nystagmus in some humans is effectively reduced with baclofen (30 mg/day) (*12*). The alternating nystagmus was abolished in both monkeys at dosages of less than 10 mg/day.

These data are consistent with the idea that there is a mechanism that can dynamically shorten the dominant time constant of the VOR in response to certain types of visual and vestibular stimulation. These include conflicting visual and vestibular stimuli or head position changes during postrotatory nystagmus or OKAN. This mechanism seems to depend on the integrity of the nodulus and uvula, as it is lost when they are removed. Whereas a single process could be responsible for the rapid discharge of activity during tilt suppression, several processes probably cause the changes in eye velocity during visual suppression. One is associated with pathways through the flocculus that directly oppose signals arising in the vestibular system to null compensatory eye movements (*1, 3, 10, 11*). It has no effect in discharging stored activity responsible for slow-phase velocity in the vestibular nuclei (*13*). Another dynamically sluggish process, using pathways from the accessory optic system and pretectum (*14*), is responsible for charging and discharging activity in the central vestibular system (*4, 11, 15*). Because it stores activity related to slow-phase velocity, it has been called a "velocity storage" mechanism (*2, 4*). Presumably, the small loss in slow-phase velocity during attempts at visual suppression during postrotatory nystagmus (Fig. 1F) or OKAN (Fig. 2A) was due to activation of this mechanism by a central representation of retinal slip. Acting on the velocity storage mechanism is the "dump" mechanism that is lost after nodulus and uvula lesions. Although it rapidly discharges residual stored activity, it does not charge the velocity storage integrator.

On the basis of these results, we propose that the flocculus and the nodulus and uvula have complementary roles in modifying the vestibulo-ocular reflex. The flocculus mediates rapid changes in eye velocity from the visual system. It aids the VOR in stabilizing gaze during ocular compensation and suppresses the VOR when watching targets or a visual surround that moves with the head. The nodulus and uvula, on the other hand, appear to have little or no effect on visual and vestibular pathways that cause rapid changes in eye velocity. Instead they affect the VOR by dynamically controlling the dominant time constant of the velocity storage integrator. This could be accomplished through their direct connections to the vestibular nuclei (*16, 17*). Differences in function between the flocculus and the nodulus and uvula may be related to the differential projections of these areas (*16*).

The nodulus and uvula may also have more global functions in controlling the VOR. It was not possible to habituate the time constant of either per- or postrotatory nystagmus or OKAN after nodulo-uvulectomy, and previous modifications of the VOR time constant were lost. There was also periodic alternating nystagmus in two of three animals after operation. Such nystagmus has been modeled as the oscillation of an unstable nonlinear system (*18*). Thus, the nodulus and uvula may also be important in habituating and stabilizing the vestibulo-ocular reflex (*19*).

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Digestive Adaptations for Fueling the Cost of Endothermy

Abstract. *Little is known about the digestive adaptations that enable mammals to sustain metabolic rates an order of magnitude higher than those of reptiles. Comparison of several features of digestion in mammals and lizards of similar size eating the same diet revealed that mammals processed food ten times faster and with the same or greater extraction efficiency. Transport kinetics and rates of nutrient absorption normalized to the quantity of intestinal tissue were similar in these two classes of vertebrates. The main basis for faster absorption in mammals is their much greater intestinal surface area.*

The differences in respiratory, circulatory, reproductive, and excretory physiology between mammals and reptiles have been much studied. However, little is known about the differences in digestive physiology that fuel the metabolic cost of endothermy. Mammals have metabolic rates and hence food requirements exceeding those of lizards by an order of magnitude (*1*), and there are at least eight types of digestive adaptations that could in theory enable mammals to meet this greater need for nutrients: faster food processing; higher extraction efficiency at the same body temperature; higher efficiency due to higher body temperature at night; greater intestinal surface area at the macroscopic, microscopic, or submicroscopic levels; and higher nutrient transport rates due to higher passive permeability or to higher capacities or binding affinities of active transport mechanisms. Although transit times (*2, 3*), extraction efficiencies (*3, 4*), and rates of transport (*5–7*) have been measured in some species of mammals and lizards, these quantities depend on diet and body size (*5–8*), and comparisons between mammals and lizards of the same size eating the same diet are lacking. The mechanisms underlying measured extraction efficiencies and transport rates in lizards remain unexplored.

Thus, quantitative assessment of the various factors that might account for the high digestive rates of mammals is

unavailable. We therefore studied two species each of herbivorous or omnivorous lizards and mammals eating the same diet of alfalfa pellets to compare them with respect to the eight digestive features listed above (Table 1). We also compared seven other species of mammals to three species of reptiles with respect to some but not all of these features (*9*).

The daily food intake required to maintain constant body weight was five to ten times greater in mammals than in reptiles of similar size (Table 1). These higher intakes were possible because transit times of individual meals through the gut (*10, 11*) were ten times faster in the mammals (Table 1). Faster transit times might be expected to yield lower extraction efficiencies because there would be less time for enzymatic digestion and absorption in the small intestine and for microbial digestion in the large intestine. However, apparent extraction efficiency (*12*) was as high or higher in the mammals compared to the lizards (Table 1).

To study extraction of individual dietary components, we compared desert woodrats and chuckwallas as follows. Plant diets consist of an inorganic component—ash (minerals)—and two primarily organic components—an easily soluble, nonfibrous fraction composed mainly of cell contents and digested in the small intestine, and a fiber fraction [neutral detergent fiber (*13*)] composed mainly of cell walls and digested in nonruminants by microbial fermentation in the hindgut. Woodrats and chuckwallas did not differ significantly in apparent extraction (*12*) of ash [56 ± 3 percent compared to 48 ± 2 percent (mean ± standard error of the mean, $n = 4$ per species); $P > 0.05$ (*t*-test)] or of the soluble fraction [70 ± 2 percent compared to 68 ± 5 percent ($n = 4$ per species); $P > 0.5$]. However, woodrats exceeded chuckwallas in apparent extraction of fiber (34 ± 2 percent compared to 21 ± 3 percent; $P < 0.05$) and therefore also in overall extraction efficiency (55 ± 2 versus 46 ± 2 percent; $P < 0.05$) (Table 1).

These results suggest that extraction efficiency of both the small and large intestine in mammals is similar to or greater than that of lizards, even though mammals must process food in shorter times. This difference was not due to the body temperatures of the ectothermic reptiles dropping to 24°C at night because extraction efficiency was not significantly different [difference, 2.2 percent ± 2.5 percentage units; $P > 0.4$ (paired *t*-test)] in chuckwallas maintained at 37°C for 24 hours per day. Thus, mammals must compensate for their faster transit times by means of greater absorptive surface area or higher rates of nutrient transport per unit area (or both).

Table 1. Digestive measurements of four lizard and mammal species. The small intestine was viewed as a smoothbore cylinder for determination of nominal area, and the microscopic area takes into account folds such as villi and ridges. Uptake capacities are transport capacities for the whole small intestine, determined by measuring uptake of glucose or proline as a function of intestinal position and integrating over the intestinal length (*6*). Values are reported as the mean ± standard error of the mean, with the number of animals given in parentheses.

Species	Body weight (grams)	Food intake (grams of dry matter per day)	Mean retention time (hours)	Apparent extraction efficiency (percent)	Small intestine			Uptake capacity (μmol/min)	
					Length (cm)	Nominal area (cm^2)	Microscopic area (cm^2)	D-Glucose	L-Proline
Desert iguana	73 ± 2 (5)	0.55 ± 0.02 (5)	96 to 177	45 ± 2 (4)	20.0 ± 1 (10)	18.2 ± 1.7 (5)	72 ± 4 (4)	2.1 ± 0.2 (5)	4.4 ± 0.4 (5)
Chuckwalla	193 ± 18 (4)	2.0 ± 0.4 (4)	59 to 118	47 ± 3 (4)	24.3 ± 4.1 (3)	31.0 ± 5.6 (3)		8.5 ± 1.5 (4)	3.6 ± 0.5 (4)
Laboratory mouse	36 ± 1 (6)	5.9 ± 1.8 (6)	8 to 18	46 ± 2 (6)	51.2 ± 1.3 (6)	43.0 ± 2.6 (6)	216 ± 22 (5)	17.8 ± 1.6 (5)	17.3 ± 1.9 (5)
Desert woodrat	125 ± 5 (5)	9.7 ± 0.2 (4)	3 to 5	55 ± 2 (4)	42.0 ± 3.0 (5)	39.6 ± 3.0 (5)	506 ± 57 (5)	14.5 ± 2.5 (5)	25.5 ± 2.9 (5)

To compare rates of nutrient transport, we used everted intestinal sleeves in vitro to measure uptake of sugar and amino acid across the apical (that is, lumen-facing) cell membrane of the intestinal epithelium (*6, 7, 14*). For all species studied (seven mammalian and five reptilian), the uptake of D-glucose or L-proline at 50 m*M*—a concentration sufficient to saturate the active transport mechanisms—was maximal in the proximal part of the small intestine. Rates of uptake in this region were similar in the species of herbivorous mammals and reptiles eating alfalfa pellets (Table 2).

Mammals and reptiles were also similar in four other aspects of nutrient transport. First, the proportion of the total uptake of glucose or proline that is active and sodium-dependent was similar. For instance, passive uptake of glucose measured by L-glucose accounts for 3 to 25 percent of total uptake in mammals (six species) and 6 to 9 percent in reptiles (three species). Second, the temperature dependencies of active glucose uptake between 25° and 40°C in desert iguana (Q_{10}, 2.51 ± 0.40; $n = 6$) and woodrats (Q_{10}, 2.28 ± 0.10; $n = 4$) were not significantly different ($P > 0.5$), even though the former is an ectothermic poikilotherm and the latter an endothermic homeotherm. Third, the kinetics of active D-glucose transport is similar: both mammals (five species) and reptiles (two species) displayed Michaelis-Menten kinetics with an apparent binding constant near 1 m*M*. Fourth, both mammals (three species) and lizards (three species) yielded low but measurable rates of active uptake of D-glucose and proline in the large intestine at less than 10 percent of the peak values for the small intestine and accounting for only 1 to 8 percent of the total transport capacity of the gut.

Because mammals and lizards have similar transport mechanisms and similar transport rates normalized to the quantity of intestinal tissue (*15*), what compensates for the faster transit times of mammals? Their intestinal surface area is about six times greater than that of reptiles of similar body weight. This difference arises from at least one, and possibly two, factors. First, although gut diameters of mammals and lizards are similar, the small intestine in mammals has more coils and hence is longer (see Table 1). The factor by which the length of the small intestine exceeds the linear dis-

Table 2. Rates of uptake (nanomoles per minute per centimeter of intestine) and total transport capacities (nanomoles per minute per gram$^{0.75}$) for three species each of mammals and reptiles. Rates of uptake were measured in the proximal part of the small intestine and are given as the range of values, with the mean value in parentheses. Transport capacities are relative to the metabolic live mass ($W^{0.75}$) of the animals and are given as the mean ± standard error of the mean.

Class	Rate of uptake (mean)		Transport capacity	
	D-Glucose*	L-Proline†	D-Glucose*	L-Proline†
Reptiles	294 to 831 (485)	249 to 377 (329)	109 ± 32	119 ± 32
Mammals	401 to 615 (487)	329 to 676 (511)	734 ± 328	800 ± 301

*Carrier-mediated uptake. †Total uptake.

tance from mouth to anus is 4.1 ± 0.5 for the eight species of small mammals studied but only 1.6 ± 0.3 for the five species of reptiles. Second, the actual surface area of the intestine is 4 to 13 times greater than that of the corresponding smoothbore cylinder (compare columns 7 and 8 of Table 1) because of elaborations of the intestinal mucosa at the microscopic level (finger-like villi in mammals and long ridges in lizards) and is increased another order of magnitude by microvilli. The factor for increase in surface area at the microscopic level may be higher for mammals (7.4 ± 1.6 for five species studied) than for lizards [4.0 for one species; see (*16*)]. When rates of uptake were integrated over the whole length of the small intestine to yield the total transport capacity [see (*6, 7*) and Table 1], these capacities, whether related to weight or to metabolic live mass, were an average of 6.8 times greater for mammals than for reptiles, for both glucose and proline (Table 2).

Thus, in the evolution of mammals from reptiles the key adaptation of the digestive system to the need for higher nutrient uptake is analogous to the key adaptation of the respiratory system to the need for higher oxygen uptake (*17*), that is, a great increase in absorptive surface area. Through lengthening of the gut (and possibly by microscopic elaborations), the intestine is enabled to process food in a shorter time without any sacrifice in extraction efficiency. This pattern of intestinal adaptation during the evolution of endothermy resembles the adaptations, within an individual animal's lifetime, to many other conditions associated with increased requirements for nutrient uptake, such as pregnancy, lactation, diabetes, intestinal resection, and perhaps reduced environmental temperatures (*5*). Under these conditions, the intestine adapts by a proliferation of mucosal surface per unit length of intestine. Such mucosal proliferation has the same result as lengthening of the gut: namely, increased rates of uptake for all nutrients. These anatomical responses contrast with the other main adaptive pattern of the gut, that is, induction or repression of specific transport mechanisms that enable animals to adapt phenotypically or evolutionarily to changes in diet (*5–7*).

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9. The four species listed in Table 1, plus box turtles (*Terrapene carolina*) and hamsters, were given a diet of alfalfa pellets and free access to water. Lizards were fed hydrated pellets by gavage to maintain constant body weight and were able to bask under heat lamps for 10 hours per day. Thus, their body temperatures were 37° to 40°C during the day and room temperature (24°C) at night. We made selected measurements on six species of herbivorous or omnivorous mammals [kangaroo rat (*Dipodomys merriami*), Belding's ground squirrel (*Spermophilus beldingi*), laboratory rat, green monkey (*Cercopithecus aethiops*), and fruit bats (*Artibeus jamaicensis* and *Carollia perspicillata*)] and on two species of carnivorous lizards [desert spiny lizard (*Sceloporous magister*) and leopard lizard (*Gambelia wislizenii*)]. These species were fed on other diets.
10. Limits for mean retention times (t_r) in Table 1 were calculated from the mass of digesta in the gut (M), the rate at which food enters the gut (R_i) and the rate at which feces leave the gut (R_o) as $(M/R_o) > t_r > (M/R_i)$ [R. M. Sibley, in *Physiological Ecology*, C. R. Townsend and P. Calow, Eds. (Sinauer, Sunderland, Mass., 1981), p. 109]. These estimated t_r values were confirmed for lizards by direct measurements with food dyed with Sudan III [desert iguanas, 95.5 ± 50.4 hours (n = 5); chuckwallas, 74.4 ± 2.4 hours (n = 4); mean ± standard error of the mean].
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12. Apparent extraction efficiency was calculated as $[(m_{food} - m_{feces})/m_{food}] \times 100$, where m is the flux of total dried weight or of a specific diet component per day. This calculation underestimates actual efficiencies if feces contain significant amounts of organic matter from intestinal secretions or microbes.
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15. Similar conclusions were obtained whether the rates of transport were normalized to the length, dry or wet weight, mucosal weight, nominal or microscopic surface area, or protein content of the tissue segment (*6*).
16. Microscopic surface area was measured as described (*7*). The ratio of microscopic to nominal area (see Table 1) is 4.0 for iguana, 5.0 for mouse, and 12.8 for woodrat; corresponding figures for three other small mammals are 7.4 (kangaroo rat), 7.1 (*Carollia perspicillata*), and 4.5 (*Artibeus jamaicensis*). Morphometric measurements and allometric analysis of gut dimensions in more species are needed to test whether mammals really do exceed reptiles in the ratio of microscopic to nominal area and to compare the contributions of an increase in this ratio and of the increased gut length to the increased gut area of mammals.
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Herbicide Resistance and Cross-Resistance: Changes at Three Distinct Sites in the Herbicide-Binding Protein

Abstract. *Plants and algae resistant to the commonly used* s-*triazine herbicides display a wide spectrum of cross-resistance to other herbicides that act in a similar manner. Analysis of uniparental mutants of the green alga* Chlamydomonas reinhardi *showed that three different amino acid residues in the 32-kilodalton thylakoid membrane protein can be independently altered to produce three different patterns of resistance to* s-*triazine and urea-type herbicides. These results clarify the molecular basis for herbicide resistance and cross-resistance. Two of the mutations do not alter normal electron transport and thus may have applications of agronomic interest.*

The light reactions of photosynthesis take place in the chloroplast thylakoid membrane, mediated in part by the membrane-bound complexes of photosystem I (PS I) and photosystem II (PS II). Many commonly used herbicides, such as atrazine [2-chloro-4-ethylamino-6-(isopropylamino)-*s*-triazine] and diuron, or DCMU [3-(3,4-dichlorophenyl)-1,1-dimethylurea], inhibit photosynthesis by preventing electron transfer at the reducing side of PS II (*1*). Recent studies (*2–4*)