutical engineering is **powder blending** in which multiple powders are mixed together to give a uniform product. In the production of a tablet, **binders** (effectively glue for powders), **fillers** (for dilution) and the **active pharmaceutical ingredients** (APIs) are blended. In a lab blender being tested, 10 parts acetaminophen to one part codeine are being fed as API. Pure starch enters at 28 mg/min along with a pure stream of microcrystalline cellulose (MCC) filler. The mixer is run continuously in order to produce 3.04 kg in 5 days at 71 wt% acetaminophen. Draw and label a flowchart and determine all mass flow rates and compositions.

C. Stewart Slater (2010), "Integrating Pharmaceutical Concepts into Introductory Chemical Engineering Courses - Part I," https://pharmahub.org/resources/360. (C. Stewart Slater – Rowan University)

Mass & Energy Balances

Solution

We begin with our flowchart:



Note the conversion of the awkward kg/5 days to kg/day.

At this point, we may examine the diagram to see where best to start. We are given enough data to solve an equation on acetaminophen ("Acet" in the figure).

$$\sum_{\text{in}} \dot{m} = \sum_{\text{out}} \dot{m}$$

$$\dot{m}_1 \times \frac{10\ \text{g Acet}}{11\ \ \text{g}} = 0.71\ \frac{\text{g Acet}}{\text{g}} \times 0.608\ \frac{\text{kg}}{\text{day}}$$

$$\dot{m}_1 = 0.475 \frac{\text{kg}}{\text{day}} \times 1000 \frac{\text{g}}{\text{kg}} \times \frac{1}{24}\frac{\text{day}}{\text{h}} \times \frac{1}{60}\frac{\text{h}}{\text{min}} = 0.330\ \frac{\text{g}}{\text{min}}$$

From this the total flow may be determined

$$\sum_{\text{in}} \dot{m} = \sum_{\text{out}} \dot{m}$$

$$0.330 \frac{\text{g}}{\text{min}} + \dot{m}_2 + 28\ \frac{\text{mg}}{\text{min}} \times \frac{1}{1000}\frac{\text{g}}{\text{mg}} = 0.608 \frac{\text{kg}}{\text{day}} \times 1000 \frac{\text{g}}{\text{kg}} \times \frac{1}{24}\frac{\text{day}}{\text{h}} \times \frac{1}{60}\frac{\text{h}}{\text{min}}$$

$$\dot{m}_2 = [0.422 - (0.330 + 0.028)]\ {}^{\text{g}}/_{\text{min}}$$

$$\dot{m}_2 = 0.064\ {}^{\text{g}}/_{\text{min}}$$

Now, since the problem asked for everything specified, this is best answered as a table:

		Mass flows (g/min)			
		m1	m2	Bind	Out
		0.330	0.064	0.028	0.422
Mass fractions	xA	0.909	0	0	0.7109
	xC	0.091	0	0	0.071
	xB	0	0	1	0.066
	xF	0	1	0	0.152

C. Stewart Slater (2010), "Integrating Pharmaceutical Concepts into Introductory Chemical Engineering Courses - Part I," https://pharmahub.org/resources/360. (C. Stewart Slater – Rowan University)

Fluid Transport

- Introduction to Mixing Equipment and Processes in Pharmaceutical Operations (Powerpoint lecture slides, Armenante, Rutgers University, 2009)
  - Location:
    - Teaching Materials → Mixing
  - Apply mixing principles to pharmaceutical processes
    - Single and multiphase mixing in pharmaceutical processes
    - Analyze pharmaceutical processes where mixing is important
    - Tools to conduct process design analysis and scale-up

Piero Armenante; Henrik Pedersen (2009), "Introduction to Mixing Equipment and Processes in Pharmaceutical Operations," https://pharmahub.org/resources/292. (Piero Armenante – Rutgers University)

Fluid Transport

Objectives

- Become familiar with the principles of single and multiphase mixing in pharmaceutical processes
- Analyze pharmaceutical processes or in which mixing is important
- Provide basic tools to conduct process design analysis and scale-up of processes or in which mixing is important

Piero M. Armenante ChE702 2

Piero Armenante; Henrik Pedersen (2009), "Introduction to Mixing Equipment and Processes in Pharmaceutical Operations," https://pharmahub.org/resources/292. (Piero Armenante – Rutgers University)

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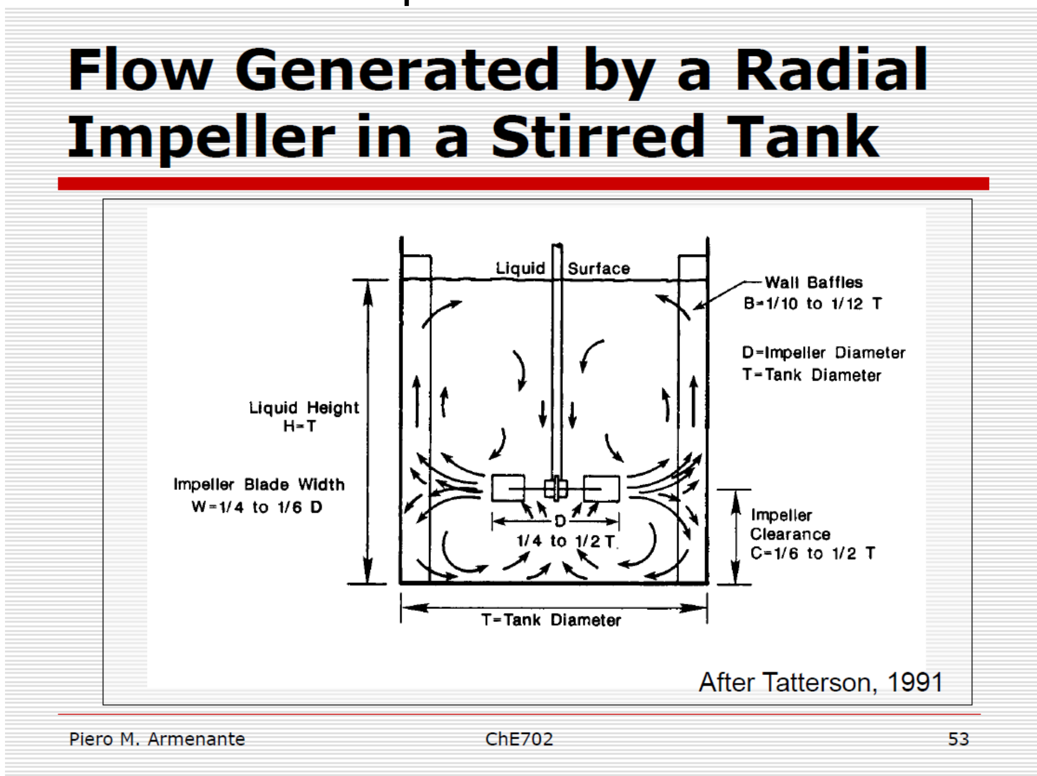
Fluid Transport

- Impeller influences flow pattern
  - How does this influence process decisions



Piero Armenante; Henrik Pedersen (2009), "Introduction to Mixing Equipment and Processes in Pharmaceutical Operations," https://pharmahub.org/resources/292. (Piero Armenante – Rutgers University)

Fluid Transport

- Introduction to the Rheology of Complex Fluids (Powerpoint lecture slides, Acevedo, Pederson, Rutgers University, 2010)
  - Location:
    - Teaching Materials → Rheology
  - Lecture
    - Mathematics behind complex fluid transport
      - Stress
      - Viscosity
      - Viscoelastic Modulus
    - Mathematical modeling approaches

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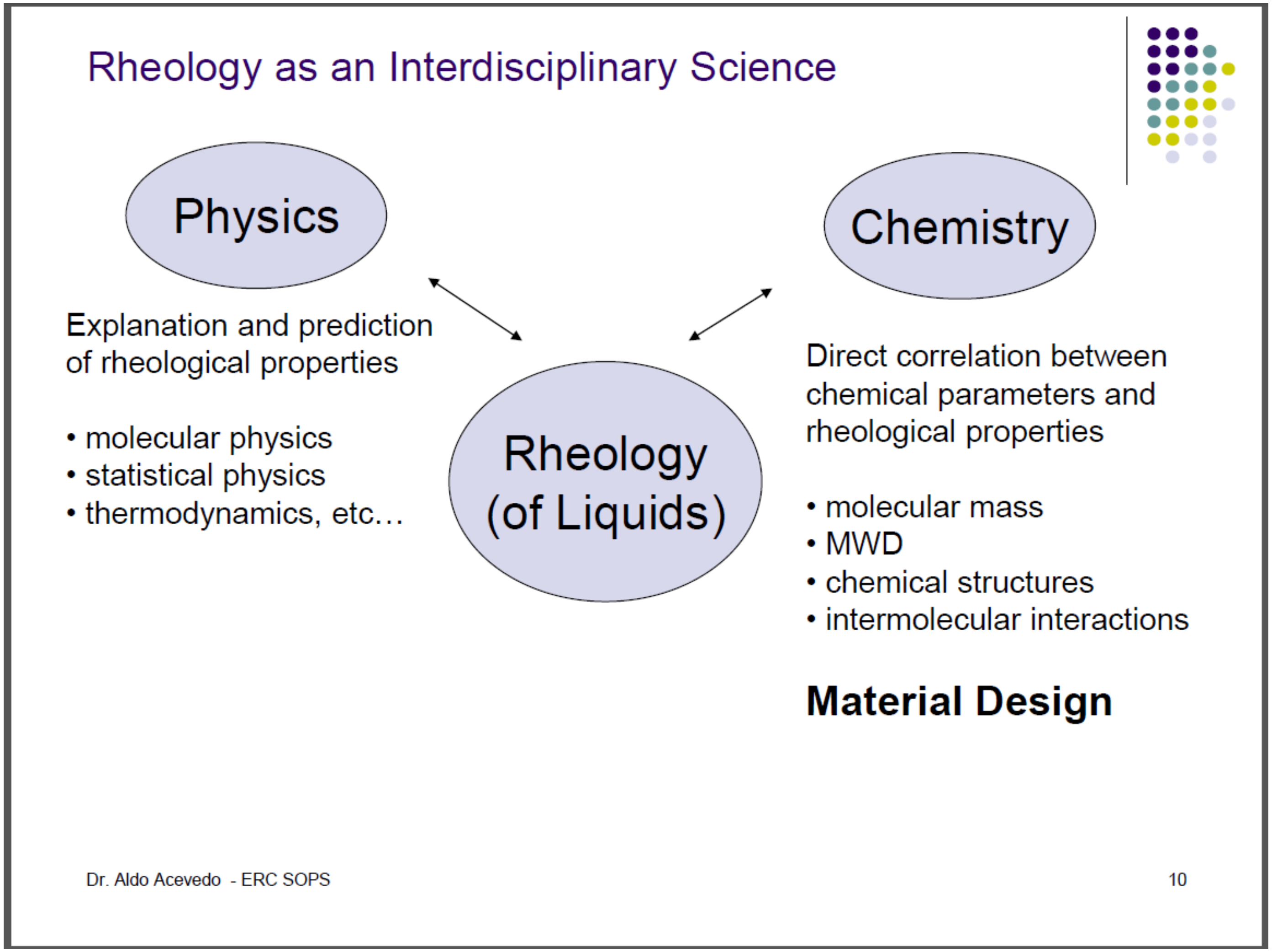
Aldo Acevedo; Henrik Pedersen (2010), "Introduction to the Rheology of Complex Fluids," https://pharmahub.org/resources/332. (Aldo Acevedo – Rutgers University)

Fluid Transport



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Aldo Acevedo; Henrik Pedersen (2010), "Introduction to the Rheology of Complex Fluids," https://pharmahub.org/resources/332. (Aldo Acevedo – Rutgers University)

Fluid Transport

Modeling of Shear Thinning and Thickening

- Carreau-Yasuda Model

$$\frac{\eta(\dot{\gamma})-\eta_{\infty}}{\eta_0-\eta_{\infty}}=[1+(\dot{\gamma}\lambda)^{a}]^{\frac{n-1}{a}}$$

a – affects the shape of the transition region

λ – time constant determines where it changes from constant to power law

n – describes the slope of the power law

η_0, η_∞ - describe plateau viscosities

- Advantages: fits most data
- Disadvantages: contains 5 parameters, do not give molecular insight into polymer behavior

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Aldo Acevedo; Henrik Pedersen (2010), "Introduction to the Rheology of Complex Fluids," https://pharmahub.org/resources/332. (Aldo Acevedo – Rutgers University)

Heat Transfer

- Introduction to API Process Simulation (Powerpoint lecture slides, Kuriyan, Purdue University, 2009)

  - Location:
    - Teaching Materials → Active Pharmaceutical Ingredient (API)

  - Presentation presenting methods to model heat transfer in pharmaceutical process
    - Heat or cool a phase with a jacket (flow)
    - Heat exchange between phases
    - Heat duty

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Kamal Kuriyan (2009), "Introduction to API Process Simulation," https://pharmahub.org/resources/319.
(Kamal Kuriyan – Purdue University)

Heat Transfer

Module Structure

- Process modeling basics
  - Model applications
  - Model types
  - Modeling procedure
- Simulation packages
  - DynoChem
- Examples
  - Heat transfer
  - Batch reactor with accumulation effects

Kamal Kuriyan (2009), "Introduction to API Process Simulation," https://pharmahub.org/resources/319.
(Kamal Kuriyan – Purdue University)

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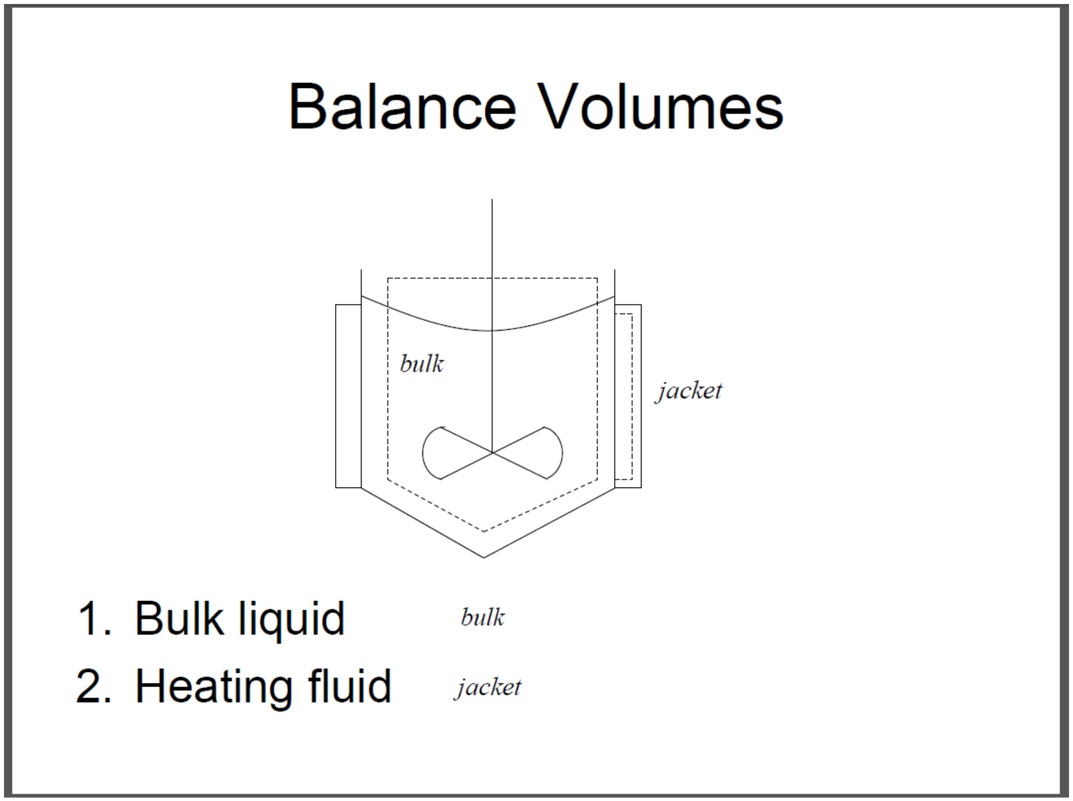
Heat Transfer

- Modeling example for heat transfer through a jacket



Kamal Kuriyan (2009), "Introduction to API Process Simulation," https://pharmahub.org/resources/319.
(Kamal Kuriyan – Purdue University)

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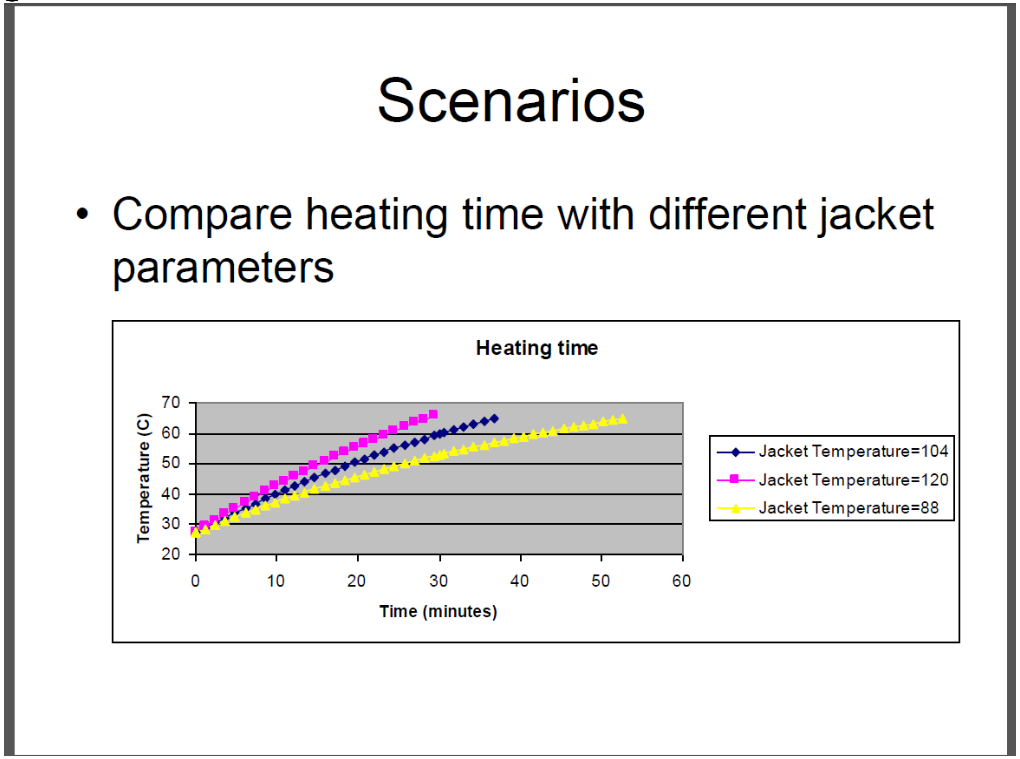
Heat Transfer

- Comparison of heating time using different heat transfer parameters



Kamal Kuriyan (2009), "Introduction to API Process Simulation," https://pharmahub.org/resources/319. (Kamal Kuriyan – Purdue University)

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Process Design

- Pharmaceutical Bulk Drug Production (Powerpoint lecture slides, Glaser, Rutgers University, 2009)
  - Location:
    - Teaching Materials→ Pharmaceutical Manufacturing
  - Two part presentation on pharmaceutical manufacturing
    - Pharmaceutical market
    - Introduction to pharmaceutical engineering
    - API synthesis
    - Process development
    - Scale-up

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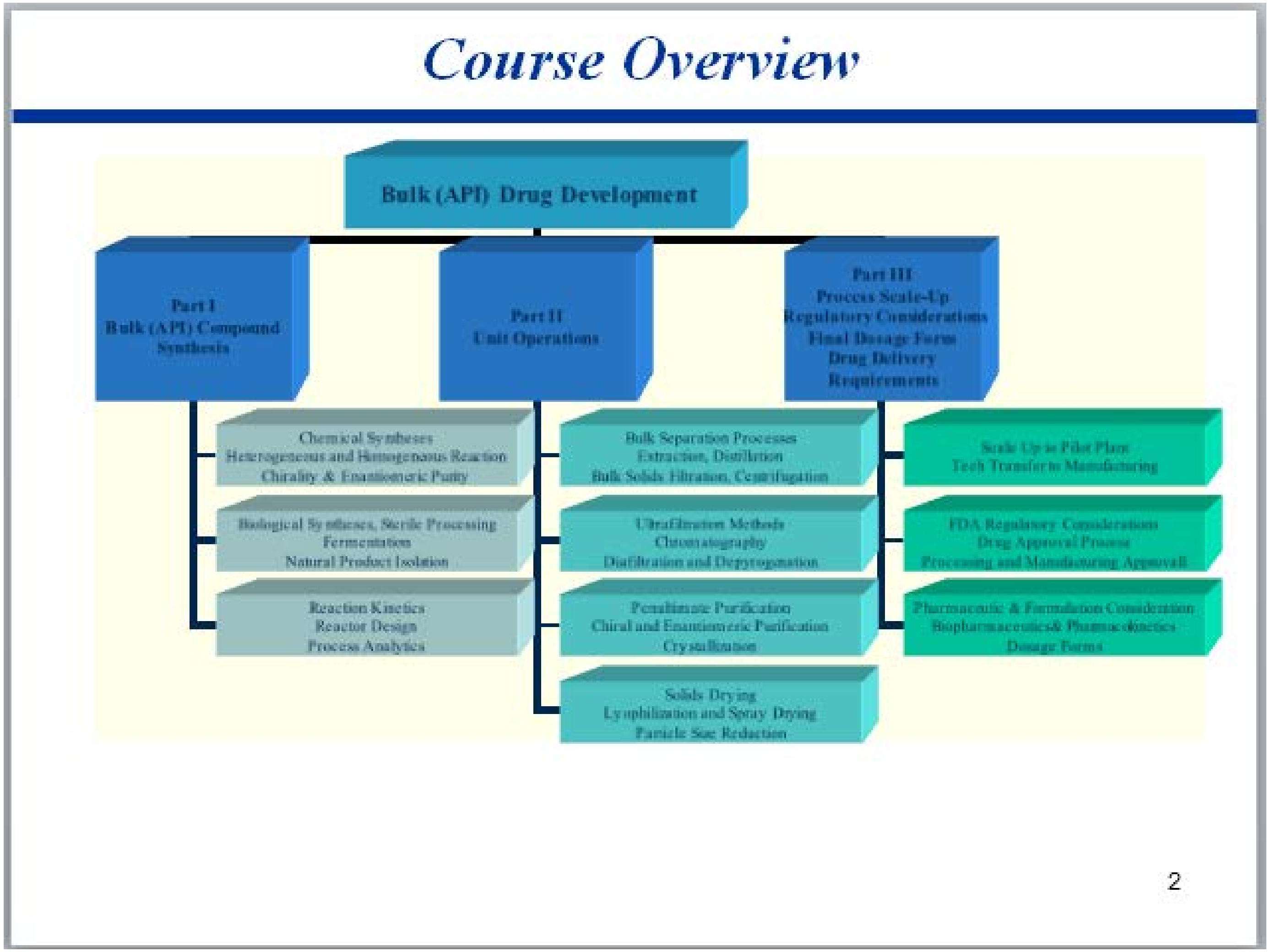
Benjamin Glasser; Henrik Pedersen (2009), "Pharmaceutical Bulk Drug Production," https://pharmahub.org/resources/286.
(Benjamin Glasser – Rutgers University)

Process Design



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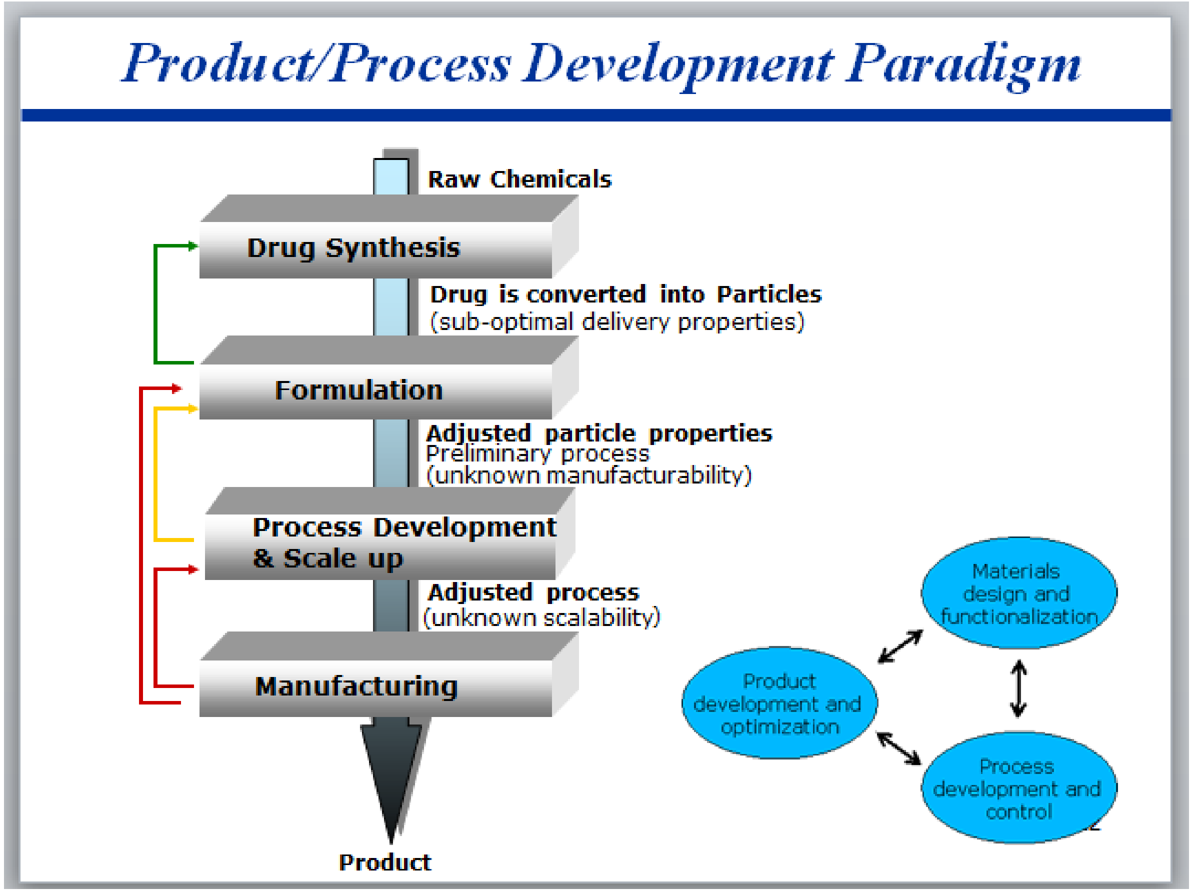
Benjamin Glasser; Henrik Pedersen (2009), "Pharmaceutical Bulk Drug Production," https://pharmahub.org/resources/286.
(Benjamin Glasser – Rutgers University)

Process Design



Benjamin Glasser; Henrik Pedersen (2009), "Pharmaceutical Bulk Drug Production,“ https://pharmahub.org/resources/286.
(Benjamin Glasser – Rutgers University)

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Process Design

Pilot plant objectives

Taken from:
Rosas, C., 2005, Process development in *Active Pharmaceutical Ingredients, Development, Manufacturing and Regulation*, Ed. Nusim, S.H., 2005, Taylor & Francis, New York. (pages 46 & 47)

1. provide ready access to scaled-up processing for the bulk drug preparative effort.
2. give the preparative effort a responsive environment to deal with the vicissitudes of the drug development programs being supported.
3. permit the rapid and convenient evaluation of processes, methods and equipment, as well as the mastery of scale-up.
4. obtain process data to support process design and the development of procedures for the eventual manufacture of the drug.
5. Demonstrate process performance at a scale that minimizes risk and the need to trigger scale-up constraints upon first manufacture.

28

Benjamin Glasser; Henrik Pedersen (2009), "Pharmaceutical Bulk Drug Production,“ https://pharmahub.org/resources/286.
(Benjamin Glasser – Rutgers University)

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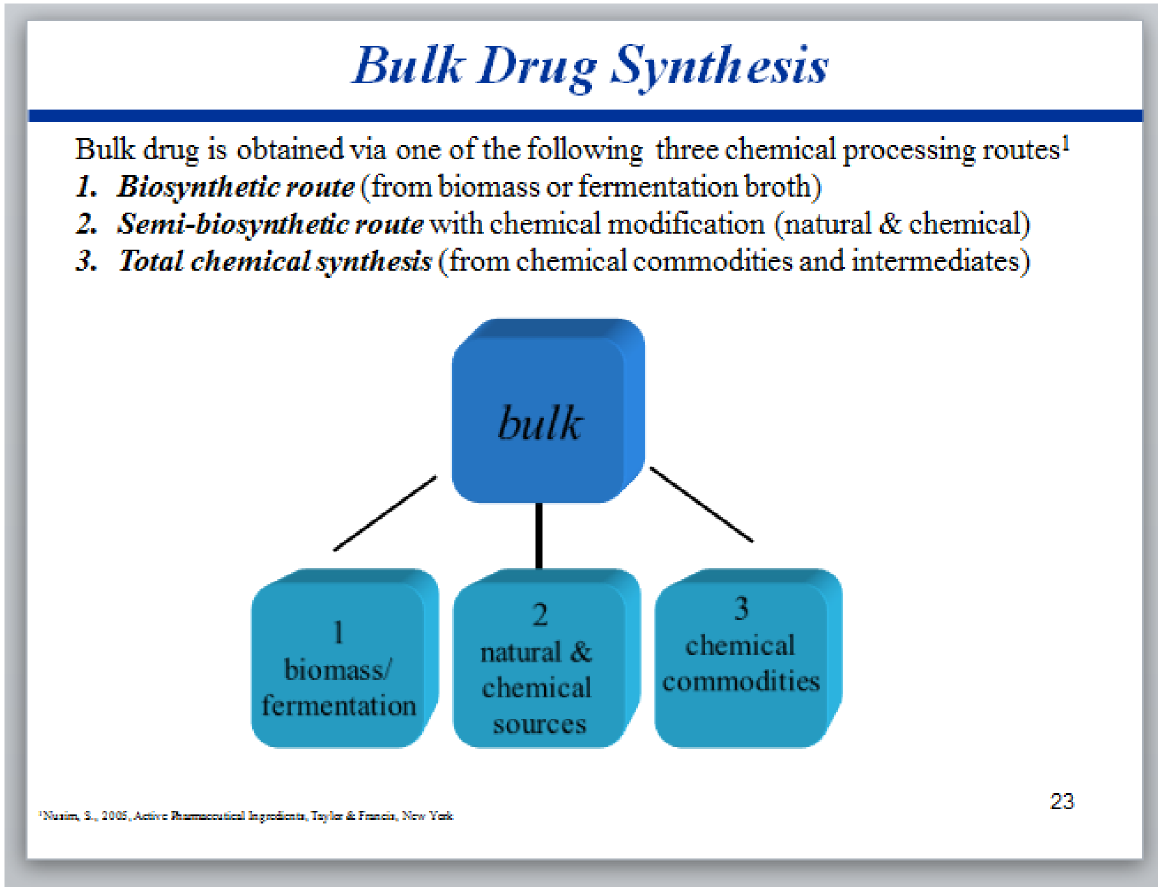
Process Design



Benjamin Glasser; Henrik Pedersen (2009), "Pharmaceutical Bulk Drug Production,“ https://pharmahub.org/resources/286.
(Benjamin Glasser – Rutgers University)

Introduction to Pharmaceutical Engineering

- Pharmaceutical Bulk Drug Production (Powerpoint lecture slides, Glasser, Rutgers University, 2009)
  - Location:
    - Teaching Materials → Pharmaceutical Manufacturing
  - Approval process for drugs
  - Application of chemical engineering principles to pharmaceutical engineering
  - Bulk pharmaceutical manufacturing techniques

Benjamin Glasser; Henrik Pedersen (2009), "Pharmaceutical Bulk Drug Production,“ https://pharmahub.org/resources/286.
(Benjamin Glasser – Rutgers University)

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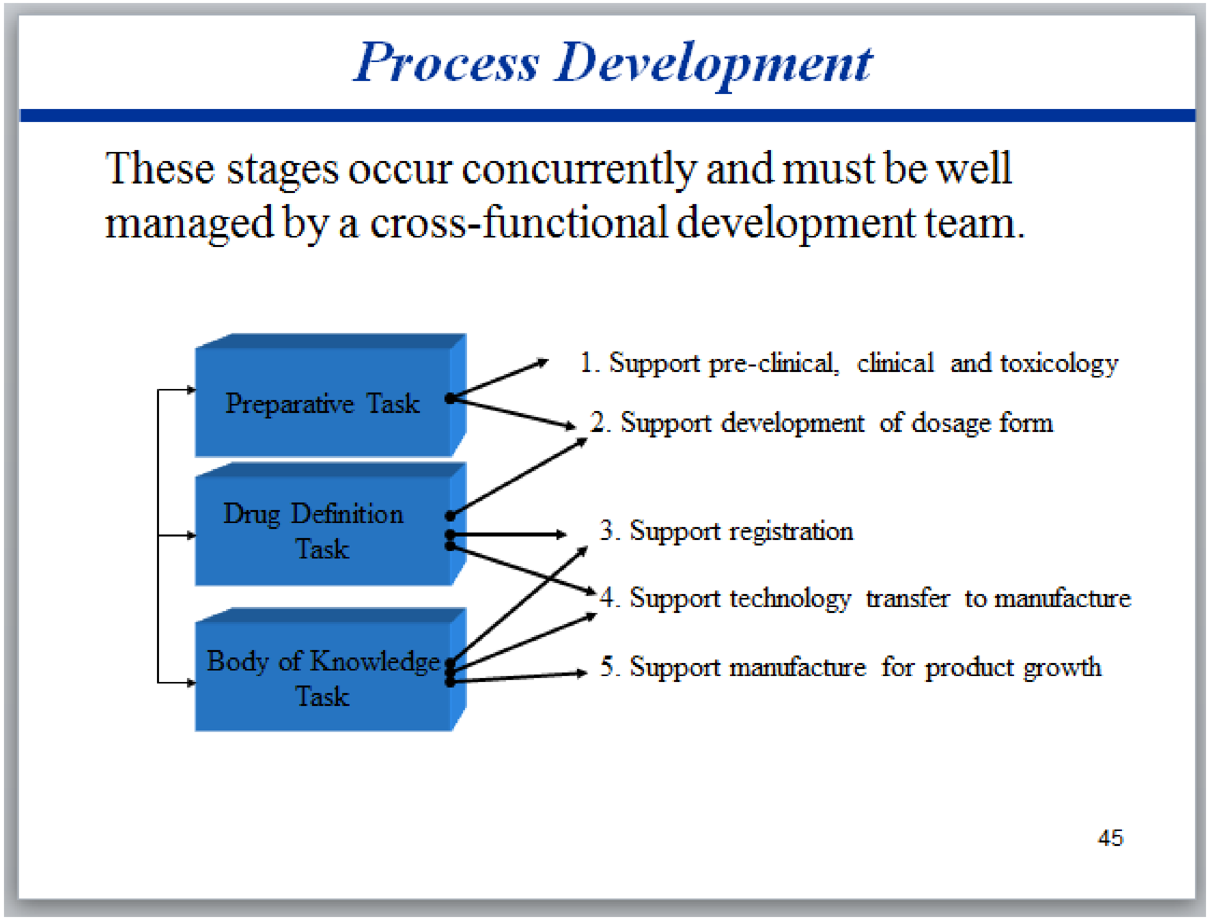
Introduction to Pharmaceutical Engineering



Benjamin Glasser; Henrik Pedersen (2009), "Pharmaceutical Bulk Drug Production,“ https://pharmahub.org/resources/286.
(Benjamin Glasser – Rutgers University)

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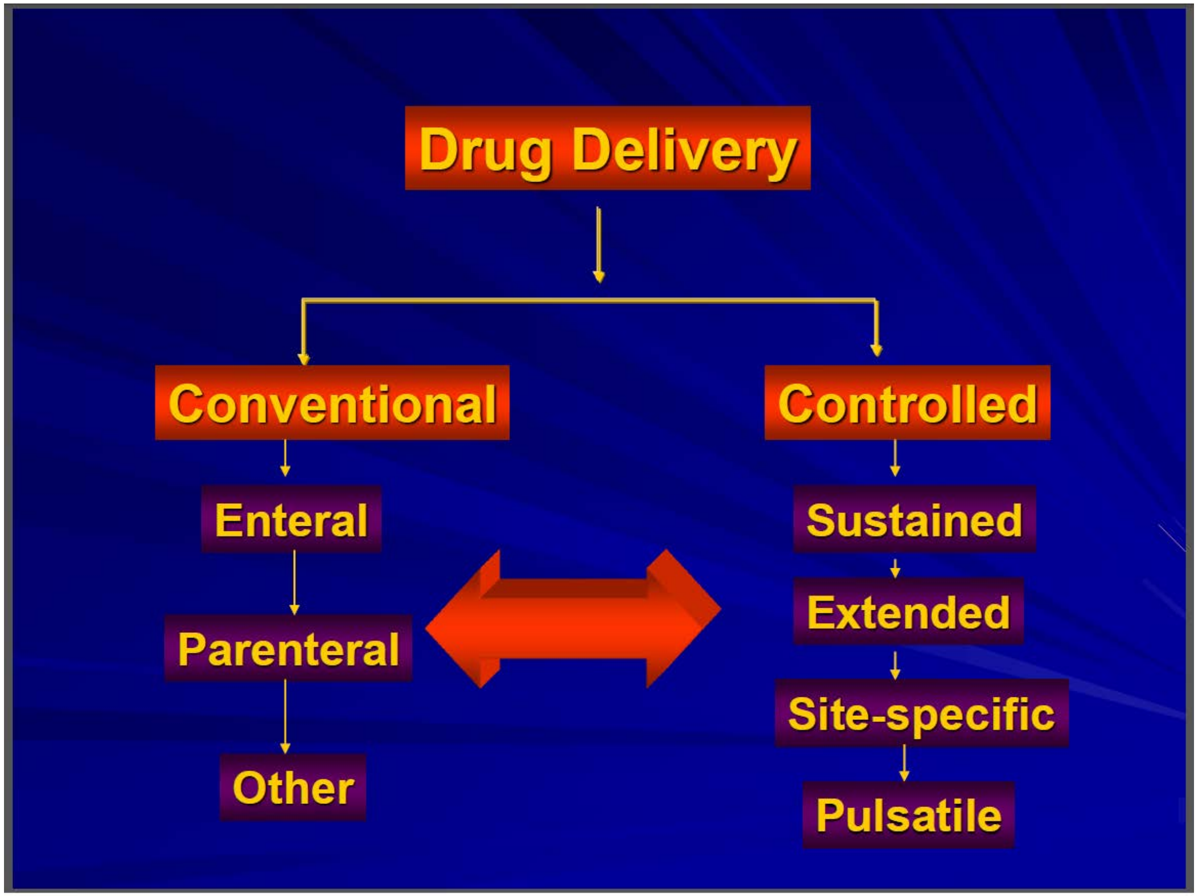
Introduction to Pharmaceutical Engineering

- Application of Chemical Engineering Principles to Drug Delivery (Powerpoint lecture slides, Torres-Lugo, Pederson, Rutgers University, 2010)
  - Location:
    - Teaching Materials→ Drug Delivery
  - Types of drug delivery
    - Oral, buccal, subcutaneous, etc
  - Use of chemical engineering principles when selecting drug delivery route
  - Body's response to drugs
    - Mathematical modeling

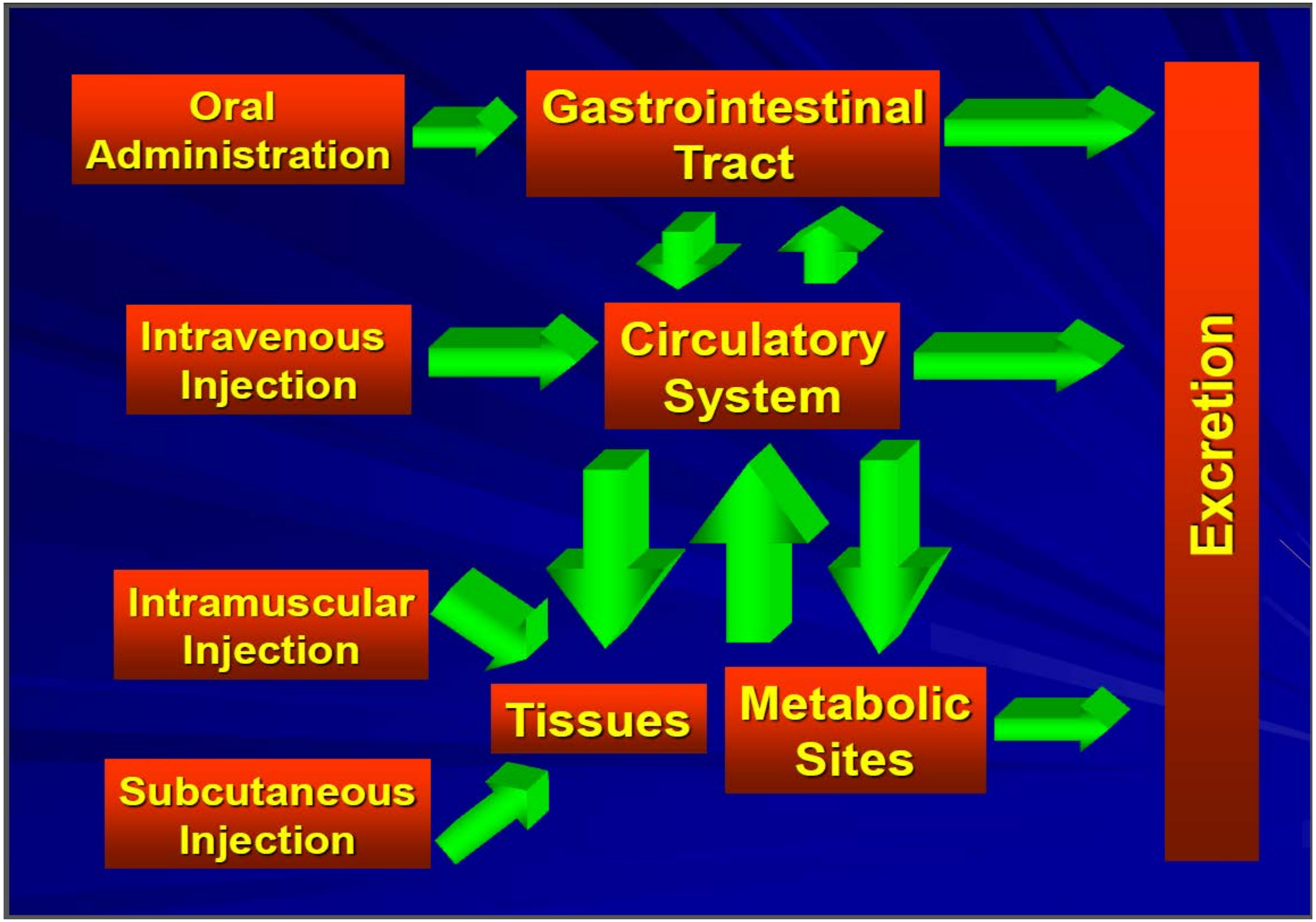
Madeline Torres-Lugo; Henrik Pedersen (2010), "Application of Chemical Engineering Principles to Drug Delivery," https://pharmahub.org/resources/339. (Madeline Torres-Lugo – Rutgers University)

Introduction to Pharmaceutical Engineering



Madeline Torres-Lugo; Henrik Pedersen (2010), "Application of Chemical Engineering Principles to Drug Delivery," https://pharmahub.org/resources/339. (Madeline Torres-Lugo – Rutgers University)

Introduction to Pharmaceutical Engineering



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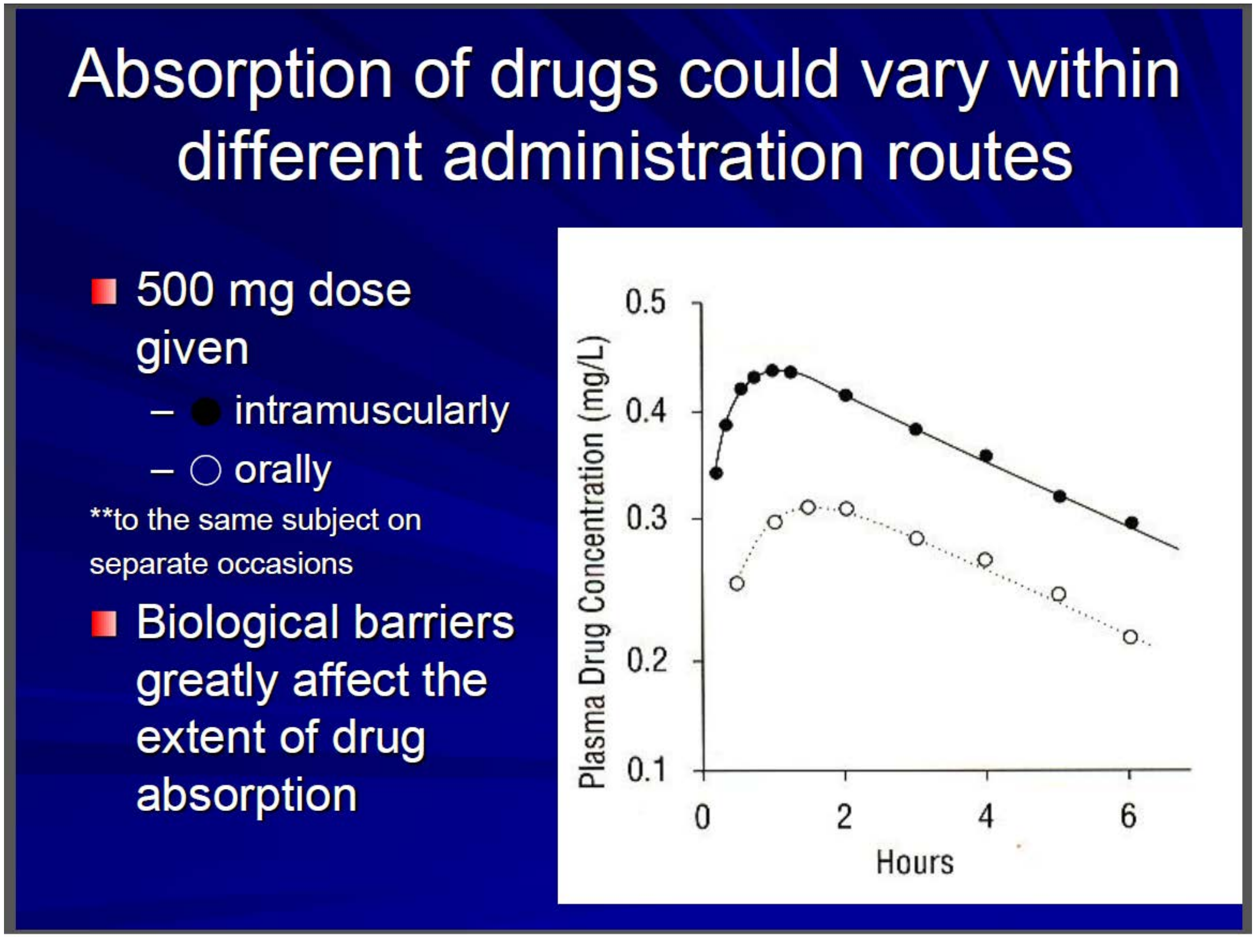
Introduction to Pharmaceutical Engineering



Madeline Torres-Lugo; Henrik Pedersen (2010), "Application of Chemical Engineering Principles to Drug Delivery," https://pharmahub.org/resources/339. (Madeline Torres-Lugo – Rutgers University)

Separations

- Solid-Liquid Separations (Powerpoint lecture slides, Kuriyan, Purdue University, 2009)
  - Location:
    - Teaching Materials → Active pharmaceutical ingredient (API)
  - Solid-Liquid separation techniques for pharmaceutical processes
    - Cake filtration
    - Centrifugation
    - Deliquoring
    - Washing

Kamal Kuriyan (2009), "Solid-Liquid Separations," https://pharmahub.org/resources/322. (Kamal Kuriyan – Purdue University)

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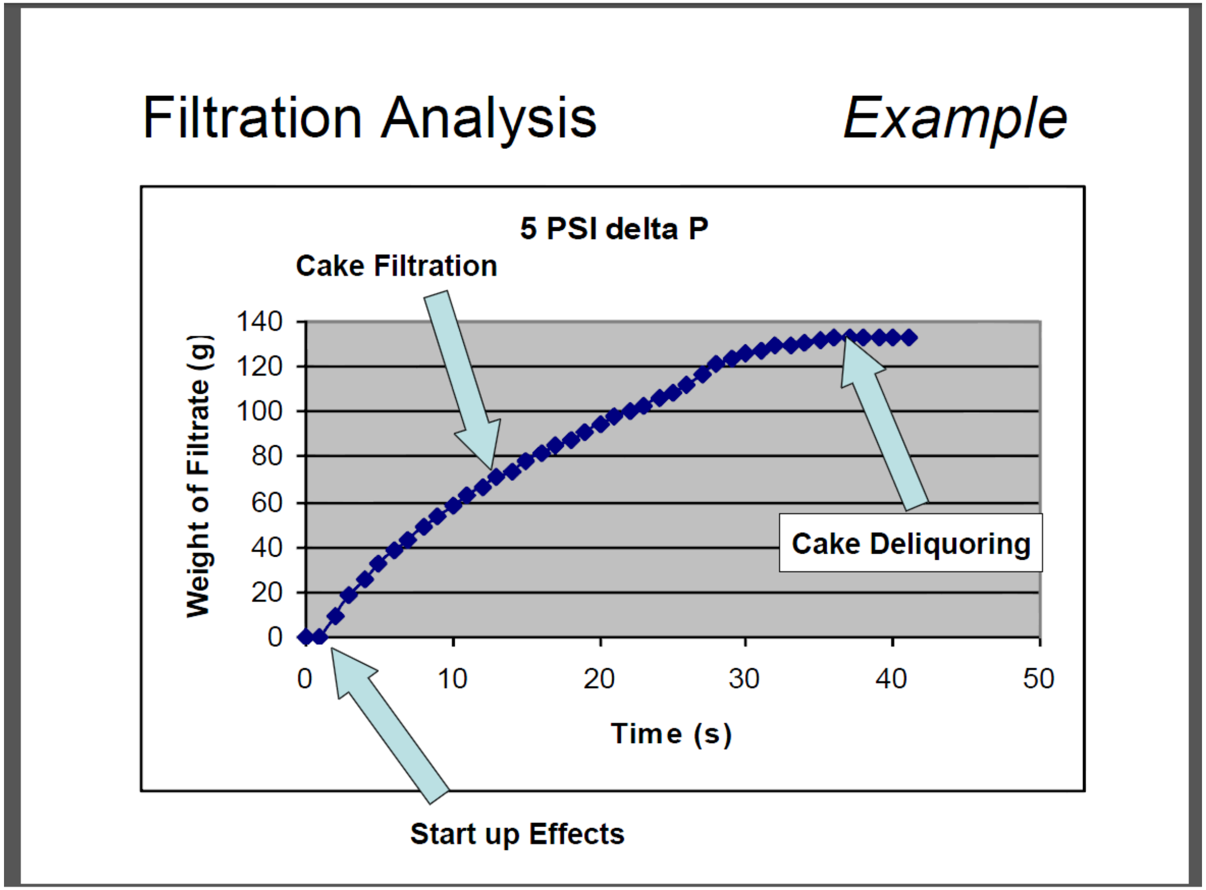
Separations

Solid-Liquid Separations

- Filtration Analysis
  - Flow in packed beds
  - Cake Filtration
  - Centrifuges
  - Deliquoring
  - Washing
- Examples
  - Cake compressibility
  - Cycle time calculations

Kamal Kuriyan (2009), "Solid-Liquid Separations," https://pharmahub.org/resources/322. (Kamal Kuriyan – Purdue University)

Separations



Separations

- Batch Distillation (Powerpoint lecture slides, Kuriyan, Purdue University, 2009)
  - Location:
    - Teaching Materials → Distillation
  - Vapor-Liquid equilibrium
  - Batch evaporation
  - Column configurations
  - Advantages of batch distillation
  - Process simulation

Kamal Kuriyan (2009), "Batch Distillaton Basics," https://pharmahub.org/resources/321.
(Kamal Kuriyan – Purdue University)

Separations

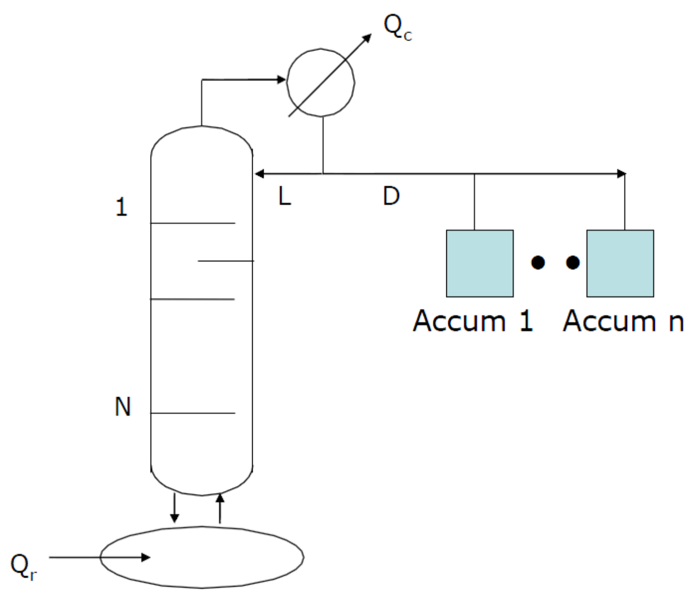
Module Structure

- Vapor Liquid Equilibrium Curves
- Rayleigh Distillation
- Column Configurations
- Column Operation
- Simulation
- Design of Batch Columns

Kamal Kuriyan (2009), "Batch Distillaton Basics," https://pharmahub.org/resources/321.
(Kamal Kuriyan – Purdue University)

Separations

Conventional Batch Distillation Column



Kamal Kuriyan (2009), "Batch Distillaton Basics," https://pharmahub.org/resources/321.
(Kamal Kuriyan – Purdue University)

Pharmaceutical Engineering Unit Operations

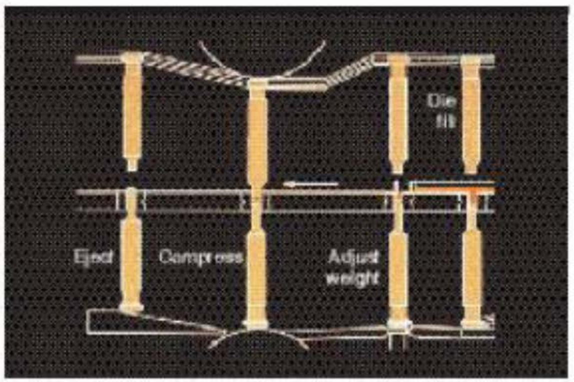
- Particle Processing and Modeling in the Pharmaceutical Industry (Powerpoint lecture slides, Glasser, Rutgers University, 2010)
  - Location:
    - Teaching Materials → Particle Modeling
  - Detailed descriptions of pharmaceutical unit operations
  - Tableting and coating
  - Particle geometry and granular flow
  - Nanoparticles
    - Drug delivery

Benjamin Glasser; Henrik Pedersen (2010), "Particle Processing and Modeling in the Pharmaceutical Industry," https://pharmahub.org/resources/356. (Benjamin Glasser – Rutgers University)

Pharmaceutical Engineering Unit Operations

Tableting Machines

Four main stages for tableting : Die fill, weight adjustment, compression, and ejection

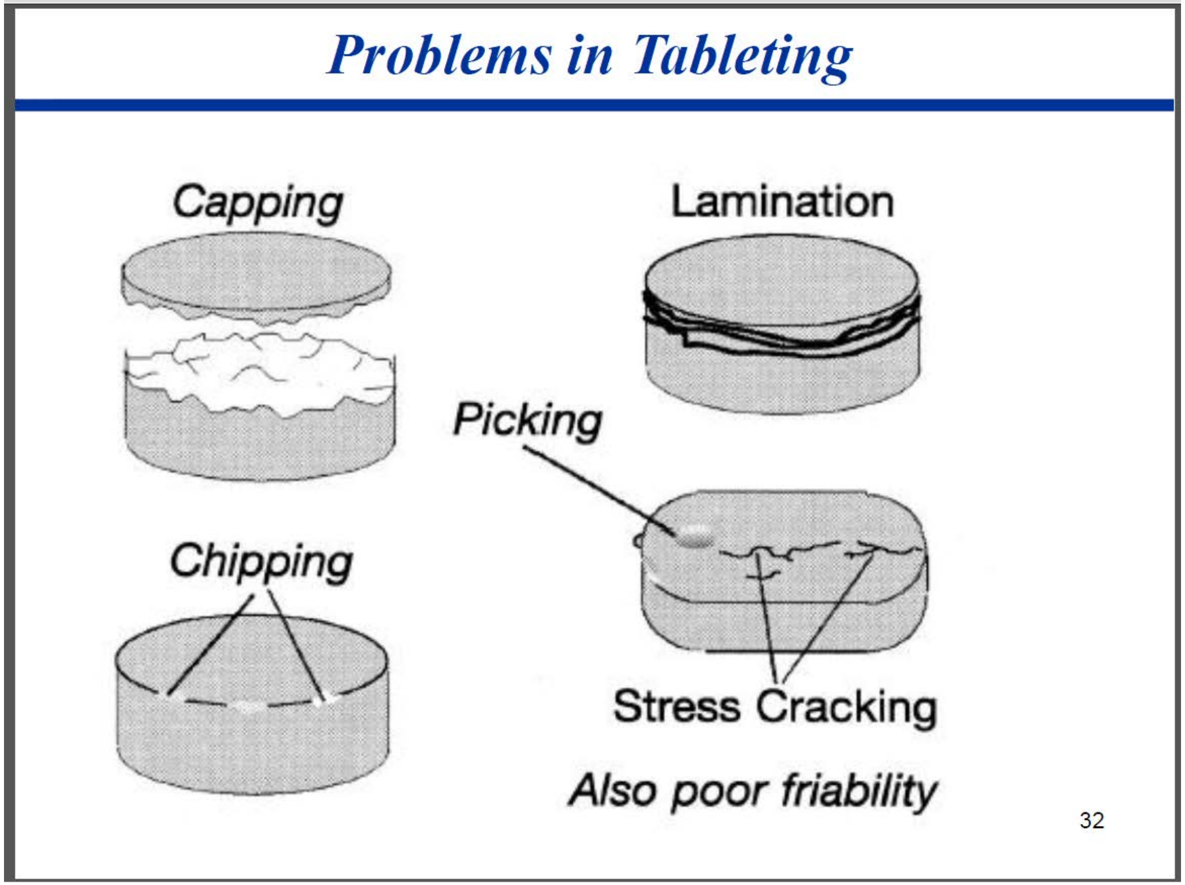


Rotary tablet presses

http://www.capsule-filling-machine.com/rimages/131/tablet-h01.jpg

Benjamin Glasser; Henrik Pedersen (2010), "Particle Processing and Modeling in the Pharmaceutical Industry," https://pharmahub.org/resources/356. (Benjamin Glasser – Rutgers University)

Pharmaceutical Engineering Unit Operations



Benjamin Glasser; Henrik Pedersen (2010), "Particle Processing and Modeling in the Pharmaceutical Industry," https://pharmahub.org/resources/356. (Benjamin Glasser – Rutgers University)

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Crystallization

- Particle Processing and Modeling in the Pharmaceutical Industry (Powerpoint lecture slides, Glasser, Rutgers University, 2010)
  - Location:
    - Teaching Materials → Particle Modeling
  - Crystal Formation
  - Crystal morphology
  - Processing of crystals
    - Drying
    - Transport
  - Crystal/granular transport devices

Benjamin Glasser; Henrik Pedersen (2010), "Particle Processing and Modeling in the Pharmaceutical Industry," https://pharmahub.org/resources/356. (Benjamin Glasser – Rutgers University)

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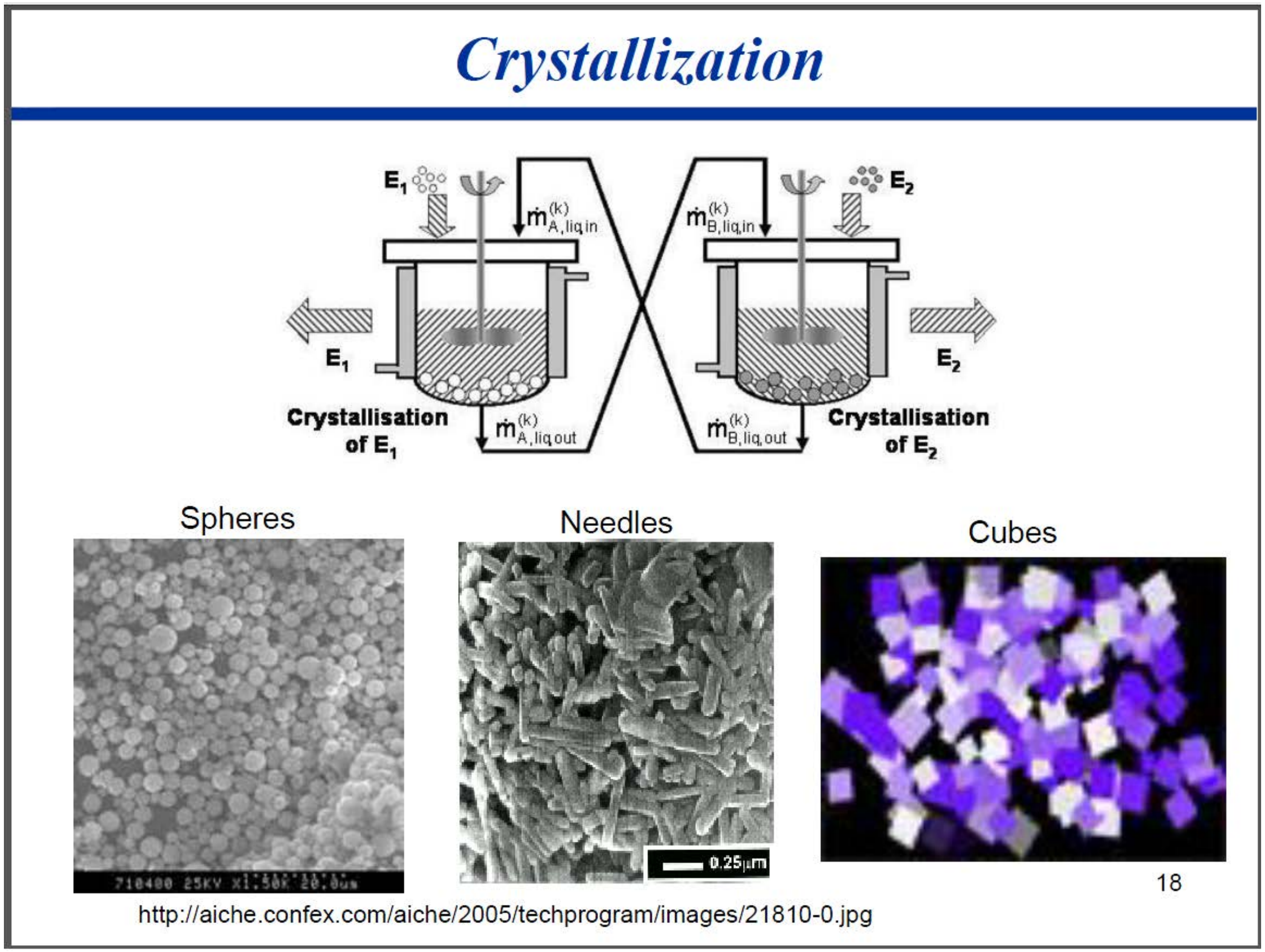
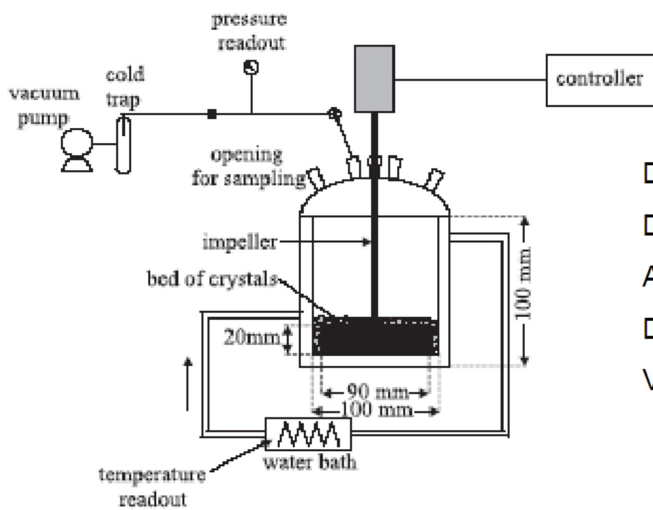
Crystallization



Benjamin Glasser; Henrik Pedersen (2010), "Particle Processing and Modeling in the Pharmaceutical Industry," https://pharmahub.org/resources/356. (Benjamin Glasser – Rutgers University)

Crystallization

Agitated Drying of Crystals



Drying Parameters:

Drying Temperature

Agitation Speed

Drying time

Vacuum

Crystal Size Distribution:

Attrition decreases the size.

Agglomeration increases the size.

Lekhal et al. Powder Technology (2003)

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Benjamin Glasser; Henrik Pedersen (2010), "Particle Processing and Modeling in the Pharmaceutical Industry," https://pharmahub.org/resources/356. (Benjamin Glasser – Rutgers University)

Thermodynamics

- Batch Distillation (Powerpoint lecture slides, Kuriyan, Purdue University, 2009)
  - Location:
    - Teaching Materials → Distillation
  - Vapor-Liquid equilibrium
  - Bubble point/dew point
  - Azeotropes
    - Homogeneous
    - Heterogeneous

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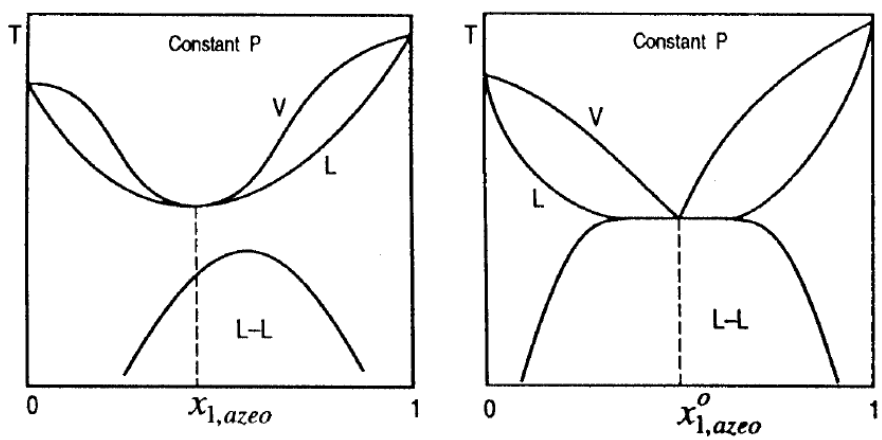
Kamal Kuriyan (2009), "Batch Distillaton Basics," https://pharmahub.org/resources/321.
(Kamal Kuriyan – Purdue University)

Thermodynamics

Heterogeneous Azeotropes

For a minimum-boiling azeotrope with large deviation from Raoult's law ($\gamma_i >> 1$), phase splitting may occur and a minimum-boiling heterogeneous azeotrope forms, having a vapor phase in equilibrium with two liquid phases.



Homogeneous Azeotrope | Heterogeneous Azeotrope

Kamal Kuriyan (2009), "Batch Distillaton Basics," https://pharmahub.org/resources/321.
(Kamal Kuriyan – Purdue University)

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Kinetics & Reaction Engineering

- Introduction to API Process Simulation (Powerpoint lecture slides, Kuriyan, Purdue University, 2009)
  - Location:
    - Teaching Materials → Active Pharmaceutical Ingredient (API)
  - Modeling example for fed-batch reaction with safety constraints
    - Reaction kinetics
    - Batch-fed and isothermal reactors
    - Exothermic reactions
    - Different operation scenarios

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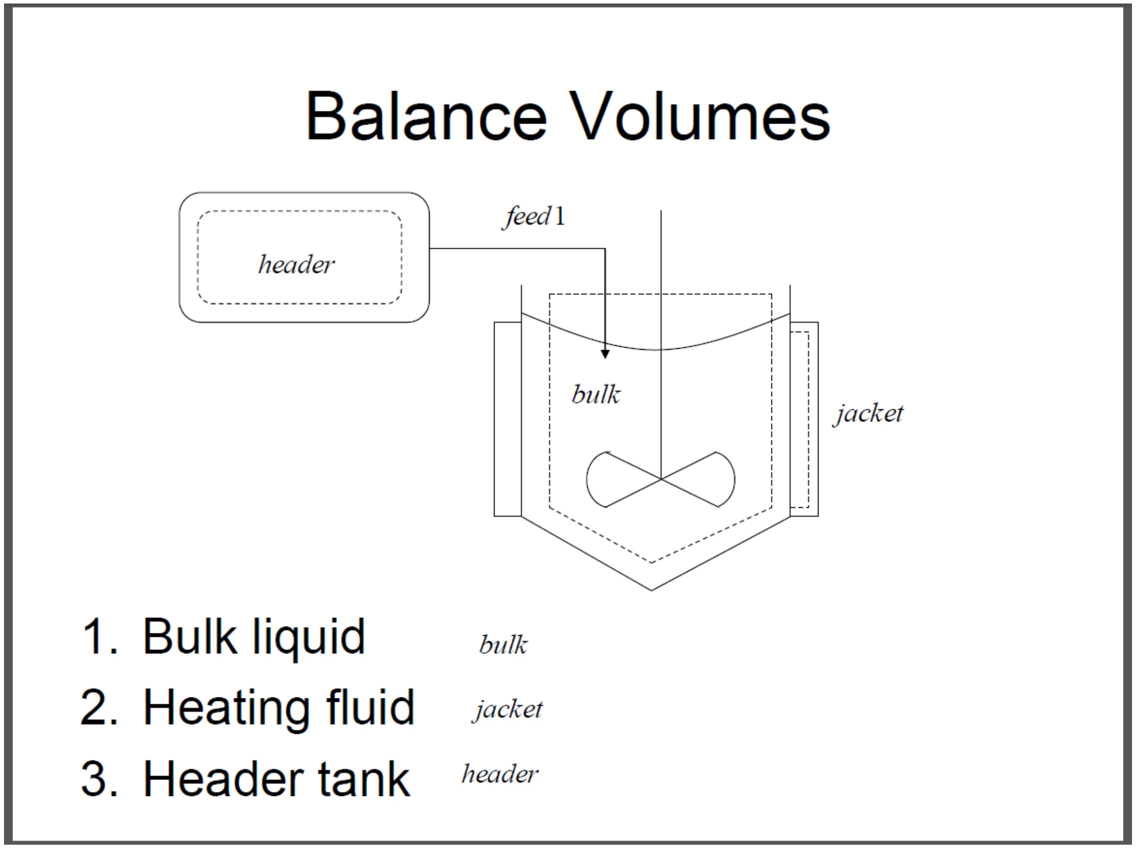
Kamal Kuriyan (2009), "Introduction to API Process Simulation," https://pharmahub.org/resources/319.
(Kamal Kuriyan – Purdue University)

Kinetics & Reaction Engineering

- Fed-batch reaction with safety constraints



Kamal Kuriyan (2009), "Introduction to API Process Simulation," https://pharmahub.org/resources/319.
(Kamal Kuriyan – Purdue University)

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Particulate Processing

- 2 Animations demonstrating Particle Processing techniques

  – Location:
    - Video #1: Animations→ Particle Modeling→ Hopper Segregation (Wassgren, Purdue University, 2007)
      – Particles behavior at hopper outlet
    - Video #2: Animations→ Particle Modeling→ Inter and Intra Tablet Coating (Wassgren, Purdue University, 2007)
      – Particle behavior in pan coater vortex

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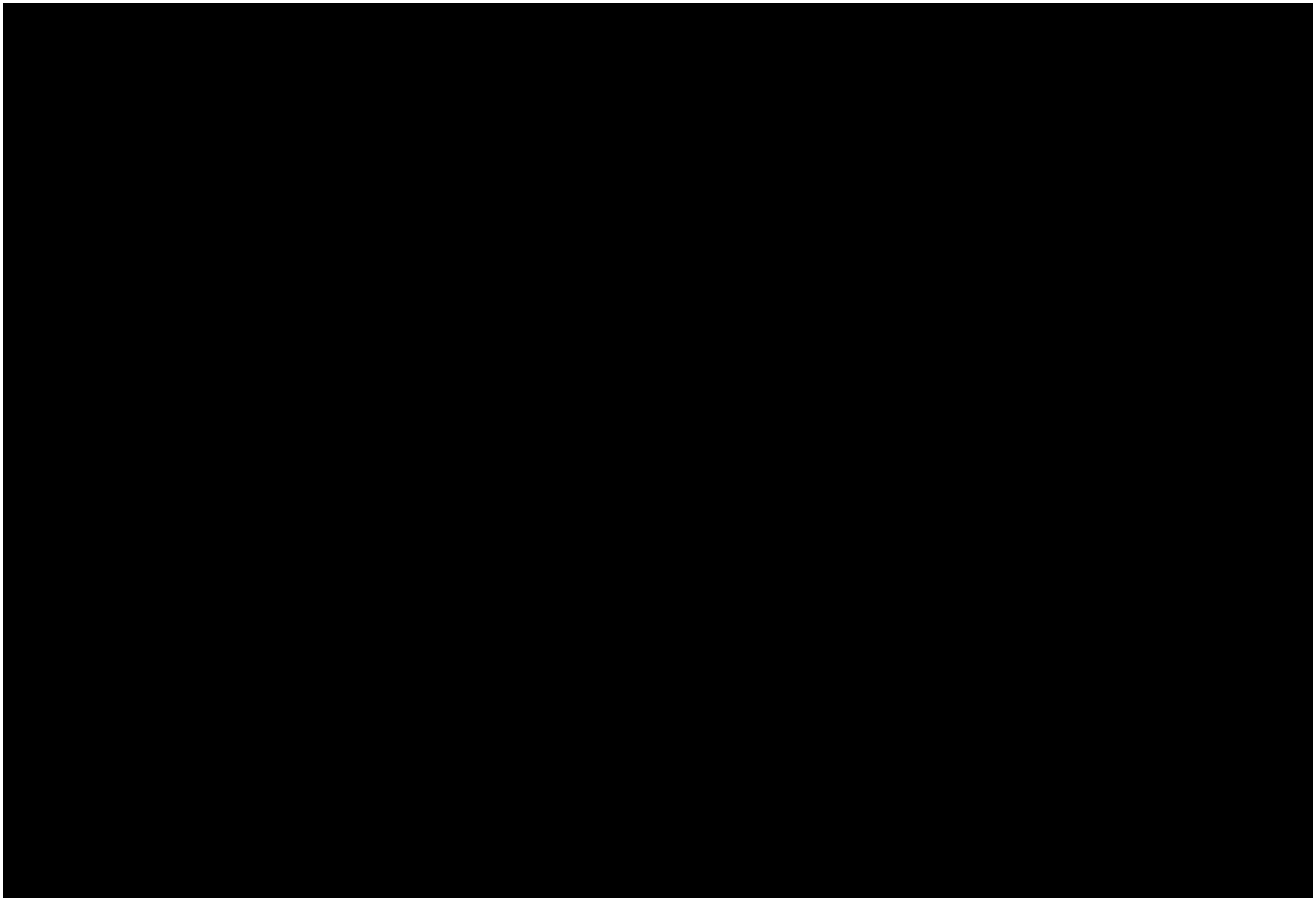
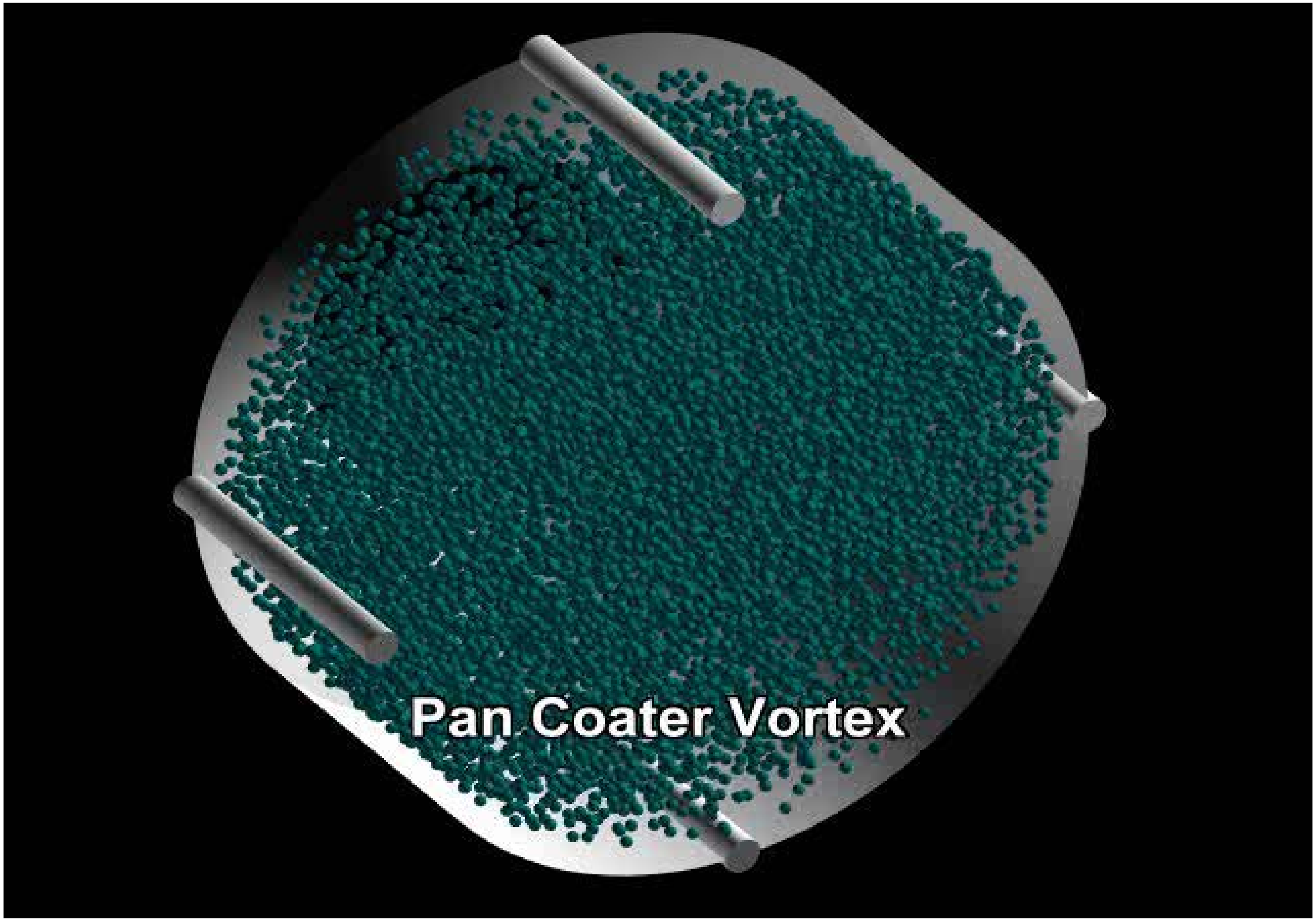
Hopper Segregation



Carl Wassgren (2007), "Hopper Segregation," https://pharmahub.org/resources/14.

Tablet Coating



Carl Wassgren (2007), "Inter- and Intra- Tablet Coating Variability," https://pharmahub.org/resources/13.