



1 **Title: Thermal mismatches explain how climate change and infectious disease**  
2 **drove widespread amphibian extinctions**

3  
4 **Authors:** Jeremy M. Cohen<sup>1\*</sup>, David J. Civitello<sup>2</sup>, Matthew D. Venesky<sup>3</sup>, Taegan A. McMahon<sup>4</sup>,  
5 and Jason R. Rohr<sup>1</sup>

6  
7 **Affiliations:**

8 <sup>1</sup>Department of Integrative Biology, University of South Florida, Tampa, FL 33620

9 <sup>2</sup>Department of Biology, Emory University, Atlanta, GA 30307

10 <sup>3</sup>Biology Department, Allegheny College, Meadville, PA 16335

11 <sup>4</sup>Biology Department, University of Tampa, Tampa, FL 33606

12 \*To whom correspondence should be addressed. E-mail: [jcohen9@mail.usf.edu](mailto:jcohen9@mail.usf.edu), 813-974-3839

13  
14 **One Sentence Summary:** Climate change and infectious disease interacted to cause widespread  
15 amphibian extinctions among species adapted to cool conditions.

16  
17 **Author contributions:** All authors contributed ideas, J.M.C. and M.D.V. wrote proposals to  
18 acquire animals, J.M.C., M.D.V. and T.A.M. conducted disease experiments, J.M.C. assembled  
19 climate database, J.M.C., D.J.C. and J.R.R. conducted statistical analyses, J.M.C. and J.R.R.  
20 wrote the paper, and all authors provided editorial advice.

21 **Abstract:**

22 Global temperatures and infectious disease outbreaks are simultaneously increasing, but linking  
23 climate change and infectious disease to modern extinctions remains difficult. The *thermal*  
24 *mismatch hypothesis* predicts that hosts should be vulnerable to disease at temperatures where  
25 the performance gap between themselves and parasites is greatest. This framework could be used  
26 to identify species at risk from a combination of climate change and disease because it suggests  
27 that extinctions should occur when climatic conditions shift from historical baselines. We  
28 conducted laboratory experiments and analyses of recent extinctions in the amphibian genus  
29 *Atelopus* to show that species from the coldest environments experienced the greatest disease  
30 susceptibility and extinction risk when temperatures rapidly warmed, confirming predictions of  
31 the *thermal mismatch hypothesis*. Our work provides evidence that a modern mass extinction  
32 was likely driven by an interaction between climate change and infectious disease.

33 **Main Text:**

34 Global climate change and emerging infectious diseases represent two of the most  
35 formidable ecological challenges in modern times, but controversy exists over whether they are  
36 causally linked (1, 2). Climatic conditions often directly influence disease outbreaks (3), and  
37 many predictive models and experiments have revealed that climate change and infectious  
38 diseases can independently drive current and future declines in biodiversity (4, 5). However,  
39 there is surprisingly little concrete evidence that interactions between climate change and  
40 infectious disease are causing widespread biodiversity losses (1, 6), possibly because of a lack of  
41 theoretical frameworks, supported by a combination of experiments and field data, that can relate  
42 climatic factors to host-parasite interactions to account for shifts in biodiversity (1). Such  
43 frameworks would be valuable in establishing causal links between climate change and  
44 extinctions mediated by disease.

45 A recently proposed hypothesis, the *thermal mismatch hypothesis* (7), suggests that  
46 infectious disease outbreaks are likely to occur at temperatures where the performance gap  
47 between pathogens and their hosts is greatest. Because parasites generally have broader thermal  
48 performance breadths than hosts (8, 9), and both hosts and parasites might be locally adapted to  
49 climatic conditions in their ranges and limited by extreme conditions, the hypothesis posits that  
50 hosts adapted to cooler climates should be especially susceptible to disease under unusually  
51 warm conditions, and vice versa (Fig. 1). Importantly, the predictions of the thermal mismatch  
52 hypothesis are robust to relaxing several of its assumptions, such as local adaptation of host and  
53 parasite and the degree and direction of the skew of the performance curves (Fig. S1). Therefore,  
54 the *thermal mismatch hypothesis* provides a framework to predict which species might be most  
55 likely to experience disease-driven declines under warming, and thus might be able to explain

56 patterns in species declines associated with climate-related outbreaks of emerging infectious  
57 diseases.

58         Although recent experimental and field evidence support the predictions of the *thermal*  
59 *mismatch hypothesis* (7), the hypothesis has not yet been applied to predict widespread host  
60 declines associated with climate change and infectious disease. In perhaps the most  
61 comprehensive spatiotemporal dataset describing a modern mass extinction, La Marca *et al.* (10)  
62 provide dates of approximately 60 extinctions in the amphibian genus *Atelopus* putatively caused  
63 by the chytrid fungus *Batrachochytrium dendrobatidis* (*Bd*), a pathogen that infects the  
64 epidermal layer of adult amphibians and is implicated in worldwide amphibian declines (11;  
65 *Table S1*). These *Atelopus* declines have been linked to climate change (12, 13), occurring in  
66 years with warm or highly variable temperatures (12, 13) despite *Bd* growing best in culture  
67 under cool or moderate conditions (7). *Bd* is sensitive to environmental conditions (14), can be  
68 locally adapted (15), and has a broad thermal breadth (16), fulfilling the assumptions of the  
69 *thermal mismatch hypothesis*. Thus, this *Atelopus* extinction dataset provides a unique  
70 opportunity to examine whether the *thermal mismatch hypothesis* can accurately predict the  
71 timing and location of disease-driven extinctions and to compete the *thermal mismatch*  
72 *hypothesis* against alternative hypotheses for these climate-related declines. Although there have  
73 been previous analyses associating climate change and *Atelopus* spp. extinctions, they relied  
74 exclusively on correlations based on broad-scale, regional climate data instead of data from  
75 individual species' ranges (12, 13; *Supplement*) and thus they failed to account for spatial  
76 heterogeneity in climate change and host adaptations to local climates. Therefore, previous  
77 analyses could not determine whether *Atelopus* spp. declines were likely caused by climate  
78 change alone or an interaction between climate change and disease. Thus, we do not yet have

79 clear, causal evidence in this system, or any system that we are aware of, that climate change  
80 caused extinctions by facilitating infectious disease (but see 17).

81 Here, we take a hypothetico-deductive approach, linking a theoretical framework,  
82 laboratory experiments, and analyses of field data to examine the relationships among  
83 extinctions, climate change, and emerging infectious disease. We simultaneously tested six  
84 hypotheses or predictors for the climate-related *Atelopus* spp. extinctions: 1) a null model, 2)  
85 pathogen alone: temperature-dependent growth of *Bd* in culture, 3) temperature variability alone:  
86 annual month-to-month variability in temperature, 4) mean climate alone: annual mean  
87 temperature, 5) climate change alone: the 5-year slope of mean temperature, and 6) the  
88 interaction between mean historical climate and climate change: because the *thermal mismatch*  
89 *hypothesis* predicts that the effect of climate change depends on whether the host is cool or warm  
90 adapted, which in turn drives the differential performance of host and pathogen.

91 Given that previous climate change analyses of the *Atelopus* dataset relied on correlating  
92 extinctions with regional climate data (12, 13), we first verified that climate change was indeed  
93 associated with these extinctions based on data from individual species' ranges. In the  
94 geographic ranges of species that went extinct, mean temperatures in the five years leading up to  
95 extinction increased ~2.5 times faster than they increased in the ranges of species that remained  
96 extant (matched pairs test:  $F_{1,45}=7.73$ ,  $p<0.01$ ; see Methods; Fig. S2; Table S2) (see 18 for a  
97 *similar approach using two species*). Hence, soon-to-be extinct species were indeed experiencing  
98 conditions that were both unusually warm for them and warmer than those experienced by  
99 species that remained extant, consistent with the hypothesis that climate change played a role in  
100 *Atelopus* spp. declines.

101           Next, we set out to parameterize our statistical model by conducting laboratory  
102 experiments to evaluate the impacts of both mean temperature and temperature variability on  
103 *Atelopus* spp. mortality risk. First, we conducted a *Temperature Gradient Experiment* in which  
104 we exposed *Atelopus zeteki*, which we consider to be cold-adapted for a variety of reasons (see  
105 Supplement), to *Bd* in replicated temperature-controlled incubators (19; Fig. S2) across a  
106 naturally relevant temperature gradient (14°, 18°, 22°, 26°, and 28°C) while simultaneously  
107 maintaining unexposed frogs and growing *Bd* in liquid cultures in the same incubators. In this  
108 experiment, the temperature gradient did not affect *A. zeteki* mortality in the absence of *Bd* (cox  
109 proportional-hazards model:  $X^2=0.54$ ,  $p=0.46$ ), but mortality increased significantly with  
110 temperature when *A. zeteki* was exposed to *Bd* (*Bd* x temperature:  $X^2=4.41$ ,  $p=0.036$ ). In fact,  
111 within a week of exposure to *Bd*, frogs at 26° and 28°C experienced 69% and 78% mortality,  
112 respectively, suggesting a temperature-dependent cost of exposure to *Bd* (see Supplement),  
113 whereas only one *Bd*-exposed animal died at the two coldest temperatures within a week of  
114 exposure (6% mortality) and only four *Bd*-negative animals died throughout the experiment  
115 (20% mortality; Fig. 2; Fig. S4). Similarly, *Bd* growth rates on frogs increased with temperature  
116 (Fig. 2a). In contrast, temperature-dependent *Bd* growth in culture closely followed previously  
117 reported patterns with growth rates increasing as temperature increased until 18.0°C (optimum)  
118 and then decreasing thereafter with little growth above 26°C (20; Fig. 2a, Fig. S5). These results  
119 demonstrate that patterns of temperature-dependent *Bd* performance in culture and on hosts  
120 differ sharply, a result consistent with the *thermal mismatch hypothesis*, which predicts that  
121 parasites should have maximum growth on host at temperatures where they most outperform the  
122 host rather than at temperatures where the parasite has the greatest absolute performance in  
123 culture. The striking monotonic positive association between temperature and both *Bd* growth on

124 frogs and *Bd*-induced host mortality contradict a common assumption that *Bd* outbreaks only  
125 occur at cool or moderate temperatures (14, 21). Importantly, although we only tested one  
126 *Atelopus* species in this experiment, the observed patterns are likely generalizable to other  
127 *Atelopus* spp., because a global analysis of *Bd* prevalence in 15,410 individuals from 598  
128 amphibian populations and 1,399 species revealed that cold- and warm-adapted amphibians  
129 generally have peak *Bd* prevalences during warm and cold spells, respectively (7; Fig. S6).

130         Second, we conducted a *Temperature Shift Experiment* in which we exposed *A. zeteki* to  
131 *Bd* at either constant or variable temperatures to evaluate how temperature variability affects host  
132 susceptibility. *A. zeteki* were exposed to *Bd* at 14°, 17°, 23°, or 26°C immediately following  
133 either two weeks of acclimation to these temperatures or two weeks of acclimation to 20°C, so  
134 that all the hosts experienced either constant or shifted temperatures before *Bd* exposure,  
135 respectively. As with the previous experiment, *Bd*-induced mortality increased with temperature  
136 (cox-proportional hazards model and ANOVA:  $X^2=4.08$ ,  $p<0.05$ ; Table S3). At the same *Bd*  
137 exposure temperatures, frogs that experienced temperature shifts had higher *Bd* loads than those  
138 that did not experience shifts (ANOVA:  $F_{1,34}=8.78$ ,  $p=0.005$ ), consistent with the findings of  
139 previous studies (19, 22). However, we did not observe any significant effect of the temperature  
140 shift treatment on mortality (Shift treatment:  $X^2=0.84$ ,  $p=0.36$ ; Shift  $\times$  temperature:  $X^2=1.03$ ,  
141  $p=0.31$ ), and the temperature gradient accounted for >6 times the variance in *Bd*-induced  
142 mortality as temperature variability (Table S4).

143         Given the results of our two laboratory experiments, we hypothesized that *Bd* growth in  
144 culture, temperature variability, and mean temperature alone would be poor predictors of  
145 *Atelopus* extinctions in the wild relative to the *thermal mismatch hypothesis*, which posits that as  
146 temperature increases, disease and extinction risk should be most pronounced among *Atelopus*

147 spp. from cooler regions because they should experience a larger performance gap relative to *Bd*  
148 than species from warmer regions (Fig. 1). This prediction of the *thermal mismatch hypothesis*  
149 would manifest as a statistical interaction between the temperature to which a species is adapted  
150 (50-year mean temperature in a species' geographic range) and the level of climate change it has  
151 experienced because cold-adapted species should experience disease-associated declines when  
152 temperatures increase, whereas warm-adapted species should not. To test these hypotheses, we  
153 utilized a time-dependent cox-proportional hazards survival model (23, see *Methods*) that  
154 concurrently evaluated the following predictors of the occurrence and timing of extinctions: *Bd*  
155 growth in culture, temperature variability, mean temperature, climate change, and the *thermal*  
156 *mismatch hypothesis* (see *Methods*). Given that extinction probabilities have repeatedly been  
157 shown to be negatively dependent on geographic range size (24), range size was included as a  
158 crossed factor with each predictor in our model. The model also controlled for two precipitation  
159 variables and altitude, which have been associated with *Atelopus* spp. extinction probabilities  
160 (12).

161 Consistent with our experiments, *Atelopus* spp. extinction risk was not significantly  
162 explained by interactions between geographic range size and *Bd* growth in culture or temperature  
163 variability but was significantly explained by the *thermal mismatch hypothesis* (Table 1).  
164 Species with large range sizes rarely experienced extinctions and thus were not strongly  
165 impacted by climate or disease. In contrast, species with smaller range sizes showed extinction  
166 patterns consistent with the *thermal mismatch hypothesis*. Increasing temperatures associated  
167 with climate change (positive slope five years before extinction) were positively associated with  
168 the occurrence and timing of the extinction of cold-adapted *Atelopus* spp. (Fig. 3a,c), whereas  
169 climate change did not predict the occurrence and timing of declines of warm-adapted species



170 (Range size  $\times$  temperature shift  $\times$  40-year mean temperature;  $\beta=11.5$ ,  $df=22$ ,  $p=0.02$ , Table 1,  
171 Fig. 3b,d). In fact, in the absence of any climate change, warm-adapted species were more likely  
172 to experience extinctions in cool rather than warm years (Fig. 3b,d), also consistent with the  
173 *thermal mismatch hypothesis* (Fig. 1). The model testing the *thermal mismatch hypothesis*  
174 explained about 2.5 times more of the variance in extinctions than a model that did not contain  
175 the interaction (Nagelkerke's pseudo- $R^2=0.466$  and  $0.189$ , respectively).

176 To gather further support for the notion that an interaction between climate change and  
177 *Bd* drove *Atelopus* extinctions, we compared the magnitude of climate change and extinctions  
178 experienced by genus *Atelopus*, which is believed to have been widely exposed to *Bd* and is  
179 found in a region of South America where *Bd* has been detected as early 1894 (25), to  
180 amphibians in Madagascar and Scandinavia, regions historically considered to be free of *Bd* (26-  
181 28). Compared to *Atelopus* spp., amphibian species in Madagascar and Scandinavia experienced  
182 similar and more climate change between 1950 and 2004, respectively (T-test:  $T=0.118$ ,  
183  $p=0.906$ ;  $T=-5.59$ ,  $p<0.0001$ ; Fig. S7). However, unlike genus *Atelopus*, there were no  
184 amphibian extinctions in these areas during this time (29). This suggests that, in the absence of  
185 *Bd*, the same level of climate change experienced in Latin America was insufficient to cause  
186 amphibian extinctions in Madagascar and Scandinavia. Although there are major differences in  
187 taxonomy and life history between these groups of amphibians, as well as differences in the  
188 potential stressors they experienced, these results are consistent with the *thermal mismatch*  
189 *hypothesis* and our laboratory findings, which suggest that *Atelopus* declines were caused by an  
190 interaction between climate change and *Bd* rather than either stressor alone. However, we  
191 caution that these analyses assume a consistent response to climate change across regions, which

192 may not be realistic given that a degree change in temperature has a greater metabolic impact on  
193 tropical species than it does on temperate species (30).

194 Our experiments and analyses of field data together suggest that *Atelopus* spp. from  
195 cooler environments are more vulnerable to mortality from chytridiomycosis under warmer  
196 conditions than those from warmer environments and thus, climate change poses a greater threat  
197 to cold-adapted *Atelopus* spp. Therefore, the *thermal mismatch hypothesis* was a useful  
198 framework for predicting which species were most likely to be impacted by an interaction  
199 between climate change and infectious disease outbreaks in this system. However, the generality  
200 of the *thermal mismatch hypothesis* is unknown, as it has only been evaluated in systems with  
201 ectothermic hosts and directly transmitted pathogens, which may be especially sensitive to  
202 environmental conditions. Further large-scale analyses of disease datasets are needed to test how  
203 well the *thermal mismatch hypothesis* applies across host-parasite systems that vary in host  
204 thermal biology or mode of transmission.

205 As global temperatures and infectious disease outbreaks have increased, these two crises  
206 have been repeatedly correlated by researchers to explain species declines and extinctions.  
207 However, evidence that they interact to cause declines has been elusive, possibly because  
208 researchers have tried to simplistically correlate increases in temperature with infectious disease,  
209 rather than looking for more nuanced patterns that depend on the host-parasite interaction (1).  
210 Here, we apply the *thermal mismatch hypothesis*, a framework that can relate environmental  
211 temperature to disease patterns while accounting for host-level variation in adaptation to climate  
212 to predict which host species are most vulnerable to infectious disease with global warming. By  
213 combining experiments with field patterns to examine how mean temperature and temperature  
214 variability impact susceptibility to *Bd* in the amphibian genus *Atelopus*, we provide the first

215 evidence that one of the greatest modern day mass extinctions was likely driven by an interaction  
216 between climate change and infectious disease.

217

## 218 **Acknowledgments:**

219 Thanks to the Maryland Zoo for providing us with the *A. zeteki* used in the experiments.

220 We thank N. Argento, K. Ebener, H. Folse, C. Gionet, T. James, C. Koshy, C. Malave, L.

221 Martinez-Rodriguez, C. Steffan, S. Rubano, and K. Vazquez for their assistance in all aspects of

222 the lab work and animal maintenance. In addition, we thank all members of the Rohr lab for

223 their helpful comments on the manuscript. Funds were provided by grants to J.R.R. from the

224 National Science Foundation (EF-1241889), the National Institutes of Health (R01GM109499,

225 R01TW010286-01), the US Department of Agriculture (2009-35102-0543), and the US

226 Environmental Protection Agency grant (CAREER 83518801).

227

## 228 **References:**

229 1. J. R. Rohr *et al.*, *Trends Ecol Evol* **26**, 270 (Jun, 2011).

230 2. C. D. Harvell *et al.*, *Science* **296**, 2158 (Jun 21, 2002).

231 3. M. Pascual, L. F. Chaves, B. Cash, X. Rodo, M. Yunus, *Clim Res* **36**, 131 (Apr 30, 2008).

232 4. X. Liu, J. R. Rohr, Y. M. Li, *Proc. R. Soc. Lond. Ser. B-Biol. Sci.* **280**, (Feb, 2013).

233 5. J. A. Patz, D. Campbell-Lendrum, T. Holloway, J. A. Foley, *Nature* **438**, 310 (Nov,

234 2005).

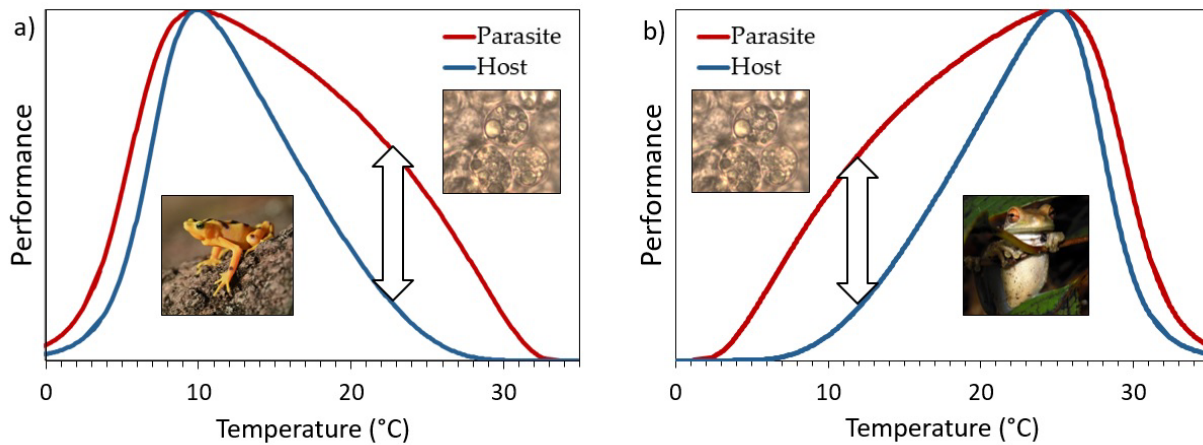
235 6. A. E. Cahill *et al.*, *Proceedings of the Royal Society B-Biological Sciences* **280**, (Jan 7,

236 2013).

- 237 7. J. Cohen *et al.*, *Ecology Letters* **20**, 184 (2017).
- 238 8. J. Rohr *et al.*, (in review).
- 239 9. L. G. M. Baas-Becking, *Geobiologie; of inleiding tot de milieukunde*. (WP Van Stockum  
240 & Zoon NV, 1934).
- 241 10. E. La Marca *et al.*, *Biotropica* **37**, 190 (Jun, 2005).
- 242 11. J. P. Collins, *Proceedings of the National Academy of Sciences of the United States of*  
243 *America* **110**, 9193 (Jun 4, 2013).
- 244 12. J. A. Pounds *et al.*, *Nature* **439**, 161 (Jan 12, 2006).
- 245 13. J. R. Rohr, T. R. Raffel, *Proceedings of the National Academy of Sciences of the United*  
246 *States of America* **107**, 8269 (May 4, 2010).
- 247 14. A. M. Kilpatrick, C. J. Briggs, P. Daszak, *Trends Ecol Evol* **25**, 109 (2010).
- 248 15. L. A. Stevenson *et al.*, *PLoS ONE* **8**, (Sep 4, 2013).
- 249 16. J. Voyles *et al.*, *Oecologia*, (2017).
- 250 17. T. Ben-Horin, H. S. Lenihan, K. D. Lafferty, *Ecology* **94**, 161 (Jan, 2013).
- 251 18. R. A. Alford, K. S. Bradfield, S. J. Richards, *Nature* **447**, E3 (May 31, 2007).
- 252 19. T. R. Raffel *et al.*, *Nature Climate Change* **3**, 146 (Feb, 2013).
- 253 20. D. C. Woodhams, R. A. Alford, C. J. Briggs, M. Johnson, L. A. Rollins-Smith, *Ecology*  
254 **89**, 1627 (2008).
- 255 21. L. Berger *et al.*, *Fungal Ecol* **19**, 89 (Feb, 2016).
- 256 22. T. R. Raffel, N. T. Halstead, T. A. McMahon, A. K. Davis, J. R. Rohr, *Proc. R. Soc.*  
257 *Lond. Ser. B-Biol. Sci.* **282**, (Feb 22, 2015).
- 258 23. T. Therneau, (2014).
- 259 24. C. D. Thomas *et al.*, *Nature* **427**, 145 (Jan 8, 2004).

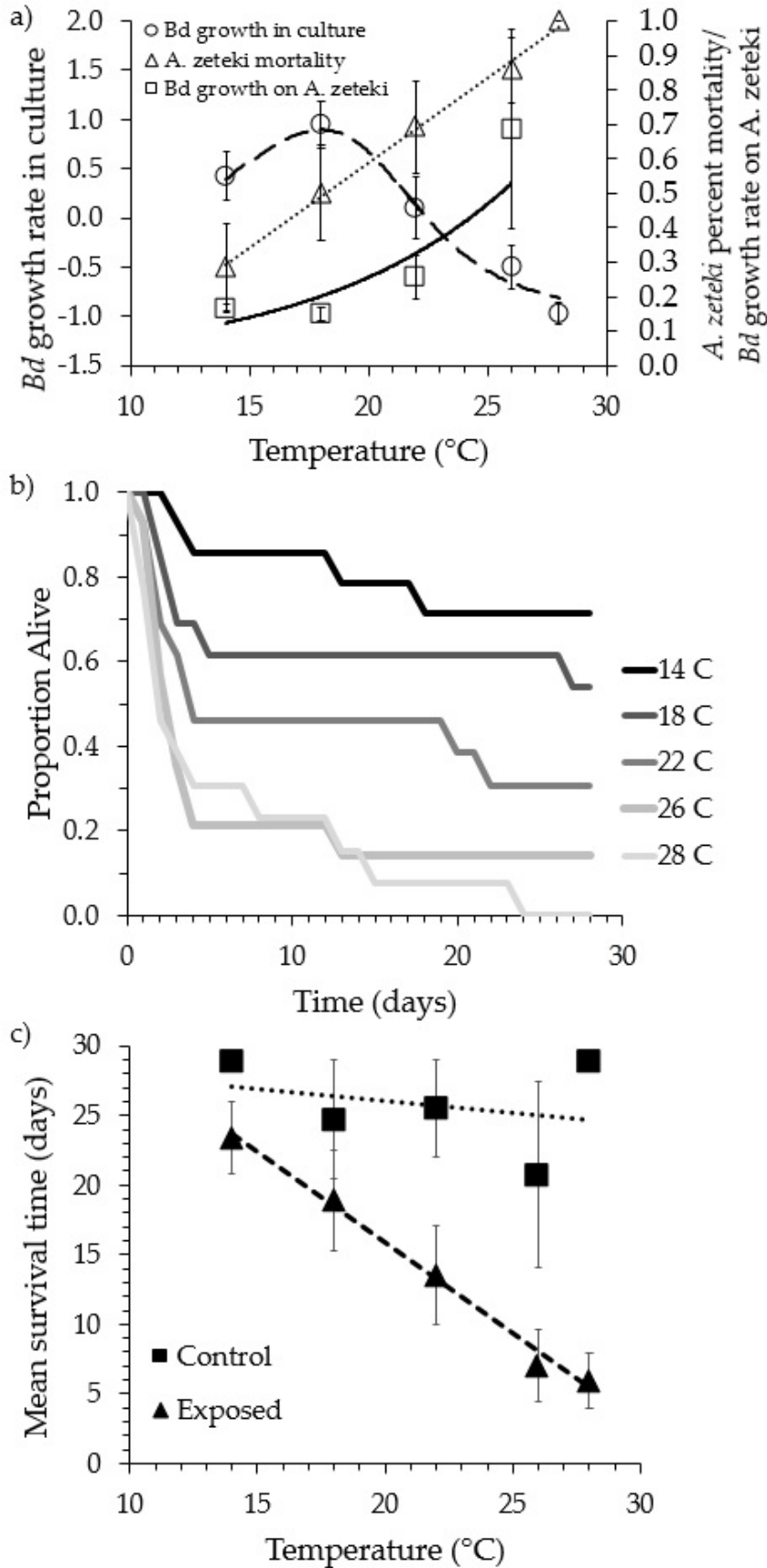
- 260 25. D. Rodriguez, C. Becker, N. Pupin, C. Haddad, K. Zamudio, *Molecular Ecology* **23**, 774  
261 (2014).
- 262 26. J. E. Kolby *et al.*, *PLoS ONE* **10**, (Jul 29, 2015).
- 263 27. F. Andreone *et al.*, *Conservation Biology* **19**, 1790 (Dec, 2005).
- 264 28. [www.bd-maps.net](http://www.bd-maps.net). (2017).
- 265 29. N. S. Sodhi *et al.*, *PLoS ONE* **3**, (Feb 20, 2008).
- 266 30. M. E. Dillon, G. Wang, R. B. Huey, *Nature* **467**, 704 (2010).
- 267
- 268

269 **Figures:**



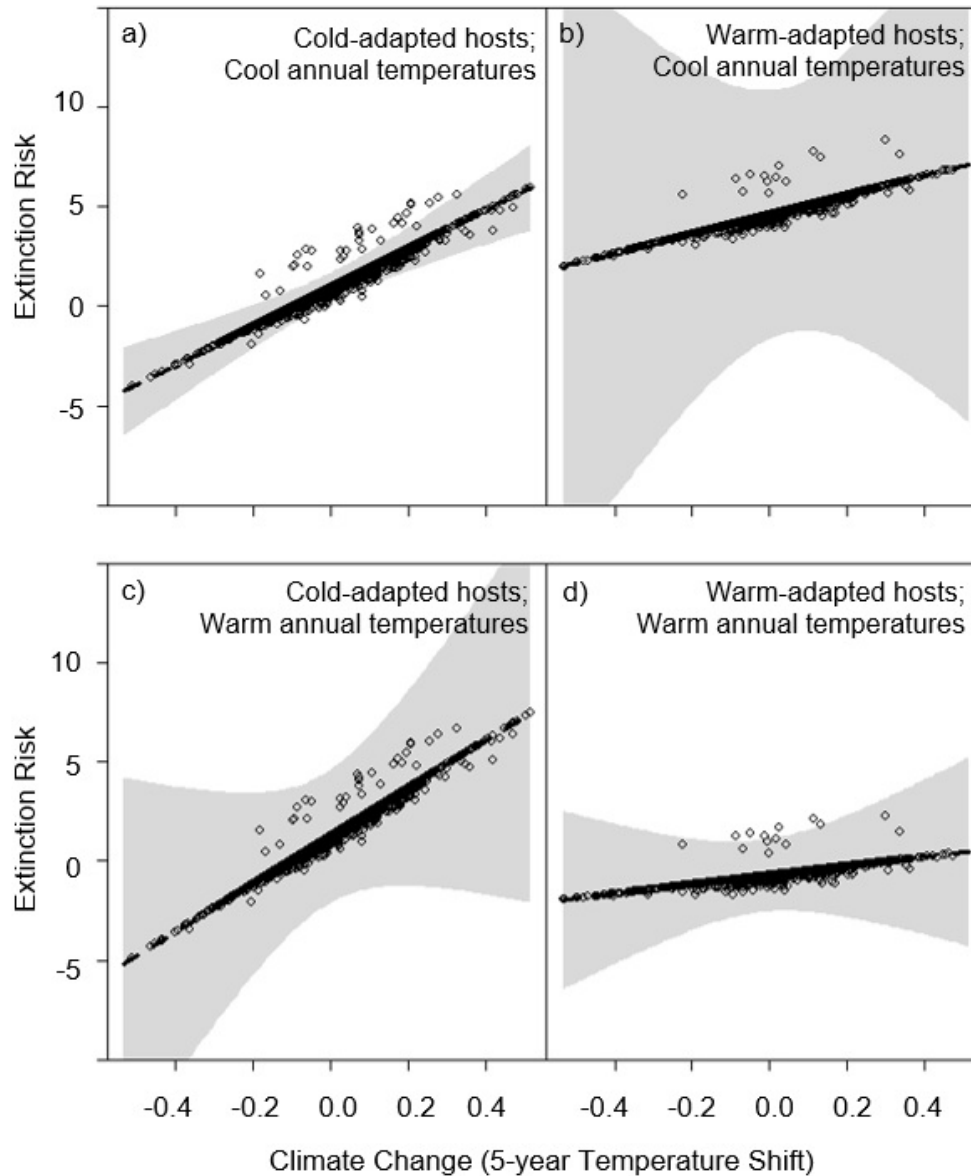
270  
271

272 **Fig. 1. Conceptual figure describing the *thermal mismatch hypothesis*.** In isolation, small  
273 organisms, such as parasites (red lines), generally have broader thermal performance curves than  
274 larger organisms, such as hosts (blue lines). Parasite growth on hosts is likely to occur at  
275 temperatures where a parasite most outperforms its host (bidirectional arrows), and not  
276 necessarily at the temperature at which a parasite performs best in isolation, providing a  
277 hypothesis for the thermal performance curve of a parasite growing on the host. For interacting  
278 cold-adapted hosts and parasites (a), parasite growth should be maximized at relatively warm  
279 temperatures, whereas for interacting warm-adapted hosts and parasites (b), parasite growth is  
280 predicted to be maximized at relatively cool temperatures.



282 **Fig. 2. Temperature-dependent patterns of *Batrachochytrium dendrobatidis* (*Bd*) growth**  
283 **and *Atelopus zeteki* mortality. (a)** *A. zeteki* experienced high mortality (triangles, dotted line)  
284 and high *Bd* growth (squares, solid line) at warm temperatures after *Bd* exposure, even though  
285 *Bd* growth rates in culture (circles, dashed line) were low at these temperatures. We could not  
286 measure *Bd* growth rates on *A. zeteki* at 28 °C because very few animals survived long enough to  
287 be tested multiple times. **(b)** Survival plot for *A. zeteki* exposed to *Bd* across two temporal  
288 blocks. **(c)** Mean survival time for *A. zeteki* at each of five temperatures when exposed to *Bd*  
289 (triangles; both temporal blocks) or not exposed (squares; 2<sup>nd</sup> temporal block). Temperature and  
290 *Bd* exposure interacted to induce high mortality in *A. zeteki* ( $X^2=4.41$ ,  $p=0.036$ ). Animals  
291 surviving the experiment are conservatively assumed to have died on day 29 for these figures  
292 only but were censored in the survival analysis. Error bars represent SEMs in all panels.





293

294 **Fig. 3. Partial residual plot displaying the effects of climate change and annual mean**  
295 **temperature on the extinction risk of cold- and warm-adapted *Atelopus* spp.** The partial  
296 residuals are from the time-dependent cox proportional-hazards model shown in Table 1 and  
297 display the significant three-way interaction among 5-year slopes in mean temperature-by-40-  
298 year mean temperature-by-annual mean temperature. Points represent individual years for each  
299 species and gray shading shows associated 95% confidence bands. The model suggests that  
300 species from typically cooler climates (**a,c**) were at greater risk of extinction (log-odds risk ratio;  
301 y-axis) after experiencing climate change (warming, or positive 5-year slope in mean  
302 temperature; x-axis) than species from warmer climates (**b,d**; breaks based on 20<sup>th</sup> and 80<sup>th</sup>  
303 percentiles). This pattern was consistent whether the annual mean temperature in a given year  
304 was relatively cool (**a,b**) or warm (**c,d**; breaks based on 20<sup>th</sup> and 80<sup>th</sup> percentiles), although  
305 species from warmer climates may be at greater risk when conditions are cooler (**b**).

306 **Tables:**

307 **Table 1.** Results of time-dependent cox-proportional hazards model predicting extinction with a  
 308 four-way interaction between log-transformed range size, long-term mean temperature  
 309 (40yr.meantemp), annual mean temperature (meantemp), and recent temperature shift  
 310 (tempchange) across both extinct and extant *Atelopus* spp. Mortality probability based on *Bd*  
 311 growth in culture (culturemortprob), log-transformed altitude (logaltitude) and a measure of  
 312 temperature variability (log-transformed AVMD, absolute value of monthly difference in  
 313 temperature) were also included. Bolded lines represent tests of the *thermal mismatch*  
 314 *hypothesis*.

	Coefficient	SE	Robust SE	z	p
Rangesize	-23.500	72.300	51.500	-0.460	0.64
Logaltitude	-0.124	0.283	0.147	-0.840	0.39
Culturemortprob (pathogen only)	-1.130	1.480	1.220	-0.930	0.35
Total precipitation	<0.001	<0.001	<0.001	0.840	0.40
Frequency of wet days	<0.001	<0.001	<0.001	-0.280	0.77
Log(AVMD) (temp. variability)	0.913	0.756	0.719	1.270	0.20
Tempchange (climate change only)	11.300	35.600	37.600	0.300	0.76
40yr.meantemp (cold or warm adapted)	1.310	0.901	0.759	1.730	0.08
Meantemp (mean temp. only)	0.564	0.972	0.756	0.750	0.45
Rangesize:Culturemortprob	-4.070	9.130	6.690	-0.610	0.54
Rangesize:log(AVMD)	-1.410	2.030	1.810	-0.780	0.43
Rangesize:Tempchange	-160.000	155.000	82.800	-1.930	0.05
Rangesize:40yr.meantemp	1.460	4.380	2.890	0.510	0.61
Tempchange:40yr.meantemp	-0.080	2.650	2.710	-0.030	0.97
Rangesize:meantemp	3.130	5.610	4.040	0.770	0.43
Tempchange:meantemp	0.420	2.380	2.200	0.190	0.84
40yr.meantemp:meantemp	-0.051	0.040	0.033	-1.580	0.11
<b>Rangesize:Tempchange:40yr.meantemp</b>	<b>11.500</b>	<b>9.800</b>	<b>5.060</b>	<b>2.280</b>	<b>0.02</b>
Rangesize:Tempchange:meantemp	5.680	9.480	6.130	0.930	0.35
Rangesize:40yr.meantemp:meantemp	-0.146	0.280	0.195	-0.750	0.45
Tempchange:40yr.meantemp:meantemp	-0.028	0.102	0.111	-0.250	0.80
<b>Rangesize:Tempchange:40yr.meantemp:meantemp</b>	<b>-0.464</b>	<b>0.467</b>	<b>0.224</b>	<b>-2.070</b>	<b>0.03</b>

315