End-to-end Biopharmaceuticals Production Process Risk and Sensitivity Analyses for Quality by Design and Stability Control

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Abstract: The biomanufacturing industry is growing rapidly and becoming one of the key drivers of personalized medicine and life science. However, biopharmaceutical production faces critical challenges, including complexity, high variability, and lengthy lead time. Driven by these challenges, we explore the bio-technology domain knowledge and propose a rigorous risk and sensitivity analysis framework for biomanufacturing innovation. Built on the causal relationships of raw material quality attributes, production process, and bio-drug properties in safety and efficacy, we develop a Bayesian Network (BN) to model the complex probabilistic interdependence between process parameters and quality attributes of raw materials/in-process materials/drug substance. It integrates various sources of data and leads to an interpretable probabilistic knowledge graph of the end-to-end production process. Then, we introduce a systematic risk analysis to assess the criticality of process parameters and quality attributes. The complex production processes often involve many process parameters and quality attributes impacting on the product quality variability. However, the real-world process data are often limited, especially for customized and personalized bio-drugs. We propose uncertainty quantification and sensitivity analysis to analyze the impact of model risk. Given very limited process data, the empirical results show that we can provide reliable and interpretable risk and sensitivity analysis. Thus, the proposed framework can provide the science- and risk-based guidance on the process monitoring, data collection, and process parameters specifications to facilitate the production process learning and stability control.

Bio-sketch: Dr. Wei Xie is an assistant professor in Northeastern University. She received her Ph.D. on Industrial Engineering and Management Sciences from Northwestern University 2014. Her research interests focus on interpretable Artificial Intelligence (AI), IoT, computer simulation, data integrity and big data analytics, design of experiments, data-driven stochastic optimization and blockchain development for complex end-to-end cyber-physical system risk management with applications, including biopharmaceutical manufacturing , industrial hemp production and supply chains, smart power grids with distributed renewable energy and battery storage, cloud computing, and 3D printing. She currently serves as Associate Editor for *ACM Transactions on Modeling and Computer Simulation* and Technical Activity Committee (TAC) for *National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL).*