Life on pause: Species capable of near-total, reversible suspension of physiological activity

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Abstract. Across the tree of life, numerous organisms have evolved the capacity to profoundly downregulate, and in extreme cases almost completely suspend, physiological activity in response to adverse environmental conditions. These reversible states, collectively referred to as dormancy, span a continuum from moderate metabolic depression (e.g. torpor, hibernation, aestivation, diapause) to the near-total metabolic arrest characteristic of cryptobiosis. This review synthesizes current knowledge on species capable of entering such extreme yet reversible physiological states, with particular emphasis on cryptobiotic meiofauna (tardigrades, rotifers, nematodes), vertebrate hibernators and aestivators, and taxa exhibiting developmental arrest through diapause. We integrate physiological, molecular and ecological perspectives to highlight common regulatory themes, including coordinated metabolic suppression, stabilization of cellular structures, molecular chaperoning, antioxidant defenses, and reversible reprogramming of gene expression. Special attention is given to cryptobiosis as the closest known biological analogue to a "paused" life state, in which metabolism becomes undetectable yet viability is preserved for years or even decades. Comparative analysis reveals that despite vast phylogenetic distances, convergent mechanisms underpin dormancy across taxa, reflecting shared evolutionary solutions to environmental unpredictability. Understanding these strategies not only expands the conceptual boundaries of life's persistence but also provides valuable models for biomedical research, biotechnology, conservation biology and resilience to global environmental change.
Key Words: dormancy, cryptobiosis, hibernation, torpor, aestivation, diapause, metabolic depression, extreme tolerance, physiological suspension, stress resistance.

Introduction. Across the tree of life, several organisms can drastically downregulate, and in extreme cases almost suspend, physiological functions to survive hostile conditions, then resume normal life when conditions improve. These states fall under the broad umbrella of dormancy, ranging from moderate metabolic depression (hibernation, torpor, diapause, aestivation) to the almost inert "latent life" of cryptobiosis (Wilsterman et al 2020; Withers & Cooper 2010; Lubzens 2015).

The aim of this work is to provide an integrative synthesis of organisms capable of near-total, yet reversible, suspension of physiological activity, examining dormancy as a continuum from hypometabolic states to cryptobiosis. By comparing physiological, molecular and ecological mechanisms across diverse taxa, the study seeks to identify shared regulatory principles, evolutionary convergences and ecological implications of extreme metabolic suppression, while highlighting the relevance of these systems as models for understanding survival, resilience and adaptation in fluctuating and extreme environments.

Conceptual and Physiological Framework. Dormancy is defined as a reversible, regulated reduction of metabolism, behaviour, development and environmental responsiveness that enhances survival in temporarily hostile environments such as cold, heat, desiccation, hypoxia or food shortage (Wilsterman et al 2020; Withers & Cooper 2010; Lubzens 2015). Physiological expression spans a continuum: from subtle hypometabolism in active mammals to profound states where metabolism is depressed to immeasurably low levels, as in cryptobiotic invertebrates (Wilsterman et al 2020; Rebecchi et al 2019; Withers & Cooper 2010; Lubzens 2015).

At the extreme end, cryptobiosis in animals such as tardigrades and certain rotifers and nematodes can entail apparent cessation of metabolic activity during desiccation, freezing, or anoxia, with recovery after years or decades once water or suitable temperature returns (Rebecchi et al 2019; Withers & Cooper 2010; Guidetti et al 2011; Lubzens 2015). Less extreme but still remarkable are hibernation and torpor in mammals and birds, in which metabolic rate can drop to <10% of resting values, body temperature is greatly reduced, and most physiological processes are slowed yet remain coordinated and reversible (Staples 2016; Giroud et al 2021; Withers & Cooper 2010). Aestivation represents an analogous hypometabolic state in response to heat and drought, documented in amphibians, reptiles, lungfish, and invertebrates (Jiang et al 2023; Staples 2016; Villadangos & Munné-Bosch 2025; Storey & Storey 1990). Diapause in invertebrates and some vertebrates halts development and strongly depresses metabolism, often at specific life stages such as embryos or larvae (Sweet & Hu 2025; Lubzens 2015; Ellis & Del Giudice 2019).

Tardigrades: Model Organisms for Cryptobiosis. Tardigrades ("water bears") are iconic for their ability to survive conditions lethal to most life forms by entering multiple dormant states, notably anhydrobiosis (desiccation), cryobiosis (freezing), anoxybiosis (anoxia), and diapause forms like encystment and resting eggs (Rebecchi et al 2019; Guidetti et al 2011; Lubzens 2015). In cryptobiosis, tardigrades contract into a tun, lose almost all body water, and biochemical activity drops to extremely low or undetectable levels, permitting survival in "hostile to life" habitats for extended periods (Rebecchi et al 2019; Guidetti et al 2011; Gagyi-Palffy & Stoian 2011; Petrescu-Mag 2016).

Cryptobiosis involves a suite of molecular protectants (e.g. specific sugars such as trehalose and late-embryogenesis abundant (LEA) proteins) that stabilize proteins and membranes and often promote intracellular glass formation, effectively arresting biochemical reactions (Rebecchi et al 2019; Guidetti et al 2011; Lubzens 2015). Survival and subsequent revival depend on the duration of the cryptobiotic state and the physical conditions during dehydration and rehydration, but many species can resume normal metabolism, growth, and reproduction upon rehydration or thawing (Rebecchi et al 2019; Guidetti et al 2011). Cryptobiosis has evolved at least twice independently within tardigrades, and its ecological advantages (persistence through desiccation, reduced predation and competition) likely contribute to their high diversity and success in ephemeral terrestrial microhabitats (Guidetti et al 2011).

Rotifers and Nematodes: Extreme Tolerance in Meiofauna. Bdelloid rotifers and some nematodes similarly exhibit anhydrobiosis and cryobiosis, surviving complete desiccation or freezing by entering a reversible state of suspended metabolism (Rebecchi et al 2019; Withers & Cooper 2010; Lubzens 2015). In rotifers, resting eggs and encysted stages can survive for decades, reactivating when hydrated (Rebecchi et al 2019; Lubzens 2015). Nematodes adopt both diapause and cryptobiotic strategies, including dauer larvae in *Caenorhabditis elegans*, which halt development and strongly depress metabolism to withstand crowding, heat or starvation (Sweet & Hu 2025; Lubzens 2015).

Mechanistically, these taxa share convergent strategies with tardigrades: accumulation of compatible solutes, LEA proteins, and robust antioxidant systems, plus global reprogramming of gene expression to favour stress resistance over growth and division (Rebecchi et al 2019; Sweet & Hu 2025; Lubzens 2015; Helena-Bueno et al 2024). Their small size and simple body plans facilitate near-complete physiological shutdown without structural damage, making them key models for understanding extreme tolerance and potential biotechnological or medical applications (Rebecchi et al 2019).

Vertebrate Hibernators and Torpid Species. Many mammals and some birds employ hibernation or daily torpor as profound but less absolute suspensions of physiological activity. Torpor is characterized by actively regulated depression of metabolic rate (often to <10% of basal) with a marked drop in body temperature and reduced responsiveness to stimuli (Staples 2016; Giroud et al 2021; Withers & Cooper 2010). Hibernation extends torpor for days to weeks, interspersed with brief arousals (Staples 2016; Giroud et al 2021).

Small mammals such as ground squirrels, bats, and some marsupials achieve deep torpor with body temperatures approaching ambient, reduced heart and respiratory rates, and systemic reprogramming of fuel use, mitochondrial function and antioxidant defences (Staples 2016; Giroud et al 2021; Storey & Storey 1990). Larger hibernators like brown bears display moderate hypothermia but still suppress metabolism, maintain organ integrity, resist muscle atrophy and bone loss, and exhibit reversible insulin resistance, resuming normal function when they arouse in spring (Shah et al 2025; Giroud et al 2021). Torpor also occurs in monotremes, marsupials, and several avian lineages, underscoring its widespread evolutionary origins (Giroud et al 2021; Withers & Cooper 2010).

Despite not reaching the near-zero metabolic rates of cryptobiosis, hibernators demonstrate coordinated multi-organ downscaling of physiology, greatly reduced protein synthesis, modified immune function, and protective mechanisms against hypoxia, ischemia–reperfusion and oxidative stress, followed by efficient rehabilitation during arousal (Shah et al 2025; Staples 2016; Giroud et al 2021; Storey & Storey 1990).

Aestivating Vertebrates and Invertebrates. In aestivation, animals enter hypometabolic states to survive hot, dry periods or resource scarcity, maintaining aerobic metabolism but at drastically reduced rates (Jiang et al 2023; Staples 2016; Villadangos & Munné-Bosch 2025; Storey & Storey 1990). Aestivating ectotherms, including lungfish, amphibians (e.g. certain frogs and toads), some fishes, reptiles, annelids and molluscs, suppress metabolism intrinsically beyond the passive effect of high temperature or dehydration, often to 10–20% of normometabolic levels (Jiang et al 2023; Staples 2016; Villadangos & Munné-Bosch 2025; Withers & Cooper 2010).

Recent syntheses highlight shared themes across aestivating lineages: shifts from carbohydrates to lipids as primary fuel, suppression of growth and reproduction, reconfiguration of immune function, and strategies to prevent oxidative damage during arousal, when oxygen consumption surges (Jiang et al 2023; Storey & Storey 1990). In vertebrate models such as African lungfish, transcriptomic analyses reveal coordinated downregulation of biosynthetic pathways and neural activity and upregulation of stress resistance genes across organs (Niu et al 2024). These animals can survive months or years in estivating cocoons or burrows, then rehydrate or re-emerge to resume feeding and reproduction within hours to days when rains return (Jiang et al 2023; Niu et al 2024).

Diapause and Developmental Arrest Across Taxa. Diapause provides another route to reversible near-suspension of physiological activity, especially in embryos, eggs, and early developmental stages of insects, crustaceans, fishes, reptiles, and some mammals (Sweet & Hu 2025; Lubzens 2015; Ellis & Del Giudice 2019). Diapause halts development and dramatically slows metabolism while maintaining viability for periods ranging from days to years, often synchronized with seasonal cues such as photoperiod (Sweet & Hu 2025; Lubzens 2015).

Examples include resting eggs of crustaceans and rotifers, insect embryos and pupae, and vertebrate embryos such as annual killifishes and some mammalian embryos that delay implantation (Sweet & Hu 2025; Lubzens 2015). Molecular studies, particularly in *C. elegans* dauer and insect diapause, reveal conserved regulatory modules involving insulin/IGF signaling, TGF-β pathways, FOXO transcription factors, and nutrient-sensing networks (e.g. mTOR), which shift physiological priorities from growth to long-term maintenance and stress resistance (Sweet & Hu 2025; Lubzens 2015; Ellis & Del Giudice 2019). These mechanisms allow developmental programs to be paused almost completely and rapidly reinitiated when environmental conditions become favourable.

Cryptobiosis and Molecular Dormancy at the Cellular Scale. Cryptobiosis is often defined as "hidden life", an extreme form of inactivity in which metabolism becomes so low it is often undetectable, associated with an altered physical state of cellular water (desiccated or frozen) (Withers & Cooper 2010; Lubzens 2015). It encompasses anhydrobiosis, cryobiosis, osmobiosis and anoxybiosis, seen in organisms ranging from bacteria and yeast spores to plant seeds and invertebrate animals (Withers & Cooper 2010; Lubzens 2015). Desiccated seeds of some plants (e.g. date palm, sacred lotus) have maintained viability for centuries to millennia, resuming growth upon rehydration (Lubzens 2015).

At the molecular level, recent work shows that during dormancy, many essential enzymes themselves enter "molecular hibernation", associating with specialized hibernation factors, forming inactive ribosome dimers or sequestered complexes that prevent unwanted activity and protect from damage (Helena-Bueno et al 2024). This concept extends from bacteria to eukaryotic cells, suggesting that reversible inactivation of core translational and transcriptional machinery is a general requirement for long-term dormancy (Helena-Bueno et al 2024).

Evolutionary and Ecological Significance. Dormancy, from moderate torpor to cryptobiosis, is not confined to any single lineage but has evolved repeatedly in animals, plants, fungi and microbes, enabling colonization of ephemeral or extreme habitats - from deserts and polar regions to temporary ponds and deep soils (Wilsterman et al 2020; Rebecchi et al 2019; Withers & Cooper 2010; Lubzens 2015; Storey & Storey 1990). A unified eco-physiological perspective emphasizes common regulatory motifs and trade-offs: organisms sacrifice immediate growth and reproduction to gain persistence and resilience, effectively "escaping in time" from inhospitable conditions (Wilsterman et al 2020; Rebecchi et al 2019; Withers & Cooper 2010; Lubzens 2015).

Comparative analyses across vertebrate dormancy states (hibernation versus aestivation) reveal convergent changes in genes controlling metabolism, neural activity, cell proliferation and stress resistance, supporting the view that similar molecular solutions underlie independently evolved dormancy strategies (Wilsterman et al 2020; Jiang et al 2023; Giroud et al 2021; Niu et al 2024; Sweet & Hu 2025; Storey & Storey 1990). At the ecological scale, these capacities shape population dynamics, community composition, and biogeography, allowing species to withstand climatic variability and, in some cases, anthropogenic environmental extremes.

Conclusions. The organisms that come closest to "stopping life" yet fully resuming normal function include cryptobiotic tardigrades, rotifers and nematodes, long-lived dormant plant seeds and spores, and a broad suite of animals using hibernation, torpor, aestivation and diapause. Although the depth of metabolic depression varies, all rely on tightly regulated, reversible suppression of physiological processes, stabilization of cellular structures, and conserved molecular pathways that prioritize survival over activity. These systems not only illuminate the boundaries of life's persistence but also provide rich models for medicine, biotechnology and understanding resilience in a rapidly changing world.

Conflict of interest. The authors declare that there is no conflict of interest.

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