SYNTHESIS

The evolutionary ecology of fatty-acid variation: Implications for consumer adaptation and diversification

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Abstract

The nutritional diversity of resources can affect the adaptive evolution of consumer metabolism and consumer diversification. The omega-3 long-chain polyunsaturated fatty acids eicosapentaenoic acid (EPA; 20:5n-3) and docosahexaenoic acid (DHA; 22:6n-3) have a high potential to affect consumer fitness, through their widespread effects on reproduction, growth and survival. However, few studies consider the evolution of fatty acid metabolism within an ecological context. In this review, we first document the extensive diversity in both primary producer and consumer fatty acid distributions amongst major ecosystems, between habitats and amongst species within habitats. We highlight some of the key nutritional contrasts that can shape behavioural and/or metabolic adaptation in consumers, discussing how consumers can evolve in response to the spatial, seasonal and community-level variation of resource quality. We propose a hierarchical trait-based approach for studying the evolution of consumers' metabolic networks and review the evolutionary genetic mechanisms underpinning consumer adaptation to EPA and DHA

distributions. In doing so, we consider how the metabolic traits of consumers are hierarchically structured, from cell membrane function to maternal investment, and have strongly environment-dependent expression. Finally, we conclude with an outlook on how studying the metabolic adaptation of consumers within the context of nutritional landscapes can open up new opportunities for understanding evolutionary diversification.

INTRODUCTION

Studies of the adaptive evolution and diversification of consumers often focus on behavioural and morphological traits associated with resource acquisition, such as consumption rates (Abrams, 2006; Wootton & Emerson, 2005), habitat selection (Abrams, 2007; Ravigne et al., 2009), prey selection (Abrams, 1999; Dudova et al., 2019; Sih & Christensen, 2001) and trophic morphology (Wainwright & Price, 2016). However, the evolution of metabolic traits underlying a broad range of both catabolic and anabolic processes is also likely to govern the origin and maintenance of consumer biodiversity (Braakman & Smith, 2012). This is partly because ecosystem- and habitat-specific differences in resource quality can contribute to divergent selection and thereby influence the evolutionary processes underlying ecological speciation and adaptive radiation (Nosil, 2012; Schluter, 2000). Considering both resource quantity and quality may help us understand additional metabolic and behavioural adaptations of consumers and their patterns of abundance and diversity (e.g., Agrawal, 2007; Kay et al., 2005; Lemaire et al., 2012; Lemmen et al., 2019). Moreover, key metabolic adaptations, such as the ability to synthesise previously essential compounds (Drouin et al., 2011; Matsushita et al., 2020), can generate ecological opportunities that enable consumer species to transition into novel adaptive zones (Simpson 1945; Simpson 1953). For example, whilst colonising freshwater ecosystems, multiple species and lineages of ancestrally marine fish have evolved the ability to synthesise fats that are comparatively scarce in freshwater food webs (e.g., Ishikawa et al., 2019; Matsushita et al., 2020).

In natural populations, consumers often face mismatches between the dietary supply of, and physiological requirements for, both inorganic elements (e.g., carbon, nitrogen and phosphorus; Elser et al., 2000a) and essential organic compounds (e.g., amino acids, lipids and vitamins; Brett & Müller-Navarra, 1997; Toupoint et al., 2012; Wilder et al., 2013). Resource quality is inherently multidimensional and can include aspects of elemental composition (Elser et al., 2000a; Elser et al., 2000b), ratios of macromolecules like carbohydrates and proteins (Raubenheimer & Simpson, 1998; Simpson & Raubenheimer, 1993) and concentrations of toxic compounds (Agrawal, 2007). There are several ways in which consumers have evolved in response to heterogeneity in the quality of available resources. Behavioural adaptations for the acquisition of limiting elemental nutrients range from moose selectively foraging in aquatic environments to obtain sodium (Belovsky, 1978) to insectivorous birds eating eggshells from compost heaps as a source of calcium during egg formation (Dhont & Hochachka, 2001). Whilst inorganic elements and minerals are strictly essential nutrients that consumers must obtain directly from their diet, organic compounds can be either essential or substitutable depending on the abilities of consumers to obtain them from other compounds in diet. This unique aspect of organic nutrients as well as toxins opens up additional avenues for metabolic adaptation. Nutritional regulation in the face of variation in the availability of organic compounds can include foraging behaviours such as consuming resources with complementary nutrients (e.g., Behmer et al., 2001; Dudová et al., 2019) as well as metabolic adaptations like breaking down proteins into sugars when carbohydrates are limiting (Thompson & Redak, 2000), repurposing dietary toxins for self-defense (e.g., Jønsson et al., 2008) or synthesising pigments from readily available dietary precursors (e.g., Badyeav et al., 2019).

In natural populations of consumers, metabolic phenotypes in general (Auer et al., 2016; Auer et al., 2015; Burton et al., 2011), and lipid phenotypes in particular (e.g., during migration in birds: McWilliams et al., 2004; Guglielmo et al., 2018), are important components of fitness variation. Lipids are fundamentally important for energy storage, cell membrane structure and cellular functions (Sunshine & Iruela-Arispe, 2017). Studies suggest that within lipids, the omega-3 (n–3) polyunsaturated fatty acids (PUFA), in particular alpha-linolenic acid (ALA; 18:3n-3), eicosapentaenoic acid (EPA; 20:5n-3), and docosahexaenoic acid (DHA; 22:6n-3), can be important for somatic development, especially for nervous and gonadal tissues (Arts & Kohler, 2009; Guo et al., 2016a; Tocher et al., 2019), cognition (Cunanne et al.,

2009; Hoffman et al., 2009; McCann & Ames, 2005), re-production (Chen et al., 2012; Martin-Creuzburg et al., 2009; Roqueta-Rivera et al., 2010; Sinendo et al., 2017) and survival (Fuiman & Perez, 2015; Kim et al., 2016; Matsunari et al., 2013; Mesa-Rodriguez et al., 2018; Twining et al., 2018).

Consumers likely face an allocation trade-off involving their enzymatic capacity to synthesise fatty acids, especially n-3 long-chain PUFA like EPA and DHA, and their capacity to acquire fatty acids from dietary sources (Figure 1a). Indeed, the behavioural and metabolic strategies to meet fatty acid requirements vary
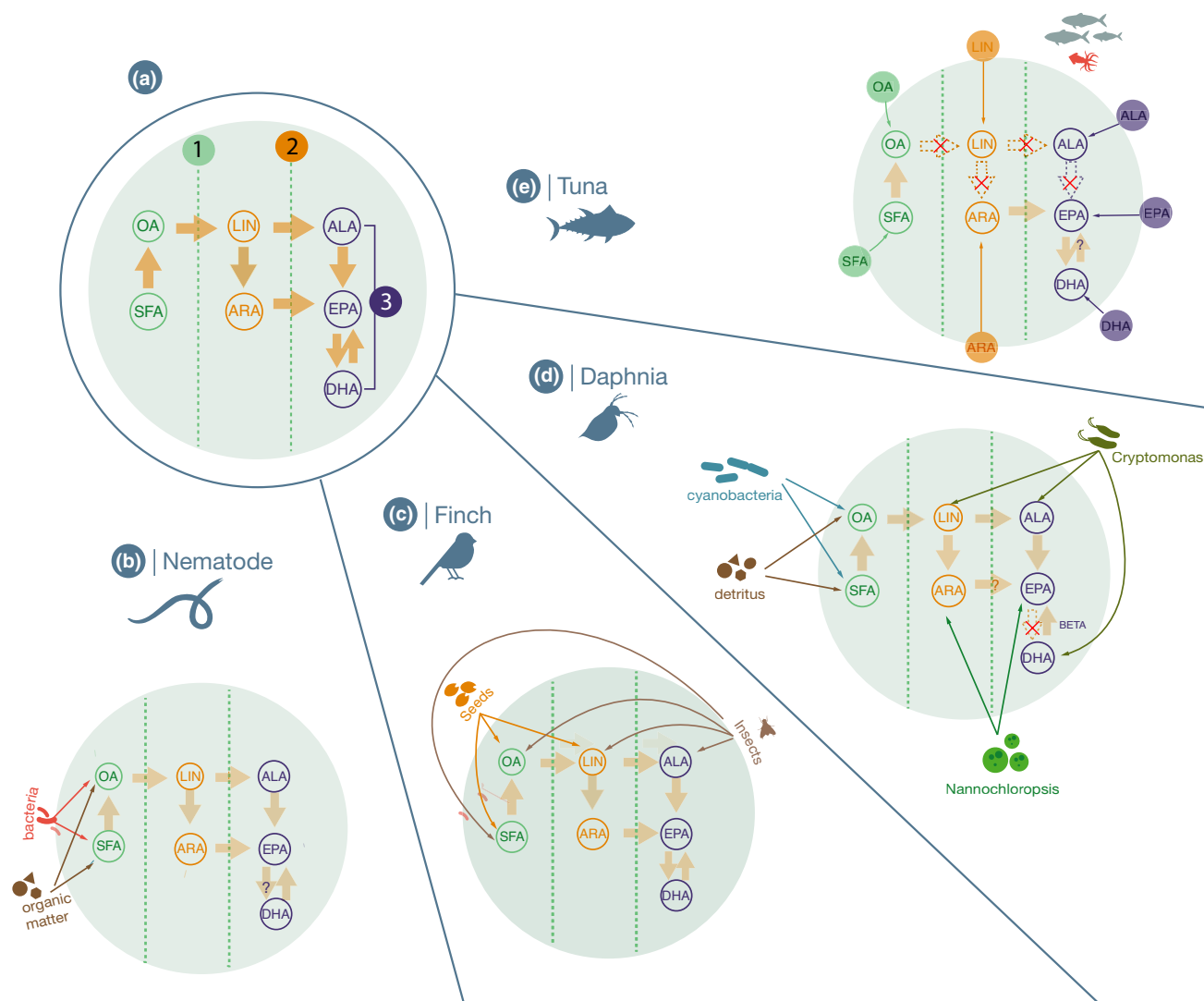
FIGURE 1 Consumers differ in their capacity to synthesise key fatty acids from precursors. Three of the major gaps in synthesis capacity (a) include: (1) conversion of saturated fatty acids (SFA), which may be derived from carbohydrates in diet, to the monounsaturated fatty acid (MUFA) oleic acid (18:1n-9; OA) and then to the omega-6 (n-6) polyunsaturated fatty acid (PUFA) linoleic acid (18:2n-6; LIN), (2) conversion of the n-6 PUFA LIN and arachidonic acid (20:4n-6; ARA) to the omega-3 PUFA alpha-linolenic acid (18:3n-3; ALA) and eicosapentaenoic acid (20:5n-3; EPA), respectively and (3) conversion of the short-chain n-3 PUFA ALA into the long-chain n-3 PUFA EPA and docosahexaenoic acid (22:6n-3; DHA). Within primary producers (a), vascular terrestrial plants are only capable of synthesising fatty acids up to ALA, whereas different species of algae and nonvascular terrestrial plants (e.g., mosses and liverworts) are also able to produce some EPA. Consumers (b–e) have evolved synthesis capabilities that differ based upon the availability of key fatty acids in their diets. Whilst some consumers (b) are capable of synthesising both short-chain and long-chain n-3 and n-6 PUFA from SFA and OA, others (c and d) require short-chain n-3 PUFA from diet, and still others (e) must receive all key fatty acids directly from diet. Some animals, such as soil nematodes (b), consume PUFA-deficient resources like bacteria and organic matter and derive only SFA and OA from their diet, which they use as precursors to synthesise LA, ARA, ALA, EPA and DHA. Others, such as finches and other terrestrial consumers (c), consume resources like seeds that contain only SFA, OA and LIN, as well as resources like terrestrial insects that also contain ALA. They must therefore convert dietary LIN into ARA and dietary ALA into EPA and DHA. Still others, like Daphnia and other aquatic invertebrates (d), consume some resources that contain both short-chain and long-chain PUFA and are incapable of converting EPA to DHA, but are capable of synthesising EPA from DHA, such as from the Cryptophyte alga Cryptomonas, through the process of beta-oxidation (BETA). Finally, some animals, like tuna (e) and other carnivorous marine fishes, consume resources that contain the full set of key fatty acids, including both EPA and DHA, and are unable to perform any of the major synthesis steps in (A)

widely across the tree of life (Figure 1). For example, detritivorous nematodes have a broad capacity to first synthesise saturated fatty acids (SFA) from dietary carbohydrates and subsequently convert SFA to monounsaturated fatty acids (MUFA) and eventually PUFA (Malcicka et al., 2018; Watts & Browse, 2002; Figure 1b). However, vertebrates and many major groups of invertebrates lack the ability to convert MUFA such as oleic acid (OA) to n–3 and n–6 PUFA (Kabeya et al., 2018). Therefore, a finch consuming seeds that lack EPA and DHA must metabolically derive these compounds from dietary precursors like ALA through enzymatic conversion processes, including desaturation and elongation (Figure 1c). Even, consumers that can synthesise some n-3 long-chain ($C_{\leq 20}$;LC-) PUFA like EPA and/or DHA from the precursor compounds (e.g., ALA) may face high metabolic costs that manifest as reduced population growth rates. For example, *Daphnia* populations grow much slower (or not all) on a diet low in EPA and DHA (e.g., cyanobacteria) compared to a diet high in EPA and DHA (e.g., *Nannochloropsis* or *Cryptomonas*; Figure 1d; Martin-Creuzburg et al., 2009; Martin-Creuzburg & von Elert, 2009). Moreover, some species of obligate carnivores, such as cats and tuna (Figure 1e), are unable to convert short-chain (C_{18}) into LC-PUFA and thus can only acquire EPA and/or DHA directly from their diet (Betancor et al., 2020; Rivers et al., 1975; Wang et al., 2020).

At the base of food chains, there are two fundamental contrasts in n-3 PUFA availability that are particularly relevant for understanding how spatiotemporal variation of resource quality can influence consumer adaptation (Figure 2). First, aquatic primary producers often contain both EPA and DHA, whereas terrestrial primary producers typically only contain shorter-chain n-3 PUFA, such as ALA (Colombo et al., 2017; Hixson et al., 2015; Twining et al., 2016a). As a result, terrestrial vertebrates, which all require EPA and DHA (Castro et al., 2016), are fundamentally more limited by dietary EPA and DHA availability than aquatic consumers and have evolved numerous adaptations to resolve this nutritional constraint. For example, some terrestrial vertebrates obtain EPA and DHA via conversion from precursors (e.g., Brenna, 2002; Raes et al., 2004) or selective retention of these compounds from aquatic resources (e.g., Broadhurst et al., 2002; Koussoroplis et al., 2008). Second, within aquatic systems, primary producers in marine ecosystems have higher DHA content than in freshwater ecosystems (Figure 2). This DHA disparity has driven multiple independent cases of consumer metabolic evolution associated with the adaptation from marine to freshwater ecosystems (Ishikawa et al., 2019). More generally, such fundamental nutritional contrasts amongst ecosystems, as well as others occurring within ecosystems (e.g., amongst habitats, and prey species), can contribute to evolutionary trade-offs involving fatty acid acquisition and metabolism.

Previous work has documented how fatty acids vary in relation to ecosystem type, trophic level, taxonomy and foraging behaviour of species (e.g., Colombo et al., 2017; Galloway & Winder, 2015; Guo et al., 2017; Hixson et al., 2015) but not how variation is important for understanding the prevailing diversity of consumer metabolism within and amongst species. Here, we review the distribution of ALA, EPA and DHA in both primary producers and consumers amongst major ecosystem (i.e., freshwater, marine and terrestrial), between adjacent habitats within ecosystems (e.g., nearshore-offshore and stream-forests) and amongst co-occurring prey species within habitats. We discuss how consumers can evolve in response to the spatial, seasonal and community-level variation of prey quality. In doing so, we consider how the metabolic traits of consumers are hierarchically structured, from cell membrane function to maternal investment, and how these traits have strongly environment-dependent expression. Finally, we discuss the evolutionary genetic mechanisms that underlie the adaptation of consumers to EPA and DHA limitation and how such metabolic evolution can be an important driver of consumer diversification in ecosystems.

HETEROGENEITY OF FATTY ACID DISTRIBUTION IN NATURE: IMPLICATIONS FOR CONSUMERS

Primary producers vary widely in their fatty acid composition across ecosystems (Figure 2a–c), but there are some stark contrasts within and amongst ecosystems (Table S1). For example, vascular land plants, such as angiosperms and gymnosperms, often contain little to no n-3 LC-PUFA, whereas aquatic algae, such as diatoms and cryptophytes, are often laden with both EPA and DHA (Figure 2a–c). However, a number of nonvascular and semi-aquatic plants, such as mosses, do contain EPA (e.g., Kalacheva et al., 2009; Figure 2b). Terrestrial primary producers also contain significantly more ALA, the precursor to EPA and DHA, compared to marine primary producers (Figure 2a; Table S1). In addition to these patterns with n-3 PUFA, terrestrial primary producers typically contain a higher proportion of n-6 PUFA, such as linolenic acid (LIN; 18:2n-6), relative to n-3 PUFA (e.g., ALA), compared to aquatic primary producers (Hixson et al., 2015), but the reasons for this are unclear. One possible explanation for these patterns in primary producers is the higher susceptibility of PUFA with more double bonds, and LC-PUFA in particular, to peroxidation (Halliwell & Gutteridge, 1985; Møller et al., 2007; Mueller, 2004), which is likely a greater risk for primary producers in terrestrial environments. Another important and well-documented pattern is that marine primary producers have a significantly higher percentage of fatty acids as EPA compared to either freshwater or terrestrial primary producers (Figure 2b and Table S1)
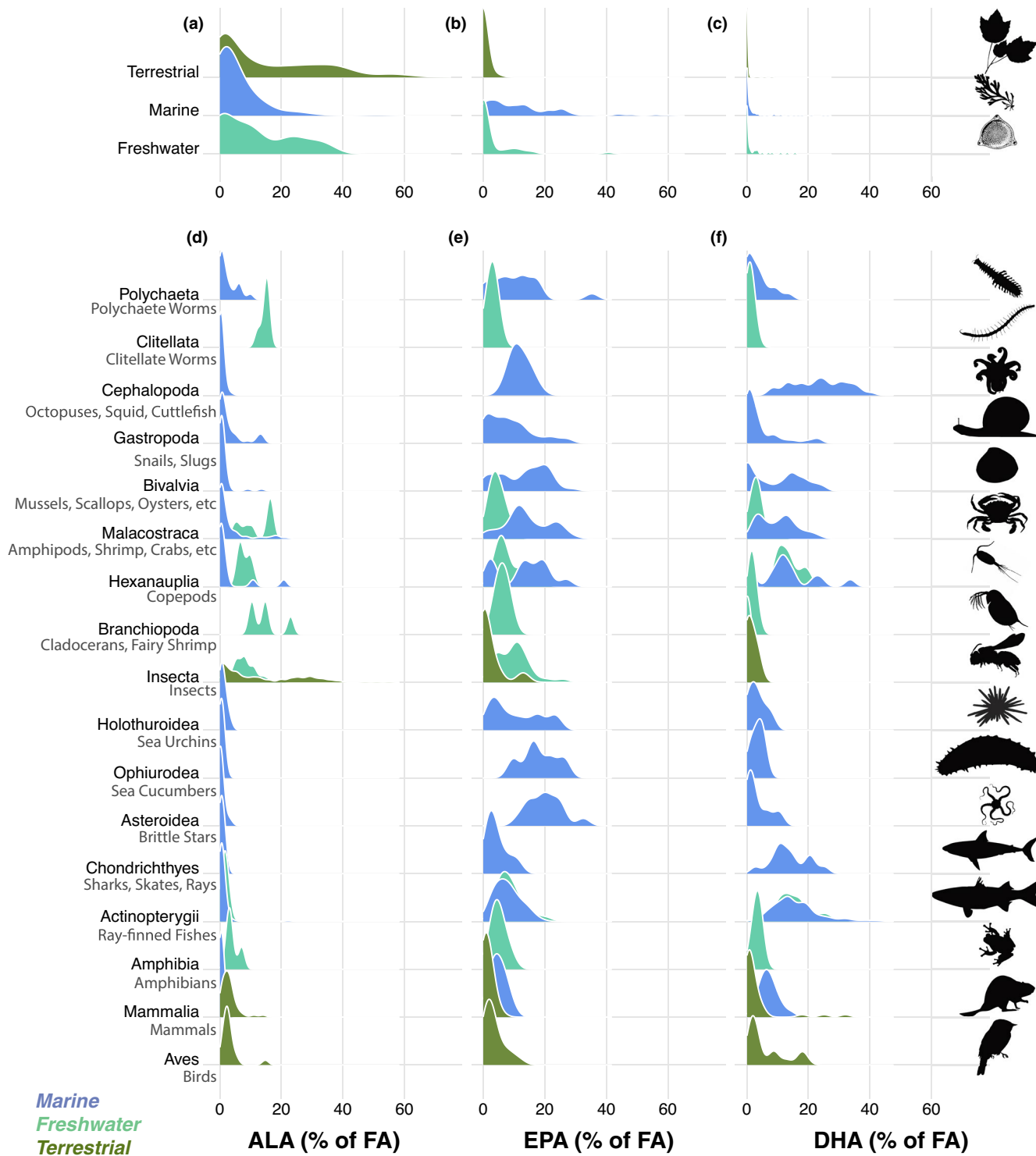
FIGURE 2 Marine, freshwater and terrestrial organisms differ in their fatty acid composition, especially in terms of the omega-3 polyunsaturated fatty acids (PUFA) alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). These ecosystem-based differences are most pronounced in (a–c) primary producers but also occur amongst (e and f) higher-order consumers. (a–c) Vascular terrestrial primary producers contain only the shorter-chain omega-3 PUFA ALA, whilst aquatic primary producers, as well as a few nonvascular terrestrial primary producers like Bryophytes, also contain the longer-chain omega-3 PUFA EPA and/or DHA. (d–f) Consumers contain more EPA and/or DHA than primary producers from the same ecosystem but also exhibit differences based on both ecosystem (e.g., terrestrial versus marine mammals and terrestrial versus freshwater insects) and trophic position (e.g., fish versus insects or Cladocerans)

as well as significantly more fatty acids as DHA compared to terrestrial primary producers (Figure 2c and Table S1). The reasons for this pattern are also unclear

but might be partly due to EPA and DHA conferring protection against high salinity (Jiang & Chen, 1999; Sui et al., 2010). Differences between marine phytoplankton

communities, which are dominated by higher EPA and DHA taxa-like diatoms and coccolithophores (e.g., Brun et al., 2015), and freshwater phytoplankton communities, which often support substantial populations of green algae and cyanobacteria (Reynolds et al., 2002), which contain ALA, but typically have negligible amounts of EPA and DHA (Twining et al., 2016a), are also likely responsible for differences in fatty acid composition amongst aquatic ecosystems.

Within ecosystems, the distribution of fatty acids of primary producers is typically attributed to both species differences (Taipale et al., 2013) and environmental conditions (Lang et al., 2011). For example, EPA and DHA are very abundant across several major groups of Eukaryotic algae (Mühlroth et al., 2013) but are absent in Cyanobacteria (Twining et al., 2016a). However, the composition and content of fatty acids can also be highly variable amongst closely related species and individuals of the same species (Charette & Derry, 2016; Galloway et al., 2012; Lang et al., 2011; Taipale et al., 2013), possibly due to the strong influence of environmental conditions (Lang et al. 2011), such as light, nutrients and temperature. LC-PUFA molecules in general are particularly unstable due to the susceptibility of their multiple double bonds to oxidation and attack by reactive oxygen species (Shchepinov et al., 2014). For instance, high temperatures increase reaction rates, such that LC-PUFA like EPA and DHA degrade faster in warm environments (Hixson & Arts, 2016). In addition, phospholipids with double bonds, such as those found in PUFA, may help cells maintain membrane fluidity at lower temperatures (homeoviscous adaptation; Feller et al., 2002; Sinensky, 1974). Thus, it may be beneficial for organisms to have more LC-PUFA when it is colder and more costly for them to protect LC-PUFA when it is warmer. In algae, n-3 LC-PUFA content is often negatively correlated with both temperature (Hixson & Arts, 2016) and light levels (Amini Khoeyi et al., 2012; Hill et al., 2011) and is also influenced by inorganic nutrient concentration (e.g., Guschina & Harwood, 2009; Piepho et al., 2012). At constant temperature and light levels, phosphorus limitation, for example, can decrease overall lipid content but increase n-3 LC-PUFA production, possibly reflecting the need to store lipids until growth conditions improve (Guschina & Harwood, 2009). However, when light, temperature and nutrients are simultaneously manipulated, fatty acid responses can be highly variable across species and systems (e.g., Cashman et al., 2013; Guo et al., 2016b; Piepho et al., 2012).

In consumers, the composition of fatty acids reflects the dietary sources of lipids (e.g., ecosystem origin, prey availability; e.g., Hiltunen et al., 2019), the capacity of consumers to metabolise different fatty acids (Figure 2; Guo et al., 2017; Hixson et al., 2015) and organ-specific fatty acid requirements (Ebm et al., 2021). Insect species with an early aquatic life stage often contain more EPA than those that are exclusively terrestrial (Twining

et al., 2018) and are thus important sources of EPA for riparian insectivores, such as Eastern Phoebes (*Sayornis phoebe*) (Twining et al., 2019). Many consumers acquire PUFA from multiple ecosystems in order to meet their own nutritional requirements. For example, mammalian carnivores can forage on aquatic resources to help increase their intake of DHA relative to linolenic acid (18:2n-6; LIN), which is an abundant n-6 PUFA in terrestrial primary producers (Koussoroplis et al., 2008). Migratory consumers can accumulate EPA and DHA from ecosystems rich in these compounds and use them for reproduction and offspring provisioning in more EPA- and DHA-depauperate ecosystems (e.g., salmon migrating from the ocean to freshwater streams; Heintz et al., 2004). Indeed, many species that experience wide temporal variation in resource quality often exhibit either plasticity (e.g., Katan et al., 2019) or genetic adaptation (Ishikawa et al., 2019) associated with fatty acid metabolism.

Within ecosystems, consumers often experience contrasting distributions of FA when foraging across multiple adjacent habitats. Within lakes, for example, ecotypes of Eurasian perch (*Perca fluviatilis*) are known to specialise on either littoral macroinvertebrates, which are DHA-poor, or pelagic zooplankton, which include species (e.g., copepods) that are DHA-rich (Figure 3a). Intriguingly, in spite of the fact that DHA is higher in pelagic prey, littoral perch typically have higher DHA than pelagic perch. This might indicate that perch can thrive on a low-DHA diet (Scharnweber et al., unpublished), via preferential DHA retention (e.g., Heissenberger et al., 2010; Hessen & Leu, 2006) and/or DHA synthesis from precursors like ALA (e.g., Bell et al., 2001; Buzzi et al., 1996). In terrestrial systems, Tree Swallows vary widely in their access to emergent aquatic insect prey (McCarty & Winkler, 1999; Michelson et al., 2018; Stanton et al., 2016), which contain substantially more EPA than terrestrial prey (Twining et al., 2019; Twining et al., 2018; Figure 3b). Controlled diet studies show that Tree Swallow chicks, which are inefficient at synthesising EPA and DHA from ALA (Twining et al., 2018b) grow faster, are in better condition and have increased survival when they consume either more aquatic insects or diets containing more EPA and DHA (Twining et al., 2016b). Because nest sites vary considerably in their distance to aquatic ecosystems, adults might trade-off food quality with quantity when provisioning their young. Although unexplored, this trade-off could select for increased efficiency of ALA to EPA and DHA conversion in populations that breed in drier, upland habitats that have a lower availability of high-quality emergent freshwater insect prey.

Contrasting distributions of fatty acids can, in some cases, drive adaptive population divergence of consumers. For example, urban and rural populations of Great Tits (*Parus major*) differ not only in their diet (Andersson et al., 2015) and their fatty acid composition (Andersson
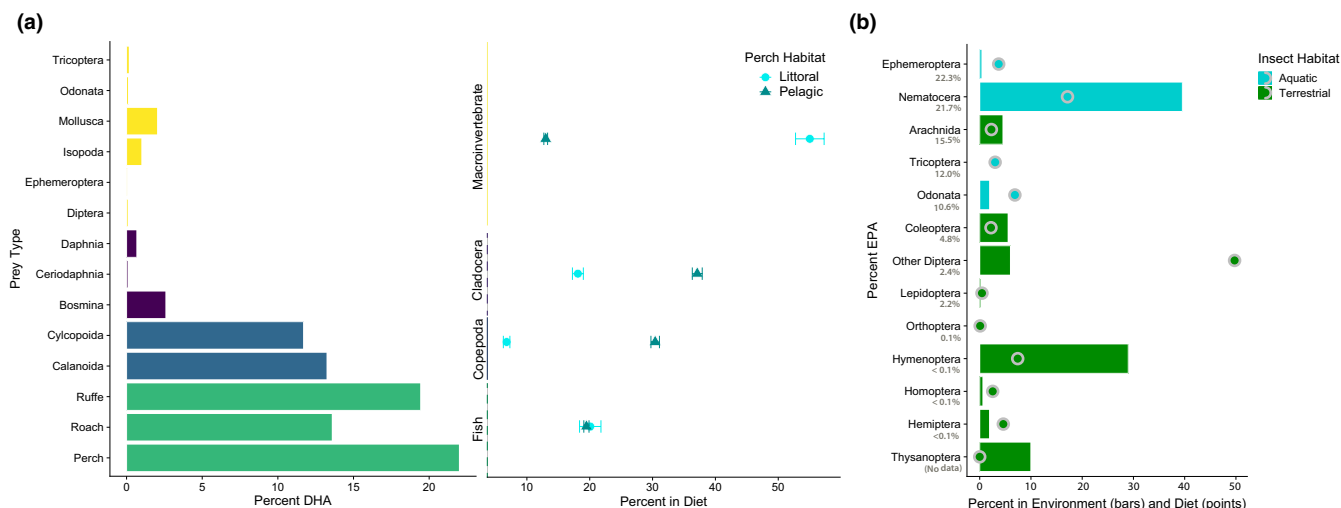
FIGURE 3 (a) The prey of Eurasian perch vary widely in their docosahexaenoic acid (DHA) content, both within and between habitats. Pelagic perch consume prey with much higher DHA content (e.g., copepods and fish), whereas littoral perch consume large amounts of DHA-poor macroinvertebrates. (b) Tree Swallows forage on insects originating from both aquatic and terrestrial habitats, but emergent aquatic insect prey tend to have higher eicosapentaenoic acid (EPA). Some EPA-poor taxa-like Hymenoptera and Thysanoptera are readily available in the environment, whereas other high-EPA taxa-like Ephemeroptera, Trichoptera and Odonata are scarce (bars denote habitat availability). All of the rare aquatic prey are preferentially selected by Tree Swallows, relative to the more EPA-poor (points reflect variation in dietary proportions). Perch prey and diet data are from Chaguaceda et al., (2020) and Tree Swallow prey and diet data are from McCarty and Winkler (1999) and Twining et al., (2018)

et al., 2015; Isaksson et al., 2017) but also in their expression of the *Elovl* and *Fads* genes (Watson et al., 2017), which code for the enzymes used to convert ALA and LIN to n-3 and n-6 LC-PUFA, respectively. Specifically, rural tits have higher plasma EPA content whilst urban tits have plasma higher in arachidonic acid (ARA, 20:4n-6) content (Andersson et al., 2015; Isaksson et al., 2017). The n-3 LC-PUFA have anti-inflammatory properties whilst n-6 LC-PUFA, which are synthesised from their shorter-chain n-6 precursor through the same pathway as n-3 PUFA, have pro-inflammatory properties (Calder et al., 2002). Urban tits experience greater oxidative stress than do rural tits (Isaksson et al., 2017; Watson et al., 2017) and also express *Elovl* and *Fads* at lower rates compared to rural tits (Watson et al., 2017). Thus, urban tits appear to suppress the production of both n-3 and n-6 LC-PUFA in order to reduce inflammation and oxidative damage in a more stressful environment (Watson et al., 2017).

THE NETWORK AND HIERARCHICAL STRUCTURE OF FATTY ACID TRAITS

The above examples illustrate the varied ways in which consumers can adapt to the heterogeneous distributions of ALA, EPA and DHA in nature (Figure 2), including via the evolution of capacity for biosynthesis of EPA and DHA and/or the foraging behaviours underlying the dietary acquisition of EPA and DHA. In light of this complexity, we suggest an integrative approach that includes both investigating the individual enzymes and processes involved in fatty acid synthesis within the metabolic

network (Figure 4 and Table 1) and situating these fatty acid synthesis traits within a hierarchical structure of functional traits leading to fitness variation (Figure 5 and Table 2).

Although all organisms share core metabolic processes for fatty acid synthesis (Figure 4), consumer species vary widely in capacity to convert: (1) MUFA to PUFA (Module C, Figure 4), (2) n–6 to n–3 PUFA (Module D, Figure 4) and (3) C_{18} n-6 and n-3 PUFA to LC-PUFA (Modules E and F, Figure 4) based upon the presence and activity or expression levels of particular enzymes and genes. SFA, such as stearic acid (18:0), can be synthesised *de novo* through the fatty acid synthase (*fasn*) and SFA elongase system (Module A, Figure 4). Stearoyl-CoA desaturase (*Scd*) can then introduce a double bond at the Δ9 position of the fatty carbon chain, producing MUFAs, such as oleic acid (OA, 18:1n-9) (Module B, Figure 4). All eukaryotes, including animals, appear to be able to synthesise OA. In contrast, the biosynthesis of PUFA with multiple double bonds, like linoleic acid (LIN; 18:2n-6) from MUFA (OA; Module C, Figure 4), only exists in a limited number of consumers with the methyl-end (ωx) desaturase, Δ12 desaturase (Blomquist et al., 1991). In addition, most consumers neither possess the related methyl-end desaturase enzyme (Δ15 desaturase) that is necessary to produce ALA from LIN nor the Δ17 and Δ19 desaturases to produce n-3 LC-PUFA from their n-6 LC-PUFA counterparts (Module D, Figure 4). The methyl-end desaturases were historically thought to exist only in plants, algae, protists, fungi and a nematode (i.e. *Caenorhabditis elegans*), but a recent study
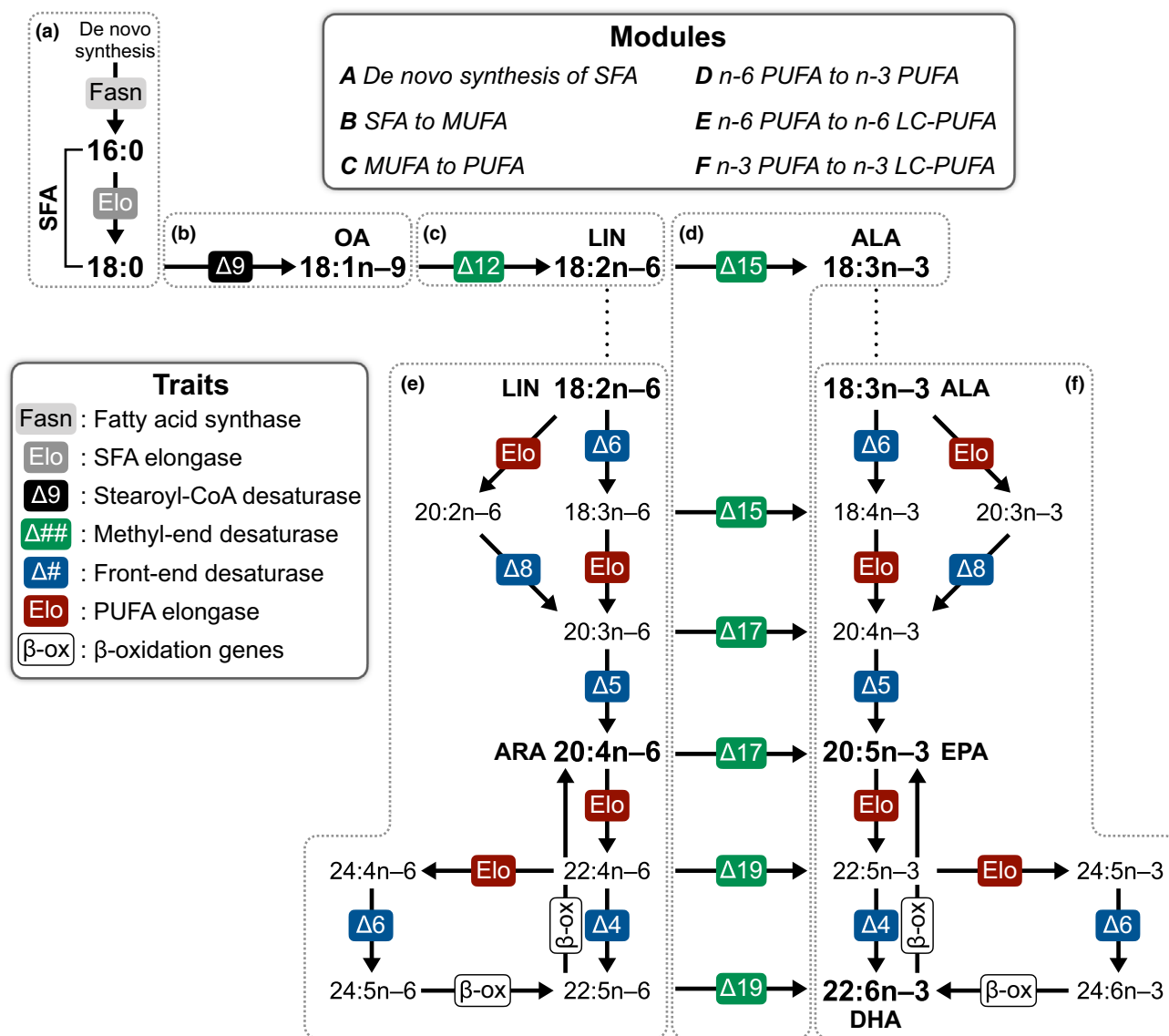
FIGURE 4 A simplified fatty acid network including the following modules: (a) *de novo* synthesis of saturated fatty acids (SFA) via fatty acid synthase and a SFA elongase (b) conversion of SFA to monounsaturated fatty acids (MUFA) via Δ9 stearoyl-coA desaturase, (c) conversion of the MUFA oleic acid (18:1n-9, OA) to the n-6 PUFA linoleic acid (18:2n-6, LIN) via Δ12 methyl-end desaturase, (d) conversion of omega-6 PUFAs like LIN and arachidonic acid (20:4n-6, ARA) to the omega-3 PUFAs ALA (18:3n-3) and to EPA (20:5n-3) via the Δ15 and Δ17 omega desaturases respectively, (e) conversion of LIN to n-6 LC-PUFAs by front-end desaturases and PUFA elongases (f) conversion of ALA to n-3 LC-PUFAs by front-end desaturases and PUFA elongases. Note that Beta-oxidation process (a multi-enzyme reaction) is also required to synthesise some LC-PUFA including DHA

suggests that this gene family also occurs in cnidarians, additional nematode species, lophotrochozoans (molluscs, annelids and rotifers) and arthropods (copepods and at least two species of insects) (Garrido et al., 2019; Kabeya et al., 2018; Kabeya et al., 2020). A much greater number of consumers, ranging from molluscs and some arthropods (Monroig & Kabeya, 2018) to chickens (Boschetti et al., 2016; Gregory & James, 2014) and humans (Leonard et al., 2002; Nakamura & Nara, 2004), are able to elongate and desaturate n-6 and n-3 C_{18} PUFA into corresponding n-6 and n-3 LC-PUFA (Modules E and F, Figure 4) using front-end desaturases as well as fatty acid elongases (elongation of very

long-chain fatty acids protein, *Elovl*), suggesting that these pathways have evolved multiple times.

In light of the complexity of fatty acid metabolic networks, identifying a set of modules and component traits can be a useful approach. As illustrated in Figure 4, we identify six core modules based on synthesis capacities (Figure 4a–f and Table 1A) and further break these down into constituent traits that define the reaction rates between specific FA substrates and products (e.g., ALA to EPA conversion capacity and efficiency, Table 1B). There is value to such simplifications because they reveal broad-scale patterns in metabolic capacity across the tree of life. However, there is also substantial pleiotropy

TABLE 1   Metabolic traits constituting the biosynthetic pathways of fatty acids

Pathway trait	Trait type	Mechanism	Gene family	Example taxa with functional pathway	Example taxa without functional pathway
1) → 18:0	0/1	De novo fatty acid synthesis	Fatty acid synthase	All eukaryotes	
		Elongation	SFA elongases	All eukaryotes	
2) 18:0 → 18:1n−9 (SFA to MUFA)	0/1	Δ9 desaturation	First desaturases (Stearoyl-CoA desaturases)	All eukaryotes	
3) 18:1n−9 → 18:2n−6 (MUFA to PUFA)	0/1	Δ12 desaturation	Omega desaturases (Methyl-end desaturases)	Plants, protists, fungi, certain invertebrates (Cnidarians, Nematodes, Lophotrochozoans, some Copepods)	Deuterostomes
4) Omega−6 → Omega−3	0/1	Δ15 desaturation (18:2n−6 → 18:3n−3)	Omega desaturases (Methyl-end desaturases)	Plants, protists, fungi, certain invertebrates (Cnidarians, Nematodes, Lophotrochozoans, some Copepods)	Deuterostomes
	0/1	Δ17 desaturation (C20 n−6 → C20 n−3)	Omega desaturases (Methyl-end desaturases)		
	0/1	Δ19 desaturation (C22 n−6 → C22 n−3)	Omega desaturases (Methyl-end desaturases)		
5) ALA → EPA and LIN → ARA	0/1	Δ6 desaturation	Front-end desaturases	Most vertebrates (Fads2 gene), invertebrates	Vascular plants (some can produce 18:4n−3)
	0/1	Δ5 desaturation	Front-end desaturases	Most vertebrates (Fads1 gene); Fish with neofunctionalisation of Fads2 (e.g., Zebrafish, Salmon); invertebrates (e.g., nematodes, molluscs, sea urchins)	Most marine teleosts except Elopomorpha (lack Fads1)
	0/1	Δ8 desaturation	Front-end desaturases	Mammals, fish (Fads2 gene), invertebrates (e.g., molluscs, sea urchins)	
	0/1	Elongation (C18 → C20)	PUFA elongases	Most animals	
6) EPA → DHA and ARA → 22:5n−6	0/1	Δ4 desaturation	Front-end desaturases	Microalgae, protists, fungi, fish with neofunctionalisation of Fads2 (e.g., Rabbit fish)	Vascular plants (no PUFA elongase) Some acanthopterygian fish (lack Δ6 desaturation to C24)
	0/1	Δ6 desaturation	Front-end desaturases	Mammals, fish (Fads2 gene)	
	0/1	Elongation (C20 → C24)	PUFA elongases	Microalgae, protists, fungi, most animals	

Abbreviations: ALA, alpha-linolenic acid; ARA, arachidonic acid; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; LIN, linolenic acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid.
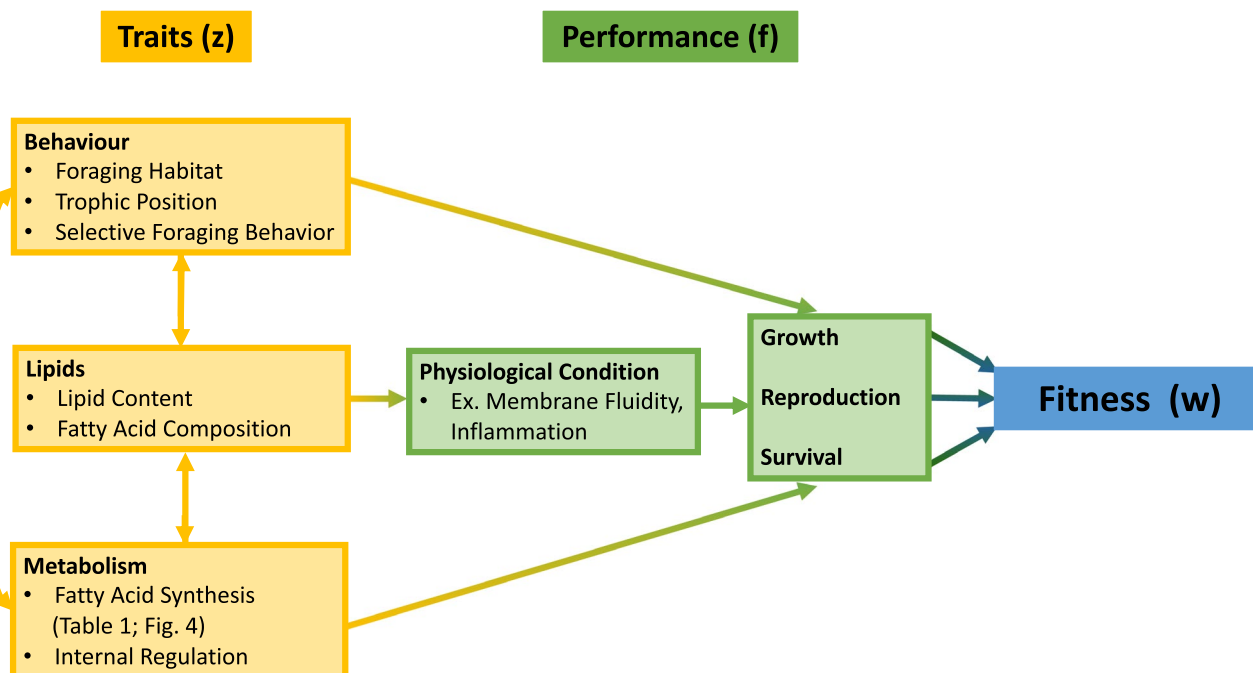
FIGURE 5 Hierarchical structure of interrelated functional fatty acid traits that can influence fitness. Shifts in traits (z; yellow boxes) involving foraging behaviour, lipid status and nutritional metabolism enable a consumer to alter performance (f, green boxes) in terms of physiological condition and vital rates, which influence fitness (w, blue box)

in that single genes that can modify the activity of numerous reaction rates across the overall metabolic network (Table 1B). For example, in many teleosts, *Fads2* gene products can influence conversion rates of LIN to a series of n-6 LC-PUFA, including ARA (Figure 4, Module E), as well as ALA to a series of n-3 LC-PUFA, including EPA and DHA (Figure 4, Module F). Nevertheless, treating both modules and their component pathways as metabolic traits permits us to document heritable variation within metabolic network modules (Box 1) and to identify both the ecological and genetic mechanisms underlying their adaptation. This is an important step for understanding the complex evolution of metabolic networks (Melián et al., 2018; Olson-Manning et al., 2012; Watson et al., 2014) and the role that nutritional metabolism plays in evolutionary diversification more broadly.

The metabolic traits (i.e., traits related to fatty acid synthesis as well as fatty acid retention and oxidation) we summarise in Table 1 are also embedded within a hierarchy of other potentially fitness-relevant consumer traits (Table 2). Natural selection acts upon the heritable intraspecific metabolic traits in the context of other subordinate and emergent functional traits in the hierarchy (Figure 5; Henshaw et al., 2020; Laughlin et al., 2020). Where there is a heritable basis for metabolic traits, there is the potential for adaptive evolution of consumer metabolism in response to natural selection. Such evolution might involve fatty acid synthesis and internal regulation and/or behavioural traits related to resource acquisition (e.g., selective foraging) and/or life history traits (e.g., migration and phenology) (see references for Table 2 and

Figure 5). Metabolic traits related to nutrient processing might evolve independently, or as a correlated response to other heritable traits, and culminate in changes in physiological performance, immunocompetence and cell membrane fluidity (Table 1 and Figure 5). Such trait change has the potential to influence numerous processes ranging from those affecting individual molecules to those affecting an individual's lifetime reproductive Darwinian fitness (Table 2 and Figure 5).

EVOLUTIONARY GENETIC MECHANISMS OF METABOLIC ADAPTATION

When consumers experience selection for EPA and DHA synthesis, they can increase enzymatic activity with three different types of genetic processes: (1) gene copy number increases, (2) enzymatic activity changes by amino acid substitutions and (3) regulatory mutations that increase transcription rates (Figure 6a). These three mechanisms differ in their effect sizes and pleiotropy (i.e., the number of phenotypic traits influenced by the gene). Copy number increases may have the strongest effects on metabolic processes like fatty acid synthesis (Loehlin et al., 2019; Loehlin & Carroll, 2016) but are also likely to have pleiotropic effects on other metabolic processes. This is because an increase in copy number may affect expression in multiple tissues throughout different ontogenetic stages (developmental pleiotropy) and/or they may change the amounts of other organic compounds

TABLE 2 Types of intraspecific fatty acid traits that occur along alternative pathways to influence individual fitness components (Figure 5)

Pathway to optimal organismal omega−3 fatty acid content	Type of functional trait	Examples	Reference(s)
Subordinate traits			
Pathway 1: individual-level intracellular fatty acid conversion and regulation			
	Fatty acid metabolic traits (Figure 4) T1: fatty acid synthase T2: SFA elongase T3: stearoyl-CoA desaturase T4: omega desaturase T5: Front-end desaturase T6: PUFA elongase T7: Beta-oxidation genes		Castro et al. (2012) Castro et al. (2016) Kabeya et al. (2018) Boyen et al. (2020)
Pathway 2: individual-level organismal resource acquisition and life history			
	Behavioural acquisition traits		
	Selective Foraging Behaviour	Between prey items within an ecosystem: Calanoid copepods Rainbow trout (*Oncorhynchus mykiss*) Between seasons within an ecosystem European whitefish (*Coregonus lavaretus*) Tuatara (*Sphenodon punctatus*) Between ecotypes within an ecosystem: Killer whales (*Orcinus orca*) Threespine stickleback (*Gasterosteus aculeatus*) Between ecosystems: Eastern Phoebes (*Sayornis phoebe*)	Eglite et al. (2019) Roy et al. (2020) Keva et al. (2019) Cartland-Shaw et al. (1998) Herman et al. (2005) Hudson et al. pers, comm.; Daneau-Lamoureux pers. comm. Twining et al. (2019)
	Consumer Trophic Position	Ontogeny in Eurasian perch (*Perca fluviatilis*) Dietary plasticity in larval anurans	Chaguaceda et al. (2020) Whiles et al. (2010)
	Life history traits		
	Body size	Freshwater calanoid copepods Round gobies and (*Neogobius melanostomus*) Monkey gobies (*Neogobius fluviatilis*)	Charette and Derry (2016) Ghomi et al. (2014)
	Maternal investment - Egg Composition (maternal effects) - Milk Composition	Daphnia egg composition Tropical nudibranch egg composition (*Aeolidilla stephanieae*) Mammalian milk composition	Schlotz et al. (2013) Leal et al. (2012); Leal et al. (2013) Brenna et al. (2009); Hibbeln et al. (2019); Muhlhausler et al. (2011)
	Migration	Migratory songbirds Migratory bats Southern hemisphere humpback whales (*Megaptera novaeanglidae*)	Pierce et al. (2005); Pierce and McWilliams (2014) McGuire et al. (2013) Waugh et al. (2012)
	Phenology	Colorado potato beetles (*Leptinotarsa decemlineata*)	Clements et al. (2020)
	Hibernation	Black bears (*Ursus americanus*) Yellow-bellied marmots (*Marmota flaviventris*)	Iverson and Oftedal (1992) Hill and Florant (1999)
	Dormancy & diapause	Harpacticoid copepods (*Heteropsyllus nunni*) Lepidopterans	Williams and Biesiot (2004) Vukašinović et al. (2015); Hemmati et al. (2017)

(Continues)

TABLE 2 (Continued)

Pathway to optimal organismal omega−3 fatty acid content	Type of functional trait	Examples	Reference(s)
	Morphology (consumer feeding traits)	Threespine stickleback	Hudson et al. pers. comm.; Daneau-Lamoureux et al. pers. comm.
Influenced by both Pathways 1 and 2			
	Lipid traits		
	Total lipids	Fairy shrimp (*Chirocephalus diaphanus*) Euphausiids (*Meganyctiphanes norvegica*) Calanoid copepods (*Diaptomus kenai*)	Bocca et al. (1998) Mayzaud et al. (1999) Butler (1994)
	Lipid classes (e.g., TAGs, polar lipids)	Euphausiids	Saito et al. (2002) Mayzaud et al. (1999)
	Fatty acid content: SFA (e.g., 16.0, 18.0) MUFA (e.g., OA) PUFAs (e.g., LA, ALA) LC-PUFA (e.g., DHA)	Daphnia EPA content Copepod DHA content Sex-specific differences: Daphnia Tuatara Southern humpback whales	Hessen and Leu (2006); Wacker and Martin-Creuzburg (2007); Sperfeld and Wacker (2012) Charette and Derry (2016) Martin-Creuzburg et al. (2018) Cartland-Shaw et al. (1998) Waugh et al. (2012)
	Body condition indexes - weight to length - fat mass	Tree Swallows (*Tachycineta bicolor*) Humans (*Homo sapiens*) Round gobies and Monkey gobies	Twining et al. (2016) Tan (2014); Elias and Innis (2001) Ghomi et al. (2014)
	Physiological traits		
	Cell membrane fluidity	Eastern newt (*Notophthalmus viridescens*) Humans and Roundworms (*Caenorhabditis elegans*)	Mineo et al. (2019) Ruiz et al. (2019)
	Mitochondrial function	Ground squirrels Red-winged Blackbirds (*Agelaius phoeniceus*) Humans	Gerson et al. (2008) Price et al. (2018) Herbst et al. (2014)
	Inflammation	Immune system performance in Wolf spiders Daphnia Largemouth bass (*Micropterus salmoides*)	Fritz et al. (2017) Schlotz et al. (2012) Schlotz et al. (2013) Schlotz et al. (2016) Zhou et al. (2020)
	Buoyancy	Calanoid copepods (*Calanoides acutus*)	Pond and Tarling (2011)
	Metabolic Rate and Exercise Performance	Thirteen-lined Ground Squirrels (*Spermophilus tridecemlineatus*) White-throated Sparrows (*Zonotrichia albicollis*) Yellow-rumped Warblers (*Setophaga coronata*) Atlantic salmon (*Salmo salar*) Mammals	Gerson et al. (2008) Price and Guglielmo (2009) Dick and Guglielmo (2019) McKenzie et al. (1998) Ruf et al. (2006)
Pathway products: Individual-level fitness component traits			
	Growth	Daphnia Tree Swallows Eastern Phoebes Freshwater fish	Brett and Müller-Navarra (1997); Müller-Navarra et al. (2000); Ilić et al. (2019) Twining et al. (2016) Twining et al. (2019) Glencross (2009); Zhou et al. (2020) Lundova et al. (2018)

(Continues)

TABLE 2 (Continued)

Pathway to optimal organismal omega−3 fatty acid content	Type of functional trait	Examples	Reference(s)
	Development	Mammalian brain development Avian embryonic development	McNamara and Arsch (2019) Pappas et al. (2007)
	Reproduction	Freshwater calanoid copepod fecundity Daphnia fecundity Eurasian perch gonad size	Charette and Derry (2016) Sperfeld and Wacker (2012); Ilić et al. (2019) Scharnweber and Gårdmark (2020)
	Survival	Tree Swallow fledge success Sterlet survival (*Acipenser ruthenus*)	Twining et al. (2018) Lundova et al. (2018)

Note: Full references are listed in our supporting information.

ALA, alpha-linolenic acid; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid.

produced as by-products when enzymes are multifunctional (biochemical pleiotropy) (Figure 6b). Pleiotropic changes may be neutral, favourable or unfavourable with respect to fitness. For instance, because n-3 and n-6 fatty acids are elongated and desaturated via the same metabolic pathway (Figure 4), increased fatty acid desaturase and/or elongase activity may result in increased production of both n-3 or n-6 LC-PUFA, depending on the relative availability of n-3 and n-6 precursors. Amino acid substitutions generally have even more pleiotropic effects than copy number increases (Carroll, 2005), but their effect sizes are reported to be smaller in some cases (Loehlin et al., 2019). Regulatory mutations may have relatively strong effects (Loehlin et al., 2019) and enable tissue- or ontogenetic stage-specific expression but may still be biochemically pleiotropic. Importantly, these three types of mutations often occur together. After gene duplication, these mutations can diverge in both functional amino acid sequences and expression patterns (Lynch, 2007; Ohno, 1970), becoming more specific (neofunctionalisation) and thus reducing pleiotropic effects whilst still having strong effect sizes (Figure 6c).

Examples of all three types of genetic mechanisms can be found within the evolution of fatty acid metabolism. Copy number variation in fatty acid desaturase (*Fads*) genes is widely observed in vertebrates (Castro et al., 2012). For instance, Ishikawa et al., (2019) recently found that freshwater threespine stickleback have increased *Fads2* copy number and thus greater capability to synthesise DHA, thereby overcoming the nutritional constraints of freshwater ecosystems. However, increased expression of *Fads2* also results in increased production of n-6 LC-PUFA, such as ARA, in sticklebacks, thus demonstrating a biochemical pleiotropic effect (Ishikawa et al., 2019). In humans, regulatory mutations are known to underlie adaptation to low EPA and DHA diets (Fumagalli et al., 2015; Tucci et al., 2018; Ye et al., 2017). Derived alleles with higher *Fads1* expression appear to have enabled humans to survive better on cultivated, terrestrial plant-derived and n-3 LC-PUFA-deficient diets,

allowing them to expand their distribution (Ameur et al., 2012; Fumagalli et al., 2015; Tucci et al., 2018). In contrast, human populations that consume EPA- and DHA-rich diets with high amounts of fish and meat have the ancestral haplotypes (Amorin et al., 2017). Amino acid changes that alter enzymatic functions can also help consumers adapt to diets that vary in EPA and DHA content. For example, although zebrafish (*Danio rerio*) have just one copy of *Fads2*, they have high Δ5 and Δ6 desaturase activities as a result of amino acid changes in *Fads2* (Hastings et al., 2001). Neo-functionalisation following duplication appears to be a common genetic process (Ohno, 1970; Zhang, 2003). In fishes, for instance, the acquisition of Δ4 activity occurred in one copy of *Fads2* after gene duplication (Li et al., 2010; Morais et al., 2012; Oboh et al., 2017). Multiple genetic mechanisms enabling n-3 LC-PUFA synthesis may arise during diversification when species colonise nutritionally novel environments. For example, Matsushita et al., (2020) found that three species of freshwater flatfish, which were ancestrally marine, each used distinct genetic mechanisms to acquire DHA synthesis ability, including gene duplication and neofunctionalisation, enabling them to synthesise DHA from ALA in freshwater environments. Further genetic analysis of variation in fatty acid metabolism across a greater diversity of taxa will help us to understand which mechanisms are the most prevalent and how mechanisms differ in their effect sizes and pleiotropy on fatty acid adaptive landscapes.

Metabolic adaptation and consumer diversification

The network structure of fatty acid metabolism, including the modularity and degree of pleiotropy, has important consequences for understanding how organisms evolve and diversify over time. For instance, whilst the primary photosynthetic pathways of plants are highly conserved, some of their components have diversified

Box 1   Why the genetics of adaptation matters for the evolutionary ecology of fatty acids.

## QUANTITATIVE GENETIC VIEW OF ADAPTATION

Quantitative genetics models generally assume that traits are continuous, normally distributed and controlled by many genes with small effects. In a model with a single trait, selection moves the trait distribution according to the breeder's equation: Response to selection (R) is a product of heritability ($h2$) and selection differential (S) (Lynch & Walsh, 1998). Any heritable traits can evolve in response to selection. In cases in which multiple traits are genetically correlated, selection on one trait can bias the evolution of another genetically correlated trait, and the evolutionary trajectories on adaptive landscapes can be biassed by a genetic variance-covariance matrix (G-matrix; Lande & Arnold, 1983; Schluter, 1996; Schluter, 2000). Although quantitative genetics models are helpful to predict short-term evolution of highly polygenic traits, genomic studies of fatty acid composition have often identified loci with moderate to large effects (Cesar et al., 2014; Horn et al., 2020; Lemos et al., 2016; Lin et al., 2018; Xia et al., 2014), suggesting that an alternative view of the genetic basis of adaptation may be more useful in some cases.

GENOMIC VIEW OF ADAPTATION

Recent advances in genomic technologies have improved our ability to elucidate the genetic details of adaptation. For instance, studies have helped document how aspects of genetic architecture, such as the number, effect sizes, pleiotropy, linkage and genomic location of adaptive loci, can influence the speed and reversibility of adaptive evolution (Barton & Keightley, 2002). Such studies also aim to identify causative genes. For instance, animal breeding studies have sought to identify genes and quantitative trait loci that control the fatty acid composition of meat (e.g., Kelly et al., 2014; Zhang et al., 2016). However, even when a locus with a major effect is identified, this does not necessarily indicate the presence of a single causative gene. Furthermore, even when a causative gene is identified, it does not necessarily mean that a single mutation causes the alteration of the gene function (Bickel et al., 2011; Stern & Frankel, 2013). Therefore, an additional goal of genetic adaptation studies is to identify specific causative mutations (Lee et al., 2014; Remington, 2015). For example, *Fads2* duplication in freshwater species derived from marine ancestors allows them to synthesise more n-3 LC-PUFA (Ishikawa et al., 2019). When adaptation occurs via standing genetic variation, it may not be necessary to further dissect it into the levels of individual mutations for predicting how adaptation proceeds. This is because such adaptation occurs by replacement of already-existing alleles with tightly linked adaptive mutations (Barrett & Schluter, 2008). However, to understand adaptation by *de novo* mutations, it is essential to determine the number and nature of responsible causative mutations (Stern & Frankel, 2013). For example, the *bab* locus explains over 60% of phenotypic variance of pigmentation in *Drosophila*, but each single SNP explains only 1% (Bickel et al., 2011). Similarly, different *Fads1* and *Fads2* gene variants in humans explain between 1% and 28.5% of the variation in the PUFA content of blood phospholipids (Schaeffer et al., 2006). Once causative mutations that alter fatty acid synthesis are identified, it is then possible to determine whether adaptive evolution has occurred through a few large steps or multiple small steps (Orr, 2005).

Box 1 Figure: Relationship between enzymatic activity and fitness in two different environments (left) and a trajectory of adaptive walk (grey arrow) biased by G-matrix on a two-dimensional adaptive landscape (right). Px, precursor of fatty acid X; Py, precursor of fatty acid Y; Plus (+), the adaptive peak
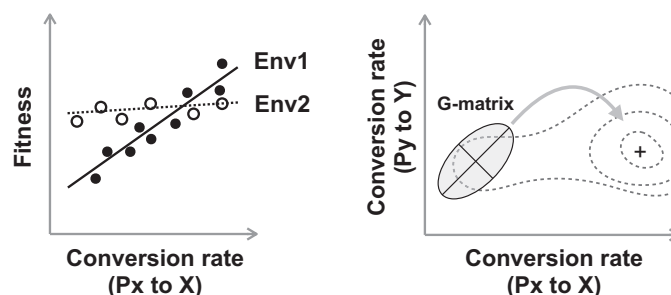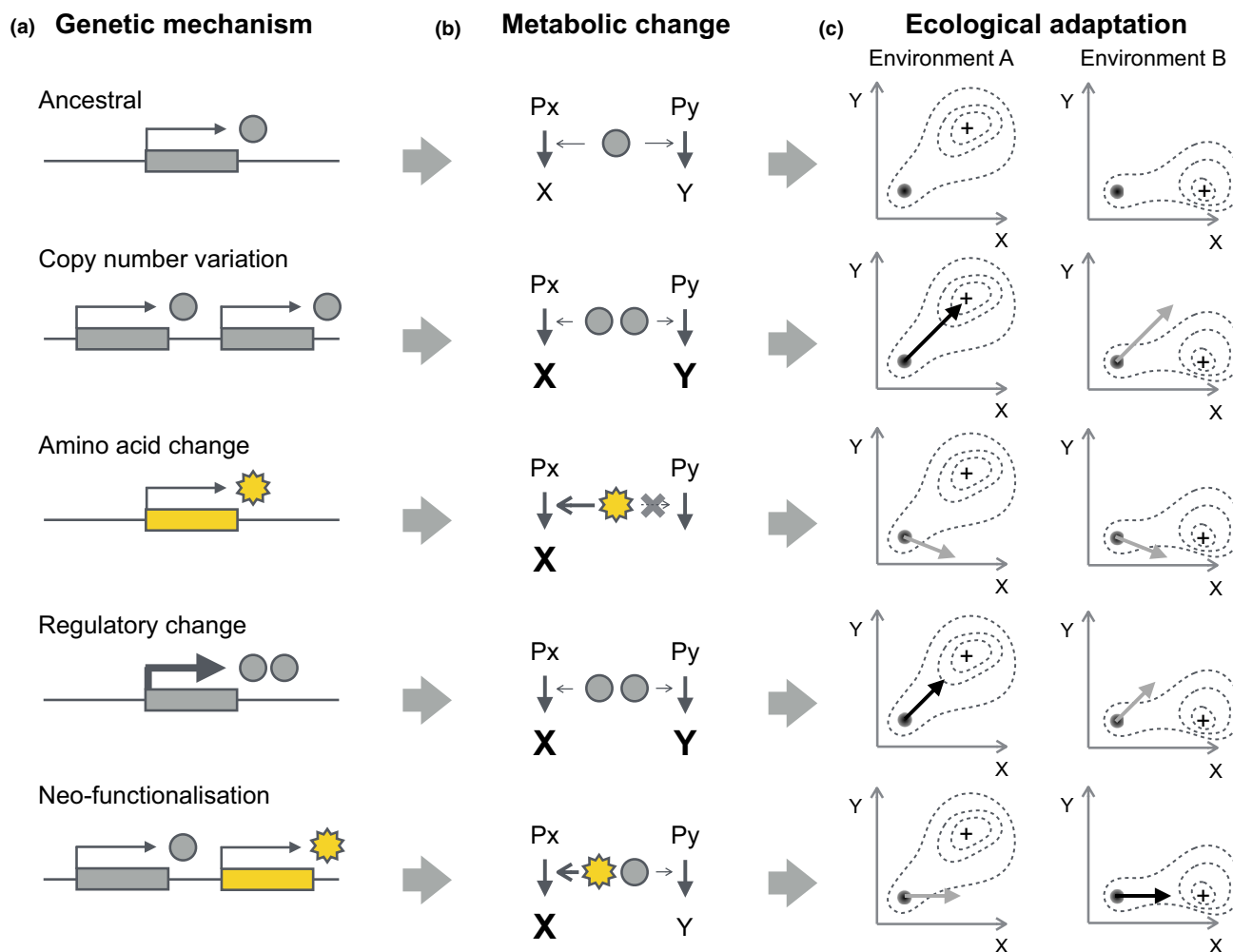
FIGURE 6 Relationship between genetics and ecology illustrated on fatty acid adaptive landscapes. (a) Different genetic mechanisms underlying increases in metabolic enzymatic activities. The arrow thickness indicates the gene expression levels. Grey circles and yellow asterisks indicate enzymes with ancestral and new functions, respectively. (b) Effects of mutations on the metabolic pathways. Because of a pleiotropic effect of the enzyme, both metabolic pathways can be influenced. Font sizes reflect the amounts of synthesised fatty acids X and Y. Px, precursor of fatty acid X; Py, precursor of fatty acid Y. (c) Adaptive (black) or nonadaptive walks (gray) on two different types of adaptive landscapes. The X and Y axes indicate the levels of fatty acids X and Y. Plus (+) indicates the adaptive peak. In Environment A, simultaneous increases of fatty acids X and Y are favoured. In Environment B, however, only an increase in fatty acid X but not fatty acid Y is favoured

widely, culminating in lineage-specific pathway regulation and structure (Maeda, 2019). As a consequence of network structure, evolutionary changes at early steps within photosynthesis can have more substantial effects on final products than those that occur in later steps (Kacser & Burns, 1981; Olson-Manning et al., 2012; Wright & Rausher, 2010). In consumers, the evolution of nutritional metabolic networks has allowed them to utilise new resources or synthesise essential organic compounds that were previously required from diet (Borenstein et al., 2008; Wagner, 2012). Within a lineage, species can differ in the number and connectivity of modules in metabolic networks as well as in synthesis activities across the network. The evolution of carotenoid networks in birds, for example, has led to considerable variation in the structure (i.e., gain and loss of modules)

and connectivity of functional modules (Morrison & Badyaev, 2016) and, interestingly, has been implicated in the diversification of avian color patterns (Badyaev et al., 2019a).

In the 1940 s, Simpson posited that species could enter new 'adaptive zones' (Simpson, 1945; Simpson, 1953) via specific events, including dispersal into new habitats, extirpation of predators, or through 'key innovations', namely, those that relax or fundamentally change the prevailing environmental sources of natural selection (Miller, 1949; Rabosky, 2017). Since then, there has been an accumulation of evidence for rapid phenotypic evolution over short time scales (Carroll et al., 2007), with perhaps some of the best examples of this phenomenon coming from range-expanding species (Miller et al., 2020). During colonisation,

consumers often encounter new food resources and undergo shifts in their trophic niche, culminating in the evolution of associated behavioural, morphological and physiological traits (Des Roches et al., 2016; Herrel et al., 2008; Leaver & Reimchen, 2012; Renaud et al., 2018). For instance, changes in jaw morphology (Burress et al., 2020), gut length (Davis et al., 2013) or even microbiome community composition (Rennison et al., 2019) can evolve rapidly, allowing consumers to profit from novel resources and persist in habitats that were previously suboptimal. Individuals from range-edge and range-core populations also frequently differ in patterns of gene expression and metabolism (Rollins et al., 2015; Van Petegem et al., 2016). Recent studies suggest that metabolic traits may be also under strong selective pressure, particularly when the colonising consumer is faced with a novel resource environment, such as when marine consumers invade freshwater ecosystems (e.g., Ishikawa et al., 2019; Matsushita et al., 2020).

Whilst microevolutionary dynamics might shape the existing structure or control of metabolic networks (Figures 4 and 5), large structural changes in the network itself, such as the internalisation of an external dependency (e.g., the ability to synthesise a formerly essential dietary fatty acid), might present a species with novel ecological opportunity. In other words, the evolution of fatty acid metabolism might afford species new opportunities to exploit novel resources (e.g., terrestrial plants containing only ALA) and allow them to persist and diversify in 'adaptive zones'. For example, freshwater threespine stickleback and freshwater flatfish have both reduced their external dependency on DHA-rich resources, which are limited outside of marine habitats (Figure 3a), by increasing their endogenous conversion rates from ALA to DHA, a key innovation. Similarly, when feeding on a low DHA diet, Arctic charr from subalpine freshwater systems endogenously converted up to 25% of ALA to DHA, which is a much higher conversion than that previously documented in marine fishes (Murray et al., 2015). Badyaev et al. (2019a) propose that such evolution in the control of metabolic networks is fundamentally associated with macroscale patterns of species diversity. Specifically, local metabolic adaptation can culminate in shifts in network topologies, potentially opening new opportunities for evolutionary diversity (Badyaev, 2019b). Currently, this is unexplored in the context of fatty acid metabolism, but there is considerable potential to do so in light of the heterogeneity of FA within and amongst ecosystems (Figure 2), variation in genes related to fatty acid synthesis across consumers, the fitness relevance of FA acquisition, retention and synthesis traits and examples of key innovations facilitating consumer diversification (Ishikawa et al., 2019; Matsushita et al., 2020).

CONCLUSION

There is a global metabolic network available for animals (Borenstein et al., 2008), and we are still in the early stages of uncovering how this network is structured across the animal tree of life (Figures 1 and 4 and Table 1) and how it is mechanistically linked to fitness variation of consumers (Table 2 and Figure 5). Empirical studies have documented substantial variation in the fatty acids of organisms, structured both within and amongst ecosystems and amongst prey communities, which creates ample opportunities for the evolution of consumer behaviour and metabolism. Whilst numerous studies have documented consumer as well as producer fatty acid content or composition, relatively few studies have explored the degree to which internal regulatory and synthesis processes versus diet drive this variation in nonmodel consumer taxa and fewer still have linked nutritional metabolism to consumer fitness variation in natural settings. However, there is growing evidence for evolutionary diversification in the primary nodes and controls of the fatty acid metabolic network (Figure 4). We suggest that researchers take an integrative approach that includes examining nutrition as an agent of natural selection acting on both behavioural foraging and metabolic traits, which are embedded in a trait hierarchy leading to fitness. Studying such metabolic diversity across multiple scales (Figures 4 and 5) will allow us to understand more broadly how consumers evolve traits related to both resource acquisition and metabolism and how they invade new environments and diversify (Figure 6).

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PEER REVIEW

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DATA AVAILABILITY STATEMENT

No new data were used in this manuscript. Data from previously published studies used to generate Figure 2 will be archived in Dryad upon article acceptance. Original references used to generate this dataset are available online (https://paperpile.com/shared/IGegrQ). Data used to generate Figure 3 from Chaguaceda et al., 2020 and Twining et al., 2018 are archived online at online (https://www.diva-portal.org/smash/record.jsf?pid=diva2%3A1434687&dswid=2927 and https://datadryad.org/stash/dataset/doi:10.5061/dryad.cr5h595).

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.