and the LGN_d (4.2 msec for the cell at 11.9° eccentricity and 4.1 msec for the cell at 10.8° eccentricity). This finding suggests that the variability in conduction velocities between cat retinal ganglion cells may have a functional basis; the variability may reflect a mechanism that ensures that visual signals arising from different areas of the retina reach their central target nuclei (in the case of X cells, primarily the LGN_d) in the same amount of time. The result, therefore, is a characteristic latency for all of the visual input arriving at the LGN_d through the X-cell pathway.

By recording simultaneously in the retina and the LGN_d, Cleland *et al.* (*11*) showed that there were latency differences in the input to the LGN_d among different classes of cat retinal ganglion cells. The mean latency between an action potential recorded in the retina and one recorded in a postsynaptic LGN_d sustained (X) cell was approximately 4.8 msec (*12*). These results are in reasonable agreement with ours when one considers that their mean latency also included the synaptic delay between the retinal ganglion cell axon and the generation of an action potential in the postsynaptic LGN_d neuron. The range of X-cell latencies that they reported was larger than ours, but this difference could be due to a number of factors. For example, their retinal recordings were obtained both from ganglion cell somata and, in some instances, from ganglion cell axons between the soma and the optic disk. The postsynaptic "jitter" that occurs in the responses of LGN_d neurons to electrical stimulation of their retinal afferents (*13*) would also increase the variability in the latencies reported by these investigators.

Our data pertain only to one (the X-cell pathway) of a number of parallel information streams between the retina and the visual areas of the central nervous system (*8*). For each of the physiological types of retinal ganglion cell, there may be a characteristic latency such as we have demonstrated for retinal X cells.

Since visual perception is a function that is presumed to occur at a central site or sites that do not receive direct retinal input, it is difficult to predict the degree of spatiotemporal precision necessary to accomplish these higher order visual functions in the central visual pathways beyond the LGN_d. Nor can we determine if, in fact, the temporal relations between retinal ganglion cell signals described here are preserved as this information is relayed along more central pathways. A scheme of retinal organization in which each pathway has a characteristic conduction time, however, could provide two relevant aspects of the timing of the visual signals relayed by retinal ganglion cells—the temporal relation among the responses of different cells in the same pathway to a changing stimulus and, on a larger scale, the relations among the visual signals from two or more parallel pathways. The maintenance of these temporal relations, both within and among these parallel information channels, may be necessary for maintaining an accurate central representation of the spatiotemporal aspects of a visual scene.

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Heritability at the Species Level: Analysis of Geographic Ranges of Cretaceous Mollusks

DAVID JABLONSKI

Geographic range has been regarded as a property of species rather than of individuals and thus as a potential factor in macroevolutionary processes. Species durations in Late Cretaceous mollusks exhibit statistically significant positive relationships with geographic range, and the attainment of a typical frequency distribution of geographic ranges in the cohort of species that originated just before the end-Cretaceous extinction indicates that species duration is the dependent variable. The strong relation between geographic ranges in pairs of closely related species indicates that the trait is, in effect, heritable at the species level. The significant heritabilities strengthen claims for processes of evolution by species-level selection, and for differential survivorship of organismic-level traits owing to extinction and origination processes operating at higher levels.

EVOLUTION BY NATURAL SELECTION can occur at any level of biological organization if three prerequisites are satisfied: for a given focal level within the hierarchy, a trait must exhibit variation, its interaction with the environment must result in differential birth or death, and the trait must be heritable, that is, offspring must significantly resemble parents for the trait in question (*1, 2*). Evolutionary research has focused primarily on the level of individuals within populations, but recently a number of authors (*1–3*) have suggested that certain traits, such as geographic range or genetic population structure, can be regarded as species-level properties subject to processes of selection and drift at that level as well (*4*). For Late Cretaceous mollusks, geographic range does meet all three prerequisites for evolution under selection: there is variation among species that gives rise to differential species survivorship, and that variation is heritable (as defined above) at the species level.

Department of the Geophysical Sciences, University of Chicago, 5734 South Ellis Avenue, Chicago, IL 60637.

The Gulf and Atlantic Coastal Plain of North America contains one of the most diverse and best-preserved molluscan faunas of the latest Cretaceous (Campanian-Maestrichtian stages). Geographic ranges and temporal durations of bivalve and gastropod species were calculated on the basis of my own and museum collections and the published literature with a series of 2 million year (m.y.) increments within the last 16 m.y. of Late Cretaceous marine deposition; species distributions were mapped on the approximately 5000-km discontinuous outcrop belt to a precision of ±20 km (*5, 6*). Sampling is inevitably incomplete, and so recorded geographic ranges should be regarded as proportional to original distributions rather than as absolute and complete measurements (*5*). Species pairs used in heritability analysis were delineated primarily on the basis of cladistic assessment of published statements (*7*) regarding evolutionary relationships. Not all speciation events are recognizable in the fossil record, but the necessary use of species distinguishable on the basis of observable morphology

(morphospecies) is conservative relative to the conclusions drawn here: members of a given pair of morphologically distinct, putative sister species are if anything likely to be less closely related than assumed for the analysis, so that their inclusion should diminish rather than artificially enhance observed correlations. To control for differences in preservation, taxonomic treatment, and morphological complexity, bivalves and gastropods were analyzed separately.

Both bivalves and gastropods exhibit a statistically significant relation between geographic range and species duration, with both Spearman rank-correlation and simple linear regression analysis (Table 1 and Fig. 1, A and B) (*8, 9*). The causal direction of the relation can be inferred from the frequency distribution of geographic ranges for the species that originated in the 2-m.y. increment just before the end-Cretaceous mass extinction. This cohort of species had its geologic durations truncated by the extinction event, but its geographic ranges are statistically indistinguishable from the frequency distribution of geographic ranges for species originating in the preceding 14 m.y. (*10*). Thus, species achieve their geographic ranges relatively early in their histories, so that geologic durations are in part a function of geographic range and not vice versa (*11, 12*). Some fluctuations in geographic range occur during the species' histories, but these appear to be relatively minor except during origination and extinction, which are brief intervals relative to the species' geologic durations (*13*). As in much of the marine invertebrate fossil record, speciation here is geologically instantaneous.

Even if species durations are directly correlated with geographic ranges, an ongoing process of evolution in geographic range magnitudes (and in traits that happen to be linked with geographic range) by selection at the species level could not occur unless geographic range is heritable, that is, unless closely related species tend to have geographic ranges more similar in magnitude than expected by chance alone. Spearman rank correlation tests indicate that this requirement is met for late Cretaceous mollusks, yielding statistically significant results for both bivalves and gastropods (Table 1).

This species-level character can be analyzed according to the procedures of quantitative genetics (*14*) to put its heritabilities in a comparative context. The analogy to quantitative genetics methodology does not depend on recognition of true ancestor-descendant (analog of parent-offspring) relationships; sister species (analog of full-sibling individuals) will also serve. Product moment correlation coefficients between sets of sibling pairs provide one estimate of heritability at the organismic level; values for species pairs of Cretaceous bivalves and gastropods are high and statistically significant, indicating species-level heritabilities comparable to values reported for many organismic traits (Tables 1 and 2) (*15*). Heritabilities are also estimated from the slope of a linear regression between parent and offspring, and Cretaceous species-level analyses yield slopes, and thus heritabilities, comparable to typical organismic values (*16*) (Fig. 1, C and D, and Table 2).

The application of quantitative genetic methods is simplified because branching of species within clades is more closely analogous to clonal reproduction than to sexual reproduction (*17*). At the same time, the analogy should not be pressed too far in quantitative terms: as noted previously, frequency distributions for geographic ranges typically violate the bivariate normality approximated by many quantitative traits at the organismic level (hence the need for nonparametric statistics), and more impor-

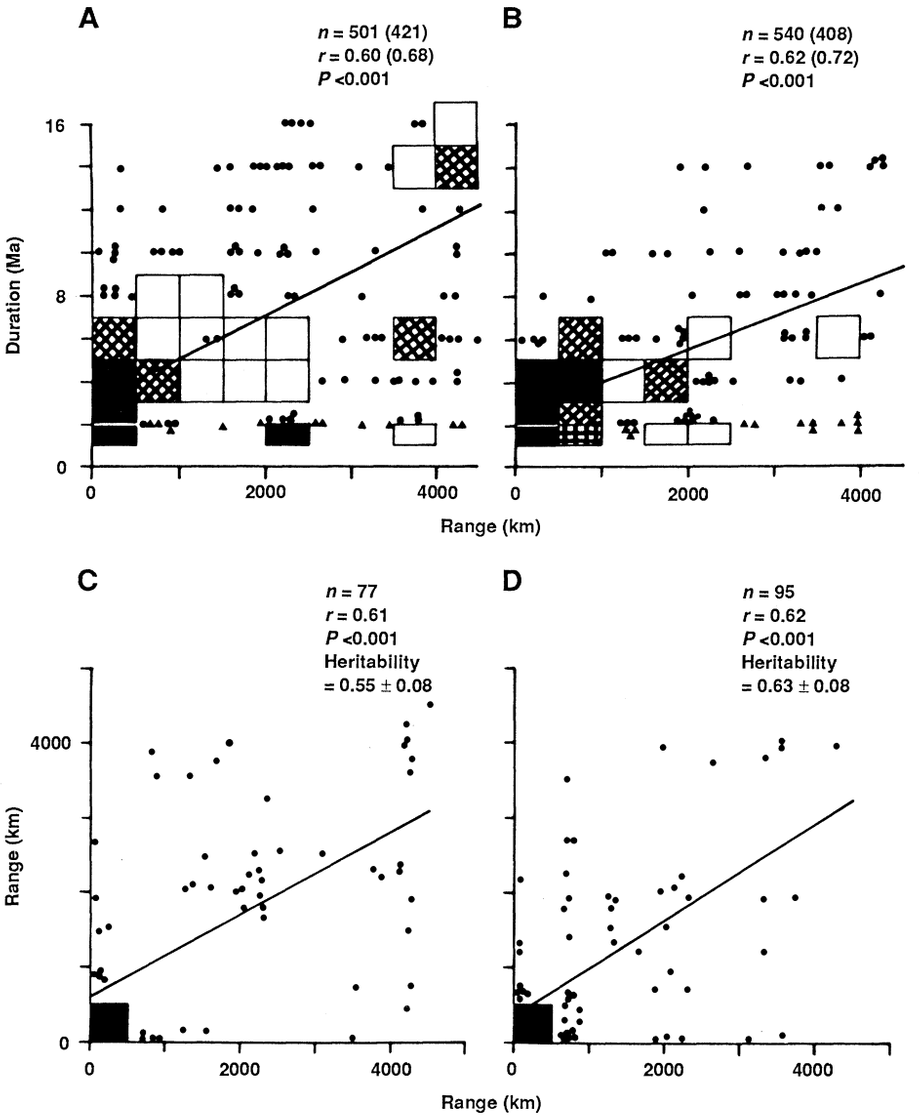

Fig. 1. Contoured scatterplots showing the relation between geographic range and species survivorship in Late Cretaceous bivalve species of the Gulf and Atlantic Coastal Plain, and heritability of that trait [nonparametric tests provide more reliable significance estimates for the relations depicted (*8, 10*)]. Solid boxes represent more than 20 species; hatchured boxes, 11 to 20 species; open boxes, 6 to 10 species. (**A** and **B**) Statistically significant positive relation between geographic range and stratigraphic duration in (A) bivalves and (B) gastropods. Lower half-boxes and triangles at 2 m.y. represent species that first appear in the 2 m.y. immediately preceding the end-Cretaceous mass extinction. Exclusion of these truncated species from the analysis lowers sample size (*n*) but yields a higher correlation coefficient (given in parentheses). (**C**) Least-squares linear regression of geographic ranges for pairs of closely related bivalve species and in (**D**) gastropods. Following the conventions of quantitative genetics, regression slopes are taken as estimates of heritability of this species-level characteristic. Product moment correlation coefficients, which provide another estimate of heritability without requiring assumptions on ancestor-descendant relationships, give statistically indistinguishable results, as do nonparametric Spearman rank correlation coefficients (Table 1).

Table 1. Correlation and regression coefficients for Late Cretaceous bivalves and gastropods. n is the number of species or species pairs, r_s is the Spearman rank-order correlation coefficient, r is the linear regression coefficient, r_p is the product moment correlation coefficient ± standard error, and m = regression slope (= "heritability") ± standard error. Significance levels: * = $P < 0.001$.

Mollusk	Parameter				
	n	r_s	r	r_p	m
Geographic range (km) versus stratigraphic duration					
Bivalves					
All species	501	0.69*	0.60*		
Truncated species omitted	421	0.80*	0.68*		
Gastropods					
All species	540	0.71*	0.62*		
Truncated species omitted	408	0.81*	0.72*		
Geographic ranges for pairs of related species					
Bivalves	77	0.63*		0.61 ± 0.09*	0.55 ± 0.08
Gastropods	95	0.65*		0.62 ± 0.08*	0.63 ± 0.08

Table 2. Heritabilities for organismic traits [in part after (*14*)] compared with species-level analog of heritability for geographic ranges of Late Cretaceous bivalves and gastropods.

Trait	Heritability	Reference
Cattle milk yield	35	(*23*)
Mouse body weight	35	(*24*)
Drosophila bristle number	50	(*23*)
Chicken egg weight	50	(*26*)
Gastropod shell diameter	53	(*27*)
Chicken body weight	55	(*26*)
Cretaceous bivalve ranges	55	
Horse racing speed	60	(*28*)
Cretaceous gastropod ranges	63	
Human stature	65	(*29*)
Cattle body weight	65	(*30*)
Gastropod shell diameter	70	(*31*)
Galapágos finch bill width	90	(*32*)

tantly, mechanisms of inheritance at the species level are complex and not readily decomposed into the additive genetic and phenotypic variances that underlie the heritabilities calculated by the quantitative geneticist. Nevertheless, it is clear that a significant correlation exists between related taxa for this species-level trait that is comparable in strength to those recorded between related individuals for organismic traits long regarded as profitable targets for artificial selection.

In marine organisms, geographic ranges are determined by a complex interaction of numerous intrinsic and extrinsic factors, for example, larval dispersal ability (*5, 18*). However, variance of geographic range within each larval mode—or any other single trait—is high. The multifactorial nature of the problem is underscored by the bivalve data, where larval mode has little detectable effect on geographic range or species duration (*12*), but the geographic range-duration relation and its heritability still holds. Mode of larval development is doubtless subject to and shaped by organismic selection as well, but if the observed species-level relations are generated because geographic range per se imparts extinction resistance [just as genetic population structure, potentially another trait above the organismic level, imparts characteristic speciation rate (*5*)], then similar evolutionary dynamics can emerge from any combination of underlying, organismic-level factors that yields the appropriate feature at higher levels (*19*). As Vrba and Gould (*2*) emphasize, the level of organization that is actually the focus of selection must be considered.

The analytical results indicate first that the spectrum of geographic ranges of species within clades can be shaped by selection at the species level; other factors being equal, mean geographic range should increase through a clade's history because widespread species are extinction-resistant and tend to give rise to similarly widespread species. However, this macroevolutionary tendency may be counteracted by mass extinctions: for the clades analyzed here, survivorship during the end-Cretaceous mass extinction was unrelated to species-level geographic range (*6*), disrupting net trends established during times of background extinction.

Second, organismic and species-level traits can "hitchhike" (*20*) on geographic range, with heritable differences among species' geographic ranges potentially giving rise to differential survival of hitchhiking traits with similar selective values at the organismic level. In a hierarchical system, heritability and its populational (*21*), species-level (*22*), and even clade-level analogs (*6*) are essential determinants of the efficacy of selection as an evolutionary force at any focal level, and of the strength of evolutionary effects across levels.

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9. The observed relation is not simply a consequence of changing geographic range-duration relations through the stratigraphic section. The proportion of geographically restricted (≤500 km) [following (*5*)], short-duration (≤2 m.y.) species remains statistically constant for bivalves and gastropods in the first and second 8-m.y. increments of the 16-m.y. study interval (bivalves 58% and 61%, respectively; gastropods 59% and 54%, respectively).
10. Kolmogorov-Smirnov test with 500-km intervals; for bivalves, $0.20 < P < 0.30$; for gastropods, $P > 0.50$. Jablonski (*5*) gives similar results for this data set in an analysis combining both bivalves and gastropods.
11. When the truncated species are omitted from the analysis, both Spearman rank correlation coefficients and regression coefficients increase as shown in Table 1 and Fig. 1, A and B.
12. In an analysis of eastern Pacific Neogene bivalves, S. M. Stanley [*Paleobiology* **12**, 89 (1986)] found that body size was a better predictor than geographic range of species extinction rates, as measured by Lyellian curve analysis. However, for Late Cretaceous mollusks, simple linear regressions for the seven bivalve and nine gastropod clades in which $n \geq 15$ (with the truncated species omitted) yielded 15 statistically significant positive correlations ($P < 0.01$) between geographic range and geologic durations, but only two significant correlations, one positive and one negative, between body size and geologic duration. This contrast in results corroborates Stanley's tentative conclusion that selective pressures were extremely different for benthic mollusks in Late Cretaceous and Neogene seas.
13. See D. Nicol [*J. Paleontol.* **28**, 22 (1954)] and A. Hoffman and B. Szubdzda-Studencka [*N. Jb. Geol. Palaeont. Abh.* **163**, 122 (1982)] on rapid attainment and relative stability of geographic ranges in Neogene bivalves.
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15. Correlations might be artificially enhanced by fossil species that are taxonomically oversplit if the conspecific variants incorrectly regarded as good species are geographically coextensive. However, among living mollusks many variants below the species level reflect geographic variation or subspeciation in which discrete populations are not constrained toward similar magnitudes of geographic ranges.

16. For the regressions on geographic ranges of Cretaceous molluscan species pairs, the member of each pair with the stratigraphically lower (that is, geologically older) first occurrence was assigned to the horizontal axis (independent variable), a relatively dependable procedure for taxa with a good fossil record [C. R. C. Paul, *Syst. Assoc. Spec. Vol.* **21**, 75 (1982); *Palaeont. Assoc. Spec. Paper 33* (1985)]; if both members of the pair first occurred in the same 2-m.y. interval, the species whose name came first alphabetically was assigned to the horizontal axis. Linear regression coefficients were statistically indistinguishable from the product moment correlation coefficients in Table 1, presumably reflecting nearly identical variances of putative sister species or ancestral-descendant pairs.
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19. See also R. R. Strathmann [*Annu. Rev. Ecol. Syst.* **16**, 339 (1985), p. 358], who argues that extensive dispersal, with "its profound evolutionary consequences," is "an accidental by-product" of organismic selection on other life-history features.
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Apolipoprotein B-48 Is the Product of a Messenger RNA with an Organ-Specific In-Frame Stop Codon

SAN-HWAN CHEN, GEETHA HABIB, CHAO-YUH YANG, ZI-WEI GU, BO RONG LEE, SHI-AI WENG, STEVEN R. SILBERMAN, SHENG-JIAN CAI, J. P. DESLYPERE, MARYVONNE ROSSENEU, ANTONIO M. GOTTO, JR., WEN-HSIUNG LI, LAWRENCE CHAN

The primary structure of human apolipoprotein (apo) B-48 has been deduced and shown by a combination of DNA excess hybridization, sequencing of tryptic peptides, cloned complementary DNAs, and intestinal messenger RNAs (mRNAs) to be the product of an intestinal mRNA with an in-frame UAA stop codon resulting from a C to U change in the codon CAA encoding Gln^{2153} in apoB-100 mRNA. The carboxyl-terminal Ile^{2152} of apoB-48 purified from chylous ascites fluid has apparently been cleaved from the initial translation product, leaving Met^{2151} as the new carboxyl-terminus. These data indicate that ~85% of the intestinal mRNAs terminate within ~0.1 to 1.0 kilobase downstream from the stop codon. The other ~15% have lengths similar to hepatic apoB-100 mRNA even though they have the same in-frame stop codon. The organ-specific introduction of a stop codon to a mRNA appears unprecedented and might have implications for cryptic polyadenylation signal recognition and RNA processing.

APOLIPOPROTEIN (APO) B HAS BEEN one of the most sought after proteins because of its important role in lipid metabolism and in the development of atherosclerosis. It is the largest protein species and an obligatory component of chylomicrons, very low density lipoproteins (VLDL), intermediate density lipoproteins (IDL), and low density lipoproteins (LDL). ApoB is heterogeneous but exists primarily in two forms: apoB-100 and apoB-48. ApoB-100 is synthesized primarily by the liver and is the major protein constituent of VLDL, IDL, and LDL. ApoB-48 is synthesized by the intestine and is found in chylomicrons and chylomicron remnants (*1*). The primary structure of human apoB-100 (4536 residues) has recently been deduced from the nucleotide sequence of overlapping liver complementary DNAs (cDNAs) (*2, 3*). The structure of apoB-48 remains elusive. It does not bind to the LDL receptor and has a molecular weight ~48% of that of apoB-100. Monoclonal antibody mapping studies indicate that apoB-48 shares antigenic determinants with the NH_2-terminal half of apoB-100 (*4*). However, complete structural analysis of apoB-48 has been hampered by its huge size, its insolubility in aqueous buffers, and difficulties in obtaining large amounts of the purified protein.

We now present the primary structure of apoB-48 obtained by nucleotide sequence analysis of cloned human intestinal apoB cDNAs and direct sequencing of human intestinal messenger RNAs (mRNAs). Our findings are corroborated by direct amino acid sequence analysis of multiple tryptic peptide fragments of purified human apoB-48, including its COOH-terminal tryptic fragment.

The adult small intestine synthesizes only apoB-48. Although apoB-48 and apoB-100 are the products of a single gene (*5*), studies indicate that apoB-48 is not the product of a post-translational cleavage of apoB-100 (*6*). It would then seem that the intestine would produce only apoB-48 mRNA. Unexpectedly, however, we found sequences identical to different regions of apoB-100 cDNA, including the COOH-terminal region, in cDNA clones from a human intestinal cDNA library (*7*).

We measured the relative concentrations of apoB-100 cDNA hybridizable sequences in the human intestine with cDNA probes corresponding to various regions of human apoB-100. In adult human small intestine the 3′ half of the apoB-100 mRNA sequence is present at ~15% of that of the 5′ half (Fig. 1). The 5′ half is at a concentration of $\sim 4.7 \times 10^7$ molecules per microgram of RNA in both human liver (Hep G2 cells) and intestine. In the intestine the concentration of mRNA sequences 3′ to those that code for amino acid residues ~1900 to 2400 drops to $\sim 7 \times 10^6$ molecules per microgram of RNA, whereas in the liver the concentration stays at $\sim 4.7 \times 10^7$ molecules per microgram of RNA. This suggests that adult intestine contains mainly an mRNA species that directs the synthesis of a protein corresponding to the NH_2-terminal half of apoB-100.

We performed direct sequence analysis of apoB-48 isolated from a patient with chylous ascites (*8*) and purified by column chromatography in SDS. The protein was found to be pure by SDS–gel electrophore-

S.-H. Chen, G. Habib, C.-Y. Yang, Z.-W. Gu, B. R. Lee, S. Weng, S. Silberman, S.-J. Cai, A. M. Gotto, Jr., L. Chan, Departments of Cell Biology and Medicine, Baylor College of Medicine, and The Methodist Hospital, Houston, TX 77030.
J. P. Deslypere, Department of Endocrinology, University Hospital, Ghent, Belgium.
M. Rosseneu, Department of Clinical Chemistry, A.Z. St. Jan, Brugge 8000, Belgium.
W.-H. Li, Center for Demographic and Population Genetics, University of Texas, Houston, TX 77030.