Arousal modulates functional connectivity through structured and hemispherically asymmetric community architecture during wakefulness

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Abstract

Arousal fluctuates continuously during wakefulness, yet how these moment-to-moment variations shape large-scale functional connectivity (FC) remains unclear. Here, we combined 7T fMRI with concurrent pupillometry to quantify, for every functional connection, how time-varying FC covaries with spontaneous arousal in the awake human brain. Rather than exerting a uniform influence across the connectome, arousal organized FC into a low-dimensional set of seven connectivity communities, each defined by characteristic network compositions. These communities exhibited systematic but community-specific hemispheric asymmetries, revealing distinct patterns of lateralized arousal modulation. Notably, the ventral attention network showed a pronounced division of labor: left-hemisphere nodes participated flexibly across multiple arousal-sensitive communities, whereas right-hemisphere nodes formed a cohesive, segregated arousal-responsive module. Importantly, hemispheric asymmetry did not arise from global shifts in connectivity strength, but instead reflected structured spatial heterogeneity embedded within community architecture. This modular and asymmetric organization was highly preserved during naturalistic movie watching, indicating that arousal-related modulation of FC reflects intrinsic principles that generalize across awake cognitive contexts. Together, these findings demonstrate that moment-to-moment arousal fluctuations shape large-scale FC through structured, hemispherically asymmetric network organization during wakefulness.

Key words: Arousal; time-resolved functional connectivity; modular organization; hemispheric lateralization; network hierarchy; spatial heterogeneity

Introduction

Arousal is a core dimension of brain state that shapes perception, attention, and the coordination of large-scale neural systems. Across major transitions—such as wakefulness to sleep, anesthesia, or disorders of consciousness—substantial reorganization of functional connectivity (FC) has been consistently observed (Chow et al., 2013; Tagliazucchi et al., 2016; Demertzi et al., 2019; Banks et al., 2020; Damaraju et al., 2020; Huang et al., 2020; Jang et al., 2024). These state-based findings demonstrate that arousal fundamentally influences whole-brain communication patterns. However, such approaches typically contrast discrete arousal states and therefore provide limited insight into how moment-to-moment fluctuations in arousal within the awake brain influence the organization of functional connectivity.

Increasing evidence shows that arousal varies continuously even during stable wakefulness, including during resting-state fMRI and ongoing cognitive engagement. These spontaneous fluctuations, often indexed by pupil diameter (Reimer et al., 2014; McGinley et al., 2015; Joshi & Gold, 2020), modulate neural gain, sensory responses, and behavioral performance. Yet despite their ubiquity and behavioral relevance, it remains largely unknown how fine-grained arousal variations are expressed across the functional connectome. Prior work has primarily examined regional signal amplitude or isolated networks (Yellin et al., 2015; Schneider et al., 2016; Breeden et al., 2017; Podvalny et al., 2021; Sobczak et al., 2021; Lloyd et al., 2023), thereby leaving unresolved the fundamental question of whether the awake brain's FC is uniformly sensitive to arousal or whether arousal instead imprints structured spatial patterns across functional networks.

A parallel question is whether arousal-related connectivity patterns show hemispheric asymmetry, given longstanding evidence for lateralized arousal, vigilance, and alerting mechanisms. Studies of unihemispheric sleep and lateralized arousal

dynamics in animals (Rattenborg et al., 2000; Lyamin et al., 2016; Mascetti, Gian Gastone, 2016; Reicher et al., 2021; Fenk et al., 2023; Libourel et al., 2023), asymmetries in human EEG-based vigilance (Tamaki et al., 2016), and right-lateralized alerting functions in attention (Heilman & Abell, 1980; Sturm & Willmes, 2001; Shulman et al., 2010; Corbetta & Shulman, 2011) all suggest that arousal may modulate left and right hemispheric systems differently. Nevertheless, these observations have yet to be linked to the organization of whole-brain functional interactions, and it remains unknown whether such asymmetries manifest at the level of large-scale FC, and whether they reflect organized connectivity patterns rather than non-specific global effects.

To address these questions, we combined high-field fMRI with concurrent pupillometry to quantify, for every functional connection, how its connectivity covaries with spontaneous arousal fluctuations during wakefulness. This edgewise measure of arousal–FC coupling provides a comprehensive map of where in the connectome arousal leaves its strongest imprint, without imposing predefined states or regional assumptions. Using this framework, we first test whether arousal sensitivity is spatially homogeneous or segregates into distinct sets of connections with similar coupling profiles. We next assess whether these spatially organized arousal-related patterns show systematic hemispheric asymmetry, with particular emphasis on attentional systems that show known lateralization. Finally, we evaluate the cross-context stability of this organizational structure by comparing resting state and naturalistic movie watching in the same participants. Together, these analyses delineate how moment-to-moment arousal fluctuations shape large-scale functional architecture in the awake human brain.

Results

The processing procedure of estimating arousal–FC coupling from fMRI and pupillometry was illustrated in Figure 1. Here, we use the term arousal–FC coupling to refer to the regression-based estimate of how spontaneous arousal fluctuations modulate each functional connection over time.

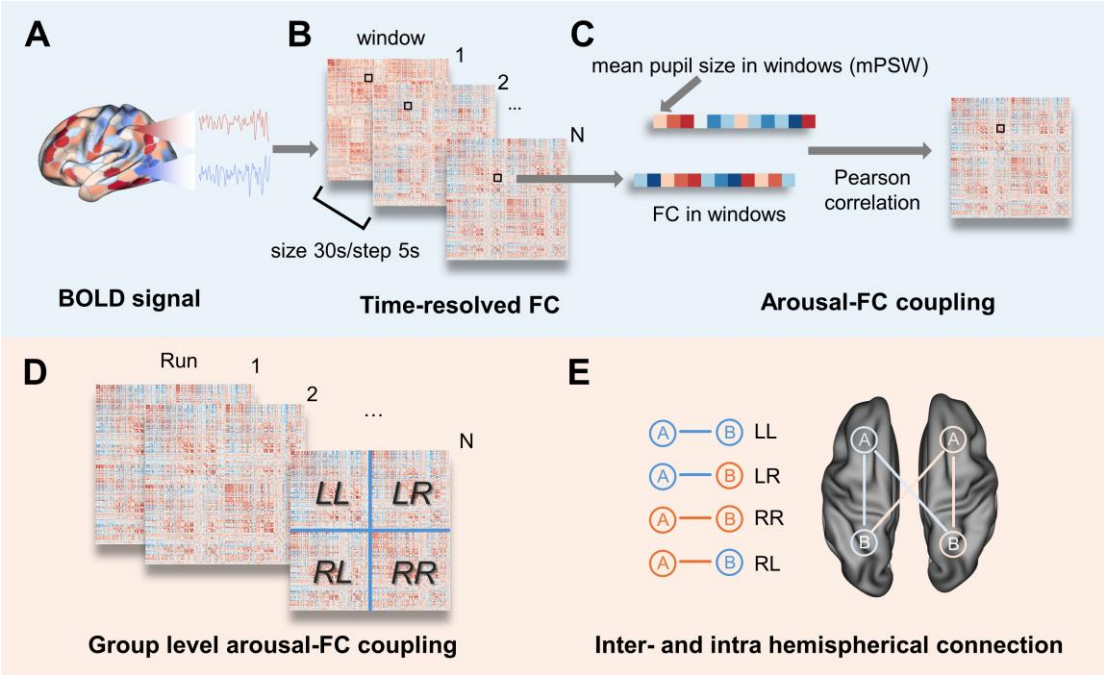

Figure 1. Pipeline for estimating arousal–FC coupling from fMRI and pupillometry. (A) Concurrent 7T fMRI and eye tracking were collected during resting state and naturalistic movie watching. **(B)** Functional connectivity (FC) was computed over sliding windows to obtain time-resolved FC for each pair of brain regions. **(C)** Pupil diameter was preprocessed to obtain a continuous arousal time series. Arousal–FC coupling for each connection was then defined as the Pearson correlation between its windowed FC time course and the corresponding arousal fluctuations. **(D)** These edgewise coupling values yielded a dense arousal–FC coupling matrix per run, which served as the input for analyses of community structure, hemispheric asymmetry, and cross-paradigm consistency. **(E)** The connections were categorized based on the hemispheres of the connected regions: Left-Left (LL) and Right-Right (RR) represent intra-hemispheric connections; Left-Right (LR) and Right-Left (RL) represent inter-hemispheric connections. This classification enabled hemisphere-specific analyses of arousal-FC coupling.

Arousal–FC coupling reveals seven distinct connectivity communities

For each functional connection, we quantified how strongly its time-varying connectivity covaried with moment-to-moment arousal, producing an edgewise

arousal–FC coupling matrix per run. Across all participants and runs, these coupling profiles showed clear structure: connections did not exhibit uniform arousal sensitivity but instead formed separable groups.

Unsupervised clustering of edgewise coupling patterns identified seven stable connectivity communities (Fig. 2A). This solution was consistently favored across a broad range of cluster numbers, indicating that arousal–FC coupling is inherently low-dimensional. The seven communities captured distinct patterns of arousal sensitivity across the connectome. Projecting each community into canonical network pairs space (Thomas Yeo et al., 2011) showed that these communities were not random mixtures of connections. Instead, each displayed a characteristic distribution across network pairs (Fig. 2B). Some communities were enriched in network pairs linking heteromodal and unimodal systems (Mesulam, 1998), while others were dominated by heteromodal–heteromodal (H-H) or unimodal–unimodal (U-U) network pairs. Community participation entropy further highlighted this structure: unimodal–unimodal connections showed low entropy, indicating a restricted participation in a few communities, whereas H-H and heteromodal–unimodal (H-U) connections showed significantly higher entropy, indicating more diverse engagement across communities ($p = 0.002$).

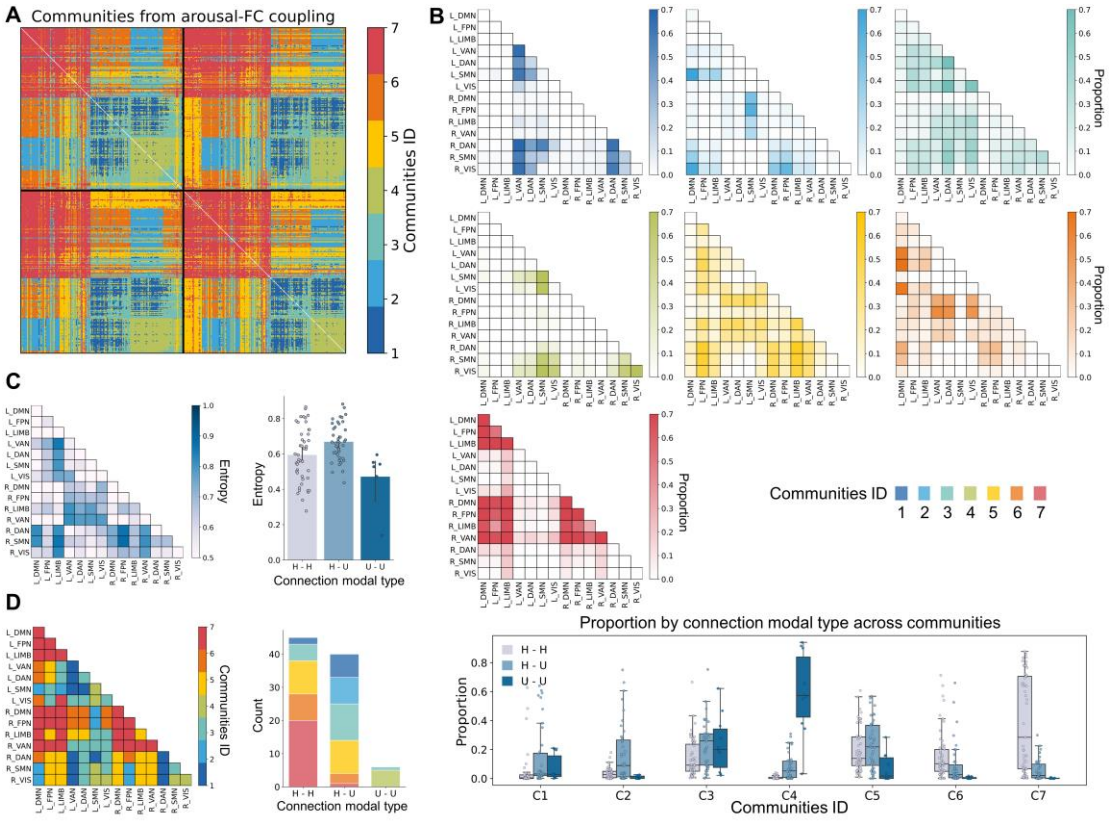

Figure 2. **Arousal–FC coupling partitions the connectome into seven distinct connectivity communities. (A)** Unsupervised clustering of edgewise arousal–FC coupling identified seven stable communities, demonstrating that arousal-linked modulation is organized into low-dimensional structure rather than uniformly distributed across connections. **(B)** Mapping communities onto network-pair space revealed distinct and reproducible composition profiles (upper panel), with some communities dominated by heteromodal interactions and others enriched in H–U or U–U network pairs (bottom panel). **(C)** Community participation entropy varied systematically across connection modal types: U–U network pairs showed lower entropy, indicating concentrated engagement in a small subset of communities, whereas H-H and H–U network pairs exhibited significantly higher entropy ($p = 0.002$), reflecting broader distribution across communities. **(D)** Dominant-community assignments confirmed this organization, showing that heteromodal interactions load onto multiple arousal-sensitive communities, whereas U–U network pairs show more restricted community involvement.

Together, these results demonstrate that arousal does not uniformly modulate the connectome but instead engages a small number of organized connectivity communities, each with distinct network-level compositions.

Arousal-related connectivity patterns exhibit systematic hemispheric asymmetry

We next asked whether these arousal-related communities express hemispheric biases. Using integration and segregation indices derived from LL, RR, LR, and RL edge categories, we quantified, for each community, whether arousal preferentially modulated intra- versus inter-hemispheric connectivity and whether these effects favored one hemisphere.

At the network-pair level, several pairs showed significant lateralization compared with a spatial permutation null model (Fig. 3A–B). Importantly, lateralization was not global: only specific network pairs within particular communities exhibited robust hemispheric biases, while others remained symmetric. Some communities showed rightward integration, indicating stronger arousal-related modulation of network pairs within the right hemisphere or between the right hemisphere and the rest of the brain, whereas others showed leftward segregation, reflecting preferential influence on within-left-hemisphere interactions.

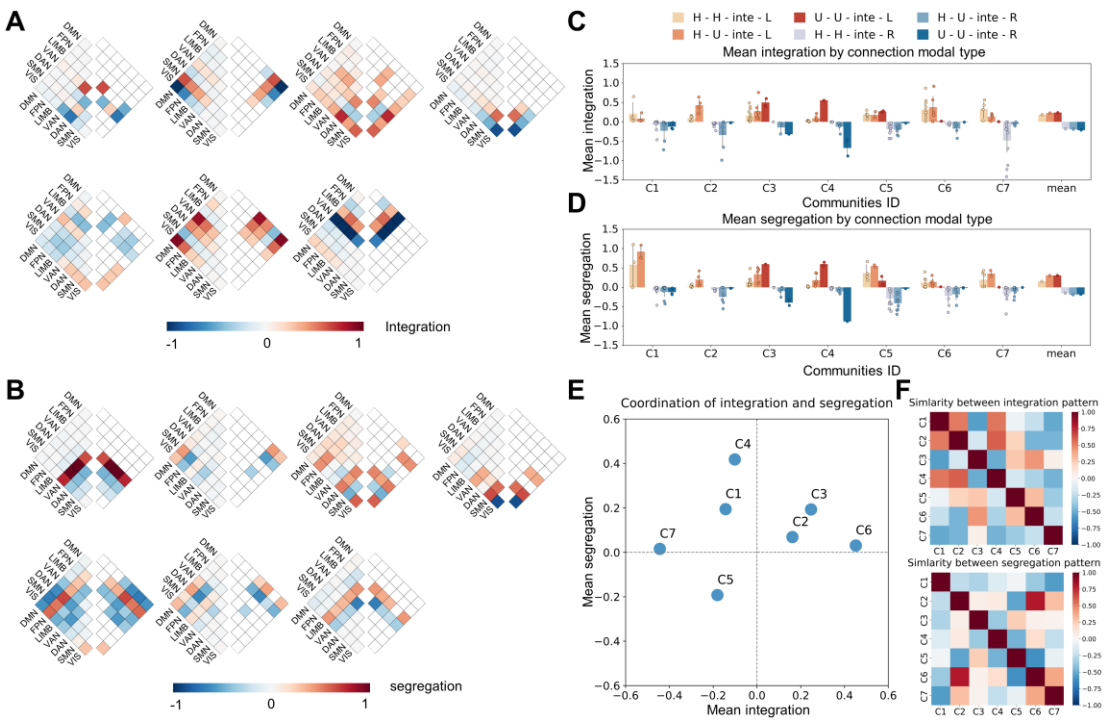

Figure 3. Arousal-related connectivity communities exhibit community-specific hemispheric asymmetry. (A) Integration indices for each network pair revealed significant leftward or rightward deviations from a spatial permutation null, indicating that arousal differentially

modulates between- and within-hemisphere interactions for specific network pairs. **(B)** Segregation indices identified network pairs showing hemisphere-specific strengthening of within-hemisphere connectivity, further demonstrating that lateralization is localized rather than global. **(C–D)** Community-averaged integration and segregation values showed that hemispheric biases vary across communities and are not determined solely by connection modal type, underscoring the community-specific nature of the asymmetry. **(E)** Aggregating all significantly lateralized network pairs, each community exhibited a distinct integration–segregation profile, revealing unique hemispheric signatures across communities. **(F)** Low similarity among communities' integration and segregation patterns confirmed that arousal imposes multiple, community-specific forms of hemispheric asymmetry, rather than a single unified left- or right-dominant pattern.

Averaging indices across connection modal types reinforced this community-specific patterning (Fig. 3C–D). Notably, identical connection modal types (e.g., H-H) could show leftward bias in one community but rightward bias in another, demonstrating that lateralization is tied to the community architecture rather than to the canonical network pair class. Aggregating all significantly lateralized network pairs, each community expressed a unique lateralization signature (Fig. 3E), and there was no clear cluster of lateralization patterns among communities (Fig. 3F), indicating heterogeneous, rather than unified, hemispheric influences of arousal on FC. Instead, arousal imprints distinct left–right biases across different connectivity motifs.

Regional affiliation patterns highlight a lateralized division of labor within the ventral attention network

Having established that arousal-modulated functional connections can be organized into modular communities with distinct hemispheric lateralization at the network level, we next explored the nodal-level mapping of these communities and the substantial variability in how regions participate in arousal-related communities. For each region, we computed its community affiliation for each brain region, defined as the proportion of edges connected to that region that were assigned to each of the seven communities, separately for LL, LR, RL, and RR edges (Fig. 4 A–B).

Next, we investigated the nodal-level community participation flexibility by

calculating the community affiliation entropy for each region. Nodal-level affiliation entropy showed a clear network gradient (Fig. 4C–D). Default modal network (DMN), frontoparietal network (FPN), and limbic (LIMB) regions exhibited lower entropy, indicating focused participation in fewer arousal-related communities. In contrast, dorsal attention network (DAN), somatomotor network (SMN), and visual (VIS) regions showed broader participation across communities ($p < 10^{-10}$).

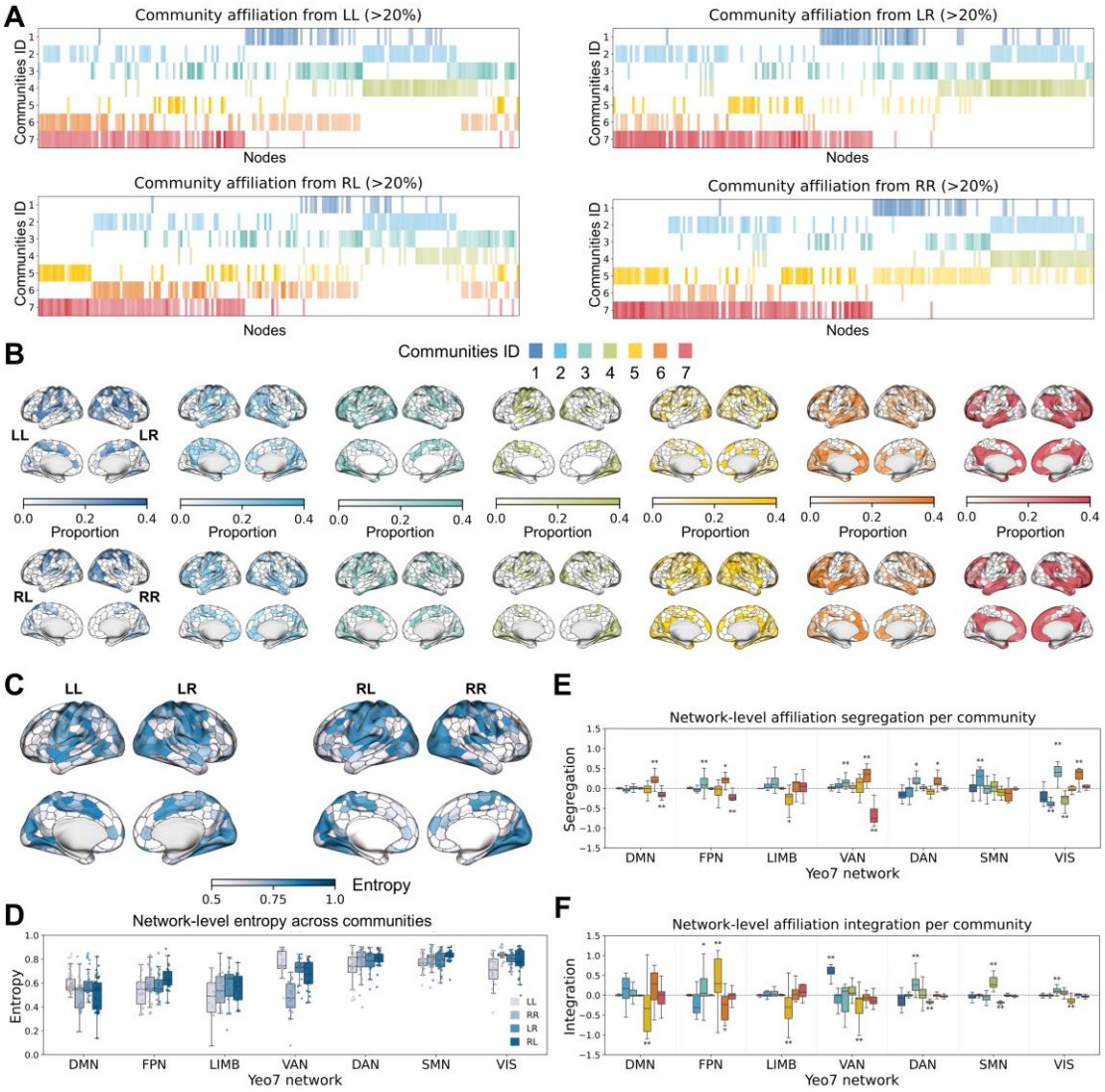

Figure 4. Regional affiliation patterns reveal a lateralized division of labor within the ventral attention network (VAN). (A–B) Nodal-level community affiliation matrices, computed separately for LL, LR, RL, and RR edges, showed substantial heterogeneity in how nodes distribute their arousal–FC coupling across the seven communities, with distinct patterns emerging across canonical networks. For visualization purposes, Figure A is restricted to displaying values where the proportion exceeds 0.2. **(C)** Nodal-level community affiliation entropy revealed a

systematic network gradient, in which heteromodal systems displayed more selective participation, whereas unimodal and dorsal attention regions showed broader, more distributed engagement across communities ($p < 10^{-10}$). **(D)** The VAN exhibited a pronounced hemispheric dissociation: the left VAN showed significantly higher entropy than the right VAN ($p < 10^{-10}$), indicating greater flexibility and broader multi-community participation. **(E)** Within the community most strongly recruiting the right VAN (community 7), we observed a significant rightward segregation bias ($p_FDR < 0.001$). **(F)** No corresponding integration bias was detected, suggesting that arousal selectively strengthens right intra-hemispheric cohesion without increasing cross-hemispheric coupling. The color of each box corresponds to the community identity. Statistical significance: * $p_FDR < 0.01$; ** $p_FDR < 0.001$.

Strikingly, the VAN showed a pronounced hemispheric dissociation: the left VAN exhibited significantly higher entropy than the right ($p < 10^{-10}$), indicating that left-hemisphere VAN nodes participate in more diverse arousal-linked connectivity patterns. Conversely, within community 7, which most strongly recruits the right VAN, we observed a significant rightward segregation bias ($p_FDR < 0.001$) but no integration bias, suggesting stronger within-right-hemisphere interactions than those in the left hemisphere when arousal modulating (Fig. 4E–F).

Together, these findings reveal a lateralized division of labor: left VAN → flexible, multi-community engagement; right VAN → cohesive, segregated arousal-related module. This asymmetry aligns with the hypothesized lateralization of alerting and reorienting functions (Corbetta & Shulman, 2002; Posner & Rothbart, 2007).

Arousal-related lateralization arises from spatial heterogeneity rather than mean shifts

In the preceding analyses, we mainly focused on the lateralization of the organizational patterns of the decomposed communities at the network-pairs and nodal levels. However, how the strength of the arousal–FC coupling is spatially distributed and whether lateralization exists in this distribution remains elusive. We therefore next examined the spatial distribution of arousal–FC coupling strength and its

lateralization properties.

To test whether hemispheric biases reflected simple shifts in mean arousal–FC coupling strength, we compared mean integration and segregation across communities and whole connectome. Although the inter-community difference for segregation was statistically significant (segregation: $p = 0.02$; integration: $p = 0.13$), the mean difference between communities was very small. This indicates limited hemispheric imbalance.

Although the mean arousal modulation on FC showed no significant lateralization, prior results suggested that its spatial pattern is highly community specific. We therefore hypothesized that the key information lies in the spatial heterogeneity (distribution gradient) of the modulation strength, not the overall strength. We therefore quantified spatial heterogeneity by ranking network pairs along a "lateralization axis" (Yang et al., 2025) and computing the slope of integration or segregation values along this axis. All communities showed slopes significantly steeper than the whole-brain baseline (all $p_{FDR} < 0.001$; Fig. 5B), demonstrating that lateralization arises from spatial heterogeneity—not uniform shifts.

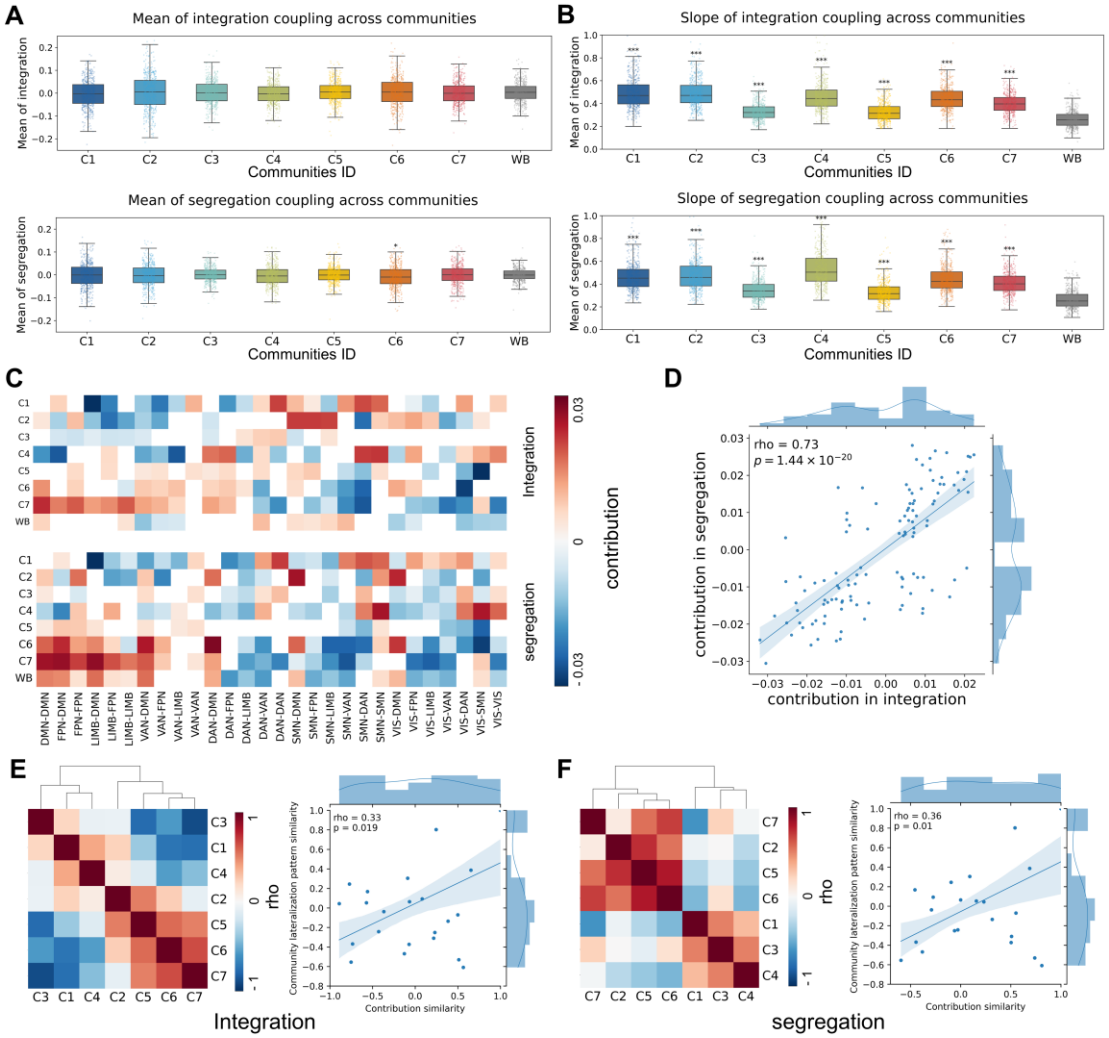

Figure 5. Spatial heterogeneity—not mean shifts—drives arousal-related hemispheric asymmetry. (A) Mean integration and segregation values showed no consistent hemispheric bias across individual communities or at the whole-brain (WB) level, indicating minimal imbalance in overall modulation strength. **(B)** Spatial heterogeneity, quantified as the slope of integration or segregation values ranked along a lateralization axis, was significantly steeper in every community compared with the whole-brain baseline (all p_FDR < 0.0001). These effects demonstrate that hemispheric asymmetry arises from spatially patterned variation, not from uniform shifts in mean modulation. **(C)** Leave-one-out analyses revealed that this heterogeneity reflects distributed contributions from many network pairs, rather than being driven by a few extreme edges. **(D)** Contribution patterns for integration and segregation were strongly correlated (rho ≈ 0.73), indicating coordinated spatial organization across metrics. **(E–F)** Similarity in contribution patterns between communities was positively associated with similarity in communities' intrinsic structure (integration: rho ≈ 0.33; segregation: rho ≈ 0.36), showing that spatial heterogeneity is constrained by each community's underlying connectivity architecture. Statistical note: * p_FDR < 0.01; ** p_FDR < 0.001; *** p_FDR < 0.0001.

Leave-one-out analyses showed that heterogeneity does not depend on a small set of

extreme network pairs. Instead, most pairs contributed modestly, producing broad, community-specific gradients (Fig. 5C). Contribution patterns for integration and segregation were highly correlated (rho ≈ 0.71). Furthermore, similarity in contribution patterns tracked similarity in intrinsic community structure (integration: rho ≈ 0.33; segregation: rho ≈ 0.36), indicating that spatial heterogeneity is shaped by underlying connectivity architecture (Fig. 5E–F).

Thus, arousal-driven lateralization is best understood as structured spatial heterogeneity within communities, rather than gross hemispheric dominance.

Community structure and hemispheric asymmetry are preserved during movie watching

To assess whether these organizational principles generalize beyond the resting state, we applied the same analytic pipeline to naturalistic movie-watching data from the same participants.

The seven-community structure was highly preserved across paradigms. After aligning communities using optimal Jaccard matching, Spearman correlations of community profiles were robust (rho ≈ 0.63; Fig. 6A–B). One heteromodal-dominated community involving the right VAN showed near-perfect correspondence (rho ≈ 0.95), suggesting that its arousal sensitivity is largely independent of external stimulation. Other communities also demonstrated strong cross-paradigm similarity, with only two showing moderate reductions—likely reflecting context-dependent modulation under rich sensory input.

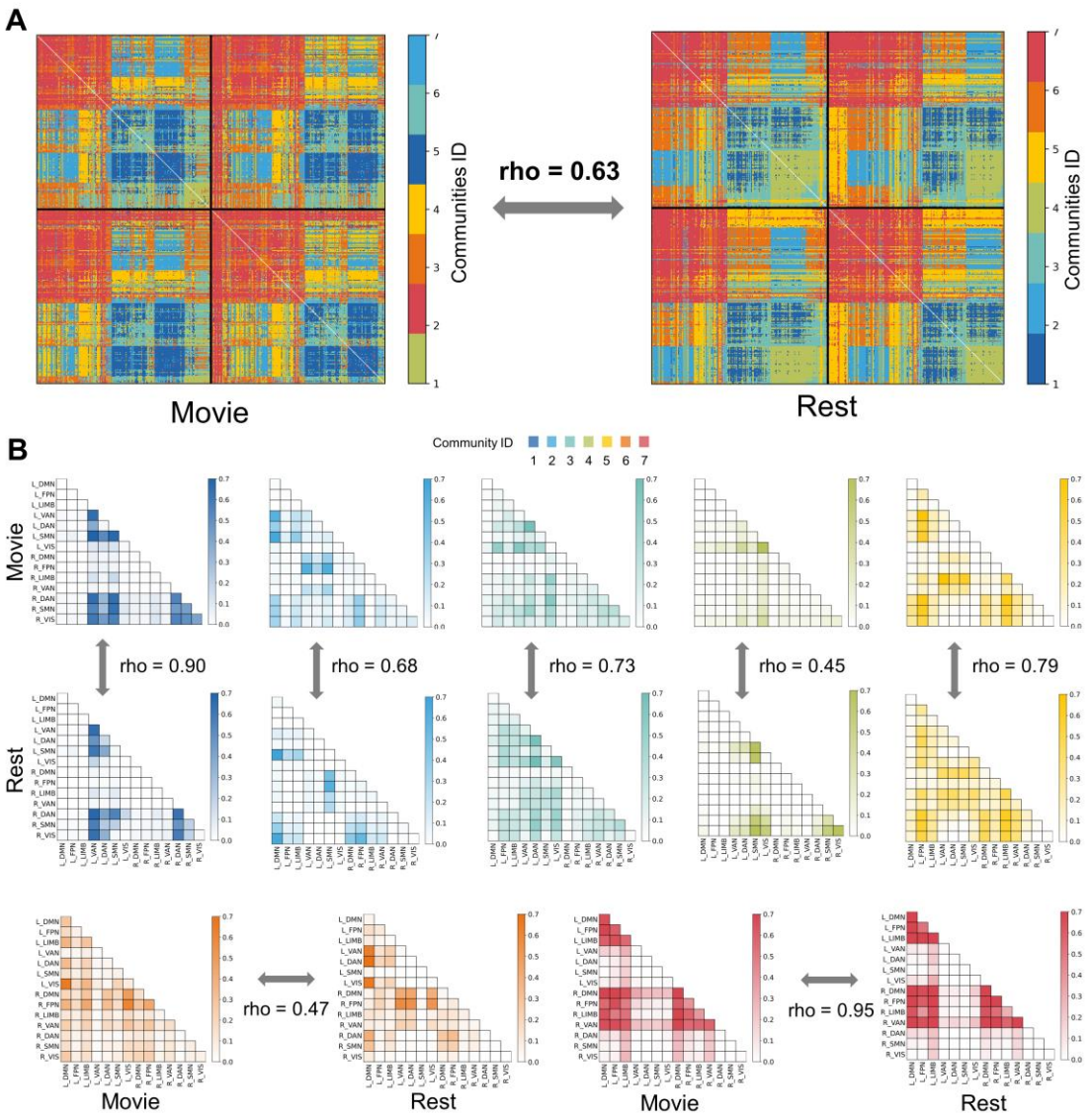

Figure 6. Community structure and hemispheric asymmetry of arousal–FC coupling are preserved across resting state and movie watching. (A) Communities derived from rest and movie data were aligned using Jaccard similarity–based optimal matching, revealing robust correspondence between paradigms (rho ≈ 0.63). (B) Network-pair composition profiles for each community were strongly correlated across paradigms (mean rho ≈ 0.72), indicating that the modular organization of arousal–FC coupling is highly stable across cognitive contexts. The heteromodal-dominated community (Community 7), which shows pronounced right-hemisphere segregation, exhibited exceptionally high cross-paradigm similarity (rho ≈ 0.95), suggesting context-independent expression of its arousal-linked lateralization pattern. Together, these findings demonstrate that arousal imposes a modular and lateralized connectivity architecture that remains highly consistent across resting and naturalistic movie-watching states.

These findings indicate that the modular, asymmetric organization of arousal–FC

coupling is not specific to rest but reflects intrinsic principles that persist across cognitive contexts.

Discussion

In this study, we investigated how moment-to-moment fluctuations in arousal shape large-scale functional connectivity in the awake human brain. By combining high-field fMRI with concurrent pupillometry, we quantified arousal–FC coupling at the level of individual edges and showed that arousal does not exert a uniform or diffuse influence across the connectome. Instead, it modulates connectivity through a set of seven distinct communities, each defined by characteristic network compositions and hemispheric patterns. These findings demonstrate that fluctuations in arousal, even within stable wakefulness, impose a structured and asymmetric organization on whole-brain functional interactions.

Although arousal is often conceptualized as a global modulatory state, our results show that its impact on FC is highly organized. The presence of low-dimensional, reproducible communities suggests that arousal modulates the connectome through coordinated motifs rather than homogeneous gain modulation, consistent with the differentiated projection patterns of modulatory systems such as the locus coeruleus–noradrenergic pathway (Aston-Jones & Cohen, 2005; Jordan, 2024) and thalamus (Magnin et al., 2010; Lewis et al., 2015; Liu et al., 2018). This organized pattern of modulation further supports the view advocated in recent years that vigilance states should be viewed as possessing spatiotemporal dynamics and regional complexity (Siclari & Tononi, 2017; Nir & De Lecea, 2023), and is strongly supported by prior work showing that spontaneous arousal fluctuations influence distributed cortical responses in selective ways (Reimer et al., 2014; McGinley et al., 2015). The hierarchical community pattern—where unimodal interactions cluster into fewer motifs while heteromodal systems participate broadly—is compatible with theories

that place heteromodal cortex at the apex of large-scale integrative gradients (Mesulam, 1998; Margulies et al., 2016). Together, these observations suggest that the arousal-sensitive connectome reflects not merely regional susceptibility but an emergent network-level architecture in which state-dependent modulation is embedded within large-scale organizational principles.

A major goal of this work was to determine whether arousal imposes systematic hemispheric asymmetry on FC. We found clear evidence that it does, but in a community-specific rather than global manner. Certain communities showed rightward integration, others leftward segregation, and others no significant bias—indicating that hemispheric asymmetry emerges from the organization of arousal-sensitive connectivity motifs rather than a single overarching hemispheric dominance. This distributed asymmetry resonates with converging evidence across species: unihemispheric vigilance in birds and marine mammals (Rattenborg et al., 2000; Lyamin et al., 2016; Mascetti, Gian Gastone, 2016; Reicher et al., 2021; Fenk et al., 2023; Libourel et al., 2023), asymmetric EEG signatures related to vigilance in humans (Tamaki et al., 2016), and classic findings of right-lateralized alerting and reorienting functions (Heilman & Abell, 1980; Sturm & Willmes, 2001; Shulman et al., 2010; Corbetta & Shulman, 2011). The VAN provided a compelling example: the left VAN displayed broad, flexible involvement across communities, whereas the right VAN formed a cohesive, segregated arousal-responsive module. This suggests that hemispheric specialization may arise from distinct modes of arousal-related reconfiguration rather than fixed structural asymmetries.

Despite the robustness of these hemispheric differences, mean integration and segregation of arousal-FC coupling strength across the entire community or whole brain showed minimal global lateralization. Instead, arousal-driven asymmetry manifested as spatially heterogeneous gradients within communities. Arousal does not uniformly shift connectivity toward one hemisphere; rather, it selectively amplifies

lateralization in specific connectivity motifs. This distributed, gradient-like pattern complements recent work highlighting macroscale cortical gradients and manifold structure as fundamental organizational principles (Margulies et al., 2016; Huntenburg et al., 2018). We further found that communities with similar intrinsic topology exhibited similar heterogeneity signatures, suggesting that baseline connectivity architecture constrains how arousal shapes hemispheric interactions. This provides a mechanistic explanation for why traditional hemisphere-level metrics often obscure arousal-related asymmetries—these effects are expressed not as global biases but as structured, topology-dependent gradients.

Another important observation is the stability of arousal–FC organization across cognitive contexts. The seven-community architecture was highly reproducible during naturalistic movie watching, and the strongly right-lateralized community involving the VAN showed near-perfect correspondence across paradigms. This robustness aligns with prior evidence that intrinsic connectivity organization persists across tasks (Cole et al., 2014; Krienen et al., 2014) and that spontaneous fluctuations in arousal modulate cortical dynamics even during rich sensory stimulation (Tanner et al., 2023). By demonstrating that arousal-driven network modulation generalizes across both internally and externally oriented states, our findings indicate that arousal acts as a stable organizing axis of large-scale brain communication, rather than merely a background physiological fluctuation.

Despite the important findings of this study, several limitations should be noted. Pupil diameter is an accessible but indirect marker of arousal (Joshi & Gold, 2020), and integrating it with EEG or brainstem imaging could refine interpretations. Sliding-window FC provides a straightforward estimate of time-varying connectivity, though alternative dynamic approaches may offer complementary perspectives. Furthermore, although we focused on group-level organization, individual differences in arousal–FC coupling likely carry behavioral or cognitive significance, presenting

opportunities for future studies. Finally, incorporating modulatory receptor maps or pharmacological perturbations may illuminate the neurochemical mechanisms underlying the connectivity communities we identified.

In summary, moment-to-moment fluctuations in arousal modulate functional connectivity through a small number of structured connectivity communities, each with distinct hemispheric characteristics. These asymmetries arise not from global shifts but from spatially heterogeneous gradients embedded within community structure. The reproducibility of these motifs across resting state and naturalistic stimulation suggests that they reflect stable and intrinsic principles by which arousal dynamically shapes large-scale brain interactions during wakefulness.

Methods and Materials

Participants and datasets

We used data from the Human Connectome Project (HCP) 7T dataset, which includes resting-state fMRI and naturalistic movie-watching runs with simultaneous eye tracking (Van Essen et al., 2013). Across participants, up to four resting runs and four movie runs were available, each approximately 15–16 minutes in length. All procedures were approved by the Washington University Institutional Review Board, and written informed consent was obtained from all participants.

MRI acquisition and preprocessing

All imaging was collected on a Siemens 7T scanner (TR = 1 s, TE = 22.2 ms, voxel size = 1.6 mm isotropic, multiband factor = 5, 900 volumes/run). We used the HCP minimally preprocessed data (Glasser et al., 2013), followed by additional denoising: linear detrending; regression of 24 head-motion parameters; regression of white

matter and CSF signals; band-pass filtering (0.01–0.1 Hz); scrubbing of frames with FD > 0.2 mm; and interpolation across removed frames. Runs were excluded if (a) more than 20% of frames exceeded motion thresholds, (b) eye tracking did not cover the full fMRI time series, or (c) more than 90% of samples were classified as eye closure. After applying these criteria, 485 of the initial 723 scans were retained for analysis. The same quality-control pipeline was applied to the movie-watching dataset, yielding 513 usable scans out of the original 725.

ROI parcellation

Analyses were performed using a 400-ROI symmetric parcellation with explicitly matched left–right homologues (Yan et al., 2023). Vertexwise BOLD signals were averaged within each ROI to obtain regional time series. All subsequent hemispheric analyses relied on this explicit homotopic structure.

Eye tracking preprocessing

Pupil diameter was extracted from the raw eye-tracking stream and cleaned following established procedures (Gonzalez-Castillo et al., 2022): Removal of samples outside MRI acquisition; detection of blinks and short missing segments (<1 s); linear interpolation across missing segments; removal of brief physiologically implausible excursions (<1 ms within long closures); smoothing with a 200 ms Hanning window; down-sampling to 1 Hz to match the temporal resolution of the fMRI data. The resulting time series served as a continuous arousal index for each run.

Time-resolved functional connectivity

Time-varying FC between each pair of ROIs was estimated using sliding-window correlations: window length: 30 s; step size: 5 s. Within each window, Pearson correlation coefficients were computed and Fisher-z transformed. This procedure yielded a FC time series for each edge in each run.

Arousal estimation from pupil size

Pupil data were processed using the same sliding-window parameters. The mean pupil size within each window was taken as an index of moment-to-moment arousal level.

Estimating arousal–FC coupling

For each functional connection, arousal–FC coupling was defined as the Pearson correlation between its time-varying FC and the pupil-derived arousal fluctuations across windows. Thus, each run produced a 400 × 400 symmetric matrix of coupling values, later vectorized into edgewise features.

These matrices were concatenated across runs to form the dataset used for community detection and all subsequent analyses.

Community detection on arousal–FC coupling

Prior to clustering, edgewise coupling values were z-scored across runs. Edges were treated as observations and runs as feature dimensions.

We applied k-means clustering (Euclidean distance), exploring k = 2–21. Each k was repeated 250 times with random initialization. Cluster number was selected by maximizing silhouette stability and reproducibility. This procedure consistently identified seven communities representing distinct arousal-sensitive connectivity motifs.

Mapping communities to networks and computing entropy

Each edge was assigned to one of seven communities. Edges were then mapped to Yeo's 7 canonical networks (visual, somatomotor, dorsal attention, ventral attention, limbic, frontoparietal, and default mode) (Thomas Yeo et al., 2011).

For each network pair (i, j), we computed the proportion $p_{i,j,k}$ of its edges

belonging to each community k. Shannon entropy $H_{i,j}$ quantified how broadly a network pair participated across communities, calculated as:

$$H_{i,j} = -\sum_{k=1}^{7} p_{i,j,k} \log_2(p_{i,j,k})$$

A higher $H_{i,j}$ indicates a broader, more uniform participation across the seven communities, while a lower $H_{i,j}$ indicates that the edges are primarily concentrated in a few communities.

Additionally, the dominant community for each network pair is defined as

$$\mathrm{Dom}(i,j) = \arg\max_{k} p_{i,j,k}$$

Entropy and dominant-community assignments jointly characterized both the diversity and primary affiliation of each network pair within the community structure.

Nodal-level community affiliation entropy A_r quantified how broadly each region r participated across communities. The entropy was calculated using the proportion $q_{r,k}$ of all incident edges of the region r belonging to the community k:

$$A_r = -\sum_{k=1}^{7} q_{r,k} \log_2(q_{r,k})$$

Quantifying hemispheric asymmetry: integration and segregation indices

To evaluate hemispheric biases in arousal–FC coupling, edges were categorized as LL, RR, LR, or RL. Using established formulations (Gotts et al., 2013), we computed:

Integration index:

$$Integartion = (LL + LR) - (RR + RL)$$

reflecting whether intra- and inter-hemispheric edges are preferentially concentrated in one hemisphere.

Segregation index:

$$Segregation = (LL - LR) - (RR - RL)$$

reflecting whether arousal preferentially strengthens within- vs. across-hemisphere connections.

Indices were computed for each network pair, each community (weighted by edge count), and all significantly lateralized subsets. Statistical significance was assessed relative to a null model (see below).

Spatial heterogeneity of lateralization

To quantify the spatial distribution characteristics of the arousal-FC coupling strength features (e.g., integration, segregation) within each community k, we first projected the edgewise coupling matrix for each participant onto the network-pair level, following the same procedure described in the previous section. The average coupling value of each network pair (i, j) within each community k is $C_{i,j,k}$. Network pairs were then sorted by their lateralization values to define the "lateralization axis" (Yang et al., 2025).

Spatial heterogeneity was quantified by performing a linear regression of the network-pair coupling values against their rank along the axis:

$$\bar{C}_{i,j,k} = \beta_k \cdot a\text{xis} + \varepsilon_{i,j,k} \,,$$

the regression slope β_k indexed the spatial heterogeneity, where a larger $|\beta_k|$ indicates a greater difference in lateralization value within the community.

The influence of each individual network pair (i, j) on the overall spatial

heterogeneity β_k was assessed using a leave-one-out method. The contribution $D_{i,j,k}$ was defined as the difference between the new slope $\bar{\beta}_{i,j,k}$ (after removing the pair) and the original slope β_k:

$$D_{i,j,k} = \bar{\beta}_{(i,j,k)} - \beta^{(k)}$$

The sign of $D_{i,j,k}$ indicates its modulatory role: positive values enhance spatial heterogeneity, whereas negative values reduce it.

Null model for hemispheric asymmetry

To determine whether observed lateralization exceeded chance, we construct a null model for hemispheric asymmetry.

For each run, ROI indices were permuted identically for rows and columns, preserving matrix symmetry and degree distribution while disrupting hemispheric structure. 10,000 permutations were performed. For each iteration, clustering and asymmetry indices were recomputed. p-values were FDR-corrected across comparisons.

Cross-paradigm validation using movie watching

To assess the context-independence of arousal–FC organization, we applied all analyses to movie-watching runs. Community structures from rest and movie data were matched using Jaccard similarity and Hungarian assignment (Kuhn, 1955). Correspondence was quantified by Spearman correlation between community-level network-pair profiles.

All analyses were implemented in Python (NumPy, SciPy, scikit-learn) using custom scripts. Visualization was performed with Matplotlib, Seaborn, and Surfplot.

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