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REVIEW

Comprehensive Review of Graph Neural Networks: Challenges, Classification, Architectures, Applications, and Potential Utility in Bioinformatics

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Received: 9 October 2024 | **Revised:** 24 April 2025 | **Accepted:** 7 June 2025

Keywords: bio-informatics | computer vision | disease prediction | drug discovery | graph neural networks | knowledge graphs | medical imaging | molecular signature analysis | natural language processing

ABSTRACT

Graphs are data structures that represent complex interactions in artificial and natural systems. While deep learning has revolutionised tasks like image processing, audio/video analysis, and natural language processing, these tasks can be viewed as special cases of graph representation learning. Real-world data is often graph-structured, representing complex dependencies in physical systems, molecular signatures, and disease prediction. Graph neural networks (GNNs) excel at processing such non-Euclidean data by capturing dependencies through message passing between graph nodes. This review provides an organised in-depth overview of existing GNN models, emphasising their applications in bioinformatics apart from most structured and unstructured GNN data utility. We provide formal mathematical foundations, compare key model variants, and evaluate their performance across real-world tasks. To enable systematic analysis, we propose a unified taxonomy based on three core axes: learning settings, expressive capacity, and aggregation mechanisms. The taxonomy defines four main GNN types: structure-agnostic, structure-aware, sparsity-optimized, and advanced learning-based models. Regarding applications, we studied them under a proposed taxonomy in detail. Additionally, we provide resources for evaluating and implementing GNN models, including open-source code, bioinformatics databases, and general GNN benchmark datasets. Finally, we propose eight GNN challenges along with corresponding research directions to advance the field. Our survey aims to establish a common reference point for researchers, empowering them to harness the full potential of GNNs in tackling the complexities of both natural and artificial systems.

1 | Introduction

Graphs are the mathematical objects (Corso et al. 2024) that can model complex relationships across diverse domains—from social networks (Ma, Chen, and Xiao 2018) to biological ecosystems (Duvenaud et al. 2015). All the real-life objects as a system can be modelled using graph structures (Veličković 2023). These objects consist of nodes (representing entities) and edges (representing relationships or interactions). Graphs effectively describe interactions in various contexts, such as molecules formed by atoms linked by chemical bonds; connectomic structure of the brain (Cui et al. 2023), where neurons connect through synapses or biomedical knowledge graphs linking genes, drugs, and diseases. Graphs serve as a universal language for depicting living organisms at all levels of organisation. They are equally crucial in representing artificial constructs like transportation networks, where intersections are connected by roads, and social networks, where individuals are connected by social links.