

# Entropic gating enables active-like transport control in passive media

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## Abstract

Precise control over mass transport is a hallmark of biological function, typically achieved through energy-dissipating active processes. In contrast, transport in equilibrium soft matter is generally governed by fixed structural parameters, lacking the adaptability of its biological counterparts. **Here, we uncover a “chemically gated state” in passive macromolecular networks that exhibits active-like, non-monotonic transport regulation without energy consumption.** By combining theory and simulation with experimental meta-analysis, we identify a reentrant dynamical transition driven by the competition between enthalpic bridging and entropic site saturation. This mechanism functions as a “diffusive transistor,” where trace amounts of a reactive mediator orthogonally switch transport from Brownian to trapped and back to Brownian modes. We demonstrate that this entropic gating follows a universal scaling law across diverse systems—from viral capture in mucus to nanoparticle sensing—and further enables programmable diffusive logic operations. Our findings define a new class of equilibrium matter that decouples structure from dynamics, offering a thermodynamic blueprint for designing zero-energy smart materials with autonomous transport functions.

**Keywords:** Entropic gating, Active-like transport, Chemically gated state, Diffusive transistor, Macromolecular networks

## Main Text

Biological systems exhibit an exquisite ability to regulate mass transport with spatiotemporal precision, a capability exemplified by the selective gating of nuclear pore complexes or the directional trafficking of synaptic vesicles [1, 2]. Such adaptability is conventionally attributed to **active matter** physics, where the consumption of metabolic energy (e.g., ATP hydrolysis) breaks detailed balance to drive transport against thermodynamic gradients [3, 4]. In stark contrast, transport in synthetic **equilibrium systems**—such as hydrogels, porous media, or intracellular fluids—is generally enslaved to the fixed structural parameters of the matrix (e.g., pore size or viscosity) and the thermal energy ( $k_B T$ ) [5]. While recent advances in active matter have successfully mimicked biological motility through energy dissipation [6], a fundamental question remains: **Can we engineer active-like, programmable transport regulation within a strictly passive, energy-conserving system?** Achieving such “zero-energy gating” would not only challenge our understanding of equilibrium statistical physics but also unlock a new paradigm for designing autonomous smart materials [7].

Current approaches to modulating passive transport typically rely on bulk environmental changes, such as altering temperature, pH, or macromolecular crowding [8, 9]. However, these modifications almost invariably lead to monotonic responses: increasing the density of obstacles or crosslinkers universally hinders diffusion via steric repulsion or hydrodynamic interactions [10]. This monotonic behavior fundamentally limits the complexity of logic operations that passive matter can perform. A largely overlooked degree of

freedom lies in the introduction of a reactive **“third component” (TC)**—trace mediators that dynamically bridge the diffusant and the matrix [11, 12]. While widely utilized in sandwich immunoassays and drug delivery [13], the microscopic physics of TC-mediated transport has been obscured by mean-field approximations that treat these interactions merely as “sticky” potentials [14]. Such simplifications fail to capture the rich, non-Gaussian fluctuations observed in recent single-particle tracking experiments [15, 16], hinting that these systems operate near a critical regime of dynamic arrest that classical theories of anomalous diffusion (e.g., continuous-time random walks) cannot fully explain [17].

Here, we combine Brownian dynamics simulations with a self-consistent mean-field theory to uncover a **“chemically gated state”** in macromolecular networks, mediated solely by the reversible binding kinetics of a third component. Contrary to the intuition that “more linkers mean slower transport,” we identify a counter-intuitive, **reentrant dynamical transition**: as the TC concentration increases, the system switches from Fickian diffusion to a transiently trapped state, and strikingly, re-emerges into a fast diffusive regime. We reveal that this non-monotonic behavior arises from a fundamental thermodynamic competition between **enthalpic bridging** (which traps particles) and **entropic site saturation** (which re-liberates them) [18]. This mechanism effectively functions as a **“diffusive transistor”** [19], where the TC concentration acts as a gating signal that orthogonally regulates the particle flux with a high on/off ratio, all while maintaining global thermodynamic equilibrium. Furthermore, we show that the intermediate regime is characterized by “punctuated” dynamics—alternating between trapped and free states—providing a microscopic origin for the “Brownian yet non-Gaussian” diffusion widely reported in heterogeneous media [20].

We demonstrate that this entropic gating is not a system-specific quirk but follows a **universal scaling law** across vast length scales, collapsing experimental data from viral capture in mucus to nanoparticle sensing onto a single master curve [21, 22]. By decoupling transport dynamics from the physical structure of the host matrix, this mechanism enables the construction of **programmable diffusive logic gates (AND/OR)** and temporal signal filters within passive fluids. These findings bridge the gap between the adaptability of active matter and the robustness of equilibrium statistical mechanics, offering a thermodynamic blueprint for “smart” soft matter that processes information through diffusion itself.

## Results

### Emergence of a chemically gated state

To explore the limits of passive transport regulation, we constructed a coarse-grained model of a tracer nanoparticle (NP) diffusing within a polymer network, modulated by a reactive third component (TC) that can reversibly bridge the NP to the matrix (Fig. 1a). Intuitively, increasing the concentration of a crosslinking agent is expected to monotonically hinder diffusion due to enhanced steric obstruction and binding avidity. Strikingly, our Brownian dynamics simulations reveal a fundamentally different phenomenology. As the TC concentration ( $\phi_{\text{TC}}$ ) is swept from dilute to dense regimes, the system undergoes a sharp, reentrant dynamical transition—a “Go-Stop-Go” behavior reminiscent of a band-stop filter or a transistor logic gate (Fig. 1b).

In the absence of the TC, the NP exhibits classical Fickian diffusion. Upon introducing the TC, the diffusivity ( $D$ ) initially plummets by orders of magnitude, driving the system into a transiently arrested state characterized by sub-diffusive scaling ( $\langle \Delta r^2 \rangle \sim t^\alpha$ ,  $\alpha < 0.5$ ). However, as  $\phi_{\text{TC}}$  exceeds a critical threshold  $\phi^*$ , the transport mobility abruptly recovers, restoring Fickian dynamics despite the highly crowded environment. This non-monotonic response yields a giant on/off switching ratio ( $D_{\text{on}}/D_{\text{off}} > 10^3$ ) within a narrow concentration window (Fig. 1c), effectively functioning as a “diffusive transistor” where the TC concentration acts as the gating signal. Crucially, this transition is reversible and hysteresis-free, distinguishing it from irreversible gelation or jamming transitions often observed in soft matter.

Microscopic trajectory analysis elucidates the topological origin of this gating effect. In the intermediate “Stop” regime, the NP trajectories display pronounced spatiotemporal heterogeneity, characterized by a “punctuated” diffusion mode where long periods of localization are interspersed with rapid bursts of displacement (Fig. 1d). This intermittent behavior indicates that the “gate” is not statically closed but fluctuates dynamically. By mapping the number of simultaneous bridges ( $N_{\text{bridge}}$ ), we observe that the arrested state corresponds to an enthalpically dominated regime where the NP is pinned to the network. Conversely, in the reentrant “Go” regime at high  $\phi_{\text{TC}}$ , both the NP surface and the network binding sites become saturated with TC molecules. This saturation creates a “passivation layer” driven by combinatorial entropy, which sterically inhibits bridge formation and effectively lubricates the NP’s motion through the crowded matrix. This chemically gated state thus represents a distinct dynamical phase where transport is orthogonally decoupled from the structural density of the host medium.

**Fig. 1 Emergence of a chemically gated state and the diffusive transistor effect.** **a**, Conceptual schematic of the “diffusive transistor.” A passive macromolecular network functions as the transport channel (Source to Drain) for tracer nanoparticles (cyan), while the concentration of a reactive third component (TC, orange) acts as the orthogonal gating signal. Unlike static obstruction, the TC dynamically modulates the permeability of the medium. **b**, Microscopic snapshots illustrating the reentrant dynamical transition. **State I (Background)**: At low TC concentrations ( $\phi < \phi_{\text{trap}}$ ), the nanoparticle diffuses freely (Brownian). **State II (Enthalpic Trap)**: In the intermediate regime, TC linkers bridge the nanoparticle to the network matrix, energetically arresting transport (“Gate Closed”). **State III (Entropic Re-entrance)**: At high concentrations ( $\phi > \phi^*$ ), stoichiometric saturation of binding sites on both the particle and network creates a passivation layer driven by combinatorial entropy, prohibiting bridge formation and restoring mobility (“Gate Open”). **c**, The gating characteristic curve. The normalized diffusivity  $D/D_0$  exhibits a giant, non-monotonic response to the gating signal  $\phi_{\text{TC}}$ , characterized by a sharp drop into an arrested state followed by a rapid recovery. The system achieves a high on/off switching ratio ( $> 10^3$ ) within a narrow concentration window. **d**, Representative particle trajectory in the intermediate gating regime, revealing “punctuated” dynamics where the particle alternates between transiently trapped (blue segments) and diffusive (cyan segments) modes, distinct from classical Gaussian motion.

## Thermodynamic origin of the reentrant gate

To elucidate the physical mechanism driving this transition, we developed a self-consistent mean-field theory (SCMFT) to map the free energy landscape  $\Delta F$  associated with the formation of particle-network bridges (Fig. 2a). The reentrant behavior emerges from a fundamental competition between the energetic gain of bonding (enthalpy,  $\Delta U$ ) and the statistical penalty of ordering (entropy,  $\Delta S$ ). We decompose the free energy difference between the trapped and free states as  $\Delta F = \Delta U - T\Delta S$ . In the dilute limit ( $\phi_{\text{TC}} < \phi^*$ ), the landscape is dominated by the binding enthalpy ( $\Delta U \ll 0$ ); the TC acts as a “sticky” linker, creating a deep potential well ( $\sim 10 k_{\text{B}}T$ ) that spatially localizes the nanoparticle (Fig. 2b, blue shaded region).

Crucially, our theory reveals that the “opening” of the gate at high concentrations is purely entropic in origin. As  $\phi_{\text{TC}}$  increases, the available binding sites on both the nanoparticle and the polymer network become progressively occupied by “capping” TC molecules. In this dense regime, forming a bridge requires the expulsion of these capping molecules to expose free reactive sites. This process incurs a prohibitive entropic cost, effectively creating a “passivation layer” driven by combinatorial saturation. Consequently, the entropic penalty  $-T\Delta S$  rises sharply, eventually overwhelming the enthalpic gain (Fig. 2b, red region). This thermodynamic inversion eliminates the trapping potential, rendering the bridged state metastable and restoring diffusive mobility.

We capture this criticality by deriving an analytical scaling law for the critical gating concentration  $\phi^*$ , defined as the point where the energetic trapping is nullified ( $\Delta F \approx 0$ ). By equating the chemical potential of the bulk TC reservoir with the effective binding affinity of the surface sites, we obtain the closed-form expression:

$$\phi^* \sim \frac{1}{K_{\text{eq}}} \left( \frac{z_{\text{eff}}}{M} \right)^\nu e^{-\beta\epsilon_b} \quad (1)$$

where  $K_{\text{eq}}$  is the equilibrium binding constant,  $M$  is the number of binding sites on the nanoparticle, and  $\epsilon_b$  represents the bond energy. This analytical prediction (dashed line, Fig. 2c) quantitatively collapses the phase boundaries observed in simulations across various interaction strengths without fitting parameters. It underscores that the “chemically gated state” is not a specific chemical effect, but a universal topological phase transition governed by the ratio of available microstates in the bridged versus passivated configurations.

**Fig. 2 Thermodynamic mechanism of entropic gating.** **a**, Three-dimensional free energy landscape  $\Delta F(\phi_{\text{TC}}, p_d)$  quantifying the thermodynamic barrier between the trapped and free states. The deep blue valley represents the enthalpically trapped regime (“Gate Closed”), while the red plateau indicates the entropically reentrant regime (“Gate Open”). The saddle point marks the critical transition threshold. **b**, Decomposition of the free energy  $\Delta F$  (black curve) into its enthalpic ( $\Delta U$ , blue) and entropic ( $-T\Delta S$ , red) components as a function of the third-component concentration  $\phi_{\text{TC}}$ . The crossover point (vertical dashed line) identifies the critical concentration  $\phi^*$  where the combinatorial entropy of site saturation overcomes the binding enthalpy, triggering the release of the nanoparticle. **c**, Phase diagram of transport regimes. Symbols represent simulation data for Brownian (circles), Trapped (triangles), and Reentrant (squares) states. The solid curve represents the theoretical prediction derived from Eq. (1), confirming that the critical gating concentration  $\phi^*$  scales exponentially with bond energy and inversely with site multiplicity, distinct from classical percolation thresholds.

## Universality and scaling collapse across diverse systems

To demonstrate that the chemically gated state is a robust universality class rather than a model-specific artifact, we validated our theoretical framework against a comprehensive library of experimental data spanning three orders of magnitude in length scale (nm to  $\mu\text{m}$ ) and diverse chemical interactions (hydrogen

bonding, antigen-antibody, and DNA hybridization) (Fig. 3a). The raw diffusivity profiles from these systems—ranging from IgG-mediated viral capture in cervicovaginal mucus to competitive linker-based drug release—appear disparate due to variations in binding affinities ( $K_{\text{eq}}$ ) and particle sizes. However, our theory suggests that the transport physics is governed by a single dimensionless control parameter: the reduced concentration  $\tilde{\phi} = \phi_{\text{TC}}/\phi^*$ , where  $\phi^*$  is the critical entropic gating threshold derived in Eq. (1).

Remarkably, rescaling the experimental control variables by  $\phi^*$  reveals a universal collapse of the data onto a single master curve (Fig. 3b). All datasets, regardless of their physicochemical origin, adhere to the theoretical prediction (solid line) without additional fitting parameters. This collapse confirms that the reentrant transition is topologically invariant: the macroscopic transport state depends solely on the thermodynamic distance from the entropic saturation point.

This scaling framework provides a unified physical basis for disparate biological functions. We identify that the immune trapping of pathogens, such as the antibody-mediated immobilization of Herpes Simplex Virus (HSV) in mucus, operates deep within the **enthalpic trap regime** ( $\tilde{\phi} \ll 1$ , Region I). Here, the immune system tunes the antibody concentration to maximize bridging probability, effectively closing the diffusive gate to pathogen invasion. Conversely, controlled release technologies exploit the **entropic reentrant regime** ( $\tilde{\phi} > 1$ , Region II). By flooding the system with competitive binders (high TC concentration), these systems drive the payload across the critical threshold  $\phi^*$ , where entropic passivation “opens” the gate, triggering a sudden release of the therapeutic agent. The ability of our theory to unify “trapping” and “release” as two sides of the same entropic gating coin highlights its predictive power for programming soft matter function.

**Fig. 3 Universal scaling laws and experimental validation.** **a**, Raw effective diffusivity data ( $D/D_0$ ) from four distinct experimental systems: antibody-mediated viral capture (circles), DNA-functionalized colloid detection (triangles), competitive drug release (squares), and protein sandwich assays (diamonds). The data span disparate concentration ranges and chemical affinities, showing no obvious correlation in their raw form. **b**, Data collapse onto a universal master curve. By normalizing the third-component concentration by the theoretical critical threshold  $\phi^*$  (Eq. 1), all experimental datasets collapse onto the predicted reentrant profile (black solid line). The shaded regions denote the theoretically defined “Enthalpic Trap” (blue,  $\phi < \phi^*$ ) and “Entropic Re-entrance” (red,  $\phi > \phi^*$ ) regimes. **c**, Schematic representation of the biological relevance of the two regimes. **Region I (Viral Capture)**: At concentrations below  $\phi^*$ , antibodies (TC) bridge the virus to the mucin network, arresting motion to prevent infection. **Region II (Drug Release)**: At concentrations above  $\phi^*$ , an excess of competitive linkers saturates binding sites, creating a passivation layer that prohibits bridging and triggers the release of the drug carrier.

## Programmable diffusive logic and autonomous smart materials

The profound nonlinearity of the entropic gating transition offers a unique opportunity to encode Boolean logic directly into the diffusive flux of matter, bypassing the need for electronic control or external energy sources. To demonstrate this **programmable transport**, we designed a dual-responsive system containing nanoparticles functionalized with two distinct receptor types ( $\alpha$  and  $\beta$ ), modulated by two orthogonal third-component inputs ( $\text{TC}_\alpha$  and  $\text{TC}_\beta$ ) (Fig. 4a). By tuning the stoichiometric ratio of these inputs relative to the critical gating threshold  $\phi^*$ , we successfully realized molecular-scale logic gates.

We first constructed a **NAND gate** for mobility. In the ground state (no inputs), the particle diffuses freely (“1”). Introduction of either  $\text{TC}_\alpha$  or  $\text{TC}_\beta$  at intermediate concentrations induces enthalpic bridging, arresting motion (“0”). Strikingly, we also achieved an **AND gate** for reentrant release (Fig. 4b). Starting from a trapped state (where the network is crosslinked by trace linkers), the system requires the simultaneous saturation of *both* receptor types by high concentrations of  $\text{TC}_\alpha$  and  $\text{TC}_\beta$  to trigger the entropic passivation layer and restore mobility (“1”). This capability to process multiple chemical signals allows the material to perform rudimentary computation: it can autonomously discern specific “chemical signatures” in a complex environment, mobilizing only when a precise combinatorial threshold is met.

Beyond static logic, the hysteresis-free nature of entropic gating enables real-time **temporal signal processing**. We subjected the system to a time-varying concentration gradient  $\phi(t)$  mimicking a chemical pulse. The system acts as a **chemical band-stop filter**: it is transparent to low-concentration background noise and high-concentration saturation signals, but selectively arrests transport only within the specific “resonant” concentration window defined by the enthalpic trap (Fig. 4c). This non-monotonic response serves as a blueprint for **autonomous smart valves** (Fig. 4d). Unlike conventional stimuli-responsive hydrogels that simply swell or collapse, our “entropic valve” can regulate permeability based on the *information content* (entropy) of the permeant, enabling sophisticated functions such as self-regulated drug release that terminates automatically upon overdose (high concentration), a safety feature unattainable by monotonic responsiveness.

**Fig. 4 Programmable diffusive logic and autonomous temporal filtering.** **a**, Schematic of a dual-input diffusive logic gate. The nanoparticle (blue) carries orthogonal receptors  $\alpha$  and  $\beta$ . The transport state  $D$  (Output) is regulated by the concentrations of two distinct third-component linkers,  $TC_\alpha$  and  $TC_\beta$  (Inputs). **b**, Implementation of a molecular **AND gate** for release. The system is initially in a trapped state (Output = 0). Adding high concentrations of only  $TC_\alpha$  or only  $TC_\beta$  is insufficient to overcome the enthalpic barrier. Only the simultaneous presence of both inputs (High/High) induces the entropic passivation necessary to restore diffusion (Output = 1), as shown by the truth table and simulation snapshots. **c**, Temporal signal processing. The top panel shows a time-varying input concentration waveform  $\phi(t)$  (black line) sweeping across the critical trapping window (shaded blue region). The bottom panel shows the instantaneous diffusivity response  $D(t)$ . The system functions as a **band-stop filter**, selectively arresting particle motion only when the chemical signal falls within the specific intermediate range, while remaining transparent to low-noise and high-saturation signals. **d**, Conceptual design of an autonomous “Smart Safety Valve.” Conventional valves (left) respond monotonically to stimuli. The proposed Entropic Valve (right) utilizes the reentrant transition to permit flow at safe concentrations but auto-shuts off (traps) at intermediate “danger” levels, before re-opening or remaining closed depending on the engineered saturation limit, enabling fail-safe fluidic control without electronics.

## Discussion

Our discovery of the chemically gated state challenges the traditional dichotomy between passive and active matter. Conventionally, high-fidelity transport regulation—such as the directional gating of nuclear pores—is assumed to require the continuous dissipation of metabolic energy to break detailed balance [23]. In contrast, our results demonstrate that **equilibrium systems possess an inherent, underutilized capacity for active-like control**, unlocked solely through the manipulation of combinatorial entropy. By exploiting the reentrant competition between enthalpic bridging and entropic saturation, we show that a passive medium can emulate the “decision-making” capability of an active gate without paying the thermodynamic cost of ATP hydrolysis. This suggests that the **“cost of control”** in soft matter need not be energetic; it can be purely entropic, paid for by the chemical potential of a regulating reservoir.

This mechanism reframes the role of the “third component” from a simple structural crosslinker to a unit of **physical information**. In our framework, the nanoparticle does not merely collide with the network; it “computes” its dynamic state based on the local stoichiometry of the mediator. The giant non-monotonic response we observe ( $D_{\text{on}}/D_{\text{off}} \gg 10^3$ ) implies that soft matter systems function as **analog computers**, where chemical concentration acts as the input variable and diffusivity as the computational output. This realization bridges the gap between statistical physics and information theory, defining a new field of **“soft matter informatics”** where logic operations are encoded in the topological fluctuations of the constituent polymers rather than in electronic states.

From an evolutionary perspective, the robustness and universality of entropic gating suggest it may represent a primordial strategy for biological transport, predating the evolution of complex protein machineries. The ability to switch from capture (viral immobilization) to release (signaling) simply by tuning a binder’s concentration offers a **“thermodynamic hack”** for early life—achieving functional complexity with minimal molecular sophistication. This may explain the widespread prevalence of multivalent interactions in biological mucins and extracellular matrices, which operate dangerously close to the sol-gel transition not by accident, but to maintain maximal entropic susceptibility to environmental signals [24].

Looking forward, the concept of the chemically gated state offers a blueprint for the next generation of **autonomous smart materials**. While current stimuli-responsive hydrogels rely on macroscopic phase transitions (swelling/collapsing) that are often slow and structurally destructive, entropic gating operates at the single-particle level with orthogonal precision. This allows for the design of “zero-energy” microfluidic logics, self-regulating drug delivery vehicles, and homeostatic membranes that maintain transport flux within a narrow safety window independent of external power. Ultimately, by decoupling transport dynamics from the immutable structural invariants of the host matrix, we unlock a new dimension of phase space where matter is not just a passive carrier of mass, but an active processor of its own environment.

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