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12-23-2022

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MANTER: Journal of Parasite Biodiversity (ISSN 2470-8224)
Occasional Papers, Number 27, December 23, 2022
doi: 10.32873/unl.dc.manter27
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MANTER: Journal of Parasite Biodiversity

This article has been produced in support of and with appreciation for the efforts by Gábor Földvári of the Institute of Evolution, Centre for Ecological Research, and the Centre for Eco-Epidemiology, National Laboratory for Health Security (both located at 1121 Budapest, Konkoly-Thege Miklós út 29-33, Hungary). Through his untiring efforts, team building, and leadership, he has secured the first EU-wide team research grant. This work was supported by the National Research, Development and Innovation Office in Hungary (RRF-2.3.1-21-2022-00006) and the COST Action CA21170 "Prevention, anticipation and mitigation of tick-borne disease risk applying the DAMA protocol (PRAGMATICK)," which represent the first funded efforts to apply the principles of the DAMA protocol.

The Stockholm Paradigm Explains the Dynamics of Darwin's Entangled Bank, Including Emerging Infectious Disease

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Abstract
Pathogens and their hosts are embedded within the larger biosphere, what Darwin called the "entangled bank." Emerging infectious disease occurs when a parasite "switches" to a new host. Understanding the dynamics of emerging disease requires understanding the dynamics of host-switching, which requires a more general understanding of how the biosphere and its constituent members cope when conditions change. The Stockholm paradigm is an integrative evolutionary framework that describes how living systems cope with change by oscillating between exploiting and exploring the geographical and functional dimensions of their environments. It combines organismal capacity, ecological opportunity, and the repeated external perturbations to the conditions that drive the interaction between capacity and opportunity, catalyzing the dynamics of the entangled bank. The Stockholm paradigm makes clear that emerging disease is an expected outcome of the expression of the same evolutionary potential that governs the response of the rest of the biosphere when conditions change.

Keywords: capacity space, ecological fitting, evolvability, fitness space, host switch, opportunity space, parasite, pathogen

Introduction

> *. . . when a parasite arrives in a new habitat, it will feed on those species whose defense traits it can circumvent because of the abilities it carries at the time.*
>
> Janzen (1980)

Parasitism may be the most common mode of life on the planet (Price, 1980; Brooks and McLennan, 1993). An enormous diversity of organisms lives and feeds on or inside other organisms, sapping energy and nutrients, and sometimes becoming pathogenic. A broad definition includes viruses, bacteria, fungi, protozoans, worms, plant-feeding insects, and plants that parasitize other plants (Nylin et al., 2018). It is safe to say that most species, including parasites, play host to at least one other species that parasitizes it and may cause disease.

An emerging infectious disease (EID) occurs when a parasite colonizes an evolutionarily novel host or an old host that it has not been in contact with for some time. Commonly referred to as *host-switching*, it is fundamentally a result of the interaction between the *capacity* of a given parasite to infect new organisms beyond their current hosts and the *opportunity* to meet these new organisms (Agosta et al., 2010; Araujo et al., 2015; Braga et al., 2018; Nylin et al., 2018; Brooks et al., 2019; Feronato et al., 2021). Traditionally, parasites have been viewed as exemplars of the evolution of specialization—they have highly intimate physiological, morphological, and ecological relationships with their hosts. Parasites *need* their hosts to survive. Combine this with the observation that most parasites are restricted to just a few closely related host species both ecologically (i.e., at a given time or place) and historically (i.e., through evolutionary time) and it is not surprising that many have assumed they are the classic evolutionary "dead end" (Moran, 1988; Wiegmann et al., 1993; Kelley and Farrell, 1998): when the host goes extinct, so does the parasite. The long-standing assumption has been that parasites are in a constant coevolutionary "arms race" with their hosts in which natural selection favors increasing specialization, leaving them with little or no capacity to colonize new hosts (for critical reviews of traditional coevolutionary theory, see Brooks and McLennan, 2002; Janz, 2011).

Yet, the world is replete with examples of parasites colonizing new hosts (Agosta, 2006; de Vienne et al., 2013; Nylin et al., 2018), often closely related to their old hosts and often as a response to a change in conditions that catalyzes the movement of species (Brooks and McLennan, 2002; Hoberg and Brooks, 2008; Agosta et al., 2010; Hoberg et al., 2017; Brooks et al., 2019; Carlson et al., 2022). EID is an emergent property of this larger phenomena of host-switching by parasites. The current EID crisis is the recognition that emerging diseases are increasing in frequency, implying that the capacity for host-switching is large and that the opportunities to do so are common (Brooks and Ferrao, 2005; Brooks et al., 2019).

The Parasite Paradox

If parasites are so highly specialized to their hosts that they lack the capacity to use new hosts, then host-switching and EID should be rare to nonexistent. This is the parasite paradox (Agosta et al., 2010): how do otherwise highly specialized parasites switch to new hosts? The answer is that parasites, like all organisms, maintain the capacity to respond in novel ways when conditions change, using what they have inherited from their ancestors to survive as best they can, including switching to new hosts (Agosta et al., 2010; Brooks et al., 2019). The assumption that high host specificity is synonymous with a lack of capacity to colonize new hosts fails to recognize that (1) parasites are specialized on *specific resources* not specific species, (2) these resources may be phylogenetically conserved across a wider array of species than the ancestral hosts, and (3) parasites have the capacity to use *any* species that contain the specific resource if given the opportunity (Brooks, 1979; Janzen, 1979, 1980; Brooks and McLennan, 1993, 2002; Agosta, 2006; Brooks et al., 2006; Agosta et al., 2010; Araujo et al., 2015; Malcicka et al., 2015; Nylin et al., 2018; Brooks et al., 2019; Boeger et al., 2022). In the case of SARS-CoV-2 and COVID-19, all mammals possess the angiotensin-converting enzyme 2 (ACE2) receptor that is the entry point for infection, and it is not surprising that it moved from its ancestral bat hosts to other mammals, including humans, when given the opportunity (Brooks et al., 2020; Low-Gan et al., 2021; Boeger et al., 2022; Ruiz-Aravena et al., 2022).

The key to understanding EID lies not in understanding how the evolution of host specialization restricts host use but in understanding how and under what conditions host-specific parasites colonize new hosts (Agosta et al., 2010; Araujo et al., 2015; Braga et al., 2018; Brooks et al., 2019). The issue is part of a more general evolutionary question: how can an organism that evolves the capacity to function under one set of conditions keep functioning when those conditions change? The short answer was provided by Darwin more than 160 years ago: it uses the information it inherited from its ancestors, which contains the potential to do something new, like switch to a new host. If this were not true, EID would not occur.

Parasites and their hosts are embedded within the larger biosphere. Understanding the dynamics of EID amounts to understanding the more general evolutionary problem of how organisms use the limited information they inherit to cope with unpredictable changes in their surroundings (Brooks et al., 2019; Agosta and Brooks, 2020). The core mechanism is "ecological fitting in sloppy fitness space" (Agosta and Klemens, 2008), a key piece of a larger theoretical framework—the Stockholm paradigm (SP)—that explains the overall evolutionary dynamics of the biosphere and how it responds to change (Brooks et al., 2014; Hoberg et al., 2015; Hoberg and Brooks, 2015; Hoberg et al., 2017; Brooks et al., 2019; Agosta and Brooks, 2020). From the perspective of the SP, it becomes clear that *EID is an expected outcome of the same Darwinian dynamics and expression of the same evolutionary potential that governs the response of the rest of the biosphere during periods of environmental change*.

The Stockholm Paradigm: Coping with Change by Changing

The SP describes the integration of the capacities for organisms to engage functionally with the environment, the ecological opportunities to use those capacities, and the repeated perturbations to the conditions of life (e.g., climate change) that drive the interaction between capacity and opportunity and catalyze evolutionary diversification and complexity in living systems (Brooks et al., 2014; Hoberg et al., 2015; Hoberg and Brooks, 2015; Hoberg et al., 2017; Brooks et al., 2019). Although only recently proposed as a synthetic framework, the SP has been under construction since 1859 when Darwin published the first edition of *On the Origin of Species* (Agosta and Brooks, 2020). He presented two major metaphors for his grand theory of "how nature works": the tree of life, depicting the selective accumulation of biodiversity and its evolutionary history of common descent, and the entangled bank, portraying the interactions among biodiversity that give rise to our modern notion of complex ecosystems. The entangled bank is the "interaction arena" where the members of the tree of life coexist, competing, cooperating, predating, and parasitizing each other.

At any given moment, the entangled bank is a snapshot of a dynamic evolutionary system with the central question being how such systems and their constituent members persist in the face of constant change (Agosta and Brooks, 2020). Coupled with the tree of life, it represents the interplay between evolutionary history and the current ecological conditions, from which emerges natural selection and the interacting web of biodiversity that we observe. This web comprises individual organisms, each with inherited capacities to interact with and engage functionally with the surroundings, including parasitizing other organisms. Understanding "how nature works" means understanding how the members of the tree of life interact to form the persistent entangled bank that characterizes the biosphere. This requires building an explanatory framework from the level of *inheritance systems* (individual organisms, populations, and species) to the emergent level of ecosystems.

Part 1. How Individual Inheritance Systems Cope with Change

For much of human history, species were largely thought of as static—the species we see today have always been here, and their characteristics that seemingly match their environments so well are evidence that they are "perfectly fit" to their surroundings. Lamarck (1809) was the first person to seriously challenge the notion of immutable species. In essence, he argued that organisms were able to evolve directly and instantaneously to changes in their surroundings, with the environment somehow driving them to get better by producing "the right adaptation at the right time." Darwin showed that this notion of evolution was wrong. He summarized his views succinctly in the second paragraph of the final edition of *Origin of Species* (1872; my boldface):

> *. . . there are two factors [in evolution]; namely, the* ***nature of the organism*** *and the* ***nature of the conditions****. The former seems to be much more important; for nearly similar variations sometimes arise under, as far as we can judge, dissimilar conditions; and, on the other hand, dissimilar variations arise under conditions which appear to be nearly uniform*

Contrary to Lamarck, Darwin rejected the notion that the environment, or "nature of the conditions," was the driver of evolution. Instead of viewing the surroundings as a creative force that "pushes" or "pulls" organisms to "get better," he viewed it as the arena into which organisms imposed themselves, using the informational capacities that they inherited from their ancestors to survive and reproduce as best they can, given the current conditions. Thus, he recognized the primacy of what he called the "nature of the organism" in evolution, and that evolution was the result of the outcome of the interaction between organisms, with their inherited capacities, and their environments, which were always changing. From this emerged *natural selection*.

Nature of the organism: metabolism plus inheritance

Organisms are cohesive functional wholes with the informational capacity to impose themselves on their surroundings in ways that facilitate survival and reproduction (Collier, 1988, 1998, 2003; Collier and Hooker, 1999). Most fundamentally, they are *combined metabolic-inheritance systems* (Gánti, 1979, 2003; Maynard Smith and Szathmàry, 1995) with the ability to both *exploit* and *explore* their environments (Brooks et al., 2019; Agosta and Brooks, 2020). Organisms use metabolism to stay alive, exploiting their surroundings as best they can with their inherited capacities and "buying" the time for reproduction to occur. Inheritance is how organisms extend themselves through time, exploring their surroundings through the production of highly similar but variable offspring. The combined metabolic-inheritance system is a functional whole with the information encoded in inheritance specifying the metabolic system, and with metabolism fueling inheritance.

Organisms are also historical entities. They form "communities of descent" with shared evolutionary history, represented by the tree of life. Organisms retain so much of their history in inheritance that common descent is always the predominant explanation for their current form and function, not the surroundings. If fruit flies are reared in the wild or in a glass bottle in a laboratory, the result is still fruit flies. The primacy of the *nature of the organism* over the *nature of the conditions* stems from four fundamental aspects of inheritance:

(1) Inheritance is highly conservative. While the inheritance system is open to change through genetic mutation, duplication, recombination, and so forth, it is highly constrained by the requirement for functional integration with the rest of the system.
(2) Inheritance produces indefinite variation. Despite its conservative nature, because of genetic mutation, imperfect copying, duplication, and recombination, all offspring are highly similar but unique. Even clones are not identical (Cepelewicz, 2020).
(3) Inheritance is highly historical. While each organism is unique, each bears a strong resemblance to their relatives. Some of these resemblances are truly ancient, like the Hox genes that specify development of metazoans.
(4) Inheritance is superfluous. Organisms produce as many offspring as possible *without regard for environmental conditions*. Therefore, there is frequent reproductive overrun, with the production of many more offspring than the environment can support.

Conservative inheritance means that history will always be the dominant causal explanation for the present in biological systems, and that a "perfect fit" between organisms and their constantly changing environments can never be achieved. Because change in the inheritance system is highly constrained, there is an inherited *evolutionary lag-load* (Maynard Smith, 1976) or *phylogenetic constraint* (Brooks and McLennan, 2002) that makes it impossible for organisms to simply evolve new capacities in the moment change occurs. Instead, as Darwin recognized, evolution requires a constant supply of preexisting variation. When the first tetrapods transitioned from water to land, for example, all the necessary traits needed for surviving on land, including lungs for breathing air, limbs for walking, and eggs capable of surviving buried in soil, had already evolved in the aquatic environment (Skulan, 2000; McLennan, 2008).

The superfluous reproduction of variable but highly similar offspring without regard for the conditions produces Darwin's "necessary misfit" (Brooks and Hoberg, 2007). The combination of reproductive overrun and conservative inheritance guarantees an imperfect fit between organisms and their environments, but within this imperfect fit lies the potential for coping with future change (Agosta and Brooks, 2020). If all organisms were "perfectly fit" to the current conditions, there would be little capacity to respond when those conditions change. For Darwin, "adaptation" was the process of coping with change by using preexisting capacities to survive as best as possible, reinforced by natural selection in the new conditions. Natural selection emerges from Darwin's necessary misfit and is proportional to the amount of mismatch between organisms and their surroundings (Brooks and Hoberg, 2007).

Life's only discernable "goal" is continued survival. This is fueled by metabolism but achieved through reproduction and inheritance. The information contained within the inheritance system specifies the development of a new organism including the metabolic system and other capacities to engage functionally with the environment (Collier, 1988, 1998, 2003; Collier and Hooker, 1999). Metabolism allows organisms to exploit the environment long enough to reproduce, but inheritance is what allows the exploration of variable and changing conditions (Agosta and Brooks, 2020). Inheritance is the essence of being evolvable.

To be a good exploiter requires functioning well enough in the current conditions. To be a good explorer requires being able to cope when those conditions change (Kováč, 2007; Popadiuk, 2012). To be evolvable, organisms need to be able to do both (Brooks et al., 2019; Agosta and Brooks, 2020; and see Page, 2011; Popadiuk, 2012). At first this might seem a paradox: there is a long history of assuming an evolutionary tradeoff between being especially good at

doing one thing (specializing) and being able to do multiple things (generalizing). The assumption is based on the premise that in the evolution of specialization, natural selection whittles variation down to such a degree that species (inheritance systems) lose the capacity to do anything else, like colonize a new host. This perspective fails to recognize that the capacity for exploration emerges and grows naturally in living systems because of the conservative but evolvable nature of the inheritance system and despite persistent natural selection for better-performing variants (Agosta and Brooks, 2020).

A conservative system of indefinitely growing capacities

Compared to metabolism, the portion of the lifetime energy budget of an organism allocated to inheritance is very small. Reproduction requires only a small fraction of the metabolic budget because replication is a recycling process of "copy from a template, rinse and repeat" and because producing gametes is inexpensive compared to maintaining an organism throughout its lifetime. Staying alive amounts to staying organized, and this is very expensive and ephemeral in an entropic universe governed by the second law of thermodynamics (Lotka, 1913, 1925; Schrödinger, 1945). But producing offspring is relatively cheap and persistent (Brooks and Wiley, 1988; Agosta and Brooks, 2020). This means that once the combined metabolic-inheritance system emerged, evolution was both highly "affordable" and probable given the routine overproduction of similar but varied propagules.

The relatively low cost of reproduction is critical for evolution, but the inherent nature of the information in the inheritance system is what produces the indefinite variation and capacity to respond when conditions change. First, mutation coupled with mistakes during replication (imperfect copying) provide a background source of de novo variation. Second, the information encoded by DNA is both digital and combinatorial. Organisms are cohesive analog wholes, but they are *digital replicators* from which the information encoding for a new organism can be recombined and read at multiple levels of the genome and at multiple times. This generates the potential for an enormous amount of information, both expressed and unexpressed, to be stored in inheritance systems (Brooks and Wiley, 1988; Smith, 1988, 1998, 2000; Maynard Smith and Szathmáry, 1995, 1999; Szathmáry, 2000, 2015; de Vladar et al., 2017). There are, of course, constraints that arise from correlations between parts of the integrated system, including molecular affinities, cell-to-cell adhesion, genetic correlations, mate recognition systems, and symbiosis (Brooks and Wiley, 1988). If, for example, one gene requires another gene to function, then the potential information (variation) that could be expressed by inheritance is constrained. If one species requires another species for survival, then entire genomes are linked, again constraining the information that can be expressed. But despite these constraints, digital replication generates enormous amounts of variation that is the source of the preexisting capacities that evolution relies on when conditions change (Brooks and Wiley, 1988; Smith, 1988, 1998, 2000; Maynard Smith and Szathmáry, 1995, 1999; Szathmáry, 2000, 2015; de Vladar et al., 2017).

Third, as the inheritance system evolves and diversifies (Figure 1), the information contained within it expands and so does the *difference* between the information that is expressed—"what's realized"—and the information that could be expressed—"what's possible"—at any given time (Brooks and Wiley, 1988; Brooks and Agosta, 2012; Agosta and Brooks, 2020). As Darwin recognized, "diversity begets diversity"—in an expanding system of accumulating information/variation/capacities, the realization of one possibility always produces new possibilities. In this way, life creates and grows its own *capacity space* to explore, or what Ulanowicz (1997) called the "window of vitality." Capacity space represents a realm of possibilities, with an abstract space proportional to the difference between *realized capacities* and *potential capacities* to engage functionally with the environment (Figure 1). This difference is tantamount to *evolutionary potential*. The greater the difference between "what's realized" and "what's possible," the greater the potential for the inheritance system to do something new, like switch to a new host, when conditions change (Brooks and Agosta, 2012; Agosta and Brooks, 2020).

Upon life's inception, it had some minimal but sufficient capacity to achieve some minimal but sufficient level of functional engagement with the surroundings (Moreno and Ruiz-Mirazo, 2009). In this moment, life emerged as a combined metabolic-inheritance system capable of exploiting the surroundings long enough for reproduction and evolution to occur, thereby catalyzing the growth of the capacity space that it continues to explore. While the buildup of historical constraints (genetic correlations, mate recognition systems, symbiotic relationships, etc.) in the inheritance system slows the overall rate of growth of diversity over time (Figure 1), the difference between potential capacity and realized capacity continues to grow. This is the Brooks-Wiley dynamic (Brooks and Wiley, 1988), and it guarantees that as evolution unfolds, "what's realized" will be an ever smaller subset of "what's possible" *regardless of persistent natural selection for better-performing variants*. From this perspective, the risk space for host-switching and EID is truly large and indefinite (Brooks and Ferrao, 2005; Brooks et al., 2014, 2019; Boeger et al., 2022).

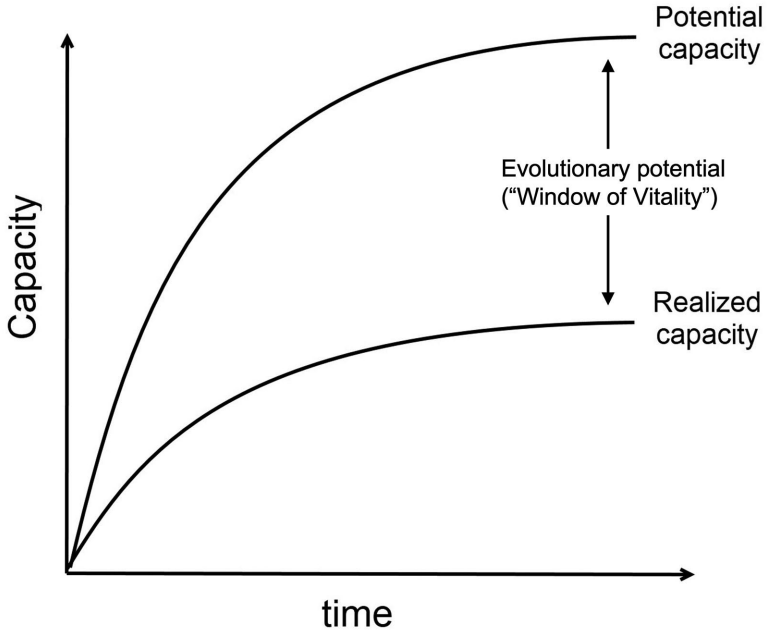

Figure 1. The Brooks-Wiley dynamic. As evolution unfolds and life diversifies, the realized capacities for organisms to engage functionally with their surroundings grow. The realization of one possibility always gives rise to new possibilities, so the potential for new capacities grows in tandem. The difference between realized and potential capacity equates to evolutionary potential, the "Window of Vitality" where reproduction and survival could occur, and it too grows as the system evolves. While the growth of all three components is indefinite, the rate of growth slows over time because of the buildup of historical correlations in the inheritance system (e.g., genetic correlations that constrain the expression of information). Modified from Agosta and Brooks (2020).

A conservative system of retained evolutionary potential

The growth of capacity space as evolution unfolds is indefinite but not unlimited. The conservative nature of inheritance produces extremely high levels of historical cohesion in biological systems. As previously mentioned, as a system expands, cohesive forces form constraints that slow the expansion. For example, gravity acts as a cohesive force that slows the expansion of the universe, allowing for the emergence of structures like stars, planets, and galaxies. In biology, the demand that all parts of the system be functionally integrated plays an analogous role (Brooks and Wiley, 1988). The essential point is that, while the inheritance system is open to change, it is severely constrained by the requirement for functional integration with the rest of the system. This is the reason that the concept of "selfish" genes driving evolution (Dawkins, 1976) is largely irrelevant—once integrated into an inheritance system, genes are part of a larger functional whole.

Across the biological hierarchy, historical correlations among various parts of the combined metabolic-inheritance system build up as evolution unfolds (Brooks and Wiley, 1988). This is the "cost of integration" and places severe constraints on both the rate of evolution and the realm of possibilities that evolution can explore. At the same time, it also facilitates evolution by lowering the "cost of innovation" in two key ways. First, conservatism significantly reduces the threshold for generating novel information because inheritance mainly recycles and recombines old information (Jacob, 1977; Gould and Lewontin, 1979; Gould and Vrba, 1982; Janzen and Martin, 1982; Brooks and McLennan, 2002; McLennan, 2008). The ability to co-opt and combine preexisting traits for new functions alleviates the inability to simply produce the "right adaptation at the right time" in response to change.

Second, conservatism slows down the entire evolutionary process. While severely limiting on one hand, this "buys time" for preexisting parts of the system to meet and become integrated into a new functional whole (Maynard Smith and Szathmáry, 1995; Brooks and Agosta, 2012; Agosta and Brooks, 2020). Conservative inheritance "stores history" long enough to produce a constant and growing lag between "what's possible" and "what's realized" for living systems (Figure 1). Because inheritance is conservative, no living system can be perfectly fit to its current conditions. And this is key to continued survival. Persisting indefinitely relies far more on having the potential to cope when conditions change and far less on how fit an inheritance

system is to the current conditions. For the SP, the essential point is that all inheritance systems retain this potential to some degree (Agosta and Brooks, 2020), even host-specific parasites (Agosta et al., 2010; Brooks et al., 2019).

Nature of the conditions: opportunities in sloppy fitness space

The capacity to exploit and explore emerges from the "nature of the organism," but the opportunities to do so are a function of the conditions in which organisms find themselves. The "nature of the conditions" gives rise to *opportunity space* where organisms find chances for survival dependent on their inherited capacities to exploit and explore (Brooks et al., 2019; Agosta and Brooks, 2020). For a given species, only a subset of the global opportunity space for the biosphere is available for survival and reproduction. This subset of opportunity space available to any given species is its *realized opportunity space* or what is more commonly referred to as *fitness space*.

Fitness space emerges when capacity space is imposed on opportunity space (Figure 2). Fitness describes how well organisms cope with their surroundings; fitness space, therefore, is analogous to "niche space" and represents the set of conditions in which survival and reproduction can occur (Hutchinson, 1957). Organisms are "fit" for any conditions in which they have the capacity to survive and reproduce. The fundamental demographic of evolution is not "survival of the *fittest*" but "survival of the *fit*" (Brooks and Agosta, 2012; Brooks et al., 2019; Agosta and Brooks, 2020). If only a single or few fittest variants survived, the stock of standing variation for evolution to act on when conditions change would be very small. There would be little potential to respond because today's fittest variant may not be fit at all in the new conditions, leaving little room for inheritance to explore new options in fitness space. Fortunately, survival does not require being the absolute best, it requires only being *good enough* to cope with the conditions at hand. All organisms that reproduce are fit, and while some are fitter than others, they all compose a *fittest collective*—a distribution of variants with adequate capacity to survive the current conditions. This fittest collective includes a range of variants—a genotypic-phenotypic distribution—that represent the evolutionary potential to cope when conditions change.

The need to achieve positive fitness dictates that organismal capacity must always complement ecological opportunity, but it does not need to perfectly match (Agosta and Brooks, 2020). Moreover, capacity cannot perfectly match opportunity because conservative inheritance ensures that evolution always lags behind the conditions (Maynard Smith, 1976), while also storing a history of past success.

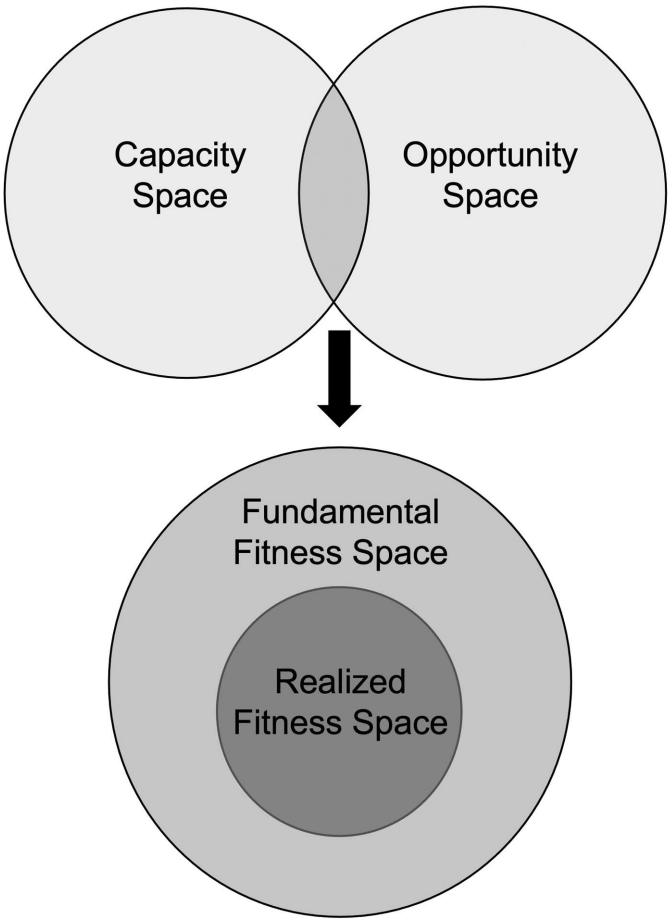

Figure 2. Fitness space emerges from the interaction of organismal capacities to engage functionally with the environment—capacity space—and the ecological chances to use those capacities—opportunity space. The difference between what organisms are doing to survive and reproduce—realized fitness space—and what they could be doing—fundamental fitness space—makes fitness space inherently "sloppy." Modified from Agosta and Brooks (2020).

Conservative inheritance therefore all but guarantees that fitness space will be "sloppy" (Agosta and Klemens, 2008) not tightly optimized to any particular set of conditions. The sloppiness is proportional to the difference between *realized fitness space*—what organisms are currently doing to survive and reproduce—and *fundamental fitness space*—what organisms could be doing if given the opportunity (Figure 2). And this difference is proportional to the capacity to cope with change.

To be evolvable, all species including parasites must maintain an inheritable difference between the actual and the possible in fitness space. This appears to be a universal feature of life emerging from the conservative but mutable nature of the organism (Brooks and Wiley, 1988; Agosta

and Klemens, 2008; Daniels et al., 2008; Brooks and Agosta, 2012; Soberon and Arroyo-Pena, 2017; Agosta and Brooks, 2020). This is how the collective biosphere has coped with constant change over the past 4 billion years.

Darwinian conflict resolution in sloppy fitness space

Understanding how species mount an initial response when conditions change is key for managing EID (Brooks et al., 2019). It boils down to a more general understanding of the dynamics of inheritance systems in sloppy fitness space (Agosta and Brooks, 2020). Since organisms will produce as many highly similar offspring as possible regardless of the conditions, reproductive overrun is inevitable. This produces Darwin's constant "struggle for survival," routinely putting organisms in *conflict* with their surroundings, including other organisms. Superfluous reproduction means that all inheritance systems may grow too much and become *victims of their own success*. If the conditions change, they may also become *victims of circumstance*. Both cases trigger *Darwinian conflict resolution* (Agosta and Brooks, 2020).

Darwin recognized that a constant "struggle for survival" was an inescapable feature of life, but for natural selection to produce the accumulated biodiversity composing the tree of life and coexisting in the entangled bank, there must be a persistent mechanism for resolving this conflict. This begins by organisms using inherited information to explore new opportunities in fitness space. Known as *ecological fitting* (Janzen, 1985), this is the general mechanism behind host-switching and the default response for all living systems when conditions change (Brooks and McLennan, 2002; Agosta, 2006; Brooks et al., 2006; Agosta and Klemens, 2008; Agosta et al., 2010; Araujo et al., 2015; Malcicka et al., 2015; Braga et al., 2018; Brooks et al., 2019; Agosta and Brooks, 2020). The capacity for ecological fitting emerges from phylogenetic conservatism (Brooks and McLennan, 2002) and other related universal aspects of inheritance, including phenotypic plasticity (West-Eberhard, 2003) and evolutionary trait co-option (the ability of existing traits to be co-opted and combined in novel ways to perform novel functions) (McLennan, 2008).

The capacity for ecological fitting affords inheritance systems critical degrees of freedom for coping with changing environments by exploring new options in under-used, less preferred, or previously inaccessible portions of fitness space. The capacity to *move away* from portions of fitness space that are densely populated, deteriorating, or disappearing into new portions of fitness space is key to indefinite persistence (see, e.g., paleontological studies by Stigall et al., 2107, 2019; Stigall, 2019), even if this leads to reduced fitness. In evolution, being fit is what matters; a marginal existence is better than not existing. *Ecological fitting in sloppy fitness space* is how life continues to apply what Agosta and Brooks (2020) called "biological assumption zero": organisms will do what they can, where they can, when they can, within the constraints of evolutionary history (inheritance) and ecological opportunity.

Reproductive overrun of highly similar offspring means there will always be a tendency for inheritance systems to be specialized in regions of highly preferred fitness space, implying the under-use of more marginal but still survivable regions (Figure 3a). When conditions are stable (e.g., when a parasite is isolated with a single host species), exploiting the surroundings as much as possible takes precedence over exploring them. During these times, conditions are largely predictable, allowing many variants to survive and reproduce by doing much of the same thing again and again, exploiting as much energy and materials as possible to make as many offspring as possible, with natural selection favoring fitter variants but with all variants that are fit enough surviving. What happens when conditions change? Exploration of new opportunities for survival becomes paramount. Inheritance systems begin to spread out in fitness space, becoming more generalized as preexisting variation "wanders" into more marginal or previously inaccessible parts of it (Figure 3b, c). Extinction occurs when an inheritance system runs out of options in fitness space, when its capacity no longer complements opportunity.

Within the SP, "specialist" and "generalist" are not nouns describing the static traits of static species but verbs describing dynamic states of inheritance systems within fitness space (Agosta and Brooks, 2020). All inheritance systems have the capacity to become more specialized or generalized in their fitness space, and, moreover, all have the capacity to oscillate between these states depending on the conditions. Species that are specializing in fitness space, in fact, have more potential to respond to a change in their conditions than those that are generalizing because they have more sloppy fitness space. Specializing in fitness space is an indicator of *evolutionary potential being stored* when conditions are stable. Generalizing in fitness space is an indicator of *evolutionary potential being spent* when conditions change (Agosta and Brooks, 2020).

Ecological fitting provides the means for inheritance systems to explore "what's possible" when the conditions change. But by itself, this only fills fitness space. Once filled, realized fitness space equals fundamental fitness space, leaving no more possibilities to explore. The propensity for organisms to exploit their surroundings as much as possible predominates, producing new conflict with no

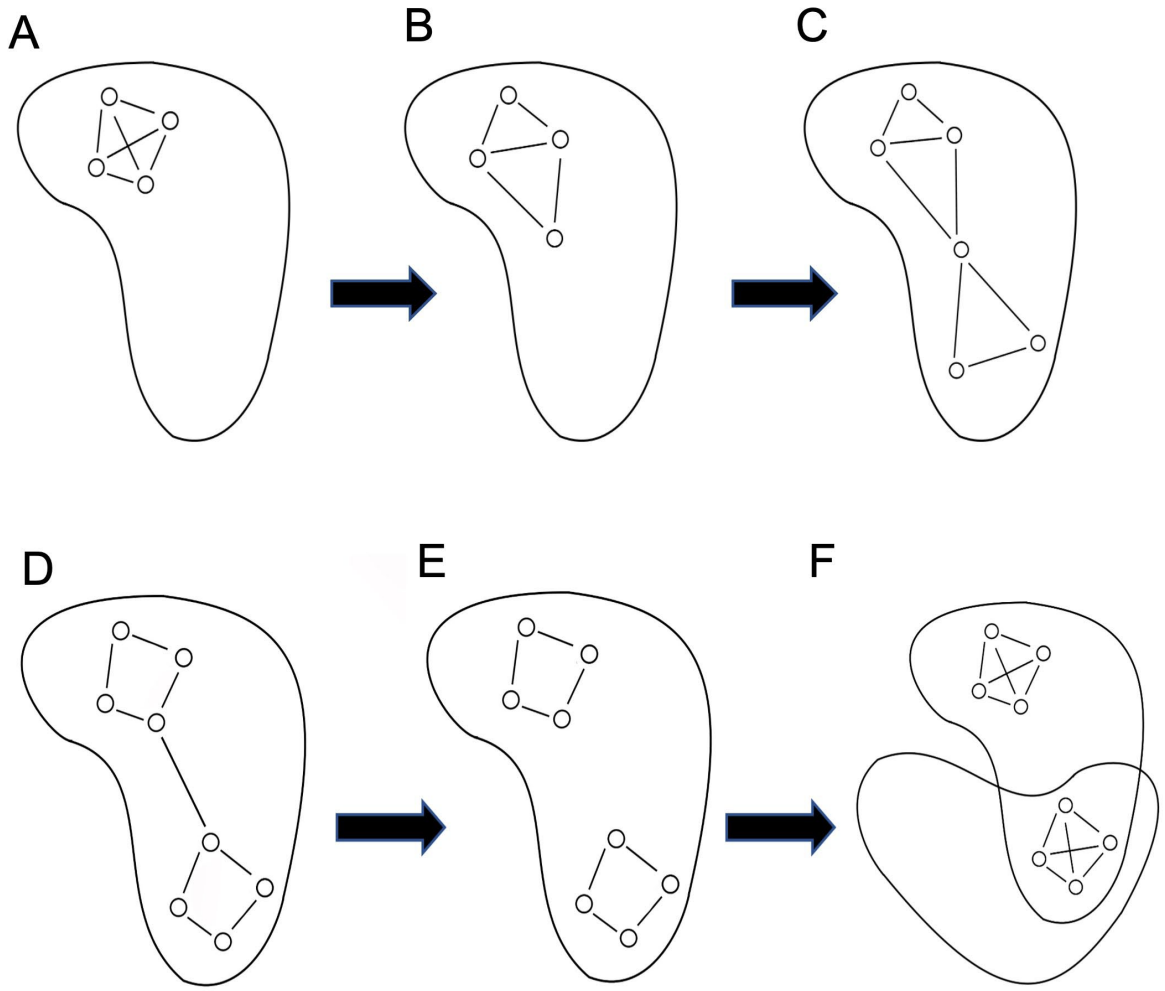

Figure 3. Darwinian conflict resolution in sloppy fitness space. The outer shape represents the fitness space of a single inheritance system. Circles represent members of the inheritance system, and lines represent connections between them; the number of connections indicates how cohesive and isolated members of the system are in fitness space. (A) When conditions are stable, preferred portions of fitness space are exploited as much as possible, causing inheritance systems to become more connected and *specialized* in isolation. (B, C) When conditions change, conflicts in fitness space manifest as a "struggle for survival," leading some members of the inheritance system to *move away* and explore new opportunities for survival, causing the system to become more disconnected and *generalized* in fitness space. (D, E) Exploration leads to the exploitation of local conditions, producing diverging subsystems, each specializing in a different part of fitness space. (F) Selection for increased cohesion with local conditions leads to speciation, producing a new inheritance system with its own fitness space, including an overlap with the original inheritance system resulting from common ancestry. Modified from Agosta and Brooks (2020).

possibility of resolution. While critical for the initial response to change, ecological fitting alone does not produce the selective accumulation of diversity represented by the tree of life and coexisting in the entangled bank. Conflict resolution requires an additional mechanism that results in previously linked subgroups permanently splitting into two or more novel inheritance systems (Figure 3d–f). When a recently generalized inheritance system becomes isolated in a new part of fitness space, selection for cohesion or *co-accommodation* (Brooks, 1979) with the new environment, including other organisms, leads to increased functional integration and increased connections within the subsystem as it becomes more specialized in its new portion of fitness space (Figure 3d). Through speciation, this may produce a newly emergent inheritance system with its own fitness space (Figure 3f). At this point, the original conflict has been resolved by diversifying and co-accommodating with the new conditions, but because the nature of the organism always predominates, conflict resolution always leads to new conflict.

Darwinian evolution is an iterative process of conflict and conflict resolution (Agosta and Brooks, 2020). Diversity accumulates rather than replaces itself because the criterion for indefinite persistence is simply to be good enough to reproduce (it is survival of the *fit*) and because each bout of conflict resolution sets the stage for new conflict. Evolution is *conflict resolution by ecological fitting in sloppy fitness space, followed by co-accommodation with the new conditions, all reinforced by natural selection*. The fuel that drives this forward is the potential emerging from preexisting capacities to first explore and then exploit new opportunities in fitness space. When conditions are stable, living systems build this potential. When conditions change, this potential is spent. Generating, maintaining, and deploying this potential is the key to individual inheritance systems coping with change, and for our purposes, is the fundamental source of EID (Brooks et al., 2019).

Part II. How Ecosystems Cope with Change

Within the SP, basic Darwinian evolutionary dynamics played out in the context of sloppy fitness space explain how individual inheritance systems, including host-specific parasites, explore new opportunities for survival when conditions change. The recent modeling work of Araujo et al. (2015), Braga et al. (2018), and Feronato et al. (2021) provides a quantitative demonstration of this exploration of infection opportunities in the context of parasites switching to new hosts. But this is only part of the story. The context of the EID crises is the interconnected web of ecosystems—the entangled bank—that comprises the biosphere and that we depend on for survival and have the capacity to alter in ways that favor EID (Brooks et al., 2019). Understanding EID as a phenomenon related to global change requires a broad evolutionary framework that describes how the collective biosphere responds when it is perturbed (Brooks and Ferrao, 2005; Hoberg and Brooks, 2008; Agosta et al., 2010; Brooks et al., 2014; Hoberg et al., 2015, 2017; Brooks et al., 2019; Boeger et al., 2022).

In the early 20th century, some believed that the entangled bank was a "superorganism"—a single entity composed of individual species working together for their collective survival, like a colony of bees or the cells that compose organisms. This view was advanced most prominently by Clements (1905, 1916). Unlike a colony of bees or a multicellular organism, however, the species that make up ecosystems do not share a singular inheritance system. Therefore, the assemblage of species that compose an ecosystem cannot be an "organism" (Tansley, 1935). Each member of an ecosystem works toward its own survival using the capacities it has inherited, including the capacity for ecological fitting. As each member degrades the surroundings to meet its own requirements, it alters the surroundings in such a way—from producers to consumers to decomposers—that converts them into new biomass that may meet the functional needs of other members. Within ecosystems, otherwise independent inheritance systems are therefore linked by a complex set of trophic interactions, with each species ensuring its own survival by indirectly providing the means for other species to survive. Each organism's fitness space represents potential fitness space for another organism; the sheer diversity of parasites exemplifies this.

Ecosystem function is an emergent property of each member's activities, each with its own inherited capacities to exploit the current conditions as best it can. Ecosystems are therefore "centers of exploitation" for their constituent members—places where organisms use metabolism to stay alive long enough to reproduce while also retaining the capacity to explore new opportunities when conditions change. This gives rise to a *collective evolutionary potential stored within ecosystems*, or what Agosta and Brooks (2020) called an *evolutionary commons*. When perturbed, expression of the evolutionary commons may result in ecological rewiring of trophic connections within ecosystems (e.g., host-switching), but on a large enough scale perturbations may cause ecosystems to break apart. When this happens, the capacity for ecological fitting stored within the evolutionary commons means there is the potential for new ecosystems to form out of the remnants of the old.

The evolutionary commons makes the biosphere extremely robust and resilient to perturbations, not fragile as some have assumed. This has dual implications for humans. No matter how much we perturb it, the biosphere is unlikely to collapse. After all, the aftermath of each great mass extinction event has been *mass evolutionary renewal*, the production of new biodiversity emerging from the species that survived. At the same time, since the biosphere is indifferent to the fate of any given species, the expression of the potential stored in the evolutionary commons may not always work in our favor. The ecosystems we depend on may disappear or change too much to support our survival, or they might give rise to the next EID. Understanding how the potential stored in the evolutionary commons is expressed when the biosphere is perturbed is the key to assessing the risk space for EID in a period of global change (Brooks et al., 2019). To do so requires going beyond explaining the dynamics of individual inheritance systems in a relatively stable, unchanging fitness space.

What happens when external perturbations change the nature of the conditions so much that the dimensions of fitness space itself change for multiple inheritance systems, including entire biotas, at once? When the dimensions of

fitness space itself are altered, old opportunities to survive and reproduce may disappear and new opportunities may arise. The nature of the organism is to take advantage of new opportunities by exploring new parts of fitness space that were previously inaccessible or nonexistent. As mentioned previously, bouts of ecological fitting in static fitness space alone would be self-limiting, leading to episodes of expansion that simply fill fitness space, and this would not lead to the indefinite diversification that characterizes the tree of life or the complexity that characterizes the entangled bank. To build a diverse, complex, persistent biosphere requires an essential ingredient: repeated systemic perturbations that routinely alter the fitness space of multiple species. These perturbations catalyze the dynamics that allow living systems to fluctuate between exploiting and exploring both the *geographical* and *functional* dimensions of fitness space (Brooks et al., 2019; Agosta and Brooks, 2020).

Fluctuating in geographical fitness space

For Darwin and Wallace, cofounder of the theory of natural selection, where a species lived was the primary component of its fitness space. Darlington (1943) extended this to include not only the places where species lived, but the movement of species to and from those places catalyzed by external changes in the conditions. He concluded that species arose in "centers of diversification," where external perturbations caused geographical ranges to fluctuate around a continuously occupied core. These fluctuations might be driven by the formation of barriers to dispersal, producing episodes of isolation leading to speciation, and the breakdown of those barriers, producing episodes of biotic expansion from the core and, as Darlington saw it, setting the stage for new species to replace older species.

The notion of new species arising in geographic centers of origin and then expanding into new areas to *replace* older species is based on the idea that the species-area relationship (Cain, 1938) is a result of the environment comprising a limited number of niches for species to fill. In this way of thinking, once an area becomes saturated, new species can be added only if another species leaves or goes extinct (e.g., MacArthur, 1969; Roughgarden and Feldman, 1975; Hairston, 1980; Case, 1981). Niches, however, are an emergent property of the nature of the organism, not the conditions, synonymous with fitness space (Hutchinson, 1957). No fixed number of niches are in the environment for species to fill; each organism's fitness space represents potential fitness space for another organism.

Following Darlington, Wilson (1959, 1961) proposed the *taxon cycle*. Multiple species from a given area may colonize new areas when a change in conditions expands the amount of suitable habitat and then may contract their ranges when another change in conditions reduces the amount of suitable habitat. MacArthur and Wilson (1963, 1967) extended this to produce the equilibrium theory of island biogeography. They proposed a one-way dynamic in which "islands" were colonized by "source areas" that contained a preexisting pool of species. Like Darlington's, their theory relied heavily on the species-area relationship and the idea of an equilibrium number of species that could fill a limited number of niches. When an island had fewer than the equilibrium number of species, it was open to colonization. When the equilibrium number of species was reached, it was closed to colonization, unless a new species displaced an old one or an old species went extinct. For MacArthur and Wilson, the available fitness space on an island was a fixed, static quantity and only preexisting species could fill it.

Erwin (1979, 1981, 1985) proposed a biogeographical theory that included both a mechanism for speciation and allowance for fitness space to be a dynamic property of the organism. The taxon pulse hypothesis posits that groups of species (biotas) experience fluctuations in their geographic ranges catalyzed by repeated changes in environmental conditions that drive diversification. When changing conditions cause dispersal barriers to break down, species expand geographically but also in fitness space as the inheritance systems generalize, spending potential in their exploration of new areas. When conditions change again, new barriers to dispersal may arise, isolating populations both geographically and in fitness space, promoting diversification and speciation. When changing conditions break down dispersal barriers again, a new phase of geographic expansion and generalization in fitness space is initiated. And so on, as changing conditions catalyze new bouts of isolation and expansion, variously isolating and mixing together species geographically, producing the historically contingent complex patterns of species distributions and coexistence that we observe.

The empirical evidence for taxon pulse–driven biotas is extensive (e.g., Spironello and Brooks, 2003; Bouchard and Brooks, 2004; Brooks and Ferrao, 2005; Halas et al., 2005; Folinsbee and Brooks, 2007; Hoberg and Brooks, 2008; Lim, 2008; Eckstut et al., 2011). A history of repeated taxon pulses, especially over large areas, produces biotas that are idiosyncratic, composed of many species that have associated with each other for varying lengths of times and have arrived under different conditions. These dynamics in geographical fitness space, catalyzed by external perturbations, cause complex mosaics of species coexisting and interacting, forming dynamic ecosystems that can break apart and reform based on the inherited capacities of the constituent members.

Fluctuating in functional fitness space

Fitness space is composed of not only the places where species can live but also the things they can do in those places. Taxon pulses lead to the mixing and matching of species in different locations, which in turn catalyzes phases of exploration of new opportunities for survival during periods of geographic expansion followed by phases of exploitation of those opportunities during periods of isolation. Thus, along with fluctuations in geographical fitness space, the oscillation hypothesis posits that inheritance systems fluctuate between generalizing and specializing in functional fitness space (Janz et al., 2006; Janz and Nylin, 2008; Nylin and Janz, 2009; Nylin et al., 2014).

The oscillation hypothesis was originally proposed to explain the evolution of host range in plant-feeding insects, but its applicability is far more general (Agosta et al., 2010; Brooks et al., 2019; Agosta and Brooks, 2020). Nonetheless, the dynamics of changes in functional fitness space are relatively easy to visualize for groups of organisms that form highly specific interactions with each other, like insects and plants or parasites and hosts. For these organisms, it is relatively easy to draw a connection between "host" and "function," and therefore between "host space"—the range of hosts that can be used—and the functional dimensions of fitness space. And since host space is a part of fitness space, there will always be a difference between *realized host range* (the set of hosts that are being used) and *fundamental host range* (the set of all hosts that could be used). As with fitness space in general, host space is inherently sloppy (Agosta, 2006; Agosta et al., 2010; Brooks et al., 2019).

The capacity for ecological fitting means that despite forming highly specific associations, parasites can always have opportunities to explore new hosts. Parasitism is not an inherent evolutionary dead end. The capacity for host-switching manifests as changes in host range that do not track phylogenetic patterns of host-relatedness directly but are constrained by the phylogenetic distribution of necessary resources found in related hosts (Brooks and McLennan, 2002; Brooks et al., 2006). The literature contains a mountain of evidence that shows this pattern, so phylogenetically conservative host-switching should be viewed as a routine phenomenon (Brooks and McLennan, 2002; Agosta, 2006; de Vienne et al., 2013; Nylin et al., 2018). Moreover, studies reveal phylogenetically conservative patterns of associations over long periods of time that alternate between increases and decreases in host range, in accordance with the oscillation hypothesis (e.g., Janz et al., 2006; Nylin et al., 2014; Jorge et al., 2018; Brooks et al., 2015; Boeger et al., 2022).

The evolution of pocket gophers (Geomyidae) and their parasitic lice (*Geomydoecus*) in North America provides a particularly instructive example (Brooks et al., 2015). Transmission of lice occurs when gophers are in their nests, so the opportunities for the parasite to switch to new hosts are limited even when external perturbations catalyze geographic expansion. Nevertheless, host-switching driven by external perturbations is a common theme in the history of these associations (Brooks et al., 2015). A burst of diversification in pocket gophers and lice 4.2 million to 1.8 million years ago coincided with a period of substantial climate and habitat change (Spradling et al., 2004). Around half of the associations that emerged during this time were the result of host-switching, followed by episodes of cospeciation. The pattern shows clear evidence of the oscillation dynamic, alternating between episodes of host range expansion by lice—generalizing in fitness space—followed by episodes of isolation and diversification—specializing in fitness space—in association with their new hosts (Brooks et al., 2015). Computer simulations have reproduced these patterns, showing how easily oscillations in sloppy fitness space can emerge from basic Darwinian dynamics in the context of opportunity space that includes the chance to encounter new hosts (Araujo et al., 2015; Braga et al., 2018; Feronato et al., 2021).

Avoiding extinction: fluctuating in combined geographical-functional fitness space

External perturbations like climate change alter both the geographical and functional dimensions of fitness space for multiple species, affecting parts of or even the entire biosphere (Brooks and Agosta, 2012; Brooks et al., 2019; Agosta and Brooks, 2020). Even without external perturbations, as dynamic complex systems, ecosystems experience continuous internal change because of "autonomous turnover" of species distributions, abundances, and interactions (O'Sullivan et al., 2021). If ecosystems were fragile, these perturbations would simply break them apart, with limited potential to form new connections within the system or to form new systems. But because of the collective capacity for coping with change retained within ecosystems—the evolutionary commons—they are relatively immune to the "butterfly effect" (Agosta and Brooks, 2020).

The butterfly effect—in which a small change in one part of a system has a large effect on the whole system (Lorenz, 1972)—has been used as a metaphor to describe the supposed fragility of the biosphere. It is, however, a truly poor way to describe a complex evolutionary system. Robustness, resiliency, and responsiveness in the face of internal and external change are hallmarks of complex systems (Kitano, 2004, 2007; Page, 2011). Complex systems are multilevel, hyperdiverse, hyperconnected, functionally redundant, and modular. All these features contribute to the *anti–butterfly effect* being a fundamental property of the

biosphere (Agosta and Brooks, 2020). While they all have vulnerability thresholds beyond which perturbations can no longer be absorbed, ecosystems do not simply collapse in response to the loss or addition of new species and, moreover, the biosphere does not collapse when ecosystems are lost or change. If living systems were this brittle, the complex persistent biosphere would not exist. Again, recall that so far the aftermath of each mass extinction event has been mass evolutionary renewal.

Ecosystems are resilient and changeable in proportion to the capacities of their constituent members for ecological fitting in sloppy fitness space, which provides species degrees of freedom for exploring new opportunities by moving to new geographic areas and by co-opting existing functions for new functions, including forming new trophic connections with other species. When perturbations lead to geographic expansion, they also catalyze intense periods of exploration of new opportunities for survival, causing species to spend evolutionary potential by generalizing in fitness space. When perturbations lead to geographic isolation, exploitation of the new opportunities is reinforced by natural selection, leading species to specialize functionally in fitness space. And since new diversity emerges in isolation when conditions are stable, new evolutionary potential to exploit new opportunities can build before the next perturbation catalyzes a new episode of geographic expansion. In this way, alternations in geographical and functional fitness space are coupled but out of phase. Each new perturbation leads to a pulse of geographic expansion, the mixing of different species, including hosts and parasites, and the spending of potential as each species generalizes, followed by episodes of isolation and then specialization when potential is restored.

The entangled bank is constructed from and persists indefinitely because of repeated and overlapping cycles of taxon pulses and correlated oscillations in functional fitness space across multiple temporal and spatial scales. The built-in capacity of individual inheritance systems to alternate between periods of specialization and generalization in combined geographical-functional fitness space is how they, and by extension the collective biosphere, avoid extinction. The biosphere is robust, resilient, and responsive. But there are limits to its evolvability. The prodigious amounts of informational capacity produced by living systems affords them the potential to cope with change, but they cannot predict the future and are therefore vulnerable to extinction. No matter how fit a species is in today's conditions, it can still be unfit tomorrow when conditions change. Individual inheritance systems and the connections between them therefore routinely go extinct, but the biosphere persists because of the capacity to absorb even massive perturbations arising from the dual exploiter-explorer nature of its constituent members and collective potential stored in the evolutionary commons (Agosta and Brooks, 2020).

Concluding Remarks

The EID crisis fundamentally involves three variables: humans, the ecosystems on which we depend and which contain the organisms that are the sources of EID, and external factors such as climate change, land conversion, urbanization, and global trade and travel that cause changes in the conditions that catalyze EID (Brooks et al., 2019). The overarching message of this paper is that we cannot disentangle EID from the overall response of ecosystems to climate change and that EID is fundamentally an expression of the same evolutionary potential that allows the rest of the biosphere to cope with change by changing. Or more simply, we cannot understand EID without a more general understanding of how nature works. This understanding is rooted in Darwinism and synthesized by the SP.

The SP tells us that in a period of global change, we should expect more host-switching and therefore more EID. It tells us the risk space for EID is very large and that the realization of these risks increases the more ecosystems are perturbed. The anti–butterfly effect, mediated by the capacity for ecological fitting in sloppy fitness space, means that cospeciation and coextinction are unlikely in parasite-host interactions, implying that pathogens routinely persist longer than their original host. For SARS-CoV-2, not only is the ACE2 receptor phylogenetically conserved among mammals, specialization on binding to the ACE2 receptor is conserved among coronaviruses (Low-Gan et al., 2021; Ruiz-Aravena et al., 2022), suggesting a large amount of sloppy fitness space in these interactions and a large potential for host-switching.

The risk space for EID is substantial, but the SP also tells us it is not random. Conservative inheritance means the traits involved in transmitting parasites to hosts, like the ACE2 binding site, are highly specific. Therefore, the community structure of parasite-host interactions should be highly conservative, even without pervasive cospeciation/coextinction dynamics. Brooks et al. (2006) examined six assemblages of lung flukes (platyhelminths) that parasitize frog species in temperate forests and grasslands in the USA and tropical dry and wet forests in Mexico and Costa Rica. They predicted that if ecological fitting was the dominant factor structuring the communities, as opposed to cospeciation/coextinction, then (1) associations should be largely determined by conservative traits related to parasite transmission rather than host phylogenetic relatedness

and (2) communities should exhibit similar patterns of associations at the generic and family levels, even though they are from widely separated areas and very different habitats. Their data corroborated both predictions: conservatism in parasite and host traits related to transmission (i.e., habitat and feeding preferences) was the primary determinant of the associations, not host phylogeny, with each community converging on a similar phylogenetic structure. The shared requirement for aquatic habitats of tadpoles for all frog species allows potential colonization by essentially any lung fluke species if given the opportunity; additional lung fluke species are associated with frog hosts largely as a function of how much time the adults spend in the aquatic habitat. The SP tells us that while the potential for EID is large, where and when EID will emerge is predictable based on knowledge of the conservative traits of parasites and hosts, suggesting proactive measures rooted in evolutionary principles (Brooks et al., 2014, 2015, 2019; Boeger et al., 2022). Knowing, for example, that malaria (1) is caused by organisms in the genus *Plasmodium* and (2) is spread to humans exclusively through bites of adult mosquitoes in the genus *Anopheles*, all of which (3) have aquatic larvae and feed on vertebrates is a large step toward narrowing the "malaria risk space." Basic natural history knowledge set in a proper theoretical framework provides humans with significant capacity to predict and preempt where the next case of emergence may occur. This is the fundamental objective of the DAMA protocol (Brooks et al., 2014, 2015, 2019; Boeger et al., 2022), which stands for Document, Assess, Monitor, and Act. DAMA is a direct application of the SP to the problem of emerging disease. It recognizes that the EID risk space is large but nonrandom because of phylogenetic conservatism. It is designed to anticipate EID before it happens, or when it does happen, to be better prepared to mitigate the spread not just among humans but among nonhuman species that may be potential suitable hosts. The combination of the SP—providing a theoretical foundation for understanding emerging disease in the context of global change—and DAMA—providing a framework for applying the SP to emerging disease—can be a powerful approach for transforming our response to the EID crisis to a more proactive, evolutionarily informed effort.

Acknowledgments – I thank the editor of this special feature for inviting me to write this paper. Thanks also to Virginia Commonwealth University, VCU Life Sciences, Center for Environmental Studies for providing a short sabbatical and to the Stellenbosch Institute for Advanced Study (STIAS) for a visiting fellowship that provided the ideal setting to develop many of the ideas in this paper.

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