

<https://doi.org/10.1038/s44260-024-00014-y>

Antifragility in complex dynamical systems



Cristian Axenie¹, Oliver López-Corona², Michail A. Makridis³, Meisam Akbarzadeh⁴, Matteo Saveriano⁵, Alexandru Stancu⁶ & Jeffrey West⁷

Antifragility characterizes the benefit of a dynamical system derived from the variability in environmental perturbations. Antifragility carries a precise definition that quantifies a system's output response to input variability. Systems may respond poorly to perturbations (fragile) or benefit from perturbations (antifragile). In this manuscript, we review a range of applications of antifragility theory in technical systems (e.g., traffic control, robotics) and natural systems (e.g., cancer therapy, antibiotics). While there is a broad overlap in methods used to quantify and apply antifragility across disciplines, there is a need for precisely defining the scales at which antifragility operates. Thus, we provide a brief general introduction to the properties of antifragility in applied systems and review relevant literature for both natural and technical systems' antifragility. We frame this review within three scales common to technical systems: intrinsic (input–output nonlinearity), inherited (extrinsic environmental signals), and induced (feedback control), with associated counterparts in biological systems: ecological (homogeneous systems), evolutionary (heterogeneous systems), and interventional (control). We use the common noun in designing systems that exhibit antifragile behavior across scales and guide the reader along the spectrum of fragility–adaptiveness–resilience–robustness–antifragility, the principles behind it, and its practical implications.

Antifragile is a term coined to describe the opposite of fragile, as defined in a recent book that generated significant interest in both the public and scientific domain¹. Although the term has a wide range of applications, it contains a precise and mathematical definition. Systems or organisms can be defined as antifragile if they derive benefit from systemic variability, volatility, randomness, or disorder². To get an intuition, we provided examples of a system's reference behaviors in Fig. 1, where three disruptions (i.e., in varying amplitude, onset and duration) occur at random times and inject volatility, randomness, or disorder in a system's dynamics.

In mathematical terms, antifragility is a nonlinear convex response to a well-defined payoff function that a system exhibits in the face of volatility. This assumes that antifragility is a local property of a dynamical system over a defined region of the system's input space. Beyond that range, the system may become fragile. This nonlinear response enables the system to not only withstand perturbations (robust) but even benefit from them (antifragile). Although the antifragility framework emerged in the context of financial

risk analysis, due to its universal mathematical formalism and principles, it has recently drawn attention and has been applied within different concepts across domains including biology³, socio-economics⁴, urban planning⁵, and risk analysis⁶. Applied antifragility theory extends Nassim Taleb's antifragility principle to the rank of system design methodology across disciplines.

Defining terms across technical and natural systems

Herein, we draw from the body of literature on technical systems (e.g., road traffic and robotics control systems) and biological systems (e.g., cancer therapy, antibiotics, and agricultural pest management) to define the scales of antifragility theory and unify definitions from natural and technical systems. The perspective manuscript describes the scales (Fig. 2) of the applied antifragility spectrum in technical systems: (1) intrinsic, (2) inherited, and (3) induced antifragility. While this taxonomy has primarily been applied to technical systems, we will show that each scale of antifragility in technical

¹Department of Computer Science and Center for Artificial Intelligence, Nuremberg Institute of Technology Georg Simon Ohm, Nuremberg, Germany. ²Investigadores por México (IxM) at Instituto de Investigaciones en Matemáticas Aplicadas y en Sistemas (IIMAS), Universidad Nacional Autónoma de México (UNAM), Ciudad Universitaria, CDMX, Mexico. ³Institute for Transport Planning and Systems (IVT), ETH Zurich, Switzerland. ⁴Department of Transportation Engineering, Isfahan University of Technology, Isfahan, Iran. ⁵Department of Industrial Engineering, University of Trento, Trento, Italy. ⁶Department of Electrical and Electronic Engineering, The University of Manchester, Manchester, UK. ⁷Department of Integrated Mathematical Oncology, H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL, USA. e-mail: jeffrey.west@moffitt.org

Fig. 1 | Figure adapted (with permission) from ref. 17—perspective on a dynamical system's behavior spectrum: Fragile–Adaptive–Resilient–Robust–Antifragile responses. Example disturbances have random onset, duration (i.e., volatility), and amplitude. Each type of system response captures the predominant traits of the spectrum members.

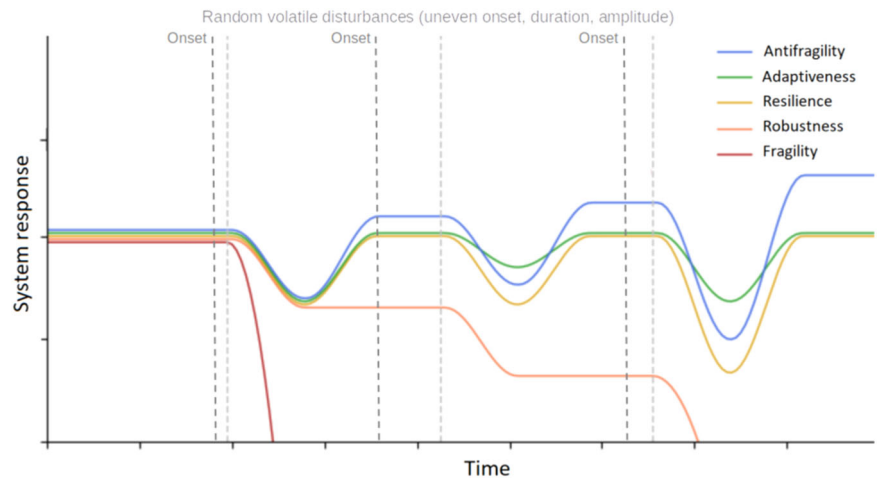
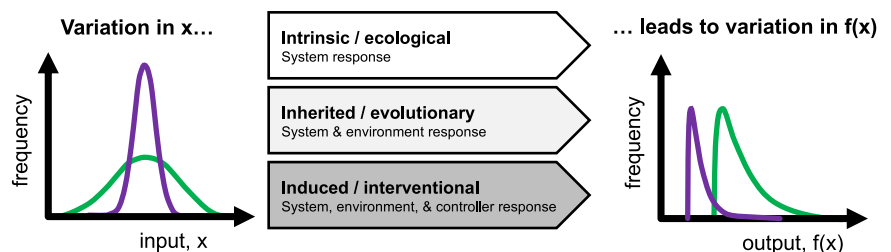


Fig. 2 | Antifragility-associated terms, defined for technical and natural (biological) systems. Variation in the system's inputs, x , (left panel) leads to variation in the system's outputs, $f(x)$ (right panel). The response to variation can be defined on three scales: intrinsic (ecological), inherited (evolutionary), and induced (interventional).



systems has its analog in natural (biological) systems: ecological, evolutionary, and interventional antifragility^{7,8}. We provide definitions for each proposed antifragility scale and review existing literature to provide examples of successful practical examples for a broad audience.

Moving along the spectrum (i.e., intrinsic, inherited, induced antifragility), the response properties of the dynamical system and its capacity to gain from stressors and anticipate random and volatile events increase. Intrinsic/ecological antifragility describes the system's internal dynamics without external interactions and intervention. Inherited/evolutionary antifragility describes the system's dynamics under external signals that modulate the system's internal dynamics. Finally, induced/interventional antifragility introduces the closed-loop (behavior) dimension of antifragility, where the system is connected to control or driving signals. Antifragility (or its converse, fragility) defines the association between nonlinearity and variability. Thus, the benefit (or harm) derived can be defined as a scale measure of volatility at the level of statistical singularities (divergence of high-order statistical moments). We note that antifragility can be quantified under a geometrical analysis of the shape of nonlinearity characterizing the payoff function (when the function is known). Across these scales, the recently formed Applied Antifragility Group (<https://antifragility.science/>) has proposed three *Paths* forward for characterizing, designing, and building systems that behave antifragile in the face of uncertainty, volatility, and randomness:

- *Path 1 to reach intrinsic/ecological antifragility*: Mathematical identification of second-order effects in the system response characterizing antifragile behavior;
- *Path 2 to reach inherited/evolutionary antifragility*: Mapping the dynamics of the system to physical principles of criticality and evolution to describe reaching an antifragile state;
- *Path 3 to reach induced/interventional antifragility*: Nonlinear control synthesis or learning of optimal driving signals to push dynamical systems to antifragile regions in their response spectrum.

It is important to note that, technical systems are typically built as homogeneous systems, i.e., all components share the same properties (i.e., spatial, temporal, structural, and functional). However, most natural systems are heterogeneous, where a few components are closer, faster, or stronger than others. Even if we analyze across scales, the common denominator is time. Each scale or property of the system evolves, be it slower or faster. When defining antifragility, time plays an important role. The study of natural systems within the antifragility concept needs special treatment as we typically use simple, limited models to describe complex, nonlinear natural phenomena^{9–11}. The study of technical systems differs because we better understand their design principles. Therefore, before discussing whether a system is antifragile or not, we need to define the environment in which the system operates and the objectives of the system. Given the environment and the objectives, there may be multiple payoff functions that can be considered for the quantification of the system's performance¹².

Depending on the indicators or metrics we adopt, the conclusions regarding the system's fragility can differ. In the following sections, we will discuss the differences between intrinsic, inherited, and induced antifragility and give certain intuitive examples in both technical and natural systems.

Intrinsic and ecological antifragility

Intrinsic/ecological antifragility (or fragility) quantifies the benefit (or harm) of input distribution unevenness, volatility, or perturbations attributed to the nonlinearity of the system's payoff function. This phenomenon is closely related to Jensen's Inequality^{13,14}, which states that the expected value of a convex function is greater than the function evaluated at the expected value:

$$\mathbb{E}(f(x)) > f(\mathbb{E}(x)). \quad (1)$$

The convex shape of the function determines the inequality. Conversely, if $f(x)$ is concave, the inequality is flipped:

$$\mathbb{E}(f(x)) < f(\mathbb{E}(x)). \quad (2)$$

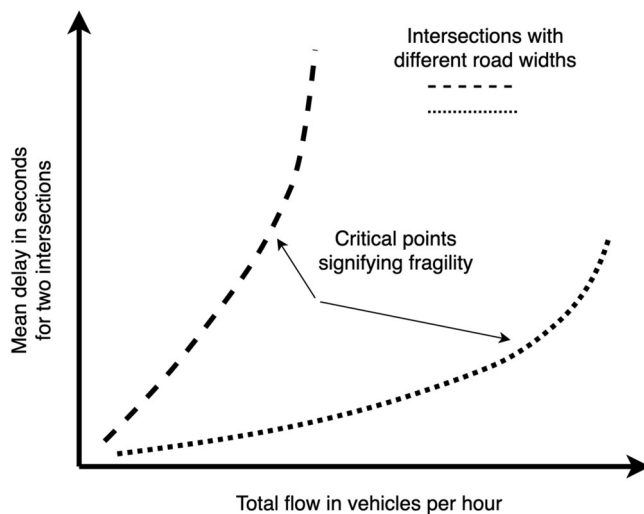


Fig. 3 | Exemplary illustration showing delays (output) at intersections with different road widths, over traffic flow (input). The long-dashed line indicates a road with a narrow average width, while the short-dashed line represents a wide-width road.

When the payoff function, $f(x)$, representing a system is known, then the inequality can be confirmed by direct observation of $f(x)$. In this section, we illustrate examples in technical and natural systems, and draw the connection between the nonlinearity of $f(x)$ and the statistical properties of the distribution of $f(x)$.

Technical systems: intrinsic (anti)-fragility

When considering intrinsic antifragility, the fundamental aspect is dynamics' timescale separation describing the input–output coupling. An example is urban intersections with different characteristics (road width), where there is a large variation in delays even in cases where the traffic state is not drastically changing, due to fluctuations in arrival and discharge rates. As shown in the exemplary Fig. 3, empirical findings show that the delays increase with traffic flow and are bounded by a maximum flow number. While approaching the flow boundary, delays (output) increase exponentially with flow (input) demonstrating empirically the fragility of the system¹⁵. The convex shape of payoff functions in Fig. 3 relates to Eq. (1), where the minimization of delays is achieved through decreasing variability, $f(\mathbb{E}(x))$, rather than increasing variability, $\mathbb{E}(f(x))$. Management strategies, such as those suggested in ref. 16, aim to push the operation of the system towards the critical density. Such strategies consider the effect of variation in input (traffic flow) on the outcome (delays), which are modulated by the shape of the input–output function (exponential), as illustrated in schematic Fig. 1 schematic.

In another example, given the interactions between multiple control loops (e.g., the internal DC motor control loop and outer robot position control loop¹⁷, the oscillators models of traffic flow inputs¹⁸, and the coupled traffic dynamics^{19,20}), antifragility is quantified in the context of input–output mappings of timescale separation performed to handle uncertainty and high-frequency phenomena. However, note that such systems employ intrinsic antifragility to achieve their prescribed objectives by design, given the specifications and constraints imposed by the physics of the operational space of the system, for example, in driver models^{21–23} or traffic dynamics^{24–26}.

When unpredictable fluctuations start developing in a dynamical system that is on the verge of losing its stability, it is commonly referred to as criticality. The ability to absorb and respond to stresses, due to the appearance of scale-free temporal fluctuations, slowing dynamics, and multistability, are the fundamental indicators of criticality. Here, antifragility can be viewed as the motion of a system from an existing steady state to a better one in the aftermath of a change in conditions. This transfer

among steady states may be continuous (second-order phase transition) or discontinuous (first-order phase transition)²⁷.

Natural systems: ecological (anti)-fragility

In biological systems, changes in environmental conditions can decrease the survival and fecundity of individuals based on a species' Darwinian fitness. The rate of change in environmental perturbations may reduce fitness in response to stochastic fluctuations and seasonal variation¹⁴. The payoff function associated with the system response to environmental variation may be concave (fragile), convex (antifragile), or linear (neutral)^{1,28}. An example is shown in Fig. 4, where there exists a dose distribution mean and variance (panel a) associated with each anticancer treatment protocol (panel b), where the outcome depends on the concave (top) or convex (bottom) dose–response function (panel c). To maximize response, concave functions (red) should employ low-variance protocols, while concave functions (blue) should employ high-variance intermittent protocols. Ecological antifragility is the natural systems counterpart to intrinsic antifragility and may be defined as the system benefit derived from input volatility⁸. Defining ecological fragility or antifragility is useful for prediction and control of a biological population. For example, mathematical models describing the response to anticancer drugs measure the ecological effect of volatile versus continuous treatment schedules⁷, with or without drug pharmacokinetics²⁹.

Neuronal processing offers a complex system that recapitulates a large repertoire of dynamics. Neural networks must keep their stability under perturbations on timescales from milliseconds to months or even years¹⁰. It seems paradoxical, but neural networks can only remain stable if they are excitable and able to adapt their response (and structure) in reaction to outside stimuli. Neuron-level excitability modifications regulate the functionality of neural networks by absorbing a broad variety of molecular and cellular parameter changes while preserving their spiking functionality. For instance, homeostatic activity regulation in single neurons enables resilience to recurrent state variable alterations that correlate with resilience to changes in parameters due to the critical slowing down phenomenon³⁰.

Similar to technical systems, criticality in natural systems also relates to antifragility. Empirical investigations have suggested that living systems operate in the proximity of critical thresholds, existing at the delicate boundary between order and randomness³¹ demonstrated across various domains including electrical heart activity and brain function, among others^{32–35}. Precise measurement of the payoff function for predicting antifragility plays a key role. López-Corona and coworkers³⁶ applied these ideas discussed above to the scale of planetary ecosystem antifragility by integrating well-established principles from nonequilibrium thermodynamics and adopting a system dynamics approach using Fisher's information on Earth's entropy production^{37–39}.

In summary, antifragility can be quantified under a geometrical analysis of the shape of nonlinearity characterizing the payoff function. Important to note here is that antifragility is a scale measure of the effect of variation at the level of statistical singularities (divergence of high-order statistical moments). Here, depending on the type of system (natural or technical) assessing antifragility is bound to the measure of benefit (or harm) of input distribution unevenness, volatility, or perturbations attributed to the nonlinearity of the system's payoff function.

Inherited and evolutionary antifragility

Inherited/evolutionary antifragility (or fragility) quantifies the benefit (or harm) of input distribution unevenness, volatility, or perturbations attributed to the system's response to external signals. In many scenarios, a system's payoff function may be unknown (or unmeasurable), or it may be known but external signals introduce additional nonlinearities. Previous work illustrated the connection⁸ between convexity (or concavity) of a payoff function, $f(x)$, and statistical properties of the distribution of $f(x)$. For example, variation in the input distribution (Fig. 2, left) passing through a convex response function, $f(x)$, results in a right-tailed outcome distribution

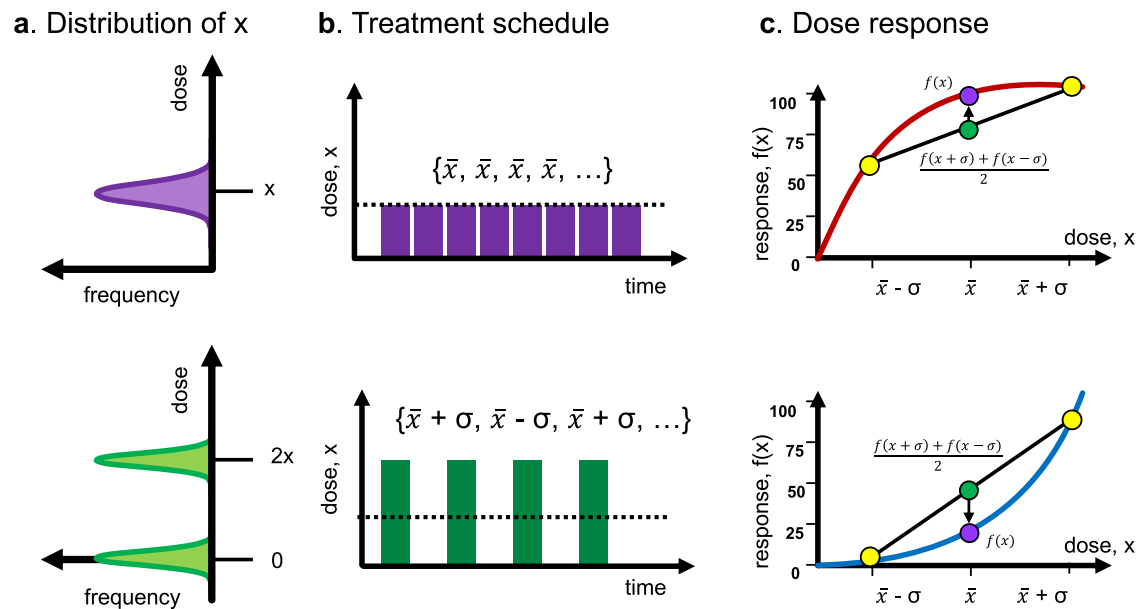


Fig. 4 | Figure reproduced with permission from ref. 8—example treatment-scheduling protocols. a Example dose distribution with low (top) or high variance (bottom). **b** Associated protocols. **c** Low-variance protocols are optimal to maximize response for concavity; high-variance protocols for convexity.

(Fig. 2, right). In contrast, a concave response function results in a left-tailed distribution. Therefore, everything fragile must be concave to harm.

Technical systems: inherited (anti)-fragility

Antifragility is correlated with increased system heterogeneity^{40,41}. This aspect comes into play when considering the system's capacity to build extra capacity in anticipation of perturbations. More precisely, to achieve inherited antifragility, a system designer builds upon the timescale separation of a redundant overcompensation component, as shown in robotics¹⁷, traffic control¹⁸, and medical⁴² applications of applied antifragility.

Similarly, machine-learning systems¹⁹ maintain timescale separation through the formulation of the learning task. More precisely, the system determines the best action at which the system yields the maximum possible discounted future reward. Isolating only the contribution of the timescale separation and the redundant overcompensation term, the machine learning inherited antifragility controller gained in the skewness (i.e., convexity) of the disruption magnitude over surging demand. In such systems, antifragility is quantified as the geometric properties of the anticipated control actions via the shape of the response to high-magnitude external perturbations.

Finally, criticality also plays a role in inherited antifragility by allowing a system to leave the current steady state, for a different one. The trigger for state switching may come from a change in the (1) parameters of the system, (2) externally enforced noise, or (3) an increase in the rates of the system from neighboring entities in a competition of cooperation with the system^{43,44}.

Natural systems: evolutionary (anti)-fragility

Evolution, defined here as the change in heritable traits within a population over time, is also influenced by environmental perturbations⁴⁵. In the previous section, ecological antifragility considered individual species in isolation to quantify the response to perturbation. Evolutionary antifragility quantifies how a heterogeneous population of interacting species is affected by perturbations. For example, in cancer, competition between heterogeneous populations of cell types modulates antifragility⁴⁶. In biological systems, we investigate complexity (which implies maximum computational capabilities) and how systems reach criticality^{47–49}. Adaptive mechanisms of living systems do more than merely react to the environment's variability through random mutations followed by selection; they must have built-in characteristics that enable them to discover alternatives to adapt to adversity, variability, and uncertainty³⁹.

Using theoretical arguments, it has been proposed that systems under eco-evolution tend to be at criticality, implying maximum complexity and inferential capabilities; and then they are also at maximum antifragility^{39,50,51}. Stability plays a central role in function, in both natural and technical dynamical systems. Paradoxically, a dynamical system can remain stable only if it is excitable and able to change its behavior in reaction to outside stimuli. It is flexible and thus stable; in fact, the organism's true stability depends on its modest instability⁵².

Inherited antifragility in natural systems is a consequence of the interactions among all components through evolutionary processes (e.g., genetic inheritance, microbiome inheritance, and social inheritance), constrained by external conditions. Antifragile natural systems derive benefits under uncertainty, stressors, and perturbations in both ecological and evolutionary scales. Evolution by natural selection itself can be thought of as an antifragile process, whereby a population is maintained amidst environmental perturbations through genetic variation. For example, although individuals within a population may die, the population evolves toward a more antifragile state, with increasingly higher fitness to address fluctuating environmental conditions^{28,53}.

Induced and interventional antifragility

Induced/interventional antifragility (or fragility) quantifies the benefit (or harm) of input distribution unevenness, volatility, or perturbations attributed to the system's response to closed-loop controllers.

Technical systems: induced (anti)-fragility

The control-theoretic approach to induced antifragility focuses on the combination of timescale separation and redundant overcompensation with variable structure control. A controller guides the system to the antifragile region of its operational domain through a judicious choice of an external control or regulation signal¹⁷. This can be accomplished by properly synthesizing a control law, which develops a redundant overcompensation capacity to handle uncertainty regarding the sensor and actuator failures by pushing the closed-loop system dynamics to prescribed dynamics. This is captured in Fig. 5, where the fragile–antifragile behavior is depicted across spatiotemporal dynamics of a robot in uncertain environments. Here, antifragility is quantified through the quality of the dynamics tracking and the speed of reaching the desired region of the desired dynamics manifold in the presence of uncertainty and volatility through adaptive control⁵⁴, robust control⁵⁵, and resilient control⁵⁶ strategies. In a large-scale traffic control

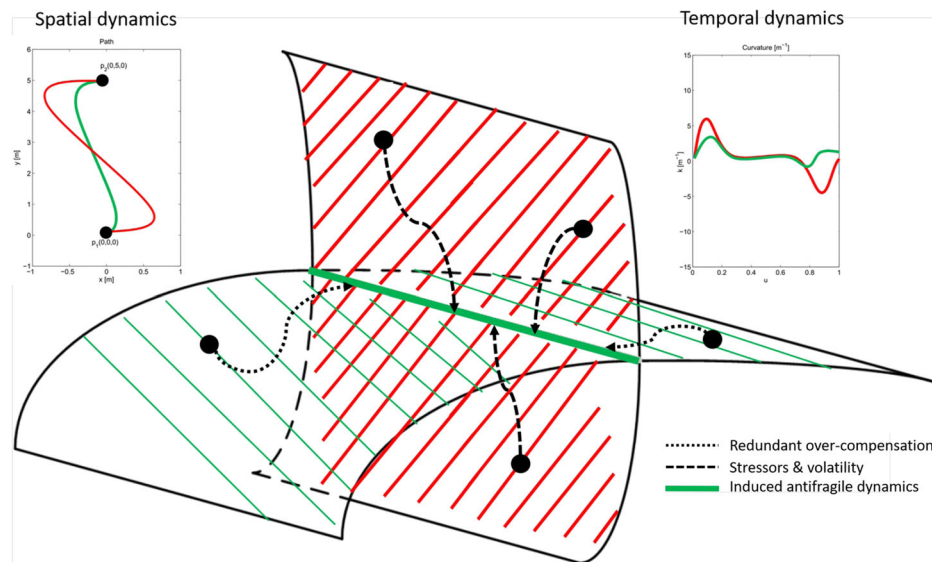


Fig. 5 | Figure reproduced with permission from ref. 17—spatial and temporal dynamics of fragile and antifragile behaviors of a robot in uncertain environments. The spatial dynamics (inset left) describe the robot's trajectory, in Cartesian (x, y) space, in the presence of uncertainty (i.e., several types of unexpected faults in the robot's motion). Red describes the strong (i.e., fragile) deviation from the goal of moving as fast as possible from point P1 to point P2 in the presence of faults. Green marks the antifragile trajectory which absorbs the uncertainty and gains a smoother trajectory. The temporal dynamics (inset right) describe the robot's trajectory tracking in the presence of uncertainty from the perspective of travel time. Travel time is implicit in the relation between the control signal sent to the robot's actuators

and the curvature of the trajectory of the robot given that signal. In this case, the fragile behavior is characterized by longer executions away from the prescribed dynamics whereas the antifragile behavior has a more straight convergence in the presence of faults. Closed-loop dynamics in the presence of stressors and volatility. The planes describe possible system dynamics motions from various initial conditions in the presence of stressors and volatility and the convergence to antifragile behavior. The redundant overcompensation refers to geometrically longer paths to reach the antifragile region (i.e., the green curve between the planes). These longer paths ensure that the system's response can cope with jitter in reaching prescribed dynamics in the presence of faults.

application¹⁸, the antifragile controller demonstrated statistically significant gains given increasing traffic disruptions amplitude over time. The systematic evaluation demonstrates that the control law selection based on the second-order effects of the signal re-computation may capture the volatile dynamics of the closed-loop system.

Machine-learning approaches can be used to induce antifragility, for example, in the design of a traffic reinforcement learning agent that learns to be conservative when regulating the controlled region¹⁹. Here, we have again a clear quantification of the system's antifragility based on a dynamics response curve to external uncertainty (i.e., amplitude of traffic disruptions) and volatility (i.e., onset and offset of traffic disruptions) overcoming the baseline approach (i.e., static police-made traffic light control), a state-of-the-art model predictive control⁵⁷, and other reinforcement learning approaches⁵⁸.

Finally, when considering criticality, the control of multistability deals with the transition of the system to a more desired steady state and also preventing it from moving to an inferior one⁵⁹. It is beneficial for a controller to anticipate the tipping points well before they occur so that remedial actions can be adopted⁶⁰.

Natural systems: interventional (anti)-fragility

Designing intervention strategies which lead to the eradication of a heterogeneous population may be exceedingly difficult due to the evolution of resistance to interventional treatments. For example, the continuous administration of anticancer drugs^{61,62} or antibiotics⁶³ selects for resistant sub-populations rendering subsequent treatments ineffective. Recent work to apply principles learned from agricultural methods known as Integrative Pest Management has shown some success in the management of cancer^{64,65}. For example, adaptive cancer therapy uses a simple rule-of-thumb protocol to adapt treatment administration and treatment break time intervals based on tumor response⁶⁶. Importantly, this adaptive protocol in an increase in dose variance (prolonged periods of high dose followed by prolonged periods of zero dose)⁶⁷. This is part of a broader effort to design treatment protocols using evolutionary

principles that increase the treatment-induced volatility that tumor cells undergo during the course of treatment to maximize tumor regression⁶⁷. Mathematical models of tumor-immune-drug interactions can drive chemotherapy optimization regimens to maximize the efficacy/toxicity ratio^{42,68}.

Furthermore, a series of recent papers have shown that dietary patterns might influence network communication along the brain-gut axis, especially at the age that both systems go through maturation processes^{69,70}. From an ecological perspective, an adequate level of connectivity dissipates the effect of perturbations in the distribution of species and enhances ecosystem stability. A loss in connectivity leads to a loss in gut microbiota ecosystem antifragility. The basic rationale is that a system's response to perturbation requires an efficient flow of information. For maximum antifragility, this flow must be optimal, implying maximum connectivity^{39,70}.

Discussion

In this perspective, we have reviewed efforts to apply antifragility theory to both technical/physical systems as well as natural/biological systems. We provide a conceptual framework to unify the language across both systems and define the relevant scales of fragility, summarized below.

Intrinsic and ecological antifragile systems benefit from internal dynamics distribution unevenness, based on the convexity of the response function of the system without external input and solely based on the internal components' heterogeneity and resilience. Features such as stability describe the most simple system response with minimal antifragile characteristics. Within this scale, precise characterization of the payoff function describing the relationship between system inputs and outputs is of foremost importance.

Homogeneity and heterogeneity play a crucial role in the design and synthesis of inherited and evolutionary antifragile systems. From criticality and multi-level interactions of multiple timescales to quantifying criticality margins, such a design scheme leverages local interactions of

the system to make it benefit from perturbations. In other words, inherited and evolutionary antifragile systems benefit from input distribution unevenness, based on the emergent system dynamics and its interactions with the operating environment (i.e., disturbances, noise, modulated perturbations).

Inducing a desired behavior within interventional antifragility requires an innovative, control-theoretic, design and synthesis approach. Here, nonlinear dynamics across both space and time can promote the system's capacity to absorb internal and external disruptions. Induced and interventional antifragile systems benefit from input distribution unevenness based on emergent system dynamics in closed-loop with a controller driving the system towards prescribed dynamics in the presence of modulated or non-stationary disturbances, noise, and volatility.

It is also important to note that we need not constrain ourselves to search only for systems that are antifragile. First, a system may be fragile on the intrinsic or inherited scales yet still be amenable to interventions that are antifragile through clever design of feedback controllers. Second, fragility (or antifragility) is a measurable quantity: the response of a system to volatility. Some systems (e.g., tumors) may respond in a fragile manner to given perturbations (e.g., chemotherapy) and thus it is critical to characterize the system along the fragile–antifragile spectrum to intervene appropriately. Finally, though we consider a discrete layering of antifragility types, we are aware that this structure can be applied systematically across scales. In other words, even the simplest systems can be subject to all three types of antifragility.

Received: 7 January 2024; Accepted: 25 June 2024;

Published online: 01 August 2024

References

1. Taleb, N. N. *Antifragile: Things That Gain from Disorder*, Vol. 3 (Random House Incorporated, 2012).
2. Taleb, N. N. & Douady, R. Mathematical definition, mapping, and detection of (anti) fragility. *Quant. Financ.* **13**, 1677–1689 (2013).
3. Pineda, O. K., Kim, H. & Gershenson, C. A novel antifragility measure based on satisfaction and its application to random and biological boolean networks. Preprint at <https://arxiv.org/abs/1812.06760> (2018).
4. de Bruijn, H., Groessler, A. & Videira, N. Antifragility as a design criterion for modelling dynamic systems. *Syst. Res. Behav. Sci.* **37**, 23–37 (2020).
5. Blečić, I. & Cecchini, A. Antifragile planning. *Plan. Theory* **19**, 172–192 (2020).
6. Johnson, J. & Gheorghe, A. V. Antifragility analysis and measurement framework for systems of systems. *Int. J. Disaster Risk Sci.* **4**, 159–168 (2013).
7. West, J. et al. Antifragile therapy. Preprint at *bioRxiv* <https://doi.org/10.1101/2020.10.08.331678> (2020).
8. Taleb, N. N. & West, J. Working with convex responses: antifragility from finance to oncology. *Entropy* **25**, 343 (2023).
9. Arnoldi, J.-F., Loreau, M. & Haegeman, B. Resilience, reactivity and variability: a mathematical comparison of ecological stability measures. *J. Theor. Biol.* **389**, 47–59 (2016).
10. Marom, S. & Marder, E. A biophysical perspective on the resilience of neuronal excitability across timescales. *Nat. Rev. Neurosci.* **24**, 640–652 (2023).
11. Ay, N. & Krakauer, D. C. Geometric robustness theory and biological networks. *Theory Biosci.* **125**, 93–121 (2007).
12. Krakovská, H., Kuehn, C. & Longo, I. P. Resilience of dynamical systems. *Eur. J. Appl. Math.* **35**, 155–200 (2024).
13. Jensen, J. L. W. V. et al. Sur les fonctions convexes et les inégalités entre les valeurs moyennes. *Acta Mathematica* **30**, 175–193 (1906).
14. Taleb, N. N. (Anti) fragility and convex responses in medicine. In *International Conference on Complex Systems*. 299–325 (Springer, 2018).
15. Wardrop, J. G. The capacity of roads. *J. Operational Res. Soc.* **5**, 14–24 (1954).
16. Papageorgiou, M., Diakaki, C., Dinopoulou, V., Kotsialos, A. & Wang, Y. Review of road traffic control strategies. *Proc. IEEE* **91**, 2043–2067 (2003).
17. Axenie, C. & Saveriano, M. Antifragile Control Systems: The Case of Mobile Robot Trajectory Tracking Under Uncertainty and Volatility. in *IEEE Access*, Vol. 11, 138188–138200, <https://doi.org/10.1109/ACCESS.2023.3339988> (2023).
18. Axenie, C. & Grossi, M. Antifragile control systems: the case of an oscillator-based network model of urban road traffic dynamics. Preprint at <https://arxiv.org/abs/2210.10460> (2023).
19. Sun, L. et al. Exploring antifragility in traffic networks: anticipating disturbances with reinforcement learning. In *23rd Swiss Transport Research Conference* (STRC, 2023).
20. Makridis, M. A., Schaniel, J. & Kouvelas, A. Rule-based on-off traffic control strategy for Caves on motorway networks: assessing cooperation level and driving homogeneity. *IEEE Access* **11**, 35111–35121 (2023).
21. Kesting, A., Treiber, M. & Helbing, D. Enhanced intelligent driver model to access the impact of driving strategies on traffic capacity. *Philos. Trans. R. Soc. A: Math. Phys. Eng. Sci.* **368**, 4585–4605 (2010).
22. Milanés, V. & Shladover, S. E. Modeling cooperative and autonomous adaptive cruise control dynamic responses using experimental data. *Transp. Res. Part C: Emerg. Technol.* **48**, 285–300 (2014).
23. Makridis, M., Fontaras, G., Ciuffo, B. & Mattas, K. Mfc free-flow model: introducing vehicle dynamics in microsimulation. *Transp. Res. Rec.* **2673**, 762–777 (2019).
24. Du, Y., Makridis, M. A., Tampère, C. M., Kouvelas, A. & ShangGuan, W. Adaptive control with moving actuators at motorway bottlenecks with connected and automated vehicles. *Transp. Res. Part C: Emerg. Technol.* **156**, 104319 (2023).
25. Daganzo, C. F. The cell transmission model: a dynamic representation of highway traffic consistent with the hydrodynamic theory. *Transp. Res. Part B: Methodol.* **28**, 269–287 (1994).
26. Messner, A. & Papageorgiou, M. Metanet: a macroscopic simulation program for motorway networks. *Traffic Eng. Control* **31**, 466–470 (1990).
27. Scheffer, M. et al. Early-warning signals for critical transitions. *Nature* **461**, 53–59 (2009).
28. Danchin, A., Binder, P. M. & Noria, S. Antifragility and tinkering in biology (and in business) flexibility provides an efficient epigenetic way to manage risk. *Genes* **2**, 998–1016 (2011).
29. Pierik, L., McDonald, P., Anderson, A. R. & West, J. Second-order effects of chemotherapy pharmacodynamics and pharmacokinetics on tumor regression and cachexia. *Bull. Math. Biol.* **86**, 47 (2024).
30. Ruggiero, A., Katsenelson, M. & Slutsky, I. Mitochondria: new players in homeostatic regulation of firing rate set points. *Trends Neurosci.* **44**, 605–618 (2021).
31. Hidalgo, J. et al. Information-based fitness and the emergence of criticality in living systems. *Proc. Natl. Acad. Sci. USA* **111**, 10095–10100 (2014).
32. Kiyono, K., Struzik, Z. R., Aoyagi, N., Togo, F. & Yamamoto, Y. Phase transition in a healthy human heart rate. *Phys. Rev. Lett.* **95**, 058101 (2005).
33. Ivanov, P. C. et al. Scaling behaviour of heartbeat intervals obtained by wavelet-based time-series analysis. *Nature* **383**, 323–327 (1996).
34. Rivera, A. L. et al. Heart rate and systolic blood pressure variability in the time domain in patients with recent and long-standing diabetes mellitus. *PLoS ONE* **11**, e0148378 (2016).
35. Goldberger, A. L., Peng, C.-K. & Lipsitz, L. A. What is physiologic complexity and how does it change with aging and disease? *Neurobiol. Aging* **23**, 23–26 (2002).
36. López-Corona, O., Kolb, M., Ramírez-Carrillo, E. & Lovett, J. Esd ideas: planetary antifragility: a new dimension in the definition of the safe operating space for humanity. *Earth Syst. Dyn.* **13**, 1145–1155 (2022).

37. Fernández, N. & Gershenson, C. Measuring complexity in an aquatic ecosystem. In *Advances in Computational Biology* (eds Castillo, L. F. et al.) 83–89 (Springer International Publishing, Cham, 2014).
38. López-Rivera, J. A., Rivera, A. L. & Frank, A. Forest complexity in the green tonality of satellite images. In *Unifying Themes in Complex Systems IX: Proceedings of the Ninth International Conference on Complex Systems 9*, 184–188 (Springer, 2018).
39. Equihua, M. et al. Ecosystem antifragility: beyond integrity and resilience. *PeerJ* **8**, e8533 (2020).
40. López-Díaz, A. J., Sánchez-Puig, F. & Gershenson, C. Temporal, structural, and functional heterogeneities extend criticality and antifragility in random boolean networks. *Entropy* **25**, 254 (2023).
41. Makridis, M., Leclercq, L., Ciuffo, B., Fontaras, G. & Mattas, K. Formalizing the heterogeneity of the vehicle-driver system to reproduce traffic oscillations. *Transp. Res. Part C: Emerg. Technol.* **120**, 102803 (2020).
42. Axenie, C., Kurz, D. & Saveriano, M. Antifragile control systems: the case of an anti-symmetric network model of the tumor-immune-drug interactions. *Symmetry* **14**, 2034 (2022).
43. Angeli, D., Ferrell Jr, J. E. & Sontag, E. D. Detection of multistability, bifurcations, and hysteresis in a large class of biological positive-feedback systems. *Proc. Natl. Acad. Sci. USA* **101**, 1822–1827 (2004).
44. Hizanidis, J., Aust, R. & Schöll, E. Delay-induced multistability near a global bifurcation. *Int. J. Bifurc. Chaos* **18**, 1759–1765 (2008).
45. López-Corona, O., Ramirez-Carrillo, E. & Magallanes-Guijón, G. The rise of the technobionts: toward a new ontology to understand current planetary crisis. *Res. ONE* (2019).
46. Bayer, P. & West, J. Games and the treatment convexity of cancer. *Dyn. Games Appl.* <https://doi.org/10.1007/s13235-023-00520-z> (2023).
47. Crosato, E., Nigmatullin, R. & Prokopenko, M. On critical dynamics and thermodynamic efficiency of urban transformations. *R. Soc. Open Sci.* **5**, 180863 (2018).
48. Gershenson, C. & Fernández, N. Complexity and information: measuring emergence, self-organization, and homeostasis at multiple scales. *Complexity* **18**, 29–44 (2012).
49. Kalloniatis, A. C., Zuparic, M. L. & Prokopenko, M. Fisher information and criticality in the kuramoto model of nonidentical oscillators. *Phys. Rev. E* **98**, 022302 (2018).
50. López-Corona, O. & Padilla, P. Fisher information as unifying concept for criticality and antifragility, a primer hypothesis. *Res. ONE* (2019).
51. Pineda, O. K., Kim, H., Gershenson, C. et al. A novel antifragility measure based on satisfaction and its application to random and biological boolean networks. *Complexity* **2019** (2019).
52. Cannon, W. B. Organization for physiological homeostasis. *Physiol. Rev.* **9**, 399–431 (1929).
53. Nichol, D., Robertson-Tessi, M., Jeavons, P. & Anderson, A. R. Stochasticity in the genotype-phenotype map: implications for the robustness and persistence of bet-hedging. *Genetics* **204**, 1523–1539 (2016).
54. Wang, H., Liu, B., Ping, X. & An, Q. Path tracking control for autonomous vehicles based on an improved mpc. *IEEE Access* **7**, 161064–161073 (2019).
55. Sola, R. & Nunes, U. Trajectory planning and sliding-mode control based trajectory-tracking for cybercars. *Integr. Computer-Aided Eng.* **14**, 33–47 (2007).
56. Antonelli, G., Chiaverini, S. & Fusco, G. A fuzzy-logic-based approach for mobile robot path tracking. *IEEE Trans. Fuzzy Syst.* **15**, 211–221 (2007).
57. Gerolimidis, N., Haddad, J. & Ramezani, M. Optimal perimeter control for two urban regions with macroscopic fundamental diagrams: a model predictive approach. *IEEE Trans. Intell. Transp. Syst.* **14**, 348–359 (2012).
58. Zhou, D. & Gayah, V. V. Scalable multi-region perimeter metering control for urban networks: a multi-agent deep reinforcement learning approach. *Transp. Res. Part C: Emerg. Technol.* **148**, 104033 (2023).
59. Pisarchik, A. N. & Feudel, U. Control of multistability. *Phys. Rep.* **540**, 167–218 (2014).
60. Grziwotz, F. et al. Anticipating the occurrence and type of critical transitions. *Sci. Adv.* **9**, eabq4558 (2023).
61. Gatenby, R. A., Silva, A. S., Gillies, R. J. & Frieden, B. R. Adaptive therapy. *Cancer Res.* **69**, 4894–4903 (2009).
62. Read, A. F., Day, T. & Huijben, S. The evolution of drug resistance and the curious orthodoxy of aggressive chemotherapy. *Proc. Natl. Acad. Sci. USA* **108**, 10871–10877 (2011).
63. Read, A. F. & Woods, R. J. Antibiotic resistance management. *Evol. Med. Public Health* **2014**, 147 (2014).
64. Whelan, C. J. & Cunningham, J. J. Resistance is not the end: lessons from pest management. *Cancer Control* **27**, 1073274820922543 (2020).
65. Cunningham, J. J. A call for integrated metastatic management. *Nat. Ecol. Evol.* **3**, 996–998 (2019).
66. Zhang, J., Cunningham, J. J., Brown, J. S. & Gatenby, R. A. Integrating evolutionary dynamics into treatment of metastatic castrate-resistant prostate cancer. *Nat. Commun.* **8**, 1816 (2017).
67. Strobl, M., Gallaher, J., Robertson-Tessi, M., West, J. & Anderson, A. Treatment of evolving cancers will require dynamic decision support. *Ann. Oncol.* **34**, 867–884 (2023).
68. West, J. B. et al. Multidrug cancer therapy in metastatic castrate-resistant prostate cancer: an evolution-based strategy. *Clin. Cancer Res.* **25**, 4413–4421 (2019).
69. Ramírez-Carrillo, E. et al. Similar connectivity of gut microbiota and brain activity networks is mediated by animal protein and lipid intake in children from a Mexican indigenous population. *PLoS ONE* **18**, e0281385 (2023).
70. Isaac, G. et al. Potential long consequences from internal and external ecology: loss of gut microbiota antifragility in children from an industrialized population compared with an indigenous rural lifestyle. *J. Dev. Orig. Health Dis.* **14**, 469–480 (2023).

Acknowledgements

Jeffrey West, PhD was supported by an Institutional Research Grant, IRG-21-145-25 from the American Cancer Society. Jeffrey West also acknowledges support from the Center of Excellence for Evolutionary Therapy at Moffitt Cancer Center. Meisam Akbarzadeh has been supported by the ETH Zurich Risk Center.

Author contributions

C.A., O.L.C., M.A.M., M.A., M.S., A.S., and J.W. all contributed to the literature review, writing, editing, and final approval of the completed version of the manuscript.

Competing interests

The authors declare no competing interests.

Additional information

Correspondence and requests for materials should be addressed to Jeffrey West.

Reprints and permissions information is available at <http://www.nature.com/reprints>

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

© The Author(s) 2024