INVITED PERSPECTIVES IN PHYSIOLOGICAL AND BIOCHEMICAL ZOOLOGY

The Provenance of Alveolar and Parabronchial Lungs: Insights from Paleoecology and the Discovery of Cardiogenic, Unidirectional Airflow in the American Alligator (*Alligator mississippiensis*)

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ABSTRACT

Birds and mammals evolved greater aerobic abilities than their common ancestor had. This required expansion of the cardiopulmonary system's capacity for gas exchange, but while directional selection for this expanded capacity resulted in extremely similar avian and mammalian hearts, strikingly different lungs arose, and the reasons for this divergence in lung morphology are not understood. In birds, gas exchange occurs in the lungs as air moves through small tubes (parabronchi) in one direction; in mammals, air flows tidally into and out of the alveoli. Here, I present a scenario for the origin of both the alveolar and parabronchial lungs that explains when and how they could have arisen by a gradual sequence of steps. I argue that (1) the alveolar lung evolved in the late Paleozoic, when high levels of atmospheric oxygen relaxed selection for a thin blood-gas barrier within the lung; (2) unidirectional flow originated in the ectothermic ancestral archosaur, the forerunner of birds and crocodilians, to enable the heart to circulate pulmonary gases during apnea. This hypothesis would be supported by a demonstration of unidirectional flow in the lungs of crocodilians, the extant sister taxon of birds. Airflow in the lungs of juvenile alligators was measured during apnea using dual thermistor flowmeters, and cardiac activity was measured with electrocardiography. Coincident with each heartbeat, a pulse of air flowed in the pulmonary conduit under study with a bias in the direction of movement, yielding a net unidirectional flow. These data suggest the internal structures requisite for unidirectional flow were present in the common ancestors of birds and crocodilians and may have preadapted the lungs of archosaurs to function advantageously during the oxygen-poor period of the early Mesozoic.

Introduction

The functional basis and historical factors underpinning the structural diversity of the vertebrate lung are not completely understood. For most vertebrates, the primary function of the lung is gas exchange, and so the question of how and why strikingly diverse lungs evolved to serve the same function has interested both scientists and laypersons and has resulted in controversy concerning the origin of these structures. Generally, scientists agree that when placed in a phyletic and historical context, the diversity of the vertebrate lung "illustrates the principle that the emergence of seemingly new structures such as the mammalian lung is due to intensification of one of the functions of the original piscine lung" (Liem 1988, p. 739). In contrast, out of a historical context, the stunning diversity appears so miraculous that the bird lung has even been propounded to refute evolution. For example, Michael Denton, who was instrumental in inspiring the intelligent design movement, states,"the structure of the lung in birds and the overall functioning of the respiratory system is quite unique. No lung in any other vertebrate species is known which in any way approaches the avian system. … Just how such an utterly different respiratory system could have evolved gradually from the standard vertebrate design is fantastically difficult to envisage" (Denton 1985, pp. 211–212). However, careful study of the crocodilian lung reveals remarkable similarity with the avian respiratory system (Perry 1988, 1990*a*, 1992). Nonetheless, some dinosaur biologists remain skeptical of this transition and suggest that the "highly efficient" lung of birds could not have arisen from the "inefficient" crocodilian-type respiratory system. To this debate about how bird lungs evolved, I contribute experimental data of unidirectional, cardiogenic airflow in the crocodilian lung that corroborates the scenario of the bird lung arising from a crocodilian-type precursor. Furthermore, I propose a scenario for lung evolution that envisages when and why the lungs gradually changed from the type presumably present in the ancestral amniote to a homogenous alveolar morphology in the synapsids, the lineage containing mammals, and to a heterogeneous form presumably present in the basal archosaur, the lineage containing both crocodilians and birds. I propose that the alveolar lung originated in Paleozoic therapsids rather than mammals as they underwent selection for greater abilities

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to sustain locomotion and that the oxygen-rich atmosphere that was apparently present during the radiation of Paleozoic therapsids relaxed selection against a relatively robust blood-gas barrier and was pivotal to the evolution of the alveolar morphology. I also hypothesize that the archosauromorphs of the Late Permian or Early Triassic evolved unidirectional airflow in their lungs because it allowed the heart to pump pulmonary gases during apnea (breath holding) and that this design was an exaptation for a respiratory system readily tailored to function in the low levels of atmospheric oxygen of the Mesozoic.

The complexity of unraveling the evolutionary history of a soft structure that has left no direct fossil record is a challenge to scientists, yet it is not an impossible undertaking. Much of the evolutionary history of the lung can be inferred by integrating the first principles that underpin the designs of gas exchangers with knowledge of how the varied respiratory systems of extant vertebrates function and their phyletic relationships (Perry 1992; Perry and Sander 2004). In the case of birds and mammals, it is clear that their lungs are very specialized for the purpose of sustaining vigorous exercise (Liem 1988; Maina 2000). Because expansion of aerobic capacity is mechanistically tied to a number of skeletal innovations that are preserved in the fossil record, it is possible to determine approximately when the lungs of these lineages underwent selection for enhanced aerobic capacity. These skeletal innovations indicate that the aerobic capacities of the lungs of synapsids greatly expanded in the late Paleozoic, while the aerobic capacities of the lungs of archosauromorphs greatly expanded in the early Mesozoic, and it is now believed that oxygen levels differed considerably during the Carboniferous and Permian periods compared with the Triassic and Jurassic periods. Levels of atmospheric oxygen could play a key role in the evolution of lung structures, and therefore, scenarios for lung evolution should be updated to include this information on the paleoatmosphere. Hence, in this article, I integrate information from the following four areas to formulate a hypothesis for the divergent evolutionary trajectories of synapsid and archosaur lungs: (1) the fossil evidence for when the aerobic capacities of the lungs expanded in synapsids and archosaurs; (2) paleoecological theories of the levels of oxygen present in the late Paleozoic and early Mesozoic; (3) first principles of lung design; and (4) neontological data of lung form and function in mammals, crocodilians, and birds.

A Synopsis of Tetrapod Evolution

Osteology reveals a great deal about how the musculoskeletal system of vertebrates gradually evolved from being specialized for movement in water to being adapted for movement over land and through air. In contrast, there is no fossil record of lungs, hearts, or many of the other soft structures that evolved in tandem with the skeletal anatomy; however, it is possible to determine something of the evolutionary history of these organs, either by phylogenetic bracketing of characters in extant groups or through osteology when these soft structures have bony correlates. A functional nexus between tetrapod posture and gait and aerobic capacity provides some insight into the evolutionary history of the soft organs that determine aerobic capacity (Perry 1992; Perry and Sander 2004).

Early tetrapods lived either a fully aquatic or an amphibious lifestyle and therefore had short, paddlelike limbs and trunks designed exclusively or primarily for locomotion in water (Romer 1966; Carroll 1988; Clack 2002). With the origin of the amniotic egg, the full conquest of the land commenced because amniotes could reproduce in a terrestrial environment, but the postcranial skeletons of the earliest amniotes remained very similar to anthracosaurian amphibians (Fig. 1), indicating that these animals still lacked advanced abilities to locomote on land and to use costal ventilation (Janis and Keller 2009). *Hylonomus*, an Early Carboniferous amniote, is representative of the early stock, with short, thick limbs, a sprawling posture, and ribs throughout the trunk. Phylogenetic bracketing indicates these animals had very large and simple saclike lungs with a few internal partitions (Perry 1998); that they breathed intermittently; that their cardiac ventricles were composed primarily of spongy myocardium and had a limited capacity to generate high systemic blood pressures, which are needed to support sustained activity (reviewed in Farmer 1999); and that the majority of the ATP needed during intense levels of exercise was made through anaerobic biochemical pathways, just as it is in many extant ectothermic tetrapods (Bennett 1978, 1991).

Amniotes are monophyletic (Clack 2002); that is, they share a single common ancestor. Thus, all extant lineages of amniotes radiated from one ancestral stock with a build and presumed physiology similar to *Hylonomus*. A gradual change from this stout skeletal morphology to forms better adapted to terrestrial locomotion is well documented in both the Synapsida and in the Archosauromorpha (Romer 1966; Carroll 1988; Benton 2005). Many members of both radiations evolved musculoskeletal specializations indicative of greater agility and an enhanced capacity for sustaining vigorous locomotion. For example, members of the Archosauromorpha and the Synapsida evolved a parasagittal posture (Brink 1956; Bakker 1971; Kemp 1978; King 1981, 1985; Parish 1986; Sereno 1991; Blob 2001; Fröbisch 2006), which is functionally correlated with an ability to sustain vigorous exercise (Carrier 1987*a*, 1987*b*). Among extant tetrapods, a sprawling posture and lateral undulatory movement of the trunk during locomotion constrain simultaneous running and costal ventilation, which in turn limits the ability of these animals to sustain vigorous locomotion (Carrier 1987*a*, 1987*b*; Owerkowicz et al. 1999; Farmer and Hicks 2000). Furthermore, later members of these lineages evolved a more cursorial form of locomotion (animals that can run efficiently and quickly). Typical characters that evolve in cursors include elongated legs, a digitigrade posture, and loss or fusion of distal bony limb elements (Romer and Parsons 1977). In summary, a suite of musculoskeletal specializations has been documented in the fossil record of Archosauromorpha and the Synapsida that makes it possible to determine when members of these lineages began to specialize as endurance athletes and expand their aerobic capacities.

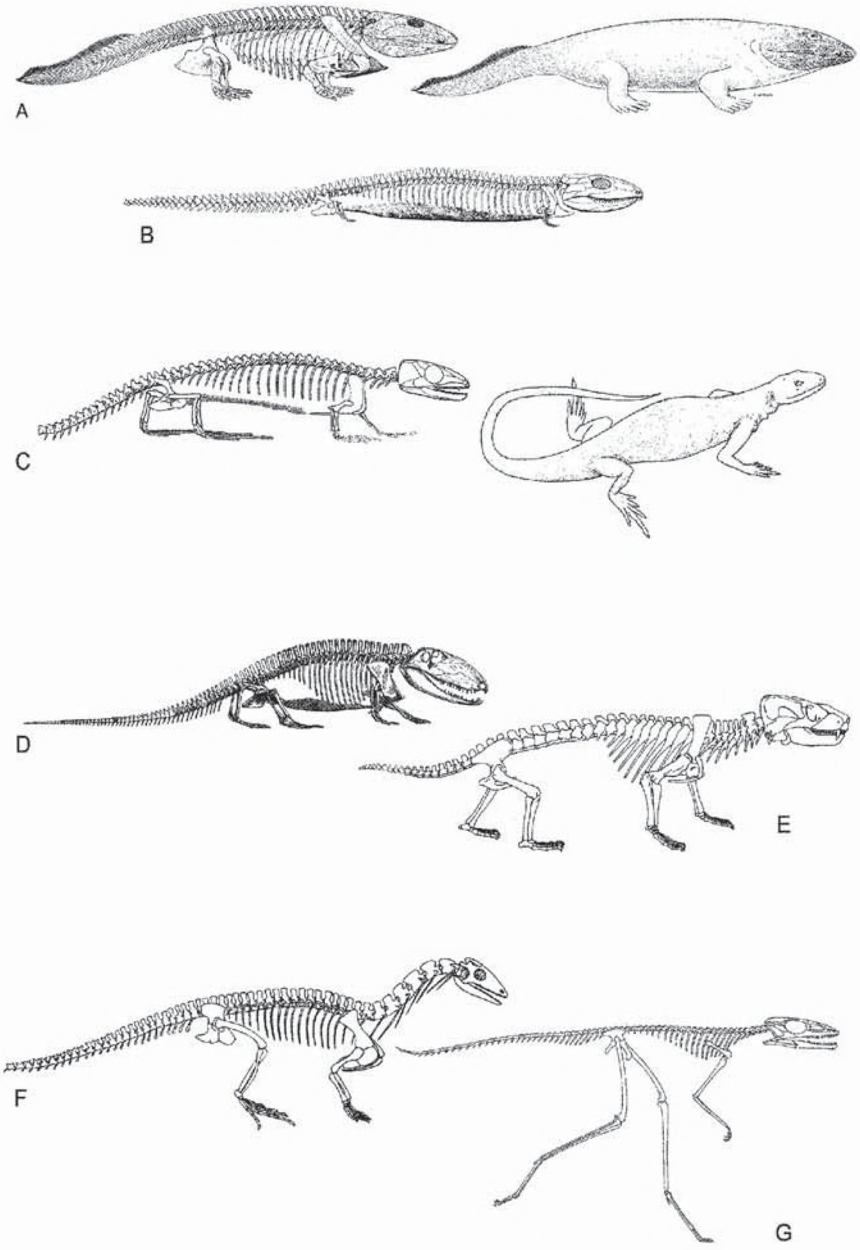

Figure 1. Illustration of the relative changes in the axial and appendicular skeletons of tetrapods. *A*, Skeletal restoration of the amphibian *Ichthyostega* (*left*) from the Upper Devonian of East Greenland, about 65 cm long (large specimens probably reached a length of about 1 m). Reconstruction of *Ichthyostega* (*right*) with soft tissues. Both images are from Jarvik (1955). *B*, Anthracosaurian amphibian *Pholidogaster*, which is a secondarily aquatic form from the Lower Carboniferous of Scotland (about 17 cm long). Image is from Romer (1966). *C*, Skeletal reconstruction of the amniote *Hylonomus lyelli* (Westphalian; *left*) from the Pennsylvanian. Skeleton as shown (without full tail) is about 21 cm long. Reconstruction of *Hylonomus lyelli* (*right*) with soft tissues. Both images are from Carroll and Baird (1972). *D*, Skeletal reconstruction of *Ophiacodon mirus*, a pelycosaurian synapsid, about 167 cm long. Image is from Romer and Price (1940). *E*, Skeletal reconstruction of the synapsid *Thrinaxodon*, about 0.5 m long. Image is from Jenkins (1984). *F*, Reconstruction of *Protorosaurus*, an early archosauromorph from the Upper Permian, 1–2 m long. Image is from Carroll (1988). *G*, Skeletal reconstruction of *Scleromochlus taylori*, a basal Avemetatarsalia from the Late Triassic (late Carnian), of Lossiemouth, northeast Scotland (approximately 18 cm long). Image is from Benton (1999).

The early synapsids are traditionally divided into a more primitive group—the pelycosaurs, which were common in the Late Carboniferous but persisted into the Late Permian—and the nonmammalian therapsids—which arose in the Permian and gave rise to true mammals in the latest Triassic (Rubidge and Sidor 2001). These mammal-like reptiles were the predominant group in the terrestrial assemblages of the late Paleozoic in the sense that they were the most diverse and most common large animals in the faunas (Rubidge and Sidor 2001). The pelycosaurs retained the ancestral sprawling posture and stocky limbs (Fig. 1), but many of the early therapsid lineages acquired features foreshadowing the mammalian condition (Brink 1956; Romer 1966; Carroll 1986, 1988; Rubidge and Sidor 2001). For example, many therapsids evolved an erect posture, steeply angled zygapophyses that restricted lateral flexion, distinct lumbar and thoracic regions of the trunk that suggest the presence of a diaphragm, longer more gracile limbs, and a shortened tail (Fig. 1). These features signal increased agility (Walter and Carrier 2002), stamina (Romer 1922; Carrier 1987*a*, 1987*b*; Carroll 1988; Owerkowicz et al. 1999; Farmer and Hicks 2000), and a general progression to a greater aerobic capacity. The lungs and hearts of these animals must have evolved in step with the musculoskeletal system because amniotes are otherwise incapable of sustaining intense locomotion.

Among the archosauromorphs, a parasagittal posture and other locomotor adaptations associated with increased stamina and agility evolved in a later geological period (Romer 1966; Parish 1986; Carroll 1988; Sereno 1991; Carrier et al. 2001; Benton 2005). The ancestry of the archosauromorphs lies in a small, terrestrial, insect-eating diapsid, and the earliest archosauromorphs were superficially lizardlike, resembling members of their sister taxon, the Lepidosauromorpha (Fig. 1). These animals (e.g., protorosaurs, trilophosaurids), which lived in the Late Permian and Early Triassic, radiated extensively in the Triassic, but many retained skeletal features that were similar to the most primitive lizardlike diapsids (e.g., *Chasmatosaurus*). However, by the Late Triassic, many archosaurs appear to have experienced selection for greater agility (Parish 1986; Carrier et al. 2001), cursorial locomotion (Romer 1966; Parish 1986; Carroll 1988; Benton 1999), and stamina. For example, *Scleromochlus* (Fig. 1), a basal archosaur from the Late Triassic, has the gracile, elongated limbs associated with a cursor (Benton 1999). Cursorial adaptations are also seen in other amniote lineages; for example, a number of fast-running species of lizards have cursorial features. However, the synapsids and the archosaurs gained the capacity to sustain high-speed terrestrial locomotion, which is only possible with a parasagittal posture and an expanded cardiopulmonary system as well.

In summary, if a parasagittal posture is a result of selection for an expanded ability to sustain higher levels of activity—and the link between this posture and expanded aerobic capacity in extant lineages supports this idea (Carrier 1987*a*, 1987*b*; Owerkowicz et al. 1999; Farmer and Hicks 2000)—and if this knowledge is integrated with other osteological evidence of activity metabolism (e.g., cursorial adaptations, specializations that enhance agility), then the fossil record suggests that the aerobic capacity of the cardiopulmonary system expanded in the synapsids in the late Paleozoic and in the archosaurs in the Triassic. Still, specific structural details of these changes (e.g., the evolution of parabronchi and alveoli) cannot be pieced together with this line of evidence. However, in all vertebrates, oxygen moves across the gas exchanger and into the blood by passive diffusion, a process that follows simple, well-known physical principles (Weibel 1999), and thus some features of these respiratory systems can be deduced ab initio.

A Synopsis of Principles of Lung Design

To sustain vigorous exercise, animals must obtain oxygen rapidly from the environment and transport it to the mitochondria of their working muscles, where it is used to produce ATP aerobically. Oxygen cascades through a series of steps, which are the same for all amniotes: (1) convection of oxygen into the lungs by ventilation, (2) diffusion of oxygen from the gases of the lung into the blood, (3) convection of oxygen-rich blood to the peripheral tissues, and (4) diffusion of oxygen to the mitochondria (Hicks and Farmer 1999). The lungs, heart, and blood determine the flux of oxygen through the first three steps of this cascade while the muscle sets the flux of the fourth. It is critical to this hypothesis to realize that oxygen is not very soluble in plasma and that almost all of the oxygen carried in the blood is bound to hemoglobin. Thus, directional selection for greater rates of maximal oxygen consumption will favor features in the lung that enhance the saturation of hemoglobin.

The rate of diffusion of a gas ($\dot{V}_{gas}$) through a tissue sheet is proportional to the surface area of the sheet (S), a diffusion constant (D) that depends on the solubility of the gas in the sheet and that is inversely related to the square root of the molecular weight of the gas, and the difference in the partial pressure of the gas on both sides of the sheet ($PA_{gas} - PC_{gas}$) but is inversely related to the thickness of the sheet (t; West 1995):

$$\dot{V}_{gas} = S \times D_{gas_2} \times \frac{PA_{gas} - PC_{gas}}{t}.$$

For rates of oxygen uptake in the lungs ($\dot{V}o_2$), the driving force for oxygen is the gradient in the partial pressure of oxygen between the gases of the lung (PA_{O_2}) and the vascular capillaries (PC_{O_2}). PA_{O_2} depends on the rate of ventilation and on the levels of oxygen in the inspired air, which are low at high altitude and in subterranean habitats and have varied considerably over the course of the earth's history (Berner 2002). PC_{O_2} depends on properties of the blood, especially the amount of hemoglobin present, the degree to which the hemoglobin is saturated, and the reaction kinetics between blood and hemoglobin. Rates of oxygen uptake in the lungs are inversely proportional to the harmonic mean thickness (t_{hh}) of the tissues and plasma separating the lung gases from the hemoglobin (Fig. 2; Weibel 1999; Maina 2000; Maina and West 2005). Importantly, for a given time of transit of a red blood cell through a capillary, the thickness of the blood-gas barrier and the gradient in partial pressures determine whether or not the hemoglobin will become saturated. Thus, one way for organisms to adapt to and compensate for a decrease in the gradient driving diffusion, such as that seen under conditions of environmental hypoxia, would be to evolve a thinner blood-gas barrier.

The capacity of the lung for gas exchange could expand with the evolution of more surface area, a thinner blood-gas barrier—although the thinner the barrier, the weaker the interface (West et al. 1991; Weibel 1999; Maina 2000; Maina and West

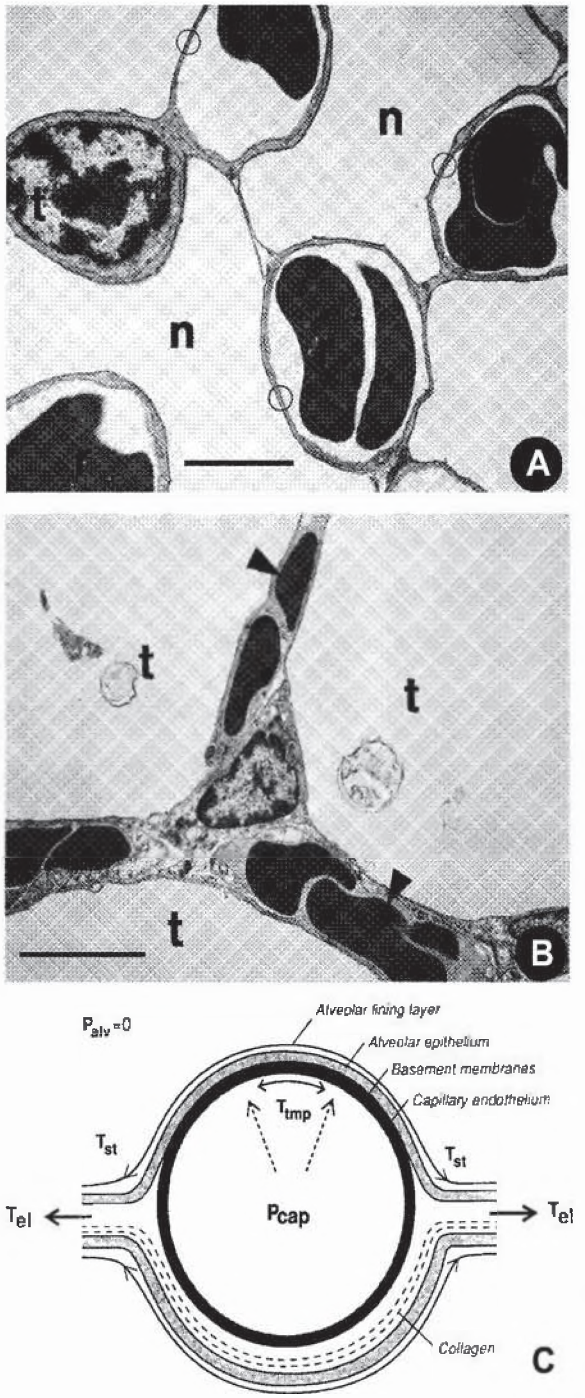

Figure 2. *A*, Photomicrograph showing the structure of the lung of a bird, *Gallus domesticus*. Air capillaries (*n*) and blood capillaries filled with red blood cells (*r*). The blood-gas barrier (*circles*) is very thin (scale bar, 8 μm). *B*, Cross section of the lung of the epauletted fruit bat, *Epomophorus wahlbergi*, alveoli (*t*; scale bar, 50 μm; arrowheads show blood capillary containing red blood cells). Both images are from Maina (2000). *C*, Model of the forces acting on the capillaries of alveolar lungs. T_{tmp}, the circumferential (*hoop*) tension caused by the transmural pressure in the capillary; T_{el}, longitudinal tension in the alveolar wall caused by lung inflation; T_{st}, surface tension of the alveolar layer; P_{alv}, alveolar pressure; P_{cap}, capillary pressure. Model from West et al. (1991).

2005)—or some combination of the two. For reasons that are unknown, mammals increased their pulmonary capacity primarily through an increase in surface area, whereas birds thinned the barrier for diffusion and increased the surface area (Fig. 3). This fact is one of the most important points of divergence in the design of the avian and mammalian lung. Given that these lungs started from the same initial condition, why did one group of amniotes respond to selection for increased aerobic capacity so differently from the other?

The shape of the terminal units of the gas exchanger in birds and mammals are also distinct from each other and from the ancestral condition. Unfortunately, the evolutionary relationships of these terminal gas-exchange units have been obscured by a specialized and sometimes confused terminology, leading to the misconception that these structures are homoplasious rather than homologous. This terminology is extensively reviewed and sorted out by Perry (1998). Here, I briefly summarize his review. Alveoli, meaning "little cavity" in Latin, traditionally refers to the gas-exchange units in the lungs of fish (Maina and Maloiy 1985), amphibians (Smith and Campbell 1976), sauropsids (Brooks 1970), and mammals. The term "sauropsids" is used here to mean diapsids + anapsids (Benton 2005). However, because the alveolar structures of fish, amphibians, and sauropsids are distinct from the mammalian alveoli, several terms have been coined to specify this variation. Trabeculae are terminal gas-exchange units that are fused with the inner wall of the lung without free septa, faveoli are deeper than they are wide, ediculae are wider than they are deep, mammalian alveoli are much smaller (up to 1,000-fold) than ediculae and faveoli, and the avian parabronchi are tubular with radiating air capillaries; the air capillaries are the true terminal respiratory units of birds (Duncker 1978*b*; Perry 1998). These distinctions are not necessarily made along species lines. Many of these terminal respiratory units are found within the same lung of one individual, and these types can merge with one another without forming distinct boundaries. For example, the saclike portions of the lung of chelonians, lizards, and amphibians often possess trabecular parenchyma, while ediculae and faveoli are found in other regions. The respiratory systems of snakes and birds contain saclike regions completely lacking gas-exchange surfaces—aparenchymal regions—and these regions are called air sacs in birds (Perry 1998). Importantly, phylogenetic bracketing indicates that the mammalian alveoli and the avian parabronchi arose through modifications of the faveoli/ediculae of their common ancestor.

The way gases move through the lung also differs among taxonomic groups, but again, these differences should not cause confusion regarding homology. I will return to this point later in the article when I discuss airflow in the lungs of alligators. Airflow is determined by the presence or absence of intrapulmonary airways, such as intrapulmonary bronchi, and by the degree and type of septation present. As mentioned previously, in some animals, the lung is a single chamber, like a balloon, and the primary bronchus terminates at the lung hilus (Perry 1998). The respiratory units line the wall or project into the lumen exclusively from the wall. In many vertebrates the lungs

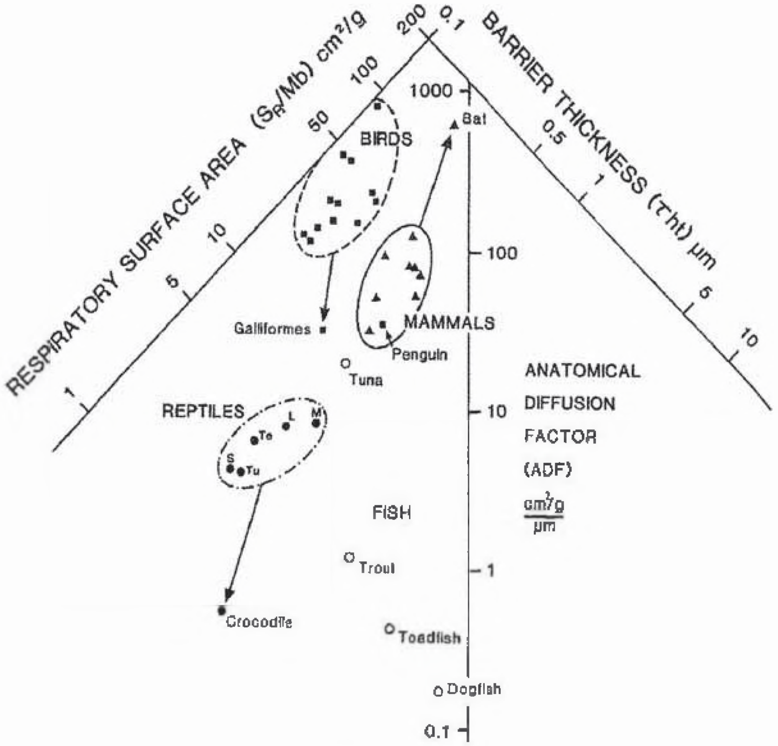

Figure 3. Triple logarithmic plot of mass-specific harmonic mean thickness of the blood gas barrier, the respiratory surface area, and the anatomical diffusion factor (ADF). *L, Lacerta* spp.; *M, Varanus exanthematicus*; *S, Pituophis melanoleucus*; *Te, Tupinambis nigropunctatus*; *Tu, Trachemys scripta elegans*. Graph is modified from Perry (1990*b*).

are partitioned, for example, in lungfish (Maina and Maloiy 1985), turtles, mammals, varanid lizards, chamaeleonid lizards, birds, and crocodilians (Perry 1983). The septa not only influence the way gases move in the lung, they also provide a base for expanding the gas-exchange surface area. As mentioned previously, the distribution of the parenchyma ranges in the respiratory system from homogeneous (e.g., mammals, *Sphenodon*) to heterogeneous (e.g., birds, snakes; Perry 1998). The parenchyma-poor saclike regions are frequently called dilations and serve for storage and distribution of gas rather than in gas exchange. Perry and Dunker have addressed at length the fact that these dilations are more compliant than regions of the system that are heavily invested with blood capillaries and therefore more readily expand and contract during ventilation (Perry and Duncker 1978, 1980; Perry 1998). In birds, all ventilation is accomplished with these nonrespiratory dilations (air sacs). This is important because it has allowed the lung to maintain a constant volume and the blood-gas barrier to become extraordinarily thin (Maina 1998; Maina and West 2005). Finally, and importantly, these differences in heterogeneity form a continuum, not distinct categories, and thus it is easy to envisage an evolutionary sequence of small modifications in the degree of heterogeneity and the degree of septation that yielded the diversity in structure seen in extant lineages (Liem 1988). The intriguing question is not how did it happen in a mechanistic sense but what were the selective pressures that caused the lungs to diverge?

Scenario for the Origin of the Alveolar Lung

Divergent evolution results from the accumulation of differences between groups that can occur as the groups adapt to different environments or different niches or by the process of random drift (Breitwisch 2001). It is tempting to try to explain the divergent lung designs of birds and mammals with random drift. However, it is unlikely that the extraordinarily convergent hearts of birds and mammals experienced directional selection but the lungs did not because both hearts and lungs serve the oxygen cascade. Because these steps occur in series, selection on the heart for an expanded ability to convey oxygen without simultaneous selection on the other steps of the cascade, such as the lung's diffusive capacity, would create a bottleneck and would not enhance gas exchange. The oxygen cascade is an extensively integrated system, and thus directional selection for expanded gas-exchange capacity must act concurrently on all steps of the cascade. Therefore, it is improbable that random drift explains the divergent lung designs of birds and mammals. It is also tempting to attribute the difference in the pulmonary designs to different niches: the use of flight in birds as a mode of locomotion (Torday et al. 2007) rather than walking and running in mammals. In this view, the same type of selective pressure yielded the parabronchial and alveolar lungs (expansion in aerobic capacity), but it was more strongly exerted on birds because flight is a more energetically demanding form of locomotion (Harrison and Roberts 2000). However, the gas-exchange capacity of the lungs of bats is as impressive as the capacities found in birds (Maina 2000), and so flight alone cannot explain the difference.

A possible third explanation for the divergent lung designs is that the divergence arose because the lineages adapted to an athletic lifestyle under different levels of environmental oxygen (Fig. 4), and the level of oxygen in the atmosphere was a pivotal factor in natural selection favoring a strong, stretchy blood-gas barrier or a very thin but fragile blood-gas barrier. Vertebrates suspend their blood vessels in the lung by a fibroskeletal framework of a three-ply design (Maina and West 2005). An extracellular matrix composed of collagen, elastic tissue, and, in many animals, smooth muscle is sandwiched between squamous endothelial and epithelial cells (Maina and West 2005). The strength and stretchiness of the matrix is due to these fibers. The matrix must be strong enough to maintain its integrity as the hydrostatic pressures generated by the heart apply pressure to the walls of the vessels and as the vessels are stretched while the lungs expand and contract during breathing (Fig. 2C; West et al. 1991; West 2000); if the integrity of the capillary walls fails, bleeding in the lung puts an end to gas exchange (West et al. 1991; Maina and West 2005). However, these structural elements thicken the barrier to diffusion and impede the movement of oxygen from the gases of the lungs to the blood. Thus, vertebrates face conflicting functional demands on this critical element of lung morphology, and a balance must be struck between opposing selective pressures. Maina and West (2005) have termed this the "bioengineering dilemma" in the design of the blood-gas barrier, but to an evolutionary biologist, this is a constraint where natural selection will constantly weigh the costs of a thin barrier against the benefits or circumvent the constraint altogether. As already mentioned, birds have partially circumvented the constraint because their capillaries are located in a lung of constant volume, and therefore these vessels can be very thin walled (Figs. 2, 3). In birds, the barrier contains fewer supportive elements than in mammalian lungs, and the extracellular matrix is often lacking altogether where the capillaries lie back-to-back (Maina and West 2005). On the other hand, in mammals, the balance between a thin or strong blood-gas barrier favored strong, because most of the increased gas-exchange capacity evolved in this lineage as a consequence of greater surface area rather than thinner barriers (Fig. 3). But the question is why should birds and mammals have evolved in such different ways?

The high levels of atmospheric oxygen present in the Carboniferous and Permian (Fig. 4) may have tipped this balance between a thin or a strong blood-gas barrier in favor of strength by relaxing selection against a thick barrier. As previously mentioned in the above discussion of first principles of lung design, the flux of oxygen ($\dot{V}O_2$) from the gases in the lung into the blood is directly proportional to the driving force for diffusion ($PA_{O_2} - PC_{O_2}$) and inversely proportional to the barrier thickness (t_{hb}):

$$\dot{V}O_2 \propto \frac{PA_{O_2} - PC_{O_2}}{t_{hb}}.$$

As previously mentioned, it is critical to appreciate the important role hemoglobin plays in the flux of oxygen. For example, the equation predicts that oxygen flux will double if the barrier thickness is reduced by a factor of two, but this is not the case once the hemoglobin that is passing through the capillaries becomes saturated with oxygen (PC_{O_2} elevates) because almost no oxygen is carried in the dissolved form in plasma. Once the hemoglobin is saturated, then neither a thinner blood-gas barrier nor a greater driving force for diffusion will increase oxygen transport significantly. In other words, when PA_{O_2} is high enough to result in complete saturation of the hemoglobin passing through the capillary, then thinning the barrier does not significantly improve gas exchange. Under these conditions, the only way to increase the diffusive capacity of the lung is to increase the number of capillaries present so that more unsaturated blood can be carried into the lung; in other words, to increase the gas-exchange surface area. In contrast, if an animal experiences selection for expanded diffusive capacity of the lung when the driving pressure (oxygen tension in the lung) is low enough that the hemoglobin is not saturated, then the animals will experience stronger selection for a thinner blood-gas barrier, and this, in turn, will favor lungs in which the blood vessels are located in regions receiving the least mechanical stress, that is, regions that change little in volume with each ventilation. Thus, I suggest that fundamentally different costs and benefits regarding this evolutionary constraint occur when a lung undergoes selection for expanded diffusive capacity under high PA_{O_2} compared with when PA_{O_2} is low. As long as the ratio of the driving pressure for oxygen to thickness of the blood-gas barrier is great enough for the hemoglobin to become saturated as the blood passes through the capillaries, then the selective pressure to thin the barrier will relax. However, because a thin barrier runs the risk of rupture, a negative selective pressure will always be exerted against thinning the barrier.

As in the case of the alveolar lung, we lack a fossil record of the avian lung. The common ancestor of modern birds (Neornithes) dates to the Cretaceous (Chiappe 2007), indicating that the minimum date for the origin of the parabronchial lung is in the Cretaceous, and we do not know the lung structure of the Jurassic *Archaeopteryx* to infer whether features such as parabronchi were present before the radiation of Neornithes occurred (O'Connor and Claessens 2005; Ward 2006). However, phylogenetic bracketing can be used to determine something of the plesiomorphic condition of the common ancestors of birds and crocodilians; these ancestors lived during the Triassic Period (Fig. 4; Sereno 1991; Gower and Sennikov 2000).

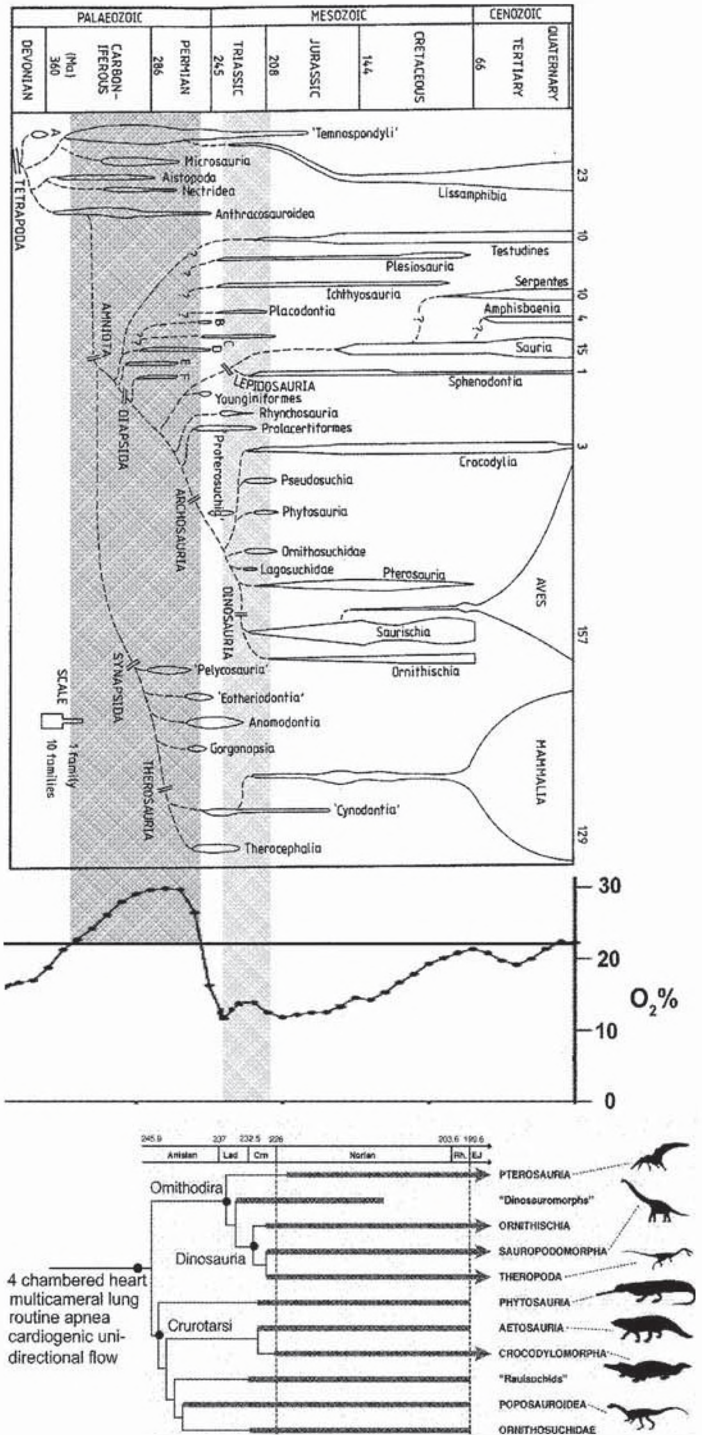

Figure 4. Percentage of Earth's atmosphere composed of oxygen as a function of millions of years before the present and in relation to the radiation of tetrapods. The top panel shows a balloon diagram of major tetrapod families from their origin in the Devonian to the present. The numbers at the top of the graph indicate millions of years ago. The panel is after Benton and King (1989). The vertical dark gray bar indicates a period of Earth's history when atmospheric levels of oxygen are thought to have been above today's values. The light gray bar indicates the point in the Triassic when oxygen values reached their nadir until the end of the Triassic. The right-hand axis of the central panel gives the percentage of oxygen in the atmosphere. The graph of oxygen was modified from Berner et al. (2007). The bottom panel shows the phylogenetic relationships of Triassic archosaurs, modified from Brusatte et al. (2009), that maps several morphological and physiological traits to before the divergence of the Crurotarsi and Ornithodira. The entire radiation occurred when atmospheric oxygen levels (*middle panel*) were below today's values (*horizontal line*). The phylogeny has been scaled to the Triassic timescale. The numbers at the top of the bottom panel are millions of years before the present; durations of major lineages are represented by horizontal gray bars.

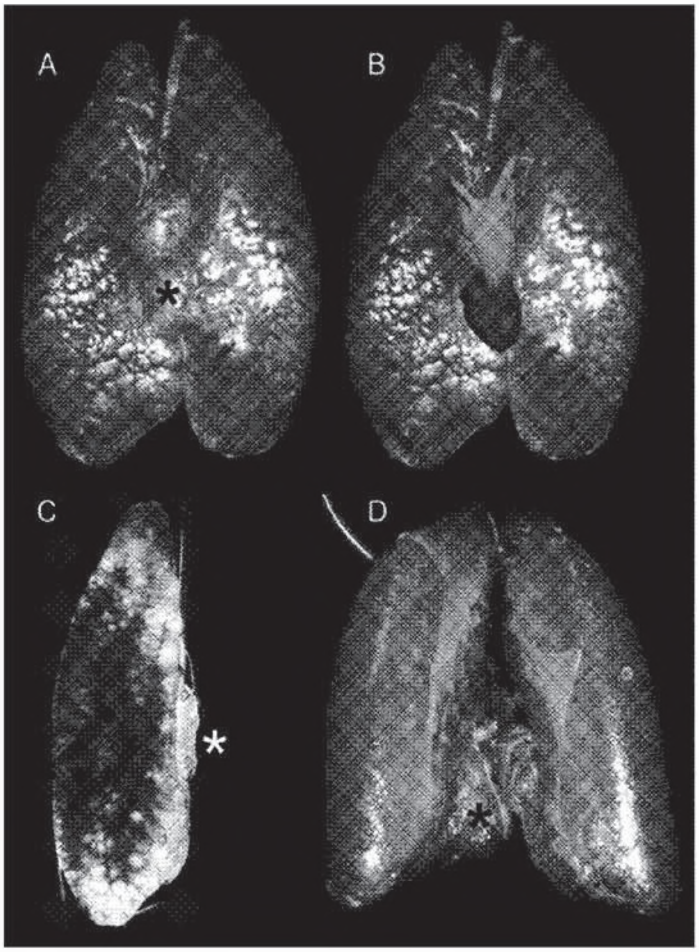

Figure 5. Photographs of an excised lung of a juvenile American alligator. *A*, Ventral view of the lungs. *B*, Ventral view but with a photograph of the heart and great vessels superimposed in the correct anatomical location. *C*, Dorsal view of the left lung with illumination from the ventral side. Apparent in this view are the spiraling bronchi, the concentration of blood capillaries in the mediodorsal regions of the lung, and the cardiac lobe (*asterisk*). *D*, Mediodorsal view of the lungs after having been dissected apart for a better view of the cardiac lobes (*asterisk*); craniad, top of page.

Structure and Function of the Archosaur Lung

Features that superficially seem unique to birds are in fact foreshadowed in the crocodilian lung. The respiratory system of birds is partitioned into air sacs, which are highly compliant and therefore readily change volume with the birds' breathing but do not contain gas-exchange vasculature (Magnussen et al. 1979), and the lung, which contains the gas-exchange vasculature and is located mediodorsally in the body cavity (Hazelhoff 1951; Duncker 1978*a*). The lungs of crocodilians are similarly partitioned. Although crocodilians do not have air sacs, ventrally and laterally the crocodilian lung contains very little gas-exchange tissue; these tissues are located dorsally (Perry 1988, 1990*b*). What are the benefits to crocodilians of this heterogeneous topography? One possible advantage is that it enables the heart to pump air when the animals are holding their breath (apnea). Crocodilians, like other ectotherms, normally hold their breath for prolonged periods of time whether or not they are diving. Thus, for ectotherms, the way that gas exchange occurs during apnea may be more important than the way gas exchange occurs during breathing.

American alligators have a lobe of the lung that is located immediately dorsal to the pericardium and is mechanically attached to it (Fig. 5), the cardiac lobe. This lobe may be an ideal bellows because it contains essentially no gas-exchange vasculature and is therefore highly compliant and because of its intimate mechanical connection with the pericardium. Thus, the cardiac lobe could transform the mechanical movement of the beating heart into airflow within the lung. If true, it would explain the benefit of a heterogeneous respiratory system; the noncompliant regions are best situated away from the heart so that the beating heart can be harnessed to pump air as well as blood. However, the cardiac stroke volume of crocodilians is only approximately 2% of the lung volume; that is, the stroke volume is less than 3 mL kg^{-1} (Franklin and Axelsson 2000), while the volume of the lungs is approximately 150 mL kg^{-1} (Bickler et al. 1985; Farmer and Carrier 2000; Farmer 2006).

If the air pumped by the cardiac lobes moves to and fro, cardiogenic flow might have little effect on gas exchange. However, if there is a bias to the direction of airflow such that with each beat the air moves in one direction (unidirectional flow), cardiogenic flow has the potential to circulate air throughout the entire lung, from avascular regions to the gas-exchange regions, even though each pulse is very small. To test some of these ideas, I undertook a study of airflow patterns within the lungs of juvenile alligators and found that cardiogenic flow does indeed exist and is primarily unidirectional. Thus, I suggest that the initial selective pressure for the evolution of unidirectional airflow was that it allowed the heart to pump pulmonary gases during apnea and that this design was an exaptation for a respiratory system readily tailored to function in the low levels of atmospheric oxygen of the Mesozoic. It is therefore easy to envisage how small modifications in the heterogeneous topography, although initially established to facilitate cardiogenic flow, would have facilitated the evolution of a very thin blood-gas barrier in regions of the lung that were not undergoing the mechanical stress associated with ventilation. Such a heterogenous lung would perform better than a homogenous one under conditions of hypoxia. It is under conditions of hypoxia that the avian lung has a greater ability to extract oxygen than the alveolar lung (Scheid and Piiper 1987). Indeed, the efficacy of the avian lung is not remarkably different from the alveolar lung when the animals are breathing air containing 21% oxygen (Fig. 6). However, unidirectional flow in conjunction with a cross-current mechanism of gas exchange (Scheid and Piiper 1972) facilitates extraction of oxygen under conditions of environmental hypoxia (Fig. 6).

Crocodilians and birds are crown group archosaurs, and the presence of unidirectional flow in crocodilians suggests that the evolution of this trait predates the divergence of the Crurotarsi, the lineage containing extant crocodilians but also phytosaurs, aetosaurs, "rauisuchians," and others, and the Ornithodira, the lineage containing extant birds but also pterosaurs and all dinosaurs, including the herbivorous ornithischians (Fig. 4). Thus unidirectional flow in the archosaur lineage evolved in the Early Triassic, or perhaps in the Archosauromorpha of the Late Permian, and predates the evolution of avian air sacs (Fig. 4). Avian air sacs do not cause unidirectional flow (Hazelhoff 1951; Scheid and Piiper 1987; Wang et al. 1992; Brown et al. 1995). These structures might serve some other function, such as facilitating control of pitch and roll (Farmer 2006).

Material and Methods

Experimental Animals

Six juvenile American alligators (2.4 ± 0.6 kg) were used in the experiments in which airflow in the lung was measured. Five animals were used for dissections. The alligators were obtained from the Louisiana Department of Wildlife and Fisheries at the Rockefeller Wildlife Refuge. At the University of Utah, the animals' housing included both basking areas and swimming tanks. The alligators ate mice and experienced a 12L : 12D photoperiod.

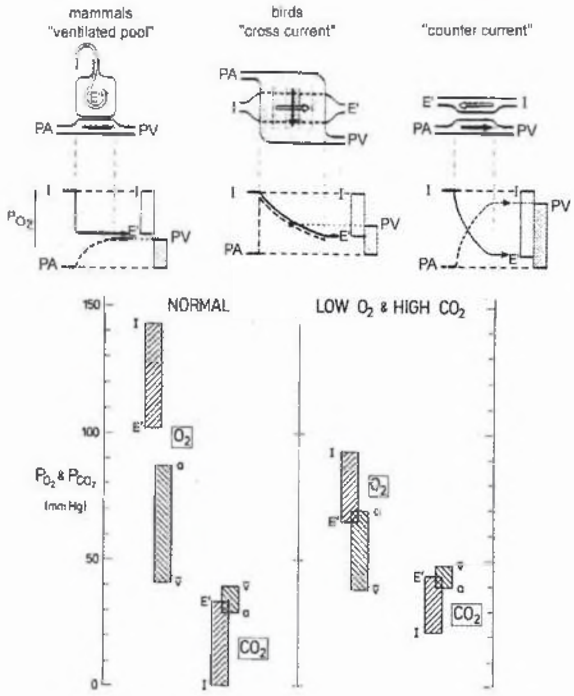

Figure 6. *Top*, models for gas exchange. In cross- and countercurrent models the O_2 tension can be greater in blood leaving the lung (pulmonary venous, *PV*) than it is in the expired gases of the lung (*E'*). *I* = inspired air, *PA* = pulmonary arterial blood. After Meyer et al. (1981). *Bottom*, tension of oxygen and carbon dioxide in the blood and lung gas in the domestic fowl, from Scheid and Piiper (1987). *I*, *E'*, *a*, and $\bar{v}$ refer to inspired, end-expired, arterial, and mixed venous partial pressure of oxygen (P_{O_2}) and carbon dioxide (P_{CO_2}) values. Note the reversal in the gradient for O_2 when the animals breathed a gas mixture low in O_2 and high in CO_2 (fraction of inspired gas: O_2 = 0.12, CO_2 = 5.0).

Surgery

The following steps were taken to implant the airflow meters in the first lateral chamber of the right lung. The alligators were intubated and then anesthetized with isoflurane and artificially ventilated with a small animal ventilator (SAR-830, CWE, Ardmore, PA) with air that had passed through a vaporizer (Dräger, Lubeck). Initially, the vaporizer was set to 4%, but that was reduced to 0.5% and maintained at this level throughout the majority of the surgery. The site where the incision was to be made was scrubbed with betadine and the rest of the animal covered with sterile drapes. The incision was approximately 6 cm long in the ventral midline. The body wall was retracted to expose the lungs. A region of the lung was cleared of connective tissue by blunt dissection, and a silk suture (6-0, Ethicon) looped around the cleared region. A small portion of the lung was pulled through the looped suture with blunt forceps, and then the lung was cut (approximately 0.5 cm in length). The airflow meter was placed into the lung through this incision, and the suture was pulled tight to seal the lung. The wires from the airflow probe were tunneled subcutaneously to exit the body dorsad, and the ventral body wall was then closed with 0 Dexon II green braided polyglycolic suture and the skin with 2-0 silk suture (Ethicon).

Data Collection

To monitor the timing of the heartbeat, the electrocardiogram (ECG) signal was recorded with subcutaneous electrodes connected to an AC amplifier (P511, Grass Instruments, West Warwick, RI). One electrode was positioned on the dorsal midline caudal to the tip of the scapula, another lead was positioned over the middle of the sternum, and a third lead, which served as a ground, was positioned on the tail. A shielded cable connected the leads to the amplifier. The ECG signal was amplified 500 or 1,000 times and filtered below 10 Hz and above 300 Hz. The signal was then transformed from analog to digital and recorded on a MacIntosh computer with a Biopac analog to digital system (Goleta, CA) and AcqKnowledge software.

To record airflow in the lung, the signal from the probe was connected to a flowmeter (HEC 132C Thermistor Flowmeter, Hector Engineering). The analog signal from the flowmeter was converted to digital and recorded on a computer as previously described for the electrocardiogram.

Experimental Protocol and Analysis

Data were collected while the alligators sat quietly in the prone position. Although lung volumes were not measured here, normally they are about 150 mL kg^{-1} during apnea in this species (Bickler et al. 1985). This is approximately the total lung volume (Perry 1988). Recordings made when the alligators were moving, including movement due to breathing, were not included in the analysis. Thus, there was no disturbance due to the musculoskeletal system of the position of the airflow meters or the electrocardiogram leads. The first 2 min at the beginning of a period of apnea were selected for analysis. The software used in the statistical analysis was JMP, release 7 (SAS Institute, Cary, NC). The raw data were used to determine the rate and direction of the flow of gases within the lung in relation to the electrocardiogram. ANCOVA with mass as a covariant was used to determine whether the airflow measured coincident with ventricular ejection, which was determined by identifying the QRS wave of the electrocardiogram, and ventricular repolarization, which was identified by the *t*-wave of the electrocardiogram, was significantly greater than no flow.

Dissection

None of the animals dissected had been preserved in formalin or other preservatives. These substances can alter the elastic properties of tissues. An animal was killed, and the trachea was then exposed through a ventral incision in the neck and cannulated with a piece of Tygone tubing with a similar outside diameter to the trachea. Suture or umbilical thread secured the tubing firmly in place in the trachea. A three-way stopcock was attached to the tubing, and a 50-mL syringe was attached to the stopcock. The lungs were gently inflated, and then the valve was sealed. A large ventral incision in the thoracoabdominal cavity was made to expose the lungs, heart, and liver. Using only blunt tools or fingers, the lungs and heart were separated from the rest of the body. During this procedure, the tissues were kept moist by misting with saline. Once the lungs and heart were excised, the heart and pericardium were separated from the lung tissue. Great care was required because the cardiac lobes of the lungs are very delicate and can easily collapse or be torn. The lungs were then dried overnight. Using a sharp scalpel, the outer tissues of the lung were peeled away so that the inner chambers were visible.

Results

Morphometric data were not collected on the lungs, but general observations of the gross morphology of the lungs were made that are in keeping with previous studies of other species of crocodilians (Perry 1988, 1990*a*). Figure 5 shows several photographs of a dried lung before removal of the outer tissues. In Figure 5*C*, the lung is backlit so that regions containing very little tissue (*bright yellow*) are distinct from those heavily invested with tissue (*dark bands*). These images illustrate the heterogeneity of the crocodilian lung; most of the tissues are concentrated medially and dorsally while the lateral and ventral regions are more vacuous. Furthermore, spiraling arching conduits, which have been described in detail for the lungs of crocodiles (Perry 1988), can be seen in this photograph. Once the outer tissues were removed, many small perforations between these conduits were apparent, the intercameral perforations described previously in crocodilians by Perry (1990*a*). A noteworthy feature observed was a saclike chamber located immediately dorsad to the heart and great vessels. The transparency of this sac, shown in Figure 5, indicates it lacks substantial gas-exchange tissues. This was confirmed visually once the lung was opened. The intimate connection of these sacs with the heart is illustrated in Figure 5*B*, where a picture of the heart has been superimposed on the ventral view of the lungs. To my knowledge, these lobes have not been described previously, and so I will refer to them as "cardiac lobes."

Airflow was measured coincident with the heartbeat in all animals that underwent surgery ($N = 6$). A sample of the raw data is provided in Figure 7. Means and SEs for heart rate and the airflow are reported in Table 1.

Discussion

Birds have long been known for their abilities to fly at altitudes where the partial pressures of oxygen are so low that mammals cannot function (Tucker 1968; Swan 1970; Faraci and Fedde 1986; Fedde et al. 1989; Schmitt et al. 2002; West 2004). In light of the recent understanding that the Mesozoic was a period of relative hypoxia, the ability of birds to exercise under hypoxia has been invoked to help unravel the evolutionary history of dinosaurs and other Mesozoic vertebrates (Huey and Ward 2005; Ward 2006; Berner et al. 2007). Although it is unclear when the avian air sacs and lung evolved, we do know that many Mesozoic archosaurs specialized to sustained aerobic ac-

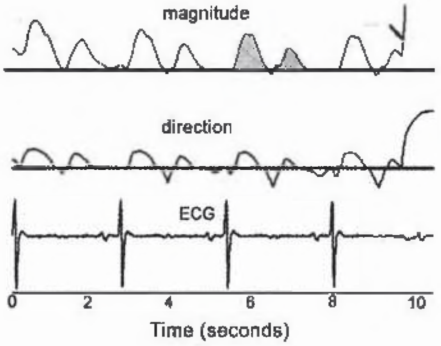

Figure 7. Sample of data of airflow measured in the lung and the electrocardiogram (ECG) measured simultaneously on a juvenile American alligator. The top and middle traces are signals from the dual thermistor flowmeter. The top trace gives the magnitude of the flow, and the middle indicates the direction of flow. The highlighted area is equivalent to a volume of 0.4 mL. This animal weighed 2.0 kg. The third trace is the ECG. The large spikes in the trace indicate the QRS wave. The arrow indicates the beginning of a respiratory cycle.

tivity; for example, many pterosaurs (Mesozoic winged archosaurs) were apparently capable of flapping flight (Padian and Rayner 1993; Padian and Chiappe 1998). Features that enable birds to function in hypoxic environments appear to have been present in the common ancestor of birds and crocodilians. I hypothesize that some of these features, such as the heterogeneous distribution of gas-exchange tissues and unidirectional airflow, initially arose because they benefited an ectothermic mode of respiration; that is, they facilitated gas exchange during apnea by taking advantage of the beating heart to stir gases within the lung. Thus, they may be exaptations and may have assumed a new function supporting strenuous exercise in the oxygen-poor Mesozoic atmosphere. If there is some truth to this, it supports the idea that the divergent lung designs of archosaurs and synapsids interplayed with levels of atmospheric oxygen to influence the Permian-Triassic faunal turnover.

The reasons for major transitions in the history of life are largely unknown and debatable. From the Late Carboniferous to the present, two clades of amniotes have dominated tetrapod evolution, the Synapsida and the Diapsida (Fig. 4; Benton and King 1989). The radiation of diapsids in the Permian and Triassic gave rise to the ancestors of lizards, snakes, crocodilians, and dinosaurs (including birds). As previously mentioned, the radiation of Synapsida gave rise to the pelycosaurs of the Carboniferous and the Permian, the therapsids of the Permian and Triassic, and the mammals toward the end of the Triassic (Benton and King 1989). The therapsids were a diverse group containing the largest terrestrial carnivores and herbivores of their assemblages. At the end of the Permian, many of the therapsids abruptly went extinct, but six or seven families survived the mass extinctions, diversified, and persisted as the dominant predators and largest land animals of the Early to Middle Triassic (Benton and King 1989; Rubidge and Sidor 2001). However, these niches were subsequently occupied by archosaurs for the remainder of the Mesozoic, the mammals remaining at low diversity until the Late Cretaceous, when they began to radiate strongly well before the end-Cretaceous extinction event (Benton and King 1989; Penny and Phillips 2004). The archosaur radiation was exceptional in its extreme morphological diversity and in its absolute dominance of large-body-size niches over a period of approximately 150 million yr. Any terrestrial vertebrate fossil found from the Jurassic or Cretaceous that is longer than a meter or two is an archosaur, while Mesozoic mammals were tiny, in the size range of mice and shrews today, with a few rare exceptions (e.g., the raccoon-sized *Repenomamus*; Bowring et al. 1999; Sereno 1999; Hu 2005; Kemp 2005). With the extinction of the large dinosaurs at the end of the Mesozoic, mammals came to dominate the large-body-size niches in the Cenozoic.

Was this turnover of fauna a historical contingency or did the archosaurs have a competitive advantage over the synapsids during the Mesozoic, an advantage that was presumably lost as mammals diversified in the Cretaceous (Sereno 1999; Penny and Phillips 2004; Ward 2006; Brusatte et al. 2009)? It has been proposed that the dinosaurs were at a competitive advantage during the Mesozoic because they had birdlike lungs (Ward 2006). However, another and slightly different way to look at this is the idea that the synapsids were disadvantaged during the Mesozoic because they had already evolved the homogenous alveolar lung during the Permian. There are no significant differences in the adult structure of the lung between extant prototherian and therian mammals (Szdzuy and Zeller 2008) or in their breathing patterns (Frappell 2003). Thus, the mammalian respiratory system has changed little since the monotreme-therian split. However, the time of this divergence is not well established. A recent analysis suggests the monotreme-therian split occurred in the Triassic (Rowe et al. 2008), but other workers date this split to the Early Jurassic (Cifelli 2001). In this article, I hypothesize that the stasis in the structure of the alveolar lung dates back to Permian therapsids. The therapsids may have embarked on a path of expanding the diffusive capacity of their lungs through an enormous elaboration of homogeneously distributed surface area, and once these evolutionary modifications had proceeded, this pathway may have handicapped the synapsids in an environment of hypoxia, because these animals would have been constrained from thinning the blood-gas barrier to the extent possible in a heterogeneously partitioned respiratory system. From this perspective, with the drop in atmospheric oxygen, a number of different diapsid lineages with heterogeneously organized respiratory systems would have been poised to supplant the synapsids as the preeminent members of the terrestrial assemblage.

Table 1: Cardiogenic airflow in the lungs of American alligators during apnea

Heart Rate (beats min^{-1})	Airflow (mL)	Body Mass (kg)	ANCOVA
22 ± 4	3.5 ± .9	2.4 ± .6	$P < .05$

Note. Data are expressed as mean ± SE.

The structure of the tarsus and foot of the Archosauromorpha, especially the articulation of the astragulus and the calcaneum, has been suggested to be indicative of selection for an upright position of the limb (Sereno 1991). Compared with the sister taxon, the Lepidosauromorpha, the Archosauromorpha apparently was trending toward the occupation of niches in which the ability to sustain locomotion was favored even though the lineage lagged behind the synapsids in this regard. However, with the end-Permian extinctions, these locomotor characters could have intertwined with the heterogeneous organization of the respiratory system to advance the archosauromophs as contenders for niches previously dominated by the synapsids. The rise to dominance of the Dinosauria (the archosaur lineage containing birds) over the Crurotarsi (the archosaur lineage containing crocodilians) appears to be a historical contingency (Brusatte et al. 2009) and suggests that both the Crurotarsi and the Dinosauria were on an equal footing to exploit similar resources of the Late Triassic (Brusatte et al. 2009) and were equally capable of dealing with the environmental conditions of the Mesozoic.

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