

Testing a developmental model in the fossil record: molar proportions in South American ungulates

Laura A. B. Wilson, Richard H. Madden, Richard F. Kay, and Marcelo R. Sánchez-Villagra

Abstract.—A developmental model, based upon murine rodents, has been proposed by Kavanagh et al. (2007) to explain lower molar proportions in mammals. We produce a clade-wide macroevolutionary test of the model using the dental evolutionary trends in a unique radiation of extinct mammals endemic to South America (“Meridiungulata”) that comprise a diverse array of molar morphologies. All of the South American ungulate groups examined follow the inhibitory cascade model with the exception of two groups: Interatheriidae (Notoungulata) and Astrapotheria. For most taxa studied, ratios between lower molar areas are greater than 1.0, indicating a weak inhibition by m1 on the subsequent molars in the tooth row, and a trend to greater absolute size of the posterior molars. Comparisons of mean ratios between clades indicate that a significant phylogenetic signal can be detected, particularly between the two groups within Notoungulata—Typotheria and Toxodontia. Body mass estimates were found to be significantly correlated with both m3/m1 and m2/m1 ratios, suggesting that the larger body size achieved the weaker inhibition between the lower molars. Molar ratio patterns are examined and discussed in relation to the independent and numerous acquisitions of hypsodonty that are characteristic of dental evolution in “Meridiungulata.”

Laura A. B. Wilson* and Marcelo R. Sánchez-Villagra. *Paläontologisches Institut und Museum, Karl Schmid-Strasse 4, CH-8006 Zürich, Switzerland. E-mail: laura.a.b.wilson@gmail.com.* *Present address: Kyoto University Museum, Yoshida-honmachi, Sakyo-ku, Kyoto 606-8501, Japan

Richard H. Madden. *Duke University, Department of Biological Anthropology and Anatomy, Duke University Medical Center, Durham, North Carolina 27710, U.S.A.*

Richard F. Kay. *Duke University, Department of Evolutionary Anthropology, Durham, North Carolina 27708, U.S.A., and Nicholas School Faculty, Department of Earth and Ocean Sciences, Durham, North Carolina 27708, U.S.A.*

Accepted: 28 July 2011

Supplementary materials deposited at Dryad: doi:10.5061/dryad.f1468

Introduction

Much of the taxonomy and diversity in extinct faunas is known through dental remains, because teeth are the most commonly recovered and best preserved elements of a fossil assemblage. Of late, evolutionary developmental biologists have begun to gain a handle upon the mechanisms that control tooth formation, number, and regeneration (e.g., Jernvall et al. 2000; Salazar-Ciudad and Jernvall 2002, 2004, 2010; Jarvinen et al. 2006; Munne et al. 2009), and have contributed to our understanding of the developmental origins of morphological variation, that is, connecting the genotype with the phenotype (Arnold 1992; Polly 2008). In practice, this provides an opportunity to reexamine the rich amount of information in the fossil record within a molecular developmental framework, and to gain insights into macroevolutionary trends (Peterson et al. 2007).

Kavanagh et al. (2007) have proposed that lower molar proportions in mammals may be predicted by a molecular developmental model. Using experimental studies conducted on mice, Kavanagh et al. (2007) demonstrated that interrupting the flow of inhibitor molecules by cutting the dental lamina at the posterior end of the first lower molar (m1), resulted in an earlier initiation and increased size of the second molar (m2). The size and initiation of lower molars were thus proposed to be the result of a dynamic balance between inter-molar inhibition and mesenchymal activation, a so-called inhibitory cascade (IC) model. Kavanagh et al. (2007) proposed that by varying the balance between activator (a) and inhibitor (i), as quantified by a ratio between the two (a/i ratio), lower molar proportions can change and different dental phenotypes are realized.

The phenotypic expression of this proposed molecular mechanism can be easily examined

through size measurements of lower molars, which can be predicted by the IC model. The predictive ability of the IC model can therefore be extended not only to extant taxa, but also to fossils (Sánchez-Villagra 2010). Initial studies to test the IC model are limited at present to one brief examination of its applicability to a few species across mammalian phylogeny (Polly 2007), and one in-depth study of the arvicoline subfamily (Renvoisé et al. 2009), which possess a peculiar lower molar phenotype with an oversized m1 in comparison to m2 and m3. The goal of this study is to examine the evolution of other dental phenotypes in the context of the IC model framework, using a clade of fossil mammals: the unique radiation of endemic South American ungulates.

For most of the Cenozoic, South America was not connected to any other major landmass. During this period of “splendid isolation” (Simpson 1980), lasting until a few million years ago when the Panama land bridge came into existence (3–3.5 Ma [Woodburne 2010]), many endemic mammals evolved in separate directions from those on other continents. Some of the archaic lineages established during the Paleocene survived to the present day, for instance the xenarthrans, represented by armadillos, sloths and anteaters (Flynn and Wyss 1998; Oliveira and Bergqvist 1998) in addition to migrants during the Early Oligocene such as caviomorph rodents (e.g., capybaras and guinea pigs) (Wilson and Sánchez-Villagra 2009; Vucetich et al. 2010), whereas others left no living descendants. Despite achieving a remarkable diversity, the endemic South American ungulates are not represented in modern faunas. In general, these animals mirrored the ungulate diversity we are familiar with today around the world, having evolved their own analogous forms of hippos, rhinos, horses, camels, and elephants (Cifelli 1985; Elissamburu 2004; Weston et al. 2004; Shockey et al. 2007; Kramarz and Bond 2009), combinations of these (Owen 1837, 1840), or completely singular forms (Scott 1937).

The evolutionary origins of the South American ungulates, collectively placed into the “Meridiungulata” (Notoungulata, Litopterna, Xenungulata, Pyrotheria and Astrapotheria) by McKenna (1975), remain largely unexplored.

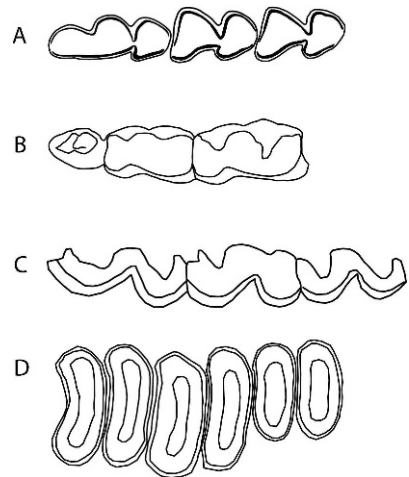


FIGURE 1. Illustrations of lower molar rows in occlusal view (anterior to posterior running left to right) for representatives of several of the major clades of South American ungulates analyzed in this study. Area values were calculated from maximum mesiodistal and buccolingual dimensions. A, *Miocochilius anamopodus* (Notoungulata). B, *Astrapothericus iheringi* (Astrapotheria). C, *Proadiantus excavatus* (Litopterna). D, *Pyrotherium romeroi* (Pyrotheria). Modified after Cifelli and Soria (1983), Kramarz (2009), and Billet (2010) (B, C, D, respectively). Molar rows illustrated are not to scale.

All five “orders” possess highly specialized dentitions, making it difficult to trace their ancestral lineages. Recently, de Muizon and Cifelli (2000) provided dental evidence linking one group, the Litopterna, with a mioclaenid “condylarth” ancestor, suggesting a migratory origin from North America at the start of the Paleocene. This event initiated a diversification of forms that survived for some 60 Myr until their extinction in the Pliocene and Pleistocene (Cifelli 1985; Bond 1999; Bond et al. 2001). Besides having a diverse array of morphologies ranging from small rodent- and rabbit-like notoungulates (Typotheria) to rhino-sized animals such as the astrapotheres—proboscis-bearing mega-herbivores with tusks and domed heads—the “meridiungulates” are perhaps most remarkable in their dental evolution (see Figure 1 for examples of diversity in lower molar morphology). Documented molar diversity ranges from brachyodont and weakly lophed (Litopterna) to bunodont and bilophed teeth (Pyrotheria); some groups had extremely massive posterior molars (Astrapotheria) and many groups evolved hypsodonty and hypselodonty (Notoungulata). Indeed, in the latter

case, at least four notoungulate clades are known to have independently evolved high-crowned teeth in parallel between the Late Eocene and Early Oligocene (Cifelli 1985; Croft and Weinstein 2008; Townsend and Croft 2008), around 15 Myr earlier than herbivorous faunas on other continents (Simpson 1980). In each case, some species from each group later developed ever-growing (hypselodont) dentitions (Marshall and Cifelli 1990; Madden 1997; Croft et al. 2004; Townsend and Croft 2008). This parallel evolution of hypselodonty is surpassed in frequency only by rodents (Croft and Weinstein 2008: p. 104).

Here we examine lower molar proportions for representatives from each of the five major groups of “Meridiungulata” in relation to the IC model framework, to produce a macro-evolutionary test of the model and its possible relation to the above-mentioned dental evolutionary trends.

Materials and Methods

Lower molar proportions were obtained for 308 specimens of fossil taxa belonging to “Meridiungulata,” comprising 64 genera and including representatives from each of the five major clades: Notoungulata (49 genera; $n = 244$), Astrapotheria (5 genera; $n = 32$), Pyrotheria (1 genus; $n = 7$), Litopterna (8 genera; $n = 23$), and Xenungulata (1 genus; $n = 2$) (see Supplementary Table 1). Measurements were compiled from the literature ($n = 161$), and from fossil collections ($N = 147$) at the following museums: AMNH (American Museum of Natural History, New York); FMNH (Field Museum of Natural History, New York); MACN (Museo Argentino de Ciencias Naturales Bernardino Rivadavia, Buenos Aires); MLP (Museo de la Plata, La Plata); NMB (Naturhistorischesmuseum Basel, Basel); SGOPV (Vertebrate Paleontology Collection, Museo Nacional de Historia Natural, Santiago); UCMP (University of California Museum of Paleontology, Berkeley); and YPM-PU (Yale Peabody Museum, New Haven). Literature sources are detailed in the Appendix. In all cases, lower molar occlusal surface area, referred to as “size” hereafter, was calculated from maximum

mesiodistal and buccolingual dimensions for m1, m2, and m3.

Additionally, because the South American ungulates are known for their precocious and frequent parallel acquisition of hypsodonty, we explored the potential interaction of crown height with the relationship between molar proportions. We examined whether the acquisition of hypsodonty is associated with the expression of specific molar proportions. A hypsodonty index (HI; height divided by width) was measured for taxa that contributed to the evolutionary increase of crown height and for which we had molar proportion data for all teeth ($n = 65$ specimens). The measurement of hypsodonty indices for the fossil “meridiungulates” examined herein does not follow the criterion adopted by Janis (1988), who used m3. Instead, we used the most complete (and least worn) isolated crowns available to us, either m1 or m2 (in the case of isolated specimens, wherein tooth position could not be unequivocally determined). Hypsodonty indices were measured only on taxa with rooted molars and are thus not comparable with HIs for taxa with ever-growing (hypselodont) teeth. For teeth with roots, unworn crown height from the apex to cement-enamel junction, just above the root, is a measure of the amount of enamel crown available to the animal during its lifetime, whereas in ever-growing (hypselodont) teeth, much of the crown height generated during an animal’s lifetime is not present in a preserved crown. Several comparable measurements from Reguero et al. (2010: Appendix 24.1) were used to supplement the data set.

Kavanagh et al. (2007) demonstrated that the development of the lower molars follows an inhibitory cascade (IC) model, which can be defined by the following equation:

$$y = 1 + [(a - i)/i](x - 1),$$

where y is the relative molar size as determined by its position in the tooth row (x), and by the relative strength of activators (a) and inhibitors (i). Because inhibition cascades from one tooth to the next, it is possible to predict the relative size of teeth along the molar row. Using simple regressions, Renvoisé et al.

(2009) showed that for murines m_3 size is calculated as $m_3 = 0.66m_1$, and similarly m_2 size has a significant influence on m_1 size ($m_2 = 0.73m_1$) and m_3 size an equally strong influence on m_2 size ($m_3 = 0.77m_2$). By plotting m_2/m_1 versus m_3/m_1 , a macroevolutionary test of the IC model can be performed because the above equation would predict a slope of 2.0 and an intercept of -1.0 (Kavanagh et al. 2007). Further, the model predicts m_2 area to be one-third of total molar area ($m_1 + m_2 + m_3$), irrespective of molar proportions; thus regression of $(m_1 + m_2 + m_3)$ area versus m_2 area would result in a slope of 3.0 and an intercept of zero.

We conducted a series of simple and multiple regressions to compare our data with the predictions of the IC model, and further to examine the evolution of molar proportions in the South American ungulate groups. To permit direct comparison with the regression results of Kavanagh et al. (2007) we use reduced major axis (RMA) methods for all linear regressions, using individuals as cases and considering only significant parameters when compiling formulae. Symmetrical line-fitting techniques (model II), such as RMA, are usually preferred (Wolpoff 1985) because error is assumed to be associated equally with both x and y variables, and simulation investigations have shown that these methods provide more stable estimates, especially if sample sizes are small (Riggs et al. 1978). Regressions were performed for the clades "Meridiungulata," Notoungulata, Astrapotheria, and Litopterna. Notoungulata is both the most speciose and the most morphologically diverse "order" among those examined herein; thus analyses were also split into eight "families" represented in the sample (of the 13 presently recognized [McKenna and Bell 1997]): Hegetotheriidae, Interatheriidae, Archaeohyracidae, Mesotheriidae, Oldfieldsthomasiidae, Toxodontidae, Leontiniidae, and Homalodotheriidae. Representatives of Litopterna were divided into Proterotheriidae and Macrauchenidae, because these two clades are ecologically and morphologically distinct from one another. Pyrotheria and Xenungulata could not be analyzed separately with regression methods because sample sizes for these

groups were small (seven individuals or fewer). Variability in molar ratios was examined across a phylogenetic framework, based upon the work of Billet (2010), and further multiple comparisons, using ANOVA and Scheffe's tests, were performed to assess the significance of differences between clades.

Results

Molar Ratios (m_2/m_1 and m_3/m_1).—Lower molar proportions (m_2/m_1 versus m_3/m_1) for each clade follow a linear relationship (Table 1), and for most species the molar ratios are greater than 1.0, indicating the posterior molars are greater in size than m_1 (Fig. 2). Only representatives from Notoungulata have molar ratios below 1.0, amounting to 9.1% of all measured specimens for m_3/m_1 ratios, and 24.2% for m_2/m_1 ratios. Among the individuals with molar ratios less than 1.0, most belonged to Interatheriidae (35% of specimens measured for m_3/m_1 , and 68% for m_2/m_1).

Variability for molar ratios was greatest for m_3/m_1 , which is expected by the IC model because the slope in the m_3 direction is twice that in the m_2 . Across the phylogenetic framework taken as reference, the members of Astrapotheria exhibited the most variation in m_2/m_1 values (range = 1.56), and Notoungulata had the most variable m_3/m_1 values (range = 2.10) (Figs. 2, 3). Mean ratios for both m_3/m_1 and m_2/m_1 were lowest for Interatheriidae (1.05 and 0.95, respectively) and outside the associated confidence intervals for Xenungulata, Astrapotheria, Pyrotheria and Homalodotheriidae. Xenungulata, represented here by two specimens of *Carodnia vieirai*, had the highest mean ratios (2.46 for m_3/m_1 and 1.85 for m_2/m_1), in all cases being outside intervals for corresponding values in all other groups (Fig. 3).

ANOVA results indicated significant differences in mean molar proportions between the five clades examined, but only for m_2/m_1 values ($p < 0.001$, $F = 82.30_{4, 308}$). Results from multiple comparisons revealed two groups with significantly different molar ratios: representatives from Notoungulata and Litopterna and representatives from Astrapotheria, Pyrotheria and Xenungulata

TABLE 1. Reduced major axis regression results for lower molar ratios (m2/m1 versus m3/m1). Values for meridiungulates are compared to those based upon the IC model derived from measurements of murines (Kavanagh et al. 2007). C.I., confidence interval. Several groups were not analyzed separately because of small sample size (Oldfieldthomasiidae (Notoungulata), Xenungulata, Pyrotheria).

	<i>n</i>	Slope	C.I. min	C.I. max	Intercept	C.I. min	C.I. max	<i>r</i>
IC model	-	2.00	-	-	0.00	-	-	1.00
Murines	29	2.150	1.772	2.688	-1.219	-1.651	-0.925	0.740
Archaeohyracidae	18	3.269	2.038	4.843	-2.263	-3.946	-1.019	0.813
Astrapotheria	32	1.270	1.057	1.484	-0.291	-0.547	-0.035	0.905
Hegetotheriidae	18	2.441	-1.509	4.386	-1.342	-3.155	2.618	0.364
Homalodotheriidae	26	1.557	1.427	2.914	-0.417	-1.935	-0.255	0.908
Interatheriidae	100	1.468	1.261	1.681	-0.347	-0.549	-0.155	0.601
Leontiniidae	23	1.952	1.374	2.608	-0.946	-1.374	2.608	0.743
Macrauchenidae	14	1.367	0.575	2.031	-0.384	-1.079	0.439	0.694
Meridiungulata	308	1.661	1.491	1.856	-0.584	-0.785	-0.411	0.782
Mesotheriidae	21	1.375	1.193	2.316	-0.345	-1.317	-0.164	0.901
Notoungulata	244	1.763	1.575	1.992	-0.655	-0.883	-0.464	0.811
Proterotheriidae	9	1.173	-1.562	1.541	-0.139	-0.528	2.768	0.469
Toxodontidae	33	1.752	1.422	3.026	-0.666	-2.010	-0.333	0.845

(in all cases Scheffe’s test, $p < 0.001$). The mean m2/m1 ratio for Notoungulata is 1.05, similar to that for Litopterns (1.06); both are lower than values for Astrapotheria (1.61), Pyrotheria (1.43), and Xenungulata (1.85). Within Notoungulata, the interatheriid taxon *Transpithecus obtentus* had lower molar ratios than all others (see Fig. 2), in which the m3/m1 value was 0.53 and the m2/m1 value was

0.63, indicating that m2 and m3 were progressively smaller than m1. Conversely, taxa with the greatest molar ratios belonged to Astrapotheria (*Granastrapotherium* sp.) and Homalodotheriidae (*Periphragmis* sp.). In the case of *Granastrapotherium* sp., both molar ratios were greater than 2.0, reflecting the condition whereby m1 is smaller than m2 and m3.

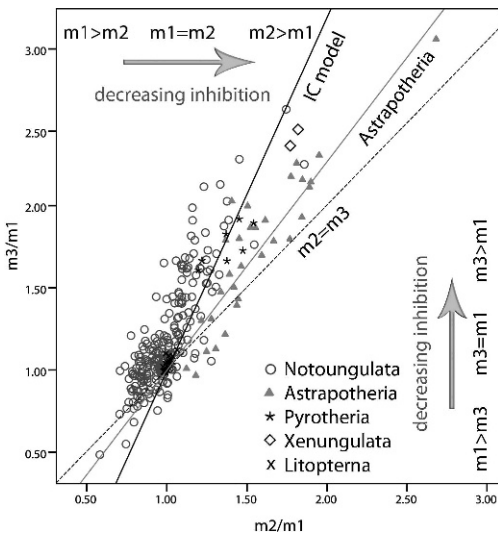


FIGURE 2. Molar ratios for South American ungulates in relation to the Inhibitory Cascade (IC) model (solid line), which was developed from values based on the lower molars of murine rodents (Kavanagh et al. 2007). Molar ratios (m3/m1 and m2/m1) are calculated from area measurements for each tooth along the lower molar row (m1–m3). Astrapotheres deviate significantly from the IC model; see Table 1 for detailed values of the regression analyses.

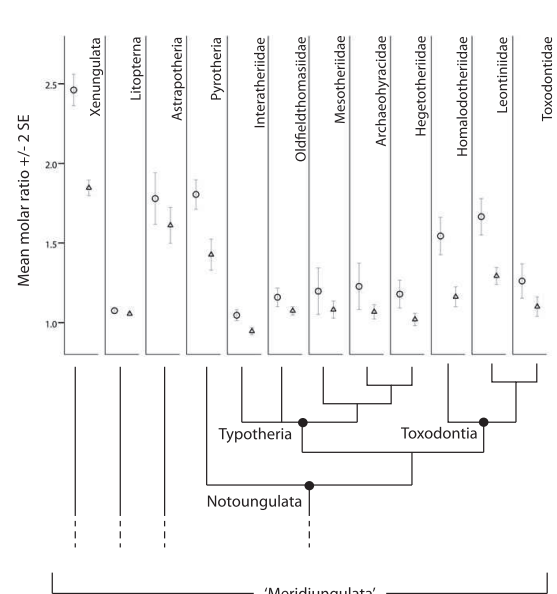


FIGURE 3. Variation in m3/m1 (open circle) versus m2/m1 (open triangle) ratios for all taxa examined in this study. Ratios are calculated from area measurements, based on maximum mesiodistal and buccolingual dimensions, for each lower molar (m1–m3). Phylogenetic relationships based upon Billet (2010).

The groups within Notoungulata show significant differences in both m_3/m_1 and m_2/m_1 mean ratios between the two divergent radiations, Typotheria and Toxodontia (Fig. 3). Scheffe's test results indicate that m_3/m_1 ratios for members of Leontiniidae and Homalodotheriidae, belonging to Toxodontia, are significantly different from those for Hegetotheriidae ($p < 0.002$), Interatheriidae ($p < 0.001$), Archaeohyracidae ($p < 0.016$) and Mesotheriidae ($p < 0.002$), all belonging to Typotheria. Typotheria are characterized by mean m_3/m_1 ratios of 1.04–1.23, compared to 1.26–1.67 for Toxodontia. A similar pattern is found for m_2/m_1 ratios, though to a lesser extent because values for both Archaeohyracidae and Mesotheriidae differed significantly only with one toxodontid group (Leontiniidae). Also, within typotheres, Interatheriidae and Mesotheriidae had significantly different m_2/m_1 values (Scheffe's test, $p = 0.006$). Mean ratios for m_2/m_1 varied between 0.95 and 1.08 for typotheres, compared with 1.10 to 1.29 for toxodontids.

Simple and Multiple Regressions.—In simple regressions of m_2/m_1 versus m_3/m_1 , slope and intercept values fall within the confidence intervals of the murine data (slope 1.772 to 2.688, intercept -1.651 to -0.925 ; Table 1) for the majority of groups, with the exception of Astrapotheria (slope 1.057 to 1.484, intercept -0.547 to -0.035 ; Table 1) and Interatheriidae (slope 1.261 to 1.681, intercept -0.549 to -0.155 ; Table 1). With the exception of Archaeohyracidae and Hegetotheriidae, absolute slope values are lower than for murines, ranging from 1.270 for Astrapotheria ($r = 0.91$, $F = 137.018$, 32) to 1.952 for Leontiniidae ($r = 0.74$, $F = 25.870$, 23), and absolute intercept values are higher, ranging from -0.291 for Astrapotheria to -0.946 for Leontiniidae. Taken together, these trends reflect a slight shift from the IC model toward a linear relationship representing a more equal size of m_2 and m_3 (Table 1, Fig. 2). Interatheriidae occupy the portion of morphospace left of the IC model line (see Fig. 2) and in contrast to other groups include a number of specimens with molar proportions that follow $m_1 > m_2 < m_3$ (28%). The regression line shown in Figure 2 for Astra-

pothoria, in contrast, reflects a shift to the right of the IC regression line, whereby m_2 is greater than m_1 and m_3 is smaller than predicted by the model.

Multiple and simple regressions of the molar area data were used to explore in more detail the relationship between molar measurements. In accordance with the IC model, it should be possible to determine m_3 size (= product of mesiodistal and buccolingual measurements) by using m_1 size, following the relationship $m_3 = 0.655m_1$ (Renvoisé et al. 2009). Among the groups examined herein, for the multiple regressions (Table 2, parts A) a significant relationship between m_3 and m_1 size was found for "Meridiungulata" and Astrapotheria. For Astrapotheria this relationship reflected a negative influence of m_1 on m_3 (Table 2) and for Meridiungulata a positive influence, and in both cases this was coupled with an added significant influence of m_2 , such that the equation for "Meridiungulata" is $m_3 = 0.370m_1 + 0.947 m_2$, and, comparably, for Astrapotheria $m_3 = -0.258m_1 + 1.288m_2$ (Table 2, parts A). Among the ten remaining groups, a positive influence of m_2 on m_3 is registered for Archaeohyracidae ($m_3 = 1.517m_2$), Homalodotheriidae ($m_3 = 0.373 + 1.051m_2$), Interatheriidae ($m_3 = 1.038m_2$), Mesotheriidae ($m_3 = 1.113m_2$), Notoungulata ($m_3 = 1.186m_2$), and Toxodontidae ($m_3 = 1.641m_2$).

Simple regressions between m_2 versus m_1 and m_3 versus m_2 reveal several broadly similar trends across the groups examined (Table 2, parts B, C). First, in all groups there is a significant influence of m_1 on m_2 and of m_2 on m_3 , and these relationships are in most instances highly linear, with r^2 values ranging between 0.566 for Macrochaenidae and 0.996 for Proterotheridae (Table 2). The high correlation between m_1 and m_2 (r^2 values between 0.747 and 0.996; Table 2, parts B) indicates that only one of these teeth is required to make a significant regression with m_3 , and the other does not need to be included in the equation. Second, the influence of m_2 on m_1 and of m_3 on m_2 is weak, because the equations generated from the b coefficients result in a combined low multiplier effect on m_1 . That is to say, for example if $m_1 =$

TABLE 2. Simple and multiple regression results of lower molar areas (length \times breadth measurements). Pyrotheria, Xenungulata, and Olfieldthomasiidae (Notoungulata) could not be analyzed separately because of low sample sizes. Regressions are as follows: A, m3 versus m1m2; B, m2 versus m1; C, m3 versus m2. Asterisk indicates $p < 0.05$. Orig. Ord., original ordinate.

			<i>b</i>	<i>p</i>	SE	<i>r</i> ²
Archaeohyracidae (<i>n</i> = 18)	Orig. ord.	A	-4.529	0.610	1.869	0.814
	m1		-0.156	0.686	0.378	
	m2		1.517*	0.001*	0.358	
	Orig. ord.	B	7.378	0.220	5.776	0.771
	m1		0.925*	0*	0.126	
	Orig. ord.	C	6.666	0.582	1.188	0.592
m2		1.248*	0*	0.107		
Astrapotheria (<i>n</i> = 32)	Orig. ord.	A	-1.31	0.92	0.75	0.992
	m1		-0.258*	0.041*	0.121	
	m2		1.288*	0*	0.12	
	Orig. ord.	B	0.471*	0*	0.076	0.978
	m1		0.997*	0*	0.027	
	Orig. ord.	C	-0.027	0.663	0.061	0.99
m2		1.035*	0*	0.019		
Hegetotheriidae (<i>n</i> = 18)	Orig. ord.	A	1.711	0.471	0.231	0.929
	m1		0.538	0.133	0.350	
	m2		0.556	0.171	0.374	
	Orig. ord.	B	-0.510	0.761	1.649	0.953
	m1		1.042*	0*	0.058	
	Orig. ord.	C	1.428	0.563	2.416	0.917
m2		1.118*	0*	0.084		
Homalodotheriidae (<i>n</i> = 26)	Orig. ord.	A	0.373*	0.007*	0.127	0.863
	m1		-0.119	0.520	0.183	
	m2		1.051*	0*	0.192	
	Orig. ord.	B	0.336*	0.007*	0.114	0.842
	m1		0.873*	0*	0.076	
	Orig. ord.	C	0.384*	0.005*	0.124	0.860
m2		0.935*	0*	0.075		
Interatheriidae (<i>n</i> = 100)	Orig. ord.	A	2.199	0.082	1.250	0.786
	m1		-0.025	0.832	0.120	
	m2		1.038*	0*	0.143	
	Orig. ord.	B	0.372*	0*	0.799	0.860
	m1		0.776*	0*	0.032	
	Orig. ord.	C	0.606*	0*	1.398	0.669
m2		0.780*	0*	0.055		
Leontoniidae (<i>n</i> = 23)	Orig. ord.	A	0.384*	0.029*	0.163	0.855
	m1		0.261	0.462	0.348	
	m2		0.696	0.056	0.343	
	Orig. ord.	B	0.280*	0.003*	0.084	0.935
	m1		0.981*	0*	0.056	
	Orig. ord.	C	0.339*	0.034*	0.150	0.851
m2		0.944*	0*	0.086		
Macrochaeriidae (<i>n</i> = 14)	Orig. ord.	A	2.271	0.170	1.547	0.590
	m1		0.601	0.233	0.476	
	m2		0.289	0.439	0.359	
	Orig. ord.	B	1.147	0.357	1.198	0.747
	m1		1.145*	0*	0.192	
	Orig. ord.	C	2.603	0.102	1.469	0.566
m2		0.932*	0.002*	0.236		
Meridiungulata (<i>n</i> = 308)	Orig. ord.	A	-8.670	0.294	0.823	0.981
	m1		0.370*	0*	0.072	
	m2		0.947*	0*	0.049	
	Orig. ord.	B	-2.40*	0.013*	0.960	0.961
	m1		1.455*	0*	0.017	
	Orig. ord.	C	-0.314*	0.011*	1.22	0.957
m2		1.747*	0*	0.021		

TABLE 2. Continued.

			<i>b</i>	<i>p</i>	SE	<i>r</i> ²
Mesotheriidae (<i>n</i> = 21)	Orig. ord.	A	0.426	0.165	0.294	0.912
	m1		-0.182	0.430	0.225	
	m2		1.113*	0*	0.250	
	Orig. ord.	B	0.681*	0.006*	0.220	0.935
	m1		0.870*	0*		
	Orig. ord.	C	0.510	0.077	0.272	0.918
m2		0.918*	0*	0.063		
Notoungulata (<i>n</i> = 244)	Orig. ord.	A	-5.012	0.321	0.504	0.967
	m1		0.171	0.140	0.116	
	m2		1.186*	0*	0.096	
	Orig. ord.	B	-2.326	0.491	0.336	0.973
	m1		1.191*	0*	0.013	
	Orig. ord.	C	-7.771	0.228	0.643	0.946
m2		1.584*	0*	0.024		
Proterotheriidae (<i>n</i> = 9)	Orig. ord.	A	1.084	0.784	3.774	0.992
	m1		0.610	0.440	0.739	
	m2		0.625	0.389	0.672	
	Orig. ord.	B	3.568	0.066	1.639	0.996
	m1		1.097*	0*	0.026	
	Orig. ord.	C	3.312	0.289	2.885	0.991
m2		1.296*	0*	0.046		
Toxodontidae (<i>n</i> = 33)	Orig. ord.	A	-0.198	0.579	1.541	0.926
	m1		-0.255	0.458	0.339	
	m2		1.641*	0*	0.298	
	Orig. ord.	B	0.232	0.276	2.093	0.939
	m1		1.103*	0*	0.050	
	Orig. ord.	C	0.182	0.710	0.485	
m2		1.555*	0*	0.116		

3.00 mm², then according to the IC model, m2 would be calculated as 2.20 mm² and m3 would be 1.70 mm² (m2 = 0.73m1 and m3 = 0.77m2 [Renvoisé et al. 2009]). For the groups studied here, in the same hypothetical situation, m2 predictions range from 2.78 mm² for Archaeohyracidae (m2 = 0.925m1; Table 2) to 3.46 mm² for Astrapotheria (m2 = 0.471 + 0.997m1; Table 2), and m3 predictions from 2.71 mm² for Interatheriidae (m3 = 0.606 + 0.78m2; Table 2) to 3.58 mm² for Astrapotheria (m3 = 1.035m2; Table 2).

One outcome of the Kavanagh et al. (2007) model is that m2 area is one-third of the total molar area; thus a regression of total molar area versus m2 area should result in a slope of

3.00 and an intercept of 0. For all groups, regression results comply closely with this prediction (Table 3).

Hypsodonty Indices.—For notoungulates, slightly reduced variability in m3/m1 (Fig. 4A) and m2/m1 (Fig. 4B) can be seen for Archaeohyracidae (*n* = 12) in comparison to other groups such as Toxodontidae and Mesotheriidae, both represented by fewer individuals. Noteworthy is the variability among the toxodontids, which include two different species of *Proadinothierium* and encapsulate ratios varying from 1.23 to 2.30 for m3/m1, and from 1.16 to 1.91 for m2/m1, with HI values of 1.98 for *Proadinothierium leptognathum* compared to 3.67 for *Proadinothierium muensteri* (Table 4).

TABLE 3. Regression results for total molar area (m1 + m2 + m3) versus m2 area, to compare values based on the predictions of the IC model with those for several of the major clades examined in this study. Xenungulata and Pyrotheria were not analyzed separately because sample sizes were too small.

	Slope	C.I. min	C. I. max	Intercept	C.I. min	C.I. max	<i>r</i> ²
IC model	3.00	-	-	0.00	-	-	1.00
Astrapotheria (<i>n</i> = 32)	3.020	2.763	3.061	-0.444	-0.595	0.235	0.998
Litopterna (<i>n</i> = 23)	2.961	2.925	2.988	0.035	-0.093	0.225	0.999
Meridiungulata (<i>n</i> = 308)	2.862	2.78	2.932	0.251	0.0638	0.484	0.996
Notoungulata (<i>n</i> = 244)	3.156	3.07	3.237	-0.265	-0.489	0.510	0.998

TABLE 4. Hypsodonty index (HI) for notoungulate and astrapothere taxa, supplemented by values taken from the literature, denoted by an asterisk.

“Order”	“Family”	Species	HI	
Notoungulata	Archaeohyracidae	<i>Protoarchaeohyrax gracilis</i>	1.73	
		<i>Archaeohyrax patagonicus</i>	2.74	
		<i>Archaeotypotherium pattersoni</i>	1.5	
	Hegetotheriidae	Interatheriidae	<i>Archaeotypotherium tinguiriricaense</i>	1.5
			<i>Hegetotherium mirabile</i>	2.42*
			<i>Miocochilius anamopodus</i>	2.47*
			<i>Santiagorothia chiliensis</i>	1.20*
			<i>Proargyrohyrax curanderensis</i>	1.20
			<i>Notpithecus adiapinus</i>	0.69
			<i>Antepithecus brachystephanus</i>	0.61
			<i>Guiliemoscottia plicifera</i>	0.86
			<i>Transpithecus obtentus</i>	0.73
			<i>Trachytherus spegazzinianus</i>	2.32*
	Toxodontiidae	<i>Proadinothierium muensteri</i>	3.67	
		<i>Proadinothierium leptognathum</i>	1.98	
Astrapotheria	Astrapotheriidae	<i>Parastrapotherium herculeum</i>	0.87	

Correlations between HI and molar ratios were significantly negative for m2/m1, providing a preliminary indication of a trend to a greater hypsodonty index associated with a lower m2/m1 (Spearman’s rank = 0.548, $p = 0.01$).

Discussion

Several insights into dental phenotypic variability among the South American “ungulates” can be summarized from the analyses of lower molar proportions: (1) the m3/m1 and m2/m1 ratios are, for most taxa studied, greater than 1.0, indicating a weak inhibition by m1 on the subsequent molars in

the tooth row, and a trend to greater absolute size of the posterior molars; (2) comparisons of mean ratios between clades suggest that a significant phylogenetic signal can be detected, particularly between Typotheria and Toxodontia (Fig. 3); (3) regression results show that all of the South American ungulate groups examined follow the IC model with the exception of two groups, which reflect the acquisition of divergent lower molar phenotypes; Interatheriidae are characterized by $m1 > m2 < m3$, whereas multiple regressions indicate that Astrapotheria are best represented by $m1 < m2 > m3$.

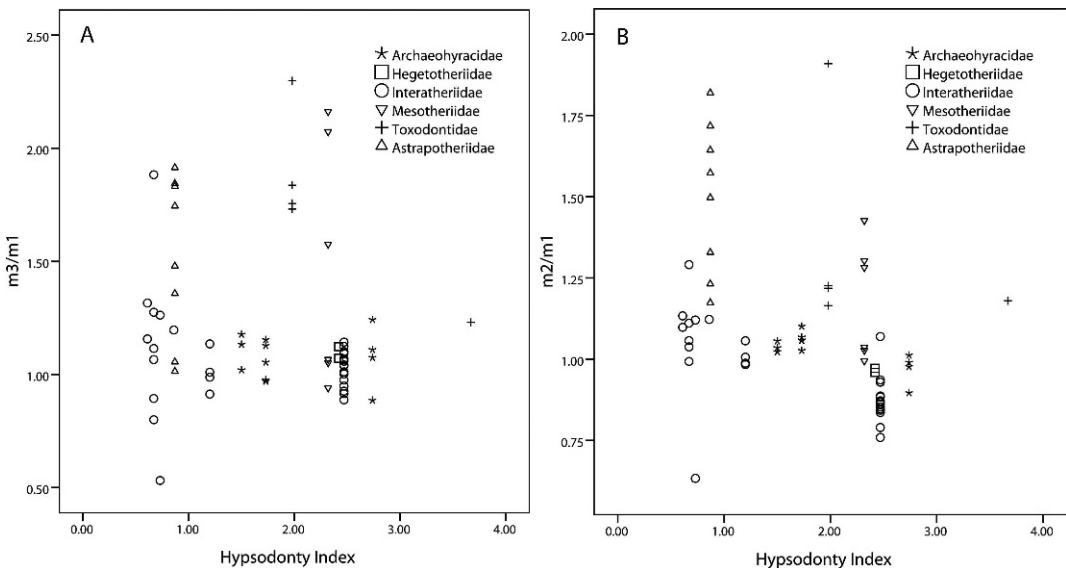


FIGURE 4. Molar ratios for m3/m1 (A) and m2/m1 (B) in relation to Hypsodonty Index (HI) values for selected taxa.

Variability and Phylogenetic Signal of Molar Ratios.—The variability of dental proportions across the South American ungulates can be illustrated in context by comparisons to within-clade data for murines and data for several species from different mammalian “orders.” Among the taxa studied here, the molar ratios are greater in range of variation than those presented by Polly (2007), who measured molars from a broad taxonomic cross-section of mammals, including animals as morphologically distinct as bats and kangaroos. Both Polly’s sample as well as our own are an array of species representing a polyphyletic group, and thus can be seen as a more or less random sampling of mammals, although in our case that sample is restricted to “ungulate” forms. Polly’s (2007) m_3/m_1 ratios ranged from 0.10 to 1.76 (range = 1.66) compared with 0.53 to 3.04 (range = 2.53) for the taxa studied herein. Likewise, m_2/m_1 ratios varied to a similar extent in terms of range magnitude, with a distribution between 0.27 and 1.50 (range = 1.23) for the taxa measured by Polly (2007), compared with 0.63 to 2.73 (range = 2.10) for our data. For further comparison, the ratios calculated by Kavanagh et al. (2007) for an ecologically diverse sample of murines were 0.55 to 0.94 (range = 0.39) for m_2/m_1 and 0 to 0.87 (range = 0.87) for m_3/m_1 . In addition to apparent high levels of diversity in lower molar proportions, our results show that plasticity in dental proportions is not equally distributed on phylogeny. Specifically, toxodontids include a much wider spectrum of molar size relationships (Fig. 3) than do other groups within Notoungulata. These differences are noteworthy because the two divergent radiations are characterized most prominently by their differences in body size. Typotheres are typically small to medium-sized animals similar in form to rabbits or rodents, whereas toxodontids include relatively large rhino- or horse-like forms (Cifelli 1985). Hence, a progression to a greater molar ratio appears to be associated with an increased body size. Kavanagh et al. (2007) did not specifically comment about whether molar proportions may be expected to differ in relation to body size. To check the significance of this trend, we

calculated body mass for all specimens, using the relationship defined by Damuth (1990) from recent non-selenodont ungulates: \log_{10} body mass = $3.17^* \log_{10}$ (m1 length) + 1.04 (Supplementary Table 1). Body mass estimates were verified where possible with data from postcranial material. Specimens that appeared to be clear outliers based on postcranial estimates were removed ($n = 15$). Body mass was significantly correlated with both m_3/m_1 (Spearman’s rank = 0.449, $p < 0.001$) and m_2/m_1 (Spearman’s rank = 0.562, $p < 0.001$), suggesting that the larger body size achieved the weaker inhibition between the lower molars.

A Model for “Meridiungulata” and Its Relation to Diversity.—The postulates of the IC model explain molar proportions for the majority of South American ungulates examined in this study. With the exception of Interatheriidae and Astrapotheria, all groups have slope and intercept values within the range predicted by the IC model. Although multiple regressions do not reveal a significant effect of m_1 size on m_3 for any of the groups, the high correlations found between m_1 and m_2 with simple regressions suggest that it is necessary for only one of these teeth to be included in the equation with m_3 for the regression to be significant. Strong evidence for the effect of the inhibitory cascade is further exemplified by comparison of b coefficients between m_2 versus m_1 and m_3 versus m_2 regressions, which reveal remarkably consistent values (Table 2).

Most taxa are characterized by molar ratios greater than 1.0, suggesting that inhibition along the molar row is weak and that posterior molars are larger than m_1 . This result does not invalidate the IC model. In cases where molar ratios are greater than 1.0, the model predicts that m_3 will be larger than m_2 and grow at a faster rate than m_2 . Several of the taxa in Polly’s (2007) analyses also possessed molar ratios greater than 1.0, including bears, rodents, and primates. Astrapotheria and Interatheriidae present two significant exceptions to the IC model; in both cases slope and intercept confidence intervals fall outside of those predicted by Kavanagh et al. (2007). For Astrapotheria, the regression line

falls to the right of the IC model (Fig. 2), indicating a smaller m_3 than would be predicted, and multiple regression results suggesting that the contributions of the m_1 and m_2 are in opposite directions (Table 2, parts A). Although Astrapotheria evolved massive posterior molars, one specimen of *Granastrapotherium* sp. in the study sample had an m_3/m_1 ratio of 3.06, representing the greatest absolute value in the data set (see Supplementary Table 1); the shape of the m_3 is somewhat pyramid-like in some members of this group (e.g., *Astrapotherculus*), meaning that the occlusal surface is much smaller than would be expected given the size of the base and the dimensions of m_2 and m_1 (Kramarz 2009). It should be noted that mean values for m_3/m_1 were quite similar between Astrapotheria and Pyrotheria (Fig. 3), reflecting the large range in values for astrapotheres (range = 2.05), which is almost comparable to that of Notoungulata (range = 2.10). Patterson and Pascual (1972) noted convergences between astrapotheres and amynodont rhinoceroses in terms of their skull and dentition, and more recently the astrapotheres have been united with Afrotheria on the basis of some shared-derived dental and postcranial characters (Agnolin and Chimento 2011), though these hypotheses require further validation (Billet and Martin 2011).

The dental phenotype best explaining molar proportions for Interatheriidae is $m_1 > m_2 < m_3$, which Kavanagh et al. (2007) suggested to be the developmentally least likely to occur. Polly (2007) found that the horse also fell into this region of the model. The interatheriids were notoungulates the size of small rodents, all possessing simplified, hypsodont molars, and in most cases with cementum. Although deviation from the IC model is apparent, it is relatively minor; the upper confidence interval of the regression slope (1.681; Table 1) falls only slightly below the lower interval for murines (1.772; Table 1) and therefore the difference is far less pronounced than for Astrapotheria. Similarly, raw tooth measurements (lengths and breadths) are in most cases less than 5% different between molars, meaning a small deviation from $m_1 = m_2 = m_3$. Because tooth areas were calculated

from length and breadth measurements, there is a chance that area values could be overestimated, for instance in the situation where molars narrow distally, and this margin of error may account for the slight deviation from the IC model in the case of Interatheriidae.

Molar placement has been hypothesized to be related to jaw mechanics in ungulates (Greaves 1978). Greaves's (1978) model proposes that halfway between the condyle and canine, a region of mechanical advantage can be recognized, which is the position where maximum forces can be exerted. This region is predicted to correspond directly to the position of the grinding tooth row length and, according to the model, is the position where simple muscle action can apply equal forces at any point (Greaves 1978, 1983). Bearing upon the schematic basis of this model, the relative sizes of the molars affect the computed linear distance to the condyle and thus the zone of maximum muscle force (see Werdelin 1987: Fig. 1). Microwear analysis of the teeth of hypsodont notoungulates has revealed that these animals chewed with strong sub-horizontal jaw movements with a wide range of orientations (Billet et al. 2009), and mesowear results suggest that even forms appearing more rabbit- or rodent-like, such as the tyotheres, also masticated in an ungulate, rather than rodent, manner (Croft and Weinstein 2008). For those taxa that are represented by cranial remains, one potentially interesting avenue for assessing molar proportions among the South American ungulates might be assessing their relation to Greaves's (1978) model.

Relation of Hypsodonty Indices to the Evolution of Molar Proportions.—The development of hypsodonty has occurred at numerous points in the evolution of herbivorous mammals, and it is widely assumed to confer a feeding advantage by extending the functional life of the tooth, which otherwise would be quickly worn down when masticating highly abrasive foods (Janis 1988). In extant ungulates, hypsodonty is hypothesized to occur under distinct selection regimes associated with open habitats and close-ground feeding, particularly the consumption of exogenous grit and/or coarse grasses (silica phytoliths) (e.g., Williams and Kay 2001; Mendoza and Palmqvist

2008). The independent and numerous acquisitions of hypsodonty among the South American ungulates is a prominent feature of their dental evolution. Often, within a species, the third molar is the tooth position having the greatest variability in size (Gingerich and Schoeninger 1979; Polly 1998). Being the last tooth to form, it is also the last to wear out under intense abrasive wear. For this reason, enhancement of its structure (for resisting abrasion) immediately prolongs the functional longevity of the entire dentition. Most basically, to improve its wear-resistance a tooth must become larger, and if enlargement is not documented in length and breadth measurements, then an alternative strategy must substitute, such as volume increase (hypsodonty). Among the six groups for which hypsodonty index information was available, a significant negative correlation was identified for $m2/m1$, suggesting that more equal sizes of these teeth may be associated with a greater degree of hypsodonty. A similar correlation was noted with $m3/m1$ values, though it was not significant. Nevertheless, this trend needs to be substantiated further, particularly because tooth dimensions for some hypsodont taxa, such as archaehyrcids, have been shown to change considerably with increasing wear (Croft et al. 2003a). This factor may have contributed to the variability noted for *Proadinothierium*, for instance, and ultimately to the results of our analyses. Explicit testing is warranted to demonstrate the significance of wear in this context.

Further investigation is required to examine the potential of the IC model to highlight active mechanisms of evolutionary change, especially in relation to hypsodonty. Reguero et al. (2010) recently showed that increasing hypsodonty is associated with increasing body size among tyotheres with complex occlusal designs. This finding, together with the evidence herein that levels of molar inhibition are correlated with body mass, suggests that testing hypotheses about the adaptive nature of hypsodonty will benefit from explicit consideration of the IC framework. Overall, the use of the IC model to examine differences and similarities in molar

proportions within “Meridiungulata” has indicated that this framework can be effectively applied to most groups. Additional analyses have provided new insights into factors that may be relevant for future considerations of the IC model and a new perspective for considering the evolution of dental development in this morphologically diverse group of extinct ungulates.

Acknowledgments

For taking several measurements of molars we thank F. Carlini (La Plata). For helpful discussions and comments we thank J. Jernvall (Helsinki), E. Renvoisé (Helsinki), A. Kramarz (Buenos Aires), L. Humphrey (London), and I. Werneburg (Kobe). We very much appreciate the thoughtful and insightful suggestions by two reviewers and especially those of D. Croft. Support for this work was provided by the Swiss National Fond (31003A_133032) to M.R.S.-V. and by the Forschungskredit of the University of Zürich (Nr. 5926) and the Japanese Society for the Promotion of Science (PE10075) to L.A.B.W.

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Appendix

Details of literature sources for specimens in Supplementary Table 1.

“Order”	“Family”	Literature sources
Astrapotheria		Sánchez-Villagra 2010
Litopterna		Cifelli 1983; Cifelli and Guerrero 1997; Scherer et al. 2009; Sánchez-Villagra 2010
Notoungulata	Archaeohyracidae	Reguero 1998; Croft et al. 2003a; Sánchez-Villagra 2010; Scarano 2010
	Hegetotheriidae	Reguero 1998; Croft and Anaya 2006; Sánchez-Villagra 2010; Scarano 2010
	Homalodotheriidae	Simpson 1967
	Interatheriidae	Reguero 1998; Scarano 2010
	Mesotheriidae	Croft et al. 2004; Billet et al. 2008; Sánchez-Villagra 2010; Townsend and Croft 2010
Xenungulata	Toxodontidae	Croft et al. 2003b; Sánchez-Villagra 2010
		Paula-Couto 1952; Sánchez-Villagra 2010