

d-c voltage. The transverse voltages were steady for as long as the magnet remained in place and showed no fluctuation synchronous with blood flow pulsations (Fig. 1). The amplitude of the voltages obtained appeared to be related to the level of anesthesia, being absent during deep anesthesia and increasing in amplitude as recovery occurred. During light anesthesia, two types of slow wave forms appeared in the voltage record. One had a period of approximately 1.25 sec, the other of 15 to 20 sec. These were usually of sufficient magnitude to mask the shifts in the base line unless their magnitude was quite high (Fig. 2C). The clearest records were obtained during moderate anesthesia prior to the appearance of the slow wave forms (Fig. 2B).

In five of the specimens, the brachial plexus was exposed through an anterior incision on the thorax, and it was found possible to section all of the nerves

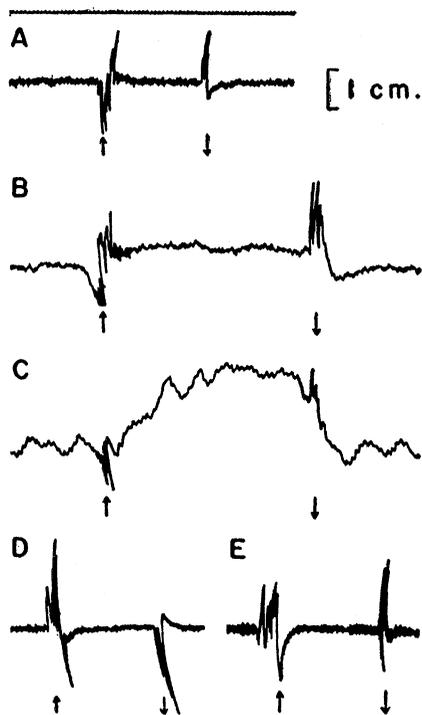


Fig. 2. Transverse voltages obtained under the conditions indicated in each case. Arrows indicate magnet movement as in Fig. 1. (A) Voltage measured from the electrodes alone with and without magnetic field. No d-c shift is observed ($50 \mu\text{v}/\text{cm}$). (B) Example of the usual Hall voltage found in moderate anesthesia ($100 \mu\text{v}/\text{cm}$). (C) Example of high magnitude Hall voltage noted during recovery phase of anesthesia; the two types of slow waves are clearly visible ($100 \mu\text{v}/\text{cm}$). (D) Transverse voltage measurements after nerve section; no evident Hall effect is visible ($50 \mu\text{v}/\text{cm}$). (E) Voltage after section of cord at medulla ($50 \mu\text{v}/\text{cm}$).

without interfering with the blood supply to the extremity. (Blood flow in the digital vessels is easily visualized with a magnification of 20 and was not markedly altered by this procedure.) After the nerve section, no transverse voltages could be obtained in response to an applied magnetic field in any stage of anesthesia, and the transverse voltages of the contralateral, nondenervated limb declined markedly. The normal d-c field voltages (longitudinal) in the intact animal average from 10 to 30 mv between the brachial area of the spine and the extremity tip, with the tip negative. After brachial plexus sectioning, these voltages drop to about 10 percent of their normal value, and frequently the voltages on the contralateral limb decrease by 50 percent or more.

In the intact animal, sectioning of the spinal cord at the level of the lower medulla results in a marked drop in the d-c field voltages in both forelimbs to about 10 percent of their normal value. In this case the transverse voltages also promptly disappeared in the same extremities along with the slow wave pattern.

Since a stationary magnetic field can have an effect only on charge carriers moving at right angles to the field, then the transverse voltages obtained are interpreted as Hall voltages, resulting from longitudinal charge carrier movement in the extremity. The independence of the observed voltages from the pulse rate, and the disappearance of these voltages after nerve section alone, indicate that the charge carrier flow is related to the peripheral nerves and that blood flow is not the parameter being measured. That the observed effect is dependent upon the functional state of the nervous system is further evidenced by the amplitude changes with different levels of anesthesia and by the change in the transverse voltages in the contralateral limb after nerve section on the opposite side. The action potential spike is presumably associated with ion movements in a direction transverse to the long axis of the axon. This direction of movement, the low mobility of ions, plus the steady state of the observed transverse voltages mediate against this activity being a factor in the production of the phenomenon.

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8 May 1961

Variable Expressivity of a Mutant Gene in Leopard Frog

Abstract. The genetic distinction between the nonspotted, or burnsi, mutant and the common-spotted, wild-type leopard frog is not simply unifactorial. The burnsi phenotype is a manifestation of genic interaction between a major pigmentary locus and a complex of modifiers (minor genes with small effects).

The disciplines of genetics and embryology converge in the search for the causality of development and differentiation. Regrettably, the paucity of genetical data in amphibians contrasts sharply with the wealth of embryological knowledge of the group. Whatever genetical information has accumulated has been admirably used to study the role of genes in development. Witness, for example, the biochemical analysis by Baker (1) of the nonspotted (burnsi) mutant of the common leopard frog (*Rana pipiens*) and the nuclear transplantation experiments by McKinnell (2) involving the mottled (kandiyohi) deviant of the common leopard frog. Each of these variant pigmentary traits is seemingly based upon a simple mode of inheritance (3, 4). However, it should be recognized that more intensive analyses would undoubtedly reveal complexities in the mode of transmission of the traits, which, in turn, would complicate embryological findings dependent upon the genetical data. This is attested by the results of a protracted investigation on the inheritance of the nonspotted (burnsi) pattern, which was heretofore thought to differ from the wild-type pattern by a single dominant gene.

J. A. Moore (3) demonstrated that the burnsi gene (designated *B*) exerts a dominance over the wild-type or

common-spotted allele (*b*). A major mutant gene is involved, but present investigations (5) reveal that modifiers (spotting genes with small effects) alter the magnitude of expression or dominance of the major burnsi gene. The action of modifiers is recognizable in the phenotypes of heterozygous burnsi frogs (*Bb*). Heterozygous burnsi frogs range from those devoid of dorsal spots (type "A" in Fig. 1) to those containing spots on the arms and legs, varying in size, shape, and number (types "B" to "E"). The spotting of the appendages of type "E" approaches the condition found in the wild-type leopard frog. Type "F" is a unique burnsi frog, possessing a large number of spots on the appendages as well as a patchwork of melanophores on the back (6).

The modifiers or minor-spotting genes (designated "+") are integral parts of the genetic system of the wild-type frog. The modifying genes most likely were established in the distant past in the wild-type stock to protect or "buffer" the main pigmentary locus against variations, both genetical and environmental. The modifiers have slight effects, virtually undetectable, in the normal genotype (*bb*). These modifying genes, however, have observable effects when the wild-type main gene is altered. The burnsi mutation (*B*) represents an alteration of the main pigmentary locus. The burnsi mutation tends to reduce pigmentation markedly, but the activity of this mutant gene is mitigated by spotting modifiers.

It has not been possible to ascertain the exact number of modifiers nor to dissociate the complex into single-gene components. This, however, does not invalidate the contention that modifiers are operative. One of several experiments is presented below that not only reveals vividly the presence of modifiers but also focuses attention on unsolved and new problems.

In the experiment, a burnsi male with heavily-spotted appendages (type "E" in Fig. 1) was crossed with a wild-type leopard frog. The cross yielded 32 common-spotted (wild-type) and 37 burnsi offspring, or 1:1 ($p > .50$). The burnsi male was thus heterozygous at the main locus (*Bb*). The spotting patterns of the burnsi progeny were variable, reflecting the segregation of spotting modifiers. Two of the 37 burnsi offspring were of type "C", 8 of type "D", and 19 of type

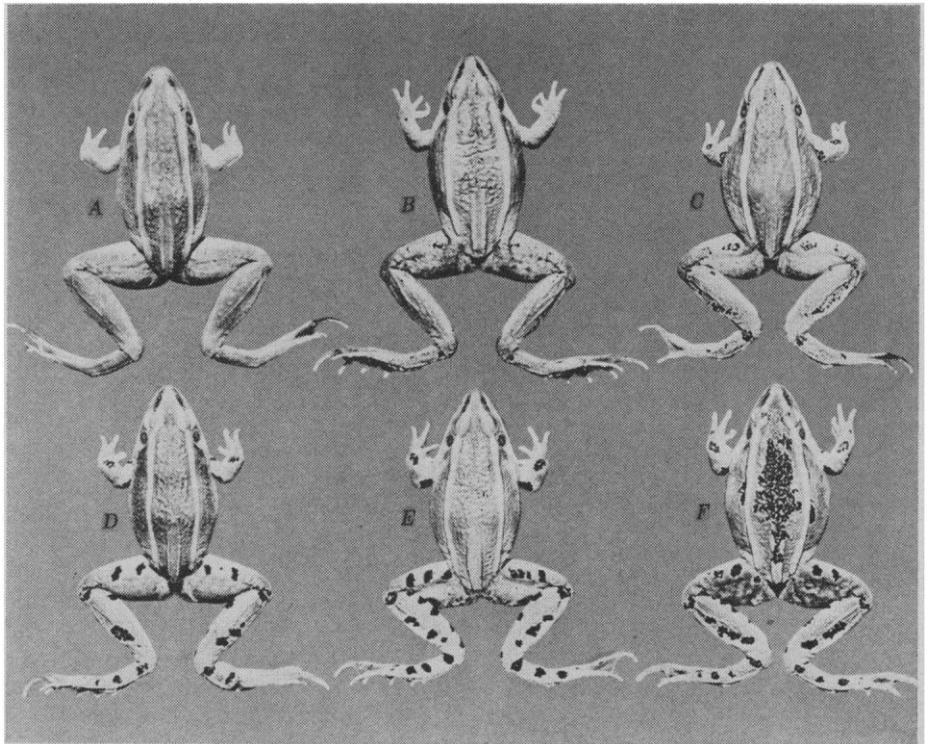


Fig. 1. Degree of variability in the expression of the burnsi character, reflecting the activity of modifiers (minor-spotting genes). No or few spotting modifiers are present in type "A"; increasing numbers of modifiers occur in types "B" to "F".

"E". No offspring specifically resembling type "F" was recovered; however, in the remaining eight burnsi offspring, the melanophores tended to aggregate or had actually aggregated into one, two, or three discrete spots on the dorsum. Apparently, these dorsum-spotted heterozygous burnsi off-

spring (Fig. 2, top row) tend in the direction of the common-spotted (wild-type) frogs because of the presence of numerous spotting modifiers.

It should be noted also that there is considerable variation in the extent of dorsal spotting (that is, between the dorsolateral folds) in wild-type indi-

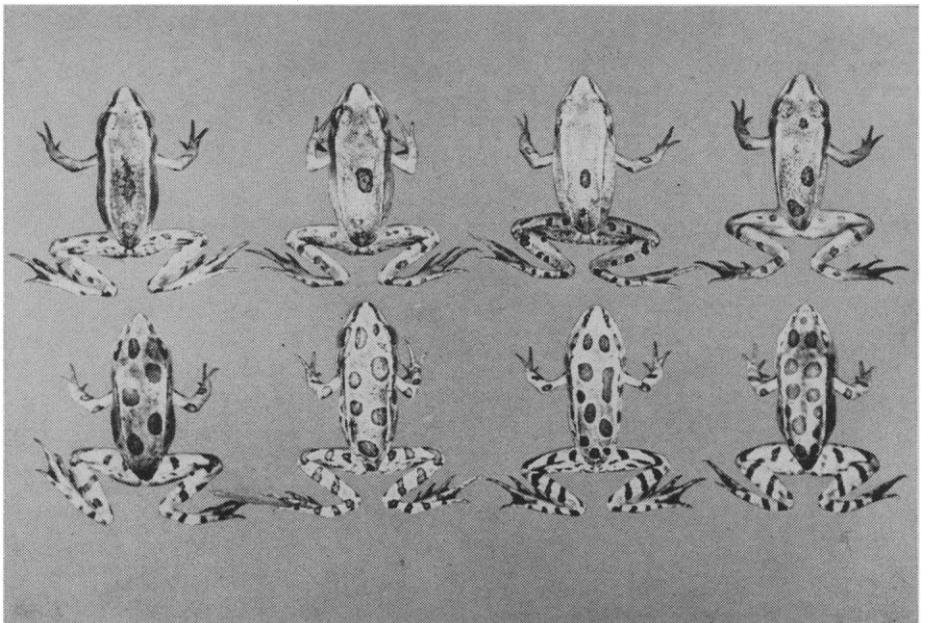


Fig. 2. Dorsally spotted heterozygous burnsi offspring (top row) and common-spotted, wild-type offspring (bottom row) derived from a cross of a type "E" burnsi frog (illustrated in Fig. 1) with a common-spotted, wild-type frog.

viduals (Fig. 2, bottom row). The number of dorsal spots among the progeny classified as wild-type ranged from 5 to 14. The gap between a burnsi and a wild-type individual is almost closed, leading to the perplexing query: How many dorsal spots must an individual contain before it is classified as a burnsi or a wild-type?

The situation is further complicated by the finding that the frequency of burnsi frogs may be as high as 10 percent in populations of leopard frogs in Minnesota (7). This supposedly rare mutant occurs too frequently in natural populations to be maintained solely by mutation pressure. The burnsi gene is probably being fostered by some selective advantage conferred upon the heterozygote. It is tempting to suggest that selection is promoting the accumulation of minor *nonspotting* genes ("—" modifiers) that enhance the activity of the burnsi gene (or counteract the effects of the "+" modifiers). Thus, it may be that there are two optimal phenotypes—the completely unspotted heterozygous burnsi frog (type "A") and the wild-type frog. The intermediate burnsi phenotypes (types "B" to "F") may be less advantageous or disadvantageous, and a sharp dimorphism may ultimately result. In essence, the burnsi gene, presently behaving as a semidominant, may eventually become completely dominant as a result of persistent selection for non-spotting modifiers.

The investigations thus far have raised more questions than have been answered, but it is apparent that an extended analysis is required to unravel the intricacies of a seemingly simple anuran trait.

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5. This research was supported by a grant from the National Science Foundation (NSF-G16317).
6. The type "F" is genetically a burnsi frog, albeit a highly modified burnsi. For details, see E. P. Volpe, *J. Heredity* **51**, 151 (1960).
7. Information on the frequency of burnsi frogs was provided by D. J. Merrell of the University of Minnesota, who is presently engaged in a study of the mutant populations in the Minnesota-Dakotas area (personal communication).

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Variations in Thermal Sensitivity

Abstract. In the past, confusion has resulted from the use of relative expressions indicative of the direction of temperature change, rather than positive identification of warm and cool sensations. Data are presented which show that at more extreme skin temperatures sudden changes in temperature may result in two readily discernible sensations. The occurrence of each sensation depends upon the magnitude of the change.

Investigations of thermal sensitivity (1), which have related changes in the thermal threshold to skin temperature, have been concerned with the quantitative aspects of the thermal sensation—for example, the occurrence of a detectable change in sensation accompanying a rapid change in skin temperature. The qualitative aspects of sensation—for example, whether the sensation is warm or cool—have not been investigated. It has been assumed that when the skin temperature is raised, warmth will be experienced, whereas reducing the skin temperature will result in a cool sensation. While this is generally true, it is

not always the case, as may be seen in the data presented here (2).

The stimulator was constructed of a hollow Lucite block 25 by 35 by 25 mm. The top was open and the bottom was a 20- by 30-mm silver plate, 0.025 mm thick. Water from constant-temperature baths was directed into the stimulator through either of two jets. Switching from one jet to the other produced a change in the temperature of the silver plate with a time constant of 0.4 sec. A thermistor inside the chamber, in contact with the middle of the silver plate, monitored the temperature of the water. Temperature changes of as little as 0.025°C could be produced with ease.

The subject was seated in an adjustable chair with the stimulator placed on the dorsal surface of the forearm 1 in. from the bend of the elbow. Water was circulated through the stimulator at the adapting temperature. After a minimum of 20 min, which allowed the subject to adapt to the room temperature and the skin beneath the stimulator to reach a reasonably stable temperature, threshold measurements were be-

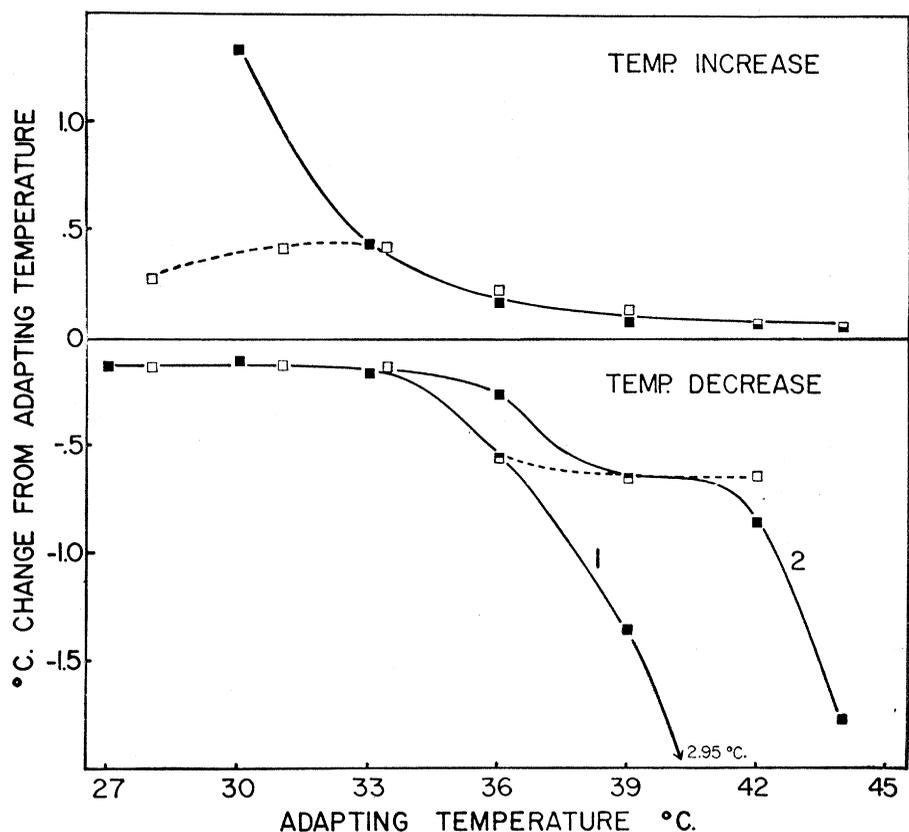


Fig. 1. Changes in the absolute threshold (solid squares, solid curves) and in the just noticeable difference threshold (open squares, broken curves) resulting from the temperature to which the skin was adapted. Male and female subjects showed the same thresholds to both increments and decrements in the adapting temperature except as shown by curve 1 (males) and 2 (females). The vertical dimension of the squares used to plot the mean thresholds represents about 0.07°C on the ordinate. The standard error of each mean threshold did not exceed the size of the square, except on curve 1 at an adapting temperature of 42°C, where it was 0.103°C.