

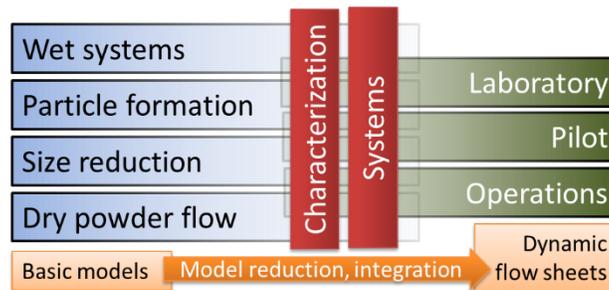
## Forward Framework for IFPRI Systems Engineering

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This is a working document, intended to become a forward-facing framework for Systems Engineering in IFPRI. It draws from personal discussions at WCPT8 (Watano, Mort, Heinrich, Litster, et al) and follow-up email (Nagy). From a timing perspective, it takes the place of an intended “Gap Analysis” that is not yet available. The authors propose to use this framework as a means of engaging IFPRI members in planning for future particle technology programs in the SE area, starting at the 2018 AGM. As a parallel next step, we have aligned to extend to the broader particle community via a Granulation Systems Engineering Workshop, to be held at PARTEC, April 2019, Nuremberg, organized jointly by the International Fine Particle Research Institute (IFPRI) and the Working Party on Agglomeration of European Federation of Chemical Engineering (EFCE).

### Context

Systems Engineering (SE) was added as a new area in the IFPRI program structure in 2015. Initially it was proposed as a means to integrate modeling and operational control frameworks over processes that encompass elements from other IFPRI focus areas (wet systems, dry powder flow, particle formation, size reduction, characterization). The initial schematic for IFPRI SE (Figure 1) displays characterization extending across the other areas and adds a system block to project the fundamental work of the original 5 areas onto multiple process scales (lab, pilot, operations) required for product development and manufacture. Models are inherent to the systems approach. Ideally, basic models developed in conjunction with IFPRI projects are translatable to dynamic flowsheets that are useful for process integration, control and optimization.



**Figure 1.** IFPRI perspective diagram on Systems as a means to integrate other focus areas (Van der Voort Maarschalk, Bermingham, Diemer and Mort, IFPRI 2015 AGM)

While the need for and application of systems engineering may vary by product and/or industry, it is typically driven by a combination of objectives including product quality (i.e., efficacy – producing the desired result) and process efficiency in both development (lab, pilot) and manufacturing operations. It seems clear that efficacy and efficiency, treated in a *pre-competitive* manner, are essential to operational sub-systems and are of relevance to IFPRI. In addition, IFPRI may choose to consider purposeful systems that are measured by their effectiveness in contributing to higher-level goals of relevance to industry-wide and/or societal systems. In this context, IFPRI’s perspective of effectiveness

toward achieving higher-level goals (e.g., safety, sustainability, life cycle management) may be considered *post-competitive*.

## Systems Engineering – exploring scope of relevance to IFPRI

The motivation for the IFPRI Systems Gap Analysis was focused on a base-level systems approach involving Process Modeling, Sensor Capability and Integration thereof;<sup>1</sup> its scope is consistent with Figure 1. In an effort to explore a broader view, this Forward Framework document selectively considers additional scope contained in the Systems Engineering Body of Knowledge (SEBoK) and many references therein.<sup>2</sup> Additional scope of potential interest to IFPRI members includes connection of Process Systems Engineering with Service, and Enterprise Systems distributed across several layers.<sup>3</sup> Depending on the operational scale and regulatory environment, a business or enterprise may need different SE approaches across relevant layers within a company or industry:

1. Process systems engineering, control and optimization – focus on technology integration.
2. Project systems -- Product systems engineering with cross-discipline and human integration.
3. Business systems – Enterprise systems engineering, service systems engineering, continuous improvement and quality management for business operations.
4. Industry systems – Long-term economic and environmental sustainability of an overall industry.
5. Societal systems – Analysis and improvement of associated issues on a societal level.

System Engineering methodologies can be classified as “Hard”, “Soft”, and “Critical Thinking”. The latter is a combination of hard and soft approaches applied situationally. In all cases, SE relies on an ability to represent problems as an integrated set of models. Hard Systems may be complex yet are solvable using available SE tools. Soft System Methodologies are better suited to handle uncertainty; rather than guaranteeing a solution to a problem, SSM provides a systematic way of organizing and exploring complex problems as learning systems.<sup>4</sup>

- Hard System methods set out to select an efficient means to achieve a well-defined and agreed objective.<sup>5</sup> There is a legacy of hard systems approaches in the aeronautical/aerospace industries, military and large civil engineering infrastructure. Hard System approaches include:
  - System Analysis - the systematic appraisal of the costs and other implications of meeting a defined requirement in various ways; a rigorous options analysis.
  - Systems Engineering (SE) - the set of activities that together lead to the creation of a complex entity and/or the procedures and information flows associated with its operation.
  - Operational Research is also considered a hard system approach, closely related to the systems analysis approach developed by the Rand Corporation.
- Soft System methods are interactive and participatory approaches to assist groups of diverse participants to alleviate a complex, problematic situation of common interest.<sup>6</sup>
  - Emergent requirements, concurrent definition of requirements and solutions, combinations of layered service-oriented and functional-hierarchy architectures, heuristics-based solutions, and evolutionary system development.

- Problem Structuring Methods use systems and systems thinking as an abstract framework for investigation, rather than a structure for creating solutions.
- Problem definition -- frame issues with an objective to achieve concise problem statement.

Regardless of the method used, simplifying assumptions are typically required for model reduction. Aligning on said assumptions may generate tension between “open” (real) systems and “closed” (model) systems. Principles to resolve said tension include:

- Consider problems holistically, setting problem boundaries though understanding of natural system relationships; try to avoid unwanted consequences.
- Create solutions based on sound system principles; create system structures which reduce organized complexity and unwanted emergent properties.
- Use understanding, judgment and models in both problem understanding and solution creation, while understanding the limitations of such views and models

As a means of assessing the success of SE projects, transformation metrics based on the “3 E’s” can be used.<sup>7</sup> Table 1 compares the “3 E’s” with an IFPRI perspective on the use of SE in Particle Technology. Efficacy (e.g., product quality) and efficiency are both clearly relevant to base-level process systems and their operation. Effectiveness may speak to a higher-level objective or goal; it may be useful to consider effectiveness in the context of expanding IFPRI’s role within the broader communities of particle science and technology.

**Table 1.** IFPRI context: 3E criteria for transformation processes, i.e., results achieved by a system.

<b>SE Transformation Metrics, 3 E’s</b>	<b>IFPRI Perspective, Particle Technology</b>
<b>Efficacy:</b> is the system producing the desired result?	Assess <i>pre-competitive</i> tools for Product Quality, Process Systems Integration and Optimization. Identify and develop fundamental capabilities needed to enable “Hard Systems” approach.*
<b>Efficiency:</b> is the system using the minimum of resources relative to the output produced?	
<b>Effectiveness:</b> is the system doing the right thing - contributing to higher-level industry-wide or societal goals?	Consider <i>post-competitive</i> IFPRI purposes relevant to higher order systems, e.g., safety, sustainability, life-cycle analyses. <sup>†</sup>

\* Consistent with the original IFPRI brief, identification of gaps in sensor, process actuation and/or modeling can be useful to the goal of enabling Hard System Methodologies. Going forward, can IFPRI better utilize Soft System Methods to identify new opportunities, e.g., for spanning said gaps?

† Going forward, should IFPRI focus only on pre-competitive content at the SE base-level, or extend scope to appropriate post-competitive topics (e.g., safety, sustainability, LCA) at higher SE levels?

## A Framework for Particulate Products and Processes\*

Specifications for particulate products may include ranges for multiple distributed characteristics, for example particle size, shape, composition, porosity or other structural attributes. On one hand, the quality and performance of products comprising particulates depends on these characteristics and structural attributes. On the other hand, processes are required to transform raw materials into particulates to meet specifications. One can frame this as an overall system of models that describe critical relationships in the chain of raw materials → processes → product structure → product function and performance (Figure 2).



**Figure 2.** Relationship diagram for Process / Structure / Performance relations. Connection symbols denote many-to-many relations among blocks in the diagram:

- Input raw materials, their specification and inherent variability;
- Processing, understanding of process capability, control and adaptability to variations in raw materials, environmental conditions, etc.;
- Structure and product characteristics as an output of processing, note specifications may have distributed attributes (e.g., particle size, shape, composition in mixtures...); and
- Derivative properties and in-use performance of products as a function of structure.

*A potential goal for the IFPRI SE effort could be to develop and/or improve tools for process/structure/performance integration, especially in ways that facilitate inverse solutions (i.e., specifying structure and process models based on performance requirements).*

*Do we have sufficient models to solve the inverse problems, i.e., for a desired product performance, what must be true of product structure, processing thereof, and materials used in that process? If so, are such solutions amenable to optimization, even multi-objective optimization?*

*Another goal can be to describe, e.g., via expert systems, details of the many-to-many relations between blocks in Figure 2. For example, detailed mapping of the relations between processes, materials and achievable structures or specifications.*

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\* inspired by W. Peukert's presentation, "Unifying Principles of Product Design," and follow up questions by B. Diemer, WCPT8, 2018.

## Process Flowsheets

A systems approach can be used to achieve quality objectives for distributed characteristics based on integrated monitoring and control. Process flowsheet models are useful in development and execution of control and optimization strategies.

Industrial systems typically include primary unit operations having control objectives (e.g., crystallization, granulation, milling) along with ancillary processes (separation, classification, recycling) that can be used to further refine output quality. Typical system models use flowsheets to integrate unit operations with flow streams having distributed characteristics. This requires a practical combination of (1) unit-op models having distributed input and output streams in sufficient detail to predict product quality objectives; and (2) sufficient measurement data to compare against the models' predicted stream distributions. On one hand, detailed models (e.g., multi-dimensional PBM's) may be challenging to implement because they require more detailed data for comparison purposes; on the other hand, grossly simplified models may not be able to adequately predict distributed characteristics relevant to product quality specifications.

Flowsheets can be used to track process efficacy, i.e., capability to meet specifications on distributed characteristics, for example particle size, shape, composition, porosity or other structural attributes of particles. A process systems approach can be used to achieve quality objectives for distributed characteristics based on integrated monitoring and control.

## Consequences of solids handling and transport

Issues with process systems startup, operating efficiency, reliability and throughput capability are often traced to problems with solids handling. This is a common experience among many IFPRI members and among the broader solids-processing community. Merrow's reports from 30 years ago cited insufficient physical understanding of solids handling, raw material feeds, and solid waste-stream handling as primary contributors to poor start-up and performance of solids-processing plants.<sup>8</sup> Specifically, Merrow cited common problems resulting from the physical tendency of solids to "plug, stick, flow unevenly, and go where they should not (often, in the form of dust)."<sup>9</sup> Pinch points were cited in feed systems, classification screens, conveyors, and bucket elevators. While IFPRI has funded considerable research in dry powder flow over the interim, these physical problems persist. In fact, challenges with solids handling, transport, and ability to control flow continue to be bottlenecks to improved process systems efficiency and efficacy (product quality).

Related to the above, many particulate process systems rely on recycle streams to achieve required product specifications while minimizing material losses. Physical handling of recycles (typically particles that are either too fine and dusty or too coarse and sticky) can be challenging. A recycle strategy that minimizes handling may seem like a good idea; however, some processes such as granulation have an undesired feedback response to direct feedback of recycles (e.g., absent other control action, increasing feedback of fines in a granulation circuit will typically drive the process to produce even more fines). In such cases, surge capacity and controlled metering of recycle streams may be needed for process control. The addition of recycle surge bins and feeders pushes against challenges with solids handling.

From a product quality and quality specification perspective, solids handling and transport can be consequential, especially in cases where quality specifications rely on distributed attributes in a mixture of particles. A product that may conform to product specifications at one sampling point may degrade simply as a consequence of de-mixing and segregation during subsequent handling, e.g., by emptying storage bins, processing through packing lines, etc. More generally, particulate products are susceptible to attrition, caking and other forms of degradation that may occur in handling and storage.

### **Forward Focus: Opportunities for advanced process system integration**

On one level, systems thinking tends to separate transformations into distinct sub-systems as a means to simplify control and optimization – i.e., a simple one-to-one relation between transformations and sub-systems may be desirable in theory. In practice, such simplified approaches often ignore the consequences of handling solid materials between sub-systems.

A “solids-handling-woke” version of systems thinking seeks to minimize consequences associated with intermediate transport and handling. Combining this awareness with flowsheet modeling, one can analyze overall system efficiency and efficacy (product quality) as a function of sub-systems choices (e.g., unit operation capability) and integration thereof.

*Are consequential transport and handling models sufficiently developed, i.e., relative to process efficiency, reliability, etc.? Are such models sufficient for use in flowsheets?*

*Recognizing the cost, operational and quality implications of solids handling, how can advances in unit operations and close-coupled integration thereof be especially advantageous to solids-processing industries?*

*In an effort to minimize negative consequences associated with handling and transport of intermediates and recycles, what are the priorities for advancing unit operations with control capability for multiple transformations? How can measurement and modeling of internal (unit-op) solids flow and stress fields promote and enable such developments?*

## Methods for Product Quality and Process Efficiency

Effective quality management assures that activities are effective and efficient with respect to a system and its performance; the focus on quality includes process and material controls, quality assurance systems, and continuous improvement. A history of quality management shows dynamic behavior regarding the balance of efficiency and quality.<sup>10</sup> Starting in the industrial revolution, production efficiency became paramount with the application of time-and-motion studies promulgated by F.W. Taylor as a “Scientific Management System.” While this system enabled higher throughput and worker productivity, it often sacrificed product quality and market adaptability. The need to achieve both quality and efficiency in more complex manufacturing systems was addressed by the adaptation of statistical methods for acceptance sampling in the 1920’s at Bell Telephone Laboratories by W.A. Shewhart et al.

W.E. Deming further developed statistical quality control, initially for agriculture, and then in support of United States’ industrial effort for World War II. Following the war, Deming was a founding member of the American Society for Quality Control.\* In the early 1950’s, Deming’s work with the Japanese Union of Scientists and Engineers enabled broad adoption of Total Quality Control (TQC) in Japan, with a rapid turnaround in both productivity and quality in many Japanese Industries. During this time, professional advocacy for quality control continued in the US, notably by J.M. Juran; however, the adoption of quality-focused methods by American industry was comparatively slow, starting only in the 1980’s with Total Quality Management (TQM). Since then, tools have continued to evolve including Six Sigma methodologies aimed at driving toward zero defects, and Lean Manufacturing aimed at just-in-time supply chain management and waste elimination.

In the context of pharmaceutical manufacturing, the US Food and Drug Administration (FDA) introduced guidance related to the use of quality-by-design (QbD) and process analytical technology (PAT) to encourage innovations and the use of more systems approaches in development and manufacturing of pharmaceutical products. In typical QbD, a process is firstly designed based on the understanding of the system to achieve a desired product quality, and then monitored and controlled using different feedback control approaches. Unlike the ‘design then control’ strategy applied in QbD, a more systems-centered approach has been recently proposed, namely the quality-by-control (QbC) concept. QbC encourages a ‘design via control’ strategy using closed-loop (feedback) control approaches to determine operating trajectories. Suitable closed-loop control approaches can reduce the influence of disturbances and decrease process and product variations, increasing the applicable design space. Development of online PAT tools with closed-loop control has enabled the QbC concept, as implemented in batch and continuous crystallization and continuous tablet manufacturing.<sup>11</sup>

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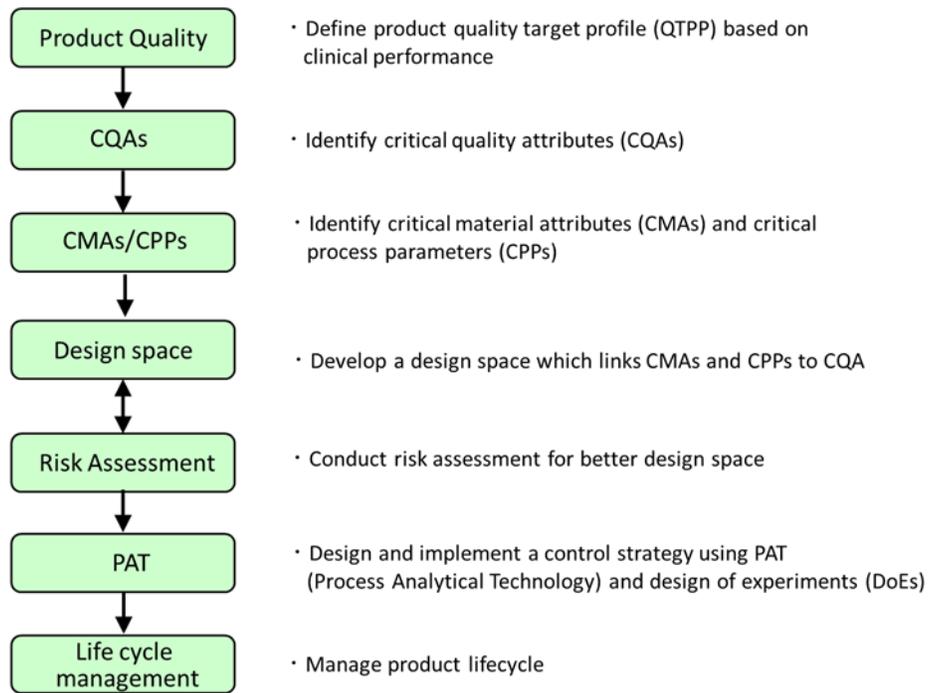
\* ASQ remains active as a global organization, <https://asq.org/>; some of its content is relevant to particles either as constituents or as contaminants across a range of manufacturing applications.

*Within IFPRI, is there interest in exploring collaboration and leverage with other professional organizations relating to common interests in systems-based tools (e.g., methods for process efficiency, product quality, safety, life-cycle analysis, etc)?*

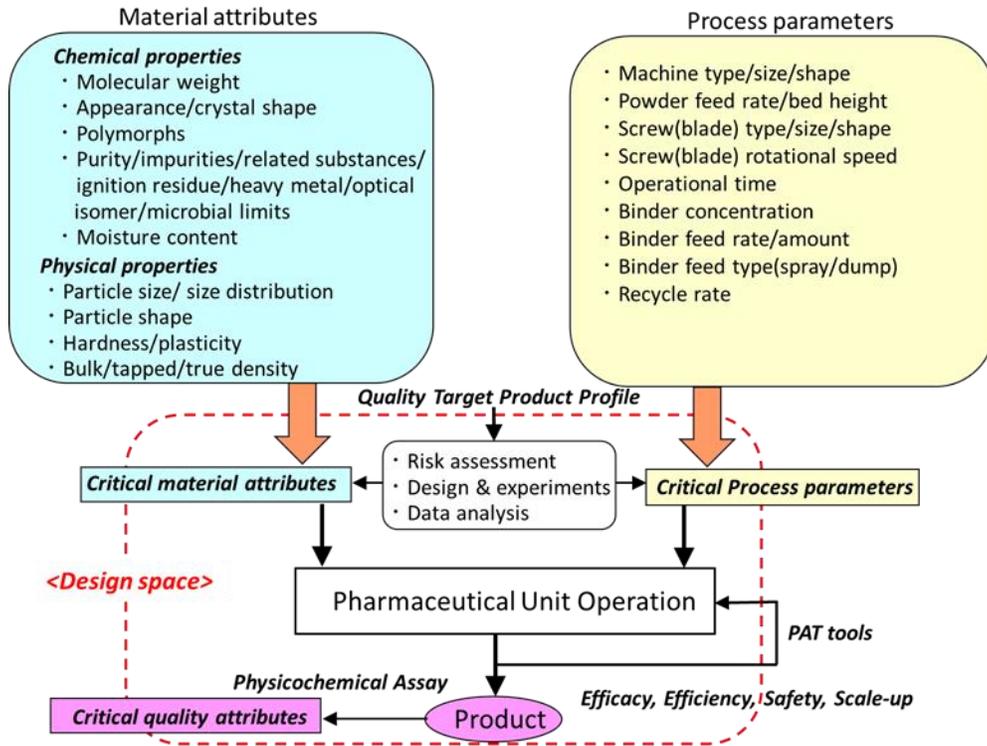
### Process systems engineering in pharmaceutical industry

Quality assurance is a major concern in pharmaceutical industry. The meaning of quality extends across process, product and service functions, and includes a wide range of concepts including product efficacy, reliability, and safety. From customer satisfaction and public health perspectives, pharmaceutical quality must be delivered at an affordable [i.e., low] cost. From an industrial R&D perspective, an effective development process is needed to better enable new drug and therapy innovation with high quality and cost-efficiency.

The concept of QbD (Quality by Design), developed by the quality pioneer J.M. Juran, embeds quality attributes in the initial product design along with quality risk assessments and lifecycle analyses. In 2005, the US Food and Drug Administration (FDA) encouraged risk-based approaches and the adoption of QbD in the drug manufacturing and its regulation. As indicated in Fig.3, the concept of pharmaceutical QbD includes following steps: 1) define product quality target profile (QTPP) based on the clinical performance and identify the critical quality attributes (CQAs) of the drug products; 2) identify critical material attributes (CMAs) and critical process parameters (CPPs) based on the process design and experiments; 3) develop a design space which links CMAs and CPPs to CQA as shown in Fig.4; 4) conduct a risk assessment for better design space; 5) Design and implement a control strategy using PAT (Process Analytical Technology) and design of experiments (DoEs); 6) Conduct product life cycle management including continual improvement.



**Figure 3.** Concept of pharmaceutical QbD



**Figure 4.** Schematics of design space

Systems Engineering (SE) is essential in the development of pharmaceutical QbD, including instrumentation of on-line monitoring and process control. While pharmaceutical design space requirements must be drawn on the commercial production scale, cost and time required to obtain design space data can be significantly reduced by using smaller-scale laboratory experiments provided one has: a) mechanistic understanding of critical quality attributes (CQAs); and b) mathematical and/or numerical modeling technologies for predictive scale-up.

The pharmaceutical industry has a legacy of batch processing for product development and manufacturing. Recently, a paradigm shift in processing pharmaceutical products has been encouraged by the US FDA (U.S. Food and Drug Administration); this requires Process Analytical Technology (PAT) to monitor and control continuous manufacturing processes. Recommended PAT's include near infrared (NIR), Raman spectroscopy, and laser detection systems. Because continuous processes are capable of higher throughput / process volume, scaling from a small batch development process to a continuous manufacturing process can avoid physical scale-up challenges associated with batch processing. On the other hand, one must address challenges inherent to continuous monitoring and control. Sensor issues include reliability, calibration drift, and fouling. Control issues include system stability, response to disturbance, recycle, and disposal of defects. Systems Engineering thinking is important to address these challenges.

## Case Studies

- Zoltan Nagy, Purdue University, “A Holistic Approach for the Model-based Control of Crystal Size, Shape and Purity in Integrated Batch and Continuous Crystallization-Wet Milling Systems,” IFPRI project, currently in progress.

A holistic proof-of-concept simulation and experimental demonstration of the real-time implementation of a full population balance model (PBM) based nonlinear predictive control (NMPC) approach for batch and continuous crystallization processes integrated with wet milling, to achieve desired crystal size and shape distribution is developed. Additionally, the effects of impurity/additive mixtures on the size, shape and crystal purity distribution will be incorporated in the model and control design to provide a system that is highly relevant to industrial crystallization where the existence of impurities is rather the norm than the exception. Typical in situ sensor models are incorporated to account for the effects of real-time measurement on parameter estimations for the process model. Further, the process model uses state-of-the-art robust and efficient numerical approaches for the solution of the multidimensional PBMs, the on-line parameter estimation and process optimization problems to achieve real-time feasibility for practical implementation of the complex nonlinear model predictive control problem.<sup>12,13</sup>

- Satoru Watano et al, Osaka Prefecture University, “Development of Continuous Manufacturing of Pharmaceuticals and Its Monitoring and Control,” WCPT8, 2018.

A novel continuous manufacturing system of pharmaceuticals with its monitoring and control systems was developed. The system consists of several unit operations such as mixing, twin screw granulation and spiral drying system. Performance of each unit operations as a function of each operating parameters was investigated experimentally. Also, a DEM (discrete element method) computer simulation was used to analyze the mechanism of twin screw granulation and a CFD (computational fluid dynamics) was used to analyze the mechanism of spiral drying system. Moisture content of granules in the twin screw granulation and the spiral drying was continuously measured and uniformity of API (Active Pharmaceutical Ingredient) content was also continuously monitored with a developed NIR (Near Infrared) sensor. Performance of the automatic manufacturing with feedback control systems of each unit operations was also investigated.

- Sudarshan Ganesh, Purdue University, “Systems Integration for Dry Granulation Based Continuous Pharmaceutical Tableting,” WCPT8, 2018.

Over the past decade, the pharmaceutical industry has seen significant progress in the mechanistic understanding of relevant unit operations, availability of multiple sensor technologies for inline monitoring of critical quality attributes and advances in data analytics to support manufacturing decision-making. These have enabled a systematic realization of continuous manufacturing for pharmaceutical tablets using the direct compaction route. However, the limitations and difficulty in handling of some particulate materials provide the impetus for investigating granulation routes to the continuous manufacturing of tablets.

In this work, the integration of dry granulation into a continuous tableting line is investigated. Specifically, the Process Analytical Technology (PAT) tools required for inline and at-line monitoring of the tableting line, and the semi-mechanistic models for the roller compactor and the tablet press are discussed. While the Kawakita model is used for the tablet press, the roller compaction process model is consisting of an integration of material balance and actuator dynamics<sup>14</sup> with a modified Johanson model.<sup>15</sup> The PAT tools, mechanistic equations, and automation system are integrated for measurement validation and data accuracy using data reconciliation in a structured ISA-95 network using DeltaV. The experimental data is presented from the operation of the continuous dry granulation line-based pilot plant at Purdue University.

- Stefan Heinrich, TUHH, “Dynamic Simulation of Interconnected Solids Processes,” WCPT8, 2018

### 1. Introduction

A novel flowsheet simulation system aimed at dynamic modelling of complex production processes in solids processing is being developed within the Priority Program SPP 1679 “Dynamic simulation of interconnected solids processes (DYNSIM-FP)” of the German Research Foundation (DFG), [www.dynsim-fp.de](http://www.dynsim-fp.de). The Priority Program consists of 29 separate projects from different German universities and is thematically divided into four main groups:

- A: Development and implementation of new dynamic models of individual apparatuses and process sub-steps;
- B: Calculation of material parameters and development of models to describe properties of solids materials;
- C: Development of advanced algorithms and methods for dynamic simulation of complex process structures;
- Z: Development of a novel framework for the flowsheet simulation of dynamic processes.

This flowsheet simulation framework, named Dyssol (DYnamic Simulation of SOLids processes), combines models, methods and algorithms, developed within the whole SPP 1679 program, into a single modelling framework that allows performing dynamic modelling of complex process structures involving solid, liquid and gaseous phases as well as their mixtures.

### 2. Calculation algorithm and applied methods

The Dyssol simulation system implements a sequential-modular approach (SMA),<sup>16</sup> where each unit is relatively independent from others and can be computed separately by its own numerical method or calculation algorithm. For each simulation time step, results of each unit model are transferred between units according to the flowsheet structure. This approach leads to a relative independence between models and provides high flexibility of the simulation system.

The SMA implies sequential computation of models in a certain order, so it is necessary to know all inlets of a model to start calculation. Flowsheets, which consist solely of serially connected modules, satisfy this condition by default. On the other hand, applying of SMA is complicated if there are recycle streams in a process structure. In this case a flowsheet must be additionally converted into sequential form by taring recycle streams.<sup>17</sup> Taring here means search for recycle streams and setting some initial values into them.

For the dynamic simulation a modified waveform relaxation method (WRM) is used.<sup>18</sup> The whole simulation time is divided into smaller non-constant time intervals, on which convergence can be reached faster. Units are solved separately on each time window using some initial guess for the solution. Calculations are repeated on the current time interval until the convergence is reached. Then, the system proceeds to the calculations on the next time window. Extrapolated values from previous time intervals are used to initialize subsequent intervals. The number of WRM iterations needed to reach convergence depends on the difference between the extrapolated and actual results. A set of extrapolation algorithms has been implemented in Dyssol to initialize the first iteration on each time interval.

### 3. Parallelization methods

Dynamic flowsheet simulation is a computationally demanding process. Sequential-modular algorithm of the Dyssol makes it relatively easy to implement different parallelization mechanisms that can significantly reduce calculation time. Several strategies are implemented:

- Parallelization of basic functions of the simulation system, such as matrix transformation and mixing of material streams.
- Parallel calculation of the model itself. Feasibility of this approach depends on the particular model, and the specific implementation is the task of a model's developer.
- Simultaneous calculation of individual time points for steady-state models. If the outlet parameters of model are independent of its internal state, and are determined only by the input parameters, model state at different time points can be computed in parallel.
- Parallel calculation of models, which are located on independent branches of a flowsheet and thereby are not directly dependent from each other.

### 4. Handling of multidimensional distributed parameters

One of the main challenges during the simulation of solids processes is related to the dispersity of granular materials: the solid phase can be distributed along several interdependent properties, such as size, shape, moisture content, density, etc. forming a multidimensional set of distributed parameters. On the other hand, each operation on the material flow, such as separation, mixing, agglomeration, etc. may require a change in one or more distributed parameters. In this case it may be necessary to calculate all dimensions from a multidimensional set even if the value of a single parameter had been changed. Therefore, the simulation must maintain interdependencies among parameters. This means that applying the same methods for calculation of solids as for liquid-gaseous systems can lead to their incorrect handling.

Dyssol represents granular material parameters in discretized form. The entire interval, on which the parameter is determined, is represented as a set of shorter intervals. To describe the distribution each such interval is associated with the number or mass of particles whose parameters fall within this interval. The discretization scheme must be fine enough that the numerical errors were small compared to the accuracy of the models.

To represent interdependency between several distributed parameters multidimensional matrixes are used,<sup>19</sup> where the number of dimensions is equal to the number of parameters. Each

cell of such matrix contains the mass fraction of the solid material with certain combination of parameters, whereas the total sum of all entities of the matrix is equal to one.

A sparse data format is used to store the discretized multidimensional distributed parameters. The multidimensional matrix is represented by a flat tree data structure, where each level of this tree is one of the dimensions. If there are some classes which are empty (contain zeroes), there is no need to store data on lower levels. This approach provides an opportunity to reduce memory consumption and calculation time. For more efficient usage, dimensions are arranged such that the more zeroes a dimension contains, the higher it is placed in the structure.

For correct handling of solids, an approach with transformation matrices is used. Each cell of a transformation matrix describes the mass fraction of material that passes from one class with a combination of parameters to some other class with another combination of parameters. This concept allows preserving information about all parameters, even those which are not considered or not changed in the current model. Thus, an explicit calculation of the model's parameters transformation matrix can be generated and applied to obtain output stream in each unit.

When using this approach, the model of each unit must follow the transformation matrix approach. While this may add complication, it ensures that all information about the distributed parameters of granular materials will be retained during the computation and properly considered.

## Selected References

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- <sup>1</sup> A. Kalbasenka, P. Vonk, S. Bermingham, and P. Mort, "Toward Systems Engineering Workshop – A Gap Analysis of Systems Modeling, Sensor Capability and Integration thereof," IFPRI AGM, 2016
- <sup>2</sup> Guide to the Systems Engineering Body of Knowledge (SEBoK), v1.9, 2017, [http://www.sebokwiki.org/wiki/Guide\\_to\\_the\\_Systems\\_Engineering\\_Body\\_of\\_Knowledge\\_\(SEBoK\)](http://www.sebokwiki.org/wiki/Guide_to_the_Systems_Engineering_Body_of_Knowledge_(SEBoK))
- <sup>3</sup> D. Hitchins, "Systems Engineering, A 21st Century Systems Methodology," Wiley, 2007.
- <sup>4</sup> P. Checkland, "Soft Systems Methodology: A Thirty-Year Retrospective," Syst. Res. 17, 2000
- <sup>5</sup> P. Checkland, "The Origins and Nature of "Hard" Systems Thinking," Journal of Applied Systems Analysis, 1978
- <sup>6</sup> P. Checkland, "Systems Thinking, Systems Practice," 1999
- <sup>7</sup> S. Burge, "An Overview of the Soft Systems Methodology," <https://www.burgehugheswalsh.co.uk/Articles-Systems-Thinking.aspx>
- <sup>8</sup> E. Merrow, "Linking R&D to Problems Experienced in Solids Processing," Rand Corporation, 1984, <https://www.rand.org/pubs/papers/P7034.html>
- <sup>9</sup> E. Merrow, "Estimating Startup Times for Solids-Processing Plants," Chemical Engineering, 1988.
- <sup>10</sup> R. Kolb, M. Hoover, "The History of Quality in Industry," Sandia Report SAND2012-7060, 2012, <http://prod.sandia.gov/techlib/access-control.cgi/2012/127060.pdf>
- <sup>11</sup> A. Koswara, Z.K. Nagy, On-Off feedback control of plug-flow crystallization: a case of quality-by-control in continuous manufacturing, IEEE Life Sciences Letters, 3 (1), 1-4, 2017.
- <sup>12</sup> B. Szilágyi, P.S. Agachi, Z.K. Nagy, Chord Length Distribution Based Modeling and Adaptive Model Predictive Control of Batch Crystallization Processes Using High Fidelity Full Population Balance Models, Ind. Eng. Chem. Res., 57 (9), 3320–3332, 2018.
- <sup>13</sup> B. Szilágyi, Z.K. Nagy, Population balance modeling and optimization of an integrated batch crystallizer–wet mill system for crystal size distribution control, Crystal Growth & Design, 18 (3), 1415-1424, 2018.
- <sup>14</sup> Hsu S-H, Reklaitis G V., Venkatasubramanian V. Modeling and Control of Roller Compaction for Pharmaceutical Manufacturing. Part I & II: Process Dynamics and Control Framework. J Pharm Innov. 2010; 5(1-2):14-36
- <sup>15</sup> Liu Y, Wassgren C. Modifications to Johanson's roll compaction model for improved relative density predictions. Powder Technol. 2016; 297:294-302.
- <sup>16</sup> Hillestad, M., Hertzberg, T.: Convergence and stability of the sequential modular approach to dynamic process simulation. Comput. chem. Engng. 12, 1988, 407-414.
- <sup>17</sup> Towler, G., Sinnott, R.: Chemical engineering design: principles, practice, and economics of plant and process design. Second edition. Butterworth-Heinemann Press, 2013.
- <sup>18</sup> Dosta, M.: Hamburg-Harburg, Techn. Univ., Diss., 2012.
- <sup>19</sup> Pogodda, M.: Hamburg-Harburg, Techn. Univ., Diss., 2007.