Original Research Article

A Formal Framework for Molecular Interaction Hyper Networks and Molecular Interaction Super Hyper Networks

Abstract

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 idea by introducing recursively nested powerset layers, thus enabling hierarchical and self-referential relationships among hyperedges. Graphs are widely used to represent networks. In this context, hypernetworks and superhypernetworks serve as the network analogues of hypergraphs and superhypergraphs, respectively. 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 introducing two new frameworks: the *Molecular Interaction HyperNetwork* and the *Molecular Interaction SuperHyperNetwork*, based on the structures of hypernetworks and superhypernetworks.

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

1 Introduction

1.1 Graph, HyperGraph, and SuperHyperGraph

Graph theory is a branch of mathematics focused on the study of networks, where nodes (called vertices) are connected by links (called edges) [23, 24]. 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. [26, 27, 45, 55]).

Mathematical structures can often be extended into *hyperstructures* and *superhyperstructures* by utilizing the power set and *n*-th iterated powerset constructions [36, 103, 104, 106]. 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* [15,18] and the *superhypergraph* [33,41,102]. A hypergraph allows each edge—called a *hyperedge*—to connect more than two vertices simultaneously, capturing complex many-to-many relationships. A superhypergraph goes further by incorporating recursively nested powerset structures, enabling hierarchical and self-referential relationships among collections of hyperedges. These models can also be extended into various directions, such as directed graphs [49,65], bidirected graphs [52,69,125], and multidirected graphs [82,83].

1.2 Graph and Networks

Network theory investigates the structure and behavior of systems composed of interconnected nodes and edges, with emphasis on the analysis of relationships, flows, and dynamic interactions in complex environments. Examples of networks include biological networks [50, 75], ecological networks [22, 73], electrical networks [13, 16], social network [78, 91, 94], telecommunications networks [31, 96], business networks [6, 56, 57], and supply networks [8, 116].

Graphs are commonly employed as foundational tools for representing such networks. In this context, *hypernetworks* and *superhypernetworks* emerge as network-based analogues of hypergraphs and superhypergraphs, respectively, allowing for the modeling of higher-order and hierarchical relationships in networked systems [38].

Graph-based and network-based approaches have also played a central role in many studies in biology [9,25,77], chemistry [46, 114, 120], and biochemistry [110]. 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 [7,48,62,74].

1.3 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.

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 [37, 39, 105]. Intuitively, the n-th powerset is a repeated application of the powerset operation. Relevant definitions and simple examples are provided below.

Definition 2.1 (Base Set). 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 2.2 (Powerset). [34, 93] 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:

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

Definition 2.3 (n-th Powerset). (cf. [34, 38, 105])

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.

Definition 2.4 (Classical Structure). (cf. [99, 105]) 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 2.5 (Hyperoperation). (cf. [92, 117–119]) 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.

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Definition 2.6 (Hyperstructure). (cf. [34, 99, 105]) 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.

Definition 2.7 (SuperHyperOperations). (cf. [105]) 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 2.8 (n-Superhyperstructure). (cf. [35, 105]) 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.

2.2 SuperHyperGraph

In classical graph theory, a hypergraph extends the idea of a conventional graph by permitting edges—called hyperedges—to join more than two vertices. This broader framework enables the modeling of more intricate relationships between elements, thereby enhancing its utility in various fields [15, 53, 54].

A *SuperHyperGraph* is an advanced extension of the hypergraph concept, integrating recursive powerset structures into the classical model. This concept has been recently introduced and extensively studied in the literature [3, 38, 76, 84].

Definition 2.9 (Hypergraph). [15, 18] 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.

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Example 2.10 (Academic Co-authorship as a Hypergraph). Consider a set of researchers

$$V(H) = \{\text{Alice, Bob, Carol, Dave, Eve}\}.$$

They have collaborated on several papers:

$$E(H) = \big\{\{\text{Alice, Bob, Carol}\}, \ \{\text{Alice, Dave}\}, \ \{\text{Bob, Dave, Eve}\}, \ \{\text{Carol, Eve}\}\big\}.$$

Here each hyperedge corresponds to the set of authors on a single paper:

- $\{\text{Alice, Bob, Carol}\}$ represents a three-author collaboration,

- $\{\text{Alice, Dave}\}$ represents a two-author paper,

- $\{\text{Bob, Dave, Eve}\}$ and $\{\text{Carol, Eve}\}$ likewise capture their multi-author works.

This hypergraph $H = (V(H), E(H))$ encodes higher-order relationships: it shows which groups of researchers have worked together, information that would be lost if we only recorded pairwise collaborations.

Definition 2.11 (n-SuperHyperGraph). [101, 102]

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

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

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 2.12 (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. [20, 67, 124]). 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 $\rightarrow$ lab groups $\rightarrow$ consortia $\rightarrow$ inter-consortium collaboration.

Example 2.13 (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

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

by setting

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

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. The formal definition of molecular interaction networks is given below.

Definition 2.14 (Network). A *network* (or *graph*) is an ordered triple

$$N = (V, E, w)$$

where

- V is a nonempty finite set of *vertices* (or *nodes*);

- $E \subseteq \{\{u, v\} \mid u, v \in V, \ u \neq v\}$ 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).

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If edges are *directed*, one instead writes

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

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 2.15 (Molecular Interaction Network). A *molecular interaction network* is a labeled hypergraph

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

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 [98], enzymatic reaction [30], 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 2.16 (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. [12, 19, 58]). Let

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

$$\mathcal{I} = \big\{\{\text{P53}, \text{MDM2}\}, \{\text{ATM}, \text{P53}\}, \{\text{ATM}, \text{CHK2}\}, \{\text{CHK2}, \text{P53}\}\big\}.$$

Define

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

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

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

If we include confidence scores:

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

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

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

where

- V is a nonempty finite set of *nodes*;

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- $\mathcal{E} \subseteq \mathcal{P}(V) \setminus \{\emptyset\}$ is the set of *hyperedges*, each hyperedge $e \in \mathcal{E}$ being a nonempty subset of nodes (allowing multi-node interactions);

- $w : \mathcal{E} \to \mathbb{R}_{\geq 0}$ 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

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

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. [14, 71, 72]). Consider the assembly and activation of the eukaryotic DNA replication pre-initiation complex. Let

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

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

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

Label each node by its functional class:

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

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.

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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. [61, 64]). Let

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

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

$$\mathcal{I} = \{ E_{\text{tetramer}}, \ E_{O_2} \},$$

where

$$E_{\text{tetramer}} = \{\alpha_1, \alpha_2, \beta_1, \beta_2\}, \quad E_{O_2} = \{\alpha_1, \alpha_2, \beta_1, \beta_2, O_2\}.$$

The labeling functions are

$$\ell_V(\alpha_i) = \text{``globin subunit''}, \quad \ell_V(\beta_i) = \text{``globin subunit''}, \quad \ell_V(O_2) = \text{``oxygen molecule''},$$

$$\ell_{\mathcal{I}}(E_{\text{tetramer}}) = \text{``hemoglobin tetramer assembly''}, \quad \ell_{\mathcal{I}}(E_{O_2}) = \text{``oxygen binding''}.$$

Optionally, assign confidence scores:

$$w(E_{\text{tetramer}}) = 1.00, \quad w(E_{O_2}) = 0.98.$$

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 [59, 85, 86, 113]. Let

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

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

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

Label each node by its type:

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

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:

$$w(I_{\text{assembly}}) = 0.ninety, \quad w(I_{\text{catalysis}}) = 0.eighty - five.$$

Here:

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- 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]. $\square$

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 $\ell_V \colon V \to L_V$ is unchanged and labels each entity by its type or identifier.

4. *Hyperedge-labeling:* The map $\ell_{\mathcal{I}} \colon \mathcal{I} \to L_{\mathcal{I}}$ likewise remains valid, assigning each interaction its category.

5. *Weight function:* The function $w \colon \mathcal{I} \to \mathbb{R}_{\geq 0}$ 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. $\square$

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)**.** [38] 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

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

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;

- $w: \mathcal{E} \to \mathbb{R}_{\geq 0}$ 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. [17, 63, 81]). Let the base set of individual responders be

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

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

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

A *molecular interaction n-superHyperNetwork* is a quintuple

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

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 $V^{(n)}$;

- $\ell_V^{(n)} : V^{(n)} \to L_V$ labels each *n*-supernode by its biological or chemical role (e.g. "multi-protein complex");

- $\ell_{\mathcal{I}}^{(n)} : \mathcal{I}^{(n)} \to L_{\mathcal{I}}$ labels each *n*-superedge by its interaction type (e.g. "cascade", "assembly");

- $w^{(n)} : \mathcal{I}^{(n)} \to \mathbb{R}_{\geq 0}$ 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. [79, 80, 97, 122, 123]). Let the base set of molecular entities be

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

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

$$E_1 = \{\text{EGF, EGFR}\}, \quad E_2 = \{\text{EGFR, GRB2, SOS}\},$$
$$E_3 = \{\text{SOS, RAS}\}, \quad E_4 = \{\text{RAS, RAF}\},$$
$$E_5 = \{\text{RAF, MEK}\}, \quad E_6 = \{\text{MEK, ERK}\}.$$

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:

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

Labeling functions assign biological roles and interaction types:

$\ell_V^{(2)}(F_R) =$ "Receptor complex assembly",

$\ell_V^{(2)}(F_S) =$ "RAS activation module",

$\ell_V^{(2)}(F_M) =$ "MAPK phosphorylation cascade",

$\ell_{\mathcal{I}}^{(2)}(\{F_R, F_S\}) =$ "Signal propagation (receptor $\to$ RAS)",

$\ell_{\mathcal{I}}^{(2)}(\{F_S, F_M\}) =$ "Signal propagation (RAS $\to$ MAPK)".

Weights (confidence scores) might be

$$w^{(2)}(\{F_R, F_S\}) = 0.95, \quad w^{(2)}(\{F_S, F_M\}) = 0.ninety,$$

reflecting high-confidence pathway activation.

In this 2-superHyperNetwork:

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- 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. [28, 115]). 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:

$\ell_V^{(2)}(F_{\text{prep}})$ = "Preparatory phase of glycolysis",

$\ell_V^{(2)}(F_{\text{payoff}})$ = "Payoff phase of glycolysis",

$\ell_{\mathcal{I}}^{(2)}\big(\{F_{\text{prep}}, F_{\text{payoff}}\}\big)$ = "Phase transition in glycolysis".

Optionally, assign a confidence score:

$$w^{(2)}\big(\{F_{\text{prep}}, F_{\text{payoff}}\}\big) = 0.ninety.$$

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.

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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:

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

Thus

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

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:

$$\ell_V^{(3)}(U_1) = \text{``EGFR}\rightarrow\text{MAPK signaling supermodule''},$$
$$\ell_V^{(3)}(U_2) = \text{``EGFR}\rightarrow\text{PI3K–AKT–mTOR supermodule''},$$

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

Optionally, assign a confidence weight:

$$w^{(3)}(\{U_1, U_2\}) = 0.ninety five.$$

- *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-SuperHyperNetwork). The insulin signaling pathway regulates glucose uptake and metabolism by transmitting signals from insulin receptors to intracellular effectors like AKT and GLUT4 (cf. [89, 95, 109]). 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:

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

Thus

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

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) = $ "Receptor-proximal and PI3K activation module", $\quad \ell_{\mathcal{I}}^{(3)}(\{U_1, U_2\}) = $ "Integrated insulin signaling cascade".
$\ell_V^{(3)}(U_2) = $ "PI3K-AKT-mediated glucose uptake module",

Optionally, assign a confidence weight:

$$w^{(3)}(\{U_1, U_2\}) = 0.ninetytwo.$$

- *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. [29, 51, 90, 121]). Let the base set of molecular entities be

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

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:

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

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

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

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

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

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

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

Then

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

Labeling functions assign:

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

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

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. [1, 2, 44, 70]). Let the base set of molecular entities be

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

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:

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

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:

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

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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 $w^{(n)} : \mathcal{I}^{(n)} \to \mathbb{R}_{\geq 0}$ 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. $\square$

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*

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

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 $\ell_{\mathcal{I}}^{(1)}(I) = \ell_{\mathcal{I}}(I)$.

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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. $\qquad\square$

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

$$\mathcal{H}^{(n-k)} = \left(\varphi_k\bigl(V^{(n)}\bigr),\, \varphi_k\bigl(\mathcal{I}^{(n)}\bigr),\, \ell_V^{(n)} \circ \varphi_k,\, \ell_{\mathcal{I}}^{(n)} \circ \varphi_k,\, w^{(n)} \circ \varphi_k\right)$$

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 $\mathcal{H}^{(n-k)}$. $\qquad\square$

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. $\qquad\square$

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. $\qquad\square$

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

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

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 Super-HyperNetwork* by integrating advanced uncertainty-handling frameworks. These include Fuzzy Sets [127,128], Intuitionistic Fuzzy Sets [10,11], Vague Sets [5,47], Rough Sets [87,88], Bipolar Fuzzy Sets [4], HyperFuzzy Sets [32,66,108], Picture Fuzzy Sets [21,60], Hesitant Fuzzy Sets [111,112], Neutrosophic Sets [100,107], Quadripartitioned Neutrosophic Sets [40,68,126], and Plithogenic Sets [36,42,43]. 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.

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.

Ethical Approval

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

Disclaimer

This work presents theoretical concepts that have not yet undergone practical testing or validation. Future researchers are encouraged to apply and assess these ideas in empirical contexts. While every effort has been made to ensure accuracy and appropriate referencing, unintentional errors or omissions may still exist. Readers are advised to verify referenced materials on their own. The views and conclusions expressed here are the authors' own and do not necessarily reflect those of their affiliated organizations.

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