Keynote Speech

On the Hybrid Approaches for Innovative Process Analysis Technology

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Abstract
This work contributes to the development of Hybrid Modelling for the purpose of Process Analysis Techniques within the Life Sciences. The hybrid modelling strategy is tailored to combine mechanistic and statistical process sensing into a hybrid abstract model. The model is developed in an abstract form such that it operates within an adequate process timeline. Within the life sciences, uncertainties are inevitable due to the complexity of the problems at hand, which cover multidisciplinary aspects of biology, chemistry and physics, thus a hybrid model is thought to provide better model diversity than a pure mechanistic or measurement- based model. From a mechanistic perspective, a model based upon different tempro-spatial levels is developed acquiring the required level of precision to model the main process characteristics. From a statistical perspective, different sensing data is analysed, correlated and calibrated with multivariate statistical algorithms to sense the main process characteristics. In a hybrid model, both types of models are combined into a high dimensional model representation (HDMR), which combines both complex paths (statistical and modelling) into an abstracted Sobol expansion. This model is trained by both measurements and mechanistic data as the input variables. The developed HDMR is thought to provide a robust alternative for process monitoring within the life sciences.

Key words: High dimensional model, Hybrid Modelling, Multivariate statistical algorithms, Life Sciences, Sobol expansion

Hybrid Approach for modeling

The statistical approach and the mechanistic approach are the two top level approaches in modelling. Particularly in statistical approach, different sensing data is analysed, correlated and calibrated with multivariate statistical algorithms to sense the main process characteristics. In statistical approach, data cleaning, data processing and feature extraction are the major steps. Extracted features may be represented as uni-variate or multi-variate models (Figure 1). However, statistical models are not capable of representing exact mechanistic properties of processes; only possible to approximate or predict the mechanistic features. Thus, this approach is not a robust approach for determining very sensitive and complicated steps of process such as understanding and determining the state transitions of biological processes. Such complicated steps are very difficult to model with a pure statistical approach. On the other hand, in statistical approach, still there are debatable selections of methods in some areas such as principle component selection and selecting a method based on the underlying assumptions and existing knowledge of the considering domain.

Particularly, statistical methods use parametric methods, which totally depend on the underlying assumptions about the process and captured data. Thus, the accuracy of statistical models totally depends on the considered underlying assumptions (Roberts, 1997), which is a major drawback of statistical methods.

Direct observation of an intended feature is one possible solution to overcome this drawback. For example, assuming the size of bubbles formed during a certain process is the determination factor of a process. Intensity of the reserving light through the bubbles is proportional to bubble diameter and can be used as a variable to determine the bubble size. However, in reality there can be unexpected situations that could reduce the intensity of light during the process, such as strange particles. If it is possible to directly observe the bubble size, this problem could be overcome. On the other hand, this approach is not a new practice for human beings. In the beginning of civilization, people used direct observation of properties such as colour, taste, smell, and hardness to determine the statuses of processes. This is the basic idea of mechanistic approach. The problem with direct or manual observation is that the approach is not precise and depends on the observer. However, due to the development of technology, now it is possible to observe physical, chemical, and biological properties.

In the concept of pure mechanistic approach, there are three levels as continuum, particle and

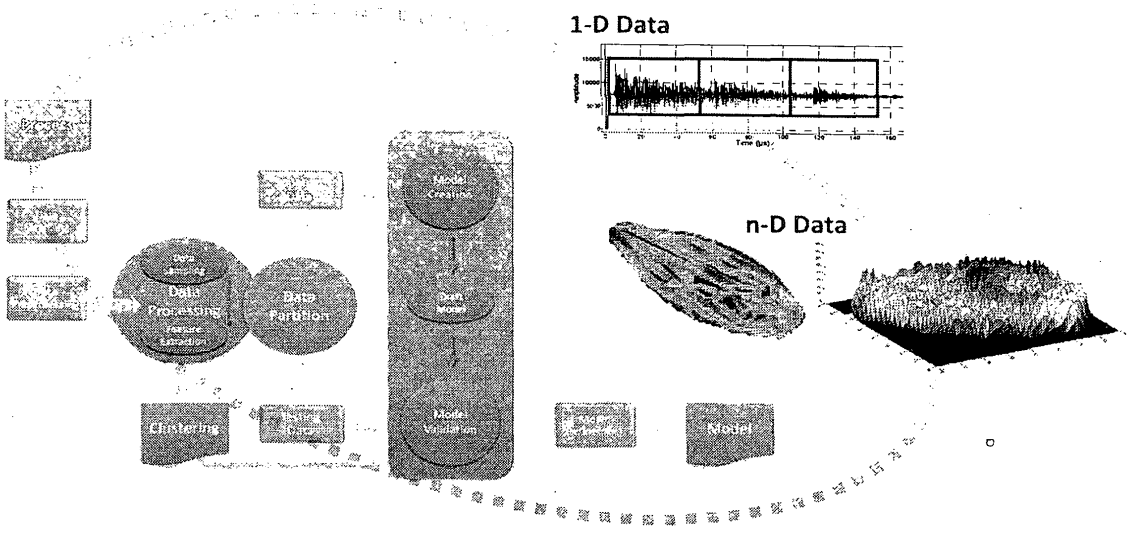

Figure 1: Basic steps of pure statistical approach

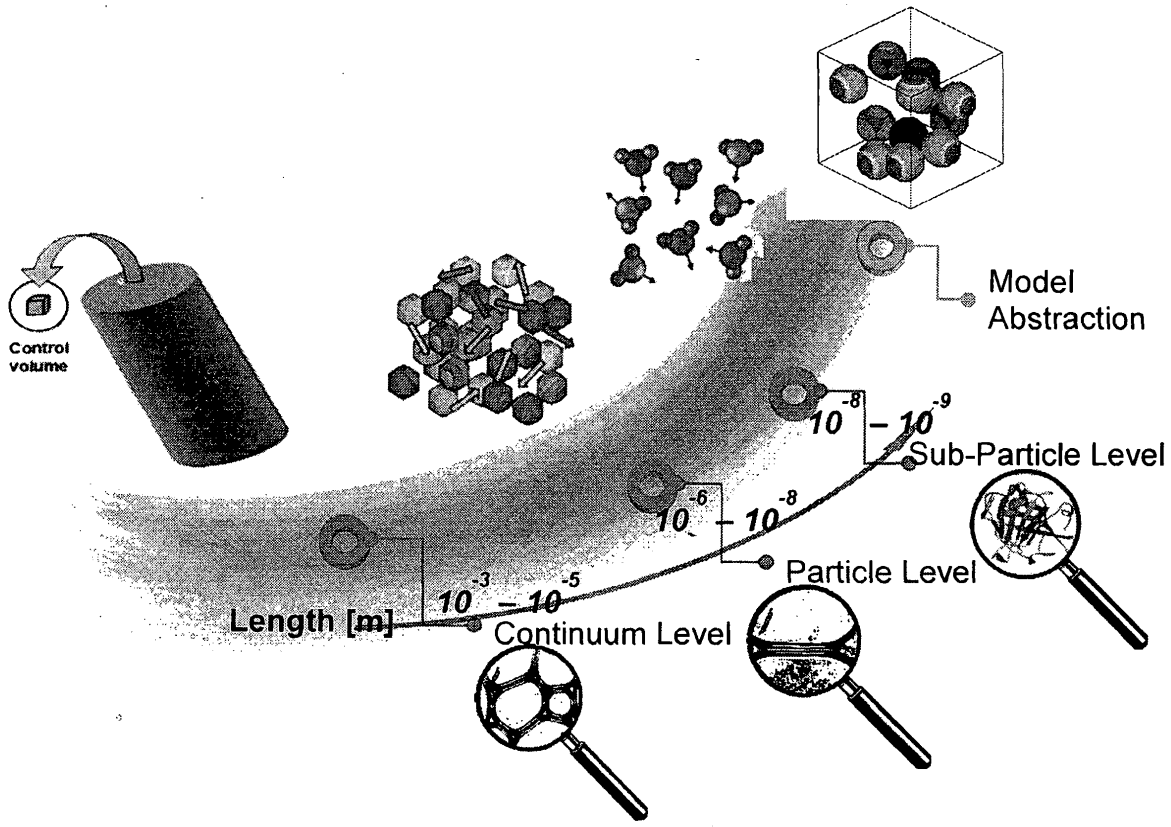

Figure 2: Basic steps of pure mechanistic approach

sub-particle levels (Figure 2). In continuum level (assumes that the substance of the object completely fills the space it occupies) considers the changes of ongoing process in terms of feature changes such as colour, magnitude of a certain cluster, etc (Verhulp et al., 2006). In particle level (atomic level) behaviour of atoms is considering, while in sub-particle level behaviour of basic atomic components (electrons, protons, and neutrons) are considering (Pornillos et al., 2011, Choi and Kang, 2013). Due to technical and financial

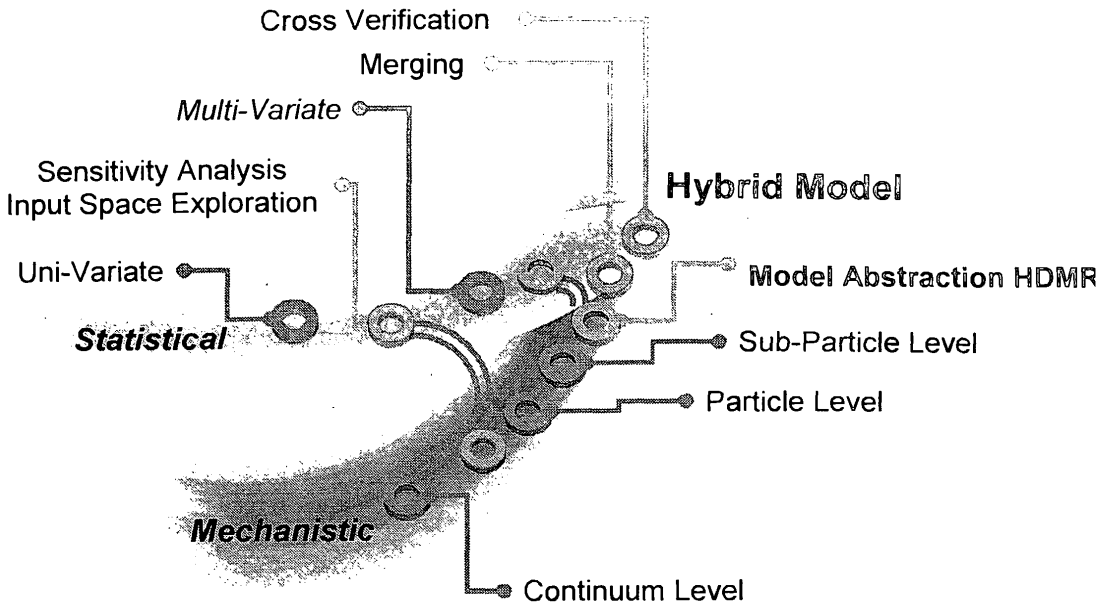

Figure 3: The hybrid approach

barriers mechanistic approach was not a feasible solution especially for online process monitoring. However, due to the development of technology, such as image processing, video processing, thermography, magnetic resonance imaging, laser, and ultra sound technologies, today it is possible to use mechanistic approach even for online process modeling at affordable costs. Furthermore, in mechanistic approach, particle level and sub particle level observation is necessary to fully understand critical stages of some processes such as bone mechanical behavior (Geris et al., 2011).

Mechanistic approach provides direct observation of features and reduces extensive multi- variate capturing done before to project and understand the same features. This is an advantage of mechanistic approach. However, the application of mechanistic approach only is not capable of modelling the whole process though it cuts off many other variables. Therefore, a statistical approach is still necessary to determine the quantitative properties. For example, using image processing, it is possible to monitor size and nature of bubbles. However, determining controlling constrains of the process, bubble density, distribution of bubbles, and / or velocity of bubbles may necessary. Using statistical approach these features can be easily mapped with the relevant mechanistic step. Thus, this approach creates hybrid model of statistical and mechanistic approaches.

In hybrid model, statistical and mechanistic models complement synergistically to overcome drawbacks of each other (Figure 3). Thus, hybrid model is known as a robust and reliable modelling method (Lounis and Madanat, 2002, Ellner et al., 1998). With hybrid approach, bubble formation of biological process was successfully modelled and proved for robustness (Mack et al., 2015a, Mack et al., 2015b).

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