pharma point

No. 2 · February 2005 Newsletter of the Swiss Society for Pharmaceutical Sciences (SSPhS)

Topic of the second edition: From Art to Science

From Art to Science: the Challenge of FDA's PAT Initiative for Academia and Industry

Prof. Dr. Hans Leuenberger
President of the Swiss Society of Pharmaceutical Scientists

Institute of Pharmaceutical Technology, Pharmacenter, Klingelbergstrasse 50, CH-4056 Basel
Hans.Leuenberger@unibas.ch www.pharmtech.unibas.ch

FDA's Initiative and update on PAT Projects can be described as a revolutionary paradigma change concerning the "Pharmaceutical cGMPs for the 21st century". FDA' PAT initiative is by far not limited to Processes and to Analytical Technologies to keep the processes within the required specifications.

FDA's initiative has a major impact on industry and academia: The main focus is no longer that product quality complies with the regulatory requirements but that there is a continuous improvement in quality of the products.

This statement includes also products on the market! The majority of the products on the market are solid dosage forms, which represent a challenge concerning manufacturing science: The performance of the pharmaceutical industry is only around Two Sigma, i.e ca. 4.5% defectives. This does not mean that the patients will receive defective samples but that the production needs to eliminate the defective samples, which can be a costly operation. The champion concerning the manufacturing performance is the chip industry with the Six Sigma value, i.e. with only 2ppb defectives, which is an enormeous advantage facilitating the production of personal computers of high quality at a reasonable prize. A high quality, i.e. Right First Time, means a low variability. This means "process understanding" and to identify critical processes. Typical problems of non-robust formulations and critical processes need to be addressed. Thus it demonstrates the necessity and the challenge of FDA's PAT initiative for the academia to develop a rigorous scientific framework especially in the area of pharmaceutical powder technology.

A kind of "Road Map" should be proposed to achieve as fast as possible the top of the "Knowledge Pyramid" often cited by FDA. The road map includes the extensive use of a multivariate design of experiments, the use of artificial neural networks (ANN), the use of the laws of physical pharmacy and percolation theory and last but not least to try to "translate" the existing laws of physical chemistry into the area of pharmaceutical powder technology, where we have the problem that the number of particles involved is much lower than the Avogadro number N_A. For this purpose the results of Nanoscience and Nanotechnology should be integrated. Thus it is important to monitor closely the progress in Nanoscience, especially in the area of mathematical modeling the fascinating special physical properties of nanoparticles, which again consist of a finite number N of atoms, respectively molecules, with $N << N_A$. The paper "Pharmaceutical Powder Technology – From Art to Science: the challenge of FDA's Process Analytical Technology (PAT) initiative" (Advanced Powder Technology, February 2005 edition) describes with typical examples the state of art.

Contents

The future importance of process modelling for the pharmaceutical industries

by Klaus Eichler

In spring 2004 the FDA (Federal Drug Administration USA) did start their PAT (Process Analytical Technology) initiative, which was already foreseen for the year before but was delayed by the outbreak of the Iraq war.

The FDA has compared the process quality standards of other industries, such as chip production or aircraft construction, with the standards of the pharmaceutical industries and using the sigma scale (1-6) were 6 is the highest mark, which stands for a failure quote of 0.000000197 %, which applies to the former industries and Sigma 2, i.e. 4.55 %, to the pharmaceutical industries, although the latter seem to be well on their way towards Sigma 3. They have so far not challenged this evaluation, which allows the conclusion that they are aware that there is not sufficient science in their processing procedures yet and that their present production is still extensively based on the empirical know-how of their production staff, hence on art.

Nevertheless, products reaching the market are, of course, of highest quality. The problem is the products not reaching the market as they do not meet the necessary quality or compliance standards.

Hence the FDA request, to change the present situation by introducing more science into production, is more than justified. Quality cannot be inspected into a product; it has to be engineered from the very beginning.

The pharmaceutical industries have to rid themselves from high inventories, low productivity, low equipment utilization and too little process understanding. At times when profits were still high, there may have been a lack of motivation to trigger changes, but the present situation makes innovation necessary for survival:

- an ever decreasing number of new chemical entities,
- ever increasing cost for launching a new product on the market (800 million US $),
- too long times between drug discovery and commercialization (9-12 years).

The FDA phrases their request neatly: Do it right the first time by building quality into the products.

To achieve this, production must be science based, i.e. we need proven data for a predictive performance and on-line quality control. We may need new sensors or even entirely new techniques to reach the target, but we cannot afford not to accept the challenge. We will also need realistic processing models to reach the target.

Process simulation will become a standard tool for process and product optimization, but to develop better models we first have to perfectly analyze our processes, understand how variability does affect product quality and performance. Understanding why things go wrong will allow us to perfectly define the optimal parameters for every process.

The artists presently working in pharmaceutical production certainly have acquired an enormous empirical know-how, which allows them to run a process more or less successful.

I knew a lady at Guangzhou Nr. 7 (Canton), who worked as production manager and did define the final moisture of a fluid bed produced granule by listening to the sound the moving granules made on the stainless steel housing of the fluid bed. When a certain frequency was achieved, she stopped the process. When product samples were subsequently analysed with an infrared scale, the residual moisture was always 2%, perfect for compression into tablets.

Our senses are true miracles of nature. Our scientists insist that the human eye can differentiate 7 million hues of colour. However, most likely this high variability is the reason why we are presently stuck with sigma 2.

There are obviously no standards for all the artist presently working in pharmaceutical production, decision criteria are at random and there cannot be any doubt, that variability is definitely desired for the arts (we could do with some more these days), but a handicap in production.

Having already a good range of hi-tech instruments and high computing power for developing processing models with high predictive power we have never before been as well equipped for accepting the FDA challenge for a science based pharmaceutical production.

I wish to repeat an aphorism from Antoine de Saint-Exupéry, who was recently quoted by Dr. Werani, a top director from Pfizer, for the conclusion of his PAT key note lecture at the Pharmacenter Basel:
PERFECTION IS ACHIEVED, NOT WHEN THERE IS NOTHING TO ADD, BUT WHEN HERE IS NOTHING LEFT TO TAKE AWAY.

The following SIGMA-TABLE is based on a process with a variability which follows the normal distribution, i.e. the estimate of error is 2 α corresponding to the amount of defects:

Sigma	Amount of defects (%)
1	31.7
2	4.55
3	0.27
4	0.00633
5	0.0000573
6	0.000000197

Klaus Eichler works since 25 years with Glatt and is Business Development Director for the group, besides running the Technology Training Center at Binzen.

Process modelling in pharmaceutical development and production: the toolbox overview

by Dr. Maxim Puchkov

The Food and Drug Administration of Department of Health and Human Services of United States of America (FDA) presents a barrier that every pharmaceutical product has to pass before it can enter the market. It warrants a high product quality but has also become a fire wall retaining products from the market. The new FDA PAT initiative for "building quality into the products" can serve as a roadmap for fast product launches www.fda.gov/cder/OPS/PAT.htm:

"There are many current and new tools available that enable scientific, risk-managed pharmaceutical development, manufacture, and quality assurance. These tools, when used within a system can provide effective and efficient means for acquiring information to facilitate process understanding, develop risk-mitigation strategies, achieve continuous improvement, and share information and knowledge. In the PAT framework, these tools can be categorized as:

- Multivariate data acquisition and analysis tools
- Modern process analyzers or process analytical chemistry tools
- Process and endpoint monitoring and control tools
- Continuous improvement and knowledge management tools".

These four types of tools have one common element that glues them together: data analysis and management technology. Modern data analysis and management is a blend of high-speed computation, mathematical modelling and "artificial intelligence".

The purpose of this article is to overview the existing modelling tools applicable to be used for pharmaceutical technology purposes. There is a number of most popular mathematical modelling techniques and "artificial intelligence" tools:

- Mapping a complex of n-dimensional functions as superposition of continuous and monotonic single segments (Artificial Neural Networks (ANN), CASE-based reasoning, Computational Fluid Dynamics (CFD), etc.);
- Multi-particulate ensembles (Percolation Theory, Dynamic Chaos Systems, etc.) ;
- Conventional mathematical description based on the idealized properties of matter (ideal mixing, plug flow, compartment models, etc.);
- Knowledge and Information Management (Information systems, Expert systems, etc);
- Imitational Modelling (Logistics, Discreet mathematics, etc.);

The amount of modelling methods is different and there is strong need to establish the rules and extents of applicability for different methods.

To fulfill the above mentioned requirement the model "evolution" levels have to be introduced:

- Empirical modelling (statistical and experimental method, "black-box" modelling)
- Analytical and experimental level (method of effective coefficients)
- Structural method (theoretical modelling assuming full understanding of the modelling object, e.g. singular unit operation or ensemble/plant)

Empirical modelling is used if the process or its nature is not known. As the modelling tools the most appropriate technologies are ANN, CASE-based reasoning, Response Surface Methodology (RSM). In pharmaceutical technology these methods are used since long time and were successful. Empirical models are representing the object as the function of inputs plus noise component. The form of criterion function is never known during the empirical modelling, thus the information about the reasons of the certain reaction of the system to the disturbance action could not be extracted. Criterion function can be a regression equation in polynomial form (RSM) or matrix of weights (ANN) or combination of logical and empirical parameters (CASE-based reasoning). The criterion function can be obtained by following 3 methods:

- Passive experiment
- Active experiment including an object response to standard disturbance (e.g. unit-impulse function disturbance)

The passive experiment is the data and process parameters acquisition of the established process. However, the variation of the dataset of such processes is very low, thus the extrapolation is not possible. Such data sets can be used as the training set for ANN of non-supervised learning (Self-Organized Feature Maps, Kohonen Networks) due to their ability to classify the unknown cases in order to detect the emergency conditions.

Active experiment assumes the variation of the process parameters according to the experimental design. Such a data can be used as well as for ANN training set or RSM. However, the combination of both methods is the most advantageous due to the possibility to evaluate the results of ANN with the corresponding RSM. The ANNs trained in this way are able to interpolate with higher regression ($R2 = 0.85 \pm 0.05$) but the extrapolation possibility is usually lower than the accepted variability.

Another application of ANN that has to be mentioned is the combination with genetic algorithms (GA). The ANN/GA technology allows fast and efficient selection of the best input variable set. In brief the method could be described as an iterative change of the different combination of the inputs according to the simplified algorithm of genitival mutations. The "stable mutation" is selected on the base of the results from ANN training: the higher the ANN correlation the better the "mutation". This process is repeated iteratively till the subsequent mutations are showing the

decrease of the correlation. Input set found at the extremum is the best. This method is also used for the screening the best ANN structure. As an example of application of such a method the robust formulation design (prediction of the influence of different excipients) or influence of process parameters during different unit operations (e.g. fluid-bed granulation) could be given.

There is a number of software products available on the market that deal with ANN/GA, RSM, CASE-based reasoning. However, in order to apply developed ANN models for on-line monitoring the specialized in-house software is often being developed. For example the ANN can be developed and trained by using STATISTICA NN package and exported to, for example, LabView module.

According to the mentioned above the ANN/GA/RSM technology is very convenient way to build up and to use the empirical models. These methods have well developed theoretical base, application examples and big variety of the software tools.

Analytical and experimental modelling is a combination of theoretical and experimental methods. By using this method the investigator is trying to determine the physics of process. This is usually done by decomposing the complex system to the elementary units in order to determine the basic process. The basic process is described by characteristic formula that is specific for given process. The influence of the other components is considered by coefficients.

As an example the modeling of the heat transfer through the powder bed of fluidized bed granulator can be examined. The heat transfer under 800K and relatively low air velocities is mainly due to heat conduction that is described by Fourier Law:

$$q = -\lambda \frac{dT}{dX}$$

However, this equation can not be used to describe the real process due to the other 2 heat transfer components (emission and convection) are not taken in to account. Thus, the experiment required to come to adapted or effective coefficient, λ_{eff}. In this case the previous equation changes as follows:

$$q = -\lambda_{eff} \frac{dT}{dX}$$

Received equation is the model of the heat transfer through the stable bed of powder, however it depends on the apparatus, scale, process and environmental conditions the experiments were carried out in order to determine the λ_{eff}.

This type of modelling has an obvious advantage over the empirical modelling; it describes the origin of the basic phenomenon. However, it includes an empirically estimated coefficients, thus could be considered as an engineering approach.

There are a number of different software tools available; unfortunately the main part of them is the in-house developments. The effectiveness of the software that works on this principle is determined by the model databank "volume". The good example is the gPROMS software package by Process System Enterprise Ltd. This package incorporates a huge library of different unit operations and the software is built with an ideology of share and exchange models. The other well-known software solutions from Aspen, MathWorks, etc. are perusing the same ideas and there are converters and connecting modules already existing.

For pharmaceutical industry this approach along with the software libraries of different unit operations are advantages for shortening the time for establishing the robust production flowchart, thus the time-to-market. Structural or theoretical modelling is the best method to develop a mathematical description of the process. However, it requires the full understanding of the process supported by the well developed and proven theory. In general this approach consists of the components as shown on the figure 1.

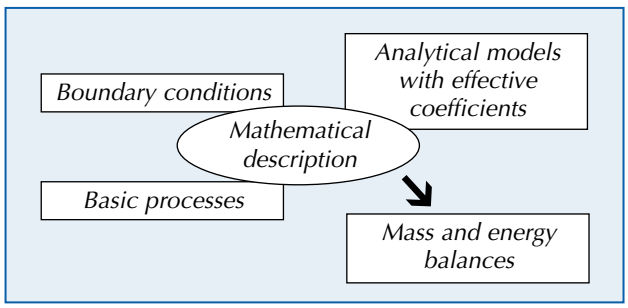

Fig. 1. Components of mathematical model according to theoretical approach.

Advantages of this method are obvious: high extrapolation possibilities, multi-level or hierarchical modeling and decomposition. However, the disadvantages are obvious as well: difficulty to create the theory of complex interactions for ensembles of multi-component systems, time-consuming development. There is no specialized software tools developed for this type of modelling. In general the combination of different software tools is used.

In the conclusion of this short overview it is important to say that the best and the ideal method for developing the mathematical description in pharmaceutical technology is the theoretical approach that incorporates the other methods and theories.

Acknowledgement

Author would like to thank Prof. H. Leuenberger (Institute of Pharmaceutical Technology, University of Basel) and Klaus Eichler (Technology Training Center) for starting the "From Art to Science" initiative that shelters all above mentioned methods.

Dr Maxim Puchkov is currently doing his postdoctoral fellowship at Institute of Pharmaceutical Technology, University of Basel. The research interests are covering application of artificial neural networks for granulation process control, modelling of pharmaceutical industry unit operations, e-learning activities at University of Basel.

TECHNOLOGY TRAINING CENTER BINZEN GERMANY

SGPhW

background

Following the recommendation of the recent PAT initiative of the FDA, the concerned industries are supposed to better the quality of the present manufacturing methods by a sound science-based understanding of all unit operations. Product quality is supposed to be designed a priori as stipulated by the FDA slogan "Do it right the first time". If quality is to be build into the products, we can no longer rely on the empirical know-how of the manufacturing artists, but have to control all possible interactions of the process parameters.
Today, having available sophisticated on-line control instruments and process simulation computer tools, we are technically better equipped than ever before. This workshop is supposed to show innovative approaches for building quality into products.

who should attend

Researchers, formulators, production managers and quality managers from the industries concerned.

Workshop
Innovative approaches for granulation coating drying

From Art to Science

speakers

Frédéric Depypere
University of Gent, Belgium
Stefan Dietrich
Parsum GmbH, Germany
Dr Samira El Mafadi
enitiaa, Nantes, France
Anja Guntermann
Pfizer GmbH, Germany
Dr Eleonore Haltner
Across Barriers GmbH, Germany
Jun-Prof Dr Stefan Heinrich
University of Magdeburg, Germany
Michael Jacob
Glatt Ingenieurtechnik GmbH, Germany
Dr Peter Kasa
University of Szeged, Hungary
Prof Dr Hans Leuenberger
University of Basel, Switzerland
Dr Bita Kolahgar
Ametek GmbH, Germany
Prof Dr Natalia Menshutina
D. Mendeleev University of Chemical Technology of Russia (MUCTR), Russia
Dr Ingela Niklasson-Bjorn
AstraZeneca, Sweden
Dr Gavin Reynolds
University of Sheffield, United Kingdom
Frauke Russel
Roche AG, Switzerland
Constantijn Sanders
University of Sheffield, United Kingdom
Prof Dr Jonathan Seville
University of Birmingham, United Kingdom
Dr Kaspar van den Dries
N.V. Organon, The Netherlands

program

Tuesday 21 June 2005

12.30 *LogIN + Snacks*
13.00 Introduction
Klaus Eichler
13.15 From art to science
Hans Leuenberger
14.00 Quality control
in high shear granulation
– a PAT perspective
Kaspar van den Dries
14.45 Optimization of the Wurster process
by accurate mass flow monitoring
Samira El Mafadi
15.30 *Coffee break*
16.00 Fluid bed coating –
a particle motion study
Frédéric Depypere
16.45 Spouted fluid bed granulation
Michael Jacob
17.30 *End of 1st day –*
bus transfer to the hotel
19.30 *Wine tasting including dinner*

Wednesday 22 June 2005

09.00 Fluid bed granulation
– from batch to continuous
processing
Stefan Heinrich
09.45 The control of solvent evaporation
from pharmaceutical products
Bita Kolahgar
10.30 *Coffee break*
11.00 Compaction and roll pressing
Jonathan Seville
11.45 The Presster – a tablet press simulator
Anja Guntermann
12.30 *Lunch break*
13.45 The benefits of process modelling
Natalia Menshutina
14.30 A rate based approach to
measuring and understanding
granulation
Gavin Reynolds
Constantijn Sanders
15.15 *Coffee break*
15.45 Industrial process modelling
Ingela Niklasson-Bjorn
16.30 A rate based approach to modelling
and understanding granulation
Gavin Reynolds
Constantijn Sanders
17.15 *End of 2nd day –*
bus transfer to the hotel
19.30 *Workshop banquet*

Thursday 23 June 2005

09.00 Cell culture as a tool to verify
coating concepts of low soluble
subtances
Eleonore Haltner
09.45 Application of an artificial
neutral network system
to predict some properties
of coated particles
and coating parameters
Peter Kasa
10.30 *Coffee break*
11.00 Dissolution testing
and NIR spectroscopy
Frauke Russel
11.45 Optical filter particle detection
(incl. demonstration)
Stefan Dietrich
12.45 *Snack buffet and LogOUT*

moderation

Prof Dr Hans Leuenberger
University of Basel, Switzerland

place of venue

Technology Training Center
Binzen, Germany

details

The participation fee is a 1.240,-- (exclusive of VAT) and includes your participation, accompanying course notes, daytime catering and evening program. All other expenses are to be borne by the attendee.

registration

Please register online
www.ttc-binzen.de

organisation

TTC (Technology Training Center)
Klaus Eichler / Jeannette Steinbach
Werner-Glatt-Strasse 1
79589 Binzen, Germany
Tel.: + 49 / 7621 / 664-308,
Fax:+ 49 / 7621 / 664-632
eMail: ttc@ttc-binzen.de

For further information
please have a look at
www.ttc-binzen.de

Application of case-based reasoning approach in tablet formulation support system

A. V. Vetrov[1], N. V. Menshutina[1], O. V. Sidorkin[1], H. Leuenberger[2]
[1]*D. Mendeleev University of Chemical Technology of Russia, 125047 Moscow, Miusskaia square 9, +7-095-973-57-49, +7-095-973-57-49 fax, chemcom@muctr.edu.ru*
[2]*Institute of Pharmaceutical Technology, University of Basel, Switzerland, tel.: +41-61-3810722, fax: +41-61-2671516, e-mail: hans.leuenberger@unibas.ch*

Introductions

Among the various formulation types for pharmaceutical preparations, the tablets by far the most popular. Over half the medicines used in the world are in the form of compressed tablets. The design of new tablet involves identifying not only an active ingredient providing curing effect, but the inert components called excipients too. Excipients play the role as fillers, binders, lubricants, disintegrants and surfactants of the tablet. Excipients are added to impart tablet with necessary physical and biological characteristics. Most tablet formulations have to meet complex and often conflicting performance criteria – e.g. high strength and rapid disintegration. Rarely can the relationships between ingredient levels, processing and product performance be quantified precisely. Formulation task is therefore a complex design task, which includes a formulator's considerable experimentation and trial batching.

The Product Formulation Support System (PFSS), which is being developed in University, will support full cycle of product formulation process and significantly reduce the amount of experimentation work. The PFSS objectives are as following:

- Collect every product formulation itself and all information concerned with it in formulation repository.
- Reduce the amount of formulator's considerable experimentation and trial batching by means of data analysis methods.
- Reuse stored information about previously formulated products in future formulations.
- Store full trace of formulator activity during formulating.

Formulation repository and data analysis unit are being developed at the first stage of work. Data analysis unit will include both an ordinary approaches (like factor analysis, for instance) and Artificial Intelligence methods as well. The Case-based reasoning (CBR) approach was the first method to implement in data analysis unit.

Approach

CBR is a problem solving technique. It imitates a human reasoning and tries to make a decision based on earlier experiences. An experience may be concerned with what was true or false, correct or incorrect, good or bad, more or less useful, etc. It can be represented by a rule, a constraint, some general law or advice, or simply by recording past event. The episode from past life can contain some decisions, which could be found useful.

Contrary to the expert systems, which rely only on general knowledge and certain rules, CBR deals with

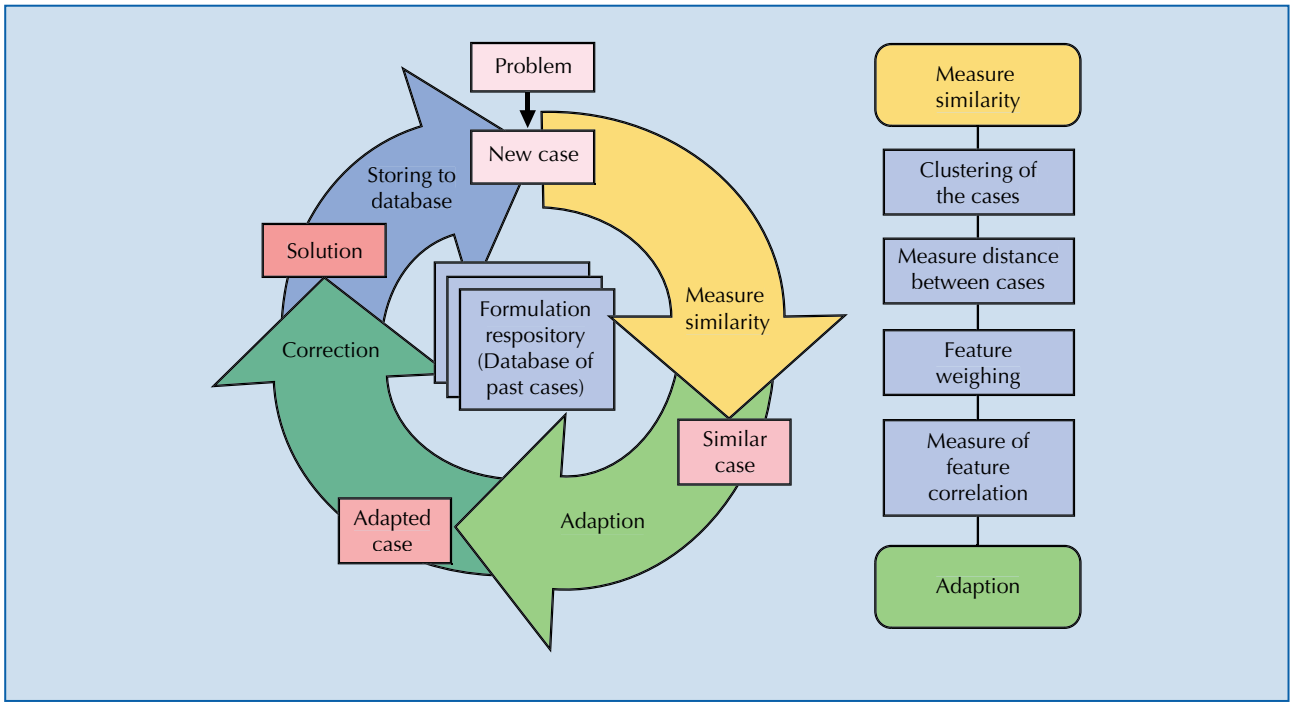

Figure 1 The application of CBR

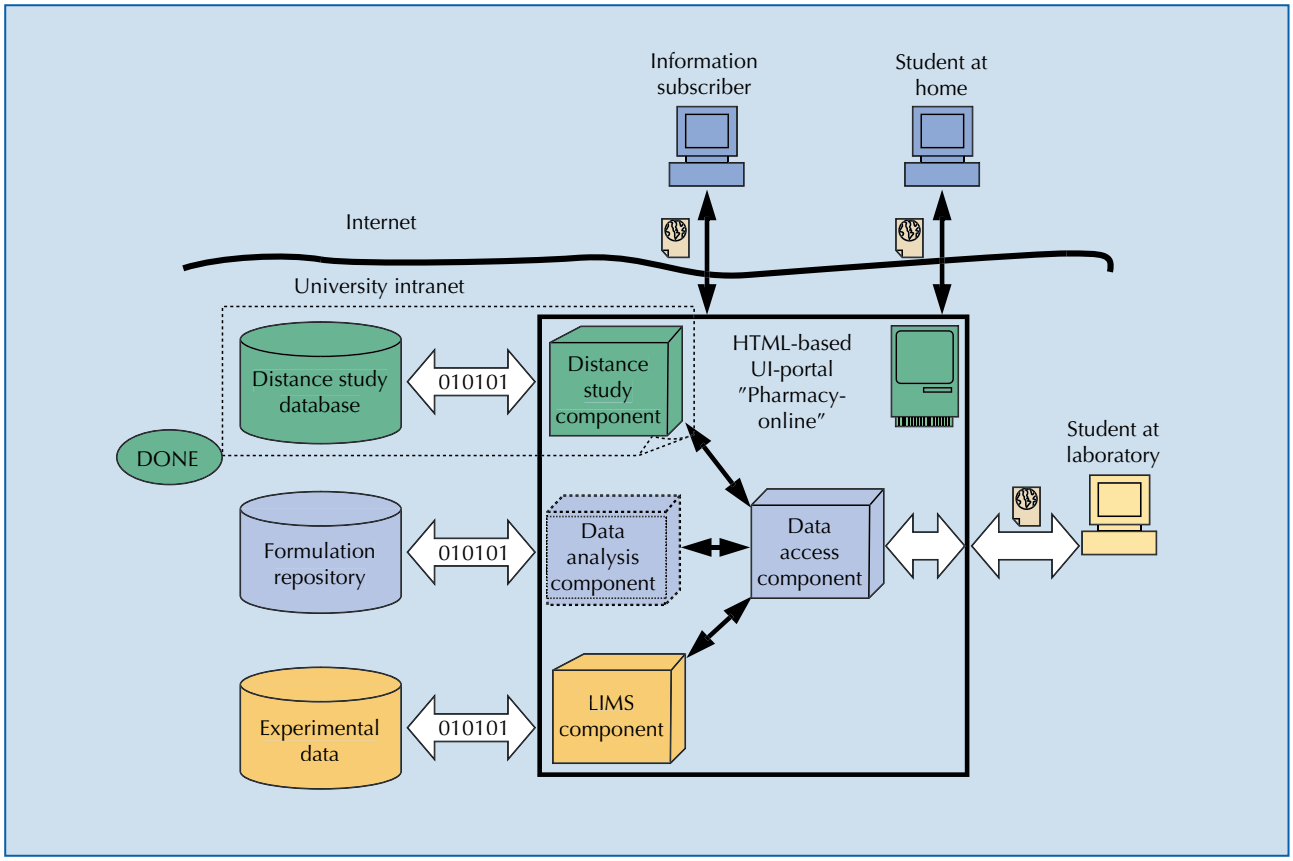

Figure 2 The structure of the PFSS

very specific data from the particular previous situations, and reuses results and experience to fit a new problem. Another advantage of CBR is ability to learn thanks to storing a newly solved problem and making it available for future use.

CBR is beneficial when the problems are not completely understood, i.e. that an exact model cannot be built, and for example experimental work, pilot studies etc. are required. The problem doesn't need to be completely defined before starting to reason possible solutions. Also failed experiences should be included in the case base because they warn about possible failures. As an approach CBR proposes solutions quickly and in this way fastens and directs the design process.

The application of CBR involved (Figure 1): a database of past case and their solutions, knowledge base for adaptation concluded in the formulation repository, a set of rules and functions for measuring similarity, rules for adaptation implemented in data analysis unit. A case base contains case attribute values that identify the problem type and that distinguish one problem type from another. The case attributes that identify the problem type are used as indices in retrieval (S. Craw, N. Wiratunga, R. Rowe, "Case-Based Design for Tablet Formulation", 4th European Work-shop on Case-Based Reasoning, pp 358-369, Springer Verlag, 1998).

The one of the basic tasks while developing the CBR systems is the development of similarity function. This function measures the degree of similarity between two different cases, or the distance between cases. Every case can be characterized by a set of its features. So the point in the N-dimension can describe every case, where N is the number of case's features. The points, describing similar cases, will reside close from one to another in clusters. These clusters can be easily recognized in N-dimension, because they have a potentially high density, if compared to non-similar case points. Mathematically the clusters can be derived by the classical clustering method – k-means.

If one of the features has unknown value, or this value is inaccurate, then this case becomes a multidimensional object. Basically, if there are no internal correlations between different features of the case, the difference between two cases can be evaluated as simple Cartesian distance between points, calculated in weighted dimension of case's features.

The method of factor analysis was involved to feature weighting. At most cases features are not detached, i.e. correlation between at least two of them can be discovered. Because of this hidden correlation the set of features affects on the result more than every feature by itself. The correlation can be both linear and non-linear. In last case, the Support Vector Machine (SVM) method can be applied to discover the hidden correlations.

The method uses hyper plane to separate cases, related to different clusters. One of the advantages of SVM is low perceptivity to noises in source data and ability to learning at low amounts of source data. Originally the SVM method has applied to pattern recognition.

Another cornerstone of CBR is the adaptation of cases. After applying the previously described function

of similarity, several most similar to requirements cases are obtained. The final result can be combined from these cases, applying the genetic algorithm iteratively (J. Yang, V. Honavar, "Feature subset selection using a genetic algorithm", 1998).

The key feature of the system is the combination of methods and approaches of artificial intelligence; those have been applied in separated tasks.

System

System is divided in several components (Figure 2):

- Distance study database. Contains information about student activity in studying process (This component has been already developed). Also the course of multimedia lectures concerning the production equipment and technologies in pharmacy has been developed.
- Formulation repository. Stores all the formulation-concerned information. It contains not only the final formulation, but all the history of declined formulations too.
- Experimental data. Holds all information about formulated product tests.
- Distance study component. It is responsible for to giving to a student learning materials, helping to completely understand the material and to examine the student's knowledge (This component has been already developed). The distance study subsystem development is fully completed, the system is deployed in Internet at http://www.muctr.edu.ru/~cache/claroline/
- Data analysis component is responsible for applying the data analysis methods (knowledge based, case-based reasoning, neural networks, etc.) on the data subset from formulation repository. With help of this component the user will reduce the amount of experimentation work during formulating. At first stage it will be case-based reasoning approach, which had been successfully used in developing water treatment information system.
- LIMS (Laboratory Information Management Systems) component is capable at least to store the experiment information connected with formulation. May be in future the functionality of this component will be extended to support full information about product testing but not only results of them.
- Data access component separates and restricts the access to information and some administrative functions between groups of users (Students, Teachers, Information subscribers)
- The user interface (UI). UI for distance learning has been developed and requires only modification for formulation and LIMS functionality. It is performed in sequence of HTML active pages.

Users of the system can be divided in the following categories: Students (who will be able to work with system both outside and inside of the University), Teaching stuff and Information subscribers. The University can distribute the charged subscription (monthly, yearly, etc.) on information stored in formulation repository. The information from Formulation repository will be very helpful to R&D departments of any pharmaceutical company. Of course the most promising formulations should be patented before being opened for information subscribers and students.

Conclusion

The PFSS system being developed will help to developer solve the following tasks:

1. Collect the formulations and all information concerned with it. At least it will be:
   - Product's physical, chemical, biological, etc. properties
   - Formulation itself
   - Experimental data. The results of different product tests like a friability test, for instance. Formulations are categorized by several different types of classification, for example, by the type of dosage form, by the way of application, etc.
2. Help formulator to reduce the amount of formulator's considerable experimentation and trial batching to obtain the end product, which will posses the required properties.
3. Help to reuse stored information about previously formulated products in future formulations.
4. Provide learning materials to a student.

Anton Vetrov graduated from the N. E. Bauman State Technical University, Moscow and received the Master of Science in Computer Science degree. Currently he is doing his PhD in D. Mendeleev University of Chemical Technology of Russia, Moscow. He is interested in application of the artificial intelligence techniques (especially case-based reasoning systems and neural networks) for optimization of the product formulation process.

Impressum

Editing Committee:
Gautam Maitra
PDA, Basel office
Klaus Eichler
TTC Binzen
Prof. Dr. Hans Leuenberger
Pharmacenter Basel
Dr. Christine Moll-Kaufmann
Novartis Basel
Dr. Claudia Reinke
MedSciences Basel

Layout:
Schmidhauser Mediengestaltung
www.schmidhauser.de

Contact:
Dr. Maxim Puchkov
Industrial Pharmacy Lab
1 Mülhauserstrasse
4056 Basel

Internet: www.sgphw.ch