Signaling SuperHypergraph

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Abstract

Graph theory studies mathematical structures of vertices and edges to model relationships and connectivity [1, 2]. Hypergraphs extend traditional graphs by allowing *hyperedges* that connect any number of vertices simultaneously [3,4]. Superhypergraphs further generalize this idea through iterated powerset layers, enabling hierarchical and self-referential connections among hyperedges [5–7].

Graph theory is also extensively used in biology, biochemistry, and related fields (cf. [8,9]). A *Signaling Graph* is a directed graph in which vertices represent entities and edges denote activation or inhibition of targets. A *Signaling Hypergraph* generalizes signaling graphs by using hyperedges that link sets of regulators to sets of targets in reactions [10–13].

In this paper, we define the *Signaling n-SuperHypergraph*, which extends these concepts using superhypergraphs, and we briefly examine its properties. Although this work is purely theoretical, we hope that future research will further advance hierarchical modeling in complex systems.

Keywords: Superhypergraph, Hypergraph, Signaling Graph, Signaling Hypergraph

1 Preliminaries

This section presents the fundamental concepts and definitions that underpin the discussions in this paper. Unless otherwise noted, all graphs considered here are *undirected*, *finite*, and *simple*. For detailed treatment of specific operations and related notions, the reader is referred to the appropriate literature.

1.1 SuperHyperGraph

In classical graph theory, a hypergraph extends the ordinary graph by permitting *hyperedges* that connect more than two vertices. This added flexibility makes hypergraphs an ideal tool for modeling complex, multi-way relationships across a variety of fields [4, 14, 15]. A *SuperHyperGraph* further enriches this framework by integrating iterated powerset constructions into the hypergraph structure, a concept that has recently garnered considerable attention in the literature [6, 16–18]. Throughout this paper, the parameter n in both the n-th powerset and the n-SuperHyperGraph is taken to be a non-negative integer.

Definition 1.1 (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 1.2 (Powerset)**.** 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 1.3 (Hypergraph)**.** [4, 19] 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 1.4 (n-th Powerset)**.** (cf. [20–22]) 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 1.5 (n-SuperHyperGraph)**.** [23–25]
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 1.6 (p53 Network as a 2-SuperHyperGraph)**.** The p53 network regulates cell cycle, DNA repair, and apoptosis through interactions between p53, MDM2, BAX, and other proteins (cf. [26, 27]). We model a simplified p53 regulatory cascade in cells as a 2-SuperHyperGraph:

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

where:

$$V_0 = \{\text{P53, MDM2, BAX}\}$$

is the finite *base set* of atomic proteins:

- P53: tumor suppressor transcription factor.
- MDM2: E3 ubiquitin ligase regulating P53.
- BAX: pro-apoptotic protein induced by P53.

For $k \geq 0$, define

$$\mathcal{P}^0(V_0) = V_0, \quad \mathcal{P}^1(V_0) =$$
$$\mathcal{P}(V_0) = \big\{ \{\text{P53}\}, \{\text{MDM2}\}, \{\text{BAX}\},$$
$$\{\text{P53}, \text{MDM2}\}, \{\text{P53}, \text{BAX}\}, \{\text{MDM2}, \text{BAX}\}, \{\text{P53}, \text{MDM2}, \text{BAX}\}\big\},$$

and

$$\mathcal{P}^2(V_0) = \mathcal{P}\big(\mathcal{P}(V_0)\big),$$

the collection of all subsets of $\mathcal{P}(V_0)$. An element of $\mathcal{P}^2(V_0)$ is thus a set of protein-complexes.

Vertices ($V \subseteq \mathcal{P}^2(V_0)$): We choose three 2-supervertices:

$$v_1 = \big\{\{\text{P53}\}, \{\text{MDM2}\}\big\}, \quad v_1 \subseteq \mathcal{P}(V_0),$$

$$v_2 = \big\{\{\text{P53, MDM2}\}\big\}, \quad v_2 \subseteq \mathcal{P}(V_0),$$

$$v_3 = \big\{\{\text{BAX}\}\big\}, \quad v_3 \subseteq \mathcal{P}(V_0).$$

Interpretation:

- $v_1 = \{\{\text{P53}\}, \{\text{MDM2}\}\}$ represents the *individual proteins* P53 and MDM2 as separate complexes.
- $v_2 = \{\{\text{P53, MDM2}\}\}$ represents the *P53–MDM2 heterocomplex*.
- $v_3 = \{\{\text{BAX}\}\}$ represents the *BAX protein* as a singleton complex.

$$V = \{v_1, v_2, v_3\} \subseteq \mathcal{P}^2(V_0).$$

Edges ($E \subseteq \mathcal{P}^2(V_0)$): We define two 2-superedges e_1 and e_2 as:

$$e_1 = \{v_1, v_2\}, \quad e_1 = \{\{\{\text{P53}\}, \{\text{MDM2}\}\}, \{\{\text{P53, MDM2}\}\}\},$$
$$e_2 = \{v_2, v_3\}, \quad e_2 = \{\{\{\text{P53, MDM2}\}\}, \{\{\text{BAX}\}\}\}.$$

Interpretation:

- $e_1 = \{v_1, v_2\}$ models the transition from the separate proteins {P53}, {MDM2} (vertex v_1) to their heterocomplex {P53, MDM2} (vertex v_2).
- $e_2 = \{v_2, v_3\}$ models the subsequent activation of BAX expression: the P53–MDM2 complex {P53, MDM2} (vertex v_2) leads to the presence of BAX {BAX} (vertex v_3).

$$E = \{e_1, e_2\} \subseteq \mathcal{P}^2(V_0).$$

Summary:

$$\text{SHT}^{(2)} = (V, E) = \Big(\{v_1, v_2, v_3\}, \{e_1, e_2\}\Big),$$

where

$$v_1 = \{\{\text{P53}\}, \{\text{MDM2}\}\}, \quad v_2 = \{\{\text{P53, MDM2}\}\}, \quad v_3 = \{\{\text{BAX}\}\},$$
$$e_1 = \{v_1, v_2\}, \qquad e_2 = \{v_2, v_3\}.$$

In this biological example:

1. v_1 captures the *unbound proteins* P53 and MDM2.
2. v_2 captures the *P53–MDM2 complex*.
3. v_3 captures the *BAX protein*, downstream of P53.
4. e_1 describes the *formation of the heterocomplex* from unbound P53 and MDM2.
5. e_2 describes the *activation of BAX expression* by the P53–MDM2 complex.

Thus $\text{SHT}^{(2)}$ is a concrete, hierarchical model of the p53 regulatory network as a 2-SuperHyperGraph.

1.2 Signaling Hypergraph

We present the formal definition of a Signaling Hypergraph [10–13].

Definition 1.7 (Hypernode)**.** Let V be a finite set of *molecular entities* (e.g., proteins, complexes, small molecules). A *hypernode* is any nonempty subset $U \subseteq V$. We denote by

$$\mathcal{V} \subseteq 2^V$$

the collection of all hypernodes under consideration, where each $U \in \mathcal{V}$ represents either a single molecule (when $|U| = 1$) or a molecular complex (when $|U| \geq 2$).

Definition 1.8 (Signaling Hyperedge)**.** (cf. [10–13]) A *signaling hyperedge* e is an ordered pair

$$e = (T(e), H(e)),$$

where

$$T(e) = \{U_1, U_2, \ldots, U_p\} \subseteq \mathcal{V} \quad \text{and} \quad H(e) = \{W_1, W_2, \ldots, W_q\} \subseteq \mathcal{V},$$

both nonempty. Here:

- $T(e)$ (the *tail*) is the set of *reactant* and *positive-regulator* hypernodes that must be simultaneously present for reaction e to occur.
- $H(e)$ (the *head*) is the set of *product* hypernodes generated by reaction e.

We require $T(e) \neq \emptyset$ and $H(e) \neq \emptyset$, and each element of $T(e) \cup H(e)$ belongs to $\mathcal{V}$.

Definition 1.9 (Signaling Hypergraph)**.** (cf. [10–13]) A *signaling hypergraph* is a triple

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

where:

- V is a finite set of *molecular entities*.
- $\mathcal{V} \subseteq 2^V$ is a chosen set of *hypernodes*, each representing a molecule or molecular complex. We assume $\bigcup_{U\in\mathcal{V}} U = V$, so that every element of V appears in at least one hypernode.
- E is a finite collection of *signaling hyperedges*, each $e = \big(T(e),\ H(e)\big)$ faithfully capturing a biochemical reaction or regulatory event.

By construction, each $e \in E$ satisfies

$$T(e) \subseteq \mathcal{V}, \quad H(e) \subseteq \mathcal{V}, \quad T(e) \neq \emptyset, \quad H(e) \neq \emptyset.$$

Definition 1.10 (Backward Star)**.** (cf. [10–13]) Given a signaling hypergraph $\mathcal{H} = (V, \mathcal{V}, E)$ and a hypernode $U \in \mathcal{V}$, the *backward star* of U is

$$\mathrm{BS}(U) \;=\; \big\{e \in E \;\big|\; U \in H(e)\big\}.$$

Definition 1.11 (B-Connection)**.** (cf. [10–13]) Let $s \in \mathcal{V}$ be a designated *source hypernode*. A hypernode $U \in \mathcal{V}$ is said to be *B-connected* to s (denoted $U \in B_{\mathcal{H}}(s)$) if either:

1. $U = s$, or
2. there exists a hyperedge $e \in E$ with $U \in H(e)$ such that *every* element of $T(e)$ is itself B-connected to s.

The set $B_{\mathcal{H}}(s)$ consists of all hypernodes reachable from s under this definition of B-connection.

Definition 1.12 (Acyclicity and B-Hyperpath)**.** (cf. [10–13]) An *acyclic B-hyperpath* from s to t in $\mathcal{H}$ is a sub-hypergraph

$$\Pi(s,t) \;=\; \big(\mathcal{V}_\Pi,\ E_\Pi\big) \quad \text{where} \quad \mathcal{V}_\Pi \subseteq \mathcal{V},\ \ E_\Pi \subseteq E,$$

satisfying:

1. *Terminal Connectivity:* $t \in B_\Pi(s)$, where $B_\Pi(s)$ denotes the B-connected set computed within $\Pi(s,t)$ itself.
2. *Minimality:* No proper sub-hypergraph of $\Pi(s,t)$ (obtained by deleting any hypernode or hyperedge) still has $t \in B_\Pi(s)$.
3. *Acyclicity:* There is no simple cycle in $\Pi(s,t)$. Equivalently, one may assign a real *ordering* $o : \mathcal{V}_\Pi \to \mathbb{R}$ such that for every $e = (T(e), H(e)) \in E_\Pi$ and every pair $(U, W) \in T(e) \times H(e)$,

$$o(U) \;<\; o(W).$$

Example 1.13 (A Simple Protein–Protein Interaction Network)**.** A Protein–Protein Interaction Network represents proteins as nodes and their physical or functional interactions as edges in biological systems (cf. [28–30]). Consider a small biochemical network involving three proteins A, B, and C. We model this as a signaling hypergraph

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

where:

$$V = \{A, B, C\}.$$

We choose the following hypernodes $\mathcal{V} \subseteq 2^V$:

$$\mathcal{V} = \big\{\{A\}, \{B\}, \{C\}, \{A, B\}\big\}.$$

Here:

- $\{A\}$ represents the free protein A.
- $\{B\}$ represents the free protein B.
- $\{C\}$ represents the free protein C.
- $\{A, B\}$ represents the $A-B$ complex.

We define two signaling hyperedges e_1 and e_2 as follows:

- **Complex formation:**
$$e_1 = \big(T(e_1), H(e_1)\big),$$
where
$$T(e_1) = \big\{\{A\}, \{B\}\big\}, \qquad H(e_1) = \big\{\{A, B\}\big\}.$$
This models the reaction in which protein A and protein B bind to form the heterodimer $A-B$.
- **Complex-mediated activation:**
$$e_2 = \big(T(e_2), H(e_2)\big),$$
where
$$T(e_2) = \big\{\{A, B\}\big\}, \qquad H(e_2) = \big\{\{C\}\big\}.$$
This models the reaction in which the $A-B$ complex activates or produces protein C.

Hence the full edge set is

$$E = \{e_1, e_2\}.$$

By construction:

$$T(e_1) = \{\{A\}, \{B\}\} \subseteq \mathcal{V}, \quad H(e_1) = \{\{A, B\}\} \subseteq \mathcal{V},$$
$$T(e_2) = \{\{A, B\}\} \subseteq \mathcal{V}, \quad H(e_2) = \{\{C\}\} \subseteq \mathcal{V}.$$

Both $T(e_1), H(e_1)$ and $T(e_2), H(e_2)$ are nonempty.

Backward Stars:

$$\mathrm{BS}(\{A, B\}) = \big\{e \in E \;\big|\; \{A, B\} \in H(e)\big\} = \{e_1\},$$

since $H(e_1) = \{\{A, B\}\}$. Similarly,

$$\mathrm{BS}(\{C\}) = \{e_2\}.$$

B-Connections: Take the source hypernode $s = \{A\}$. Then:

- $\{A\} \in B_{\mathcal{H}}(s)$ trivially because it is the source.

- $\{B\} \notin B_{\mathcal{H}}(s)$ unless $\{B\}$ is produced by some edge whose tail is already B-connected to $\{A\}$. Here, no hyperedge has $\{B\}$ in its head, so $\{B\} \notin B_{\mathcal{H}}(s)$.
- $\{A, B\} \in B_{\mathcal{H}}(s)$ because e_1 has $\{A, B\} \in H(e_1)$ and every element of $T(e_1) = \{\{A\}, \{B\}\}$ must be B-connected to $\{A\}$. While $\{A\} \in B_{\mathcal{H}}(s)$, $\{B\} \notin B_{\mathcal{H}}(s)$, so in fact $\{A, B\}$ is *not* in $B_{\mathcal{H}}(s)$ under strict definition (both tail-elements must be B-connected). Thus $\{A, B\} \notin B_{\mathcal{H}}(s)$ here.
- $\{C\} \in B_{\mathcal{H}}(s)$ only if $\{A, B\}$ were B-connected to $\{A\}$. Since $\{A, B\} \notin B_{\mathcal{H}}(s)$, it follows $\{C\} \notin B_{\mathcal{H}}(s)$.

Acyclicity Check: The underlying directed graph $\mathcal{D}(\mathcal{H})$ has vertices $\{A\}$, $\{B\}$, $\{A, B\}$, $\{C\}$. Its directed edges are:

$$\{A\} \to \{A, B\}, \quad \{B\} \to \{A, B\}, \quad \{A, B\} \to \{C\}.$$

There is no directed cycle in this small digraph, so $\mathcal{H}$ is acyclic.

2 Result: Signaling n-SuperHypergraph

We present the formal definition of a Signaling n-SuperHypergraph.

Definition 2.1 (Signaling n-SuperHypergraph)**.** Fix an integer $n \geq 2$. Let $\mathcal{P}^k(V_0)$ be defined as above. A *signaling n-SuperHypergraph* is a quadruple

$$\mathrm{SNHT}^{(n)} = \big(V_n, \mathcal{V}_{n-1}, E_n, \{T(e), H(e)\}_{e \in E_n}\big),$$

satisfying all of the following:

1. $V_n \subseteq \mathcal{P}^n(V_0)$. We call each $v \in V_n$ an *n-supervertex*. In particular, every $v \in V_n$ is a subset of $\mathcal{P}^{n-1}(V_0)$.
2. $\mathcal{V}_{n-1} \subseteq \mathcal{P}^{n-1}(V_0)$. We call each $U \in \mathcal{V}_{n-1}$ an $(n-1)$*-hypernode*. Equivalently, each $(n-1)$-hypernode U is an element of V_n if and only if $U \in v$ for some $v \in V_n$.
3. $E_n \subseteq V_n \subseteq \mathcal{P}^n(V_0)$. Thus each $e \in E_n$ is itself an n-superedge, i.e. a set
$$e \subseteq \mathcal{P}^{n-1}(V_0), \quad e \in V_n.$$
4. For each $e \in E_n$, there are two nonempty subsets
$$T(e), H(e) \subseteq e \subseteq \mathcal{P}^{n-1}(V_0),$$
called the *tail* and *head* of the signaling edge e. These must satisfy:
$$T(e) \neq \emptyset, \quad H(e) \neq \emptyset, \quad T(e) \cup H(e) = e.$$
In other words, each n-superedge e is *partitioned* (not necessarily disjointly) into its reactant/regulator hypernodes $T(e)$ and product hypernodes $H(e)$. Since $e \subseteq \mathcal{P}^{n-1}(V_0)$, it follows that $T(e)$ and $H(e)$ are sets of $(n-1)$-hypernodes.

Remark 2.2 (Signaling n-SuperHypergraph)**.**
- By construction, each n-superedge e is an element of $\mathcal{P}^n(V_0)$, and each $(n-1)$-hypernode is an element of $\mathcal{P}^{n-1}(V_0)$. Thus
$$T(e), H(e) \subseteq e \subseteq \mathcal{P}^{n-1}(V_0), \quad e \in E_n \subseteq V_n \subseteq \mathcal{P}^n(V_0).$$
- Intuitively, a signaling n-SuperHypergraph replaces the $(n-1)$-level "simple hypernodes" (which generalize molecular complexes) with $(n-1)$-hypernodes, and the n-level "hyperedges" now carry the same tail/head semantics as in an ordinary signaling hypergraph, but one level higher.
- When $n = 2$, one recovers the usual *signaling hypergraph* as follows:
$$\mathcal{P}^1(V_0) = 2^{V_0} \quad \text{and} \quad \mathcal{P}^2(V_0) = \mathcal{P}(2^{V_0}).$$
In that case, each $(n-1)$-hypernode is just a simple subset of V_0, and each 2-superedge is a subset of $\mathcal{P}(V_0)$. The partition $e = T(e) \cup H(e)$ with $T(e), H(e) \subseteq 2^{V_0}$ exactly matches the classical signaling-hyperedge notion. We make this precise in Theorem 2.5 below.

Example 2.3 (T-Cell Receptor Signaling as a 3-SuperHypergraph)**.** T-Cell Receptor Signaling is the cellular process by which TCRs recognize antigens and trigger intracellular immune activation pathways (cf. [31–33]). We model a simplified T-cell receptor (TCR) activation cascade as a signaling 3-SuperHypergraph

$$\mathrm{SNHT}^{(3)} = \big(V_3,\ \mathcal{V}_2,\ E_3,\ \{T(e),\ H(e)\}_{e\in E_3}\big).$$

Below, we describe each level concretely.

Base set (V_0): Let

$$V_0 = \{\,\mathrm{TCR},\ \mathrm{pMHC},\ \mathrm{CD3},\ \mathrm{ZAP70}\,\}$$

be the set of *atomic molecular entities*:

- TCR: T-cell receptor protein.
- pMHC: peptide-MHC complex on antigen-presenting cell.
- CD3: CD3 co-receptor complex.
- ZAP70: cytosolic tyrosine kinase ZAP-70.

First-level hypernodes ($\mathcal{V}_1 \subseteq \mathcal{P}(V_0)$): We select these subsets of V_0:

$$\mathcal{V}_1 = \big\{\{\mathrm{TCR}\},\ \{\mathrm{pMHC}\},\ \{\mathrm{CD3}\},\ \{\mathrm{ZAP70}\},\ \{\mathrm{TCR},\mathrm{pMHC}\},\ \{\mathrm{CD3},\mathrm{ZAP70}\}\big\}.$$

Interpretation:

- {TCR}, {pMHC}, {CD3}, {ZAP70} are *single-protein* hypernodes.
- {TCR, pMHC} is the *ligand–receptor* complex hypernode.
- {CD3, ZAP70} is the *co-receptor–kinase* complex hypernode.

Second-level hypernodes ($\mathcal{V}_2 \subseteq \mathcal{P}^2(V_0)$): Each element of $\mathcal{V}_2$ is a subset of $\mathcal{V}_1$. Choose:

$$\mathcal{V}_2 = \Big\{U_a,\ U_b\Big\} \quad \text{where} \quad U_a = \big\{\{\text{TCR, pMHC}\},\ \{\text{CD3}\}\big\}, \quad U_b = \big\{\{\text{CD3, ZAP70}\}\big\}.$$

Interpretation:

- U_a is the *receptor–co-receptor assembly* hypernode, containing both {TCR, pMHC} and {CD3}.
- U_b is the *co-receptor–kinase* hypernode already formed at level 1.

Third-level vertices ($V_3 \subseteq \mathcal{P}^3(V_0)$): Each element of V_3 is a subset of $\mathcal{V}_2$. We choose:

$$V_3 = \Big\{v^{(3)}\Big\}, \quad v^{(3)} = \big\{U_a,\ U_b\big\}.$$

Interpretation:

- $v^{(3)}$ is the *assembled signaling scaffold* hypervertex, consisting of both the receptor–co-receptor assembly U_a and the co-receptor–kinase complex U_b.

Third-level superedges ($E_3 \subseteq V_3$): Since $V_3 = \{\,v^{(3)}\}$, we set

$$E_3 = \big\{e^{(3)}\big\}, \quad e^{(3)} = v^{(3)}.$$

This single 3-superedge $e^{(3)}$ is partitioned into:

$$T\big(e^{(3)}\big) = \{U_a\}, \qquad H\big(e^{(3)}\big) = \{U_b\}.$$

Thus:

- $T(e^{(3)}) = \{U_a\} = \{\{\{\text{TCR, pMHC}\},\{\text{CD3}\}\}\}$ represents the requirement that {TCR, pMHC} and {CD3} both be present to form the assembled scaffold.

- $H(e^{(3)}) = \{U_b\} = \{\{\{\text{CD3, ZAP70}\}\}\}$ represents the downstream formation of the co-receptor–kinase complex {CD3, ZAP70}.

Here $T(e^{(3)}) \cup H(e^{(3)}) = \{U_a, U_b\} = e^{(3)} \subseteq \mathcal{V}_2$, satisfying the definition.

Summary of the Example:

$$\text{SNHT}^{(3)} = \Big(V_3 = \{\{U_a, U_b\}\},\ \mathcal{V}_2 = \{U_a, U_b\},\ E_3 = \{e^{(3)}\},\ T(e^{(3)}) = \{U_a\},\ H(e^{(3)}) = \{U_b\}\Big).$$

Concretely, this models the biological process in which:

1. The receptor–ligand complex {TCR, pMHC} and the CD3 co-receptor {CD3} assemble together to form the higher-order scaffold U_a.
2. That scaffold U_a then recruits the CD3–ZAP70 complex U_b, producing ZAP70 phosphorylation events.

Hence $\text{SNHT}^{(3)}$ is a concrete, biologically motivated example of a signaling 3-SuperHypergraph, illustrating hierarchical assembly from atomic proteins up to multi-protein complexes and their signaling transitions.

Example 2.4 (Transcription Initiation as a 3-SuperHypergraph)**.** Gene transcription initiation is the process where transcription machinery assembles at a gene promoter to begin RNA synthesis from DNA (cf. [34–36]). We model a simplified gene transcription initiation cascade in eukaryotes as a signaling 3-SuperHypergraph:

$$\text{SNHT}^{(3)} = \big(V_3,\ \mathcal{V}_2,\ E_3,\ \{T(e),\ H(e)\}_{e \in E_3}\big).$$

Below, each level is described in detail.

Base set (V_0): Let

$$V_0 = \{\text{TF, P, M, R}\}$$

be the set of *atomic molecular entities*:

- TF: a specific transcription factor protein.
- P: a promoter DNA region upstream of the gene.
- M: the Mediator coactivator complex.
- R: RNA Polymerase II enzyme.

First-level hypernodes ($\mathcal{V}_1 \subseteq \mathcal{P}(V_0)$): We choose these subsets of V_0:

$$\mathcal{V}_1 = \Big\{\{\text{TF}\},\ \{\text{P}\},\ \{\text{M}\},\ \{\text{R}\},\ \{\text{TF}, \text{P}\},\ \{\text{P}, \text{M}\}\Big\}.$$

Interpretation:

- {TF}, {P}, {M}, {R} are *singleton* hypernodes.
- {TF, P} represents the *transcription factor–promoter* complex (TF bound to DNA).
- {P, M} represents the *promoter–Mediator* complex (Mediator bound at the promoter).

Second-level hypernodes ($\mathcal{V}_2 \subseteq \mathcal{P}^2(V_0)$): Each element of $\mathcal{V}_2$ is a subset of $\mathcal{V}_1$. We pick:

$$\mathcal{V}_2 = \big\{U_a,\ U_b\big\}, \quad U_a = \big\{\{\text{TF}, \text{P}\},\ \{\text{M}\}\big\}, \quad U_b = \big\{\{\text{P}, \text{M}\},\ \{\text{R}\}\big\}.$$

Interpretation:

- U_a is the *pre-initiation assembly* hypernode, containing both the TF–promoter complex {TF, P} and the free Mediator {M}.
- U_b is the *elongation assembly* hypernode, containing the promoter–Mediator complex {P, M} and the free RNA Polymerase II {R}.

Third-level vertices ($V_3 \subseteq \mathcal{P}^3(V_0)$): Each element of V_3 is a subset of $\mathcal{V}_2$. We choose:

$$V_3 = \{v^{(3)}\}, \quad v^{(3)} = \{U_a, U_b\}.$$

Interpretation:

- $v^{(3)}$ is the *full transcription initiation scaffold* hypervertex, containing both the pre-initiation assembly U_a and the elongation assembly U_b.

Third-level superedges ($E_3 \subseteq V_3$): Since $V_3 = \{v^{(3)}\}$, we set

$$E_3 = \{e^{(3)}\}, \quad e^{(3)} = v^{(3)}.$$

This single 3-superedge $e^{(3)}$ is partitioned into:

$$T(e^{(3)}) = \{U_a\}, \qquad H(e^{(3)}) = \{U_b\}.$$

Thus:

- $T(e^{(3)}) = \{U_a\} = \{\{\{\text{TF, P}\}, \{\text{M}\}\}\}$ represents the requirement that the TF–promoter complex and free Mediator assemble into the pre-initiation complex.
- $H(e^{(3)}) = \{U_b\} = \{\{\{\text{P, M}\}, \{\text{R}\}\}\}$ represents the downstream recruitment of RNA Polymerase II to form the elongation assembly.

Note that $T(e^{(3)}) \cup H(e^{(3)}) = \{U_a, U_b\} = e^{(3)} \subseteq \mathcal{V}_2$, satisfying the requirement that $T(e) \cup H(e) = e$.

Summary of the Example:

$$\text{SNHT}^{(3)} = \Big(V_3 = \{\{U_a, U_b\}\},\ \mathcal{V}_2 = \{U_a, U_b\},\ E_3 = \{e^{(3)}\},\ T(e^{(3)}) = \{U_a\},\ H(e^{(3)}) = \{U_b\}\Big).$$

Concretely, this models the biological process:

1. {TF, P} (TF bound to promoter) and {M} (Mediator) form the pre-initiation assembly U_a.
2. That pre-initiation assembly U_a then recruits {R} (RNA Polymerase II) and {P, M} (promoter–Mediator) to generate the elongation assembly U_b.

Thus $\text{SNHT}^{(3)}$ provides a concrete, hierarchical illustration of gene transcription initiation in eukaryotes as a signaling 3-SuperHypergraph.

Theorem 2.5. *Let $\mathcal{H} = (V_0, \mathcal{V}, E_{\text{orig}})$ be an ordinary signaling hypergraph in the sense of Definition 2.4, where*

$$\mathcal{V} \subseteq 2^{V_0} = \mathcal{P}^1(V_0), \quad E_{\text{orig}} \subseteq \Big\{ (T(e), H(e)) \ \Big|\ T(e), H(e) \subseteq \mathcal{V},\ T(e) \neq \emptyset,\ H(e) \neq \emptyset \Big\}.$$

Define

$$V_2 = \mathcal{P}^2(V_0) \quad \text{and} \quad E_2 = \big\{ e \in \mathcal{P}^2(V_0) \ \big|\ \exists\, (T, H) \in E_{\text{orig}} \text{ with } T \cup H = e \big\}.$$

Then

$$\text{SNHT}^{(2)} = \big(V_2, \mathcal{V}, E_2, \{T(e), H(e)\}_{e \in E_2}\big)$$

is a signaling 2-SuperHypergraph in the sense of Definition 2.1. In particular, there is a one-to-one correspondence between the original signaling hyperedges $(T(e), H(e))$ and the new 2-superedges $e = T(e) \cup H(e)$. Hence every signaling hypergraph is exactly a signaling 2-SuperHypergraph.

Proof. We check each requirement of Definition 2.1 when $n = 2$:

1. By construction, $V_2 = \mathcal{P}^2(V_0)$. Clearly, $V_2 \subseteq \mathcal{P}^2(V_0)$.
2. We take $\mathcal{V}_1 = \mathcal{V} \subseteq 2^{V_0} = \mathcal{P}^1(V_0)$. Thus each $(n-1)$-hypernode (with $n = 2$) is precisely one of the original simple hypernodes.

3. We set
$$E_2 \;=\; \big\{\, e \in \mathcal{P}^2(V_0) \;\big|\; \exists (T,H) \in E_{\mathrm{orig}},\, T \cup H = e \big\}.$$
By construction, each such e is an element of $\mathcal{P}^2(V_0)$, and since $\mathcal{P}^2(V_0) = V_2$, it follows that $E_2 \subseteq V_2$. Hence $E_2 \subseteq \mathcal{P}^2(V_0)$.

4. For each original signaling hyperedge $\big(T(e), H(e)\big) \in E_{\mathrm{orig}}$, form
$$e \;=\; T(e) \,\cup\, H(e) \;\in\; \mathcal{P}^2(V_0).$$
Define $T(e)$ and $H(e)$ in $\mathrm{SNHT}^{(2)}$ exactly as in the original pair. Since $T(e), H(e) \subseteq \mathcal{V} = \mathcal{P}^1(V_0)$ and $T(e) \cup H(e) = e$, all hypotheses of Definition 2.1 are satisfied for $n = 2$. In particular, $T(e) \neq \emptyset$ and $H(e) \neq \emptyset$ by assumption.

Therefore $\mathrm{SNHT}^{(2)}$ is a signaling 2-SuperHypergraph, and one sees immediately that every original signaling hyperedge $\big(T(e), H(e)\big)$ corresponds bijectively to the 2-superedge $e = T(e) \cup H(e)$. □

Theorem 2.6. *Every signaling n-SuperHypergraph*
$$\mathrm{SNHT}^{(n)} \;=\; \big(V_n,\, \mathcal{V}_{n-1},\, E_n,\, \{\,T(e),\, H(e)\}_{e \in E_n}\big)$$
is, in particular, an n-SuperHyperGraph. That is, if $n \geq 2$ *and*
$$V_n \;\subseteq\; \mathcal{P}^n(V_0), \qquad E_n \;\subseteq\; \mathcal{P}^n(V_0),$$
then $\big(V_n,\, E_n\big)$ *automatically satisfies the definition of an n-SuperHyperGraph.*

Proof. By Definition 2.1, we have:
$$V_n \;\subseteq\; \mathcal{P}^n(V_0), \quad E_n \;\subseteq\; V_n \;\subseteq\; \mathcal{P}^n(V_0).$$
An n-SuperHyperGraph is *precisely* any pair (V, E) with $V \subseteq \mathcal{P}^n(V_0)$ and $E \subseteq \mathcal{P}^n(V_0)$. In our case, both V_n and E_n lie inside $\mathcal{P}^n(V_0)$. Hence
$$\big(V_n,\, E_n\big)$$
meets the requirements of an n-SuperHyperGraph. The additional data $\{\,T(e), H(e)\}$ places no extra restriction on $\big(V_n, E_n\big)$ regarding the underlying hypergraph structure; it only endows each edge $e \in E_n$ with a distinguished *tail* and *head*. Consequently, every signaling n-SuperHypergraph is indeed an n-SuperHyperGraph. □

Definition 2.7 (Underlying Directed Graph)**.** Let $\mathrm{SNHT}^{(n)} = (V_n,\, \mathcal{V}_{n-1},\, E_n,\, \{T(e), H(e)\}_{e \in E_n})$ be a signaling n-SuperHypergraph. Define the *underlying directed graph* $\mathcal{D}(\mathrm{SNHT}^{(n)})$ as follows:

Vertices: $\mathcal{V}_{n-1}$. Directed edges: $\big(U \;\longrightarrow\; W\big)$ whenever there exists $e \in E_n$ with $U \in T(e),\ W \in H(e)$.

That is, for each $e \in E_n$ and each ordered pair $(U, W) \in T(e) \times H(e)$, we include a directed arc $U \to W$ in $\mathcal{D}(\mathrm{SNHT}^{(n)})$.

Definition 2.8 (Acyclic Signaling n-SuperHypergraph)**.** A signaling n-SuperHypergraph $\mathrm{SNHT}^{(n)}$ is said to be *acyclic* if its underlying directed graph $\mathcal{D}(\mathrm{SNHT}^{(n)})$ (as in Definition 2.7) has no directed cycles. Equivalently, there exists a function
$$o \colon \mathcal{V}_{n-1} \;\longrightarrow\; \mathbb{R}$$
such that for every $e \in E_n$ and every $(U, W) \in T(e) \times H(e)$, one has
$$o(U) \;<\; o(W).$$

Theorem 2.9. *Let* $\mathrm{SNHT}^{(2)} = (V_2,\, \mathcal{V}_1,\, E_2,\, \{T(e), H(e)\}_{e \in E_2})$ *be a signaling* 2*-SuperHypergraph as in Definition 2.1, where*
$$V_2 \subseteq \mathcal{P}^2(V_0), \quad \mathcal{V}_1 \subseteq \mathcal{P}^1(V_0) = 2^{V_0}, \quad E_2 \subseteq V_2.$$
Then $\mathrm{SNHT}^{(2)}$ *is exactly equivalent to a classical signaling hypergraph* $\big(V_0,\, \mathcal{V}_1,\, E_{\mathrm{orig}}\big)$ *with*
$$E_{\mathrm{orig}} \;=\; \big\{\, \big(T(e),\, H(e)\big) \;\big|\; e \in E_2 \text{ and } T(e) \cup H(e) = e \big\}.$$
In particular, there is a bijection between the 2*-superedges* $e \in E_2$ *and the classical signaling hyperedges* $\big(T(e), H(e)\big)$.

Proof. By Definition 2.1 for $n = 2$:

$$\mathcal{V}_1 \subseteq \mathcal{P}^1(V_0) = 2^{V_0}, \quad E_2 \subseteq \mathcal{P}^2(V_0) = \mathcal{P}(2^{V_0}).$$

Each 2-superedge $e \in E_2$ satisfies $e \subseteq \mathcal{P}^1(V_0)$ and is partitioned into $T(e),\ H(e) \subseteq \mathcal{P}^1(V_0)$ with $T(e) \cup H(e) = e$. Hence the pair $\big(T(e), H(e)\big)$ is precisely a signaling hyperedge on the vertex-set $\mathcal{V}_1 \subseteq 2^{V_0}$. Collecting all such pairs for $e \in E_2$ yields

$$E_{\mathrm{orig}} \ = \ \big\{ (T(e), H(e)) \ \big| \ e \in E_2 \big\}.$$

Since every classical signaling hyperedge is by definition an ordered pair of nonempty subsets of $\mathcal{V}_1 \subseteq 2^{V_0}$, and since each such pair $\big(T(e), H(e)\big)$ determines a unique 2-superedge $e = T(e) \cup H(e)$, the correspondence

$$e \ \longleftrightarrow \ \big(T(e),\ H(e)\big)$$

is bijective. Therefore $\mathrm{SNHT}^{(2)}$ and $\big(V_0,\ \mathcal{V}_1,\ E_{\mathrm{orig}}\big)$ encode exactly the same signaling relationships, proving the claim. □

Theorem 2.10. *Let* $\mathrm{SNHT}^{(n)} = (V_n,\ \mathcal{V}_{n-1},\ E_n,\ \{T(e), H(e)\}_{e \in E_n})$ *be a signaling n-SuperHypergraph as in Definition 2.1. Then the pair*

$$\big(V_n,\ E_n\big)$$

is an n-SuperHyperGraph in the sense of Definition 1.4, since

$$V_n \subseteq \mathcal{P}^n(V_0), \quad E_n \subseteq V_n \subseteq \mathcal{P}^n(V_0).$$

Proof. By hypothesis, $V_n \subseteq \mathcal{P}^n(V_0)$ and $E_n \subseteq V_n$. By Definition 1.4 of an n-SuperHyperGraph, any pair (V', E') with

$$V' \subseteq \mathcal{P}^n(V_0), \quad E' \subseteq \mathcal{P}^n(V_0)$$

is itself an n-SuperHyperGraph. Here we take $V' = V_n$ and $E' = E_n$. Clearly $E_n \subseteq V_n \subseteq \mathcal{P}^n(V_0)$. Thus $\big(V_n,\ E_n\big)$ satisfies all requirements to be an n-SuperHyperGraph. The extra data $\{T(e), H(e)\}$ does not interfere with the underlying set-theoretic structure: it simply enriches each superedge with a distinguished *tail* and *head*. Hence every signaling n-SuperHypergraph is in particular an n-SuperHyperGraph. □

Theorem 2.11 (Acyclicity Equivalence)**.** *Let* $\mathrm{SNHT}^{(n)} = (V_n,\ \mathcal{V}_{n-1},\ E_n,\ \{T(e), H(e)\}_{e \in E_n})$ *be a signaling n-SuperHypergraph, and let* $\mathcal{D}(\mathrm{SNHT}^{(n)})$ *be its underlying directed graph on the vertex-set* $\mathcal{V}_{n-1}$ *as in Definition 2.7. Then the following are equivalent:*

(a) $\mathcal{D}(\mathrm{SNHT}^{(n)})$ *has no directed cycles (i.e.* $\mathrm{SNHT}^{(n)}$ *is acyclic by Definition 2.8).*

(b) There exists a function

$$o\colon \mathcal{V}_{n-1} \ \longrightarrow \ \mathbb{R}$$

such that for every $e \in E_n$ *and every* $(U, W) \in T(e) \times H(e)$*, one has*

$$o(U) \ < \ o(W).$$

(c) One can list the $(n-1)$*-hypernodes in* $\mathcal{V}_{n-1}$ *as* $U_1, U_2, \ldots, U_m$ *so that for every* $e \in E_n$ *and every* $(U, W) \in T(e) \times H(e)$*, the index of* U *is strictly less than the index of* W*.*

Proof. We show $(a) \Rightarrow (b) \Rightarrow (c) \Rightarrow (a)$.

(a) $\Rightarrow$ **(b)** : If $\mathcal{D}(\mathrm{SNHT}^{(n)})$ has no directed cycles, then it is a directed acyclic graph (DAG) on the finite vertex-set $\mathcal{V}_{n-1}$. A standard result about DAGs guarantees the existence of a *topological ordering* (real-valued or integer-valued) of its vertices. Concretely, one may define

$$o(U) \ = \ (\text{length of the longest directed path in } \mathcal{D} \text{ ending at } U).$$

Since there are no directed cycles, each such "longest path" is well-defined and finite, so $o(U) \in \mathbb{N} \subset \mathbb{R}$. Whenever (U, W) is a directed arc (i.e. $U \to W$ in $\mathcal{D}(\mathrm{SNHT}^{(n)})$), this construction ensures

$$o(U) \ < \ o(W).$$

But by the definition of directed arcs, $U \in T(e)$ and $W \in H(e)$ for some $e \in E_n$. Hence o satisfies the required inequality $o(U) < o(W)$ for every $(U, W) \in T(e) \times H(e)$. This yields (b).

(b) $\Rightarrow$ **(c)** : Assume $o\colon \mathcal{V}_{n-1} \to \mathbb{R}$ satisfies

$$o(U) \ < \ o(W), \quad \forall\, e \in E_n,\ \forall\,(U, W) \in T(e) \times H(e).$$

Since $\mathcal{V}_{n-1}$ is finite, the values $\{\, o(U) \mid U \in \mathcal{V}_{n-1}\}$ are finitely many real numbers. Order them in strictly increasing order:

$$o(U_1) \ < \ o(U_2) \ < \ \cdots \ < \ o(U_m),$$

where $\mathcal{V}_{n-1} = \{\, U_1, U_2, \ldots, U_m\}$. Then for any $(U, W) \in T(e) \times H(e)$, we have $o(U) < o(W)$, which immediately implies the index of U is less than the index of W, because the ordering by real values corresponds to the numbering. Thus (c) holds.

(c) $\Rightarrow$ **(a)** : Suppose there is a labeling $\mathcal{V}_{n-1} = \{U_1, \ldots, U_m\}$ such that

$$\text{if } (U, W) \in T(e) \times H(e) \text{ for some } e \in E_n, \text{ then } \mathrm{index}(U) < \mathrm{index}(W).$$

If a directed cycle existed in $\mathcal{D}(\mathrm{SNHT}^{(n)})$,

$$U_{i_1} \ \longrightarrow \ U_{i_2} \ \longrightarrow \ \cdots \ \longrightarrow \ U_{i_k} \ \longrightarrow \ U_{i_1},$$

then along this cycle we would have

$$\mathrm{index}(U_{i_1}) < \mathrm{index}(U_{i_2}) < \cdots < \mathrm{index}(U_{i_k}) < \mathrm{index}(U_{i_1}),$$

which is impossible (an integer cannot be strictly less than itself). Hence no directed cycle can exist in $\mathcal{D}(\mathrm{SNHT}^{(n)})$. This proves (a).

Combining the three implications, we conclude $(a) \Leftrightarrow (b) \Leftrightarrow (c)$. □

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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.

Conflicts of Interest

The authors confirm that there are no conflicts of interest related to the research or its publication.

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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