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Case studies using Artificial Intelligence (A.I) Tools

Manufacturing process optimisation

Case study

A pharmaceutical company approached the IPI, to investigate potential changes to their formulation and process to increase the robustness of a tableted product. They were facing a problem with the efficiency of large scale manufacturing as relatively slow compression speeds were required in order to produce satisfactory tablets to required specifications for hardness and friability.

The IPI carried out compression studies on the samples provided using our small-scale formulation laboratory in order to assess the effect of scale and compression force on differing formulations.

Initial analyses showed informative results in the behaviour of the alternative formulations. Further data interrogation was carried out to understand more about the manufacturing conditions required to produce robust tablets.

The IPI recommended data-mining of these experimental results, together with the manufacturer's own data, using A.I tools (neural networks and genetic algorithms) in order to generate meaningful patterns and relationships from the data, which the client can use to their advantage.

A.I Tools - Rule Generation

Case study on data-mining exercise

Using the AI software from *Intelligensys* a data-mining exercise was carried out to generate rules from experimental data supplied by a large multinational pharmaceutical company. The company was surprised by the rules generated, as they were not consistent with their own perceptions of their manufacturing process. However the company repeated their experimental work and the results showed that the knowledge generated from the AI tools was correct. This is because data-mining aims to extract hidden knowledge from data, and this knowledge may be new to the formulator and outside the realm their expertise and experience. Without using these AI tools, knowledge that is hidden in data can easily be lost and not be capitalised on.



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A.I Tools – Neural Network Modelling and Optimisation

Case study

Last month the IPI was invited to visit a company in China in order to present the IPI's capability in using Artificial Intelligence tools to solve problems in formulation system design. After a demonstration of the A.I software, the client requested the IPI to analyse one of their own datasets, which was the result of a series of nine experiments (with both input and output variables). This dataset was fed into the software and the neural networks were then built. Based on these neural networks optimisation task was carried out using genetic algorithms in order to generate an optimal formulation and processing conditions. The results obtained from the software were in the same range as those results obtained from the clients' own analytical methods. The client felt that "the tools were powerful", as the results obtained from the IPI's software tools were generated in a much shorter time than for their current analysis method.

Modelling and Simulation Tools

By modelling and simulating a process, manufacturers gain improved understanding of that process without having to actually run that process in real time. This can result in a more effective and efficient use of limited resources and assist in the reduction in costs and time of producing newer products.

The IPI, in conjunction with *Intelligensys* one of its software partners, is developing software products designed to simulate manufacturing processes. Current products include prediction of cracking in film coatings; optimisation of capsule filling (and other drug containment systems); and modelling powder packing to simulate tablet compaction.

- Tablet cracking simulator

The cracking simulator is able to simulate crack propagation in viscoelastic materials. The simulator is able to model crack propagation in compacted porous materials as well as for filled polymer systems enabling researchers to simulate the cracking of tablets as well as of tablet film coatings. Cracking can have profound effects on the release of an active ingredient especially if the tablet has been coated with an enterosoluble or a sustained release film.

With the visualisation function, the simulator enables researchers to view how the crack propagates; at what speed and to what degree the cracking occurs across the simulation box. This cracking simulator has been validated against electron micrographs of real materials in a number of cases and has been applied to understand issues important in drug formulation and have been used in a variety of materials e.g. aspirin, microcrystalline cellulose, and for pigment-filled tablet film coatings.





- Powder packing simulator

The IPI and *Intelligensys* are able to offer useful bespoke simulation software that integrates analysis and visualisation to let you examine features of the packing system. This software is useful in solving problems involving particulates and particle packing to help understand the behaviour of particulates in materials, for example; how they pack and how this affects microstructure and end-use properties. The software is able to solve problems associated with the variability in the filling process e.g. estimating volumes, materials handling loads and mixing problems etc.

Visualisation is especially useful and both 2D and 3D representations can be obtained. The visualisation coupled with the analysis give powerful insights into local ordering, behaviour at boundaries, and overall packing densities.

The knowledge gained can underpin aspects of formulation design e.g. capsule design and filling, ratios and distribution parameters.

- Tablet compaction simulator

The modelling of powder packing enables the simulation of tablet compaction. A tablet compaction simulator is currently being developed in AstraZeneca in order to simulate compaction of particulates on a large-scale manufacturing. This simulation package will be able to address the variability of a multi-particulate system and calculate stresses in the system to generate knowledge as to how the compaction would behave during large-scale manufacture.

This tablet compaction simulation software can be used to:

- Avoid mechanical failure (capping, lamination)
- Optimise process conditions e.g. rate, waste, rejects
- Scale up
- Avoid the need for expensive time consuming experimentation (materials and personnel, time to market etc)





Expert Systems

An expert system provides formulators an affordable means to capture knowledge in a documented form available to all. They are transforming the way in which pharmaceutical companies manage and retain formulation data and know-how.

The IPI has established a partnership with *KnowledgeBench*, a software company, to offer an expert system which manages information and optimises decision-making at all stages of the formulation process.

KnowledgeBench is an intelligent information workbench, offering a fully integrated decision support framework covering all aspects of product development. *KnowledgeBench* is designed to bring better quality, control and effectiveness to new product development and this is achieved by acknowledging the deficiencies of previous tightly regulated approaches, and allowing a high-level process to be mapped and then supported via:

- ✚ advanced decision support (to encapsulate and model decision processes within an organisation)
- ✚ knowledge management
- ✚ datamining and
- ✚ goal-centric workflow in order to provide targeted information and guidance on all aspects of the new product development lifecycle.

The benefits of engaging the IPI services supported by the *KnowledgeBench* platform include;

- Capturing data to be incorporated into an expert system
- Knowledge management
- Knowledge protection and availability
- Consistency in decision making
- Access to software products designed to simulate the manufacturing process
- Identifying opportunities to improve formulation e.g. product line extensions
- Solving formulation/processing problems
- Capturing knowledge which may be lost due to staff turnover

Both GlaxoSmithKline (GSK) and AstraZeneca (AZ) are currently implementing this product formulation expert system.

