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REVIEW

SPECIAL ISSUE
THE INTEGRATIVE BIOLOGY OF EXERCISE

The sugar oxidation cascade: convergent metabolic strategies in hovering vertebrate nectarivores

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ABSTRACT

The smallest flying vertebrate pollinators, including hummingbirds and nectar bats, exist at an energetic extreme. Nectarivores must balance the need for high rates of metabolic power output to sustain comparatively high costs of thermoregulation and the intense energetic demands of forward and hovering flight with the constraint against building and carrying large, heavy energy stores. Work over the past half century has quantified metabolic rate and daily energy requirements for these animals and revealed that hummingbirds and nectar bats achieve energy homeostasis through exceptional physiological flexibility. They can rapidly and completely switch from fueling costly flight with lipid oxidation, when fasted, to oxidizing nectar sugar, ingested minutes prior, at rates that completely support hovering while foraging. This physiological capacity for rapid flux and oxidation of dietary sugar to completely fuel intense exercise, termed the 'sugar oxidation cascade', stands in stark contrast to models of fuel use in running mammals. Remarkably, the capacity for rapid absorption and oxidation of fructose is as elevated in hummingbirds and nectar bats as is their capacity to use glucose. Here, we review insights into convergently and divergently evolved features of the sugar oxidation cascade among hummingbirds and nectar bats, as revealed by advances in comparative genomic, molecular and biochemical techniques. We then review available evidence and hypothesize that additional groups of nectar and fruit-eating bats and birds exhibit similar fuel use patterns during exercise, and we call on researchers to develop techniques to assess fuel use during forward flight in these non-hovering taxa.

KEY WORDS: Hummingbird, Bat, Sugar, Fuel use, Exercise, Nectar

Introduction

Powered, flapping flight is one of the most striking innovations in vertebrate evolution. Although it generally demands high power output (work per unit time), it is a relatively efficient mode of locomotion, allowing flying animals to move more quickly than running ones (Norberg, 1990). Powered flight has evolved independently in two vertebrate classes: Aves and Mammalia (Rayner, 1988). Of the more than 10,000 bird species, over 99% are capable of powered flight. In mammals, powered flight is far rarer, having evolved only in the order Chiroptera, which contains more than 1498 recognized species of bat – all capable of flight (Simmons and Cirranello, 2025; Thewissen and Babcock, 1992). For centuries, humans have been captivated by the speed and maneuverability of birds and bats in flight, although we only engineered our own means of aerial travel within the past 150 years. Among birds and bats, certain aerial performers command even greater appreciation, standing out for their highly specialized form of flight: hovering.

Hovering is the most energetically demanding mode of locomotion in animals, even more so than forward flapping flight. Most birds and bats cannot sustain this level of power output for more than a few seconds, if at all. However, over 360 species of hummingbird (Trochilidae family) possess the ability to hover, seemingly indefinitely (Warrick et al., 2012). Unlike forward flight, hovering involves remaining airborne in the absence of forward motion and, thus, requires continuous lift production to counteract gravity (Weis-Fogh, 1972). Hummingbirds achieve this by sweeping their wings in a characteristic figure-eight pattern, generating lift on both the upstroke and downstroke – a stark contrast from most other birds. which produce lift primarily during the downstroke (Houghton, 1966). The ability to hover is crucial to their foraging behavior, as it permits access to nectar from flowers that cannot support a perched visitor. Less well appreciated is the fact that some nectar-feeding bats have convergently evolved the ability to hover, similarly allowing access to flower nectar that would be otherwise inaccessible (Clark, 1977). However, the biomechanics of hovering differs between hummingbirds and nectar-feeding bats. Hummingbird wings remain relatively rigid throughout their figure-eight stroke cycle, whereas bats tend to exhibit extensive wing flexion, particularly during the upstroke (Håkansson et al., 2015). Consequently, bats generate far less lift during the upstroke than do hummingbirds, but they compensate by producing greater aerodynamic force during a lengthened downstroke (Håkansson et al., 2015; Ingersoll et al., 2018). This hovering strategy is energetically costly, but bats partially offset this cost with disproportionally large wings relative to their body mass (Ingersoll et al., 2018) in comparison to those of hummingbirds. The fact that hummingbirds and nectar bats have evolved distinct kinematic solutions to the same aerodynamic challenge offers rich insights into how different evolutionary paths can arrive at functionally similar outcomes under shared ecological pressures.

The minimum power required for flight increases more quickly with body size than does the power-generating ability of the musculoskeletal system (Marden, 1990, 1994). Thus, there is an upper limit in body size above which animals cannot achieve powered flight. Hovering, which demands more power than forward flight at even moderate speeds, further constrains body size (Chai and Millard, 1997). It is, therefore, no surprise that birds and bats that can hover are all clustered near the low end of the size range for their respective group (Fernandez et al., 2011). Indeed, all hummingbird species weigh less than ∼12 g, apart from the Southern giant hummingbird (*Patagona gigas*), which reaches a mere 20 g (Fernandez et al., 2011). Similarly, nectar bats that hover tend to be small, typically weighing less than 30 g (Voigt and Winter, 1999). For small animals with high mass-specific metabolic rates (see

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Glossary

Advanced glycation end-products (AGEs)
Molecules formed when proteins, lipids or nucleic acids react non-enzymatically with sugars. AGEs accumulate with age and/or high-sugar diets and have been linked to various metabolic pathologies.

Aerobic power
The rate at which muscles can produce ATP via aerobic metabolism.

Cardiac output
The volume of blood pumped by the heart per unit time.

C_3 and C_4 plants
Plants that differ in their photosynthetic carbon fixation pathways, resulting in distinct stable carbon isotope ratios ($\delta^{13}C$) in their nectar and tissues.

Crossover concept
A general model describing how fuel use shifts from primarily fats to carbohydrates with increasing exercise intensity in many vertebrates.

Glycation
The non-enzymatic attachment of sugars to proteins or lipids, which can impair function and form AGEs.

Headgut
The anterior portion of the digestive tract, including the mouth and pharynx, responsible for food acquisition, mechanical processing and the initiation of digestion.

Maximum enzyme activity
The highest rate at which an enzyme can catalyze a reaction.

Mass-specific metabolic rate
Metabolic power production required to sustain a given behaviour per unit animal weight (e.g. W kg^{-1}).

Nectarivory
A dietary strategy in which an animal derives most or all of its energy and nutrients from sugar-rich nectar produced by flowers.

Paracellular absorption
Passage of molecules between intestinal cells, rather than through them, allowing for the rapid uptake of nutrients and other small molecules.

Respiratory exchange ratio
The ratio of CO_2 produced to O_2 consumed; values near 1.0 indicate predominant carbohydrate oxidation, whereas values closer to 0.7 indicate primarily lipid oxidation.

Rostrum
The anterior portion of the skull, often elongated in nectarivores to access floral nectar.

Thermoregulatory cost
The energy an organism expends to maintain a stable core body temperature within its preferred range, which is minimal within the thermal neutral zone but increases when environmental temperatures deviate from the optimum.

Transcellular absorption
Movement of molecules through intestinal cells via specific transporters or channels, as opposed to between cells.

Glossary), nectar is an energy-rich resource, and the ability to feed on nectar by hovering reinforces the requirement for small body size. Just as hummingbirds and nectar bats have converged on the ability to hover, they have also independently evolved physiological adaptations to support a diet dominated by simple sugars. The combination of small body size, hovering ability and diet specialization have made hummingbirds and nectar-feeding bats attractive models for comparative exercise physiologists interested in understanding the energetic cost of flight. In this Review, we integrate insights from across levels of biological organization, from genomic to whole-organism measurements, to highlight the sugar metabolism adaptations that support hovering flight in nectarivorous birds and bats.

Early experiments to understand hovering metabolism

The first experiments to evaluate metabolism during hovering flight were conducted on hummingbirds using simple, yet effective, techniques. In a pioneering study in 1950, Pearson placed birds inside a glass jar ∼6 in in diameter and 10 in tall – just large enough for a hummingbird to hover in place (Fig. 1A). The jar contained soda lime and calcium chloride to absorb carbon dioxide (CO_2) and water vapor, along with a fan to circulate the air and ensure accurate oxygen (O_2) measurements. The most reliable measurements came from the Allen's hummingbird (*Selasphorus sasin*), which was most amenable to hovering in the confined jar. Although this early experiment involved only short bouts of hovering, it revealed that these tiny birds achieve some of the highest mass-specific metabolic rates recorded among vertebrates (Pearson, 1950). Over the next few decades, longer bouts of hovering were achieved in other hummingbird species using similar closed-chamber setups, yielding more robust estimates of the extraordinary energetic costs of sustained hovering (Epting, 1980; Lasiewski, 1963; Schuchmann, 1979; Wolf and Hainsworth, 1971).

In 1972, Berger and Hart introduced an innovative experimental approach by designing a mask-based respirometry setup that took advantage of the hummingbird's natural foraging behavior (Berger and Hart, 1972). Specifically, they designed a respirometry 'mask' resembling a large conical-shaped flower angled downward, with a sugar water reservoir placed deep inside to mimic a nectary. An artificial flower or red-painted 'nectary' within coaxed hummingbirds to hover while feeding, causing them to effectively 'wear' the mask. While birds fed, air samples from within the mask were collected to measure O_2 consumption and CO_2 production (Berger, 1974, 1985; Berger and Hart, 1972). It was not until the mid-1990s that similar mask respirometry techniques were first applied to hovering bats (Fig. 1B). These initial studies found that the mass-specific metabolic rate of hovering Jamaican long-tongued bats (*Glossophaga soricine*, now *Glossophaga antillarum*) was approximately half that of the hummingbirds studied by Pearson (1950) and others (Fig. 1B; Winter, 1998; Winter et al., 1998).

Another major advancement in the study of hovering vertebrate metabolism came in the mid-2000s with the integration of stable isotope tracking in hummingbirds with mask-based respirometry. In these early studies, animals were maintained on diets with a stable isotope ratio ($^{13}C/^{12}C$) characteristic of photosynthetic C_3 plants (see Glossary $\delta^{13}C \approx -25$ to $-20‰$). During experiments, they were offered sugar solutions derived from C_4 plants, which have a markedly different $^{13}C/^{12}C$ signature ($\delta^{13}C \approx -15$ to $-10‰$), to distinguish between the use of recently ingested versus stored fuels during hovering flight (Voigt and Speakman, 2007; Welch and Suarez, 2007; Welch et al., 2006, 2008). For example, Welch et al. (2006) maintained broad-tailed hummingbirds (*Selasphorus platycercus*) on a beet sugar diet (C_3), then switched to cane sugar (C_4) during mask respirometry trials. Measurements of CO_2 production, O_2 consumption and the $^{13}C/^{12}C$ signature of exhaled CO_2 during hovering revealed that, within 20 min, ∼75% of the hummingbirds' hovering metabolism was fueled by ingested sugar. Parallel studies in nectar-feeding bats showed similar patterns. Notably, Voigt and Speakman (2007) showed that *G. soricina* (now *G. antillarum*) rapidly oxidized dietary sugars, relying almost exclusively on ingested carbohydrates with just 10–15 min of feeding. Subsequent studies refined this experimental approach by using artificially ^{13}C-enriched sugars. For example, Chen and Welch (2014) fed ruby-throated hummingbirds (*Archilochus colubris*) ^{13}C-enriched glucose and fructose, and found that, within 60 min of feeding, 81% and 88%

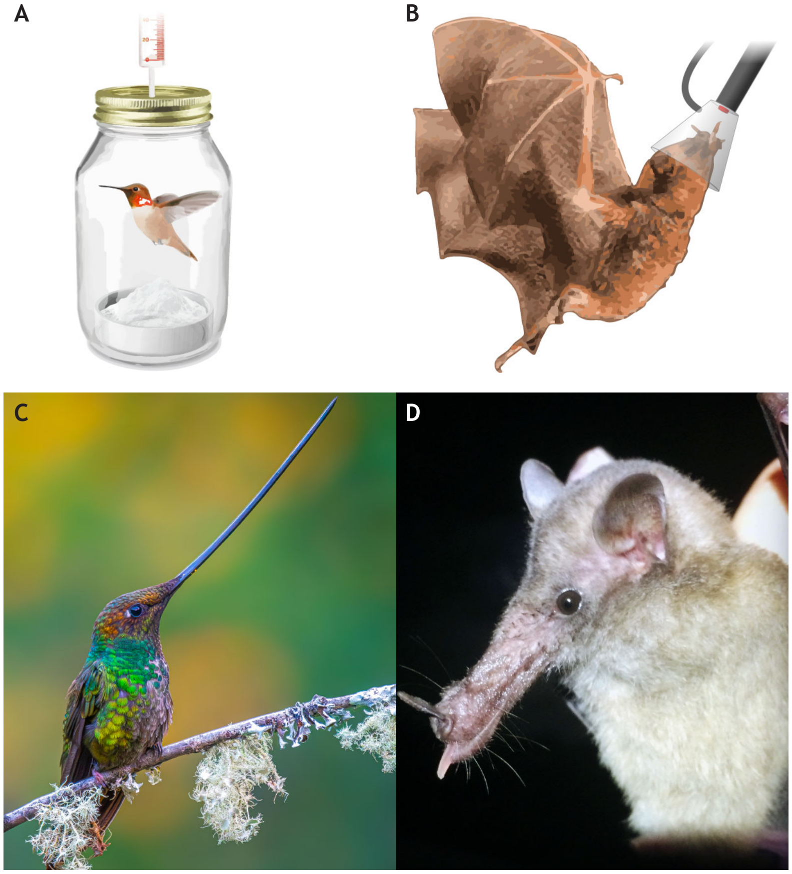

Fig. 1. Approaches used to quantify hovering metabolic rate in hummingbirds and small nectarivorous bats and examples of convergent evolution of cranial morphology in vertebrate nectarivores. (A) An Allens' hummingbird (*Selasphorus sasin*) hovers within a bell jar that is set up to operate as a closed-system, volumetric respirometer (Pearson, 1950). (B) A Jamaican long-tongued nectar bat (*Glossophaga antillarum*) hovers at a 'feeder mask' (Berger and Hart, 1972; Winter, 1998). By inserting its head into the cone to access sugar water, the bat effectively 'wears' the mask, which comprises part of a flow-through respirometer. (C,D) The sword-billed hummingbird (*Ensifera ensifera*) (C) and trumpet-nosed bat (*Musonycteris harrisoni*) (D) exemplify the most extreme headgut (i.e. rostrum or bill) elongation in each group. Image credits: Soumyadeep Chatterjee (C); Luis Viquez Rodriguez (D). Photos used with permission.

of hovering metabolism was supported by exogenous glucose and fructose, respectively. Collectively, these findings underscore the exceptional capacity of hummingbirds and nectar bats to rapidly and efficiently oxidize dietary sugars to meet the energetic demands of hovering – an ability far beyond the carbohydrate oxidation capacities of humans and other vertebrates. However, this apparent deviation from the 'crossover concept' (see Glossary) may not be unique to nectarivores and could be more broadly shared among small, fast-metabolizing vertebrates (e.g. Rossi and Welch, 2024), representing a fascinating avenue for future work.

The ability to rapidly oxidize dietary carbohydrates to fuel hovering represents a metabolic strategy that deviates sharply from the conventional crossover concept observed in most vertebrates, in which carbohydrate reliance increases gradually with exercise intensity (Fig. 2A,B; Brooks and Mercier, 1994). In nectarivorous birds and bats, fuel use during hovering appears to be uncoupled from exercise intensity and instead tightly linked to dietary status (i.e. fed versus fasted; Fig. 2C,D). Understanding the mechanisms that support rapid sugar oxidation during hovering has emerged as an exciting area of research for many comparative exercise physiologists. The pathway of carbon flux – from flowers, through the digestive and cardiovascular systems, across muscle membranes and into mitochondria – has been termed the 'sugar oxidation cascade', an analog to the well-established 'oxygen transport cascade' (for a review, see Suarez et al., 2011). In the sections that follow, we use the sugar oxidation cascade as a conceptual framework to highlight the morphological, physiological and molecular adaptations that facilitate this remarkable metabolic feat (Fig. 3). We begin by examining adaptations that enhance sugar ingestion and absorption, followed by those supporting vascular delivery and cellular uptake, and, finally, those that enable the rapid oxidation of sugars in flight muscle. Throughout, we highlight both convergent and divergent traits among nectarivorous birds and bats, from classical metabolic measurements to new insights provided by modern genomic and transcriptomic tools. Importantly, we acknowledge that small, flying vertebrates, regardless of diet, share adaptations of the oxygen transport cascade that support their shared high aerobic capacity. We discuss whether specializations along the sugar oxidation cascade are broadly observed among small fliers, and conclude that similar capacities to rapidly oxidize ingested sugar to fuel flight may be more widespread than previously understood. Because some bat species complexes have undergone reorganization, we list both the species as originally reported and the corrected species name, where it can be determined based on capture location.

Maximizing flux: the sugar oxidation cascade in hummingbirds and nectar bats

Sugar ingestion and absorption

Perhaps only behind their hovering flight, tiny size and brilliant colors, hummingbirds are noted for their elongated bills and tongues, with the sword-billed hummingbird (*Ensifera ensifera*) being the most extreme example (Fig. 1C). Many nectar bats have convergently evolved elongated cranial features, such as an elongated rostrum (see Glossary) and tongue, to similarly access nectaries deep within flowers (Dumont, 2004; Winter and Von Helversen, 2003), the most extreme example in this group being the trumpet-nosed bat (*Musonycteris harissoni*; Fig. 1D). In both hummingbirds and nectar bats, the distal portions of

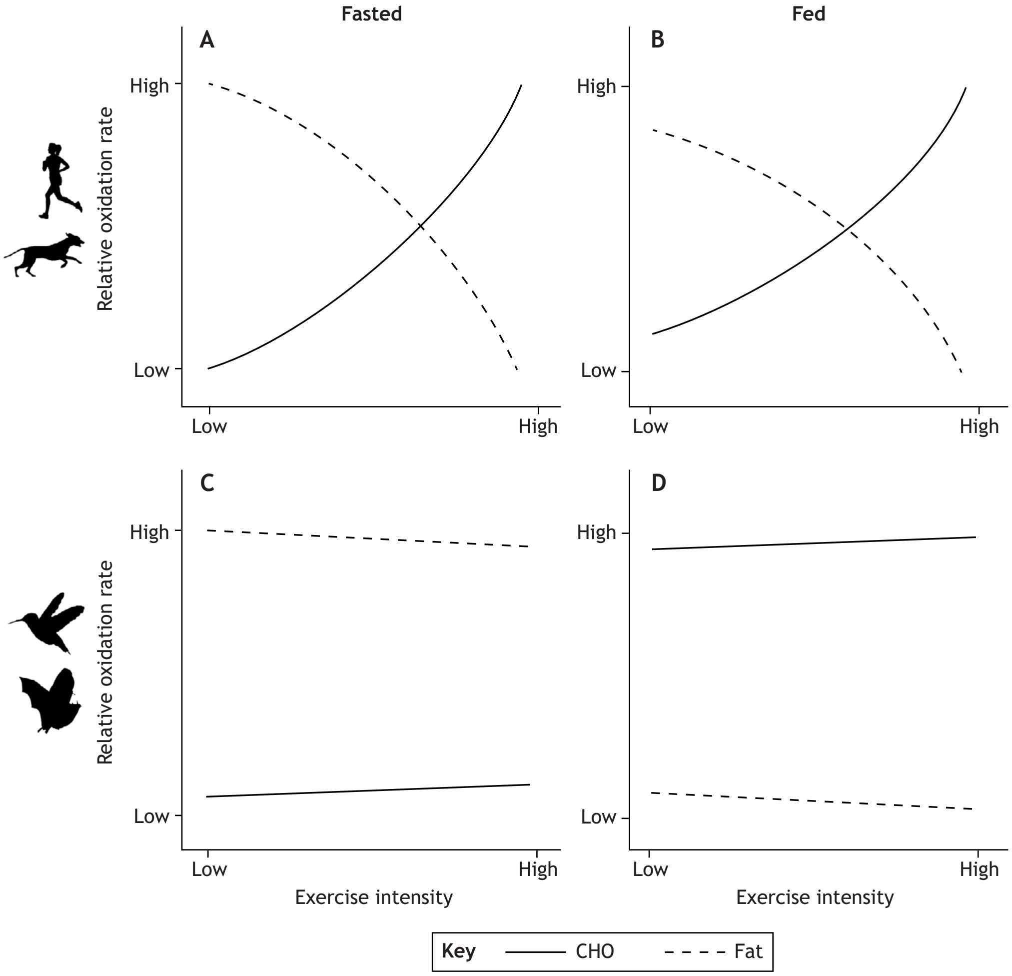

Fig. 2. A comparison of the 'crossover concept' model of fuel use during exercise with the 'sugar oxidation cascade'. (A,B) Relative reliance on oxidation of lipid versus carbohydrate (CHO) as a function of exercise intensity in the fasted state in non-flying mammals. (C,D) Relative reliance on oxidation of lipid versus CHO in relation to exercise intensity when animals have recently fed on a simple sugar meal in hummingbirds and nectar bats. In the case of non-flying mammals (A,B), dietary status causes a subtle shift towards greater reliance on CHO (largely ingested sugar) oxidation at low to medium intensities. At highest exercise intensities, oxidation of intramuscular glycogen dominates. In contrast, in hummingbirds and nectar bats (C,D), dietary status almost entirely predicts what fuels are oxidized. These animals almost exclusively oxidize lipids when fasted, and CHO (almost exclusively recently ingested sugar) when they are feeding regularly, regardless of exercise (flight) intensity.

the tongue are highly specialized to enhance nectar loading, but the morphology and action of the tongue differ between these two groups. Hummingbirds generally share a common morphology and mode of action: forked, rolled tongue tips that rapidly expand in diameter and trap fluid upon breaking the nectar meniscus (Rico-Guevara and Rubega, 2011). By contrast, bats that have independently evolved a nectar-based diet show at least two distinct morphologies and associated mechanisms. In some species, exemplified by *G. soricina*, the tongue enters the nectar pool in repeated cycles (as in hummingbirds), and, with each cycle, hemodynamically expanded papillae 'mop' up the nectar (Harper et al., 2013). In others, such as *Lonchophylla robusta*, the tongue lacks papillae, but features distinct lateral grooves. These bats plunge their tongue into the nectar and keep it there as nectar moves along the grooves by a pumping mechanism that remains incompletely understood (Tschapka et al., 2015).

Although their headguts (see Glossary) are highly morphologically specialized for a floral nectar diet, the digestive systems of hummingbirds and nectar bats face a conundrum common to all small, flying vertebrates. Their diminutive size, and therefore relatively high thermoregulatory costs (see Glossary), combined with their energetically intensive mode of locomotion, means that they must achieve relatively high rates of energy intake, despite constraints on the size of their digestive machinery imposed by the need to minimize supported weight. In effect, these smallest flying animals have proportionately less digestive tissue and reduced surface area for nutrient absorption than do similarly sized non-flying animals, yet they have higher absorption demands. Using *in vitro* approaches, such as the everted sleeve technique (Karasov and Diamond, 1983), researchers have shown that both hummingbirds and nectar bats have evolved higher maximal rates of transcellular absorption (see Glossary) of hexose (e.g. glucose) than have non-fliers (Brun et al., 2014; Karasov et al., 1986; McWhorter et al., 2006; Price et al., 2015). This capacity is supported by comparatively higher activities of intestinal disaccharidases (Hernandez and Martinez del Rio, 1992; Martínez del Rio, 1990; Napier et al., 2013), relatively elaborated villi and microvilli that enhance the available surface area (Camacho et al., 2024; Lavin et al., 2015), and presumably elevated expression and activity of glucose transporters in the solute carrier family 2 (SLC2A, commonly referred to as GLUT proteins). For example, Camacho et al. (2024) report elevated expression of GLUT2 in two nectar bat species relative to that in insectivorous species, although similar studies on hummingbird intestinal transporters have not yet been undertaken. Despite these adaptations, the elevated capacities for cellular-mediated absorption of nectar sugars do not fully compensate for the deficit in intestinal length and absorptive surface area. Thus, both hummingbirds and nectar bats – and small, flying vertebrates more broadly – rely extensively on paracellular absorption (see Glossary) of small molecules, such as glucose and fructose, and, to much lesser extent, sucrose, because of its greater molecular mass (Brun et al., 2014; Karasov et al., 1986; McWhorter et al., 2006; Price et al., 2015) (Fig. 3).

Notably, nectar bats possess elevated sucrase activity compared with that of non-flying mammals or an insectivorous bat species, but activity levels per unit of intestinal surface area in nectar and fruit

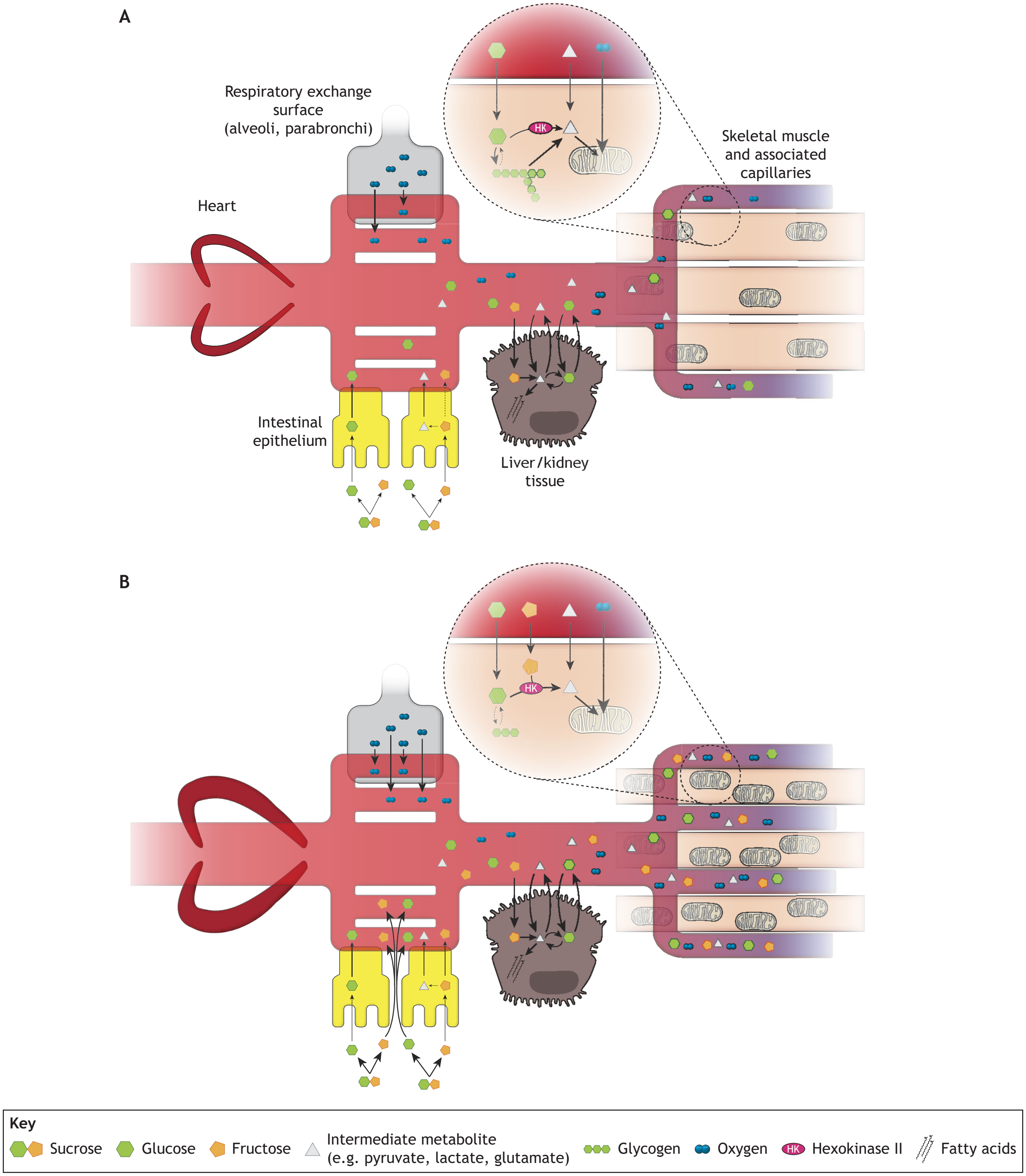

Fig. 3. Schematic representations highlighting aspects of the oxygen transport cascade and sugar oxidation cascade in non-flying mammals (e.g. rodents, humans) and hummingbirds and nectar bats. (A,B) Aspects of the oxygen transport and sugar oxidation cascades in a non-flying mammal (e.g. running rodent; A) and a flying nectarivorous (and possibly frugivorous) hummingbird (or passerine; e.g. sunbird, honey eater) or bat (B). In B, we highlight enhancements of the sugar oxidation cascade, including greater reliance on paracellular absorption of sugars in the intestine, enhanced absorption and higher systemic circulating levels of glucose and fructose, and comparatively high rate of sugar phosphorylation by hexokinase II in skeletal muscles. We also highlight enhancements that augment both the sugar oxidation and oxygen transport cascades, including larger heart sizes that drive greater cardiac output, higher muscle capillary densities and greater mitochondrial content. Notably, these latter features are also broadly observed among small, non-nectarivorous flying birds and bats, owing to their shared high energetic costs associated with flight. Figures made using assets from National Institute of Allergy and Infectious Diseases (NIAID) National Institutes of Health (NIH) BioArt Source (bioart.niaid.nih.gov/bioart/203; bioart.niaid.nih.gov/bioart/352).

bats are about half those measured in hummingbirds (Hernandez and Martinez del Rio, 1992). In both taxa, surface area-specific sucrase activity scales negatively with body mass, whereas intestinal surface area scales positively (Hernandez and Martinez del Rio, 1992; McWhorter et al., 2021). Thus, because total capacity depends on both activity per unit area and total intestinal surface area (McWhorter et al., 2021), hummingbirds and nectar and fruit-eating bats exhibit nearly identical allometric scaling of summed sucrase activity with body mass. Although it has been understood for some time that, on average, hummingbird-pollinated flowers produce nectar with higher concentrations of sucrose relative to monosaccharides than flowers pollinated by bats (Baker et al., 1998), this does not seem to be the result of digestive constraint in bats. Nectar bats show no preference for equicaloric monosaccharide solutions over disaccharide solutions (Ayala-Berdon et al., 2008), and they oxidize sugars in sucrose or hexose nectar meals equally rapidly and to a similar extent (Voigt and Speakman, 2007).

Fuel delivery to muscle

Cardiovascular adaptations

The oxygen transport and sugar oxidation cascades converge at the convective step of the circulatory system. Thus, adaptations to the cardiovascular system that enhance oxygen delivery to meet the elevated demand of exercising flight muscles can simultaneously enhance sugar delivery. The delivery of oxygen and sugars to flight muscles depends on the extent of vascularization, the rate of convective flow of blood and the concentration of substrate being delivered (Suarez et al., 2011). Although the cardiovascular physiology of nectar-feeding bats is far less studied than that of hummingbirds, we can infer relevant adaptations from other bat species. For example, in both an insect-eating bat (*Eptesicus fuscus*; Mathieu-Costello et al., 1992a) and a hummingbird (*Selaphorus rufus*; Mathieu-Costello et al., 1992b), flight muscle capillary density is two to six times greater than that of the leg muscles of small, non-flying mammals. Despite reaching heart rates of 480–1200 beats min^{-1} during flight (Didio, 1967; Lasiewski, 1964), hummingbirds have relatively low heart rates for their body size, but their enlarged hearts support high cardiac output (see Glossary; Johansen et al., 1987; Nespolo et al., 2018) (Fig. 3). Heart rates and cardiac output during hovering have not been reported for nectar bats, but it is reasonable to expect similar elevations, considering that larger fruit-eating (*Uroderma bilobatum*, now *Uroderma convexum*; O'Mara et al., 2017) and insect-eating bats (*Molossus molussus*; Dechmann et al., 2011) can reach heart rates near 900 beats min^{-1} during flight. Moreover, like hummingbirds, bats possess relatively large hearts – in fact, they are reported to have the largest relative heart size of all mammals (Canals et al., 2005). In terms of oxygen-carrying capacity, hematocrit can exceed 55% in hummingbirds (Johansen et al., 1987; Williamson et al., 2024), the nectar bat *Glossophaga commissarisi* and several other bat species (Jürgens et al., 1981; Schinnerl et al., 2011), which is higher than in most non-flying mammals. Finally, it is important to note that many cardiovascular traits scale strongly with body mass (Dawson, 2003), and, therefore, many features we have highlighted reflect the general demands of powered flight in small vertebrates rather than nectarivory (see Glossary). That said, nectarivory requires the rapid transport of dietary sugars, a demand for which enhanced cardiovascular capacity can play a critical role (Suarez et al., 2011).

Blood sugar levels during feeding and fasting

Concentrations of sugar in the blood vary with dietary status in all vertebrates, and the same is true for hummingbirds and nectar bats. When fasted, nectar bats (*G. soricina*, now *G. antillarum*) exhibit relatively low blood glucose levels of ∼3.5 mmol l^{-1} (Kelm et al., 2011). In glucose tolerance tests on 29 species of neotropical bat, similarly low fasting blood glucose levels were observed broadly across all dietary guilds represented in the sampling, including in three nectar bat and four frugivorous bat species (Camacho et al., 2024). Keegan (1977) was the first to publish blood sugar values in fasted *Rousettus aegypticus*, reporting a value of just 1.6 mmol l^{-1}. Similarly, the fruit bats *Eonycteris spelaea* and *Cynopterus sphinx* exhibit fasting blood glucose levels of 4.5 and 4.6 mmol l^{-1}, respectively (Peng et al., 2017). These values are comparable to those reported for fasted laboratory rats (∼4 mmol l^{-1}; Wang et al., 2010) and align with broader patterns observed among mammals. By contrast, Beuchat and Chong (1998) reported blood glucose levels of ∼17 mmol l^{-1} in three species of North American hummingbird (*Calypte anna*, *Calypte costae* and *A. colubris*) fasted overnight. Fasting blood glucose levels among birds typically range from 1.5 to 2.5 times higher than those of comparably sized mammals (Braun and Sweazea, 2008), and this difference is attributed, in part, to the absence of the gene encoding GLUT4 in birds and the broad insulin insensitivity of this group (Braun and Sweazea, 2008; Welch et al., 2013).

Supported by high rates of active and passive absorption of hexoses (Price et al., 2015), blood sugar levels in recently fed hummingbirds and nectar and fruit bats reach some of the highest absolute values observed among all vertebrates. Indeed, Beuchat and Chong (1998) measured blood glucose concentrations ranging from 28 to 41 mmol l^{-1} in three species of North American hummingbird (*C. anna*, *C. costae* and *A. colubris*) shortly after feeding. Similarly, Camacho et al. (2024) recorded glucose concentrations between 16 and 33 mmol l^{-1} just 10 min after feeding on glucose solutions in three neotropical nectar bats (*Glossophaga* sp., *Lonchophylla* sp. and *Choeroniscus godmani*; some taxa were only identified to genus in the report). Importantly, the handheld glucometer used by Camacho et al. (2024) had a detection limit of 33 mmol l^{-1}, indicating that blood glucose levels may have risen higher in some individuals. Kelm et al. (2011) reported post-feeding blood glucose levels of 20–30 mmol l^{-1} in captive *G. soricina* (now *G. antillarum*) nectar bats, with variation depending on both the volume of glucose solution offered and the bats' activity levels. High blood glucose concentrations are also observed in fruit bats following a nectar meal. For example, Keegan (1977) observed peak blood glucose levels of >40 mmol l^{-1} in *R. aegypticus* fed 1.5 g of glucose in solution. Moreover, Camacho et al. (2024) found comparable blood glucose levels in neotropical fruit bats after feeding on a glucose solution, with peak glucose values between 20 and 33 mmol l^{-1} – again reaching the glucometer detection limit – in *Sturnira* sp., *Uerodema* sp., *Artibeus* sp. and *Dermanura phaotis*. Interestingly, when fed equicaloric sucrose meals rather than glucose, the nectar and fruit bats examined by Camacho et al. (2024) only reached blood glucose values of 11–17 mmol l^{-1}. Similarly, Peng et al. (2017) observed peak blood glucose levels of 24 and 15 mmol l^{-1}, respectively, in the fruit bats *C. sphinx* and *E. spelaea* after feeding on sucrose solutions. These lower peak blood glucose levels likely reflect the reduced glucose content of the meal (as sucrose comprises only 50% glucose). Importantly, although absolute glucose concentrations in hummingbirds and nectar bats are higher than those in most vertebrates, when body size is accounted for, both fall within the expected range for small vertebrates (Martinez del Rio and Gutiérrez-Guerrero, 2020). Nonetheless, their high absolute blood glucose levels remain biologically relevant, helping to support the extreme metabolic demands of hovering flight.

Absorption of fructose

On average, floral nectar contains an equal amount of fructose and glucose, occurring individually as monosaccharides or together as sucrose (Baker et al., 1998). Fructose is a rarer component of most vertebrate diets, and its level in the blood is usually unquantified, because it is typically present at much lower concentrations and varies less dynamically than glucose. The first measurement of fructose in a vertebrate nectivore was reported in 1977, when Keegan measured blood fructose levels in the Egyptian fruit bat (*Rousettus aegyptiacus*). Keegan (1977) found that, as in fasted rats, blood fructose levels in partially fasted *R. aegyptiacus* were below detectable limits. Decades later, using untargeted metabolomics, Ali et al. (2020) found that after just 1 h of fasting, blood fructose levels in ruby-throated hummingbirds (*A. colubris*) averaged 0.21 mmol l^{-1}. In a follow-up study, Muhammad (2021) reported that hummingbirds fasted for an additional hour (i.e. for 2 h in total) exhibited blood fructose levels nearly 10-fold lower, averaging ∼0.025 mmol l^{-1}. Given the relatively higher capacity for paracellular fructose absorption in hummingbirds and most bats compared with that in non-flying animals with much lower (transcellular or paracellular) capacities for fructose absorption, it is unsurprising that blood fructose levels would rise higher in fed hummingbirds and fruits bats (Fig. 3). Although blood fructose levels have not been reported in any nectar bats (as far as we are aware), insights can be inferred from the available data on *R. aegyptiacus*. Upon ingestion of a small amount of fructose solution by this species, Keegan (1977) observed that plasma fructose concentrations peaked at ∼11 mmol l^{-1} just 5 min after feeding, whereas levels remained nearly undetectable for at least 30 min in rats fed the same solution. When glucose and fructose are offered in an equicaloric solution, *R. aegyptiacus* exhibits peak blood glucose levels above 27 mmol l^{-1} at 10 min, whereas blood fructose peaks at just ∼3 mmol l^{-1} after 5 min (Keegan, 1977). Although blood fructose levels have not been reported in hummingbirds fed a pure fructose solution, those fed a sucrose solution (effectively, an equicaloric mixture of glucose and fructose, given the high sucrase activity in the hummingbird intestine) show plasma fructose levels of ∼5.5 mmol l^{-1} (Ali et al., 2020). Thus, it may be reasonable to assume that if nectar bats or hummingbirds were given a meal of fructose calorically equivalent to the glucose or sucrose solutions used in previous studies, plasma fructose levels might approach the value of 11 mmol l^{-1} reported in *R. aegyptiacus* by Keegan (1977).

The role of GLUT proteins

Although glucose and fructose may enter the circulatory system of nectar bats or hummingbirds by paracellular movement across both the intestinal brush border and from extracellular fluid into capillaries, the movement of hydrophilic sugars across cell membranes is almost exclusively transporter mediated. In vertebrate skeletal muscle, various isoforms of the GLUT family of proteins facilitate this crucial function (Fueger et al., 2004). The ligand specificity and transport kinetics of the various GLUT isoforms seem to be highly conserved among vertebrate groups. Therefore, although the substrate affinities and transport kinetics of nectar bat and hummingbird GLUTs are not known, we can assume *a priori* that their functions are similar to those described in well-studied vertebrate species. In mammals, such as humans and rodents, GLUT4 is abundantly expressed in skeletal muscle and plays a crucial role in postprandial blood glucose regulation. In these animals, insulin signaling leads to massive translocation of GLUT4 from intracellular vesicles to the cell membrane (Shepherd and Kahn, 1999). Because GLUT4 has higher affinity for glucose than for other hexoses, this dynamic translocation increases the glucose uptake capacity of the tissue. Increasing muscle activity can also independently trigger the translocation of intracellular GLUT4 stores to the cell surface (Osorio-Fuentealba et al., 2013). GLUT1 and GLUT3, isoforms that similarly prefer glucose over other hexoses, are also present in mammalian skeletal muscle, although at comparatively lower levels (Gaster et al., 2000). Although some information on the expression patterns of GLUTs and related transporters in bat intestinal tissue is now available (Camacho et al., 2024), there are few reports of GLUT expression in bat muscle tissue. Suarez and Welch (2017), with help from Robert Lee-Young and the late David Wasserman, showed that GLUT4 abundance in nectar bat (*G. soricina*, now *Glossophaga mutica*) pectoralis is approximately six times greater than that in mouse gastrocnemius muscle, presumably providing the enhanced glucose uptake capacity of nectar bat flight muscle that is necessary to support the high rates of oxidation of recently ingested sugar during hovering (Voigt and Speakman, 2007; Welch et al., 2008). To the best of our knowledge, expression of no other GLUT isoform in bat skeletal muscle has been assessed, although the continued accumulation of high-quality reference bat genomes will surely address this deficit in knowledge.

In contrast to nectar bats, GLUT expression in the flight muscle of ruby-throated hummingbird (*A. colubris*) muscle has been investigated more thoroughly. There is no evidence of the gene encoding GLUT4 in hummingbirds (Workman et al., 2018), nor have researchers detected expression of any mRNA similar to mammalian *Glut4* sequences in hummingbird tissues (Welch et al., 2013). Interestingly, the absence of GLUT4 may be ancestral to birds, although some species possess a GLUT12 isoform that has evolved to take on an insulin-sensitive role, compensating for the absence of GLUT4 by translocating to the cell surface after insulin stimulation to increase glucose uptake (for a review, see Martinez del Rio and Gutiérrez-Guerrero, 2020). In ruby-throated hummingbirds, GLUT1, GLUT2, GLUT3 and GLUT5 proteins can be detected by immunoblotting the flight muscle, heart and liver (Ali et al., 2020). Among these three tissues, GLUT1 – an isoform with high affinity for glucose and that is expressed at low levels in most animal tissues – is expressed at relatively higher levels in hummingbird flight muscle than in heart and liver (Ali et al., 2020). Similarly, Ali et al. (2020) detected GLUT2 and GLUT3 – isoforms with relatively low and high glucose affinity, respectively – at roughly similar levels in flight muscle as in heart and liver. Interestingly, GLUT2 is typically expressed mainly in enteric and splanchnic tissue (Thorens, 2015), and GLUT3 is typically expressed only in muscle, brain and testes, in other animals (Simpson et al., 2008). The presence of these three isoforms in the plasma membrane of hummingbird flight muscle – possibly at comparatively greater levels than those in most other vertebrates – may support the glucose uptake capacity required to sustain complete reliance on recently ingested sugar to fuel hovering. In nectar bats, this role is assumed to be largely fulfilled by high GLUT4 expression.

Fuel oxidation

To sustain high rates of aerobic power (see Glossary) during flight, small- to medium-sized bats and birds generally possess flight muscles with relatively high mitochondrial density (Fig. 3). Given their small size and energetically costly mode of flight, it is not surprising that hummingbird pectoralis muscle exhibits the highest mitochondrial density reported for vertebrate skeletal muscle, at ∼35% of muscle fiber volume (Mathieu-Costello et al., 1992b). Because oxygen and sugar metabolites ultimately converge at the mitochondria, adaptations that enhance the sugar oxidation cascade in hummingbirds and nectar bats are often shared to varying degrees by other small- to medium-sized flying vertebrates. For example, the negative allometry observed in the minimum and maximum cost of flight with body mass is reflected by similar scaling patterns in the maximum activity of mitochondrial enzymes, such as citrate synthase, expressed per gram of flight muscle tissue. Accordingly, maximum flight muscle citrate synthase activity in nectar- and fruit-feeding hummingbirds and bats is indistinguishable from that of similarly sized birds and bats with other diets, yet generally higher than that in the skeletal muscles (e.g. gastrocnemius) of non-flying mammals (Fig. 4A). This elevated flight muscle oxidative capacity is likely to reflect the very high mass-specific metabolic rates needed to support costly hovering flight.

Hummingbirds and nectar bats are somewhat unique among vertebrates in that there is clear evidence that they can fuel hovering flight directly with recently ingested sugars. In other volant species, far less is known about fuel use during flight, with most available evidence coming from migratory species that primarily fuel flight using endogenous lipids and intramuscular glycogen stores (for a review, see Guglielmo, 2010). In hummingbirds and other small, flying vertebrates, intramuscular glycogen stores can be very low (Didio, 1967; Sweazea and Braun, 2005), especially compared with those of larger, relatively non-volant species (e.g. broiler chickens; Edwards et al., 1999), although available data are limited. These low

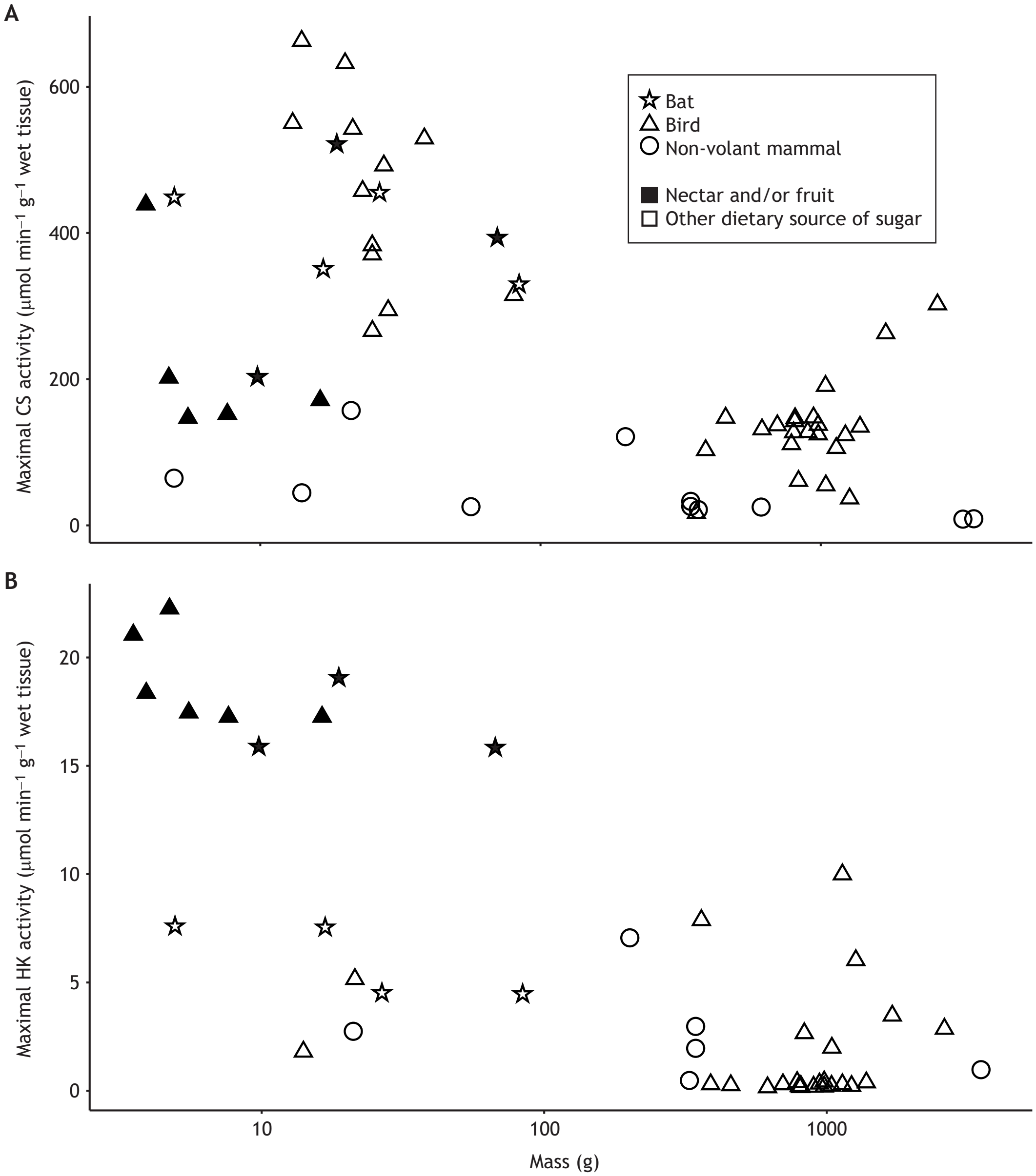

Fig. 4. Maximal activities of mitochondrial enzymes citrate synthase and hexokinase in flying vertebrates and non-volant mammals. (A,B) Maximal activities of citrate synthase (CS; A) and hexokinase (HK; B) are shown in µmol min^{-1} g^{-1} wet tissue, and values relate to the pectoralis muscles of small- to medium-sized birds and bats or the leg muscle (typically gastrocnemius) of similarly sized non-volant mammals, plotted against body mass (g). Small, flying vertebrates (birds and bats) generally exhibit elevated citrate synthase activities, regardless of diet type and associated sugar intake load, consistent with their shared need for high oxidative capacity to support flight. However, hexokinase activity is higher in the flight muscles of species known to oxidize dietary sugar at high rates during flight (nectar bats and hummingbirds) and those suspected of similar abilities (frugivorous species) than in birds, bats and non-volant mammals with different diets (e.g. insectivory, herbivory or omnivory). Note, because enzyme assays reported in the literature were performed at varying temperatures (25–41°C), we correct enzyme activities (assuming a Q_{10} of 2) to temperatures of active muscles *in vivo* (37°C in mammals and 39°C in birds). Please see Table S1 for included data and citations.

intramuscular glycogen levels may reflect both the high energetic turnover of flight muscles and the disadvantage of glycogen's obligatory water content, which would add excess weight. In hovering nectarivores and other small flying nectarivores and frugivores, this constraint may further contribute to reliance on the rapid oxidation of dietary sugars. Despite their elevated oxidative enzyme activities, non-nectarivorous and non-frugivorous birds and bats possess only modest maximum activities of hexokinase (a key sugar oxidation cascade and glycolytic enzyme) in their flight muscles, consistent with their limited capacity to utilize circulating sugars at rates sufficient to support the high rates of ATP turnover required for flight (Fig. 4B). Both frugivorous and nectarivorous birds and bats, by contrast, express hexokinase activities that are well above those of other flying birds and bats, and non-flying mammals (Fig. 4B). Hexokinase activities in the pectoralis of frugivorous and nectarivorous birds and bats range between 15.9 and 21.1 μmol min^{-1} g^{-1} wet tissue, whereas in other birds and bats, values range from 0.2 to 10.0 μmol min^{-1} g^{-1} wet tissue – similar to the range of activities seen in skeletal muscles (e.g. gastrocnemius) of non-volant mammals (0.5 to 7.1 μmol min^{-1} g^{-1} wet tissue). These differences underscore the key importance of hexokinase as a component of the sugar oxidation cascade (Fig. 3). Indeed, overexpression of hexokinase in mouse muscle is associated with a greater capacity for glucose uptake from the circulation (Chang et al., 1996). Even in the leg muscles of non-volant mammals, high capacities for anaerobic or aerobic glycogenolysis are not accompanied by high maximal hexokinase activity. Instead, the much lower hexokinase activity, and comparatively lower glucose transport capacity, of these muscles is sufficient to support glucose phosphorylation rates that underlie glycogenesis during periods of low activity and a fraction of glycolysis during exercise.

It is also notable that the flight muscles of small, flying vertebrates tend to have much smaller glycogen stores than the muscles of non-volant mammals (Potter et al., 2021; Suarez et al., 1990). For example, Potter et al. (2021) performed metabolomic analyses on the pectoralis muscles of 16 New World bats and found that glycogen levels are <1 μmol g^{-1} across nectarivorous, frugivorous and insectivorous species (Potter et al., 2021). In contrast, the gastrocnemius muscle of rats (*Rattus norvegicus*) contains ∼20–30 μmol g^{-1} of glycogen (Coderre et al., 2007). The low glycogen levels in bats further emphasize the fact that muscle glycogen stores probably function to buffer intracellular flux through glycolysis rather than serving as the principal carbohydrate store fueling flight.

The recent explosive growth in available genomic data from diverse taxa has ushered in a new era of molecular evolution studies, including investigations into the evolution of high-sugar diets. In a study examining signatures of selection on genes in several genera of hummingbirds and across three independent evolutions of nectarivory in bats, Potter et al. (2021) identified 49 genes – out of 13,500 examined – showing evidence of parallel positive selection in nectarivorous birds and bats. Many of the genes under positive selection encode key metabolic enzymes associated with carbohydrate metabolism (Potter et al., 2021). However, for most enzymes under positive selection, the activity and regulation of their protein products remain unknown. Potter et al. (2021) performed enzyme activity assays on two such proteins and found that activity of pyruvate dehydrogenase (PDH; a mitochondrial enzyme linking glycolysis to the citric acid cycle) is highest in nectarivorous bats, intermediate in frugivorous bats and lowest in insectivorous bats. Importantly, Potter et al. (2021) did not detect a positive signature of selection on hexokinase, which we highlighted above as an enzyme for which activity is critical to supporting high rates of dietary sugar oxidation in nectar- and fruit-eating bats and hummingbirds. This suggests that the elevated hexokinase activity in these species may result from increased protein levels, rather than changes in catalytic efficiency underpinned by animo acid substitutions. Although 49 genes were found to be under positive selection in at least two of the nectarivorous lineages, none showed consistent positive selection across all four independently evolved nectar-feeding groups (Potter et al., 2021). This pattern suggests that there may be distinct evolutionary 'solutions' to the metabolic challenges posed by specialization on high-sugar diets and highlights the need for continued comparative work to connect genomic changes to physiological function. Indeed, recent work by Osipova et al. (2024) reported that the gene encoding fructose bisphosphatase 2 (FBP2) was inactivated in the ancestral hummingbird lineage, a modification not observed in nectar or fruit bats. FBP2 is a gluconeogenic enzyme expressed in skeletal muscle, and its knockdown in an avian cell line increases glycolysis, enhances mitochondrial respiration and abundance, and upregulates genes involved in mitochondrial respiration and organization (Osipova et al., 2023). The loss of FBP2 in hummingbird flight muscle may be an adaptation that enhances flux through the oxygen transport cascade rather than the sugar oxidation cascade. Still, these findings serve as a reminder that convergent and divergent evolutionary trajectories coexist among vertebrate nectarivores.

Unlike in their hovering counterparts, pattens of fuel use during flight have not yet been reported in other frugivorous bats or birds. Because these species cannot hover as well as hummingbirds and nectar bats (or at all), such investigations have been hampered by the significant logistical challenges associated with studying forward flight. Nonetheless, several lines of evidence suggest that similar metabolic strategies are at play. Notably, fruit bats exhibit similar maximal flight muscle hexokinase activities and post-nectar feeding blood glucose spikes as in nectar bats and hummingbirds. At rest, they oxidize newly ingested glucose as quickly and extensively as nectar bats (Amitai et al., 2010). Likewise, nectarivorous passerines, such as sunbirds, show similar daily fluctuations in respiratory exchange ratio (see Glossary) as hummingbirds, with values ≥1.0 during foraging periods, suggesting a reliance on carbohydrate catabolism (Mata, 2010; Prinzinger et al., 1992). Further study is warranted to test whether these metabolic patterns of fuel use during flight extend to frugivorous and nectarivorous birds, and to bats more broadly.

Fructose, the other nectar sugar

As noted above, blood sugar levels in recently fed hummingbirds and nectar bats reach values that appear to exceed those observed in almost any other vertebrate. In many cases, these measurements are obtained using hand-held blood glucometers, which are favored for their low cost and ease of use (Beuchat and Chong, 1998; Camacho et al., 2024; Kelm et al., 2011). The biochemistry employed in these readers is highly specific to the quantification of glucose. In human blood, in which concentrations of other sugars are typically negligible, this specificity provides an accurate measure of total blood glucose. However, this assumption is clearly violated in nectarivores, in which glucose and fructose are typically equally abundant in the diet and digestive system (Baker et al., 1998; Nicolson and Fleming, 2003). Moreover, the rapid absorption of both glucose and fructose, particularly through the non-discriminating paracellular pathway (Price et al., 2015), ensures that absorption rates of the two sugars are more similar than in most vertebrates. High cardiac output (Suarez et al., 2011) further promotes rapid systemic distribution of both sugars. Indeed, circulating fructose levels of at least 5–10 mmol l^{-1} have been reported in *R. aegypticus* fed fructose solutions (Keegan, 1977) and in *A. colubris* fed sucrose solutions (Ali et al., 2020). Similar circulating fructose levels can be reasonably predicted for nectar bats and other nectarivorous or frugivorous bats and birds.

The presence of circulating fructose at levels that rival mammalian blood glucose levels raises questions about how that fructose is metabolized. In mammals, the intestine plays a central role in fructose metabolism; a substantial portion of absorbed fructose is metabolized in enterocytes before reaching the liver, where it can be converted to glucose, lactate or other intermediates (Herman and Birnbaum, 2021). Comparable data are lacking for nectarivorous birds and bats, highlighting the need for studies quantifying intestinal fructose absorption and metabolism under ecologically relevant feeding conditions. The ability of hummingbirds and nectar bats to rely as much on ingested fructose as on glucose to fuel hovering flight could reflect exceptional capacities for the uptake and use of fructose for gluconeogenesis in the liver or kidneys; fructose would then be remobilized into the circulation as glucose or a partial metabolite for use by flight muscles. However, it could also reflect the direct uptake and utilization of fructose by the exercising flight muscle, a phenomenon that does not occur in the skeletal muscles of other vertebrates to any significant extent. Although direct evidence for substantial fructolysis in the flight muscles of hummingbirds and nectar bats is lacking, several lines of evidence provide some support for this idea. In both hummingbirds and nectar bats, CO_2 derived from fructose oxidation appears in the exhaled breath of hummingbirds and nectar bats as quickly as for glucose (Chen and Welch, 2014; Voigt and Speakman, 2007). If fructose were first metabolized in splanchnic tissue before reaching the muscle, this would presumably delay its full metabolism to CO_2. Immunohistochemical approaches reveal that ruby-throated hummingbird (*A. colubris*) expresses the GLUT5 transporter in the pectoralis at levels that are higher than those in liver, and the transporter is enriched in the plasma membrane sample fraction relative to the cytosolic sample fraction, suggesting substantial fructose uptake capacity (Ali et al., 2020). In contrast, GLUT expression profiles in bat flight muscle have not been thoroughly examined, and expression of GLUT5 in nectar or fruit bat flight muscle remains unknown. Importantly, although Potter et al. (2021) reported convergent positive selection on key fructolytic genes – aldolase B (*ALDOB*) and fructokinase [i.e. ketohexokinase (*KHK*)] – these enzymes are not expressed in flight muscle in hummingbirds (Workman et al., 2018) or in nectar bats (Potter et al., 2021). Nevertheless, hummingbird hexokinase exhibits a maximum enzyme activity (V_{max}; see Glossary) when catabolizing fructose that is ~50% of that observed when catabolizing glucose (12.94 versus 21.09 μmol min^{-1} g^{-1} wet tissue, respectively; Myrka and Welch, 2018). This activity *in vivo* could permit fructose to enter glycolysis as fructose-6P at substantial rates, skipping the catalytic steps that are limited by the absence of ALDOB.

Why evolve the ability to catabolize fructose (along with glucose) in skeletal muscles? In most vertebrates, chronically elevated blood glucose levels can lead to several pathologies, and high levels of fructose are suspected to be equally, if not more, harmful. Specifically, chronically elevated levels of reducing sugars in tissues lead to protein glycation (see Glossary) and crosslinking, resulting in the formation of advanced glycation end-products (AGEs; see Glossary), which are linked to pathologies such as metabolic disease and diabetes mellitus (Goh and Cooper, 2008). In particular, *in vitro*, fructose glycates hemoglobin 7.5 times more rapidly (Bunn and Higgins, 1981) and crosslinks proteins 10 times more rapidly (McPherson et al., 1988) than identical concentrations of glucose. In most vertebrates, low intestinal absorption capacity and rapid uptake by first-pass splanchnic tissues keep circulating fructose levels very low, minimizing glycation risk in systemic tissues. However, the much higher peak postprandial blood fructose levels observed in flying vertebrate nectarivores and frugivores would presumably constitute a substantial glycation stressor. Typically, insulin helps limit glycation risk by rapidly lowering the postprandial peak in blood glucose, but this response is absent in hummingbirds and insufficient in nectar or fruit bats to manage extreme sugar loads. Consequently, blood glucose levels remain elevated for at least 1 h in resting, fasting hummingbirds (Ali et al., 2020) and nectar bats (Camacho et al., 2024). Indeed, Kelm et al. (2011) showed that relative flight activity is strongly correlated with how rapidly blood glucose levels decline from the post-feeding peak in the nectar bat *G. soricina* (now *G. antillarum*), suggesting that flight muscles are a key tissue for absorption and clearance of blood glucose. The relative temporal dynamics of blood glucose and fructose levels have only been reported for a few species of hummingbird (Ali et al., 2020; Beuchat and Chong, 1998; Muhammad, 2021) and one species of fruit bat (Keegan, 1977); in both cases, blood fructose levels drop more quickly during a fast than do blood glucose levels. Together, these findings support the hypothesis that the flight muscles of flying nectarivores and frugivores may have evolved a unique capacity to directly oxidize fructose during exercise, not just to meet energetic demand, but also to mitigate fructose toxicity by rapidly clearing it from the blood. This role is likely to complement continued clearance of fructose by the liver and kidney, and may support the idea that chronically elevated blood glucose levels in these animals are, in part, a result of gluconeogenesis associated with this rapid fructose clearance.

Conclusions and future directions

Although genomic approaches have greatly expanded our ability to detect signatures of selection in gene-coding sequences, identifying positive selection alone does not predict how protein function or metabolic pathway flux may differ *in vivo*. Thus, physiological and behavioral data will continue to be invaluable in understanding how nectar- and fruit-feeding animals manage energy homeostasis despite the various challenges of small body size and high energetic demand. They are also essential for uncovering how these species tolerate or mitigate the adverse consequences of chronically elevated blood sugars. Future efforts must also be turned towards frugivorous bats, birds and even small mammals. Emerging evidence suggests that frugivores, particularly those that can fly, share many, if not all, of the same enhancements to the sugar oxidation cascade seen in nectar bats and hummingbirds. Thus, we hypothesize that nectarivores and frugivores more broadly may possess a remarkable ability to mobilize and oxidize ingested sugars to power energetically demanding behaviors such as forward flight or mating displays. Moving forward, comparative physiologists will need to adopt creative approaches to interrogate fuel use during exercise in these less conveniently studied, but equally fascinating, groups.

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ECR Spotlight

This article has an associated ECR Spotlight interview with Giulia S. Rossi.

Special Issue

This article is part of the special issue 'The Integrative Biology of Exercise', guest edited by Erika Eliason, Christopher Guglielmo, Natalie Holt and Monica Daley. See related articles at https://journals.biologists.com/jeb/issue/229/7.

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