Maternally-transferred thyroid hormones and life-history variation in birds

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Abstract

Life-history traits vary largely across species and several physiological parameters have been proposed to be associated with life-history variation, such as metabolic rates, glucocorticoids, and oxidative stress. Interestingly, the association between thyroid hormones (THs) and life history variation has never been considered, despite a close interaction between THs and these physiological traits. Because of the crucial effects on embryonic development, THs can also induce transgenerational plasticity when transferred to developing offspring, for instance, via egg yolks in birds. In this study, we compiled a unique data set of maternal yolk THs in 34 bird species across 17 families and 6 orders, and tested for associations with various life-history traits. Our phylogenetic mixed models indicated that both concentrations and total amounts of the two most important forms of THs (T3 and T4) were higher in the eggs of migratory species than in those of resident species, and that there were higher total amounts of T3 in the eggs of precocial species than in those of altricial species. However, maternal THs did not show clear associations with any traits of the pace-of-life syndrome, such as developmental duration, growth rate, or lifespan. When taking environmental factors into account, we found that captive species deposited higher TH concentrations and larger amounts in the egg yolks than wild species. These findings suggest that maternal THs are likely involved in the evolution of life-history variation, or vice versa.

Key words: life-history variation, yolk hormones, maternal hormone transfer, phylogenetic comparative analysis, phenotypic plasticity

Introduction

Life-history variation constitutes a large part of biodiversity. Across species, life-history traits are often inter-correlated and present along several continuums. For example, many life-history traits, such as lifespan, fecundity and growth rates, co-vary with one another and constitute a continuum representing the 'pace of life' (Ricklefs and Wikelski 2002; Dammhahn et al. 2018). On the one end of this continuum, species exhibit fast growth and development, early maturation, but also fast senescence and short lifespan ("fast" species). On the other end, species have slow growth and development, late maturation and first reproduction, but also live longer ("slow" species). Other life-history continuums, such as the nutrient source for developing embryos (from yolk or via placenta), income versus capital breeders, precocial to altricial developmental modes, and various degrees of migratory tendencies, also exist across various taxa in the animal kingdom.

Identifying the mechanisms underlying the evolution of life history differences has fascinated evolutionary biologists for decades. For example, metabolic rate has been proposed as a mediator for the pace-of-life (POL) continuum, as it exhibits a parallel pattern with fast species usually having higher basal and resting metabolic rates (BMR and RMR), while slow species having lower metabolic rates (e.g. Wikelski et al. 2003; Auer et al. 2018). Some studies also proposed other possible mediators, such as glucocorticoids (Hau et al. 2010), oxidative stress (Vágási et al. 2019), and blood glucose level (Tomasek et al. 2019). We propose that thyroid hormones (THs), which have regulatory functions on metabolism (Mullur et al. 2014) and interactions with glucocorticoids (Darras et al. 1996; Kulkami and Buchholz 2012; Cortés et al. 2014), may be an additional mechanism underlying life-history variation, such as the POL continuum, or explain previously observed associations between metabolic rate or circulating glucocorticoids and life-history variation.

THs do not only regulate metabolisms in adults, but they are also transferred from mothers to developing offspring in all vertebrates (Ruuskanen and Hsu 2018). Such maternally-derived THs (hereafter "maternal THs") play a critical role for early embryonic development (Moog et al. 2017; Darras 2019). In humans, the levels of maternal THs are associated with new-born body mass and

66 children's IQ (Medici et al. 2013; Korevaar et al. 2016). This suggests that variation in maternal THs
67 can induce transgenerational phenotypic plasticity, which can constitute an important part of
68 phenotypic variation in wild animals (Mousseau and Fox 1998; Moore et al. 2019). Nevertheless, the
69 ecological and evolutionary significance of maternal THs in wild animals has been almost totally
70 neglected (Ruuskanen and Hsu 2018). Recently, several experimental studies manipulating maternal
71 THs reported variable effects of yolk TH on nestling traits across species (Ruuskanen et al. 2016a;
72 Hsu et al. 2017, 2019a). These intriguing species differences suggest species might respond
73 differently to elevated yolk TH levels and thus that maternal yolk THs might have co-evolved with
74 life-history differences.

75 In this study, we explored the potential associations between maternal yolk TH levels and
76 life-history strategies across 34 bird species. In birds, two maternally derived THs – triiodothyronine
77 (T3) and thyroxine (T4) are transferred and stored in the egg yolk (Sechman and Bobek 1988; Prati et
78 al. 1992). We asked whether the inter-specific variation of yolk THs would be associated with life-
79 history traits across species, while accounting for environmental factors that may potentially
80 contribute to the variation in yolk THs. The associations between maternal THs and life-history traits,
81 if they exist, probably reflect the involvement of maternal THs in the evolution of life-history
82 differences or vice versa.

83 Based on the known functions of THs, we considered three life-history continuums for which
84 we hypothesized that maternal yolk THs may be associated with the related life-history traits. The
85 first is the altricial-precocial developmental spectrum. At the two ends of this life-history continuum,
86 precocial species and altricial species show distinctive ontogenetic patterns of visual and locomotory
87 ability (Starck and Ricklefs 1998c), hypothalamic-pituitary-adrenal (HPA) axis (Wada 2008),
88 hypothalamic-pituitary-thyroid (HPT) axis (McNabb 2006; de Groef et al. 2013) and
89 thermoregulation (Price and Dzialowski 2018). In precocial species, the thyroid function already
90 starts in the middle of incubation and the TH levels in thyroid gland and blood circulation both peak
91 around hatching. By contrast, the thyroid function of altricial species starts days after hatching, and

92 their circulating blood TH levels slowly increase towards the adult level (McNabb 2006; de Groef et
93 al. 2013). Therefore, we hypothesized that such differences in the mode of development may be
94 associated with yolk TH levels, either because higher maternal THs are required for a comparatively
95 advanced development at hatching or because the developmental modes at least partly determine
96 the transfer process of maternal THs, or both.

97 Second, we considered the life-history differences between migratory and resident species.
98 THs have been known to regulate seasonal physiology and reproduction (Dardente et al. 2014;
99 McNabb and Darras 2015; Nishiwaki-Ohkawa and Yoshimura 2016) and also moulting and feather
100 regeneration (Vézina et al. 2009; Pérez et al. 2018). Several studies have also considered THs as part
101 of the hormonal mechanism underlying migration (Pérez et al. 2016) and in general migratory
102 species have higher BMR than resident species (Jetz et al. 2008). We thus hypothesized that
103 maternal TH levels may be associated with a species' migratory status.

104 Third, we considered the slow-fast pace-of-life (POL) continuum (Ricklefs and Wikelski 2002;
105 Dammhahn et al. 2018). As introduced above, metabolic rates (Wikelski et al. 2003; Auer et al.
106 2018), glucocorticoids (Hau et al. 2010), and oxidative stress (Vágási et al. 2018) have been proposed
107 to mediate the POL-related life-history variation. Interestingly, THs appear to have associations with
108 all of them. It is well known that THs have regulatory function on metabolism (Mullur et al. 2014),
109 and in wild birds, within-species studies have confirmed positive correlations between blood THs
110 and BMR and RMR (e.g. Chastel et al. 2003; Elliott et al 2013; Welcker et al. 2013). THs also have
111 cross-talks with the HPA axis (Cortés et al. 2014) and may induce higher oxidative stress due to the
112 metabolic effects (Villanueva et al. 2013). Therefore, it seems possible that THs may also be a
113 mediator of pace of life.

114 In addition to life-history differences, some environmental factors may also contribute to the
115 inter-specific variation of maternal yolk THs and should be taken into account. First, we expected
116 that the foraging environment, through its direct influence on food composition, may influence the
117 inter-specific variation of maternal yolk THs. For example, food conditions before and during the

118 egg-laying of captive wild-type rock pigeons (*Columba livia livia*) affected maternal yolk TH levels
119 (Hsu et al. 2016). A possible explanation for this finding is the iodine content in the diet, as iodine is
120 an essential ingredient for TH production (Bizhanova and Kopp 2009). In humans, even mild iodine
121 deficiency during pregnancy has been shown to lead to deficiency of maternal T4 and hence
122 detrimental effects on foetal development (Bath et al. 2013; Trumpff et al. 2013). In wild animals,
123 environmental iodine availability is associated with antler weights of roe deer (*Capreolus capreolus*)
124 via its influence on TH production (Lehoczki et al. 2011), and freshwater alligators (*Alligator*
125 *mississippiensis*) have on average lower plasma T3 and T4 concentrations than their estuarine
126 conspecifics (Boggs et al. 2011). Therefore, we hypothesized that iodine availability from the
127 environment and diet (e.g. Eckhoff and Maage 1997) could contribute to part of the variation in
128 maternal yolk THs. Moreover, captive environments differ in many aspects from wild environments,
129 such as in food availability and safety from predators. Confinement and regular human disturbance
130 might also pose as chronic stressors, which may influence THs (e.g. Angelier et al. 2016) and
131 therefore maternal TH deposition. We therefore hypothesized that captivity may also influence
132 maternal yolk THs.
133 To test these hypotheses, we collected information on life-history traits pertaining to each
134 hypothesis from the literature. The environmental variables were assigned for each species based on
135 the sampled population. We measured maternal THs in egg yolks, constructing the first interspecific
136 maternal TH data set. By combining data of life-history traits and maternal THs, we were able to run
137 phylogenetic mixed-effects models using a Bayesian framework to test our hypotheses.

Materials and Methods

Sample collection

We collected unincubated eggs from 34 species of birds across 17 families and 6 orders (n = 1-21 per species, median=7, Table S1). Nests of wild species were located by extensive nest searches in the known breeding habitats of each species or from nest-box populations during 2016-2017. We aimed at collecting eggs from species with varying body sizes and life-history traits and included both precocial and altricial species. All eggs were collected before clutch completion (i.e. when found, the eggs were cold and clutch was not completed) and one, randomly sampled egg per clutch was collected. Therefore, in most of the cases, the laying order of the sampled egg was unknown. Most of the wild species were sampled from Finnish populations near Turku (60°27'N, 22°16'E), Oulu (65°01'N, 25°28'E) and Kauhava (63°06'N, 23°04'E) regions, except thorn-tailed rayaditos (*Aphrastura spinicauda*, sampled mostly from Chiloé island, Chile, 42°40'S, 73°59'W) and collared flycatchers (*Ficedula albicollis*, from Burgsvik, Gotland, Sweden, 57°02'N, 18°16'E). The eggs of captive homing pigeons (*C. l. domesticus*) and domesticated chicken (*Gallus domesticus*) and eggs of semi-captive pheasants (*Phasianus colcichus*) and grey partridges (*Perdix perdix*) were sampled from local breeders in Finland. The eggs of red jungle fowl (*G. g. gallus*) and rock pigeons (*C. l. livia*) were sampled from the captive colonies at the University of Groningen, the Netherlands, and the eggs of captive zebra finches (*Taeniopygia guttata*) were from the University of Glasgow, UK. All collected eggs were first frozen and stored at -20°C until further analysis. For most of the species, the frozen eggs were shipped to the University of Turku, where we separated the yolk for hormone analysis (see *Yolk TH analysis*). Two exceptions are the collared flycatchers and the rock pigeons, for which the eggs had been dissected and the yolk had been homogenized and mixed in known amount of milli-Q (MQ) water before shipped to University of Turku and were already ready for extraction. Eggs of wild species were collected under licenses from the environmental authorities in each country: Finland, VARELY/665/2016, POPELY/61/2016, VARELY/63/2016, VARELY/412/2016, VARELY/6085/2016, and Finnish Wildlife Agency 84/2016; Chile, Agricultural Ministry 404/2017,

164 Sweden, National Board for Laboratory Animals. Captive species were housed and eggs were
165 collected following all national and international guidelines.
166
167 Yolk TH analysis
168 We extracted THs from the egg yolks and measured two THs (T3 and T4) at the University of
169 Turku and Turku Centre of Biotechnology. Yolk was separated from albumen after a short period of
170 thawing. A few eggs showed signs of very early development and all such eggs were discarded from
171 the analysis. After dissection, yolks were weighed (~0.01 g), and a half (for passerines) or a quarter
172 (for other species) of the yolk was weighed for extraction and we added an equal amount of MQ to
173 facilitate homogenizing.
174 We used the extraction protocol described previously (Ruuskanen et al. 2016b). In brief, we
175 first added 2 ml methanol to the yolk-MQ mixture (ca. 300 mg) and homogenized the sample. A
176 known amount of $^{13}C_{12}$-T4 (Larodan) was added to each sample as an internal tracer, which allowed
177 us to correct for extraction efficiency (i.e. recovery). Four ml of chloroform was then added and
178 samples were centrifuged at +4°C 1900g for 15 min. The supernatant was then collected and the
179 pellet was re-extracted in 2:1 chloroform-methanol mixture, back-extracted with 0.05% $CaCl_2$ into
180 aqueous phase, and re-extracted with chloroform:methanol:0.05% $CaCl_2$ mixture (3:49:48). The
181 aqueous phase was further purified on Bio-Rad AG 1-X2 resin columns, eluted with 70% acetic acid,
182 and then vacuum-evaporated overnight. Samples from different species were spread over extraction
183 batches and the extraction batch ID was included as a random intercept in the statistical models.
184 We used a validated nano-flow liquid chromatography-mass spectrometry (LC-MS) protocol
185 to measure yolk T3 and T4 simultaneously (Ruuskanen et al. 2018). In brief, the dry TH extracts were
186 re-suspended in 150 µl 0.1% NH_3 and further diluted with 0.01% NH_3. The dilution factor depended
187 on the expected amount of T3 and T4 in each sample. Internal standards $^{13}C_6$-T3 and $^{13}C_6$-T4 were
188 added to identify and also quantify T3 and T4 in the samples. A triple quadruple mass spectrometer
189 (TSQ Vantage, Thermo Scientific, San Jose, CA) and nano-flow HPLC system Easy-nLC (Thermo

190 Scientific) were used for the measurements. The on-column quantification limits were 10.6 amol and
191 17.9 amol for T4 and T3, respectively (Ruuskanen et al. 2018). The data was acquired automatically
192 using Thermo Xcalibur software (Thermo Fisher Scientific) and subsequently analysed by Skyline
193 (MacLean et al. 2010). TH concentrations were calculated using the peak area ratios of sample to
194 internal standard, corrected for recovery, and expressed as pg/mg yolk. We further calculated the
195 total amount of THs per yolk and expressed it as ng/yolk.
196
197 Life-history traits and environmental factors
198 *I. Altricial-Precocial continuum (i.e. developmental mode)*
199 We specified each species as precocial or altricial, following Starck and Ricklefs (1998a). The four
200 semi-precocial species, which all belong to the family Laridae (gulls and terns) and one semi-altricial
201 species (the kestrel, *Falco tinnunculus*) were pooled with precocial or altricial species, respectively.
202
203 *II. Migratory status*
204 Each species was categorized as either migratory or resident, based on data compiled in Lehikoinen
205 et al. (2003), McNab (2009) and Pap et al. (2015). When needed, the migratory status assignment
206 was made based on the population from which we collected eggs.
207
208 *III. Pace-of-life continuum*
209 The pace-of-life continuum incorporates many related life-history traits, including a species'
210 developmental duration, fecundity, metabolic rate, growth rate, and the rate of maturation and
211 senescence.
212 (i) The data on **developmental duration** was collected mainly from the amniote life-history
213 database compiled by Myhrvold et al. (2015) with supplementation from other literature
214 (see *supplementary materials*). We collected the **incubation duration** and **the time to**
215 **fledging** (from hatching) to represent the prenatal and postnatal part of the developmental

period. We additionally calculated two more variables: **the total length of development** (incubation duration + time to fledging) and **the proportion of prenatal development** (incubation duration / total developmental length).

(ii) The **growth rate** data originated from Starck and Ricklefs (1998b) and was supplemented with other literature (see *supplementary materials*). For comparability, the logistic growth rate constants were used to represent the growth rate of each species. Whenever multiple sources of the growth rates are available for a species, an average was used.

(iii) **Species' body mass, clutch size** and **number of clutches per year** were obtained from Myhrvold et al. (2015).

(iv) **Basal metabolic rates** (BMR) were mainly obtained from McKechnie et al. (2006) and McNab (2009), supplemented by other literature (see *supplementary materials*).

(v) **Maximum lifespan** and **ages at first reproduction** originated from the database AnAge (Tacutu et al. 2013), except for the thorn-tailed rayaditos (*Aphrastura spinicauda*), for which the data was obtained from Moreno et al. (2005) and Quirici et al. (2019).

IV. Environmental factors

For environmental factors, we created two variables to represent a species' **foraging environment** and **captivity status.** Respectively, species were categorized as marine-bound (foraging on marine food resources) or terrestrial (foraging on non-marine bound resources) based on the breeding territory and diet, and wild or captive. Semi-captive species (the pheasant and the grey partridge) were categorized as captive.

All life-history and environmental data we compiled for this study, the sources we consulted, and the final values used in all our models, can be found in the supplementary materials.

<u>Phylogenetic mixed models</u>

Model specifications

242 Following Hadfield and Nakagawa (2010), we ran phylogenetic mixed models with the R package
243 *MCMCglmm* (Hadfield 2010). T3 and T4 concentrations (pg/mg yolk) as well as total contents
244 (ng/yolk) were ln-transformed and standardized and used as dependent variables in separated
245 univariate models. Species body mass and other life-history and environmental variables (see *Life-*
246 *history traits and environmental factors*) were treated as fixed factors and covariates. In order to
247 facilitate model fitting, body mass was also ln-transformed and standardized. Before fitting models,
248 all two-level categorical variables were first dummy-coded as -0.5 and 0.5 (Table S2), to facilitate
249 model mixing/convergence. The life-history traits that are known to be associated with body mass
250 (BMR, growth rate, maximum lifespan, age at first reproduction) were first corrected for body mass
251 and phylogenetic relatedness among species using the R package *phytools* (Revell 2009, 2012). BMR
252 data, in particular, was first converted to mass-specific BMR (KJ/h/g) and ln-transformed and
253 corrected for body mass and phylogeny.

254 The four variables of developmental duration were strongly correlated with one another.
255 Therefore, we conducted a phylogeny-corrected principal component analysis (PCA) using R package
256 *phytools* (Revell 2009, 2012). The first two PCs explained 99.74% of the variance (Table S3). The
257 loadings suggested that PC1 is highly positively correlated with the time to fledging and the total
258 length of developmental period, and negatively correlated with the proportion of prenatal
259 development, while PC2 is negatively correlated with the duration of prenatal development (Table
260 S3). In subsequent phylogenetic mixed models, we therefore used the scores of PC1 and PC2 for
261 each species to represent the developmental duration.

262 Because the data of life-history traits were not available for all species, we defined several
263 sets of models depending on data availability, listed in Table 1. Each model and data set was thus
264 pruned for the specific set of species where data was available. Each model set consists of separate
265 models to analyse the concentrations and total contents of T3 and T4, respectively. This is because in
266 oviparous species, the total contents of maternal hormones in the yolk is fixed after yolk formation.

267 Therefore, the total content of hormones represents an initial maximum hormone availability and
268 may represent different biological significance from the concentration.
269 In all models, the phylogenetic relatedness among all species included was treated as
270 random effects, following Hadfield and Nakagawa (2010). Additionally, species name was also
271 included as a random factor to control for within-species non-independence among the multiple
272 eggs from the same species. For this random factor, homing pigeons and domesticated chickens
273 were coded separately from their wild-type ancestor rock pigeons and red jungle fowl, despite that
274 they were not distinguished in the phylogeny (i.e. coded with the same scientific names, *Columba*
275 *livia* and *Gallus gallus*). The batch of hormone extraction was also included as an additional random
276 factor. Response variables were all assumed to follow Gaussian distributions. All models were run
277 for 750000 iterations with a 350 thinning interval and burn-in of 50000, aiming for an approximately
278 2000 effective sample size for all parameters. Following Houslay and Wilson (2017), we used an
279 uninformative parameter-expanded prior following a Cauchy distribution (V=1, nu=1, alpha.mu=0,
280 alpha.V=25^2) for all random factors. Tests using an uninformative inverse-Wishart prior or
281 improper flat prior gave qualitatively same results, suggesting the results are robust against the
282 choice of priors.
283
284 *Phylogenetic trees and phylogeny uncertainty*
285 Each phylogeny set (Table 1) was correspondingly pruned and obtained from BirdTree.org (Jetz et al.
286 2012) based on two phylogenetic backbones (Ericson et al. 2006; Hackett et al. 2008). For each
287 backbone, 100 possible trees were generated and downloaded. All models were tested repeatedly
288 across the 100 possible trees in each backbone and the posterior means of parameter estimates and
289 their 95% credible intervals (CIs) were stored. The average posterior mean and the average
290 boundaries of the 95% CIs were calculated to account for phylogenetic uncertainty (Rubolini et al.
291 2015) and reported. The results are highly similar across all possible trees (see Fig. S1 for examples)

292 and between the two backbones. Therefore we only reported the results based on the Hackett
293 backbone.
294
295 *Model diagnostics*
296 As models across all possible phylogenetic trees produced highly similar results, we examined model
297 performance by re-fitting all models with a consensus tree. The consensus tree was derived using
298 the R package *phytools* (Revell 2012) for each phylogeny set. Model diagnostics were conducted by
299 visual inspection on the trace plots for proper mixing and on autocorrelations. Model convergence
300 was also checked using Gelman diagnostics provided in the R package *coda* (Plummer et al. 2006).
301 For all models, visual inspection did not raise any red flags for poor mixing or substantial
302 autocorrelation and all models passed the Gelman diagnostics with all potential scale reduction
303 factors < 1.05.
304
305 *Phylogenetic signals*
306 Phylogenetic signal, a.k.a. phylogenetic heritability (H^2), was calculated as
307 $$H^2 = \frac{\sigma_a^2}{\sigma_a^2 + \sigma_s^2 + \sigma_e^2}$$
308 where σ_a^2 represents the variance of the phylogeny; σ_s^2 represents the variance accounted by
309 individual species; σ_e^2 represents the residual variance. The H^2 calculated this way is equivalent to
310 the Pagel's λ (Hadfield and Nakagawa 2010).
311 Because phylogenetic signal is in fact the proportion of the phylogenetic variance over the
312 total phenotypic variance, the fixed factors included in the model will influence the value of the
313 phylogenetic signal by changing the estimates of all variance components (Nakagawa and Schielzeth
314 2010). Therefore we calculated the phylogenetic signals for yolk T4 and T3 based on the
315 phylogenetic mixed model that only included the life-history traits whose 95% CIs did not encompass
316 0 (i.e. having credible associations). These are the developmental mode, migratory status, captivity,

317 and body mass (see *Results*). In these models, all 34 species and the full phylogeny set was included

318 and we used a consensus tree from the Hackett backbone, derived by using the *phytools* package

319 (Revell 2012).

320

321 **Table 1.** Model, phylogeny and data sets defined in this study

Model set	Phylogeny	Data set	Model structure (fixed factors)	Remark
1	All 34 species	Full data set	~developmental mode + migration + body mass + maximum lifespan + foraging environment + captivity	
2a	Excluding *Coturnix japonica**	Excluding domesticated Japanese quails and domesticated chicken	~developmental mode + migration + body mass + clutch size + clutches per year + captivity	Domesticated quails and chicken do not lay clear "clutches" of eggs.
2b	Excluding *Coturnix japonica*	Excluding Japanese quails	~developmental mode + migration + body mass + PC1 and PC2 of developmental period + captivity	Time to fledging data was missing for Japanese quails
3	Excluding *Gallus gallus*	Excluding red jungle fowl and domesticated chicken	~developmental mode + migration + body mass + age at first reproduction + captivity	Age at first reproduction data was missing for both jungle fowl and chicken
4	28 species with BMR data	Species with BMR data	~developmental mode + migration + body mass + BMR + captivity	
5	29 species with growth rate data	Species with growth rate data	~developmental mode + migration + body mass + growth rate + captivity	

322 * In Model set 2a, both Japanese quails and domesticated chicken were removed from the "data

323 set" but only *Coturnix japonica* was removed from the phylogeny because *Gallus gallus* was still

324 needed in the phylogeny for the data from red jungle fowl.

325 **Results**

326 Inter-specific variation in yolk THs and phylogenetic signals

327 We observed substantial inter-specific variation in both T3 and T4 concentrations (Fig. 1,
328 Table S1). Great tits (*Parus major*) and redshanks (*Tringa totanus*) had the lowest and highest
329 concentrations of yolk T3 and T4 among the 34 species, respectively. Between the two species, the
330 difference in average yolk THs reached 100-fold for T3 (great tit, mean ± SD = 0.112 ± 0.032 pg/mg
331 yolk, n = 11; redshank, mean ± SD = 11.242 ± 5.067 pg/mg yolk, n = 4), and 18-fold for T4 (great tit,
332 mean ± SD = 0.989 ± 0.292 pg/mg yolk, n = 12; redshank, mean ± SD = 18.101 ± 4.125 pg/mg yolk, n =
333 4).

334 The moderate to strong phylogenetic signals indicated that the phylogenetic relatedness
335 among species accounted for 60%-85% of the inter-specific variation in yolk THs (Table 2). On
336 average, T3 has stronger phylogenetic signals than T4, although their 95% CIs overlapped.

337

338 **Table 2.** Phylogenetic signals (i.e. phylogenetic heritability) for maternal yolk T3 and T4.

Hormone	Parameter	Posterior mean [95% CI]
T3	concentration	0.84 [0.68, 0.95]
	total content	0.84 [0.71, 0.95]
T4	concentration	0.60 [0.25, 0.87]
	total content	0.75 [0.54, 0.91]

339

340 Associations between yolk THs and life-history variables

341 The estimated posterior means and 95% CIs from all models are presented in Fig. 2.
342 Precocial species deposited larger total amounts of THs in the egg yolks than altricial species (Fig. 3),
343 but not higher TH concentrations. The model set 1 supported this difference with positive posterior
344 means and 95% CIs, when controlling for species body mass and other covariates, especially for T3
345 contents (Fig. 2D). Also, migratory species generally deposited higher concentrations and also larger
346 amounts of both THs in the egg yolks than resident species (Fig. 4), which were supported by the
347 model set 1 (Fig. 2). Species body mass also strongly correlated with yolk TH content, but not with

348 yolk TH concentration (Fig. 2). Along the slow-fast pace-of-life continuum, however, no traits were
349 found to be credibly associated with maternal yolk TH concentrations or contents (Fig. 2)
350
351 Associations between yolk THs and environmental variables
352 Although the raw data suggested that marine-bound species deposited larger amounts of yolk THs
353 than terrestrial species (Fig. S2), this was not supported by the phylogenetic mixed models (Fig. 2).
354 Between captive and wild species, credible differences in both yolk T3 and T4, and in both
355 concentrations and total contents (Fig. 2) were found. This suggested that captive species deposited
356 higher concentrations and larger amounts of yolk THs than wild species (Fig. 5).

357 **Discussion**

358 Maternal THs and life-history variation

359 Among the three life-history continuums, our phylogenetic mixed models estimated
360 credible differences in maternal yolk THs between the migratory and resident life histories, and
361 between precocial and altricial developmental modes. However, contrary to our expectation, none
362 of the pace-of-life (POL) related traits were found credibly associated with maternal yolk THs, after
363 controlling for body mass. The moderate to strong phylogenetic signals also indicate that a
364 substantial proportion of variation in maternal THs is accounted for by the phylogeny itself. This
365 suggests a substantial extent of phylogenetic inertia, which may present some evolutionary
366 constraints in maternal TH deposition. Despite the constraint, the credible differences of maternal
367 THs between precocial and altricial species, and between migratory and resident species still suggest
368 that maternal THs are associated with the evolution of these two life-history continuums or vice
369 versa.

370

371 *THs and migration*

372 Migration is a critical and demanding life-history stage. Many physiological changes occur
373 both before and after migration, such as fat deposition, gonadal regression and recrudescence
374 (Hahn et al. 2015). The temporal overlap with other seasonal activities, such as breeding and moult,
375 also tends to be minimized over evolutionary history in migratory species (Hahn et al. 2015). By
376 contrast, resident species usually have a relatively longer time window to coordinate the
377 physiological transition before and after reproduction compared with migratory species. Therefore,
378 migratory species may require a higher sensitivity or accuracy to fine-tune the transition. THs play a
379 central role in the molecular mechanisms of photoperiodic response. The photoperiodic change
380 influences the expression levels of the thyroid-stimulating hormones (TSH) in the hypothalamus,
381 which subsequently induces reciprocal switching of two deiodinases (DIO2, converting T4 to active
382 T3 and DIO3, converting T4 and T3 to inactive THs) that activate and inactivate T3, respectively

383 (Nakao et al. 2008; Dardente et al. 2014). This photoperiodic DIO2/DIO3 expression pattern further
384 regulates the seasonal maturation of gonads. Interestingly, the photoperiodic DIO2/DIO3 gene
385 expression pattern of great tits was only evident in a Swedish population but not in a southern
386 German population (Perfito et al. 2012), in which the duration of the breeding seasons are likely to
387 differ. Our result of higher yolk TH levels in migratory than resident species, not only in terms of
388 higher concentrations but also larger amounts, is therefore in line with the notion that the
389 differences in maternal THs could have some organizational effects on TH responsiveness later in
390 life. There may still be species differences in the seasonal regulation of DIO2/DIO3 expression, as a
391 similar pattern was not found in European starlings (*Sturnus vulgaris*, Bentley et al. 2013).
392 Comparison of TH-related gene expression between conspecific populations that possess different
393 migratory propensity, potentially in combination with TH manipulation, may help to identify the
394 elements responsible for such differences.
395
396 *Does precocial development require more maternal THs?*
397 We found that precocial species deposited higher amounts of THs (accounted for body
398 mass), particularly T3, in the egg yolks than altricial species, which fits their distinct developmental
399 trajectories (Starck and Ricklefs 1998c). Compared with altricial species, precocial species temporally
400 shift their physiological maturity to an earlier life stage in terms of visual and locomotory ability
401 (Starck and Ricklefs 1998c), HPA and HPT axis (McNabb 2006; Wada 2008; de Groef et al. 2013) and
402 thermoregulation (Price and Dzialowski 2018). Our result may suggest the requirement of a larger
403 amount of maternal THs for such an advanced ontogenetic trajectory in precocial birds.
404 An alternative way to look at the contrasting ontogenetic differences between precocial and
405 altricial development may be the placement of hatching on the ontogenetic timeline. Regardless of
406 the developmental modes, the event of hatching requires a lot of physiological changes to prepare
407 the chick for the “outside” world and therefore marks a major life-stage transition. As the altricial
408 developmental mode is assumed to have evolved later than the precocial mode (Starck and Ricklefs

409 1998c; de Groef et al. 2013), one way to look at the shift is that the event of hatching is moved
410 earlier along the ontogenetic timeline in the altricial development so that hatching occurs when the
411 young is still poorly developed. Whether maternal THs mediate such a shift during the evolution
412 from precocial to altricial development requires further studies, but according to our data such a
413 change may coincide with a reduction in TH deposition over the evolutionary course. We therefore
414 could expect intermediate levels of maternal THs in semi-precocial and semi-altricial species.
415 Interestingly, the only semi-altricial species we measured, the Eurasian kestrel, indeed has higher
416 maternal TH content than most other altricial species, but lower than most semi-precocial and
417 precocial species (Fig. 3).
418
419 *No size-independent associations between maternal THs and pace of life (POL)*
420 Given the known function of THs on metabolism and interactions with glucocorticoids, it is
421 surprising that we did not detect any associations between maternal THs and all tested POL-related
422 traits (Fig. 2). Although yolk TH contents show strong correlations with species body mass, this is
423 because large species produce large eggs and large yolks, hence higher total amounts of yolk THs.
424 After controlling for body mass and phylogenetic relatedness, only clutch size showed a potential
425 trend with T4 contents. The model estimated a negative posterior mean and the 95% CI was slightly
426 overlapped with 0 (Fig. 2B), implying that species with larger clutch sizes tended to deposit less T4 in
427 the egg yolks. Such a trend is probably driven by the difference between passerines and shorebirds
428 (Fig. S3). Confirming such a relationship perhaps would require a larger sampling scheme that
429 includes more species.
430 The lack of associations between maternal yolk THs and POL-related traits does not support
431 our hypothesis that THs were mediators of POL. This result therefore implies that either (i) the
432 effects of maternal THs may not be translated directly to blood THs or (ii) blood THs are not
433 associated with POL-related traits. The former could be due to limited organizational effects of
434 maternal THs on the HPT axis or a more complex manifestation, such as sex-specific effects. To our

435 knowledge, there are only few experimental studies that have examined how maternal THs
436 influenced blood THs and metabolic rates during the nestling phase. In the great tit, yolk TH
437 elevation did not influence nestling RMR before fledging (Ruuskanen et al. 2016a). In the rock
438 pigeon, yolk TH elevation raised the RMR in female nestlings but reduced it in males on hatching
439 day, a pattern that was consistent with the effects on plasma T4 concentrations (but not T3) at day
440 14 after hatching (in the middle of the nestling phase, Hsu et al. 2017). Although elevated yolk THs
441 showed consistent effects on nestling RMR and plasma T4, the sex-specific pattern remains
442 unexplained. Nevertheless, in domesticated chicken embryos the injection of THs into the yolk
443 influenced the expression of two TH-transporters in the brain (van Herck et al. 2012). This suggests
444 that differential exposure to maternal THs may influence brain TH availability. Such changes might
445 have the potential to alter the sensitivity and responsiveness of the HPT axis in the long term.
446 Therefore, the notion that maternal THs may organizationally shape the HPT axis cannot yet be ruled
447 out. Another possibility to explain the lack of associations between maternal THs and POL-related
448 traits is that blood THs are not associated with POL-related traits. This would be quite surprising
449 considering the close associations between THs with metabolic rates, glucocorticoids, and oxidative
450 stress. As POL-related traits are usually strongly associated with body mass, perhaps a much larger
451 number of species is required to detect such potential associations after accounting for species body
452 mass.
453
454 *Maternal THs and life-history variation: cause or consequence?*
455 Above, we have discussed the potential role of maternal THs as mediators of life-history variation.
456 However, it is possible that differences in life-histories, particularly in migratory behaviour and
457 developmental mode, may result in physiological differences that cause differential maternal TH
458 deposition during egg formation across species. For example, migratory birds generally have higher
459 BMR than residents (Jetz et al. 2008). Given the close relationship between BMR and THs, migratory
460 species probably also have higher circulating blood TH levels. One study in two closely-related

461 skylark species indeed found that the migratory Eurasian skylarks (*Alauda arvensis*) had higher pre-
462 breeding blood T3 levels than the resident Asian short-toed larks (*Calandrella cheleensis*, Zhao et al.
463 2017). A meta-analysis on the available blood TH data from the literature should be promising to test
464 the associations between life-history variation and TH physiology but to our knowledge, such a
465 meta-analysis has not yet been done. If in general migratory species keep comparatively higher
466 circulating TH levels than resident species, the higher maternal TH deposition could be simply
467 mirroring the circulating TH levels in the system of migratory birds.

468 Even if maternal yolk THs are a physiological consequence induced by different life histories,
469 differential yolk TH deposition may still reinforce the evolution of the life-history variation. Due to
470 the critical role in embryonic development, maternal THs likely have short-term and long-term
471 effects on offspring phenotype, such as nestling development, growth, and physiology (Ruuskanen
472 et al. 2016a; Hsu et al. 2017, 2019a). If higher maternal THs would lend beneficial effects for a
473 certain life-history strategy, and physiologically such a life history results in a higher maternal TH
474 transfer, maternal THs may speed up the evolution of associated life-history traits (McGlothin and
475 Galloway 2014). At the moment, this is a bold speculation. However, considering that yolk T3
476 deposition has a moderate heritability (h^2 = 0.25, Ruuskanen et al. 2016c) and clear between-
477 individual difference (Hsu et al. 2019b), there might be evolutionary potential for this to happen.
478 Future studies may examine the temporal and quantitative differences in the expression patterns of
479 TH-related genes in embryonic brains between migratory and resident species, and between
480 precocial and altricial species, to know if there has been fundamental differences during the early
481 developmental stage. Another angle would be examining whether birds hatching from eggs with
482 elevated yolk THs may deposit higher yolk THs than control birds to test if maternal TH can induce
483 any non-genetic inheritance.

484

485 <u>Maternal THs and environment</u>

486 In terms of environmental factors, our models suggested differences in maternal yolk THs between
487 captive and wild species, but not between terrestrial and marine-bound species.
488
489 *Captive life has favoured higher maternal TH deposition*
490 Life in captivity is characterised by space confinement, (usually) unlimited food availability and a
491 predator-free environment (Mason 2010). The contrast to life in the wild can influence phenotypic
492 expression (i.e. phenotypic plasticity) and even cause selection for certain traits (Driscoll et al. 2009).
493 For example, captive zebra finches, domesticated or not, started incubating earlier and therefore
494 induced a stronger degree of hatching asynchrony than wild zebra finches (Gilby et al. 2013). In our
495 study, all the captive species have acclimated to captive lives for generations. Therefore the result
496 that captive species deposit higher levels of THs in the egg yolks likely reflects some selection under
497 captivity. The actual selective force is elusive at the moment, but probably related to traits like faster
498 acclimation/habituation for anthropogenic diet or perhaps dampened stress response to confined
499 space and constant human disturbance, which should be favoured in captivity.
500
501 *Lack of evidence for the potential link with proximity to the sea*
502 The larger yolk TH contents in marine-bound species compared to terrestrial species, apparent from
503 the raw data, were not supported by the phylogenetic mixed models. Our data likely lacked the
504 power to statistically partition the effects of environment and phylogeny because all sampled
505 marine-bound species were from the order Charadriiformes. Future studies should therefore
506 broaden the sampling scheme to overcome this problem. An alternative to test the relationship
507 between foraging environment and maternal THs is to focus on a smaller clade, such as a single
508 order or a single species inhabiting both inland and marine-bound populations. In the present study,
509 the eggs of the little ringed plover (*Charadrius dubius*) were sampled from an inland population. The
510 species, interestingly, had the lowest T4 content among all Charadriiform species, which implies
511 possible influence from the environment. Experimentally manipulating the iodine content of diet in a

512 captive model system or supplementing iodine-rich food to a wild population would be also an
513 effective approach in this respect.
514
515 Conclusion
516 Our phylogenetic mixed models suggested that migratory species deposited higher levels of both
517 THs in the egg yolks than resident species, and precocial species deposited higher total content of T3
518 in the egg yolks than altricial species. In addition, captive species also consistently deposited higher
519 levels of yolk THs, suggesting some selection process under captivity. These identified patterns
520 suggest that maternal THs may be involved in the process of life-history evolution and can respond
521 to on-going selective forces. Further effort should be invested to uncover the underlying
522 physiological mechanisms.
523
524 **Acknowledgement**
525 We thank Jon Brommer for his kind and helpful statistical advice in the beginning stage of data
526 analysis. We thank Jorma Nurmi for excellent nest-finding skills and effort in the field. Mass
527 spectrometry analyses were performed at the Turku Proteomics Facility, University of Turku and Åbo
528 Akademi University. The facility is supported by Biocenter Finland. This study was funded by a grant
529 from the Academy of Finland to SR (grant no. 286278).

530

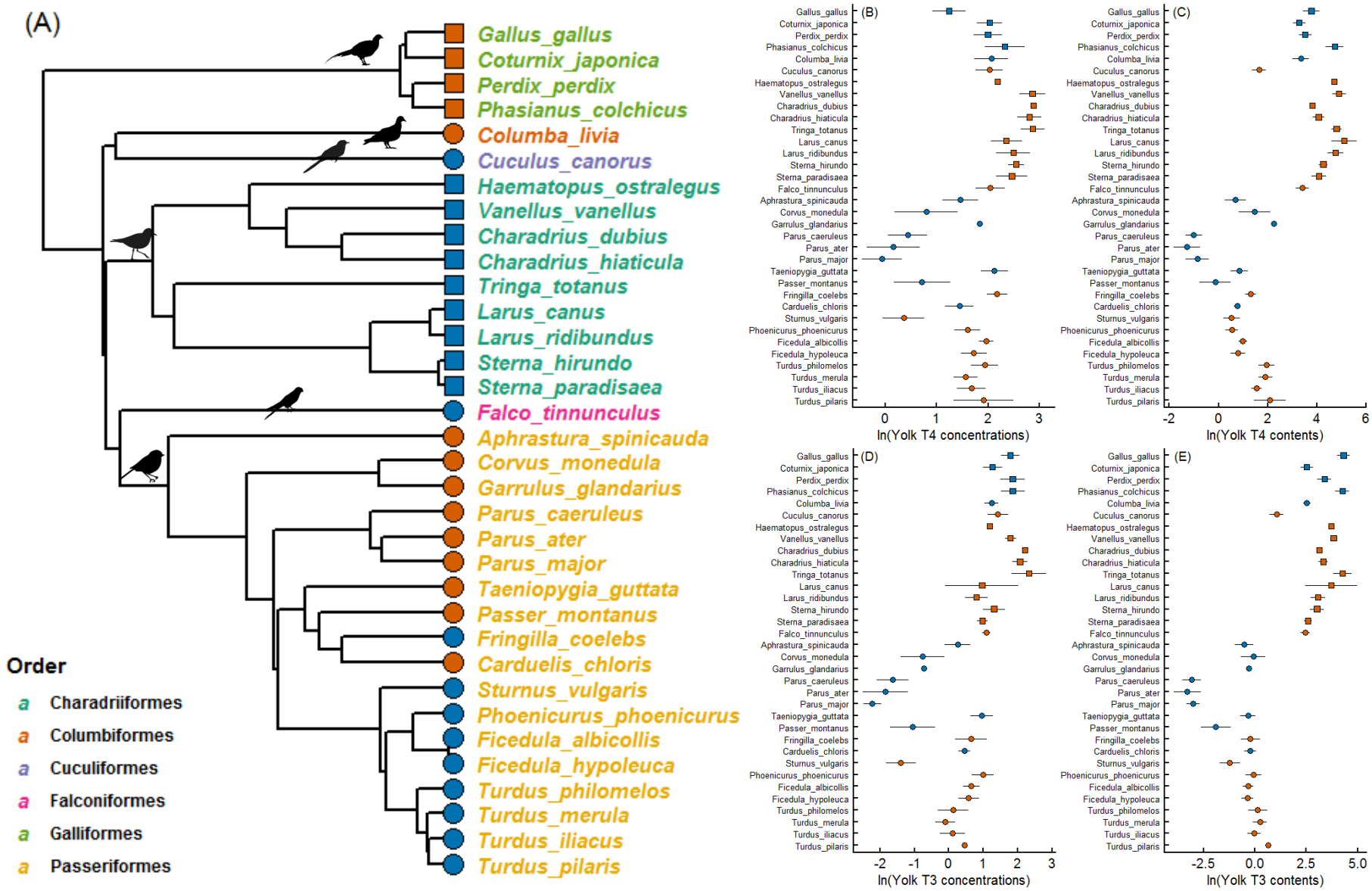

(A)
Gallus_gallus
Coturnix_japonica
Perdix_perdix
Phasianus_colchicus
Columba_livia
Cuculus_canorus
Haematopus_ostralegus
Vanellus_vanellus
Charadrius_dubius
Charadrius_hiaticula
Tringa_totanus
Larus_canus
Larus_ridibundus
Sterna_hirundo
Sterna_paradisaea
Falco_tinnunculus
Aphrastura_spinicauda
Corvus_monedula
Garrulus_glandarius
Parus_caeruleus
Parus_ater
Parus_major
Taeniopygia_guttata
Passer_montanus
Fringilla_coelebs
Carduelis_chloris
Sturnus_vulgaris
Phoenicurus_phoenicurus
Ficedula_albicollis
Ficedula_hypoleuca
Turdus_philomelos
Turdus_merula
Turdus_iliacus
Turdus_pilaris
Order
Charadriiformes
Columbiformes
Cuculiformes
Falconiformes
Galliformes
Passeriformes
(B)
ln(Yolk T4 concentrations)
(C)
ln(Yolk T4 contents)
(D)
ln(Yolk T3 concentrations)
(E)
ln(Yolk T3 contents)

Figure 1. Phylogenetic tree, yolk TH concentrations and total contents of the avian species included in this study. The phylogenetic tree (A) is one possible tree derived from the Hackett backbone (see text). Different colours in species names represent different orders they belong to. Yolk TH concentrations (B, D) and total contents (C, E) exhibited substantial inter-specific variation (mean ± SD, see Table S1 for exact values and sample sizes). Red symbols represent resident species, while blue symbols migratory species. Circles represent altricial species, and squares precocial species.

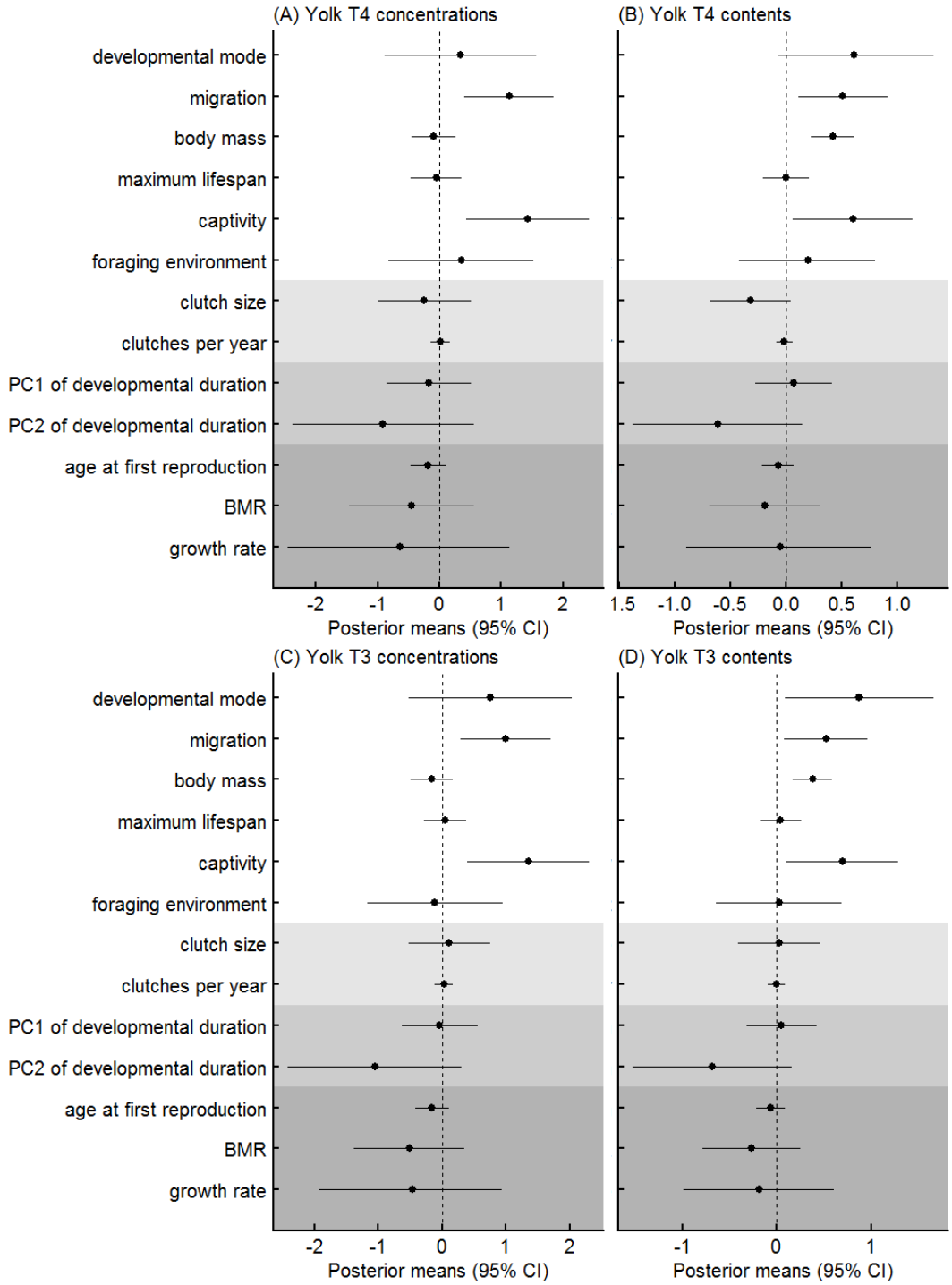
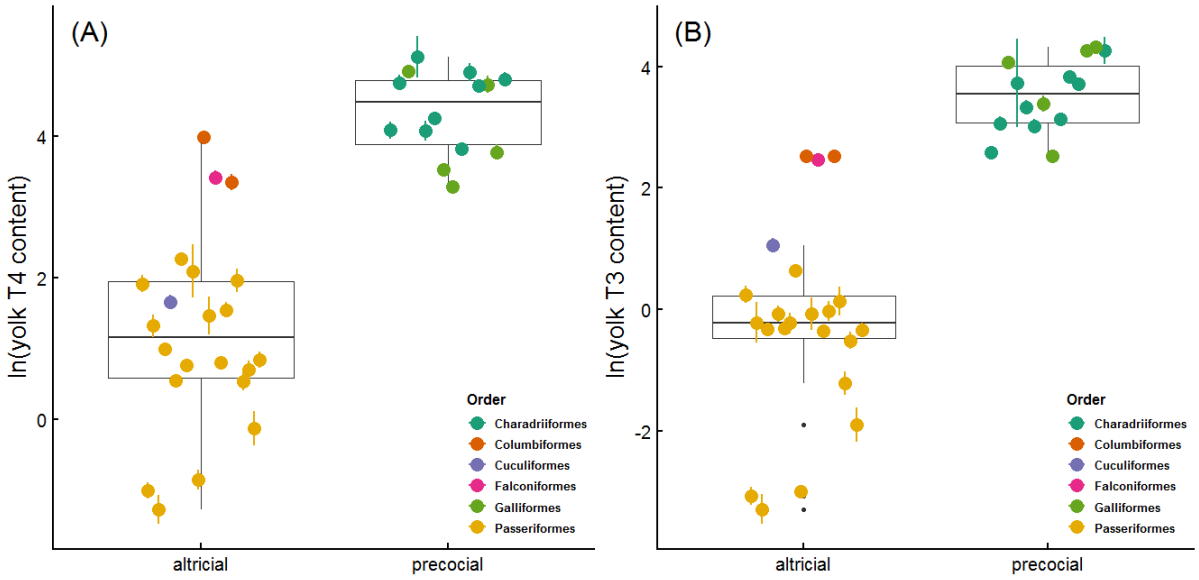


Figure 2. Posterior means (± 95% credible intervals) between yolk THs and all life-history variables tested in this study. White area presents the estimates from model set 1 (see text and Table 1). The shaded areas present the variables tested in model set 2 (the light and medium grey areas) and model set 3-5 (the darkest grey area). In models 2-5, the estimates of the variables that had been tested in model set 1 are not redundantly presented. For developmental mode, the estimate represents the difference of yolk THs in precocial species from altricial species. For migration, the

541 estimate represents the difference in migratory species from resident species. For captivity, the

542 estimate represents the difference in captive species from wild species. For foraging environment,

543 the estimate represents the difference in marine-bound species from terrestrial species.



544

545 **Figure 3.** Boxplots and species-specific averages of yolk T4 (A) and T3 (B) contents (ng/yolk, ln-

546 transformed raw data) according to developmental mode. Boxplots represent the median (the

547 middle line) and the first and the third quartiles (the box), and the whiskers extend to 1.5 times of

548 the interquartile range. Colored dots represent species-specific means (±SE).

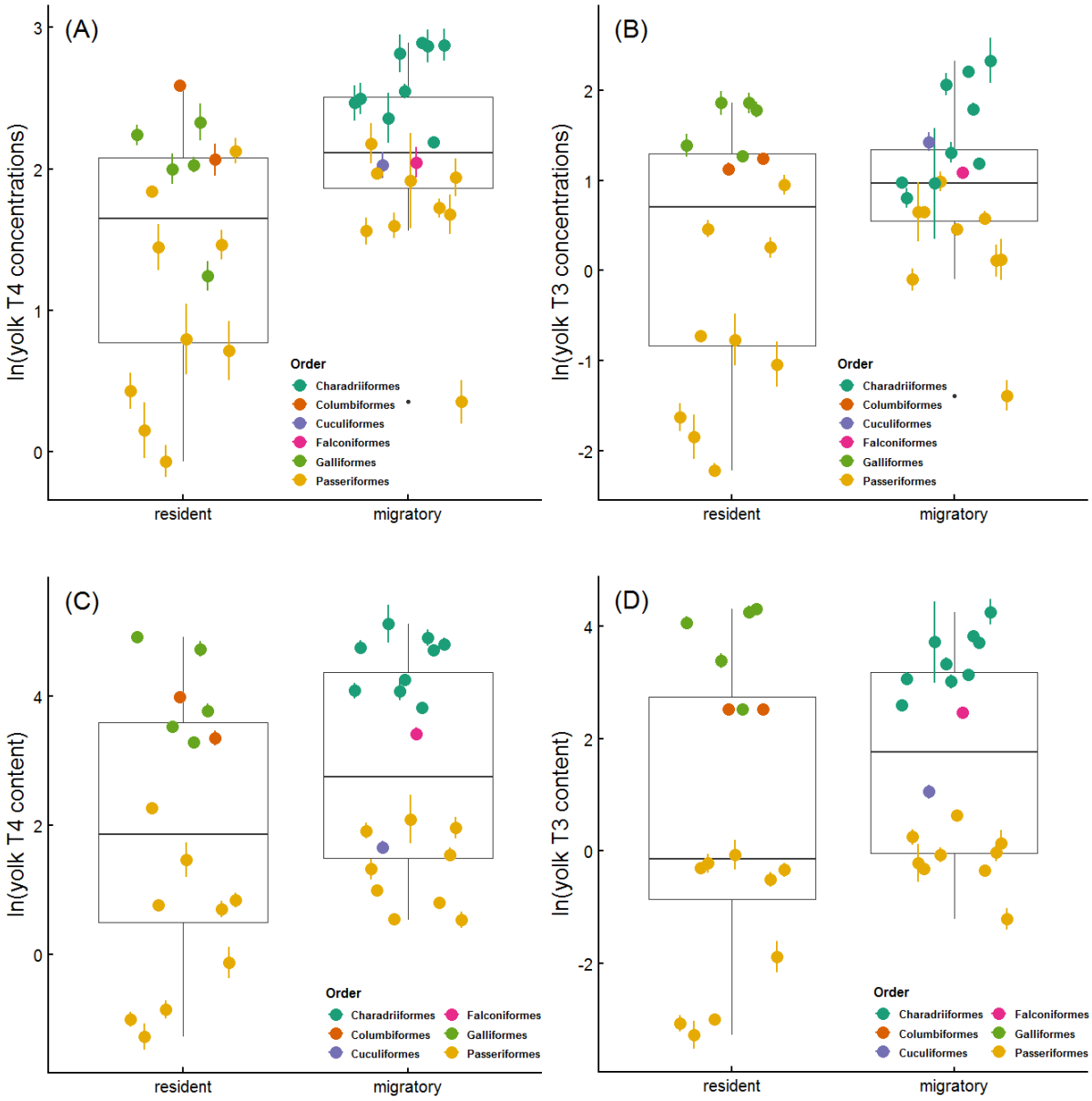


Figure 4. Boxplots and species-specific averages of yolk TH concentrations (A, B, pg/mg, ln-transformed raw data) and total contents (C, D, ng/yolk, ln-transformed raw data) between migratory and resident species. Boxplots represent the median (the middle line) and the first and the third quartiles (the box), and the whiskers extend to 1.5 times of the interquartile range. Colored dots represent species-specific means (±SE).

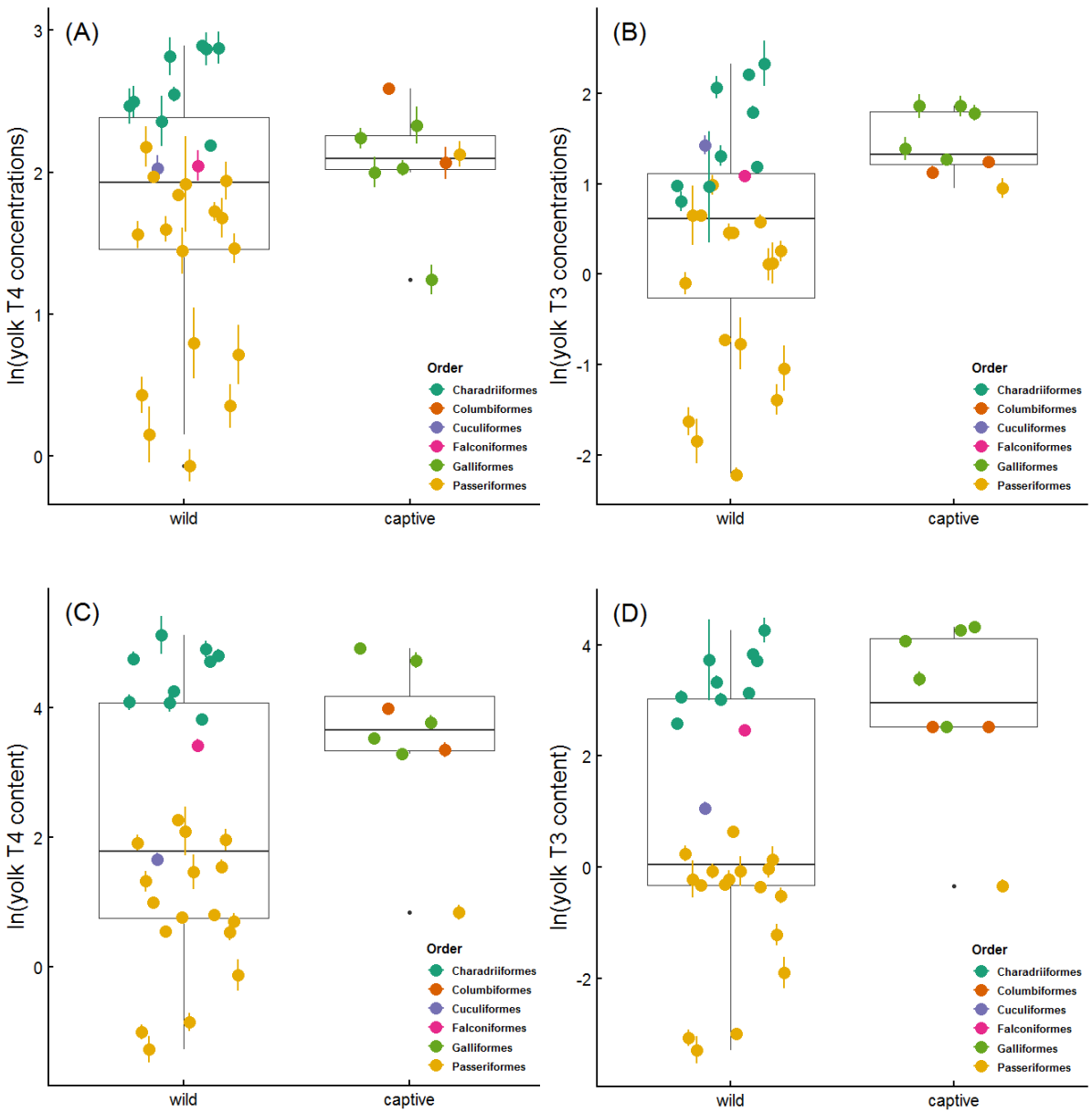


Figure 5. Boxplots of yolk TH concentrations (A, B, pg/mg, ln-transformed raw data) and total contents (ng/yolk, ln-transformed raw data) in between captive and wild species. Boxplots represent the median (the middle line) and the first and the third quartiles (the box), and the whiskers extend to 1.5 times of the interquartile range. Colored dots represent species-specific means (±SE).

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