

# Trend of the Application of Hybrid Artificial Neural Network Models in Bioprocesses

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## Abstract

Due to the complexity of biological transformations, developing model-based strategies to optimize and control bioprocesses is nontrivial. Hybrid models combining a mechanistic description of known influential factors with machine learning to infer the missing influential factors from data have been reported as powerful tools for bioprocesses applications. The artificial neural network is one of the most popular machine learning methods in this case. This paper presents a systematic literature review by computerized search across two databases: Scopus and Web of Science, and backward citation. The PRISMA method was applied to selecting the publications and 159 research articles were categorized as hybrid model applications to bioprocesses problems. It was found that hybrid models were mainly applied in upstream operation steps with a predominance of bioreaction steps. In downstream processing, chromatography appeared as a more recent research topic, with a relatively small number of publications. Furthermore, holistic hybrid modeling applications that integrate data and knowledge from several bioprocess steps will likely emerge in the future, enabling better optimization and control of the bioprocess's platform. The combination of other machine learning methods with the hybrid neural network model is another opportunity that could improve the output of the model.

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