



Invited Review

Sex Ratios in a Warming World: Thermal Effects on Sex-Biased Survival, Sex Determination, and Sex Reversal

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Abstract

Rising global temperatures threaten to disrupt population sex ratios, which can in turn cause mate shortages, reduce population growth and adaptive potential, and increase extinction risk, particularly when ratios are male biased. Sex ratio distortion can then have cascading effects across other species and even ecosystems. Our understanding of the problem is limited by how often studies measure temperature effects in both sexes. To address this, the current review surveyed 194 published studies of heat tolerance, finding that the majority did not even mention the sex of the individuals used, with <10% reporting results for males and females separately. Although the data are incomplete, this review assessed phylogenetic patterns of thermally induced sex ratio bias for 3 different mechanisms: sex-biased heat tolerance, temperature-dependent sex determination (TSD), and temperature-induced sex reversal. For sex-biased heat tolerance, documented examples span a large taxonomic range including arthropods, chordates, protists, and plants. Here, superior heat tolerance is more common in females than males, but the direction of tolerance appears to be phylogenetically fluid, perhaps due to the large number of contributing factors. For TSD, well-documented examples are limited to reptiles, where high temperature usually favors females, and fishes, where high temperature consistently favors males. For temperature-induced sex reversal, unambiguous cases are again limited to vertebrates, and high temperature usually favors males in fishes and amphibians, with mixed effects in reptiles. There is urgent need for further work on the full taxonomic extent of temperature-induced sex ratio distortion, including joint effects of the multiple contributing mechanisms.

Subject area: Genotype to phenotype

Key words: global warming, phylogeny, sex conversion, temperature-dependent sex determination

Global warming can affect sex ratios through a range of mechanisms. Distorted sex ratios can then increase mate shortages, sexual aggression, and breakdown in parental cooperation (Le Galliard et al. 2005; Eberhart-Phillips et al. 2018). Distortion is also expected to alter effective population size, limit sexual selection and adaptive potential, and increase extinction risk (Wedekind 2002; Godwin et al. 2020). Biased sex ratios may be particularly common at the end of species ranges. This is expected to

reduce a species' ability to track shifting climate envelopes if distortion is male biased, but can enhance it if distortion is female biased (Miller and Inouye 2013; Boyle, Hone, et al. 2014; Boyle, Schwanz, et al. 2014; Boyle et al. 2016). Because males and females are not always ecologically equivalent, sex ratio distortion can also have cascading effects on other species and even ecosystems. For example, female-biased populations of mosquitofish induce stronger trophic cascades than male-biased populations,

including effects on primary productivity, zooplankton abundance, pH, and temperature (Fryxell et al. 2015). Similarly, in dioecious plants, skewed sex ratios can alter ecosystem function through impacts on community structure, photosynthesis, water use, and nutrient cycling (Munné-Bosch 2015; Hultine et al. 2016, 2018; Olano et al. 2017; Zhang et al. 2018). Importantly, male- and female-biased sex ratios are expected to have different consequences, with male bias expected to be more detrimental to population growth and viability, as both are often constrained by female fecundity (e.g., Wedekind 2002).

This review focuses specifically on how high temperature affects sex ratio. Although a few examples have received considerable attention (e.g., warming-induced feminization of turtle populations), the full extent of the problem across different taxa and mechanisms has not been well documented. There are 3 main mechanisms through which high temperature can distort sex ratios. One mechanism is sex-biased heat tolerance, which refers to sex differences in the ability to survive high-temperature exposure. A second mechanism is temperature-dependent sex determination (TSD), meaning cases in which sex is not determined genetically, and is instead controlled by the environmental temperature experienced during development. A third mechanism is temperature-induced sex reversal, which refers to cases in which sex is initially determined genetically, but is then altered by environmental temperature. It is important to consider these mechanisms jointly because they can interact. That is, temperature-dependent sex determination can be either relieved or aggravated by sex-biased thermal tolerance (Geffroy and Wedekind 2020). This review is the first to assess broad phylogenetic patterns for all 3 contributing mechanisms. The review begins with a survey of the frequency that both sexes are considered in publications on heat tolerance. For each of the 3 mechanisms, I then review existing information on taxonomic and evolutionary patterns, with examples plotted onto phylogenetic trees. This allows assessment of data gaps and evolutionary lability for different mechanisms of warming-induced sex ratio distortion.

Sex-Biased Heat Tolerance

Survey of the Treatment of Sex Differences

In biomedicine, sex differences were understudied for decades, with a preponderance of work focusing only on males to reduce variation from hormonal cycles, standardize the study population, and/or protect females of reproductive age (e.g., Beery and Zucker 2011). The problems with this approach and the practice of extrapolating results from males to females have since been realized, and the biomedical community is making considerable effort to study both sexes. For example, research funded by the United States National Institutes of Health (NIH) is now required to account for sex as a biological variable (Clayton 2016; Woitowich and Woodruff 2019; Woitowich et al. 2020).

Although biomedical research is beginning to address the importance of studying both sexes, the study of sex differences in physiological tolerance across taxa lags far behind, albeit for different reasons. Here I focus specifically on heat tolerance, which is estimated by survival-related metrics (e.g., Bennett et al. 2018; Kingsolver and Umbanhowar 2018) including critical thermal maximum (the upper temperature causing physiological failure), median lethal temperature (the temperature resulting in death of 50% of exposed individuals), and upper lethal temperature (the upper temperature causing death of a specified fraction of exposed individuals). To gauge the level of attention given to sex differences in studies of heat tolerance, I surveyed ISI Web of Science (Thompson Scientific) for publications in 2 time periods (1997–1999 and 2017–2019) using search terms “critical thermal maxim*,” “median lethal temperature,” or “upper lethal temperature.” Search results were further refined to include only those with original data on heat tolerance. Publications were then examined to determine the sex of the experimental subjects (search terms “sex,” “gender,” “male,” “female,” “hermaphrodite”), as well as their life stage (search terms “egg,” “embryo,” “larva,” “juvenile,” “adult”). A total of 38 publications were retained for 1997–1999 and 156 for 2017–2019 (Figure 1, Supplementary Appendix 1), suggesting increased recent interest in heat tolerance. However, attention to sex differences in heat tolerance shows only a modest

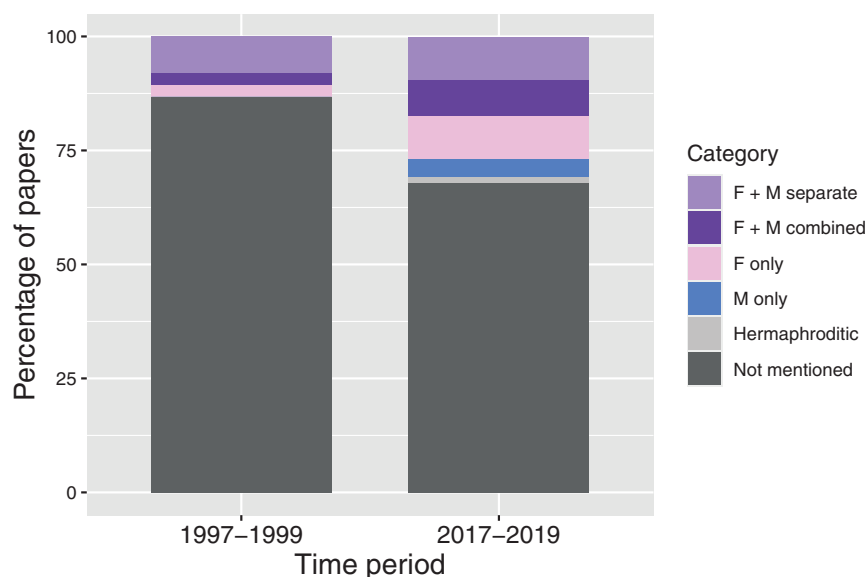


Figure 1. Survey of the treatment of sex in papers on heat tolerance published during 2 time periods: 1997–1999 (38 papers) and 2017–2019 (156 papers). F, females; M, males.

increase, with the majority of studies in both time periods not mentioning the sex of their subjects (86.8% in 1997–1999, 67.9% in 2017–2019) and less than 10% reporting results for males and females separately (7.9% in 1997–1999, 9.6% in 2017–2019).

Why do so few studies address sex differences in thermal tolerance? Of the 176 studies that did not assess sex differences, only 14 offered explanations. These explanations included the species being hermaphroditic, one sex being more common in collections, the desire to eliminate confounding effects of sex or reproductive status, concern that sex identification would require excessive manipulation of samples, research questions focused on only one sex, and previous work that did not find a statistical difference between sexes. However, for another 63 studies the tested organisms were in early-life stages (eggs, embryos, larvae, juveniles) that were presumably too young to be sexed, although this was not discussed. Many studies of stress tolerance focus on early-life stages because they are expected to be more sensitive, although there are certainly cases where this assumption is not valid (e.g., Rodnick et al. 2004; Tangwancharoen and Burton 2014; Clark et al. 2017; Vidal et al. 2017). Although this approach focusing on early-life stages may aim to identify the “weakest links” in climate response (Pandori and Sorte 2019), if sex identification is not feasible or not undertaken for the studied organisms, it may have the unintended consequence of obscuring our understanding of the sex-biased results of rising temperatures.

Taxonomic and Evolutionary Patterns

Global warming may alter sex ratios due to sex-biased tolerance of factors such as water deficiency and high temperature. In dioecious plants, males are quite often more drought tolerant, in part due to lower reproductive investment, and drought-induced masculinization of plant populations can have cascading effects on soil carbon flux, nutrient transformation rates, photosynthesis, and community composition (Munné-Bosch 2015; Hultine et al. 2016, 2018; Olano et al. 2018; Zhang et al. 2018). Here I instead focus on sex differences in high-temperature tolerance. Such differences have been reported to cause severe sex ratio distortion in some natural populations, such as in tropical black flying foxes where 84% of adults killed by an extreme high-temperature event were females (Welbergen et al. 2008). This review is the first to compile studies of sex-biased heat tolerance across a broad range of taxa. Publications were surveyed on ISI Web of Science (Thompson Scientific) using search terms “sex” and (“thermal tolerance” or “temperature tolerance” or “thermal performance” or “heat tolerance” or “critical thermal maximum” or “CTmax” or “upper lethal temperature” or “median lethal temperature” or “LT50”). A total of 73 publications were found with original data on sex-biased heat tolerance, spanning 99 different species (Supplementary Appendix 2). Sex-biased tolerance for a species was scored as “Equivocal” if no significant sex differences were found within a publication or if conflicting conclusions were found in different publications.

Phylogenetic relationships among the 99 species were reconstructed using the “rotl” package, v3.0.10 (Michonneau et al. 2016) interfaced to the “Open Tree of Life” or OTL (Hinchliff et al. 2015), using R v3.6.0 (R Core Team 2019). Species names were matched to those in the OTL database using the Taxonomic Name Resolution Service (TNRS). The resultant tree was redrawn using ggtree v1.16.1 (Yu et al. 2017), and sex differences in high temperature tolerance were then mapped onto the tree (Figure 2). Results show that data on sex-biased heat tolerance spans a diversity of taxa (arthropods,

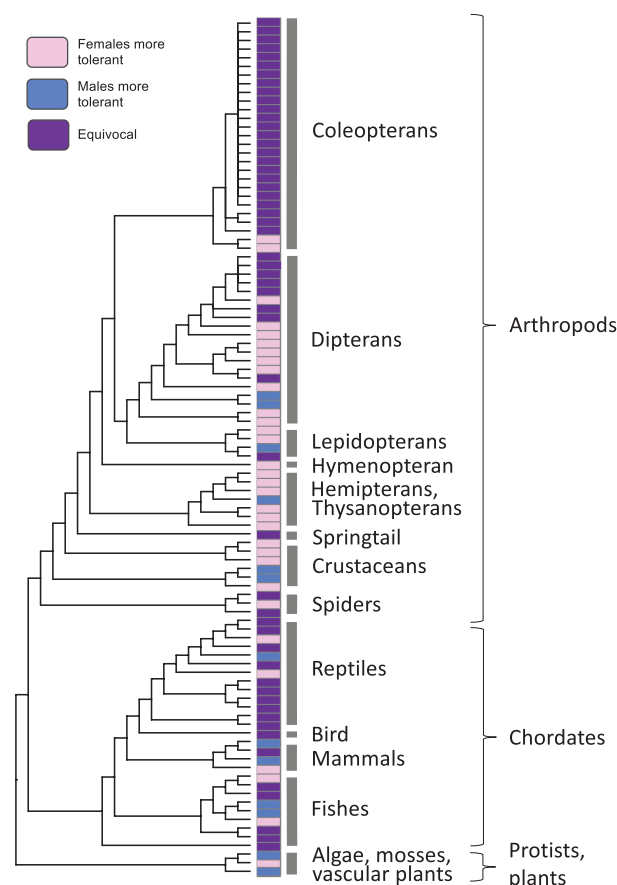


Figure 2. Phylogeny of 99 species tested for sex-specific heat tolerance.

chordates, protists, plants) but is dominated by arthropod species, which are popular subjects for experimental assessment of heat tolerance. When sex differences were found, higher tolerance was more common in females (32/99) than in males (13/99); however, results were equivocal for the majority of species (54/99). The general trend toward greater tolerance in females is the relatively less problematic direction in terms of population viability. Across the tree, the direction of sex-biased tolerance appears highly labile, with both higher-female and higher-male tolerance found within many taxonomic groups, including dipterans, lepidopterans, hemipterans, crustaceans, reptiles, mammals, and fishes.

The phylogenetic fluidity of sex-biased heat tolerance seen in Figure 2 may reflect the large number of variables contributing to this trait. One factor that might be expected to make a major contribution is sex chromosomes. The expectation here is that the heterogametic sex (males in an XY system and females in a ZW system) will be more vulnerable due to the unmasking of deleterious recessives on their unprotected sex chromosomes (e.g., Trivers 1985; Pipoly et al. 2015). Contrary to this prediction, frequencies of sex-biased heat tolerance in the current dataset (Supplementary Appendix 2) do not differ between species known to have male heterogamety (13 females more tolerant:5 males more tolerant:14 equivocal) and those known to have female heterogamety (3 females more tolerant:1 males more tolerant:5 equivocal) (Fisher's exact test, $N = 41$, $P = 0.88$). Although there is strong evidence that the sex with heterogametic sex chromosomes is more likely to die earlier (Xiracostas et al. 2020), it is not clear from this limited dataset that the heterogametic sex exhibits lower heat tolerance.

Another factor that may contribute to sex differences in heat tolerance is body size, although effects may go in either direction. In some cases, smaller organisms may be more heat tolerant, due to factors such as greater surface to volume ratios allowing better heat dissipation in endotherms (e.g., Gardner et al. 2011) or greater oxygen dissolution in ectotherms (e.g., Atkinson 1994). In other cases, smaller organisms may be less tolerant due to greater vulnerability to dehydration and overheating during acute exposure to extremely high temperature (McKechnie and Wolf 2010). It has therefore been predicted that gradual warming may favor smaller size, whereas extreme high-temperature spikes may favor larger body size (Gardner et al. 2011). In the current dataset (Supplementary Appendix 2), body size is mentioned as a possible factor affecting sex-biased heat tolerance in 4 species where the larger sex was more tolerant (all ectotherms) and 3 species where the smaller sex was more tolerant (2 ectotherms, 1 endotherm).

Many other factors may contribute to sex differences in heat tolerance. The sex with higher metabolic rate and/or activity level can be expected to exhibit lower tolerance, assuming that oxygen is limiting (Pörtner 2010). Hormones are another factor in sex-biased heat tolerance, with estrogen generally being beneficial (Tower et al. 2020), whereas cortisol (Jeffries et al. 2012) and testosterone (Chen and Yu 2018) are generally detrimental. Heat tolerance may also trade off with sex-biased investments in growth, mating, reproduction and offspring care (Marshall and Sinclair 2010; Roze et al. 2013).

Temperature-Dependent Sex Determination

TSD is a subset of environmental sex determination (ESD) in which sex is determined after conception by the environmental temperature experienced during embryogenesis (Charnier 1966; Bull 1983; Valenzuela 2004). The possibility that global climate change will wreak havoc with sex ratios in TSD species has long been recognized. It has even been suggested that sex determination in dinosaurs may have been temperature dependent and that warming-induced sex ratio distortion may have played a significant role in their extinction (Miller et al. 2004). Recent data suggest climate change can result in extreme sex ratio distortion for TSD species. For example, loggerhead sea turtle populations in warmer areas are reported to be up to 99% female (Jensen et al. 2018), and single-sex populations are projected for the near future in other TSD reptiles including lizards, crocodilians, and tuatara (Valenzuela et al. 2019).

Environmental sex determination has been suggested in a range of taxa including invertebrates (Bull 1983), but unambiguous cases of TSD are so far limited to vertebrates, specifically reptiles and fish (Ashman et al. 2014). After vigorous debate, there is no clear conclusion as to whether TSD or genotypic sex determination (GSD) is the ancestral state in vertebrates, as both appear to have evolved multiple times (Bull 1983; Janzen and Paukstis 1988; Pokorná and Kratochvíl 2014). The exact molecular mechanisms underlying TSD have long remained elusive. Recently, it has been proposed that cellular calcium and redox status acts as a conserved sensor of environmental conditions mediating vertebrate ESD (Castelli et al. 2020). In the case of red-eared slider turtles (*Trachemys scripta*), it has been shown that temperature-dependent calcium signaling regulates a transcription factor (STAT3) controlling *Kdm6b*, which in turn effects methylation at the promoter to the male sex-determining gene *Dmrt1* (Ge et al. 2017, 2018; Weber et al. 2020).

True cases of TSD do not include examples of genotypic sex determination with temperature effects (GSD + TE). For a species

to be unambiguously identified as having TSD, it should (1) not have sex chromosomes and (2) exhibit sex ratio shifts in response to temperature fluctuations within the “range of natural temperature” (Valenzuela et al. 2003; Conover 2004; Ospina-Álvarez and Piferrer 2018). For reptiles, cases of TSD have been further subdivided into 1 of 3 patterns (Ewert and Nelson 1991). In TSD Ia, low temperature produces males and high temperature produces females (MF). In TSD Ib, low temperature produces females and high temperature produces males (FM). In TSD II, both low and high temperatures produce females, whereas intermediate-temperature produces males (FMF). Fish with TSD have traditionally been grouped into patterns equivalent to Ia and Ib, as well as an additional pattern (MFM) wherein males are produced at both low and high temperatures, whereas females are produced at intermediate temperatures (Conover 2004). However, more recent examination of the data showed that all unambiguous cases of TSD in fish fall into the FM pattern (Ospina-Álvarez and Piferrer 2008). Although there is no explicit support, it has been proposed that the FMF pattern is the underlying pattern for all TSD species and that the FM and MF patterns are a byproduct of the limited temperature range over which developing animals are viable (Webb and Smith 1984).

To assess the evolutionary lability of TSD patterns, I mapped examples onto a phylogenetic tree. The dataset includes TSD species with information on TSD pattern in the vertebrate Tree of Sex database (Ashman et al. 2014), excluding cases listed as “equivocal,” “tentative,” or “questionable.” This dataset was extended and modified with additional information on TSD patterns in fish from Ospina-Álvarez and Piferrer (2008) and in reptiles from Godfrey et al. (2003), Gamble (2010), Charruau (2012), and González et al. (2019). The 3 reptile TSD labels (Ia, Ib, and II) were used to categorize all taxa in the dataset. This yielded a total of 149 TSD species with information on TSD pattern (Supplementary Appendix 3). A phylogenetic tree was generated using the same methods described for Figure 2, and TSD patterns for each species were mapped onto this tree (Figure 3).

Figure 3 shows that all 70 turtle species with TSD produce females at higher temperatures (patterns MF and FMF). In crocodilians, high temperature favors females in 10 species (pattern FMF) and males in 3 species (FM). In clade 2 (Squamata, tuatara), high temperature favors females (pattern FMF) in the majority of species, with 4 exceptions: for 3 species in the order Squamata and the single tuatara species (order Rhynchocephalia), males are favored at high temperature (pattern FM). And finally, for all 37 fish species (clade 3) high temperature favors males (pattern FM). Based on this analysis, crocodilians and squamates show the greatest evolutionary lability in high-temperature effects, and thus the greatest hope for escaping deadly effects of climate warming through evolution of a different TSD pattern. Alternatively, TSD species may be able to avoid warming-induced sex ratio distortion through the evolution of sex chromosomes (e.g., Grossen et al. 2010).

The adaptive significance of ESD (including TSD) continues to be debated. With sexual reproduction, population sex ratios are generally expected to be 1:1, as individuals of the rarer sex should have an advantage until an equilibrium is reached (Darwin 1871; Düsling 1884a, 1884b; Fisher 1930; Edwards 2000). In GSD species, 1:1 sex ratios are also enforced by random meiotic segregation of the primary sex-determining element (Williams 1979; Charnov 1982). However, when sex is determined environmentally, sex ratios can be highly skewed, a pattern that can theoretically be explained by environmental effects on fitness (Bull 1981; Freedberg et al. 2001). The most widely accepted evolutionary explanation for ESD remains

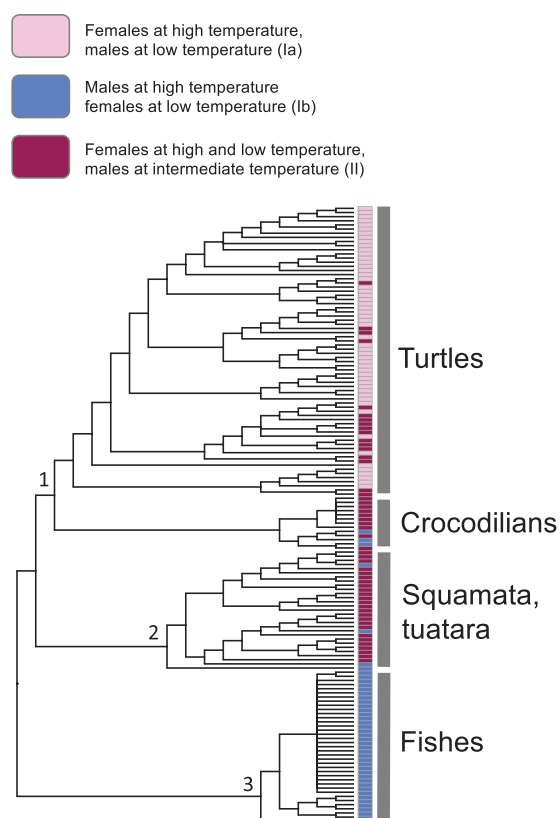


Figure 3. Phylogeny of 149 vertebrate species known to have temperature-dependent sex determination. Numbers indicate clades 1–3.

the Charnov–Bull model (Charnov and Bull 1977; with subsequent variants reviewed in Schwanz et al. 2016), which posits that selection favors ESD when the fitness of individuals depends on the environment in a sex-biased manner. For example, in the painted turtle *Chrysemys picta*, one of many MF species in clade 1 of Figure 3, the sex determination system may be adaptive in that it allows embryos to develop into the sex best suited to its environment due to sex-biased overwintering physiology (Spencer and Janzen 2014). The concern is that with rapid global warming, distorted sex ratios in TSD species may lead to demographic collapse. Indeed, extreme sex ratio distortion has been reported recently for all 3 TSD patterns, reaching up to 75% males in FM fish species (Ospina-Álvarez and Piferrer 2018), up to 89% females in FMF species like *Crocodylus niloticus* (Bókonyi et al. 2019), and up to 99% females in MF species like the green sea turtle, *Chelonia mydas* (Jensen et al. 2018).

Temperature-Induced Sex Reversal

Although the potential effects of climate change on sex ratios of TSD species are well established, less attention has been given to how climate change may alter sex ratio in GSD species exhibiting environmentally induced sex reversal. In these taxa, sex is determined genetically at fertilization, but can be overridden during a critical period of ontogeny by environmental factors including pH, photoperiod, density, water availability, endocrine disrupting chemicals, and, especially, temperature (Quinn et al. 2009; Bhandari et al. 2015; Baroiller and D’Cotta 2016; Flament 2016; Holleley et al. 2016; Li et al. 2016; Weber and Capel 2018). This leads to a mismatch between genetic sex and phenotypic sex. Documented cases of sex

reversal are likely to increase as we continue to develop sex-linked molecular markers that can reveal these genetic/phenotypic mismatches. In fact, it has been estimated that one third of the fish species thought to have TSD actually exhibit GSD + TE (Ospina-Álvarez and Piferrer 2008). Although the data for natural populations are still sparse, environmentally induced sex reversal has been shown to cause extreme sex ratio distortion in some cases. For example, in the flounder *Paralichthys lethostigma*, where warm temperatures masculinize genetic females, sex ratios have been found to reach as high as 94% male in some southern populations (Honeycutt et al. 2019).

Global warming can induce sex reversal through both temperature effects and water restriction. For example, in 2 reptile species, water restriction promotes conversion to males (Baroiller and D’Cotta 2016; Dupoué et al. 2019). Here I focus specifically on temperature-induced sex reversal, termed GSD + TE. The mechanism(s) underlying temperature-induced sex reversal remain an area of active research, with key factors including levels of cortisol and aromatase (Uchida et al. 2004; Fernandino et al. 2013; Holleley et al. 2016; Castañeda Cortés et al. 2019), with cellular calcium and redox status proposed as a sensor of environmental signals (Castelli et al. 2020). In several cases, epigenetic control of promotion/inhibition has been demonstrated (Baroiller and D’Cotta 2016; Ma et al. 2016; Zhou et al. 2019). Behavior may also play an important role, as sex reversal has been shown to be impacted by individual temperature preferences of sexually undifferentiated juveniles (Nivelle et al. 2019).

Because thermal sex reversal is easily manipulated, it is frequently used to alter sex ratios in managed populations. In many fish species, one sex grows faster than the other so aquaculturists often use thermal sex reversal (as well as hormone-induced reversal) to create cost-effective monosex populations (Baroiller and D’Cotta 2016; Cui et al. 2018; Zhou et al. 2019). Thermal sex reversal can also be manipulated for pest management. For example, fruit flies have been genetically engineered to produce sterile male populations at high temperature (Li and Handler 2017).

Well-documented natural cases of GSD + TE are largely limited to vertebrates, specifically poikilotherms. Here I focus on 38 vertebrate species found to exhibit thermal sex reversal under natural conditions, including 22 fish, 11 amphibians, and 5 reptiles (Figure 4, Supplementary Appendix 4). Phylogenetic relationships among these taxa were reconstructed using the same procedure used for Figure 2. Type of temperature effect and GSD for each species was then mapped onto the tree (Figure 4).

The most common pattern of thermal sex reversal in vertebrates is a masculinizing effect of high temperature, which is found in 76% of the species shown in Figure 4. Masculinization at high temperature was found to predominate in fishes and amphibians, but not in reptiles. An excess of males is, unfortunately, the more problematic direction of sex ratio distortion in terms of population viability. Male-biased sex ratios may become particularly common in fishes (Geffroy and Wedekind 2020), where high temperature favors males in cases of TSD (Figure 3) as well as GSD + TE (Figure 4). For cases of sex reversal, the demographic consequences will also depend on the underlying form of GSD (Bókonyi et al. 2017). When high temperature masculinization is combined with male-heterogametic sex chromosomes (47% of the species in Figure 4), homogametic pseudo-males (“XX”) mating with homogametic females (“XX”) will produce 100% genetically female (“XX”) offspring, thereby countering the masculinizing distortion. Greater distortion is expected when high temperature masculinization is combined with female heterogamety (16% of the species in Figure 4). Here, heterogametic

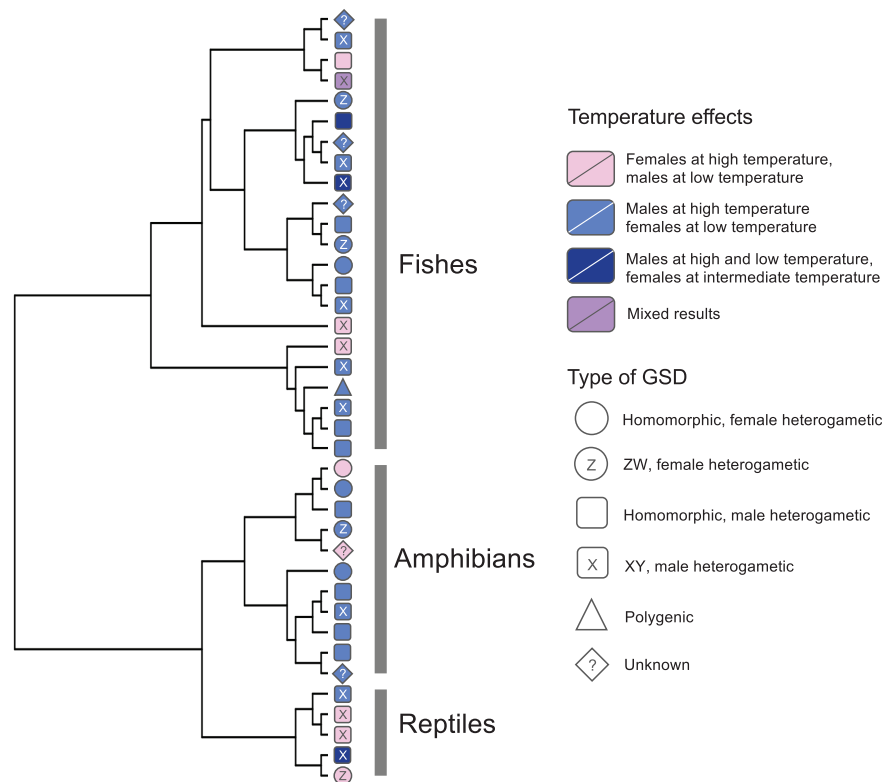


Figure 4. Phylogeny of 38 vertebrate species known to exhibit temperature-induced sex reversal (GSD + TE). Type of temperature effect (TE) shown by color and type of GSD (genetic sex determination) shown by shape.

(“ZW”) pseudo-males mating with heterogametic (“ZW”) females should produce a ratio of 1 “ZZ”:2 “ZW”:1 “WW,” resulting in 25% “ZZ” males or 33% “ZZ” males if the “WW” female genotype is not viable. The actual phenotypic sex ratio consequences of such a cross are more difficult to predict. For example, in tongue sole (*Cynoglossus semilaevis*), most ZW females from this type of cross develop into ZW pseudo-males even without temperature induction (Chen et al. 2014; Cui et al. 2018). Under these scenarios, high-temperature masculinization causes greater excess of males when females are heterogametic. Alternatively, if the WW genotype is resistant to masculinization, the female-heterogametic system can maintain balanced sex ratios by evolving male heterogamety (Nemesházi et al. 2021). High-temperature feminization is considerably less common (21% of the species in Figure 4), but its effect on sex ratio is also expected to depend on the type of GSD. Here, greater excess of females is expected when males are heterogametic. Based on empirical data for amphibians over the past 60 years (Bókonyi et al. 2017), adult sex ratios shifted toward males in ZZ/ZW species but did not change significantly in XX/XY species.

Temperature-induced sex reversal may also have important consequences over evolutionary time scales. One major outcome may be accelerated transitions between sex determination systems, eventually leading to elimination of sex chromosomes (Holleley et al. 2016; Schwanz et al. 2020). For example, frequent crosses between ZZ males and ZZ pseudo-females could lead to loss of the W chromosome. Modeling work (Schwanz et al. 2020) shows that such sex chromosome loss is buffered by immigration, heritable variation for thermal sensitivity, and reduced reproductive fitness in sex-reversed individuals. The actual fitness effects of sex reversal are incompletely known. There are cases where sex-reversed individuals have been

found to have reduced fitness, such as in the frog *Rana dalmatina* (Nemesházi et al. 2020). In contrast, in the case of the bearded lizard *Pogona vitticeps*, ZZ pseudo-females have novel, male-like behaviors that can increase reproductive fitness relative to genetic (ZW) females, potentially favoring replacement of the old GSD + TE system with pure TSD (Li et al. 2016). Between these 2 extremes, a systematic survey of fishes found little evidence for fitness differences between sex-reversed and wild-type individuals (Senior et al. 2016).

A second major evolutionary consequence of sex reversal is the potential for rejuvenating degenerating sex chromosomes. According to the “fountain of youth” hypothesis (Perrin 2009), XY or ZW recombination in sex-reversed individuals can block the decay of Z and W chromosomes, thereby keeping the sex chromosomes homomorphic. This may help explain the high frequency of homomorphic sex chromosomes in Figure 4 (14 of 38 species) and in amphibians and fish in general, where sex reversal is relatively common. This recombination may also help explain the high lability of sex determination systems among ectothermic vertebrates.

The Future of Sex Ratios on a Warming Planet

There are already examples of severely distorted sex ratios in natural populations caused by each of the 3 mechanisms discussed above (e.g., Welbergen et al. 2008; Jensen et al. 2018; Honeycutt et al. 2019), and such examples are likely to become more common. Can we expect species to adjust their sex ratios in response to warming temperatures? In some cases, species will be able to shift their geographic or elevational distribution (e.g., Lenoir and Svenning 2015; Sunday et al. 2017). Other taxa will stay in place but buffer sex ratio distortion through changes in

behavior. For TSD species like turtles, there is evidence of adjustment of primary sex ratio by choosing cooler locations or seasons for nesting (Mainwaring et al. 2017; Patrício et al. 2017) and by embryos moving within the egg to select specific thermal regimes (Ye et al. 2019). Similarly, GSD + TE species such as Nile tilapia have been shown to induce sex reversal through their temperature preference during the juvenile phase (Nivelle et al. 2019). Fish have also been shown to mitigate sex ratio distortion in their offspring through nonbehavioral maternal effects (Donelson and Munday 2015).

Thermal disruption of sex ratio may also be ameliorated by microevolutionary change, particularly in taxa with short generation times. Evolutionary adjustments for sex-biased mortality are expected to be constrained by Fisherian sex ratio selection, which predicts equal investment in male and female offspring, even if males and females have very different chances of surviving to adulthood (Fisher 1930; Székely et al. 2014). For GSD species, balanced sex ratios are also imposed by meiotic segregation of sex chromosomes or other sex-determining elements (Williams 1979; Charnov 1982). For TSD species, however, we might predict evolutionary changes in factors such as the pivotal temperature of sex determination, or maternal choice of nesting site or season (Refsnider and Janzen 2016; Blechschmidt et al. 2020). Similarly, for GSD + TE species, evolution might adjust sex ratios through genetic changes underlying thermal sensitivity of sex reversal (Grossen et al. 2010) or preference for normal versus sex-reversed mates (Nemesházi et al. 2021).

If sex ratio adjustments do not occur naturally, human intervention may be justified, particularly for small and declining populations. The goal here could be either to balance sex ratios to maximize effective population size and adaptive potential or to create female-biased ratios, at least temporarily, to increase population growth (Wedekind 2002). For TSD species like some reptiles and fishes, this could be done by manipulating the thermal environment during critical developmental stages (Wedekind 2002; Esteban et al. 2018; Jensen et al. 2018). Environmental sex reversal, found in amphibians, fishes, and reptiles, can also be manipulated by altering temperature or other extrinsic factors (Baroiller and D'Cotta 2016; Cui et al. 2018; Zhou et al. 2019). Sex ratio manipulation in cases where sex determination is strictly genetic will require different approaches, such as supplementation with individuals of the desired sex from captive breeding programs (Lenz et al. 2007). All of these strategies for sex ratio manipulation are temporary solutions, which are likely to fall short if underlying threats to population viability are not addressed.

Conclusions

Our understanding of sex-biased consequences of temperature is obscured by the widespread practice of “sex-blind” physiological tolerance assays, as illustrated by the above survey of literature on heat tolerance, in which less than 10% of studies reported results for males and females separately. The situation could be improved if studies of thermal biology begin seriously addressing sex as a biological variable, an approach that is now mandated for biomedical research funded by the NIH. Although the data are far from complete, this review assessed phylogenetic patterns of thermal effects on sex ratio for 3 separate mechanisms: sex-biased heat tolerance, TSD, and temperature-induced sex reversal

(GSD + TE). Studies of sex-biased heat tolerance are dominated by arthropods, with additional examples in chordates, protists, and plants. When sexes differ in high-temperature tolerance, high female tolerance is more common. However, the direction of sex-biased tolerance appears to be phylogenetically fluid, perhaps due to the variety of contributing factors including sex chromosomes, body size, metabolism, hormones, and life-history traits. Examples of TSD are limited to cases where genetic sex determination can be definitively ruled out, and are currently restricted to vertebrates. Effects are fairly phylogenetically constrained, with high temperature usually feminizing reptiles and always masculinizing fishes. Definitive examples of GSD + TE are also currently limited to vertebrates. In these examples, high-temperature sex reversal usually masculinizes fishes and amphibians, with more mixed effects in reptiles. The type of GSD is important here, as temperature-induced sex reversal is expected to have very different consequences in male-heterogametic systems versus female-heterogametic systems. Overall, the potential for warming-induced sex ratio distortion appears to be an understudied yet taxonomically widespread problem. Risks are particularly large when high temperature favors males, as is found across multiple mechanisms in fishes (Geffroy and Wedekind 2020), for example. Avoiding population collapse due to warming-induced sex ratio bias will require much greater attention to the taxonomic extent of sex-biased thermal effects, as well as management strategies for cases that have already reached the emergency level.

Supplementary Material

Supplementary data are available at *Journal of Heredity* online.

Supplementary Appendix 1. Survey of publications on heat tolerance during two time periods: 1997–1999 and 2017–2019.

Supplementary Appendix 2. Information on species included in Figure 2, showing the phylogeny of species tested for sex-biased heat tolerance. Species are listed by rank order in the tree, from top to bottom, with information on sex determination when available. For each publication on a particular species, the entry includes citation for heat tolerance, metric of heat tolerance, sex with higher tolerance (Female, Male or Equivocal; including consensus for species with multiple publications) and comments.

Supplementary Appendix 3. Species included in the phylogeny of temperature-dependent sex determination (TSD) in Figure 3, listed in order from top to bottom. Ia = females at high temperature, males at low temperature; Ib = males at high temperature, females at low temperature; II = females at high and low temperature, males at intermediate temperature.

Supplementary Appendix 4. Information on species included in Figure 4, showing the phylogeny of species with genetic sex determination (GSD) with temperature effects (TE). Species are listed by rank order in the tree, from top to bottom. GSD + TE types: M = males favored at high temperature; M2 = males favored at low and high temperature; F = females favored at high temperature; Mixed = mixed results.

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Data Availability

All data generated in this study have been reported within the main text or in the supplementary files.

References

- Ashman T-L, Bachtrog D, Blackmon H, Goldberg EE, Hahn MW, Kirkpatrick M, Kitano J, Mank JE, Mayrose I, Ming R, *et al.* 2014. Tree of Sex: a database of sexual systems. *Sci Data*. 1:140015.
- Atkinson D. 1994. Temperature and organism size: a biological law for ectotherms? *Adv Ecol Res*. 25:1–58.
- Baroiller JF, D'Cotta H. 2016. The reversible sex of gonochoristic fish: insights and consequences. *Sex Dev*. 10:242–266.
- Beery AK, Zucker I. 2011. Sex bias in neuroscience and biomedical research. *Neurosci Biobehav Rev*. 35:565–572.
- Bennett JM, Calosi P, Clusella-Trullas S, Martínez B, Sunday J, Algar AC, Araújo MB, Hawkins BA, Keith S, Kühn I, *et al.* 2018. GlobTherm, a global database on thermal tolerances for aquatic and terrestrial organisms. *Sci Data*. 5:180022.
- Bhandari RK, Deem SL, Holliday DK, Jandegian CM, Kassotis CD, Nagel SC, Tillitt DE, Vom Saal FS, Rosenfield CS. 2015. Effects of the environmental estrogenic contaminants bisphenol A and 17 α -ethinyl estradiol on sexual development and adult behaviors in aquatic wildlife species. *Gen Comp Endocrinol*. 214:195–219.
- Blechschmidt L, Wittmann MJ, Bluml C. 2020. Climate change and green sea turtle sex ratio – preventing possible extinction. *Gene*. 11:588.
- Bókony V, Köver S, Nemesházi E, Liker A, Székely T. 2017. Climate-driven shifts in adult sex ratios via sex reversals: the type of sex determination matters. *Philos Trans R Soc B*. 372:20160325.
- Bókony V, Milne G, Pipoly I, Székely T, Liker A. 2019. Sex ratios and bimaturism differ between temperature-dependent and genetic sex determination systems in reptiles. *BMC Evol Biol*. 19:57.
- Boyle M, Hone J, Schwanz LE, Georges A. 2014. Under what conditions do climate-driven sex ratios enhance versus diminish population persistence? *Ecol Evol*. 4:4522–4533.
- Boyle M, Schwanz LE, Hone J, Georges A. 2014. How do climate-linked sex ratios and dispersal limit range boundaries? *BMC Ecol*. 14:19.
- Boyle M, Schwanz LE, Hone J, Georges A. 2016. Dispersal and climate warming determine range shift in model reptile populations. *Ecol. Model*. 328:34–43.
- Bull JJ. 1981. Sex ratio evolution when fitness varies. *Heredity*. 46:9–26.
- Bull JJ. 1983. *Evolution of sex determining mechanisms*. Menlo Park (CA): Benjamin Cummings.
- Castañeda Cortés DC, Arias Padilla LF, Langlois VS, Somoza GM, Ferdinando JI. 2019. The central nervous system acts as a transducer of stress-induced masculinization through corticotropin-releasing hormone B. *Development*. 146:dev172866.
- Castelli MA, Whiteley SL, Georges A, Holleley CE. 2020. Cellular calcium and redox regulation: the mediator of vertebrate environmental sex determination? *Biol Rev Camb Philos Soc*. 95:680–695.
- Charnier M. 1966. Action de la température sur la sex-ratio chez l'embryon d'*Agama agama* (Agamidae: Lacertilien). *C R Séances Soc Biol L'Ouest Afr*. 160:620–622.
- Charnov EL. 1982. *The theory of sex allocation*. Princeton (NJ): Princeton University Press.
- Charnov EL, Bull J. 1977. When is sex environmentally determined? *Nature*. 266:828–830.
- Charruau P. 2012. Microclimate of American crocodile nests in Banco Chinchorro Biosphere Reserve, Mexico: effect on incubation length, embryos survival and hatchlings sex. *J Therm Biol*. 37:6–14.
- Chen S, Zhang G, Shao C, Huang Q, Liu G, Zhang P, Song W, An N, Chalopin D, Volff JN, *et al.* 2014. Whole-genome sequence of a flatfish provides insights into ZW sex chromosome evolution and adaptation to a benthic lifestyle. *Nat Genet*. 46:253–260.
- Chen Y, Yu T. 2018. Testosterone mediates hyperthermic response of mice to heat exposure. *Life Sci*. 214:34–40.
- Clark TD, Roche DG, Binning SA, Speers-Roesch B, Sundin J. 2017. Maximum thermal limits of coral reef damselfishes are size dependent and resilient to near-future ocean acidification. *J Exp Biol*. 220:3519–3526.
- Clayton JA. 2016. Studying both sexes: a guiding principle for biomedicine. *FASEB J*. 30:519–524.
- Conover DO. 2004. Temperature-dependent sex determination in fishes. In: Valenzuela N, Lance VA, editors. *Temperature-dependent sex determination in vertebrates*, Vol. 1. Washington (DC): Smithsonian Books. p. 1–4.
- Cui Y, Wang W, Ma L, Jie J, Zhang Y, Wang H, Li H. 2018. New locus reveals the genetic architecture of sex reversal in the Chinese tongue sole (*Cynoglossus semilaevis*). *Heredity (Edinb)*. 121:319–326.
- Darwin C. 1871. *The descent of man and selection in relation to sex*. London (UK): Murray.
- Donelson JM, Munday PL. 2015. Transgenerational plasticity mitigates the impact of global warming to offspring sex ratios. *Glob Chang Biol*. 21:2954–2962.
- Dupoué A, Lourdaïs O, Meylan S, Brischoux F, Angelier F, Rozen-Rechels D, Marcangeli Y, Decenière B, Agostini S, Le Galliard JF. 2019. Some like it dry: water restriction overrides heterogametic sex determination in two reptiles. *Ecol Evol*. 9:6524–6533.
- Düsing C. 1884a. Die Regulierung des Geschlechtsverhältnisses bei der Vermehrung der Menschen, Tiere und Pflanzen. *Jena. Z. Naturwiss*. 17:594–940.
- Düsing C. 1884b. *Die Regulierung des Geschlechtsverhältnisses bei der Vermehrung der Menschen, Tiere und Pflanzen*. Jena, Germany: Gustav Fischer.
- Eberhart-Phillips LJ, Küpper C, Carmona-Isunza MC, Vincze O, Zefania S, Cruz-López M, Kosztolányi A, Miller TEX, Barta Z, Cuthill IC, *et al.* 2018. Demographic causes of adult sex ratio variation and their consequences for parental cooperation. *Nat Commun*. 9:1651.
- Edwards AW. 2000. Carl Düsing (1884) on the regulation of the sex-ratio. *Theor Popul Biol*. 58:255–257.
- Esteban N, Laloë JO, Kiggen FSPL, Ubels SM, Becking LE, Meesters EH, Berkel J, Hays GC, Christianen MJA. 2018. Optimism for mitigation of climate warming impacts for sea turtles through nest shading and relocation. *Sci Rep*. 8:17625.
- Ewert MA, Nelson CE. 1991. Sex determination in turtles: diverse patterns and some possible adaptive values. *Copeia*. 1:50–69.
- Ferdinando JI, Hattori RS, Moreno Acosta OD, Strüssmann CA, Somoza GM. 2013. Environmental stress-induced testis differentiation: androgen as a by-product of cortisol inactivation. *Gen Comp Endocrinol*. 192:36–44.
- Fisher R. 1930. *The genetical theory of natural selection*. Oxford: Oxford University Press.
- Flament S. 2016. Sex reversal in amphibians. *Sex Dev*. 10:267–278.
- Freedberg S, Ewert MA, Nelson CE. 2001. Environmental effects on fitness and consequences for sex allocation in a reptile with environmental sex determination. *Evol Ecol Res*. 3:953–967.
- Fryxell DC, Arnett HA, Apgar TM, Kinnison MT, Palkovacs EP. 2015. Sex ratio variation shapes the ecological effects of a globally introduced freshwater fish. *Proc Biol Sci*. 282:20151970.
- Gamble T. 2010. A review of sex determining mechanisms in geckos (Gekkota: Squamata). *Sex Dev*. 4:88–103.
- Gardner JL, Peters A, Kearney MR, Joseph L, Heinsohn R. 2011. Declining body size: a third universal response to warming? *Trends Ecol Evol*. 26:285–291.
- Ge C, Ye J, Weber C, Sun W, Zhang H, Zhou Y, Cai C, Qian G, Capel B. 2018. The histone demethylase KDM6B regulates temperature-dependent sex determination in a turtle species. *Science*. 360:645–648.
- Ge C, Ye J, Zhang H, Zhang Y, Sun W, Sang Y, Capel B, Qian G. 2017. *Dmrt1* induces the male pathway in a turtle species with temperature-dependent sex determination. *Development*. 144:2222–2233.

- Geffroy B, Wedekind C. 2020. Effects of global warming on sex ratios in fishes. *J Fish Biol.* 97:596–606.
- Godfrey MH, Delmas V, Girondot M. 2003. Assessment of patterns of temperature-dependent sex determination using maximum likelihood model selection. *Écoscience.* 10:265–272.
- Godwin JL, Lumley AJ, Michalczyk Ł, Martin OY, Gage MJG. 2020. Mating patterns influence vulnerability to the extinction vortex. *Glob Chang Biol.* 26:4226–4239.
- González EJ, Martínez-López M, Morales-Garduza MA, García-Morales R, Charruau P, Gallardo-Cruz JA. 2019. The sex-determination pattern in crocodilians: a systematic review of three decades of research. *J Anim Ecol.* 88:1417–1427.
- Grossen C, Neuenschwander S, Perrin N. 2010. Temperature-dependent turnovers in sex determination: a quantitative model. *Evolution.* 65:64–78.
- Hinchliff CE, Smith SA, Allman JF, Burleigh JG, Chaudhary R, Coghill LM, Crandall KA, Deng J, Drew BT, Gazis R, et al. 2015. Synthesis of phylogeny and taxonomy into a comprehensive tree of life. *Proc Natl Acad Sci USA.* 112:12764–12769.
- Holleley CE, Sarre SD, O'Meally D, Georges A. 2016. Sex reversal in reptiles: reproductive oddity or powerful driver of evolutionary change? *Sex Dev.* 10:279–287.
- Honeycutt JL, Deck CA, Miller SC, Severance ME, Atkins EB, Luckenbach JA, Buckel JA, Daniels HV, Rice JA, Borski RJ, et al. 2019. Warmer waters masculinize wild populations of a fish with temperature-dependent sex determination. *Sci Rep.* 9:6527.
- Hultine KR, Bush SE, Ward JK, Dawson TE. 2018. Does sexual dimorphism predispose dioecious riparian trees to sex ratio imbalances under climate change? *Oecologia.* 187:9210921.
- Hultine KR, Grady KC, Wood TE, Shuster SM, Stella JC, Whitham TG. 2016. Climate change perils for dioecious plant species. *Nat Plants.* 2:16109.
- Janzen FJ, Paukstis GL. 1988. Environmental sex determination in reptiles. *Nature.* 332:790.
- Jeffries KN, Hinch SG, Martins EG, Clark TD, Lotto AG, Patterson DA, Cooke SJ, Farrell AP, Miller KM. 2012. Sex and proximity to reproductive maturity influence the survival, maturation, and blood physiology of Pacific salmon when exposed to high temperature during a simulated migration. *Physiol Biochem Zool.* 85:62–73.
- Jensen MP, Allen CD, Eguchi T, Bell IP, LaCasella EL, Hilton WA, Hof CAM, Dutton PH. 2018. Environmental warming and feminization of one of the largest sea turtle populations in the world. *Curr Biol.* 28:154–159.e4.
- Kingsolver JG, Umbanhowar J. 2018. The analysis and interpretation of critical temperatures. *J Exp Biol.* 221:jeb167858.
- Le Galliard JF, Fitze PS, Ferrière R, Clobert J. 2005. Sex ratio bias, male aggression, and population collapse in lizards. *Proc Natl Acad Sci USA.* 102:18231–18236.
- Lenoir J, Svenning JC. 2015. Climate-related range shifts – a global multidimensional synthesis and new research directions. *Ecography.* 38:15–28.
- Lenz TL, Jacob A, Wedekind C. 2007. Manipulating sex ratio to increase population growth: the example of the Lesser Kestrel. *Anim Conserv.* 10:236–244.
- Li J, Handler AM. 2017. Temperature-dependent sex-reversal by a *transformer-2* gene-edited mutation in the spotted-wing drosophila, *Drosophila suzukii*. *Sci Rep.* 7:12363.
- Li H, Holleley CE, Elphick M, Georges A, Shine R. 2016. The behavioral consequences of sex reversal in dragons. *Proc R Soc B.* 283:20160217.
- Ma WJ, Rodrigues N, Sermier R, Brelsford A, Perrin N. 2016. *Dmrt1* polymorphism covaries with sex-determination patterns in *Rana temporaria*. *Ecol Evol.* 6:5107–5117.
- Mainwaring MC, Barber I, Deeming DC, Pike DA, Roznik EA, Hartley IR. 2017. Climate change and nesting behavior in vertebrates: a review of the ecological threats and potential for adaptive responses. *Biol Rev.* 92:1991–2002.
- Marshall KE, Sinclair BJ. 2010. Repeated stress exposure results in a survival-reproduction trade-off in *Drosophila melanogaster*. *Proc Biol Sci.* 277:963–969.
- McKechnie AE, Wolf BO. 2010. Climate change increases the likelihood of catastrophic avian mortality events during extreme heat waves. *Biol Lett.* 6:253–256.
- Michonneau F, Brown JW, Winter DJ. 2016. rotl: an R package to interface with the Open Tree of Life data. *Methods Ecol Evol.* 7:1476–1481.
- Miller D, Summers J, Silber S. 2004. Environmental versus genetic sex determination: a possible factor in dinosaur extinction? *Fertil Steril.* 81:954–964.
- Miller TE, Inouye BD. 2013. Sex and stochasticity affect range expansion of experimental invasions. *Ecol Lett.* 16:354–361.
- Munné-Bosch S. 2015. Sex ratios in dioecious plants in the framework of global change. *Environ. Exp. Bot.* 109:99–102.
- Nemesházi E, Gál Z, Ujhegyi N, Verebélyi V, Mikó Z, Üveges B, Lefler KA, Jeffries DL, Hoffmann OI, Bókony V. 2020. Novel genetic sex markers reveal high frequency of sex reversal in wild populations of the agile frog (*Rana dalmatina*) associated with anthropogenic land use. *Mol. Ecol.* 29:3607–3621.
- Nemesházi E, Kövér S, Bókony V. 2021. Evolutionary and demographic consequences of temperature-induced masculinization under climate warming: the effects of mate choice. *BMC Evol Biol.* 21:16.
- Nivelle R, Gennotte V, Kalala EJK, Ngoc NB, Muller M, Mélard C, Rougeot C. 2019. Temperature preference of Nile tilapia (*Oreochromis niloticus*) juveniles induces spontaneous sex reversal. *PLoS One.* 14:e0212504.
- Olano JM, González-Muñoz N, Arzac A, Rozas V, von Arx G, Delzon S, García-Cervigón AI. 2017. Sex determines xylem anatomy in a dioecious conifer: hydraulic consequences in a drier world. *Tree Physiol.* 37:1493–1502.
- Ospina-Álvarez N, Piferrer F. 2018. Temperature-dependent sex determination in fish revisited: prevalence, a single sex ratio response pattern, and possible effects of global climate change. *PLoS One.* 3:e2837.
- Pandori LM, Sorte CJB. 2019. The weakest link: sensitivity to climate extremes across life stages of marine invertebrates. *Oikos.* 128:621–629.
- Patricio AR, Marques A, Barbosa C, Broderick AC, Godley BJ, Hawkes LA, Rebelo R, Regalla A, Catry P. 2017. Balanced primary sex ratios and resilience to climate change in a major sea turtle population. *Mar Ecol Prog Ser.* 577:189–203.
- Perrin N. 2009. Sex reversal: a fountain of youth for sex chromosomes? *Evolution.* 63:3043–3049.
- Pipoly I, Bókony V, Kirkpatrick M, Donald PF, Székely T, Liker A. 2015. The genetic sex-determination system predicts adult sex ratios in tetrapods. *Nature.* 527:91–94.
- Pokorná MJ, Kratochvíl L. 2014. What was the ancestral sex-determining mechanism in amniote vertebrates? *Biol Rev.* 91:1–12.
- Pörtner HO. 2010. Oxygen- and capacity-limitation of thermal tolerance: a matrix for integrating climate-related stressor effects in marine ecosystems. *J Exp Biol.* 213:881–893.
- Quinn AE, Radder RS, Sarre SD, Georges A, Ezaz T, Shine R. 2009. Isolation and development of a molecular sex marker for *Bassiana duperreyi*, a lizard with XX/XY sex chromosomes and temperature-induced sex reversal. *Mol Genet Genomics.* 281:665–672.
- R Core Team. 2019. *R: a language and environment for statistical computing*. Vienna (Austria): R Foundation for Statistical Computing. Available from: <https://www.R-project.org/>
- Refsnider JM, Janzen FJ. 2016. Temperature-dependent sex determination under rapid anthropogenic environmental change: evolution at a turtle's pace? *J Hered.* 107:61–70.
- Rodnick KJ, Gamperl AK, Lizars KR, Bennett MT, Rausch RN, Keeley ER. 2004. Thermal tolerance and metabolic physiology among redband trout populations in south-eastern Oregon. *J Fish Biol.* 64:310–335.
- Roze T, Christen F, Amerand A, Claireaux G. 2013. Trade-off between thermal sensitivity, hypoxia tolerance and growth in fish. *J. Therm. Biol.* 38:98–106.
- Schwanz LE, Cordero GA, Charnov EL, Janzen FJ. 2016. Sex-specific survival to maturity and the evolution of environmental sex determination. *Evolution.* 70:329–341.
- Schwanz LE, Georges A, Holleley CE, Sarre SD. 2020. Climate change, sex reversal and lability of sex-determining systems. *J Evol Biol.* 33:270–281.

- Senior AM, Johnson SL, Nakagawa S. 2016. Sperm traits of masculinized fish relative to wild-type males: a systematic review and meta-analyses. *Fish Fish.* 17:143–164.
- Spencer RJ, Janzen FJ. 2014. A novel hypothesis for the adaptive maintenance of environmental sex determination in a turtle. *Proc Biol Sci.* 281:20140831.
- Sunday JM, Bates AE, Dulvy NK. 2017. Thermal tolerance and the global redistribution of animals. *Nat Clim Change.* 2:686–690.
- Székely T, Liker A, Freckleton RP, Fichtel C, Kappeler PM. 2014. Sex-biased survival predicts adult sex ratio variation in wild birds. *Proc Biol Sci.* 281:20140342.
- Tangwancharoen S, Burton RS. 2014. Early life stages are not always the most sensitive: heat stress responses in the copepod *Tigriopus californicus*. *Mar Ecol Prog Ser.* 517:75–83.
- Tower J, Pomatto LCD, Davies KJA. 2020. Sex differences in the response to oxidative and proteolytic stress. *Redox Biol.* 31:101488.
- Trivers R. 1985. *Social evolution*. Menlo Park (CA): Benjamin/Cummings.
- Uchida D, Yamashita M, Kitano T, Iguchi T. 2004. An aromatase inhibitor or high water temperature induce oocyte apoptosis and depletion of P450 aromatase activity in the gonads of genetic female zebrafish during sex-reversal. *Comp Biochem Physiol A Mol Integr Physiol.* 137:11–20.
- Valenzuela N. 2004. Introduction. In: Valenzuela N, Lance VA, editors. *Temperature-dependent sex determination in vertebrates*, Vol. 1. Washington (DC): Smithsonian Books. p. 1–4.
- Valenzuela N, Adams DC, Janzen FJ. 2003. Pattern does not equal process: exactly when is sex environmentally determined? *Am Nat.* 161:676–683.
- Valenzuela N, Literman R, Neuwald JL, Mizoguchi B, Iverson JB, Riley JL, Litzgus JD. 2019. Extreme thermal fluctuation from climate change unexpectedly accelerate demographic collapse of vertebrates with temperature-dependent sex determination. *Sci Rep.* 9:4254.
- Vidal MA, Novoa-Muñoz F, Werner E, Torres C, Nova R. 2017. Modeling warming predicts a physiological threshold for the extinction of the living fossil frog *Calyptocephalella gayi*. *J Therm Biol.* 69:110–117.
- Webb GJ, Smith AM. 1984. Sex ratio and survivorship in the Australian freshwater crocodile *Crocodylus johnstoni*. In: Ferguson MWJ, editor. *The structure, development and evolution of reptiles*. London (UK): Academic Press.
- Weber C, Capel B. 2018. Sex reversal. *Curr Biol.* 28:R1234–R1236.
- Weber C, Zhou Y, Lee JG, Looger LL, Qian G, Ge C, Capel B. 2020. Temperature-dependent sex determination is mediated by pSTAT3 repression of *Kdm6b*. *Science.* 368:303–306.
- Wedekind C. 2002. Manipulating sex ratios for conservation: short-term risks and long-term benefits. *Anim Conserv.* 5:13–20.
- Welbergen JA, Klose SM, Markus N, Eby P. 2008. Climate change and the effects of temperature extremes on Australian flying-foxes. *Proc Biol Sci.* 275:419–425.
- Williams GC. 1979. The question of adaptive variation in sex ratio in out-crossed vertebrates. *Proc R Soc B.* 205:567–580.
- Woitowich NC, Beery A, Woodruff T. 2020. A 10-year follow-up study of sex-inclusion in the biological sciences. *eLife.* 9:e56344.
- Woitowich NC, Woodruff TK. 2019. Research community needs to better appreciate the value of sex-based research. *Proc Nat Acad Sci USA.* 116:7154–7156.
- Xiracostas ZA, Everingham SE, Moles AT. 2020. The sex with reduced sex chromosome dies earlier: a comparison across the tree of life. *Biol Lett.* 16:20190867.
- Ye YZ, Ma L, Sun BJ, Li T, Wang Y, Shine R, Du WG. 2019. The embryos of turtles can influence their own sexual destinies. *Curr Biol.* 29:2597–2603.e4.
- Yu G, Smith D, Zhu H, Guan Y, Lam TT. 2017. ggtree: an R package for visualization and annotation of phylogenetic trees with their covariates and other associated data. *Methods Ecol Evol.* 8:28–36.
- Zhang R, Liu J, Liu Q, He H, Xu X, Dong T. 2018. Sexual differences in growth and defence of *Populus yunnanensis* under drought stress. *Can J For Res.* 49:491–499.
- Zhou H, Zhuang ZX, Sun YQ, Chen Q, Zheng XY, Liang YT, Mahboob S, Wang Q, Zhang R, Al-Ghanim KA, et al. 2019. Changes in DNA methylation during epigenetic-associated sex reversal under low temperature in *Takifugu rubripes*. *PLoS One.* 14:e0221641.