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Not peer-reviewed version

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Posted Date: 23 January 2026

doi: 10.20944/preprints202601.1851.v1

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Article

Towards Enzymatic-Like Control of Cellular Physical Processes

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Abstract

Cellular dynamics rely on numerous physical processes, including phase separation, membrane remodeling, stress relaxation, transport and stochastic fluctuation control, which are commonly treated as passive consequences of thermodynamics, mechanics or statistical physics. Here we advance the hypothesis that living systems can actively regulate such processes through biologically produced, reusable agents that act analogously to enzymes, but target physical state transitions rather than chemical reactions. We introduce the concept of enzymatic-like control, defined as the localized and saturable lowering of kinetic, topological or statistical barriers in configuration space by endogenous cellular components. Among the many cellular physical phenomena to which this concept may apply, we focus on biomolecular condensate nucleation and dissolution as a concrete and analytically tractable example. Condensate dynamics are conceived as barrier-limited physical reactions whose kinetic rates can be selectively modulated by putative enzyme-like Phase-Kinetases without altering equilibrium phase behavior. Using hazard-based inference and survival analysis, we present simulations demonstrating how these putative enzyme-like agents could generate small effective free-energy shifts on the order of a few kT, resulting in orders-of-magnitude changes in nucleation rates and yielding explicit, falsification-oriented criteria. Our framework complements existing biochemical and mechanical models by providing a testable perspective on the active regulation of physical dynamics without invoking new chemistry or nonstandard physics. It reframes cellular organization as the selective control of physical state transitions, rather than their passive accommodation within fixed physical laws.

Keywords: mesoscopic catalysis; hysteresis; energy landscape surgery; soft matter biology; organizational kinetics

1. Introduction

Cellular organization relies on a wide range of physical processes, including phase separation, membrane remodeling, stress relaxation, transport and stochastic fluctuation dynamics. In current state-of-the-art descriptions, these physical processes are attributed to thermodynamics, continuum mechanics, polymer physics or stochastic kinetics, while their biological control is reduced to boundary conditions, material parameters or externally applied forces. This perspective has been highly successful in capturing generic behaviors and scaling laws, yet it faces persistent limitations when confronted with the speed, selectivity, spatial localization and reversibility observed in living systems. Empirically, many cellular physical transitions occur orders of magnitude faster than predicted by passive models, display saturable dependence on specific molecular components and exhibit strong context sensitivity that cannot be explained by global energetic inputs alone. Existing explanations invoke increasingly complex material descriptions or active forcing, but these approaches blur the distinction between force generation and rate control, lacking a unifying principle comparable to enzymatic catalysis in chemistry. As a result, there is currently no systematic framework for interpreting how biology may actively regulate physical state transitions without

invoking new chemical reactions or abandoning physical consistency. These limitations motivate a reconsideration of how biological activity interfaces with physical dynamics at mesoscopic scales. Our approach introduces the concept of enzymatic-like control as a theoretical perspective on biological regulation of physical processes. Within our framework, cells are assumed to produce endogenous, reusable and localized agents that act by lowering effective kinetic, topological or statistical barriers in configuration space, rather than by modifying equilibrium states or generating macroscopic forces. This notion extends the logic of enzymatic catalysis beyond chemistry, while remaining fully compatible with established physical laws. Recent evidence that random heteropolymers can exhibit enzyme-like catalytic behavior without sequence optimization supports the plausibility of enzymatic-like control, suggesting that reusable, non-specialized biological structures may lower effective barriers for physical state transitions, analogously to chemical catalysis (Yu et al., 2026).

Our aim is to identify shared operational signatures of active regulation, including saturability, exponential sensitivity to small free-energy shifts and spatially confined action and to use these signatures to reinterpret the dynamics of biomolecular condensation, a process often labeled as a passive consequence of phase separation physics.

We will proceed as follows. We first apply the concept of enzymatic-like control directly to biomolecular condensate nucleation and dissolution, treating condensation as a barrier-limited physical reaction subject to localized kinetic modulation. Building on this focused analysis, we present a quantitative case study of condensate nucleation from which explicit, falsification-oriented predictions are derived. We conclude by integrating these results into a broader perspective on how enzymatic-like regulation may operate in cellular physical dynamics.

2. Phase Separation Nucleation and Dissolution as an Enzymatic-Like Process

We provide here a concrete example of enzyme-like regulation acting on a physical process rather than on a chemical reaction. We focus on biomolecular condensates, whose nucleation and dissolution arise from well-characterized physical phase transitions, yet display a degree of precision, spatial localization, reversibility and context dependence that is difficult to reconcile with passive thermodynamic control alone. Condensate dynamics thus provide a tractable and experimentally accessible setting to explore the possibility that biological agents actively modulate the kinetics of physical state transitions by biasing rates, barriers and pathways without redefining the underlying thermodynamic landscape.

Physical description of biomolecular phase separation. Phase separation of biomolecules into membraneless condensates is commonly described as a mesoscopic physical process governed by polymer physics and nonequilibrium thermodynamics (Alberti and Dormann 2019). In this framework, liquid–liquid phase separation (LLPS) arises from multivalent, weak interactions among proteins and nucleic acids, leading to demixing once concentration or interaction thresholds are exceeded (Hyman, Weber and Jülicher 2014; Banani et al. 2017; Dai et al. 2024). Mean-field approaches and extensions of Flory–Huggins theory account for coexistence regions, interfacial tension and material properties such as viscosity and elasticity and have been instrumental in rationalizing condensate formation in simplified in vitro systems (Choi, Holehouse and Pappu 2020; Dignon et al. 2018; Guillén-Boixet et al. 2020).

These physical descriptions predict that nucleation and dissolution kinetics are determined primarily by diffusion-limited encounters and by free-energy barriers depending smoothly on concentration and interaction strength. Within this view, condensate dynamics are expected to scale continuously with thermodynamic parameters and reversibility is governed by proximity to coexistence boundaries.

Empirical limits of passive thermodynamic accounts. Nevertheless, a growing body of experimental evidence indicates that purely physical accounts are insufficient to explain condensate

behavior in living cells. Condensates often nucleate at reproducible, spatially restricted sites such as transcriptional loci, centrosomes or stress granule seeds, even when bulk concentrations are uniform (Alberti and Dormann 2019; Shin and Brangwynne 2017). Assembly and dissolution frequently occur on timescales far shorter than predicted by diffusion alone and condensates can persist or dissolve despite remaining well within predicted coexistence regimes (Snead and Stachowiak 2019; Riback et al. 2020).

Moreover, condensates display strong hysteresis and memory effects: prior assembly history influences subsequent nucleation probability and material state, incompatible with equilibrium phase diagrams (Klosin et al. 2020; Jawerth et al. 2020). Condensates with similar molecular composition can exhibit sharply different lifetimes, internal dynamics or viscoelastic properties depending on cellular context, post-translational state or metabolic conditions. These observations support the hypothesis that cells can actively regulate the kinetics of phase transitions, rather than merely tuning thermodynamic control parameters.

Enzymatic-like interpretation of nucleation and dissolution. Phase separation nucleation and dissolution could be interpreted as an enzymatic-like process acting on mesoscale assembly dynamics. Specific biological agents could catalyze transitions between mixed and demixed states by selectively lowering or raising effective free-energy barriers in configuration space, without altering the equilibrium phase diagram.

This role is analogous to enzymatic catalysis in chemistry, where reaction pathways are accelerated while equilibrium constants remain unchanged. Applied to LLPS, enzymatic-like control implies that relatively small effective barrier shifts, on the order of a few kT, could generate orders-of-magnitude changes in nucleation or dissolution rates, consistent with experimentally observed kinetics. This interpretation does not require new physical principles or exotic interactions but reassigns an active regulatory role to biological components.

Putative phase-kinetases as hidden regulators. Putative agents of this control, which we collectively refer to as phase-kinetases, may include a range of biological structures capable of modulating condensate nucleation and dissolution kinetics.

- a. In our context, RNA helicases of the DEAD-box family would act as localized, ATP-driven remodeling agents that could continuously reshuffle RNA–protein interaction topologies inside condensates (Cargill, Venkataraman, and Lee 2021; Naineni et al. 2023; Hirth et al. 2024; Li et al. 2024). Rather than globally dissolving assemblies, their activity would selectively lower kinetic barriers for rearrangement by transiently weakening RNA-mediated crosslinks, thereby potentially preventing topological trapping while preserving condensate identity. Such action would effectively tune the internal relaxation time of the condensate without altering its macroscopic composition, allowing rapid switching between metastable organizational states in response to small energetic inputs (Zhang et al. 2026).
- b. ATP-dependent chaperones would be expected to operate in a closely related but mechanistically distinct manner (Trösch et al. 2015; Alfi et al. 2019; Wang et al. 2025). In our framework, they would transiently destabilize multivalent protein–protein contacts that might otherwise accumulate into long-lived kinetic bottlenecks. By repeatedly injecting energy at specific interaction nodes, chaperones would locally flatten the free-energy landscape, accelerating escape from arrested configurations while leaving the overall phase-separated state intact. This behavior would support a view of condensates as dynamically maintained nonequilibrium structures whose stability depends on continuous, spatially confined energy dissipation rather than on static affinity balances.
- c. Post-translational modification systems acting on low-complexity domains would provide an additional layer of fine-grained control (Wang, Osgood, and Chatterjee 2022; Gong et al. 2024; Tao et al. 2024; Zhang et al. 2025). In our context, phosphorylation, acetylation, or methylation

would not merely shift average interaction strengths but would modulate the lifetime and cooperativeness of specific contact motifs. Because such modifications could be rapidly written and erased, they would function as reversible kinetic regulators that bias assembly or disassembly pathways without requiring large concentration changes. This would enable sharp, switch-like responses of condensate dynamics to weak upstream signals, consistent with an enzymatic-like mode of regulation ().

- d. ATP-driven disaggregases would extend this logic to the active dissolution regime (Wentink et al. 2020; Low et al. 2021; Mahapatra et al. 2023). Rather than functioning solely as emergency cleanup factors, they would behave as controlled sinks that selectively remove over-stabilized interaction clusters, thereby maintaining condensates near a regime of high responsiveness. By targeting specific substructures, disaggregases would preserve the overall compartment while preventing irreversible aging or pathological solidification, stabilizing condensates as long-lived yet dynamically renewable entities ().
- e. A complementary mechanism would involve metabolic enzymes and cofactors regulating local ATP, ADP, or NADH availability within condensates. In our context, such local metabolic tuning would modulate interaction lifetimes and reaction barriers without altering bulk cytosolic concentrations. Condensates would thus act as microreactors with partially autonomous energetic states, where small metabolic fluctuations could be amplified into large kinetic effects on assembly or dissolution. This would provide a direct physical route by which cellular metabolic state might bias condensate behavior without invoking global energy shifts (Dai et al. 2024).
- f. Scaffold proteins with conformational switching capabilities would further sharpen this regulation (Greenwald et al. 2014; Yang et al. 2022; Ball, Barnett, and Goult 2024). In our framework, conformational transitions would selectively expose or occlude multivalent binding motifs, effectively acting as gating mechanisms that control access to interaction networks. Because such switches are often ligand- or energy-sensitive, they would allow condensates to behave as conditional reaction platforms, assembling or relaxing only when specific structural states are populated, reinforcing a barrier-controlled rather than equilibrium-driven interpretation (Abyzov, Blackledge, and Zweckstetter 2022; DiRusso, Dashtiahanger, and Gilmore 2022; Li, Tresset, and Zandi 2025).
- g. Finally, intrinsically disordered regions themselves could acquire enzyme-like roles when embedded in heterogeneous macromolecular environments (Nussinov et al. 2017; Blundell, Gupta, and Hasnain 2020; Djulbegovic et al. 2022; Djulbegovic et al. 2023). In our context, disorder would not merely be permissive but functionally active: by sampling broad conformational ensembles, IDRs could stabilize transition states or destabilize intermediates along assembly and disassembly pathways. Crucially, such catalytic behavior would not require sequence-level optimization in the classical enzymatic sense but would emerge from collective interactions within the condensate milieu, consistent with a physical rather than biochemical notion of catalysis (Gupta et al 2026).

These components are typically described as regulators of condensate composition, material state or turnover. However, these descriptions implicitly assume that their primary role is to shift equilibrium properties or material parameters. Within our framework, they can instead be coherently reinterpreted as catalytic modulators of phase-transition kinetics, repeatedly biasing nucleation, coalescence or dissolution pathways without being consumed. Phase-kinetases could act analogously

to enzymes by lowering effective free-energy barriers between metastable mesoscale states, while leaving the underlying phase diagram largely intact.

This reinterpretation is reinforced by several converging observations. First, perturbations of candidate phase-kinetases frequently produce strongly nonlinear and saturable effects on condensate lifetimes, nucleation rates or dissolution kinetics, inconsistent with simple proportional control of interaction strength. Second, the same agent can accelerate both assembly and disassembly depending on context, a hallmark of kinetic rather than thermodynamic regulation. Third, recent demonstrations that structurally heterogeneous or even random macromolecular assemblies can display enzyme-like catalytic behavior support the plausibility of reusable, non-specialized biological structures acting as kinetic catalysts at the mesoscale (Yu et al, 2026).

Together, these findings strengthen the view that condensate dynamics are governed not only by passive phase behavior, but by an active, catalysis-like layer of control operating on the rates of physical state transitions.

Conceptual implications and outlook. Rather than treating condensation as a process governed solely by equilibrium thermodynamics, our enzymatic-like interpretation of condensate nucleation and dissolution emphasizes kinetic regulation. Equilibrium phase behavior is not overridden, but the rates at which phase boundaries are crossed appear subject to selective biological modulation. The evidence discussed above is consistent with the existence of reusable cellular agents that bias assembly and disassembly pathways without being consumed, acting on transition dynamics rather than on material composition. Within this view, phase separation could emerge as a regulated variable rather than a passive consequence of molecular properties. Biological organization may thus exploit catalysis-like control over existing physical degrees of freedom, selectively accelerating, slowing or redirecting transitions within constrained configuration spaces. Our interpretation does not invoke new forces or departures from established physical laws; instead, it reframes familiar regulatory components as agents acting on kinetic barriers, thereby reshaping physical dynamics from within.

By focusing on barrier modulation, our enzymatic-like perspective implies specific and testable signatures in kinetics, scaling behavior and sensitivity to perturbation that can be evaluated independently of biological interpretation. Whether these signatures are ultimately confirmed or refuted, treating condensate dynamics as potential targets of kinetic regulation sharpens the conceptual distinction between passive material behavior and biological control.

At this stage, the emphasis remains conceptual. While barrier modulation naturally suggests the existence of sharp kinetic signatures, a rigorous formulation of quantitative predictions requires explicit modeling choices, including how nucleation events are operationally defined, how waiting-time distributions are constructed and how effective free-energy barriers are inferred from empirical data. For this reason, a systematic quantitative treatment is developed in the following chapter, where condensate nucleation is analyzed as a barrier-limited physical reaction and explicit rate laws, scaling relations and falsification criteria are derived.

3. A Quantitative Case Study: Barrier Modulation in Condensate Nucleation

We develop here a quantitative case study in which condensate nucleation is treated as a barrier-limited physical reaction whose kinetics can be modulated by biologically produced putative Phase-Kinetases. The objective is to derive explicit rate laws, parameter mappings and falsification thresholds directly from measurable time series and perturbation series.

Problem setup and observable definitions. We begin by fixing observables and a minimal stochastic description so that each subsequent calculation has a precise empirical target. Condensate nucleation is represented as a stochastic first-passage event in configuration space, observed as the time T at which a compartment (cell, nucleus, subregion) first exhibits a condensate satisfying a predefined detection criterion. Let $N(t)$ denote the cumulative number of nucleation events observed across M independent compartments up to time t and let $F(t) = \mathbb{P}(T \leq t)$ be the nucleation-time cumulative distribution. The survival function is $S(t) = 1 - F(t) = \mathbb{P}(T > t)$. A

minimal assumption used in our approach is that conditional on fixed experimental condition θ (concentrations, temperature, genotype, ATP level), nucleation events in distinct compartments are independent and identically distributed with hazard function $h_\theta(t)$. The baseline “passive” model is time-homogeneous nucleation with constant hazard $h_\theta(t) = \lambda_\theta$, giving $S(t) = \exp(-\lambda_\theta t)$. This choice is not asserted as universally correct; rather it is a controlled starting point that permits exact inversion from data. The observable rate λ_θ is estimated from M waiting times $\{T_i\}$ by maximum likelihood, including right-censoring at observation horizon $t_{\max}$. If $\delta_i \in \{0,1\}$ indicates whether nucleation occurred before censoring, the log-likelihood is $\ell(\lambda) = \sum_i \delta_i \log \lambda - \lambda \sum_i \min(T_i, t_{\max})$, yielding $\hat{\lambda} = \frac{\sum_i \delta_i}{\sum_i \min(T_i, t_{\max})}$. We establish here the measurable objects that will carry all subsequent barriers and catalyst inferences.

Barrier-limited kinetics and effective free-energy shifts. We now need to map rates to effective barriers so that biological modulation can be expressed as quantitative barrier shifts in units of kT . We treat nucleation as barrier crossing with an effective activation free energy ΔG_θ^* governing the rate. The central kinetic ansatz is Arrhenius/Eyring-like:

$$\lambda_\theta = \lambda_0 \exp\left(-\frac{\Delta G_\theta^*}{kT}\right),$$

where k is Boltzmann’s constant and T the absolute temperature and λ_0 is a prefactor representing attempt frequency in the relevant coarse-grained coordinate. The passive reference condition $\theta = \theta_0$ defines $\Delta G_{\theta_0}^*$ and any perturbation defines an effective barrier shift $\Delta\Delta G^*(\theta) = \Delta G_\theta^* - \Delta G_{\theta_0}^*$. Eliminating λ_0 gives an experimentally invertible relation:

$$\Delta\Delta G^*(\theta) = -kT \ln\left(\frac{\lambda_\theta}{\lambda_{\theta_0}}\right).$$

Thus a rate ratio of 10 corresponds to $\Delta\Delta G^* = -kT \ln 10 \approx -2.30 kT$, while a 50-fold ratio corresponds to $-3.91 kT$. Our framework uses these conversions as falsification primitives: if Phase-Kinetase perturbations yield rate changes that cannot be summarized by a stable $\Delta\Delta G^*$ across replicates and measurement windows, the barrier-modulation hypothesis is rejected in its minimal form. When time-dependent hazards are needed, our approach generalizes to $h_\theta(t) = \lambda_\theta \exp(-\Delta G_\theta^*(t)/kT)$ and uses piecewise-constant hazards over bins $[t_j, t_{j+1})$, estimating λ_j by the same likelihood formula applied per bin. This preserves direct mapping from measured hazards to barrier profiles $\Delta G^*(t)$, enabling detection of history dependence while maintaining quantitative interpretability.

Incorporating phase-kinetases via saturable barrier modulation. We next specify a catalyst-like dependence yielding sharp, parameter-identifiable predictions rather than descriptive post hoc fits. To represent biologically produced Phase-Kinetases, our approach introduces an endogenous agent concentration C (measured or proxied by fluorescence/abundance) modulating the effective barrier. The simplest saturable form mirrors catalytic saturation without asserting molecular Michaelis–Menten chemistry:

$$\Delta G^*(C) = \Delta G_\infty^* + (\Delta G_0^* - \Delta G_\infty^*) \frac{K}{K + C},$$

equivalently expressed as a saturating barrier reduction

$$\Delta\Delta G^*(C) = \Delta G^*(C) - \Delta G^*(0) = -\Delta G_{\max} \frac{C}{K + C},$$

with $\Delta G_{\max} = \Delta G_0^* - \Delta G_\infty^* > 0$. Substituting into the rate law yields

$$\lambda(C) = \lambda(0) \exp\left(-\frac{\Delta G_{\max}}{kT} \frac{C}{K + C}\right).$$

Two identifiability features follow. First, the log-rate is linear in $C/(K + C)$: $\ln \lambda(C) = \ln \lambda(0) + (\Delta G_{\max}/kT) C/(K + C)$. Second, the high- C plateau gives $\lambda(\infty) = \lambda(0) \exp(\Delta G_{\max}/kT)$, so measuring the plateau rate fixes $\Delta G_{\max}/kT = \ln(\lambda(\infty)/\lambda(0))$. Falsification thresholds become explicit: if $\ln \lambda(C)$ does not approach a finite asymptote as C increases or if the inferred K differs systematically across replicates beyond uncertainty, the saturable Phase-Kinetase model fails. In our simulations used to

generate the diagnostic plots, we chose normalized units with $kT = 1$, $\Delta G_{\max} = 4kT$ and $K = 2$ (Figure 1B), so the maximum predicted rate ratio is $\exp(4) \approx 54.6$, while $C = K$ yields $\exp(2) \approx 7.4$. These numerical separations define experimentally resolvable regimes.

Regime classification and rate-ratio diagnostics. We now translate the equations into regime maps supporting direct interpretation of experimental perturbations as distinct kinetic classes. Our approach classifies control strength by the inferred barrier reduction $\Delta G_{\max}/kT$ or by measured rate ratios. The regime map follows from $\lambda/\lambda_0 = \exp(\Delta\Delta G^*/kT)$ (Figure 1A). A weak-modulation regime corresponds to $|\Delta\Delta G^*| < 1kT$ (rate ratios $< e \approx 2.72$), typically difficult to distinguish from modest passive variability. A moderate regime corresponds to $1-3kT$ (rate ratios $e-e^3 \approx 20.1$) and a strong regime corresponds to $> 3kT$ (rate ratios > 20). For a perturbation series $\{C_m\}$, the predicted fold-change curve is $R(C) = \lambda(C)/\lambda(0) = \exp((\Delta G_{\max}/kT) C/(K+C))$ (Figure 1B). Our framework uses two quantitative diagnostics. The first is curvature: $d^2 \ln R/dC^2 < 0$ for all $C > 0$ under saturable modulation; empirically, convexity in $\ln R$ falsifies the model. The second is the half-saturation point: $C = K$ implies $R = \exp(\Delta G_{\max}/2kT)$. Thus measuring C at which $\ln R$ reaches half its plateau estimates K without fitting the full curve. For uncertainty, if $\hat{\lambda}$ is estimated from n events over exposure time E , then $\hat{\lambda} = n/E$ with approximate standard error $\text{SE}(\ln \hat{\lambda}) \approx 1/\sqrt{n}$ for Poisson counting, yielding $\text{SE}(\Delta\Delta G^*/kT) \approx \sqrt{1/n_\theta + 1/n_{\theta_0}}$. This provides an explicit planning rule: to resolve $\Delta\Delta G^* = 2kT$ against zero with $z \approx 2$, one needs n such that $2/\sqrt{2/n} \gtrsim 2$, i.e. $n \gtrsim 2$ per condition at minimum, but robust discrimination typically requires $n \geq 25$ to shrink uncertainty below $0.3kT$.

Waiting-time distributions and survival-based inference. We next shift from point estimates of rates to full distributional tests that sharpen falsification by exploiting the entire time series. A core prediction of our approach is that barrier modulation should reorganize waiting-time distributions in a way that is describable by a small number of parameters. Under constant hazard λ , the waiting time T is exponential with density $f(t) = \lambda e^{-\lambda t}$, survival $S(t) = e^{-\lambda t}$ and median $t_{1/2} = (\ln 2)/\lambda$. Barrier modulation changes λ multiplicatively; therefore, survival curves for different conditions should be related by a time rescaling $t \mapsto t(\lambda/\lambda_0)$. In our simulations (Figure 1C), we used $\lambda_0 = 0.1$ and $\Delta\Delta G^* \in \{0, 2, 4\}kT$, implying $\lambda \in \{0.1, 0.739, 5.46\}$ and medians $t_{1/2} \in \{6.93, 0.94, 0.127\}$. These numerically separate regimes by almost two orders of magnitude. Empirically, our framework proposes testing whether survival curves satisfy $\ln S_\theta(t) \approx -\hat{\lambda}_\theta t$ over the observation window. Deviations can be evaluated via the Kolmogorov-Smirnov statistic on rescaled times $u_i = \hat{\lambda}_\theta T_i$, which should be exponentially distributed with unit rate if the constant-hazard assumption holds. For comparisons among conditions, a log-rank test on survival data quantifies whether λ_θ differs significantly from λ_{θ_0} ; the test statistic is approximately χ^2_1 under the null. Importantly, saturable Phase-Kinetase control predicts ordered survival curves with diminishing incremental shifts at high C , while non-saturating forcing predicts continued shifting. The median-based test $t_{1/2}(C) = (\ln 2)/\lambda(0) \exp((\Delta G_{\max}/kT) C/(K+C))$ yields a direct falsification: if $t_{1/2}(C)$ does not approach a positive asymptote as $C \rightarrow \infty$, the saturable model is rejected.

Time-resolved fractions nucleated and hazard reconstruction. We now connect individual waiting times to population-level fractions in a way that yields parameter recovery from standard imaging assays. Many experiments measure the fraction of compartments exhibiting condensates over time rather than individual nucleation times. Under the exponential model, the fraction nucleated by time t is $F(t) = 1 - e^{-\lambda t}$. With Phase-Kinetase concentration dependence, the prediction becomes $F(t; C) = 1 - \exp[-\lambda(C)t]$ (Figure 1D). In our simulations, using the same $\lambda_0 = 0.1$, $K = 2$, $\Delta G_{\max} = 4kT$ and concentrations $C \in \{0, 1, 2, 5, 10\}$, the implied rates are $\lambda(C) = 0.1 \exp(4C/(2+C))$, yielding approximate values $0.1, 0.38, 0.74, 2.78, 4.28$. The corresponding $t_{50} = \ln 2/\lambda$ values are $6.93, 1.82, 0.94, 0.25, 0.16$. These numbers provide sharp falsification: measured t_{50} should compress strongly between $C = 0$ and $C = 2$ and then change weakly between $C = 5$ and $C = 10$. Our approach reconstructs the hazard from fraction data by $\hat{\lambda} = -\frac{d}{dt} \ln [1 - \hat{F}(t)]$. With discrete time points t_j , one uses finite differences: $\hat{\lambda}_j \approx -\frac{\ln(1-\hat{F}_{j+1}) - \ln(1-\hat{F}_j)}{t_{j+1} - t_j}$. Under the model, $\hat{\lambda}_j$

should be approximately constant in j and departures indicate time-varying hazards or heterogeneous subpopulations. The same inversion gives barrier profiles: $\widehat{\Delta G}^*(t_j) = -kT \ln(\hat{\lambda}_j/\lambda_0)$ up to a constant. These steps provide a precise algorithmic pathway from imaging-derived fractions to inferred barrier reductions, enabling the quantitative evaluation of Phase-Kinetase action.

Simulation protocol and computational tools. We used a minimal stochastic simulator to generate regime-comparison plots independent of any peculiar molecular mechanism.

Step 1 defined a grid of barrier reductions $\Delta\Delta G/kT \in [0,5]$ and computed rate ratios $R = \exp(\Delta\Delta G/kT)$, producing the exponential regime map (Figure 1A).

Step 2 defined a concentration axis $C \in [0,10]$ and a saturable barrier function $\Delta\Delta G(C) = \Delta G_{\max}C/(K + C)$ with $K = 2$ and $\Delta G_{\max} = 4$, then computed $R(C) = \exp(\Delta\Delta G(C))$ (Figure 1B).

Step 3 generated survival curves using the exponential survival function $S(t) = \exp(-\lambda t)$ on a time grid $t \in [0,60]$ with $\lambda = \lambda_0 \exp(\Delta\Delta G)$ and $\lambda_0 = 0.1$ for three barrier settings $\Delta\Delta G \in \{0,2,4\}$ (Figure 1C).

Step 4 computed nucleated fractions $F(t; C) = 1 - \exp[-\lambda(C)t]$ using the same time grid and concentrations $C \in \{0,1,2,5,10\}$ (Figure 1D).

The computational tools were NumPy for vectorized evaluation of rate laws and distribution functions and Matplotlib for plotting. No parameter fitting was performed in the simulations; all curves were direct evaluations of the equations stated above, ensuring that the plots encode only the theoretical assumptions of barrier modulation and saturability. For extension to data, our framework uses maximum-likelihood estimation for exponential hazards and standard survival-analysis routines for censored data; these can be implemented with SciPy or statsmodels, but the present simulations required only closed-form expressions.

Overall, our approach specifies a fully quantitative route from condensate nucleation time series to inferred barrier shifts and to saturable Phase-Kinetase response curves. The section provided explicit hazard-based likelihood estimation, barrier inversion in kT units, distributional survival tests, fraction-based hazard reconstruction and a reproducible simulation protocol yielding Figure 1A–D. These elements jointly define sharp numerical thresholds for falsifying barrier-modulated nucleation control.

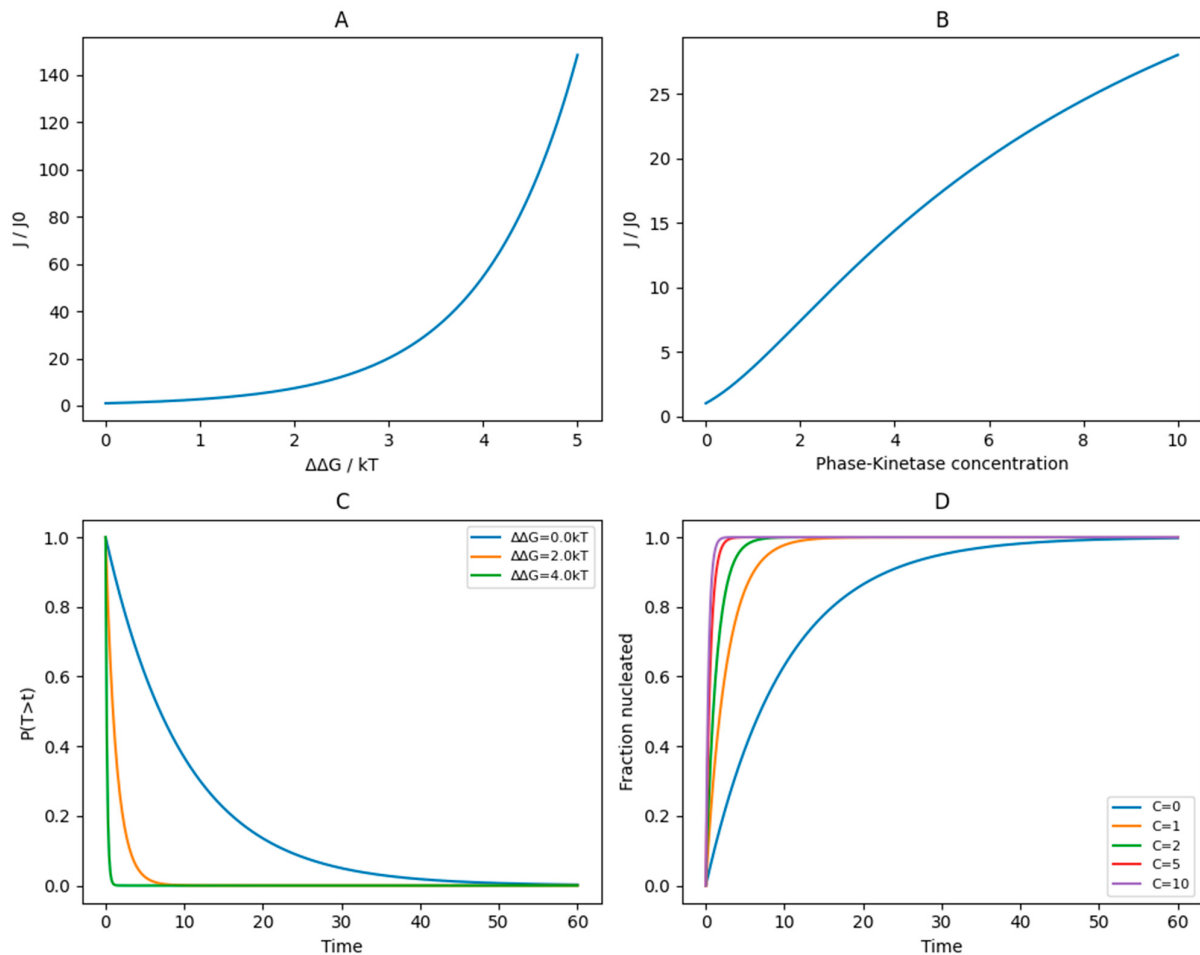


Figure 1. Quantitative regimes of enzymatic-like control in condensate nucleation. (A) Nucleation rate enhancement J/J_0 as a function of effective free-energy barrier reduction $\Delta\Delta G/kT$. The exponential dependence produces clearly separated regimes: weak modulation (<1 kT), biologically accessible enzymatic-like control ($1-3$ kT) and strong acceleration (>3 kT), yielding order-of-magnitude rate changes. (B) Nucleation rate enhancement as a function of Phase-Kinetase concentration, assuming saturable barrier modulation $\Delta\Delta G(C) = \Delta\Delta G_{\max}C/(K + C)$. The response displays an onset regime, a region of maximal sensitivity near $C \approx K$ and a high-concentration plateau, distinguishing barrier-lowering catalysis from non-saturating physical forcing. (C) Waiting-time survival curves $P(T > t)$ for condensate nucleation at fixed baseline rate and different barrier reductions. Barrier shifts of 2–4 kT yield sharply separated survival profiles, allowing direct inference of $\Delta\Delta G$ from kinetic data. (D) Fraction of nucleated compartments as a function of time for increasing Phase-Kinetase concentration. Time-to-half nucleation decreases with concentration but approaches an asymptote, providing a falsification criterion for saturable enzymatic-like control.

4. Conclusions

Our results suggest that a broad class of cellular physical processes can be understood as barrier-limited reactions whose kinetics are actively modulated by biologically produced agents acting in an enzymatic-like manner. We have focused explicitly on biomolecular condensate nucleation and dissolution as a concrete example of this principle. Rather than introducing new physical principles or invoking nonstandard forms of energy input, we reframe familiar biological components involved in condensate regulation as agents that locally and repeatedly lower effective kinetic barriers in configuration space. This shift allows condensate dynamics to be treated within a quantitative approach analogous to chemical catalysis. We identify explicit observables for condensate nucleation and dissolution, mapping them to effective barrier parameters in units of kT and define falsifiable

relationships between biological perturbations and measurable rate or waiting-time distributions. Our approach does not reinterpret biology as violating physics, but as actively shaping which physical transitions are realized and at what rates.

Condensate regulation could exemplify a more general mode of cellular organization, in which physical reactions are subject to layered kinetic control. We provide a language for biological regulation of physical dynamics that differs from strategies based on force generation, parameter tuning or purely material descriptions. Standard accounts of condensate behavior emphasize changes in interaction strengths, viscosities or global energy fluxes, often requiring system-specific models with limited transferability. In contrast, our framework centers on barrier modulation as a shared operational principle, allowing condensate nucleation and dissolution to be compared on a common energetic scale with other physical processes. This yields conceptual advantages. First, it naturally explains why modest biological perturbations can induce order-of-magnitude changes in nucleation or dissolution kinetics, through the exponential sensitivity of rates to barrier shifts. Second, it provides explicit saturation criteria distinguishing catalysis-like control from additive or force-driven mechanisms. Third, it enables direct inversion from data to effective energetic parameters, facilitating quantitative falsification. We do not introduce new entities but rather reorganize existing knowledge into a barrier-centric perspective that enables comparison, inference and testing. In terms of classification, our approach can be situated among mesoscopic theories of biological organization explicitly bridging molecular activity and emergent physical behavior. It differs from equilibrium thermodynamic treatments by focusing on kinetics rather than state functions, from continuum active matter models by emphasizing localized and saturable control and from purely biochemical frameworks by targeting physical state transitions instead of chemical reactions.

While we develop this approach in detail only for condensate dynamics, the same framework may plausibly extend to other cellular physical processes. We summarize in Table 1 additional, more speculative physical processes that may be amenable to enzymatic-like control and warrant future investigation.

Several limitations must be acknowledged. Several numerical thresholds stand for representative regimes rather than empirically validated constants. The assumption of constant or piecewise-constant hazards simplifies inference but may fail in systems with strong history dependence or spatial coupling. Idealizations concerning compartment definition, detection thresholds and event independence may not hold universally. The saturable functional forms used for barrier modulation are minimal hypotheses rather than mechanistic derivations and alternative nonlinearities could fit some data equally well. Finally, our figures are model-driven simulations rather than empirical measurements.

Despite these constraints, our approach suggests potential applications and future research directions. Experimentally, our framework motivates perturbation series that hold equilibrium or mean-state properties fixed while measuring nucleation kinetics, waiting-time distributions and saturation behavior. Testable hypotheses include the existence of finite plateaus in nucleation-rate enhancement under increasing concentrations of putative phase-kinetases, consistent barrier shifts inferred across independent observables and exponential relationships between inferred barriers and measured kinetics. Future work may extend our formalism to coupled barriers, heterogeneous populations or time-dependent modulation, integrating high-resolution imaging with survival and hazard reconstruction.

In summary, we addressed whether cellular activity could regulate condensate phase transitions through mechanisms analogous to enzymatic catalysis. We showed how localized, saturable and reusable biological agents can be modeled as modulators of effective kinetic barriers, yielding sharp and falsifiable quantitative predictions concerning condensate dynamics. Overall, viewing cellular physical dynamics through the lens of enzymatic-like control could provide a testable perspective on how living systems shape physical processes from within.

Table 1. Candidates potentially subject to enzymatic-like control. This table summarizes eight biophysical reactions that, while not analyzed in detail in the main text, could represent theoretical and speculative extensions of our enzymatic-like control framework. For each process, the table contrasts standard physical interpretations with empirical or conceptual limitations and proposes a coherent class of hidden enzymatic-like activities, defined as biological agents that could catalyze transitions between physical regimes without directly altering mean-state variables. The listed candidates are intended as hypothesis-generating examples. Falsification-oriented quantitative signatures are formulated in terms of variance modulation, effective temperature shifts, kinetic barrier reductions, threshold behavior or relaxation-time scaling, allowing these possibilities to be experimentally tested.

Possible candidate (fundamental biophysical reaction)	Usually attributed to physics	Why this is insufficient	Hidden enzymatic-like activity (coherent name + plausible biological candidates)	Testable quantitative signature (falsification-oriented)
Noise shaping and fluctuation control (variance, burstiness, spectra)	Thermal noise, Poisson statistics, stochastic chemical kinetics	Cells selectively tune variance, noise spectra and burstiness without changing mean values; fluctuations are context-dependent and heritable	Stochastases – chromatin remodelers (SWI/SNF-like complexes), RNA-binding proteins buffering transcriptional bursts, metabolic buffering metabolites (ATP/ADP, NADH/NAD ⁺ pools), phase-separated transcriptional hubs	Variance and power spectra change independently of mean; noise modulation shows saturability and exponential sensitivity consistent with $\Delta\Delta G \approx 1\text{--}3\text{ kT}$
Anomalous and biased intracellular diffusion (transport statistics)	Crowding, fractal geometry, viscoelastic media	Diffusion exponents and directionality change dynamically in time and space for identical molecules, incompatible with static physical environments	Diffusases – transient scaffolding proteins, RNA granules acting as dynamic obstacles, metabolite-regulated crowding modulators, weak multivalent binders that restructure local geometry	Diffusion exponent $\alpha(t)$ changes without altering viscosity; directional bias appears with saturable dependence on agent abundance
Local modulation of effective temperature (“active thermalization”)	Active matter noise, ATP-driven agitation	Effective temperature changes are spatially confined and reversible, not	Thermokatalysts – ATP-dependent chaperones (Hsp70/Hsp90-like systems), RNA helicases and remodelers,	Local violation of fluctuation–dissipation relations; inferred $\Delta T_{\text{eff}}/T \approx 0.1\text{--}0.3$

Possible candidate (fundamental biophysical reaction)	Usually attributed to physics	Why this is insufficient	Hidden enzymatic-like activity (coherent name + plausible biological candidates)	Testable quantitative signature (falsification-oriented)
		globally driven by energy input	metabolon-associated enzymes with oscillatory ATP/ADP or NADH/NAD ⁺ cycling, active cytoskeletal remodeling complexes, phase-separated activity hubs	without bulk heating
			Topo-Catalysts –	Event rates increase
Membrane fusion/fission initiation (stalk or neck nucleation)	Lipid elasticity, spontaneous curvature, thermal membrane fluctuations	Fusion and fission occur too fast, too selectively and at specific sites to be explained by rare thermal lipid fluctuations alone	curvature-sensing or inserting proteins (BAR-domain proteins), short amphipathic helices in fusion factors, dynamin-like GTPases, locally acting lipid-modifying enzymes	exponentially with catalyst concentration and saturate; inferred barrier reduction $\Delta\Delta G \approx 3\text{--}5$ kT from rate ratios
			Topolysins – SMC-family complexes	Loop formation and release rates
Topology control of chromatin and polymer loops	Polymer entropy, random collisions, loop extrusion models	Loop lifetimes and boundaries are sharply defined and cell-type specific	(cohesin- and condensin-like), topoisomerases (topology-level role), chromatin remodeling complexes, RNA-binding architectural proteins, phase-separated architectural scaffolds	show exponential sensitivity to small perturbations; barrier reductions of $\sim 2\text{--}4$ kT inferred from kinetics
		Length distributions shift faster than monomer turnover allows and without corresponding changes in synthesis or degradation rates	Polymodases – filament severing factors (cofilin, katanin-like), annealing and end-to-end exchange mediators, length-redistribution complexes acting on actin, microtubules or RNA	Mean length $\langle L \rangle$ scales inversely with agent concentration and saturates; redistribution kinetics exceed monomer turnover rates
Polymer length distribution reshaping (without synthesis or degradation)	Steady-state polymerization kinetics, critical concentration arguments			

Possible candidate (fundamental biophysical reaction)	Usually attributed to physics	Why this is insufficient	Hidden enzymatic-like activity (coherent name + plausible biological candidates)	Testable quantitative signature (falsification-oriented)
Cytoplasmic or cortical stress relaxation (viscoelastic response)	Passive rheology, jamming/unjamming, polymer physics	Relaxation times change abruptly, locally and reversibly, far beyond what changes in bulk force or composition predict	Rheolysins – actin-severing proteins (cofilin-like), crosslink turnover regulators, ATP-dependent cytoskeletal remodelers	Stress relaxation time τ decreases exponentially with agent concentration; τ ratios imply $\Delta\Delta G \approx 2\text{--}3\text{ kT}$; effect is local and reversible
		Wave nucleation sites and arrest points are highly reproducible, cell-type specific and history-dependent	Wave-Kinetases – scaffolded signaling complexes (MAPK, Rho-family GTPase modules), localized phosphatase-kinase feedback pairs, membrane- or cortex-anchored excitability regulators	Sharp all-or-none changes in wave frequency from small parameter shifts; effective threshold changes of $\sim 5\text{--}10\%$
Reaction–diffusion wave initiation and arrest (excitable dynamics)	Reaction–diffusion equations, threshold instabilities			

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Data Availability Statement: All data and materials generated or analyzed during this study are included in the manuscript. The Author had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis.

Conflicts of Interest: The Author does not have any known or potential conflict of interest including any financial, personal or other relationships with other people or organizations within three years of beginning the submitted work that could inappropriately influence or be perceived to influence their work.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Acknowledgments: During the preparation of this work, the author used ChatGPT 4o to assist with data analysis and manuscript drafting and to improve spelling, grammar and general editing. After using this tool, the author reviewed and edited the content as needed, taking full responsibility for the content of the publication.

Author Contributions: The Author performed: study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, statistical analysis, obtained funding, administrative, technical and material support, study supervision.

References

- Abyzov, Anton, Martin Blackledge, and Markus Zweckstetter. 2022. "Conformational Dynamics of Intrinsically Disordered Proteins Regulate Biomolecular Condensate Chemistry." *Chemical Reviews* 122 (6). <https://doi.org/10.1021/acs.chemrev.1c01088>.
- Alberti, Simon and Dorothee Dormann. 2019. "Liquid-Liquid Phase Separation in Disease." *Annual Review of Genetics* 53: 171–194.
- Alfi, A., B. Zhu, J. Damjanović, T. Kojima, Y. Iwasaki, and H. Nakano. 2019. "Production of Active Manganese Peroxidase in Escherichia coli by Co-Expression of Chaperones and In Vitro Maturation by ATP-Dependent Chaperone Release." *Journal of Bioscience and Bioengineering* 128 (3): 290–295. <https://doi.org/10.1016/j.jbiosc.2019.02.011>
- Ball, N. J., S. F. H. Barnett, and B. T. Goult. 2024. "Mechanically Operated Signalling Scaffolds." *Biochemical Society Transactions* 52 (2): 517–527. <https://doi.org/10.1042/BST20221194>
- Banani, Salman F., Hyun O. Lee, Anthony A. Hyman and Michael K. Rosen. 2017. "Biomolecular Condensates: Organizers of Cellular Biochemistry." *Nature Reviews Molecular Cell Biology* 18 (5): 285–298.
- Blundell, T. L., M. N. Gupta, and S. E. Hasnain. 2020. "Intrinsic Disorder in Proteins: Relevance to Protein Assemblies, Drug Design and Host-Pathogen Interactions." *Progress in Biophysics and Molecular Biology* 156: 34–42. <https://doi.org/10.1016/j.pbiomolbio.2020.06.004>
- Cargill, M., R. Venkataraman, and S. Lee. 2021. "DEAD-Box RNA Helicases and Genome Stability." *Genes* 12 (10): 1471. <https://doi.org/10.3390/genes12101471>.
- Choi, Jae-Hyung, Alex S. Holehouse and Rohit V. Pappu. 2020. "Physical Principles Underlying the Complex Biology of Intracellular Phase Transitions." *Annual Review of Biophysics* 49: 107–133.
- Dai, Yifan, Zhengqing Zhou, Wen Yu, Yuefeng Ma, Kyer Kim, Nelson Rivera, et al. 2024. "Biomolecular Condensates Regulate Cellular Electrochemical Equilibria." *Cell* 187 (21): 5951–5966.e18. <https://doi.org/10.1016/j.cell.2024.08.018>.
- DiRusso, Christopher J., Maryam Dashtiahangar, and Thomas D. Gilmore. 2022. "Scaffold Proteins as Dynamic Integrators of Biological Processes." *Journal of Biological Chemistry* 298 (12): 102628. <https://doi.org/10.1016/j.jbc.2022.102628>.
- Dignon, Gregory L., Wenwei Zheng, Young C. Kim and Jeetain Mittal. 2018. "Sequence Determinants of Protein Phase Behavior from a Coarse-Grained Model." *PLoS Computational Biology* 14 (1): e1005941.
- Djulbegovic, M. B., D. J. Taylor, V. N. Uversky, A. Galor, C. L. Shields, and C. L. Karp. 2022. "Intrinsic Disorder in BAP1 and Its Association with Uveal Melanoma." *Genes* 13 (10): 1703. <https://doi.org/10.3390/genes13101703>
- Djulbegovic, M., D. J. Taylor Gonzalez, M. Antonietti, V. N. Uversky, C. L. Shields, and C. L. Karp. 2023. "Intrinsic Disorder May Drive the Interaction of PROS1 and MERTK in Uveal Melanoma." *International Journal of Biological Macromolecules* 250: 126027. <https://doi.org/10.1016/j.ijbiomac.2023.126027>
- Gong, H., H. Zhong, L. Cheng, L. P. Li, and D. K. Zhang. 2024. "Post-Translational Protein Lactylation Modification in Health and Diseases: A Double-Edged Sword." *Journal of Translational Medicine* 22 (1): 41. <https://doi.org/10.1186/s12967-023-04842-9>
- Greenwald, E. C., J. M. Redden, K. L. Dodge-Kafka, and J. J. Saucerman. 2014. "Scaffold State Switching Amplifies, Accelerates, and Insulates Protein Kinase C Signaling." *Journal of Biological Chemistry* 289 (4): 2353–2360. <https://doi.org/10.1074/jbc.M113.497941>
- Guillén-Boixet, Jordi, et al. 2020. "RNA-Induced Conformational Switching and Clustering of G3BP Drive Stress Granule Assembly by Condensation." *Cell* 181 (2): 346–361.
- Gupta, Munishwar Nath, and Vladimir N. Uversky. 2026. "The Functional Significance of Intrinsic Disorder in Enzymes." *Biochimie* 241 (February): 116–124. <https://doi.org/10.1016/j.biochi.2025.10.016>.
- Hirth, A., E. Fatti, E. Netz, S. P. Acebron, D. Papageorgiou, A. Švorinić, C. M. Cruciat, E. Karaulanov, A. Gopanenko, T. Zhu, I. Sinning, J. Krijgsveld, O. Kohlbacher, and C. Niehrs. 2024. "DEAD Box RNA Helicases Are Pervasive Protein Kinase Interactors and Activators." *Genome Research* 34 (6): 952–966. <https://doi.org/10.1101/gr.278264.123>.
- Hyman, Anthony A., Clifford A. Weber and Frank Jülicher. 2014. "Liquid-Liquid Phase Separation in Biology." *Annual Review of Cell and Developmental Biology* 30: 39–58.

- Jawerth, Louise M., et al. 2020. "Protein Condensates as Aging Maxwell Fluids." *Science* 370 (6522): 1317–1323.
- Klosin, Adam, et al. 2020. "Phase Separation Provides a Mechanism to Reduce Noise in Cells." *Science* 367 (6476): 464–468.
- Li, S., T. Feng, H. Yuan, Q. Li, G. Zhao, and K. Li. 2024. "DEAD-Box RNA Helicases in the Multistep Process of Tumor Metastasis." *Molecular Biology Reports* 51 (1): 1006. <https://doi.org/10.1007/s11033-024-09912-9>.
- Li, Siyu, Guillaume Tresset, and Roya Zandi. 2025. "From Disorder to Icosahedral Symmetry: How Conformation-Switching Subunits Enable RNA Virus Assembly." *Science Advances* 11 (39). <https://doi.org/10.1126/sciadv.ady7241>.
- Low, K. J. Y., A. Venkatraman, J. S. Mehta, and K. Pervushin. 2021. "Molecular Mechanisms of Amyloid Disaggregation." *Journal of Advanced Research* 36: 113–132. <https://doi.org/10.1016/j.jare.2021.05.007>
- Mahapatra, S., A. Sarbahi, N. Punia, A. Joshi, A. Avni, A. Walimbe, and S. Mukhopadhyay. 2023. "ATP Modulates Self-Perpetuating Conformational Conversion Generating Structurally Distinct Yeast Prion Amyloids That Limit Autocatalytic Amplification." *Journal of Biological Chemistry* 299 (5): 104654. <https://doi.org/10.1016/j.jbc.2023.104654>
- Naineni, S. K., F. Robert, B. Nagar, and J. Pelletier. 2023. "Targeting DEAD-Box RNA Helicases: The Emergence of Molecular Staples." *Wiley Interdisciplinary Reviews: RNA* 14 (2): e1738. <https://doi.org/10.1002/wrna.1738>.
- Nussinov, R., H. Jang, C. J. Tsai, T. J. Liao, S. Li, D. Fushman, and J. Zhang. 2017. "Intrinsic Protein Disorder in Oncogenic KRAS Signaling." *Cellular and Molecular Life Sciences* 74 (17): 3245–3261. <https://doi.org/10.1007/s00018-017-2564-3>
- Riback, Joshua A., et al. 2020. "Composition-Dependent Thermodynamics of Intracellular Phase Separation." *Nature* 581: 209–214.
- Shin, Yongdae and Clifford P. Brangwynne. 2017. "Liquid Phase Condensation in Cell Physiology and Disease." *Science* 357 (6357): eaaf4382.
- Snead, William T. and Jeanne C. Stachowiak. 2019. "Structure versus Stochasticity—The Role of Molecular Crowding and Phase Separation in Membraneless Organelles." *Journal of Molecular Biology* 431 (23): 4711–4725.
- Tao, J., J. Li, X. Fan, C. Jiang, Y. Wang, M. Qin, Z. Nikfard, F. Nikfard, Y. Wang, T. Zhao, N. Xing, M. Zille, J. Wang, J. Zhang, X. Chen, and J. Wang. 2024. "Unraveling the Protein Post-Translational Modification Landscape: Neuroinflammation and Neuronal Death after Stroke." *Ageing Research Reviews* 101: 102489. <https://doi.org/10.1016/j.arr.2024.102489>
- Trösch, R., T. Mühlhaus, M. Schroda, and F. Willmund. 2015. "ATP-Dependent Molecular Chaperones in Plastids: More Complex than Expected." *Biochimica et Biophysica Acta* 1847 (9): 872–888. <https://doi.org/10.1016/j.bbabi.2015.01.002>
- Wang, S., A. O. Osgood, and A. Chatterjee. 2022. "Uncovering Post-Translational Modification-Associated Protein-Protein Interactions." *Current Opinion in Structural Biology* 74: 102352. <https://doi.org/10.1016/j.sbi.2022.102352>
- Wang, J., Y. Xiang, Y. Youhuan, X. Ma, Y. Gu, D. Zhang, J. Wang, Y. Fu, F. Shi, J. Sun, M. H. Hansen, M. H. Hansen, P. Wang, Y. Xu, and W. Yang. 2025. "The Mitochondrial DNAJC Co-Chaperone TCAIM Reduces Alpha-Ketoglutarate Dehydrogenase Protein Levels to Regulate Metabolism." *Molecular Cell* 85 (3): 638–651.e9. <https://doi.org/10.1016/j.molcel.2025.01.006>
- Wentink, A. S., N. B. Nillegoda, J. Feufel, G. Ubartaitė, C. P. Schneider, P. De Los Rios, J. Hennig, A. Barducci, and B. Bukau. 2020. "Molecular Dissection of Amyloid Disaggregation by Human HSP70." *Nature* 587 (7834): 483–488. <https://doi.org/10.1038/s41586-020-2904-6>
- Yang, Y., S. Liu, S. Egloff, C. D. Eichhorn, T. Hadjian, J. Zhen, T. Kiss, Z. H. Zhou, and J. Feigon. 2022. "Structural Basis of RNA Conformational Switching in the Transcriptional Regulator 7SK RNP." *Molecular Cell* 82 (9): 1724–1736.e7. <https://doi.org/10.1016/j.molcel.2022.03.001>
- Yu, H., M. Eres, S. L. Hilburg, et al. 2026. "Random Heteropolymers as Enzyme Mimics." *Nature* 649: 83–90. <https://doi.org/10.1038/s41586-025-09860-9>.
- Zhang, P., D. Wang, G. Zhou, S. Jiang, G. Zhang, L. Zhang, and Z. Zhang. 2025. "Novel Post-Translational Modification Learning Signature Reveals B4GALT2 as an Immune Exclusion Regulator in Lung

Adenocarcinoma." *Journal for ImmunoTherapy of Cancer* 13 (2): e010787. <https://doi.org/10.1136/jitc-2024-010787>

Zhang, Ziyin, Daqian Li, Bo Zheng, and Jia-feng Liu. 2026. "DEAD-box ATPase-Marked Condensates Coordinate Compartmentalized Translation and Antibiotic Persistence." *Science Advances* 12 (1): eady1930. <https://doi.org/10.1126/sciadv.ady1930>.

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