New Jersey Institute of Technology

Otto H. York Department of Chemical Engineering

Course: PhEn 606 Pharmaceutical Unit Operations: Solids Processing (3 credits)

Prerequisites: PhEn601: Principles of Pharmaceutical Engineering, PhEn603: Pharmaceutical Processing and Manufacturing or completion of the bridge program

Reason for prerequisites: Understanding of the basic concepts of pharmaceutical engineering is required for the quantification of pharmaceutical powder technology

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Course description: The course focuses on fundamentals of particulate processing, such as the particle characterization, blending, milling, granulation, tableting, and coating. The emphasis is on the application of macro- and micro-scale models of granular materials to quantify and scale up manufacturing pharmaceutical processes.

The course combines lectures, problem-solving, labs, and project assignment to provide students with

- Fundamentals of particulate processing in pharmaceutical technology
- Societal and economic impacts of pharmaceutical powder technologies
- Ability to communicate effectively the acquired knowledge in written & verbal form

The course objectives

- Identify the fundamental macro- and micro-scale phenomena underlying particulate processing
- Introduce the basic operating principles of solids processing units
- Apply basic concepts to analyze and scale up manufacturing pharmaceutical processes

Course outline

• Introduction		Pharmaceutical Powder Technology Main Challenges of Pharmaceutical Technologies FDA Process Analytical Technology Initiative
• Particle & Granule Micrometrics		Particle Size Characterization Static and Dynamic Powder Sampling Particle Size Measurement Characterization of the Powder Bed Density, Porosity, Permeability, and Surface Area
• Continuum Mechanics of Particulate Solids	Flow of Powders	Flow of Granular Materials Mohr's Circle for Normal and Shear Stresses The Mohr-Coulomb Failure Criterion Active and Passive Rankine States Angle of Repose The Effective Wall Yield Locus Shear Testing Equipment Cohesionless and Cohesive Materials Stress-Strain Diagram Jenike's Method for Flow of Cohesive Powders Mass Flow Rate of Free-Flowing Materials

		Discharge Devices Janssen's Analysis of Stresses and Forces in Silos
	Powder Compaction	Basic Methods of Tablet Manufacturing Diagram of Forces in a Punch-Die Assembly Characterization of Powder Compressibility Densification Behavior of Soft Powders Work Involved in Compression of Powders Optimization of Force-Displacement Diagram Mechanical Tests of Formed Compacts Indentation Hardness
• Micromechanics of Particulate Solids	Interparticle Forces	Dry Vs. Wet Granular Materials Van der Waals Intermolecular Forces Interaction of Elastically and Plastically Deformed Spherical Particles Adhesion Model for Particle Friction Types of Electrostatic Forces Two Spheres Joined by a Liquid Bridge Liquid Bridge Between a Cone and a Plane Viscous Force Between Two Colliding Spheres Impact and Rebound of Particles Classification of Interparticle Forces Particle Assembly Elasticity
	Wet and Dry Granulation	Wetting and Nucleation Drop Controlled Regime Granule Consolidation and Growth Characteristic Dimensionless Parameters Operating Regime Map Breakage of Wet and Dried Granules Measurements of Fracture Properties High and Low Shear Mixer Granulators Scale-Up, Endpoint Determination and Control Fluid Bed Granulation Geldart's Diagram of Fluidization Behavior Scale-up and Granulation Endpoint Dry Granulation Roller Compaction Pressure Distribution Between Rolls
	Mixing of Granular Materials	Mixing and Segregation Characterization of Powder Mixture Mixing Mechanisms Powder Mixers
	Particle Size Reduction	Mechanisms of Size Reduction Properties Affecting Size Reduction Classification of Mills Low- and High-Energy Mills

Tentative weekly listing of topics (15-week schedule)

Week	Topic	Subtopic
1	Introduction	
2	Particle & Granule Micrometrics Continuum Mechanics of Particulate Solids	
3, 4		Flow of Powders
4, 5		Powder Compaction
6	Midterm Micromechanics of Particulate Solids	
7, 8		Interparticle Forces
9, 10		Wet and Dry Granulation
11		Labs
12		Mixing of Granular Materials
13		Particle Size Reduction
14	Project Presentations	
15	Final Exam	

Midterm and final exam

- There will be a midterm exam. Exact date of the midterm exam will be announced a week before.
- There will be a final exam during Finals' week, covering all of the course materials.
- The midterm and final exams must be completed individually, in accordance with the NJIT Honor Code.
- Each problem will be graded independently.

A missed midterm exam will be averaged into the final grade as *zero*, unless an excuse is obtained in advance. Excuses are granted only for very serious circumstances attested to by the NJIT administration, verifiable and significant medical problems, religious holidays, and also serious personal situations, such as deaths in the family. A student who has been excused will be required to take a makeup exam.

Laboratory work

Labs will be conducted at the National Science Foundation Engineering Research Center on Structured Organic Particulate Systems located in The Otto H. York Center for Environmental Engineering and Science.

A missed lab will be averaged into the final grade as *zero*, unless an excuse is obtained. Excuses are granted only for very serious circumstances attested to by the NJIT administration, verifiable and significant medical problems, religious holidays, and also serious personal situations, such as deaths in the family. A student who has been excused will be required to take a makeup lab.

Project assignment

Students will work as a team by cooperating in a group to carry out a short research project on specific applications of solids processing and prepare a written report and a verbal presentation at the seminar. Topics for research projects may include but are not limited to:

- Particle size analysis and control for process quality
- Powder processing equipment
- Pharmaceutical powder mixing, compaction, fluidization
- Pharmaceutical powder testing
- Pharmaceutical powder blends

- Properties of pharmaceutical powders (adhesion, wetting, flowability, etc) and their effects on powder processing
- Powder coating for pharmaceutical applications

Project grading

Peer evaluation of an oral presentation by the seminar participants will include

- Mastery of the subject
- Presentation of the subject matter
- Preparation for the presentation
- Capture of the audience's attention
- Quality of visuals
- Quality of the write-up

Assessment criteria and grading

This course has been designed so that lectures, problem-solving, project assignment, and laboratory work are integral and essential parts of the learning process. Final grades will be determined from scores as follows:

▪ Project, written report and oral presentation	50%
▪ Laboratory reports and oral presentations	10%
▪ Midterm exam	20%
▪ Final exam	20%

The final grade will be assigned on the basis of "*a curve*".

Course Materials

Lecture notes, lab manuals, relevant publications and websites

Relevant publications

- M. Rhodes, Introduction to Particle Technology, Wiley, 1998.
- H.C. Ansel, L.V. Allen, Jr., N.G. Popovich, Pharmaceutical Dosage Forms and Drug Delivery Systems, Lippincott Williams & Wilkins, 1999.
- MRS Bulletin, Pharmaceutical Materials Science, 31 (11) 870, 2006
- Pharmaceutical Online http://www.pharmaceuticalonline.com
- FDA Process Analytical Technology (PAT) Initiative http://www.fda.gov/cder/OPS/PAT.htm
- J.P.K. Seville, U. Tuzun, R. Clift, Processing of Particulate Solids, Chapman & Hall, 1997.
- M. Deleuil, D. Chulia, Y. Pourcelot, Particle and Powder Dynamics, In Powder Technology and Pharmaceutical Processes, Elsevier, 1998, Chapter 5
- J. Litster, B. Ennis, The Science and Engineering of Granulation Processes, Kluwer, Dordrecht, 2004.
- M. Deleuil, Sampling, In Powder Technology and Pharmaceutical Processes, Elsevier, 1998, Chapter 1
- H.G. Brittain. Particle-size distribution II: The problem of sampling powdered solids. Pharmaceutical Technology, July 2002, 67
- R. Xu, Particle Characterization: Light Scattering Methods, Kluwer, 2000
- N.A. Armstrong, Tablet Surface Area, In Pharmaceutical Powder Compaction Technology, Marcel Dekker, 1996
- R.M. Nederman, Statics and Kinematics of Granular Materials, Cambridge Univ Press, 1992
- J.T. Carstensen, Pharmaceutics of Solids and Solid Dosage Forms, J Wiley & Sons, 1977
- J.K. Prescott, R.A. Barnum, On powder flowability, Pharmaceutical Technology, Oct 2000, 60-84
- R.L. Brown J.C. Richards, Principles of Powder Mechanics, Pergamon Press, 1970
- D. Schulze, Storage, Feeding, Proportioning, In Powder Technology and Pharmaceutical Processes, Elsevier, 1998, Chapter 9

- E. Doelker, Assessment of Powder Compaction, In Powder Technology and Pharmaceutical Processes, Elsevier, 1998, Chapter 13
- G. Ragnarsson, Force-Displacement and Network Measurements, In Pharmaceutical Powder Compaction Technology, Marcel Dekker, 1996
- P. Paronen, J. Ilkka, Porosity-Pressure Functions, In Pharmaceutical Powder Compaction Technology, Marcel Dekker, 1996
- P.N. Davies, J.M. Newton, Mechanical Strength. In Pharmaceutical Powder Compaction Technology, Marcel Dekker, 1996
- N. Mitarai, F. Nori, Wet granular materials, Advances in Physics, 55 (1-2), 1-45, 2006
- C. Führer, Interparticulate Attraction Mechanisms, In Pharmaceutical Powder Compaction Technology, Marcel Dekker, 1996
- J.N. Israelachvili, Intermolecular and Surface Forces, 2nd Ed, Academic Press, London, 1991.
- J.P.K. Seville, C.D. Willett, P.C. Knight, Interparticle forces in fluidization: a review, Powder Technology 113, 261–268, 2000.
- G. Barnocky, R.H. Davis, Elastohydrodynamic collision and rebound of spheres: Experimental verification. Phys Fluids 31, 1324, 1988
- M.D.Tousey, The Granulation Process. Basic technologies for tablet making, Pharmaceutical Technology 8-13, 2002
- S.M. Iveson, J.D. Litster, K. Hapgood, B.J. Ennis, Nucleation, growth and breakage phenomena in agitated wet granulation processes: a review, Powder Technology 117, 3–39, 2001
- K.P. Hapgood, J.D. Litster, S.R. Biggs, T. Howes, Drop penetration into porous powder beds, J. Colloid & Interface Sci, 253, 353-366, 2002
- D.G. Bika, M. Gentzler, J.N. Michaels, Mechanical properties of agglomerates, Powder Technology 117, 98–112, 2001
- D.M. Parikh, Introduction, In Handbook of Pharmaceutical Granulation Technology, Marcel Dekker, New York, 1997, 1-6.
- P. Holm, High Shear Mixer Granulators, In Handbook of Pharmaceutical Granulation Technology, Marcel Dekker, New York, 1997, 59-73
- T. Chirkot, C.W. Propst, Low Shear Granulators, In Handbook of Pharmaceutical Granulation Technology, Marcel Dekker, New York, 1997, 205-225
- D.M. Parikh, J.A. Bonck, M. Mogavero, Batch Fluid Bed Granulation, In Handbook of Pharmaceutical Granulation Technology, Marcel Dekker, New York, 1997, 227-302
- R.W. Miller, Roller Compaction Technology, In Handbook of Pharmaceutical Granulation Technology, Marcel Dekker, New York, 1997, 99-150
- M. Summers, M. Aulton, Granulation, In Pharmaceutics: Science of Dosage Form Design , Churchill Livingstone , 2001
- G. Bindhumadhavan, J.P.K. Seville, M.J. Adams, R.W. Greenwood, S. Fitzpatrick, Roll compaction of a pharmaceutical excipient: Experimental validation of rolling theory for granular solids, Chemical Engineering Science 60, 3891 – 3897, 2005
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- J.M. Ottino, D.V. Khakhar, Mixing and Segregation of Granular Materials, Annual Rev. Fluid Mech. 32, 55-91, 2000
- N. Harnby, M.F. Edwards, A.W. Nienow, Mixing in the Process Industries, Butterworth-Heinemann, Oxford, 1997
- C.W. Clump, Mixing of Solids, In Mixing: Theory and Practice, Eds. V.W. Uhl, J.B. Gray, Academic Press, 1967, v II, p. 263-287
- G.S. Rekhi, M.K. Vuppala, Sizing of Granulation, In Handbook of Pharmaceutical Granulation Technology, Marcel Dekker, New York, 1997, 389-418.