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Autonomic Determinism: The Modes of Autonomic Control, the Doctrine of Autonomic Space, and the Laws of Autonomic Constraint

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Contemporary findings reveal that the multiple modes of autonomic control do not lie along a single continuum extending from parasympathetic to sympathetic dominance but rather distribute within a 2-dimensional space. The physiological origins and empirical documentation for the multiple modes of autonomic control are considered. Then a formal 2-dimensional conception of autonomic space is proposed, and a quantitative model for its translation into a functional output surface is derived. It is shown that this model (a) accounts for much of the error variance that has traditionally plagued psychophysiological studies, (b) subsumes psychophysiological principles such as the law of initial values, (c) gives rise to formal laws of autonomic constraint, and (d) has fundamental implications for the direction and interpretation of a wide array of psychophysiological studies.

Revolutionary perspectives on the organization and control of the autonomic nervous system (ANS) are rapidly emerging from the contemporary literature. The discovery of peripheral ganglionic reflexes, the identification of cotransmitters and peptide modulators, and the increasing delineation of central autonomic controls promise substantive advances in the understanding of autonomic regulation. Unfortunately, the evolution of conceptual models of autonomic organization has fallen dramatically behind the explosion of empirical developments. In the absence of a contemporary overarching conceptual framework, novel issues and findings may be neglected or denigrated, through assimilation into archaic views of autonomic organization. An example is the doctrine of autonomic reciprocity, which maintains that sympathetic and parasympathetic outflows are subject to tightly coupled reciprocal control, with increasing activity in one branch associated with decreasing activity in the other. Although this reciprocal model may represent one common mode of ANS regulation, exceptions to this pattern of autonomic control have been demonstrated repeatedly. It is now apparent that activity in the two ANS divisions may be either coupled or uncoupled. Moreover, coupled responses may be either reciprocal or nonreciprocal, the latter entailing concurrent increases (coactivation) or decreases (coinhibition) in both vagal and sympathetic outflows.

The maxim of autonomic determinism maintains that the functional state of visceral organs is governed in part by autonomic influences. Indeed, much of the psychophysiological enterprise is based on this maxim, together with the assumption that autonomic controls reflect broader adaptive states of the organism. A further implicit assumption is that functional measures of visceral organs provide veridical reflections of autonomic states. In this article, we show that the veracity of this assumption may relate to the specific autonomic dimensions measured and that adequate interpretation of such measures is dependent on an accurate model of ANS organization and control. We begin by describing the possible modes of autonomic control, the empirical data documenting these modes, and the potential physiological origins of these patterns. A principal thesis will be that autonomic functions cannot adequately be viewed as lying along a single vector or continuum extending from parasympathetic to sympathetic control. Rather, a two-dimensional autonomic surface is the minimal representation required to capture the complexities of autonomic control. Given an appropriate understanding of this autonomic space, a number of subordinate principles or laws that govern specific dimensions or boundary conditions can be derived.

We propose that the doctrine of autonomic reciprocity be subsumed by the broader *doctrine of autonomic space,* whose elements include principles of autonomic organization and control that are consistent with a two-dimensional autonomic space. We further derive a quantitative model that describes the translation of this autonomic space into a functional output surface. The model is shown to account for much of the error variance that has plagued psychophysiological studies. The model further demonstrates that psychophysiological principles, such as the law of initial values, can be subsumed by the doctrine of autonomic space as special case instantiations. Implicit in the concept of autonomic space is that both tonic autonomic state and phasic reactivity are constrained by the dimensions and features of this space, and that baseline effects are not mere artifacts or confounds to be dealt with experimentally. Indeed, we show that the dual-vector model gives rise to formal laws of autonomic constraint that have fundamental implications for the psychophysiological enterprise.

Modes of Autonomic Control

The potential patterns of autonomic control over dually innervated target organs are outlined in Table 1, which depicts all

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combinations of increased, decreased, or unaltered activity in the two ANS divisions. The nine cells of Table 1 can be further grouped into three major categories: (a) coupled reciprocal modes, in which activities of the two divisions are negatively correlated; (b) coupled nonreciprocal modes, in which activities are positively correlated; and (c) uncoupled modes, in which activity changes are uncorrelated. The classical reciprocal patterns, in which the divisions are negatively correlated, are represented by the cells in the upper right (*reciprocal sympathetic* mode) and the lower left (*reciprocal parasympathetic* mode). Coupled responses in which the activities of the two divisions are positively correlated are represented by the cells in the upper left (*coactivation*) and lower right (*coinhibition*). The remaining cells (except baseline) depict autonomic responses in one ANS division that are uncorrelated with changes in the other (*uncoupled sympathetic* and *uncoupled parasympathetic* modes).

The cells of Table 1 exhaust the potential modes of autonomic response at any given moment. These autonomic modes are intended as taxonomic descriptors of empirical patterns of ANS response, and may not map isomorphically onto functionally distinct underlying mechanisms. As we discuss later, the elemental modes of control, represented by the individual cells of Table 1, may distribute along a functional dimension extending from reciprocal to nonreciprocal coupling.

Doctrine of Autonomic Reciprocity: A Historical Perspective

In his 1939 treatise, *The Wisdom of the Body,* Cannon declared that "it is characteristic of the smooth muscles and glands that they are supplied with nerve fibers from two (autonomic) sources" and that "the two divisions which supply the viscus are, as a rule, opposed in their effects" (Cannon, 1939, p. 252). Even prior to the turn of the century, and before Langley proposed the phrase *autonomic nervous system* to refer to the visceral nerves of the thoracic, cranial, and sacral outflows, it was recognized that separate components of this system could exert opposing actions on target organs. By the mid 1800s, it was known that vagal stimulation could slow, and sympathetic stimulation could speed, the beat of the heart. Furthermore, Gaskell (1990) noted that sympathetic stimulation decreased, whereas vagal activation increased, the demarcation (injury) potential of the atrial myocardium, indicating that antagonistic influences could be manifest at a common cellular level. The concept of functional antagonism between sympathetic and parasympathetic systems was further solidified by the discovery of distinct postganglionic neurochemical mediators having differential excitatory/inhibitory actions on target organs (*sympathin,* Cannon & Rosenbleuth, 1937; Dale, 1934; *vagusstoff,* Loewi, 1921).

Although early conceptions of the "involuntary" or "vegetative" nervous system generally focused on the peripheral nervous components, the discovery of multiple central controls over visceral activities mandated an expansion of the concept of the ANS to include its central components (Cannon, 1928; Langley, 1921). Since the writings of Langley and Cannon, these central mechanisms have frequently been considered to exert *reciprocal control* over the sympathetic and vagal outflows, offering a functional parallel to Sherrington's (1906) concept of reciprocal innervation within the somatic system.

Collectively, these and other perspectives led to the view of the ANS as a dichotomous system, with its sympathetic and parasympathetic (vagal) divisions exerting functionally opposing influences under reciprocal central control. This conception, which we will term the *doctrine of autonomic reciprocity,*[1] entails three fundamental, and closely related, principles: (a) the principle of *dual innervation* of visceral target organs, (b) the principle of *functional antagonism* of the dual innervations, and (c) the principle of *reciprocal control* over the ANS divisions.

The pupillary control system serves as a simple exemplar of these principles: (a) Pupillary muscles are dually innervated by both sympathetic and parasympathetic systems, (b) the two ANS divisions exert opponent constrictor and dilator influences on the pupil, and (c) the ANS innervations are often subject to reciprocal central control (Beatty, 1986; Brodal, 1981). Anomalous features, however, emerge even in this relatively simple system (Beatty, 1986; Brodal, 1981). Although exerting functionally opponent effects, sympathetic and parasympathetic systems, in fact, innervate separate muscle groups (radial and sphincter muscles, respectively). Moreover, although these innervations may operate reciprocally in "psychosensory" or pain reflexes, light and accommodation reflexes are mediated almost exclusively by selective variations in parasympathetic control.

Although considerable evidence supports the general concept of a reciprocal, opponent organization of the ANS, deviations from this model were recognized even by early researchers. These exceptions included the following: (a) Some target organs are not dually innervated, (b) sympathetic and parasympathetic influences on some dually innervated organs are synergistic or orthogonal rather than antagonistic, and (c) parasympathetic and sympathetic actions are not always subject to reciprocal variation. Rosenbleuth and Bard (1932) and Rosenbleuth and Cannon (1932) offered evidence that the cat nictitating membrane was innervated largely or exclusively by the sympathetic division of the ANS, and Richter and colleagues drew a similar conclusion for sweat glands (Richter, 1927; Tower & Richter, 1932). In addition, both ANS divisions were known to exert mutually supportive influences on erection/ejaculation reflexes (Root & Bard, 1947). Finally, Gellhorn and colleagues demonstrated that certain conditions, including emotional states, could yield coactivation of both vagal and sympathetic divisions of the ANS (Gellhorn, Cortell, & Feldman, 1941). These exceptions to the doctrine of autonomic reciprocity presaged the emergence of contemporary perspectives

[1] The doctrine of autonomic reciprocity is offered as a heuristic, against which contemporary perspectives can be viewed. We do not suggest that anyone would slavishly defend the universal applicability of each of its features. As we point out, clear exceptions to this model of autonomic nervous system organization have been historically recognized, and are now well documented. Most remarkable is that, in spite of this documentation, its collective features have survived as general organizational principles. Even in the contemporary literature, deviations from this model are frequently acknowledged as exceptions to the general rule of reciprocity.

Table 1
Modes of Autonomic Control

Sympathetic response	Parasympathetic response		
	Increase	No change	Decrease
Increase	Coactivation	Uncoupled sympathetic activation	Reciprocal sympathetic activation
No change	Uncoupled parasympathetic activation	Baseline	Uncoupled parasympathetic withdrawal
Decrease	Reciprocal parasympathetic activation	Uncoupled sympathetic withdrawal	Coinhibition

that more appropriately emphasize the interactive influences among sympathetic and vagal divisions of the ANS.

In spite of the recognized limitations of the doctrine of reciprocity, no overarching conceptual framework has emerged that captures the complexities of autonomic control. A quantitative conceptual framework is important for the strategic guidance of experimental studies and the promotion of hypothesis testing rather than exploratory approaches. Such a framework may offer important parameters for quantifying the effects of tasks, examining the dimensions of individual differences, or identifying sources of error variance in psychophysiological studies. A broader conceptual framework may also confer a more integrated perspective on autonomic processes, minimizing the proliferation of microtheories related to specific autonomic innervations. This broader perspective would likely facilitate the elucidation of psychophysiological relationships with more molar behavioral processes.

We outline here a general conception of autonomic organization that subsumes the veridical features of the doctrine of autonomic reciprocity while incorporating demonstrated violations of this doctrine. We further show that this conception, together with a derived quantitative model, can illuminate psychophysiological inquiries ranging from environmental effects on autonomic activity to individual differences in autonomic reactivity. First, however, we consider some methodological approaches to the study of the autonomic modes and the empirical data that document these modes of control.

Empirical Hallmarks of the Modes of Autonomic Control

Methodological considerations in the identification of differing modes of autonomic response have probably contributed to the relative neglect of nonreciprocal or uncoupled ANS responses. Indeed, the dependent measures of most psychophysiological studies do not reveal the underlying autonomic adjustments that give rise to a target-organ response. The dual ANS innervation of many visceral organs renders end-point measures of the functional state of the organ equivocal. Because sympathetic cardiac nerves increase heart rate and vagal innervations slow the beat of the heart, for example, an increase in heart rate could emerge from multiple sources. As illustrated in Table 2, tachycardia could arise from uncoupled sympathetic activation, uncoupled parasympathetic withdrawal, or a reciprocal sympathetic mode of response. Moreover, depending on the relative magnitude of sympathetic and parasympathetic responses, tachycardia could also result from coactivation or coinhibition. In view of the ambiguity of end-point measures of the functional state of an organ, alternate indices of the underlying modes of autonomic response are desirable.

Direct Recording of Peripheral Nerve Activity

One of the most definitive methods of identifying the modes of autonomic control is the direct physiological recording of concurrent activity in relevant vagal and sympathetic nerves. This approach is generally not feasible in human subjects, however, and may be applicable only to animal preparations. Although promising, recent developments in the recording of discrete autonomic nerves by transcutaneous electrodes (Wallin & Fagius, 1988) are thus far limited to relatively superficial nerves of the sympathetic division.

Selective Blockade of Peripheral Autonomic Nerves

Alternative approaches include the selective surgical or pharmacological blockade of sympathetic or parasympathetic innervations of target organs. For illustration, Table 2 details the expected heart rate responses arising from different modes of autonomic control, together with the expected consequences of functional blockade of the sympathetic and vagal innervations. As is apparent, the direction of heart rate change in untreated subjects is relatively uninformative as to the underlying mode of control. Differential effects of autonomic blockade, however, would be predicted for alternate control modes.

As indicated in Table 2, heart rate changes arising from uncoupled autonomic response modes would be eliminated by blockade of the active division but would be relatively unchanged by blockade of the alternate division. In contrast, responses arising from reciprocal modes should be attenuated, but not eliminated, by blockade of either division. They would be eliminated only by dual blockade (any residual responses would probably be attributable to local metabolic or hormonal influences). Finally, heart rate responses arising from nonreciprocal modes (coactivation and coinhibition) would be expected to change direction or become larger, with blockade of either division alone. Again, they would be eliminated only by blockade of both divisions. Thus, for identical heart rate changes

Table 2
Expected Effects of Functional Blockade on Heart Rate Responses Arising From Different Modes of ANS Control

Sympathetic response and autonomic blockade	Parasympathetic response		
	Increase	No change	Decrease
Increase	Coactivation	Sympathetic activation	Reciprocal sympathetic activation
None	↑ ↔ ↓	↑	↑↑
Sympathetic	↓ ↓ ↓↓	↔	↑
Vagal	↑↑ ↑ ↑	↑	↑
No change	Parasympathetic activation		Parasympathetic withdrawal
None	↓		↑
Sympathetic	↓	Baseline	↑
Vagal	↔		↔
Decrease	Reciprocal parasympathetic activation	Sympathetic withdrawal	Coinhibition
None	↓↓	↓	↑ ↔ ↓
Sympathetic	↓	↔	↑↑ ↑ ↑
Vagal	↓	↓	↓ ↓ ↓↓

Note. Multiple columns within cells indicate alternate response patterns. ANS = autonomic nervous system. ↔ indicates no response; ↑ and ↓ indicate increases and decreases in heart rate, respectively; ↑↑ and ↓↓ indicate larger increases and decreases, respectively.

arising from different modes of ANS response, distinct patterns of effects would be anticipated with functional blockade of the ANS divisions.

These approaches are not without limitations, however. Although surgical procedures offer a high degree of anatomical specificity, they are irreversible and are not applicable to human subjects. For these reasons, pharmacological approaches have frequently been used in both human and animal studies. Because of the potential importance of this approach, caveats and limitations warrant consideration. First, sympathetic antagonists block both sympathetic neural and sympathoadrenal actions. Under conditions of adrenomedullary catecholamine secretion, sympathetic blockade would tend to overestimate the level of sympathetic neural control. This may not be particularly troublesome for investigations of transient responses, because adrenomedullary actions are typically delayed and have a slow rise time. Moreover, under typical laboratory conditions, the contributions of adrenomedullary catecholamines may be rather modest for many organs, including the heart.[2] In other cases, however, these effects may be more significant.

In addition, many pharmacological agents can have effects on multiple classes of receptors, at both central and peripheral sites. Central nervous system (CNS) actions of pharmaceuticals are especially problematic, because central autonomic systems use receptor populations that overlap extensively with those of peripheral autonomic nerves (Feldman & Ellenberger, 1988; Loewy & Spyer, 1990). In fact, pharmacological agents can potentially alter autonomic responding through numerous routes, including (a) peripheral autonomic blockade, (b) indirect peripheral actions, (c) antagonism of central autonomic mechanisms, and (d) indirect effects on CNS behavioral substrates that alter the organism's functional response to a stimulus or context. Although no pharmacological agent is absolutely specific, relatively selective peripheral post-ganglionic receptor antagonists are currently available.[3] With any pharmacological ap-

[2] Denervation of the heart eliminates the rapid rise in heart rate and contractility to a conditioned stimulus in animals, although smaller, delayed changes are still apparent (D. C. Randall, Kaye, Randall, Brady, & Martin, 1976). These residual responses are presumably mediated by adrenal catecholamines. Studies on the denervated hearts of cardiac transplant patients suggest that heart rate changes to mental arithmetic or reaction time tasks, of presumptive adrenal origin, were less than 15% of those of control subjects (Sloan, Shapiro, & Gorman, 1990). In fact, this may be an overestimate of adrenal contributions, because cardiac denervation results in a sensitization of the heart to catecholamines (Vatner et al., 1985).

[3] The quaternary salts of the muscarinic antagonists scopolamine (e.g., scopolamine methylnitrate) and atropine (atropine methylnitrate) do not readily cross the blood–brain barrier (Gilman, Goodman, Rall, & Murad, 1985). At moderate doses, these compounds produce a relatively selective blockade of postganglionic parasympathetic receptors. Specific adrenergic blockers are also available. The β_1 adrenergic antagonist atenolol is considered to be a relatively "cardioselective" beta blocker, because it has little activity on other adrenergic receptor types, minimal nonreceptor-mediated effects on target organs, and minimal central nervous system (CNS) actions (Cruickshank, 1980; Frishman,

proach, however, careful attention must be paid to the selectivity of the antagonists used, the dosage employed, and potentially confounding drug actions.

An additional complication arises from the fact that peripheral autonomic blockade eliminates tonic as well as phasic influences of the ANS division on target organs. On the basis of the law of initial values (Wilder, 1967), variations in basal activity of an organ may alter phasic responses of that organ. This may not preclude meaningful interpretation, however, if both sympathetic and vagal antagonists are used. Alternate modes of autonomic response yield differential predictions of the effects of ANS blockade on phasic target-organ responses (see Table 2) that may be opposite those of the law of initial values. For example, blockade of the sympathetic control of the heart would be expected to decrease heart rate, and this decreased basal rate may tend to minimize further deceleratory responses. The expected effect of the loss of phasic sympathetic drive under conditions of coactivation, however, would be an exaggeration of deceleratory responses (Table 2). This outcome is opposite of that predicted by the law of initial values and would provide strong evidence for coactivation.

The importance of employing both sympathetic and parasympathetic antagonists is illustrated by the reciprocal sympathetic mode of response. The potential decrease in heart rate associated with loss of sympathetic tone would again tend to minimize bradycardic responses, which is precisely the pattern predicted for blockade of phasic sympathetic influences under a reciprocal sympathetic mode (Table 2, lower left cell). Thus, attenuation of evoked bradycardia, although consistent with a reciprocal sympathetic mode, would not be definitive. On the other hand, a parallel finding of attenuated bradycardia with vagal blockade would substantially strengthen the interpretation. In the latter case, the increase in heart rate resulting from loss of vagal tone would be expected to potentiate deceleratory responses, whereas blockade of phasic vagal responses should yield an attenuation of evoked bradycardia (under a reciprocal sympathetic mode of control). Thus, adequate interpretation of the effects of autonomic blockade requires an appreciation of the pattern of results obtained with both sympathetic and parasympathetic antagonists.

Altered basal activity in a target organ arising from autonomic blockade may also introduce an indirect confound, by triggering reflexive changes in the functional state of the other ANS division. An example derives from the common use of propranolol to investigate the origin of heart rate responses. Because propranolol is a nonspecific beta blocker, it antagonizes cardiac β_1 receptors as well as vascular β_2 vasodilators. As a result, propranolol not only blocks the sympathetic innervation of the myocardium, but it may yield increases in blood pressure that can lead to baroreflex-induced changes in the vagal control of the heart (McDevitt, 1987). In this case, potential confound by pressor responses could be minimized by the use of a cardioselective β_1 antagonist ("vascular-sparing agent," such as atenolol) that has minimal effects on tonic blood pressure or phasic blood pressure responses (McDevitt, 1987; Quigley & Berntson, 1990). In other cases, however, confounding reflex effects may arise directly from the blockade of the organ of interest. This is especially problematic for those autonomic functions, such as blood pressure, that are directly monitored and regulated physiologically. Although these confounds can often be experimentally circumvented, they must be carefully considered in pharmacological investigations.

In summary, the selection of appropriate pharmacological blockers requires consideration not only of receptor selectivity and possible confounding drug actions, but of potential indirect reflex consequences or other functional interactions among the ANS divisions. Because these considerations will vary across organ systems, no single set of optimal agents or procedures can be specified. Nevertheless, if experimental procedures can adequately control or account for these potential sources of confound, pharmacological blockade can provide a powerful approach to the identification of autonomic modes of control.

Indirect Measures

A number of noninvasive measures of sympathetic and parasympathetic control have been proposed in the literature, including respiratory sinus arrythmia (Porges, 1986; Porges & Bohrer, 1990), T-wave amplitude (Heslegrave & Furedy, 1979), pulse transit time (Weiss, Bo, Reichek, & Engelman, 1980), and derivations from the impedance cardiogram (Kelsey & Guethlein, 1990; Sherwood et al., 1990). Although the status of these measures as specific indicators of the activity within a single ANS division has yet to be fully established, further development of these or other noninvasive measures could offer important experimental tools. This approach will be considered later.

Empirical Documentation of the Modes of Autonomic Control

The elemental modes of autonomic control, as detailed in Table 1, fall into three major categories: coupled reciprocal modes, coupled nonreciprocal modes, and uncoupled modes. In the present section, we present empirical documentation of the existence of each of these three major classes of autonomic control.

Coupled Reciprocal Modes

Reciprocal patterns of sympathetic/parasympathetic change represent a common form of autonomic adjustment, and can be observed widely in behavioral and physiological contexts (Cohen & Randall, 1984; Galosy, Clarke, Vasko, & Crawford, 1980; Weise, Heydenreich, & Runge, 1987). The opposite influences of baroreceptor reflexes on sympathetic and vagal control of the heart represent a prototypic example of reciprocal control (Koizumi, Terui, & Kollai, 1983; Spyer, 1981). Indeed, this mode of control may be particularly adaptive in the critical baroreflex control of circulation. The reciprocal modes would

1981; McDevitt, 1987). In contrast, other commonly used beta blockers, such as propranolol, may antagonize multiple receptor types (cardiac β_1 as well as vascular β_2), exert local anesthetic action directly on the myocardium, or have notable CNS actions. In addition to the selection of specific agents, dosage becomes an important consideration, because receptor selectivity is often dose dependent.

be expected to maximize the gain and dynamic range of target-organ responses, because an increase in activity of one ANS division is associated with a decrease in the opponent activity of the other.

A similarly well-documented demonstration of reciprocal control is provided by the studies of Cohen and associates on the neural mechanisms underlying classically conditioned bradycardia in the pigeon (Cohen, 1982; Gold & Cohen, 1981). Through direct physiological recordings and transections of peripheral autonomic nerves, these authors demonstrated that the conditioned bradycardia was attributable to an increase in vagal activity and a reciprocal decrease in sympathetic outflow. Reciprocal patterns of ANS response, in fact, have been widely reported in behavioral contexts (Cohen & Randall, 1984; Galosy et al., 1980).

Coupled Nonreciprocal Modes

In contrast to the principle of reciprocity, Cannon (1939) recognized that adaptive challenges could induce concurrent sympathetic and parasympathetic responses in separate target organs. Strong fear reactions were noted to yield signs of sympathetic arousal in some organs (e.g., increases in heart rate and blood pressure) and simultaneous indications of parasympathetic activation in other organ systems (e.g., bowel and bladder emptying). A more serious challenge to the generality of the concept of reciprocal control came from subsequent studies of Gellhorn et al. (1941) that indicated that joint vagal and sympathetic activation could be manifested concurrently in the same target organ. In the intact rat, distressing stimuli yielded a moderate decrease in pancreatic insulin secretion associated with sympathetic activation. After sympathectomy, however, the same stimuli yielded a notable increase in insulin secretion that could be blocked by vagotomy. These findings were interpreted to reflect a stress-evoked coactivation of both sympathetic and vagal controls over pancreatic secretions.[4]

More recent studies document numerous instances of coactivation (or coinhibition) of sympathetic and vagal controls of visceral organs, and it is now clear that both reciprocal and nonreciprocal autonomic influences can arise directly from central reflex mechanisms. Furedy, Randall, Fitzovich, and Shulhan (1989) provided indirect evidence of coactivation of the autonomic controls of the heart, in response to increased cephalic blood pressure (negative body tilt) in dogs. More direct measures of coactivation to mechanoreceptor stimuli were provided by Kollai, Koizumi, Yamashita, and Brooks (1978). These authors examined the effects of atrial and carotid sinus distention on autonomic controls of the heart by direct physiological recordings of activity in both vagal and sympathetic cardiac nerves. Bradycardia induced by baroreflex activation (carotid sinus distention) yielded an increase in activity of vagal cardiac efferents, coupled with the expected reciprocal decrease in sympathetic nerve traffic. In contrast, activation of atrial stretch receptors yielded tachycardia, which was associated with a coactivation of both vagal and sympathetic cardiac outflows.[5] Specific chemoreceptor reflexes can also induce either reciprocal or nonreciprocal alterations in autonomic control of the heart. Chemoreceptor stimulation by marked hypoxia or hypercapnia evokes reciprocal autonomic adjustments, in part through indirect baroreflex interactions (Fukuda, Sato, Suzuki, & Trzebski, 1989; Kollai & Koizumi, 1979). As illustrated in Figure 1, however, mild hypoxia or hypercapnia can result in sustained coactivation of autonomic controls of the heart. This is evidenced by concurrent increases in activity of both vagal and sympathetic cardiac nerves with decreases in ventilatory volume, or with variations in the composition of inspired gasses (Fukuda et al., 1989; Koizumi et al., 1983; Kollai & Koizumi, 1979).

In addition to these findings with basic reflexive controls, nonreciprocal changes in autonomic activity are also manifest in behavioral contexts. Early evidence comes from the study of Obrist, Wood, and Perez-Reyes (1965) on the autonomic origin of the cardiac response to a conditioned aversive stimulus in human subjects. These authors reported that the bradycardia evoked by the conditioned stimulus (CS) could be blocked by the parasympathetic antagonist atropine. Under parasympathetic blockade, in fact, the heart rate response to the CS reverted to a notable cardioacceleration. This finding led the authors to conclude that the CS evoked concurrent sympathetic activation that was normally masked by a more potent vagal response. A subsequent classical conditioning study in monkeys, although reporting an acceleratory conditioned response, also provided evidence of autonomic coactivation to the CS (Schoenfeld, Kadden, Tremont, McCullough, & Steele, 1980). The initial response to the CS appeared to arise from reciprocal autonomic adjustments because it was attenuated by either vagal or sympathetic blockade and was eliminated by dual blockade. A longer latency coactivation, however, was suggested by the de novo appearance of deceleratory components to the CS after administration of the sympathetic antagonist propranolol.

A more recent study in animals supports these general find-

[4] At the time, it could not be definitively ascertained whether the stress-induced inhibition of insulin was due to sympathetic neural or sympathoadrenal action. It has now been demonstrated that the splanchnic sympathetic innervation of the pancreas can directly inhibit insulin secretion by means of alpha adrenergic receptors (Holst, Schwartz, Knuhtsen, Jensen, & Nielsen, 1986).

[5] Coactivation of autonomic controls of the heart, in response to atrial stretch, probably contributed to a historical controversy associated with the Bainbridge reflex. Following the description by Bainbridge (1915) of tachycardia in response to atrial volume loading, several studies failed to demonstrate this reflex or reported an opposite bradycardia to atrial distention (e.g., Daly, Ludany, Todd, & Verney, 1937). Although it now appears that atrial stretch may consistently yield tachycardia in quiescent, wakeful subjects (Horwitz & Bishop, 1972), subjects with high baseline heart rates may evidence bradycardia (Edis, Donald, & Sheperd, 1970; Kurz, Wead, & Roberts, 1990). The explanation for this discrepancy may relate to an important property of nonreciprocal modes of control. Depending on the relative dominance of the two autonomic divisions, nonreciprocal modes can yield diametrically opposite organ responses. Coactivation of vagal and sympathetic controls of the heart could result in either tachycardia or bradycardia depending on the degree of activation of the two autonomic nervous system divisions. In this regard, high basal heart rates may minimize further cardioacceleratory lability, unmasking the concordant vagal actions. Under these conditions, autonomic coactivation to atrial stretch may foster the appearance of bradycardia (Edis et al., 1970).

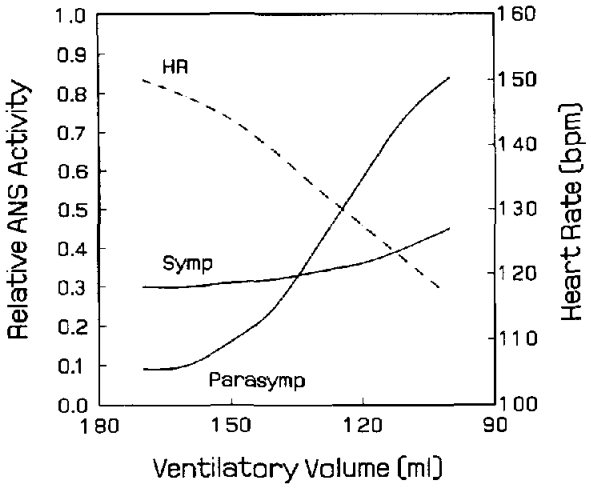

Figure 1. Coactivation of the sympathetic and parasympathetic controls of the heart. (Relative changes in activity of sympathetic [Symp] and parasympathetic [Parasymp] cardiac nerves, together with heart rate [HR], are illustrated as a function of ventilatory volume in the dog. From "Reciprocal and non-reciprocal action of the vagal and sympathetic nerves innervating the heart" by M. Kollai and K. Koizumi, 1979, *Journal of the Autonomic Nervous System, 1,* Figure 7. Copyright 1979 by Elsevier Science Publishing Co., Inc. Adapted by permission.)

ings, and also suggests an important contribution of psychological variables to autonomic coactivation in associative paradigms (Iwata & LeDoux, 1988). Rats given unpaired presentation of an auditory CS and a shock unconditioned stimulus (US) uniformly displayed tachycardia in response to the CS, reflecting a nonspecific sensitization. This cardioacceleratory response was largely eliminated by the sympathetic antagonist propranolol but was unaltered by the parasympathetic blocker atropine (see Figure 2). The results in control animals are consistent with a CS-induced increase in sympathetic drive to the heart (uncoupled sympathetic mode).

As a group, the forward-paired experimental animals showed a statistically similar mean acceleratory response to the CS. The heart rate response of the conditioned animals, however, appeared to have a fundamentally different autonomic origin from the similar response of controls. Greater variability was apparent among the experimental animals, and several of the subjects evidenced bradycardic components to the heart rate response. Moreover, in contrast to control animals, parasympathetic blockade dramatically increased the acceleratory components of cardiac response, suggesting that the CS evoked a concurrent vagal activation that normally dampened the acceleratory response of experimental subjects. As further illustrated in Figure 2, whereas sympathetic blockade resulted in a simple attenuation of the CS-induced tachycardia in control animals, it unmasked a notable bradycardia to the CS in conditioned subjects. This represents the prototypic pattern of coactivation. If considered from the perspective of heart rate responses in untreated animals, no evidence of conditioning was apparent. Vagal blockade, however, revealed a considerably larger sympathetically driven response to the CS in the conditioning group that was normally masked by the apparent vagal coactivation.

Together, these results support the suggestion that conditioned aversive stimuli can evoke coactivation of both sympathetic and vagal chronotropic controls of the heart. Indeed, autonomic coactivation to conditioned aversive stimuli may contribute to the variable reports in the literature of tachycar-

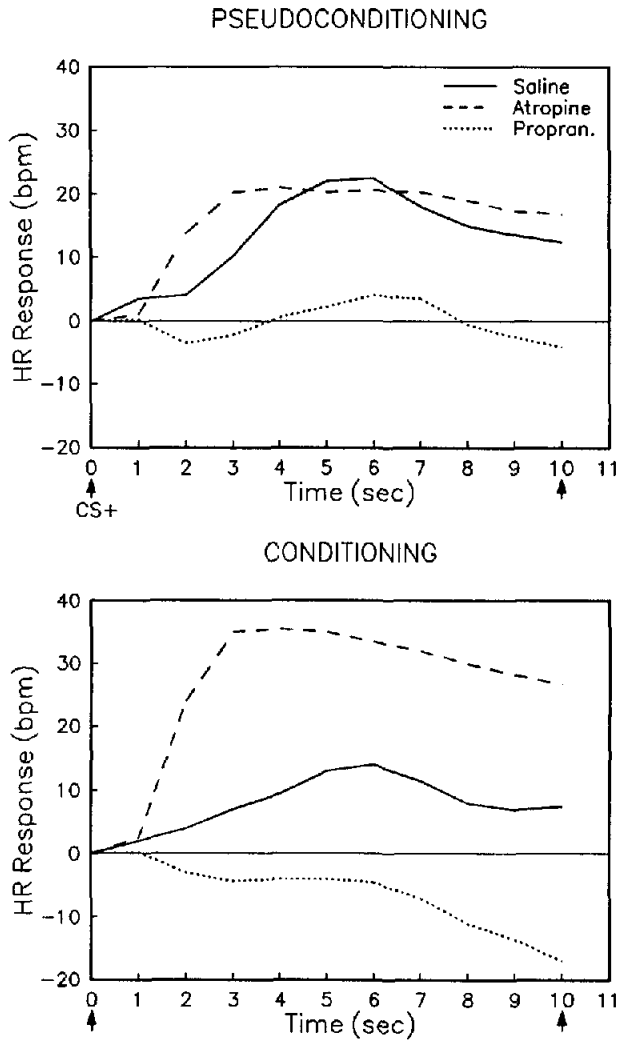

Figure 2. Autonomic coactivation to a conditioned stimulus (CS) as revealed by the effects of pharmacological blockade. (Coactivation was apparent to the CS in the conditioning group, as evidenced by enhancement of the heart rate [HR] response with muscarinic blockade [atropine] and the reversal of response direction with beta adrenergic blockade [propranolol]. Although the control group showed a similar cardioacceleratory response to the CS, it appeared to arise from uncoupled sympathetic activation, because it was largely eliminated by sympathetic blockade but minimally affected by vagal blockade. CS onset and offset are indicated by the arrows on the abscissa. The solid horizontal line indicates baseline. From "Dissociation of associative and nonassociative concomittants of classical fear conditioning in the freely behaving rat" by J. Iwata and J. E. LeDoux, 1988, *Behavioral Neuroscience, 102,* pp. 72–73. Copyright 1988 by the American Psychological Association, Inc. Adapted by permission.)

dia, bradycardia, or biphasic responses to such stimuli (Cohen & Randall, 1984; Galosy et al., 1980; see also Iwata & LeDoux, 1988, Table 3). Under conditions of coactivation, the dominant autonomic influence (sympathetic positive chronotropy or vagal negative chronotropy) may be dependent on the experimental context, baseline heart rate, or other variables. Because it is also clear that reciprocal autonomic changes frequently occur in conditioning contexts (Cohen & Randall, 1984), the behavioral and neural determinants of coactivation during conditioning remain to be clarified.[6] Although additional work is sorely needed in this area, it is apparent that varying modes of autonomic control, including coactivation, can be observed in conditioning contexts.

Apparent coactivation of sympathetic and vagal chronotropic controls of the heart can also be seen in response to simple attentional stimuli (Quigley & Berntson, 1990). Consistent with the distinction between orienting and defensive reactions, nonsignal acoustic stimuli of two intensities (55 vs. 75 db SPL) yielded equivalent vasopressor but distinct cardiac responses in rats. Whereas the high-intensity stimulus evoked notable tachycardia, the lower intensity stimulus resulted in a predominant bradycardia (Figure 3, solid lines). The autonomic origins of these cardiac responses were investigated by the administration of the postganglionic parasympathetic antagonist scopolamine methylnitrate and the sympathetic β_1 adrenergic antagonist atenolol.

As illustrated in Figure 3 (bottom panel), pharmacological blockade revealed characteristic features of coactivation in response to the low-intensity stimulus.[7] The deceleratory response to this stimulus was eliminated by parasympathetic blockade. Consistent with the finding of Obrist et al. (1965), however, scopolamine not only eliminated the stimulus-induced bradycardia, but unmasked a notable tachycardiac response to the stimulus. The cardioacceleratory response emerging under parasympathetic blockade likely reflected a concurrent sympathetic activation that was normally masked by the more potent vagal response. This was further indicated by the finding that sympathetic blockade increased the magnitude of the stimulus-induced bradycardia to the low-intensity stimulus (Figure 3, bottom panel).

In contrast to this pattern of coactivation to the low-intensity stimulus, the high-intensity stimulus yielded a more complex temporal pattern that included a predominant uncoupled sympathetic (or slight reciprocal sympathetic) component, beginning within a few seconds of stimulus onset. The acceleratory response during this period was dramatically attenuated by atenolol but only marginally affected by scopolamine. In fact, on the basis of the responses obtained under scopolamine, both stimuli yielded approximately equivalent sympathetic activation throughout the poststimulus period. The primary difference between the responses to the two stimuli appeared to be in the parasympathetic contribution (see atenolol curves, Figure 3).

The studies just outlined illustrate multiple instances of autonomic coactivation emerging in a single target organ (the heart) within a rather limited range of paradigms. Nonreciprocal autonomic control, however, has also been revealed by direct neural recordings in other target organs (Matsuo & Yamamoto, 1989), and may be a rather ubiquitous feature of ANS organization.

Uncoupled Modes

In addition to the modes of correlated autonomic discharge just outlined, responses can be observed in one ANS division in the absence of change in the other. Whereas "psychosensory" pupillary responses arise from reciprocal autonomic adjustments, pupillary light and accommodation reflexes are mediated largely or exclusively by variations in parasympathetic control (Beatty, 1986). Through the use of pharmacological blockades, Pollak and Obrist (1988) found that whereas the heart rate increase during sustained handgrip arose from reciprocal autonomic adjustments, a similar heart rate change during reaction time tasks was attributable to an uncoupled sympathetic response.

Apparent functional uncoupling of the autonomic divisions may arise from differences in threshold or gain. Thus, one division may show a relatively low activational slope, so that modest phasic variations have minimal effects on the functional state of the organ, relative to the other division. Alternatively, the two ANS divisions may have different thresholds for activation, so that at moderate levels of provocation, only the division with the lower threshold exerts functional effects. In this case, functionally significant variations of both divisions may be apparent only at higher levels of activity. Although exercise in humans ultimately leads to a reciprocal pattern of sympathetic activation and vagal withdrawal, the initial heart rate response to moderate exercise appears to derive largely from vagal inhibition (Rowell, 1986). As an additional example, the baroreceptor–heart rate reflex is mediated largely by alterations in vagal activity at high blood pressures (with the associated baroreflex inhibition of sympathetic tone). At low blood pressures, however, the baroreflex appears to be mediated predominantly by changes in sympathetic activity (Head & McCarty, 1987). Both divisions are active at intermediate pressures (Furedy et al., 1989; Head & McCarty, 1987).

It is apparent that notable changes can be seen in the activity of one ANS division in the absence of appreciable changes in the other. An example of such apparent uncoupling in behavioral contexts has already been mentioned for the control group in the conditioning study of Iwata and LeDoux (1988). Both the

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[6] One variable that may be relevant to the pattern of autonomic change during conditioning is the nature of the associated somatomotor response. If the conditioned stimulus evokes somatic activation, the cardiac response may be tachycardia, whereas bradycardia may be associated with somatic suppression (Cohen & Randall, 1984; Schneiderman, 1974). A related determinant may be the basal levels of vagal and sympathetic tone, because studies observing bradycardia to conditioned stimuli have frequently reported higher baseline heart rates than those reporting tachycardia (see Iwata & LeDoux, 1988, Table 3). In fact, the autonomic mode may even change over the course of conditioning, as the discriminative stimulus becomes well differentiated and the response well defined.

[7] Doses illustrated in Figure 3 were those yielding asymptotic effects in a dose by response study. Drug effects were dose dependent, and all major drug effects reported were significant. No significant effects of these antagonists were apparent on either basal blood pressure or phasic blood pressure responses.

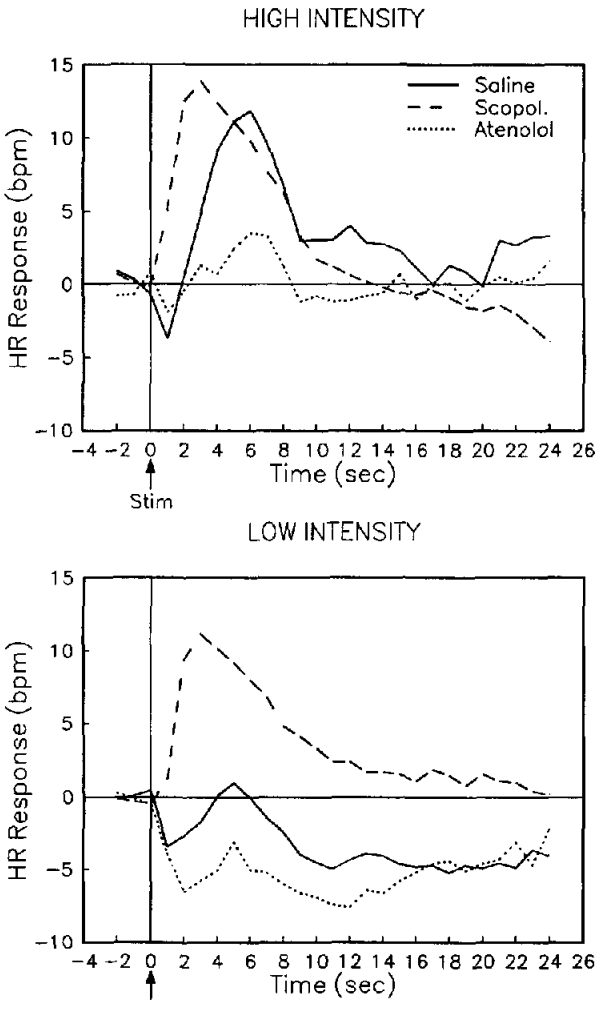

Figure 3. Coactivation of the autonomic controls of the heart in response to a low-intensity nonsignal stimulus (Stim). (Coactivation was apparent in the enhancement of the deceleratory response with β_1 adrenergic blockade [atenolol] and the reversal of response direction with muscarinic blockade [scopolamine]. In contrast, a predominant uncoupled sympathetic activation, or slight reciprocal sympathetic pattern, was seen to the high-intensity stimulus. The arrows on the abscissa and the vertical line indicate the time of stimulus presentation. HR = heart rate. From "Autonomic origins of cardiac responses to nonsignal stimuli in the rat" by K. S. Quigley and G. Berntson, 1990, *Behavioral Neuroscience, 104*, p. 758. Copyright 1990 by the American Psychological Association, Inc.)

experimental and control groups in their study evidenced comparable baseline blood pressure and heart rate, and both responded to the CS with a similar cardioacceleratory response. Nevertheless, whereas the conditioning group evidenced coactivation of both sympathetic and vagal controls of the heart, the control group displayed a relatively uncoupled sympathetic activation. Unlike the conditioning group, CS-induced tachycardia in control subjects was completely blocked by sympathetic antagonism (propranolol) but was neither increased nor decreased by parasympathetic blockade (atropine). This is the prototypic pattern of results for uncoupled responses.

Neural Origins of Autonomic Modes of Control

Although the role of specific neural systems in behavior is not the focus of this article, the existence of multiple modes of autonomic control is most relevant to behavioral scientists if these modes are linked to or influenced by neural systems underlying behavioral processes. In the present section, we briefly review evidence indicating that rostral brain areas, which have been implicated in behavioral processes, can alter or modulate the modes of autonomic control.

Neural mechanisms for autonomic control are represented at the lowest levels of the central nervous system, and many sympathetic and sacral parasympathetic reflexes are apparent even in spinal organisms. Early studies by Brooks (1933) in animals, and Kuhn (1950) in humans, documented the return of an array of autonomic reflexes after spinal transections. It was noted, however, that these reflexes were often relatively isolated and incomplete. Indeed, it has become increasingly apparent that supraspinal mechanisms play a prominent role not only in the integration of phasic reflexive controls, but in the maintenance of autonomic tone (Calaresu & Yardley, 1988; Loewy & Spyer, 1990; Mathias & Frankel, 1988).

Brain-stem autonomic mechanisms constitute a primary source of reciprocal control over sympathetic and vagal outflows. For the cardiovascular system, baroreflexes and respiratory reflexes serve as important sources of reciprocal control, which is exerted through relatively direct opponent influences on sympathetic and vagal motor neurons (Kollai & Koizumi, 1979, 1981). The basic neural circuitry of the baroreflex, for example, is beginning to be understood in some detail (Loewy & Spyer, 1990; Spyer, 1981). Afferents from the carotid and aortic baroreceptors terminate in and around the nucleus tractus solitarius (NTS), which plays an important integrative role in autonomic regulation. The NTS, in turn, gives rise to direct excitatory projections to vagal motor neurons and indirect inhibitory influences to spinal sympathetic neurons. This opponent innervation of vagal and sympathetic motor neurons constitutes an important mechanism of reciprocal central control of the ANS.

Central systems can also exert nonreciprocal influences over autonomic outflows. To some extent, these influences may arise directly from basic brain-stem reflexes, as evidenced by the coactivation attendant on hypoxia or atrial distention (discussed earlier). Of potentially greater importance for the present consideration, however, are descending influences from higher telencephalic and diencephalic systems. Bard (1960) suggested that suprabulbar systems may inhibit baroreceptor reflexes under conditions of emotional excitement, which could account for the reflex-inconsistent increases in both heart rate and blood pressure in such states. Consistent with this suggestion, it now appears that even mild stressors, including mental arithmetic, can lead to a reduction in the sensitivity or gain of the baroreceptor–heart rate reflex (Conway, 1984; Nosaka, Nakase, & Murata, 1989; Stephensen, Smith, & Scher, 1981; Steptoe & Sawada, 1989).

This modulation of baroreflex mechanisms appears to arise, at least in part, through descending influences from rostral brain systems. One model system for the study of descending autonomic influences is the hypothalamic defense response

(see Hess, 1957). This response can be elicited by electrical stimulation of a descending system extending from the amygdala, through the hypothalamus, to the midbrain central gray and lower brain-stem areas (Berntson, 1972, 1973; DeMolina & Hunsperger, 1962; Hilton & Zbrozyna, 1963; Yardley & Hilton, 1986). The evoked response includes both somatic (e.g., growling, piloerection, and escape) and cardiovascular features (increased heart rate and blood pressure, hind-limb vasodilation, and renal and splanchnic vasoconstriction) reminiscent of natural defense reactions. As with stress reactions, the concurrent increase in heart rate and blood pressure observed during this response is in direct contrast to the baroreflex pattern.[8]

Direct anatomical projections have now been demonstrated from the amygdala and the hypothalamus to cardiovascular control mechanisms in the NTS, dorsal motor nucleus, nucleus ambiguus, raphe nuclei, medullary vasomotor areas, parabrachial nucleus, and intermediolateral cell column of the spinal cord (Danielsen, Magnuson, & Gray, 1989; Hamilton, Ellenberger, Liskowsky, & Schneiderman, 1981; Holstege, 1987; Loewy & Spyer, 1990; Onai, Takayama, & Miura, 1987). Moreover, stimulation of the rostral "defense" areas in the hypothalamus or amygdala has been shown to suppress the baroreflex through two mechanisms: (a) a direct inhibition of NTS neurons that receive baroreflex afferents and (b) an indirect gamma-aminobutyric acid (GABA)-mediated inhibition of vagal motor neurons (Coote, Hilton, & Perez-Gonzales, 1979; Nosaka et al., 1989; Spyer, 1989). Thus, rostral limbic mechanisms appear to have multiple routes by which they can influence cardiovascular functions.

Stimulation of rostral brain areas can also yield an opposite pattern of bradycardia, hypotension and facilitated baroreflexes in the rabbit. Active areas include the prefrontal cortex (Hardy & Holmes, 1988), lateral hypothalamus (Gellman, Schneiderman, Wallach, & Le Blanc, 1981; Hardy & Mack, 1990; Spencer, Sawyer, & Loewy, 1989), and central nucleus of the amygdala[9] (Applegate, Kapp, Underwood, & McNall, 1983; Cox et al., 1986; Gellman et al., 1981; Iwata, Chida, & LeDoux, 1987; Pascoe, Bradley, & Spyer, 1989). These areas have been heavily implicated in emotional processes and in learning in affective contexts (Kapp, Pascoe, & Bixler, 1984; Sarter & Markowitsch, 1985). Indeed, the amygdala may play a pivotal role in both the behavioral and cardiovascular components of conditioned aversive reactions. It has been shown that (a) activity of amygdaloid neurons to a CS is selectively altered during conditioning (Applegate, Frysinger, Kapp, & Gallagher, 1982; Pascoe & Kapp, 1985), (b) amygdaloid lesions can block both the behavioral and cardiovascular components of conditioned emotional responses without impairing cardiac orienting responses or the unconditioned cardiac response to the US (Gentile, Jarrell, Teich, McCabe, & Schneiderman, 1986; Kapp et al., 1984; Sananes & Campbell, 1989), and (c) blockade of specific output pathways of the amygdala can selectively eliminate either the cardiovascular or behavioral components of the conditioned response (CR) without altering the other (Jarrell et al., 1986; LeDoux, Iwata, Cicchetti, & Reis, 1988).

In fact, a wide array of specific autonomic patterns can be evoked by stimulation of different loci within the hypothalamus (Gellman et al., 1981; Koizumi & Kollai, 1981). Through direct recordings of vagal and sympathetic cardiac nerves, Koizumi and Kollai (1981) have reported four general classes of response to hypothalamic stimulation in dogs that represent all major classes of the autonomic modes of control. The first entailed a reciprocal pattern of vagal inhibition and sympathetic excitation, accompanied by increases in heart rate and blood pressure, increased muscle blood flow, and inhibition of the baroreflex (the "defensive" response). A second reciprocal pattern consisted of an increase in vagal discharges and a decrease in sympathetic outflow, accompanied by bradycardia and hypotension. Stimulation at other points yielded nonreciprocal patterns of increased traffic in the cardiac nerves of both ANS divisions (coactivation) or decreased activity in both sympathetic and vagal cardiac nerves (coinhibition).

Although it is apparent that rostral brain systems can exert a wide array of modulatory effects on central autonomic mechanisms, it remains less clear what specific behavioral conditions are associated with different modes of autonomic control. This is an especially important area for future investigation, and one to which we will return later.

The Doctrine of Autonomic Space

The concept of a sympathetic–parasympathetic continuum represents a conceptual advance over the implicit dichotomies of sympathotonia versus vagotonia or ergotropic versus trophotropic. As documented earlier, however, it is now clear that the autonomic modes similarly cannot map onto a single linear vector. Consequently, the doctrine of autonomic reciprocity must yield to a multidimensional model of autonomic control. Given the two basic autonomic divisions, a two-dimensional surface is minimally necessary to represent the autonomic modes of control. Although two-dimensional autonomic surface may still neglect nonneural metabolic and hormonal effects, it exhaustively represents the potential graded combinations of sympathetic and parasympathetic influences.

The doctrine of autonomic reciprocity is not entirely vacuous, because it does capture a subset of the autonomic modes of control. Consequently, it must be subsumable under an alternative conception. We propose an expansion of the doctrine of reciprocity to the doctrine of autonomic space, which entails a two-dimensional surface representation of sympathetic and parasympathetic controls and incorporates the recognized complexities of autonomic control. As illustrated in Figure 4, this surface (a) subsumes the doctrine of reciprocity as one diagonal vector, (b) represents the nonreciprocal modes on the alternate diagonal, and (c) depicts the uncoupled modes as vectors lying along the axes. In addition, the families of vectors parallel to those just mentioned represent the general categories of auto-

[8] Cardiovascular responses are not secondary to respiratory or other somatic reactions, because similar cardiovascular effects are obtained in paralyzed animals and with experimental control of respiratory drive (Pascoe, Bradley, & Spyer, 1989).

[9] In view of the potential functional role of the amygdala in aversive reactions, it is interesting to note that freezing is a common response to threat in the rabbit. In this species, amygdaloid stimulation yields bradycardia and hypotension through excitation of nucleus tractus solitarius cells receiving baroreceptor afferents (Cox et al., 1986).

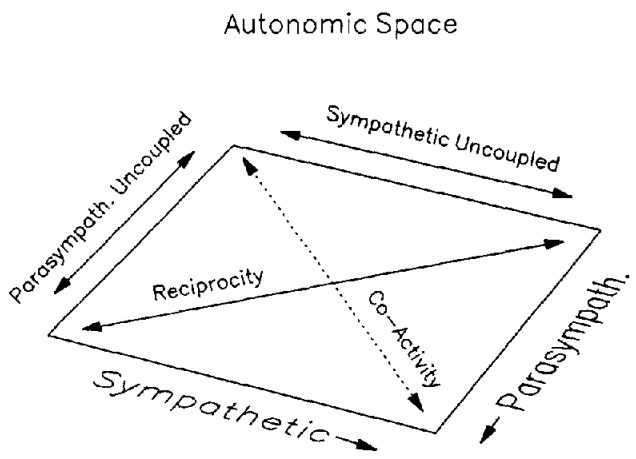

Figure 4. Two-dimensional model of autonomic space. (Axes represent the level of activity in sympathetic and parasympathetic innervations. The solid arrow extending from the left to the right axis intersections depicts the diagonal of reciprocity. The dotted arrow extending from the back to the front axis intersections represents the diagonal of coactivity. The arrows alongside the axes depict uncoupled changes in the single autonomic nervous system divisions. These arrows, and vectors parallel to them, illustrate the major modes of autonomic control. Parasympath. = parasympathetic.)

nomic control expressed from varying starting points within the two-dimensional space.

A feature of the doctrine of autonomic space is that it is indifferent as to the nature of the functional impacts of the autonomic innervations on the target organ. Although the nature of the autonomic influences clearly governs the translation from autonomic space to functional effects on organs, it does not alter the basic representations within autonomic space. Moreover, the concept of autonomic space can accommodate singly innervated organs, in which case the space simplifies to a single vector lying along the relevant sympathetic or parasympathetic axis.

The three principles of the doctrine of autonomic reciprocity are subsumed by the broader perspective of the doctrine of autonomic space. Specifically:

1. The principle of dual innervation is subsumed by the broader *principle of innervation,* which asserts that a visceral organ may be either singly or dually innervated by the ANS.
2. The principle of functional antagonism is absorbed by the *principle of conjoint action,* which maintains that the two ANS divisions may exert either antagonistic or synergistic influences on dually innervated organs. The functional nature of these influences is relevant only in the translation of autonomic space into functional actions on target organs.
3. The principle of reciprocal control is assimilated by the more general *principle of multiple modes,* which asserts that the mode of control over sympathetic and parasympathetic innervations may be reciprocal, nonreciprocal, or uncoupled.

We will next consider the formal implementation of these principles into a quantitative model of autonomic space and its translation into a functional output surface.

Formal Properties of the Autonomic Modes

Although a comprehensive account of the significance of various modes of autonomic control is not yet possible, some general properties of these modes can be derived from the perspective of a two-dimensional autonomic space.

Functional Properties and Derived Principles

As illustrated in Table 3, the modes of autonomic control appear to differ on at least three dimensions: (a) the functional direction of the organ response, (b) the dynamic range of response, and (c) the response lability within the dynamic range. As is apparent in this table, these properties evidence a high degree of functional coherence within the general categories of reciprocal, non-reciprocal, and coupled autonomic modes.

Directional stability. Reciprocal modes of autonomic control yield a directionally stable pattern of target organ response. Because these modes entail activation of one ANS division and inhibition of the other (antagonistic) division, the actions of both divisions synergistically promote the same directional response in the target organ. Consequently, variations in the magnitude of the response of either division, although probably affecting response amplitude, would not be expected to alter the basic direction of the target-organ change. Because either sympathetic activation or vagal withdrawal is sufficient to produce an increase in heart rate, for example, the tachycardia associated with reciprocal sympathetic activation would be attenuated, but not eliminated, by blockade of the functional impact of either of the ANS divisions. Indeed, this feature constitutes a hallmark of the reciprocal mode of control.

In contrast, nonreciprocal modes (coactivation or coinhibition) yield a fundamentally variable directional response, or may yield no response at all if the changes in the two divisions are functionally equivalent. Thus, coactivation of the chronotropic controls of the heart could yield either tachycardia (sympathetic dominance) or bradycardia (vagal dominance). With covarying antagonistic influences, blockade of the dominant division would result in a reversal of the response direction, whereas blockade of the other division would be expected to increase response amplitude.

Like reciprocal patterns, uncoupled autonomic modes yield unidirectional responses, because only one ANS division undergoes active change. In contrast to other modes, therefore, uncoupled responses can be eliminated by blockade of the active ANS division but are relatively unaltered by blockade of the inactive division.

These differences can be summarized by the *principle of directional stability,* which asserts that there are fundamental differences in the nature of the target-organ response under alternate modes of autonomic control. Specifically, the reciprocal modes are characterized by a high directional consistency of the target-organ response, whereas organ responses under nonreciprocal modes are fundamentally variable in direction.

Dynamic range. Autonomic modes of control are also characterized by differences in the dynamic range of the target-organ response. For antagonistic innervations, the changes in activity of the two ANS divisions result in concordant effects on the target organ. Consequently, the reciprocal modes can yield the greatest dynamic range of organ response. Sympathetic reciprocal activation, for example, entails an increase in the positive chronotropic effects of the sympathetic innervation and a decrease in the negative chronotropic actions of the vagus. Both

Table 3
Operating Characteristics of the Modes of Autonomic Control

Sympathetic response and functional dimension	Parasympathetic response		
	Increase	No change	Decrease
Increase	Coactivation	Sympathetic activation	Reciprocal sympathetic activation
Directional stability	↓	↑	↑
Dynamic range	↓	↔	↑
Reactive lability	↓	↔	↑
None	Parasympathetic activation	Baseline	Parasympathetic withdrawal
Directional stability	↑		↑
Dynamic range	↔		↔
Reactive lability	↔		↔
Decrease	Reciprocal parasympathetic activation	Sympathetic withdrawal	Coinhibition
Directional stability	↑	↑	↓
Dynamic range	↑	↔	↓
Reactive lability	↑	↔	↓

Note. ↔ indicates intermediate levels; ↑ and ↓ indicate increases and decreases, respectively.

of these changes synergistically promote a cardioacceleratory response. Consequently, this phasic acceleratory response would be eliminated only by blockade of both ANS divisions. Blockade of either division alone, however, would reduce the dynamic range of the response to a level comparable to that of the uncoupled modes.

In contrast, nonreciprocal modes of control in antagonistic innervations may evidence a substantially restricted dynamic range of the target-organ response. This is attributable to the mutually opponent actions of the ANS divisions. In coactivation of the sympathetic and vagal controls of the heart, for example, the positive (sympathetic) and negative (vagal) chronotropic effects oppose the functional impact of the other division. Under these conditions, blockade of one division would increase or unmask the functional manifestations of the other division. Consequently, blockade of a single division would expand the dynamic range of the target-organ response to a level comparable to that of uncoupled modes.

The uncoupled autonomic modes would be expected to display intermediate characteristics, because only one ANS division undergoes active change. In uncoupled modes, the response of the active division is neither enhanced nor restrained by corresponding changes in the alternate division. Consequently, the uncoupled modes are characterized by an intermediate dynamic range of the target-organ response. For uncoupled modes, blockade of the active ANS division would eliminate responses, whereas blockade of the other division would be expected to have little effect on the dynamic range.

These properties of the autonomic modes of control are captured by the *principle of dynamic range,* which asserts that basic differences exist in the dynamic range of organ response under alternate modes of control. These differences lie along a continuum from a wide dynamic range (reciprocal modes) to a restricted range (nonreciprocal modes), with uncoupled modes again being intermediate.

Reactive lability. Differences in the lability of the target-organ response (irrespective of direction) also characterize varying modes of autonomic control. This is illustrated, for example, by the effects of a given increment of sympathetic activity under different modes of control. The slope of the target-organ response would be expected to be greatest in the reciprocal sympathetic pattern, because the functional effect of a given increment in sympathetic activity would be enhanced by the concurrent decrement in vagal control. This high degree of response lability would be decreased by blockade of either ANS division, which would yield a reduction in lability to a level comparable to that of uncoupled modes of control.

In contrast, target-organ lability would be expected to be minimal for nonreciprocal modes, because a given increment in sympathetic activity would be countered by a concurrent increase in vagal control. In further contrast to the reciprocal modes, blockade of either ANS division would be expected to increase target organ lability to a level comparable to that of the uncoupled modes.

The uncoupled modes would again be expected to yield an intermediate level of target-organ lability, because they are driven by a single active division that is neither enhanced nor opposed by the alternate division. This lability would be eliminated by selective blockade of the active division, but would be relatively unaltered by blockade of the inactive division.

These relationships are subsumed by the *principle of reactive lability,* which maintains that fundamental differences exist in the response lability of an organ system under alternate modes of control. These differences would lie along a continuum from

a high lability under reciprocal modes to a low lability with nonreciprocal modes.

Summary of formal properties. A high degree of functional coherence emerges among the formal properties of the autonomic modes of control, as illustrated in Table 3. The nonreciprocal modes of coactivation and coinhibition would tend to stabilize the functional state of the target organ, because both the dynamic range and the response amplitude lability are reduced. At the same time, these nonreciprocal modes evidence a fundamental instability in response direction that may afford a degree of flexibility in the directional response to physiological or behavioral conditions. In contrast, the reciprocal modes of control feature high directional stability, a wide dynamic range, and a high response lability. The uncoupled modes evidence features intermediate to those of the reciprocal and nonreciprocal modes of control. (The properties just described apply for antagonistic actions of the ANS divisions. With synergistic actions, the properties of reciprocal and nonreciprocal modes would be reversed.)

A Quantitative Model of the Formal Properties of Autonomic Modes

The distinct properties of the general modes of autonomic control are illustrated in Figure 5, which depicts models of the target-organ responses arising from different autonomic modes. The target-organ response functions (right panels) were derived from standardized input functions (left panels) by a simple additive model. Inputs to the model were typical sigmoidal activity functions of the two ANS divisions, varying along an activation continuum (as illustrated, for example, in Figure 1). A single sympathetic function was input, and a family of parasympathetic inputs was used to capture different lead–lag relationships between the divisions (or different vagal baselines in the case of the uncoupled sympathetic modes). The output functions were derived from an adaptation of the quantitative model of Levy and Zieske (1969) for the autonomic control of the heart.[10] We used the following model:

$$f_{ij} = \beta + c_{si} \cdot s_i + c_{pj} \cdot p_j + c_{sipj} \cdot s_i p_j + e, \qquad (1)$$

where f_{ij} is the functional state of the target organ at point ij on an activation continuum, β is the basal functional state in the absence of autonomic input, s_i and p_j are the independent functional activities of the sympathetic and parasympathetic innervations at activation point ij (the input sigmoids of Figure 5), c_{si} and c_{pj} are coupling coefficients that reflect the relative functional impact of sympathetic and parasympathetic activities on the target organ (at activation point ij), $c_{sipj} \cdot s_i p_j$ is a term representing potential interactions among the ANS divisions, and e is an error term that includes, among other things, local (nonneural) metabolic and hormonal effects. Although Equation 1 is a linear model, the indexes (i, j) on the coefficients can accommodate potential nonlinearities in the functional impact of the ANS on the target organ (which translate into variations in the coupling coefficients at different activation levels, i.e., i, j become vectors).

Although relatively comprehensive, this model simplifies some dynamic features of autonomic control by including a number of variables in the error term. Currently evolving models of the chronotropic controls of the heart, for example, will ultimately need to incorporate frequency transfer functions and baseline dependencies of sympathetic and vagal innervations, activity patterning within autonomic nerves, and local (nonneural) metabolic[11] and circulatory effects (Berger, Saul, & Cohen, 1989; Billman & Bickerstaff, 1986; Furukawa & Levy, 1984; Warner & Russell, 1969). Variance associated with these factors is here included in the error term. Many of these variables will differ from organ to organ, however, and specific implementations of this general model may benefit by a further parsing of the components of the error term variance. Our intention, however, is not to model autonomic control of a particular organ, but rather to illustrate general properties of the modes of autonomic control.

The terms of Equation 1 reflect each of the principles of the doctrine of autonomic space. The principle of innervation is expressed in the presence of the terms s_i and p_j, which assume a fixed value of zero in the absence of the relevant input. The principle of conjoint action is manifest in the signs of the coefficients c_{si} and c_{pj}, which are equivalent for concordant actions and opposite for antagonistic actions. Finally, the principle of multiple modes is captured by the relative changes in the values of s_i and p_j with variations in activation (i.e., the relative changes of the input functions, as illustrated in Figure 5). For the response functions in Figure 5, we have assumed a basal state (β) of 0, symmetrically opponent ANS influences (coupling coefficients are equal and of opposite sign, ± 1), constancy of the coefficients across the activation continuum, and an interaction term of zero. Deviations from these assumptions will be considered subsequently.

As illustrated in Figure 5, notable differences emerge in the

[10] Although all potential combinations of autonomic nervous system influences within the two-dimensional autonomic space may not be represented in nature, this is an empirical question, and may vary from organ to organ. That possibility does not pose a serious complication for the present model.

[11] The body is adapted for movement and the maintenance of posture in gravitational space. Hence, Cannon (1928) suggested that among the most important roles of the autonomic nervous system were its sustenance of the metabolic needs of the muscles and its preparation of the organism for action. The flight or fight response is served, Cannon argued, by autonomic (primarily sympathetic) and hormonal outpourings during physical activity. Obrist (1981) has elaborated on these somatovisceral connections, suggesting that cardiac–somatic coupling and passive coping responses are controlled primarily by parasympathetic activity, whereas active coping responses are controlled primarily by sympathetic activity (e.g., Obrist, 1981, pp. 200–210). The important point is that cardiac–somatic links are largely achieved by central control over the autonomic nervous system (ANS) divisions, and these influences are appropriately represented in the ANS terms of Equation 1. The error term includes only somatic metabolic influences of peripheral nonneural origin, such as those arising secondarily from local changes in blood flow (Billman & Bickerstaff, 1986). It is the centrally mediated cardiac–somatic link that may be the most potent in behavioral contexts. This is evidenced by the fact that autonomic changes frequently exceed peripheral metabolic demands (Carroll, Turner, & Rogers, 1987; Obrist, 1981; Turner, 1989) and typical autonomic responses persist in somatically paralyzed subjects (Berntson & Boysen, 1990; Dworkin & Dworkin, 1990).

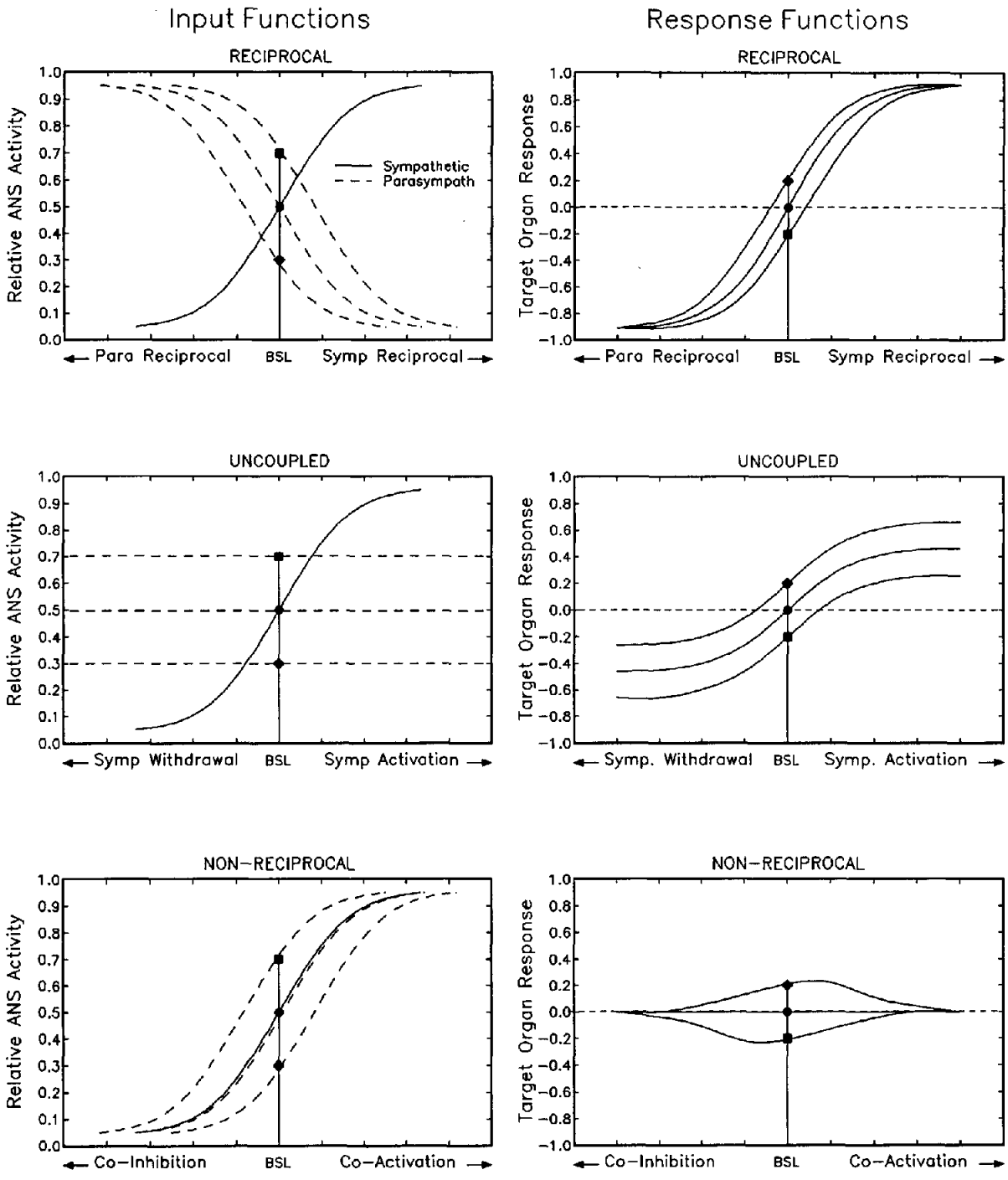

Figure 5. Autonomic nervous system [ANS] inputs (left panels) and organ-response functions (right panels) illustrating reciprocal, uncoupled, and nonreciprocal modes of autonomic control. (Input functions include a single sympathetic [Symp] sigmoid and three parasympathetic [Para] functions having different baseline offsets [or lags]. Response functions were derived from Equation 1 [sympathetic coefficient = 1.0 and parasympathetic coefficient = −1.0]. The solid symbols demarcate functions obtained with the three parasympathetic inputs. All axes are in relative units. BSL = baseline.)

target-organ response functions under different autonomic modes. These differences are in accord with the formal properties outlined earlier. Given identical functional inputs, the target organ response in reciprocal modes has a higher slope (high response lability) and a wider dynamic range than either nonreciprocal or uncoupled modes. Moreover, the response functions under reciprocal control are monotonic (directionally stable). At the other extreme, the nonreciprocal modes evidence the smallest dynamic range, the lowest rate of change (low response lability), and nonmonotonic response functions (directional instability). Uncoupled modes are generally intermediate.

The intermediate appearance of the uncoupled modes may not be adventitious. Rather, the uncoupled modes assume a transitional status between reciprocal and nonreciprocal modes. This is evidenced by the consequences of varying the coupling coefficients of Equation 1, which would correspond to differences in the functional impact of the two ANS divisions on the target organ (equivalent effects would also be produced by varying the inputs, s_i or p_j). Figure 6 illustrates the effects of variations in the coupling coefficients of Equation 1, maintaining the input functions depicted in Figure 5. Although it is clear that different coefficients can yield different patterns of target organ response, they do not alter the relative characteristics of the three general modes of autonomic control.

In all cases, uncoupled modes yield outputs that lie intermediate between the two coupled modes because one ANS division is invariant, neither enhancing nor opposing the functional changes associated with the other division. The functional outputs of both reciprocal and nonreciprocal modes approach the effects of uncoupled modes, however, as one of the coefficients in Equation 1 approaches zero. This is illustrated in the bottom row of Figure 6, where target organ responses under the different modes are identical when the parasympathetic coefficient is zero. (This is not the case in the top row, however, because different parasympathetic functions are input.) An additional point, apparent in Figure 6, is that for all non-zero values of the coefficients, the nonreciprocal modes yield nonmonotonic functions, which evidence the smallest dynamic range and the lowest response lability.

An additional variation in the pattern of autonomic control may arise from differences in the slopes of the autonomic activation (input) functions for the two ANS divisions (e.g., see Figure 1). Thus, even if coupling coefficients are similar, differences in the functional impact on a target organ can arise from differences in the ANS inputs. Figure 7 illustrates the consequences of an exemplar slope difference among the ANS divisions. The resulting target-organ response functions were derived from Equation 1, using input functions having slopes differing by a factor of two (see the inserts of Figure 7). As is apparent in Figure 7, differences in the activation slope can alter the shape of the response functions. Again, however, they do not disturb the relative differences in the formal properties of the modes.

At the limit, a decrease in slope yields a nonvarying state in one division, and the coupled modes yield target responses that converge on each other and on those of the uncoupled modes. Furthermore with progressively increasing slopes, the response functions of the coupled modes become increasingly steep. At the limit, reciprocal and nonreciprocal responses again become equivalent (but have a different sign or direction).

Functional Features of the Autonomic Modes

The formal properties of the autonomic modes, as outlined earlier, may be associated with distinct adaptive features. Of particular interest are those features that differ among the general modes of control.

Reciprocal Modes

Reciprocal modes can yield large, directionally stable shifts in the functional state of the target organ. They may therefore be suited for well-defined adaptive adjustments to survival challenges. Thus, it is not surprising that critical baroreflex compensatory adjustments to perturbations in blood pressure evidence a reciprocal pattern (Koizumi et al., 1983; Spyer, 1981). Moreover, as recognized by Cannon (1929, 1939), highly evocative survival challenges may precipitate a striking and pervasive reciprocal sympathetic pattern. This reciprocal sympathetic mode can extend across organ systems with sufficient authority to inhibit or override even baroreflex-mediated facilitation of vagal controls (Bard, 1960; Stephensen et al., 1981). Thus, stressors can lead to an increase in heart rate, in spite of an elevated blood pressure that would normally serve to suppress sympathetic output and enhance vagal control.

One adaptive feature of reciprocal modes of control is a shift in the relative dominance of the two ANS divisions. During behavioral quiescence, the parasympathetic system may predominate in the autonomic control of heart rate, and responses to moderate challenges may be determined largely by activation or withdrawal of vagal tone (Haroutunian & Campbell, 1982; Levy, 1984; Obrist, 1981; Rowell, 1986). Autonomic activation, however, can reverse this relative dominance and shift the chronotropic control of the heart to the sympathetic system. This is illustrated in the reciprocal model presented in Figure 5 (top panels). As is apparent, a shift to the right along the abscissa (reciprocal sympathetic mode) is associated with an increase in sympathetic control and a reciprocal decrease in parasympathetic influences. The result is a transition from tonic parasympathetic to tonic sympathetic system control of the target organ. This transition would be characterized by a notable increase in heart rate (see Figure 5). Thus, phasic reciprocal responses generally lead to changes in tonic level, unless they are followed by a shift to another control mode (such as an opposite reciprocal pattern, which would lead to a restoration of baseline).

Nonreciprocal Modes

Dissociation of tonic versus phasic controls. The adaptive significance of nonreciprocal controls is less immediately apparent, however, because these modes tend to preserve the baseline functional state of the organ. In fact, with coactivation, no change in basal state may be seen if the ANS divisions evidence equal thresholds, slopes, and coefficients of coupling. Identical parameters across the two divisions are improbable, however, and varying degrees of coactivation (or coinhibition) are more

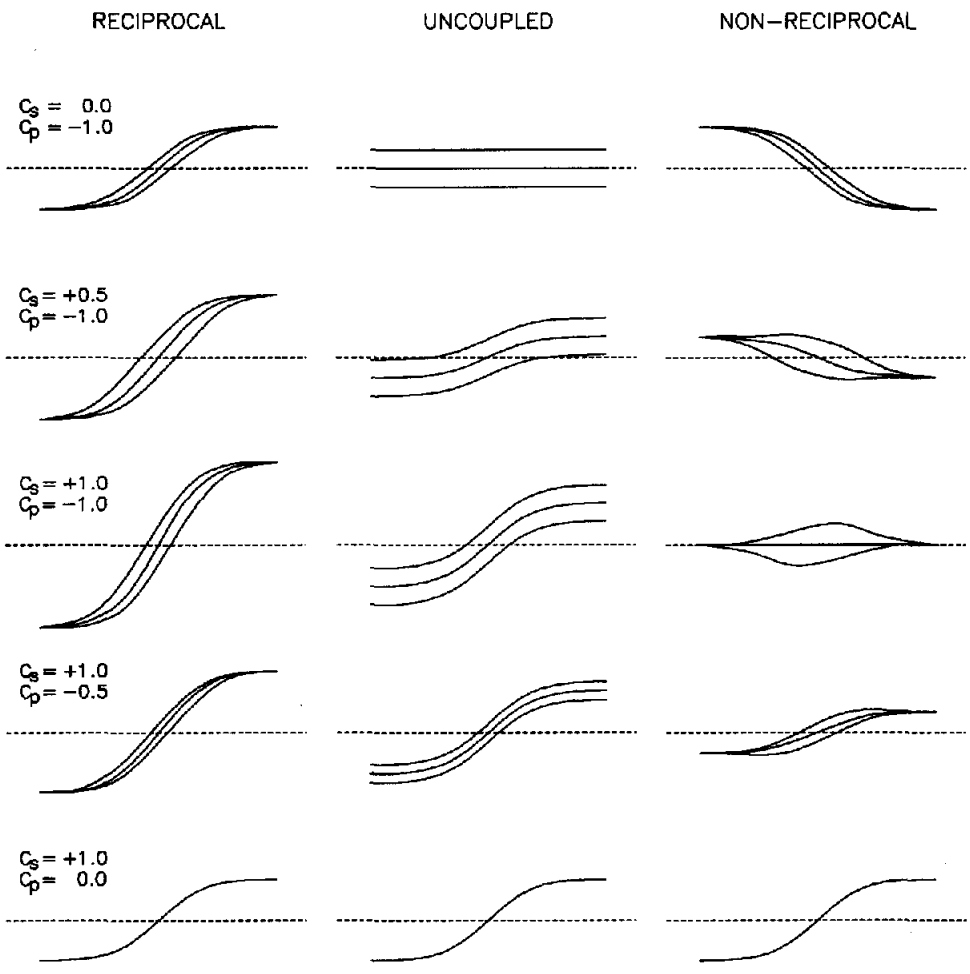

Figure 6. Effects of variations in coupling coefficients on response functions under reciprocal, uncoupled, and nonreciprocal modes of control. (Functions were derived from Equation 1, using input functions depicted in Figure 5. Sympathetic and parasympathetic coefficients were varied as indicated.)

likely the norm. An example can be seen in Figure 1, where notable differences are apparent in the thresholds and slopes of the activation functions for sympathetic and vagal cardiac nerves.

Disparities among coactivated ANS divisions reveal functional properties unique to nonreciprocal modes of control. Shifts in tonic and phasic ANS controls are correlated in reciprocal modes, but they can become dissociated in nonreciprocal modes. The distinction between tonic and phasic controls over a target organ is apparent in Figure 1. In this experimental context, the tonic functional state of the heart under basal conditions (left end of abscissa) may have been under predominant sympathetic control, given the appreciably greater activity in the cardiac sympathetic nerves. In contrast, the phasic or reactive heart rate response to the chemoreceptor challenge appeared to derive largely from parasympathetic changes, given the substantively higher slope (first derivative) of the vagal function (see Figure 1). This is evidenced by the decreasing heart rate emerging in association with the increase in vagal activity. At the peak of vagal activation, the basal heart period was largely determined by the vagus, and the tonic control of the heart would have undergone a shift from sympathetic to vagal control. At the point where vagal activation reached a plateau, however, the slope of the sympathetic activity was increasing. Consequently, further variations in activation would be manifested largely by changes in sympathetic activity, and the phasic control of the heart, at this point, would have shown an opposite shift to the sympathetic system.

This dissociation between tonic and phasic controls is further illustrated by the response functions of Figure 8. These functions were derived from the linear model of Equation 1, with the slopes of the input functions (upper panels) differing for the ANS divisions. Progressive slope differences enhance the magnitude of the shift in phasic control from the sympathetic to the parasympathetic system, for both reciprocal and nonreciprocal modes. This is indicated by the differences in the first derivative of the response functions of the two divisions (Figure 8, bottom panels). In fact, the first derivative functions of the reciprocal and nonreciprocal modes are identical, indicating that these modes yield comparable shifts among the divi-

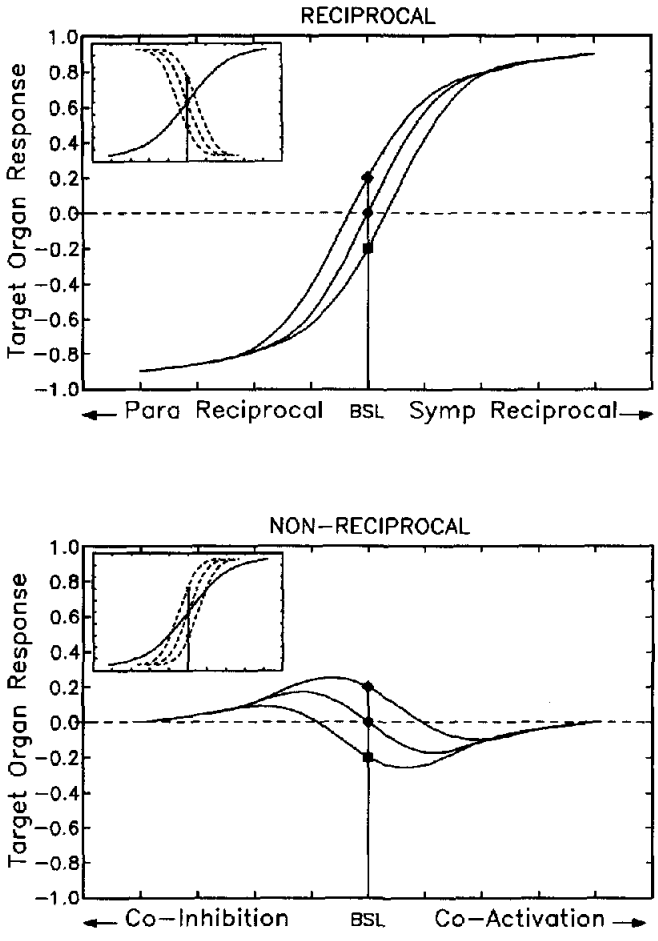

Figure 7. Exemplar response functions resulting from differences in slope of the input functions of the two autonomic nervous system divisions. (Input slopes differed by a factor of two, and are illustrated in the inserts. Solid symbols again depict functions associated with differing time lags in the parasympathetic [Para] input. BSL = baseline; Symp = sympathetic.)

sions in phasic autonomic control. (The opposite shift, from parasympathetic to sympathetic control, would be evidenced if the parasympathetic division displayed the steeper slope.)

A distinction emerges between these modes, however, in the tonic control of the target organ. An index of tonic control could be derived from the relative difference in activity of the ANS divisions across the activation functions, whereas phasic control is determined by differences in the slopes of the activation functions (the first derivatives). As is apparent in Figure 8 (middle panels), the reciprocal sympathetic pattern is associated with a progressive, monotonic shift from the parasympathetic to the sympathetic system in the tonic control of the organ. With chronotropic controls, for example, this would be manifested in a progressive increase in heart rate. In fact, a monotonic shift in baseline would be an invariable consequence of movement along the activation continuum under a reciprocal mode of control.

As discussed earlier, however, nonreciprocal modes tend to preserve baseline functional states, and this is again apparent in Figure 8. Although nonreciprocal changes can yield a moderate alteration in tonic control, this is considerably smaller than the parallel shift under reciprocal modes. Moreover, this alteration in tonic controls is nonmonotonic and limited to the regions of dynamic response of the ANS divisions. In contrast to reciprocal modes, the associated heart rate change would be modest.

Thus, two effects of reciprocal modes of activation are (a) a shift in tonic autonomic controls and the associated basal state, and (b) a shift among divisions in the dynamic or phasic control of the heart. With comparable input functions, however, nonreciprocal modes can yield an equivalent shift in phasic ANS controls with minimal changes in tonic control or in the basal state of the organ.

Autonomic synergism. An additional contribution of nonreciprocal controls may be in the organ-specific or dimension-specific tuning of autonomic actions that can arise from asymmetries in autonomic influences on distinct functional dimensions of a target organ. Given the relatively greater inotropic action of the sympathetic division (Levy, 1984), coactivation of both sympathetic and vagal controls may maximize cardiac contractility while minimizing increases in rate. This could yield an increase in stroke volume by increasing ventricular filling time, a possibility that was confirmed in a study using direct electrical activation of vagal and sympathetic cardiac nerves (Koizumi, Terui, Kollai, & Brooks, 1982). Vagal stimulation alone resulted in bradycardia and reduced cardiac output, whereas sympathetic stimulation alone yielded tachycardia and increased cardiac output. Simultaneous activation of the vagal and sympathetic nerves, however, produced an even greater increment in cardiac output that was associated with an intermediate heart rate and a larger stroke volume.

An additional example of synergism in nonreciprocal modes is found in the autonomic control of salivation, where both vagal and sympathetic innervations contribute to salivary secretion. The actions of the autonomic divisions are not completely concordant, however, because vagal inputs promote the volume secretion of aqueous saliva, whereas sympathetic stimulation yields a reduction in volume with an increase in amylase and other enzymes (Emmelin, 1987; Garrett, 1987). In this case, coactivation may be advantageous, as suggested by the fact that gustatory stimuli result in a notable concurrent activation of both the sympathetic and vagal innervations of salivary glands (Matsuo & Yamamoto, 1989).

Summary of functional features. A comprehensive account of the functional features of various modes of autonomic control, exerted over specific organ functions in particular behavioral contexts, is not possible at the present time. Although this is clearly an important issue that warrants vigorous study, the exhaustive detailing of potential functional features of the ANS modes is not the purpose of this article. Rather, a broader perspective on the doctrine of autonomic space and its implications may, more important, serve to guide general approaches to these issues.

Autonomic Space and Its Functional Surface

In the present section, we expand the two-vector model of autonomic space by considering its translation into functional effects on organs. Figure 9 depicts a two-dimensional represen-

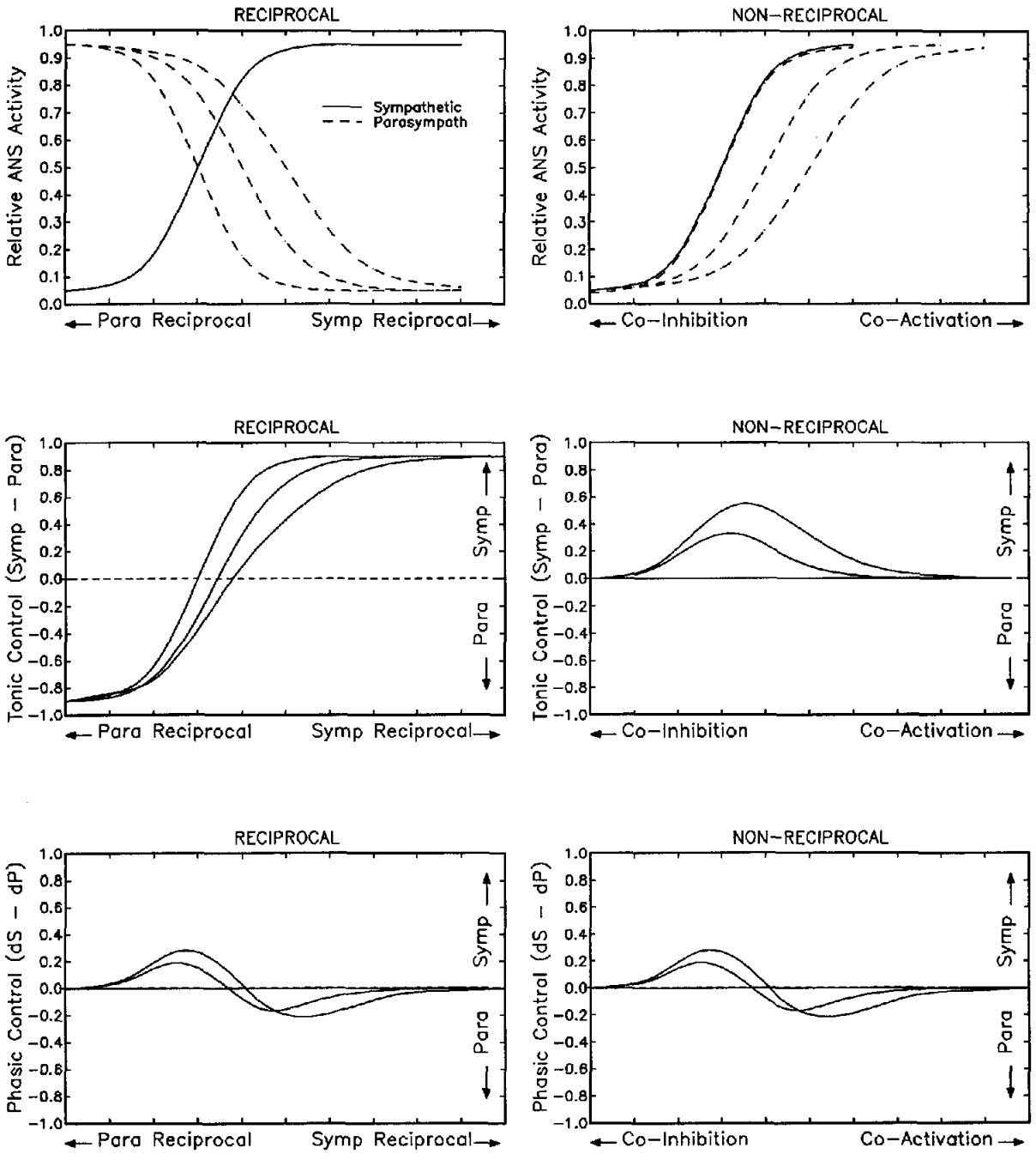

Figure 8. Effects of different input slopes on tonic and phasic autonomic controls. (Top panels illustrate input functions with common thresholds but differing slopes in the parasympathetic division. Middle panels depict the relative autonomic nervous system [ANS] contributions to basal organ state, as derived from the simple difference in the input functions of the two ANS divisions. Bottom panels illustrate relative contributions to reactive change in the target organ, as derived from differences in the first derivatives of the input functions. Para = parasympathetic; Symp = sympathetic; ds = sympathetic change; dp = parasympathetic change.)

tation of autonomic space, bounded by sympathetic and parasympathetic continua. The overlying surface illustrates the functional state of an organ, for each point within autonomic space. This surface was derived from Equation 1, together with the sigmoidal input functions of Figure 5 (coefficients of coupling = ±1 and coefficient of interaction = 0). The input functions are apparent at the edges of the functional surface, where one ANS division varies and the other remains constant. The

autonomic space depicted in Figure 9 exhaustively represents the variations in sympathetic and parasympathetic activation, and the overlying functional surface exhaustively depicts the functional state of the target organ for all locations within autonomic space. This surface is not intended to represent a specific target organ, but rather to illustrate general features of autonomic control that transcend specific coefficients and input functions. As discussed earlier, changes in the parameters varied in Figures 5–8, or interactions among the ANS divisions, could affect the specific shape of this functional surface but would not alter the general relational features of the surface topography.

Modes of tonic control. The functional surface of Figure 9 represents the baseline functional state of an organ, associated with all possible loci within autonomic space. This baseline state may arise from varying degrees of reciprocal or nonreciprocal tonic activities among the ANS divisions. Thus, basal functional states represent a tonic counterpart to phasic responses, relative to the autonomic modes of control. In Figure 9, the diagonal extending from the back to the front represents the continuum of coactivity in tonic controls, the diagonal from the left to the right represents the continuum of reciprocity in tonic control, and the sympathetic and parasympathetic axes depict potential uncoupled contributions to tonic control.

Isofunctional contours. An important feature of the surface depicted in Figure 9 is that a given functional state of the organ is ambiguous with regard to its autonomic origins. This is evident in the isofunctional contour lines projected onto the autonomic plane of this figure. These contours illustrate the multiple loci within autonomic space that yield an equivalent functional output of the target organ. Because identical psychophysiological outcomes may arise from different autonomic

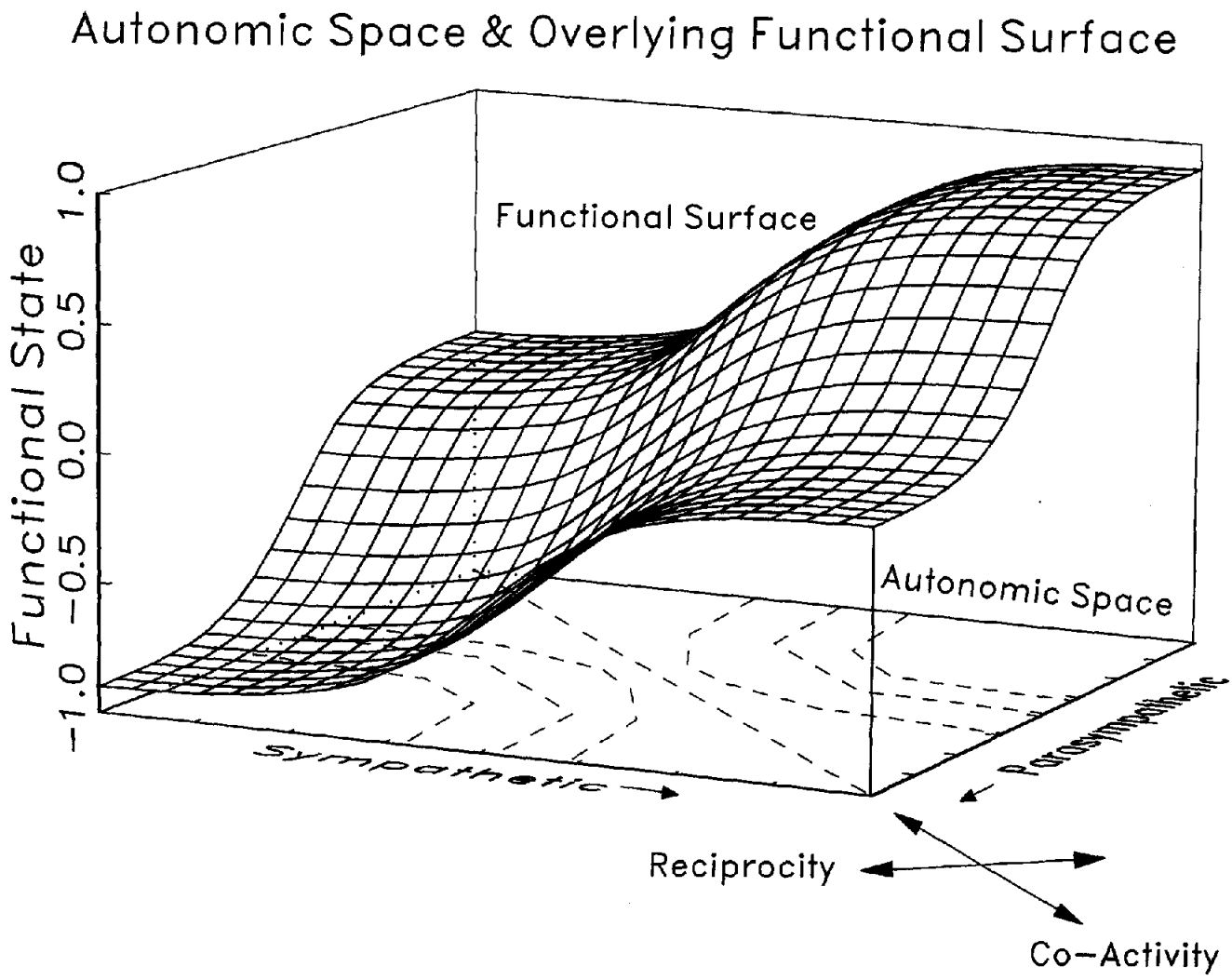

Figure 9. Two-dimensional autonomic space and its associated functional surface. (The functional surface represents the operational state of the target organ, expressed in relative units, as derived from Equation 1 [weighting coefficients = ±1.0]. The axes dimensions are in decile units of functional activation. Dotted lines represent isofunctional contour lines projected on the autonomic space, illustrating loci within autonomic space that have equivalent functional outputs.)

loci, it is apparent that information beyond a simple measure of target state may be necessary to disambiguate autonomic origins.

Phasic reactivity as movements within autonomic space. The functional surface of Figure 9 can be viewed as a static representation of the tonic state of a target organ at different autonomic loci. Phasic movements within autonomic space, however, are translated into a response trajectory across the functional surface. This is illustrated in Figure 10, which maps the input functions of Figure 5 onto the two-dimensional autonomic space and depicts the translation of these inputs into corresponding response functions on the overlying surface. If these inputs were time-varying signals, this surface depiction would provide a representation of phasic response in the spatial domain. Indeed, any change in the location in autonomic space would necessarily translate into a corresponding movement on the functional surface. Given the existence of isofunctional contours, however, this may or may not be expressed as a change in the functional state of the organ. Consequently, time-varying locations in autonomic space provide an unambiguous account of autonomic response, whereas changes in functional state of the target organ do not.

Summary and empirical status of the model. The preceding discussion leads to at least two conclusions. First, a two-dimensional conception of autonomic space provides a much more comprehensive account of autonomic control and consequence than can a single-vector model. Given a two-dimensional autonomic space, the existence of surface features in functional outputs is a logical consequence. Second, the proposed two-dimensional model of autonomic space, expressed in Equation 1, offers a powerful quantitative approach to investigations of psychophysiological relationships. Importantly, the elements of Equation 1, as well as the proposed features of autonomic space and the functional surface, are subject to empirical confirmation. Sigmoidal activation functions, such as those used as inputs to Equation 1, have routinely been demonstrated in neurophysiological and neuropharmacological systems. For any specific organ system, the precise form of the input functions (sympathetic and parasympathetic nerve traffic, s_i and p_j) and the relative functional coupling between these neural activities and the target organ (c_{si} and c_{pj}) could be empirically determined. Direct recordings of autonomic nerve traffic along an activation continuum, would describe s_i and p_j. Concurrent measures of functional organ state under selective blockade, or with selective driving of a given ANS division, would allow specification of the coupling between neural activities and functional effects on organs (c_{si} and c_{pj}). This level of specification would not be necessary, however, for the model to be theoretically and pragmatically useful. The resultant functional impacts of the sympathetic ($S_i = c_{si} \cdot s_i$) and parasympathetic ($P_j = c_{pj} \cdot p_j$) innervations could be determined, along the activation continuum, by measures of functional organ state during selective blockade of the ANS divisions. Alternatively, similar information could be obtained by indirect and noninvasive measures of sympathetic and parasympathetic control in untreated subjects. Relative measures of these terms have already been suggested for some organs (these measures are discussed later).

The interaction term ($c_{sipj} \cdot s_i p_j$) can also be empirically derived by a determination of the functional influences of a given

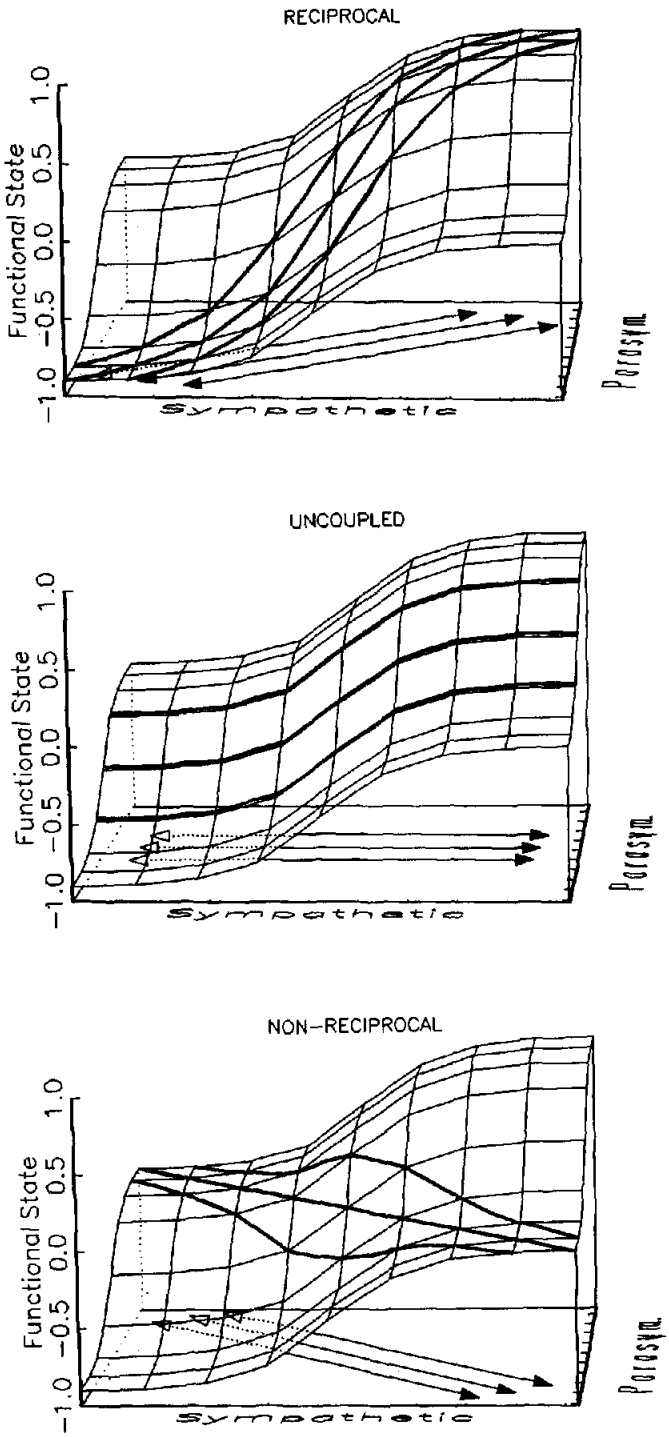

Figure 10. Patterns of movement within autonomic space and their translation onto the functional surface. (Arrows on the autonomic space depict the movement vectors associated with the input functions of Figure 5. The translation of these autonomic vectors to functional changes in the target organ is depicted on the functional surfaces. The functions are those of Figure 5, here plotted on the three-dimensional functional surface of Figure 9. For illustrative purposes, the viewpoint has been changed somewhat from Figure 9. The sympathetic axes are toward the front and the parasympathetic axes are on the right. Parasym. = parasympathetic.)

ANS division under differing levels of activity in the other division. Levy and colleagues (Levy, 1984; Levy & Zieske, 1969), for example, have demonstrated interactions among sympathetic and vagal controls of the heart. Specifically, high levels of vagal activity inhibit sympathetic influences. This yields a negative coefficient of interaction in Equation 1 that would cant the surface of Figure 9 downward at the front axis intersection. Direct concurrent activation of cardiac sympathetic and vagal nerves, by electrical stimulation at different frequencies, was shown to yield a functional surface with precisely this feature[12] (Levy & Zieske, 1969).

The quantitative mapping of the functional surfaces of target organs would allow a specification of the terms of Equation 1 and would permit an evaluation of its predictive accuracy. Equation 1 provides an expedient descriptive model of autonomic relationships, and its utility lies in its ability to approximate the features of functional surfaces. Discrepancies in predicted and observed outcomes would require modifications to this equation, or an alternate formulation, to more closely approximate the veridical features of functional surfaces. Importantly, the theoretical and practical issues raised here, the conceptual advantages of the doctrine of autonomic space, and the conclusions derived therefrom do not hinge on Equation 1. It is used here as a first approximation, to illustrate the general features of autonomic space and its output surface.

Tonic Determinants of Phasic Response: The Laws of Autonomic Constraint

As a representation of the tonic, basal state of an organ, the functional surface of Figure 9 illustrates the variance that may be associated with a psychophysiological "baseline." Indeed, any point on this surface, or even the entire surface, may be mapped into the center (baseline) cells of Table 1–3. Importantly, these tonic variations set fundamental constraints on the phasic modes of control depicted in the remaining cells of these tables. The laws of autonomic constraint capture three fundamental sets of constraints on autonomic response.

The First Law of Autonomic Constraint: The Law of Dynamic Range

The law of dynamic range derives from physiological limits on the extremes of autonomic activity. Because autonomic space is bounded by the dynamic range of the ANS divisions, the extent to which each division can vary is constrained by proximity to its physiological boundaries. The law of dynamic range imposes constraints not only on the modes of autonomic control, but on target-organ manifestations as well.

The effect of baseline state on psychophysiological reactivity has long been recognized (Lacey & Lacey, 1962; Wilder, 1931, 1967). The law of initial values (Wilder, 1931, 1967) asserts that, given limitations in the range of a functional response, variations in basal state can exert directionally specific constraints on reactive changes. Results consistent with the law of initial values are frequently apparent in psychophysiological studies, although they may not be universally observed (Furedy & Scher, 1989; Scher, Furedy, & Heslegrave, 1985; Stern, Ray, & Davis, 1980). The law of initial values is empirically based, being inferred from changes in the functional state of the end organ. It is subsumable by the more general law of dynamic range, however, where it is explicated in terms of the boundaries of the underlying autonomic space. When viewed within the context of the functional surface and the laws of constraint, it becomes apparent that exceptions to the empirical form of the law of initial values are to be expected.

The law of initial values is represented by the (reciprocal) diagonal that extends from the left to the right axes intersections of Figure 9. Changes in baseline state along this diagonal serve to directionally constrain the potential reactivity of the target organ. At the extreme left of this diagonal, reactive decreases in functional state cannot be observed, because the system is already at its dynamic limit. At this point, neither of the nonreciprocal modes (coactivation or coinhibition) are possible. Similarly, a reciprocal parasympathetic pattern is precluded, as are uncoupled modes of sympathetic withdrawal and parasympathetic activation. Only three reactive modes of control remain—reciprocal sympathetic, uncoupled sympathetic activation, and uncoupled parasympathetic withdrawal. Each of these modes yields an increase in the functional state of the organ. Conversely, at the extreme right of this diagonal, reactive increases in functional state are precluded by the upper limit of the dynamic range. At this point in autonomic space, only uncoupled sympathetic withdrawal, uncoupled parasympathetic activation, or a reciprocal parasympathetic mode could be manifest. Each of these modes yields a decrease in the functional state of the organ. This is the essence of the law of initial values, but here is expressed in terms of the boundaries of autonomic space rather than the functional surface (i.e., target-organ baseline).

As is apparent in Figure 9, autonomic locations along the reciprocal diagonal are associated with different functional states of the organ. Consequently, the autonomic constraints along the reciprocal diagonal could be couched either in terms of the boundaries of autonomic space or of basal functional state (i.e., the law of initial values). A fundamental difference, however, arises from the fact that each point in autonomic space is unique, defined by two Cartesian coordinates (sympathetic and parasympathetic). In contrast, the functional surface is indexed by a single dimension (functional state) that may not specify a unique location on that surface. The baseline functional state is invariant along the coactivity diagonal. At the same time, different locations along this diagonal are associated with widely differing constraints on reactive change of the two ANS divisions. At the extreme front of this diagonal, neither reciprocal modes, uncoupled activation modes, nor coactivation are possible. Uncoupled sympathetic withdrawal, uncoupled parasympathetic withdrawal, and coinhibition are the only modes of control that could be manifest. In contrast, at the far end of this continuum, neither reciprocal modes, uncoupled withdrawal modes, nor coinhibition can be evidenced. All modes of control, however, are possible in the center of the diagonal.

[12] Unfortunately, only three stimulation frequencies were used in this study, which precluded identification of the fine features of the functional surface.

The law of initial values is blind to the varying constraints on reactivity, in which the functional state of the organ does not change. Moreover, even with baseline variations that are associated with changes in functional state, predictions of the law of initial values will be straightforward only for reactive changes that lie along a given vector in autonomic space. This is illustrated by an uncoupled sympathetic mode of response, entailing a movement vector lying on the sympathetic axis of Figure 9. As long as movement is restricted to that vector, the law of initial values would apply. For baseline locations approaching the sympathetic maxima, further increases would be constrained by the autonomic boundaries. At the extreme, no further increases would be observed. The functional state of the organ, however, would not be at its maximum at this point. Further increases in functional state, and increases in reactivity, would be associated with movements along the parasympathetic axis. The law of initial values is wedded to a reciprocal model of autonomic control, and loses much of its predictive authority in a two-dimensional autonomic space.

Because the constraints on reactivity (along the coactivity dimension) are not associated with notable variations in the tonic state of the organ, the broader set of autonomic constraints on reactivity cannot be derived from baseline measures. Moreover, the isofunctional contours in Figure 9 reveal multiple loci within autonomic space where varying autonomic constraints are apparent in the absence of differences in the functional state. Thus, although target-organ states may not reliably reveal autonomic constraints, these constraints become intuitively obvious, and empirically documentable, from a two-dimensional model of autonomic space.

The Second Law of Autonomic Constraint: The Law of Reactive Lability

In addition to the limits of dynamic range, constraints on lability are imposed by the direction of movement within autonomic space. As considered earlier, movement along the reciprocal diagonal is associated with notable changes in the functional state of the target organ, whereas similar movements along the coactivity diagonal are accompanied by minimal or no changes in organ state. Thus, variations in target-organ lability, to a given displacement in autonomic space, are apparent even at loci remote from dynamic range boundaries. The law of reactive lability is illustrated in Figure 11, which shows the expected variations in the lability of a target organ with different directional movements (modes of control) in autonomic space.

The surfaces in Figure 11 depict the directional derivatives of the functional surface of Figure 9, which correspond to the instantaneous rate of target-organ change with the indicated movements through autonomic space (the first derivatives along directional movement vectors). What becomes apparent is that the magnitude of target-organ response for a unit movement in autonomic space is dependent not only on the autonomic starting point, but on the specific direction of movement within autonomic space (i.e., the autonomic mode of control). For each mode of control, minimal lability is seen at the four corners, because autonomic influences have reached plateau at those points. For the uncoupled modes, the surface gradients depicting reactive lability peak at the center of the dynamic range of the active division, where activation slopes are maximal (see Figure 5). For these modes, the surface gradients are uniform for variations in baseline activity on the inactive dimension. For reciprocal modes, the peak reactivity lies in the center of autonomic space, at the intersection of the (synergistic) sympathetic and parasympathetic gradients. Finally, for coupled nonreciprocal modes, there is a notable reactivity trough extending along the diagonals. In fact, movements along the coactivity diagonal yield no changes in target-organ state (see also Figure 10). On the basis of the law of reactive lability, a given displacement in autonomic space can yield wide variations in the magnitude of the target-organ response. These variations are related not only to the starting location within autonomic space, but to the direction of movement from that point associated with the specific mode of autonomic control.

In summary, for a unit movement along a given vector within autonomic space, the magnitude of the resulting functional response of the organ will vary depending on both the autonomic starting point and the direction of the movement vector. The law of reactive lability comprises a set of constraints distinct from those of dynamic range. These constraints could seriously obscure the empirical manifestations of the law of initial values.

The Third Law of Autonomic Constraint: The Law of Directional Stability

The law of directional stability constitutes a final set of constraints on target-organ responses, related to the directional coherence of target-organ change with movements through autonomic space. As illustrated in Figure 10, movements along any vector parallel to the reciprocal diagonal yield similar directional responses in the target organ (although they may vary in amplitude). They also yield comparable directional responses throughout the length of the vectors. These features do not hold for movements along the coactivity diagonal. First, movements directly along this diagonal yield no organ response. Second, movements along parallel vectors may result in organ responses, but vectors on opposite sides of this coactivity diagonal yield responses of opposite direction. Finally, the direction of the target-organ response is not uniform, even for movements along vectors parallel to the coactivity diagonal. Rather, the target-organ response changes sign as the vector crosses the reciprocal diagonal (see Figure 10).

The law of directional stability cautions against a rigid interpretation of a specific directional response in a visceral organ, in the absence of knowledge of the origin and trajectory of the movement in autonomic space.

Summary of the Laws of Autonomic Constraint

The laws of autonomic constraint impose fundamental limitations on visceral responses. In some cases, these constraints are intuitive, such as for the law of dynamic range. In other instances, constraints are far from obvious. The law of directional stability, for example, asserts that a specific movement within autonomic space can yield diametrically opposite organ responses, depending on the locus from which the movement begins. The law of reactive lability further qualifies the magni-

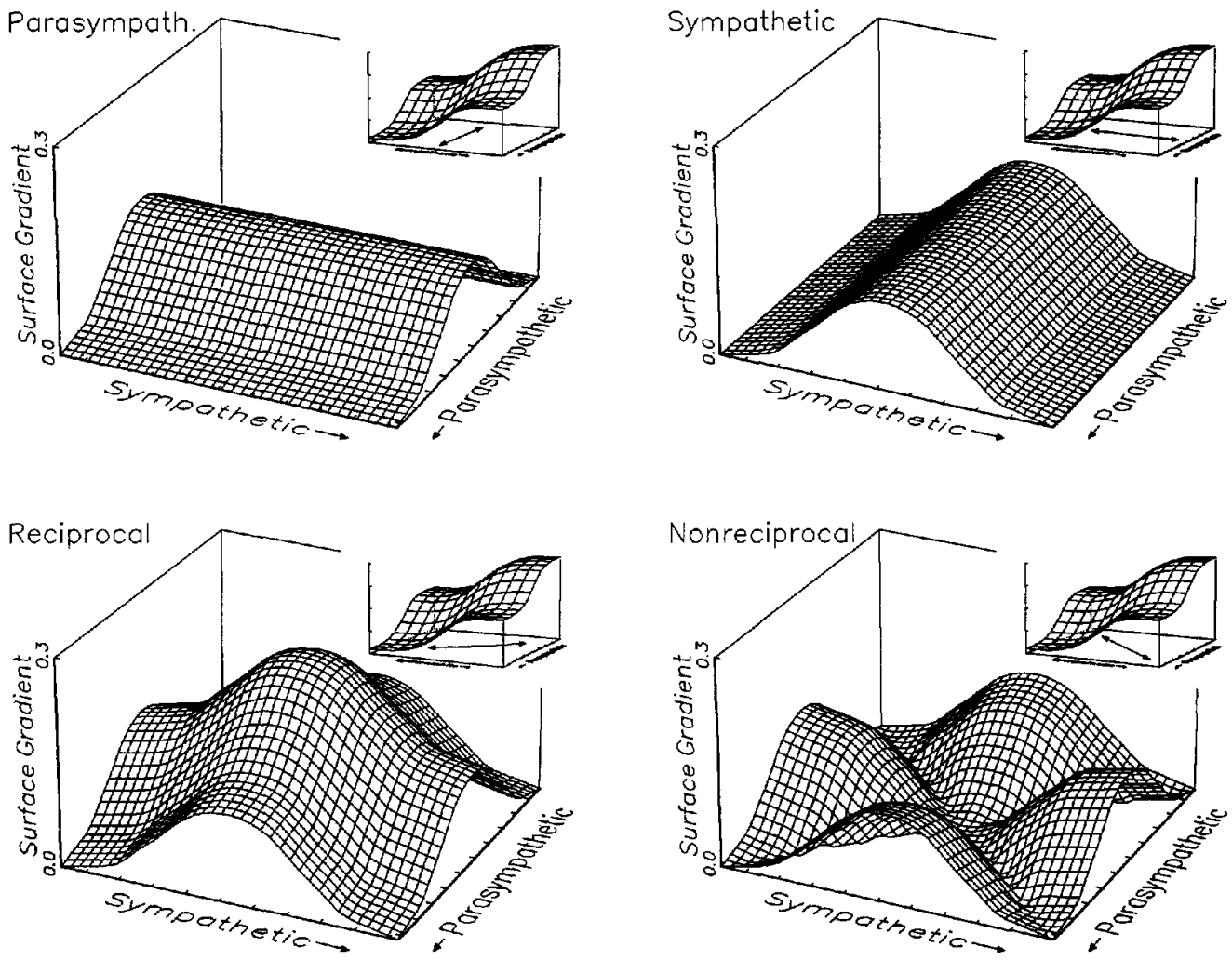

Figure 11. Surface plots of reactive lability as a function of the direction of movement (mode of control) within autonomic space. (Small insets show the functional surface of Figure 9, and the arrows on the autonomic plane depict the direction of movement. The larger plots depict the gradients [sum of the partial derivatives] of the functional surface across autonomic space. Variations in the surface amplitude in these figures illustrate the instantaneous changes in organ state associated with the indicated movement from any point in autonomic space. Parasympath. = parasympathetic.)

tude of this organ response depending on the specific direction of movement from a given point. These nuances of autonomic determinism can contribute substantially to variance in psychophysiological measures. If accounted for, that variance may translate into important experimental effects. If neglected, it appears as error variance. Accounting for this variance, however, may require knowledge of the underlying autonomic space.

Overview and Selected Implications for Psychophysiology

The axiom of autonomic determinism asserts that the functional state of an innervated visceral organ is governed in large part by autonomic influences.[13] An important corollary of this axiom is that the functional state of a target organ is constrained by the dimensions and features of autonomic space. Given an adequate understanding of this autonomic space, the principles and laws that dictate its operations and boundary conditions can be derived.

[13] Although central processes contribute substantially to the control of visceral organs, the activity of many organs is also sensitive to local metabolic and hormonal conditions, and a vast number of regulatory peptides have now been identified within these organs. These local metabolic and hormonal factors may exert direct regulatory influences over visceral activity, and can also modulate postganglionic autonomic transmission (Campbell, 1987; Franco-Cereceda, Bengtsson, & Lundberg, 1987; Needleman et al., 1989; Re & Rovigatti, 1988). Moreover, recent evidence suggests that interneurons within autonomic ganglia may participate in local and relatively isolated autonomic reflexes, even in the absence of central nervous system inputs (Amour, 1987).

In this regard, a single-vector model of an autonomic continuum leads to an overly restrictive conception of autonomic controls that is belied by established empirical findings. Although the single-vector model has been recognized as deficient, a coherent alternative has not previously been advanced. Consequently, demonstrated violations of autonomic reciprocity have generally been addressed within the limited context of specific neural pathways or mechanisms (e.g., the baroreflex), rather than the more general features of autonomic organization or the modes of control. From empirical studies on specific organ functions, one finds clear evidence for multiple modes of phasic variation in autonomic control, including both reciprocal and nonreciprocal adjustments, as well as uncoupled responses limited to a single ANS division. It is also clear that these alternate modes of control may evidence divergent properties and functional consequences. The doctrine of reciprocity, with its single-vector model of ANS organization, is unable to capture this autonomic diversity. The two-dimensional model of the doctrine of autonomic space represents an important and necessary expansion of the doctrine of reciprocity. The doctrine of autonomic space can readily assimilate the veridical features of the earlier doctrine, but provides a more comprehensive representation of psychophysiological relationships. Although the specific details of the present model may undergo revision or renunciation, current understandings of autonomic organization preclude the resurrection of a single-vector concept of autonomic control.

A major obstacle to specifying psychological events as a function of physiological processes $\{\psi = f(\phi)\}$ is the many-to-one mappings that may obtain between autonomic space and organ response on the one hand, and between behavioral variables and autonomic space on the other (Cacioppo & Tassinary, 1990). The present model represents a solution for one of these two major sources of error variance—the loss of fidelity in the translation between autonomic space and organ responses. For instance, each of the isofunctional contour lines of Figure 9 represents a many-to-one mapping between autonomic space and the autonomic response of an end organ. Difficulties in identifying reliable relationships between psychological and physiological events can be compounded by restricting measures to the functional surface rather than to points and movements within autonomic space. Representations of autonomic responses in the terms of autonomic space would therefore constitute a significant advance in psychophysiology.

Differential patterns of response of the two autonomic divisions across organ systems or functional dimensions are now well recognized. A notable example is the orienting response, which is frequently associated with cardiac deceleration (vagal activation), pupillary dilation (vagal withdrawal), and electrodermal responses (sympathetic activation; Beatty, 1986; Lynn, 1966; Siddle, Stephenson, & Spinks, 1983; van der Molen, Boosma, Jennings, & Nieuwboer, 1989). Such patterns of autonomic response across target organs serve as the basis of more refined attempts to derive lawful relationships between behavioral states and autonomic functions (Cacioppo & Tassinary, 1990). A further refinement in the characterization of autonomic response patterns has come from efforts to identify the ANS division that dominates the control of a given organ (Allen & Crowell, 1989; Allen, Obrist, Sherwood, & Crowell, 1987; Johnson & Anderson, 1990; Obrist, 1981; Pollak & Obrist, 1988; Stemmler, Grossman, Schmid, & Foerster, in press). Thus, responses of an organ system can be specified in terms of their beta adrenergic, alpha adrenergic, or muscarinic origins. For a reciprocal mode of control, quantification of the contribution of the dominant ANS division to a response may suffice, because reciprocal changes in the other division are implicit. Although this represents an important advance, it has limitations within a two-dimensional autonomic space, where the activity of the dominant ANS division does not adequately characterize the influence of the other division. Quantification of the dominant ANS influence on dually innervated organs does not uniquely specify a location in autonomic space. Consequently, response measures may remain confounded by the differential impact of the laws of autonomic constraint.

Importantly, these confounds cannot be extracted using conventional response measures of functional state. Lacey (1959) noted that simple change scores can yield misleading results owing to the law of initial values, and he recommended regression (residualized change) procedures to deal with this problem. In the present conception, however, the law of initial values is a special case instantiation of only a single dimension of one of the three major sources of autonomic constraint. In many cases, this broader set of constraints relates to the mode of autonomic control, rather than tonic levels, and may not be differentiated by variations in preevent baseline. Residualized change scores are inept at dealing with this class of autonomic constraints.

What is needed are independent measures of the relative activities of both ANS divisions within an organ or functional dimension. This would permit specification of the organ state, or its reactive change, in the dimensions of autonomic space. Unfortunately, quantification of the specific activities of the ANS divisions can be problematic. For human studies, pharmacological blockade may represent the most viable current approach to documentation, if the design includes evaluation of the contribution of both divisions of the ANS. This approach is exemplified by Stemmler et al. (1990).

Alternate possibilities include more indirect indices of autonomic action that can be derived from the functional state of the organ. A number of noninvasive indices of sympathetic and vagal controls of the heart have been proposed, including T-wave amplitude, pulse-transit time, respiratory sinus arrhythmia, and the amplitude of the Mayer wave in heart period variance (Akselrod et al., 1981; Grossman, Stemmler, & Meinhardt, 1990; Heslegrave & Furedy, 1979; Pagani et al., 1986; Porges, 1986; Porges & Bohrer, 1990; Saul, Rea, Eckberg, Berger, & Cohen, 1990; Shin, Tapp, Reisman, & Natelson, 1989; Weiss et al., 1980). Developments in impedance cardiography also hold promise for selective indices of ANS activities (Kelsey & Guethlein, 1990; Sherwood et al., 1990). It is not our intention to advocate specific indices, however, because debates over these measures continue in the literature, and measures are continually being refined. Rather, it may be more informative to consider the essential criteria for meaningful measures of autonomic space. Clearly, independent indices of activities of both the sympathetic and parasympathetic divisions are required. Moreover, in view of the highly specific patterns of autonomic activity that can be seen across organ systems, measures of the

two autonomic divisions should be derived from the same target organ. Finally, even chronotropic and inotropic influences on the heart, for example, are mediated by separate efferent pathways that may be subject to differential central control (Billman et al., 1989; W. C. Randall & Ardell, 1985). Consequently, indices should optimally be derived from the same functional dimension of the target organ.

This is not to suggest that the outlined model is mute, pending the refinement of indirect measures. On the contrary, the model offers specific predictions that are amenable to empirical test and reorients thought on a number of empirical anomalies. These include empirical inconsistencies with the law of initial values, as discussed earlier. Additionally, Equation 1 parses autonomic control into components that may have immediate utility in psychophysiology. Recent research has revealed not only that there are individual differences in cardiovascular reactivity, but that reactive individuals may fall into at least two subgroups (Kasprowicz, Manuck, Malkoff, & Krantz, 1990; Sherwood, Dolan, & Light, 1990). Some individuals show particularly strong alpha adrenergic responses (e.g., increased total peripheral resistance), whereas others show exaggerated beta adrenergic responses (e.g., increased myocardial contractility). Recognition of these differences can reduce what otherwise would appear as between-subjects (error) variance on psychophysiological measures and outcomes. An understanding of the origins of these individual differences could have significance for both basic and applied questions. In terms of Equation 1, the following differences could arise: (a) centrally, reflected in relative differences in the degree of sympathetic nerve traffic to the heart and vasculature (i.e., in the s_i for each organ); (b) peripherally, reflected by differences in the transfer functions between sympathetic inputs and functional outputs (i.e., in the c_{si} for the organs); or (c) from both sources (i.e., the term $c_{si} \cdot s_i$ for the organs). Alternate origins would have substantial implications for the basic understanding of these individual differences and for their health implications.

An additional example derives from the study of Richardson, Siegel, and Campbell (1988), who found that the transfer of adult or preweanling rats to an unfamiliar testing environment inhibited both the heart rate and behavioral components of the orienting response (OR) to a pulsating tone. Saiers, Richardson, and Campbell (1990) replicated these observations in preweanling rats, and also observed similar inhibitory effects of a prior shock. They stated that "the incongruity of the present experimental findings with both past (e.g., Razran, 1961) and current (e.g., Kahneman, 1973) conceptions of the orienting response cannot be overemphasized" (p. 53). These authors suggested that the experimental conditions may have elicited unidentified competing responses that either inhibit or mask the orienting response (pp. 54–55). Saiers et al. offered no suggestion regarding what these competing responses might be, whereas the present model points to an important qualification to and a potential source of "competing responses" in this line of research.

Saiers et al.'s (1990) conclusion that new or stressful environments could inhibit the OR was based largely on their observation of attenuation of the heart rate deceleration to a novel tone. As we have noted, heart rate is influenced by both sympathetic and parasympathetic inputs, and these influences are antagonistic. If one assumes a reciprocal mode of ANS control throughout, then the inference by Saiers et al. is appropriate. Alternatively, novel or challenging environments—environments in which optimal or adaptive behavioral responses are unclear—may be more likely to evoke or promote coactivation of both the sympathetic and parasympathetic divisions than are familiar environments. Hence, the attenuated cardiac orienting responses reported by Siegel, Sananes, Gaddy & Campbell (1987) and Saiers et al. (1990) could reflect greater conjoint parasympathetic and sympathetic activation (i.e., coactivation), rather than attenuation of the vagal response associated with the OR (Quigley & Berntson, 1990). Examination of the second-by-second heart rate changes in the Saiers et al. study (Figure 6) supports this interpretation. The sympathetic system is known to have a longer latency than vagal influences on the heart. Although vagal influences can be apparent within the beat in which a triggering event occurs, sympathetic manifestations are typically delayed by 2–3 s (Karemaker, 1985; Warner & Russell, 1969). In the Saiers et al. study, the experimental manipulations (shock or context change) did not alter the heart rate response during the first second after the stimulus; rather, experimental curves progressively diverged from the control condition over the subsequent 2 to 3 s. This is consistent with a concurrent (longer latency) sympathetic activation that could obscure the vagal response. Autonomic coactivation is also consistent with the absence of baseline increases in heart rate in the Saiers et al. study, even after repeated shocks. If research bears out this interpretation, then measures of the orienting response derived from organs that are not dually and antagonistically innervated (e.g., eccrine glands in humans) may be valuable under these conditions. Alternatively, independent estimates of sympathetic and vagal control of the heart could be used to address this issue.

The two-dimensional concept of autonomic space also raises an important issue as to the fundamental nature of psychophysiological adjustments in orienting and other behavioral contexts. At least three possibilities arise. In some instances, psychophysiological responses may be best characterized by a directional vector through autonomic space. These vector-specific (or mode-specific) adjustments may evidence considerable variance in the functional response of the organ, depending on the basal starting point in autonomic space (see Figures 10–11). They would, however, show commonalities in the direction and magnitude of the movement through that space (i.e., in the autonomic mode of control). In other cases, the specific directional vector may be less germane than the ultimate end point of movement within autonomic space. For these locus-targeted adjustments, both the optimal mode of control and the related functional changes in the organ may vary widely depending on the starting point within autonomic space. The common feature of these responses would be the end locus of the autonomic trajectory. Finally, a psychophysiological response may have as an end point a specific functional state of the organ. In this case, the autonomic mode or response vector could vary with the autonomic starting point, and the autonomic end point could vary along any isofunctional contour. It is only for these output-targeted responses that the common feature could be discerned from the functional end point of a visceral response. For present considerations, it is of relevance that output-targeted adjustments are probably the least represented in the autonomic con-

trol of the viscera, because they necessitate an explicit physiological monitoring and feedback regulation of the functional state of the organ. Although this may be the case for blood pressure (by means of baroreceptors), it does not appear to hold for many other organ systems. Consequently, it becomes increasingly important to specify psychophysiological relationships within the dimensions of autonomic space.

In summary, the present model has taken as a starting point questions about autonomic organization and control posed early in this century by Cannon (1930), Gaskell (1900), and Langley (1921). Cannon (1930) raised the question "Why this double innervation?" (p. 1109). Cannon's answer was that the sympathetic nervous system influenced visceral activity generally, and the parasympathetic nervous system modulated the activity of individual viscera, up or down, from the level established by sympathetic input. Subsequent research revealed that the sympathetic nervous system could also have rather specific effects on autonomic organs, although its peripheral anatomy enables more diffuse actions than those of the parasympathetic system (Johnson & Anderson, 1990; Wallin & Fagius, 1988).

Although dual innervation may allow both general and specific inputs to the viscera through the actions of the two autonomic branches, its significance may not be limited to this feature. Importantly, innervation by a single ANS division enables only three modes of action: increases, decreases, or maintenance of the existing activity. In contrast, dual innervation can appreciably expand the modes of autonomic control. The expansion of the modes of control associated with a two-dimensional autonomic space and the differential functional properties of these modes associated with the functional output surface provide a complementary answer to the question of the significance of dual innervation. Dual innervation of the viscera affords greater flexibility and precision in adjusting internal states to meet the challenges of anticipated or realized environmental challenges, not only by the patterning of autonomic actions across organs, but by the patterning of these actions within organ systems.

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