

## Peer Review

# Review of: "Aging as Cybernetic Attractor Decay: Beyond the Stochastic-Programmed Dichotomy"

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The manuscript presents an ambitious and, in several respects, intellectually stimulating proposal that aims to move beyond the classical programmed–stochastic dichotomy in aging by introducing a framework based on regulatory architectures and attractor dynamics. The integration of epigenetic clock predictability, partial rejuvenation, and the role of developmental gene regulation constitutes a relevant and potentially impactful theoretical effort.

However, the central argument relies on the use of entropy as the explanatory variable for aging, and at this point, the manuscript shows a fundamental weakness at both the operational and epistemological levels.

In its current form, “regulatory network entropy” is not defined as a measurable quantity. Shannon entropy is not an intrinsic property of a network but of an explicitly specified probability distribution. The manuscript does not define the state space, the underlying distribution, or how such a quantity would be computed in real biological data. As a consequence, entropy functions here as a general metaphor for disorganization rather than as a falsifiable scientific variable.

More importantly, even if formally defined, entropy cannot distinguish between functional variation and variation that degrades system performance. In biological systems, variability is a condition of adaptability rather than a thermodynamic residue. An increase in entropy may reflect functional plasticity as well as a loss of regulatory control. Therefore, it cannot by itself serve as an explanation for aging without an explicit reference to the conditions under which such variation is required for the maintenance of function.

This is not merely a technical issue but a structural one: by locating the cause of aging in an internal property of the system (entropy increase), the model remains at the same explanatory level as damage-accumulation theories, despite the change in language. In both cases, decline is explained by an internal system state rather than by a loss of the capacity to sustain coherences under specific constraints.

From a strictly operational perspective, the phenomenon described throughout the manuscript is more accurately captured by a different formulation: aging as the increase of **variety that is no longer processed by the regulatory architecture and that progressively overlaps with the variety required to sustain function**. This does not correspond to generalized disorder but to interference within the viability domain: activation of regulatory trajectories out of context, loss of cellular identity exclusivity, hybrid states, and increased transitions toward paths that previously remained suppressed.

This situation can be formalized through the distinction between **Required Variety (RV)** and **Non-Required Variety (NRV)** in a functional sense. If the system state is represented as  $X$  and the performance required under its constraints as  $Y$ , then:

$$X = X_{\text{req}} + X_{\text{nr}}$$

and

$$NRV = \frac{\|X_{\text{nr}}\|^2}{\|X\|^2}$$

NRV does not measure abstract dispersion but the fraction of variation that interferes with the maintenance of regulatory coherence. In single-cell data, this is directly observable as the increasing occupation of off-lineage or hybrid states and as the rise in transitions toward trajectories that do not belong to the functional domain. This quantity is measurable with current technologies and allows the formulation of falsifiable hypotheses that can be directly compared with mutational load or network-based metrics.

In its present form, the manuscript contains a powerful theoretical intuition, but its main explanatory variable remains at the level of analogy. As long as entropy is not replaced by an operational quantity that explicitly distinguishes functional from interfering variation, the model cannot empirically sustain its claim of providing an alternative to existing aging theories.

In summary, this is a work with remarkable conceptual integrative capacity, but its scientific consistency depends on an explicit reformulation of its central variable. The incorporation of a metric based on the

distinction between required and non-required variety would transform what is currently a largely metaphorical proposal into an empirically testable and comparative framework.

## **Declarations**

**Potential competing interests:** No potential competing interests to declare.