International Journal of Advanced Engineering and Technology Research
ISSN: 3106-8677 (Print), ISSN: 3106-8685 (Online) | Vol. 1, No. 3, 2026

Exploring Structure–Function Coupled Brain Network Construction for Brain Disease-Aided Identification

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Abstract: Brain disorders are often associated with coordinated abnormalities in brain structure, functional interactions, and cross-regional connectivity patterns rather than isolated changes in single regions. Conventional single-modality brain network analysis usually captures only one side of these alterations, either from the perspective of anatomical organization or from the perspective of statistical functional coupling, and therefore may not fully characterize the complexity of disease-related network disruption. With the rapid development of multimodal neuroimaging techniques, especially structural magnetic resonance imaging (sMRI), diffusion tensor imaging (DTI), and functional magnetic resonance imaging (fMRI), increasing attention has been paid to how structural information and functional information can be jointly organized into a unified brain network representation. This paper discusses structure–function coupled brain network construction for brain disease-aided identification. First, the complementary roles of structural connectivity, functional connectivity, and morphology-related association information are analyzed. Second, several representative coupling paradigms are summarized, including structure-prior-constrained construction, graph-level cooperative fusion, and coupling strategies for time-varying functional connectivity. Their respective characteristics are compared in terms of representational completeness, topological stability, and interpretability. Finally, major open issues are discussed, including modality heterogeneity, bias in connectivity estimation, the reliability of dynamic coupling, and the biological interpretability of coupled graphs. The purpose of this paper is to examine multimodal brain network representation from the perspective of coupled graph construction rather than classification model design, and to provide a focused methodological reference for future studies on brain disease-aided identification.

Keywords: Brain disease-aided identification, Structural connectivity, Functional connectivity, Coupled brain network, Multimodal neuroimaging.

1. Introduction

Brain disorders are increasingly understood as system-level abnormalities rather than isolated regional lesions. In many neurological and neurodegenerative conditions, structural degeneration, white matter disruption, and functional dysregulation emerge together and influence one another across distributed brain systems. This makes brain network analysis an attractive framework for brain disease-aided identification, since it explicitly models inter-regional relationships instead of relying only on local measurements [1].

Existing studies commonly describe brain organization from two major perspectives. One perspective emphasizes anatomical connectivity and relatively stable structural pathways between brain regions. The other emphasizes statistical dependence and coordinated activity patterns across regions. The first perspective offers a more stable description of the brain's topological scaffold, while the second is more sensitive to state-dependent fluctuations and disease-related functional disturbances. Both are informative, yet neither is sufficient on its own. Structural connectivity may fail to capture subtle short-term functional abnormalities, whereas functional connectivity is often sensitive to noise, subject state, preprocessing strategy, and graph construction parameters [2].

For this reason, structure–function coupled brain network construction has gradually emerged as an important topic. Instead of simply concatenating multimodal features at the representation level, this line of research attempts to coordinate structural and functional information directly at the graph construction stage. The goal is to obtain a brain graph that remains topologically plausible while preserving sensitivity to disease-related abnormalities. Compared with studies that mainly focus on increasingly sophisticated classifiers, coupled brain network construction places greater emphasis on the quality of the graph input itself, namely, whether the constructed brain network is stable, informative, and biologically meaningful.

Another reason this topic deserves separate discussion is that graph quality often determines the upper limit of subsequent analysis. Even a sophisticated downstream model may fail to recover meaningful disease-related patterns if the input graph is poorly constructed, unstable, or conceptually inconsistent. In contrast, a well-designed coupled graph can serve as a more reliable substrate for feature extraction, statistical comparison, and disease-aided identification. In this sense, the problem of how to construct a brain graph should not be treated as a minor preprocessing detail but as a central methodological issue.

Accordingly, this paper focuses on coupled graph construction rather than downstream model design. It discusses the complementarity of structural and functional information, representative paradigms for structure–function coupling, their value in brain disease-aided identification, and the major challenges that remain unresolved.

Figure 1 presents the general logic of structure–function coupled brain network construction. The left side of the framework contains three major sources of neuroimaging evidence: sMRI, fMRI, and DTI. After ROI parcellation, these modalities contribute different forms of graph-relevant information, including morphology-related descriptors, functional interactions, and structural pathways. The middle part of the figure illustrates that these heterogeneous signals

are not merely concatenated at the feature level but are reorganized into a coupled brain graph in which structural priors and functional dependencies are jointly considered. The right side emphasizes the role of the coupled graph as an intermediate representation for brain disease-aided identification, indicating that graph construction itself is a crucial part of the analytical pipeline rather than a passive input generation step.

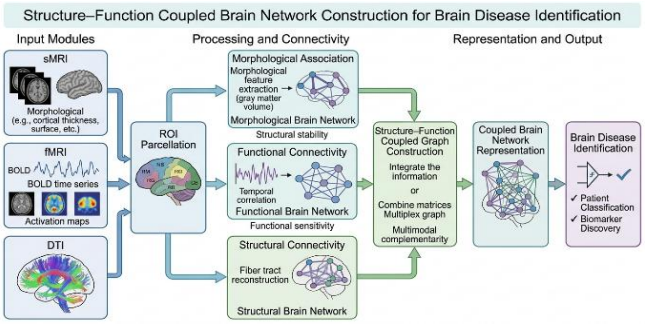

Figure 1. Basic framework of structure–function coupled graph construction for brain disease-aided identification

2. Complementary Representations of Structural and Functional Information

2.1. Two Perspectives for Describing Inter-Regional Brain Relationships

From the perspective of brain network modeling, the relationship between brain regions can be described in at least two ways. The first emphasizes whether two regions are anatomically connected through relatively stable physical pathways. The second emphasizes whether the activities of two regions exhibit statistical coordination or dependence over time. These two perspectives correspond, respectively, to structural connectivity and functional connectivity.

A brain network is commonly represented as a weighted graph:

$$G = (V, E, A) \tag{1}$$

Where $V = \{v_1, v_2, \dots, v_N\}$ denotes the set of brain regions, E denotes the edge set, and $A = [a_{ij}]_{N\times N}$ is the adjacency matrix. In structural graphs, a_{ij} usually represents anatomical connection strength or morphology-related similarity. In functional graphs, a_{ij} usually reflects the degree of statistical coupling between regional signals.

To characterize basic graph properties, a degree matrix D is often defined by

$$D_{ii} = \sum_{j=1}^{N} a_{ij} \tag{2}$$

and the graph Laplacian can be written as

$$L = D - A \tag{3}$$

Although the present paper does not focus on graph neural network design, these standard graph quantities help clarify an essential point: once inter-regional relations are encoded in graph form, the research problem becomes not only "which regions are abnormal" but also "how the regions are connected," "whether the connectivity is reliable," and "whether the resulting topology is disease-relevant."

More importantly, these two perspectives should not be regarded as competing alternatives. Anatomical pathways and statistical functional coordination reflect different aspects of brain organization. The former indicates whether large-scale communication has a plausible physical substrate, while the latter reveals whether two regions actually co-vary in a way that may be clinically relevant. Therefore, a coupled graph representation is not simply a technical fusion strategy; it is an attempt to encode the dual nature of brain organization itself [3].

2.2. Stability-oriented Properties of Structural Connectivity

Structural connectivity is commonly derived from diffusion tensor imaging. By analyzing anisotropic water diffusion in white matter tracts, DTI provides indirect evidence regarding the existence and strength of anatomical pathways between brain regions. If the number of reconstructed fiber tracts between regions i and j is denoted by n_{ij}, one simple normalized structural edge weight can be defined as

$$s_{ij} = \frac{n_{ij}}{\max\limits_{p,q} n_{pq}} \tag{4}$$

The corresponding structural adjacency matrix is then given by

$$A^{(s)} = [s_{ij}]_{N\times N} \tag{5}$$

The major advantage of structural connectivity lies in its relatively strong biological grounding. Structural topology tends to be more stable than functional topology and is less affected by transient state changes. For this reason, structural information is often treated as a low-frequency, relatively stable prior in brain network modeling. In practice, when one aims to suppress noisy or weakly supported functional edges, structural connectivity provides a natural reference for topological plausibility.

However, structural connectivity should not be viewed as noise-free or absolute. Tractography results depend on acquisition quality, reconstruction algorithms, atlas definition, and thresholding strategy. In regions with crossing fibers or weak pathways, structural edges may be underestimated or inconsistently recovered. Therefore, structural information is highly useful as a constraint or reference, but not necessarily as a complete and definitive description of brain communication.

Another point worth emphasizing is that structural connectivity often reflects long-term network organization rather than momentary communication efficiency. A preserved white matter pathway does not guarantee that the corresponding functional interaction is normal; similarly, the absence of a strong reconstructed tract does not always imply the absence of meaningful coordination at the systems level. This means that structure is necessary but not sufficient as a standalone descriptor, which further motivates coupled construction.

2.3. Sensitivity-oriented Properties of Functional Connectivity

Functional connectivity is usually derived from fMRI time series and aims to describe statistical dependence among regional neural activities. If the BOLD time series of brain regions i and j are denoted by $x_i(t)$ and $x_j(t)$, respectively, their Pearson correlation coefficient can be written as

$$r_{ij} = \frac{\sum_{t=1}^{T}(x_i(t)-\bar{x}_i)(x_j(t)-\bar{x}_j)}{\sqrt{\sum_{t=1}^{T}(x_i(t)-\bar{x}_i)^2}\sqrt{\sum_{t=1}^{T}(x_j(t)-\bar{x}_j)^2}} \quad (6)$$

Which leads to the functional connectivity matrix

$$A^{(f)} = [r_{ij}]_{N\times N} \quad (7)$$

Functional connectivity is often more sensitive than structural connectivity to disease-related disruption. In some brain disorders, abnormal coordination patterns emerge earlier than clear anatomical damage, which makes functional connectivity particularly relevant to early-stage identification. This is especially important in conditions where pathological changes affect network communication efficiency or synchronization before causing obvious tissue loss.

At the same time, functional graphs are more vulnerable to noise and variability. Motion artifacts, physiological fluctuations, scan duration, subject condition, and preprocessing choices may all substantially affect connectivity estimates. Weak or spurious edges are common, especially when graph construction relies on noisy or limited observations. Consequently, functional connectivity is highly informative but requires stabilization, which is one reason why structural information is frequently introduced during coupled graph construction.

In addition, the meaning of a functional edge is not always uniform across subjects or acquisition sessions. A connection that appears strong in one time interval may weaken in another, and this instability can be either biologically meaningful or methodologically undesirable. Therefore, functional connectivity is best understood as a high-sensitivity but relatively high-variance representation, which benefits from being contextualized by more stable structural evidence.

2.4. The Supplementary Role of Morphology-Related Association

Besides white matter structural connectivity and functional coupling, morphology-related association provides an additional source of information. Based on sMRI, one can extract regional measures such as gray matter volume, cortical thickness, or morphological descriptors and construct a region-to-region association graph according to similarity.

If m_i and m_j denote morphological feature vectors of regions i and j, a Gaussian-kernel-based similarity can be defined as

$$\mathrm{sim}(i,j) = exp\left(-\frac{\|m_i-m_j\|_2^2}{2\sigma^2}\right) \quad (8)$$

And the corresponding morphology-related adjacency matrix is

$$A^{(m)} = [\mathrm{sim}(i,j)]_{N\times N} \quad (9)$$

Morphology-related association does not directly encode physical tracts, nor does it represent dynamic coordination. Instead, it reflects whether two regions exhibit similar structural variation patterns. This is especially relevant in neurodegenerative disorders, where multiple regions often undergo coordinated atrophy. Therefore, morphology-related information can serve as an important supplement to both structural and functional representations.

Compared with DTI-based structural connectivity, morphology-related association is less tied to explicit anatomical pathways but may better capture distributed co-degeneration. Compared with functional connectivity, it is less sensitive to transient fluctuations and may reflect slower disease-related changes. As a result, morphology-related graphs often occupy an intermediate role in coupled construction: they are not a replacement for anatomical structure or functional interaction, but rather an additional cue that helps describe regional co-abnormality in a more complete manner.

Table 1. Comparison of structural connectivity, functional connectivity, and morphology-related association

Connectivity type	Data source	Main target of description	Main advantage	Main limitation
Structural connectivity	DTI	Physical pathways between regions	Relatively stable, biologically grounded	Sensitive to tractography settings and image quality
Functional connectivity	fMRI	Statistical coupling of regional activity	Sensitive to abnormal interactions	More vulnerable to noise and subject-state variation
Morphology-related association	sMRI	Coordinated structural variation	Reflects co-degeneration patterns	Physical interpretation is indirect

Table 1 summarizes the distinct but complementary roles of the three major connectivity-related representations used in multimodal brain network analysis. Structural connectivity provides anatomically grounded information about physical pathways and is therefore relatively stable, but it may be affected by tractography uncertainty. Functional connectivity is more sensitive to network-level abnormalities and is particularly useful for capturing interaction disturbances, yet it is also more vulnerable to noise and physiological variation. Morphology-related association contributes a third perspective by describing coordinated structural variation patterns across regions, which is valuable in disorders characterized by distributed atrophy. The comparison highlights why coupled graph construction is appealing: it allows these different representations to be jointly exploited rather than separately interpreted [4].

3. Major Paradigms for Structure–Function Coupled Brain Network Construction

3.1. Structure-Prior-Constrained Graph Construction

One of the most common strategies in coupled graph construction is to build a functional graph first and then constrain it using structural priors. The rationale is straightforward: functional connectivity is sensitive but unstable, whereas structural connectivity is stable but less responsive to short-term pathological changes. A coupled graph should ideally preserve the former's sensitivity while borrowing the latter's topological plausibility.

A simple coupled adjacency matrix can be expressed as

$$A^{(sf)} = \alpha A^{(f)} + (1-\alpha)A^{(s)} \quad (10)$$

Where $A^{(sf)}$ is the coupled graph, $A^{(f)}$ is the functional adjacency matrix, $A^{(s)}$ is the structural adjacency matrix, and $\alpha \in [0,1]$ is the fusion coefficient.

To reduce scale mismatch between graphs, normalization is often applied:

$$\hat{A} = D^{-\frac{1}{2}} A D^{-\frac{1}{2}} \quad (11)$$

Where D is the degree matrix. Such normalization helps align propagation scale and reduces the dominance of extremely large edge weights.

Besides direct weighted combination, another common strategy is structural filtering. In this case, structural edges are used to retain, suppress, or reweight functional connections. For example, functional edges lacking structural support may be downweighted, while those supported by strong structural pathways may be preserved with higher confidence. The benefit of this family of methods is conceptual clarity and improved graph stability. The limitation is that if structural constraints are too strong, functionally meaningful but anatomically weak relationships may be suppressed.

A more general optimization-oriented form of constrained coupling can be written as

$$\min_{A^{(sf)}} \| A^{(sf)} - A^{(f)} \|_F^2 + \lambda \| A^{(sf)} - A^{(s)} \|_F^2 + \gamma \Omega(A^{(sf)}) \quad (12)$$

Where $\|\cdot\|_F$ denotes the Frobenius norm, λ controls the strength of structural consistency, and $\Omega(\cdot)$ is a regularization term that may encourage sparsity, smoothness, or prior-specific constraints. This formulation is useful because it makes explicit that coupled graph construction is essentially a trade-off problem: the final graph should remain close to the observed functional structure, but not so close that it loses topological plausibility [5].

In practice, the success of structure-prior-constrained construction depends strongly on how "support" is interpreted. Hard masking based on structural edges is strict and simple but may discard meaningful weak interactions. Soft reweighting is more flexible but requires careful calibration. Therefore, although this paradigm is intuitive and widely applicable, it also demands careful balance between preservation and correction.

3.2. Graph-Level Cooperative Fusion

Unlike structure-prior-constrained construction, graph-level cooperative fusion does not treat structure merely as an auxiliary regularizer. Instead, it attempts to let structural graphs, functional graphs, and sometimes morphology-related graphs jointly participate in the formation of a coupled representation.

Let $A^{(s)}$, $A^{(f)}$, and $A^{(m)}$ denote structural, functional, and morphology-related adjacency matrices, respectively. A general graph-level fusion form can be written as

$$A^{(joint)} = \phi(A^{(s)}, A^{(f)}, A^{(m)}) \quad (13)$$

Where $\phi(\cdot)$ may represent weighted summation, gating, adaptive edge selection, low-rank integration, or other graph combination mechanisms.

A linear weighted version is

$$A^{(joint)} = \beta_1 A^{(s)} + \beta_2 A^{(f)} + \beta_3 A^{(m)}, \beta_1 + \beta_2 + \beta_3 = 1 \quad (14)$$

The appeal of graph-level fusion lies in representational completeness. Instead of privileging only one graph and treating others as supplements, it attempts to form a more balanced multimodal network representation. This is particularly useful when different disorders are characterized by abnormalities distributed across anatomical, functional, and morphological levels.

However, graph-level fusion is also challenging. Edge weights from different graphs have different meanings. A strong structural edge and a strong functional edge are not interchangeable concepts. Therefore, although graph-level fusion can be informative, interpretability becomes more complicated unless the fusion mechanism is carefully designed.

To address this issue, adaptive weighting can be introduced. For example, if q_1, q_2, q_3 are relevance scores estimated for structural, functional, and morphology-related graphs, one may define:

$$\beta_k = \frac{exp\ (q_k)}{\sum_{l=1}^{3} exp\ (q_l)},\ k = 1,2,3 \quad (15)$$

Which enables the model or algorithm to assign different importance to different graph sources in a data-dependent manner. Although such adaptive fusion increases flexibility, it also introduces additional complexity and may reduce transparency unless the resulting weights are explicitly analyzed.

Overall, graph-level cooperative fusion is attractive because it aims to model the brain network as a genuinely multimodal object rather than a function-dominant graph corrected by structure. Its weakness is that it makes the interpretation of edge composition more difficult, especially when multiple graph types are merged into one final adjacency matrix.

3.3. Coupled Graph Construction for Time-Varying Functional Connectivity

Because brain function is inherently dynamic, structure–function coupling has increasingly moved from static graph construction to dynamic graph construction. In this setting, structural information is usually treated as a relatively stable prior, while functional connectivity evolves across temporal windows.

Suppose $A_t^{(f)}$ is the functional adjacency matrix in the t-th temporal window. Then a time-varying structure–function coupled graph can be defined as

$$A_t^{(sf)} = \alpha_t A_t^{(f)} + (1-\alpha_t)A^{(s)}, t = 1,2,\dots,T_w \quad (16)$$

Where α_t can be fixed or adaptively determined for each time window. This formulation allows the coupling strength to vary according to the distribution or reliability of the current functional connectivity estimate.

To further suppress weak or noisy edges, sparsification is often introduced. If $\mathcal{S}(\cdot)$ denotes a sparsification operator, then the refined dynamic coupled graph can be written as

$$\tilde{A}_t^{(sf)} = \mathcal{S}(A_t^{(sf)}) \quad (17)$$

$\mathcal{S}(\cdot)$ may correspond to thresholding, Top-k edge retention, adaptive pruning, or related operations. These steps are especially important because dynamic functional connectivity estimates are often unstable in short windows.

The core difficulty of this paradigm lies in balancing structural stability and temporal flexibility. If structural constraints dominate, meaningful time-varying abnormalities

may be weakened. If the functional component dominates, the resulting graph sequence may become noisy and less reliable.

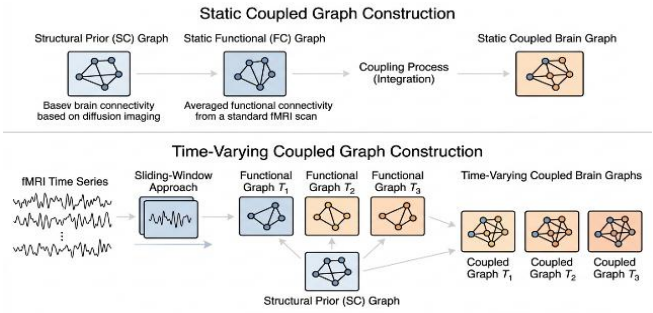

Figure 2. Comparison between static structure–function coupling and time-varying structure–function coupling.

Figure 2 contrasts two major scenarios of structure–function coupling. In the upper branch, structural and functional information are combined into a single static coupled graph, which is suitable for representing average or global connectivity organization. In the lower branch, the functional component is first decomposed into multiple temporal windows, and a structure-guided coupling operation is then performed for each window to generate a sequence of coupled graphs. This comparison highlights an important methodological distinction: static coupling emphasizes topological integration at one graph level, whereas time-varying coupling emphasizes the joint treatment of graph reliability and temporal evolution. The figure therefore clarifies why dynamic coupled construction is methodologically richer but also more demanding than static graph coupling [6].

3.4. Comparison of Different Coupling Strategies

In general, structure-prior-constrained methods prioritize stability, graph-level cooperative fusion prioritizes representational completeness, and time-varying coupled graph construction attempts to balance stability and temporal sensitivity. None of these paradigms is universally optimal. Their suitability depends on the research objective.

If the goal is to obtain a relatively robust graph representation under small-sample conditions, structure-prior-constrained construction may be preferable. If the goal is to integrate multiple graph sources as comprehensively as possible, graph-level cooperative fusion is more suitable. If the target is to characterize evolving pathological network patterns, dynamic coupling becomes more valuable.

A further distinction concerns interpretability. Structure-prior-constrained graphs often remain easier to explain because the role of structural information is relatively explicit. In contrast, graph-level fusion may be more expressive but often blurs the semantic boundary between edge types. Dynamic coupled graphs add another level of complexity because both multimodal coupling and temporal variation must be interpreted simultaneously. Therefore, choosing a coupling strategy should involve not only performance considerations but also representational goals and interpretability requirements.

Table 2. Comparison of representative structure–function coupling paradigms.

Coupling paradigm	Core idea	Main advantage	Main limitation
Structure-prior-constrained construction	Functional graph is adjusted by structural prior	Clear rationale, better stability	Sensitive to weighting strength
Graph-level cooperative fusion	Multiple graphs jointly form a coupled graph	More complete multimodal representation	Different edge semantics are harder to unify
Time-varying coupled construction	Structural prior is applied window by window	Balances temporal sensitivity and topological stability	Higher complexity and stronger reliability requirements

Table 2 compares the major structure–function coupling paradigms from the viewpoints of construction logic, practical advantage, and methodological limitation. Structure-prior-constrained construction is attractive because it has a clear rationale and usually improves graph stability, but its effect depends heavily on how strongly structure is allowed to influence function. Graph-level cooperative fusion is more comprehensive and may better preserve multimodal information, yet it raises greater challenges in aligning edge semantics across graph sources. Time-varying coupled construction is particularly valuable for dynamic brain analysis because it preserves temporal sensitivity while using structure as a stabilizing prior, although it also introduces more parameters and higher reliability demands. The table shows that coupled graph construction is not a single technique but a family of design choices with different trade-offs [7].

4. Value for Brain Disease-Aided Identification

4.1. Improving Representational Completeness

Disease-related abnormalities are often distributed across several levels. Some are more visible in white matter pathways, some in functional interactions, and others in coordinated morphological degeneration. A representation built from only one of these perspectives may miss complementary disease evidence. Structure–function coupled graphs help gather these different forms of information into a more unified brain network representation [8].

From this viewpoint, coupled graphs are not merely a technical fusion product. They represent an attempt to shift from modality-isolated description toward network-level integration. This may provide a more appropriate foundation for brain disease-aided identification, especially when abnormality is subtle and distributed.

Representational completeness is especially relevant when disease effects are weak at the single-region level but more visible in cross-regional organization. A coupled graph can retain a broader range of abnormality-related evidence by jointly considering support pathways, coordinated activity, and morphology-related trends. In this sense, coupled graph construction expands the descriptive capacity of brain network analysis rather than simply increasing the dimensionality of the input [9].

4.2. Enhancing the Stability of Connectivity Estimation

Functional graphs are often informative but unstable. When the signal-to-noise ratio is low, when graph edges are weak,

or when dynamic windows are short, estimated functional connectivity can fluctuate considerably. If such graphs are directly used as the basis for downstream analysis, uncertainty in graph construction may propagate to later stages.

By introducing structural constraints or morphology-related associations, coupled graph construction can reduce clearly implausible connections and stabilize network topology. Even before any classifier is applied, this improvement in graph reliability is itself an important contribution. In that sense, coupled graph construction should be recognized not only as a pre-processing choice but as a central component of network representation design.

This stabilizing effect is particularly important in small-sample neuroimaging studies, where graph estimation uncertainty may significantly affect observed group differences. A more stable graph representation can improve reproducibility across folds, sessions, and preprocessing variants. Therefore, the value of structure–function coupling should also be assessed in terms of graph robustness, not only downstream prediction metrics.

4.3. Improving the Characterization of Disease-Related Abnormality

Some disorders are characterized by a mismatch between structural organization and functional coordination. For example, anatomical pathways may remain partly preserved while their associated functional interactions become disrupted, or conversely, abnormal synchronization may emerge among regions without strong direct structural links. A coupled graph is particularly useful in such situations, because it can distinguish between support topology and operating interaction.

This makes coupled representation especially relevant when the goal is not merely to classify subjects, but to describe how pathological network organization differs from healthy organization. In this broader sense, structure–function coupling contributes not only to identification but also to interpretation.

In addition, coupled graphs may help separate disease-relevant abnormality from incidental fluctuation. A functional edge that is statistically strong but structurally implausible may deserve different interpretation from one that is both functionally strong and structurally supported. Likewise, a region pair showing coherent morphological degeneration and altered functional interaction may be more biologically meaningful than one that appears abnormal in only one graph view. Thus, coupled construction does not merely merge information; it can also refine the interpretive hierarchy of abnormal patterns.

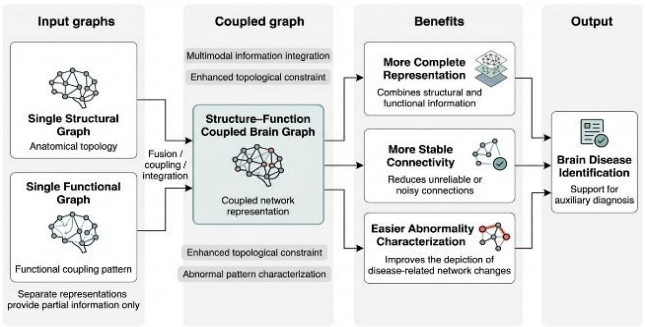

Figure 3. The role of structure–function coupled graphs in brain disease-aided identification

Figure 3 illustrates the practical value of coupled graphs in brain disease-aided identification. Compared with single structural or single functional graphs, a coupled brain network provides a representation that is more complete, more stable, and more capable of expressing disease-related mismatch patterns between topology and interaction. The figure is intended to show that the benefit of coupling is not restricted to data fusion in a narrow sense; rather, it lies in improving how brain abnormalities are organized and interpreted at the graph level. This is why coupled graph construction can contribute both to downstream identification performance and to the broader understanding of pathological network organization [10].

5. Open Problems and Future Directions

5.1. Modality Heterogeneity and Scale Inconsistency

A major challenge in coupled graph construction is modality heterogeneity. Structural connectivity, functional connectivity, and morphology-related association differ in biological meaning, numerical scale, and noise mechanism. Even when they are all represented as adjacency matrices, they do not naturally live in the same semantic space. This means that edge-level combination is not just a numerical problem but also a representation problem.

Future research needs to address how to preserve modality-specific meaning while enabling principled cross-modal alignment. Otherwise, coupled graphs may be mathematically convenient yet conceptually ambiguous. This issue becomes more serious when additional sources such as phenotype information or cognitive scores are introduced, because the question is no longer only how to combine different graphs but also how to relate graph-derived structure to non-graph clinical descriptors [11].

5.2. Bias in Connectivity Estimation and Graph Sensitivity

Brain graph construction is highly sensitive to atlas definition, edge estimation strategy, preprocessing decisions, and thresholding. In coupled graph settings, these uncertainties accumulate rather than disappear. Structural graphs may contain tractography bias, functional graphs may contain spurious coupling, and morphology-related graphs may be affected by feature selection and similarity design.

Accordingly, future studies should pay more attention to the robustness of graph construction itself instead of focusing exclusively on downstream performance. A graph representation that yields a strong classification score under one setting but is unstable across settings may not be reliable enough for broader scientific or clinical use.

One promising direction is to explicitly model uncertainty during graph construction. Instead of treating every edge as equally trustworthy, future coupled construction frameworks may assign confidence estimates to edges or to graph components. Such confidence-aware design could help distinguish stable disease-related relationships from method-induced fluctuations [10].

5.3. Reliability of Dynamic Coupled Graph Construction

Dynamic coupling is promising because it can describe

evolving network patterns, but it is also more fragile than static coupling. Window length, step size, sparsification strategy, and temporal fluctuation all influence the resulting graph sequence. If consecutive coupled graphs vary too dramatically due to estimation noise, dynamic analysis may become unreliable.

Potential future directions include adaptive windowing, temporal smoothness constraints, and confidence-aware edge update mechanisms. These could improve the repeatability of dynamic coupled graph sequences and make them more suitable for studying disease-related temporal variation.

Another challenge is that dynamic coupling requires one to distinguish true temporal evolution from graph estimation instability. Without this distinction, a sequence of graphs may appear dynamic even when part of the observed variation is only methodological. Therefore, future work should pay more attention to validating whether detected temporal changes correspond to biologically meaningful shifts rather than artifact amplification.

5.4. Biological Interpretability and Clinical Usefulness

For brain disease-aided identification, improved graph construction is valuable only if the resulting graphs can eventually support meaningful interpretation. A coupled graph that is mathematically effective but biologically opaque may have limited clinical usefulness. Therefore, future work should place greater emphasis on identifying key regions, key pathways, and key structure–function relationships that contribute most strongly to pathological differentiation.

This also suggests that evaluation criteria should not be limited to predictive performance. Interpretability, robustness, and biological plausibility should play a much larger role in judging the quality of structure–function coupled brain network construction.

In clinical settings, the usefulness of a coupled graph is not determined solely by whether it improves a numerical score. It also depends on whether clinicians and researchers can understand why a subject is flagged as abnormal, whether the highlighted regions and pathways align with known disease mechanisms, and whether the method remains stable across sites and scanners. These broader requirements make interpretability and generalizability central rather than optional goals.

5.5. Toward More Reliable Coupled Graph Representation

Looking forward, future advances may come less from simply increasing model complexity and more from improving representational principles. More reliable coupled graph construction may require subject-specific adaptive fusion, uncertainty-aware edge modeling, biologically informed regularization, and better integration between static structural priors and dynamic functional evidence. Rather than asking only how to fuse graphs, future studies may increasingly ask what kind of graph should be constructed for a specific scientific or clinical purpose [12].

This shift in emphasis would help reposition coupled graph construction as a core methodological problem in multimodal brain network analysis. Such a perspective is likely to be especially valuable in brain disease-aided identification, where the quality of the graph representation strongly influences both downstream performance and interpretability [13].

6. Conclusion

Structure–function coupled brain network construction provides an alternative research path to approaches that focus mainly on increasingly complex classifiers. Its central concern is not simply how to maximize predictive performance, but how to construct a brain network representation that is more stable, more informative, and more consistent with disease-related abnormalities. From this perspective, structural connectivity, functional connectivity, and morphology-related association should be regarded as complementary sources rather than competing descriptions.

Although current coupling methods have shown promise in improving graph stability, integrating multimodal information, and enhancing the characterization of network abnormalities, substantial challenges remain in modality alignment, graph reliability, dynamic coupling, and biological interpretation. Continued work on these issues is likely to further strengthen the value of coupled graph construction in brain disease-aided identification.

Acknowledgements

We thank all the anonymous reviewers for their hard reviewing work

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