SFI TRANSMISSION

COMPLEXITY SCIENCE FOR COVID-19

STRATEGIC INSIGHT: **Pandemics rapidly reshape the evolutionary and ecological landscape and have cascading social, economic, and other system-level effects.**

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In the 1950s, the planet still had isolated islands, in both geographical and cultural terms — lands of unique mysteries, societies, and resources. By the end of the 20th century, expanding numbers of people, powerful technology, and economic demands had linked Earth's formerly isolated, relatively nonindustrialized places with highly developed ones into an expansive and complex network of ideas, materials, and wealth. —Julianne Lutz Warren and Susan Kieffer (2010)

Believe me who have tried. Thou wilt find something more in woods than in books. Trees and rocks will teach what thou canst not hear from a master. —St. Bernard of Clairvaux (1841)

This oak tree and me, we're made of the same stuff. —Carl Sagan (1980)

It is remarkable how closely the history of the apple tree is connected with that of man. —Henry David Thoreau (1862)

Among the most pressing ecological and socioeconomic imperatives of our time is that of assessing the impact of novel external perturbations to manage complex systems for resilience. Broadly defined, resilience is the capacity of a system to maintain function in response to perturbation.

Pandemics — the spread of epidemic disease around the world — are a signature of the Anthropocene. Before the rise of an interconnected world, epidemics were largely contained to a limited area and pandemics were rare. Pre-Anthropocene biology was defined by splendid isolation. As continents moved, mountains formed, and rivers eroded, populations, species, and clades become isolated and gene flow was limited. Indeed, the amazing biodiversity of the planet is due largely to this isolation. Within isolated regions, separate co-evolutionary dynamics between individuals and their enemies produced much of Earth's biological diversity. The co-evolution of host populations and pathogens is a stepwise reciprocal evolutionary interaction and, if transmissible, can result in epidemics. Epidemics result in intense co-evolutionary selection pressures on both host and pathogen populations, ultimately allowing long-term persistence and ecosystem stability. In the new biology of the Anthropocene, however, the barriers of isolation and limited geneflow are now rapidly disappearing.[1] Global dispersal and immigration of species between regions are now increasingly frequent, entirely due to human movement, human-caused changes to the environment, and economic trade connections. The new biology is a biology of panmixia, or random mating within a population, writ large.

A pathogen is any agent that disrupts homeostasis in an individual. When a pathogen spreads among hosts, the effects on the total population can be substantial. Novel pathogen introductions can impact both host and pathogen unpredictably, often resulting in associations with no previous co-evolutionary history. When geographically isolated pathogens and their hosts are suddenly transported great distances and mixed with new hosts and pathogens, remarkable and unpredictable pathways of evolution are possible. A science of the Anthropocene necessarily would include a description of complete biological planetary interconnectedness. This is a lofty goal given the degree of global interconnectedness; indeed, the biosphere has never experienced panmixia and pandemics on the scale we see today.

August Krogh, a Danish professor at the department of zoophysiology at the University of Copenhagen from 1916 to 1945, specialized in comparative physiology, particularly areas relating to cellular respiration. In 1920 he was awarded the Nobel Prize in Physiology for his discovery of the mechanism regulating capillaries in skeletal muscle. Krogh also succinctly encapsulated the idea of comparative biology, which recognizes that parts or processes that are difficult or impossible to study in one species may be much more accessible in an alternate species.[2] To paraphrase the Krogh principle, for many problems there is another organism or organisms on which it can be most conveniently studied. Krogh's principle is the guiding foundation of comparative biology — the use of biological variation and disparity to understand the patterns and rules of life at all levels.

Given the global impact of COVID-19, the pandemic is often compared to past pandemics. For example, the news is filled with references to the Spanish influenza, smallpox, and the potential pandemic of Ebola. These past human pandemics have helped guide our current response to COVID-19. However, there is more to a viral disease pandemic than the human host and pathogens. Spread or transmission of an infectious agent relies on interactions of individuals and populations.

Stepping back to earlier concepts, we can use Krogh's principle to assess and build a comparative science that addresses a world of complete biological planetary interconnectedness. Specifically, we ask: what can other organisms reveal about how biological systems respond to the rise of a massively connected biosphere? Plants, and trees in particular, are remarkable teachers — like us, they are dominant, cover most of the earth, and disproportionately impact the functioning of the biosphere. They also prefer environments similar to those most habitable for humans, and their life cycles span time frames relatively close to our own. They, too, have experienced an increase in pandemics, some with disastrous consequences.

There are at least three immediate lessons from a comparison of pandemics in humans with pandemics in trees. These lessons point to common threads for a science of the Anthropocene as well as a focus on the need to rigorously assess the concept of resilience.

(1) Pandemics cause sudden rapid transformations across interconnected ecological and economic systems.

The parallels between COVID-19 and the 1904 blight of chestnut trees are striking. COVID-19 (caused by the SARS-CoV-2 coronovirus) and chestnut blight (caused by the Ascomycota fungus *Cryphonectrica parasitica*) both likely arose in Southeast Asia and were transported via international travel networks that enable pathogens to circumnavigate the globe. Over the course of about a month, both spread rapidly and simultaneously across Europe and North America, causing a broad spectrum of disease, from mild to severe and even death. In the U.S., both pathogens first devastated the New York region. Both infections first revealed their presence by several symptoms, but ultimately the more stressed and susceptible individuals died first as the pathogen more easily blocked and "suffocated" the vascular network. The collateral damage of both pandemics was remarkable. Spreading unimpeded, the chestnut blight decimated what had been one of the most dominant species of trees. Similarly, the novel coronavirus hit the local subsistance economies, mainly in the poor areas of the continent. Spikes in unemployment and dramatic changes in the traditional ways of life left culture irreversibly altered and shifted economic models.

For years, the American chestnut tree largely defined American deciduous forests, ranging from Maine to Georgia and west to the prairies. It survived all evolutionary adversaries for 40 million years, but then, within 40 years, it effectively disappeared. The American chestnut had no evolutionary history of interaction with this new exotic fungal pathogen. First discovered in 1904 in New York City, the chestnut blight was a global pandemic hitting forests around the world. In fact, it has been called the first great ecological disaster to strike the world's forests. It is estimated that in some places, such as the Appalachians, one in every four trees was an American chestnut. Within the span of a generation the North American forests had no chestnut trees. Chestnut blight spread rapidly and caused significant tree loss on different continents. The primary plant tissues targeted by *C. parasitica* are the vascular tissue and the cambium, a layer of actively dividing cells. The fungus girdles the stem, severing the flow of nutrients and water to the vital vegetative tissues. The absence of nutrient dispersal from leaves to roots causes the main stem to die, though, ironically, the root system may survive. The American chestnut still exists, but poorly; its individuals are continuously knocked back by a resurgence of the pathogen when any one grows bigger than a sapling.

The wood of mature chestnut trees was lightweight, soft, easy to split, and resistant to decay. For three centuries, barns and homes on the East Coast were made from American chestnut. Chestnut wood literally made the new American colony — industries grew up around making posts, poles, piling, lumber, railroad ties, and split-rail fences. In 1907, approximately 600 million board feet of chestnut were cut in the United States. The estimated modern retail value of wood exceeds three billion dollars. But the edible nut was also a significant contributor to the rural economy. A *New York Times* article from 1892 describes how the gathering of chestnuts represented perhaps the best opportunity for a family to make money and to help enable self-sufficient agriculture. Domestic hogs and cattle could be fattened for market quickly by allowing them to forage in chestnut-dominated forests.

The chestnut pandemic had a devastating economic and cultural impact on communities in the eastern United States that we are still trying to understand.[3,4,5,6] In the first half of the 20th century, an estimated four billion chestnut trees were killed. It is clear that the chestnut blight brought about the rapid decline of American subsistence culture and expedited the rise of industrialization. Despite these major societal and cultural changes, the ecological and evolutionary impacts of the chestnut blight are surprisingly understudied. Subsequent studies of forest succession show that biodiversity equilibrium still has not been attained. Furthermore, they indicate that no single species will replace the role of the chestnut in the foreseeable future. The impacts on native wildlife and ecology are still being assessed.

Pandemics offer a sober reminder that no matter how dominant the host or how grand and impressive the ecological or economic impact of a species, the exponential growth of a highly transmissible pathogen can be overwhelming. Pandemics rapidly reshape the evolutionary and ecological landscape and have cascading social, economic, and other system-level effects. They remind us that selective pressures are not a mere abstraction: they can happen quickly and are a grim reality of mortality and adaptation. A pandemic represents the impact of novel selective events that change the rules of interactions and allow some genotypes and phenotypes to be favored at the expense of others.

(2) The impact of novel pathogens on complex systems can be quantified by assessing deviations from scaling laws.

How does one measure the impact of a novel pathogen, or, for that matter, how does one define a healthy forest? How does one predict where the system will go once the perturbation has subsided? One powerful way to determine the impact of pathogens on a population is to assess age-dependent population dynamics, where the impact is measured in changes in birth and death rates.

In 1898, François de Liocourt published a manuscript in *De l'amenagement des sapinières Bulletin trimestriel, Société forestière de Franche-Comté et Belfort* called "The management of silver fir forests."[7] The pattern he discovered, now known as the law of de Liocourt, was that, in unimpacted forests, the distribution of tree sizes in different forests converged to a similar distribution or J-shaped curve. In such a forest there is an uneven age and size structure. De Liocourt argued that if disturbed forests were left alone, they would converge on distributions common to other unmanaged forests, as shown in the bottom curve of Figure 1.

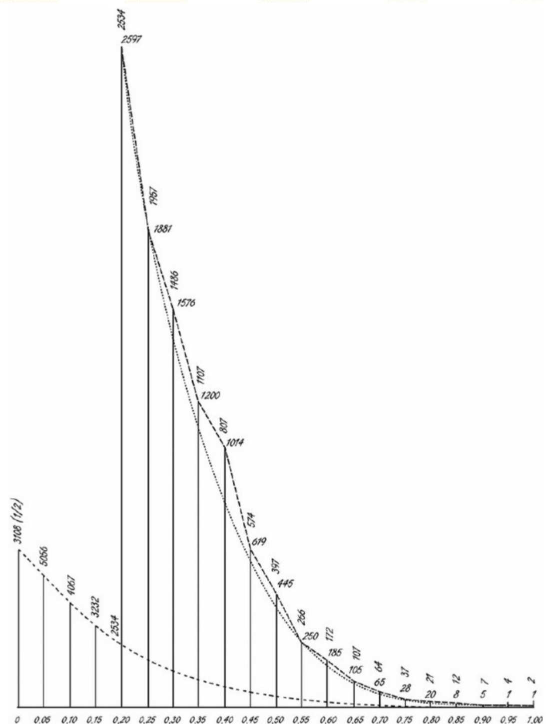

Figure 1. *From de Liocourt's 1898 paper showing the frequency distribution of tree sizes and the mean number of trees in a healthy forest (solid line and horizontal numbers) and his "fitted distribution" (dotted line and vertical numbers). The x -axis legend is diameter (cm), and the y -axis legend is frequency.*

It was not until 1931 when the roots of quantitative models of demography emerged, due in part to the insight of Soviet mathematician Andrei Kolmogorov. Kolmogorov was working on the problem of diffusion starting from the theory of discrete-time Markov processes.[8] Now known as the Chapman–Kolmogorov equation, he sought to develop a theory of continuous-time Markov processes by extending this equation. Kolmogorov detailed two versions of his theory for discrete-time Markov processes — a forward and backward system applied to many areas of biology. For the life sciences, the forward equation, also known as the Fokker–Planck equation, has been the most useful. Specifically, here *n* is the population index, with reference to the initial population, *\beta* is the birth rate, and finally *{\ p_{n}(t)=\Pr(N(t)=n)}{ p_{n}(t)=\Pr(N(t)=n)}* is the probability of achieving a certain total population size, *N*. This foundational work has been extended across biology and used to model population growth with birth, cell growth, and epidemiology. The insight from this work is that in populations, if disturbance and external mortality is low, we expect to see an age or size structure that is a balance between size-dependent growth and mortality.[9,10] The result is a characteristic age or size distribution, also called a size spectra. The implication is that an increasing impact of disturbance will increasingly shift that spectra as older or younger individuals are disproportionately impacted by the pathogen until a new population equilibrium emerges.[11] In the case of a plant pathogen that does not cause 100 percent mortality, we expect the new size structure to mirror a new demographic equilibrium, as was seen in the American chestnut.

Today botanists and forest ecologists often turn to de Liocourt for a useful definition of a "healthy" sustainable forest ecosystem.[12] The balance of size-dependent birth and death in the absence of a major disturbance, such as a new lethal pathogen, might indeed be characterized by a size distribution with a characteristic mathematical signature — one that mains a stable size–structure relationship by balancing growth with mortality.

An accurate quantification of the impact caused by novel pathogens forms the basis for management strategies.[12] For fungal forest pathogens, tree mortality is the most commonly used variable to quantify losses. Since tree mortality is an inherent process of forest dynamics, defining a baseline against which mortality caused by a new pathogen can be compared presents a major challenge. Changes in the population of the host would occur if the new pathogen caused a higher mortality or changes in birth or death rate than that occurring under pre-pathogen conditions in the forest. Foresters are now obtaining the baseline mortality from a de Liocourt curve calculated from tree inventories carried out over large areas to use as a baseline to quantify the impact of a pathogen.[13] In other words, shifts in size distributions are perhaps the best general measure to link pathogen impacts on death, growth, and birth — the fundamental biological processes that apply across all living organisms. These patterns need not apply only to biology; similar inverse size spectra appear in the distribution of city and settlement size as well as the distribution of businesses, social networks, and groups.[14] De Liocourt's Law and the Chapman–Kolmogorov equation offer a novel way to define resilience of a system to external impacts and quantify pandemic impacts on age and size structure. The hypothesis is that exogenous disturbance produces systematic deviations from size spectra and provides a link between the dynamics of complex systems and their age or size dependent scaling properties.

(3) There is no going back – our management systems are now faced with "adaptive management" of sudden rapid transformations across interconnected ecological and economic systems.

> *That all the [chestnut] trees in the United States are doomed to destruction by a mysterious disease called chestnut blight . . . is the gloomy prediction of Dr. W.A.Murrill . . . now he asserts there is nothing to be done against it; that it must run its course like all epidemics . . . a vast loss will be entailed on the eastern forest region should this disease prove as destructive as is at present threatened. —The New York Times*, Sunday May 31st, 1908

Like human pandemics, plant pandemics are also associated with the coming of the Anthropocene and first started appearing with the rise of an interconnected world.[15] Some of the first recorded pathogen outbreaks were associated with wheat, as recorded by the Romans (2100-1950 B.P.). In fact, the Romans had a god/goddess of rust (Robigus/Robigine) because these new pathogens were so feared.[15] Feasts, processions, and sacrifices in their name were conducted in order to prevent crop destruction and stop future waves of reinfection. Over the past 200 years the number and severity of plant diseases has increased exponentially.[16] Once a pathogen spreads globally, eradication becomes difficult or even impossible. Pathogens do not respect international boundaries. Efforts to reduce the movement of pathogens across borders or by quarantines are easily frustrated by globalization, travel, and trade.

Governmental plans to deal with plant pandemics — mainly associated with agriculture — now largely revolve around prevention, response, and recovery. The effort to protect the food supply and human health[17] is largely focused on limiting spread and impact. The chestnut blight was one of the first major pandemics in forests, but there are many more that impact wild ecosystems. Dutch elm disease, sudden oak death, *Phytophthora cinnamomi*, and *Armillaria* honey fungus are all pathogens in an age of pandemics with potential to alter ecology and cultures, if not entire civilizations. Human pathogens and the threat of new pandemics reveal a sobering reality. While considerable effort is now expended on learning how pathogens emerge and identifying potential pandemic pathogens, less has been done to recognize the general signatures of pathogens within and across populations. So this raises the question: what, in terms of ecological and cultural impact, will the next chestnut blight or COVID-19 bring? In particular, what lessons have we learned from trees that inform our ability to deal with the losses and envision a recovery from any pandemic pathogen?

An accurate quantification of the impacts caused by transmissible pathogens must form the basis for management strategies. Developing a general theory of ecological or system resilience is critical. Resilience is a dynamical property that depends on both the trajectory and the rate of change through time.[18] A distinct but related dynamical property is termed "engineering resilience," and is the return time of the system to a steady, or equilibrium, state. Resilience relates to the degree of perturbation that a system can tolerate. The regularities embodied by both empirically documented and theoretically derived emergent properties of systems, with and without disturbance, provide important baselines for understanding resilience and change in complex systems.[11] In the context of adaptive management, such baselines can be used to formulate hypotheses and derive surrogate parameter estimates in the absence of more specific data. Furthermore, ecological scaling relationships such as de Liocourt's Law, which often (but not always) takes the form of power laws, may describe attractors for, or constraints on, the structure and dynamics of complex systems.[11] Deviations from scaling relationships can be used as a signature of specific underlying structuring processes — such as the impact of a pathogen — or may indicate the transient reorganization of the system. Although the focus here has been on forest communities, the concepts and research opportunities described should apply more generally to human and economic systems.

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ENDNOTES

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