Table 1. Results of six experiments with wooden models (see Fig. 1). The end-third model with yellow and red rings received significantly more pecks at the unpatterned end (Fig. 1c) than at the patterned end ($P < .01$); in addition, the response to this model was significantly different at $P < .01$ from the responses to either of the other two end-third models.

Pattern	Pecks at end-third models				Pecks at solid models
	Total	Percentage at			
		a	b	c	
Yellow and red ring	79	15.19	5.06	79.75	0
Yellow and red stripe	90	46.81	14.89	38.30	60
Green and blue ring	33	66.67	0.00	33.33	89

Evidently this aversion to a yellow and red ring pattern is innate; since motmots are burrow nesters, the experimental birds had had no opportunity to see this pattern prior to their capture.

It seems unlikely that this is a response to a wasp pattern, as adult motmots regularly take a wide variety of hymenopterans, including the inch-long *Pepsis*, with no apparent difficulty (*7*). Indeed, motmots seem remarkably resistant to the chemical defenses of most insects (*5, 7*). However, coral snakes might well prove dangerous to motmots. They tend to be secretive and during the day are sometimes encountered partly concealed in forest litter. A motmot attacking a small exposed portion of a coral snake would be in danger of being bitten, especially if that portion did not include the head. Motmots have a heavy, powerful bill but very small feet which lack the heavy, protecting scutes of a hawk or an owl. Thus even a small-mouthed rear-fanged snake might successfully inject its venom if a motmot failed in its initial attack.

The motmots used in these experiments came from northwestern Costa Rica, where both the elapid *Micrurus nigrocinctus* and the very similar rear-fanged colubrid *Erythrolamprus bizona* occur (*2*). Venom from either of these could propably kill a turquoise-browed motmot. Moreover, there is apparently no mildly poisonous species with a coral snake pattern living in this area, and hence no opportunity for motmots of this population to learn by experience to avoid this pattern. Their innate ability to recognize and avoid such a pattern is thus adaptive.

There have been a few published reports of other avian predators capturing either *Micrurus* (*8*) or a non-venomous mimic (*9*). This negative evidence shows that in these instances there was no safety to be gained by being a member of the coral snake complex. In order for mimicry to be effective, there must be predator avoidance of the character mimicked, and provided there is also generalization by the predator, it is irrelevant to the safety of the mimics whether this avoidance is innate or learned. The motmots' innate aversion to a generalized coral snake pattern is the first positive evidence that such protection exists for members of the coral snake complex against avian predators. An innate response to coral snakes has been suggested for at least one mammalian predator (*10*); further tests should be done with other small potential predators to find out whether this recognition is a more general phenomenon. Perhaps the complicated mechanism of Mertensian mimicry is unnecessary to explain the existence of the coral snake complex in the neotropics.

SUSAN M. SMITH
Departamento de Biología,
Universidad de Costa Rica,
Ciudad Universitaria,
Costa Rica, Central America

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Single Gene Cricket Mutations: Effects on Behavior, Sensilla, Sensory Neurons, and Identified Interneurons

Abstract. *Crickets are suitable for studying the effects of single gene mutations on single nerve cells. In one mutant, three classes of sensilla are lost sequentially. The absence of one class of mechanoreceptors throughout postembryonic development deprives certain sensory neurons of normal stimulation and results in abnormal physiological and structural development of an identified interneuron.*

Genetic manipulations can be used to investigate the role of genes in the construction of the nervous system and to produce lesions for analyzing the operation or the development of neural circuits. Current neurogenetics is based primarily on research with animals such as mice, *Drosophila, Paramecium, Daphnia*, and nematodes, in which it is difficult or impossible to study the physiology of particular neurons (*1, 2*). Mutations can be easily generated in crickets, however, and their neurons are amenable to physiological analysis. They are fecund, with females producing up to 2000 offspring, and have a reasonably short generation time (~ 6 weeks at 35°C). Eggs hatch into *Drosophila*-sized nymphs, which have a large behavioral repertoire and can be subjected to mass selection techniques. Interesting mutants can be studied as adults, when their many large, identified neurons are easily accessible for physiological and structural investigation (*3–6*).

In this report, techniques are described for inducing mutations and screening for behavioral mutants. Mutants that fail to make the evasion response to stimulation of the cerci (posterior sensory appendages) have been isolated. The behavior involves an intensively studied circuit including sensilla, sensory neurons, identified interneurons, and identified motor neurons. One such mutant lacks filiform hairs, the mechanoreceptors that initiate the evasion response. After molting to adulthood, it selectively loses each additional class of sensilla save one. This allows selective study of the behavioral roles and connectivity within the nervous system of each class of sensilla.

The absence of filiform hairs during postembryonic development prevents stimulation of filiform sensory neurons, which in turn deprives some identified interneurons, such as the medial giant interneuron (MGI), of normal synaptic activation. Filled with dye, the MGI appears withered and markedly reduced in cell volume compared to the MGI of a wild type. Evidently the establishment of synaptic connectivity with the sensory neurons is insufficient to induce normal growth of MGI unless the synapses maintain normal electrical activity.

These experiments were conducted on the Polynesian field cricket, *Teleogryllus oceanicus*, obtained from laboratory stock. After molting to adulthood, males and females were kept in separate containers for 1 week. They were deprived of food and water for 48 hours and then provided with sponges soaked in 0.025*M* ethyl methanesulfonate for an additional 48 hours (the sponges were changed once). Animals were mated in isolated pairs so that spermatophore transfers could be confirmed, and eggs were collected for 7 days.

Various screening techniques were used to test nymphs for behavioral mutations on the day after hatching. For example, to test for grooming mutants, several hundred nymphs were shaken in a bag with a fine, orange powder (Procion yellow dye), spread on a screen, and sifted gently to remove excess dye; when checked in about 2 hours, normal individuals had groomed themselves clean and nongroomers appeared orange. Since the neural circuitry for the evasion response has been well studied, screening was concentrated on mutations for this behavior. A few hundred nymphs were scattered over a shallow pan; the area was then scanned with a tube delivering rapid air puffs, which was trailed by a vacuum tube leading to a disposal flask. Normal nymphs jumped in response to the air puffs and were sucked into the vacuum tube, while nonjumpers remained in place. From about 40,000 nymphs, several dozen nonjumpers were detected by this method. Of those surviving to adulthood and used in testcrosses, two proved to be single gene mutants.

When testcrossed with a wild-type female, one nonjumping, male, putative mutant (filiform, *fl*) produced an F_1 with essentially all wild-type offspring (1415 wild type to 2 *fl*). Self-cross of the F_1 yielded a ratio of wild-type to mutant offspring of 3.72 : 1 (517 : 139). All mutants were male. Crosses of F_2 mutant males with some F_2 wild-type females resulted in a ratio of wild-type to mutant offspring of 1.1 : 1 (422 : 376), with mutants being both male and female (crosses with other F_2 wild-type females yielded all wild-type offspring). Crosses of F_3 mutant males with F_3 mutant females produced all mutant offspring. These results indicate that *fl* is a single gene, sex-linked, recessive mutation with slightly reduced viability (crickets have X0 sex determination). Similar testcrosses showed the second nonjumper (Hairless, *Hr*) to be a single gene autosomal dominant mutation.

The cause of the behavioral failure in these mutants was traced to the cercal sensilla. In normal adult crickets, four classes of cercal sensilla have been described: (i) campaniform sensilla (cuticular stress receptors), (ii) appressed hairs (chemoreceptors and possible contact mechanoreceptors), (iii) clavate hairs (function unknown), and

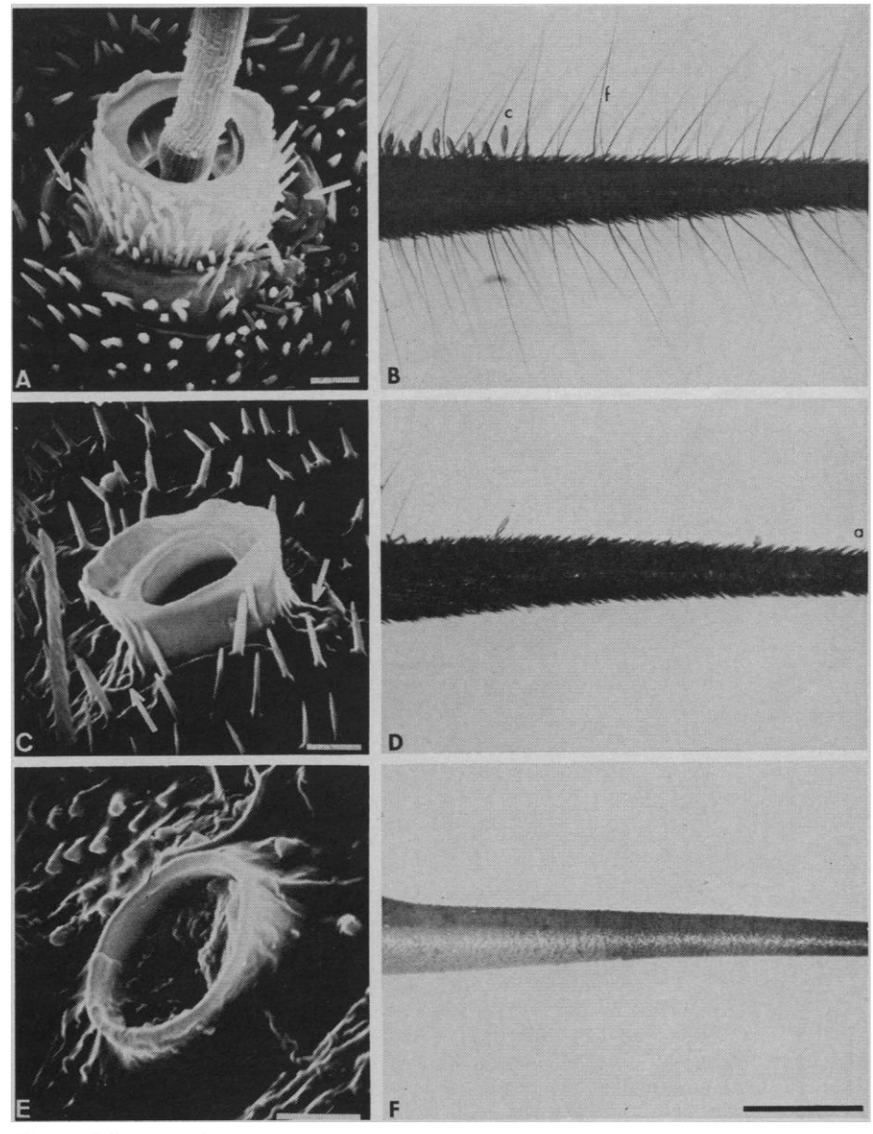

Fig. 1. Effects of *fl* mutation on sensilla. (A) Wild-type filiform hair and socket, first instar cercus (arrows indicate campaniform sensilla). (B) Wild-type adult cercus (*f*, filiform hair; *c*, clavate hair). (C) Empty filiform socket of *fl* mutant, first instar (arrows indicate campaniform sensilla). (D) Young *fl* mutant adult cercus (*a*, appressed hairs). Filiform and clavate hairs (save one) are missing (the long hairs at the base of the cercus are a special subclass of appressed hairs). (E) Empty appressed hair socket of mature adult *fl* mutant. (F) Mature adult *fl* mutant cercus. All hairs are missing. Calibrations: (A), (C), and (E), 5 μm; (B), (D), and (F), 1 mm.

(iv) filiform hairs (distance mechanoreceptors) (*4, 7*). Filiform hairs, which initiate the evasion response, respond to air puffs and to sound waves up to 2000 hertz (*4, 8*). They are frequency-specific according to their length and directionally specific according to their plane of vibration, either longitudinal to the cercus (L-hairs) or transverse (T-hairs) (*4, 8*). Adult *T. oceanicus* have about 100 clavate hairs, 650 filiform hairs, 1300 campaniform sensilla, and 3000 appressed hairs on each cercus (Fig. 1, A and B). Cerci of first instar nymphs average 1 clavate hair, 14 appressed hairs, 52 filiform hairs, and 104 campaniform sensilla. Inspection of the mutants with scanning electron and optical microscopes revealed that *Hr*, the autosomal dominant, averages only 8.8 filiform hairs in the first instar, and the sex-linked recessive, *fl*, has no filiform hairs at all (Fig. 1, C and D). Both have the normal complement of other hair types. The loss of the filiform hairs and consequent uncoupling of the evasion response circuitry accounts for the behavioral abnormality of these mutants.

Filiform hairs remain absent during postembryonic development of *fl*, and newly molted adults still have the normal number of other sensilla except for a slight reduction in the number of clavate hairs. In the ensuing 4 weeks, first the clavate hairs and then the appressed hairs are lost (with some overlap) leaving a completely bald cercus which retains only campaniform sensilla embedded in the cuticle (Fig. 1, E and F). As a result of this selective loss, five stages of adult crickets are available for examining the connectivity and behavioral roles of the different sensilla: (i) wild types with all four classes of sensilla; (ii) young *fl* adults lacking only filiform hairs; (iii) intermediate *fl* adults lacking every filiform and clavate hair, but retaining about 2000 appressed hairs and all campaniform sensilla; (iv) mature *fl* adults lacking filiform, clavate, and appressed hairs, but retaining campaniform sensilla; and (v) animals with cerci removed or with young cercal regenerates which lack all types of sensilla.

The effects of the *fl* mutation on sensory neurons were also examined. Filiform hairs, clavate hairs, and campaniform sensilla are known to be singly innervated by sensory neurons whose dendrites extend to the hair or sensillar base and whose axons terminate ipsilaterally in the last abdominal ganglion (*4, 7*). Appressed hairs are multiply innervated by three to six neurons whose dendrites differ in reaching the length of the hair shaft to a pore at the tip (*4, 7*). In *fl*, plastic sections 1 μm thick show an apparently normal neuron cell body, a truncated dendrite, and a normal looking axon underlying each filiform hair socket. Transmission electron micrographs showed 246 axons with normal fine structure in an *fl* first instar cercal nerve and 276 axons in a wild-type first instar cercal nerve. When the diameter of each axon of these nerves was measured and displayed in a histogram,

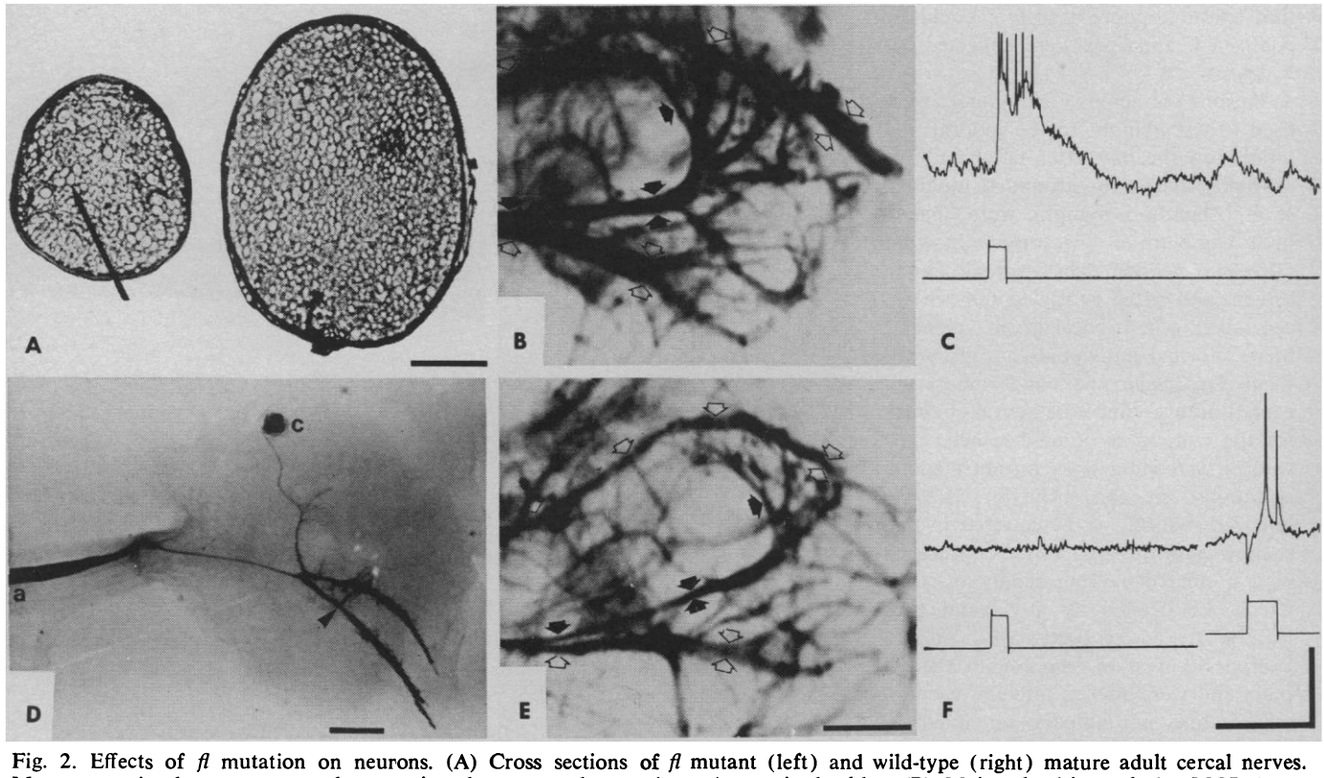

Fig. 2. Effects of *fl* mutation on neurons. (A) Cross sections of *fl* mutant (left) and wild-type (right) mature adult cercal nerves. Most axons in the mutant are degenerating, but some clusters (arrow) remain healthy. (B) Major dendrites of the MGI (open arrows indicate two branches) and LGI (solid arrows) filled with cobalt dye, showing normal size in the wild type (ventrolateral aspect). (C) Intracellular recording in dendrites of the MGI showing response to a standardized air puff in the wild type. (D) Adult *fl* mutant MGI filled with cobalt through the recording electrode (dorsal aspect; *c*, cell body; *a*, axon; arrow, third order dendrite where measurements were taken: see text). (E) Major dendrites of the MGI (open arrows) and LGI (solid arrows) in *fl* mutant showing reduced diameter; the age, magnification, and aspect are the same as in (B). (F) Intracellular recording in dendrites of the MGI in an *fl* mutant, showing the absence of response to a standardized air puff stimulus (lower trace indicates delivery of stimulus). The inset (right) shows an action potential in the MGI elicited by current injection (lower trace) through a microelectrode. Calibrations: (A), (B), and (E), 50 μm; (D), 100 μm; (C) and (F), 100 msec, 20 mv, 2×10^{-9} amp.

profiles of wild-type and *fl* histograms were very similar and no group of axons seemed to be missing. The T-hair axons normally connect to MGI in the terminal ganglion (*9*). Since the neurons are present in the *fl* mutant and have normal structure and enter the ganglion, the simplest hypothesis is that they are normally connected to the MGI. This view is supported by the observation that electrical stimulation of the cercal nerve does elicit postsynaptic potentials in the MGI (filiform sensory axons are the only components of the cercal nerve known to connect to the MGI, but not all axon types have been tested).

In adult *fl*, loss of the appressed hairs is accompanied by atrophy of the cercal nerve (Fig. 2A). Electron micrographs and semithin sections of the cercal nerve show that about 90 percent of the axons degenerate, while some bundles of axons remain healthy. While the mutation could be affecting neurons directly, it seems more likely that the degenerating axons are from appressed hair sensory cells damaged by the loss of their dendrites.

What is the developmental consequence of the *fl* mutation for interneurons of the evasion response circuit? The transversely vibrating filiform hairs provide the major afference to the MGI and LGI (lateral giant interneuron), two of the several identified interneurons in the terminal ganglion (*4–6, 10*). The MGI has a massive dendritic arborization in the terminal ganglion and sends its axon to the head (Fig. 2D); it has a large arborization in the thoracic ganglia, where it excites and inhibits interneurons and is thought to provide a first step in organizing the evasion response; and it is under efferent control from the thoracic ganglia and is involved in several inhibitory circuits within the terminal ganglion (*4–6, 10*).

In the wild type, intracellular recording from the MGI (identified by subsequent injection of cobalt dye through the microelectrode) shows a 20- to 30-mv depolarization and a brief train of impulses in response to a standardized air puff stimulus to the cercus (Fig. 2C). In *fl*, the standard stimulus produces no response at all in the MGI (Fig. 2F); this confirms that the T-hair sensory neurons are uncoupled from their normal stimulus and are unable to activate the MGI in response to it. Action potentials can be initiated in the MGI by intracellular current pulses, so the interneuron is still excitable (Fig. 2F).

The structure of the MGI was examined by axonal diffusion of cobalt dye (intracellular injection was not used for measurements because of cell volume distortion). Compared to the wild type, *fl* mutants have a strikingly withered or shriveled MGI (Fig. 2, B and E). In ten mutants and ten wild type (young adults), the width and depth of the large dorsolateral dendrite were measured just posterior to a particular third order branch (Fig. 2D, arrow). The cross-sectional area of the wild-type neuron at this point averaged about 400 percent of the comparable areas in *fl* ($361 \pm 41 : 97 \pm 16$ μm^2), confirming the visual impression of size difference. No significant difference in the lengths of the major dendrites or the diameter of the axon was detected. First order, second order, and certain third order branches are consistent in position and shape in the wild type, and these were also present and similar in the mutant; fewer fourth order branches were found in *fl*, but this could be because diminished size rendered them too small for visualization in the optical microscope. In general, MGI in the mutant appeared to have the normal number and shape of major dendrites, but to have failed to grow to normal cell volume.

What are the factors whose absence results in the failure of MGI to grow? Two kinds of factors can be distinguished in the interaction between presynaptic and postsynaptic cells. The first simply require the successful establishment of a connection between the cells. These include (i) formation of postsynaptic specializations, (ii) occupation of synaptic space, (iii) miniature or quantal synaptic potentials, and (iv) exchange of "trophic substances," and can be grouped under the heading of connectivity factors. The second require the impulse traffic in the presynaptic cells. These include (i) large amounts of transmitter and possibly other substances released by the arrival of impulses in the presynaptic terminals and interacting with the postsynaptic membrane, (ii) postsynaptic potentials, and (iii) action potentials caused by the postsynaptic potentials, and can be grouped under the heading of activity factors. In *fl*, connectivity factors between T-hair sensory neurons and the MGI are normal, as far as is known, but activity factors are greatly reduced (some spontaneous activity of the sensory neurons may remain). Therefore, the former appear inadequate to stimulate normal growth of the cell, and one or more of the activity factors seem necessary.

It is possible to discover which of these factors are critical for the development of the MGI. The role of action potentials independent of synaptic potentials could be tested by antidromically stimulating the axon of the MGI in the thorax of *fl* mutants with continuously implanted electrodes. Alternatively, the role of synaptic potentials could be tested by chronic stimulation of the cercal nerve. Connectivity factors and activity factors can both be eliminated simply by removing the cerci of newly hatched crickets and preventing regeneration, thereby causing degeneration of the sensory neurons (*9*). The effect of this operation on the structure of the MGI has recently been studied in a closely related cricket species, *Acheta domesticus* (*11*). A marked shortening of the major dendrites (20 to 40 percent) specific to the deprived side of the ganglion was found. This shortening could be a specific effect of deafferentation on the MGI or, since the neuropil of a ganglion after deafferentation is much smaller than normal, MGI dendrites could be growing to maintain a specified relative size within the available volume of neuropil (*11*). The results from the *fl* mutant are consistent with either of these hypotheses.

Two interesting comparisons can be drawn between these results and recent analyses of vertebrate neurons. First, several types of vertebrate neurons have now been shown to suffer various sorts of growth failures as a consequence of deafferentation. Affected features include cell body size, growth of large dendrites, spread of the arborization, and number of dendritic spines (*2, 12*). Second, in the vertebrate visual system several investigators have shown that the loss of normal physiological activity without the apparent loss of connectivity, a situation comparable to that of the MGI in the *fl* mutant, has severe consequences for the development of the nervous system (*13*). It may be that in the control of their development vertebrate and arthropod neurons have more in common than has previously been thought.

DAVID BENTLEY
Department of Zoology,
University of California,
Berkeley 94720

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Pattern Recognition May Resolve Management of Breast Cancer: Limited Mastectomy versus Radical Mastectomy

In the 7 October 1974 issue of the *Journal of the American Medical Association* two surgeons debated the methods of management of breast cancer. Crile (*1*) took the position that limited mastectomy was the method of choice, while Anglem (*2*) took the position that management of breast cancer should be by radical mastectomy. Both surgeons cited their own studies as well as those of others to support their respective positions.

However, the data base structures cited by the two surgeons were apparently not the same, and as a result it is not possible to compute survival probabilities which are conditioned on different assumptions. I now propose a method for organizing the data base and then evaluating the outcome of different treatments. The method can be applied to existing data as well as to data that may be collected in the future.

Pattern recognition theory and practice is based on classes, features of these classes, and the statistical distribution of these features for the respective classes. In the problem of breast cancer survival there are two basic classes (a class will be generally denoted C).

C_{RY} = survival for Y years after radical mastectomy

C_{LY} = survival for Y years after limited mastectomy

Additional classes can be defined in terms of other treatments or features.

The features of the classes will be inferred from the discussion by the two surgeons and other studies: f_1, cancer stage; f_2, patient age; f_3, histopathology; f_4, lymph node involvement; f_5, treatment; f_6, family history of breast cancer; f_7, immunological status; f_8, patient's cause of death; f_9, location of primary lesion; f_{10}, duration of disease at diagnosis; f_{11}, pre- or postmenopause; f_{12}, associated pregnancy; f_{13}, antibody to breast cancer antigen; and f_{14}, tumor growth rate.

The patient's feature vector may be denoted as

$$\mathbf{f} = [f_1, f_2, \ldots, f_{14}]$$

a column vector. Let the joint probability distribution of $\mathbf{f}$ be $p(\mathbf{f} \mid C_{RY})$ and $p(\mathbf{f} \mid C_{LY})$ for the two classes, respectively.

Given a patient with a particular feature vector $\mathbf{f}$, what is the probability of the occurrence of C_{RY} or C_{LY}?

To answer this question, we must ask what is the probability of C_{RY} or C_{LY} for a patient with breast cancer before we look at $\mathbf{f}$ for that patient? These a priori probabilities will be denoted $p(C_{RY})$ and $p(C_{LY})$, respectively. Then, the probability of C_{RY} or C_{LY} for a patient after looking at his feature vector, called an a posteriori probability, will be denoted $p(C_{RY} \mid \mathbf{f})$ and $p(C_{LY} \mid \mathbf{f})$ for the two respective classes. For the latter notation, the $\mid$ in $p(C_{RY} \mid \mathbf{f})$ is used to mean given: that is, probability of C_{RY} given $\mathbf{f}$.

The well-known Bayes theorem relates the a posteriori probability to the a priori probability as

$$p(C_{RY}|\mathbf{f}) = \frac{p(\mathbf{f}|C_{RY})\ p(C_{RY})}{p(\mathbf{f})}$$

For class C_{RY} (1)

$$p(C_{LY}|\mathbf{f}) = \frac{p(\mathbf{f}|C_{LY})\ p(C_{LY})}{p(\mathbf{f})}$$

For class C_{LY} (2)

where

$$p(\mathbf{f}) = p(\mathbf{f}|C_{LY})\ p(C_{LY}) + p(\mathbf{f}|C_{RY})\ p(C_{RY}) \quad (3)$$

A standard pattern recognition problem is, given "training samples" for class C_{RY} and "training samples" for class C_{LY}, to estimate the respective probability distributions $p(\mathbf{f} \mid C_{RY})$ and $p(\mathbf{f} \mid C_{LY})$. This is not an easy task. First, a model for the probability distribution must be assumed a priori; or in the language of pattern recognition, a "family structure" must be assumed for the probability distribution. Patrick considers such estimation of probability distribution in detail (*3*). There is not one currently available computer procedure that can be used to construct the required estimated probability density functions $p(\mathbf{f} \mid C_{RY})$ and $p(\mathbf{f} \mid C_{LY})$. Any procedure assumes some structure about the functional form of p, whether it is a multivariate Gaussian assumption at one extreme or a "nonparametric" structure at the other extreme (*4–6*). Up to now, analyses of breast cancer data have been dependent on the formation of one-dimensional or two-dimensional probability distributions; for example, with f_1 (that is, the cancer stage) or with the two features f_1 and f_3 (that is, histopathology). Probability distributions might have been constructed for f_1 and f_3, with the use of different values of f_2 (that is, patient age). Another problem is how to use a priori knowledge that two features are statistically dependent.

Thus, given the number of training samples N_R for class C_{RY} and the number of training samples N_L for class C_{LY}, we can estimate $p(\mathbf{f}|C_{RY})$ and $p(\mathbf{f}|C_{LY})$. Once these are estimated and a priori probabilities $p(C_{RY})$ and $p(C_{LY})$ specified, then the a posteriori probabilities $p(C_{RY} \mid \mathbf{f})$ and $p(C_{LY}) \mid \mathbf{f})$ can be calculated for any patient $\mathbf{f}$, where $p(\mathbf{f})$ is calculated from Eq. 3.

However, difficulties can be anticipated. First, what are the a priori probabilities $p(C_{RY})$ and $p(C_{LY})$? Might one assume $p(C_{RY}) = p(C_{LY}) = 1/2$? Did Crile (*1*) and Anglem (*2*) cause a priori