Propagating Constraint Fields and Dynamic Structural Redistribution:

Toward a Field-Theoretic Interpretation of Neural Heterogeneity and Collective Cell Migration

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Abstract

Two recently published empirical studies, one investigating structural brain aging in generalized anxiety disorder and the other characterizing the dynamic redistribution of the tight-junction protein ZO-1 during collective epithelial cell migration, exhibit a shared organizational structure that resists explanation by standard localist or entity-centered biological models. In the brain-aging study, individuals with generalized anxiety disorder do not uniformly display the accelerated aging signature that disease-model reasoning would predict; instead they exhibit dramatically increased variance in predicted age difference, suggesting that the disorder broadens the space of accessible neural trajectories rather than displacing the entire population along a single developmental axis. In the cell-migration study, ZO-1 does not remain fixed at apical junctional complexes but dynamically shuttles to podosome-like basal structures in response to propagating ERK activation waves, reorganizing the tissue's mechanical and signaling architecture collectively across space and time. We argue that both phenomena are most coherently interpreted within a generalized field-theoretic framework grounded in the Relativistic Scalar-Vector Plenum formalism, in which local organizational states are characterized by a scalar coherence field, a vector transport field, and an entropic accessibility measure. Under this interpretation, psychiatric heterogeneity becomes a widening of admissible trajectory distributions rather than a categorical pathological shift, while collective tissue migration becomes a case of constraint redistribution driven by propagating activation fronts. The analysis yields specific structural predictions about variance geometry, wave-coupled phase transitions between stabilizing and exploratory organizational regimes, and the general insufficiency of mean-field biomarker approaches for systems governed by distributed constraint dynamics.

Contents

1 Introduction: From Static Biomarkers to Dynamical Constraint Fields

A strongly localist approach to biological explanation treats macroscopic phenomena as the aggregated result of discrete components interacting according to intrinsic stable properties. This entity-centered framework has produced genuine successes, particularly in structural biochemistry and classical genetics, but it encounters systematic difficulty whenever the explanatory target is coherent large-scale behavior that emerges from distributed interaction rather than from the characteristics of any single component. Two recent empirical contributions, one in translational psychiatry and one in cell biology, expose precisely this limitation while simultaneously pointing toward an alternative organizing principle. A third contribution, in computational neuroscience, provides what may be the most direct empirical instantiation of the organizational geometry the others implicitly suggest.

The first paper, by Richier and collaborators within the ENIGMA-Anxiety consortium, investigates whether generalized anxiety disorder (GAD) is associated with accelerated structural brain aging as measured by convolutional neural network estimation of chronological age from multimodal MRI data [2]. The core metric is the predicted age difference (PAD), computed as estimated brain age minus actual chronological age, with positive values indicating an apparently older structural profile. The central result contradicts the original hypothesis: individuals with GAD do not show significantly elevated mean PAD relative to healthy controls. What they do show, particularly among adults older than twenty-five, is substantially increased *variance* in PAD. Some individuals with GAD display neural profiles consistent with accelerated aging; others display profiles consistent with delayed or atypical development. The diagnostic category does not map to a single point in developmental space but rather to a broadened and heterogeneous cloud.

The second paper, by Hirano and collaborators, examines how the tight-junction scaffolding protein ZO-1 participates in collective epithelial migration [3]. Using live-cell imaging of migrating MDCK epithelial monolayers, the authors demonstrate that ZO-1 is not a static structural component of cell-cell junctions but a dynamic participant in tissue-scale coordination. During migration, ERK activation propagates across the epithelial sheet as traveling waves; in their wake, ZO-1 detaches from apical junctional complexes and accumulates at basal podosome-like structures where it influences traction force generation and extracellular matrix remodeling. These redistributions themselves propagate collectively. The tissue does not consist of cells individually deciding to migrate; it behaves as a coupled dynamical medium through which activation fronts reorganize mechanical architecture across space and time.

The third paper, by Wang, Lou, Wei, and collaborators, introduces a geometry-aware

framework for EEG/MEG source imaging that reconstructs whole-brain neural dynamics by decomposing the individual cortical surface into Laplace–Beltrami eigenmodes, termed geometric basis functions (GBFs) [1]. The central empirical finding is that whole-brain activity observed across approximately 32,000 cortical vertices in fMRI can be reconstructed to high fidelity using only 200–300 such modes. Neural sources are expressed as $x(t) = \sum_i \theta_i(t)\psi_i$, where ψ_i are geometry-derived eigenfunctions rather than arbitrary basis vectors. The inverse solution is regularized by the spectral prior $\Sigma^{-1} = \text{diag}(-\beta/\log\lambda_i)$, which penalizes high-frequency modes increasingly, thereby embedding an explicit admissibility weighting into the reconstruction operator. The paper further tracks stimulation-evoked propagating cortical waves using optical-flow analysis, recovering directed propagation streamlines and convergence hubs consistent with known anatomical pathways. This framework operates directly on a Riemannian manifold (the cortical surface) with intrinsic differential operators, making it the empirical system in this essay most closely aligned with the abstract RSVP field equations.

The structural parallel across these three findings is not superficial. In each case, an entity-centered account that assigns stable properties to diagnosable individuals, to protein molecules, or to individual cortical sources fails to capture the dominant organizational signal. In each case, the explanatory work is done by distributed field-like dynamics: trajectory-space variance geometry in the psychiatric case; traveling wave-coupled phase transitions in the cell biology case; and geometry-constrained eigenmode compression with wave propagation in the neuroimaging case. The present essay develops these parallels systematically, arguing that all three phenomena can be interpreted within a common generalized field-theoretic framework without reducing any to the others or making implausible claims about ontological identity across biological scales.

The interpretive framework we employ, the Relativistic Scalar-Vector Plenum (RSVP) formalism, was developed originally in the context of cosmological field theory and has been extended progressively to problems in cognition, political economy, and collective computation. We do not claim that the cellular ERK system, the anxious brain, and the cortical eigenmode structure are literally implementing the same physical equations. We claim something more modest and more defensible: that the organizational principles visible in all three systems are instances of a common mathematical structure, namely the propagation of constraint redistribution across coupled fields defined over organizational manifolds, and that formalizing this structure yields genuine predictive and explanatory leverage that entity-centered models cannot provide.

Section 2 develops the RSVP-theoretic interpretation of the GAD brain-age findings. Section 3 analyzes the ZO-1 and ERK wave dynamics. Section 4 develops a unified account of structural phase transitions between stabilizing and exploratory organizational regimes. Section 5 establishes admissibility as a cross-domain mathematical primitive. Section 6 presents the formal framework including interpretation of all three empiri-

cal systems. Section 7 draws implications for psychiatry, developmental biology, and collective intelligence research. Section 9 addresses conceptual boundaries, theoretical distinctions, and the scope of the framework's claims. Section 10 acknowledges limitations explicitly. Section 11 derives experimentally discriminable predictions. Section 8 concludes.

2 Brain-Age Variability and Heterogeneous Neural Trajectories

2.1 The PAD Geometry of Anxiety

The brain-age framework rests on a simple and elegant idea: a machine learning model trained to estimate chronological age from structural neuroimaging can be applied to clinical populations, and the residual discrepancy between predicted and actual age provides a measure of how structurally atypical that population's brains are relative to healthy developmental norms [2]. Positive predicted age difference implies a neurologically older-appearing structure; negative PAD implies relative youth or atypicality in a different direction. The implicit model is that pathology acts as an accelerant, pushing brains prematurely toward configurations typical of older healthy individuals.

This model is intuitively appealing and has shown positive results in conditions such as schizophrenia and major depression. Its failure in GAD is therefore informative. The absence of a significant mean PAD elevation does not merely show that GAD is neurologically undetectable at the group level; it reveals that the appropriate description of the GAD population in trajectory space is not a translation (a shift of the mean) but a dilation (an expansion of the variance). The population is more spread out in the space of structural brain configurations, not more concentrated in a pathological direction.

Let $\mathcal{T}$ denote the space of structural brain configurations reachable across a healthy lifespan, parameterized by chronological age $t \in [t_0, t_\infty]$ and by a high-dimensional morphometric state vector $\mathbf{x} \in \mathbb{R}^n$. The healthy control population traces a distribution μ_{HC} over $\mathcal{T}$, which the CNN model approximates by learning to invert the projection $\pi : \mathcal{T} \to [t_0, t_\infty]$ that extracts chronological age from structural configuration. The PAD for an individual is then $\hat{t}(\mathbf{x}) - t$, where $\hat{t}$ is the learned inverse map.

The Richier et al. findings can be formalized as follows.

Definition 2.1 (PAD Geometry)**.** Let μ_{HC} and μ_{GAD} denote the distributions of structural configurations in healthy controls and GAD individuals respectively, projected to PAD values via $\delta(t, \mathbf{x}) = \hat{t}(\mathbf{x}) - t$. The GAD population exhibits *trajectory-space dilation* rather than translation if

$$\mathbb{E}_{\mu_{GAD}}[\delta] \approx \mathbb{E}_{\mu_{HC}}[\delta] \quad \text{while} \quad \mathrm{Var}_{\mu_{GAD}}[\delta] > \mathrm{Var}_{\mu_{HC}}[\delta],$$

with the inequality becoming more pronounced in adult subpopulations.

This is precisely what Richier et al. report. The finding suggests that GAD does not primarily operate by shifting the brain's developmental trajectory in a single direction but by increasing the dispersion of trajectories across individuals. Some individuals consolidate neural architecture prematurely in response to chronic threat-anticipation; others remain in more developmentally diffuse or plastic states. The disorder does not produce a single neurological signature because it does not impose a single developmental pressure but rather amplifies the sensitivity of developmental trajectories to individual variation in symptom severity, comorbidity, medication, and life history.

2.2 Admissibility Geometry and Trajectory Variance

The entity-centered biomarker model implicitly assumes that GAD is a fixed point in diagnostic space corresponding to a fixed region in brain-configuration space. The PAD results falsify this assumption. A more adequate model treats the condition as a deformation of the admissibility geometry of developmental trajectories: a change in which configurations are dynamically accessible, and with what probability, rather than a change in the mean configuration.

Definition 2.2 (Admissibility Field)**.** An admissibility field over $\mathcal{T}$ is a non-negative function $S : \mathcal{T} \to [0, \infty)$ that assigns to each configuration $\mathbf{x}$ at age t the local volume of accessible future trajectories. High S corresponds to high developmental plasticity or instability; low S corresponds to a consolidated, constrained future trajectory.

In healthy development, S typically decreases with age as neural architecture consolidates. Critical periods are intervals during which S is locally elevated, permitting major structural reorganization. Pathological processes can alter S in two ways: by globally elevating it (increasing plasticity or instability), by globally suppressing it (premature consolidation), or by increasing its *variance* across individuals without strongly shifting its mean.

The third pattern is what the GAD results suggest. The disorder does not uniformly elevate or suppress developmental plasticity; it increases the heterogeneity of admissibility profiles across individuals. Some GAD brains show signatures of suppressed S (premature consolidation, positive PAD); others show elevated S (delayed consolidation, negative PAD); the population-level mean remains close to zero.

Proposition 2.3. *If GAD acts primarily through increased variance in the admissibility field rather than through a directional shift in its mean, then the PAD distribution of the GAD population will be approximately mean-zero but with elevated variance relative to controls, and symptom severity will correlate with the magnitude of individual PAD rather than with its sign.*

Argument. Let S_i denote the admissibility profile of individual i. If GAD shifts S_i by a zero-mean random perturbation ξ_i with $\mathrm{Var}[\xi_i] > \mathrm{Var}[\xi^{HC}]$, then the resulting PAD distribution inherits the increased variance without inheriting a directional mean shift.

Symptom severity, as a monotone function of the perturbation magnitude $|\xi_i|$, will then correlate with $|\delta_i|$ regardless of sign. The exploratory analyses reported by Richier et al. showing symptom-PAD correlations after controlling for medication and comorbidity are consistent with this structure. □

2.3 The Insufficiency of Univariate Reduction

A secondary finding of Richier et al. is that their CNN-based multivariate approach detects the heterogeneity signal more clearly than traditional univariate neuroimaging analyses would. This is not a minor methodological footnote. It reflects a deep point about the relationship between representational dimensionality and the detectability of distributed organizational structure.

Traditional univariate analyses project the high-dimensional brain-configuration manifold $\mathcal{T}$ to a collection of scalar measurements at individual voxels or regions. These projections preserve local amplitude information but destroy the distributed relational structure that encodes developmental state. The CNN model, by learning spatially distributed nonlinear functions of the full three-dimensional input, retains more of this relational structure and therefore detects organizational patterns invisible to univariate methods.

This is exactly what should be expected if the relevant organizational signal is carried by the admissibility geometry of the manifold rather than by the marginal distributions at individual measurement sites. Variance in trajectory space is a property of the manifold's global structure; collapsing the manifold to independent scalars destroys precisely the information that makes this variance detectable.

One important epistemic limitation of the trajectory-space dilation interpretation deserves explicit acknowledgment. The Richier et al. data are cross-sectional: each individual contributes a single PAD measurement at a single time point. The dilation interpretation treats increased cross-sectional PAD variance as evidence for increased variance in developmental trajectories, but this inference requires the additional assumption that the cross-sectional distribution reflects the underlying longitudinal dynamics. Individuals with high positive PAD may have followed a consistently accelerated trajectory, or may have undergone a recent acute consolidation event; the cross-sectional measurement cannot distinguish these. Longitudinal imaging designs, in which the same individuals are followed across developmental transitions, would be required to confirm that the trajectory-space dilation is a genuine dynamical feature rather than an artifact of population heterogeneity in initial developmental state. This limitation motivates the experimental predictions developed in Section 11.

3 ERK Activation Waves as Distributed Coordination Dynamics

3.1 The Tissue as a Coupled Dynamical Medium

The standard model of epithelial cell migration treats cells as semi-autonomous agents that respond to local chemical gradients, express motility machinery, and collectively produce directed movement as a statistical aggregate of individual decisions. This model works reasonably well for loosely coupled populations but becomes inadequate when describing the highly coordinated collective migration observed in wound healing, embryonic development, and cancer invasion. The Hirano et al. paper on ZO-1 and ERK wave dynamics provides a particularly clear demonstration of why [3].

The central observation is that ERK activation does not arise independently in each cell in response to local stimuli but propagates across the epithelial monolayer as a traveling wave. The tissue, as a coupled dynamical medium, supports the propagation of biochemical activation fronts in ways that individual cells, considered in isolation, cannot generate. This propagating activation then triggers a second-order dynamical event: the redistribution of ZO-1 from apical junctional complexes to basal podosome-like structures. This redistribution itself propagates collectively, following the ERK wave with a characteristic delay.

The result is a tissue that reorganizes its structural architecture in a wave-like fashion across space and time. The tight-junction protein that normally maintains epithelial barrier integrity transiently relocates to structures associated with invasive migration and extracellular matrix remodeling. The collective consequence is directed migration driven not by independent cellular decisions but by a distributed signaling computation performed across the entire monolayer.

3.2 ERK Waves as Constraint-Propagating Fronts

From a field-theoretic perspective, the ERK activation wave is best understood not as a simple diffusion front but as a constraint-propagating front: a traveling region of local dynamical reorganization that alters the admissibility structure of each cell it passes through, enabling configurations (podosome formation, ZO-1 redistribution, elevated traction force) that were not accessible before the wave arrived.

Definition 3.1 (Constraint-Propagating Front)**.** A constraint-propagating front in a coupled spatial dynamical system is a traveling region $\mathcal{F}(t) \subset \Omega$ such that passage of $\mathcal{F}$ through a local neighborhood U alters the local admissibility structure $S|_U$, enabling transitions between organizational regimes that are suppressed in the pre-wave state.

The ERK wave is a constraint-propagating front because it enables the ZO-1 redistribution transition: MEK inhibition, which suppresses ERK wave propagation, also suppresses ZO-1 translocation to podosomes, demonstrating that the wave is not merely

correlated with the structural reorganization but is causally required for it [3]. The wave opens a dynamical window during which the cell can exit the tight-junction maintenance regime and enter the podosome-mediated invasive regime.

This is structurally different from simple diffusion or gradient-driven migration. In diffusion, the signal spreads to enable a quantitative response whose direction is determined by concentration. In constraint propagation, the wave alters the qualitative topology of local accessible state space: it enables regime transitions rather than merely modulating continuous response intensity. The analysis of admissible and non-classical waves in hyperbolic systems provides formal precedent for precisely this kind of topology-changing wave structure, in which the wave selects among formally permissible branches of evolution rather than simply transporting energy [30].

3.3 Wave Mechanics and Propagation Velocity

The mathematical structure of ERK waves in epithelial systems has features consistent with reaction-diffusion dynamics of the excitable medium type [9]. A minimal model treats local ERK activation $u(\mathbf{r}, t)$ as satisfying

$$\frac{\partial u}{\partial t} = D\nabla^2 u + f(u, v), \quad \frac{\partial v}{\partial t} = \epsilon g(u, v), \tag{1}$$

where v is a recovery variable, f and g are nonlinear kinetic functions specifying the local excitable dynamics, D is the effective coupling coefficient (which in an epithelial sheet combines intracellular signaling diffusion with paracrine coupling through gap junctions and extracellular ligands), and $\epsilon \ll 1$ is the timescale separation between the fast activation variable and the slow recovery. Equation (1) supports traveling wave solutions of the form $u(\mathbf{r}, t) = U(\mathbf{r} - c\mathbf{n}t)$ for wave speed c and propagation direction $\mathbf{n}$.

The ZO-1 redistribution dynamics can be coupled to this wave by treating the local fraction of ZO-1 at apical junctions as a slow structural variable $\phi(\mathbf{r}, t)$ satisfying

$$\frac{\partial \phi}{\partial t} = -k_+(u)\phi + k_-(\phi)(1 - \phi), \tag{2}$$

where $k_+(u)$ is the wave-dependent redistribution rate (increasing in u) and k_- is the restoration rate returning ZO-1 to junctions after the wave passes. The coupled system (1)–(2) produces the qualitative behavior observed by Hirano et al.: ZO-1 redistribution following the ERK wave with a delay determined by the ratio k_+/k_- and the wave speed c.

Proposition 3.2. *In the coupled system (1)–(2), the ZO-1 redistribution front propagates at the same velocity as the ERK wave in the quasi-static limit $\epsilon \to 0$ of slow recovery dynamics.*

Proof. In the quasi-static limit, the recovery variable v varies slowly relative to the wave

transit time, so the ERK wave passes through any local neighborhood U before v has significantly changed. During the transit, u rises from rest to peak activation and falls again on the timescale c^{-1} (per unit distance). The ZO-1 variable ϕ responds according to (2); since k_+ is concentrated in the wave region, ϕ decreases during wave passage and recovers at rate k_- afterward. The spatial locus of minimum ϕ therefore propagates with the wave front at velocity c. □

4 ZO-1 Redistribution and Structural Phase Transitions

4.1 Two Organizational Regimes

The Hirano et al. findings identify two distinct organizational regimes for a migrating epithelial cell: a junction-maintenance regime, in which ZO-1 localizes at apical tight-junction complexes and the cell participates in maintaining epithelial barrier integrity and collective cohesion; and a podosome-invasive regime, in which ZO-1 relocalizes to basal podosome-like structures and the cell participates in extracellular matrix remodeling and directed invasive movement [3].

These are not merely quantitatively different states along a continuum. They involve qualitatively different organizational principles: different spatial localization of key proteins, different cytoskeletal configurations (cortical actin for junction maintenance versus actin-rich podosome cores), different extracellular interactions (paracellular barrier maintenance versus matrix degradation and substrate adhesion), and different contributions to collective behavior (cohesion versus migration). The transition between them is triggered by the ERK wave and is therefore externally induced rather than arising from purely internal fluctuation.

Definition 4.1 (Organizational Phase)**.** An organizational phase for a cell in a coupled epithelial monolayer is an equivalence class of structural configurations with qualitatively similar protein localization patterns, cytoskeletal architectures, and mechanical interactions with the environment. A phase transition occurs when the cell moves from one equivalence class to another in response to a constraint-propagating front.

The ERK wave is the trigger for the phase transition from junction-maintenance to podosome-invasive. The molecular requirements identified by Hirano et al. specify the mechanism: ERK phosphorylation of ZO-1 releases it from junctions (phospho-deficient mutants fail to redistribute), and the actin-binding and cortactin-binding regions of ZO-1 are required for podosome localization. The transition is therefore a phosphorylation-dependent structural reorganization with both energetic and spatial components.

4.2 Constraint Density Reallocation

The RSVP-theoretic interpretation of this transition treats it as a reallocation of constraint density between organizational modes. In the junction-maintenance phase, the dominant structural constraint is the maintenance of intercellular cohesion through tight-junction complexes; ZO-1's contribution to this constraint is local and apical. In the podosome-invasive phase, the dominant structural constraint shifts to the generation of directed traction forces and matrix remodeling; ZO-1's contribution becomes basal and protrusive.

Let $\rho_J(\mathbf{r}, t)$ and $\rho_P(\mathbf{r}, t)$ denote the constraint densities associated with junction maintenance and podosome activity respectively at position $\mathbf{r}$ and time t. The total constraint density $\rho_T = \rho_J + \rho_P$ is approximately conserved on the timescale of ZO-1 redistribution, since the total ZO-1 concentration does not change rapidly. The ERK wave drives a local transfer from ρ_J to ρ_P by enabling the phosphorylation- dependent redistribution.

Theorem 4.2 (Constraint Reallocation)**.** *Under the coupled dynamics* (1)–(2)*, the passage of an ERK activation front through a local neighborhood* U *drives a transient reallocation of constraint density from junction-maintenance to podosome-invasive modes, with the magnitude of reallocation proportional to the local ERK peak amplitude* $\max_t u(\mathbf{r}, t)$ *for* $\mathbf{r} \in U$*.*

Argument. The redistribution rate $k_+(u)$ is monotone increasing in u by the phosphorylation mechanism. Therefore the total ZO-1 displaced from junctions during the wave transit is

$$\Delta\phi(U) = \int_0^\infty k_+(u(\mathbf{r}, t))\phi(\mathbf{r}, t)\, dt,$$

which is bounded below by $k_+(\max_t u) \cdot \int_0^\infty \phi\, dt$ and above by $k_+(\max_t u) \cdot \phi(0) \cdot T_{wave}$, where T_{wave} is the wave transit time through U. Both bounds are monotone in $\max_t u$, establishing the claimed proportionality. The displaced ZO-1 localizes to podosome structures by the actin-binding pathway, completing the reallocation from ρ_J to ρ_P. □

4.3 Reversibility and Restoration

The phase transition induced by the ERK wave is not permanent. After the wave passes, the recovery variable v in equation (1) suppresses further ERK activation, and the restoration term $k_-(1 - \phi)$ in equation (2) drives ZO-1 back toward junctions. The cell returns to the junction-maintenance phase on a timescale determined by k_- and the ERK recovery dynamics.

This reversibility is crucial for collective migration. If the phase transition were irreversible, cells would permanently lose junction-maintenance capacity and the epithelial sheet would disintegrate. Instead, the wave induces a transient invasive window: a period during which the cell can participate in directed migration and matrix remodeling, after which it restores its junction-maintenance function and contributes to the cohesion that keeps the migrating sheet intact.

The collective consequence is a tissue that can simultaneously maintain structural integrity and achieve directed migration: different spatial regions are in different phases at any given time, determined by the local passage of the ERK wave front. The wave coordinates migration not by bringing all cells into the invasive phase at once but by propagating the invasive phase through the tissue in a controlled temporal sequence.

5 Admissibility as a General Principle of Constraint Selection

The concept of admissibility appears across several independent mathematical domains as a mechanism for restricting formally possible trajectories, morphisms, or solutions to those that preserve coherent structural evolution under transformation, perturbation, or propagation. This recurrence is not terminological coincidence. Before introducing the RSVP field equations, it is worth surveying these appearances systematically, because they provide independent mathematical legitimacy for treating accessibility as a dynamical field variable rather than as a derived property of state evolution. The novelty of the RSVP framework does not lie in the concept of admissibility itself but in treating the volume of admissible trajectories as a primary distributed dynamical quantity rather than as a fixed background constraint.

5.1 Admissibility in PDE Theory and Weak Solutions

In the theory of nonlinear hyperbolic partial differential equations, classical solutions can fail to exist globally due to shock formation and discontinuities. The resulting weak solutions are generally non-unique; additional selection criteria, called admissibility conditions, are required to identify physically or organizationally meaningful solutions among the many that satisfy the equations in the distributional sense. Classical admissibility conditions include the Lax entropy condition, the viscosity condition, and the kinetic relation, each embodying a different physical principle for selecting coherent evolution from formally valid but structurally unstable alternatives.

Recent work has extended admissibility analysis to action rate criteria, formalizing the selection of weak solutions through the rate at which the system's action functional is consumed at discontinuities [25]. This approach is especially relevant to the present framework because it treats admissibility as a local-in-time property, selecting dynamically coherent evolutions at each instant rather than requiring global minimization. The parallel to RSVP-style constraint-propagating fronts is direct: the front itself functions as a traveling admissibility criterion, selecting at each spatial location the organizational regime that preserves coherent structural evolution. The analysis of hyperbolic equations and non-classical wave structures in related systems further shows that admissibility conditions govern the emergence of composite waves and phase boundaries of the type observed in the ERK-ZO-1 transition [30].

5.2 Admissibility and Nonuniform Hyperbolicity

In the theory of dynamical systems, admissibility conditions arise naturally in the characterization of nonuniform hyperbolicity. A dynamical system exhibits nonuniform hyperbolicity when the rates of expansion and contraction along trajectories vary in a measurable but non-constant way, and admissibility conditions for associated operators are precisely what determine whether the observed trajectory structure is consistent with a given Lyapunov-exponent profile [26]. The key structural feature is that admissibility in this context is not a property of individual states but of *weighted trajectory spaces*: the question is not whether a given orbit is possible but whether the entire family of orbits is organized in a way consistent with the underlying hyperbolicity structure.

This is directly analogous to the RSVP interpretation of GAD developmental trajectories. The disorder does not render individual neural configurations impossible; it alters the organizational geometry of the trajectory family, widening the accessible trajectory space in ways that are visible at the population level rather than the individual level. Admissibility in the dynamical-systems sense operates on the same object — the space of trajectories rather than the space of states — as the RSVP accessibility field S.

The analysis of admissibility through delay-equation induction offers a complementary perspective [27]. By embedding lower-dimensional trajectory dynamics into higher-dimensional delay systems, admissibility conditions acquire a natural geometric interpretation in terms of the lifted trajectory space, where organizational constraints become visible as curvature or confinement properties that are not apparent at the original dimensionality. This is structurally consistent with the RSVP claim that distributed organizational constraints operating on the trajectory manifold cannot be reduced to point-wise state properties.

5.3 Inferential Admissibility and Organizational Coherence

Admissibility conditions also appear in philosophical logic and inferential semantics as constraints on which inference rules preserve the coherence of a logical or semantic system. The classic example is the tonk connective introduced by Prior: a connective defined by an introduction rule and an elimination rule that, taken together, allow the derivation of any proposition from any other, collapsing the inferential structure of the system entirely. Admissibility constraints are what prevent such inferential collapse by requiring that transition rules preserve the organizational integrity of the consequence relation [29].

The structural parallel to biological admissibility is not superficial. An inferential system that loses its admissibility constraints undergoes unbounded expansion of derivable conclusions — an explosion of accessible states — exactly analogous to a biological system that loses its organizational constraints on trajectory-space accessibility. In both

cases, the failure mode is not incorrect evolution but unconstrained evolution: the system reaches states that are formally reachable but organizationally incoherent. The RSVP accessibility field S functions in the biological domain as an admissibility measure functions in the inferential domain: it bounds the volume of accessible evolution and thereby preserves the structural coherence that makes organized behavior possible. This parallel suggests that admissibility is not merely a technical device in each domain but a general invariant of systems that must maintain coherent organizational structure under ongoing state evolution.

5.4 Categorical Admissibility and Structural Preservation

In category theory and its applications to algebraic topology and localization theory, admissibility conditions govern which morphisms or localizations preserve relevant structural properties under functorial transformation. The admissibility of localizations of crossed modules, for example, determines which localization maps preserve the higher-dimensional algebraic structure of crossed-module diagrams under pullback [31]. Admissibility in this setting is a condition on the transformations themselves rather than on the objects: it distinguishes structure-preserving mappings from formally valid but structurally destructive ones.

This categorical sense of admissibility connects to the RSVP framework through the question of which constraint-transport operations preserve organizational coherence across spatial or temporal projection. The vector field $\mathbf{v}$ in the RSVP equations does not merely carry activation; it carries the organizational regime through the tissue. Admissibility, in the categorical sense, would require that this transport preserve the relevant structural relationships among the $(\Phi, \mathbf{v}, S)$ fields rather than merely relocating activation energy. The multivalued fixed-point and coincidence-point results that arise in metric fixed-point theory under admissibility conditions provide further formal grounding for the idea that admissibility restricts which dynamical correspondences are structurally stable [28].

5.5 Admissibility as a Cross-Domain Invariant

Across these otherwise disconnected mathematical domains, admissibility repeatedly emerges as a mechanism for restricting formally possible trajectories to those preserving coherent structural evolution under transformation, perturbation, or propagation. Whether the relevant objects are weak PDE solutions, inferential rule systems, hyperbolic cocycles, localization functors, or collective biological states, admissibility functions as a constraint-selection principle operating over spaces of possible organizational evolution. The RSVP framework interprets this recurrence not as terminological coincidence but as evidence that admissibility is a general invariant of distributed dynamical organization. The framework's specific contribution is to treat the volume of admissible trajectories not

as a fixed background constraint but as the primary dynamical variable S, a distributed field that evolves under the same coupled equations as coherence and transport. In the two biological systems examined here, this dynamical admissibility field is what distinguishes the RSVP interpretation from both standard diffusion theory and localist entity-centered accounts: the question is not which states a system can occupy but which *trajectory structures* it can sustain, and how the volume of those structures evolves under propagating organizational perturbations.

6 The RSVP Framework and Constraint Propagation Across Biological Scales

6.1 The Field Triple

The term *field* is used throughout this section in the phenomenological dynamical-systems sense: a distributed quantity defined over a spatial or configuration-space domain whose local evolution depends on neighboring states and transport structure, rather than in the sense of a fundamental gauge or particle field in high-energy physics. This distinction matters because the RSVP framework is equally applicable to literal physical space (as in the epithelial monolayer) and to abstract state manifolds (as in the developmental configuration space relevant to the GAD findings). In each case, the field triple $(\Phi, \mathbf{v}, S)$ describes the organizational geometry of the system rather than its physical substrate.

The Relativistic Scalar-Vector Plenum framework characterizes organizational states through a triple $(\Phi, \mathbf{v}, S)$ defined over an admissible trajectory manifold $\mathcal{M} \times [0, T]$, where $\mathcal{M}$ is the relevant organizational state space rather than necessarily a Euclidean domain. In the epithelial migration setting, $\mathcal{M} \approx \mathbb{R}^2$ is the physical tissue surface. In the neural developmental setting, $\mathcal{M}$ is the high-dimensional configuration manifold of structural brain states, which may be reconstructed from imaging or transcriptomic data via nonlinear dimensionality reduction. In general:

$$(\Phi, \mathbf{v}, S) : \mathcal{M} \times [0, T] \to \mathbb{R}_{\geq 0} \times T\mathcal{M} \times [0, \infty),$$

where $T\mathcal{M}$ denotes the tangent bundle of $\mathcal{M}$, accommodating transport along the manifold's intrinsic geometry rather than through ambient Euclidean space. This abstraction unifies what would otherwise appear as domain-specific models into instances of a single organizational-geometric framework.

Definition 6.1 (RSVP Field Triple)**.** The RSVP organizational state at $(x, t) \in \mathcal{M} \times [0, T]$ is the triple $(\Phi, \mathbf{v}, S)$ where:

1. $\Phi(x, t)$ measures local organizational density or coherence: the degree to which the system at $x \in \mathcal{M}$ is organized around a specific structural configuration.

2. $\mathbf{v}(x,t) \in T_x\mathcal{M}$ specifies the local transport or propagation direction and magnitude along $\mathcal{M}$: the direction and rate of constraint redistribution or signaling flow.

3. $S(x,t)$ measures geometric accessibility: the logarithmic local volume of dynamically reachable configurations under finite-energy perturbation from the current state, approximated operationally as

$$S(x,t) \approx -\log \rho(x,t),$$

where $\rho(x,t)$ is the local trajectory density on $\mathcal{M}$ at time t. High S implies a large accessible future trajectory bundle and high organizational plasticity; low S implies a consolidated, narrow trajectory distribution.

Remark 6.2. The quantity S should not be identified directly with thermodynamic entropy in the statistical-mechanical sense. It functions as a geometric accessibility measure over dynamically reachable organizational trajectories. In the biological applications considered here, S operates at the level of geometric entropy S_{geom}: the logarithmic volume of admissible trajectory bundles on a reconstructed organizational manifold. This is distinct from informational entropy S_{info} (uncertainty over discrete symbolic states) and from thermodynamic entropy S_{phys} (microstate counts at the molecular level). Thermodynamic and informational interpretations are optional specializations rather than foundational commitments of the framework. The operationalization $S \approx -\log \rho$ is practical precisely because it makes S_{geom} inferable from data through inverse local trajectory density estimation on experimentally reconstructed state manifolds.

The governing equations couple these three fields over $\mathcal{M}$:

$$\frac{\partial \Phi}{\partial t} = -\text{div}_{\mathcal{M}}(\Phi \mathbf{v}) + \lambda R(\Phi, S), \tag{3}$$

$$\frac{\partial \mathbf{v}}{\partial t} = -\nabla^{\mathbf{v}}_{\mathcal{M}}\mathbf{v} - \alpha\, \text{grad}_{\mathcal{M}}\, \Phi + \beta\, \text{grad}_{\mathcal{M}}\, S + \mathbf{F}_{ext}, \tag{4}$$

$$\frac{\partial S}{\partial t} = \kappa \Delta_{\mathcal{M}} S - \gamma \Phi S + \delta Q(\mathbf{v}), \tag{5}$$

where $\text{div}_{\mathcal{M}}$, $\text{grad}_{\mathcal{M}}$, and $\Delta_{\mathcal{M}}$ are the divergence, gradient, and Laplace–Beltrami operators on $\mathcal{M}$; $R(\Phi, S)$ is a regeneration term encoding how organized structures rebuild under favorable accessibility conditions; $\mathbf{F}_{ext}$ represents external forcing; $Q(\mathbf{v})$ represents the accessibility generated by transport flows; and $\lambda, \alpha, \beta, \gamma, \delta, \kappa > 0$ are coupling constants whose values are substrate-dependent.

Equation (3) states that coherence is transported along $\mathcal{M}$ by the vector field and locally regenerated at a rate depending on existing coherence and accessibility. Equation (4) states that transport evolves under coherence gradients (regions of high coherence attract transport) and accessibility gradients (transport is directed toward regions of higher organizational openness). The $\beta\, \text{grad}_{\mathcal{M}}\, S$ term encodes the tendency of propagating

organizational dynamics to preferentially expand into regions of higher reorganizational permissibility, analogous to how activation fronts in excitable media preferentially propagate through regions below refractory threshold: since $S \approx -\log \rho$, the accessibility gradient $\mathrm{grad}_{\mathcal{M}} S \approx -\mathrm{grad}_{\mathcal{M}} \log \rho$ points away from dense trajectory basins toward regions where organizational restructuring remains possible. Equation (5) states that accessibility diffuses over $\mathcal{M}$, is suppressed by high coherence (organized structures close off alternatives), and is generated by active transport.

A derived quantity of particular interest is the *constraint-flux law*, which describes how the organizational domain evolves under coupled transport and accessibility:

$$\partial_t x = F(x, \mathbf{v}, \mathrm{grad}_{\mathcal{M}} S), \quad x \in \mathcal{M}, \tag{6}$$

capturing the key insight that accessibility gradients shape the directionality of organizational evolution on $\mathcal{M}$. Because $\mathrm{grad}_{\mathcal{M}} S \approx -\mathrm{grad}_{\mathcal{M}} \log \rho$, this law describes how constraint fronts preferentially drive organizational evolution away from trajectory concentration basins. An empirically tractable invariant associated with this law is the ratio

$$\mathcal{I} = \frac{|\mathbf{v}|}{|\partial_t S|}, \tag{7}$$

which measures organizational conversion efficiency: the transport expenditure required to collapse a unit volume of accessible trajectory space. In the epithelial setting, $|\mathbf{v}|$ corresponds to wave-front propagation speed and $|\partial_t S|$ to the rate of junctional ZO-1 departure. In the neural developmental setting, $|\mathbf{v}|$ corresponds to developmental drift velocity on the neural configuration manifold and $|\partial_t S|$ to attractor-collapse or pruning rate. The hypothesis that $\mathcal{I}$ takes approximately substrate-invariant values across organizational systems is a candidate universality claim that would require longitudinal, multi-system empirical data to evaluate.

Two candidate functional forms for the unspecified terms deserve mention as the most natural choices consistent with the framework's organizational logic. For the regeneration term $R(\Phi, S)$, a logistic-exponential form

$$R(\Phi, S) = \Phi(1 - \Phi)\, e^{-S} \tag{8}$$

captures the core phenomenology: regeneration is maximal at intermediate coherence (logistic factor $\Phi(1-\Phi)$, vanishing both at full disorganization $\Phi = 0$ and at full saturation $\Phi = 1$) and suppressed exponentially by high accessibility (exponential factor e^{-S}, since high S corresponds to a plastic, uncommitted state in which coherent structure cannot easily rebuild). For the accessibility generation term $Q(\mathbf{v})$, a local kinetic energy density

$$Q(\mathbf{v}) = \tfrac{1}{2}|\mathbf{v}|^2 \tag{9}$$

is the most parsimonious choice: transport flows generate accessible future states at a rate proportional to their squared magnitude, which is consistent with the Constraint-Flux Law (6) and with the operationalization $S \approx -\log \rho$, since fast transport redistributes trajectory density and thereby raises S in the downstream region. These forms are proposed as minimal candidates for future parameterization rather than as derivable consequences of the biological mechanisms.

It should be emphasized that equations (3)–(6) are phenomenological field equations over an organizational manifold rather than mechanistic biochemical models. They are intended to capture the organizational logic of constraint redistribution at a level of abstraction above specific molecular pathways. The equations are offered as structural scaffolding for interpreting the qualitative dynamics and generating experimentally discriminable predictions, not as a predictive mechanistic model awaiting parameter fitting.

6.2 RSVP Interpretation of the GAD Findings

In the neural trajectory setting, $\mathcal{M}$ is the high-dimensional manifold of structural brain configurations; $\Phi(x,t)$ represents the local coherence of structural neural organization at configuration $x \in \mathcal{M}$ and developmental time t; $\mathbf{v}(x,t)$ represents the developmental drift velocity along $\mathcal{M}$; and $S(x,t) \approx -\log \rho(x,t)$ represents the geometric accessibility of the local developmental trajectory bundle, with ρ the local density of developmentally observed neural configurations.

Healthy development corresponds to a smooth decreasing profile of S along the typical developmental trajectory: high plasticity in early development, progressive consolidation in adolescence, stable low plasticity in mature adulthood. The PAD measurement captures where on this trajectory a given individual's structural configuration falls at their chronological age.

The GAD population's increased PAD variance, in RSVP terms, corresponds to increased variance in S across individuals at any given chronological age. The disorder amplifies inter-individual heterogeneity in the accessibility profile: some individuals consolidate more rapidly (low S, high Φ, positive PAD), others more slowly or atypically (high S, lower Φ, negative PAD). The coupling constant γ in equation (5), which governs the rate at which high coherence suppresses accessibility, would show elevated inter-individual variance in the GAD population.

Proposition 6.3 (RSVP Variance Amplification)**.** *If GAD increases the variance of the coupling parameter γ across individuals without strongly shifting its mean, then the PAD distribution of the GAD population will satisfy* $\mathrm{Var}_{GAD}[\delta] > \mathrm{Var}_{HC}[\delta]$ *with* $|\mathbb{E}_{GAD}[\delta] - \mathbb{E}_{HC}[\delta]| \approx 0$*, consistent with the Richier et al. findings.*

The exploratory finding that symptom severity correlates with PAD magnitude

after controlling for medication is consistent with this interpretation: symptom severity reflects the magnitude of the perturbation to γ, which drives the individual toward either extreme of the accessibility distribution. High symptom severity corresponds to large $|\xi_i|$, pushing the individual toward either early consolidation or prolonged plasticity.

6.3 RSVP Interpretation of the ERK Wave Dynamics

In the tissue migration setting, $\mathcal{M} \approx \mathbb{R}^2$ is the physical epithelial surface; $\Phi(x,t)$ represents local organizational coherence of the junction-maintenance architecture (tight junctions, apical ZO-1 localization, cortical actin organization); $\mathbf{v}(x,t)$ represents the local transport of signaling activation (ERK wave propagation direction and velocity along the tissue surface); and $S(x,t) \approx -\log \rho(x,t)$ represents local structural accessibility, with ρ the local density of observed cellular configurations at (x,t), with high S enabling the transition to podosome-invasive organization and low S enforcing junction-maintenance.

The resting epithelial monolayer corresponds to high Φ (well-organized junctions), low $\mathbf{v}$ (no directed transport), and low S (junction maintenance is the dominant organizational attractor, podosome formation is suppressed). The ERK wave corresponds to a propagating region of elevated $\mathbf{v}$, which through equation (5) generates elevated S in its wake (transport flows open up accessibility). This elevated S, through the term $-\gamma\Phi S$ in equation (5), reduces Φ locally, enabling the regime transition to podosome-invasive organization.

After the wave passes, $\mathbf{v}$ returns to low amplitude, S decays through the $\kappa\nabla^2 S$ diffusion term (accessibility spreads and diminishes), and the regeneration term $\lambda R(\Phi, S)$ in equation (3) drives Φ back toward its junction-maintenance value. The tissue restores junction-maintenance organization while the wave front continues propagating through downstream regions.

The RSVP framework thus captures the key qualitative features of the Hirano et al. system: wave-triggered regime transitions, ZO-1 redistribution as a transient suppression of Φ, and restoration to junction-maintenance after wave passage.

6.4 RSVP Interpretation of the GBF Neuroimaging Framework

The Wang et al. geometric basis function framework provides what is in some respects the most direct empirical instantiation of the RSVP manifold formalism [1]. In that paper, $\mathcal{M}$ is not an abstract organizational manifold but a literal Riemannian surface: the individual's cortical mesh reconstructed from structural MRI and endowed with the intrinsic metric of the cortical geometry. The Laplace–Beltrami operator $\Delta_{\mathcal{M}}$ is computed explicitly on this surface, yielding eigenmodes ψ_i that are precisely the harmonic basis of the manifold. Neural activity is then expressed as $x(t) = \sum_i \theta_i(t)\psi_i$, a decomposition that is RSVP-compatible at the level of notation: the coherence field Φ corresponds to the

spatially organized amplitude distribution $x(t)$ over $\mathcal{M}$, and the eigenmode coefficients $\theta_i(t)$ carry the temporal dynamics.

The spectral prior $\Sigma^{-1} = \text{diag}(-\beta/\log\lambda_i)$ is the most directly interpretable component from the RSVP accessibility perspective. Because λ_i increases with spatial frequency, $-\beta/\log\lambda_i$ decreases with λ_i, assigning smaller prior variance (higher regularization) to high-frequency modes. Equivalently, high-frequency eigenmodes are penalized not because they are physically forbidden but because they correspond to high-curvature, short-wavelength configurations that are dynamically inaccessible under realistic signal-to-noise and physiological constraints. In RSVP terms, this prior is an admissibility weighting: $S(\psi_i) \propto -\log\lambda_i$, assigning lower accessibility to configurations that oscillate rapidly over the cortical surface. The logarithmic form is significant: it matches the RSVP operationalization $S \approx -\log\rho$ if the local eigenmode density on the spectral manifold is taken to scale as $\rho \propto \lambda_i$ in the high-frequency regime, consistent with the Weyl law for Laplace–Beltrami eigenvalue asymptotics.

The finding that approximately 200–300 modes suffice to reconstruct whole-brain dynamics with high fidelity is directly interpretable as an empirical upper bound on the dimensionality of the admissible trajectory manifold $\mathcal{M}_{adm}$. Of the approximately 32,000 spatial degrees of freedom in the cortical vertex representation, only a low-dimensional submanifold is dynamically admissible under the cortical geometry prior. The remaining dimensions are not activated because they are admissibility-suppressed: their high curvature places them in regions of low S, making them dynamically inaccessible rather than merely unexplored. This is structurally identical to the RSVP prediction that organized biological systems maintain low effective dimensionality by suppressing high-S organizational modes through the coupling term $-\gamma\Phi S$ in equation (5).

The optical-flow wave propagation analysis in the Wang et al. paper maps directly onto the RSVP vector field $\mathbf{v}$. Phase gradients across the cortical surface define a local velocity field

$$\mathbf{v}(\mathbf{r}, t) = -\frac{|\partial_t\phi|}{|\nabla\phi|^2}\,\nabla\phi,$$

which is precisely a surface-intrinsic transport field of the type $\mathbf{v} \in T\mathcal{M}$ in the RSVP formalism. The convergence hubs identified by DBSCAN clustering of streamline endpoints correspond to attractor basins in the Φ field: regions of high coherence density where transport trajectories terminate. This gives the invariant $\mathcal{I} = |\mathbf{v}|/|\partial_t S|$ a direct operationalization in the GBF framework: $|\mathbf{v}|$ is the optical-flow propagation speed (reported in mm/ms), and $|\partial_t S|$ can be approximated by the rate of change of the effective mode dimensionality as the wave passes through a cortical region.

The GBF paper therefore functions simultaneously as an empirical confirmation of the RSVP manifold geometry and as a methodological blueprint for operationalizing the abstract fields $(\Phi, \mathbf{v}, S)$ in neural data. The cortical manifold is the organizational

substrate; the eigenmodes are the admissible trajectory basis; the spectral prior is the accessibility field; and the propagating cortical waves are constraint-propagating fronts carrying organizational transitions across the cortical surface. The representational framing of the GBF paper — cortical geometry as a prior constraining inverse solutions — is, from the RSVP perspective, a special case of a more general claim: cortical geometry is constitutive of the admissibility structure of neural trajectories, not merely a useful regularization device.

6.5 Cross-Scale Structural Invariants

The RSVP interpretation of all three systems reveals a shared set of structural invariants that persist across substantial differences in biological scale, mechanism, and measurement modality.

The first invariant is the primacy of constraint propagation over signal diffusion. In all three systems, the causally relevant dynamics involves the propagation of regime-enabling fronts or admissibility-selecting operators rather than the diffusion of quantitative signals. ERK waves enable qualitative phase transitions in the tissue; developmental perturbations in GAD alter the qualitative topology of accessible trajectory space; cortical eigenmodes select admissible neural configurations by suppressing high-curvature trajectories through the spectral prior. In no case is the dominant organizational signal a concentration gradient or a mean-field intensity; it is either a traveling boundary between dynamical regimes or an admissibility operator that restricts the accessible configuration space.

The second invariant is variance amplification as the primary signature of altered organizational dynamics, rather than mean-field displacement. Increased PAD variance in GAD and increased heterogeneity in wave propagation velocity and ZO-1 redistribution magnitude across individual cells are both expressions of this pattern. The GBF paper provides the complementary case: reconstruction quality saturates at approximately 300 modes and degrades when higher-order modes are included, because expanding the active dimensionality beyond the admissible manifold amplifies ill-conditioning and noise rather than adding signal. The systems do not shift their average behavior; they are governed by the geometry of the admissible distribution, and it is departures from this geometry — whether through pathological dilation in GAD, constrained ERK wave propagation in migration, or inadmissible mode inclusion in source imaging — that constitute the observable signatures of organizational disruption or miscalibration.

The third invariant is the identification of reversibility with organizational competence. In all three systems, the capacity to undergo regime transitions and return to baseline functions as a marker of health. GAD involves a loss of developmental trajectory focus without a corresponding loss of the mean trajectory; disrupted ERK-ZO-1 coupling,

whether through MEK inhibition or phospho-deficient ZO-1 mutants, impairs not the static structure of junctions but the dynamic capacity for coordinated migration. In the GBF setting, the logarithmic spectral prior achieves precisely this: it permits moderate excursions into higher spatial frequencies (reversible activation of finer-grained modes) without permanently committing to configurations outside the admissible manifold. The prior moderates penalization rather than truncating modes absolutely, preserving the capacity for controlled excursion and return.

The fourth invariant is distributed coordination without centralized control. In none of the three systems does a central controller direct the macroscopic behavior. Neural developmental trajectories are shaped by distributed gene expression, environmental input, and accumulated experience; collective tissue migration is shaped by distributed ERK wave propagation and intercellular mechanical coupling; cortical source dynamics are shaped by the distributed eigenmode structure of the cortical geometry itself, with no single region or module imposing the admissibility constraint. Coherent global behavior emerges from local dynamics and their spatial coupling through the manifold geometry, not from any supralocal supervisory process.

7 Implications for Psychiatry, Development, and Collective Intelligence

7.1 Psychiatric Taxonomy and Field Geometry

The GAD brain-age findings suggest a reconsideration of psychiatric taxonomy that has broader implications. Standard diagnostic categories in psychiatry implicitly assume that conditions correspond to relatively discrete regions of neurobiological state space, distinguishable from health and from each other by characteristic mean-field features. The accumulating evidence from large-scale neuroimaging consortia increasingly challenges this assumption.

The RSVP framework suggests an alternative: psychiatric conditions correspond primarily to deformations of the accessibility geometry of developmental trajectory space rather than to specific locations in neural configuration space. A condition may manifest predominantly as trajectory-variance amplification (GAD, perhaps; also consistent with the enormous heterogeneity reported across autism spectrum studies), or as trajectory-compression into a narrow pathological attractor (some features of OCD or addiction), or as loss of trajectory-regeneration capacity (aspects of treatment-resistant depression).

This reframing has direct implications for biomarker development. If the primary neurobiological signal is a geometric deformation of trajectory space rather than a mean-field configuration shift, then effective biomarkers must capture distributional properties of neural trajectories rather than point estimates of brain state. The CNN approach

used by Richier et al. represents a step in this direction, but even more powerful would be methods that directly estimate the local dimensionality, curvature, or accessibility volume of the individual's trajectory space from longitudinal imaging data.

7.2 Collective Intelligence and Wave-Mediated Coordination

The ZO-1 and ERK findings have implications beyond wound healing and embryonic development. They contribute to an emerging picture of tissues as genuinely computational systems that solve coordination problems through distributed wave-mediated signal processing rather than through cellular autonomy or central control.

This picture is continuous with work on morphogenetic fields [14], bioelectric coordination [17], and the general theory of self-organization in biological systems [15]. The RSVP framework positions these observations within a common mathematical language that facilitates comparison across systems and scales. The propagating constraint front is a mathematical object that appears both in neural developmental dynamics and in epithelial collective migration; recognizing this shared structure opens possibilities for cross-domain theoretical transfer.

In particular, the wave-mediated coordination mechanism raises the question of whether similar constraint-propagating fronts play organizational roles in systems traditionally modeled without reference to wave dynamics: neural circuits during learning, immune system coordination, and social coordination in human groups. The RSVP framework predicts that wherever distributed coordination is achieved without central control, constraint-propagating fronts of some form will be identifiable. It should be emphasized that this essay does not claim these systems share mechanistic identity with the ERK wave or neural developmental systems discussed here; only that they may instantiate homologous organizational invariants, in the sense that their dynamical organization may be governed by structurally similar admissibility constraints operating over analogous trajectory spaces. Whether this homology is deep or shallow is an empirical question that requires system-specific analysis.

7.3 Developmental Timing and Phase Transition Windows

Both papers implicate temporal dynamics as a crucial organizational variable. The GAD findings show that the increased PAD variance is more pronounced in adults over twenty-five than in younger individuals, suggesting that the developmental timing of GAD onset and consolidation shapes the neurological trajectory in ways that diverge over time. The ERK wave findings show that the phase transition from junction-maintenance to podosome-invasive organization occurs in a temporally precise window defined by the wave transit time.

The concept of a constraint-propagating front provides a unified language for

both: developmental trajectories pass through constraint-propagating fronts associated with maturational transitions (critical periods, hormonal reorganization, experience-dependent consolidation), and the organizational consequences of these fronts depend on the system's admissibility structure at the time of passage. GAD may alter the admissibility structure in ways that amplify the divergence of trajectories at subsequent constraint- propagating fronts, producing the increasing variance observed in adults.

7.4 Extracellular Matrix Remodeling as Environmental Constraint Writing

A further implication of the Hirano et al. findings concerns the bidirectional nature of the interaction between cell and environment. Podosomes are not merely sensors of the extracellular matrix; they actively remodel it through proteolytic degradation and physical deformation. The migrating tissue therefore continuously rewrites the substrate it inhabits while simultaneously reorganizing itself in response to that substrate.

This bidirectional coupling is a specific instance of the general principle that organized systems do not merely respond to environmental constraints but modify them through their activity. In RSVP terms, the vector field $\mathbf{v}$ does not merely propagate through a fixed domain Ω but through a domain whose admissibility structure is itself being modified by the system's activity. This self-referential modification of the constraint environment is a general feature of living systems and represents a fundamental limitation of any modeling framework that treats the environment as a fixed external input.

7.5 Relation to Existing Theoretical Frameworks

The RSVP interpretation developed here does not emerge from a theoretical vacuum, and situating it relative to adjacent frameworks clarifies both what it contributes and where its claims remain genuinely distinctive.

The closest established framework is Friston's Free Energy Principle [4], which also treats biological systems as minimizing a scalar quantity (variational free energy) over generative model parameters and sensory states. The RSVP framework shares with the Free Energy Principle the emphasis on distributed inference and the rejection of passive stimulus-response causation, but differs in its explicit treatment of spatial field dynamics: the Free Energy Principle does not naturally accommodate propagating constraint fronts or spatially distributed phase transitions without additional architectural assumptions. The ERK wave system, where the organizational transition is intrinsically spatial and wave-mediated, is more naturally described by a field-theoretic formalism than by a variational inference framework applied locally.

Morphogenetic field theory in the tradition of Turing [8] and its contemporary descendants in bioelectric field research [14] also address spatially distributed coordination in biological systems. Reaction-diffusion systems of the Turing type produce spatial

pattern through local activation and long-range inhibition, and the ERK wave system has features consistent with this class of dynamics. The distinction is that standard Turing pattern formation produces static spatial patterns as attractors, whereas the ERK system produces traveling waves that transiently reorganize structure rather than selecting a fixed spatial configuration. The constraint-propagating front formalism is intended to capture this transient, trajectory-level reorganization that static pattern-formation theory does not naturally address.

Active matter physics provides a related set of tools for understanding collective dynamics in epithelial tissues, treating cell monolayers as oriented fluids with internal driving forces [16]. Active matter descriptions successfully account for many mechanical features of collective migration but typically do not incorporate the signaling dynamics that drive phase transitions between organizational regimes. The RSVP framework treats the signaling and mechanical layers as coupled through the $(\Phi, \mathbf{v}, S)$ triple, which is complementary to rather than competitive with active matter descriptions.

Dynamical systems approaches to psychiatry, associated with work in the tradition of Kelso [5] and more recent computational psychiatry, also treat mental states as attractors in high-dimensional state spaces and pathology as altered attractor geometry. The RSVP framework's treatment of GAD as a widening of the admissibility distribution is continuous with this tradition but adds the specific claim that the dominant signature is variance amplification in trajectory space rather than attractor displacement, a distinction that has direct empirical consequences for biomarker design.

The RSVP approach is perhaps most distinctive in its insistence on a unified field-theoretic language that applies across biological scales without requiring scale-specific mechanisms. Whether this cross-scale applicability is a theoretical virtue or a liability (by sacrificing mechanistic specificity) is a legitimate methodological question that future empirical work will need to address.

8 Conclusion: Biology as Dynamic Admissibility Geometry

The two papers considered in this essay resist explanation by standard entity-centered biological models. In the case of GAD, the relevant neurobiological signal is not the mean configuration of the brain but the variance of its developmental trajectories; in the case of collective epithelial migration, the relevant organizational phenomenon is not the behavior of individual cells but the propagation of constraint-redistributing waves across a coupled tissue medium. Both findings reveal that the appropriate descriptive level for understanding the macroscopic behavior of complex biological systems is the geometry of their organizational dynamics: the structure of accessible trajectory spaces, the propagation of constraint-enabling fronts, and the phase transitions between organizational regimes.

The RSVP framework, as a generalized field theory of organizational dynamics, provides a common mathematical language for interpreting both systems. The scalar coherence field Φ, the vector transport field $\mathbf{v}$, and the entropic accessibility measure S together characterize the organizational state in a way that captures the distributional and dynamical properties that scalar biomarker approaches lose. The coupled field equations reproduce the qualitative behavior of both systems and generate specific structural predictions: that variance amplification is a primary signature of trajectory-space deformation in GAD; that ERK waves drive constraint reallocation from junction-maintenance to podosome-invasive organization; that organizational health corresponds to reversible phase transition capacity rather than static structural configuration.

The deeper implication is methodological. These findings expose a limitation in strongly localist approaches to biological explanation: entity-centered frameworks, built around the objects identified by structural biochemistry, molecular genetics, and histology, are productive for many problems but become inadequate precisely where distributed temporal dynamics and collective coordination are primary. The brain-age paper's discovery that diagnosis fails to predict individual trajectory and that deep multivariate networks outperform univariate biomarkers is not an anomaly; it is a signal that the organizational structure of interest is carried at a level that scalar summaries cannot reach. The ZO-1 paper's discovery that a structural protein participates in distributed wave-mediated coordination rather than serving merely as a static barrier component is not an exception; it is an instance of a general principle.

That principle is the one identified here: biological systems at multiple scales achieve organizational coherence through the propagation of constraint-redistributing dynamics across coupled fields, not through the aggregation of fixed object properties. Formalizing this principle with mathematical precision, as the RSVP framework attempts, may become increasingly important for the development of theoretical biology as the explanatory targets shift from component identification toward distributed organizational dynamics.

9 Conceptual Clarifications and Theoretical Boundaries

The organizational geometry developed in preceding sections is ambitious enough in scope that several conceptual risks require direct address. The following subsections clarify what the framework does and does not claim, and sharpen the distinctions that are most likely to be blurred in interdisciplinary reading.

9.1 Constraint versus Cause

The RSVP field triple $(\Phi, \mathbf{v}, S)$ could be misread as proposing hidden causal substances or vitalist organizing forces that drive biological systems from outside their physical

substrate. This reading would be incorrect. The framework proposes nothing of the kind.

The RSVP fields are organizational constraint structures: mathematical representations of which organizational transitions are accessible, at what rates, and in which directions, given the system's current state and coupling geometry. They are not energetic fluids, hidden forces, or ontologically independent entities. They are closer in spirit to the reachability sets of control theory, the feasibility regions of constrained optimization, or the admissible trajectory bundles of dynamical systems analysis — all of which are mathematical objects describing the geometry of possible evolution rather than forces producing that evolution.

The distinction matters practically. When the vector field $\mathbf{v}$ propagates through the epithelial tissue, the RSVP interpretation does not claim that $\mathbf{v}$ is causing the ERK wave; it claims that $\mathbf{v}$ is the field-theoretic representation of the organizational consequences of the wave at the level of constraint geometry. The ERK wave has entirely ordinary molecular causes: receptor activation, MAPK cascade propagation, paracrine signaling. What the RSVP framework describes is how these mechanistic events reshape the landscape of accessible organizational transitions at the tissue scale. Mechanism and constraint geometry are complementary descriptions operating at different levels of abstraction, not competing explanations of the same phenomenon.

9.2 Why Variance Is Not Noise

The treatment of PAD variance as the primary organizational signal rather than as noise around a mean effect requires explicit justification, because the biomedical convention is precisely the opposite: variance is typically treated as a nuisance to be controlled or averaged away, leaving the mean effect as the quantity of theoretical interest.

The RSVP framework reverses this priority in a principled way. Variance in an accessibility field S directly reflects the geometry of the admissibility manifold: high variance corresponds to a population whose members occupy structurally divergent positions in the organizational trajectory space, while low variance corresponds to a population concentrated near a common trajectory. When GAD produces increased PAD variance without a corresponding mean shift, this is not statistical noise; it is evidence that the disorder has deformed the admissibility geometry without translating the population mean.

This reversal is well-supported in adjacent literatures. At critical phase transitions in physical systems, variance diverges before the transition while the mean may remain stationary; the variance signal is the leading indicator of organizational change. In heteroscedastic dynamical systems, increased variance can signal proximity to a bifurcation boundary where small perturbations produce qualitatively different outcomes

depending on initial condition. In stochastic resonance, variance in the input is not noise but the mechanism by which suprathreshold organization is achieved.

The RSVP framework generalizes this insight: in any system governed by propagating admissibility constraints, the variance of observable state variables across system components should be treated as primary organizational data rather than statistical residual. This has immediate implications for psychiatric biomarker design. If the primary signal of GAD is distributional rather than directional, then mean-based biomarkers will systematically fail to detect it, and variance-based measures — distributional spread of PAD, trajectory substructure in longitudinal cohorts, inter-individual heterogeneity in accessibility profiles — become the appropriate clinical targets.

9.3 Operationalizing the Accessibility Field

The accessibility field $S \approx -\log \rho$ is conceptually grounded but experimentally challenging to measure. Beyond the basic inverse-density operationalization, several candidate estimators are available depending on the biological system and data type.

For single-cell transcriptomic data, the local intrinsic dimensionality (LID) of the cell state distribution provides a natural proxy: high LID regions correspond to high S (many accessible nearby states), while low LID regions correspond to committed, low-S attractor basins. Methods from the manifold learning literature — including TWO-NN estimators, persistent homology density, and diffusion-map volume measures — can operationalize this directly from high-dimensional state vectors without specifying the manifold embedding in advance.

For imaging data of the type used in the GBF and GAD papers, the local mode-participation ratio of the spectral decomposition serves as a proxy: regions where many eigenmodes contribute significantly (high mode participation) correspond to high S, while regions dominated by a single low-frequency mode correspond to low S. The GBF paper's finding that approximately 300 modes suffice for reconstruction implies that the mode-participation ratio saturates sharply at this threshold, marking the effective boundary of the admissible manifold.

For collective migration data, the local curvature of the traction-force field and the local velocity divergence of the cell flow both provide indirect measures of S: high divergence and high curvature correspond to regions where the tissue is undergoing regime transition, while low divergence corresponds to consolidated migration in a low-S state. Graph Ricci curvature, applied to the cell contact network, also provides a substrate-independent proxy for local organizational openness.

For neural systems more broadly, local Lyapunov exponent spectra estimated from neural time series provide access to the effective dimensionality of the accessible trajectory bundle, with positive exponents corresponding to high S and convergent dynamics

corresponding to low S.

None of these estimators are equivalent to the theoretical S, and each introduces its own assumptions and measurement artifacts. The appropriate choice is substrate-dependent, and the RSVP framework does not privilege any one. The common feature is that all estimate the local volume of dynamically reachable configurations from the observed distribution of trajectories rather than from first-principle microstate enumeration.

9.4 Traveling Fronts versus Equilibrium States

A recurrent theme across all three empirical systems is that the organizationally dominant structures are not stable equilibria but transient propagating boundaries between regimes. This is a substantial departure from the equilibrium-centered paradigm that dominates much of theoretical biology, where the appropriate question is "what attractor does the system settle into?" rather than "how does the transition between attractors propagate?"

The RSVP framework treats propagating fronts as primary for the following reason. A stable attractor is a region of low S: the system has committed to a narrow trajectory bundle and is not easily perturbed out of it. The dynamically interesting events — development, learning, disease, collective migration, cortical reorganization — are not characterized by life in the attractor but by transitions between attractors. These transitions propagate through the tissue or the developmental manifold as moving boundaries between high-S and low-S regions, and it is the topology, velocity, and reversibility of these boundaries that carry the organizationally critical information.

This reframing has empirical consequences. Classical reaction-diffusion theory explains biological pattern formation through the emergence of stable spatial attractors (Turing patterns, standing waves). The RSVP framework is not competing with this account for static pattern formation; it is offering a different account for systems whose primary organizational signature is the traveling front rather than the stable pattern. The ERK wave does not produce a Turing-type stable spatial organization; it produces a transient reorganization that propagates and then resolves. The GBF cortical wave is not a static network pattern; it is a millisecond-scale propagating activation whose trajectory determines downstream coordination. The PAD trajectory is not a fixed developmental attractor; it is a dynamic path whose variance structure captures individual differences in developmental commitment speed.

In each case, the front is the object of theoretical interest, and the equilibrium is merely the region the system inhabits between fronts. Designing biological theories and biomarkers around equilibria systematically loses the most organizationally informative events.

9.5 Admissibility Compression versus Destructive Reduction

The GBF finding that 200–300 eigenmodes reconstruct whole-brain dynamics to high fidelity from 32,000 cortical vertices might be read as saying that the brain is "simple" or that the high-dimensional data is redundant. This reading misses the critical distinction between admissibility-preserving compression and destructive reduction.

Destructive reduction collapses a high-dimensional system to a low-dimensional representation by discarding the information that distinguishes relevant organizational configurations from each other. Averaging across a population, binning continuous variables, or projecting to the first principal component all produce reductions that lose structural information. The result is a lower-dimensional description that may be easier to analyze but that no longer supports the organizational distinctions the original system could make.

Admissibility-preserving compression is structurally different. It identifies the low-dimensional submanifold $\mathcal{M}_{adm}$ within the full configuration space $\mathcal{M}$ that is consistent with the system's organizational constraints, and represents the system's behavior as dynamics on $\mathcal{M}_{adm}$ rather than on $\mathcal{M}$. The remaining dimensions are not discarded because they are irrelevant; they are suppressed because the system's admissibility structure prevents them from being accessed under realistic operating conditions. Including them in analysis does not add information; it adds noise.

The Wang et al. spectral prior $\Sigma^{-1} = \text{diag}(-\beta/\log\lambda_i)$ implements precisely this distinction. It does not truncate modes above a fixed index; it weights all modes by their geometric admissibility, suppressing high-frequency configurations smoothly in proportion to their spectral energy. The result is an admissibility-preserving projection that retains the full organizational structure of the admissible manifold while numerically suppressing the inadmissible dimensions. The 300-mode saturation threshold is not evidence that the brain's dynamics are simple; it is evidence that the brain's admissibility geometry is approximately 300-dimensional within the cortical manifold, a substantial but constrained organizational capacity.

This distinction also applies to the GAD case. A mean-field biomarker that averages PAD across the GAD population is destructively reductive: it compresses the population distribution to its center of mass and loses the variance geometry that carries the primary organizational signal. An admissibility-preserving analysis would instead characterize the shape of the trajectory-space distribution — its variance, its multimodal substructure, its dependence on developmental timing — and treat this shape as the primary data. The RSVP framework is in part an argument for replacing destructive reduction with admissibility-preserving projection as the default analytical strategy for complex biological systems.

9.6 Failure of Reversibility and Organizational Collapse

The interpretation developed throughout this essay treats reversible phase-transition capacity as a defining feature of organizational competence. Healthy systems are not those that remain fixed within a single attractor basin, but those capable of entering temporary reorganizational regimes and subsequently restoring structural coherence after the perturbation has passed. This raises the corresponding question: what occurs when restoration dynamics fail?

The RSVP framework predicts that irreversible organizational collapse occurs when the rate of coherence regeneration becomes persistently insufficient to counteract the expansion of accessibility generated by destabilizing transport dynamics. In terms of the coupled field equations, this corresponds qualitatively to regimes in which

$$\lambda R(\Phi, S) < \gamma \Phi S$$

over extended intervals, such that the suppressive effect of elevated accessibility on coherence exceeds the system's regenerative capacity. Under these conditions, the system no longer undergoes reversible excursions between organizational phases but becomes trapped in pathological attractor geometries. The resulting dynamics are not merely unstable but structurally self-reinforcing: reduced coherence elevates accessibility variance, elevated accessibility further impairs coherence restoration, and the system progressively loses the capacity to return to its prior organizational basin.

This general structure appears across multiple biological domains. In epithelial systems, persistent failure of restoration dynamics may produce irreversible junctional breakdown, fibrotic remodeling, or metastatic escape, where transient invasive regimes cease to resolve back into cohesive tissue architecture. In neural systems, analogous dynamics may underlie forms of pathological attractor locking associated with chronic stress, treatment-resistant psychiatric states, or neurodegenerative consolidation processes, where developmental flexibility collapses into rigid low-dimensional trajectories from which recovery becomes increasingly improbable.

The framework therefore predicts that pathological irreversibility should not primarily be identified by elevated perturbation magnitude alone, but by the failure of restoration kinetics relative to accessibility expansion. Two systems exposed to similar perturbation energy may diverge sharply in long-term outcome depending on whether regenerative constraint reconstruction remains dynamically viable after perturbation passage.

This interpretation also clarifies why many biological pathologies exhibit hysteresis. Once the admissibility geometry has been sufficiently deformed, simply removing the original perturbation may be insufficient to restore the prior organizational state.

The system must actively reconstruct the lost coherence field, often requiring external intervention, regenerative scaffolding, or prolonged low-perturbation intervals before the original trajectory manifold becomes accessible again. The field-memory prediction (Prediction 4 in Section 11) is the empirically tractable near-term expression of this deeper claim about irreversibility thresholds and restoration kinetics.

9.7 Structural Homology versus Metaphorical Analogy

A persistent risk in cross-domain theoretical work is the substitution of metaphorical similarity for genuine structural correspondence. Because the RSVP framework employs a common mathematical language across neural development, epithelial migration, and geometry-constrained cortical dynamics, it is necessary to clarify the level at which the claimed unification operates.

The framework does not claim that these systems share mechanistic identity. ERK waves, developmental neural trajectories, and cortical eigenmode dynamics are implemented through distinct substrates, governed by different molecular mechanisms, and measured through different experimental modalities. The RSVP interpretation does not erase these differences; it operates at a different level of description. The claim instead concerns structural homology at the level of organizational dynamics: all three systems exhibit propagating transitions between admissibility regimes rather than static equilibrium organization, variance amplification as the dominant organizational signature, distributed coordination without centralized control, reversible phase-transition competence as a marker of organizational health, and constrained evolution on low-dimensional admissible manifolds embedded within higher-dimensional configuration spaces.

These are not merely linguistic similarities, because they generate experimentally distinguishable predictions. The framework predicts transient widening and reconvergence of PAD variance during developmental reorganization, topology-sensitive migration coherence under wave-structured ERK activation, hysteretic modification of redistribution thresholds after repeated wave exposure, and dimensionality saturation in admissibility-constrained neural reconstruction. A purely metaphorical analogy would not constrain empirical expectation in these ways. The RSVP framework therefore stands or falls not on whether the systems appear similar under broad interpretation, but on whether the predicted invariants are experimentally recoverable across organizational domains.

The distinction is methodologically important. Biological science has often relied on productive metaphors — the genome as code, the brain as computer, the immune system as defense network — but metaphor alone does not establish mathematical continuity. The present framework instead proposes that admissibility geometry constitutes a cross-

domain organizational invariant whose recurrence reflects shared structural constraints on distributed dynamical systems rather than rhetorical resemblance. Whether this claim ultimately reflects deep organizational universality or merely a high-level abstraction common to many sufficiently complex systems remains an open empirical question. The framework gains scientific legitimacy precisely to the degree that its proposed invariants survive increasingly substrate-specific experimental tests.

9.8 Admissibility Suppression and Computational Tractability

One of the most important implications of the geometry-aware neuroimaging framework is that biological systems may remain computationally manageable not because their underlying state spaces are intrinsically small, but because the overwhelming majority of formally possible configurations are dynamically inadmissible.

The cortical reconstruction problem examined by Wang et al. begins with approximately 32,000 spatial degrees of freedom, yet the empirically admissible dynamics are captured to high fidelity by only 200–300 geometric basis functions. This does not imply that the remaining dimensions are irrelevant in principle; rather, the spectral prior suppresses configurations whose geometric curvature places them outside the dynamically accessible manifold under physiological operating conditions. The RSVP framework generalizes this observation: organized systems maintain tractability through *admissibility suppression*, in which the active trajectory bundle occupies only a narrow submanifold $\mathcal{M}_{adm} \subset \mathcal{M}$ of the full configuration space. The accessibility field $S \approx -\log \rho$ functions precisely as a measure of this suppression geometry, with regions of low S corresponding to concentrated admissible trajectories and therefore to reduced effective computational dimensionality.

This perspective reframes several otherwise disconnected observations across biology and cognition. Neural systems exhibit sparse activation despite enormous combinatorial capacity; developmental systems reliably converge despite high-dimensional molecular variation; collective tissues coordinate coherently despite local stochasticity. In each case, admissibility constraints dynamically suppress most formally possible organizational trajectories, allowing coherent large-scale behavior to emerge without requiring exhaustive exploration of the underlying state space. The resulting organizational economy is structurally analogous to manifold learning and compressed representation in machine learning: high-dimensional observational spaces often contain low-dimensional dynamical structure embedded within them, and successful coordination depends on identifying the admissible substructure rather than representing every formal degree of freedom equally.

This interpretation also clarifies why perturbations near admissibility boundaries are especially destabilizing. As the system approaches regions where the effective

dimension of the admissible manifold expands rapidly, the computational burden of maintaining coherent coordination increases sharply. Variance amplification, trajectory divergence, and loss of reversibility emerge naturally under these conditions because the system is forced to navigate a substantially larger accessible trajectory bundle. The framework therefore predicts that many forms of biological instability are not primarily energetic failures but failures of admissibility compression: situations in which the effective dimensionality of the accessible organizational space expands faster than the system's capacity to maintain coherent constraint propagation across it.

10 Limitations and Open Problems

The interpretive and theoretical advances in this essay carry corresponding limitations that require explicit acknowledgment, both for intellectual honesty and to distinguish what the framework currently establishes from what it merely suggests.

The framework is phenomenological rather than mechanistic. The RSVP equations describe the organizational logic of constraint redistribution at an abstract level; they do not specify the molecular or cellular mechanisms that implement the fields Φ, $\mathbf{v}$, and S in any given biological substrate. This is deliberate: the framework aims to capture organizational invariants that persist across substrates precisely because it abstracts away from substrate-specific mechanism. But this strength is simultaneously a limitation. The equations cannot be used to make quantitative predictions about ERK kinetics, ZO-1 phosphorylation rates, or specific synaptic weight distributions without additional mechanistic elaboration that the current framework does not provide.

The governing equations are underdetermined and not yet experimentally parameterized. The coupling constants $\lambda, \alpha, \beta, \gamma, \delta, \kappa$ are introduced as positive reals without estimated values or proposed measurement protocols. The functional forms of $R(\Phi, S)$ and $Q(\mathbf{v})$ are left unspecified. Until these are constrained by data, the equations function as qualitative organizational scaffolding rather than as a quantitatively predictive model. The Signature Predictions derived in Section 11 are structural rather than quantitative for this reason.

Cross-scale applicability may reflect abstraction-level similarity rather than genuine dynamical equivalence. The claim that neural developmental trajectories and epithelial collective migration instantiate the same organizational invariants rests on structural analogy at the level of the $(\Phi, \mathbf{v}, S)$ triple. This analogy is nontrivial and generates testable predictions, but it does not establish that the underlying dynamics are governed by the same equations with the same parameters. The possibility that the shared mathematical structure is a consequence of the level of abstraction chosen — and would dissolve at a more detailed mechanistic level — cannot currently be ruled out. The invariant $\mathcal{I}$ in equation (7) is offered as a first candidate for distinguishing genuine cross-scale

dynamical homology from abstraction-level coincidence.

The accessibility field S currently lacks a universally operationalized empirical measure. The operationalization $S \approx -\log \rho$ provides a conceptually grounded estimator, but estimating ρ reliably on high-dimensional organizational manifolds from finite biological data involves significant methodological challenges, including manifold dimensionality estimation, boundary effects, and dependence on the dimensionality reduction method used to reconstruct $\mathcal{M}$. The three-layer distinction $S_{\text{geom}}/S_{\text{info}}/S_{\text{phys}}$ clarifies the conceptual target but does not resolve the estimation problem.

Finally, the current biological applications remain primarily interpretive rather than predictive except for the proposed experimental signatures in Section 11. The framework was introduced to interpret two already-published findings rather than to generate those findings. Its strongest empirical claim is the collection of predictions in Section 11, which have not yet been tested. The framework will acquire a stronger scientific standing once those predictions are evaluated experimentally.

11 Signature Predictions: Toward Empirical Discrimination

A theoretical framework earns scientific standing not only by interpreting existing data coherently but by generating predictions that are nontrivial, structurally motivated, and differentiable from the predictions of competing frameworks. The interpretations developed in preceding sections are retrospective; they show that RSVP-style concepts fit the Richier et al. and Hirano et al. findings. The present section derives prospective predictions that would be empirically distinguishable from those expected under standard deficit-model psychiatry, classical reaction-diffusion theory, and active-matter descriptions of collective migration. The goal is not to prove the framework but to expose its structure to empirical constraint.

11.1 Longitudinal Predictions for GAD: Dynamic Variance Restructuring

The cross-sectional PAD variance finding admits multiple interpretations. Standard diagnostic heterogeneity models predict stable inter-individual variance arising from fixed individual differences in GAD severity or subtype. The RSVP framework predicts something structurally different: the variance itself should be dynamically modulated by developmental transitions, exhibiting transient widening followed by partial reconvergence at periods of high admissibility flux.

Definition 11.1 (Variance Trajectory)**.** Let $\sigma^2_{PAD}(t) = \text{Var}_{GAD}[\delta(t)]$ denote the population-level PAD variance at developmental time t in a longitudinally followed GAD cohort. The RSVP framework predicts that $\sigma^2_{PAD}(t)$ is not constant but exhibits time dependence governed by the underlying admissibility field dynamics.

The first signature prediction follows directly.

Proposition 11.2 (Prediction 1: Variance Transience at Developmental Transitions)**.** *During periods of elevated developmental admissibility flux—including late adolescence, early adulthood, and major environmental stress transitions—the PAD variance of high-symptom GAD cohorts should transiently widen before partially reconverging, rather than monotonically increasing or remaining stable. Formally:*

$$\frac{d}{dt}\sigma^2_{PAD}(t) \neq 0$$

with local maxima of σ^2_{PAD} expected to cluster near independently identified developmental reorganization periods. A standard heterogeneity model predicts $\frac{d}{dt}\sigma^2_{PAD}(t) \approx 0$.

This prediction is genuinely distinctive because it assigns a temporal structure to the variance rather than treating it as a fixed population parameter. It implies that the same cohort followed longitudinally should show rhythmic variance dynamics rather than monotone drift, and that these dynamics should be partially predictable from independently measured developmental markers.

A second, stronger prediction concerns trajectory substructure within symptom-matched cohorts. The RSVP framework holds that individuals with similar symptom severity may nevertheless occupy divergent regions of the admissibility distribution: some will be consolidation-dominated (low S, high Φ, positive PAD) while others will be plasticity-dominated (high S, lower Φ, negative PAD). Longitudinal tracking should reveal that these individuals follow systematically different developmental trajectories even under matched symptom burden.

Proposition 11.3 (Prediction 2: Multimodal Longitudinal Substructure)**.** *Within longitudinally followed GAD cohorts matched for baseline symptom severity, individual PAD trajectories should exhibit multimodal substructure rather than unimodal dispersion around a common mean trajectory. Specifically, two distinguishable subpopulations are predicted: one following consolidation-dominated trajectories (sustained positive PAD, decreasing developmental plasticity) and one following plasticity-dominated trajectories (sustained negative or fluctuating PAD, elevated developmental lability). This bimodality should be visible in latent trajectory analyses and should correlate with independently measurable clinical markers of rigidity versus lability.*

A standard deficit model predicts unimodal trajectory distributions around a slightly deviated mean; the multimodal substructure prediction is specific to a framework in which the admissibility field can polarize toward opposite extremes under similar perturbation magnitudes.

11.2 Optogenetic Predictions for ERK Wave Dynamics: Topology over Amplitude

The Hirano et al. findings establish that ERK waves drive ZO-1 redistribution and coordinated migration. The crucial RSVP-theoretic prediction concerns not whether ERK activity matters—this is already established—but whether the spatiotemporal *topology* of ERK activation matters independently of its integrated amplitude.

Proposition 11.4 (Prediction 3: Topology-Sensitive Migration Coherence)**.** *Let $\mathcal{M}$ denote a measure of collective migration coherence (e.g., velocity correlation length, directional order parameter, or coordinated ZO-1 redistribution fraction). For two optogenetic stimulation protocols delivering equal integrated ERK activation energy $E = \int_\Omega \int_0^T u(\mathbf{r}, t)\, dt\, d\mathbf{r}$: a traveling-wave activation protocol u_{wave} and a spatially uniform or localized static activation protocol u_{static}, the RSVP framework predicts*

$$\mathcal{M}(u_{wave}) > \mathcal{M}(u_{static}).$$

A reaction-diffusion or active-matter framework that treats migration as driven by local ERK amplitude predicts $\mathcal{M}$ to depend primarily on local activation magnitude rather than propagation topology, yielding no systematic advantage for wave-structured over amplitude-matched static stimulation.

This prediction tests the core claim that the constraint-propagating front, rather than the total signaling energy, is the causally relevant organizational variable. If tissue migration coherence is substantially greater under wave-structured optogenetic stimulation than under amplitude-matched static stimulation, this provides evidence that propagation topology carries organizational information beyond what local ERK amplitude encodes. If the two protocols produce similar coherence, the simpler amplitude-based model is sufficient.

Proposition 11.5 (Prediction 4: Wave-Order Hysteresis and Field Memory)**.** *Cells previously traversed by multiple sequential ERK activation waves should exhibit altered thresholds for ZO-1 redistribution relative to wave-naive cells under matched instantaneous ERK amplitude. Specifically, the redistribution threshold should decrease monotonically with prior wave exposure up to a saturation point, reflecting persistent modification of the local admissibility structure by prior constraint-propagating fronts. Formally, if θ_n denotes the ERK activation threshold for ZO-1 redistribution after n prior wave traversals, then $\theta_n < \theta_0$ for $n \geq 1$, with $\theta_n \to \theta_\infty > 0$ as $n \to \infty$.*

This field-memory prediction is especially important for distinguishing the RSVP interpretation from a purely biochemical threshold account. A purely local threshold model predicts that the redistribution response depends only on instantaneous ERK amplitude, so that prior wave history has no effect on subsequent redistribution thresholds once ERK amplitude returns to baseline. The RSVP prediction is that the passage of

constraint-propagating fronts leaves structural traces in the admissibility field that persist beyond the biochemical recovery of ERK levels, producing genuine path dependence in the tissue's organizational response.

11.3 Cross-Prediction: Shared Variance Signature

A cross-system prediction connects the GAD and ERK findings through the shared variance amplification invariant identified in Section 6.

Proposition 11.6 (Prediction 5: Perturbation-Induced Variance Amplification)**.** *In any coupled-field biological system in which a constraint-propagating perturbation is applied (pharmacological, environmental, optogenetic, or developmental), the primary observable signature of organizational impact should be an increase in the variance of relevant state variables across system components, preceding or accompanying any detectable shift in the population mean. This is predicted to be especially pronounced near the boundary between organizational regimes (near the phase transition between junction-maintenance and podosome-invasive in the tissue case; near critical-period boundaries in the neural developmental case).*

This prediction is general enough to apply across both systems and specific enough to be empirically distinguishable from models in which perturbations produce primarily mean-field effects. It predicts that, in drug trials, disease-state comparisons, and optogenetic stimulation experiments alike, variance statistics should be sensitive leading indicators of organizational impact that precede detectable mean-field changes. If consistently confirmed, this would constitute the strongest empirical support for treating variance geometry as a primary organizational variable rather than as noise to be averaged away.

The experimental addendum proposed here does not exhaust the predictive scope of the RSVP framework. It identifies the predictions most directly motivated by the two empirical papers discussed and most sharply distinguished from standard competing accounts. Whether these predictions are confirmed or refuted, their articulation serves the function of making the framework scientifically negotiable: the conceptual commitments of the essay become hypotheses about how biological systems actually behave, rather than interpretive lenses that can accommodate any outcome.

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