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domestication syndrome were real [16]. Although it is a long-standing hypothesis, the domestication syndrome has not yet been rigorously tested, as any scientific hypothesis must be, and cannot be assumed to be true.

¹Bioinformatics and Integrative Biology, University of Massachusetts Medical School, 368 Plantation Street, Worcester, MA 01605, USA

²Broad Institute of MIT and Harvard, 415 Main Street, Cambridge, MA 02142, USA

³The Palaeogenomics and Bio-Archaeology Research Network, Research Laboratory for Archaeology and History of Art, University of Oxford, 1 South Parks Road, Oxford OX1 3TG, UK

⁴Program in Molecular Medicine, University of Massachusetts Medical School, 368 Plantation Street, Worcester, MA 01605, USA

*Correspondence:

elinor@broadinstitute.org (E.K. Karlsson).

©Twitter: @Greger_Larson (G. Larson) and @eenork (E.K. Karlsson).

<https://doi.org/10.1016/j.tree.2020.10.004>


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Forum

Beyond Infection: Integrating Competence into Reservoir Host Prediction

Daniel J. Becker ^{1,*},
Stephanie N. Seifert ² and
Colin J. Carlson ³



Most efforts to predict novel reservoirs of zoonotic pathogens use information about host exposure and infection rather than competence, defined as the ability to transmit pathogens. Better obtaining and integrating competence data into statistical models as covariates, as the response variable, and through postmodel validation should improve predictive research.

Predicting Reservoir Hosts

Epidemics of zoonotic disease beget questions about origins: from where did a pathogen originate? Rapid research during the coronavirus disease 2019 (COVID-19) pandemic has focused on identifying likely **reservoir hosts** (see [Glossary](#)) of severe acute respiratory syndrome coronavirus (SARS-CoV)-2. High nucleotide identity between this virus and related viruses found in horseshoe bats (e.g., *Rhinolophus affinis*) implies a wildlife origin, yet divergence of these viral lineages decades ago suggests hosts involved in spillover remain unknown [1]. Searching for closely related pathogens

in wildlife is a labor-intensive process made all the more difficult by the diversity of possible hosts to sample. Given such challenges, ecologists and data scientists have developed statistical models to predict likely reservoir hosts, which can forecast sources of cross-species transmission and prioritize surveillance targets [2].

Predictive studies typically use parametric or semiparametric models (e.g., generalized linear or additive models) or machine learning algorithms (e.g., boosted regression trees), where the predictor matrix (i.e., X) includes life history, taxonomic, and geographic traits of hosts. In most cases, the response (i.e., y) is pathogen positivity or richness using data on the detection of pathogen antigen or pathogen-specific antibody [3]. Given many logistical hurdles in sampling wildlife, **serology** and PCR are often the first data available for predictive models. By indicating recent exposure, serology in particular remains useful for pathogens with short infectious periods and high temporal variability in infection [4]. However, such data do not necessarily reflect host **competence**, the ability to transmit pathogens [5]. In turn, even the best models using such data could generate spurious predictions. For example, broad serological sampling of bats has led to many bat–flavivirus associations in model-ready datasets, despite evidence that many bats are not competent reservoirs [6]. We here suggest that the use of serology and PCR data must be considered as a starting point for identifying likely reservoirs and emphasize how host competence data can be better integrated into all aspects of predictive research, including as covariates in the predictor matrix, as the response, and through post-model validation (Figure 1).

Host Competence Data

Competence can be defined most strictly as the host capacity to transmit pathogens to new hosts or vectors [7]. This definition

restricts competence to only those infection processes that occur within the host: establishment of infection given exposure, pathogen development (i.e., replication), and pathogen survival until transmission. The former process is equivalent to host **susceptibility**, whereas the latter processes are contained within **suitability** and are mediated by resistance and tolerance mechanisms [5]. As competence encompasses several stepwise processes, this trait is continuous [8]. For some purposes, it may be approximated as binary [9].

As a composite trait, competence is difficult to determine in natural systems. Frequent detection of pathogen-specific antibodies or antigen alone cannot be interpreted as competence, as such patterns can instead reflect transmission from a true maintenance host. In wild hosts, competence can instead be inferred by detecting **shedding** of live virus (Figure 1). For vector-borne diseases, shedding may be less informative for ability to transmit. Instead, the susceptible state of vectors prior to feeding can be assumed in some systems, such that the infection status of engorged vectors can inform host competence. For example, as ticks are born free of *Borrelia burgdorferi* (the cause of Lyme borreliosis) and only become infectious from feeding, pathogen presence in engorged larvae implies competent hosts [8,9]. Competence can also be inferred by combining pathogen diagnostics of hosts and fed vectors with blood meal analyses [6].

In many cases, however, quantifying competence in field systems remains challenging. For example, despite bats being suggested reservoirs for Ebola virus and African henipaviruses, live virus has yet to be isolated despite frequent detection of antigen and antibody. Data on within-host components of competence, such as susceptibility and suitability (e.g., pathogen replication), could provide mechanistic

covariates for predictive models using serology and PCR data as the response (Figure 1). As one example, species means in immunological covariates, such as leukocyte concentrations or *ex vivo* responses to pathogen challenge [10], could represent these within-host processes better than many currently used traits (e.g., body mass and fecundity).

Host genetic variation can also shape susceptibility and suitability, especially for factors that enable pathogen entry into host cells and replication. For the former, *in silico* methods can characterize receptor binding. For example, by focusing on angiotensin-converting enzyme (ACE)2, the receptor involved in SARS-CoV-2 host cell entry, *in silico* studies predicted various primate, rodent, and deer species as susceptible to the virus [11]. Analogous comparative data on receptor use for other pathogens could provide invaluable within-host covariates (Figure 1). However, *in vitro* studies are necessary to functionally validate *in silico* results and can further characterize host factors required for pathogen replication. As another example, reverse genetic assays were recently used to show functional compatibility of the spike glycoprotein from various novel SARS-like CoVs to enter cells with ACE2 from potential host species [12].

Lastly, *in vivo* pathogen challenge studies are the gold standard to determine shedding (i.e., productive infection) and onward transmission in a given host-pathogen system (Figure 1). For example, in the West Nile virus system, exposure of 25 bird species to infectious mosquitoes or virus challenge established greater competence of songbirds and shorebirds [13].

Integration into Predictive Research

These competence data can be integrated into different aspects of predictive research (Figure 1). Field-based measures

Glossary

Competence: host ability to transmit pathogens to new susceptible hosts or arthropod vectors.

Reservoir host: populations or species in which a pathogen can be maintained and that serve as a source of infection for the recipient host.

Serology: detection of pathogen-specific antibodies in serum or plasma to infer exposure history.

Shedding: Release of pathogen in excreta (e.g., saliva, feces, and urine) following successful replication within the host.

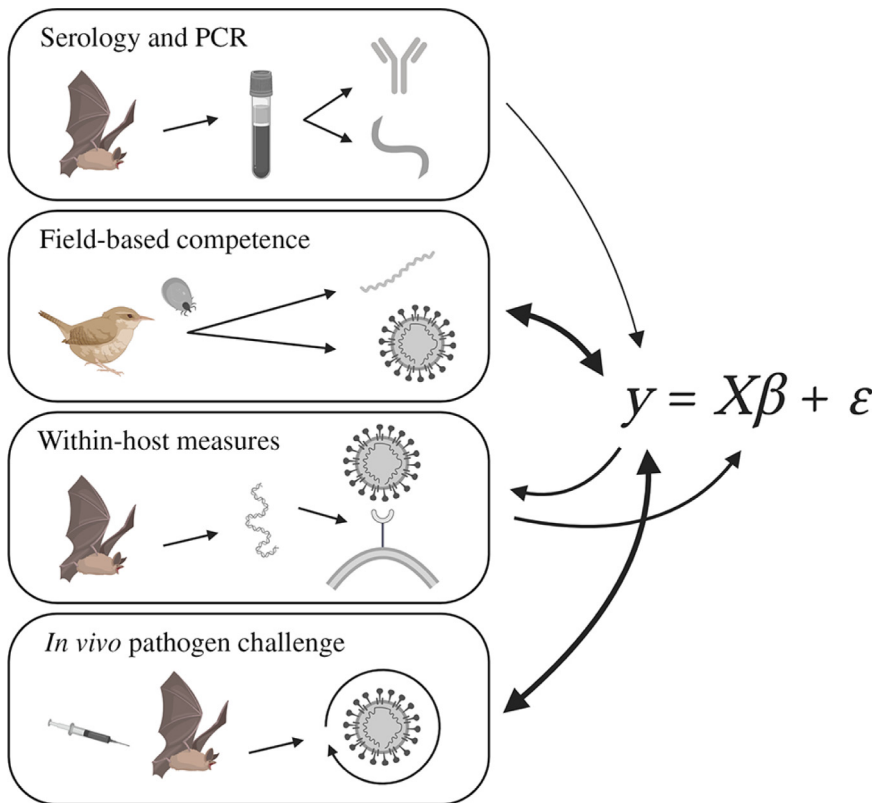
Suitability: ability of a host to support pathogen development (i.e., replication) and survival until transmission.

Susceptibility: probability of an infection establishing in the host given exposure to a pathogen.

of competence (i.e., detection of live virus or pathogens in recently fed vectors) can be prone to false negatives owing to short or highly variable periods of active infection or host seeking [4]. Longitudinal sampling is important to capture host shedding or transmission, yet such studies are logistically difficult. One clear contribution of predictive modeling based on serology and PCR is therefore to narrow the scope of hosts to then sample longitudinally for virus isolation and to understand transmission dynamics [2,3]. Resulting data on host competence could then allow confirming or refuting model predictions (Figure 1).

Similarly, within-host data can inform parameterizing (e.g., receptor use for susceptibility covariates) and validating predictive models. As *in vivo* pathogen challenge trials are costly, labor intensive, and can be limited to high-containment laboratories, they may be most useful for robustly testing model predictions (Figure 1). In one example, experimentally infected Egyptian fruit bats (*Rousettus aegyptiacus*) did not support *in vivo* replication of Nipah virus [14], despite prior serology-based predictive models suggesting this species could be a likely reservoir [3].

Iteratively integrating field studies, predictive models, and experimental trials could build a



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Figure 1. Integrating Competence into Reservoir Host Predictive Models. We take a simplified statistical model (in matrix notation, where β represents regression coefficients and ε represents errors) and illustrate how data can be used as the response (arrows towards y), covariates (arrows towards X), and/or validation (arrows from y). Presence of pathogen antibody or antigen is commonly used as the response but conflates competence with exposure. Predictions from these models can be validated by field measures of competence, such as isolating live virus or diagnostics of certain arthropod vectors, both of which can also be more informative response variables. Both *in silico* and *in vitro* analyses can characterize receptor binding (i.e., informing susceptibility) and reveal host factors required for viral replication, which can be used as covariates or validation for models using PCR or serology responses. Lastly, *in vivo* experimental challenge studies can confirm pathogen replication and transmission to susceptible hosts or vectors, and results can serve as either the response or model validation.

systematic dataset of host competence for select pathogens, which would facilitate including competence as the response in statistical models (Figure 1). To date, competence has been analyzed in several comparative frameworks (e.g., how host life history shapes the proportion of infected larval ticks per species [8]). Such data have generally yet to be included in larger predictive models, although doing so may generate more meaningful forecasts of likely reservoirs. In one recent example, the presence of infected larval ticks was integrated into machine learning algorithms

to determine the taxonomic and life history correlates of competence for *Borrelia burgdorferi* across bird species, which allowed predicting likely but unsampled avian reservoirs [9]. A key research priority moving forward will be to determine how statistical models trained on serology, PCR, and competence response variables differ in performance and predictions.

Improving Reservoir Host Prediction

Efforts to predict reservoirs of zoonotic pathogens are expected to increase

dramatically following the emergence of SARS-CoV-2 and the COVID-19 pandemic. On their own, traditional modeling approaches using data on antigen detection and seropositivity will likely provide limited insights into the underlying competence of proposed reservoir hosts. Being agnostic to host susceptibility and suitability, such models could fail to identify true reservoirs and lead to unnecessary responses (e.g., culling). Here, we have outlined how competence data could be better integrated into predictive research, through an iterative combination of testing model predictions, including within-host data as covariates, and eventually modeling competence itself as the response (Figure 1). Such work could produce more relevant forecasts of reservoirs, identify host traits with causative physiological links to infection, and enhance our understanding of how different wildlife species contribute to pathogen transmission in host communities. To accomplish such aims, we emphasize a broader need for close collaboration between ecologists, data scientists, microbiologists, and immunologists to ensure that data and methods are used and interpreted accurately and to foster better dialogue between prediction and validation.

Acknowledgments

D.J.B. was supported by an appointment to the Intelligence Community Postdoctoral Research Fellowship Program at Indiana University, administered by Oak Ridge Institute for Science and Education through an interagency agreement between the US Department of Energy and the Office of the Director of National Intelligence. S.N.S. was supported by the Intramural Research program of the National Institute of Allergy and Infectious Diseases. The authors were supported by funding to the Viral Emergence Research Initiative (VERENA) consortium, including NSF BII 2021909 and a grant from Institut de Valorisation de Données (IVADO). We thank members of the Ketterson Laboratory and two anonymous reviewers for helpful feedback on earlier versions of this manuscript.

¹Department of Biology, Indiana University, Bloomington, IN, USA²Laboratory of Virology, Division of Intramural Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Hamilton, MT, USA³Center for Global Health Science and Security, Georgetown University Medical Center, Washington, D.C., USA

*Correspondence:

danbeck@iu.edu (D.J. Becker).

<https://doi.org/10.1016/j.tree.2020.08.014>

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Forum**The Silver Lining of Extreme Events**M.A. Coleman^{1,2,3,*} and T. Wernberg³

Extreme climatic events cause devastating impacts to species and ecosystems, precipitating significant mortality. However, emerging empirical evidence is revealing that such mortality can drive directional selection and result in increased tolerance. We discuss the novel opportunities for promoting climate resilience presented by this ‘silver lining’ of extreme events.

The Destructive Nature of Extreme Events

Extreme climatic events such as floods, cyclones, heatwaves, and cold spells have precipitated significant impacts to species and ecosystems over evolutionary and contemporary time scales [1] and are predicted to increase in intensity and frequency under climate change [2]. By definition, extreme events exceed the norms of environmental conditions and therefore drive significant mortality, resulting in range shifts, local extinctions, and transitions to novel ecosystem states [3]. This causes significant loss of economic, social, and ecological values derived from natural systems. Consequently, extreme events are overwhelmingly perceived as negative and receive significant scientific, societal, financial, and media attention. However, emerging empirical research is demonstrating that mortality induced by extreme events is often not random but can drive directional selection and rapid adaptation to climate stressors [1,4–7]. Acknowledging this positive ‘silver lining’ of extreme events presents unique opportunities to boost resilience of natural populations under future climates.

Extreme Events Promote Selection and Increased Resilience

Theory predicts that extreme events cause selection against weak phenotypes and, where species maximum thresholds are approached, but not exceeded, promote the persistence of stress tolerant

phenotypes (Figure 1). When this has a heritable basis, rapid adaptation to the prevailing stressor can occur. As such, selection driven by extreme events may be one of the few natural mechanisms through which species and populations can increase their resilience to the rapid advance of climate change. However, despite a strong theoretical basis for extreme events driving selection, studies have empirically demonstrated this process only recently. For example, comparisons of genomic and physiological data before and after a severe cold snap demonstrated increased cold tolerance in green anole lizards (*Anolis carolinensis*) [4]. Similarly, cyclones induced widespread selection favouring heritable traits in group-living spiders that enhanced competitive resource acquisition, reproduction, and survival (*Anelosimus studiosus*) [6]. In the marine environment, an extreme marine heatwave caused significant loss of genetic diversity and signatures of directional selection towards increased thermal tolerance in kelp forests (*Scytothalia dorycarpa*, *Sargassum fallax*, and *Ecklonia radiata*) [5,7]. In all cases, these extreme events precipitated significant, but nonrandom mortality, favouring certain traits or genotypes that confer greater fitness to the climate stressors (e.g., cold, heat) underpinning the extreme events. With extreme events predicted to increase in the future [2], selection may confer increased resilience and accelerated adaptation under climate change by increasing the frequency of strong, climate-proof genotypes. This ‘silver lining’ of the otherwise destructive impacts of extreme events is only just being realised, but provides novel opportunities for managing future resilience of species and ecosystems under climate change (Figure 1).

Harnessing the ‘Silver Lining’ of Extreme Events

There is increasing support for conservation, restoration, and management of natural ecosystems to proactively anticipate future climatic conditions. This involves strategies