Nanotechnology Perceptions
ISSN 1660-6795
www.nano-ntp.com

Graph Theory Across Disciplines: A Review

Poonam Chawla

Assistant Professor, Department of Mathematics, Mata Gujri College, Fatehgarh Sahib, Punjab

Graph theory models complex systems as networks of vertices and edges. This review synthesizes applications across neuroscience, materials science, structural biology, ecology, and engineering. Key concepts like connectivity, phase transitions, and small-world networks unify these fields. Applications include EEG brain network analysis, alloy passivity modeling, protein structure prediction, and sensor network connectivity. Graph theory enables quantitative analysis and cross-disciplinary knowledge transfer.

Keywords: Graph theory; small-world networks; percolation; protein structure prediction.

Introduction

Definition of Graph Theory

Graph theory, as applied across the reviewed research papers, is a branch of mathematics that studies the structure, connectivity, and properties of networks by representing them as graphs collections of vertices (nodes) connected by edges (links).

Graph theory: It is the mathematical study of networks composed of vertices (representing discrete elements) and edges (representing relationships or interactions between them). A graph G=(V,E) consists of a nonempty set V of vertices and a set E of unordered pairs of distinct vertices called edges [22].

Key Concepts from the Papers

Graph Invariants

Invariants are properties independent of vertex labeling that characterize network topology. Common invariants include:

- **Order (n)** and **size (t)**: Number of vertices and edges [22].
- **Vertex degree**: Number of edges incident to a vertex
- **Cycle rank** ($\beta = t - n + 1$): Number of independent cycles, indicating network complexity
- **Eccentricity, radius, diameter**: Distance-based measures of network spread
- **Planarity**: Whether a graph can be drawn without edge crossings

Connectivity and Phase Transitions: Graph theory reveals critical thresholds in network connectivity. In random graphs (Erdős–Rényi model) and percolation models, a phase transition occurs at a critical probability $p_c$below this threshold, the graph consists of small, isolated components; above it, a giant connected component emerges [8]. This behavior mirrors physical phase transitions and is fundamental to understanding wireless sensor network reliability.

Biconnected Components and Articulation Points: Graphs can be decomposed into biconnected components subgraphs that remain connected even after removing any single vertex. Articulation points are vertices whose removal disconnects the graph. This decomposition reduces combinatorial complexity in protein side-chain prediction by allowing independent optimization of smaller subgraphs [3].

Constraint Networks and Rigidity: In protein flexibility analysis, graph theory models molecular interactions as constraint networks where vertices are atoms and edges represent covalent bonds, hydrogen bonds, or salt bridges. The rigidity or flexibility of regions is determined by counting floppy modes (degrees of freedom) and redundant constraints, using algorithms like FIRST to identify rigid clusters and flexible hinge joints [19].

Small-World Networks: Graph theory also characterizes small-world networks, which combine high local clustering with short characteristic path lengths. Such networks are considered optimal for balancing functional segregation and integration in neural systems [14].

EEG (Electroencephalography) is a non-invasive neurophysiological technique that records electrical activity generated by the brain using electrodes placed on the scalp. It captures the synchronized activity of large populations of neurons, providing a direct measure of cortical dynamics with high temporal resolution [14].

LU factorization: It is a matrix decomposition method that factors a square matrix A into the product of a lower triangular matrix L and an upper triangular matrix U:
$A=L\cdot U$
TARIS refers to a concept from

- **Graph theory:** Tarjan's algorithm for biconnected components
- **Network analysis**: A specific metric or software
- **Bioinformatics**: A protein structure analysis tool

1. Introduction

The ability to model and analyze complex systems is fundamental to scientific progress across disciplines. Whether examining the synchronized firing of neurons during cognitive tasks, the stability of oxide films protecting metal alloys, the folding pathways of proteins, or the connectivity of wireless sensor networks, researchers face a common challenge: understanding how the structure of a system determines its function. Graph theory the mathematical study of networks composed of vertices (nodes) and edges (connections) provides a unifying framework for addressing this challenge.

A graph G=(V,E) consists of a nonempty set V of vertices and a set E of unordered pairs of distinct vertices called edges [22].This simple abstraction has proven remarkably powerful. By representing components as vertices and their interactions as edges, graph theory enables the quantification of network topology through invariants such as order, size, degree distribution, cycle rank, and distance-based measures. More importantly, graph theory reveals universal principles, phase transitions in connectivity [8], the optimality of small-world architecture ([14]; [6]), the power of hierarchical decomposition through biconnected components [3], and the ability to extract meaningful patterns from complex data via spectral methods ([23]; [24]).
The past two decades have witnessed an explosion of graph-theoretic applications across disciplines. In neuroscience, graph theory has transformed our understanding of brain connectivity, revealing that functional brain networks exhibit small-world properties that balance local specialization with global integration ([14]; [15]). In materials science, graph models of oxide networks have provided quantitative explanations for the critical alloy compositions required for passivity ([12]; [13]). In structural biology, graph decomposition algorithms have enabled rapid protein side-chain prediction ([3]) and flexibility analysis ([19]; [21]). In ecology, graph theory has offered powerful tools for assessing landscape connectivity and guiding conservation planning ([20]; [25]). In engineering, graph methods have optimized structural design [9], finite element analysis [10], and multi-domain system modeling [17]. In pattern recognition, spectral graph theory has enabled correspondence-free graph comparison and classification ([23]; [24]). In medical diagnostics, graph invariants have differentiated normal from pathological microvascular networks [22]. In computational chemistry, graph-based similarity measures have enabled alignment-free molecular comparison ([11]; [16]). And in network security, pursuit-evasion games modeled on graphs have provided insights into distributed computing and robotics [5].
This review aims to synthesize these diverse applications, highlighting both the common mathematical foundations and the field-specific adaptations that make graph theory such a versatile tool. By examining papers spanning the period 2000–2009, we demonstrate how graph theory serves as a bridge discipline a universal language for describing, analyzing, and predicting the behavior of complex systems.
We begin with foundational concepts, then explore applications across domains, and conclude by identifying emerging trends and future directions. Sudbø et al [18] in 2000 presented an important and innovative approach to improve prognosis in oral squamous cell carcinoma (OSCC) using graph theory and quantitative image analysis. The study addressed a key limitation in traditional histological grading, which often suffered from poor reproducibility and limited prognostic value. To overcome this, the authors applied graph theoretical methods to quantitatively analyze tissue architecture. Using digitized histological images from 193 OSCC cases, they constructed graphs based on the spatial arrangement of cell nuclei through Voronoi diagrams and their subgraphs. Two main structural features were evaluated: average Delaunay Edge Length (DEL_av) and average homogeneity of the Ulam Tree (ELH_av). A major contribution of the study was the demonstration that these graph-based features provided significant prognostic information, particularly when analyzed at the invasive front of tumors. The results showed strong statistical significance for both DEL_av and ELH_av in predicting relapse-free and overall survival, especially in deeper tumor regions. Interestingly, ELH_av also showed prognostic value in normal-appearing mucosa, suggesting that subtle structural

changes not visible to the human eye may carry clinical importance. The study demonstrated high reproducibility of the computed features, addressing one of the main shortcomings of conventional grading systems. The use of Kaplan–Meier survival analysis further supported the clinical relevance of the results. However, the paper had some limitations, the analysis was retrospective, and the model relied on certain assumptions regarding tissue structure and graph construction. Moreover, although the results were promising, clinical application would require validation through prospective studies and integration into routine diagnostic workflows. The study highlighted the potential of graph theory in medical diagnostics and opened new directions for research in computational pathology and cancer prognosis. McCaerty [12] in 2000 presented a novel theoretical approach to explain the passivity behavior of binary alloys using graph theory. The study modelled the oxide film formed on alloy surfaces as a network of metal–oxygen–metal (M–O–M) bonds and represented this structure using mathematical graphs. By applying graph theoretical concepts such as connectivity and the Randic index, the study evaluated the insertion of different metal ions that disrupted the oxide network. A stochastic method was used to determine the critical concentration at which the network loosed connectivity, which corresponded to the breakdown of passivity. The model was applied to several important binary alloy systems, including Fe–Cr, Ni–Cr, Cu–Ni, and Fe–Si. In each case, the calculated critical concentrations of alloying elements required for passivity showed strong agreement with experimental observations. This demonstrated the effectiveness of the graph theory approach in predicting corrosion behavior and understanding oxide film stability. A major strength of the paper was its innovative integration of mathematics and materials science, providing a clear and quantitative explanation for the existence of critical alloy compositions. The use of graph theory offered a fresh perspective compared to traditional chemical or electrochemical models. However, the approach relied on simplifying assumptions about oxide structure and randomness, which might limit its applicability to more complex or real-world systems. Overall, the paper made a significant contribution by introducing a rigorous and predictive framework for analyzing passivity in binary alloys, and it opened the way for further research combining graph theory with corrosion science. Hayes [6] in 2000 provided an insightful and accessible exploration of application of graph theory to large real-world networks such as the World Wide Web, social networks, and communication systems. The study emphasized key properties of large networks, including sparseness, clustering, and small diameter, which together characterized small-world networks. The study used previous literature to explain real networks that lied between regular lattices and random graphs. A major contribution of the study was its explanation of different graph models. It compared lattice structures (highly ordered but inefficient) with random graphs (efficient but lacking clustering), and introduced the Watts–Strogatz model, which combined both features to produce small-world networks. The study also discussed advanced models such as the Paul Erdős–Alfréd Rényi random graph model and the Albert-László Barabási model of scale-free networks, which explained power-law degree distributions observed in real systems. The study further explored concepts such as rewiring, network navigation, and preferential attachment, showing how these mechanisms influence network structure and behavior. It also highlighted practical applications, including modeling the internet, social connections, and communication networks, making the discussion highly relevant and interdisciplinary. One of the strengths of the study was its clarity and ability to simplify complex mathematical ideas without losing depth. It effectively bridged theory and real-world applications, making graph theory more understandable to a broad audience. However, as a survey-style study, it did not provide detailed mathematical proofs or empirical validation, which may limit its depth for advanced researchers. Urban and Keitt [20] in 2001 introduced graph theory as a powerful analytical framework for assessing landscape connectivity in conservation biology and metapopulation ecology. It was suggested that traditional landscape representations like vector polygons and raster grid could be complemented by a third data structure, the graph. In this representation, habitat patches were nodes, and edges represented functional connectivity between patches (for example via dispersal). Graph theory provided a rich set of tools for analyzing connectivity, including measures of shortest paths, graph components, diameter, minimum spanning trees, and node/edge connectivity. The study illustrated graph-based analyses using a hypothetical landscape of 50 habitat patches, demonstrating the way edge removal (thinning) and node removal (patch loss) affect overall connectivity. Key metrics included the number of graph components, size of the largest component, and graph diameter. The minimum spanning tree the shortest set of edges connecting all nodes emerged as a useful construct for identifying the structural backbone of a landscape. Node sensitivity analysis identified which patches were most critical for recruitment, dispersal flux, and traversability. The approach was applied to a real-world conservation scenario: the Mexican Spotted Owl (Strix occidentalis lucida) in the southwestern United States. Using habitat data from satellite imagery and an incidence-function metapopulation model, the study simulated habitat loss under different patch removal strategies (random, smallest-area first, and minimum spanning tree pruning). Results showed that protecting the minimum spanning tree maintained metapopulation persistence even with substantial habitat loss, whereas random or area-based removal lead to rapid declines. The study concluded that graph theory offered a computationally efficient, process-based framework for landscape analysis that could guide conservation planning even with limited data. Thorpe et al [19] in 2001 presented a constraint-based approach, implemented in the software FIRST (Floppy Inclusion and Rigid Substructure Topography), for analyzing protein flexibility and dynamics. The method modeled strong local interactions of covalent bonds (bond-stretching and bond-bending), salt bridges, and hydrogen bonds as distance constraints within a graph-theoretic framework. In this study Hydrogen bonds were included or excluded based on an energy threshold using a geometry-dependent energy function. The constraint network was analyzed to identify rigid clusters, flexible joints (hinge joints), and the distribution of floppy modes and redundant constraints. A flexibility index f_i quantified local flexibility (positive values) or rigidity (negative values). The authors extended this static analysis to explore protein motions through Monte Carlo sampling of dihedral angles in flexible regions while maintaining all constraints. Ring closure in cyclic structures was handled using Go-Scheraga equations solved via fictitious energy minimization. Simplex method ensured branch atoms avoid van der Waals overlaps. Application to HIV protease demonstrated that the flexible flaps and loops (colored red) exhibited significant motion, while the core remains rigid (colored blue). The method produced 300 allowed conformations in hours, capturing motions consistent with crystallographic interpolations. This constraint-based approach offered a fast, computationally efficient alternative to molecular dynamics for exploring large-scale conformational flexibility in proteins. Vishveshwara et al [21] in 2002 reviewed the application of graph theory to analyze protein structures, folding, stability, function, and dynamics. The study introduced fundamental graph concepts like vertices, edges, adjacency and Laplacian matrices, graph spectra, and isomorphism and demonstrated that these could be translated to biological problems. Protein graphs were constructed with nodes representing secondary structures, residues, or atoms, and edges representing spatial proximity or non-covalent interactions. Key applications included structure comparison via subgraph isomorphism to identify conserved motifs like the catalytic triad in serine proteases, cluster identification using spectral analysis of the Laplacian matrix to detect active sites, folding nuclei, hydrophobic cores, and protein-protein interaction hot spots, folding and topology analysis of α/β barrel proteins and aromatic clusters in thermophiles, dynamics through the Gaussian Network Model (GNM) and constrained graph theory (FIRST) to predict B-factors and flexible regions and inverse folding and comparative modeling using clique detection algorithms. The review concluded that graph theory provided powerful, computationally efficient tools for extracting biologically meaningful information from protein structures, with future potential in fold classification, allosteric network analysis, and structure prediction.

In 2003 Canutescu et al [3] presented a novel algorithm for protein side-chain prediction based on graph theory, implemented in SCWRL3.0, a widely used software tool for homology modeling and protein structure prediction. The study addressed the combinatorial challenge of selecting optimal side-chain rotamers (discrete conformations) for a given protein backbone by modeling the problem as an undirected graph. In this graph, vertices represented residues, and edges indicated pairwise interactions between rotamers. The key innovation lied in decomposing the interaction graph into biconnected components subgraphs that could not be disconnected by removing a single vertex using Tarjan's depth-first search algorithm. These components were solved recursively: for each articulation point (a vertex connecting multiple components), the minimum energy configuration of the component was computed for each rotamer of the articulation point using a branch-and-bound backtracking algorithm. Solved components were then collapsed onto the articulation point, progressively reducing the problem size. This approach, combined with dead-end elimination (DEE) to prune improbable rotamers, reduced the computational complexity from exponential to manageable levels. The algorithm was tested on a benchmark set of 180 proteins with 34,342 side chains. SCWRL3.0 completed all predictions in fewer than 7 minutes, achieving χ_1 and χ_{1+2} dihedral angle accuracies of 82.6% and 73.7%, respectively, using a simple energy function based on a backbone-dependent rotamer library and linear repulsive steric terms. The method was significantly faster than previous versions and alternative approaches such as generalized DEE, completing predictions for large proteins (for example 2,462 residues) in minutes rather than hours. The authors attribute the speed and reliability improvements to the decomposition into biconnected components, which reduces the largest subproblem size and eliminates the need for heuristic cutoffs that compromised global optimality in earlier versions. The study concluded that the graph-theoretic framework provides foundation for future extensions, including more complex energy functions and side-chain flexibility, without sacrificing computational efficiency. Wahl et al [22] in 2004 applied graph theory to analyze and compare the topological structure of renal glomerular microvascular networks. The study represented glomerular blood vessels as edges and branch points as vertices, constructing mathematical graphs from previously published network reconstructions. Using graph theory invariants including order (number of vertices), size (number of edges), cycle rank (number of independent cycles), radius, diameter, root distance, eccentricity distribution, vertex degree distribution, and planarity the study compared six normal adult rat glomeruli with one uremic adult rat glomerulus and one newborn rat glomerulus. The analysis revealed that normal adult glomeruli exhibited consistent topological characteristics: average order of 278 vertices, average size of 445 edges, cycle rank averaging 168, and a predominance of degree 3 vertices (bifurcations) comprising approximately 82% of all branch points. All adult networks were non-planar, indicating three-dimensional structural complexity. The uremic glomerulus showed a distinct shift in vertex degree distribution, with only 64% degree 3 vertices and a higher proportion of higher-degree vertices, along with a wider, more uniform eccentricity distribution. The newborn glomerulus was planar, had a significantly smaller network (24 vertices, 35 edges), and exhibited higher rd/n and rd/t ratios, suggesting developmental progression from a simple planar structure to a complex nonplanar network along a shortest path between afferent and efferent arterioles. The study concluded that graph theory invariants could effectively differentiate between normal adult, pathological (uremic), and developing (newborn) glomerular networks providing a quantitative framework for characterizing microvascular topology. Kawahigashi et al [8] in 2004 applied random graph theory, specifically percolation theory, to model connectivity in ad hoc sensor networks where node positions and link availability were uncertain. The study contrasted two models. The classical Erdős–Rényi random graph, where edges between any node pairs form with uniform probability p, was unsuitable for wireless networks because it ignored geographic constraints. Instead, they proposed a percolation model on a 2D square lattice where nodes connected only to their four nearest neighbors with probability p, capturing the spatial locality of wireless links. A key feature was the phase transition at a critical probability p_c=1/2, below this threshold, the network consisted of small isolated fragments; above it, a large connected component emerged. Numerical simulations on grid areas of 10×10to 100×100 confirmed this sharp transition, which became clearer as area size increased. Relating p to physical distance using a simplified radio propagation model (E=−20log d), the study showed that connectivity dropped sharply at distances around 10–20 m, indicating that node spacing or transmission power must be carefully chosen for reliable network connectivity. The study concluded that percolation theory provided a useful framework for understanding connectivity thresholds in ad hoc sensor networks, with practical implications for network design. Wilson et al [23] in 2005 presented a method for converting graphs into pattern vectors using spectral graph theory, eliminating the need for node correspondences. They constructed feature vectors from the spectral decomposition of the Laplacian matrix by applying symmetric polynomials (elementary and power polynomials) to the components of the spectral matrix. These polynomials produced permutation-invariant features that uniquely represented the graph and allowed comparison of graphs with different sizes by padding smaller graphs with zeros. For attributed graphs, the method was extended using a Hermitian property matrix, where edge attributes were encoded as complex numbers (magnitude for weights, phase for additional measurements). The eigenvectors of this matrix were complex, and symmetric polynomials were applied to both real and imaginary parts. Three embedding techniques Principal Component Analysis (PCA), Multidimensional Scaling (MDS), and Locality Preserving

Projection (LPP) were used to project the feature vectors into low-dimensional spaces. Experiments on synthetic random graphs, view-based object recognition (Delaunay graphs from 2D views), and shock graphs (shape skeletons) demonstrated that the method produced well-separated clusters and captured structural variations effectively. The approach provided a computationally efficient, correspondence-free framework for graph clustering, classification, and manifold learning in pattern recognition applications. Allesina et al [1] in 2005 used graph theory to analyze energy flow in ecological food webs. The study applied the concept of strongly connected components (SCCs) subsets of species where energy could cycle among all members to 17 published ecosystem networks. SCCs were identified using depth-first search, then aggregated into a directed acyclic graph (DAG), and topologically sorted to reveal linear energy flow pathways from sources to sinks. It was found that most networks contained one large SCC plus several single-node SCCs (sources, sinks, or cross-vertices) and four aquatic ecosystems (Chesapeake Bay, Baltic Sea, Charca de Maspalomas, Upper Chesapeake) showed clear separation between benthic and pelagic subcommunities, with cycling confined within each subsystem. Weak energy flows were critical for maintaining cycling; their removal quickly fragments SCCs and compartmentalization was not universal, suggesting it depended on specific ecosystem conditions. The study concluded that SCC analysis efficiently identified functional subsystems and hierarchical energy pathways, offering insights into ecosystem structure, stability, and disturbance propagation. Micheloyannis et al [14] in 2006 presented an in-depth investigation of difference of brain network organization according to cognitive ability during working memory tasks. The study employed EEG recordings and applied graph theoretical analysis to examine functional connectivity across different brain regions. By converting synchronization likelihood values into network graphs, they evaluated key parameters such as clustering coefficient and characteristic path length, which help identify small-world network properties. These properties were considered indicators of optimal brain organization, balancing local and global information processing. The study compared individuals with lower education levels to those with university degrees while performing a 2-back working memory task and revealed that individuals with lower education showed stronger small-world network characteristics, whereas more educated individuals exhibited less pronounced small-world organization during the task. This result supported the neural efficiency hypothesis, suggesting that individuals with higher cognitive ability or education performed tasks with less complex or less widespread neural activation. In other words, their brains operated more efficiently, requiring fewer coordinated connections to achieve similar or better performance. A key strength of the paper was its integration of neuroscience and mathematical modeling, particularly the use of graph theory to analyze brain connectivity. It also contributed to the understanding of how working memory and intelligence are related at the neural level. However, the study was limited by its relatively small sample size and the fact that some observed differences were not statistically significant. Additionally, the use of a single, relatively simple working memory task might not fully capture the complexity of cognitive processing. Overall, the study provided valuable insights into neural efficiency and demonstrates the potential of graph theoretical methods in cognitive neuroscience and laid a foundation for future research, especially studies involving larger samples and more diverse cognitive tasks to strengthen and expand the findings.

De Almeida et al [4] in 2007 presented a graph-theoretic framework for analyzing urban scene topology using LiDAR data. The study aimed to extract structured spatial information from unstructured point clouds by constructing polygon regions, building adjacency graphs, and applying graph traversal algorithms. The methodology begun with generating a TIN from LiDAR points, classifying facets by slope threshold (steep vs. flat), and merging adjacent facets of the same class into polygonal regions. An adjacency graph was then constructed where vertices represent polygons and edges represent adjacency (sharing at least one arc). The authors compared depth-first search (DFS) and breadth-first search (BFS) for graph traversal, concluding that BFS yielded more meaningful results for urban scene interpretation because its broad, shallow branches corresponded better to individual urban features. A key challenge addressed was detecting containment relationships not explicit in the graph such as a polygon surrounded by a ring of polygons meeting only at nodes leading to the proposed containment-first search (CFS). The study also described an interactive visualization tool being developed within ArcGIS to link graph traversal trees with the original map, enabling users to explore topological relationships dynamically. This study offered a solid methodological foundation for integrating graph theory with GIS for urban scene analysis. The systematic workflow from unstructured LiDAR to graph-based topology analysis was clearly presented, and the emphasized on visualization and interactive tools was a notable strength. While the approach shows promise, it required further validation, refinement of classification methods, and full implementation of the analytical components to achieve its stated goals. Ponten et al [15] in 2007 analyzed intracerebral EEG (SEEG) recordings from patients with mesial temporal lobe epilepsy and investigate functional connectivity using synchronization likelihood. By transforming these connectivity patterns into graphs, they evaluated key network measures such as clustering coefficient (C) and characteristic path length (L), which were essential for identifying small-world network properties. The study examined multiple stages of seizure activity, including interictal, preictal, ictal, and postictal periods, providing a dynamic view of brain network changes. The results showed that synchronization between brain regions increased significantly during seizures across various frequency bands. At the same time, both clustering coefficient and path length increased, particularly in lower frequency bands (delta, theta, and alpha). This indicated that the brain network shifted from a more random configuration in the interictal state toward a more ordered, small-world-like structure during and after seizures. These findings suggested that seizure activity was associated with increased local connectivity and slightly reduced global efficiency, supporting the idea that network topology played a crucial role in seizure generation and propagation. A key strength of the paper was its rigorous methodology, including the use of intracerebral recordings, multiple frequency band analysis, and comparison with random networks to validate results. The study also effectively integrated concepts from neuroscience, nonlinear dynamics, and graph theory, providing a deeper understanding of epileptic brain function. However, the study had some limitations. The sample size was relatively small, and the analysis is based on fixed time windows, which may overlook finer temporal dynamics of seizure evolution. Additionally, the functional connectivity derived from EEG did not directly represented anatomical connections, which might affect interpretation of the network structure. The study highlighted the importance of graph theoretical analysis in understanding epilepsy and offered a promising framework for future research in brain network dynamics and seizure prediction. Iturria-Medina et al [7] in 2007 presented a graph-theoretic method to characterize anatomical brain connections using diffusion-weighted MRI (DW-MRI). The brain was modeled as a weighted, non-directed graph where voxels were nodes and arcs between neighboring voxels represented potential fiber connections. Arc weights combined probabilistic tissue segmentation (from anatomical MRI) and orientational distribution functions (from DW-MRI) to reflect the probability of actual fiber connectivity. A tractography algorithm found the most probable path between any two nodes, with node-to-node connectivity defined as the minimum arc weight along that path. To quantify connections between gray matter regions, three measures were introduced first was anatomical connection strength (ACS) to estimate information flow based on connected surface voxels, second was anatomical connection density (ACD) to study the fraction of surface area involved and third was anatomical connection probability (ACP) to find maximum probability of at least one connection. The method was validated on artificial diffusion data (crossing tracts, branching) and was applied to five healthy subjects. Reconstructed fiber pathways for example occipital connections through corpus callosum, corticospinal tract aligned with known anatomy. Mean connectivity maps for 71 gray matter regions showed consistent patterns across subjects. It was concluded that graph theory offered a flexible framework for quantifying brain anatomical connectivity from DW-MRI, with potential applications in studying white matter disorders. Wilson and Zhu [24] in 2008 investigated the effectiveness of graph spectra (eigenvalues) as a representation for comparing graphs and trees in pattern recognition tasks. They evaluated several matrix representations like adjacency matrix (A), combinatorial Laplacian (L), signless Laplacian (|L|), normalized Laplacian ($\hat{L}$), heat kernel (H), and path length distribution (D_k) across three criteria: cospectrality, stability under structural changes, and performance in classification and clustering. The study extended previous studies to quantify the fraction of graphs and trees that shared the same spectrum (cospectral). For general graphs up to 11 vertices, the normalized Laplacian produced the fewest cospectral pairs approximately 0.2%, outperforming the signless Laplacian (3.8%), Laplacian (9%), and adjacency matrix (21%). For trees up to 26 vertices, the combinatorial Laplacian showed the lowest cospectral fraction (as low as 0.00005% at 26 vertices), contradicting Schwenk's theorem that almost all trees are cospectral this only holds for very large trees beyond this size. The Euclidean distance between spectra correlated strongly with graph edited distance across all representations. The heat kernel showed the smallest relative deviation (≈1–3.5%), indicating the most stable relationship. Using synthetic random graphs, shape skeletons (trees), and Delaunay graphs from the COIL image database, the combinatorial Laplacian consistently achieved the lowest classification error rates and best cluster compactness. The adjacency matrix performd worst, while normalized Laplacian and heat kernel showed intermediate results. The study concluded that the combinatorial Laplacian spectrum was the most practical representation for graph comparison tasks, offering a good balance of uniqueness, stability, and discriminative power, despite the normalized Laplacian's theoretical advantage in cospectrality. Kaveh and Shahrouzi [9] in 2008 presented a hybrid optimization method combining genetic algorithms (GAs) with graph theory to optimize the topology and sizing of bracing systems in steel frames. The study addressed the high computational cost of conventional GAs by incorporating problem-specific topological knowledge as memes cultural learning units that guided the search. Key contributions of study included the graph-theoretic algorithms to assess load path connectivity from lateral loads to supports using priority-grown multiple shortest route trees (PMSRT), two memetic evolution strategies Lamarckian (direct chromosome modification) and Baldwinian (fitness adjustment) to enforce topological quality, dynamic mutation band control for refined local search and extraction of an optimal design family using ant colony-inspired memory, rather than a single pseudo-optimum. The method was tested on two steel frame examples under wind and seismic loading. Results showed that Baldwinian memetic learning achieved the best balance of convergence and diversity, producing lighter structures (for example 50,782 N vs. 64,065 N with standard GA) while satisfying design code constraints. Super bracing systems (connected bracing graphs) consistently outperformed conventional patterns. The authors concluded that graph-theoretic memetic algorithms offer an efficient framework for structural layout optimization, providing diverse high-quality designs for engineering decision-making. In 2008 Kaveh and Koohestani [10] presented a graph-theoretical method for efficiently computing null basis matrices in the force method of finite element analysis for plate bending problems using triangular and rectangular elements. The force method required a sparse and banded null basis matrix (self-stress matrix) for computational efficiency, but traditional algebraic methods like LU factorization became computationally expensive for large models. The study developed a systematic graph-based algorithm that identified self-equilibrating stress systems (SESS) of four types using two graph representations: an associate digraph (nodes = elements, edges = shared sides) and an interface graph. These SESS types corresponded to adjacent element interfaces, elements with single negative incidence, triple-element configurations and openings (cycles) in the model. The non-zero pattern of the null basis was determined through these subgraphs, and numerical values were computed using minimal algebraic operations on small submatrices. The method was tested on triangular and rectangular plate examples. Results showed that the graph-theoretical approach produced null basis matrices that were significantly sparser (for example 17,350 vs. 398,389 non-zero entries) and more banded than LU factorization, with up to 80% reduction in computational time and higher numerical accuracy. It was concluded that the graph-theoretical force method offered an efficient, accurate, and scalable alternative to algebraic methods for plate bending finite element analysis.

Fomin and Thilikos [5] in 2008 provided a comprehensive annotated bibliography of research on guaranteed graph searching, a pursuit-evasion problem where searchers must capture a fugitive hiding in a graph (representing rooms and corridors). The field originated with Parsons (1976) and Petrov, inspired by cave rescue problems, and had since expanded into numerous variants driven by applications in computer science, discrete mathematics, and robotics. The bibliography classified graph searching models along several dimensions such edge search, node search, mixed search; visible vs. invisible fugitives; lazy vs. agile fugitives; directed graphs; hypergraphs; connected search; cop and robber games; games with restricted speed or radius of capture. Whether a search strategy could avoided recontaminating clear areas. Classic edge, node, and mixed search were monotone; connected search and multi-fugitive variants are not. Search numbers were equivalent to graph parameters such as pathwidth, treewidth, branchwidth, and hypertree-width. Determining search numbers was NP-complete in general but linear-time solvable for fixed k and for trees. The bibliography cited key results on complexity, algorithms for special graph classes, minimal graphs with given search numbers, and obstructions. It was highlighted the rapid growth of the field, with contributions spanning discrete mathematics, algorithmic graph theory, and applications in network security, robotics, and distributed computing. The annotated format provided researchers with a structured entry point into the literature, summarizing foundational papers, key theorems, and open problems. This work served as an essential reference for understanding the diverse landscape of graph searching problems and their interconnections with width parameters and pursuit-evasion games. In 2008 Schmitke and McPhee [17] presented a unified graph-theoretic formulation for systematically generating the governing symbolic equations of multibody, multi-domain systems (mechanical, electrical, hydraulic, etc.). The approach was based on the principle of orthogonality a generalization of the principle of virtual work and virtual power and leveraged linear graph theory to separate component physics from system topology. The key innovation was the consistent treatment of all energy domains within a single framework. The formulation used linear graphs where nodes represented reference frames or connection points, and edges represented components with across variables (for example voltage, angular velocity, translational velocity) and through variables (for example current, torque, force). A tree selection determined the primary variables of system like branch across variables and chord through variables. Fundamental cutset and circuit equations provided the topological constraints, with the orthogonality relationship Af=−Bf linking the two. The principle of orthogonality stated that the sum of the dot products of across and through variables over all edges was zero, representing conservation of energy or power. By substituting virtual through and across variables, the authors derived the system's dynamic and constraint equations without ever forming a single large symbolic expression instead, equations were generated directly for each modeling variable by projecting cutset equations onto across spaces and circuit equations onto through spaces. The formulation was implemented in the software package DynaFlexPro. Validation was provided through a forward dynamic analysis of a flexible parking lot barrier system, which included a three-phase induction motor, a six-bar mechanism, and a flexible beam. Simulation results for motor currents matched those published in the literature, demonstrating the ability of approach to handle tightly coupled multi-domain systems with complex kinematics and flexibility. The study concluded that linear graph theory combined with the principle of orthogonality provided a powerful, flexible, and computationally efficient framework for modeling multi-domain systems, with the ability to use joint, absolute, or hybrid coordinate sets based on tree selection. Marín et al [11] in 2008 introduced TARIS, a graph-theoretical method for comparing molecular electrostatic potentials (MEPs) without requiring molecular alignment. The method encoded successive negative molecular isopotential surfaces (NMISs) into weighted rooted trees, where nodes represented connected components and edges represented parent-child relationships as components merged with decreasing potential. Node weights were the surface areas of components. Molecular similarity was measured using tree edit distance the minimum cost of node insertions, deletions, and changes with costs based on node areas. The resulting similarity matrix was used for hierarchical clustering and QSAR analysis. The method was validated on two datasets first was 46 small organic molecules representing eight functional groups, where hierarchical clustering correctly grouped molecules by functional class; and second was 31 steroids with known corticosteroid-binding globulin (CBG) affinities, where partial least-squares regression yielded cross-validated q2q2 values of 0.71 (full set) and 0.84 (first 21 steroids, outlier removed), comparable to or better than other MEP-based methods.

Hierarchical clustering also partitioned steroids into high, intermediate, and low activity groups. Key advantages included alignment independence, systematic encoding of the full MEP field, metric behavior, and low parameter sensitivity. The study concluded that TARIS provided an effective, alignment-free approach for molecular similarity assessment with applications in chemical classification and SAR/QSAR studies. Sahu and Lee [16] in 2008 introduced a new topological index called the net-sign identity information index (I_e) derived from chemical signed graph theory. The index was defined as the sum of squares of information measures I_K over all molecular orbital levels, where I_K was based on the distribution of positive and negative signs in edge-signed graphs. The predictive performance of I_e, along with $\sqrt{I_e}$ and $\sqrt{I_b}$ (square root of bonding information index), was evaluated against three classical descriptors Wiener index (WW), Randić's connectivity index (χ), and Balaban's index (J) using QSPR models for 12 alkanes and 13 alkenes. Properties modeled included molar volume (MV), boiling point (BP), molar refraction (MR), critical pressure (PC), and critical temperature (TC). Key results showed that $\sqrt{I_e}$ and $\sqrt{I_b}$ perform comparably to (χ) for bulk properties (MV, BP, PC, TC), for molar refraction (optical property), I_e and $\sqrt{I_e}$ outperform all classical indices, achieving correlation coefficients up to R=0.971R=0.971 for alkanes and 0.9330.933 for alkenes. It was conclude that the net-sign identity information index was particularly effective for modeling optical properties and offered a promising alternative to traditional topological descriptors in QSPR studies. In 2008 McCafferty [13] applied graph theory to explain the passivity of Ni-Cr-Mo ternary alloys by modeling the oxide film as a network of metal-oxygen-metal bridges. Two competing models were evaluated first passivity due to a continuous network of -Cr-O-Cr- bridges (with Ni^{2+} and Mo^{4+} ions inserted), and second passivity due to a continuous network of -Ni-O-Ni- bridges (with Cr^{3+} and Mo^{4+} ions inserted). The oxide structure was represented as a mathematical graph where vertices were metal ions and edges were oxygen ions. Using graph theory and stochastic edge deletion to simulate incorporation of foreign ions, the author calculated the critical cation fractions required for network connectivity. For the -Cr-O-Cr- model, a continuous network formed when the Cr^{3+} cation fraction in the oxide reached 0.35 or greater. For the -Ni-O-Ni- model, a continuous network required a Ni^{2+} cation fraction of 0.55 or greater. Experimental XPS surface analysed from the literature for various Ni-Cr-Mo alloys (for example Alloy C276, Alloy 625, Alloy 59) showed that passive films were consistently enriched in Cr^{3+} (cation fractions typically 0.5–0.9) with low Ni^{2+} content (generally <0.5). These compositions lied within the region predicted by the -Cr-O-Cr- model but not the -Ni-O-Ni- model, indicating that passivity in Ni-Cr-Mo ternary alloys was primarily due to a continuous network of -Cr-O-Cr- bridges in the oxide film. The study concluded that graph theory provided a quantitative framework for understanding critical alloy compositions for passivity in ternary systems, consistent with experimental observations. Assenov et al [2] 2008 presented Network-Analyzer, a versatile Cytoscape plugin for computing topological parameters of biological networks. As high-throughput experiments generated large molecular interaction networks, there was a growing need for user-friendly tools to characterize network structure through graph-theoretic properties. Network-Analyzer computed a comprehensive set of topological parameters for both directed and undirected networks, including simple parameters such as number of nodes, edges, connected components, network diameter, radius, density, centralization, heterogeneity, clustering coefficient, characteristic path length, and average number of neighbors and complex parameters such as distributions of node degrees, neighborhood connectivity, average clustering coefficients, topological coefficients, shortest path lengths, and shared neighbors. The plugin extended existing definitions to directed networks for example three types of neighborhood connectivity and introduced novel features such as enumeration of shared neighbors for all node pairs. Results were displayed as customizable histograms or scatter plots using JFreeChart, with options for linear/logarithmic scales, power law fitting, and export to image or text formats. Computed parameters were stored as node attributes, enabling visual mapping within Cytoscape for example node size proportional to clustering coefficient, color based on degree. Additional functionality included network modification (intersection, union, difference), extraction of connected components, and removal of self-loops. The plugin was designed for biologists with no graph theory expertise, offering an intuitive interface while maintaining computational efficiency. Network-Analyzer was freely available via the Cytoscape website and has become a widely used tool for analyzing biological networks such as protein-protein interaction networks. Wu and Murray [25] in 2008 introduced a new quantitative measure of spatial contiguity a key property in land allocation, reserve design, and forest management using graph theory and spatial interaction. The authors reviewed 11 existing contiguity measures and identified two major limitations: bias toward compact shapes and failure to account for inter-patch relationships in fragmented landscapes. The proposed measure, C (ranging 0 to 1), combined intra-patch contiguity (α) (direct linkages within patches), inter-patch contiguity (β) (spatial interaction between patches) using minimum spanning tree (MST) path lengths and maximum contiguity (λ) (linkages in a complete graph single patch) the method constructed adjacency graphs, MST graphs, and full contiguity graphs to capture both intra- and inter-patch relationships without shape bias. Empirical testing on hypothetical configurations and a real reserve design case study in Virginia showed that C rated completely contiguous configurations equally regardless of shape, differentiated fragmented configurations by inter-patch distance and produced consistent values for equivalent spatial arrangements. It was conclude that this measure provided a direct, unbiased, and shape-insensitive alternative to existing contiguity proxies, with potential applications in landscape planning and conservation.

Conclusion

Graph theory has proven to be a powerful unifying tool across diverse scientific disciplines. Network topology reveals system function, graph methods enable prediction at critical thresholds, and algorithmic innovations continue to expand applications. As data complexity grows, graph theory will remain essential for understanding and designing complex systems

References:

[1] Allesina, S., Bodini, A. and Bondavalli, C.: Ecological Subsystems via Graph Theory: The Role of Strongly Connected Components, Oikos, (2005), pp. 164-176.

[2] Assenov,Y., Ramirez, F., Schelhorn, S. E., Lengauer, T., and Albrecht, M.: Computing Topological Parameters of Biological Networks, Bioinformatics, Volume 24(2),(2008), pp. 282–284.

[3] Canutescu, A.A., Shelenkov, A. A. and Dunbrack Jr., R. L.: A Graph-Theory Algorithm for Rapid Protein Side-Chain Prediction, Protein Science, Volume 12, (2003), pp. 2001–2014.
[4] De Almeida, J. P., Morley, J.G. and Dowman, D.: Graph Theory in Higher Order Topological Analysis of Urban Scenes, Computers, Environment and Urban Systems 31 (2007), pp. 426–440
[5] Fomin, F. V. and Dimitrios M. Thilikos: An Annotated Bibliography on Guaranteed Graph Searching, Theoretical Computer Science, Volume 399, (2008), pp. 236–245
[6] Hayes, B.: Graph Theory in Practice: Part II,, American Scientist, Volume 88, Number 2, (March–April, 2000),pp. 104–109.
[7] Iturria-Medina, Y., Canales-Rodriguez, E.J., Melie-Garcia, L., Valdés-Hernández, P.A., Martínez-Montes ,E., Alemán-Gómez Y., and Sánchez-Bornot, J.M.: Characterizing Brain Anatomical Connections Using Diffusion Weighted MRI and Graph Theory, NeuroImage, Volume 36, (2007),pp. 645–660
[8] Kawahigashi, H., Terashima, Y., Miyauchi, N. and Nakakawaji, T. :Modeling Ad hoc Sensor Networks using Random Graph Theory, IEEE (Mitsubishi Electric Corporation), 2004
[9] Kaveh, A. and Shahrouzi, M.: Graph Theoretical Implementation of Memetic Algorithms in Structural Optimization of Frame Bracing Layouts, Engineering Computations, Volume 25 (1), (2008), pp. 55 – 85.
[10] Kaveh, A. and Koohestani, K.: Efficient Finite Element Analysis by Graph-Theoretical Force Method; Triangular and Rectangular Plate Bending Elements, Finite Elements in Analysis and Design, Volume 44, (2008), pp. 646 – 654.
[11] Marín, R. M., Aguirre, N. F., and Daza E. E. Graph Theoretical Similarity Approach To Compare Molecular Electrostatic Potentials, Journal of Chemical Information and Modeling, Volume 48, (2008), pp. 109-118
[12] McCaerty, E.: Graph theory and the passivity of binary alloys, Corrosion Science 42 (2000), pp. 1993-2011.
[13] McCafferty, E.: Oxide Networks, Graph Theory, and the Passivity of Ni-Cr-Mo Ternary Alloys, Corrosion Science, Volume 50, (2008), pp. 3622–3628.
[14] Micheloyannis, S., Pachou, E., Stam, C. J., Vourkas, S. and Tsirka, V.: Using graph theoretical analysis of multichannel EEG to evaluate the neural efficiency hypothesis, Neuroscience Letters, 402 (2006) pp. 273–277.
[15] Ponten, S. C., Bartolomei, F. and Stam, C. J.: Small-World Networks and Epilepsy: Graph Theoretical Analysis of Intracerebrally Recorded Mesial Temporal Lobe Seizures, Clinical Neurophysiology 118 (2007), pp. 918–927.
[16] Sahu, P. K. and Lee, S. L.: Net-Sign Identity Information Index: A Novel Approach Towards Numerical Characterization of Chemical Signed Graph Theory, Chemical Physics Letters, Volume 454 (2008), pp. 133–138
[17] Schmitke ,C. and McPhee, J.P: Using Linear Graph Theory and the Principle of Orthogonality to Model Multibody, Multi-Domain Systems, Advanced Engineering Informatics, Volume 22, (2008), pp. 147–160.
[18] Sudbø, J., Bankfalvi, A., Bryne, M., Marcelpoil, R., Boysen, M. Piffko, J., Hemmer, J. Kraft, K. and Reith, A.: Prognostic Value of Graph Theory-Based Tissue

Architecture Analysis in Carcinomas of the Tongue, Laboratory Investigation, Volume 80(Number 12), (December 2000).

[19] Thorpe, M.F., Lei, M., Rader, A.J., Jacobs, D. J., and Kuhn, L. A.: Protein Flexibility and Dynamics Using Constraint Theory, Journal of Molecular Graphics and Modelling, Volume 19, (2001), pp. 60–69.

[20] Urban, D. and Keitt, T.: Landscape Connectivity: A Graph-Theoretic Perspective, Ecology, Volume 82(5), (2001), pp.1205–1218

[21] Vishveshwara, S., Brinda, K.V., and Kannan, N.: Protein Structure: Insights from Graph Theory, Journal of Theoretical and Computational Chemistry, Volume 1(1), (2002), pp. 187–211

[22] Wahl, E. M., Quintas, L. V., Lurie, L L., and Gargano, M. L.: A Graph Theory Analysis of Renal Glomerular Microvascular Networks, Microvascular Research, Volume 67, (2004), pp. 223–230.

[23] Wilson, R. C., Hancock, E. R., and Luo, B.: Pattern Vectors from Algebraic Graph Theory, IEEE Transactions on Pattern Analysis and Machine Intelligence, Volume 27(7), (2005).

[24] Wilson R. C. and Zhu P.: A Study of Graph Spectra for Comparing Graphs and Trees, Pattern Recognition, Volume 41, (2008), pp. 2833–284.

[25] Wu, X. and Murray, A.T.: A New Approach to Quantifying Spatial Contiguity Using Graph Theory and Spatial Interaction, International Journal of Geographical Information Science, Volume 22(4), (2008), pp. 387–407.