ability of the residual voltage-insensitive conductance. This component is sufficiently small that passage of Lucifer might not have been detected during the experiment even if the junctions were permeable to it.

The voltage sensitivity described here is found in three amphibian families of two orders. Less marked sensitivity is observed in blastomeres of the teleost *Fundulus* (unpublished observations). Rectification is uncommon at electrotonic synapses, but where it occurs it is generally much faster and probably operates by a different mechanism (*2, 11*). Records similar to those in Fig. 1 have been obtained from pairs of *Limulus* retinula cells, but the morphological basis is unclear and the mechanism may be quite distinct (*2, 12*).

The significance of voltage dependence of junctional conductance remains to be established. One of the major questions about early development is how coupled blastomeres acquire and maintain individual developmental programs. In several instances specific cells or cell groups are known to uncouple or lose their gap junctions at specific times (*13*), and a large difference in resting potential can develop between different regions of an embryo (*14*).

The phenomena described here would allow a cell to determine the extent to which its cytoplasm communicates with that of its neighbors by making small changes in its membrane potential. Changes in relative ion permeability, ion concentration, or electrogenic pumping could all lead to differences in resting potential that rapidly uncoupled the cells from each other (*15*). Additional mechanisms are required to account for disappearance of gap junctions, but the relatively rapid changes reported here provide a possible mechanism for short-term regulation of cellular communication during development.

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4. Physiological saline contained, in millimoles per liter: NaCl, 58.2; KCl, 0.7; $Ca(NO_3)_2 \cdot 4H_2O$, 0.3; $MgSO_4 \cdot 7H_2O$, 0.8; Na_2HPO_4, 0.8; KH_2PO_4, 0.1; and $NaHCO_3$, 0.4 [M. C. Niu and V. C. Twitty, *Proc. Natl. Acad. Sci. U.S.A.* **39**, 985 (1953)].
5. The coupling coefficient is V_2/V_1, where V_1 is the voltage in the cell in which current is injected and V_2 is the potential in the other cell [M. V. L. Bennett, *Ann. N.Y. Acad. Sci.* **137**, 509 (1966)].
6. The voltage-sensitive component of junctional conductance can be well fit by an expression of the form $g_j/(g_m - g_j) = \exp[-A(V - V_0)]$, where g_m is the maximum conductance, V is the transjunctional voltage, V_0 is the voltage at half-maximal conductance, and A is a constant. This result is consistent with a Boltzmann distribution of open and closed channels where $A(V - V_0)kT$ is the energy difference between the two states. The movement of about six electron charges through the entire transjunctional potential would account for the energy differences and the ratio $g_j/(g_m - g_j)$ changes e-fold for a 4-mV change in V. Similar analyses are given for channels in artificial membranes by G. Ehrenstein, H. Lecar, and E. R. Nossal [*J. Gen. Physiol.* **55**, 119 (1970)] and S. J. Schein, M. Colombini, and A. Finkelstein [*J. Membr. Biol.* **30**, 99 (1976)]. The voltage-insensitive component of junctional conductance may arise from a small population of channels which are not voltage-sensitive or from incomplete closure of channels. Alternatively, there may be a small amount of coupling by way of extracellular space in the large area of apposition between cells.
7. Junctional conductance decays exponentially to its steady-state value. As transjunctional voltage increases, the time constant increases then decreases. The recovery of conductance with both cells at the resting potential is also exponential. We conclude that junctional conductance changes by a first-order process.
8. Lucifer Yellow is a substituted 4-aminonaphthalimide dye with high fluorescent yield and good retention by nonjunctional membranes. It was designed by W. W. Stewart [*Cell* **14**, 741 (1978)] for cell marking and has been shown by him and others to cross electronic junctions [Bennett *et al.* (*9*); S. B. Kater and J. J. Galvin, *J. Cell Biol.* **79**, 20 (1979)]. We are indebted to W. W. Stewart for providing the dye.
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10. Impermeability to fluorescein or Procion Yellow has been asserted for gap junctions in several other early embryonic systems [C. Slack and J. F. Palmer, *Exp. Cell Res.* **55**, 416 (1969); M. V. L. Bennett, M. E. Spira, G. D. Pappas, *Dev. Biol.* **29**, 419 (1972); J. T. Tupper and J. W. Saunders, Jr., *ibid.* **27**, 546 (1972)]. The recent demonstration of Lucifer Yellow CH and fluorescein passage in *Fundulus* (*9*) suggests that reevaluation of previous negative and ambiguous [J. D. Sheridan, *Dev. Biol.* **26**, 627 (1971)] findings would be worthwhile.
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15. The voltage dependence is sufficiently great that a decrease in junctional conductance can occur regeneratively under constant-current conditions, such as might be provided by an electrogenic pump. (Compare Fig. 1.) We have seen stable uncoupling induced by brief pulses when resting potentials of cells differed sufficiently. Although in these cases the resting potential differences were probably due to injury produced by microelectrode penetration, greater differences have been observed in situ at later stages (*14*).
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Comparisons of Frogs, Humans, and Chimpanzees

A few minutes with a basic text on amphibians (*1*) reveal that the frogs *Rana* and *Xenopus* differ in at least the following six basic structural traits: (i) tongue (present in *Rana*, absent in *Xenopus*); (ii) centra of anterior vertebrae (procoelus in *Rana*, opisthocoelus in *Xenopus*); (iii) ribs (absent in *Rana*, present in *Xenopus*); (iv) urostyle (articulated to sacral vertebra by a double condyle in *Rana*, fused to sacral vertebra in *Xenopus*); (v) eyelids (functional in *Rana*, nonmovable in *Xenopus*); and (vi) tadpoles (with horny mouthparts and one ventral spiracle in *Rana*, without horny mouthparts and with two lateral spiracles in *Xenopus*). To the extent that we can compare *Pan* and *Homo* with respect to these traits we would find them identical. Moreover, there are no morphological differences between man and chimpanzee of comparable magnitude to those which distinguish the two anurans. An unbiased assessment of morphological differences between *Rana* and *Xenopus* or *Pan* and *Homo* would show just what the genetic data show: trenchant differences between the two frogs and great similarity between the two primates. The external shape comparisons recently presented by Cherry, Case, and Wilson (*2*) seem wanting. By comparing external shape of selected anguilliform vertebrates such as eels (Osteichthyes), snakes and limbless lizards (Reptilia), and caecilians (Amphibia), it could be demonstrated that all of these show greater resemblance to one another than do humans and chimpanzees.

By selecting appropriate anatomical features among vertebrates, one could show great similarity between taxa wide-

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ly separated genetically and the converse. For example, if erythrocyte shape were selected, camels and amphibians would appear more similar to each other (both having ovoid or elliptical erythrocytes) than would camels and other mammals. Presence of enucleated erythrocytes would link other mammals with some salamanders (*1*, *3*); absence of erythrocytes would separate ice fish from all other fishes and cause them to resemble some invertebrates.

At one time numerical taxonomists espoused a notion referred to as the nonspecificity hypothesis (*4*), which held that detailed analysis of any structure or organ system of a set of organisms would reveal the same picture of affinities that would emerge from analysis of any other structure or system. A multitude of findings have caused this hypothesis to be abandoned (*5*, *6*), and systematists have more and more come to use data from the entire phenotype to predict genotypic affinities. Students interested in comparing rates of morphological and biochemical evolution could do worse than to be attentive to a diversity of phenotypic as well as of genotypic traits before drawing their conclusions.

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Evolutionary biology is in need of a yardstick or metric with which to measure morphological evolution in creatures as diverse as frogs and mammals. Two types of metric have been suggested to measure morphological distance, one based on quantal traits and the other on quantitative traits. Quantal traits are those whose state varies and is scored as 0 or 1 (presence or absence of a tongue). Quantitative traits are those whose state varies continuously (length of leg), and in this case the degree of difference between states is measured quantitatively.

Findley (*1*) recommends that quantal traits be used for comparing the magnitude of the morphological difference between humans and chimpanzees with that between frogs. He chooses six quantal traits such that the state in *Xenopus* differs from that in *Rana*, whereas the state in humans is identical to that in chimpanzees (*1*). We present a counter list of six quantal traits, for which the opposite result is obtained. For these traits, chimpanzees and humans differ, whereas *Xenopus* and *Rana* are the same. Table 1 records the results of comparing additional pairs of species with respect to the 12 traits. Frogs belonging to different species, genera, or families are identical for all 12 of the traits, confirming the hypothesis that phenotypically chimpanzees differ more from humans than one frog family differs from another.

Table 1. Morphological comparisons for 12 quantal traits. The traits examined include the six listed by Findley (*1*) and the following six: cranium (ethmoid meets or does not meet parietal); upper jaw (premaxilla fused or unfused to maxilla); lower jaw (simian shelf present or absent); ribs (number of pairs, 13 or less than 13); pelvis (sciatic notch present or absent); and foot (first digit opposable or nonopposable).

Species compared	Number of traits different
Primates	
Human versus chimpanzee	6
Frogs	
Different suborders	
Xenopus versus *Rana*	6
Different families	
Hyla versus *Rana*	0
Different genera	
Hyla versus *Acris*	0
Different species	
Hyla regilla versus *eximia*	0

Most numerical taxonomists, however, would argue that 12 quantal traits are too few for an adequate test. As chimpanzees and humans are reported to differ by at least 312 quantal traits (*2*), it occurred to us to invite Findley to try to come up with a similar number of quantal traits by which *Xenopus* and *Rana* could be distinguished. An exercise like this could be entertaining, but it might not have scientific value. We are not convinced that it is valid to use quantal traits for estimating overall degree of morphological difference between species. Our skepticism stems chiefly from considering the problem of how to avoid bias in the picking of quantal traits. This problem is illustrated by the contrasting results obtained in the above example. Depending on which of the two sets of six traits one picks, the chimpanzee-human difference seems either small or large relative to the *Xenopus-Rana* difference.

We feel that quantitative traits may be more appropriate than quantal traits for obtaining reliable estimates of morphological distance. It is well known from studies of quantitative genetics that such linear traits usually exhibit continuous variation in genetic tests. Furthermore, in our own morphological work with hundreds of species (*3*, *4*), every quantitative trait examined varies in length both within and among species. Variability within a particular taxonomic group is therefore not a criterion for choosing among quantitative traits.

Cherry *et al.* (*3*) have developed a morphological distance metric based on quantitative traits from all major parts of the body. The metric is monotonically related to traditional zoological estimates of phenotypic distance among frogs (*3*). Findley (*1*) seems to have overlooked the significance of this empirical demonstration of the utility of the metric based on quantitative traits.

Regardless of the approach preferred, it seems from the information already available that, relative to differences among frog families, the morphological difference between humans and chimpanzees is large. However, at the protein sequence level, the chimpanzee-human difference is very small by frog standards. As pointed out before, species within a genus of frogs usually differ far more from each other in their protein sequences than do humans from chimpanzees (*3*, *5*). Thus morphological evolution and protein sequence evolution can proceed at contrasting rates. This contrast has important implications for our understanding of the mechanism of evolution (*6*).

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