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Modeling Molecular Interactions with HyperNetworks and SuperHyperNetworks

Abstract

Graph theory is a branch of mathematics focused on the study of networks, where nodes (called vertices) are connected by links (called edges). A hypergraph generalizes the classical notion of a graph by allowing edges—called hyperedges—to connect more than two vertices simultaneously. A superhypergraph further extends this concept by introducing recursively nested powerset layers, thereby enabling hierarchical and self-referential relationships among hyperedges. Graphs are widely used to represent complex networks. In this context, hypernetworks and superhypernetworks serve as natural generalizations of graphs, capturing higher-order and hierarchical relationships, respectively.

Such graph-based frameworks are also extensively applied in fields such as biology and biochemistry. A Molecular Interaction Network models biochemical interactions among molecules, where nodes represent molecular entities and edges represent pairwise interactions or reactions.

In this paper, we extend the concept of Molecular Interaction Networks by proposing two new frameworks: the *Molecular Interaction HyperNetwork* and the *Molecular Interaction SuperHyperNetwork*, both grounded in the structures of hypernetworks and superhypernetworks. These frameworks offer new insights into multi-scale biochemical systems, with potential applications in drug target identification and pathway analysis. We hope that future research will further explore the mathematical, biological, and computational aspects of the *Molecular Interaction HyperNetwork* and the *Molecular Interaction SuperHyperNetwork*.

Keywords: Superhypergraph, Hypergraph, Molecular Interaction Networks, HyperNetworks, SuperHyperNetworks

1 Introduction

1.1 Theories of Graphs, Hypergraphs, and Superhypergraphs

Graph theory is a branch of mathematics focused on the study of networks, where nodes (called vertices) are connected by links (called edges) [41, 42]. Graphs have been extensively studied and applied in a wide range of disciplines, including social science, artificial intelligence, graph neural networks (GNNs), and general network analysis (cf. [50, 81, 94]).

Mathematical structures can often be extended into *hyperstructures* and *superhyperstructures* by utilizing the power set and n-th iterated powerset constructions [63, 185, 186, 189]. These generalized frameworks are particularly useful for modeling hierarchical and multi-layered systems in both theoretical and practical contexts.

When applied to graph theory, these extensions give rise to two important generalizations: the *hypergraph* [25, 29, 49, 49] and the *superhypergraph* [60, 77, 183, 184]. A hypergraph allows each edge—called a *hyperedge*—to connect more than two vertices simultaneously, capturing complex many-to-many relationships. A superhypergraph

1.3 Graph in biology and biochemistry

Graph-based and network-based approaches have also played a central role in many studies in biology [17, 45, 150], chemistry [82, 201, 208], biophysics [194], bioelectricity [86], bioinformatics [104, 221, 227], and biochemistry [197]. Examples of graph concepts in biology and biochemistry include the Molecular Graph [48, 100, 136], Protein–Protein Interaction (PPI) Graph [30, 128, 196], Signal Transduction Network [80, 174, 211], Phylogenetic Tree [108, 120, 148], and RNA Secondary Structure Graph [124, 132]. Hypergraphs are likewise employed in fields such as biology and biochemistry [38, 49, 54, 117]. As such, graph-based models are widely utilized across various domains in the life sciences.

In this paper, we focus on a class of graph-based models known as *Molecular Interaction Networks*, which describe biochemical interactions among molecules. In such models, nodes represent molecular entities (e.g., proteins, genes, or metabolites), and edges represent pairwise interactions or chemical reactions [14, 85, 110, 133].

1.4 Our Contributions

This paper introduces two novel generalizations: the *Molecular Interaction HyperNetwork* and the *Molecular Interaction SuperHyperNetwork*, which extend the structure of Molecular Interaction Networks using the frameworks of hypernetworks and superhypernetworks, respectively. We present their formal definitions, investigate their mathematical properties, and provide concrete real-world examples. These newly proposed models are intended to support future research on hierarchical and multi-scale representations of molecular interaction networks.

1.5 Structure of this paper

This subsection outlines the structure of the paper. Section 2 presents the *Preliminaries and Definitions*, including foundational concepts such as Classical Structure, Hyperstructure, and n-Superhyperstructure, as well as Hypergraph, SuperHyperGraph, and Molecular Interaction Networks. Section 3 introduces and defines *Molecular Interaction HyperNetworks*, while Section 4 focuses on the definition and analysis of *Molecular Interaction SuperHyperNetworks*. For each, concrete examples and related mathematical theorems are discussed. Finally, Section 5 provides the *conclusion* of the paper along with directions for *future work*.

2 Preliminaries and Definitions

This section provides an overview of the fundamental concepts and definitions essential for the discussions presented in this paper. For the sake of simplicity, all graphs considered herein are assumed to be *simple*, *undirected*, and *finite*, unless stated otherwise.

2.1 Classical Structure, Hyperstructure, and n-Superhyperstructure

A *Classical Structure* represents a general mathematical concept, while a *Hyperstructure* can be defined using the power set, and an n*-Superhyperstructure* can be defined using the n-th powerset [1, 64, 72, 188]. Intuitively, the n-th powerset is a repeated application of the powerset operation [12,64,65,187]. Relevant definitions and simple examples are provided below.

Definition 2.1 (Set)**.** [103, 116, 134] A *set* is a well-defined collection of distinct objects, called elements or members.

Definition 2.2 (Subset)**.** [103,116,134] Let A and B be sets. We say that A is a *subset* of B, written $A \subseteq B$, if every element of A is also an element of B; that is,

$$A \subseteq B \quad \Longleftrightarrow \quad \forall x\,(x \in A \Rightarrow x \in B).$$

Definition 2.3 (Base Set)**.** [61] A *base set* S is the foundational set from which complex structures such as powersets and hyperstructures are derived. It is formally defined as:

$$S = \{x \mid x \text{ is an element within a specified domain}\}.$$

All elements in constructs like $\mathcal{P}(S)$ or $\mathcal{P}_n(S)$ originate from the elements of S.

Definition 2.4 (Powerset)**.** [61] The *powerset* of a set S, denoted $\mathcal{P}(S)$, is the collection of all possible subsets of S, including both the empty set and S itself. Formally, it is expressed as:

$$\mathcal{P}(S) = \{A \mid A \subseteq S\}.$$

Example 2.5 (Post-translational Modification Combinations)**.** Post-translational modifications are chemical changes made to proteins after synthesis, altering their activity, localization, stability, or interaction with other molecules (cf. [127,142,172]). Consider a protein domain that can undergo three types of post-translational modifications:

$$S = \{\text{P, Ac, Me}\},$$

where P = phosphorylation, Ac = acetylation, Me = methylation. Then the powerset $\mathcal{P}(S)$ enumerates all possible modification states:

$$\mathcal{P}(S) = \big\{\, \emptyset,\ \{\mathrm{P}\},\ \{\mathrm{Ac}\},\ \{\mathrm{Me}\},\ \{\mathrm{P},\mathrm{Ac}\},\ \{\mathrm{P},\mathrm{Me}\},\ \{\mathrm{Ac},\mathrm{Me}\},\ \{\mathrm{P},\mathrm{Ac},\mathrm{Me}\} \big\}.$$

[left=1em]$\emptyset$: unmodified protein. $\{\mathrm{P}\}$, $\{\mathrm{Ac}\}$, $\{\mathrm{Me}\}$: single modification states. $\{\mathrm{P}, \mathrm{Ac}\}$, $\{\mathrm{P}, \mathrm{Me}\}$, $\{\mathrm{Ac}, \mathrm{Me}\}$: dual-modification states. $\{\mathrm{P}, \mathrm{Ac}, \mathrm{Me}\}$: fully modified protein.

This enumeration guides the design of experiments probing cross-talk between different modifications and their combinatorial effects on protein function.

Definition 2.6 (n-th Powerset)**.** (cf. [61, 66, 188])

The n-th powerset of a set H, denoted $P_n(H)$, is defined iteratively, starting with the standard powerset. The recursive construction is given by:

$$P_1(H) = P(H), \quad P_{n+1}(H) = P(P_n(H)), \quad \text{for } n \geq 1.$$

Similarly, the n-th non-empty powerset, denoted $P_n^*(H)$, is defined recursively as:

$$P_1^*(H) = P^*(H), \quad P_{n+1}^*(H) = P^*(P_n^*(H)).$$

Here, $P^*(H)$ represents the powerset of H with the empty set removed.

Example 2.7 (Gene Regulatory Programs via n-th Powersets)**.** In eukaryotic gene regulation [43, 230], a gene's expression is controlled by combinations of regulatory elements such as promoters Pr, enhancers En, and silencers Si. Let

$$H = \{\text{Pr, En, Si}\}.$$

First powerset $P^1(H)$: all subsets of regulatory elements regulating a single gene:

$$P^1(H) = \mathcal{P}(H) = \{\,\emptyset, \{\mathrm{Pr}\}, \{\mathrm{En}\}, \{\mathrm{Si}\}, \{\mathrm{Pr}, \mathrm{En}\}, \{\mathrm{Pr}, \mathrm{Si}\}, \{\mathrm{En}, \mathrm{Si}\}, \{\mathrm{Pr}, \mathrm{En}, \mathrm{Si}\}\}.$$

Second powerset $P^2(H)$: sets of regulatory programs for multiple genes. For instance, choose two programs:

$$A_1 = \{\mathrm{Pr}\}, \quad A_2 = \{\mathrm{Pr}, \mathrm{En}\}, \quad A_3 = \{\mathrm{En}, \mathrm{Si}\}.$$

Then

$$P^2(H) = \mathcal{P}\big(P^1(H)\big), \quad M_1 = \{A_1, A_2\}, \quad M_2 = \{A_2, A_3\}.$$

Third powerset $P^3(H)$: meta-programs across cell types or tissues:

$$P^3(H) = \mathcal{P}\big(P^2(H)\big), \quad T = \{M_1, M_2\},$$

where T might represent a tissue-specific regulatory program comprising two distinct gene-level programs M_1 and M_2.

This hierarchy

$$\underbrace{\text{Regulatory Elements}}_{H} \to \underbrace{P^1(H)}_{\text{Gene Programs}} \to \underbrace{P^2(H)}_{\text{Multi-gene Programs}} \to \underbrace{P^3(H)}_{\text{Tissue-level Programs}}$$

illustrates how iterated powersets capture increasingly higher-order combinations in gene regulatory networks.

Definition 2.8 (Classical Structure)**.** (cf. [181, 188]) A *Classical Structure* is a mathematical framework defined on a non-empty set H, equipped with one or more *Classical Operations* that satisfy specified *Classical Axioms*. Specifically:

A *Classical Operation* is a function of the form:

$$\#_0 : H^m \to H,$$

where $m \geq 1$ is a positive integer, and H^m denotes the m-fold Cartesian product of H. Common examples include addition and multiplication in algebraic structures such as groups, rings, and fields.

Definition 2.9 (Hyperoperation)**.** (cf. [173, 205–207]) A *hyperoperation* is a generalization of a binary operation where the result of combining two elements is a set, not a single element. Formally, for a set S, a hyperoperation $\circ$ is defined as:

$$\circ : S \times S \to \mathcal{P}(S),$$

where $\mathcal{P}(S)$ is the powerset of S.

Definition 2.10 (Hyperstructure)**.** (cf. [61, 181, 188]) A *Hyperstructure* extends the notion of a Classical Structure by operating on the powerset of a base set. Formally, it is defined as:

$$\mathcal{H} = (\mathcal{P}(S), \circ),$$

where S is the base set, $\mathcal{P}(S)$ is the powerset of S, and $\circ$ is an operation defined on subsets of $\mathcal{P}(S)$. Hyperstructures allow for generalized operations that can apply to collections of elements rather than single elements.

Example 2.11 (Metabolic Pathway Hyperstructure of Glycolysis)**.** A metabolic pathway is a series of enzyme-catalyzed biochemical reactions that convert substrates into products, sustaining cellular processes and energy flow (cf. [31, 146]). In biochemistry, metabolic pathways involve sequences of enzyme-catalyzed reactions converting substrates into products. We model part of the glycolysis pathway as a hyperstructure

$$\mathcal{H} = \big(\mathcal{P}(S), \circ\big),$$

where the *base set* of metabolites is

$$S = \big\{\text{Glucose, ATP, ADP, Glucose-6-Phosphate, Fructose-6-Phosphate, Fructose-1,6-Bisphosphate}\big\},$$

and the *hyperoperation*

$$\circ : S \times S \longrightarrow \mathcal{P}(S)$$

is defined on single metabolites by the stoichiometry of key reactions:

$$\begin{aligned}
\text{Glucose} \circ \text{ATP} &= \{\text{Glucose-6-Phosphate, ADP}\}, \\
\text{Fructose-6-Phosphate} \circ \text{ATP} &= \{\text{Fructose-1,6-Bisphosphate, ADP}\}, \\
x \circ y &= \{\, x, y\} \quad \text{if no direct reaction occurs.}
\end{aligned}$$

We extend $\circ$ to mixtures by

$$A \circ B = \bigcup_{a \in A,\; b \in B} (a \circ b), \quad A, B \subseteq S.$$

Concrete computations:

$$\{\text{Glucose}\} \circ \{\text{ATP}\} = \{\text{Glucose-6-Phosphate, ADP}\},$$

$$\begin{aligned}
&\{\text{Glucose, ATP}\} \circ \{\text{Fructose-6-Phosphate, ATP}\} \\
&= (\text{Glucose} \circ \text{Fructose-6-Phosphate}) \;\cup\; (\text{ATP} \circ \text{ATP}) \;\cup\; \dots \\
&= \{\text{Glucose, Fructose-6-Phosphate}, \dots\}.
\end{aligned}$$

Thus $\mathcal{H}$ captures the many-to-many relationships of metabolites in glycolysis: combining substrates yields all possible products, and mixing mixtures yields the union of individual reaction outcomes, modeling both single-step and multi-step biochemical processes within one algebraic framework.

Definition 2.12 (SuperHyperOperations)**.** (cf. [188]) Let H be a non-empty set, and let $\mathcal{P}(H)$ denote the powerset of H. The n-th powerset $\mathcal{P}^n(H)$ is defined recursively as follows:

$$\mathcal{P}^0(H) = H, \quad \mathcal{P}^{k+1}(H) = \mathcal{P}(\mathcal{P}^k(H)), \quad \text{for } k \geq 0.$$

A *SuperHyperOperation* of order (m, n) is an m-ary operation:

$$\circ^{(m,n)} : H^m \to \mathcal{P}^n_*(H),$$

where $\mathcal{P}^n_*(H)$ represents the n-th powerset of H, either excluding or including the empty set, depending on the type of operation:

- If the codomain is $\mathcal{P}^n_*(H)$ excluding the empty set, it is called a *classical-type* (m, n)*-SuperHyperOperation*.
- If the codomain is $\mathcal{P}^n(H)$ including the empty set, it is called a *Neutrosophic* (m, n)*-SuperHyperOperation*.

These SuperHyperOperations are higher-order generalizations of hyperoperations, capturing multi-level complexity through the construction of n-th powersets.

Definition 2.13 (n-Superhyperstructure)**.** (cf. [62,188]) An n-*Superhyperstructure* further generalizes a Hyperstructure by incorporating the n-th powerset of a base set. It is formally described as:

$$\mathcal{SH}_n = (\mathcal{P}_n(S), \circ),$$

where S is the base set, $\mathcal{P}_n(S)$ is the n-th powerset of S, and $\circ$ represents an operation defined on elements of $\mathcal{P}_n(S)$. This iterative framework allows for increasingly hierarchical and complex representations of relationships within the base set.

Example 2.14 (2-Superhyperstructure of Protein Complex Assembly)**.** Protein complex assembly is the biological process where multiple protein subunits interact and bind to form a functional multi-protein complex (cf. [109, 139, 153]). In cellular biochemistry [23], many functional units arise by hierarchical assembly of protein subunits.

- **Base set** S of protein subunits:

$$S = \{\text{Actin, Myosin, Tropomyosin, Troponin}\}.$$

- **First-level complexes** $\mathcal{P}^1(S)$:

$$C_1 = \{\text{Actin, Myosin}\} \quad \text{(actomyosin)},$$
$$C_2 = \{\text{Actin, Tropomyosin, Troponin}\} \quad \text{(thin filament regulatory unit)},$$
$$C_3 = \{\text{Myosin, Troponin}\} \quad \text{(myosin–troponin interaction)}.$$

- **Second-level supervertices** $\mathcal{P}^2(S)$:

$$M_1 = \{C_1, C_2\}, \quad M_2 = \{C_1, C_3\}, \quad M_3 = \{C_2, C_3\}.$$

Define the superhyperoperation

$$\star : \mathcal{P}^2(S) \times \mathcal{P}^2(S) \longrightarrow \mathcal{P}\big(\mathcal{P}^2(S)\big)$$

by

$$X \star Y = \big\{\, X \cup Y,\ X \cap Y,\ X \triangle Y \,\big\}, \quad X, Y \subseteq \mathcal{P}^2(S),$$

where $X \triangle Y$ is the symmetric difference. For example,

$$M_1 \star M_2 = \big\{\, \{C_1, C_2, C_3\},\ \{C_1\},\ \{C_2, C_3\} \big\}.$$

Thus $\big(\mathcal{P}^2(S), \star\big)$ is a 2-Superhyperstructure modeling the hierarchical assembly of protein complexes—first forming binary and ternary subcomplexes, then organizing them into larger functional modules such as the sarcomeric apparatus in muscle fibers.

2.2 SuperHyperGraph

In classical graph theory, a hypergraph generalizes the notion of a standard graph by allowing each edge—known as a hyperedge—to connect more than two vertices. This generalized framework enables the representation of complex, higher-order relationships among elements, making it particularly valuable across various scientific domains [25, 92, 93]. The literature recognizes several well-established extensions of HyperGraphs, including Directed HyperGraphs [9, 170, 219], Fuzzy HyperGraphs [149,177,210], Regular HyperGraphs [44,46], Soft HyperGraphs [10,15,88], and Neutrosophic HyperGraphs [8, 11, 137, 140]. A *SuperHyperGraph* further extends the concept of a hypergraph by incorporating recursively defined powerset structures into the classical formulation. This advanced model captures hierarchical and self-referential relationships within data and has recently been introduced and actively explored in the literature [33, 59, 66, 162]. Related concepts include the Fuzzy SuperHyperGraph [98] and the Plithogenic SuperHyperGraph [113, 143, 147, 191], which further expand the model to handle uncertainty and multi-valued logic in hierarchical structures.

The concepts of HyperGraph, SuperHyperGraph, along with their related extensions and concrete examples, are presented below.

Definition 2.15 (Graph)**.** [35,41,52,203] A graph is a mathematical structure consisting of a set of vertices and a set of edges, where each edge connects a pair of distinct vertices.

Definition 2.16 (Subgraph)**.** [35,41] Let $G = (V, E)$ be a graph. A *subgraph* of G is a graph $G' = (V', E')$ such that

$$V' \subseteq V, \quad E' \subseteq \big\{\{u, v\} \in E \mid u, v \in V'\big\}.$$

In other words, G' is obtained by selecting a subset of vertices and retaining only those edges of G whose endpoints both lie in V'.

Definition 2.17 (Hypergraph)**.** [25, 29] A *hypergraph* $H = (V(H), E(H))$ consists of:

- A nonempty set $V(H)$ of vertices.
- A set $E(H)$ of hyperedges, where each hyperedge is a nonempty subset of $V(H)$, thereby allowing connections among multiple vertices.

Unlike standard graphs, hypergraphs are well-suited to represent higher-order relationships. In this paper, we restrict ourselves to the case where both $V(H)$ and $E(H)$ are finite.

Definition 2.18 (Subhypergraph)**.** (cf. [25, 29]) Let $H = (V, E)$ be a hypergraph. A *subhypergraph* of H is a hypergraph $H' = (V', E')$ such that

$$V' \subseteq V, \quad E' \subseteq \big\{\, e \in E \mid e \subseteq V' \big\}.$$

Equivalently, H' is obtained by choosing a subset of vertices and keeping only those hyperedges of H that lie entirely within V'.

Example 2.19 (Citric Acid Cycle as a Hypergraph)**.** The Citric Acid Cycle is a central metabolic pathway that generates energy by oxidizing acetyl-CoA into carbon dioxide and high-energy molecules (cf. [6, 157, 209, 217]). Model the key steps of the citric acid (TCA) cycle as a hypergraph $H = (V, E)$:

Vertices (metabolites):

$$V = \{\,\text{Acetyl-CoA},\ \text{Oxaloacetate},\ \text{Citrate},\ \text{Isocitrate},\ \alpha\text{-KG},\ \text{Succinate},\ \text{Fumarate},\ \text{Malate}\,\}.$$

Hyperedges (enzyme-catalyzed reactions):

$$\begin{aligned} e_1 &= \{\text{Acetyl-CoA},\ \text{Oxaloacetate},\ \text{Citrate}\},\\ e_2 &= \{\text{Citrate},\ \text{Isocitrate}\},\\ e_3 &= \{\text{Isocitrate},\ \alpha\text{-KG}\},\\ e_4 &= \{\alpha\text{-KG},\ \text{Succinate}\},\\ e_5 &= \{\text{Succinate},\ \text{Fumarate}\},\\ e_6 &= \{\text{Fumarate},\ \text{Malate}\},\\ e_7 &= \{\text{Malate},\ \text{Oxaloacetate}\}. \end{aligned}$$

Here each hyperedge e_i connects all substrates and products of the i-th step simultaneously, capturing the stoichiometry of that reaction.

Interpretation:

[left=1em]e_1 (citrate synthase) consumes Acetyl-CoA + Oxaloacetate to form Citrate. e_4 (α-ketoglutarate dehydrogenase) transforms α-KG into Succinate (via intermediates), etc. Representing each reaction as a hyperedge highlights multi-component interactions in one step, unlike a simple pairwise graph.

This hypergraph formalism aids pathway analysis by recognizing reactions involving more than two metabolites as single cohesive units.

Definition 2.20 (n-SuperHyperGraph)**.** [183, 184]

Let V_0 be a finite base set of vertices. For each integer $k \geq 0$, define the iterative powerset by

$$\mathcal{P}^0(V_0) = V_0, \quad \mathcal{P}^{k+1}(V_0) = \mathcal{P}(\mathcal{P}^k(V_0)),$$

where $\mathcal{P}(\cdot)$ denotes the usual powerset operation. An *n-SuperHyperGraph* is then a pair

$$\mathrm{SHT}^{(n)} = (V, E),$$

with

$$V \subseteq \mathcal{P}^n(V_0) \quad \text{and} \quad E \subseteq \mathcal{P}^n(V_0).$$

Each element of V is called an *n-supervertex* and each element of E an *n-superedge*.

Example 2.21 (Global Climate Research Consortia as a 2-SuperHyperGraph)**.** Global climate refers to the long-term patterns and averages of temperature, humidity, wind, and precipitation across the entire Earth(cf. [36, 121, 218]). Let the base set of researchers be

$$V_0 = \{\text{Alice, Bob, Carol, Dave}\}.$$

First-level research groups (1-supervertices in $\mathcal{P}^1(V_0)$) are:

$$R_1 = \{\text{Alice, Bob}\}, \quad R_2 = \{\text{Bob, Carol}\}, \quad R_3 = \{\text{Carol, Dave}\}.$$

Second-level consortia (2-supervertices in $\mathcal{P}^2(V_0)$) are:

$$C_\alpha = \{R_1, R_2\}, \quad C_\beta = \{R_2, R_3\}.$$

We then form the 2-SuperHyperGraph

$$\text{SHT}^{(2)} = (V, E)$$

by

$$V = \{ C_\alpha, C_\beta\}, \qquad E = \big\{\{ C_\alpha, C_\beta\}\big\}.$$

Here:

- Each 2-supervertex C_α and C_β represents a research consortium composed of overlapping labs.
- The single 2-superedge $\{C_\alpha, C_\beta\}$ models a joint international summit bringing together both consortia.
- This structure captures three hierarchical levels: individual researchers $\to$ lab groups $\to$ consortia $\to$ inter-consortium collaboration.

Example 2.22 (2-SuperHyperGraph of Protein Complex Hierarchies)**.** Protein complex hierarchy refers to the multi-level organization of proteins into subunits, complexes, and higher-order assemblies with distinct biological functions (cf. [144, 145, 169]). In muscle contraction, proteins assemble hierarchically into complexes and higher-order modules. We model this as a 2-SuperHyperGraph:

Base set of proteins:

$$V_0 = \{\text{MyosinII}, \ \text{Actin}, \ \text{Tropomyosin}, \ \text{Troponin}\}.$$

First-level complexes ($\mathcal{P}^1(V_0)$):

$$C_1 = \{\text{MyosinII, Actin}\}, \quad C_2 = \{\text{Actin, Tropomyosin, Troponin}\}, \quad C_3 = \{\text{MyosinII, Troponin}\}.$$

Second-level supervertices ($\mathcal{P}^2(V_0)$):

$$M_1 = \{C_1, C_2\}, \quad M_2 = \{C_1, C_3\}, \quad M_3 = \{C_2, C_3\}.$$

Define the 2-SuperHyperGraph

$$\mathrm{SHT}^{(2)} = (V, E),$$

with

$$V = \{M_1, M_2, M_3\}, \quad E = \big\{\{M_1, M_2\}, \{M_2, M_3\}\big\}.$$

Interpretation:

[left=1em]Each M_i is a *2-supervertex* representing a higher-order module of protein complexes (e.g. thick vs. thin filament assemblies). Each $\{M_i, M_j\} \in E$ is a *2-superedge* linking modules that coexist or interact within the sarcomeric unit during contraction.

Thus $\big(\mathcal{P}^2(V_0), E\big)$ captures the hierarchical organization from individual proteins to complexes and then to functional modules in muscle biochemistry.

Example 2.23 (Corporate Hierarchy as a 3-SuperHyperGraph)**.** Let the base set of employees be

$$V_0 = \{\text{Alice, Bob, Carol, Dave, Eve, Frank}\}.$$

First-level committees (1-supervertices in $\mathcal{P}^1(V_0)$) might be:

$$C_1 = \{\text{Alice, Bob}\}, \quad C_2 = \{\text{Carol, Dave}\}, \quad C_3 = \{\text{Eve, Frank}\}, \quad C_4 = \{\text{Bob, Carol}\}.$$

Second-level departments (2-supervertices in $\mathcal{P}^2(V_0)$) could group these committees into:

$$D_{\text{Sales}} = \{C_1, C_4\}, \quad D_{\text{Engineering}} = \{C_2, C_3\}.$$

Third-level divisions (3-supervertices in $\mathcal{P}^3(V_0)$) then organize departments into:

$$U_{\text{Commercial}} = \{D_{\text{Sales}}\}, \quad U_{\text{Technical}} = \{D_{\text{Engineering}}\}.$$

We form the 3-SuperHyperGraph

$$\mathrm{SHT}^{(3)} = (V, E)$$

by setting

$$V = \{\, U_{\text{Commercial}}, U_{\text{Technical}} \,\}, \qquad E = \big\{\{\, U_{\text{Commercial}}, U_{\text{Technical}} \,\}\big\}.$$

Interpretation:

- $\mathcal{P}^0(V_0)$: individual employees.
- $\mathcal{P}^1(V_0)$: cross-functional committees C_i.
- $\mathcal{P}^2(V_0)$: departments D_{Sales} and $D_{\text{Engineering}}$.
- $\mathcal{P}^3(V_0)$: top-level divisions $U_{\text{Commercial}}$ and $U_{\text{Technical}}$.
- The single 3-superedge $\{U_{\text{Commercial}}, U_{\text{Technical}}\}$ models a company-wide strategic initiative linking both divisions.

This example illustrates how a 3-SuperHyperGraph captures four hierarchical layers—employees, committees, departments, divisions—and their inter-division collaboration in one unified structure.

2.3 Molecular Interaction Networks

Molecular interaction networks represent biochemical relationships, where nodes correspond to molecules (such as proteins, genes, or metabolites), and edges denote physical or functional interactions among them [40, 141, 152, 159]. Due to their biochemical significance, molecular interaction networks have been the subject of extensive research across various disciplines [107,135,215,216]. The formal definition of molecular interaction networks is provided below.

Definition 2.24 (Network)**.** (cf. [47, 171]) A *network* (or *graph*) is an ordered triple

$$N = \bigl(V,\, E,\, w\bigr)$$

where

- V is a nonempty finite set of *vertices* (or *nodes*);
- $E \subseteq \bigl\{\{u, v\} \mid u, v \in V,\ u \neq v\bigr\}$ is the set of *undirected edges*, each joining two distinct vertices;
- $w\colon E \to \mathbb{R}_{\geq 0}$ is a *weight function* assigning a nonnegative real weight to each edge (omitted if unweighted).

If edges are *directed*, one instead writes

$$N = \bigl(V,\, A,\, w\bigr), \quad A \subseteq V \times V,$$

and each $(u, v) \in A$ is an *arc* from u to v. In either case, one may also include an optional *vertex-labeling* $\ell_V : V \to L_V$ to record vertex types.

Definition 2.25 (Molecular Interaction Network)**.** (cf. [40,141,152,159]) A *molecular interaction network* is a labeled hypergraph

$$\mathcal{N} \;=\; \bigl(V,\,\mathcal{I},\,\ell_V,\,\ell_{\mathcal{I}}\bigr)$$

where

- V is a finite set of *molecular entities* (e.g. proteins, metabolites, genes);
- $\mathcal{I} \subseteq \mathcal{P}(V) \setminus \{\emptyset\}$ is a set of *interactions*, each interaction $I \in \mathcal{I}$ being the subset of entities participating simultaneously in a biochemical event (e.g. complex formation [180], enzymatic reaction [55], regulatory effect);
- $\ell_V : V \to L_V$ is a *vertex-labeling* function assigning to each entity its type or identifier (e.g. "kinase", "ligand", "metabolite");
- $\ell_{\mathcal{I}} : \mathcal{I} \to L_{\mathcal{I}}$ is an *interaction-labeling* function assigning to each interaction its category or attributes (e.g. "binding", "phosphorylation", confidence score).

Optionally, one may equip $\mathcal{N}$ with a weight function $w : \mathcal{I} \to \mathbb{R}_{\geq 0}$ to record interaction strengths or probabilities.

Example 2.26 (Yeast Protein–Protein Interaction Network)**.** Yeast protein–protein interaction refers to physical or functional associations between yeast proteins, essential for cellular processes and regulatory networks (cf. [21,34,99]). Let

$$V = \{\mathrm{P53}, \mathrm{MDM2}, \mathrm{ATM}, \mathrm{CHK2}\},$$

$$\mathcal{I} = \bigl\{\{\mathrm{P53}, \mathrm{MDM2}\},\ \{\mathrm{ATM}, \mathrm{P53}\},\ \{\mathrm{ATM}, \mathrm{CHK2}\},\ \{\mathrm{CHK2}, \mathrm{P53}\}\bigr\}.$$

Define

$$\ell_V(x) = \text{“protein”} \quad (\forall x \in V),$$

$$\ell_{\mathcal{I}}(\{\mathrm{P53}, \mathrm{MDM2}\}) = \text{“ubiquitination”}, \quad \ell_{\mathcal{I}}(\{\mathrm{ATM}, \mathrm{P53}\}) = \text{“phosphorylation”},$$

$$\ell_{\mathcal{I}}(\{\mathrm{ATM}, \mathrm{CHK2}\}) = \text{“activation”}, \quad \ell_{\mathcal{I}}(\{\mathrm{CHK2}, \mathrm{P53}\}) = \text{“phosphorylation”}.$$

If we include confidence scores:

$$w(\{\mathrm{P53}, \mathrm{MDM2}\}) = 0.95,\ w(\{\mathrm{ATM}, \mathrm{P53}\}) = 0.80,\ w(\{\mathrm{ATM}, \mathrm{CHK2}\}) = 0.85,\ w(\{\mathrm{CHK2}, \mathrm{P53}\}) = 0.90.$$

Then $\mathcal{N} = (V, \mathcal{I}, \ell_V, \ell_{\mathcal{I}}, w)$ models a small yeast protein–protein interaction network, capturing both the participants and the types and strengths of their interactions.

3 Molecular Interaction HyperNetwork

A *Molecular Interaction HyperNetwork* is a mathematical framework developed to represent complex biochemical systems, where interactions may involve multiple molecular entities simultaneously. We now present the formal definition of a Molecular Interaction HyperNetwork.

Definition 3.1 (Hypernetwork)**.** A *hypernetwork* is an ordered triple

$$H = \big(V, \mathcal{E}, w\big)$$

where

- V is a nonempty finite set of *nodes*;
- $\mathcal{E} \subseteq \mathcal{P}(V)\setminus\{\emptyset\}$ is the set of *hyperedges*, each hyperedge $e \in \mathcal{E}$ being a nonempty subset of nodes (allowing multi-node interactions);
- $w\colon \mathcal{E} \to \mathbb{R}_{\geq 0}$ is a *weight or attribute function* on hyperedges (omitted if unweighted).

A *directed hypernetwork* may be defined by replacing $\mathcal{E} \subseteq \mathcal{P}(V)$ with a set of *ordered* tuples of nodes or by equipping each $e \in \mathcal{E}$ with a head-tail partition. One can further add a *node-labeling* $\ell_V : V \to L_V$ and a *hyperedge-labeling* $\ell_{\mathcal{E}} : \mathcal{E} \to L_{\mathcal{E}}$ to record types or properties.

Definition 3.2 (Molecular Interaction HyperNetwork)**.** A *molecular interaction hypernetwork* is a tuple

$$\mathcal{H} \;=\; \big(V, \mathcal{I}, \ell_V, \ell_{\mathcal{I}}, w\big)$$

where

- V is a finite set of *molecular entities* (e.g. proteins, metabolites, genes);
- $\mathcal{I} \subseteq \mathcal{P}(V)\setminus\{\emptyset\}$ is a set of *interaction hyperedges*, each $I \in \mathcal{I}$ being a nonempty subset of entities participating in a single biochemical event (e.g. complex formation or multi-enzyme reaction);
- $\ell_V : V \to L_V$ labels each node by its type or identifier (e.g. “kinase”, “ligand”);
- $\ell_{\mathcal{I}} : \mathcal{I} \to L_{\mathcal{I}}$ labels each hyperedge by its interaction category (e.g. “binding”, “phosphorylation cascade”);
- $w : \mathcal{I} \to \mathbb{R}_{\geq 0}$ assigns a nonnegative weight or confidence score to each interaction.

Example 3.3 (Eukaryotic DNA Replication Pre-Initiation as a Molecular Interaction HyperNetwork)**.** DNA replication is the biological process of copying a cell's DNA, producing two identical DNA molecules before cell division (cf. [24, 126, 129]). Consider the assembly and activation of the eukaryotic DNA replication pre-initiation complex. Let

$$V = \{\,\mathrm{ORC},\ \mathrm{Cdc6},\ \mathrm{Cdt1},\ \mathrm{MCM2–7},\ \mathrm{CDK2},\ \mathrm{DDK}\}$$

be the set of molecular entities: the origin recognition complex (ORC), loading factors Cdc6 and Cdt1, the MCM2–7 helicase, and the two kinases CDK2 and DDK. Define two interaction hyperedges:

$$\mathcal{I} = \{\, I_{\text{loading}},\ I_{\text{activation}}\,\},$$

where

$$I_{\text{loading}} = \{\mathrm{ORC}, \mathrm{Cdc6}, \mathrm{Cdt1}, \mathrm{MCM2–7}\}, \quad I_{\text{activation}} = \{\mathrm{MCM2–7}, \mathrm{CDK2}, \mathrm{DDK}\}.$$

Label each node by its functional class:

$$\ell_V(x) = \begin{cases} \text{“origin-binding factor”}, & x = \mathrm{ORC}, \\ \text{“helicase loader”}, & x = \mathrm{Cdc6}, \mathrm{Cdt1}, \\ \text{“replicative helicase”}, & x = \mathrm{MCM2–7}, \\ \text{“kinase”}, & x = \mathrm{CDK2}, \mathrm{DDK}. \end{cases}$$

Label each hyperedge by its biological process:

$$\ell_{\mathcal{I}}(I_{\text{loading}}) = \text{“MCM2–7 helicase loading”}, \quad \ell_{\mathcal{I}}(I_{\text{activation}}) = \text{“helicase activation by phosphorylation”}.$$

Optionally, assign confidence scores based on experimental evidence:

$$w(I_{\text{loading}}) = 0.92, \quad w(I_{\text{activation}}) = 0.88.$$

- I_{loading} models the coordinated loading of the MCM2–7 helicase onto origin DNA by ORC, Cdc6, and Cdt1.
- $I_{\text{activation}}$ captures the subsequent activation of the loaded helicase by CDK2 and DDK phosphorylation.

This hypernetwork illustrates a multi-step, multi-protein process in which hyperedges represent higher-order interactions essential for DNA replication initiation.

Example 3.4 (Human Hemoglobin Interaction HyperNetwork)**.** Human hemoglobin is a protein in red blood cells that transports oxygen from the lungs to body tissues and organs(cf. [106, 112]). Let

$$V = \{\alpha_1,\ \alpha_2,\ \beta_1,\ \beta_2,\ \mathrm{O_2}\}$$

be the set of molecular entities (four globin subunits and oxygen). Define the set of interaction hyperedges

$$\mathcal{I} = \{\, E_{\text{tetramer}},\ E_{\text{O}_2} \,\},$$

where

$$E_{\text{tetramer}} = \{\alpha_1, \alpha_2, \beta_1, \beta_2\}, \quad E_{\text{O}_2} = \{\alpha_1, \alpha_2, \beta_1, \beta_2, \text{O}_2\}.$$

The labeling functions are

$$\ell_V(\alpha_i) = \text{“globin subunit”}, \quad \ell_V(\beta_i) = \text{“globin subunit”}, \quad \ell_V(\text{O}_2) = \text{“oxygen molecule”},$$

$$\ell_{\mathcal{I}}(E_{\text{tetramer}}) = \text{“hemoglobin tetramer assembly”}, \quad \ell_{\mathcal{I}}(E_{\text{O}_2}) = \text{“oxygen binding”}.$$

Optionally, assign confidence scores:

$$w(E_{\text{tetramer}}) = 1.00, \quad w(E_{\text{O}_2}) = 0.98.$$

Here:

- E_{tetramer} captures the multi-protein assembly of two α and two β chains into the functional hemoglobin tetramer.
- E_{O_2} captures the cooperative binding of molecular oxygen to the assembled tetramer.

This example illustrates a molecular interaction hypernetwork where hyperedges represent complex biochemical events involving more than two entities.

Example 3.5 (Pyruvate Dehydrogenase Complex as a Molecular Interaction HyperNetwork)**.** Pyruvate Dehydrogenase Complex is a multi-enzyme system that converts pyruvate into acetyl-CoA, linking glycolysis to the Krebs cycle [101, 163, 164, 200]. Let

$$V = \{\, \text{E1, E2, E3, Pyruvate, CoA, NAD}^+ \},$$

be the set of molecular entities: the three enzyme subunits of the pyruvate dehydrogenase complex (E1, E2, E3) and its substrates/cofactors (pyruvate, coenzyme A, NAD^+). Define the interaction hyperedges

$$\mathcal{I} = \{\, I_{\text{assembly}},\ I_{\text{catalysis}} \,\},$$

where

$$I_{\text{assembly}} = \{\text{E1}, \text{E2}, \text{E3}\}, \quad I_{\text{catalysis}} = \{\text{E1}, \text{E2}, \text{E3}, \text{Pyruvate}, \text{CoA}, \text{NAD}^+\}.$$

Label each node by its type:

$$\ell_V(\text{E1}) = \ell_V(\text{E2}) = \ell_V(\text{E3}) = \text{“enzyme subunit”}, \quad \ell_V(\text{Pyruvate}) = \ell_V(\text{CoA}) = \ell_V(\text{NAD}^+) = \text{“substrate/cofactor”}$$

Label each hyperedge by its biological process:

$$\ell_{\mathcal{I}}(I_{\text{assembly}}) = \text{“complex assembly”}, \quad \ell_{\mathcal{I}}(I_{\text{catalysis}}) = \text{“oxidative decarboxylation reaction”}.$$

Optionally, assign confidence scores:

$$w(I_{\text{assembly}}) = 0.90, \quad w(I_{\text{catalysis}}) = 0.85.$$

Here:

- I_{assembly} models the multi-enzyme assembly of E1, E2, and E3 into the functional pyruvate dehydrogenase complex.
- $I_{\text{catalysis}}$ captures the coordinated catalytic event converting pyruvate plus CoA and NAD^+ into acetyl-CoA and NADH.

This example demonstrates a molecular interaction hypernetwork in which hyperedges represent both the assembly of a multi-protein complex and its multi-participant enzymatic reaction.

Theorem 3.6 (Hypernetwork Property)**.** *Every molecular interaction hypernetwork $\mathcal{H} = (V, \mathcal{I}, \ell_V, \ell_{\mathcal{I}}, w)$ is a hypernetwork in the sense of Definition [Hypernetwork].*

Proof. Let $\mathcal{H} = (V, \mathcal{I}, \ell_V, \ell_{\mathcal{I}}, w)$ be a molecular interaction hypernetwork. We verify each condition of Definition [Hypernetwork]:

1. **Node set:** By hypothesis, V is a nonempty finite set of molecular entities.
2. **Hyperedge set:** By construction,

   $$\mathcal{I} \subseteq \mathcal{P}(V) \setminus \{\emptyset\},$$

   and each $I \in \mathcal{I}$ is a nonempty subset of V.
3. **Weight function:** The map $w \colon \mathcal{I} \to \mathbb{R}_{\geq 0}$ assigns a nonnegative real weight or confidence score to each hyperedge, as required.
4. **Optional labels:** The node-labeling $\ell_V \colon V \to L_V$ and hyperedge-labeling $\ell_{\mathcal{I}} \colon \mathcal{I} \to L_{\mathcal{I}}$ are admissible extensions under the general hypernetwork definition and do not violate any axioms.

Since all structural requirements of a hypernetwork are satisfied, $\mathcal{H}$ is indeed a hypernetwork in the sense of Definition [Hypernetwork]. □

Theorem 3.7 (Generalization of Molecular Interaction Networks)**.** *Let $\mathcal{N} = (V, \mathcal{I}_2, \ell_V, \ell_{\mathcal{I}}, w)$ be a molecular interaction network in which every interaction involves at most two entities, i.e. $\mathcal{I}_2 \subseteq \big\{\{u, v\} \mid u, v \in V\big\} \cup \{\{v\} \mid v \in V\}$. Then $\mathcal{N}$ is a special case of the molecular interaction hypernetwork $\mathcal{H}$ obtained by setting $\mathcal{I} = \mathcal{I}_2$.*

Proof. Let $\mathcal{H} = (V, \mathcal{I}, \ell_V, \ell_{\mathcal{I}}, w)$ be the candidate hypernetwork obtained by taking $\mathcal{I} = \mathcal{I}_2$. We check that $\mathcal{H}$ satisfies the definition of a molecular interaction hypernetwork:

1. *Node set:* By hypothesis, V is a finite set of molecular entities.
2. *Hyperedges:* Since $\mathcal{I}_2 \subseteq \big\{\{u, v\} \mid u, v \in V\big\} \cup \{\{v\} \mid v \in V\}$, we have
$$\mathcal{I} \subseteq \mathcal{P}(V) \setminus \{\emptyset\},$$
and each element of $\mathcal{I}$ is a nonempty subset of V of cardinality one or two.
3. *Node-labeling:* The map $\ell_V : V \to L_V$ is unchanged and labels each entity by its type or identifier.
4. *Hyperedge-labeling:* The map $\ell_{\mathcal{I}} : \mathcal{I} \to L_{\mathcal{I}}$ likewise remains valid, assigning each interaction its category.
5. *Weight function:* The function $w : \mathcal{I} \to \mathbb{R}_{\geq 0}$ assigns a nonnegative score to each interaction.

All conditions of Definition [Molecular Interaction HyperNetwork] are thus met. Moreover, because every interaction in $\mathcal{I}$ involves at most two entities, $\mathcal{H}$ is precisely the original molecular interaction network $\mathcal{N}$, viewed as a special case of a hypernetwork where hyperedges have size ≤ 2. Therefore, $\mathcal{N}$ embeds directly into the hypernetwork framework without alteration. □

Theorem 3.8 (Induced Subhypernetwork)**.** *Let $\mathcal{H} = (V, \mathcal{I}, \ell_V, \ell_{\mathcal{I}}, w)$ be a molecular interaction hypernetwork and let $U \subseteq V$ be any nonempty subset of molecular entities. Define*
$$\mathcal{I}_U = \{ I \in \mathcal{I} : I \subseteq U \},$$
and restrict labels and weights accordingly. Then
$$\mathcal{H}[U] = (U,\ \mathcal{I}_U,\ \ell_V|_U,\ \ell_{\mathcal{I}}|_{\mathcal{I}_U},\ w|_{\mathcal{I}_U})$$
is itself a molecular interaction hypernetwork.

Proof.

1. U is nonempty and finite since $U \subseteq V$.
2. $\mathcal{I}_U \subseteq \mathcal{P}(U) \setminus \{\emptyset\}$ by construction, and each $I \in \mathcal{I}_U$ remains a nonempty interaction hyperedge.
3. The restricted maps $\ell_V|_U$ and $\ell_{\mathcal{I}}|_{\mathcal{I}_U}$ still assign valid labels to nodes and hyperedges.

4. The restricted weight $w|_{\mathcal{I}_U}$ remains a nonnegative function on $\mathcal{I}_U$.

Thus $\mathcal{H}[U]$ satisfies all axioms of Definition [Molecular Interaction HyperNetwork]. □

Theorem 3.9 (Primal Graph Theorem). *Let $\mathcal{H} = (V, \mathcal{I}, \ell_V, \ell_{\mathcal{I}}, w)$ be a molecular interaction hypernetwork. Its* primal graph *$G(\mathcal{H})$ is the labeled simple graph*

$$G(\mathcal{H}) = \big(V,\ E,\ \ell_V,\ \psi\big)$$

where

$$E = \big\{\{u,v\} \subseteq V : \exists\, I \in \mathcal{I},\ \{u,v\} \subseteq I\big\}, \quad \psi(\{u,v\}) = \max_{I \ni u,v} w(I).$$

Then $G(\mathcal{H})$ is a molecular interaction network.

Proof.

- V is finite and nonempty.
- Each $\{u,v\} \in E$ arises from some hyperedge $I \subseteq V$, so $E \subseteq \{\{u,v\} \mid u,v \in V\}$.
- The node-labeling ℓ_V is unchanged.
- The bond-order labeling ψ assigns a nonnegative weight to each edge, taking the maximum confidence among all hyperedges that contain both u and v.

Hence $G(\mathcal{H})$ meets the definition of a molecular interaction network (a special case of Definition [Hypernetwork] with hyperedges of size at most two). □

Theorem 3.10 (Coverage of Entities). *In any molecular interaction hypernetwork $\mathcal{H} = (V, \mathcal{I}, \ell_V, \ell_{\mathcal{I}}, w)$, every entity participates in at least one interaction:*

$$\bigcup_{I \in \mathcal{I}} I \ = \ V.$$

Proof. By the biochemical semantics of molecular interaction hypernetworks, each entity $v \in V$ must appear in at least one biochemical event $I \in \mathcal{I}$. Formally, if some v did not appear in any I, then v would be isolated and never part of an interaction—contradicting the intended modeling. Therefore the union of all hyperedges equals V. □

4 Molecular Interaction n-SuperHyperNetwork

A *Molecular Interaction n-SuperHyperNetwork* is a mathematical framework designed to model hierarchical biochemical systems. It captures multi-scale molecular interactions using n-level nested groupings of molecular entities and their associated interaction events. We formally define a Molecular Interaction n-SuperHyperNetwork as follows.

Definition 4.1 (n-SuperHypernetwork)**.** [66] Let V_0 be a finite base set of *nodes*. Define the n-th iterated powerset recursively by

$$\mathcal{P}^0(V_0) = V_0, \qquad \mathcal{P}^{k+1}(V_0) = \mathcal{P}\big(\mathcal{P}^k(V_0)\big) \quad (k \geq 0).$$

An *n-superhypernetwork* is a tuple

$$\mathcal{N}^{(n)} \;=\; \big(V,\; \mathcal{E},\; w\big)$$

where

- $V \subseteq \mathcal{P}^n(V_0)$ is a finite set of *n-supernodes*;
- $\mathcal{E} \subseteq \mathcal{P}^n(V_0)$ is a finite set of *n-superedges*, each superedge $e \in \mathcal{E}$ being a nonempty subset of V;
- $w\colon \mathcal{E} \to \mathbb{R}_{\geq 0}$ is an optional *weight function* assigning a nonnegative real weight (or confidence) to each superedge.

In other words, both vertices and hyperedges of the network are drawn from the n-th powerset of the base node set, capturing up to n levels of hierarchical grouping.

Example 4.2 (Disaster Response as a 2-SuperHypernetwork)**.** Disaster response involves coordinated actions by emergency services, governments, and communities to manage and mitigate the impact of disasters (cf. [27, 111, 156]). Let the base set of individual responders be

$$V_0 = \{\text{Alice},\ \text{Bob},\ \text{Carol},\ \text{Dave}\}.$$

First-level collections (teams, in $\mathcal{P}^1(V_0)$) are

$$T_1 = \{\text{Alice}, \text{Bob}\}, \quad T_2 = \{\text{Bob}, \text{Carol}\}, \quad T_3 = \{\text{Carol}, \text{Dave}\}.$$

Second-level collections (task forces, in $\mathcal{P}^2(V_0)$) are

$$F_A = \{T_1, T_2\}, \quad F_B = \{T_2, T_3\}.$$

Define the 2-superhypernetwork

$$\mathcal{N}^{(2)} = (V, \mathcal{E}, w)$$

by

$$V = \{ F_A, F_B \}, \qquad \mathcal{E} = \big\{ \{F_A, F_B\} \big\},$$

with weights

$$w(\{F_A, F_B\}) = 0.85.$$

Here:

- Each supernode $F_A, F_B \in V$ is a *2-supernode*, representing a pair of overlapping teams working together.
- The single superedge $\{F_A, F_B\}$ connects these two task forces, modeling a joint multi-team operation.
- The weight 0.85 might represent the confidence or coordination efficiency of that joint operation.

This construction captures individual responders $\to$ teams $\to$ task forces and the cooperative relations among those forces, all within a single unified 2-superhypernetwork framework.

Definition 4.3 (Molecular Interaction n-SuperHyperNetwork)**.** Let V_0 be a finite set of molecular entities (e.g. proteins, metabolites, genes). For each integer $n \geq 1$, define the iterated powerset

$$\mathcal{P}^0(V_0) = V_0, \quad \mathcal{P}^{k+1}(V_0) = \mathcal{P}\big(\mathcal{P}^k(V_0)\big) \quad (k \geq 0).$$

A *molecular interaction n-superHyperNetwork* is a quintuple

$$\mathcal{H}^{(n)} \; = \; \big(V^{(n)}, \mathcal{I}^{(n)}, \ell_V^{(n)}, \ell_{\mathcal{I}}^{(n)}, w^{(n)}\big)$$

where

- $V^{(n)} \subseteq \mathcal{P}^n(V_0)$ is a finite set of *n-supernodes*;
- $\mathcal{I}^{(n)} \subseteq \mathcal{P}^n(V_0) \setminus \{\emptyset\}$ is a finite set of *n-superedges*, each $I \in \mathcal{I}^{(n)}$ being a nonempty subset of $V^{(n)}$;
- $\ell_V^{(n)} \colon V^{(n)} \to L_V$ labels each n-supernode by its biological or chemical role (e.g. “multi-protein complex”);
- $\ell_{\mathcal{I}}^{(n)} \colon \mathcal{I}^{(n)} \to L_{\mathcal{I}}$ labels each n-superedge by its interaction type (e.g. “cascade”, “assembly”);
- $w^{(n)} \colon \mathcal{I}^{(n)} \to \mathbb{R}_{\geq 0}$ assigns a nonnegative confidence score to each n-superinteraction.

Example 4.4 (EGF Receptor Signaling Pathway as a Molecular Interaction 2-SuperHyperNetwork)**.** The EGF receptor signaling pathway is a molecular cascade activated by epidermal growth factor, regulating cell growth, differentiation, survival, and proliferation through kinase-mediated interactions (cf. [154, 155, 179, 213, 214]). Let the base set of molecular entities be

$$V_0 = \{\,\mathrm{EGF},\ \mathrm{EGFR},\ \mathrm{GRB2},\ \mathrm{SOS},\ \mathrm{RAS},\ \mathrm{RAF},\ \mathrm{MEK},\ \mathrm{ERK}\}.$$

First-level interaction hyperedges (in $\mathcal{P}^1(V_0)$) are the elementary binding or activation events:

$$\begin{aligned} &E_1 = \{\mathrm{EGF},\ \mathrm{EGFR}\}, \quad E_2 = \{\mathrm{EGFR},\ \mathrm{GRB2},\ \mathrm{SOS}\},\\ &E_3 = \{\mathrm{SOS},\ \mathrm{RAS}\}, \quad E_4 = \{\mathrm{RAS},\ \mathrm{RAF}\},\\ &E_5 = \{\mathrm{RAF},\ \mathrm{MEK}\}, \quad E_6 = \{\mathrm{MEK},\ \mathrm{ERK}\}. \end{aligned}$$

These form the set of 1-supernodes:

$$V^{(1)} = \{E_1, E_2, E_3, E_4, E_5, E_6\} \ \subseteq\ \mathcal{P}^1(V_0).$$

Next, group related events into functional modules (2-supernodes in $\mathcal{P}^2(V_0)$):

$$F_R = \{E_1, E_2\}, \quad F_S = \{E_3, E_4\}, \quad F_M = \{E_5, E_6\}.$$

Thus

$$V^{(2)} = \{\,F_R,\ F_S,\ F_M\}\ \subseteq\ \mathcal{P}^2(V_0).$$

Finally, define the 2-superinteraction hyperedges (in $\mathcal{P}^2(V_0)$) linking these modules:

$$\mathcal{I}^{(2)} = \bigl\{\{F_R, F_S\},\ \{F_S, F_M\}\bigr\}.$$

Labeling functions assign biological roles and interaction types:

$$\begin{aligned} \ell_V^{(2)}(F_R) &= \text{“Receptor complex assembly”},\\ \ell_V^{(2)}(F_S) &= \text{“RAS activation module”},\\ \ell_V^{(2)}(F_M) &= \text{“MAPK phosphorylation cascade”}, \end{aligned}$$

$$\begin{aligned} \ell_{\mathcal{I}}^{(2)}(\{F_R, F_S\}) &= \text{“Signal propagation (receptor} \to \text{RAS)”},\\ \ell_{\mathcal{I}}^{(2)}(\{F_S, F_M\}) &= \text{“Signal propagation (RAS} \to \text{MAPK)”}. \end{aligned}$$

Weights (confidence scores) might be

$$w^{(2)}(\{F_R, F_S\}) = 0.95, \quad w^{(2)}(\{F_S, F_M\}) = 0.90,$$

reflecting high-confidence pathway activation.

In this 2-SuperHyperNetwork:

- Level 0 (V_0) are individual proteins.
- Level 1 ($V^{(1)}$) are elementary interactions.
- Level 2 ($V^{(2)}$) are functional modules grouping those interactions.

- Hyperedges $\mathcal{I}^{(2)}$ connect modules to model the hierarchical signal-transduction cascade.

Example 4.5 (Glycolytic Pathway as a Molecular Interaction 2-SuperHyperNetwork)**.** The glycolytic pathway is a series of enzymatic reactions that convert glucose into pyruvate, generating ATP and NADH in cells (cf. [51, 202]). Let the base set of molecular entities be

$$V_0 = \{\,\text{Glucose, ATP, HK, G6P, PGI, F6P, PFK, FBP, ALD, GAP, TPI}\}.$$

Define the first-level interaction hyperedges (1-supernodes in $\mathcal{P}^1(V_0)$) corresponding to the elementary enzymatic steps:

$$\begin{aligned}
E_1 &= \{\text{Glucose, HK, ATP}\},\\
E_2 &= \{\text{G6P, PGI}\},\\
E_3 &= \{\text{F6P, PFK, ATP}\},\\
E_4 &= \{\text{FBP, ALD}\},\\
E_5 &= \{\text{GAP, TPI}\}.
\end{aligned}$$

Thus

$$V^{(1)} = \{\,E_1, E_2, E_3, E_4, E_5\} \;\subseteq\; \mathcal{P}^1(V_0).$$

Next, group these into two functional modules (2-supernodes in $\mathcal{P}^2(V_0)$):

$$F_{\text{prep}} = \{\,E_1,\, E_2,\, E_3\}, \qquad F_{\text{payoff}} = \{\,E_4,\, E_5\}.$$

Hence

$$V^{(2)} = \{\,F_{\text{prep}},\, F_{\text{payoff}}\} \;\subseteq\; \mathcal{P}^2(V_0).$$

Finally, define the second-level interaction hyperedges (2-superedges):

$$\mathcal{I}^{(2)} = \big\{\,\{F_{\text{prep}},\, F_{\text{payoff}}\}\big\}.$$

Label each 2-supernode and the 2-superedge:

$$\begin{aligned}
\ell_V^{(2)}(F_{\text{prep}}) &= \text{“Preparatory phase of glycolysis”},\\
\ell_V^{(2)}(F_{\text{payoff}}) &= \text{“Payoff phase of glycolysis”},
\end{aligned}
\qquad
\ell_{\mathcal{I}}^{(2)}\big(\{F_{\text{prep}}, F_{\text{payoff}}\}\big) = \text{“Phase transition in glycolysis”}.$$

Optionally, assign a confidence score:

$$w^{(2)}\big(\{F_{\text{prep}}, F_{\text{payoff}}\}\big) = 0.90.$$

In this 2-SuperHyperNetwork:

- Level 0 (V_0): individual metabolites and enzymes.
- Level 1 ($V^{(1)}$): elementary enzymatic interactions.
- Level 2 ($V^{(2)}$): functional modules (preparatory vs. payoff phase).
- 2-superedge $\{F_{\text{prep}}, F_{\text{payoff}}\}$ models the hierarchical linkage between the two phases of glycolysis.

Example 4.6 (EGFR Signaling as a Molecular Interaction 3-SuperHyperNetwork)**.** Let the base set of entities be

$$V_0 = \{\, \text{EGF, EGFR, GRB2, SOS, RAS, RAF, MEK, ERK, PI3K, AKT, mTOR}\}.$$

First-level interaction hyperedges (1-supernodes in $\mathcal{P}^1(V_0)$) correspond to elementary binding or activation events:

$$\begin{aligned} &E_1 = \{\text{EGF}, \text{EGFR}\}, && E_2 = \{\text{EGFR}, \text{GRB2}, \text{SOS}\}, \\ &E_3 = \{\text{SOS}, \text{RAS}\}, && E_4 = \{\text{RAS}, \text{RAF}\}, \\ &E_5 = \{\text{RAF}, \text{MEK}\}, && E_6 = \{\text{MEK}, \text{ERK}\}, \\ &E_7 = \{\text{EGFR}, \text{PI3K}\}, && E_8 = \{\text{PI3K}, \text{AKT}\}, \\ &E_9 = \{\text{AKT}, \text{mTOR}\}. \end{aligned}$$

Thus

$$V^{(1)} = \{E_1, E_2, \dots, E_9\} \ \subseteq\ \mathcal{P}^1(V_0).$$

Second-level modules (2-supernodes in $\mathcal{P}^2(V_0)$) group these into functional units:

$$F_R = \{E_1, E_2\}, \quad F_M = \{E_3, E_4, E_5, E_6\}, \quad F_P = \{E_7, E_8, E_9\}.$$

Hence

$$V^{(2)} = \{F_R, F_M, F_P\} \ \subseteq\ \mathcal{P}^2(V_0).$$

Third-level supermodules (3-supernodes in $\mathcal{P}^3(V_0)$) capture overarching signaling branches:

$$U_1 = \{F_R, F_M\}, \quad U_2 = \{F_R, F_P\}.$$

Thus

$$V^{(3)} = \{U_1, U_2\} \ \subseteq\ \mathcal{P}^3(V_0).$$

Define the single 3-superinteraction hyperedge

$$\mathcal{I}^{(3)} = \{\{\, U_1, U_2\}\}.$$

Labeling functions record functional roles:

$$\begin{aligned} \ell_V^{(3)}(U_1) &= \text{“EGFR→MAPK signaling supermodule”}, \\ \ell_V^{(3)}(U_2) &= \text{“EGFR→PI3K–AKT–mTOR supermodule”}, \end{aligned}$$

$$\ell_{\mathcal{I}}^{(3)}\big(\{U_1, U_2\}\big) = \text{“Integrated proliferative and survival signaling”}.$$

Optionally, assign a confidence weight:

$$w^{(3)}(\{U_1, U_2\}) = 0.95.$$

- *Level 0* (V_0): individual molecular entities.
- *Level 1* ($V^{(1)}$): elementary interactions (ligand–receptor, adapter binding, kinase activation).
- *Level 2* ($V^{(2)}$): functional modules (receptor complex, MAPK cascade, PI3K–AKT–mTOR branch).
- *Level 3* ($V^{(3)}$): supermodules integrating MAPK-driven proliferation and PI3K–AKT–mTOR-driven survival pathways.
- $\mathcal{I}^{(3)}$ captures the coordination between these two critical signaling branches.

Example 4.7 (Insulin Signaling Pathway as a Molecular Interaction 3-SuperHyper-Network)**.** The insulin signaling pathway regulates glucose uptake and metabolism by transmitting signals from insulin receptors to intracellular effectors like AKT and GLUT4 (cf. [167, 176, 195]). Let the base set of molecular entities be

$$V_0 = \{\,\text{Insulin, IR, IRS, PI3K, PDK1, AKT, AS160, GLUT4}\}.$$

First-level interaction hyperedges (1-supernodes in $\mathcal{P}^1(V_0)$) correspond to elementary signaling steps:

$$\begin{aligned} E_1 &= \{\text{Insulin, IR}\}, & E_2 &= \{\text{IR, IRS}\}, \\ E_3 &= \{\text{IRS, PI3K}\}, & E_4 &= \{\text{PI3K, PDK1}\}, \\ E_5 &= \{\text{PDK1, AKT}\}, & E_6 &= \{\text{AKT, AS160}\}, \\ E_7 &= \{\text{AS160, GLUT4}\}. \end{aligned}$$

Thus

$$V^{(1)} = \{E_1, E_2, \dots, E_7\} \;\subseteq\; \mathcal{P}^1(V_0).$$

Second-level modules (2-supernodes in $\mathcal{P}^2(V_0)$) group these steps into functional blocks:

$$F_R = \{E_1, E_2\}, \quad F_K = \{E_3, E_4, E_5\}, \quad F_T = \{E_6, E_7\}.$$

Hence

$$V^{(2)} = \{F_R, F_K, F_T\} \;\subseteq\; \mathcal{P}^2(V_0).$$

Third-level supermodules (3-supernodes in $\mathcal{P}^3(V_0)$) capture the two main signaling arms:

$$U_1 = \{F_R, F_K\}, \quad U_2 = \{F_K, F_T\}.$$

Thus

$$V^{(3)} = \{U_1, U_2\} \;\subseteq\; \mathcal{P}^3(V_0).$$

Define the 3-superinteraction hyperedge

$$\mathcal{I}^{(3)} = \big\{\{\,U_1, U_2\}\big\}.$$

Labeling functions record biological roles:

$$\ell_V^{(3)}(U_1) = \text{“Receptor-proximal and PI3K activation module”},$$
$$\ell_V^{(3)}(U_2) = \text{“PI3K-AKT-mediated glucose uptake module”},$$

$$\ell_{\mathcal{I}}^{(3)}\big(\{U_1, U_2\}\big) = \text{“Integrated insulin signaling cascade”}.$$

Optionally, assign a confidence weight:

$$w^{(3)}(\{U_1, U_2\}) = 0.92.$$

- *Level 0* (V_0): individual molecules.
- *Level 1* ($V^{(1)}$): elementary binding and phosphorylation events.
- *Level 2* ($V^{(2)}$): functional blocks—receptor activation (F_R), kinase cascade (F_K), and transporter regulation (F_T).
- *Level 3* ($V^{(3)}$): supermodules integrating early PI3K activation (U_1) and downstream GLUT4 translocation (U_2).
- $\mathcal{I}^{(3)}$ models the coordination between these two critical modules in the insulin response.

Example 4.8 (26S Proteasome Complex as a Molecular Interaction 4-SuperHyperNetwork)**.** The 26S proteasome complex is a large protein structure that degrades ubiquitinated proteins, maintaining cellular protein homeostasis and regulating various biological processes (cf. [53, 90, 168, 212]). Let the base set of molecular entities be

$$V_0 = \{\, A_1, \dots, A_7,\ B_1, \dots, B_7,\ \mathrm{Rpt}_1, \dots, \mathrm{Rpt}_6,\ \mathrm{Rpn}_1, \dots, \mathrm{Rpn}_{13}\},$$

where A_i and B_i are the seven α- and β-subunits of the 20S core particle, Rpt_j the six ATPase subunits, and Rpn_k the thirteen non-ATPase regulatory subunits.

First-level groupings (1-supernodes in $\mathcal{P}^1(V_0)$) are the fundamental subcomplexes:

$$F_\alpha = \{A_1, \dots, A_7\}, \qquad F_\beta = \{B_1, \dots, B_7\},$$
$$F_{\text{base}} = \{\mathrm{Rpt}_1, \dots, \mathrm{Rpt}_6\}, \quad F_{\text{lid}} = \{\mathrm{Rpn}_1, \dots, \mathrm{Rpn}_{13}\}.$$

Second-level assemblies (2-supernodes in $\mathcal{P}^2(V_0)$) combine rings into particle subunits:

$$M_{\text{CP}} = \{F_\alpha,\, F_\beta\}, \quad M_{\text{RP}} = \{F_{\text{base}},\, F_{\text{lid}}\}.$$

Third-level super-assemblies (3-supernodes in $\mathcal{P}^3(V_0)$) isolate each particle:

$$S_{\text{core}} = \{M_{\text{CP}}\}, \quad S_{\text{reg}} = \{M_{\text{RP}}\}.$$

Fourth-level 4-supernodes (in $\mathcal{P}^4(V_0)$) represent the complete 26S proteasome components:

$$U_1 = \{S_{\text{core}}\}, \quad U_2 = \{S_{\text{reg}}\}.$$

Then

$$V^{(4)} = \{\, U_1,\, U_2\}, \quad \mathcal{I}^{(4)} = \big\{\{\, U_1,\, U_2\}\big\}.$$

Labeling functions assign:

$$\ell_V^{(4)}(U_1) = \text{“20S core particle”}, \quad \ell_V^{(4)}(U_2) = \text{“19S regulatory particle”},$$

$$\ell_{\mathcal{I}}^{(4)}\big(\{U_1, U_2\}\big) = \text{“26S proteasome assembly”},$$

and optionally

$$w^{(4)}(\{U_1, U_2\}) = 1.00.$$

Here:

- *Level 0 (V_0)*: individual proteasome subunits (α, β, ATPase, non-ATPase).
- *Level 1 ($\mathcal{P}^1$)*: fundamental rings and subcomplexes (α-ring, β-ring, base, lid).
- *Level 2 ($\mathcal{P}^2$)*: core particle (M_{CP}) and regulatory particle (M_{RP}).
- *Level 3 ($\mathcal{P}^3$)*: isolated core (S_{core}) and regulatory (S_{reg}) super-assemblies.
- *Level 4 ($\mathcal{P}^4$)*: top-level supernodes (U_1, U_2) representing the two principal 26S components, connected by a single 4-superedge modeling the intact proteasome.

Example 4.9 (E. coli 70S Ribosome as a Molecular Interaction 4-SuperHyperNetwork)**.** The E. coli 70S ribosome is a molecular machine composed of 30S and 50S subunits, responsible for protein synthesis during translation (cf. [2, 3, 79, 125]). Let the base set of molecular entities be

$$V_0 = \{\, S_1, \dots, S_{21},\ \text{16S rRNA},\ L_1, \dots, L_{23},\ \text{23S rRNA},\ \text{5S rRNA}\},$$

where S_i are the 21 small-subunit proteins, L_j the 23 large-subunit proteins, and the three ribosomal RNAs.

Level 1 (1-supernodes in $\mathcal{P}^1(V_0)$). Group individual components into four functional clusters:

$$F_S = \{S_1, \dots, S_{21}\}, \quad F_{rS} = \{\text{16S rRNA}\},$$
$$F_L = \{L_1, \dots, L_{23}\}, \quad F_{rL} = \{\text{23S rRNA, 5S rRNA}\}.$$

Level 2 (2-supernodes in $\mathcal{P}^2(V_0)$). Assemble each ribosomal subunit's core components:

$$M_{30\text{S}} = \{F_S,\, F_{rS}\}, \quad M_{50\text{S}} = \{F_L,\, F_{rL}\}.$$

Level 3 (3-supernodes in $\mathcal{P}^3(V_0)$). Encapsulate each subunit as a single supermodule:

$$U_{30S} = \{ M_{30S} \}, \quad U_{50S} = \{ M_{50S} \}.$$

Level 4 (4-supernodes in $\mathcal{P}^4(V_0)$). Define the two top-level supernodes and their interaction:

$$V^{(4)} = \{ U_{30S}, U_{50S} \}, \qquad \mathcal{I}^{(4)} = \big\{ \{ U_{30S}, U_{50S} \} \big\}.$$

Labeling functions assign:

$$\ell_V^{(4)}(U_{30S}) = \text{“30S ribosomal subunit”}, \quad \ell_V^{(4)}(U_{50S}) = \text{“50S ribosomal subunit”},$$

$$\ell_{\mathcal{I}}^{(4)}\big(\{U_{30S}, U_{50S}\}\big) = \text{“70S ribosome assembly”}, \quad w^{(4)}\big(\{U_{30S}, U_{50S}\}\big) = 1.00.$$

- *Level 0 (V_0)*: individual proteins and rRNAs.
- *Level 1 ($\mathcal{P}^1$)*: four component clusters (small-subunit proteins, 16S rRNA, large-subunit proteins, 23S+5S rRNAs).
- *Level 2 ($\mathcal{P}^2$)*: 30S and 50S subunit assemblies.
- *Level 3 ($\mathcal{P}^3$)*: supermodules representing each subunit.
- *Level 4 ($\mathcal{P}^4$)*: top-level supernodes and the superhyperedge capturing the intact 70S ribosome.

This example illustrates how a molecular interaction 4-superHyperNetwork encodes the hierarchical assembly of the bacterial ribosome from individual proteins and RNAs up to the fully assembled complex.

Theorem 4.10 (n-SuperHyperNetwork Property)**.** *Every molecular interaction n-superHyperNetwork $\mathcal{H}^{(n)}$ is an n-superhypernetwork in the sense of Definition [n-SuperHypernetwork].*

Proof. By construction:

- $V^{(n)} \subseteq \mathcal{P}^n(V_0)$ and $\mathcal{I}^{(n)} \subseteq \mathcal{P}^n(V_0) \setminus \{\emptyset\}$, so both supernodes and superedges lie in the n-th iterated powerset of the base set.
- Each element of $\mathcal{I}^{(n)}$ is a nonempty subset of $V^{(n)}$, matching the requirement that superedges connect supernodes.
- The weight function $w^{(n)} \colon \mathcal{I}^{(n)} \to \mathbb{R}_{\geq 0}$ and the labelings $\ell_V^{(n)}, \ell_{\mathcal{I}}^{(n)}$ are exactly the optional data permitted in the general n-superhypernetwork framework.

Hence all axioms of an n-superhypernetwork are satisfied. □

Theorem 4.11 (Generalization of Molecular Interaction HyperNetworks)**.** *Let $\mathcal{H} = (V_0, \mathcal{I}, \ell_V, \ell_\mathcal{I}, w)$ be any molecular interaction hypernetwork (the case $n = 1$). Then there is a natural identification of $\mathcal{H}$ with a molecular interaction 1-superHyperNetwork $\mathcal{H}^{(1)}$ given by*

$$V^{(1)} = \{\{v\} \mid v \in V_0\}, \quad \mathcal{I}^{(1)} = \mathcal{I} \subseteq \mathcal{P}^1(V_0),$$

with $\ell_V^{(1)}(\{v\}) = \ell_V(v)$, $\ell_\mathcal{I}^{(1)} = \ell_\mathcal{I}$, and $w^{(1)} = w$. Under this identification, $\mathcal{H}^{(1)}$ is isomorphic to $\mathcal{H}$.

Proof. Define

$$\Phi_V : V_0 \longrightarrow V^{(1)}, \quad v \mapsto \{v\}, \quad \Phi_\mathcal{I} : \mathcal{I} \hookrightarrow \mathcal{I}^{(1)}$$

where we simply regard each hyperedge $I \subseteq V_0$ as an element of $\mathcal{P}^1(V_0)$. Then:

1. Φ_V is a bijection from the original nodes V_0 onto $V^{(1)}$.
2. $\Phi_\mathcal{I}$ is the identity embedding of $\mathcal{I}$ into $\mathcal{P}^1(V_0)$.
3. Labels are preserved since $\ell_V^{(1)}(\{v\}) = \ell_V(v)$ and $\ell_\mathcal{I}^{(1)}(I) = \ell_\mathcal{I}(I)$.
4. Weights are preserved: $w^{(1)}(I) = w(I)$.

Thus the data of $\mathcal{H}$ and $\mathcal{H}^{(1)}$ coincide under the natural isomorphism $(\Phi_V, \Phi_\mathcal{I})$. Therefore every molecular interaction hypernetwork is a special case of a molecular interaction n-superHyperNetwork for $n = 1$, and the class of n-superHyperNetworks strictly generalizes that of hypernetworks. □

Theorem 4.12 (Flattening Theorem)**.** *Let*

$$\mathcal{H}^{(n)} = \left(V^{(n)}, \mathcal{I}^{(n)}, \ell_V^{(n)}, \ell_\mathcal{I}^{(n)}, w^{(n)}\right)$$

be a molecular interaction n-SuperHyperNetwork over base entities V_0. For each k with $0 \le k \le n$, define the k-flattening map

$$\varphi_k : \mathcal{P}^n(V_0) \longrightarrow \mathcal{P}^{n-k}(V_0), \quad X \mapsto \bigcup_{Y \in X} Y,$$

iterated k times. Then

$$\mathcal{H}^{(n-k)} = \Big(\varphi_k\big(V^{(n)}\big),\ \varphi_k\big(\mathcal{I}^{(n)}\big),\ \ell_V^{(n)} \circ \varphi_k,\ \ell_\mathcal{I}^{(n)} \circ \varphi_k,\ w^{(n)} \circ \varphi_k\Big)$$

is a well-defined molecular interaction $(n-k)$-SuperHyperNetwork.

Proof. Since $V^{(n)} \subseteq \mathcal{P}^n(V_0)$ and $\mathcal{I}^{(n)} \subseteq \mathcal{P}^n(V_0)$, applying φ_k yields $\varphi_k(V^{(n)}) \subseteq \mathcal{P}^{n-k}(V_0)$ and $\varphi_k(\mathcal{I}^{(n)}) \subseteq \mathcal{P}^{n-k}(V_0)$. Each $\varphi_k(I)$ remains a nonempty subset of $\varphi_k(V^{(n)})$. Composing the label functions and weights with φ_k preserves their codomains and assignments. Thus all axioms of Definition [Molecular Interaction n-SuperHyperNetwork] hold for $\mathcal{H}^{(n-k)}$. □

Theorem 4.13 (Entity Coverage Theorem)**.** *In any molecular interaction n-SuperHyperNetwork $\mathcal{H}^{(n)}$ over V_0, the union of the fully flattened hyperedges covers the entire base set:*

$$\bigcup_{I \in \mathcal{I}^{(n)}} \varphi_n(I) \;=\; V_0.$$

Proof. We proceed by induction on n.

Base case $n = 1$. Then $\mathcal{H}^{(1)}$ is a molecular interaction hypernetwork, and by definition each base entity participates in at least one interaction hyperedge, so $\bigcup_{I \in \mathcal{I}^{(1)}} I = V_0$.

Inductive step. Assume the statement holds for $n-1$. Consider $\mathcal{H}^{(n)}$. Its 1-flattening $\mathcal{H}^{(n-1)}$ satisfies $\bigcup_{J \in \varphi_1(\mathcal{I}^{(n)})} \varphi_{n-1}(J) = V_0$ by the induction hypothesis. Since $\varphi_n = \varphi_{n-1} \circ \varphi_1$ and $\varphi_1(\mathcal{I}^{(n)}) = \varphi_1(\mathcal{I}^{(n)})$, we obtain

$$\bigcup_{I \in \mathcal{I}^{(n)}} \varphi_n(I) = \bigcup_{J \in \varphi_1(\mathcal{I}^{(n)})} \varphi_{n-1}(J) = V_0.$$

This completes the induction. □

Theorem 4.14 (Connectivity Equivalence)**.** *Let $\mathcal{H}^{(n)}$ be a molecular interaction n-SuperHyperNetwork, and let $G^{(n)}$ be its primal graph on n-supernodes. Then $G^{(n)}$ is connected if and only if the primal graph of the fully flattened network, $G^{(0)}$, is connected.*

Proof. In the primal graph $G^{(n)}$, two distinct n-supernodes u, v are adjacent if they both lie in some n-superedge I. Under each flattening step φ_k, adjacency is preserved: if $\{u, v\} \subseteq I$ then $\{\varphi_k(u), \varphi_k(v)\} \subseteq \varphi_k(I)$. Thus any path in $G^{(n)}$ projects to a path in $G^{(n-1)}$, and iterating down to $G^{(0)}$ yields a corresponding path. Conversely, any path in $G^{(0)}$ lifts to paths at higher levels by inverse images under the φ_k. Hence connectedness is equivalent at all levels. □

Theorem 4.15 (Induced Subnetwork Theorem)**.** *Let $\mathcal{H}^{(n)}$ be a molecular interaction n-SuperHyperNetwork on V_0, and let $B \subseteq V_0$ be a nonempty subset of base entities. Define*

$$V' = \{\, v \in V^{(n)} : v \subseteq \mathcal{P}^n(B) \,\}, \quad \mathcal{I}' = \{\, I \in \mathcal{I}^{(n)} : I \subseteq \mathcal{P}^n(B) \,\}.$$

Then

$$\mathcal{H}^{(n)}[B] \;=\; \bigl(V', \mathcal{I}', \ell_V^{(n)}|_{V'}, \ell_{\mathcal{I}}^{(n)}|_{\mathcal{I}'}, w^{(n)}|_{\mathcal{I}'}\bigr)$$

is a molecular interaction n-SuperHyperNetwork on base set B.

Proof. By construction, $V' \subseteq \mathcal{P}^n(B)$ and $\mathcal{I}' \subseteq \mathcal{P}^n(B) \setminus \{\emptyset\}$. Each induced hyperedge I' remains a nonempty subset of V'. The restrictions of $\ell_V^{(n)}, \ell_{\mathcal{I}}^{(n)}, w^{(n)}$ to the smaller sets preserve their codomains and assignments. Therefore all axioms of Definition [Molecular Interaction n-SuperHyperNetwork] hold for the induced subnetwork $\mathcal{H}^{(n)}[B]$. □

5 Conclusion and Future Works

In this paper, we introduced two novel mathematical frameworks: the *Molecular Interaction HyperNetwork* and the *Molecular Interaction SuperHyperNetwork*. We provided formal definitions, illustrative real-world examples, and a preliminary discussion of their structural and mathematical properties.

As future work, we aim to extend the *Molecular Interaction HyperNetwork* and *Molecular Interaction SuperHyperNetwork* by integrating advanced uncertainty-handling frameworks. These include Fuzzy Sets [223, 225, 226], Intuitionistic Fuzzy Sets [18–20], Vague Sets [7, 32, 84], Rough Sets [165, 166], HyperRough Sets [67, 69, 75], SuperHyperRough Sets [58, 71], Bipolar Fuzzy Sets [5], HyperFuzzy Sets [57, 119, 193], Picture Fuzzy Sets [37, 102], Hesitant Fuzzy Sets [198, 199], Neutrosophic Sets [182, 192], Quadripartitioned Neutrosophic Sets [74, 122, 222], and Plithogenic Sets [63, 78, 190]. Building on these extensions, we plan to investigate applications in AI [4, 28, 68, 76], linear programming [114, 115, 229], algorithm design [73, 224, 228], neural networks [95, 105, 131], and decision-making [83, 158]. Incorporating these frameworks will potentially enhance the descriptive power and applicability of our models, especially for representing complex and hierarchical biochemical systems under various forms of uncertainty.

Ethical Approval

As this research is entirely theoretical in nature and does not involve human participants or animal subjects, no ethical approval is required.

Data Availability

This research is purely theoretical, involving no data collection or analysis. We encourage future researchers to pursue empirical investigations to further develop and validate the concepts introduced here.

Research Integrity

The authors hereby confirm that, to the best of their knowledge, this manuscript is their original work, has not been published in any other journal, and is not currently under consideration for publication elsewhere at this stage.

Disclaimer (Artificial Intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

Disclaimer (Note on Computational Tools)

No computer-assisted proof, symbolic computation, or automated theorem proving tools (e.g., Mathematica, SageMath, Coq, etc.) were used in the development or verification of the results presented in this paper. All proofs and derivations were carried out manually and analytically by the authors.

Disclaimer (Limitations and Claims)

The theoretical concepts presented in this paper have not yet been subject to practical implementation or empirical validation. Future researchers are invited to explore these ideas in applied or experimental settings. Although every effort has been made to ensure the accuracy of the content and the proper citation of sources, unintentional errors or omissions may persist. Readers should independently verify any referenced materials.

To the best of the authors' knowledge, all mathematical statements and proofs contained herein are correct and have been thoroughly vetted. Should you identify any potential errors or ambiguities, please feel free to contact the authors for clarification.

The results presented are valid only under the specific assumptions and conditions detailed in the manuscript. Extending these findings to broader mathematical structures may require additional research. The opinions and conclusions expressed in this work are those of the authors alone and do not necessarily reflect the official positions of their affiliated institutions.

Competing interests

Author has declared that no competing interests exist.

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References

[1] Sunday Adesina Adebisi and Adetunji Patience Ajuebishi. The order involving the neutrosophic hyperstructures, the construction and setting up of a typical neutrosophic group. *HyperSoft Set Methods in Engineering*, 3:26–31, 2025.

[2] Rajendra K Agrawal, Pawel Penczek, Robert A Grassucci, and Joachim Frank. Visualization of elongation factor g on the escherichia coli 70s ribosome: the mechanism of translocation. *Proceedings of the National Academy of Sciences*, 95(11):6134–6138, 1998.

[3] Rajendra K Agrawal, Manjuli R Sharma, Michael C Kiel, Go Hirokawa, Timothy M Booth, Christian MT Spahn, Robert A Grassucci, Akira Kaji, and Joachim Frank. Visualization of ribosome-recycling factor on the escherichia coli 70s ribosome: functional implications. *Proceedings of the National Academy of Sciences*, 101(24):8900–8905, 2004.

[4] Muhammad Rayees Ahmad and Usman Afzal. Mathematical modeling and ai based decision making for covid-19 suspects backed by novel distance and similarity measures on plithogenic hypersoft sets. *Artificial Intelligence in Medicine*, 132:102390, 2022.

[5] Muhammad Akram. Bipolar fuzzy graphs. *Information sciences*, 181(24):5548–5564, 2011.

[6] Muhammad Akram. Citric acid cycle and role of its intermediates in metabolism. *Cell biochemistry and biophysics*, 68(3):475–478, 2014.

[7] Muhammad Akram, A Nagoor Gani, and A Borumand Saeid. Vague hypergraphs. *Journal of Intelligent & Fuzzy Systems*, 26(2):647–653, 2014.

[8] Muhammad Akram and Anam Luqman. Bipolar neutrosophic hypergraphs with applications. *Journal of Intelligent & Fuzzy Systems*, 33(3):1699–1713, 2017.

[9] Muhammad Akram and Anam Luqman. Certain networks models using single-valued neutrosophic directed hypergraphs. *Journal of Intelligent & Fuzzy Systems*, 33(1):575–588, 2017.

[10] Muhammad Akram and Hafiza Saba Nawaz. Implementation of single-valued neutrosophic soft hypergraphs on human nervous system. *Artificial Intelligence Review*, 56(2):1387–1425, 2023.

[11] Muhammad Akram, Sundas Shahzadi, and Arsham Borumand Saeid. Single-valued neutrosophic hypergraphs. *viXra*, pages 1–14, 2018.

[12] Adel Al-Odhari. A brief comparative study on hyperstructure, super hyperstructure, and n-super superhyperstructure. *Neutrosophic Knowledge*, 6:38–49, 2025.

[13] Juan Alcácer, John A. Cantwell, and Lucia Piscitello. Internationalization in the information age: A new era for places, firms, and international business networks? *Journal of International Business Studies*, 47:499–512, 2016.

[14] C. Alfarano, C. E. Andrade, Kira Anthony, Neil Bahroos, M. Bajec, K. Bantoft, Doron Betel, B. Bobechko, K. Boutilier, E. Burgess, K. Buzadzija, R. Cavero, C. D'Abreo, Ian M. Donaldson, D. Dorairajoo, Michel Dumontier, Michel Dumontier, V. Earles, R. Farrall, Howard J. Feldman, E. Garderman, Y. Gong, R. Gonzaga, V. Grytsan, E. Gryz, V. Gu, E. Haldorsen, A. Halupa, Robin Haw, Anthony Hrvojic, L. T. Bazzano Hurrell, Ruth Isserlin, F. Jack, F. Juma, A. Khan, T. Kon, S. Konopinsky, V. Le, E. Lee, S. Ling, M. Magidin, J. Moniakis, Jason Montojo, Susan Moore, B. Muskat, I. Ng, J. P. Paraiso, Benjamin D. Parker, Greg Pintilie, R. Pirone, John J. Salama, S. Sgro, Tong Shan, Y. Shu, J. Siew, D. Skinner, Kevin A. Snyder, Robert Stasiuk, D. Strumpf, Brigitte Tuekam, S. Tao, Z. Wang, M. White, R. Willis, Cheryl Wolting, S. Wong, A. Wrong, Chenwei Xin, R. Yao, B. Yates, Shudong Zhang, K. Zheng, Tony Pawson, B. F. Francis Ouellette, and Christopher W. V. Hogue. The biomolecular interaction network database and related tools 2005 update. *Nucleic Acids Research*, 33:D418 – D424, 2004.

[15] Abbas Amini, Narjes Firouzkouhi, Ahmad Gholami, Anju R Gupta, Chun Cheng, and Bijan Davvaz. Soft hypergraph for modeling global interactions via social media networks. *Expert Systems with Applications*, 203:117466, 2022.

[16] Erjie Ang, Daniel Iancu, and Robert Swinney. Disruption risk and optimal sourcing in multitier supply networks. *Manag. Sci.*, 63:2397–2419, 2017.

[17] Banda Ashton. Graph theory in dna sequencing: Unveiling genetic patterns. *International Journal of Biology and Life Sciences*, 2023.

[18] Krassimir Atanassov and George Gargov. Elements of intuitionistic fuzzy logic. part i. *Fuzzy sets and systems*, 95(1):39–52, 1998.

[19] Krassimir T Atanassov and Krassimir T Atanassov. *Intuitionistic fuzzy sets*. Springer, 1999.

[20] Krassimir T Atanassov and G Gargov. *Intuitionistic fuzzy logics*. Springer, 2017.

[21] Gary D Bader and Christopher WV Hogue. Analyzing yeast protein–protein interaction data obtained from different sources. *Nature biotechnology*, 20(10):991–997, 2002.

[22] Norman Balabanian and Theodore A. Bickart. Electrical network theory. 1969.

[23] Salman F Banani, Hyun O Lee, Anthony A Hyman, and Michael K Rosen. Biomolecular condensates: organizers of cellular biochemistry. *Nature reviews Molecular cell biology*, 18(5):285–298, 2017.

[24] Stephen P Bell and Anindya Dutta. Dna replication in eukaryotic cells. *Annual review of biochemistry*, 71(1):333–374, 2002.

[25] Claude Berge. *Hypergraphs: combinatorics of finite sets*, volume 45. Elsevier, 1984.

[26] Eilert Berglind and Lars Gillner. Quantum noise treated with classical electrical network theory. 1994.

[27] Djamel Berkoune, Jacques Renaud, Monia Rekik, and Angel Ruiz. Transportation in disaster response operations. *Socio-Economic Planning Sciences*, 46(1):23–32, 2012.

[28] Abderrahmane Bettayeb and Muhammad Eid Balbaa. Success factors in adopting ai in human resource management in uae firms: Neutrosophic analysis. *International Journal of Neutrosophic Science (IJNS)*, 21(3), 2023.

[29] Alain Bretto. Hypergraph theory. *An introduction. Mathematical Engineering. Cham: Springer*, 1, 2013.

[30] Gaëlle Brevier, Romeo Rizzi, and Stéphane Vialette. Pattern matching in protein-protein interaction graphs. In *International Symposium on Fundamentals of Computation Theory*, pages 137–148. Springer, 2007.

[31] Dustin G Brown, Sangeeta Rao, Tiffany L Weir, Joanne O'Malia, Marlon Bazan, Regina J Brown, and Elizabeth P Ryan. Metabolomics and metabolic pathway networks from human colorectal cancers, adjacent mucosa, and stool. *Cancer & metabolism*, 4:1–12, 2016.

[32] Humberto Bustince and P Burillo. Vague sets are intuitionistic fuzzy sets. *Fuzzy sets and systems*, 79(3):403–405, 1996.

[33] Yan Cao. Integrating treesoft and hypersoft paradigms into urban elderly care evaluation: A comprehensive n-superhypergraph approach. *Neutrosophic Sets and Systems*, 85:852–873, 2025.

[34] Barry Causier and Brendan Davies. Analysing protein-protein interactions with the yeast two-hybrid system. *Plant molecular biology*, 50:855–870, 2002.

[35] Gary Chartrand. *Introductory graph theory*. Courier Corporation, 2012.

[36] David Coen, Julia Kreienkamp, and Tom Pegram. *Global climate governance*. Cambridge University Press, 2020.

[37] Bui Cong Cuong and Vladik Kreinovich. Picture fuzzy sets-a new concept for computational intelligence problems. In *2013 third world congress on information and communication technologies (WICT 2013)*, pages 1–6. IEEE, 2013.

[38] Qionghai Dai and Yue Gao. Hypergraph computation for medical and biological applications. In *Hypergraph Computation*, pages 191–221. Springer, 2023.

[39] Eva Delmas, Mathilde Besson, Marie-Hélène Brice, Laura A. Burkle, Giulio V. Dalla Riva, Marie-Josée Fortin, Dominique Gravel, Paulo Roberto Guimarães, David H. Hembry, Erica A. Newman, Jens M. Olesen, Mathias Mistretta Pires, Justin D. Yeakel, and Timothée Poisot. Analysing ecological networks of species interactions. *Biological Reviews*, 94, 2018.

[40] Lorenzo Di Rocco, Umberto Ferraro Petrillo, and Simona E Rombo. Diamin: a software library for the distributed analysis of large-scale molecular interaction networks. *BMC bioinformatics*, 23(1):474, 2022.

[41] Reinhard Diestel. Graduate texts in mathematics: Graph theory.

[42] Reinhard Diestel. Graph theory 3rd ed. *Graduate texts in mathematics*, 173(33):12, 2005.

[43] Niall Dillon and Pierangela Sabbattini. Functional gene expression domains: defining the functional unit of eukaryotic gene regulation. *Bioessays*, 22(7):657–665, 2000.

[44] Ioana Dumitriu and Yizhe Zhu. Spectra of random regular hypergraphs. *arXiv preprint arXiv:1905.06487*, 2019.

[45] Siddarth Durga, M. Durgadevi, and Kannan Rama Devi. Graph theory applications in biology. 2019.

[46] David Ellis and Nathan Linial. On regular hypergraphs of high girth. *arXiv preprint arXiv:1302.5090*, 2013.

[47] Ernesto Estrada. Graph and network theory in physics. *arXiv preprint arXiv:1302.4378*, 2013.

[48] Jean-Loup Faulon. Isomorphism, automorphism partitioning, and canonical labeling can be solved in polynomial-time for molecular graphs. *Journal of Chemical Information and Computer Sciences*, 38(3):432–444, 1998.

[49] Song Feng, Emily Heath, Brett Jefferson, Cliff Joslyn, Henry Kvinge, Hugh D Mitchell, Brenda Praggastis, Amie J Eisfeld, Amy C Sims, Larissa B Thackray, et al. Hypergraph models of biological networks to identify genes critical to pathogenic viral response. *BMC bioinformatics*, 22(1):287, 2021.

[50] Yifan Feng, Haoxuan You, Zizhao Zhang, Rongrong Ji, and Yue Gao. Hypergraph neural networks. In *Proceedings of the AAAI conference on artificial intelligence*, volume 33, pages 3558–3565, 2019.

[51] Linda A Fothergill-Gilmore. The evolution of the glycolytic pathway. *Trends in Biochemical Sciences*, 11(1):47–51, 1986.

[52] Leslie R Foulds. *Graph theory applications*. Springer Science & Business Media, 1995.

[53] Sarah Frankland-Searby and Sukesh R Bhaumik. The 26s proteasome complex: an attractive target for cancer therapy. *Biochimica et Biophysica Acta (BBA)-Reviews on Cancer*, 1825(1):64–76, 2012.

[54] Nicholas Franzese, Adam Groce, TM Murali, and Anna Ritz. Hypergraph-based connectivity measures for signaling pathway topologies. *PLoS computational biology*, 15(10):e1007384, 2019.

[55] Perry A Frey and Adrian D Hegeman. *Enzymatic reaction mechanisms*. Oxford University Press, 2007.

[56] Victor S. Frost and Benjamin Melamed. Traffic modeling for telecommunications networks. *IEEE Communications Magazine*, 32:70–81, 1994.

[57] Takaaki Fujita. Some types of hyperfuzzy set: Bipolar, m-polar, q-rung orthopair, trapezoidal, linguistic, intuitionistic, picture, hesitant, spherical, type-m, offset, overset, and underset. *Preprint*.

[58] Takaaki Fujita. Hyperrough cubic set and superhyperrough cubic set. *Prospects for Applied Mathematics and Data Analysis*, 4(1):28–35, 2024.

[59] Takaaki Fujita. Review of some superhypergraph classes: Directed, bidirected, soft, and rough. *Advancing Uncertain Combinatorics through Graphization, Hyperization, and Uncertainization: Fuzzy, Neutrosophic, Soft, Rough, and Beyond (Second Volume)*, 2024.

[60] Takaaki Fujita. Short note of supertree-width and n-superhypertree-width. *Neutrosophic Sets and Systems*, 77:54–78, 2024.

[61] Takaaki Fujita. Superhypergraph neural networks and plithogenic graph neural networks: Theoretical foundations. *arXiv preprint arXiv:2412.01176*, 2024.

[62] Takaaki Fujita. A theoretical exploration of hyperconcepts: Hyperfunctions, hyperrandomness, hyperdecision-making, and beyond (including a survey of hyperstructures). 2024.

[63] Takaaki Fujita. *Advancing Uncertain Combinatorics through Graphization, Hyperization, and Uncertainization: Fuzzy, Neutrosophic, Soft, Rough, and Beyond*. Biblio Publishing, 2025.

[64] Takaaki Fujita. Antihyperstructure, neutrohyperstructure, and superhyperstructure. *Advancing Uncertain Combinatorics through Graphization, Hyperization, and Uncertainization: Fuzzy, Neutrosophic, Soft, Rough, and Beyond*, page 311, 2025.

[65] Takaaki Fujita. Concise note of z-number, hyper z-number, and superhyper z-number. *Advancing Uncertain Combinatorics through Graphization, Hyperization, and Uncertainization: Fuzzy, Neutrosophic, Soft, Rough, and Beyond*, 6(25):352, 2025.

[66] Takaaki Fujita. Exploration of graph classes and concepts for superhypergraphs and n-th power mathematical structures. 2025.

[67] Takaaki Fujita. Forest hyperplithogenic set and forest hyperrough set. *Advancing Uncertain Combinatorics through Graphization, Hyperization, and Uncertainization: Fuzzy, Neutrosophic, Soft, Rough, and Beyond*, 2025.

[68] Takaaki Fujita. Natural n-superhyper plithogenic language. *Advancing Uncertain Combinatorics through Graphization, Hyperization, and Uncertainization: Fuzzy, Neutrosophic, Soft, Rough, and Beyond*, page 294, 2025.

[69] Takaaki Fujita. Neighborhood hyperrough set and neighborhood superhyperrough set. *Pure Mathematics for Theoretical Computer Science*, 5(1):34–47, 2025.

[70] Takaaki Fujita. Review of rough turiyam neutrosophic directed graphs and rough pentapartitioned neutrosophic directed graphs. *Neutrosophic Optimization and Intelligent Systems*, 5:48–79, 2025.

[71] Takaaki Fujita. Short introduction to rough, hyperrough, superhyperrough, treerough, and multirough set. *Advancing Uncertain Combinatorics through Graphization, Hyperization, and Uncertainization: Fuzzy, Neutrosophic, Soft, Rough, and Beyond*, page 394, 2025.

[72] Takaaki Fujita. Short note of superhyperstructures of partitions, integrals, and spaces. *Advancing Uncertain Combinatorics through Graphization, Hyperization, and Uncertainization: Fuzzy, Neutrosophic, Soft, Rough, and Beyond*, page 384, 2025.

[73] Takaaki Fujita. A short note on the basic graph construction algorithm for plithogenic graphs. *Advancing Uncertain Combinatorics through Graphization, Hyperization, and Uncertainization: Fuzzy, Neutrosophic, Soft, Rough, and Beyond*, page 274, 2025.

[74] Takaaki Fujita. Some types of hyperneutrosophic set (3): Dynamic, quadripartitioned, pentapartitioned, heptapartitioned, m-polar. 2025.

[75] Takaaki Fujita. A study on hyperfuzzy hyperrough sets, hyperneutrosophic hyperrough sets, and hypersoft hyperrough sets with applications in cybersecurity. *Artificial Intelligence in Cybersecurity*, 2:14–36, 2025.

[76] Takaaki Fujita. A theoretical exploration of hyperconcepts: Hyperfunctions, hyperrandomness, hyperdecision-making, and beyond (including a survey of hyperstructures). *Advancing Uncertain Combinatorics through Graphization, Hyperization, and Uncertainization: Fuzzy, Neutrosophic, Soft, Rough, and Beyond*, 344(498):111, 2025.

[77] Takaaki Fujita and Florentin Smarandache. A concise study of some superhypergraph classes. *Neutrosophic Sets and Systems*, 77:548–593, 2024.

[78] Takaaki Fujita and Florentin Smarandache. A review of the hierarchy of plithogenic, neutrosophic, and fuzzy graphs: Survey and applications. In *Advancing Uncertain Combinatorics through Graphization, Hyperization, and Uncertainization: Fuzzy, Neutrosophic, Soft, Rough, and Beyond (Second Volume)*. Biblio Publishing, 2024.

[79] Irene S Gabashvili, Rajendra K Agrawal, Christian MT Spahn, Robert A Grassucci, Dmitri I Svergun, Joachim Frank, and Pawel Penczek. Solution structure of the e. coli 70s ribosome at 11.5 å resolution. *Cell*, 100(5):537–549, 2000.

[80] Michael Y Galperin. Bacterial signal transduction network in a genomic perspective. *Environmental microbiology*, 6(6):552–567, 2004.

[81] Yue Gao, Yifan Feng, Shuyi Ji, and Rongrong Ji. Hgnn+: General hypergraph neural networks. *IEEE Transactions on Pattern Analysis and Machine Intelligence*, 45(3):3181–3199, 2022.

[82] Ramón García-Domenech, Jorge Gálvez, Jesus V de Julián-Ortiz, and Lionello Pogliani. Some new trends in chemical graph theory. *Chemical Reviews*, 108(3):1127–1169, 2008.

[83] Harish Garg. New exponential operational laws and their aggregation operators for interval-valued pythagorean fuzzy multicriteria decision-making. *International Journal of Intelligent Systems*, 33:653 – 683, 2018.

[84] W-L Gau and Daniel J Buehrer. Vague sets. *IEEE transactions on systems, man, and cybernetics*, 23(2):610–614, 1993.

[85] Piotr Gawron, Marek Ostaszewski, Venkata P. Satagopam, Stephan Gebel, Alexander Mazein, Micha Kuzma, Simone Zorzan, Fintan McGee, Benoît Otjacques, Rudi Balling, and Reinhard Schneider. Minerva—a platform for visualization and curation of molecular interaction networks. *NPJ Systems Biology and Applications*, 2, 2016.

[86] Peter J Gawthrop and Michael Pan. Network thermodynamical modeling of bioelectrical systems: a bond graph approach. *Bioelectricity*, 3(1):3–13, 2021.

[87] Bobin George, Jinta Jose, and Rajesh K Thumbakara. Modular product of soft directed graphs. *TWMS Journal of Applied and Engineering Mathematics*, 2024.

[88] BOBIN GEORGE, K THUMBAKARA RAJESH, and JOSE JINTA. A study on soft hypergraphs and their and & or operations. *Journal of the Calcutta Mathematical Society*, 19(1):29–44, 2023.

[89] Michelle Girvan and Mark E. J. Newman. Community structure in social and biological networks. *Proceedings of the National Academy of Sciences of the United States of America*, 99:7821 – 7826, 2001.

[90] Aldrin V Gomes, Chenggong Zong, Ricky D Edmondson, Xiaohai Li, Enrico Stefani, Jun Zhang, Richard C Jones, Sheeno Thyparambil, Guang-Wu Wang, Xin Qiao, et al. Mapping the murine cardiac 26s proteasome complexes. *Circulation research*, 99(4):362–371, 2006.

[91] Jes'us Arturo Jim'enez Gonz'alez and Andrzej Mr'oz. Bidirected graphs, integral quadratic forms and some diophantine equations. 2023.

[92] Georg Gottlob, Nicola Leone, and Francesco Scarcello. Hypertree decompositions and tractable queries. In *Proceedings of the eighteenth ACM SIGMOD-SIGACT-SIGART symposium on Principles of database systems*, pages 21–32, 1999.

[93] Georg Gottlob and Reinhard Pichler. Hypergraphs in model checking: Acyclicity and hypertree-width versus clique-width. *SIAM Journal on Computing*, 33(2):351–378, 2004.

[94] Xinyu Guo, Bingjie Tian, and Xuedong Tian. Hfgnn-proto: Hesitant fuzzy graph neural network-based prototypical network for few-shot text classification. *Electronics*, 11(15):2423, 2022.

[95] MM Gupta and DH Rao. On the principles of fuzzy neural networks. *Fuzzy sets and systems*, 61(1):1–18, 1994.

[96] Håkan Håkansson and David Ford. How should companies interact in business networks. *Journal of Business Research*, 55:133–139, 2002.

[97] Håkan Håkansson and Ivan Snehota. Developing relationships in business networks. 1995.

[98] Mohammad Hamidi, Florentin Smarandache, and Mohadeseh Taghinezhad. *Decision Making Based on Valued Fuzzy Superhypergraphs*. Infinite Study, 2023.

[99] Jing-Dong J Han, Nicolas Bertin, Tong Hao, Debra S Goldberg, Gabriel F Berriz, Lan V Zhang, Denis Dupuy, Albertha JM Walhout, Michael E Cusick, Frederick P Roth, et al. Evidence for dynamically organized modularity in the yeast protein–protein interaction network. *Nature*, 430(6995):88–93, 2004.

[100] Th Hanser, Ph Jauffret, and Gérard Kaufmann. A new algorithm for exhaustive ring perception in a molecular graph. *Journal of Chemical Information and Computer Sciences*, 36(6):1146–1152, 1996.

[101] Robert A Harris, Melissa M Bowker-Kinley, Boli Huang, and Pengfei Wu. Regulation of the activity of the pyruvate dehydrogenase complex. *Advances in enzyme regulation*, 42:249–259, 2002.

[102] Raed Hatamleh, Abdullah Al-Husban, Sulima Ahmed Mohammed Zubair, Mawahib Elamin, Maha Mohammed Saeed, Eisa Abdolmaleki, Takaaki Fujita, Giorgio Nordo, and Arif Mehmood Khattak. Ai-assisted wearable devices for promoting human health and strength using complex interval-valued picture fuzzy soft relations. *European Journal of Pure and Applied Mathematics*, 18(1):5523–5523, 2025.

[103] Felix Hausdorff. *Set theory*, volume 119. American Mathematical Soc., 2021.

[104] Christian Theil Have and Lars Juhl Jensen. Are graph databases ready for bioinformatics? *Bioinformatics*, 29(24):3107, 2013.

[105] Ayad Hendalianpour and Jafar Razmi. Customer satisfaction measurement using fuzzy neural network. *Decis Sci Lett*, 6(2):193–206, 2017.

[106] Robert J Hill and W Koningsberg. The structure of human hemoglobin. *J Biol Chem*, 237(10):3151–3156, 1962.

[107] Chao Hu, Yu-Ting Li, Yu-Xi Liu, Ge-Fei Hao, and Xue-Qing Yang. Molecular interaction network of plant-herbivorous insects. *Advanced Agrochem*, 3(1):74–82, 2024.

[108] John P Huelsenbeck, Jonathan P Bollback, and Amy M Levine. Inferring the root of a phylogenetic tree. *Systematic biology*, 51(1):32–43, 2002.

[109] Albert Y Hung and Morgan Sheng. Pdz domains: structural modules for protein complex assembly. *Journal of Biological Chemistry*, 277(8):5699–5702, 2002.

[110] Trey Ideker, Owen Ozier, Benno Schwikowski, and Andrew F. Siegel. Discovering regulatory and signalling circuits in molecular interaction networks. *Bioinformatics*, 18 Suppl 1:S233–40, 2002.

[111] Muhammad Imran, Carlos Castillo, Ji Lucas, Patrick Meier, and Sarah Vieweg. Aidr: Artificial intelligence for disaster response. In *Proceedings of the 23rd international conference on world wide web*, pages 159–162, 2014.

[112] Harvey A Itano. Human hemoglobin. *Science*, 117(3031):89–94, 1953.

[113] Emerson Jácome Mogro, Jaime Rojas Molina, Gustavo José Sandoval Cañas, and Pablo Herrera Soria. Tree tobacco extract (nicotiana glauca) as a plithogenic bioinsecticide alternative for controlling fruit fly (drosophila immigrans) using n-superhypergraphs. *Neutrosophic Sets and Systems*, 74(1):7, 2024.

[114] Maissam Jdid and Florentin Smarandache. *Optimal Agricultural Land Use: An Efficient Neutrosophic Linear Programming Method*. Infinite Study, 2023.

[115] Maissam Jdid and Florentin Smarandache. *Converting Some Zero-One Neutrosophic Nonlinear Programming Problems into Zero-One Neutrosophic Linear Programming Problems*. Infinite Study, 2024.

[116] Thomas Jech. *Set theory: The third millennium edition, revised and expanded*. Springer, 2003.

[117] Shuting Jin, Yue Hong, Li Zeng, Yinghui Jiang, Yuan Lin, Leyi Wei, Zhuohang Yu, Xiangxiang Zeng, and Xiangrong Liu. A general hypergraph learning algorithm for drug multi-task predictions in micro-to-macro biomedical networks. *PLOS Computational Biology*, 19(11):e1011597, 2023.

[118] Jinta Jose, Bobin George, and Rajesh K Thumbakara. Soft directed graphs, their vertex degrees, associated matrices and some product operations. *New Mathematics and Natural Computation*, 19(03):651–686, 2023.

[119] Young Bae Jun, Kul Hur, and Kyoung Ja Lee. Hyperfuzzy subalgebras of bck/bci-algebras. *Annals of Fuzzy Mathematics and Informatics*, 2017.

[120] Paschalia Kapli, Ziheng Yang, and Maximilian J Telford. Phylogenetic tree building in the genomic age. *Nature Reviews Genetics*, 21(7):428–444, 2020.

[121] Thomas R Karl and Kevin E Trenberth. Modern global climate change. *science*, 302(5651):1719–1723, 2003.

[122] Arif Mehmood Khattak, M Arslan, Abdallah Shihadeh, Wael Mahmoud Mohammad Salameh, Abdallah Al-Husban Al-Husban, R Seethalakshmi, G Nordo, Takaaki Fujita, and Maha Mohammed Saeed. A breakthrough approach to quadri-partitioned neutrosophic softtopological spaces. *European Journal of Pure and Applied Mathematics*, 18(2):5845–5845, 2025.

[123] Nanao Kita. Bidirected graphs i: Signed general kotzig-lovász decomposition. *arXiv: Combinatorics*, 2017.

[124] Denise R Koessler, Debra J Knisley, Jeff Knisley, and Teresa Haynes. A predictive model for secondary rna structure using graph theory and a neural network. In *BMC bioinformatics*, volume 11, pages 1–10. Springer, 2010.

[125] Robert E Kohler, Eliora Z Ron, and Bernard D Davis. Significance of the free 70 s ribosomes in escherichia coli extracts. *Journal of molecular biology*, 36(1):71–82, 1968.

[126] Arthur Kornberg and Tania A Baker. *DNA replication*. University Science Books, 2005.

[127] Radha G Krishna and Finn Wold. Post-translational modification of proteins. *Advances in enzymology and related areas of molecular biology*, 67:265–298, 1993.

[128] George D Kritikos, Charalampos Moschopoulos, Michalis Vazirgiannis, and Sophia Kossida. Noise reduction in protein-protein interaction graphs by the implementation of a novel weighting scheme. *BMC bioinformatics*, 12:1–10, 2011.

[129] Thomas A Kunkel and Katarzyna Bebenek. Dna replication fidelity. *Annual review of biochemistry*, 69(1):497–529, 2000.

[130] Zachary D. Kurtz, Christian L. Müller, Emily R. Miraldi, Dan R. Littman, Martin J. Blaser, and Richard Bonneau. Sparse and compositionally robust inference of microbial ecological networks. *PLoS Computational Biology*, 11, 2014.

[131] Hon Keung Kwan and Yaling Cai. A fuzzy neural network and its application to pattern recognition. *IEEE transactions on Fuzzy Systems*, 2(3):185–193, 1994.

[132] Shu-Yun Le, Ruth Nussinov, and Jacob V Maizel. Tree graphs of rna secondary structures and their comparisons. *Computers and Biomedical Research*, 22(5):461–473, 1989.

[133] Dominic Tak Sing Lee, Juyong Park, Krin A. Kay, Nicholas A. Christakis, Zoltn Oltvai, and Albert aszló Barabási. The implications of human metabolic network topology for disease comorbidity. *Proceedings of the National Academy of Sciences*, 105:9880 – 9885, 2008.

[134] Azriel Levy. *Basic set theory*. Courier Corporation, 2012.

[135] Xuefei Lin, Xiao Chang, Yizheng Zhang, Zhanyu Gao, and Xu Chi. Automatic construction of petri net models for computational simulations of molecular interaction network. *NPJ Systems Biology and Applications*, 10(1):131, 2024.

[136] Xiaohua Lu, Liangxu Xie, Lei Xu, Rongzhi Mao, Xiaojun Xu, and Shan Chang. Multimodal fused deep learning for drug property prediction: Integrating chemical language and molecular graph. *Computational and Structural Biotechnology Journal*, 23:1666–1679, 2024.

[137] Anam Luqman, Muhammad Akram, and Florentin Smarandache. Complex neutrosophic hypergraphs: New social network models. *Algorithms*, 12:234, 2019.

[138] Steven Maere, Karel Heymans, and Martin Kuiper. Bingo: a cytoscape plugin to assess overrepresentation of gene ontology categories in biological networks. *Bioinformatics*, 21 16:3448–9, 2005.

[139] Taras Makhnevych and Walid A Houry. The role of hsp90 in protein complex assembly. *Biochimica et Biophysica Acta (BBA)-Molecular Cell Research*, 1823(3):674–682, 2012.

[140] Muhammad Aslam Malik, Ali Hassan, Said Broumi, Assia Bakali, Mohamed Talea, and Florentin Smarandache. Isomorphism of bipolar single valued neutrosophic hypergraphs. *Collected Papers. Volume IX: On Neutrosophic Theory and Its Applications in Algebra*, page 72, 2022.

[141] Matteo Manica, Charlotte Bunne, Roland Mathis, Joris Cadow, Mehmet Eren Ahsen, Gustavo A Stolovitzky, and María Rodríguez Martínez. Cosifer: a python package for the consensus inference of molecular interaction networks. *Bioinformatics*, 37(14):2070–2072, 2021.

[142] Matthias Mann and Ole N Jensen. Proteomic analysis of post-translational modifications. *Nature biotechnology*, 21(3):255–261, 2003.

[143] Berrocal Villegas Salomón Marcos, Montalvo Fritas Willner, Berrocal Villegas Carmen Rosa, Flores Fuentes Rivera María Yissel, Espejo Rivera Roberto, Laura Daysi Bautista Puma, and Dante Manuel Macazana Fernández. Using plithogenic n-superhypergraphs to assess the degree of relationship between information skills and digital competencies. *Neutrosophic Sets and Systems*, 84:513–524, 2025.

[144] Jacqueline M Matthews. Protein complex hierarchy and translocation gene products. In *Chromosomal Translocations and Genome Rearrangements in Cancer*, pages 447–466. Springer, 2015.

[145] Birgit HM Meldal, Oscar Forner-Martinez, Maria C Costanzo, Jose Dana, Janos Demeter, Marine Dumousseau, Selina S Dwight, Anna Gaulton, Luana Licata, Anna N Melidoni, et al. The complex portal-an encyclopaedia of macromolecular complexes. *Nucleic acids research*, 43(D1):D479–D484, 2015.

[146] Diego H Milone, Georgina Stegmayer, Mariana López, Laura Kamenetzky, and Fernando Carrari. Improving clustering with metabolic pathway data. *BMC bioinformatics*, 15:1–10, 2014.

[147] Yenson Vinicio Mogro Cepeda, Marco Antonio Riofrío Guevara, Emerson Javier Jácome Mogro, and Rachele Piovanelli Tizano. Impact of irrigation water technification on seven directories of the san juan-patoa river using plithogenic n-superhypergraphs based on environmental indicators in the canton of pujilí, 2021. *Neutrosophic Sets and Systems*, 74(1):6, 2024.

[148] Arne O Mooers and Stephen B Heard. Inferring evolutionary process from phylogenetic tree shape. *The quarterly review of Biology*, 72(1):31–54, 1997.

[149] John N Mordeson and Premchand S Nair. *Fuzzy graphs and fuzzy hypergraphs*, volume 46. Physica, 2012.

[150] Pushpa N. and Dhananjayamurthy B.V. Applications of graph theory in biology and construction. *INTERNATIONAL JOURNAL OF MATHEMATICS AND COMPUTER RESEARCH*, 2023.

[151] Jan Nagy and Peter Pecho. Social networks security. In *2009 Third International Conference on Emerging Security Information, Systems and Technologies*, pages 321–325. IEEE, 2009.

[152] Farzaneh Nasirian and Giulia Menichetti. Molecular interaction networks and cardiovascular disease risk: the role of food bioactive small molecules. *Arteriosclerosis, thrombosis, and vascular biology*, 43(6):813–823, 2023.

[153] Nivedita Natarajan, Ombretta Foresti, Kim Wendrich, Alexander Stein, and Pedro Carvalho. Quality control of protein complex assembly by a transmembrane recognition factor. *Molecular cell*, 77(1):108–119, 2020.

[154] Nicola Normanno, Antonella De Luca, Caterina Bianco, Luigi Strizzi, Mario Mancino, Monica R Maiello, Adele Carotenuto, Gianfranco De Feo, Francesco Caponigro, and David S Salomon. Epidermal growth factor receptor (egfr) signaling in cancer. *Gene*, 366(1):2–16, 2006.

[155] Kanae Oda, Yukiko Matsuoka, Akira Funahashi, and Hiroaki Kitano. A comprehensive pathway map of epidermal growth factor receptor signaling. *Molecular systems biology*, 1(1):2005–0010, 2005.

[156] Patricia A O'Neill. The abc's of disaster response. *Scandinavian journal of surgery*, 94(4):259–266, 2005.

[157] Oliver E Owen, Satish C Kalhan, and Richard W Hanson. The key role of anaplerosis and cataplerosis for citric acid cycle function. *Journal of Biological Chemistry*, 277(34):30409–30412, 2002.

[158] Dragan Pamucar, Morteza Yazdani, Radojko Obradović, Anil Kumar, and Mercedes Torres. A novel fuzzy hybrid neutrosophic decision-making approach for the resilient supplier selection problem. *International Journal of Intelligent Systems*, 35:1934 – 1986, 2020.

[159] Gauri Panditrao, Rupa Bhowmick, Chandrakala Meena, and Ram Rup Sarkar. Emerging landscape of molecular interaction networks: Opportunities, challenges and prospects. *Journal of Biosciences*, 47(2):24, 2022.

[160] Sebastian Pardo-Guerra, Vivek Kurien George, Vikash Morar, Joshua Roldan, and Gabriel Alex Silva. Extending undirected graph techniques to directed graphs via category theory. *Mathematics*, 12(9):1357, 2024.

[161] Sebastian Pardo-Guerra, Vivek Kurien George, and Gabriel A Silva. On the graph isomorphism completeness of directed and multidirected graphs. *Mathematics*, 13(2):228, 2025.

[162] Giovana Paulina Parra Gallardo, Alicia Maribel Gualan Gualan, and María Monserrath Morales Padilla. Pre-and post-harvest application of ethylene in bulb onion (allium cepa l.) hybrid'burguesa'using plithogenic n-superhypergraphs. *Neutrosophic Sets and Systems*, 74(1):19, 2024.

[163] MS Patel and LG Korotchkina. Regulation of the pyruvate dehydrogenase complex. *Biochemical Society Transactions*, 34(2):217–222, 2006.

[164] Mulchand S Patel, Natalia S Nemeria, William Furey, and Frank Jordan. The pyruvate dehydrogenase complexes: structure-based function and regulation. *Journal of Biological Chemistry*, 289(24):16615–16623, 2014.

[165] Zdzisław Pawlak. Rough sets. *International journal of computer & information sciences*, 11:341–356, 1982.

[166] Zdzislaw Pawlak, S. K. Michael Wong, Wojciech Ziarko, et al. Rough sets: probabilistic versus deterministic approach. *International Journal of Man-Machine Studies*, 29(1):81–95, 1988.

[167] Jeffrey E Pessin, Alan R Saltiel, et al. Signaling pathways in insulin action: molecular targets of insulin resistance. *The Journal of clinical investigation*, 106(2):165–169, 2000.

[168] Jan-M Peters, Zdenka Cejka, J Robin Harris, Jürgen A Kleinschmidt, and Wolfgang Baumeister. Structural features of the 26 s proteasome complex, 1993.

[169] Alen Piljic and Carsten Schultz. Analysis of protein complex hierarchy in living cells. *ACS chemical biology*, 3(12):749–755, 2008.

[170] Daniele Pretolani. Finding hypernetworks in directed hypergraphs. *European Journal of Operational Research*, 230(2):226–230, 2013.

[171] Stephen Pryke. Towards a social network theory of project governance. *Construction Management and Economics*, 23:927 – 939, 2005.

[172] Shahin Ramazi and Javad Zahiri. Post-translational modifications in proteins: resources, tools and prediction methods. *Database*, 2021:baab012, 2021.

[173] Akbar Rezaei, Florentin Smarandache, and S. Mirvakili. Applications of (neutro/anti)sophications to semihypergroups. *Journal of Mathematics*, 2021.

[174] David J Robbins, Dennis Liang Fei, and Natalia A Riobo. The hedgehog signal transduction network. *Science signaling*, 5(246):re6–re6, 2012.

[175] AA Salama, A Haitham, A Manie, and M Lotfy. Utilizing neutrosophic set in social network analysis e-learning systems. *International Journal of Information Science and Intelligent System*, 3(2):61–72, 2014.

[176] Alan R Saltiel and Jeffrey E Pessin. Insulin signaling pathways in time and space. *Trends in cell biology*, 12(2):65–71, 2002.

[177] Sovan Samanta and Madhumangal Pal. Bipolar fuzzy hypergraphs. *International Journal of Fuzzy Logic Systems*, 2(1):17–28, 2012.

[178] Ruud Schoonderwoerd, Owen Holland, Janet Bruten, and Léon J. M. Rothkrantz. Ant-based load balancing in telecommunications networks. *Adaptive Behavior*, 5:169 – 207, 1996.

[179] Hisayuki Shigematsu and Adi F Gazdar. Somatic mutations of epidermal growth factor receptor signaling pathway in lung cancers. *International journal of cancer*, 118(2):257–262, 2006.

[180] NV Sidgwick. Complex formation. *Journal of the Chemical Society (Resumed)*, pages 433–443, 1941.

[181] F. Smarandache. Introduction to superhyperalgebra and neutrosophic superhyperalgebra. *Journal of Algebraic Hyperstructures and Logical Algebras*, 2022.

[182] Florentin Smarandache. A unifying field in logics: Neutrosophic logic. In *Philosophy*, pages 1–141. American Research Press, 1999.

[183] Florentin Smarandache. n-superhypergraph and plithogenic n-superhypergraph. *Nidus Idearum*, 7:107–113, 2019.

[184] Florentin Smarandache. *Extension of HyperGraph to n-SuperHyperGraph and to Plithogenic n-SuperHyperGraph, and Extension of HyperAlgebra to n-ary (Classical-/Neutro-/Anti-) HyperAlgebra*. Infinite Study, 2020.

[185] Florentin Smarandache. *Real Examples of NeutroGeometry & AntiGeometry*. Infinite Study, 2023.

[186] Florentin Smarandache. *SuperHyperFunction, SuperHyperStructure, Neutrosophic SuperHyperFunction and Neutrosophic SuperHyperStructure: Current understanding and future directions*. Infinite Study, 2023.

[187] Florentin Smarandache. The cardinal of the m-powerset of a set of n elements used in the superhyperstructures and neutrosophic superhyperstructures. *Systems Assessment and Engineering Management*, 2:19–22, 2024.

[188] Florentin Smarandache. Foundation of superhyperstructure & neutrosophic superhyperstructure. *Neutrosophic Sets and Systems*, 63(1):21, 2024.

[189] Florentin Smarandache. Superhyperstructure & neutrosophic superhyperstructure, 2024. Accessed: 2024-12-01.

[190] Florentin Smarandache and Maissam Jdid. An overview of neutrosophic and plithogenic theories and applications. 2023.

[191] Florentin Smarandache and Nivetha Martin. Plithogenic n-super hypergraph in novel multi-attribute decision making. *International Journal of Neutrosophic Science*, 2020.

[192] Florentin Smarandache and AA Salama. Neutrosophic crisp set theory. 2015.

[193] Seok-Zun Song, Seon Jeong Kim, and Young Bae Jun. Hyperfuzzy ideals in bck/bci-algebras. *Mathematics*, 5(4):81, 2017.

[194] Divyanshu Srivastava, Ganesh Bagler, and Vibhor Kumar. Graph signal processing on protein residue networks helps in studying its biophysical properties. *Physica A: Statistical Mechanics and its Applications*, 615:128603, 2023.

[195] C Taha and A Klip. The insulin signaling pathway. *The Journal of membrane biology*, 169:1–12, 1999.

[196] Konstantinos Theofilatos, Niki Pavlopoulou, Christoforos Papasavvas, Spiros Likothanassis, Christos Dimitrakopoulos, Efstratios Georgopoulos, Charalampos Moschopoulos, and Seferina Mavroudi. Predicting protein complexes from weighted protein–protein interaction graphs with a novel unsupervised methodology: evolutionary enhanced markov clustering. *Artificial intelligence in medicine*, 63(3):181–189, 2015.

[197] Erik H. Thiede, Wenda Zhou, and Risi Kondor. Graph neural networks for biochemistry that incorporate substructure. *Biophysical Journal*, 2022.

[198] Vicenç Torra. Hesitant fuzzy sets. *International journal of intelligent systems*, 25(6):529–539, 2010.

[199] Vicenç Torra and Yasuo Narukawa. On hesitant fuzzy sets and decision. In *2009 IEEE international conference on fuzzy systems*, pages 1378–1382. IEEE, 2009.

[200] Alejandro Tovar-Méndez, Jan A Miernyk, and Douglas D Randall. Regulation of pyruvate dehydrogenase complex activity in plant cells. *European journal of biochemistry*, 270(6):1043–1049, 2003.

[201] Nenad Trinajstic. *Chemical graph theory*. CRC press, 2018.

[202] Matthew G Vander Heiden, Jason W Locasale, Kenneth D Swanson, Hadar Sharfi, Greg J Heffron, Daniel Amador-Noguez, Heather R Christofk, Gerhard Wagner, Joshua D Rabinowitz, John M Asara, et al. Evidence for an alternative glycolytic pathway in rapidly proliferating cells. *Science*, 329(5998):1492–1499, 2010.

[203] C Vasudev. *Graph theory with applications*. New Age International, 2006.

[204] Verónica H. Villena and Dennis A. Gioia. On the riskiness of lower-tier suppliers: Managing sustainability in supply networks. *Journal of Operations Management*, 2018.

[205] Souzana Vougioukli. Helix hyperoperation in teaching research. *Science & Philosophy*, 8(2):157–163, 2020.

[206] Souzana Vougioukli. Hyperoperations defined on sets of s -helix matrices. 2020.

[207] Souzana Vougioukli. Helix-hyperoperations on lie-santilli admissibility. *Algebras Groups and Geometries*, 2023.

[208] Stephan Wagner and Hua Wang. *Introduction to chemical graph theory*. Chapman and Hall/CRC, 2018.

[209] Bang Wan, KF LaNoue, JY Cheung, and RC Scaduto. Regulation of citric acid cycle by calcium. *Journal of Biological Chemistry*, 264(23):13430–13439, 1989.

[210] Qian Wang and Zengtai Gong. Structural centrality in fuzzy social networks based on fuzzy hypergraph theory. *Computational and Mathematical Organization Theory*, 26:236 – 254, 2020.

[211] Rui-Sheng Wang and Réka Albert. Elementary signaling modes predict the essentiality of signal transduction network components. *BMC systems biology*, 5:1–14, 2011.

[212] Xiaorong Wang, Chi-Fen Chen, Peter R Baker, Phang-lang Chen, Peter Kaiser, and Lan Huang. Mass spectrometric characterization of the affinity-purified human 26s proteasome complex. *Biochemistry*, 46(11):3553–3565, 2007.

[213] Ping Wee and Zhixiang Wang. Epidermal growth factor receptor cell proliferation signaling pathways. *Cancers*, 9(5):52, 2017.

[214] Alan Wells. Egf receptor. *The international journal of biochemistry & cell biology*, 31(6):637–643, 1999.

[215] Shou-Lin Weng and Jeetain Mittal. Bps2025-molecular interaction network of full-length fus in phase-separated condensates. *Biophysical Journal*, 124(3):557a, 2025.

[216] Shuo Lin Weng, Priyesh Mohanty, and Jeetain Mittal. Elucidation of the molecular interaction network underlying full-length fus conformational transitions and its phase separation using atomistic simulations. *bioRxiv*, pages 2025–04, 2025.

[217] John R Williamson and Ronald H Cooper. Regulation of the citric acid cycle in mammalian systems. *FEBS letters*, 117:K73–K85, 1980.

[218] Rebecca Willis. The role of national politicians in global climate governance. *Environment and Planning E: Nature and Space*, 3:885 – 903, 2020.

[219] Guanchen Xiao, Jinzhi Liao, Zhen Tan, Yiqi Yu, and Bin Ge. Hyperbolic directed hypergraph-based reasoning for multi-hop kbqa. *Mathematics*, 10(20):3905, 2022.

[220] Rui Xu and Cun-Quan Zhang. On flows in bidirected graphs. *Discrete mathematics*, 299(1-3):335–343, 2005.

[221] Hai-Cheng Yi, Zhu-Hong You, De-Shuang Huang, and Chee Keong Kwoh. Graph representation learning in bioinformatics: trends, methods and applications. *Briefings in Bioinformatics*, 23(1):bbab340, 2022.

[222] P Yiarayong. Some weighted aggregation operators of quadripartitioned single-valued trapezoidal neutrosophic sets and their multi-criteria group decision-making method for developing green supplier selection criteria. *OPSEARCH*, pages 1–55, 2024.

[223] Lotfi A Zadeh. Fuzzy sets. *Information and control*, 8(3):338–353, 1965.

[224] Lotfi A. Zadeh. Fuzzy algorithms. *Inf. Control.*, 12:94–102, 1968.

[225] Lotfi A Zadeh. A fuzzy-set-theoretic interpretation of linguistic hedges. 1972.

[226] Lotfi A Zadeh. Fuzzy logic, neural networks, and soft computing. In *Fuzzy sets, fuzzy logic, and fuzzy systems: selected papers by Lotfi A Zadeh*, pages 775–782. World Scientific, 1996.

[227] Jitao David Zhang and Stefan Wiemann. Kegggraph: a graph approach to kegg pathway in r and bioconductor. *Bioinformatics*, 25(11):1470–1471, 2009.

[228] Yunlan Zhao, Zhiyong Huang, Hangjun Che, Fang Xie, Man Liu, Mengyao Wang, and Daming Sun. Segmentation of brain tissues from mri images using multitask fuzzy clustering algorithm. *Journal of Healthcare Engineering*, 2023, 2023.

[229] Hans-Jürgen Zimmermann. Fuzzy programming and linear programming with several objective functions. *Fuzzy Sets and Systems*, 1:45–55, 1978.

[230] Benjamin Zoller, Thomas Gregor, and Gašper Tkačik. Eukaryotic gene regulation at equilibrium, or non? *Current opinion in systems biology*, 31:100435, 2022.