finding indicates that bacteria of the intestinal tract probably play a prominent role in degradation of MTX and may be responsible for the changed MTX toxicity observed during antibiotic treatment in mice.

Another interesting finding is the change in the relative excretion of radioactivity in urine as compared to feces. In Table 1, the percentage of the dose that appears in the urine decreased approximately 50 percent, from 42 percent in normal mice to 19 percent in animals treated with antibiotics. This change in the urine was paralleled by an inverse change in feces, in which there was an increase from 39 percent in normal animals to 54 percent in those treated with antibiotics. A possible explanation for this observation is that neomycin has been shown to alter the intestinal absorption of several substances (*9*) and may have a similar effect on MTX. In order to test whether this inhibition of MTX absorption was due to neomycin, several mice (male DBA/2) that had been raised in a germ-free environment were tested in a similar manner. After an intraperitoneal injection of tritiated MTX, 80 to 99 percent of the radioactive dose appeared in the feces. This abnormal fecal excretion was attributed to the inevitable injection directly into the characteristic, enormously enlarged cecum of these animals (*10*). Similar experiments with a subcutaneous injection into germ-free and normal animals indicate that the distribution of radioactivity between urine and feces of germ-free animals was similar to that of normal mice—52 to 61 percent in the urine and 20 to 34 percent in the feces of germ-free mice. These findings indicate that neomycin probably inhibits the intestinal absorption of MTX. The fraction of radioactivity representing MTX in the urine of the germ-free mice rose to 86 to 94 percent, which suggests that little metabolism of MTX was taking place. Unfortunately, feces of germ-free mice were not amenable to separation into identifiable radioactive components by various organic solvent extraction and chromatographic procedures.

Our findings support the hypothesis that an antibiotic regimen given along with MTX affects absorption from the intestinal tract and the metabolism of MTX by intestinal flora. This kind of drug-host-drug interaction may have far-reaching significance in chemotherapy during which antibiotics are used extensively along with anticancer drugs and perhaps other chemotherapeutic agents. The choice of the proper antibiotic may be crucial for successful chemotherapeutic treatment.

DANIEL S. ZAHARKO
HOWARD BRUCKNER
VINCENT T. OLIVERIO

Laboratory of Chemical Pharmacology,
National Cancer Institute,
Bethesda, Maryland 20014

References and Notes

1. D. G. Johns, A. T. Iannotti, A. C. Sartorelli, J. R. Bertino, *Biochem. Pharmacol.* **15**, 555 (1966).
2. H. M. Redetzki, J. E. Redetzki, A. L. Elias, *ibid.*, p. 425.
3. E. S. Henderson, R. H. Adamson, C. Denham, V. T. Oliverio, *Cancer Res.* **25**, 1008 (1965).
4. R. R. Scheline, *J. Pharm. Sci.* **57**, 2021 (1968).
5. H. Bruckner, *Fed. Proc.* **28**, 263 (1969).
6. V. T. Oliverio, *Anal. Chem.* **33**, 263 (1961).
7. D. G. Johns, J. W. Hollingsworth, A. R. Cashmore, I. H. Plenderleith, J. R. Bertino, *J. Clin. Invest.* **43**, 621 (1964).
8. P. Goldman and C. C. Levy, *Biochem. Pharmacol.* **17**, 2265 (1968).
9. E. D. Jacobsen, R. B. Chodos, W. W. Faloon, *Amer. J. Med.* **28**, 524 (1960).
10. M. E. Coates, H. A. Gordon, B. S. Wastmann, Eds., *The Germ-Free Animal in Research* (Academic Press, New York, 1968), pp. 145–151.
11. Supported in part by NIH fellowship 1-F3-GM39 700-01 from the National Institute of General Medical Sciences. We thank Noreen Considine for technical assistance.

4 September 1969

Lissamphibian Origins: Possible Protolissamphibian from the Lower Permian of Oklahoma

Abstract. *A new genus and family of rhachitomous labyrinthodont amphibian, related to the Upper Paleozoic Dissorophidae and Trematopsidae, may be ancestral to some or all of the modern Amphibia.* Doleserpeton *occurs in Lower Permian fissure fill deposits in southwestern Oklahoma. It is unique among nonlissamphibian tetrapods in that it possesses pedicellate, bicuspid teeth together with nearly monospondylous vertebrae in which the main central element is a pleurocentrum.* Doleserpeton *may have been utilizing the food resources of the upland, terrestrial environment in a novel fashion for rhachitomes.*

The phylogeny of most higher taxa of living tetrapods is now known at least in broad outline. The three orders of modern Amphibia (hereafter to be referred to as Lissamphibia for convenience—no phyletic judgment is intended) constitute one of the few exceptions. Various investigators have suggested a taxonomically and structurally diverse series of groups as ancestors of part or all of the Lissamphibia, but no consensus on their origins presently exists. The major reason for this is the lack of recognizable transitional forms in the fossil record. A variety of fragmentary specimens have been hopefully assigned to an ancestral position, but all are open to other interpretations. This paper presents the first report of a species which is represented by abundant and well-preserved material and possesses characters otherwise confined to the Lissamphibia among tetrapods.

All specimens come from Lower Permian fissure fillings in Ordovician limestones from the Wichita Mountains in southwestern Oklahoma. Almost all are from the Fort Sill locality of Gregory *et al.* (*1*), which is the Richards Spur site of Olson (*2*). A few fragmentary specimens came from the South Carnegie locality of Olson (*2*). Both Fort Sill and Carnegie are limestone quarries; the latter is not being worked at present. Preservation at Fort Sill is exceptional; both surface markings and histological details, such as calcified cartilage in the ends of long bones, are easily observed. My material came from fissure fill which had been discarded in a corner of the quarry; no accessible fossil-bearing fissures are presently exposed in the quarry walls. Most specimens came from a single clay mound of the many in the spoil heap. This clay contains remains of many thousands of individuals but virtually no genera other than *Doleserpeton.* I will hereafter refer to it as the "D-concentrate."

Class Amphibia
Subclass Labyrinthodontia
Order Temnospondyli
Suborder Rhachitomi
Superfamily Dissorophoidea, n. superf.
Family Doleserpetontidae, n. fam.

Diagnosis: The same as for the genus; presently a monogeneric family.

Doleserpeton, n. gen.

Diagnosis: Small rhachitomous amphibian. The marginal teeth are nonlabyrinthine, bicuspid with labial and lingual cuspules, and pedicellate in the sense of Parsons and Williams (*3*). Postatlantal vertebral centra consist of two ossifications: (i) a cylindrical pleurocentrum, which may or may not be open dorsally but is always complete ventrally in adults; and (ii) a small, crescentic, ventral intercentrum. The generic name refers to Dolese Brothers Company, the operator of the Fort Sill quarry.

Doleserpeton annectens, n. sp.

Holotype: Field Museum of Natural History UR 1308 (Fig. 1), a nearly complete skull with the dorsal and lateral surfaces exposed, with anterior part of vertebral column and partial right forelimb. Referred specimens are too numerous to list; all are in the Field Museum.

Diagnosis: The same as for the genus. The specific name refers to its possible annectent position with respect to some or all of the Lissamphibia.

Locality and horizon: Dolese Brothers Company quarry, Richards Spur plant, southwest quarter, section 31, township 4 north, range 11 west, Comanche County, Oklahoma. The fissure fills contain Lower Permian tetrapods, but more exact stratigraphic correlation is difficult. Olson (*2*) probably concurred with majority opinion when he tentatively correlated these fills with the Arroyo formation of Texas on the basis of similarity between tetrapod faunas. Most specimens from the D-concentrate are probably subadult. Sculpturing on the dermal cranial roof bones is weakly developed, thus corresponding to juvenile stages as described by Bystrow (*4*). A few of the larger elements, however, many of which are not from the D concentrate, show typical labyrinthodont reticulate sculpturing. Except for differences in dermal sculpturing, the smallest and largest elements are identical. Thus, if *Doleserpeton* underwent metamorphosis, the available material is probably all postmetamorphic, despite the weak sculpturing. Sutures between roofing bones are squamous, even on the larger specimens. The largest skull in my collection, measured parallel to the midline between the quadrate bone and the tip of the snout, is some 20 mm long. The smallest skull is about 12 mm long. Most of the elements in the D-concentrate are appropriate to animals with a skull length of about 15 mm.

Description: The skull (Figs. 2 and 3) is slightly longer than broad and rather flattened as reconstructed. Measured vertically, the height from the bottom of the quadrate to the dorsal surface of the parietal bone is approximately one-third of the interquadrate width. Small bony rods scattered around the postcranial skeleton in several specimens probably represent remains of scales (*5*). With the exception of the intertemporal bone, all the usual labyrinthodont dermal roofing bones are present. There seems to have been a small internasal fenestra. The otic notch is well developed; a small but definite semilunar flange of the supratemporal bone projects into the notch. The frontal bones participate in the orbital margins. The lacrimal bone is pierced posteriorly by several foramina which lead into a single canal for the lacrimal duct. A striking feature is the lateral exposure of the palatine bone at the anteroventral corner of the orbit, above the maxilla and separating the jugal and lacrimal bones. Both lacrimal and palatine have, in addition, a broad exposure within the orbit. Each quadrate bears posteromedially a stout dorsal process, and a short flange from the quadratojugal bone wraps around the base of the process posteriorly. Prootic and opisthotic bones are well ossified, although rarely fused. The occipital condyle is partly subdivided into two lateral condyles, connected by a ventral bony strip. Several tiny foramina, presumably for cranial nerve XII, are present in the exoccipital bone. There is no supraoccipital bone, and indeed no room for one, as the opisthotics cover the tops of the exoccipitals and, in maturer specimens, fuse above the foramen magnum. The stapes consists of a rodlike columella and an approximately circular footplate, perforated by a stapedial foramen. No dorsal process has been identified. Postmortem separation of braincase elements precludes observation of the fenestra ovalis and determination of the presence or absence of an ossified operculum. The lower jaw as reconstructed does not differ greatly from that of other Lower Permian rhachitomes, although the symphyseal pit teeth are identical with those of palatal bones. Both lower jaws are present in two specimens, with well-preserved symphyseal regions. No mentomeckelian bones are present in either specimen.

Interpterygoid vacuities (Fig. 3) are large, and the pterygoid bones appear to make contact only with the most posterior parts of the palatines. The basipterygoid joint was probably mobile, although the pterygoid and the parasphenoid-basisphenoid complex are always poorly preserved at the joint. The ectopterygoid bone is missing, even in the more mature specimens, and no toothed bone which could be an ectopterygoid occurs in the D-concentrate. The vomer and palatine bones each have a single tooth pit. In each pit there were three to five simultaneously functioning pit teeth similar to the marginal teeth. The ventral surfaces of both

Fig. 1. *Doleserpeton annectens*. Type UR 1308. Skull in dorsal view, with associated partial postcranium. Scale equals 1 cm. (Upper inset) UR 1323. Posteriorly placed tooth on left maxilla in medial view. Crown is tilted laterally and has almost completely dropped off. Scale equals 0.1 mm. (Lower inset) FMNH 5254. Separated crown from D-concentrate in anteroposterior view. Scale equals 0.1 mm.

vomer and pterygoid bear numerous unicuspid, conical, recurved denticles. There are a few denticles on the palatine anterior to the tooth pit. Parasphenoidal denticles are restricted to a raised triangle at the base of the cultriform process. In section some of the parasphenoidal denticles, in particular, seem pedicellate, but the evidence is equivocal. As preserved, marginal teeth usually lack crowns (insets, Fig. 1), which occur separately scattered through the D-concentrate. No pit-tooth crowns have been identified. The few marginal-tooth crowns on skull UR 1323 are bicuspid and join the tooth bases (pedicels) at a definite line of potential abscession. Pedicels of both marginal and pit teeth are essentially cylindrical and are composed of dentine near the junction with the crown. In thin section, neither teeth nor denticles show any development of labyrinthine structure. Marginal teeth are pleurodont; pit teeth are fused to the lateral wall of the pit.

There are approximately 25 presacral vertebrae, including the atlas. All but the atlas represent variations on the pattern exemplified by the dorsal vertebrae (Fig. 4). The atlas has a single, solid centrum of uncertain homologies. It is fused without trace of suture to its neural arches, which fail to meet dorsally and do not bear diapophyses. The neurocentral suture is closed in larger, presumably more mature, vertebrae. There is a single sacral rib. All ribs are bicipital, and all presacral vertebrae except the atlas bear ribs.

The appendicular skeleton, including carpal and tarsal elements and phalanges, is well ossified. Long bones of the fore- and hindlimb, plus the pelvis and scapulocoracoid, are identical with those previously ascribed to Fort Sill microsaurian amphibians (*1*). These elements are now either unknown for the Fort Sill microsaurs or are indistinguishable from those of *Doleserpeton*. The tarsus is known only from individual elements. The two partial carpi found can be interpreted as being in good agreement with that of *Eryops* as reconstructed by Gregory *et al.* (*6*). Terminal phalanges are hooked, and the downturned portion is somewhat expanded.

Discussion: *Doleserpeton* is probably related to the rhachitomous amphibians of the Family Dissorophidae, which ranges in time from the Middle Pennsylvanian to the Lower Triassic. The family may be informally characterized as follows: Terrestrial animals with a well-developed appendicular skeleton; body is not elongated; there are 26 or fewer rhachitomous presacral vertebrae where the column is known; the intertemporal bone is absent; orbits are large, the frontal bone participating in the orbital margin in all but the primitive *Amphibamus* (*7*); otic notch is well developed in all and is closed posteriorly in some genera. All but *Tersomius* and *Amphibamus* (which are early members) have a semilunar flange from the supratemporal bone projecting into the otic notch (*8*). Most later genera are armored, with a row of dermal bony plates above the neural spines. Lateral exposure of the palatine is probably characteristic of dissorophids (*8, 9*), as is the combination of a dorsal process on the quadrate and a posteromedial process on the quadratojugal (*9*).

Doleserpeton is very likely related also to the rhachitomous amphibians of the Family Trematopsidae, a Lower Permian group. My analysis of this family is incomplete, but thus far the laterally exposed palatine and the quadrate and quadratojugal processes have been found in *Acheloma whitei,* and there is evidence for their occurrence in *Trematops* (*9*).

The dissorophids and trematopsids at present are placed in the Superfamily Eryopoidea. This superfamily is a "grade," whose members have departed from the presumably primitive rhachitome structure to a comparable degree and in similar fashion. The members of the Superfamily Eryopoidea differ somewhat from the group as proposed by Romer (*10*), but Romer's comments as to its possibly polyphyletic nature are still applicable. Romer proposed that the dissorophids, termatopsids, and zatracheids might be closely related. The latter are Pennsylvanian and Lower Permian rhachitomes remarkable for their development of bony fringes and spines on the skull. They appear not to possess the characteristics of palatine, quadrate, and quadratojugal discussed above, nor is there any other strong indication of relationship to dissorophids and trematopsids (*11*), although further study may validate Romer's suggestion. In any case, available evidence warrants separation of the dissorophids, trematopsids, and doleserpetontids as a phyletically based Superfamily Dissorophoidea.

Doleserpeton possesses no characters which would debar it from protolissamphibian status, but this is true of many other Paleozoic amphibians. There are three positive features suggestive of relationship to lissamphibians: (i) nearly monospondylous vertebrae, (ii) pedicellate

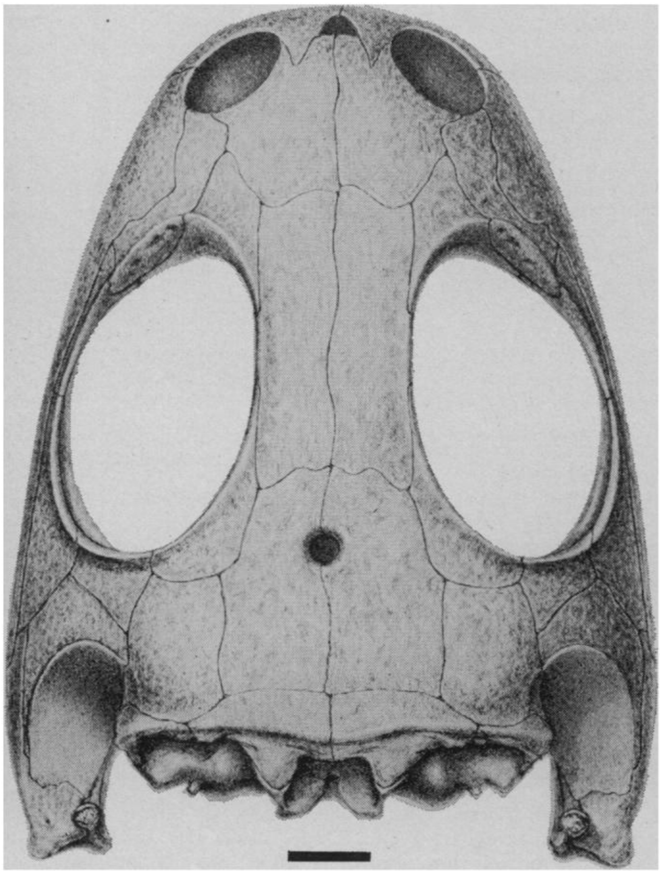

Fig. 2. Composite drawing of skull of *Doleserpeton annectens* in dorsal view. Scale equals approximately 1 mm.

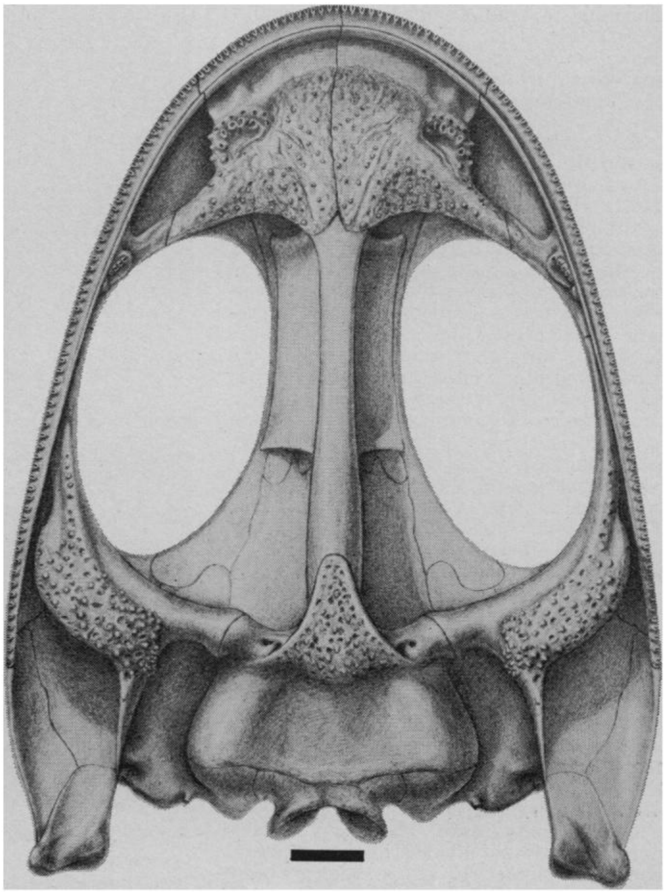

Fig. 3. Composite drawing of skull of *Doleserpeton annectens* in ventral view. Scale equals approximately 1 mm.

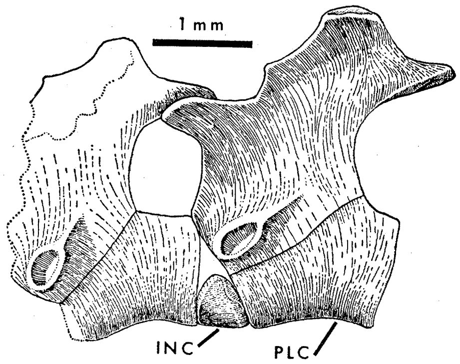

Fig. 4. *Doleserpeton annectens* UR 1332, two dorsal vertebrae in left lateral view; *INC*, intercentrum; *PLC*, pleurocentrum.

teeth, and (iii) bicuspid teeth. The first character is not particularly convincing by itself, as it is shared with other fossil amphibian groups [although among rhachitomes in the broad sense, only with *Peltobatrachus* (*12*), which otherwise does not seem to resemble *Doleserpeton* very closely (*9*)]. Parsons and Williams (*13*, p. 48) have listed seven characters which they feel "most clearly and uniquely link the three modern orders"; I would add an eighth, corresponding to (iii) above. Three of these eight characters might be determinable in a fossil. Two correspond to (ii) and (iii) above; the third, an operculum-plectrum complex, may or may not be present in *Doleserpeton.* Characters (ii) and (iii) have not been observed previously in any nonlissamphibian fossil tetrapod. Parsons and Williams argue for the recognition of Lissamphibia as a phyletic unit. They list 19 characters [I would expand this to 20, by including (iii) above] which might be present in an ancestral lissamphibian and might be recognizable in a fossil. [I question the advisability of postulating that pleurocentra would be "the dominant, if not the only, central elements." Despite Williams' (*14*) review, the homology of central elements in living amphibians is not secure (*15*). Rather, the vertebral centra should be monospondylous, or nearly so, thus leaving in abeyance the question of homologies.] On the basis of either the amended or original list, *Doleserpeton* has a higher "score" than any other nonlissamphibian tetrapod (*15*). *Doleserpeton* does not appear to possess any characters which clearly point to exclusive affinity with any one modern order. It is thus structurally a "protolissamphibian." Whether it is also such phyletically is an open question. Although a morphologically plausible protolissamphibian, *Doleserpeton* might well be ancestral to only part of the Lissamphibia. Its discovery does not solve the problem of the phyletic unity of the Lissamphibia.

The tetrapod faunas of upland, terrestrial environments are poorly represented in Upper Paleozoic deposits in North America. Most of our knowledge of such faunas comes from occasional finds of animals which were transported into lower-lying, more aquatic areas and buried there. The Fort Sill deposits, however, contain large numbers of upland terrestrial tetrapods, especially the reptile *Captorhinus,* and lack significant numbers of stream and pond dwellers. With the exception of the extremely rare aïstopod *Phlegethontia,* the only amphibians identified in the fissure fills were two genera of gymnarthrid microsaurs whose habits are problematic (*1, 16*). Labyrinthodonts other than *Doleserpeton* occur at Fort Sill but are comparatively quite rare. *Doleserpeton* is probably second in abundance only to *Captorhinus.* Bones of *Doleserpeton* in the D-concentrate generally show no signs of transportation. This and their abundance indicate that *Doleserpeton* is a member of the terrestrial fauna.

Throughout their long history, labyrinthodonts have occurred in association with aquatic or periaquatic vertebrate faunas. Several groups experimented with a more terrestrial mode of life, however, the best-studied case being that of the dissorophids and trematopsids (*8*). In certain respects, *Doleserpeton* was possibly adapted more completely to terrestrial existence than any other known labyrinthodont. *Doleserpeton* shows striking differences from other labyrinthodonts in both dentition and vertebrae. These changes in locomotor and feeding systems, together with its occurrence in a presumably very terrestrial situation, suggest that *Doleserpeton* was exploiting the terrestrial environment in a basically different fashion, and perhaps more fully than most contemporary labyrinthodonts. This could be a fundamental reason for the persistence of the Lissamphibia to the present. In this view the doleserpetontid protolissamphibians were a terrestrial group in the sense that early members were dependent for food on animals that lived on land (possibly insects, by analogy with living amphibians). If insects did constitute their major food source, then by implication most labyrinthodonts either fed upon insects in a basically different way, or did not feed upon them to the same extent, or both.

JOHN R. BOLT

Department of Anatomy, University of Illinois at the Medical Center
and *Department of Geology,*
University of Illinois at
Chicago Circle, Chicago, Illinois

References and Notes

1. J. T. Gregory, F. E. Peabody, L. I. Price, *Bull. Peabody Mus. Natur. Hist. 10* (1956).
2. E. C. Olson, *Okla. Geol. Surv. Circ. 74* (1967).
3. T. S. Parsons and E. E. Williams, *J. Morphol.* **110**, 375 (1962).
4. A. P. Bystrow, *Acta Zool. Stockholm* **16**, 65 (1935).
5. E. H. Colbert, *Amer. Mus. Novitates No. 1740* (1955).
6. W. K. Gregory, R. W. Miner, G. K. Noble, *Bull. Amer. Mus. Natur. Hist.* **48**, 279 (1923).
7. R. L. Carroll, *Bull. Mus. Comp. Zool. Harvard Univ.* **131**, 161 (1964).
8. R. E. DeMar, *J. Paleontol.* **42**, 1210 (1968).
9. J. R. Bolt, thesis, University of Chicago (1968).
10. A. S. Romer, *Bull. Mus. Comp. Zool. Harvard Univ.* **99**, 3 (1947).
11. W. L. Langston, *Univ. Calif. Publ. Geol. Sci.* **29**, 349 (1953).
12. A. L. Panchen, *Phil. Trans. Roy. Soc. London Ser. B Biol. Sci.* **242**, 207 (1959).
13. T. S. Parsons and E. E. Williams, *Quart. Rev. Biol.* **38**, 26 (1963).
14. E. E. Williams, *ibid.* **34**, 1 (1959).
15. R. Estes, *Amer. Zool.* **5**, 319 (1965).
16. E. C. Olson, *Evolution* **6**, 181 (1952).
17. I thank Drs. H. Barghusen, R. DeMar, E. Olson, and D. Wake for criticism and discussion, A. Gorman for photography, and Miss M. Moran and R. Parshall for drawings. A. Graffham supplied several fine skulls. J. Yingling, superintendent of the Dolese Brothers Richards Spur plant, allowed me to collect in the quarry on several occasions and aided in other ways. Supported by a NSF graduate fellowship at the University of Chicago and by a grant from the University of Illinois at the Medical Center, College of Medicine.

12 June 1969; revised 29 July 1969

Acoustic Synchrony: Two Mechanisms in the Snowy Tree Cricket

Abstract. *Snowy tree crickets synchronize their chirps by responding to the preceding chirp of their neighbors. If a neighbor's chirp precedes his own, a cricket shortens his chirp and the following interval. If it follows his own, he lengthens his chirp interval and sometimes the following chirp. A single response of the first type may advance his phase of chirping 160° and one of the second type may retard it 200°.*

The snowy tree cricket *Oecanthus fultoni* Walker (*1*) is a common dooryard species throughout most of the United States. Since 1889, its synchronous chirping has been a subject for comment in scientific literature (*2, 3*). However, only two previous investigators have reported experimental approaches to the phenomenon, and both established only that the synchrony is real and depends on auditory stimuli—Fulton found that males without tympanic organs chirped asynchronously, and Allard noted that individuals quickened their chirps in response to rapidly delivered imitations (*4*). I now report the first quantitative description of synchrony in the snowy tree cricket and the first detailed account of stimulus-response mechanisms in this or any other insect with comparable synchrony (*5*).

The song of the snowy tree cricket

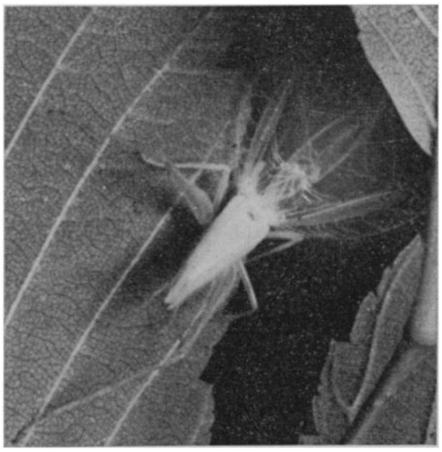

Fig. 1. Posterior view of male snowy tree cricket stridulating with elevated forewings. Neighboring males synchronize their chirps and the chirp rate varies directly with temperature. The chirp rhythm attracts sexually responsive females. After the female accepts a spermatophore from the male, she feeds 10 to 30 minutes at the glandular cavity visible at the base of the male's forewings. She then removes the just-emptied spermatophore and eats it.