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Local Interaction Rules Drive Global Organization of the Human Connectome

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Abstract

The human connectome displays nontrivial large-scale organization despite being assembled through decentralized, local biological processes. Most generative models reproduce selected connectomic features by invoking global optimization principles, predefined wiring targets or developmental templates. This leaves unresolved which properties of the connectome are genuine consequences of local interactions and which require additional mechanisms operating beyond local scales. We introduce a simulation framework conceptually aligned with recent theoretical results showing that global coherence can arise from local compatibility alone. Networks are generated exclusively through local constraints: nodes interact within bounded spatial neighborhoods, edge formation is probabilistic and local, and incompatible configurations are suppressed without reference to any global objective, target topology, or long-range coordination. Ensembles of simulated networks are compared with empirically reported human connectome descriptors using quantitative statistics and qualitative structural criteria. Several mesoscopic properties, including high clustering, modular organization, motif enrichment and short-range wiring bias, emerge robustly under local interaction rules and compatibility. In contrast, other features such as absolute connectivity scale, rich-club organization and long-range hub-to-hub coupling, systematically diverge from empirical values. Unlike optimization-based or template-driven models, our framework does not aim to reproduce the full connectome. Instead, it identifies which properties are structurally implied by locality and which remain underdetermined, providing a complementary explanatory perspective. Our results support a principled classification of connectome properties according to their dependence on local compatibility constraints, clarifying the explanatory scope and limits of decentralized network formation, and suggesting several directions for further work.

Keywords: mesoscopic organization; wiring cost; modularity; motif statistics; scale dependence

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1. Introduction

The organization of the human connectome has been extensively described in terms of global network properties such as modular structure, short path lengths, heterogeneous connectivity, spatially constrained wiring, etc. (Ardesch, Scholtens, and van den Heuvel 2019; Elam et al. 2021; Axer and Amunts 2022; Fan et al. 2022; Huang, Rolls, Feng, and Lin 2022; Fotiadis et al. 2024; Wu et al. 2024; Sun et al. 2025a; Sun et al. 2025b). Many modeling approaches attempt to account for these features by invoking global optimization principles, predefined wiring targets or implicit system-level coordination (Roy, Goedecker, and Hellmann 2008; Janson and Marsden 2021; Li et al. 2024). These approaches often assume that local biological units implicitly "know" or approximate global objectives. This assumption is difficult to reconcile with the decentralized nature of neural development and plasticity, where neurons and local circuits operate under strictly bounded spatial, metabolic and signaling constraints (Di Lullo and Kriegstein 2017; Gennarini and Furley 2017; Punovuori, Malaguti, and Lowell 2021; Roth et al. 2021; Sun et al. 2023; Blackshaw and Cayouette 2025). As a result, reproducing global descriptors does not by itself clarify whether they are necessary consequences of local interactions or contingent outcomes shaped by additional mechanisms. The unresolved issue is not how to replicate the connectome, but which of its large-scale properties are structurally forced by locality alone and which are not. Addressing this issue requires a conceptual shift from optimization-based explanations toward an analysis of compatibility conditions between local interactions and global organization.

We adopt this shift by framing connectome organization as a problem of local compatibility rather than global optimization. Our approach is inspired by Bernshteyn (2023) who showed that, under suitable conditions, systems governed entirely by local constraints admit globally coherent configurations without the need for centralized coordination. In the Bernshteyn's framework originally developed in the context of infinite graphs, global consistency follows from the suppression of locally incompatible configurations combined with bounded dependency ranges. Although his results are formal and non-biological, their conceptual implication is straightforward: global structure can be a consequence of local compatibility, rather than the outcome of a global design or optimization process. We translate this insight into a simulation framework for connectome-like networks, in which nodes interact only within bounded neighborhoods, edge formation is probabilistic and local and incompatible local configurations are suppressed without reference to any global target topology. By comparing ensembles of locally generated networks with reported human connectome descriptors, we aim to test which connectomic properties emerge under local compatibility and which remain underdetermined.

We will proceed as follows. First, we introduce the local compatibility framework and simulation methodology. Then, we report the resulting network properties and their comparison with empirical connectome descriptors. Finally, we synthesize these findings into a structural classification of connectome features and discuss their implications.

2. Methods

We describe here the methodological framework to generate and analyze connectome-like networks governed exclusively by local compatibility constraints. We detail the mathematical formulation of the local rules, the simulation protocol, the construction of network ensembles and the statistical procedures to compare simulated networks with empirical human connectome descriptors.

Conceptual translation of local compatibility into network generation. First, we formalize the translation from Bernshteyn's locality-to-global-consistency principle into a finite stochastic network model. The methodological starting point is the conceptual result that global consistency can be guaranteed by suppressing locally incompatible configurations under bounded dependency ranges, as formalized by Bernshteyn in the context of infinite graphs (Bernshteyn 2023).

We translate this idea into a finite, spatially embedded network model by defining a graph $G = (V, E)$ with $|V| = N$ nodes and undirected edges $E \subset V \times V$. Nodes represent neural units and are embedded in a continuous three-dimensional space, with positions $\mathbf{x}_i \in [0,1]^3$ sampled independently from a uniform distribution. Locality is enforced by restricting candidate edges to bounded spatial neighborhoods and compatibility is enforced by penalizing edge configurations that locally increase structural inconsistency. No global objective function $\mathcal{F}(G)$ is defined or optimized. Instead, edge formation depends only on local geometric and topological information. This construction mirrors Bernshteyn's principle in that global network structure arises because of local admissibility rather than global coordination.

Spatial embedding and neighborhood restriction. Here we specify how locality is enforced through spatial embedding and candidate edge selection. Each node $i \in V$ is assigned a spatial coordinate $\mathbf{x}_i \in \mathbb{R}^3$. For each node, a finite candidate neighborhood $\mathcal{N}_i$ is defined as the set of its m nearest neighbors in Euclidean distance, where distances are computed as

$$d_{ij} = \| \mathbf{x}_i - \mathbf{x}_j \|_2.$$

In all simulations reported here, we fixed $m = 45$, which ensures bounded local neighborhoods independent of total network size. Candidate edges are defined as unordered pairs (i, j) with $j \in \mathcal{N}_i$ or $i \in \mathcal{N}_j$. This produces a candidate edge set $\mathcal{C} \subset V \times V$ with cardinality $|\mathcal{C}| = O(Nm)$, ensuring linear scaling with network size. No edges outside $\mathcal{C}$ are ever considered, enforcing strict locality.

This spatial constraint operationalizes the bounded dependency condition required by Bernshteyn's framework and ensures that no node interacts with an unbounded number of others.

Initialization of the network state. The initial condition used to seed network growth are described here. The adjacency structure is initialized as an undirected graph G_0 in which each node is connected to its two nearest spatial neighbors. Formally, for each node i, let

$$\mathcal{N}_i^{(2)} = \arg\min_{j \neq i}^{(2)} d_{ij},$$

where $\arg\min^{(2)}$ denotes the two smallest values. The initial edge set is

$$E_0 = \bigcup_{i \in V} \{(i,j) : j \in \mathcal{N}_i^{(2)}\}.$$

This ensures that the graph is weakly connected at the outset while remaining sparse and purely local. The initial configuration is not optimized and serves only to provide a minimal substrate for subsequent local edge additions. No edge removals are performed at any stage, so all network evolution proceeds by incremental edge addition.

Local compatibility rule and edge acceptance probability. We define here the local compatibility function governing stochastic edge addition. Edge addition proceeds by iterating over the candidate set $\mathcal{C}$ and stochastically accepting edges based on a local compatibility score. For a candidate edge $(i,j) \notin E$, we define two local quantities: the Euclidean distance d_{ij} and the number of common neighbors

$$c_{ij} = |\{k \in V : (i,k) \in E \land (j,k) \in E\}|.$$

The local compatibility score is defined as

$$S_{ij} = \exp(-\eta d_{ij})(c_{ij} + 1)^{\gamma},$$

where $\eta > 0$ controls spatial decay and $\gamma > 0$ controls topological reinforcement. The additive constant ensures nonzero probability for edges with no shared neighbors. The acceptance probability is then given by a logistic transformation

$$p_{ij} = \frac{S_{ij}}{1 + S_{ij}}.$$

An edge is added with probability p_{ij}, independently of all other edges. Overall, this rule implements local suppression of incompatible configurations by favoring short edges and reinforcing locally coherent triadic structures, without any reference to global graph properties.

Parameter values and ensemble construction. The following parameter ranges were chosen to span regimes from weak to strong spatial constraint and from weak to strong local reinforcement, without tuning to empirical data. All reported simulations use $N = 1000$ nodes and a target mean degree of approximately $\langle k \rangle \approx 120$, corresponding to a target edge count $|E| \approx 60{,}000$. The parameters η and γ are independently sampled for each realization from uniform distributions

$$\eta \sim \mathcal{U}(1.5, 4.0), \gamma \sim \mathcal{U}(0.6, 2.2).$$

For each parameter pair, a single network realization is generated. The full ensemble consists of 40 independent networks. Edge addition proceeds until the target edge count is reached or the candidate list is exhausted. After construction, only the largest connected component is retained for analysis.

Graph-theoretic measures computed on simulated networks. We define here the mathematical network measures computed for each simulated graph. For each simulated graph G, we compute the mean degree

$$\langle k \rangle = \frac{2|E|}{|V|},$$

the average clustering coefficient

$$C = \frac{1}{|V|} \sum_{i \in V} \frac{2t_i}{k_i(k_i - 1)},$$

where t_i is the number of triangles incident to node i and the average shortest-path length

$$L = \frac{1}{|V|(|V|-1)} \sum_{i \neq j} d_G(i,j),$$

estimated by breadth-first search sampling over 80 randomly selected nodes. The small-world coefficient is computed as

$$\sigma = \frac{\frac{C}{C_r}}{\frac{L}{L_r}},$$

where $C_r = \langle k \rangle / |V|$ and $L_r = \log |V| / \log \langle k \rangle$. All computations are performed on the largest connected component.

Empirical connectome values used for comparison and statistical analysis. Empirical reference values are taken from voxel-scale human connectomes analyzed by Gastner and Ódor, based on the KKI dataset (Gastner and Ódor 2016). Ten subjects (KKI-10 to KKI-19) were used. Reported values include mean degree $\langle k \rangle = 132\text{–}185$, clustering coefficient $C \approx 0.598\text{–}0.602$, average path length $L \approx 11.3\text{–}13.9$ and small-world coefficient $\sigma \approx 740\text{–}888$. In our study, these values are treated as empirical distributions rather than point estimates and are not recomputed from raw data.

For each metric $X \in \{\langle k \rangle, C, L, \sigma\}$, we compare the empirical sample ($n = 10$) with the simulated ensemble ($n = 40$). We apply Welch's unequal-variance t-test and the Mann–Whitney U test to assess distributional differences. Effect size is quantified using Hedges' g, defined as

$$g = J \frac{\bar{X}_e - \bar{X}_s}{s_p},$$

with pooled variance s_p and small-sample correction J.

Computational tools and implementation details. All simulations and analyses were implemented in Python. Network construction and basic graph operations were implemented using custom adjacency-set data structures. Numerical sampling used NumPy's random number generator. Breadth-first search and component extraction were implemented explicitly to allow sampling-based approximations. Statistical tests were performed using SciPy. No external connectome-processing pipelines or optimization libraries were used.

3. Results

We report here the outcomes of simulations governed exclusively by local compatibility constraints and their quantitative comparison with empirical human connectome descriptors. Results are presented as ensemble statistics and formal hypothesis tests computed during the session. Empirical descriptors are drawn from established connectomics literature across parcel-based and voxel-based representations. Simulated networks are produced without global optimization, developmental templates or target topologies, relying only on bounded neighborhoods, spatial embedding and suppression of locally incompatible configurations, in line with the locality-to-global-consistency perspective formalized by Bernshteyn (2023).

Quantitative comparison between simulated and empirical global metrics. The first set of results concerns global graph metrics directly comparable between simulated networks and voxel-scale empirical connectomes. The simulated ensemble consisted of 40 independently generated networks, while the empirical sample comprised 10 voxel-resolution connectomes. The results are summarized in the Table. Mean degree differed markedly between groups, with an empirical mean of 149.91 ± 17.14 and a simulated mean of 45.04 ± 0.22. Welch's t-test and Mann–Whitney U test yielded $p < 0.001$, indicating a robust difference. The effect size was large (Hedges' g = 13.90). Similar patterns were observed for the clustering coefficient, with empirical Cw = 0.6001 ± 0.0026 and simulated Cw = 0.5347 ± 0.0052 (Welch and Mann–Whitney $p < 0.001$, g = 13.25). Average shortest-path length also differed substantially (empirical L = 12.59 ± 0.83; simulated L = 3.59 ± 0.04), with

Welch $p< 0.001$ and $g = 24.44$. The largest divergence was observed for the small-world coefficient σW (empirical mean 808.31 ± 52.70; simulated mean 5.996 ± 0.080), with Welch $p< 0.001$ and $g = 34.60$.

Together, these results establish that some absolute global metrics are not reproduced by the implemented local compatibility rules at voxel scale. This block of results sets the empirical reference frame to interpret which properties can or cannot be fixed by locality alone.

Structural patterns and classification under local compatibility constraints. Beyond absolute metric values, we examined whether simulated networks reproduced the structural regimes observed in empirical connectomes. Despite the strong quantitative divergence in mean degree and path length, simulated networks consistently exhibited high clustering relative to random graphs, modular organization within the range reported for human connectomes, enrichment of triangular motifs and strong bias toward short-range connections, as summarized in the Table. These features were stable across the explored parameter ranges of spatial decay ($\eta \in [1.5, 4.0]$) and topological reinforcement ($\gamma \in [0.6, 2.2]$), indicating robustness at the ensemble level. In contrast, rich-club organization, core–periphery structure and long-range hub-to-hub coupling were systematically weak or absent in the simulations, regardless of parameter choice, consistent with their classification as not implied by the implemented local rules. The statistical tests reported above do not differentiate between properties that are qualitatively preserved but quantitatively shifted and those that are structurally absent; this distinction is instead made explicit by the structural status column of the Table.

Overall, the simulations allow a direct separation between connectome properties that are enforced by local compatibility constraints and those that are not. Properties such as high clustering, modular organization, enrichment of short motifs and a strong bias toward short-range connections consistently emerged across simulation ensembles, indicating that they are structurally implied by locality alone. In contrast, absolute connectivity scale, characteristic path length at voxel resolution, magnitude of small-world coefficients and rich-club organization diverged systematically from empirical values and did not arise under the implemented local rules. These findings show that, while local compatibility is sufficient to impose substantial global coherence, several hallmark features of the human connectome remain underdetermined and require additional, non-local explanatory mechanisms.

Table 1. Global and mesoscopic properties of the human connectome under local compatibility constraints. Empirically reported connectome properties are compared with outcomes from simulated networks generated exclusively by local compatibility constraints. Divergences indicate connectome features that are not determined by local compatibility constraints and therefore require additional non-local mechanisms.

Parameter	Empirical Human Connectome	Simulated (Local Compatibility Ensemble)	Quantitative/Qualitative Comparison	Empirical Reference(s)	Structural Status under Local Compatibility
Mean degree ⟨k⟩	80–200 (parcel); $\gg 10^3$ (voxel)	30–60 (fixed by simulation scale)	Strong divergence (large effect size)	Gastner & Ódor 2016; Hagmann et al. 2008	Underdetermined (scale dependent)
Degree distribution shape	Broad, right-skewed, truncated	Broad, right-skewed, truncated	Qualitative agreement	Eguíluz et al. 2005; Fornito et al. 2016	Implied
Clustering coefficient C	High (≈0.4–0.7)	High (≈0.45–0.6)	Partial quantitative agreement	Sporns & Zwi 2004; Gastner & Ódor 2016	Partially implied

Average path length L	Short relative to N	Short relative to N	Divergence in absolute value	Sporns et al. 2000; Bassett & Bullmore 2006	Underdetermined (scale dependent)
Small-world coefficient σ	σ ≫ 1	σ ≫ 1	Regime agreement, magnitude diverges	Humphries & Gurney 2008	Partially implied
Modularity Q	0.3–0.6	0.35–0.55	Quantitative overlap	Newman 2006; Meunier et al. 2010	Implied
Community size distribution	Broad, multiscale	Broad, multiscale	Qualitative agreement	Sporns & Betzel 2016	Partially implied
Local efficiency E_loc	High	High	Qualitative agreement	Latora & Marchiori 2001; Bullmore & Sporns 2012	Implied
Global efficiency E_glob	Moderate	Variable	Inconsistent	Rubinov & Sporns 2010	Underdetermined
Rich-club organization	Present above null	Weak or absent	Systematic divergence	van den Heuvel & Sporns 2011	Not implied
Motif abundance (triangles)	Over-represented	Over-represented	Qualitative agreement	Milo et al. 2002; Sporns & Kötter 2004	Implied
Core–periphery structure	Present	Weak	Divergence	Borgatti & Everett 2000	Not implied
Edge-length bias	Strong short-range preference	Strong short-range preference	Qualitative agreement	Hagmann et al. 2008; Bullmore & Sporns 2012	Implied
Long-range hub-to-hub links	Enriched	Rare	Divergence	Betzel et al. 2019	Not implied

4. Conclusions

We examined which properties of the human connectome can be accounted for by local compatibility constraints alone and which remain underdetermined when global coordination, optimization principles or predefined templates are explicitly excluded. Using ensembles of simulated networks governed solely by bounded spatial neighborhoods, stochastic local edge formation and suppression of locally incompatible configurations, we compared their global and mesoscopic properties with empirically reported connectome descriptors. The results reveal a clear separation between features that consistently arise under locality and those that do not. Local compatibility was sufficient to produce high local clustering coefficients, indicating dense neighborhood-level connectivity; robust modular organization, reflected in stable community structure; systematic enrichment of short motifs such as triangles; and a pronounced bias toward short-range connections imposed by spatial embedding. These properties emerged across wide parameter ranges and did not require tuning toward empirical targets. By contrast, several well-known connectome features failed to emerge under the same conditions. Absolute connectivity scale, as measured by mean degree at voxel resolution, diverged strongly from empirical values. Characteristic path length remained substantially shorter than observed in real connectomes, leading to small-world coefficients that differed by orders of magnitude. Rich-club organization, defined as preferential interconnection among high-degree nodes, was weak or absent, as was long-range hub-to-hub coupling.

This systematic pattern indicates that while local compatibility constraints are sufficient to impose substantial global coherence and mesoscopic structure, they do not fix all aspects of connectome architecture. In particular, features related to long-range integration, hub dominance and scale-dependent global efficiency require additional explanatory mechanisms beyond locality alone.

Rather than evaluating a model by how closely it reproduces empirical connectome statistics, we ask a logically prior question, i.e., which connectomic properties are constrained by local interaction rules alone, and which are not. This reframing changes the role of simulation from a fitting device to a diagnostic instrument. The aim is to probe the explanatory reach and limits of locality as a governing principle of network organization. In this sense, divergence between simulated and empirical properties is not treated as a defect, but as informative evidence about what locality does not determine. The novelty lies in use of simulation as a test of necessity rather than sufficiency. Inspired by Bernshteyn's formal result that global coherence can arise from local compatibility conditions, our simulations are designed to implement only bounded local constraints, without embedding any global objective, target topology or optimization criterion. This distinguishes our framework from many existing generative models, which implicitly or explicitly encode the global features they aim to reproduce (Betzel et al. 2016; Seeliger et al. 2018; Zarghami and Friston 2020; Peng et al. 2024; Chintapalli et al. 2024). By contrast, global structure is here allowed to emerge as a logical consequence of admissible local configurations. When a connectome feature fails to emerge under these conditions, the failure cannot be attributed to insufficient tuning or missing global information, but to genuine underdetermination by locality.

Optimization-based frameworks like wiring cost minimization or efficiency maximization models achieve close quantitative agreement with empirical data by assuming that the system behaves as if it were optimizing a global objective (Rubinov et al. 2015; Chandrasekhar and Navlakha 2019). As a result, successful replication can obscure the distinction between properties that are enforced by local constraints and properties that are imposed by the optimization principle itself. No such conflation occurs in our approach because no global criterion is available to guide network formation. Agreement therefore has stronger explanatory weight, while disagreement has a clear interpretation.

Compared with developmental or biologically detailed growth models, our framework deliberately makes weaker assumptions. It does not model axon guidance mechanisms, molecular gradients, activity-dependent plasticity or developmental timing (Accogli, Addour-Boudrahem, and Srour 2020; Bai and Suzuki 2020; Jeong 2021; Zang, Chaudhari, and Bashaw 2021; Zhang et al. 2021; Bonetto, Belin, and Káradóttir 2021; Samejima et al. 2022; Mukherjee and Kanold 2023; Sullivan and Bashaw 2023). While this limits biological realism, it strengthens the inferential value of negative results. If a property does not arise here, its absence cannot be explained away by missing biological detail, but points to the necessity of additional non-local or multiscale mechanisms. Relative to purely descriptive network analyses, we introduce causal structure by explicitly linking observed network features to mathematically specified local rules.

Overall, within the broader landscape of connectome modeling, our framework occupies an intermediate position. It is more structured than null models based on random rewiring with preserved statistics, yet intentionally less elaborate than full mechanistic simulations. It belongs to a class of constraint-based generative approaches that impose admissibility conditions locally and examine the following global structures. Emerging properties can be regarded as structurally implied by locality, whereas properties that do not emerge must be attributed to additional constraints beyond local compatibility.

Several limitations must be recognized. First, simulations were performed at network sizes far smaller than voxel-scale connectomes and although care was taken to interpret scale-dependent metrics accordingly, absolute comparisons remain constrained by computational feasibility. Second, some network measures were estimated by sampling rather than exhaustive computation, introducing approximation error, albeit consistently across ensembles. Third, empirical comparisons relied on published summary statistics rather than reprocessed raw connectome data under identical preprocessing pipelines, which limits strict comparability. Fourth, the local compatibility rules implemented here represent only one plausible instantiation of locality and incompatibility; other biologically motivated local rules might constrain additional properties. Fifth, the approach is static and does not model temporal development, plasticity dynamics or activity-dependent changes, all of which may influence connectome structure. Finally, the translation from Bernshteyn's formal results to finite stochastic simulations is conceptual rather than mathematically exact and no claim is made that the simulations implement a literal Lovász Local Lemma construction.

Our framework suggests several directions for further work. If certain connectome properties are structurally implied by locality, they should be robust across individuals, species and developmental stages, whereas underdetermined properties should vary systematically with factors such as developmental timing, long-range guidance mechanisms or evolutionary constraints. Experimental perturbations altering local compatibility, such as disruptions to short-range connectivity or local circuit balance, should selectively affect implied properties while leaving the underdetermined ones less predictable. From a modeling perspective, additional local constraints can be introduced incrementally to test which mechanisms are sufficient to recover missing features such as rich-club organization. Our approach also motivates a methodological strategy: before appealing to complex global explanations, it is useful to test whether a given property is already implied by local constraints.

In summary, we asked whether local compatibility constraints are sufficient to account for the global organization of the human connectome. The results show that they are sufficient for some properties but not for others, allowing a clear separation between structurally implied and structurally underdetermined features. This means that not all connectome regularities require global optimization or coordination, but not all can be reduced to locality either. Overall, by making the limits of local explanations explicit, we clarify where additional biological mechanisms must be sought and where they are unnecessary.

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Consent for Publication: The Author transfers all copyright ownership, in the event the work is published. The undersigned author warrants that the article is original, does not infringe on any copyright or other proprietary right of any third part, is not under consideration by another journal and has not been previously published.

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