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Recovery physiology: a testable systems framework for preserving the capacity to function

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Living systems must restore function after perturbation while operating under finite energetic, structural, regulatory, and environmental constraints. This Hypothesis and Theory article proposes Recovery Physiology as a testable framework for studying that problem. Recovery is defined narrowly as the time-dependent response following a prospectively specified perturbation that measurably displaces one or more prespecified functional variables from a relevant reference state. Recovery Capacity (RC) is defined separately as a hypothetical latent, context-dependent property that may influence the magnitude, rate, completeness, coordination, and cost of that response; favorable outcomes are not evidence of high RC by definition. Three candidate domains—bioenergetic capacity, biological information integrity, and systems coordination—are proposed as a parsimonious but revisable architecture. The framework makes three separable claims: recovery phenotypes may contain reliable challenge-specific latent structure and possibly a higher-order cross-challenge factor; the proposed domain architecture may explain recovery beyond simpler alternatives; and dynamic trajectories may add prognostic information beyond baseline state and established constructs. Each claim is paired with competing models and falsification criteria. A standardized exercise protocol illustrates how reliability, construct validity, incremental predictive validity, cross-challenge generalization, and intervention responsiveness could be tested. Recovery Physiology is not presented as a new discipline or clinical system. Its value depends on whether prespecified recovery measures outperform parsimonious models based on age, baseline function, disease burden, frailty, physiological reserve, intrinsic capacity, allostatic load, and established resilience measures.

KEYWORDS
intrinsic capacity, longitudinal phenotyping, network physiology, perturbation-response, physical resilience, recovery capacity, recovery physiology

1 Introduction

Physiology has explained how living systems generate, regulate, and coordinate function. A complementary question is how function is restored after a defined perturbation and why apparently similar individuals or systems can follow different recovery trajectories. This is fundamentally a physiological problem because restoration, compensation, or

persistent deficit may depend on interacting processes operating across molecular, cellular, tissue, organ, system, and whole-organism levels. A central motivation for Recovery Physiology is therefore to provide a testable framework for relating recovery-relevant processes that are often investigated separately (Mitchell, 1961; Holloszy, 1967; von Bertalanffy, 1968; Maturana and Varela, 1980; Prigogine and Stengers, 1984; Goldberger et al., 2000; Ideker et al., 2001; Goldberger et al., 2002a; Kitano, 2002a; Kitano, 2002b; Hood et al., 2004; Noble, 2006; Pedersen, 2009; Dibner et al., 2010; Bashan et al., 2012; Booth et al., 2012; Noble, 2012; Pedersen and Febbraio, 2012; Egan and Zierath, 2013; Noble, 2013; Hawley et al., 2014; Peake et al., 2017; Ivanov, 2021).

The framework does not claim novelty for perturbation-response measurement, repeated physiological assessment, recovery trajectories, dynamic stimulation testing, resilience analysis, network physiology, or longitudinal phenotyping. These approaches already have substantial precedents. The proposed contribution is narrower: to separate antecedent determinants, a possible latent recovery capacity, biological recovery processes, observed trajectories, immediate outcomes, and later consequences within an explicitly comparative and falsifiable model (Seeman et al., 1997; Goldberger et al., 2002b; Scheffer et al., 2009; Bashan et al., 2012; Hood and Flores, 2012; Chen et al., 2012; Ashley, 2015; Collins and Varmus, 2015; World Health Organization, 2015; FDA-NIH Biomarker Working Group, 2016; Whitson et al., 2016; Price et al., 2017; Dunn et al., 2018; Varadhan et al., 2018; Coravos et al., 2019; Ivanov and Bartsch, 2014; Cesari et al., 2018).

Recovery is used here only when a defined perturbation measurably displaces a prespecified functional variable or multidimensional state from a relevant reference condition. Routine cycling, maintenance, repair, adaptation, and environmental exposure may influence recovery but are not automatically classified as recovery themselves. This boundary is intended to prevent semantic expansion in which nearly any physiological fluctuation is retrospectively labeled a recovery event.

Recovery Capacity (RC) is a named hypothetical latent construct. It is not directly observed, not defined by a favorable endpoint, and not assumed to be organism-wide. Challenge-specific capacities may exist for exercise, infection, surgery, sleep deprivation, metabolic challenge, or cognitive stress. A higher-order general RC would require reproducible cross-challenge covariance and prediction across independent perturbations.

The proposed incremental contribution can be expressed as three separable propositions. First, recovery phenotypes may contain a challenge-specific latent component and, potentially, a higher-order cross-challenge factor that explains variance beyond challenge dose, baseline state, and established constructs. This proposition would be weakened if phenotypes are unreliable, exclusively challenge-specific, or add no predictive information beyond comparator models. Second, bioenergetic capacity, biological information integrity, and systems coordination may provide a useful but provisional architecture for explaining recovery. This proposition would require revision if simpler or alternative architectures are more reproducible, interpretable, or predictive. Third, prespecified recovery-trajectory features may improve prediction of independent outcomes beyond baseline physiological measurements and established constructs. This proposition would be rejected if they do not produce reproducible out-of-sample or independently validated improvement.

Criterion for distinct construct validity. Correlation with age, baseline function, disease burden, frailty, physiological reserve, intrinsic capacity, allostatic load, or resilience would not establish a new construct. To support RC as distinct, a prespecified RC model must demonstrate reproducible incremental explanatory or predictive value after these competing variables and constructs are included. Failure to do so should lead to narrowing, reformulation, or rejection of RC as a distinct construct.

Literature selection and evidentiary scope. This Hypothesis and Theory article uses a purposive narrative synthesis rather than a systematic or scoping review. Sources were selected to develop and critically contextualize the framework, compare it with established constructs, and identify representative mechanisms, perturbation-response paradigms, and measurement approaches. Seminal conceptual papers were combined with representative empirical and methodological studies. The literature set was not intended to be exhaustive, and no formal systematic-review screening or study-quality assessment was performed. Citations therefore support the established physiological observations to which they are attached; they do not by themselves validate RC, the three-domain architecture, or a higher-order general factor.

2 Relation to existing constructs and competing explanations

The principal novelty question is not whether recovery has been studied before, but whether the proposed organization provides information not already contained in established constructs. Homeostasis concerns regulated stability; allostasis concerns stability through adaptive change and allostatic load concerns cumulative regulatory burden; physiological reserve concerns capacity beyond ordinary demand; physical resilience concerns resistance to or recovery from health stressors; intrinsic capacity integrates physical and mental capacities; frailty describes vulnerability; dynamical resilience examines return dynamics and stability; and systems/network physiology examines interactions among physiological components (Cannon, 1929; Cannon, 1932; Selye, 1936; Selye, 1956; Sterling and Eyer, 1988; Seeman et al., 1997; McEwen, 1998; Fried et al., 2001; Goldberger et al., 2002b; McEwen and Wingfield, 2003; Barabási and Oltvai, 2004; Rockwood and Mitnitski, 2007; Scheffer et al., 2009; Bashan et al., 2012; World Health Organization, 2015; Whitson et al., 2016; Varadhan et al., 2018; Ivanov, 2021; Ivanov and Bartsch, 2014; Cesari et al., 2018).

Intrinsic capacity is an especially important comparator because it is multidomain, may be represented using latent-variable methods, and is considered in relation to environmental context. RC therefore cannot be distinguished from intrinsic capacity merely by being multidimensional or latent. The proposed distinction is perturbation-conditioned and temporal: RC would need to explain reproducible recovery dynamics and independent outcomes beyond

intrinsic capacity itself (World Health Organization, 2015; Beard et al., 2016; World Health Organization, 2019; World Health Organization, 2021; Cesari et al., 2018).

The comparison clarifies that perturbations, repeated measurements, recovery rates, completeness, network interactions, and dynamical-stability metrics are not unique to Recovery Physiology. The comparison with established constructs is summarized in Table 1. The proposed framework is useful only if it yields discriminating predictions against rival explanations.

2.1 Competing models and discriminating predictions

To evaluate whether Recovery Capacity (RC) represents a distinct and scientifically useful construct, the proposed framework must be tested against competing explanations rather than assumed to be valid. Table 2 summarizes six competing models, their distinguishing predictions, the evidence that would favor each model, and the implications for retaining, revising, or rejecting the RC hypothesis. This comparative approach establishes explicit criteria for evaluating the proposed framework and helps prevent circular reasoning or unsupported claims of novelty.

3 Operational definitions and boundaries

Terminology convention. Recovery Physiology is capitalized as the name of the proposed framework, and Recovery Capacity (RC) denotes the specifically defined hypothetical latent construct. Candidate domains and generic physiological processes, including bioenergetic capacity, biological information integrity, systems coordination, recovery, adaptation, compensation, and resilience, are written in lowercase except where capitalization is grammatically required.

3.1 Classification of demand and perturbation

Not every change in physiology is a recovery challenge. We distinguish five operational categories: (1) routine physiological demand, such as ordinary metabolic or behavioral fluctuations; (2) experimentally standardized perturbation, deliberately administered with a reproducible protocol; (3) acute stressor, a discrete time-limited event causing measurable displacement; (4) chronic

TABLE 1 Comparison of recovery physiology with adjacent physiological constructs.

Construct	Primary dependent variable	Level/ timescale	Role of perturbation	Typical measurement	Distinction from Recovery Physiology (RP)
Homeostasis	Regulated-state deviation	Cell-system/sec-hours	Displacement from regulated range	Physiological variables; feedback responses	Relevant to restoration; does not by itself define a latent recovery-capacity construct.
Allostasis/allostatic load	Adaptive regulation/ cumulative burden	Multisystem/hours-years	Repeated or chronic demand	Multisystem biomarker indices	Potential antecedent determinant or cost; short-term adaptation may carry long-term burden.
Physiological reserve	Capacity above basal demand	Organ-multisystem/ min-years	Challenge reveals functional headroom	Stress tests; functional reserve measures	May influence recovery but does not specify restoration kinetics, coordination, completeness, or cost.
Physical resilience	Functional response after a health stressor	Whole person/days-months	Central	Repeated pre/post-stressor trajectories	Closest adjacent construct; RP must add value beyond established resilience measures.
Frailty	Vulnerability/deficit burden	Whole person/ months-years	Stressor may expose vulnerability	Phenotype; deficit index	Comparator and antecedent predictor; not equivalent to the observed trajectory.
Intrinsic capacity	Physical and mental capacities	Whole person/ months-years	Not required	Multidomain/latent assessment	Major competing construct; RP must add perturbation-conditioned predictive information beyond it.
Stress-response phenotyping	Dynamic physiological response	Molecular-multisystem/min-days	Central, often standardized	Serial challenge-response measurements	Strong methodological overlap; novelty cannot rest on repeated measurements themselves.
Network physiology	Inter-system coupling	Multisystem/sec-days +	Optional or informative	Coupling, synchronization, network metrics	Provides candidate measures of systems coordination.
Dynamical resilience	Return/stability after displacement	Multiscale/context dependent	Central	State-space and dynamic-stimulation models	Strong conceptual overlap; RP must outperform established dynamic metrics.
Critical slowing down	Declining return rate/ stability	Multiscale/repeated observations	Disturbances reveal stability loss	Return rate, autocorrelation, variance	Candidate dynamic indicator; not synonymous with RP.

TABLE 2 Competing models and discriminating predictions.

Model	Distinct prediction	Finding favoring model	Consequence
Baseline/established-construct model	Age, baseline function, disease burden, frailty, reserve, intrinsic capacity, allostatic load, and resilience adequately explain recovery.	Candidate RC measures add no reproducible validated information.	Distinct RC not supported.
Challenge-specific model	Reliable recovery phenotypes exist within perturbation classes but generalize weakly across classes.	Good within-challenge reliability; weak cross-challenge covariance/prediction.	Retain challenge-specific capacities; reject organism-wide RC.
Additive-composite model	A weighted combination of component measures adequately explains recovery.	Nonlinear, network, or latent models do not outperform a parsimonious additive score.	Weak-emergence claim not supported; a composite may remain useful.
Alternative-architecture model	Recovery determinants are organized differently from the proposed three domains.	One-, two-, expanded-, hierarchical-, or network models replicate better.	Combine, subdivide, add, remove, or replace domains.
Hierarchical RC model	Challenge-specific capacities share a reproducible higher-order component.	Reliable within-challenge phenotypes + cross-challenge covariance/prediction + incremental validity.	Supports continued testing of a higher-order RC.
No stable phenotype	Observed trajectories are dominated by measurement error or transient state variation.	Poor test-retest reliability under standardized conditions.	Do not construct RC from these measures.

exposure, a sustained or recurrent condition that may alter baseline state or vulnerability; and (5) pathological insult, disease- or injury-related dysfunction. Aging is not treated as a discrete perturbation; it is a longitudinal context that may modify antecedent state, reserve, RC, and response to later challenges.

A perturbation used to estimate a recovery phenotype should, wherever feasible, be specified prospectively by type, dose or severity, duration, expected response, biological domain(s) perturbed, reference state, sampling schedule, and observation window. A trajectory should not be classified as recovery solely because it follows a physiological change.

3.2 Routine cycling, maintenance, repair, recovery, and adaptation

Routine resetting and cyclical physiology, such as repolarization within an action-potential cycle, diastole within the cardiac cycle, or expiration within the respiratory cycle, are not by themselves post-perturbation recovery. Maintenance refers to ongoing preservation of structural and functional integrity. Repair refers to restoration or reconstruction of damaged components and may contribute to recovery without being synonymous with it. Adaptation is a persistent later change and may occur with complete recovery, incomplete recovery, compensation, or sustained exposure. This separation prevents the framework from becoming universal by semantic expansion.

3.2.1 Normal physiological cycles as candidate measurement tools

Cardiac, respiratory, neural, circadian, and endocrine cycles are established regulatory processes, not independent evidence of Recovery Physiology or a generalized RC. With a prospectively specified perturbation, features of these cycles—such as heart-rate recovery after standardized exercise, autonomic reactivation, or the return of circadian timing after sleep disruption—may provide candidate indicators of challenge-specific recovery phenotypes. Their usefulness depends on reproducible measurement and incremental predictive value beyond baseline dynamics and established constructs; routine cycling alone does not establish RC.

The biological hierarchy used here terminates at the whole organism: molecule → organelle → cell → tissue → organ → physiological system → organism. Environmental conditions are treated as contextual modifiers, exposures, and constraints on this hierarchy rather than as an eighth level. References to ecosystem-level organization are outside the present model.

3.2.2 Key concept

The framework separates six causal roles: antecedent state/resources; defined perturbation; hypothetical RC; recovery processes; measured trajectory and immediate outcome; and future consequences. These roles should not be collapsed into a single latent construct (Figure 1).

3.3 Multiscale biological basis without semantic expansion

The framework retains a multiscale physiological perspective because mechanisms relevant to post-perturbation recovery operate at many levels, even though not every process at those levels should be called recovery. At the molecular level, DNA repair, proteostasis, autophagy, mitochondrial quality control, and redox regulation preserve the components needed for subsequent function. At the cellular level, energy restoration, organelle turnover, stress responses, and regulated cell survival can influence whether a perturbed cell returns toward function, is replaced, or remains impaired. At tissue level, extracellular-matrix remodeling, vascular responses, inflammation resolution, stem/progenitor-cell activity, and structural repair can shape restoration after injury. These mechanisms are well established in their respective fields;

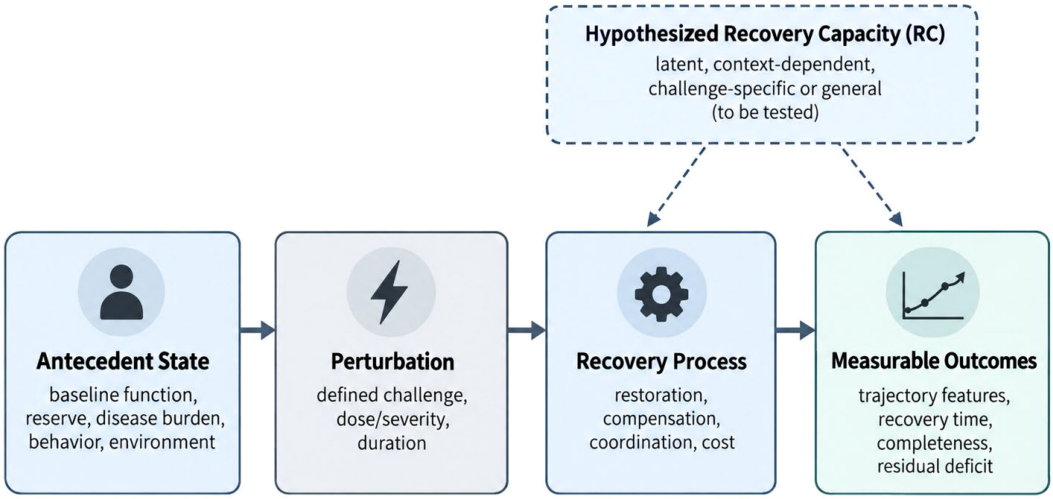

FIGURE 1
Simplified conceptual framework for recovery physiology. An antecedent physiological state precedes a defined perturbation, recovery processes, and measurable outcomes. Antecedent variables include baseline function, reserve, disease burden, behavior, and environmental context; challenge characteristics include dose, severity, and duration. Outcomes include prespecified trajectory features, recovery time, completeness, and residual deficit. Hypothesized Recovery Capacity (RC) is displayed separately as a latent, context-dependent property that may influence recovery processes and outcomes; dashed arrows are hypotheses, not demonstrated causal effects. Challenge-specific RC and any higher-order general RC require independent validation. Measured outcomes test, rather than define, RC.

Recovery Physiology does not rename them as a new mechanism but asks how their state before and after a defined perturbation contributes to a measured recovery trajectory (Mitchell, 1961; Till and McCulloch, 1961; Gurdon, 1962; Lindahl, 1993; Sánchez Alvarado, 2000; Nathan, 2002; Serhan and Savill, 2005; Hotamisligil, 2006; Rando, 2006; Scadden, 2006; Takahashi and Yamanaka, 2006; Harper and Elledge, 2007; Mizushima, 2007; Serhan, 2007; Balch et al., 2008; Gurtner et al., 2008; Levine and Kroemer, 2008; Medzhitov, 2008; Morrison and Spradling, 2008; Orkin and Zon, 2008; Rossi et al., 2008; Yamanaka, 2008; Hoeijmakers, 2009; Jackson and Bartek, 2009; Murphy, 2009; Powers et al., 2009; Houtkooper et al., 2010; Poss, 2010; Chawla et al., 2011; Galli et al., 2011; Hartl et al., 2011; Rubinsztein et al., 2011; Tanaka and Reddien, 2011; Youle and Narendra, 2011; Atala, 2012; Chan, 2012; Hardie et al., 2012; Nunnari and Suomalainen, 2012; Suda et al., 2011; Wallace, 2012; López-Otín et al., 2013; Nicholls and Ferguson, 2013; Buckley et al., 2014; Chandel, 2014; Lancaster and Knoblich, 2014; Ohsumi, 2014; Blau et al., 2015; Cantó et al., 2015; Clevers, 2015; Iwasaki and Medzhitov, 2015; Kaushik and Cuervo, 2015; Clevers, 2016; O'Neill et al., 2016; Picard et al., 2016; Wynn and Vannella, 2016; Dalli and Serhan, 2017; Franceschi et al., 2017; Saxton and Sabatini, 2017; Dikic and Elazar, 2018; Herzig and Shaw, 2018; Klaips et al., 2018; Furman et al., 2019; Takebe and Wells, 2019; Netea et al., 2020; López-Otín et al., 2023).

Organ-specific recovery provides further examples of why function and mechanism should be separated. Neurological recovery after stroke can involve spontaneous biological repair, altered excitability, plasticity, and compensation; restoration of performance need not mean restoration of the original neural configuration. Skeletal muscle after exercise or injury can show metabolic restoration, protein synthesis, inflammatory responses, and remodeling over different timescales. Acute tissue injury can resolve through structural repair, functional compensation, or persistent deficit. These examples support the need to specify the dependent variable and observation window rather than assume that one generic recovery endpoint captures all levels of organization (Hebb, 1949; Holloszy, 1967; Bliss and Lømo, 1973; Merzenich et al., 1983; Kandel, 2001; Cramer, 2008; Murphy and Corbett, 2009; Pedersen, 2009; Booth et al., 2012; Carmichael, 2012; Krakauer et al., 2012; Pedersen and Febbraio, 2012; Egan and Zierath, 2013; Nedergaard, 2013; Nudo, 2013; Hawley et al., 2014; Peake et al., 2017).

Sleep and circadian physiology illustrate the same boundary problem. Sleep is associated with neural, metabolic, and homeostatic processes relevant to restoration, and sleep deprivation provides a standardized perturbation paradigm. However, ordinary sleep-wake cycling is not itself proof of a latent RC. Similarly, circadian feedback and endocrine regulation create time-dependent physiological states that can alter baseline and response kinetics; they should be modeled as antecedent or contextual variables unless a specific perturbation-response question is defined (Borbély, 1982; Reppert and Weaver, 2002; Tononi and Cirelli, 2006; Haus, 2007; Scheer et al., 2009; Dibner et al., 2010; Czeisler, 2013; Xie et al., 2013; Buysse, 2014; Dallmann et al., 2014; Tononi and Cirelli, 2014; Bass and Lazar, 2016; Panda, 2016; Foster and Kreitzman, 2017; Hall et al., 2017; Takahashi, 2017; Walker, 2017; Hastings et al., 2018; Ruben et al., 2018; Patke et al., 2020).

Immune and inflammatory biology is particularly informative because recovery after infection, vaccination, or tissue injury can involve both activation and active resolution. Resolution of inflammation is not passive return to baseline; it includes regulated termination and repair processes. Yet chronic or dysregulated inflammatory states can preserve short-term defense while increasing longer-term cost. This makes immune-inflammatory regulation a plausible candidate determinant of recovery and also a serious competing candidate domain that the current three-domain

architecture must accommodate or explicitly fail to accommodate (Nathan, 2002; Serhan and Savill, 2005; Hotamisligil, 2006; Serhan, 2007; Medzhitov, 2008; Chawla et al., 2011; Galli et al., 2011; Buckley et al., 2014; Iwasaki and Medzhitov, 2015; O'Neill et al., 2016; Wynn and Vannella, 2016; Dalli and Serhan, 2017; Franceschi et al., 2017; Ferrucci and Fabbri, 2018; Furman et al., 2019; Netea et al., 2020).

At the whole-organism level, recovery trajectories can reflect interactions among cardiovascular, respiratory, autonomic, endocrine, immune, metabolic, musculoskeletal, and behavioral systems. The systems perspective is therefore not that every organ possesses a single recovery variable, but that a defined challenge can generate coupled changes across systems whose timing, coordination, and trade-offs may matter for functional outcome. Network physiology provides established tools for analyzing such interactions and therefore serves both as a methodological resource and as a competing explanatory framework (Goldberger et al., 2000; Goldberger et al., 2002a; Goldberger et al., 2002b; Barabási and Oltvai, 2004; Bashan et al., 2012; Ivanov, 2021; Ivanov and Bartsch, 2014).

Environmental and behavioral context enters this multiscale model through exposure and constraint rather than hierarchy. Temperature, oxygen availability, nutrition, light, pollutants, pathogens, psychosocial conditions, habitual activity, and sleep can alter antecedent state, challenge dose, resource availability, and the meaning of a subsequent trajectory. Because these influences can shift reference states or create chronic exposures rather than discrete perturbations, they should be modeled explicitly rather than absorbed into RC after the fact (Sterling and Eyer, 1988; McEwen, 1998; Reppert and Weaver, 2002; McEwen and Wingfield, 2003; Haus, 2007; Scheer et al., 2009; Dibner et al., 2010; Czeisler, 2013; Shalev et al., 2013; Buysse, 2014; Dallmann et al., 2014; Fontana and Partridge, 2015; Bass and Lazar, 2016; López-Lluch and Navas, 2016; Panda, 2016; Foster and Kreitzman, 2017; Hall et al., 2017; Takahashi, 2017; Epel and Prather, 2018; Hastings et al., 2018; Picard et al., 2018; Ruben et al., 2018; Madeo et al., 2019; Patke et al., 2020).

4 The three-domain architecture as a revisable hypothesis

The proposed three-domain architecture was derived conceptually rather than statistically. The starting question was what broad functional requirements recur when a biological system must restore or re-establish function after perturbation. This reasoning suggested three provisional requirements: usable energy and material flux to perform restorative work; sufficiently preserved and faithfully executed biological specification to guide repair, regulation, rebuilding, or adaptation; and dynamic coordination and resource allocation across interacting components so that local responses produce coherent system-level function. These requirements motivate bioenergetic capacity, biological information integrity, and systems coordination as a parsimonious starting architecture (Mitchell, 1961; Lindahl, 1993; Goldberger et al., 2002b; Barabási and Oltvai, 2004; Harper and Elledge, 2007; Mizushima, 2007; Balch et al., 2008; Levine and Kroemer, 2008; Hoeijmakers, 2009; Jackson and Bartek, 2009; Murphy, 2009; Powers et al., 2009; Houtkooper et al., 2010; Hartl et al., 2011; Rubinsztein et al., 2011; Youle and Narendra, 2011; Bashan et al., 2012; Chan, 2012; Hardie et al., 2012; Nunnari and Suomalainen, 2012; Wallace, 2012; López-Otín et al., 2013; Nicholls and Ferguson, 2013; Chandel, 2014; Ohsumi, 2014; Cantó et al., 2015; Kaushik and Cuervo, 2015; Picard et al., 2016; Saxton and Sabatini, 2017; Dikic and Elazar, 2018; Herzig and Shaw, 2018; Klaips et al., 2018; Ivanov and Bartsch, 2014; López-Otín et al., 2023).

The domains are not claimed to be mutually exclusive, statistically independent, necessary, sufficient, or exhaustive. Structural/material resources could warrant separation from bioenergetics; immune-inflammatory regulation could form an independent domain; behavior and organism-environment interaction could be modeled separately; and resource allocation could remain within systems coordination or become another dimension. The architecture should therefore be selected empirically rather than fixed conceptually.

A domain should be added if a reproducible class of recovery-relevant variation is not represented by existing domains and improves explanatory or predictive performance. A domain should be removed if its indicators are unreliable or add no independent value. Domains should be combined if their indicators consistently form one latent or network structure, and subdivided if reproducible subdimensions show distinct mechanisms, challenge specificity, or prognostic consequences. Competing factor, hierarchical, network, and predictive models should be compared prospectively.

Biological information integrity is deliberately narrower than in earlier formulations. It concerns preservation and faithful execution of biological specification. Signal transmission, feedback, coupling, and network integration are assigned primarily to systems coordination. Candidate information-integrity measures include DNA-damage/repair responses, mutation burden, epigenetic stability or drift, transcriptional/translational fidelity, proteostasis, and molecular regulatory specificity. Candidate coordination measures include signaling fidelity, signal-to-noise relationships, autonomic and cardiorespiratory recovery, endocrine-immune coupling, feedback dynamics, synchronization, network connectivity, and network entropy. Boundary measures may load differently depending on biological level and empirical model.

The framework does not assume that these domains optimize a single objective. Recovery occurs under finite resources and competing demands. Improvement in one variable can impose energetic, reproductive, immune, metabolic, or other costs elsewhere or at another timescale. The model therefore evaluates function under prevailing constraints rather than global biological optimization.

4.1 Biological rationale and candidate measurements

Bioenergetic capacity is motivated by the energetic requirements of repair, ion transport, biosynthesis, remodeling, immune activity, and coordinated organ function. Mitochondrial respiration, substrate utilization, phosphocreatine recovery, oxygen-uptake kinetics, lactate clearance, redox state, and metabolic flexibility are examples of measurable processes that could contribute to

a challenge-specific phenotype. None is proposed as a universal RC biomarker. Their relevance depends on perturbation type, tissue, sampling time, and whether they add information beyond baseline fitness or disease status (Mitchell, 1961; Holloszy, 1967; Murphy, 2009; Pedersen, 2009; Houtkooper et al., 2010; Youle and Narendra, 2011; Booth et al., 2012; Chan, 2012; Hardie et al., 2012; Nunnari and Suomalainen, 2012; Pedersen and Febbraio, 2012; Wallace, 2012; Andreux et al., 2013; Egan and Zierath, 2013; Nicholls and Ferguson, 2013; Chandel, 2014; Hawley et al., 2014; Cantó et al., 2015; Picard et al., 2016; Sun et al., 2016; Peake et al., 2017; Saxton and Sabatini, 2017; Herzig and Shaw, 2018; Picard et al., 2018).

Biological information integrity is motivated by the requirement that restoration depends on sufficiently preserved instructions and molecular quality control. DNA damage and repair, epigenetic state, transcriptional and translational fidelity, protein folding, proteostasis, and selective degradation are plausible components. The domain does not include all biological communication. A change in endocrine coupling or inter-organ signaling belongs primarily to systems coordination unless the experiment specifically measures fidelity of information encoding or execution at a molecular level (Lindahl, 1993; Harper and Elledge, 2007; Mizushima, 2007; Balch et al., 2008; Levine and Kroemer, 2008; Hoeijmakers, 2009; Jackson and Bartek, 2009; Powers et al., 2009; Hartl et al., 2011; Rubinsztein et al., 2011; López-Otín et al., 2013; Ohsumi, 2014; Kaushik and Cuervo, 2015; Dikic and Elazar, 2018; Klaips et al., 2018; López-Otín et al., 2023).

Systems coordination is motivated by the observation that organism-level responses depend on timing, feedback, allocation, and coupling across physiological systems. Candidate measures may include autonomic reactivation, heart-rate and blood-pressure recovery, cardiorespiratory coupling, endocrine-immune relationships, circadian alignment, inter-system phase relationships, and network topology or connectivity. The domain is therefore closer to dynamic communication and control than to storage of biological information (Goldberger et al., 2000; Goldberger et al., 2002a; Goldberger et al., 2002b; Nathan, 2002; Reppert and Weaver, 2002; Barabási and Oltvai, 2004; Serhan and Savill, 2005; Hotamisligil, 2006; Haus, 2007; Serhan, 2007; Medzhitov, 2008; Scheer et al., 2009; Dibner et al., 2010; Chawla et al., 2011; Galli et al., 2011; Bashan et al., 2012; Czeisler, 2013; Buckley et al., 2014; Buysse, 2014; Dallmann et al., 2014; Iwasaki and Medzhitov, 2015; Bass and Lazar, 2016; O'Neill et al., 2016; Panda, 2016; Wynn and Vannella, 2016; Dalli and Serhan, 2017; Foster and Kreitzman, 2017; Franceschi et al., 2017; Hall et al., 2017; Takahashi, 2017; Hastings et al., 2018; Ruben et al., 2018; Furman et al., 2019; Netea et al., 2020; Patke et al., 2020; Ivanov, 2021; Ivanov and Bartsch, 2014).

The three domains also generate explicit rival predictions. If structural substrate availability or extracellular-matrix integrity explains recovery independently of bioenergetic measures, a material/structural domain may be needed. If immune-inflammatory regulation forms a reproducible factor not captured by information integrity or coordination, it should be separated. If behavior or organism-environment interaction adds independent structure, a higher-level contextual domain may be warranted. Conversely, if candidate indicators from two domains repeatedly load on one factor and no intervention or perturbation dissociates them, the two-domain distinction should be abandoned. The point of the architecture is therefore to structure comparison, not to protect a preferred taxonomy.

5 Recovery capacity as a hierarchical and weak-emergence hypothesis

RC should be considered hierarchically. At a lower level, individuals may possess partially distinct challenge-specific capacities for exercise, infection, surgery, sleep deprivation, metabolic challenge, or cognitive stress. These may share determinants but need not covary strongly. A higher-order general RC is a separate empirical hypothesis supported only if prespecified recovery phenotypes demonstrate reproducible covariance and prediction across independent perturbation classes after adjustment for challenge characteristics and baseline state.

Failure to identify a stable higher-order factor would not invalidate Recovery Physiology as a framework; it would argue for domain- or challenge-specific capacities rather than an organism-wide RC. Conversely, evidence for general RC would require reliable within-challenge phenotypes, reproducible cross-challenge associations or latent structure, replication in independent cohorts, and incremental predictive value beyond age, baseline function, disease burden, frailty, physiological reserve, intrinsic capacity, allostatic load, and established resilience measures.

RC is proposed as weakly emergent only in a testable sense. Emergence does not imply philosophical irreducibility. Evidence could include reproducible nonlinear interactions among determinants, network-level properties that predict recovery beyond component values, a latent structure that generalizes across challenges, or incremental prediction beyond a conventional weighted composite. If a parsimonious additive or weighted health score performs equally well, the weak-emergence claim is unsupported and RC should be treated as a composite or abandoned as a distinct systems-level construct.

Core requirement against circular inference. A favorable outcome must not be interpreted retrospectively as evidence of high RC. Before outcomes are known, studies should prespecify, wherever feasible, the perturbation, reference state, antecedent covariates, candidate RC indicators, recovery variables, sampling schedule, trajectory features, comparator constructs, primary outcomes, competing models, and criteria for support or rejection. Candidate RC measures should then be tested against independent outcomes or appropriately separated training and validation data.

5.1 Distinguishing RC from current physiological function

Current physiological function and recovery capacity answer different empirical questions. Resting cardiac output, glomerular filtration, pulmonary function, muscle strength, cognitive performance, or inflammatory markers characterize aspects of current state. Recovery research asks how those or other prespecified variables respond after a defined perturbation and whether the response contains reproducible information not already encoded in

baseline values. Individuals with similar baseline performance may show different trajectories, but that observation alone does not establish RC; differences could reflect challenge dose, measurement error, unmeasured disease, reserve, frailty, intrinsic capacity, or other established factors. The RC hypothesis begins only after those alternatives are modeled.

This distinction also implies that RC should not be estimated from a single favorable endpoint. A latent model would require multiple prespecified indicators or repeated challenges, explicit handling of measurement error and challenge characteristics, and validation against outcomes not used to construct the score. Depending on the data, the appropriate representation may be a latent factor, several correlated challenge-specific factors, a network state, a conventional composite, or no summary score at all.

6 Recovery trajectories and longitudinal measurement

Longitudinal physiological assessment is an established methodological strategy, not a new discipline introduced here. Repeated-measures challenge studies, dense phenotyping, ambulatory monitoring, time-series analysis, and recovery-trajectory modeling provide the methods needed to test the framework. The proposed contribution lies in the hypotheses tested with these methods, not in longitudinal measurement itself (Goldberger et al., 2000; Goldberger et al., 2002a; Bashan et al., 2012; Chen et al., 2012; Ashley, 2015; Collins and Varmus, 2015; FDA-NIH Biomarker Working Group, 2016; Li et al., 2017; Price et al., 2017; Dunn et al., 2018; Coravos et al., 2019; Ivanov, 2021; Schüssler-Fiorenza Rose et al., 2019).

For a functional variable F(t) with prespecified reference F0 and perturbation beginning at t = 0, deviation can be represented as D(t) = F(t) - F0. Candidate trajectory features include maximum displacement Dmax, time to peak/nadir, time to return within a prespecified tolerance, restoration rate or fitted time constant, completeness at a fixed endpoint, residual deficit, overshoot, post-recovery stability, inter-system synchrony, and energetic or behavioral cost. These are observed features, not RC itself.

The same challenge can lead to distinct immediate outcomes. Restoration describes movement toward the reference state; compensation describes preservation or restoration of function through an altered configuration; residual deficit indicates incomplete recovery. Longer-term consequences are separate and can include beneficial adaptation, little persistent change, maladaptation, altered reserve or vulnerability, or cumulative loss. Short-term functional success can therefore coexist with long-term biological cost, as emphasized in the allostasis literature (Sterling and Eyer, 1988; Seeman et al., 1997; McEwen, 1998; McEwen and Wingfield, 2003).

6.1 Trajectory modeling and measurement strategy

Trajectory analysis should be matched to the biology of the endpoint. Fast variables such as heart rate or blood pressure may require second-to-minute sampling, whereas inflammatory, transcriptional, tissue-repair, or functional outcomes may evolve over hours to weeks. A single universal recovery time is therefore unlikely to be meaningful. Studies should specify the expected response phases and sampling density before data collection and avoid selecting favorable time points retrospectively.

Several modeling strategies may be appropriate depending on the data: mixed-effects models for repeated measurements, nonlinear recovery curves, functional data analysis, state-space models, time-to-threshold approaches, multivariate latent-variable models, or network methods. Model complexity should be justified by improvement over simpler alternatives and evaluated with validation data. Critical-slowing-down measures such as return rate, autocorrelation, or variance may be informative in some systems but should be treated as candidate dynamic features rather than evidence for RC by definition (Goldberger et al., 2000; Goldberger et al., 2002a; Goldberger et al., 2002b; Scheffer et al., 2009; Bashan et al., 2012; Varadhan et al., 2018; Ivanov, 2021; Ivanov and Bartsch, 2014).

Longitudinal monitoring between formal challenges may also be informative. Wearables and dense phenotyping can characterize baseline variability, sleep, activity, autonomic state, and other contextual factors that may influence challenge response. Their role in the framework is to improve estimation of antecedent state and dynamic phenotype, not to create a new methodological discipline (Chen et al., 2012; Ashley, 2015; Collins and Varmus, 2015; FDA-NIH Biomarker Working Group, 2016; Li et al., 2017; Price et al., 2017; Dunn et al., 2018; Coravos et al., 2019; Schüssler-Fiorenza Rose et al., 2019).

7 Proof-of-concept protocol: standardized exercise recovery

A first empirical test should use a perturbation that can be standardized, repeated, densely sampled, and administered with relatively low risk. A controlled exercise challenge is suitable for testing whether a reliable exercise-specific recovery phenotype exists. It is not assumed to measure organism-wide RC. The proposed experimental sequence is summarized in Figure 2.

Exercise is particularly useful because external workload can be controlled while internal physiological load is measured, recovery begins at a defined time, and the protocol can be repeated for reliability. It also engages multiple systems without requiring that every measured response be combined into one score. The primary objective is methodological: determine whether a small set of prespecified trajectory features can be measured reliably and whether a candidate latent or multivariate phenotype has incremental value beyond baseline fitness and established constructs.

Eligibility criteria should be chosen to minimize avoidable safety risk and interpretive heterogeneity while preserving enough variation to test construct validity. An initial study might enroll clinically stable middle-aged and older adults capable of cardiopulmonary exercise testing, document medications and chronic conditions, and exclude acute infection, unstable cardiopulmonary disease, recent major surgery or hospitalization, or other

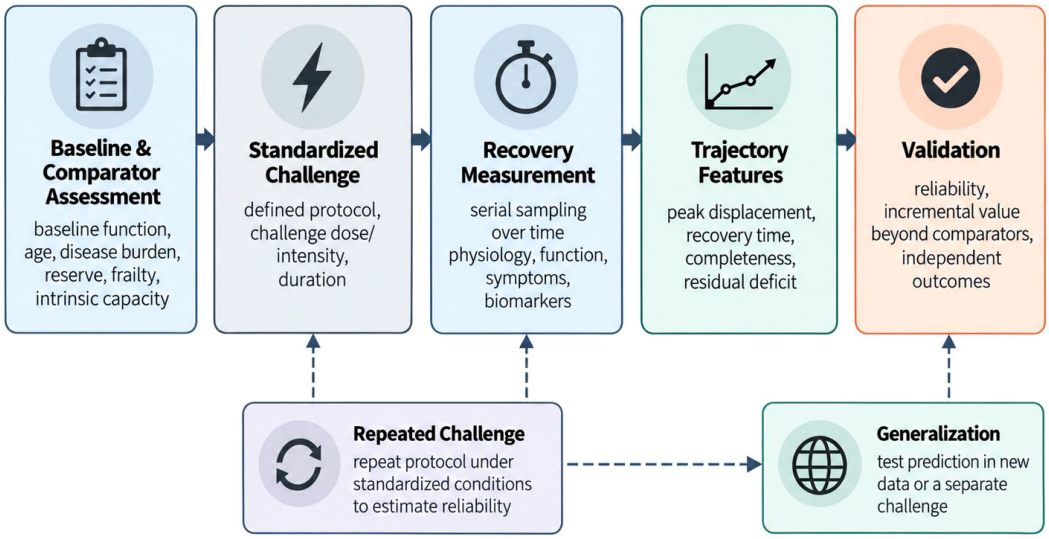

FIGURE 2
Simplified standardized protocol for testing recovery phenotypes. Baseline function and comparator constructs are assessed before a defined challenge. Serial measurements generate prespecified trajectory features that may be subjected to repeated-challenge reliability testing and evaluation of incremental explanatory or predictive validity against parsimonious comparator models. Independent data assess replication; generalization to other challenge classes requires separate testing. The initial objective is a reliable challenge-specific phenotype, not a universal Recovery Capacity Index.

contraindications. A later replication program should deliberately broaden age, sex, disease, fitness, and population diversity rather than assuming transportability from the development cohort.

The challenge should be normalized to individual capacity, for example by workload relative to peak oxygen uptake or ventilatory threshold, while also recording delivered workload, heart rate, perceived exertion, and other internal-load measures. Hydration, recent meals, caffeine, alcohol, prior exercise, sleep, medication timing, ambient temperature, and time of day should be standardized where feasible or measured prospectively. This is essential because unexplained variation in challenge dose would otherwise be misattributed to RC.

The sampling schedule should be endpoint-specific. Rapid autonomic and cardiorespiratory variables can be captured continuously or within minutes; metabolic variables may require minutes to hours; inflammatory or molecular responses may require hours to days. A core protocol could collect baseline, end-exercise, 5, 15, 30, and 60 minutes, 2 and 6 hours, and 24 and 48 hours, with fewer or additional time points justified for each variable. Predefined missing-data rules and minimum sampling density should be established before modeling trajectories.

The repeat challenge should occur after a sufficient washout and under comparable conditions. Reliability should be evaluated at the level of individual trajectory features before a latent score is built. Features with unacceptable within-person reliability or large measurement error should be removed even if they correlate with outcomes in the discovery sample. This separates biomarker discovery from measurement validation.

Incremental validity requires a comparator model that is strong enough to be clinically credible. At minimum it should include age, relevant sex effects, baseline functional capacity, disease burden, frailty, physiological reserve, intrinsic capacity, allostatic load, and established resilience measures where available. Candidate RC measures must improve prespecified out-of-sample or external-validation performance beyond this model. A statistically significant coefficient in the same dataset used to construct RC is not sufficient.

8 Seven testable propositions

The framework is summarized as propositions rather than established principles. Each proposition should be linked to an empirical prediction and a condition that would require revision or rejection.

9 Adaptation, trade-offs, and future consequences

Recovery after perturbation does not necessarily improve future capacity. A challenge-response-recovery episode may lead to restoration toward a prior reference state, compensation, or residual deficit. Persistent later changes may be beneficial, neutral, costly, or maladaptive. These outcomes are not mutually exclusive across physiological systems or timescales. The three hypothetical immediate recovery outcomes are illustrated schematically in Figure 3; possible longer-term consequences are discussed below.

Adaptation is distinguished from recovery by persistence beyond the immediate recovery interval and, ideally, by an altered response to a subsequent standardized exposure or challenge. Acclimatization is a context-dependent form of adaptation during sustained or repeated environmental exposure; conditioning is adaptation induced by repeated or structured exposure; maladaptation is a persistent change associated with adverse consequences

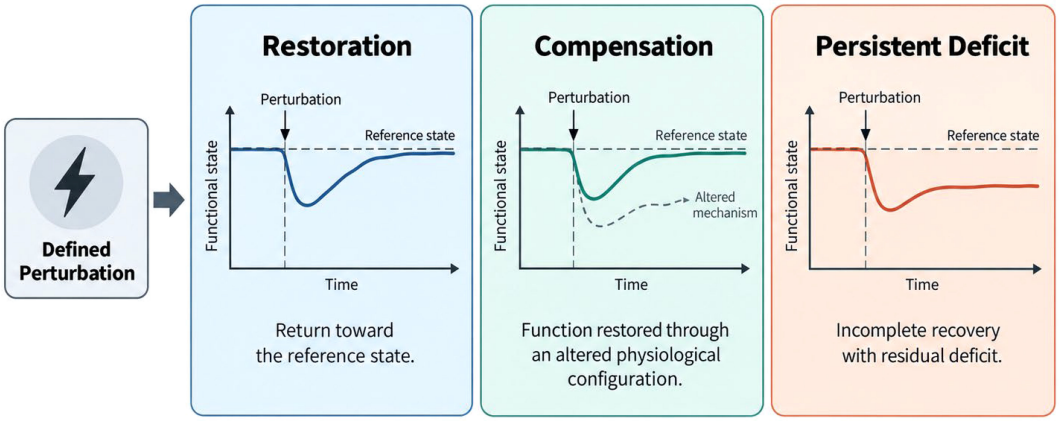

FIGURE 3
Illustrative alternative recovery outcomes after a defined perturbation. Conceptual trajectories (not empirical data and not to scale) illustrate three possible outcomes of a defined perturbation: restoration toward a prespecified functional reference state; compensation in which function is restored or maintained through an altered physiological configuration; and a persistent deficit characterized by incomplete recovery. Functional trajectory alone may not distinguish restoration from compensation; mechanistic assessment may be necessary. Outcomes depend on the perturbation, antecedent state, observation period, and physiological costs. Recovery does not inherently imply improvement.

under a prespecified outcome, domain, or timescale. Adaptation can occur despite incomplete recovery or continued exposure, while complete restoration may occur without durable adaptation.

Allostatic responses illustrate why outcome neutrality is essential. Regulatory adjustments can preserve immediate function while accumulating biological cost when repeatedly activated, prolonged, or inefficiently terminated. A favorable short-term endpoint should therefore not be equated with improved RC or organism-wide benefit. Recovery phenotypes should be evaluated with respect to physiological cost, cross-system consequences, temporal persistence, and competing demands (Sterling and Eyer, 1988; Seeman et al., 1997; McEwen, 1998; McEwen and Wingfield, 2003).

9.1 Examples of divergent consequences

Exercise illustrates a beneficial but nonobligatory adaptation pathway: repeated appropriately dosed training with adequate recovery can improve cardiovascular and skeletal-muscle performance, but excessive load or insufficient recovery can produce persistent fatigue, injury, or impaired performance. The adaptive outcome therefore depends on dose, context, and recovery opportunity rather than challenge alone (Holloszy, 1967; Pedersen, 2009; Booth et al., 2012; Pedersen and Febbraio, 2012; Egan and Zierath, 2013; Hawley et al., 2014; Peake et al., 2017).

Immune responses provide another example. Vaccination or infection can generate immune memory, yet inflammatory responses can also be prolonged or dysregulated, and resolution processes are distinct from activation. A successful short-term defensive response may coexist with tissue damage or later cost. Likewise, compensation after organ injury can preserve function despite altered mechanisms, making apparent functional restoration an incomplete description of underlying state (Nathan, 2002; Serhan and Savill, 2005; Hotamisligil, 2006; Serhan, 2007; Medzhitov, 2008; Chawla et al., 2011; Galli et al., 2011; Buckley et al., 2014; Iwasaki and Medzhitov, 2015; O'Neill et al., 2016; Wynn and Vannella, 2016; Dalli and Serhan, 2017; Franceschi et al., 2017; Furman et al., 2019; Netea et al., 2020).

These examples motivate a two-stage interpretation. Immediate outcomes should be classified relative to the prespecified reference state and function; later consequences should be assessed with separate measurements. Adaptation should be inferred only when a persistent change is demonstrated beyond the immediate recovery window or when response to a later standardized challenge is altered. This prevents every favorable recovery episode from being reclassified as beneficial adaptation after the fact.

9.1.1 Key concept

Recovery is not synonymous with improvement. Immediate outcomes and later consequences must be distinguished, and the significance of either depends on the prespecified functional domain, timescale, energetic or physiological cost, and cross-system trade-offs.

10 Falsification, validation, and research priorities

Directional predictions are insufficient unless paired with null hypotheses and decision rules. Numerical thresholds should be justified prospectively for each endpoint and use case rather than treated as universal constants. Reliability criteria should be prespecified with attention to confidence intervals, measurement error, intended use, and the consequences of misclassification.

Intervention responsiveness should be tested only after adequate reliability and construct validity are established. Responsiveness does not itself establish that RC is a causal therapeutic target or clinically actionable. Clinical utility would require later evidence that using the measure improves decisions or outcomes.

10.1 Staged research priorities

A staged validation and falsification pathway is summarized in Figure 4. Stage 1 defines the recovery phenotype prospectively, including the perturbation, reference state, measured variables, and outcomes. Stage 2 establishes measurement reliability under standardized repeated challenges. Stage 3 evaluates validity against baseline function, disease burden, frailty, physiological reserve, intrinsic capacity, allostatic load, physical resilience, and relevant dynamical metrics. Stage 4 tests incremental predictive value beyond parsimonious comparator models. Stage 5 evaluates replication in independent datasets and, where a generalized RC is proposed, generalization across distinct challenges. Stage 6 examines intervention responsiveness, conditional on acceptable prior measurement and construct validity. Core operational definitions, an illustrative standardized exercise proof-of-concept protocol, and the framework's testable propositions and revision criteria are presented in Tables 3–5, respectively. Detailed falsification criteria are provided in Table 6.

Within Stage 5, cross-challenge generalization should be considered only after reliable within-challenge measurement, construct validity, and incremental predictive value have been established. A higher-order RC hypothesis requires at least two independent perturbation classes and is stronger when supported across several biologically distinct challenges. The aim is not to find one universal correlation threshold but to establish a reproducible shared component whose magnitude and predictive value are large enough to survive measurement error, challenge-specific effects, and established comparator constructs. Weak, unstable, or cohort-specific correlations should be interpreted as evidence for challenge specificity rather than as partial proof of a general factor.

Intervention studies form a later stage. A validated recovery phenotype may be responsive to exercise training, sleep intervention, rehabilitation, treatment of disease, or other interventions, but responsiveness alone does not establish causal mediation. The next question would be whether modifying the candidate phenotype changes independent functional or clinical outcomes and whether benefits outweigh costs or trade-offs. Only after such evidence would clinical utility or an index intended for decision-making become appropriate research targets.

A Recovery Capacity Index is therefore not assumed by the framework. If validation supports several challenge-specific capacities, separate scores may be preferable. If a reproducible higher-order factor exists, a latent score may be appropriate. If network organization explains outcomes better, a network representation may be preferred. If a conventional composite performs equally well, the simpler measure should be favored. If none of these structures add value beyond established constructs, no RC index should be created.

11 Discussion

Recovery Physiology is best understood as a proposed framework for organizing a specific physiological question: how prespecified functional variables change after defined perturbations and whether those changes reveal reliable latent structure beyond established constructs. Its strongest rationale is integrative rather than proprietary. Recovery-relevant mechanisms span multiple levels of biological organization, yet the existence of multilevel mechanisms does not itself establish RC, a three-domain taxonomy, or an organism-wide factor.

The revised framework therefore places competing explanations at its center. Recovery may be adequately explained by baseline health and established constructs; it may be challenge-specific; it may be represented by a conventional composite; the proposed domains may be wrong; or no sufficiently reliable phenotype may emerge. These alternatives are not peripheral limitations but direct empirical competitors. RC is supported only to the extent that prespecified models outperform them.

The framework also narrows the meaning of recovery. Routine physiological cycling, maintenance, repair, and adaptation are related processes but are not synonyms. Environment is a contextual modifier rather than an added biological level. “Optimization” is not assumed because physiological responses manage trade-offs under constraints. Likewise, longitudinal measurement is an established strategy rather than a new discipline, and clinical concepts such as Recovery Medicine or a Recovery Capacity Index are premature before construct validation.

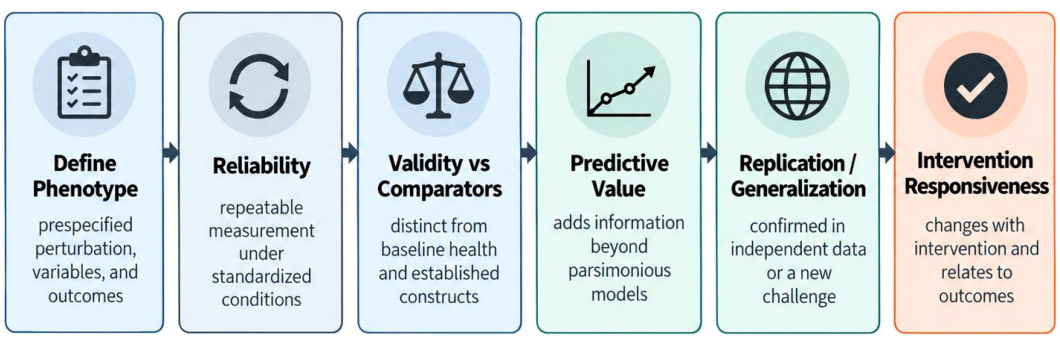

FIGURE 4
Simplified validation pathway for recovery capacity. Six major empirical stages are shown: (1) define the recovery phenotype; (2) establish measurement reliability; (3) compare validity with baseline and established constructs; (4) evaluate incremental predictive value; (5) test replication and, where warranted, generalization; and (6) examine intervention responsiveness. Each stage is conditional on evidence from preceding stages; failure requires narrowing or rejecting the corresponding claim rather than assuming confirmation. Clinical usefulness or actionability is not established by this proposed pathway.

TABLE 3 Core operational definitions.

Term	Operational definition
Recovery Physiology	A proposed physiological framework for studying mechanisms and trajectories by which a prespecified functional variable or state changes following a defined perturbation, and for testing whether latent recovery capacities add information beyond established constructs.
Recovery	The time-dependent post-perturbation process evaluated relative to prespecified functional variables, a reference state, and an observation window. It may lead to restoration, compensation, or residual deficit.
Recovery Capacity (RC)	A hypothetical latent, context-dependent property that exists independently of the eventual outcome and may influence the magnitude, rate, completeness, coordination, and cost of recovery after a defined perturbation.
Recovery trajectory	The observed time series of prespecified variables before, during, and after perturbation; candidate features include response magnitude, time to nadir/peak, restoration rate, threshold time, overshoot, residual deficit, coordination, and cost.
Restoration	Movement of a prespecified variable or state toward a prespecified reference condition.
Compensation	Preservation or restoration of function through an altered physiological configuration; compensation may carry energetic, regulatory, or cross-system cost.
Adaptation	A persistent change in physiological state or subsequent response characteristics that extends beyond the immediate recovery interval and alters response to later exposure or challenge.
Maladaptation	A persistent change associated with adverse consequences under a prespecified outcome, biological domain, or timescale, even if it preserves short-term function.
Bioenergetic capacity	Candidate domain describing the availability, distribution, and utilization of energy and substrates required for restorative biological work.
Biological information integrity	Candidate domain describing preservation, accessibility, and faithful execution of biological specification in genetic, epigenetic, transcriptional, translational, and proteostatic states.
Systems coordination	Candidate domain describing dynamic signaling, feedback regulation, temporal coupling, resource allocation, and integration across cells, tissues, organs, and physiological systems.
Environment	External context and coupled influence—not a higher biological organizational level—that can modify antecedent state, perturbation exposure, resources, constraints, and recovery trajectories.

TABLE 4 Illustrative standardized exercise proof-of-concept protocol.

Component	Prespecified design
Population	Clinically stable adults able to complete cardiopulmonary exercise testing; prespecified exclusions for unstable disease, acute infection, recent major surgery/hospitalization, or contraindications.
Challenge standardization	Individualized exercise dose based on peak oxygen uptake, ventilatory threshold, or another validated relative workload; standardize or record time of day, hydration, food/caffeine, prior activity, environment, and medication timing.
Baseline/comparators	Repeated resting physiology where appropriate; functional capacity; disease burden; frailty; physiological reserve; intrinsic capacity; allostatic load; established resilience measures; recent sleep/activity; relevant laboratory measures.
Sampling times	Illustrative schedule: baseline, end-exercise, 5, 15, 30, 60 min, 2 h, 6 h, 24 h, and 48 h, adapted prospectively to endpoint kinetics.
Bioenergetic candidates	VO2 recovery, phosphocreatine recovery where feasible, lactate clearance, substrate utilization/metabolic flexibility, mitochondrial measures in substudy.
Information-integrity candidates	DNA-damage/repair responses, epigenetic stability, transcriptional or translational fidelity, proteostatic markers.
Systems-coordination candidates	Heart-rate recovery/HRV, blood-pressure recovery, cardiorespiratory coupling, endocrine-immune/autonomic coupling, feedback and network metrics.
Trajectory features	Magnitude, peak/nadir time, restoration rate, half-time or time constant, threshold time, completeness, overshoot, residual deficit, coordination, post-recovery stability, cost.
Reliability	Repeat standardized challenge under comparable conditions; exclude features that fail prespecified test-retest criteria.
Primary proof-of-concept outcomes	Reliability of prespecified trajectory features; explanatory contribution of candidate domains beyond challenge dose and baseline; incremental prediction of an independent subsequent outcome.
General-RC test	Use an independent perturbation class; exercise-derived measures must show reproducible cross-challenge covariance/prediction before supporting a higher-order RC.
Failure conditions	Poor reliability; no incremental validity; simpler model performs equally well; no cross-challenge structure where general RC is claimed.

TABLE 5 Testable propositions and revision criteria.

Proposition	Empirical prediction	Revision/rejection condition
1. Defined perturbation	Recovery phenotypes require a prospectively characterized perturbation, reference state, variable, and observation window.	Retrospective relabeling of arbitrary fluctuations as recovery does not support the framework.
2. Reproducible trajectory	Some recovery features are sufficiently stable within individuals under comparable challenges to support phenotype construction.	Poor test-retest reliability argues against use of that feature or challenge model.
3. Multiscale contribution	Recovery can depend on mechanisms operating across multiple biological levels without every routine cycle being classified as recovery.	If higher-level outcomes are fully explained by one local mechanism, broad multiscale claims should be narrowed.
4. Provisional domains	Bioenergetic capacity, biological information integrity, and systems coordination provide useful explanatory structure.	If simpler/alternative architectures replicate better, add/remove/combine/subdivide domains.
5. Incremental validity	Dynamic recovery measures add explanatory or predictive value beyond established comparator constructs.	No reproducible improvement after comparators are included argues against distinct RC.
6. Recovery-adaptation relationship	Some challenge-recovery experiences produce persistent changes in subsequent responses, but adaptation is not required for restoration.	If no persistent change is present, classify as restoration without adaptation; maladaptation and compensation remain alternatives.
7. Hierarchical RC	Challenge-specific capacities may share a higher-order factor.	Weak or unstable cross-challenge covariance supports challenge-specific rather than organism-wide RC.

TABLE 6 Decision rules for falsification and validation.

Question	Null hypothesis	Evidence to reject null	Consequence if null not rejected
Trajectory reproducibility	Features are dominated by measurement error or transient state variation.	Prespecified acceptable reliability under standardized repeated challenge.	Features failing reliability criteria are excluded from RC construction.
Incremental validity	RC adds no value beyond a parsimonious comparator model.	Replicated improvement in out-of-sample/independent performance exceeding a prespecified meaningful threshold.	No meaningful improvement => distinct RC not supported.
Cross-domain value	Three-domain measures do not outperform a simpler model.	Validated advantage with acceptable calibration and complexity.	Equivalent simpler model => domain structure not justified.
General RC	Recovery is challenge-specific.	Reproducible cross-challenge covariance/latent structure plus prediction across independent perturbations.	Weak/unstable generalization => retain challenge-specific model only.
Three-domain architecture	Proposed architecture is not distinguishable from alternatives.	Reproducible fit/interpretability and advantage over competing structures.	Redundant, unstable, or inferior domains => combine, subdivide, add, remove, or replace.
Intervention responsiveness	Validated phenotype is not modifiable by the tested intervention.	Prospectively specified change beyond measurement error with appropriate controls.	No responsiveness does not invalidate measurement validity; it limits claims of modifiability.

The immediate research objective is therefore construct validation. A staged program should establish reliable challenge-specific phenotypes, compare them with intrinsic capacity, reserve, frailty, allostatic load, resilience, and baseline function, test candidate domain architectures against alternatives, and evaluate cross-challenge generalization only after within-challenge measurement is robust. A generalized index should be considered only if a stable and incrementally valid structure is demonstrated.

Potential translation is explicitly conditional. If validated recovery phenotypes later prove modifiable and clinically useful, applications in rehabilitation, geroscience, preventive medicine, or precision health could be tested. The present article does not establish clinical discipline, therapeutic target, or actionable index.

11.1 Strengths, limitations, and scope

A strength of the framework is that it converts an integrative physiological intuition into explicit construct boundaries and competing hypotheses. It encourages investigators to separate baseline state from response dynamics, immediate outcome from later adaptation, and latent capacity from the variables used to estimate it. It also makes negative findings informative: unreliable trajectories argue against the phenotype; lack of incremental validity argues against a distinct construct; absence of cross-challenge structure argues against organism-wide RC; and failure of the three-domain architecture supports a different organization.

Several limitations remain. The literature synthesis is purposive rather than systematic and may underrepresent relevant fields. The

proposed domains are intentionally broad and could conceal mechanistically distinct subdomains. Different perturbations may require different variables and timescales, limiting comparability. Chronic exposures that shift reference states may not fit acute challenge-recovery models. Compensation can mimic restoration, and cross-system costs may be difficult to observe within a short study. Latent-variable models can also create apparently coherent factors from correlated measurement procedures rather than biology, making external replication and mechanistic dissociation essential.

The framework is also deliberately restricted to organismal physiology. Comparative physiology may help test whether similar constraints or recovery motifs occur across species, but the present article does not propose an ecological or ecosystem-level recovery theory. Environmental context is included because it shapes exposures, resources, and constraints on organisms, not because the environment is treated as a biological level above the organism (Cabello-Rivera and del Nogal Avila, 2026).

Finally, the framework should not be judged by whether every proposed term survives. A useful outcome of empirical testing could be rejection of a general RC in favor of several challenge-specific capacities, replacement of the three-domain architecture, or demonstration that established constructs already explain the relevant variation. Such results would narrow the theory while still improving conceptual clarity about recovery.

12 Conclusion

Recovery Physiology proposes a testable physiological framework for studying restoration, compensation, residual deficit, and later consequences after defined perturbations. Recovery Capacity is a hypothetical latent construct, not an outcome label. The framework is supported only if prespecified recovery phenotypes are reliable, add explanatory or predictive value beyond established constructs, and—where a higher-order general RC is claimed—generalize across independent perturbation classes.

The three candidate domains are a revisable architecture rather than an established taxonomy. The organism-level hypothesis is likewise conditional: if cross-challenge structure is absent, challenge-specific capacities are the appropriate model; if simple composites perform equally well, weak emergence is unsupported; if comparator constructs explain outcomes equally well, a distinct RC construct is unnecessary. These failure conditions are integral to the framework.

The central value of the proposal is therefore not that it declares a new discipline, but that it organizes an integrative physiological question into competing models that can be prospectively measured, compared, falsified, and refined.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material. Further inquiries can be directed to the corresponding author.

Author contributions

JL: Investigation, Visualization, Conceptualization, Writing – original draft, Project administration, Writing – review & editing, Supervision. HG: Conceptualization, Investigation, Visualization, Writing – review & editing, Writing – original draft.

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Conflict of interest

The author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declared that generative AI was used in the creation of this manuscript. The authors used OpenAI ChatGPT (Version: GPT-5.6, Model: GPT-5.6 Sol; OpenAI, https://chatgpt.com/) to assist with language editing, structural revision, and formatting. The authors reviewed and verified the scientific content, citations, and final text and take full responsibility for the manuscript. Conceptual figures were prepared with generative-AI-assisted design and reviewed by the authors for scientific accuracy.

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