

The coevolutionary mosaic of betacoronavirus emergence risk

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Driven by the need to understand the ecological factors involved in the emergence of *Betacoronavirus* (the genus causing the SARS, MERS, and COVID-19 in human) through bat hosts, we develop an approach to the assessment of spillover risk based on the Geographic Mosaic Theory of Coevolution. In doing so, we provide a global mapping of the spillover risk posed by betacoronaviruses, reflecting the fact that this risk is best understood through the multi-faceted prism of ecological and evolutionary mechanisms. Our framework reveals that host richness alone, although a component of viral hazard, is not a sufficiently integrative predictor of risk. We offer alternative insights based on viral sharing, host compositional uniqueness, and host phylogenetic diversity and phylogeographic regions. By comparing our aggregated measure of risk to a proxy for human density, namely the proportion of each pixel that is covered by urban or built land, we provide a synthetic risk map, allowing the identification of hotspots where the bat-betacoronavirus interaction network may facilitate the emergence of novel viruses and their spillover into human populations.

1 Disease emergence is complex, and is driven not only by animal-human contact, but also by the
2 underlying evolutionary dynamics in viral reservoirs.¹ Although host richness is often used as a superficial
3 proxy for spillover risk,^{2,3} these approaches oversimplify the relevant interspecific heterogeneity in
4 immunology, behavior, and other traits, and therefore overlook unique host pools that allow for the rapid
5 evolution of highly divergent viruses.⁴ In the case of generalist pathogens like betacoronaviruses, there is
6 conceptual and empirical support to the idea that these community-level mechanisms are even more
7 important,⁵ particularly given that cross-species transmission may, as a rule, structure viral evolution
8 more than co-divergence with hosts.⁶ This creates a disconnect between coevolutionary theory (including
9 empirical evidence from virology) and most existing ecological frameworks for mapping spillover risk.

10 The Geographic Mosaic Theory of Coevolution (GMTC) attempts to explicitly connect microevolutionary
11 dynamics to the macroecology and biogeography of symbiotic interactions.⁷ The GMTC posits that
12 coevolutionary processes among pairs⁸ or complexes⁹ of species are structured in space by the rippling
13 effects of abiotic conditions onto evolutionary mechanism, giving rise to fragmented systems with
14 different structure and ecologically dynamics over large spatial extents.¹⁰ The GMTC predicts a spatial
15 fragmentation of coevolutionary dynamics under the joint action of three processes:¹¹ coevolutionary hot-
16 and coldspots, which appear when the intensity of *interaction* (in terms of reciprocal fitness consequences)
17 varies spatially; selection mosaics, wherein the intensity of *selection* varies across space, driven by both the
18 biotic complexity of the community (locally diverse hosts and viruses are more biotically complex) and the
19 local favorability of the environment;¹² and trait remixing, which occurs when coevolutionary dynamics
20 are driven by the arrival (or departure) of *functional traits*, through changes in community composition
21 due to invasions, meta-community dynamics, and dispersal.

22 Here, we apply the GMTC to explore and explain the global biogeography of betacoronaviruses, the group
23 that includes SARS-CoV, MERS-CoV, and SARS-CoV-2. In their bat reservoirs, coronaviruses evolve
24 through a mix of host jumps, recombination among disparate lineages, and, to a lesser degree,
25 co-divergence with their hosts—²a mix of mechanisms that creates a complex and nonlinear relationship
26 between host diversity and viral emergence. Working from a recently published database of bat hosts of
27 betacoronaviruses, we test whether spatial structure in bat-betacoronavirus coevolution is identifiable at a
28 global scale. Aiming to explain these patterns, we develop a generalized framework for applying the
29 GMTC to host-virus interactions, with a specific emphasis on the potential to create independent
30 coevolutionary dynamics (and therefore spatial fragmentation in risk) through heterogeneity. We develop

31 a trivariate risk assessment system that connects each GMTC mechanism to a quantifiable aspect of
32 host-virus interactions: (i) viral sharing rates in host communities, representing the strength of potential
33 interaction between viruses and any one host (i.e., places where viruses undergo constant host switching
34 may be coevolutionary coldspots); (ii) the phylogenetic diversity of hosts, as a proxy for variation in the
35 immunological mechanisms that antagonize viruses (i.e., the selection mosaic); and (iii) the local
36 uniqueness of the bat community, representing the potential for viruses to be exposed to novel host traits
37 (e.g., variation in receptor sequences). Together, we argue that these can be used to identify and map the
38 evolutionary drivers that—in conjunction with transmission processes (e.g., viral prevalence in reservoirs
39 and animal-human contact rates)—determine disease emergence risk.

40 Results and Discussion

41 Hotspots of host richness and viral diversification are distinct

42 Bats, the second most diverse group of mammals, are found worldwide; gradients in their species
43 richness generally track broader patterns of mammal diversity, with a striking Neotropical hotspot
44 (especially in the Amazon basin) and a secondary hotspot centered in the southeast Asian peninsula.
45 These hotspots of bat diversity are generally presumed to be hotspots of viral adaptive radiation, and
46 therefore areas of concern for human health.^{2,13} However, the hotspots of bat betacoronavirus reservoirs
47 show a distinct pattern, with primary hotspots (both in terms of size and higher values) of host richness
48 situated primarily southeast Asia, parts of southern Europe, and to a lesser extent parts of Africa in the
49 -25-0 range of latitudes (fig. 1; top). Although hundreds of species likely host undiscovered
50 betacoronaviruses, machine learning predictions have suggested that these undiscovered reservoirs should
51 follow the same diversity gradient.¹⁴ In principle, these hotspots of locally-diverse, virus-rich bat
52 communities should drive more adaptive diversification in their viruses.

53 [Figure 1 about here.]

54 However, we find that the global pattern of betacoronavirus phylogenetic distinctiveness is quite distinct
55 from both bat host richness and phylogenetic distinctiveness (fig. 1; bottom). In contrast to the sparsity of
56 Neotropical betacoronavirus hosts, South America has the most evolutionary distinct hosts *and* viruses,

57 followed by secondary hotspots in southeast Asia and the Rift Valley region have mostly distinct viruses.
58 Some degree of sampling bias may contribute to these patterns: for example, South-America is one of the
59 places where the fewest bat betacoronavirus sequences have been generated,^{2,13,15} resulting in a sparser
60 phylogenetic tree, and artificially inflating distinctiveness; conversely, disproportionate research effort in
61 eastern China¹⁶ may have led to a more complete inventory of the local diversity of coronaviruses, again
62 inflating these metrics relative to underlying patterns. Even accounting for these potential biases, though,
63 there is obvious heterogeneity in betacoronavirus evolutionary distinctiveness that is distinct from overall
64 bat diversity.

65 On closer inspection, these patterns recapitulate the evolutionary history of both the order Chiroptera and
66 the genus *Betacoronavirus*. Horseshoe bats (Rhinolophidae) are both the reservoirs of the SARS-like
67 viruses (subgenus *Sarbecovirus*) and a possible ancestral host of *Betacoronavirus*.¹⁷ The hotspots of host
68 richness and viral diversity in southeast Asia—both of which are disproportionately high, considering the
69 global landscape of bat species richness—are almost entirely driven by viral adaptive radiation through
70 host switching within this clade^{3,14}. In contrast, the Neotropical hotspot of viral distinctiveness is driven
71 by isolation by host vicariance. Out of the four main groups of betacoronaviruses, only the subgenus
72 *Merbecovirus* (MERS-like viruses) has been found in animals in the Americas—an introduction that is
73 generally presumed to be ancient.³ While comparatively understudied, New World merbecoviruses have
74 been found in the ghost-faced bats (Mormoopidae), New World leaf-nosed bats (Phyllostomidae), and
75 free-tailed bats (Molossidae) (add cite: Olival 2020 PLoS Pathogens). The former two groups are endemic
76 to the Neotropics, while the explosive adaptive radiations of the latter two (and particularly the
77 phyllostomids) are responsible for the hotspot of bat diversity in the Amazon. Together, these clades of
78 New World bats play host to a distinct regime of betacoronavirus coevolution.

79 Global biogeographic regions are consistent for bats and betacoronaviruses

80 Most previous work has assumed that coronavirus biogeography is driven by coevolutionary regimes that
81 form at finer taxonomic scales, treating the presence or richness of key bat host groups as predictive of
82 these viruses' distribution.^{2,3} Projecting bat and betacoronavirus phylogeny over space (fig. 2), we find
83 further support for the idea that bat community assembly is directly responsible for spatial heterogeneity
84 in viral coevolutionary regimes. The distinct groupings (represented by different colors, symbolizing
85 positions in a subspace formed by the first two phylogenetic principal components) are essentially

86 equivalent between the two groups, and can be coarsely delineated as (1) south and southeast Asia, (2)
87 east Asia (including northern China), west Asia, and the Mediterranean coast; (3) Eurasia above a
88 northing of 40; and (4) Africa and south America. These results suggest that, although the evolutionary
89 distinctiveness of the bat-betacoronavirus complex varies spatially, biogeographic regions are consistent
90 between bats and their viruses. In some cases, this may diverge from expectations about coronavirus
91 biogeography: for example, previous work has rarely flagged India as a region of concern, but for both bats
92 and betacoronaviruses, the subcontinent falls into the same phylogeographic regions as the southeast
93 Asian peninsula (and indeed, the region is home to known bat hosts of nobecoviruses, sarbecoviruses, and
94 merbecoviruses [Ruiz-Aravena2022EcoEvo]).

95 [Figure 2 about here.]

96 **Coevolution-informed emergence risk is different in space**

97 As host richness, joint distinctiveness, or phylogeographic structure suggest that the bat-betacoronaviruses
98 complex is globally fragmented enough to give rise to both different levels of risk (as evidenced by the
99 spatial location of spillover events) and different types of co-evolutionary dynamics, we turn to the
100 Geographic Mosaic Theory of Coevolution to provide a measure of risk accounting for multiple processes.
101 In fig. 3, we overlapped three components of spillover risk: viral sharing, *i.e.* the chance that two bats will
102 share viruses overall; Local Contribution to Beta Diversity, *i.e.* the fact that a bat community is
103 compositionally unique compared to the average compositional similarity across the entire system; finally,
104 host phylogenetic diversity, *i.e.* how dispersed the bats in a location are within the tree of life. This
105 approach leads to the definition of broad biogeographic regions of risk, where the same color represents
106 the same type of risk. By way of contrast to figures fig. 1 and fig. 2, these regions do not necessarily
107 overlap with previous spatial partitions of the bat-betacoronaviruses complex.

108 [Figure 3 about here.]

109 From the perspective of spillover risk, the most important combination of factors is a high phylogenetic
110 diversity of hosts with low viral sharing; this, essentially, means that very different betacoronaviruses
111 could co-exist within the same place. This is particularly the case given that betacoronaviruses often
112 evolve and even achieve host shifts through recombination, which requires the co-occurrence of

113 sufficiently distinct viruses to be a major driver of emergence. In fig. 3, this corresponds to yellow to pale
114 green areas, which are essentially limited to South-Eastern Asia, and to some part of Sub-Saharan Africa.
115 Adopting a geographic mosaic theory perspective on risk, other regions of the world are of lesser concern
116 (fig. 4). Our risk decomposition does not account for viral diversity or distinctiveness. The simple
117 rationale behind it is that the acquisition of viral data is rarely disconnected from the acquisition of host
118 data. There are more sources of information on hosts than on viruses, allowing to develop a host-centric
119 perspective on risk (although this estimate would be more accurate with viral traits related to e.g. ability to
120 switch hosts or pathogenic potential). Areas with high bat diversity and high turnover *may* facilitate the
121 evolutionary radiation of viruses, matching previous findings that the diversification of bat coronaviruses
122 is driven largely by host shifts (inter-genus or higher levels of cross-species transmission) and, to a lesser
123 degree, cospeciation and sharing, representing intra-genus cross-species transmission.² This
124 diversification is not an actual risk factor for spillover itself, but acts downstream of a spillover event by
125 increasing the random chance of the emergence of a virus with the raw genomic components required for
126 the potential to infect humans.

127 [Figure 4 about here.]

128 From another perspective, areas of high host uniqueness and virus sharing (red-to-pink) could provide
129 hotspots of *Betacoronavirus* risk through mixing of unique viruses (via codivergence) and in turn
130 recombination. Under our framework, such a hotspot was identified in Madagascar, where most bat
131 species are endemic following evolutionary divergence from sister species in both African and Asian
132 continents.¹⁸ Recent surveillance¹⁹ has identified a novel *Betacoronavirus* (in the subgenus *Nobecovirus*) in
133 Madagascar-endemic pteropid bat species (*Pteropus rufus*, *Rousettus madagascariensis*), emphasizing
134 strong proof of principle in model predictions.

135 **Human occupancy drives different levels of effective risk globally**

136 Based on the previous result, we extracted the risk component from the composite map (see Methods), to
137 provide a single measure of risk varying between 0 and 1. This measure is presented in fig. 4. As this map
138 represents the potential risk, it must be weighed by the potential for contacts with humans. As a proxy for
139 this measure, we used the proportion of build/urban land from the EarthEnv dataset: this is a reasonable
140 proxy for the density of humans per unit area, which increases the probability of pathogen spread more

widely.²⁰ Since human activity is required to amplify the frequency of virus encounters and thus create areas of viral amplification, mapping the potential risk against measures of land use is required to generate a more actionable assessment of risk. This map is presented in fig. 5. Most of South America and Europe are at comparatively lower risk, as although densely populated, settlements tend to be in areas with lower potential risk. Regions like Malaysia and the North coast of Australia have a high risk component, but should represent a relatively lower effective risk due to low human density. However, this mapping reveals that South-East Asia, the Indian subcontinent, and parts of sub-Saharan Africa, are at high risk due to the overlap between built areas and bat communities representing more opportunities for cross-species transmission of betacoronaviruses. In looking for the origins of SARS in China,²¹ present serological evidence that strongest human-animal contact results in higher risk of virus exposure, regardless of the animal species, but that different types of contact had different impacts. Ideally, finer-grained information about human activity (rather than human presence through anthropisation) could allow to partition this risk further, albeit at the cost of more hypotheses required to estimate the amount of risk represented by each activity. Our map of purported high risk/diversitifcation potential (Madagascar, South-America) overlay with sampling gaps for *Betacoronavirus*,¹⁶ stressing the need for spatially targeted monitoring and discovery.

[Figure 5 about here.]

PUT THIS SOMEWHERE: Available information describing the spillover of zoonotic betacoronaviruses of bat origin where data was available before and up through the COVID-19 pandemic puts spillover events of SARS-CoV-2 in Wuhan, China; SARS-CoV in Guangdong, China based on the presence of closest known viruses circulating in nature, and a nearby location where serological (antibody) evidence has indicated human exposure to SARS-like viruses;²² MERS-CoV in Saudi Arabia based on index cases available from a recently-published compendium of cases.²³ For the latest event, most if not all index cases are presumed to be camel-to-human transmission, and the precise origin point (if it exists) of MERS-CoV in bats is uncertain. Recent recombinant canine coronavirus spillover events in Haiti²⁴ and Europe²⁵ are not relevant here, as bats' involvement in these cycles of transmission have been supposed to be non-existent. These index cases fall within different phylogeographic bioregions (fig. 2), which further highlight the issue that different host-virus sub-systems may lead to widespread emergence.

169 **Conclusion**

170 Bats are important reservoir hosts for different classes of microorganisms, many of which a threat to
171 human health.^{26,27} Chiropterans emerged around 64 million years ago and are one of the most diverse
172 mammalian orders, with an estimated richness of more than 1400 species.^{28,29} They exhibit a broad variety
173 of habitat use, behaviour, and feeding strategies, putting them at key positions in the delivery and
174 provisioning of several ecosystem services, tied to important ecosystem-derived benefits to human.³⁰ For
175 example, bats are an essential component of many seed-dispersal networks.³¹ Over two-thirds of bats are
176 know to be either obligate or facultative insectivores, therefore actively contributing for agricultural pest
177 control,^{32,33} and vectors of pathogens that put a risk on human health.^{34,35} Because bats are globally
178 distributed and have a long evolutionary history, phylogeographic and biogeographic approaches are
179 required to shed light on the contemporary distribution of coevolutionary processes between bats and the
180 pathogens they host. Not all areas in which bats, viruses, and human are co-occurring are facing a risk of
181 spillover towards human populations, and the areas in which this risk exist may not be facing risks of the
182 same nature and magnitude.

183 Here, we propose a simple framework with broad explanatory power that helps contextualize discoveries
184 like highly divergent nobecoviruses in Madagascar and the previously-neglected adaptive radiation of
185 sarbecoviruses outside of southern China and throughout southeast Asia. In doing so, it advances
186 ecological theory beyond the current state of the art for global maps of emergence risk. For example,
187 previous studies that have used host richness as proxy have predicted a high diversity of unsampled bat
188 viruses,¹³ bat coronaviruses,² and even specifically betacoronaviruses¹⁴ in both the Amazon and southeast
189 Asia. While we find that both regions are characterized by highly divergent host and viral communities,
190 our framework identifies key differences between the regions. We find that Latin America is a hotspot of
191 both host and viral distinctiveness, suggesting that this branch of the bat-betacoronavirus complex may be
192 undergoing independent evolutionary dynamics from the rest of the global pool, but with limited potential
193 for viral diversification—a finding that is supported by previous work indicating a higher rate of
194 codivergence in Latin America.² In contrast, in southeast Asia, host richness and viral distinctiveness are
195 high but sharing is low; this suggests a different type of evolutionary dynamics that could generate high
196 local diversity of viruses through host switching and viral recombination (see e.g.,¹⁷ as well as the
197 discovery of recombinant viruses that share genetic material from both the SARS-CoV and SARS-CoV-2

198 branches of the Sarbecovirus lineage).³⁶ Both of these regions are priority areas for sampling, especially
199 given predictions that they contain many bat hosts of undiscovered betacoronaviruses.^{14,16} However, both
200 the evolutionary and ecological aspects of emergence risk are likely higher in southeast Asia—a fact that
201 will only become more relevant, as bats track shifting climates and exchange viruses with other species,
202 creating a hotspot of cross-species transmission unique to the region.³⁷

203 The diversity and diversification potential of bats responds to anthropogenic factors others than shifting
204 climates.³⁸ Land use changes could significantly decrease bat suitability, notably through effects on diet
205 and availability of habitats.³⁹ As our results establish that the diversification of bats betacoronaviruses
206 happens on top of processes affecting hosts, biogeographic variation in human population density and
207 anthropogenic disturbances may feed into co-evolutionary dynamics. Increase in humans-hosts contacts
208 also increase the risk of emergence of novel diseases,⁴⁰ so does the changes in landscape connectivity at
209 local/regional scales.⁴¹ This represents a challenge for both conservation strategies and disease ecology:
210 some areas can a high emergence risk and more potential for the acquisition of zoonotic viruses through
211 bat-human encounters.⁴² In particular, the challenge ahead lies in the need to quantify actual exposure
212 (and risk) accounting for several transmission scenarios, including both direct and indirect bat - human
213 interactions, and feeding back into the provision of ecosystem services by bats.

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224 **Methods**

225 **Known *Betacoronavirus* hosts**

226 We downloaded the data on bats hosts of *Betacoronavirus* from
227 <https://www.viralemergence.org/betacov> on Apr. 2022,¹⁴ and filtered it to “known” hosts (established
228 before the emergence of SARS-CoV-2) and “novel” hosts (confirmed through sampling and competence
229 assays since the initial data collection). The original database was assembled by a combination of data
230 mining and literature surveys, including automated alerts on the “bats” and “coronavirus” keywords to
231 identify novel empirical evidence of bats-betacoronaviruses associations; this yielded a total of 126 known
232 hosts, 47 of which were novel hosts.

233 **Bat occurrences**

234 We downloaded the rangemap of every current bat species that was classified as an empirically
235 documented host of *Betacoronavirus* from the previous step, according to recent IUCN data.⁴³ The range
236 maps were subsequently rasterized using the rasterize function from GDAL⁴⁴ at a resolution of
237 approximately 100kmx100km. For every pixel in the resulting raster where at least one bat host of
238 *Betacoronavirus* was present, we extract the species pool (list of all known bat hosts), which was used to
239 calculate the following risk assessment components: bat phylogenetic diversity, bat compositional
240 uniqueness, and predicted viral sharing risk.

241 **Bat phylogenetic diversity**

242 For every pixel, we measured Faith’s Phylogenetic Diversity⁴⁵ based on a recent synthetic tree with robust
243 time calibration, covering about 6000 mammalian species.⁴⁶ Faith’s PD measures the sum of unique
244 branches from an arbitrary root to a set of tips, and comparatively larger values indicate a more
245 phylogenetic diverse species pool. We measured phylogenetic diversity starting from the root of the entire
246 tree (and not from Chiroptera); this bears no consequences on the resulting values, since all branches
247 leading up to Chiroptera are only counted one per species pool, and (as we explain when describing the
248 assembly of the composite risk map), all individual risk components are ranged in [0,1]. This measure
249 incorporates a richness component, which we chose not to correct for; the interpretation of the

250 phylogenetic diversity is therefore a weighted species richness, that accounts for phylogenetic
251 over/under-dispersal in some places.

252 **Bat compositional uniqueness**

253 For every species pool, we measured its Local Contribution to Beta-Diversity;⁴⁷ LCBD works from a
254 species-data matrix (traditionally noted as \mathbf{Y}), where species are rows and sites are columns, and a value of
255 1 indicates occurrence. We extracted the \mathbf{Y} matrix assuming that every pixel represents a unique location,
256 and following best practices⁴⁸ transformed it using Hellinger's distance to account for unequal bat
257 richness at different pixels. The correction of raw community data is particularly important for two
258 reasons: first, it prevents the artifact of richer sites having higher importance; second, it removes the effect
259 of overall species richness, which is already incorporated in the phylogenetic diversity component. High
260 values of LCBD indicate that the pixel has a community that is on average more dissimilar in species
261 composition than what is expected knowing the entire matrix, i.e. a more unique community. Recent
262 results by⁴⁹ shows that LCBD measures are robust with regards to spatial scale, and are therefore
263 applicable at the global scale.

264 **Viral sharing between hosts**

265 For all bat hosts of *Betacoronavirus*, we extracted their predicted viral sharing network, generated from a
266 previously published generalized additive mixed model of virus sharing by a tensor function of
267 phylogenetic distance and geographic range overlap across mammals.⁵⁰ This network stores pairwise
268 values of viral community similarity. To project viral sharing values into a single value for every pixel, we
269 averaged the pairwise scores. High values of the average sharing propensity means that this specific extant
270 bat assemblage is likely to be proficient at exchanging viruses.

271 **Composite risk map**

272 To visualize the aggregated risk at the global scale, we combine the three individual risk components
273 (phylogenetic diversity, compositional uniqueness, and viral sharing) using an additive color model.⁵¹ In
274 this approach, every risk component gets assigned a component in the RGB color model (phylogenetic
275 diversity is green, compositional uniqueness is red, and viral sharing is blue). In order to achieve a valid

276 RGB measure, all components are re-scaled to the [0,1] interval, so that a pixel with no sharing, no
277 phylogenetic diversity, and no compositional uniqueness is black, and a pixel with maximal values for
278 each is white. This additive model conveys both the intensity of the overall risk, but also the nature of the
279 risk as colors diverge towards combinations of values for three risk components. Out of the possible
280 combinations, the most risky in terms of rapid diversification and spillover potential is high phylogenetic
281 diversity and low viral sharing,⁵² in that this allows multiple independent host-virus coevolutionary
282 dynamics to take place in the same location. In the colorimetric space, this corresponds to yellow – because
283 the HSV space is more amenable to calculations for feature extraction,⁵³ we measured the risk level by
284 calculating the angular distance of the hue of each pixel to a reference value of 60 (yellow), and weighted
285 this risk level by the value component. Specifically, given a pixel with colorimetric coordinates (h, s, v) , its
286 ranged weighted risk value is

$$v \times \left[1 - \frac{|\text{atan}(\cos(\text{rad}(h)), \sin(\text{rad}(h))) - X|}{2\pi} \right],$$

287 where X is $\text{atan}(\cos(\text{rad}(60)), \sin(\text{rad}(60)))$, a constant approximately equal to 0.5235.

288 Viral phyogeography and evolutionary diversification

289 To next represent phyogeography of betacoronaviruses in bats, we aggregated and analyzed
290 betacoronavirus sequence data. We used the following query to pull all *Betacoronavirus* sequence data
291 from the GenBank Nucleotide database except SARS-CoV-2; (“Betacoronavirus”[Organism] OR
292 betacoronavirus[All Fields]) NOT (“Severe acute respiratory syndrome coronavirus 2”[Organism] OR
293 sars-cov-2[All Fields]). We added a single representative sequence for SARS-CoV-2 and manually curated
294 to remove sequences without the RNA-dependent RNA polymerase (RdRp) sequence or that contained
295 words indicating recombinant or laboratory strains including “patent”, “mutant”, “GFP”, and
296 “recombinant”. We filtered over-represented taxa including betacoronavirus 1, hCoV-OC43, Middle East
297 respiratory syndrome coronavirus, Murine hepatitis virus, and hCoV-HKU1. Curated betacoronavirus
298 RdRp sequences were then aligned using MAFFT⁵⁴ v1.4.0 (Algorithm FFT-NS-2, Scoring matrix 200PAM /
299 k=2, gap open penalty 1.53m offset value 0.123) and a maximum likelihood tree reconstructed in
300 IQ-TREE⁵⁵ v1.6.12 with ModelFinder⁵⁶ ultrafast bootstrap approximation⁵⁷ with a general time reversible
301 model with empirical base frequencies and the 5-discrete-rate-category FreeRaye model of nucleotide

302 substitution (GTR+F+R5).

303 We first tested the hypothesis that hotspots of viral diversification would track hotspots of bat
304 diversification. To do so, we plotted the number of known bat hosts (specifically only those included in the
305 phylogeny, so there was a 1:1 correspondence between data sources) against the “mean evolutionary
306 distinctiveness” of the associated viruses. To calculate this, we derived the fair proportions evolutionary
307 distinctiveness⁵⁸ for each of the viruses in the tree, then averaged these at the bat species level, projected
308 these values onto their geographic distributions, and averaged across every bat found in a given pixel. As
309 such, this can be thought of as a map of the mean evolutionary distinctiveness of the known viral
310 community believed to be associated with a particular subset of bats present.

311 **Co-distribution of hosts and viral hotspots**

312 Subsequently, we tested the hypothesis that the biogeography of bat betacoronaviruses should track the
313 biogeography of their hosts. To test this idea, we loosely adapted a method from,^{59,60} who proposed a
314 phylogenetic method for the delineation of animal biogeographic regions. In their original method, a
315 distance matrix - where each row or column represents a geographic raster’s grid cell, and the dissimilarity
316 values are the “beta diversity similarity” of their community assemble - undergoes non-metric
317 multidimensional scaling (NMDS); the first two axes of the NMDS are projected geographically using a
318 four-color bivariate map. Here, we build on this idea with an entirely novel methodology. First, we
319 measure the phylogenetic distance between the different viruses in the betacoronaviruses tree by using the
320 cophenetic function in ape;⁶¹ subsequently, we take a principal components analysis of that distance
321 matrix (readily interchangeable for NMDS in this case) to project the viral tree into an n-dimensional
322 space. We then take the first two principal components and, as with the evolutionary distinctiveness
323 analysis, aggregated these to a mean host value and projected them using a four-color bivariate map.

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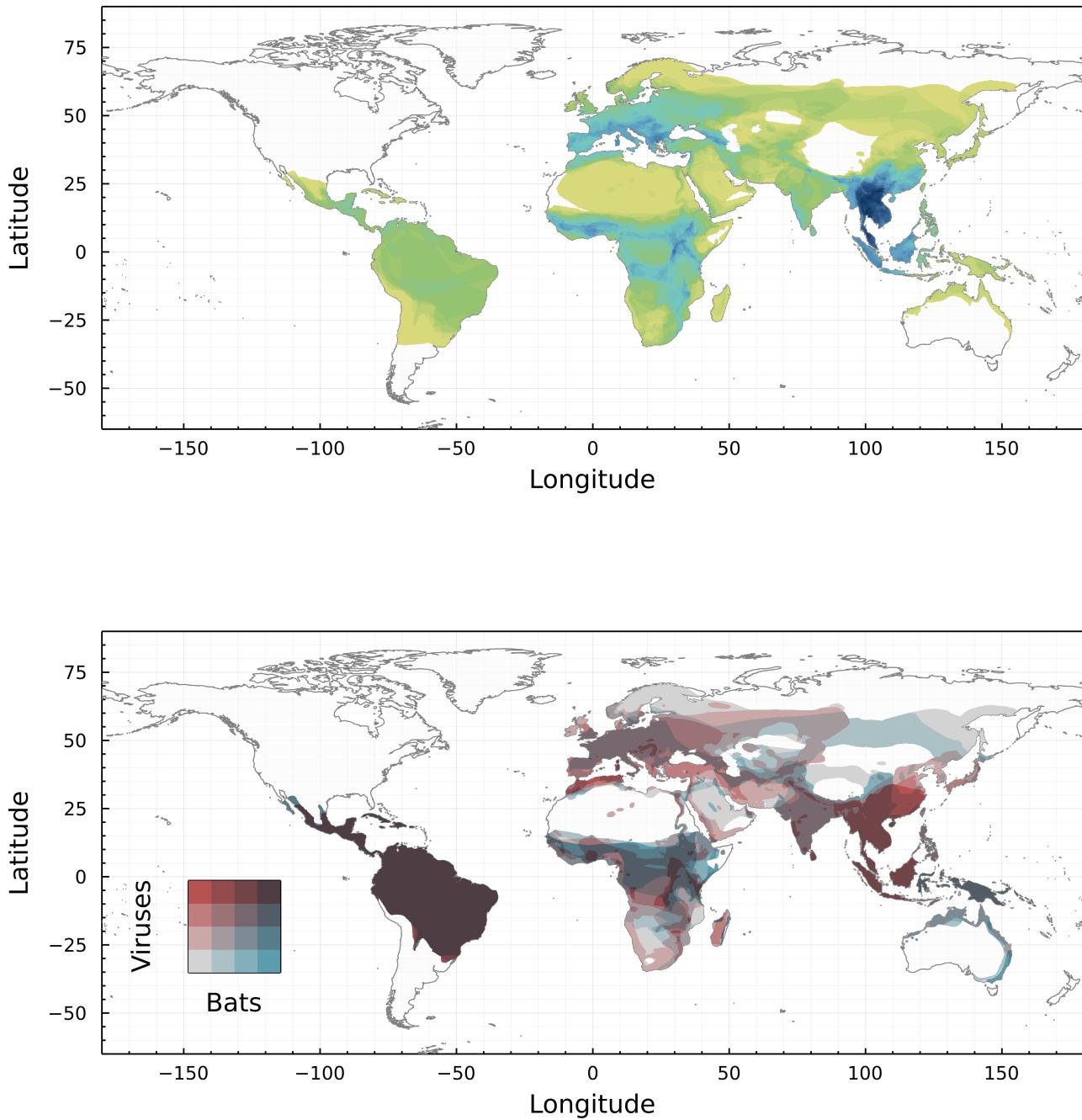


Figure 1: Top panel: relative diversity of known bat hosts of betacoronaviruses. This map shows that the region with the largest number of possible hosts is South-Eastern Asia. Bottom panel: congruence between the evolutionary distinctiveness of the hosts (grey to blue) and the viruses (grey to red).

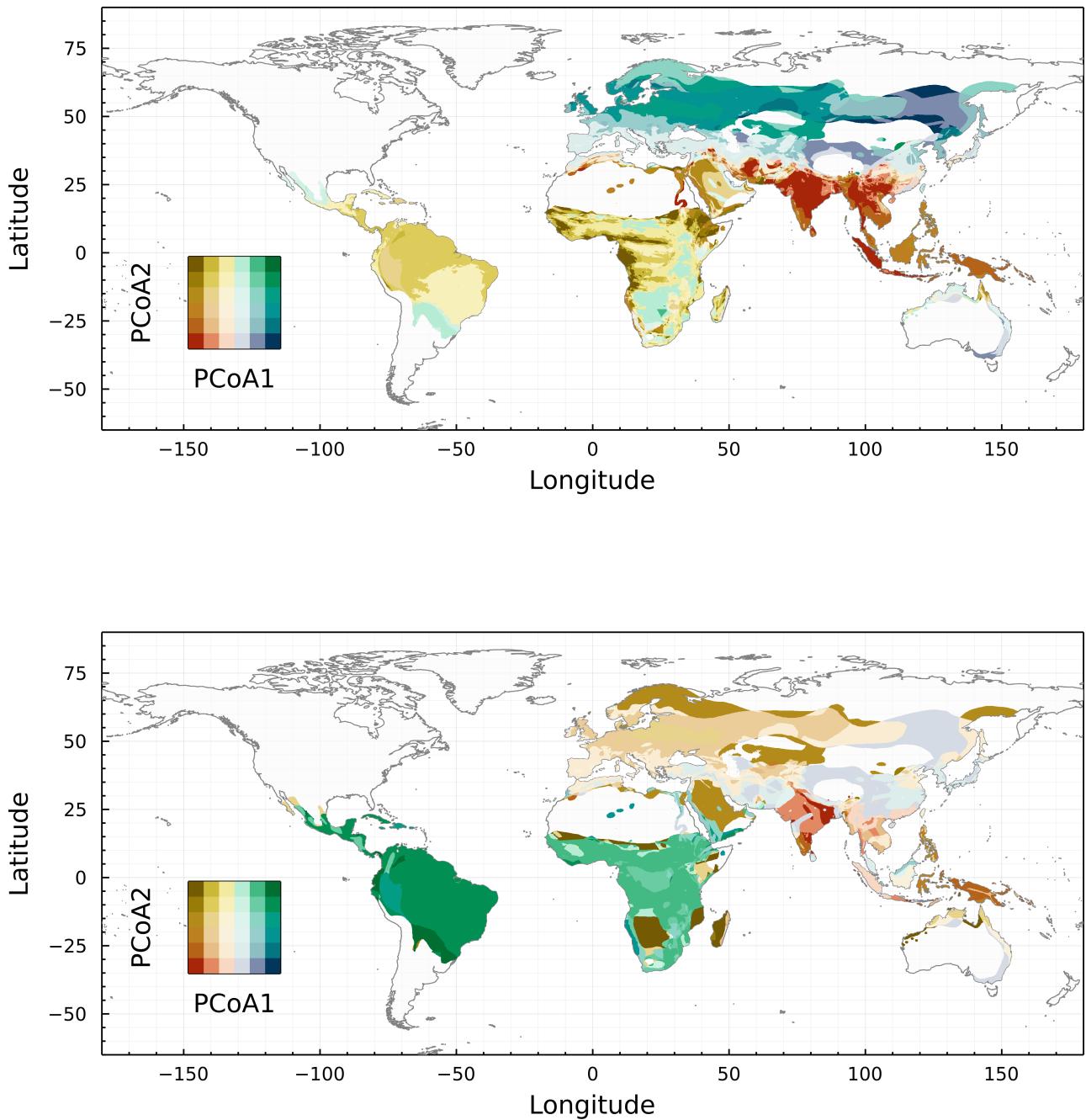


Figure 2: Phylogeographic regions of bats (top) and viruses (bottom) based on the joint analysis of their occurrence and phylogenetic relatedness. The different colors show tendencies to separate alongside the first two components of a PCoA. Note that the PCoA for the bats and viruses are independent, and so cannot be compared directly – that being said, the regions can be compared across maps.

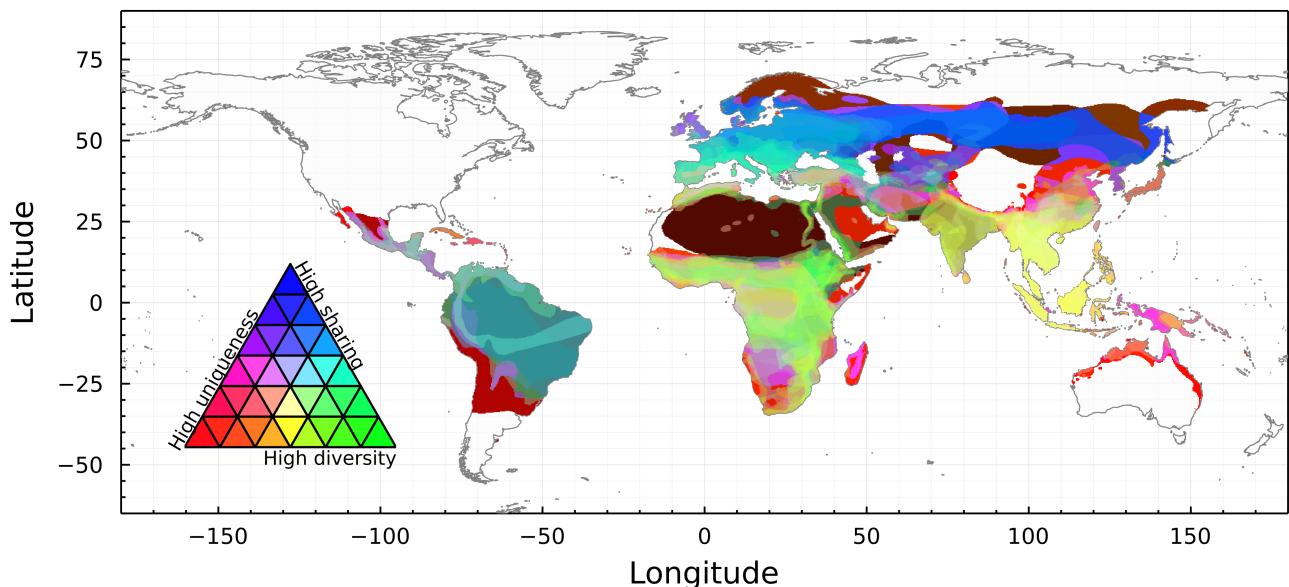


Figure 3: Trivariate additive mapping of the components of risk in the red/green/blue, where high virus sharing is encoded in the blue channel, host phylogenetic diversity in the green channel, and compositional uniqueness in the red channel. A pixel that would maximize all measures (highest possible risk) would be a pure white (specifically $\text{RGB}(1.0, 1.0, 1.0)$), and a pixel with the lowest possible values would be pure black (specifically $\text{RGB}(0.0, 0.0, 0.0)$). Therefore, lighter values (the sum of the three channels gets closer to 3) indicate higher risk, and the color indicates the proportional distribution of the factors making up the total risk.

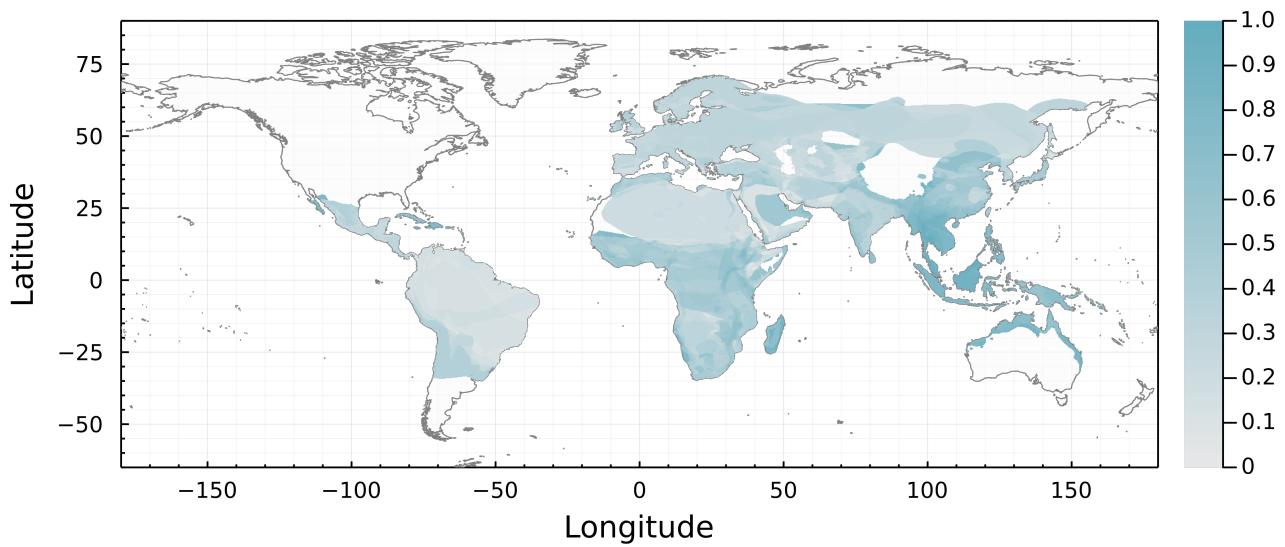


Figure 4: Extraction of a measure of *Betacoronavirus* spillover risk from bat hosts based on the colorimetric space from fig. 3. The risk is a composite measure of the color value and angular distance to the yellow hue, as defined in the methods, ranged in the unit space. Based on this analyses, regions at high risk of spillover are southeast Asia and Madagascar.

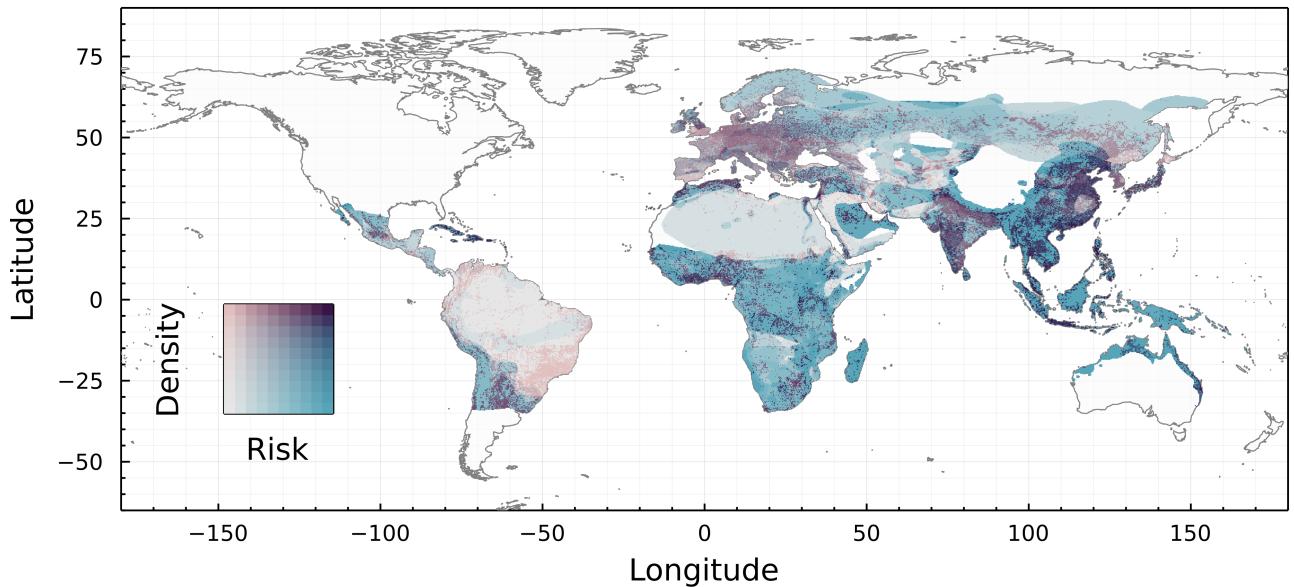


Figure 5: Overlap of the percent of each pixel occupied by urbanized structures, representing the degree of settlement, on the spillover risk map (where the risk comes only from wildlife, and ignores multi-hosts chains of transmissions including non-bats hosts). Darker pixels correspond to more risk, in that the GMTC-derived risk of fig. 4 is high *and* the pixel is densely occupied by human populations. This approach increases the relative risk of several regions in Africa, and highlights the risk in India, southeast China, and the Arabian peninsula where areas of high to moderate risk overlap with areas of denser population.