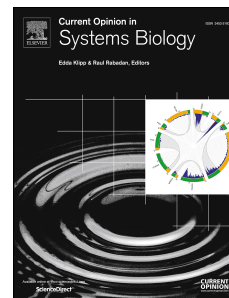


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Higher-order assembly and emergent persistence in biology

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Abstract

Biological systems often maintain functional organization for far longer than the molecular, cellular, or ecological interactions from which it emerges. How such organization persists despite rapid dynamics and continuous component turnover remains poorly understood. Here we review examples from genomics, neuroscience, development, and ecology, and distinguish the timescale over which organization assembles from the timescale over which it persists. Classical mechanisms based on slow variables, conserved quantities, or weak coupling explain important aspects of this separation, but persistence can also reside in relationships that remain stable as their underlying components change. We propose that interaction-modulating architectures provide one mechanism for this form of persistence by making interactions depend on additional components or context. A multilayer stochastic framework illustrates how these conditional relationships can be

maintained across separated timescales. This perspective shifts the focus from the lifetime of individual components to the organization that persists through their turnover.

Highlights:

- Persistence reflects stabilized interaction constraints
- Rapid turnover coexists with stable mesoscale organization
- Higher-order interactions modulate effective couplings
- Interaction-modulating layers can maintain organization across separated timescales

The problem of time in biological organization

Biological systems are inherently multiscale and dynamically active. Molecular interactions unfold on sub-second timescales, cellular processes over minutes to hours, yet functional organization—such as cell identity, anatomical structure, ecological communities, or collective behavior—can persist for years or longer. This separation of timescales underlies the capacity of living systems to maintain reliable function under noise, turnover, and environmental variability (Kitano 2004; Gunawardena 2014).

Mechanisms capable of generating slow dynamics are well established in physics and dynamical systems theory. However, these explanations typically rely on slow state variables, conserved quantities, special parameter regimes, or structural symmetries. By contrast, biological systems are open, adaptive, and far from equilibrium: they sustain rapid microscopic activity while maintaining long-lived organization (Prigogine and Nicolis 1985; Ramaswamy 2017). In such regimes, intrinsically slow processes provide only part of the explanation for persistence.

This contrast highlights a conceptual gap. The central challenge is not only to explain how slow modes emerge but also to understand what remains invariant as fast dynamics unfold. Persistence, in this sense, concerns the maintenance of organizational features that continue to constrain system behavior despite ongoing turnover and reconfiguration. Explanations of biological persistence must therefore address how such constraints are stabilized in systems that remain dynamically active. It is at this intermediate scale—between individual components and whole-system outcomes—that fast activity and long-term organization are reconciled.

Box 1. Glossary

Higher-order assembly. The formation of biological organization through multicomponent interaction structure. Such organization may arise from higher-order interactions or from pairwise interactions under appropriate conditions; the term refers to the assembly process rather than to a specific interaction mechanism.

Higher-order organization. A coordinated pattern involving several components at an intermediate or whole-system scale. It can emerge from pairwise interactions alone under particular conditions (e.g., criticality or symmetry breaking), but may also be supported by higher-order interactions.

Higher-order interaction. An interaction in which the influence of one component on another depends on additional components or on context. In other words, the relationship itself can change with the situation, rather than remaining fixed.

Assembly timescale (τ_a). The time required for a specified organizational constraint C to become detectable, defined by a prespecified detection threshold and measured from a specified assembly onset.

Persistence timescale (τ_p). The average duration, measured from detection, during which the same organizational constraint C remains predictive of system dynamics despite fluctuations and component turnover, before changing beyond a prespecified tolerance.

Constraint. A stable pattern of relationships—a constraint structure—that limits the system’s possible behaviours without fixing the state of every component. Here, it can be represented by a context-dependent transition rule or stationary distribution that remains stable despite turnover.

Conditional dependence. A relationship in which an interaction depends on the state or presence of other components or on context. It determines which interactions are effective in which situations.

Interaction-modulating architecture. An arrangement in which some components regulate the interactions among others, rather than acting directly on their states.

Mesoscale organization. Organization at an intermediate scale: larger than individual components but smaller than the whole system, where collective constraints can emerge and persist.

Emergent persistence. The maintenance of an organizational constraint while components continue to change or turn over. It can be supported by interaction structure rather than slow variables alone.

Mechanisms of timescale separation

A wide range of mechanisms capable of generating slow dynamics and timescale separation are well established in physics and dynamical systems theory (Strogatz 2015; Hohenberg and Halperin 1977). These mechanisms have been applied across biological and ecological systems, yet their explanatory scope is uneven in open, adaptive contexts. Below we briefly review the principal classes of explanation for persistent biological organization under rapid internal dynamics.

Critical slowing down and proximity to bifurcations. Near bifurcation points, dominant eigenvalues approach zero, producing slow recovery from perturbations and long correlation times (Strogatz 2015). This phenomenon underlies early-warning signals preceding regime shifts (Scheffer et al. 2009; Sardanyés et al. 2024). However, critical slowing requires operation near special regions of parameter space. Biological systems often function across broad parameter ranges without apparent fine-tuning (Goldbeter 1996; Kitano 2004). Moreover, critical slowing predicts globally slow state variables, whereas many biological systems exhibit rapid component turnover alongside persistent organization (Gunawardena 2014).

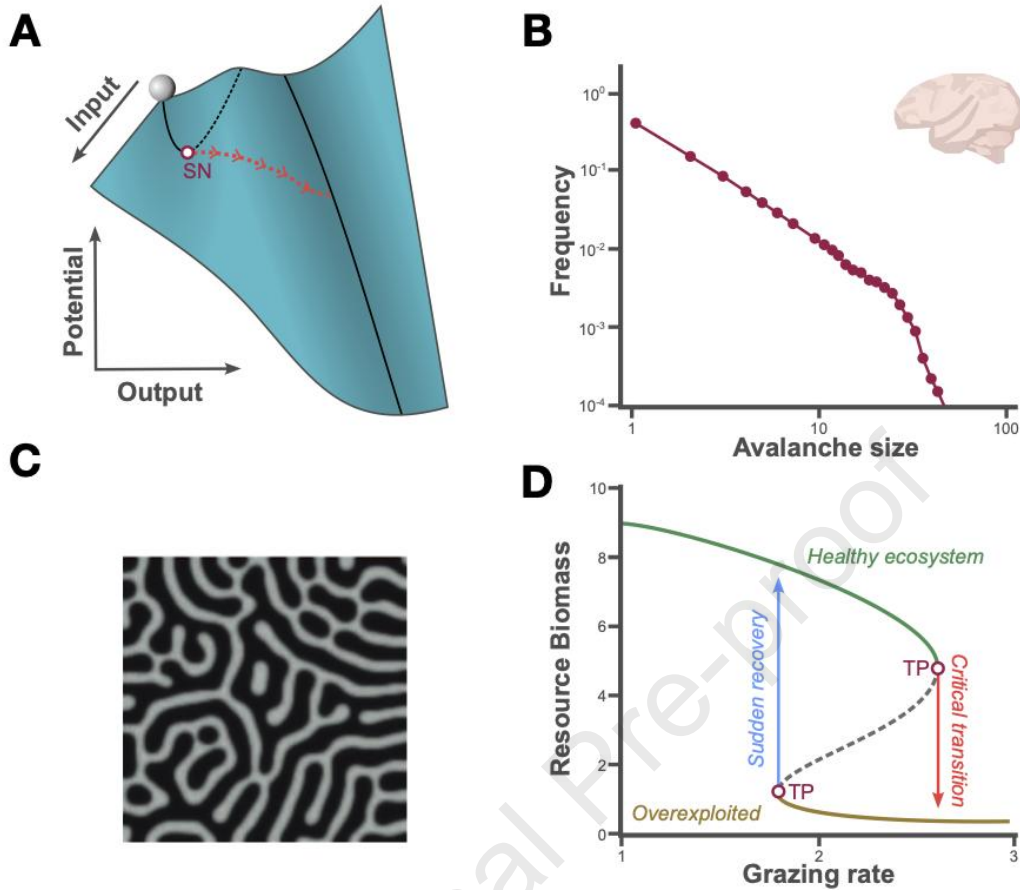
Conservation laws and slow variables. Conservation laws generate slow relaxation modes by restricting the evolution of conserved quantities (Hohenberg and Halperin 1977). In near-equilibrium physical systems, such constraints yield long-lived correlations. Biological systems, however, are open and continuously driven, maintained far from equilibrium by sustained fluxes of matter and energy (Prigogine and Nicolis 1985). While approximate conservation may hold locally or transiently, open biological systems continually exchange matter and energy with their surroundings (Ramaswamy 2017).

Broken continuous symmetries and soft modes. Systems with broken continuous symmetries exhibit Goldstone modes—soft directions in state space along which dynamics are slow (Cross and Hohenberg 1993). This mechanism explains slow collective modes in many physical systems. Biological regulatory architectures, however, are typically discrete, heterogeneous, and context-dependent (Anderson 1972; Alon 2006). Symmetry-based arguments therefore apply in restricted settings rather than as a general principle for biological organization.

Weak coupling, modularity, and spatial separation. Slow dynamics can also arise when subsystems interact weakly or are separated in space, delaying the propagation of perturbations. Modularity and near-decomposability are important organizing principles in complex systems (Simon 1962; Hartwell et al. 1999). However, many biological functions rely on dense and context-dependent interactions rather than weak coupling alone (Barabasi and Oltvai 2004). In such systems, structured interdependence becomes relevant to robustness and functional stability alongside the isolation afforded by modular organization.

Empirical signatures and limits of existing mechanisms

Across biological domains, empirical studies document forms of organization that remain functionally stable despite ongoing component turnover and internal dynamics. We examine representative systems in which this decoupling is well documented, considering how established slow-mode mechanisms operate in each context and which empirical features remain difficult to reconcile within them (see Figure 1).



Canonical mechanisms generating slow dynamics and timescale separation. (A) Saddle-node bifurcation in a positive-feedback gene regulatory circuit, adapted from (Ferrell 2012). (B) Scale-free neuronal avalanches observed in awake primate cortex, adapted from (Petermann et al. 2009). (C) Reaction-diffusion instability yielding a stationary Turing pattern, adapted from (Kondo and Miura 2010). (D) Bifurcation diagram of an ecological resource-consumer system, adapted from (Dakos et al. 2012).

Genome organization and gene regulation

Genome regulation exhibits higher-order organization across spatial and temporal scales, including transcriptional hubs, enhancer–promoter assemblies, chromatin loops, and regulatory condensates formed by coordinated genomic loci and regulatory proteins. These structures can assemble rapidly—often within seconds to minutes—through stochastic chromatin motion and transient molecular interactions (Lieberman-Aiden et al. 2009; Belmont 2014; Mirny and Goloborodko 2019). Yet they can persist as effective constraints on gene expression across cell cycles and developmental timescales (Dekker et al. 2013; Bonev and Cavalli 2016), despite continuous turnover of their molecular components.

Several mechanisms are commonly invoked to account for this stability. Regulatory network models associate stable expression patterns with bifurcations underlying cell-fate

decisions (Huang et al. 2005; Ferrell 2012) (see Figure 1A). Spatial compartmentalization and topologically associating domains partially decouple loci and can slow large-scale reorganization (Dixon et al. 2012; Mirny et al. 2019). Finite pools of transcription factors and chromatin modifiers may also transiently constrain regulatory dynamics (Voss and Hager 2014).

Nevertheless, regulatory architectures often remain functionally stable far from specific bifurcation regimes (Kitano 2004), and gene expression programs are robust to substantial molecular fluctuations (Elowitz et al. 2002; Raj and Van Oudenaarden 2008). At the same time, chromatin interactions form and dissolve on short timescales (Misteli 2007; Mirny et al. 2019). The persistence of regulatory dependencies under such rapid molecular turnover extends beyond what is captured by state-based attractors or spatial decoupling alone.

Neural systems

Neural systems exhibit coordinated cell assemblies, population-level motifs, and large-scale activity patterns that emerge rapidly through synaptic coupling and recurrent network dynamics (Harris and Shepherd 2015; Luppi et al. 2022). Despite ongoing neuronal variability and synaptic plasticity, such functional organizations—associated with perception, learning, and behavior—can remain stable over extended timescales (Buzsáki 2010; Bassett and Sporns 2017).

Several dynamical mechanisms have been proposed to account for these observations. Operation near critical regimes can generate long temporal correlations and extended recovery times (Beggs and Plenz 2003; Mora and Bialek 2011) (see Figure 1B). Hierarchical modularity and weak coupling between subnetworks may permit slow global fluctuations alongside fast local activity (Wang et al. 2011; Bassett and Sporns 2017). Attractor and low-dimensional manifold models further demonstrate how structured population activity can arise from recurrent pairwise interactions (Khona and Fiete 2022).

Recent empirical work complements these perspectives by showing that multivariate dependencies contribute to neural computation. Incorporating higher-order functional interactions among multiple brain regions improves task decoding and individual identification compared to dyadic models (Santoro et al. 2024). Information-theoretic analyses likewise reveal synergistic triplet and quadruplet interactions that encode task-relevant information not fully captured by pairwise connectivity alone (Combrisson et al. 2025). These results indicate that neural coordination often involves structured multivariate dependencies beyond simple pairwise coupling.

Importantly, neural assemblies can remain functionally stable despite substantial synaptic turnover and continuous remodeling at the level of individual connections (Ziv et al. 2013). Critical and attractor-based accounts explain persistent activity patterns, yet they generally presuppose an interaction architecture that is comparatively stable over the timescale of the attractor. The critical question is how specific coordination or routing structures remain constrained while synaptic connectivity itself is in flux (Tognoli and Kelso 2014; Betzel 2022; Gallos et al. 2012).

Anatomical and developmental systems

Anatomical and developmental organization involves the emergence of coherent tissue- and organ-level structures from local cellular interactions, spanning timescales from hours to weeks (Gilbert 2010). Processes such as axis specification, segmentation, and organogenesis assemble higher-order structures through coordinated genetic, biochemical, and mechanical interactions. Once formed, these structures typically persist over the lifetime of the organism, constraining physiology and behavior far beyond the timescales of individual cell cycles or signaling events.

Symmetry-breaking instabilities underlie many patterning processes, and reaction–diffusion models illustrate how diffusion-driven instability can generate stationary spatial patterns (Figure 1C) (Kondo and Miura 2010). Persistence under cellular turnover or remodeling poses a distinct problem: the relevant constraint must be maintained as cells are replaced, rearranged, or change state.

More recent work situates such mechanisms within broader multiscale developmental frameworks that integrate biochemical and mechanical coupling (Sozen et al. 2021; Lenne et al. 2021). Conservation constraints and growth-coupled transport processes introduce intrinsic slow modes (Kicheva and Briscoe 2023), while oscillatory gene regulatory circuits generate explicit developmental clocks, such as the segmentation clock in somitogenesis (Cooke and Zeeman 1976; Pourquié 2003; Clark 2021). Spatial separation between organizing centers and diffusive coupling across tissues further contributes to extended coordination timescales (Sozen et al. 2021).

Even in these contexts, developmental robustness cannot be attributed solely to a single slow variable or clock. Anatomical structures often maintain functional organization despite extensive cellular turnover and remodeling, as seen in renewing tissues such as epidermis and intestinal epithelium (Blanpain and Fuchs 2009; Simons and Clevers 2011). Moreover, cell-fate decisions frequently depend on combinatorial integration of signaling level, duration, and competence rather than on one dominant temporal parameter (Sagner and Briscoe 2017; Warmflash et al. 2014). The persistence of developmental organization thus reflects not only intrinsic slow processes but also stable constraint structures governing how multiple inputs jointly delimit admissible trajectories.

Ecological systems

Ecological systems display higher-order organization at the level of communities, food webs, and spatially structured populations. Community assembly typically unfolds over seasons to years as species colonize, compete, and adapt, yet established interaction structures—such as coexistence patterns or trophic roles—can persist over much longer timescales even as individual abundances fluctuate (Billick and Case 1994; Grilli et al. 2017).

Several slow-mode mechanisms are well documented in ecological contexts. Critical slowing has been observed near regime shifts, where recovery from perturbations

becomes progressively slower and variance increases (Scheffer et al. 2009; Dakos et al. 2012) (see Figure 1D). Spatial structure and limited dispersal can delay system-wide responses in metapopulations (Hanski 1999; Gouhier et al. 2010), and conservation constraints such as nutrient or biomass budgets introduce slow recycling modes in tightly coupled ecosystems (Hessen et al. 2013; DeAngelis 1980).

At the same time, many ecological communities remain stable far from critical transitions (Hastings et al. 2018; Vidiella et al. 2021). Modularity and spatial separation can buffer perturbations, yet they do not by themselves guarantee the persistence of specific interaction patterns as environmental conditions and species abundances change (Stouffer and Bascompte 2011). Empirical and theoretical studies increasingly show that context-dependent and non-pairwise effects—where one species modifies the interaction between others—reshape coexistence outcomes beyond predictions from pairwise models (Bailey et al. 2016; Grilli et al. 2017; Vidiella et al. 2026). Studies of multitrophic communities further demonstrate that such higher-order interaction modifications can redistribute interaction strengths and promote species persistence in ways not captured by additive pairwise coefficients (Buche et al. 2024).

Assembly and persistence across biological systems

Across the four empirical domains, assembly and persistence refer to the same specified organizational constraint C , rather than to characteristic timescales of the system as a whole. The relevant constraint is necessarily domain-specific: a regulatory dependency in genome organization, a functional coordination structure in neural systems, a patterning relation in development, or a conditional interaction structure in ecological communities. Its dynamics can nevertheless be described in common terms: τ_a measures the time required for the constraint to emerge, whereas τ_p measures how long it remains predictive once established.

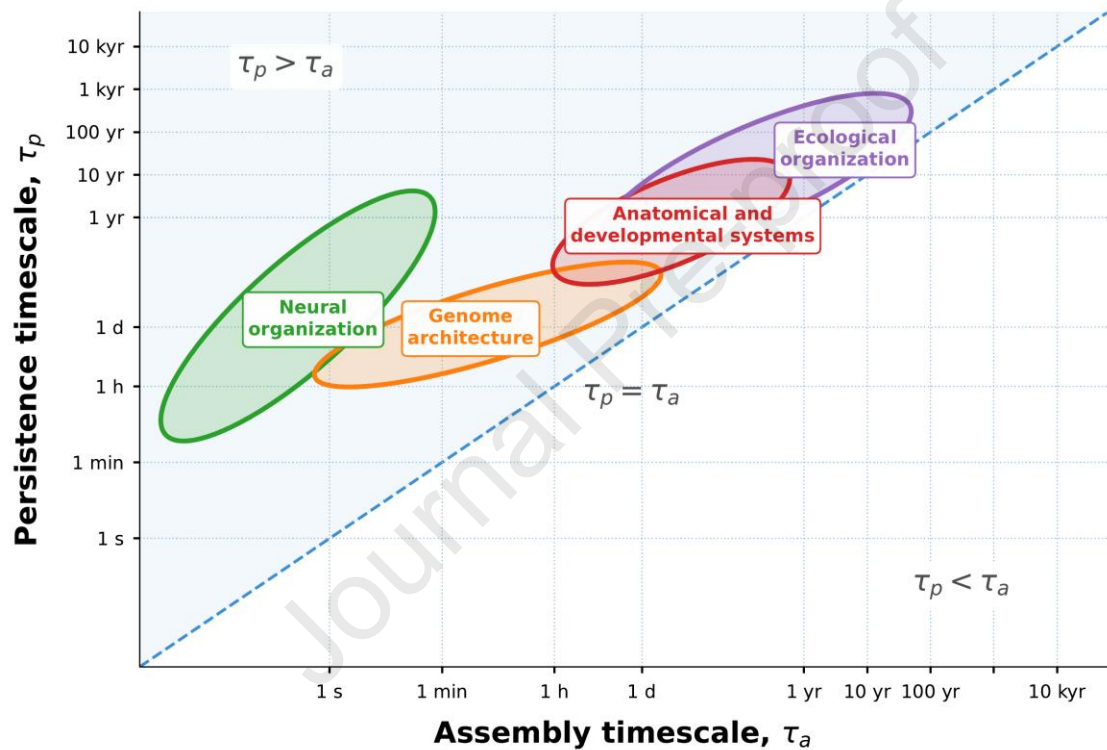
Measuring these timescales requires domain-specific observables that identify both the emergence and continued validity of C . Assembly onset, detection threshold, and persistence tolerance must therefore be specified for each domain, relative to the temporal resolution and statistical uncertainty of the relevant observable rather than as universal thresholds across systems. Table 1 summarizes candidate observables for tracking the same organizational constraint through assembly and persistence.

The relationship between these timescales can be represented in an assembly–persistence space (Figure 2). Persistence exceeds assembly time when $\tau_p > \tau_a$, while $\tau_p/\tau_a \gg 1$ identifies a strong separation between the timescale over which an organizational constraint forms and the timescale over which it persists.

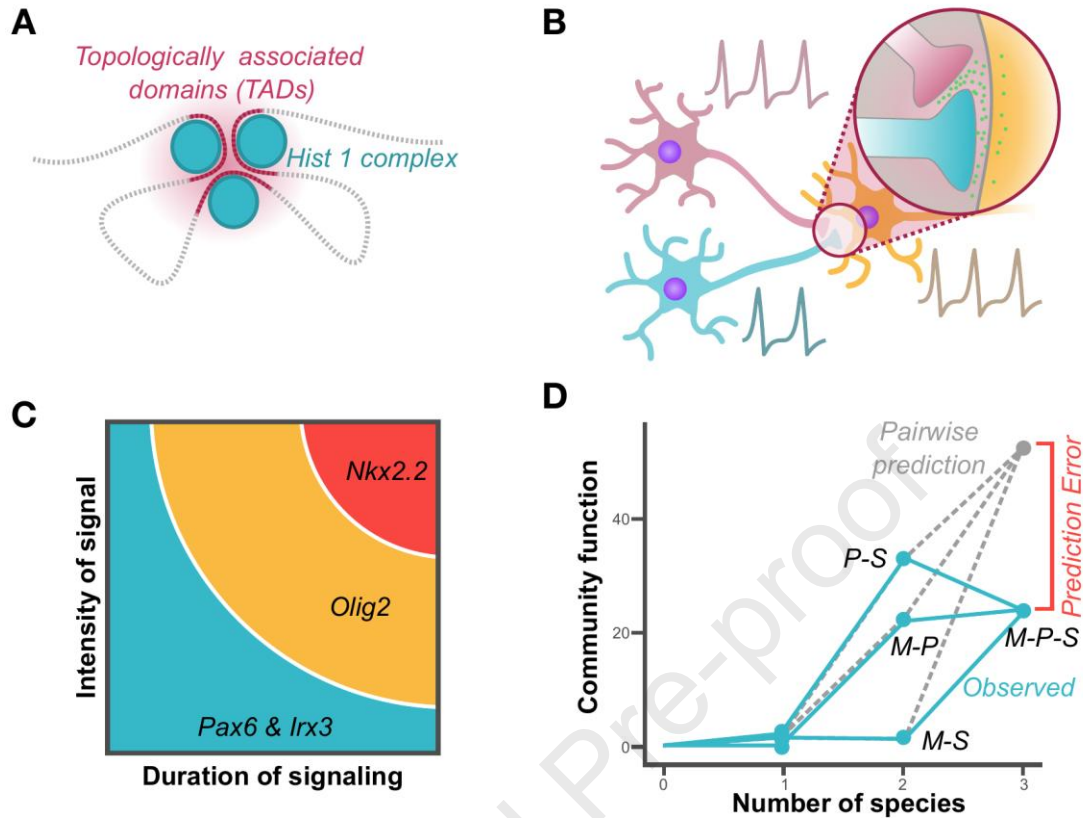
Table 1. Operationalizing assembly and persistence across empirical domains.

Candidate observables for tracking the assembly and persistence of a specified organizational constraint C .

System	Assembly observable (τ_a)	Persistence observable (τ_p)	Constraint C
Genome	Multi-locus configuration	Regulatory dependence	Accessibility/express ion logic
Neural	Population motif	Functional dependence	Transmission/coordi nation
Developmental	Joint-input relation	Maintained patterning relation	Fate/morphological trajectories
Ecological	Interaction configuration	Functional dependence	Conditional species relations



Assembly–persistence space across biological organization. Schematic ranges of assembly (τ_a) and persistence (τ_p) timescales for the same specified organizational constraint C within each empirical example. The dashed diagonal denotes $\tau_p = \tau_a$; systems above it satisfy $\tau_p > \tau_a$, and increasing distance above the diagonal corresponds to stronger separation between assembly and persistence timescales. Ellipses are schematic ranges for organizational constraints rather than component lifetimes; they are not quantitative estimates or sharply defined empirical bounds.



Empirical examples of higher-order interaction structures across biological systems. (A) Genome: multi-way chromatin contacts detected by SPRITE (Quinodoz et al. 2018). (B) Neural: triadic synaptic configuration (Millán et al. 2025). (C) Anatomical/developmental: neural-tube patterning through joint integration of signaling level and duration (Sagner and Briscoe 2017). (D) Ecological: microbial-consortium function versus additive and pairwise predictions (Sanchez-Gorostiaga et al. 2019).

From higher-order assembly to emergent persistence

How, then, can an organizational constraint remain effective once established, despite ongoing component turnover? One possibility is that a regulatory context modulates which fast interactions are effective, allowing a stable conditional interaction structure to outlast the states, components, or edges that instantiate it.

Persistence can be understood as the maintenance of admissible dynamical relations, that is, limits on how components may influence one another without loss of function (Aubin et al. 2011). These limits are encoded in patterns of conditional dependence that determine which interactions are effective under particular contextual configurations (Montévil and Mossio 2015). Long-lived organization, in this view, reflects stability of relational constraints rather than intrinsic slowness of state variables.

Higher-order interactions provide one architectural mechanism for maintaining these constraints. In interaction-modulating architectures, the influence of one component on another depends explicitly on additional components or contextual variables. When interactions are mediated by such contextual variables or higher-level regulators, rewiring or replacement of individual elements need not in principle disrupt the conditional transition structure that governs admissible trajectories. Persistence can therefore reside in relational structure without requiring the relevant fast states, pairwise edges, or parameters themselves to remain fixed.

This principle is visible in three-dimensional genome organization. Multi-way chromatin conformation methods, including SPRITE, GAM, Multiplex-GAM, MC-3C, and CiFi, reveal coordinated multi-locus configurations in which enhancers, promoters, and transcriptional machinery are simultaneously co-localized (Quinodoz et al. 2018; Beagrie et al. 2017, 2023; Tavares-Cadete et al. 2020; McGinty et al. 2025; Dotson et al. 2022). These observations reveal regulatory configurations that cannot be represented as isolated pairwise contacts alone. Cooperative binding and multi-protein assemblies can thereby support regulatory logic despite continuous synthesis, degradation, and exchange of molecular components (Figure 3A).

Neural systems exhibit a parallel organization. Large-scale brain state transitions display structured temporal dynamics (Vidaurre et al. 2017), while local propagation patterns are shaped by multi-neuron motifs such as triadic synaptic configurations (Song et al. 2005; Perin et al. 2011). In these motifs, effective transmission depends on joint activity patterns, biasing routing and information flow even under continuous synaptic plasticity (Harris and Mrsic-Flogel 2013; Litwin-Kumar and Doiron 2012) (Figure 3B).

Developmental organization likewise depends on combinatorial integration of signaling level, duration, and cellular competence (Sagner and Briscoe 2017; Sozen et al. 2021). Admissible cell fates correspond to regions in multi-input configuration space rather than to a single dominant temporal variable. At anatomical scales, coordinated ensembles of tissues constrain viable morphological trajectories through their collective configuration (Klingenberg 2008; Fostowicz-Frelik and Tseng 2023; Lenne et al. 2021) (Figure 3C).

Ecological communities show analogous structure, with hypergraphs providing a natural representation of feasible interacting sets whose realization depends on species composition and environmental context (Vidiella et al. 2026). Non-pairwise interaction modifications—where one species alters the interaction between others—reshape coexistence and functional output (Bairey et al. 2016; Grilli et al. 2017). Experimental microbial systems demonstrate systematic deviations between observed community function and predictions derived from pairwise measurements (Sanchez-Gorostiaga et al. 2019; Morin et al. 2022), indicating that interaction effects depend on overall community composition (Figure 3D). Persistence of coexistence and function thus reflects stability of structured interaction dependencies rather than constancy of abundances.

Classical attractor-based explanations typically assume that coupling architecture remains relatively stable over the lifetime of the attractor. In interaction-modulating

architectures, by contrast, conditional dependency structure may remain stable even when specific couplings are rewired or replaced, because admissible interactions are defined by modulatory context rather than fixed edges. The distinction is therefore not between attractors and non-attractors, but between persistence grounded in stable parameters and persistence grounded in stable patterns of modulation.

Together, these examples reveal a common empirical pattern: rapid local dynamics coexist with persistent mesoscale dependency structures. The multilayer framework of Box 2 formalizes one architectural mechanism through which interaction modulation can maintain this organization across already-separated intrinsic relaxation times τ_μ . These describe layer dynamics, whereas τ_a and τ_p describe the assembly and persistence of a specified organizational constraint. In the corresponding timescale-separation limit, interaction-modulating couplings yield a conditional probabilistic decomposition, directional asymmetry between slow regulators and fast subsystems, and propagation of dependency structure without direct pairwise coupling (Nicoletti and Busiello 2024).

Box 2. A multilayer stochastic model of interaction-modulated persistence

Following Nicoletti and Busiello, consider N finite-state stochastic layers with states $\mathbf{x} = (x_1, \dots, x_N)$. Layer μ has M_μ nodes, intrinsic relaxation time τ_μ , and a transition operator $\hat{\Omega}^\mu$ that contains both intralayer transitions and higher-order triadic interactions. The joint dynamics obey the master equation (Nicoletti and Busiello 2024)

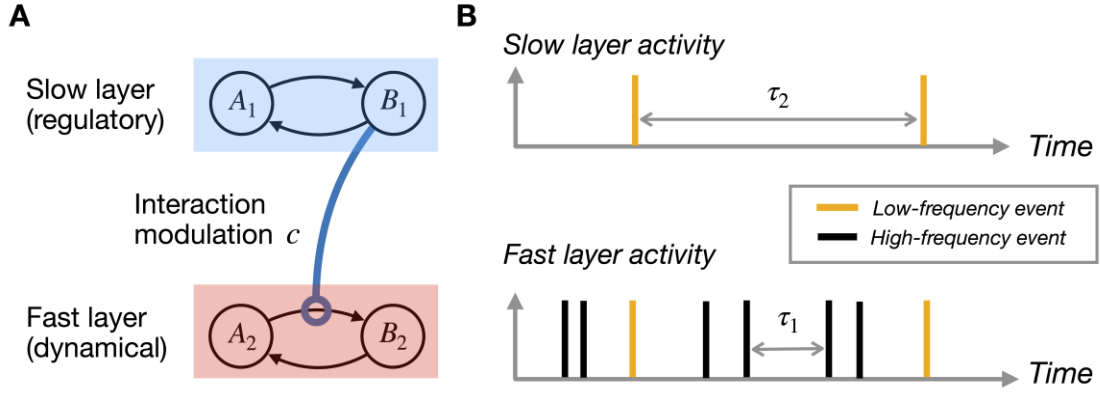
$$\partial_t p_{1,\dots,N}(t) = \sum_{\mu=1}^N \frac{\hat{\Omega}^\mu(\{\mathbf{x}\}_{\Rightarrow\mu})}{\tau_\mu} p_{1,\dots,N}(t).$$

Here $\{\mathbf{x}\}_{\Rightarrow\mu}$ denotes the states of all layers connected to μ by higher-order interactions.

A triadic higher-order interaction is present when a state x_ν in a regulating layer changes the transition rate $i \rightarrow j$ within another layer μ :

$$\hat{W}_{i \rightarrow j}^{H\mu}(\{\mathbf{x}\}_{\Rightarrow\mu}) = (\hat{W}^\mu)_{i \rightarrow j} + \sum_{\nu \neq \mu} \sum_{k=1}^{M_\nu} C_{k;i \rightarrow j}^{\nu\mu} \phi_k^\mu(x_\nu).$$

Here $\hat{W}^\mu$ is the intralayer transition matrix, $C_{k;i \rightarrow j}^{\nu\mu}$ is a triadic interaction specifying how node k in layer ν modulates the $i \rightarrow j$ edge in layer μ , and ϕ_k^μ quantifies the state dependence of that modulation. Together, they determine the transition operator $\hat{\Omega}^\mu$ of the μ -th layer. Thus, the regulator acts on an interaction, rather than directly on a target state. Nicoletti and Busiello analyze a fixed multilayer architecture; in biological applications, this provides a baseline for asking whether the context-conditioned kernel $\hat{W}^{H\mu}$ (and the conditional dependencies it induces) remains functionally invariant as underlying components are replaced or rewired.



The two-layer illustration (panel A) depicts interaction modulation across a fast and a slow layer. Black ticks mark high-frequency events in the fast layer, and yellow ticks mark low-frequency events in the slow layer (panel B). Yellow ticks also appear on the fast trace to indicate when changes in the slow context modify the fast transition kernel; they do not denote additional fast-layer events.

Generalizing this illustration, order the N layers from fast to slow, $\tau_1 \ll \tau_2 \ll \dots \ll \tau_N$. In the timescale-separation limit $\tau_\mu / \tau_{\mu+1} \rightarrow 0$, the joint distribution factorizes into conditional stationary distributions of the faster layers and an effective distribution for the slowest layer,

$$p_{1,\dots,N}(t) = p_N^{\text{eff}}(t) \prod_{\mu=1}^{N-1} p_{\mu|\rho(\mu)}^{\text{st,eff}}$$

where the superscript ‘‘eff’’ denotes that these probabilities are built from the effective operators $\hat{\Omega}_{\text{eff}}^\mu$, obtained by averaging $\hat{\Omega}^\mu$ over the conditional stationary distributions of all faster layers. The surviving conditional dependencies are determined by the set $\rho(\mu)$, which contains slower layers connected to μ through a single feedback link or a minimal propagation path. The decomposition is exact in the timescale-separation limit, not an unconditional identity. It makes the constraint explicit: fast layers relax rapidly, but to distributions conditional on a comparatively stable regulatory context.

The induced dependence between layers μ and ν can be measured by their mutual information,

$$I_{\mu\nu} = \sum_{x_\mu, x_\nu} p_{\mu\nu} \log_2 \left(\frac{p_{\mu\nu}}{p_\mu p_\nu} \right)$$

with $p_{\mu\nu}$, p_μ and p_ν the stationary marginal probabilities of $p_{1,\dots,N}$. In this model and separation limit, slow-to-fast triadic feedback can generate nonzero stationary mutual information, whereas fast-to-slow interactions alone do not generate it. Fast-to-slow interactions can nevertheless propagate information generated by a slow regulatory layer along minimal propagation paths (Nicoletti and Busiello 2024).

The intrinsic relaxation times τ_μ define the model's dynamical hierarchy, whereas τ_a and τ_p characterize the assembly and persistence of an organizational constraint C . The framework therefore links conditional dependencies across dynamical timescales to the empirical persistence of organization. Exogenous turnover can be represented as an additional layer with its own timescale, modulating the regulatory architecture through which the constraint is maintained. Endogenously generated turnover, by contrast, would require extending the framework to include the dynamics through which that architecture itself assembles and reorganizes. Such an extension would provide a natural setting for studying regimes in which $\tau_p/\tau_a \gg 1$.

Implications and outlook

If biological organization can outlive the components that instantiate it, where does persistence reside? One possibility is that it resides in the interaction structure that constrains collective dynamics. This suggests experimentally separating changes in components from changes in their organization. Functional persistence under component or edge turnover, together with sensitivity to perturbations of modulatory interactions, would provide evidence that long-term organization is maintained relationally rather than through the stability of individual components or state variables.

An open theoretical problem is to explain how such interaction structures assemble, persist, and reorganize. Models with dynamic interaction architectures could establish the conditions under which organization survives turnover, identify architectures that produce long persistence relative to assembly, and determine which of these properties depend on higher-order interactions rather than effective pairwise dynamics.

Empirically, the main challenge is to identify the relevant organizational constraints and follow them through time. Which relationships remain predictive as components change? How robust are they to turnover and environmental variability? Can the same constraint be identified during both assembly and persistence across genomic, neural, developmental, and ecological systems? Resolving these questions would allow assembly and persistence to be mapped quantitatively across biological domains, while directly testing whether persistence resides in states, components, or their organization. The same distinction between component turnover and organizational persistence may also provide a useful lens for cultural and technological systems, where enduring structures can likewise outlive the particular agents or artifacts that instantiate them.

In conclusion, biological persistence need not require microscopic stability. By preserving organization while its constituents change, living systems can maintain function across timescales far longer than those of the processes from which that organization emerges.

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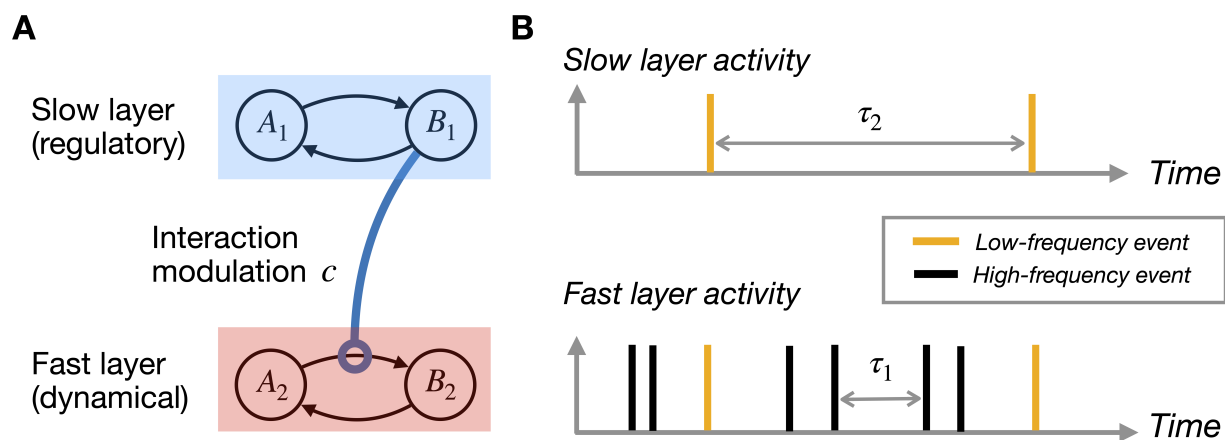
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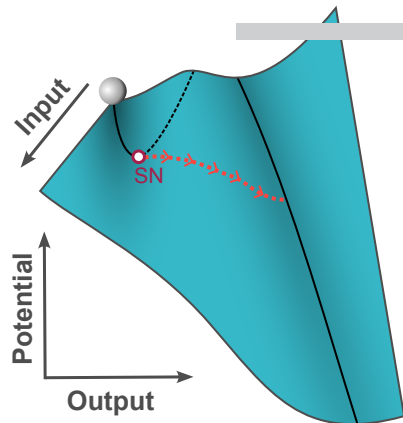
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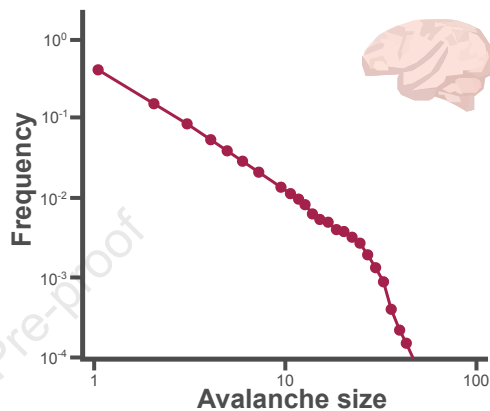
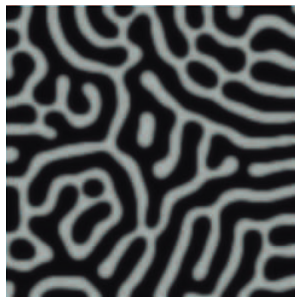
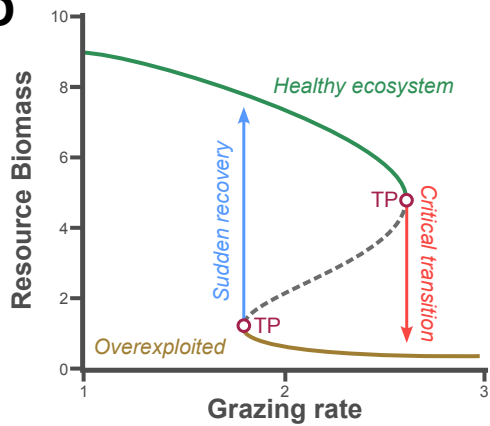
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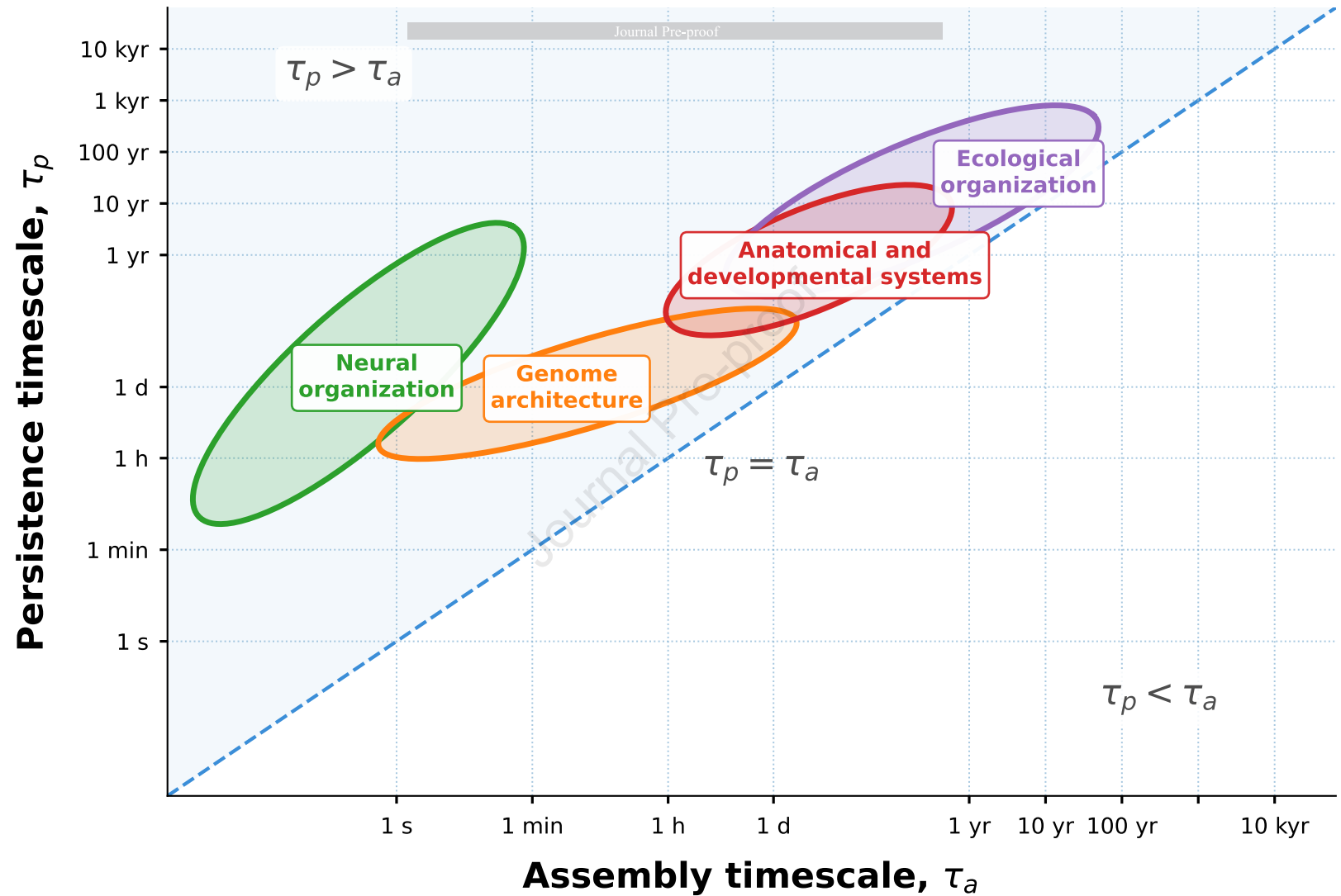
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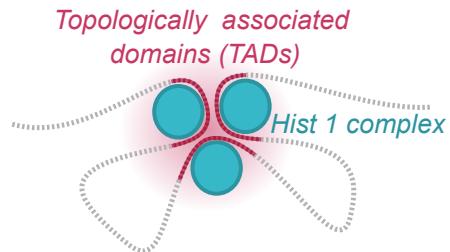


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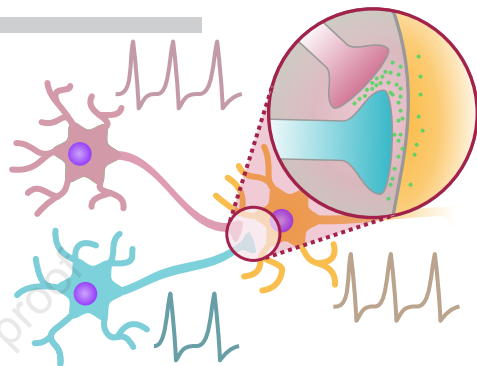
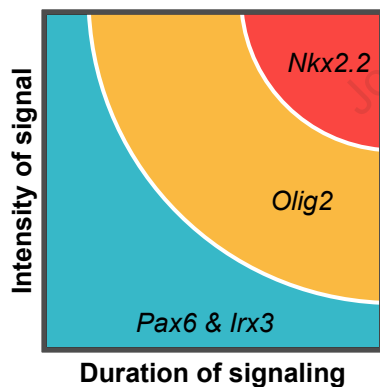
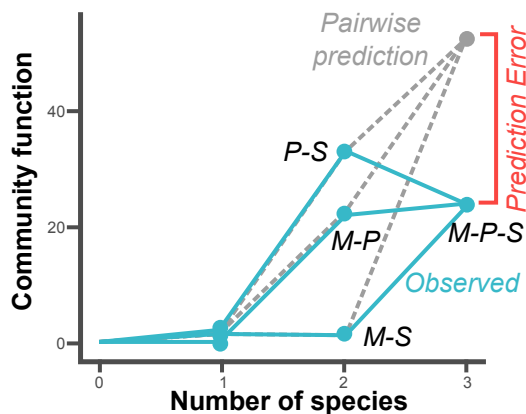
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The authors declare no conflict of interest.