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Perspective

A Climate BioStress Sentinel System: Identifying climate impacts from the genome to the urbanized biosphere

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SUMMARY

The impacts of climate change are pervasive across the biosphere, stressing virtually all biotic kingdoms and supporting habitats. Contemporary lifeforms respond to climate stress and are early sentinels of how the biosphere could evolve over the longer term. Our capacity to detect biostress has improved markedly with new genetic, biochemical, and biogeochemical techniques; model organisms; ubiquitous *in situ* and remote sensors; simulations; artificial intelligence tools; socio-environmental perspectives; and global-scale data analytics. Based on these advancements, we present a conceptual climate biostress model, together with an integrative Climate BioStress Sentinel System (CBS3). The sentinel system represents a vehicle for uncovering synergistic and cumulative climate effects in urban settings and their biological, built, and social infrastructures. Developing an integrated CBS3 constitutes a pan-scientific grand challenge requiring integration

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across traditional disciplinary perspectives spanning at least 12 orders of magnitude each in space and time. By providing operational tracking of the success or failure of commitments to long-term climate and environmental action, CBS3 can provide insights into necessary policy investments and adjustments.

INTRODUCTION

A changing climate is the hallmark of Earth's history, but over the past century its pace and scope have greatly accelerated in response to the collective human enterprise.[1] Major technological, social, economic, environmental, and geopolitical forces are transforming the planet across many scales, yet these remain incompletely understood. Contemporary climate change is identified as a pervasive and existential threat,[1–3] compounded by society's mismanagement of the challenge. The global scope of climate change begs the question of how prolific, pervasive, and important are its impacts on a major building block of the Earth system—the biosphere.

Climate biostress (CBS), as referred to here, provokes responses from living systems activated directly or indirectly by excessive heat, changes in water availability, elemental and energy cycling, elevated air pollutants, and carbon dioxide (CO_2) exposure. It produces selective pressures on individuals, groups of individuals, and different species by altering the availability of habitat and other resources necessary for survival.[3] CBS embodies interactions with fundamental genetic and biochemical processes but also includes the less deterministic behavior of communities and ecosystems, which are regulated by the physical, biogeochemical, and behavioral interactions created by life itself. Thus, CBS goes well beyond the more recognizable, human-centered notion of psychological stress or the idea of stress-to-strain in a mechanical engineering sense.

Across the biosphere, CBS manifests itself at multiple levels, from molecules, cells, and organisms to ecosystems and society. Recent reviews consider multi-scale gene-to-function and gene-to-organism impacts[4–6] as well as the metabolic foundation of ecosystem properties,[7] life evolving in contemporary urban settings,[8] and the whole biosphere.[9] Additionally, human health studies today recognize the interconnections of people, animals, plants, and their shared environments, collectively encompassing the One Health approach.[10] Our perspective builds on these and similar studies to develop an observational strategy to detect multi-scale CBS. While environmental stress responses are more-or-less universal, our emphasis here is on urban areas where climate-forced physical changes can rapidly transform into human health and social emergencies affecting billions.[11]

Climate stresses have already imposed significant impacts on urban systems globally, directly on people and through impairments to their supporting ecological services.[12,13] Latest United Nations estimates to mid-century place nearly all global population growth into urbanized areas (i.e., city cores and surrounding metropolitan regions), mostly small and medium-sized cities in low-to-moderate income countries. For the first half of the century, this translates into an additional 3.5 B people living in cities, rising from about half in 2000 to two-thirds of the global population in 2050.[14] Cities will serve not only as a major source of ongoing greenhouse gas emissions but also as a primary recipient of their accumulated impacts. Better monitoring of climate-biology interactions will be invaluable not only in designing long-term climate policy options but also in managing extreme weather emergencies.

While evolution unfolds over generations and can span millions of years, the geological record shows ample evidence of sudden shifts, including multiple mass extinctions like the K-Pg event that led to the demise of dinosaurs and subsequent rise of new life forms.[15] Thus, despite the modern assault on biodiversity,[16] today's species richness constitutes clear evidence that the biosphere contains a storehouse of genetic, phenotypic, and functional building blocks to draw upon when responding to a diversity of new climates. Recent climate warming is essentially a planetary-scale biology experiment with trends, extremes, and nearly endless derivative impacts that are testing our capacity to monitor, understand, and keep pace with the change. Too sluggish a societal response to climate stress runs the risk of activating major geophysical tipping points.[17–19] There are also anticipated biotic[20,21] tipping points, which, if transcended, will take many forms: physiological impairment, competitive disadvantage, structural and functional reorganization, migration, extinction, and/or collapsing food webs. Coupled to these are costly socioeconomic disruptions[22] but also plausible socially beneficial tipping points.[23] Hence, we need conceptual and practical approaches to identify the nature and extent of CBS so they can be understood, minimized, and potentially avoided.

These subtleties require a multi-scale, interdisciplinary approach to improve understanding of how climate affects life throughout the living kingdoms. Our perspective samples a range of issues that our planet and its urban systems face and synthesizes key findings from the existing literature to design an essential CBS detection system. We draw on established initiatives like One Health and integrate them into a climate impacts domain. The product of this observational strategy we call the Climate BioStress Sentinel System (CBS3). A well-designed CBS3 can stimulate basic research yet ultimately support initiatives like intergovernmental science-to-policy platforms on climate and biodiversity.

We guide the design of such a system using three questions: *how does contemporary climate change shape the biosphere, from its subcellular underpinnings through individual life forms, ecological systems, and, ultimately, a human-dominated planet? To what degree are we scientifically and technically prepared to select candidate climate sentinels and then monitor and assess their sensitivities to the broad dimensions of climate change? How might a notional CBS3 be configured?*

We begin by briefly defining the climate stressors themselves, then move to an overview of climate impacts across scales from the subcellular to the Earth system. While not seeking to be fully comprehensive, this perspective does aim to identify some major signatures of living system response to CBS, informing the

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choice of candidate sentinels within a proposed CBS3. While we recognize the fully global dimension of climate change and its impacts, for tractability we focus much of our attention on a critical and rapidly changing 21st-century habitat, the major urban complex. We present this as a science rationale and planning document for CBS3, but where necessary we explore some of its implementation aspects. The main themes underpinning our CBS3 strategy are discussed in the supplemental information.

A HEURISTIC MODEL OF URBAN CLIMATE BIOSTRESS

Our overall conceptual framework for CBS3 (Figure 1) emphasizes linkages between climate change, the enabling socioeconomic environment, and the biotic and abiotic infrastructures upon which the climate stresses are simultaneously imposed. Depending on the city in question, all three infrastructures will be present, but to varying degrees. For example, an urban center will be dominated by human-built and social components but nonetheless support green infrastructure in the form of plants, animals, and less apparent lifeforms, including microorganisms. By contrast, a regional mix of urban-suburban-exurban landscapes will display prominent biotic infrastructures.

Global climate trends and extremes embody a huge array of exogenous physical drivers, imposing stress onto the three infrastructures over more local domains. These more direct climate impacts include shifts in the timing, geography, and severity of heat waves; drought; excessive precipitation, humidity, and flooding; hurricanes and tornadoes; freeze-thaw events; and, in coastal settings, sea level rise and storm surge.

The socioeconomic backdrop is critical in shaping responses to climatic stress, attenuating or amplifying its impacts on the resident urban infrastructures and thus helping to define the system's vulnerability and resilience. This enabling context differs greatly across urban settings. For example, a major hurricane will define two starkly different endpoints as it hits a climate-ready, wealthy city equipped with advanced warning systems and well-engineered flood protection versus a poor city dominated by unplanned, rapidly expanding informal neighborhoods likely to be devastated by the storm's immediate impacts and a difficult recovery. The socioeconomic context also sets the stage for synergistic effects, as when background levels of poor air quality combine with heat stress to produce public health emergencies.[24] Additional amplifying factors include existing urban soil and water degradation, socioeconomic disparities, inequitable land use and zoning, and any historical losses of green infrastructure.[13]

HOW LIFE CONFRONTS A CHANGING CLIMATE

Climate stress and its biospheric responses play out over a range of scales and complexity, spanning (1) molecular genetics, epigenetics, and protein biochemistry; (2) cellular processes; (3) the physiology and fitness of individual tissues, organs, and organisms; (4) ecosystems, including cities; (5) regional dynamics; and ultimately (6) the full Earth System (Figure 1). The supplemental information describes in more detail many of the commonalities of CBS response across the biosphere.

Disciplinary studies of these phenomena together span at least 12 orders of magnitude in scale each over space and time. As a result, the collective body of documented evidence strongly reflects unique subdisciplinary perspectives, with non-trivial nomenclature and methodological differences challenging our ability to assemble a holistic picture of change.[6,25] The multifaceted elements of climate change are fertile ground for convergent studies that break down scale-focused perspectives to reveal patterns and processes that may well be coincident across many life forms and produce systemic responses operating over nested scales.[26]

Figure 1 illustrates bi-directional interactions between climate and the biosphere across multiple scales. Thus, biochemical changes at the finest of scales mix with an increasing number of complex chemistries that define organismal physiology, which in turn determines the still more complex biology and behaviors of individuals, populations, ecosystems, social systems, and eventually the entire Earth system. As these systems themselves change, the character of their linkages is also transformed through the physical, chemical, physiological, behavioral, and ecosystem connections uniting them all. In principle, climate impact should display itself within clearly delineated living components but also as coordinated biospheric responses across scales.

Nature can overcome climate pressures through biological detection and response strategies that have evolved over the long term. Cellular stress reactions are highly conserved over evolutionary time and multiple life forms,[26–28] with initial feedbacks emphasizing cell defense and recovery. These mechanisms include DNA-damaging agents, heat shock, and the production of reactive oxygen species, leading to altered metabolic and proteomic responses.[27] For instance, common to many prokaryote and eukaryote life forms is the use of lipid-mediated signaling pathways that can be detected in soil and water.[29] Shifts in the production of lipids and other metabolites caused by CBS change the ecology of microbial communities,[30] altering the character of resident soils, water, plants, and animals. Yet, insufficient cellular response to counteract external stressors may lead to apoptosis or other forms of cell death.[28] Cellular responses can also include epigenetic modifications of DNA and chromatin, leading to long-term changes in reproductive success and the behavioral and phenotypic adaptations of animals and plants at the level of individuals and populations.[4–6] Longer-term biostress and continued selection over several generations may lead to irreversible evolutionary changes.[27]

CBS can also set in motion more rapid feedbacks between ecological and evolutionary processes (''eco-evolutionary feedbacks'') that modulate the response of urban ecosystems to stress.[8,31,32] A prime example is the complex interactions among plants and their soil microbial symbionts. Soil microbial communities can quickly change during periods of abnormally hot or dry conditions and promote plant stress tolerance through physical modifications of the environment, secretion of phytohormones, modification of plant gene expression, and improved nutrient acquisition. At the same time, plants can release chemical exudates from roots to create more favorable environments for beneficial soil microbes.[33] These rapid responses likely impart a longer-term ''ecological memory,'' leaving detectable markers

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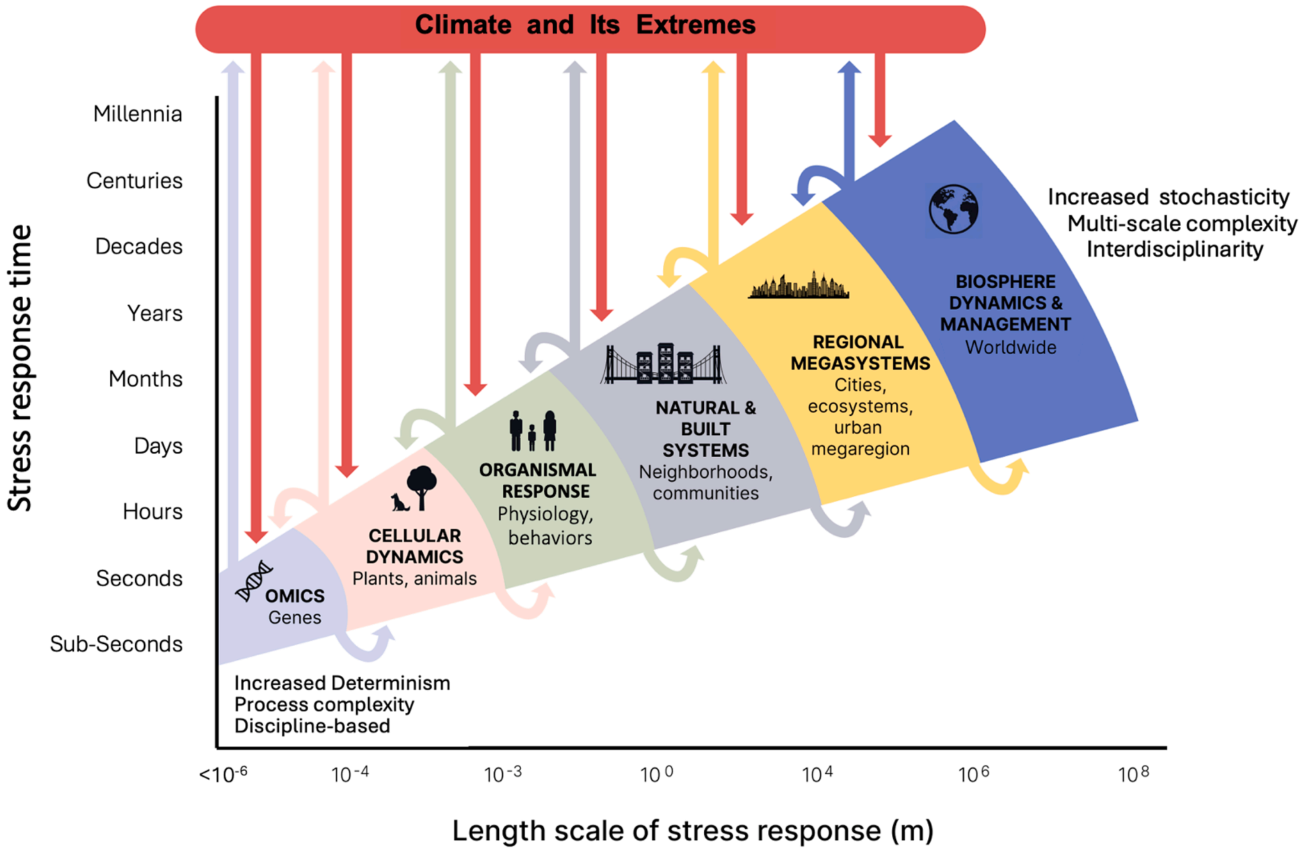

Figure 1. Approximate time and space scales of characteristic CBS response across the biosphere
Narratives describing key components of the CBS3 in the text and in Table S1 follow the general sequence traced diagonally from bottom left to upper right. The narratives summarize how the complexity of their interactions, the number of disciplines required for improved understanding, the stochasticity of the inherent processes, and the space-time horizons of feedbacks all increase when moving from organismal studies toward macro-system domains. Human and non-human behavioral and social systems must also be considered, together with emerging climate management strategies, as we move toward larger domains.

in the soil that can lead to altered trajectories of ecosystem function and ultimately evolution.

Beyond biology, CBS also affects social systems. In humans, we find that the poor, young, old, and sick are most at risk from both negative health and social outcomes.[34] Comprehensive CBS monitoring should therefore consider these social vulnerabilities, extending the purely biological monitoring aims of CBS3 to include a detection system for environmental justice.[35]

AN ABUNDANCE OF CBS SENTINELS

Table S1 gives observational evidence supporting our contention that CBS acts across all scales of life and provides raw material for assembling a catalog of useful sentinels. This section provides an overview of some emblematic CBS sentinels, sequentially moving forward from subcellular to intermediate to macro scales (Figure 1). The table also pairs the sentinels with existing methodologies for their detection.

Sentinel biochemistry across species

Having common markers facilitates direct comparisons within single and across multicellular organisms, communities, and biomes. They also open the door to assembling system-wide CBS detection strategies. For example, sugars, amino acids, polyamides, lipids, and metabolic byproducts such as reactive oxygen species are common across all living organisms responding to stress.[36] The soil metabolome also reveals tracers associated with warming, for example, saccharides and amino acids accumulating in heated soils that represent an imbalance between primary growth metabolism and protective metabolism in response to physical forcings.[37]

An important stress indicator is a class of lipids called sphingolipids. They are components of membranes that serve as structural and bioactive signaling molecules in organisms ranging from yeast to animals. Recently, they have been identified as signaling molecules for microbial pathogens,[38] anaerobic marine bacteria,[39] and soil bacteria.[40] Sphingolipids in cellular membranes and organ tissues can be synthesized or degraded to modulate cellular responses based on environmental cues. In yeasts they produce potential heat stress signatures.[41] They also have been shown to play a role in human disease.[42] Studies of human intestinal bacteria suggest that the same molecules could also play a role in stress response[43] and in turn modify the epigenome of human cells.[44]

Sentinel organisms and species

The presence or absence of select species/taxa is a relatively straightforward indicator of climate-induced stress. But beyond a simple dichotomy, other informative metrics can be assembled. Four examples are given below, illustrating how different life forms could serve within an omnibus detection system.

Single-celled organisms

Microorganisms constitute the "unseen majority" of lifeforms, well recognized both to produce and consume greenhouse gases, adapt to climate change, and contribute to environmental sustainability.[45] The value of microbes as sentinel measures of climate change, including the monitoring of microbial pathogens and beneficial microbes, has been established.[46] From a microbial perspective, an additional candidate sentinel comprises biofilms, which enable bacteria to survive changing or hostile environments. Biofilm formation in human pathogens is closely associated with infectivity and antibiotic resistance that is already monitored through existing healthcare infrastructure.[47] Biofilm formation in marine bacteria routinely causes large economic losses in a variety of industries.[48] Climate warming also, and obviously, alters the balance of microbiomes in otherwise cold environments.[49]

As another example, microscopic phytoplankton form the base of most freshwater and marine food webs, with a nearly ubiquitous biogeographical distribution. They assimilate both natural and anthropogenic CO_2 and generate >50% of the world's annual oxygen production through photosynthesis, making them important biosentinels owing to their links with global climate, ecosystem productivity, and biogeochemical cycling.[50] Given their short generation times (typically hours to days), phytoplankton are highly responsive to stressors like seasonal heating and episodic weather events that modulate the physical environment and resource availability. Their ecophysiology and species composition react to stress and can be targeted for both short-term (days-weeks: primary production, nutrient availability, and algal bloom formation) and longer-term (months-years: biogeochemical cycling, food web alterations, and acidification) monitoring, as well as over spatial domains from restricted water bodies (lakes and lagoons) to coastal waterways to seas and the oceans using remote sensing.[51]

In urban environments, human pressures from pollution and eutrophication accentuate the stress of warming waters on phytoplankton growth. This provides ideal conditions for the proliferation of additional waterborne sentinels—harmful algal blooms (HABs), hypoxia, and their cascading socioeconomic impairments like shellfish poisoning, closed beaches, and elevated health care costs[52–54] that disproportionately fall on vulnerable populations like coastal fishing communities.[55] In a CBS3 context, phytoplankton could help determine the magnitude and severity of climate sensitivity through tangible outcomes (e.g., monitoring HAB or hypoxia risk) and triggering early warnings across climate-threatened coastlines.

Multicellular sentinel species

A rich variety of multicellular life expands the sentinel playing field based on biochemistry, physiology, and behavior. Amphibians are the metaphorical canaries in the coal mine for environmental sensitivity, having undergone well-documented population declines and extinction events in response to abiotic and biotic stresses.[56] Their permeable skin that is essential for oxygen capture, life cycles in water and on land, and limited dispersal capacity make them particularly vulnerable to climate and habitat shifts, lending themselves to straightforward presence/absence inventories.

Behavioral changes are another organismal response to CBS. Climate change impacts have been recorded on nervous systems through sensory and cognitive determinants of fitness that ultimately drive rapid evolutionary change.[57] Marine species, from benthic invertebrates[58] to cetaceans,[59] have already been used in ecotoxicology assessments as pollution indicators and thus sentinels of risk exposure to humans. Some behavioral responses to CBS can also be detected by monitoring chemicals in the appropriate medium. For example, the persistence and concentration of volatile organic carbon (VOC) compounds normally provide cues for prey location in oceanic primary consumers, but rising ocean temperatures provoke miscues.[57] Yet, overall, the direct links between behavior and its neurocellular and molecular determinants have to date been incompletely explored.[60] This gap in mechanistic knowledge argues for monitoring behavioral change in selected, sensitive organisms as phenomenological evidence for climate stress, similar to the observation of changed swimming behaviors and activity levels in aquatic organisms exposed to river pollution.[61] The phenology of animal behaviors is also a practical CBS sentinel—for example, the seasonal shift in the onset of migration and breeding by short-distance (intracontinental) migrant birds.[62]

Sessile organisms

Stationary lifeforms often have distinct annual growth markers reflecting long-term multi-year or generational climate impacts. Corals, for example, have been used in this way in paleoclimatology studies,[63] capitalizing on their propensity to thrive in narrow, stable thermal ranges close to their upper physiological limits.[64] On land, plants are reliable sessile sentinels. Tree rings are a first and obvious example of using a physiological signature of growth as an indicator of CBS. Across many tree species and forest biomes, heat stress has been linked to declines in tree growth, with the timing and severity of extremes (e.g., early versus late in the growing season) producing physiological signatures of response as recorded in these markers.[65] Heat stress has been linked to histone modification in plants, DNA methylation and the expression of heat-tolerant genes, and additionally epigenetic memory for intergenerational coping capacity for heat stress, produced by both transient and more persistent transcriptions.[66] Plant synthesis of protective biochemicals like antioxidants to maintain cell membrane function is a sentinel of heat stress, as in fruit.[67] In oaks (*Quercus spp.*), heat stress can trigger production of isoprene—a biologically produced volatile organic compound believed to improve thermotolerance—but which can interact with fossil fuel pollutants to create harmful ground-level ozone pollution.[68] The disappearance of particular species, the emergence of pioneer vegetation, or changes in greenness indices following disturbance are imminently observable through ground surveys and remote sensing.[69]

Symbionts as sentinels

Since the 1800s, lichens have been used as biomonitors of environmental stress in terrestrial systems, particularly in the context of air pollution. Lichen symbioses between a fungus and an alga that form perennial multicellular organisms lack some of the protective features of many plants (e.g., cuticle and stomata) and thus can be highly sensitive to environmental conditions[70] like excessive heat.[71] Another potential symbiont sentinel is represented by the links between plants and mycorrhizal fungi, with studies showing that a low diversity of arbuscular mycorrhizal fungi—a key to plant water and nutrient uptake and resistance to stress—is an indicator of climate-disturbed soil.[72]

Synthetic biology, microcosms, and mesocosms

The ability to study complex CBS-relevant phenomena on organisms can be facilitated by controlled experimental systems. These range from mimicking specific environmental conditions in rodent experiments[73] to the use of free-air CO_2 enrichment (FACE) mesocosms in metabolomic and transcriptomic studies.[27] Researchers have even studied synthetic microbial communities in manipulable enclosures.[6] Bioengineering of synthetic microbes holds promise to mimic signaling and responses to stress at higher levels of biotic organization, including in organs and even ecosystems.[6] A relatively unexplored domain of synthetic biology involves thermophilic microbes and the proposed development of a "thermochassis" species[74]—using a microbe to transfer and modify genetic information to yield particular metabolites. Such bioengineered life systems could indicate the fitness of particular molecular biochemistries in response to global warming and extreme heat waves.

Ecosystems as sentinels

Ecosystems are environmental integrators of the subordinate-scale biology associated with individuals and populations. Combined with highly variable natural physical and chemical conditions, these become more-or-less open systems, far less deterministic and potentially more plastic in their response to climate stresses than biochemistry, tissues and organs, and individual organisms (Figure 1).

Microbial communities in soil ecosystems exhibit rapid turnover times and large, diverse populations that enable them to rapidly trigger detectable CBS responses. They also have inherent phenologies that modify their dynamics under climate sensitivities.[75] In turn, plants can use soils as sentinels of change to trigger responses in their own physiological processes.[75] Additionally, through eco-evolutionary feedbacks, interactions among plants and their soil microbial symbionts during periods of CBS result in the production of a variety of chemical compounds and alterations to the physical environment.[37,40]

Much of the world's population—nearly half—resides within today's coastal zones.[14] Estuarine health can be a sensitive indicator of CBS, particularly when combined with indicators of elevated urban water pollution, HABs, hypoxia, public health warnings, and resultant losses to economic livelihoods.[52,76] Wetland ecosystems occupy a relatively narrow band of the coastal zone defined by elevation and tidal inundation, making their spatial redistribution a good indicator of sea level rise.[77] Their soils additionally give a record of longer-term historical change from environmental and anthropogenic factors. In or around urban areas, wetland disappearance or deteriorating condition provides an early warning of sea level rise that can eventually presage damage to built infrastructure.[77]

On land, changes in the transition zones (ecotones) of forest ecosystems are themselves promising ecosystem-scale sentinels. Tree species near the warmer end of their climatic range limit tend to be more sensitive to heat stress than their higher-latitude counterparts and also more sensitive than co-occurring tree species positioned farther away from their climatic range limit.[78] Forests adjacent to non-forested land also tend to experience hotter and drier conditions than the interior of forests, which exacerbates extreme climate impacts.[78] Additionally, urban forests are found to be more sensitive to climate stress than their rural counterparts,[78,79] making them optimal candidates for CBS impact comparison studies.

Regional to larger-scale sentinels

Regional perspectives can provide a useful integration of otherwise innumerable local-scale climate sensitivities. In the urbanized United States (US) Northeast, population growth, land-use change, and economic development create persistent thermal signatures in land,[80] long-lived carbon balances, and water and its ecosystem services, all detectable over the fully regional domain through remote sensing and modeling.[81]

Over still larger macro-regional to continental domains, satellite remote sensing can be used to detect signs of diminished resilience. For example, analyses of the normalized difference vegetation index (NDVI) from satellite imagery[69] was used to quantify the general response of forest productivity to the 2017 summer drought across southern Europe while pinpointing particularly sensitive oaks and forests. Biodiversity monitoring (e.g., species-based inventories) also provides an integrated bio-response to CBS and could serve as a central component of any continental-to-global-scale monitoring effort.[16] Large-scale "biodiversity informatics" projects have arisen in the last several decades to tackle longstanding challenges with developing up-to-date distribution models for key taxa. These include iNaturalist,[82] eBird,[83] and Global Ant Biodiversity Informatics (GABI),[83] which creatively combine data from museums, published literature, and citizen science observations.

Detection of such large-scale shifts in state may be harbingers of even more consequential climate impacts. A recent satellite-based analysis concluded that over 75% of the Amazon has lost some degree of resilience since the early 2000s,[84] with the decline occurring mostly closer to human disturbance and areas moving toward a possible alternative climate-ecosystem regime.[17] Such disturbances can be detected statistically in time series of field observations, remote sensing, surveys, simulated data, and data analytics as early warning signals of approaching tipping points at a range of scales (e.g., Earth system geophysics, ecosystem regime shifts, brain seizures, and market crashes).[85] Across urbanized regions, large-scale greenness change can track the expansion and severity of heat waves from the urban core to "archipelagos."[80] Deep learning algorithms have uncovered commonalities among tipping points drawn from multiple disciplines and can be used to construct early warnings of climate regime change.[86,87]

Emergent properties from multi-scalar and systems modeling

Castiglione et al.[5] describe a strategy for multi-scale biotic modeling. They review simple top-down and process-laden bottom-up approaches to conclude that the integration aspect of

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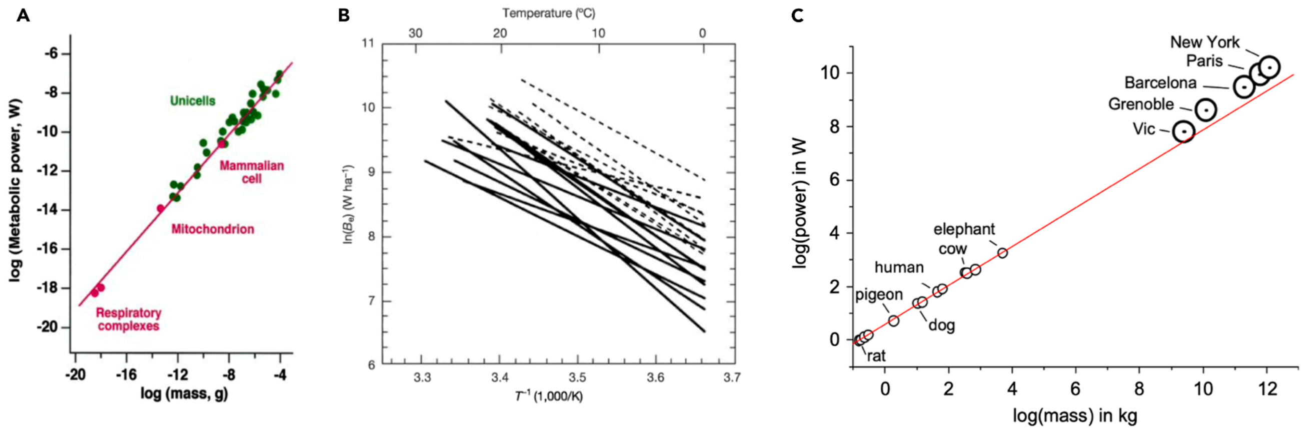

Figure 2. Power law dependencies in biological and social human systems often follow well-defined trajectories, with small-scale complexities subsumed and synthesized into macro-scale behaviors

Gross metabolic relationships often transcend biotic scales from the (A) subcellular[90] to (B) terrestrial ecosystems[91] to (C) urban agglomerates.[92] Careful monitoring of these patterns and their deviation from the original relationship over time could be used to assemble multi-scale aggregate change arising from CBS.

the problem rather than its mechanistic sophistication is essential. They review an alternate "middle-out" strategy that preserves any required complexity necessary to articulate the individual model components while honoring the need for simpler synthesis afforded through the top-down approach. Revisiting earlier notions of how life is organized, in the sense of seeing biomolecules as molecular rule-based computations, this approach has enabled different modalities of biotic stress response to be revealed.[88] These have been tested successfully in scaling from cells to the organismal level in heart and brain research.[4] An understanding of intercellular communication in shaping CBS response can be built using differential equations and cellular automata.[4] Some of these interactions can be captured by existing software that generates networks of these higher-level transformations using kinetics based on foundational biochemical properties of molecules and their binding sites.[4] Allometric scaling, used in many domains of science (Figure 2), subsumes intermediate and lower-level complexity processes that ultimately express themselves as multi-scalar outcomes.[89] This forms a CBS strategy for establishing sentinel-based benchmarks against which deviations over time can be monitored.

The anticipated advances represented by CBS3 will arguably be fueled by AI, just as this new technology has done in the worlds of finance, biomedicine, and complex environmental chemistry, and will make available more than 20 relevant techniques.[93] Protein language models (PLMs), analogous to natural language processing used in machine learning, are based on the likelihood of encountering a particular amino acid at a particular site in a broader sequence and then evaluating the probability of a mutation as a surrogate for fitness.[94] Machine learning with genetic sequencing has also identified biological regime shifts, for example, tracking genetic markers integrated within urban wastewater.[45]

Paleo, historical, and observatory records

Proxy data in the form of sediment cores, palynological, tree ring, and ice core data provide detailed time series records of past climate and linked biological response that can detect regime shifts and tipping points.[26] Dendrochronology and other techniques provide a useful historical perspective on prior climate states.[65]

For more contemporary sentinels, there are well-established programs that support scientific observatories and infrastructure. For example, the National Ecological Observatory Network (NEON) provides highly coordinated data on ecological change for representative terrestrial and aquatic sites across the continental US,[95] producing immediate and publicly available data from flux tower measurements of carbon, nutrients, and water; airborne remote sensing; detailed measurements of soil and aquatic conditions; and standardized protocols for organismal sampling. The National Oceanic and Atmospheric Association (NOAA)'s National Estuarine Research Reserve (NERR) and the National Science Foundation (NSF)'s Long-Term Ecological Research (LTER) also provide a rich observational history of ecosystem-climate data. The National Aeronautics and Space Administration-Global Learning and Observations to Benefit the Environment (NASA-GLOBE) program has developed a 30-year environmental archive using citizen-collected measurements from more than 120 countries.[96] New AI approaches, in particular those that can decipher long-term versus short-term patterns in environmental time series,[97] will play important roles in developing strategies to uncover climate-sensitive patterns from CBS3 archives.

As we described earlier, a single stressor alone may be insufficient to generate a system-level response but becomes significant when linked to other enabling factors, particularly socioeconomic ones (Figure 1). Urban environmental history provides a valuable repository of human responses to social and environmental stress and crisis.[13,98] Narratives of urbanization are replete with illustrations of how stress responses erupt within cities and how pathways emerge in attempts to resolve them. Recognizing explicitly interactions between engineered and social resilience has been the focus of a large international consortium of cities (C40) assembled to improve climate preparedness.[99]

Detecting socioeconomics

Social media and telecommunications have revolutionized our ability to take the pulse of urban society.[100] Such digital information can be used to reveal communication patterns during heat waves, floods, and other emergencies,[101] which can detect an urban population's sentiments, preparedness, and responsiveness to actual climate events. Socioeconomic as well as racial disparities (through redlining in the US and continued patterns of systematic bias) have led to large numbers of people living in arguably less than desirable, climate-sensitive places, simultaneously experiencing high levels of air, noise, and heat pollution as well as crime. These patterns are well-documented in government survey data and financial transactions, which, when coupled with climate change forecasts, are likely to confirm uneven impacts on the poorest and most marginalized groups.[102] A CBS3 could be engineered to identify gradual or abrupt shifts in these societal risks, particularly with changes in climate hazard exposure, frequency, and intensity. Discrepancies in the number of hospitalizations during heatwaves, stratified by neighborhood or socioeconomic conditions, are one such example.[103] A component of a CBS3 could therefore be dedicated to monitoring the state and dynamics of climate justice, including information reported by citizens as part of a transition toward data democratization.[104]

URBAN CLIMATE STRESS TESTS

Stress tests are widely used in the medical and financial fields to identify vulnerabilities that may not otherwise be obvious under "normal" conditions. Based on currently available knowledge, Table S1 suggests that to varying degrees there is an ongoing, universal biotic response to climate change. Signals generated by existing *in situ* and remote sensing studies, biosystem observatories, mesocosms, modeling, and data synthesis appear today sufficient to identify a reasonably representative set of sentinels across different lifeforms, from the subcellular to global biosphere. From this collection and a suitable staging framework (Box 1), we anticipate being able to identify CBS hot spots and moments, commonalities in biotic response, and emergent trajectories of the full system.

How could a CBS3 stress test be implemented? Consider uncovering the impacts of an extreme urban heatwave using the CBS3 framework. Heat stress is among the pre-eminent climate concerns,[12] as urban "heat island" effects have increased rapidly in recent decades and now conservatively affect 1.7 billion people.[11] In Beijing and New York City, socio-ecological frameworks are being used to identify the distribution of urban heat hazards, heat exposure, social vulnerability, and the best allocation of urban green spaces for climate adaptation.[112] An opportunity exists to go beyond such human-centered impacts, uncovering heat stress effects on the many interconnected life forms of the city.

Technology innovation makes possible a vision for just-in-time monitoring and forecasts of potential sources of CBS, their biological responses, and societal feedbacks at the hyperlocal level.[109] We would first apply geophysical information associated with the heat wave. Each day, 100s of terabytes of data shower down upon us from Earth-observing satellites,[80,113] making it possible to monitor the spatial distribution and intensity of extreme weather events based on remotely sensed imagery and *in situ* monitors (Figure 3). In addition, ubiquitous microsensors united through telecommunication networks and meshes[114] can identify urban temperature patterns[115] and air pollution.[116] Citizens experiencing these events can also participate in CBS monitoring through prolific and low-cost sensors. Citizen science platforms, like iNaturalist,[82] can uncover changes in the appearance and relative abundances of species, particularly in cities where routine biological observations by a trained public can be made.[117] These data plus high-resolution weather nowcasts for essential meteorological variables can then be combined with virtual renderings of a city[118] to geolocate hot spots of heat exposure and their attendant biotic and socioeconomic impacts.

The biological components of the CBS search would begin at the subcellular biochemistry level, recognizing that most proteins are marginally stable and therefore may encounter harsh limits under different climate extremes.[119] Machine learning on rRNA gene sequences can make the important distinction between regime shifts and more typical natural fluctuations in microbial communities.[87] Additionally, variations in large protein sequences can be monitored, reflecting differences in fitness conveyed by organismal activity, stability, and structural biochemistry, playing out across diverse life forms (Figure 1).[120] Considering life forms that display behavioral responses, we see special stressors operating in urbanized settings, for example, triggering changes in animal cranial capacity and behavioral plasticity, possibly an attempt to adapt to ever-changing anthropogenic environments.[121] Communication is also affected, as with birds changing their songs in response to environmental changes, increasing their frequency to overcome city noise.[122,123] Humans also express responses communicated through their behaviors and opinions. Online monitoring of urban services like hospitalizations can be coupled with data on CBS-relevant human behavior and sentiment, commutation patterns, and neighborhood-level energy use and economic activity.[100,106]

A PATH FORWARD THROUGH SENTINEL PARTNERSHIPS

Establishing an urban CBS detection system constitutes a quintessential topic for cross-disciplinary collaboration. Notions of networked research partnerships and collaborations[124] become particularly important as CBS surveillance requires a pan-scientific framing.[6,60] Existing and forthcoming community reference databases, like the *Metabolomics Standards Initiative*,[83] can provide keystone metabolite identification.[125] Similarly, within-taxa open-access registries can capture changes in population responses to CBS through time, as has been done for invertebrates and vertebrates.[83] To keep pace with climate change and the massive demographic transition to an urbanized planet now under way,[14] a successful CBS3 needs to capitalize on the success of climate-resilient development, smart cities

Box 1. Digital twins, advanced GIS, and artificial intelligence

Recent advances in observatory capabilities, data analytics, and computational infrastructure enable virtual worlds to be constructed and analyzed. *Digital twins* are particularly promising in the urban planning domain, with several applications already addressing decarbonization, air pollution, optimizing transportation, renewable energy potential, and streamlining city services.[105] Digital representations of the physical setting can be assembled now at cm-scale resolution, yielding highly realistic 3D renderings of a city's built infrastructure (aboveground and subterranean), which, when monitored over time, gives a 4D picture of urban CBS evolution. Onto these digital renderings can be draped a wide array of spatially and temporally coded urban data to quantify the physical, biological, and social infrastructure state. The constellation of sentinels described in this perspective could be derived from ground-based stationary and mobile samplers, remote sensing, field and laboratory experiments, and models of climate extremes and their biotic impacts (Table S1).

Socioeconomic sentinels are secured by deep dives into social media sources, as well as traditional government agency records, financial transactions, traffic and mobility assessments, and opinion surveys.[106] Together, these information resources constitute a multi-dimensional data source that can be analyzed using AI and machine learning (ML) for comprehensive urban climate monitoring.[107,108] Deep learning approaches enable automated classification of urban infrastructure and vegetation from high-resolution imagery with unprecedented accuracy,[109] while ML algorithms detect complex spatiotemporal patterns in sensor networks for predictive enhanced resolution modeling of climate extremes.[108,110] AI-powered digital twins will combine these data streams with dynamic models of urban ecosystem responses under CBS.[111] For biological early warning, relative rates of change and indices normalized to benchmarks will also be highly useful in revealing the places, times, and impacts of CBS on living systems. Applying CBS "scaling laws," via carefully chosen sentinels and recording their departure over time relative to baseline relationships (Figure 3; supplemental information), is also a promising approach.[90–92]

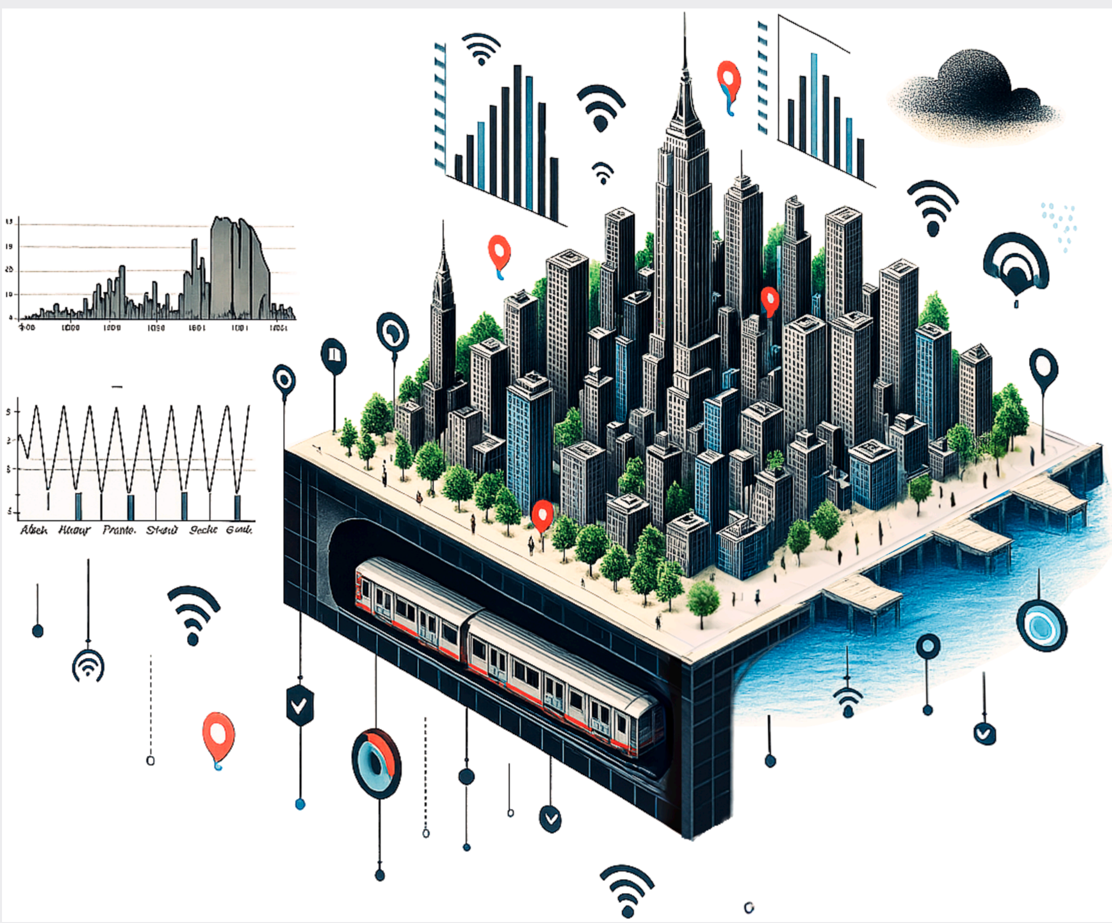

Image courtesy of: P. Setayesh/FloodNet NYC.

technology, urban social equity, circular city economies, and next-generation planning and design initiatives.[13,99]

There, of course, will be numerous obstacles in realizing a functional CBS3. These include the many technical challenges in organizing heterogeneous data collected from intrinsically different sources, for example, *in situ* meteorological variables, species/taxa inventories, on-the-ground microsensors, satellite observations, urban socioeconomic records, or the huge data

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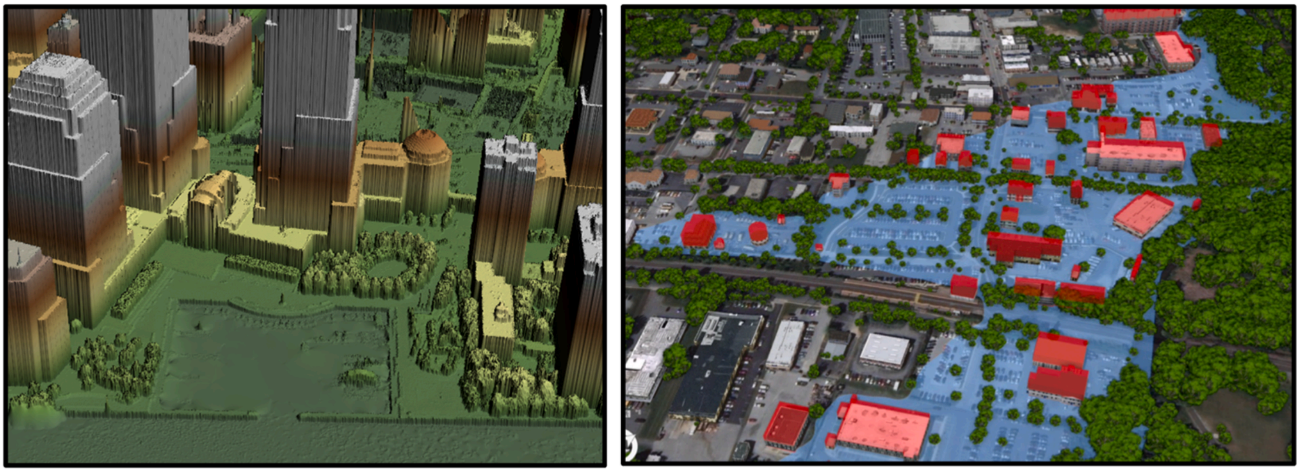

Figure 3. Ultra-high-resolution renditions of cityscapes derived from airborne radar can provide a "digital twin" template (left) for multivariable observations and simulated climate extremes, here, shown for urban flooding (right)
Images courtesy of S.C. Ahearn and H. Ahn, Center for Advanced Research of Spatial Information, Hunter College; K. McMaster (SymGEO).

volumes from genetic sequencing data alone. Harmonizing across distinct time and space scales, with the additional aim of establishing a near real-time CBS3, creates a sizable digital integration challenge, but one with which the science community has successfully grappled.[81,104,126] A CBS-based system would also need to rely on durable collaborations across academia and other technical partners and financial support from government, non-governmental organizations (NGOs), and the private sector. Policy initiatives over the past decade focusing on ecosystem, infrastructure, and community have demonstrated the need for robust, meaningful indicators to assess urban sustainability.[127] Key metrics for policy support are those that can highlight trade-offs, co-benefits, and the effectiveness of interventions (i.e., net positive benefits), which could be integrated directly into the CBS3 framework.[128]

To improve the value of a bioclimatic surveillance system in shaping climate policy per se, ongoing dialog between the research community and policymakers will be essential. Too often, scientific realities are lost in climate debates that have catalyzed political mistrust and stymied action—witness the sluggish, decades-long response to the continuing exponential rise in atmospheric CO_2.[129] Paradoxically, exposure of humans to information on climate change may be the very source for behavioral inaction through neurally based trauma-response mechanisms[57]; thus, studies on appropriate biostress messaging to activate societal response make this a fertile topic for additional study.[130]

CBS planning could in principle fit well into newly established, high-level forums. For example, the United Nations has begun discussions on how best to embed science into the broader sustainable development agenda, in which climate action figures prominently. In 2023, the General Assembly hosted direct scientist-to-policymaker briefings on climate economics, conflict, and human health,[131] and the UN-convened group *Science for Action* was recently established together with the *U.N. International Decade of Sciences for Sustainable Development, 2024–2033*.[132] The CBS3 we describe here would also gain traction by assembling its data outputs into a climate de-risking framework[133] in which anomalous interactions among the sentinels could be detected systematically and routinely reported as early warning signals of sensitive parts of the biosphere. The system could also be cast to better estimate positive and negative externalities of climate response options.[1,2,23] Outputs from such a near real-time bio-surveillance system could also be incorporated more formally into the Intergovernmental Panel on Climate Change (IPCC) process, amplifying its urban climate impact dimensions.[12]

To promote public engagement and policy formulation, CBS3 can follow the lead of integrated, thematic surveillance systems akin to the *Global Carbon Project*, *Global Heat Health Information Network*, and *Global Drought Monitor*.[134] It thus could be trained to identify particularly sensitive or rapidly changing impact areas and highlight emblematic and newsworthy case studies. Postings of annual CBS report cards for researchers, the public, and policymakers would provide timely tracking of the success or failure of climate resilience policies[23] and CBS-related business opportunities[135] across cities.

CONCLUSIONS

We find that responses to CBS are deeply encoded into the mechanics of the biosphere, with many commonalities but also essential differences as we move across the living kingdoms. Developing a climate sentinel system thus constitutes a grand research challenge requiring integration across traditional disciplinary perspectives spanning at least 12 orders of magnitude each in space and time. Numerous technical and operational details remain to be worked out, including sampling protocols, error control, and data integration, which constitutes future work. We propose that the research community is, at the same time, technically ready to adopt a sufficiently broad, initial set of sentinels.

The urban environment, relatively well-contained spatially and with dense legions of people, could also be an ideal testbed for deploying networks of citizen scientists in data collection, curation, and analysis, thus supporting important data access efforts[104] during an era of retrenchment by government observatories. The real challenge will be in system-wide integration, requiring a union of experts in advanced instrumentation, mathematics, information technologies, artificial intelligence, and machine language. Recent international collaborations provide a positive signal that such integration could indeed materialize.

An important, ongoing debate around the global climate challenge centers on mitigation versus adaptation, with broad consensus that we must do both.[1] While intuitive and well-intentioned, we see current investments in climate adaptation per se as a decidedly anthropocentric remedy, driven fundamentally by economics and human well being,[22,34,136,137] as when we climate-proof cities against loss of life and economic casualty or deploy new drought-resistant urban water delivery systems. These human-focused adaptations can indeed benefit other living systems, as when we design tidal surge infrastructure to protect low-lying cities and simultaneously preserve coastal wetlands. However, from a global biospheric perspective, such adaptation responses are highly targeted to and essentially benefit but a single species—humans. In practical terms, the multi-scale complexity of CBS is likely to frustrate foreseeable efforts to design a truly universal climate adaptation strategy, likely stranding huge elements of the natural world and its biodiversity inside a rising tide of climate change.[16]

We simply do not have the current knowledge, technical wherewithal, or financial resources to adapt to climate change across the full spectrum of life, from its fundamental genetics to its role in shaping the biosphere. A long-term commitment to climate mitigation may therefore be the only practicable, all-embracing solution to counter the vast number of climate impacts affecting the biotic kingdoms. Pursuing this long-term strategy can be accelerated by investing in an essential CBS3.

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DECLARATION OF INTERESTS

The authors declare no competing interests.

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