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Matching Gas Exchange in the Bat from Flight to Torpor[1]

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SYNOPSIS. **Many microchiropteran bats can reduce their metabolic rate three orders of magnitude during heterothermic torpor. This extraordinary range provides a unique insight into the adaptability of mammalian ventilatory control and function. To enable powered flight, bats have developed the highest capacity gas exchange system among mammals. However, starving during winter may account for the greatest mortality among bats that hibernate, thus imposing a strong selective pressure to decrease metabolic cost during torpor. This high capacity gas exchange system must therefore operate efficiently at very reduced rates, despite conflicting mechanical constraints imposed by an enormous functional overhead. The bat surmounts this dilemma by adjusting its control strategy to breathe intermittently during torpor. This allows instantaneous breathing rates and tidal volumes near predicted optimal levels. In addition, a passive oxygen influx coupled with a high acidotic tolerance facilitates longer intervals between the breathing bouts. The acidotic tolerance supports the endurance of these apneas because the passive efflux of carbon dioxide does not match the rate of oxygen influx. The acidotic tolerance further helps by allowing carbon dioxide to enrich the alveolar gas during apnea to levels above that of a nonacidotic, continuous pattern of breathing. Thus, the bat's carbon dioxide load can be cleared in fewer breaths when breathing resumes. By efficiently controlling a high capacity gas exchange system to meet the minuscule demands during torpor, the bat demonstrates how physiological control strategies can adapt to overcome limitations imposed by conflicting selection pressures.**

INTRODUCTION

In taking to the air, bats have developed the highest capacity gas exchange system among mammals (Maina *et al.*, 1991). Flying bats can maintain metabolic rates 2.5 to 3 times the maximal rates attainable by similar-sized non-flying mammals (Thomas, 1975). In the opposite extreme, many bat species routinely employ heterothermic torpor, thereby matching their lofty metabolic capacity with an equally impressive metabolic reduction. For the 15 g bat *Eptesicus fuscus*, the highest metabolic cost of flight, based upon Thomas' data and scaling relationships, would be 30.4 mmol O_2/hr (Thomas, 1975). In contrast, at a body temperature of 5°C, this bat consumes only 24.0 μmol O_2/hr (Szewczak and Jackson, 1992*c*), for a total metabolic range of 1,270! Flight is, of course, essential for the livelihood of a bat. However, starving during winter may account for the greatest mortality among bats that hibernate (Wimsatt, 1977; Tuttle and Stevenson, 1987). We should thus expect a strong selective pressure for reducing metabolism during torpor. Yet during torpor the functional overhead of the bat's high capacity gas exchange system could constitute a potential metabolic penalty from inefficiency, just as we might expect when using a jet's engine to slowly taxi along a runway rather than fly.

The mechanical constraints of the bat's ventilatory system may yield energetic compromises, or may have provoked elegant solutions to the contrary selective pressures of flight and torpor. I will review our understanding of the bat's control of blood gases and acid-base state during tor-

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por, and then interpret whether these strategies compromise or enhance metabolic reduction during torpor.

INTERMITTENT BREATHING AND THE WORK OF BREATHING

Intermittent breathing in vertebrates typically occurs during the hypometabolic states of ectothermy, sleep, and torpor (see Malan, 1982; Milsom, 1988), and can best be interpreted as an energy-sparing strategy. The metabolic energy that euthermic mammals devote to breathing comprises only 0.6 to 2% of their total metabolic rate, a level generally regarded to be of minor metabolic significance (Otis *et al.*, 1950; Otis, 1954). However, during heterothermic torpor, somatic metabolism is reduced to pilot-light levels during which breathing and cardiac activity become the primary mechanical energetic expenditures for the animal. Breathing costs the torpid bat *E. fuscus* 5 to 10% of total metabolism, demonstrating an elevated relative cost over euthermia and an arguably significant portion of a tight energy budget (Szewczak, 1991).

The benefits of intermittent breathing follow from pulmonary mechanics. Reducing the cost of breathing requires matching the dynamics of the respiratory system with sufficient tidal volume to overcome dead space volume. The pace at which respiratory muscles move and the velocity of airflow through conducting airways constrain allowable frequencies of ventilation. Low tidal volume breathing wastes disproportionate effort ventilating dead space volume, whereas high tidal volume breathing loses effort overcoming elastic recoil forces. As a result, cost per unit volume of alveolar ventilation rises at the low and high end of an animal's range of alveolar ventilation (Otis *et al.*, 1950; Crossfill and Widdicombe, 1961). Thus, supporting the low metabolic demands of torpor with continuous breathing would usurp the energy-sparing objective of torpor. The bat solves this dilemma by supplanting continuous breathing with intermittent bouts in which the tidal volume and frequency within these bouts (instantaneous frequency) are at more optimal values.

For torpid *E. fuscus*, the observed frequencies within these intermittent bouts are similar to predicted optimal frequencies (Szewczak, 1991). Thus, by cycling its ventilation on and off, the bat uses its high capacity system efficiently, just as a high capacity furnace is cycled on and off to warm a small home. Although the relative cost of breathing during torpor is still high compared to euthermia, the intermittent strategy keeps the *absolute* cost of breathing reasonable, as measured by the ventilation-specific oxidative cost of ventilation. At a body temperature of 10°C, breathing cost *E. fuscus* 0.87 ml O_2 for one liter of ventilation (Szewczak, 1991), comparable to values reported for resting euthermic mammals, 0.2 to 1 mlO_2/L (Otis *et al.*, 1950; Robertson *et al.*, 1977).

LENGTHENING APNEAS WITH PASSIVE OXYGEN FLUX

Calculations of the oxygen stores available to *E. fuscus* suggest that apneas no longer than 17 minutes should be expected at a body temperature of 10°C, despite observed apneas as long as 147 minutes (Fig. 1) (Malan, 1982; Szewczak, 1991; Szewczak and Jackson, 1992*c*). The bat has two options available to replenish oxygen during apnea: cutaneous uptake or passive tracheal flux. The large cutaneous surface of the bat's wing membranes would seem to support the former, but the torpid bat keeps its wings folded during torpor. Even with outstretched wings, however, cutaneous uptake cannot account for the required oxygen replenishment during apnea (Herreid *et al.*, 1968; Szewczak and Jackson, 1992*c*). Thus the latter option of passive tracheal flux demands consideration.

Passive tracheal flux of oxygen functions by oxygen following a concentration gradient down an open airway and is enhanced by a convective influx of air. The convective influx occurs to replace alveolar volume lost to oxygen absorbed, but not entirely replaced by an equivalent volume of carbon dioxide. The mechanical action of the bat's heartbeat likely benefits this process by mixing gases in the small airways. Calculations of the passive tracheal flux of oxygen based upon this model compare favorably with direct measurements of oxy-

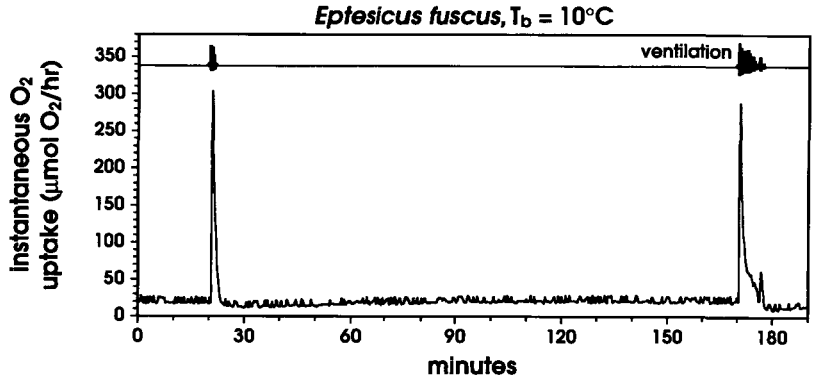

FIG. 1. Simultaneous recording of ventilation and oxygen uptake showing a 147 minute period of apnea from a big brown bat (*Eptesicus fuscus*) torpid at a body temperature of 10°C. Note that oxygen uptake remained above zero during apnea. Minor fluctuations are instrument artifact. More refined measurements with improved signal-to-noise have confirmed this pattern of oxygen uptake during apnea, but this remains the longest apnea recorded to date.

gen uptake during apnea for this bat (*cf.*, Fig. 1) (Szewczak and Jackson, 1992*c*).

The time course of instantaneous oxygen uptake during apnea typically rises sharply from a non-zero rate at the onset of ventilation, reaches a peak and then falls, presumably as depleted oxygen stores are replenished (Fig. 2). The continued ventilation past repayment of the oxygen debt is also consistent with the tracheal flux model because the passive efflux of carbon dioxide does not match the passive influx of oxygen. Carbon dioxide has only a third of the concentration gradient of oxygen, one quarter less diffusivity than oxygen, and must move contrary to the convective influx. Therefore the bulk of the animal's carbon dioxide production must remain sequestered until the next ventilatory bout, accounting for both the continued ventilation and acidosis of blood samples taken toward the end of apneas, as described in the next section.

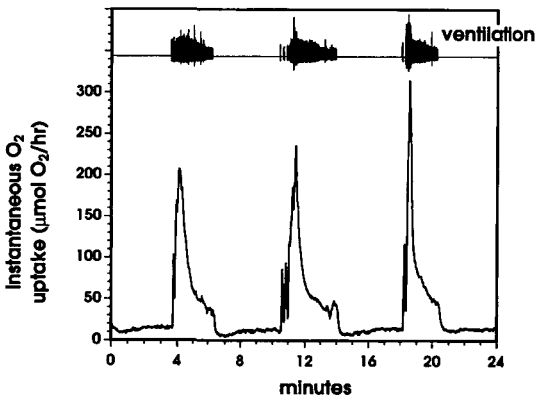

FIG. 2. Simultaneous recording of ventilation activity and oxygen uptake by a 4 g western pipistrelle bat, *Pipistrellus hesperus*. The body temperature of the torpid animal was 10°C. Note that oxygen stores depleted during apnea were apparently quickly abolished (large initial spike) when ventilation resumed. The oxygen uptake during the ventilatory bout then fell to a lower level as ventilation continued, presumably to flush out stored carbon dioxide.

E. fuscus can acquire up to 79% of their total oxygen consumption by this non-ventilatory process. Although the rate of passive tracheal flux moves only a minuscule 21.3 µmol O_2/hr at 10°C, it becomes significant at the reduced metabolic rate of torpor, 35.2 µmol O_2/hr at 10°C (Szewczak and Jackson, 1992*c*). It should be noted, however, that this is a very scale-dependent process. The exponential decrease in diffusional flux with linear distance limits the practical significance of tracheal flux to animals under 100 g (Szewczak, 1994*a*).

INTERMITTENT BREATHING, TORPOR, AND ACID-BASE STATE

The first arterial blood pH samples obtained from torpid *E. fuscus* revealed a disconcerting lack of control. For example, at a body temperature of 20°C, arterial pH varied from 7.30 to nearly 7.60 (Szewczak and Jackson, 1992*a*). This apparent discrepancy in precise physiological control was resolved by coordinating blood sampling with ventilatory state. As previously mentioned,

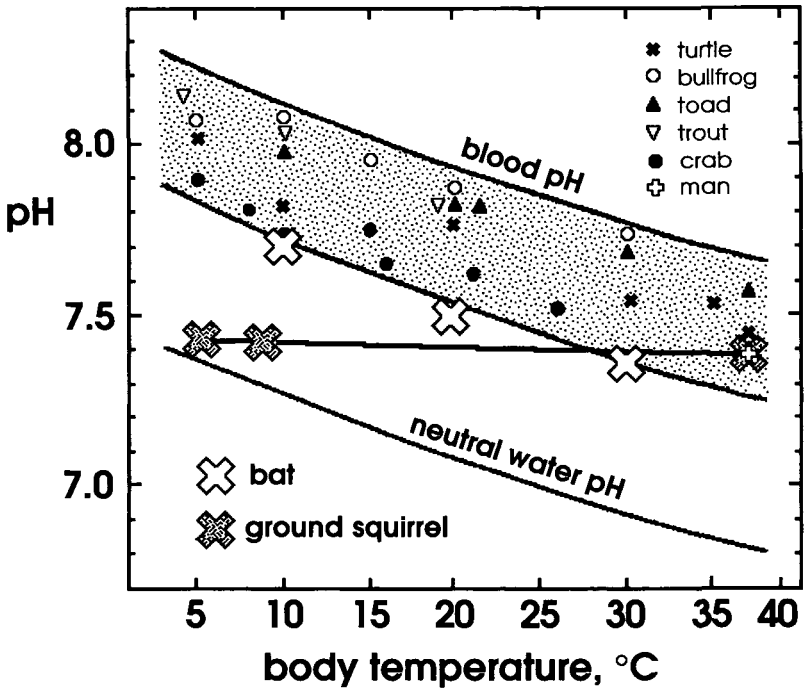

FIG. 3. Arterial blood pH *vs.* body temperature for a variety of ectotherms (from Dejours, 1981) and two heterothermic mammals, a ground squirrel Musacchia and Volkert (1971), and bat (Szewczak and Jackson, 1992*a*). Bat data are end-ventilatory values for *Eptesicus fuscus*.

E. fuscus breathes intermittently during torpor. At a body temperature of 20°C, apneic intervals of 4–12 mins follow ventilation periods lasting 1–2 mins (Szewczak and Jackson, 1992*a*). Arterial blood sampling coordinated with the end of ventilatory bouts revealed an ectotherm-like arterial pH change of −0.011 units per °C body temperature from 10 to 37°C (Fig. 3). Such a pH-temperature relationship maintains a constant [H+]/[OH−] ratio and hence a constant charge state on proteins (Reeves, 1972; Somero, 1981). This acid-base strategy is consistent with the obligation shared by most ectotherms to maintain functional capacity over a range of temperatures.

Because mammalian heterothermy developed out of a selective pressure to reduce metabolism, maintaining biochemical function at euthermic capacity is unnecessary. In fact, alterations that inhibit biochemical function may be desirable. Most heterothermic mammals maintain a nearly constant arterial pH with decreasing body temperature (Reeves, 1969; Musacchia and Volkert, 1971; Malan *et al.*, 1973; Malan, 1982; Heisler, 1986). However, because the pH of neutral water increases with a fall in temperature (Fig. 3), this strategy actually elicits a progressive acidosis with decreasing body temperature. This acidosis has been implicated in reducing metabolism (Malan, 1986; Malan *et al.*, 1988). In this regard, the less acidotic, ectotherm-like, arterial pH regulation of *E. fuscus* may do less to reduce metabolism during torpor. However, this bat still incurs a considerable acidosis during apnea, accounting for the variability in the original acid-base measurements which were made without regard for ventilatory state.

Arterial blood sampled at the end of apneas averaged 0.15 and 0.10 pH units lower than end-ventilatory values at body temperature of 20 and 10°C, respectively (Szewczak and Jackson, 1992*a*). The maximum pH swing during a ventilatory cycle was 0.24 pH unit. Such high fluctuations in arterial pH during a ventilatory cycle have not been observed in torpid rodents or insectivores (Malan *et al.*, 1973; Tähti and Soivio, 1975). Above a body temperature of 30°C,

the thirteen-lined ground squirrel (*Spermophilus teritacaudus*) showed a tendency that was more ectotherm-like than the nearly constant arterial pH of other mammalian hibernators, but did not follow this pattern down to the colder body temperatures at which it typically hibernates (Bickler, 1984). Other studies that considered acid-base state with ventilatory cycle in torpid mammals used subjects at least ten times larger than *E. fuscus*. Perhaps the bat experiences greater swings in arterial pH during apnea because of its comparatively small size and consequent higher mass-specific metabolic rate. However, the thorough ectotherm-like strategy of *E. fuscus* may be unique to chiropteran heterotherms. Nevertheless, the apneic acidosis contributes to reducing metabolic cost in one more way, as described in the next section.

Putting It All Together to Reduce Metabolic Cost

What advantage does passive oxygen uptake confer if the bat must still ventilate to remove carbon dioxide? To interpret this, let us compare how the bat would clear carbon dioxide if, instead of intermittent breathing, it matched metabolic demand with equally-spaced breaths of identical tidal volume to its intermittent breathing (disregard for the moment that such a pattern would be inherently inefficient, as discussed above). For this comparison I will take data from a body temperature of 20°C, and I will assume that the bat regulates in both cases toward the end-ventilatory state of 21.9 torr arterial partial pressure of carbon dioxide (Szewczak and Jackson, 1992*a*). I will also assume a tidal volume of 170 μL (Szewczak and Jackson, 1992*b*) and scaled alveolar ventilation of 150 μL (Leith, 1982).

For the bat that is breathing intermittently, a typical bout of 50 breaths would begin with an arterial carbon dioxide partial pressure of 34.8 torr and end at 21.9 torr. Assuming sea level pressure and alveolar gas concentrations to be equilibrated with arterial blood, the first breath of the bout would expire 6.87 μL of carbon dioxide (at body temperature and pressure) in the 150 μL alveolar ventilation, and the final breath would expire 4.32 μL. Simply modeling an exponential washout over the course of the bout yields a total carbon dioxide expiration of 275 μL (Fig. 4A). For the bat that is breathing continuously, maintaining the desired arterial carbon dioxide level of 21.9 torr means that each breath would only expire 4.32 μL of carbon dioxide. Therefore, to remove the same 275 μL of carbon dioxide would require 64 breaths, 28% more than for the intermittent breather (Fig. 4B). Because breathing is already relatively expensive for the torpid bat, avoiding this extra cost through intermittent breathing is clearly advantageous.

Of course, a third possibility exists if the bat could tolerate a chronic acidosis near the end-apneic arterial carbon dioxide partial pressure of 34.8 torr. With a pattern of appropriately-delayed single breaths, each breath could move the same 6.87 μL of carbon dioxide as the first breath of the intermittent pattern above. Such a pattern would require only 40 breaths to remove the 275 μL of carbon dioxide in the above example, 20% less than for the intermittent breather. Why then does torpid *E. fuscus* not breathe in this pattern? The arrangement of the ventilatory controller may preclude this pattern developing, or there may be some imperative for at least periodically abolishing the acidotic state through the ventilatory bouts. Some rodent hibernators breathe in a single breath pattern, and thus may exploit the advantage offered by this pattern.

Nevertheless, mechanisms that enhance the duration of apnea and permit carbon dioxide accumulation will also reduce the total volume of ventilation and hence its cost. The tolerance of the bat for progressive acidosis permits the retention of carbon dioxide that might otherwise trigger an early end to apnea. However, the bat lacks a matching capacity for storing oxygen. The passive tracheal oxygen flux fulfills this role by supporting apneas beyond what endogenous oxygen stores could achieve. Together with the intermittent breathing pattern, these adaptations satisfy the gas exchange requirements of the torpid bat at minimal energy expenditure despite using a physiological system with tremendous excess capacity.

The acidosis observed in non-chiropteran heterothermic mammals would similarly

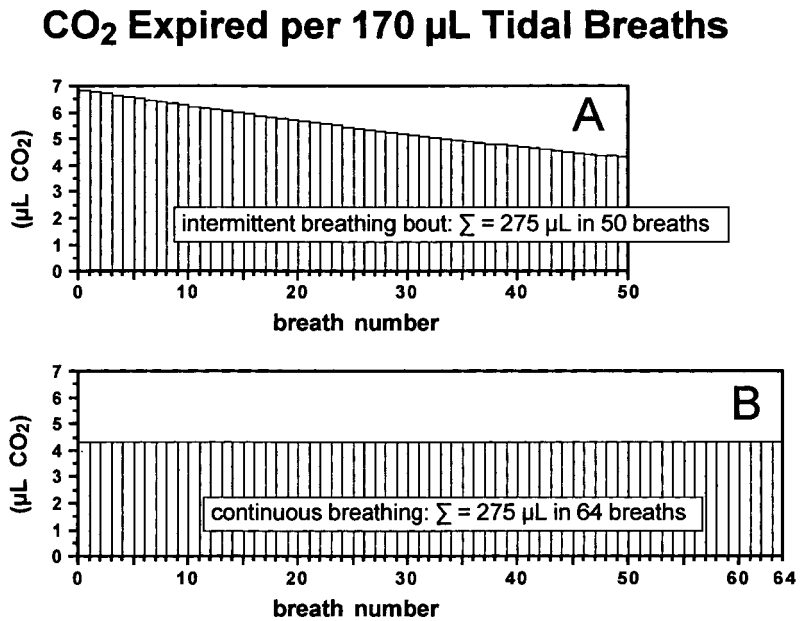

FIG. 4. Comparison of carbon dioxide expired per breath following an apnea (A) with carbon dioxide expired per breath from a hypothetical continuous breather (B) to achieve the same 275 µliter volume of carbon dioxide removal; presuming in each case a final goal of 21.9 torr arterial partial pressure of carbon dioxide in the alveolar gas (see text). For the intermittent breather, the carbon dioxide-enriched alveolar gas at the onset of ventilation reduces the number of breaths required to clear an equivalent volume of carbon dioxide, compared to the continuous breather.

expire more carbon dioxide with each breath and therefore reduce total ventilatory requirement. This effect will benefit animals maintaining an acidotic state independent of whether they incorporated an intermittent pattern of breathing. Furthermore, the ventilatory benefits of high alveolar carbon dioxide concentrations will reduce total metabolic cost in a torpid animal independent of any acidosis-mediated metabolic effects (Malan *et al.*, 1985, 1988).

AN UNREFINED RESPONSE DURING TORPOR

The preceding sections discussed how the bat has responded to the dual selective pressures of flight and torpor with a strategy for gas exchange that functions to meet its needs during either condition, despite the limitations of a single physiological system. In the absence of strong selective pressures, however, refined responses may not develop, or may depart from a previously refined response, *i.e.*, if a vestigial response. Such a response apparently occurs in torpid *E. fuscus* when exposed to hypoxia.

Eptesicus fuscus hibernates in well-ventilated caves and tree trunks where hypoxic conditions would not normally be encountered (Barbour and Davis, 1969). As a consequence, the bat has probably not experienced selective pressure during torpor to refine its hypoxic ventilatory response. Furthermore, the reduced body temperatures of torpor left-shifts the hemoglobin-oxygen dissociation curve (Maginniss and Milsom, 1994). This increases the oxygen affinity of the blood to partially or completely compensate for any hypoxic exposure. This mechanism further reduces the expectation of any hypoxic selective pressure during torpor under natural conditions. Thus, hypoxic exposure in the laboratory is a novel encounter for this animal.

Eptesicus fuscus does, however, remain sensitive to changing inspired gas mixtures during torpor, and its unconscious condition in this state provides consistent, repeatable responses (Szewczak and Jackson, 1992*b*). Interestingly, hypercapnia and hypoxia elicit distinctive patterns of breathing. Hypercapnia tends to elicit rhythmic, steady tidal volumes whereas hypoxia elicits irregular tidal

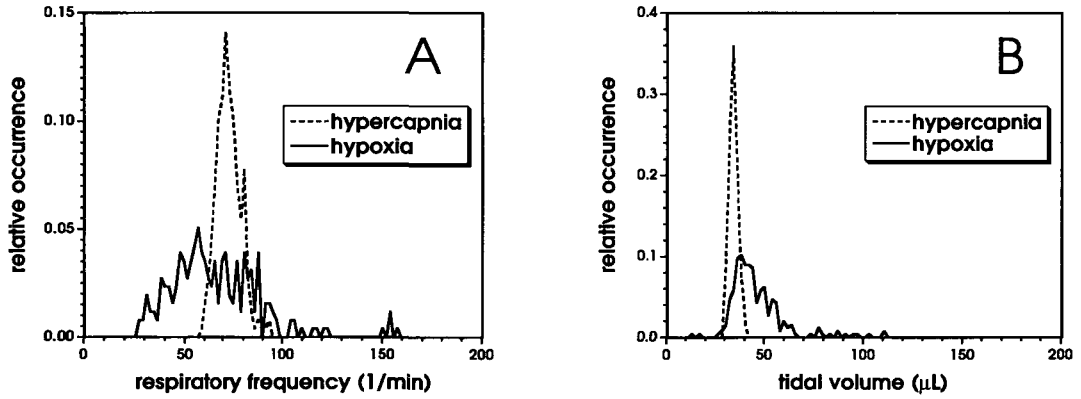

FIG. 5. Comparison of relative occurrence of respiratory frequency (A) and tidal volumes (B) from hypoxic and hypercapnic-stimulated breathing from a 20°C *E. fuscus*. Despite approximately equivalent minute volumes in each case of triple the normoxic normocapnic level, the bat displays less regulatory precision in response to hypoxia. The total fractional occurrences under each curve sum to unity.

volumes and arrhythmic breath intervals (Figs. 5A and 5B). Despite approximately equivalent minute volumes from each case, the bat arrives at these levels very differently. In response to hypoxia, the bat apparently lacks the regulatory precision to achieve a presumed optimal frequency or tidal volume as required to minimize the cost of breathing (see discussion above).

Fractal analysis can help determine whether the observed variation in the hypoxic ventilatory response signifies the random fluctuations of imprecise control or an intended regulatory strategy. Instantaneous respiratory frequency and tidal volumes can be collected into time series and then interpreted using the relative dispersion dimension, dim(RD). A dim(RD) value of 1.0 indicates a perfectly correlated series and 1.5 perfectly uncorrelated, as from a random process (Bassingwaighte *et al.*, 1994). In 6 bats at a body temperature of 20°C, hypercapnia that tripled minute volume over normoxic normocapnic levels had identical dim(RD)'s of 1.08 ± 0.01 for both frequency and tidal volume. However, hypoxia that tripled minute volume over normoxic normocapnic levels had significantly greater dim(RD) of 1.24 ± 0.02 for frequency and 1.22 ± 0.02 for tidal volume. (Gas levels were adjusted to triple the minute volume of individual bats: approximately 22 torr carbon dioxide for hypercapnia, and 34 torr oxygen for hypoxia; Szewczak, 1994. This bat can withstand hypoxia down to 22 torr oxygen at this temperature.)

The lower correlation of hypoxic-stimulated breathing indicates less regulatory precision compared with the hypercapnic response. This may result from the manner in which the ventilatory controller processes oxygen chemoreception, or a pathological response to hypoxia or the consequential respiratory alkalosis. Nevertheless, the irregular tidal volumes and instantaneous frequencies of hypoxia constitute a more energetically-costly response according to the cost of breathing analysis discussed earlier (Otis *et al.*, 1950; Crossfill and Widdicombe, 1961).

CONCLUSIONS

Eptesicus fuscus presents an interesting example of an organism that has adapted to changing needs by adapting its available resources. By efficiently controlling a high capacity gas exchange system to meet the minuscule demands during torpor, this bat demonstrates that the method by which an animal regulates a physiological system can be as influential as the physical arrangement of that system. Bartholomew (1987) noted that natural selection produces systems that function no better than they must. The crude hypoxic response of torpid *E. fuscus* functions adequately for an animal with limited hypoxic exposure. But controlling its gas

exchange system efficiently during torpor is a greater *must* that provided the selective pressure for a more refined solution. Although the morphometry of this bat's gas exchange system provides a system that can function better than it must during torpor, it meets the selective imperative of efficient function by the manner of its control rather than its functional capacity.

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