

**SENSORY CONFLICT IN MOTION SICKNESS:
AN OBSERVER THEORY APPROACH**

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SUMMARY

"Motion sickness" is the general term describing a group of common nausea syndromes originally attributed to motion-induced cerebral ischemia, stimulation of abdominal organ afferent, or overstimulation of the vestibular organs of the inner ear. Sea-, car-, and airsickness are the most commonly experienced examples. However, the discovery of other variants such as Cinema-, flight simulator-, spectacle-, and space sickness in which the physical motion of the head and body is normal or absent has led to a succession of "sensory conflict" theories which offer a more comprehensive etiologic perspective. Implicit in the conflict theory is the hypothesis that neural and/or humoral signals originate in regions of the brain subserving spatial orientation, and that these signals somehow traverse to other centers mediating sickness symptoms. Unfortunately, our present understanding of the neurophysiological basis of motion sickness is far from complete. No sensory conflict neuron or process has yet been physiologically identified. To what extent can the existing theory be reconciled with current knowledge of the physiology and pharmacology of nausea and vomiting? This paper reviews the stimuli which cause sickness, synthesizes a contemporary Observer Theory view of the Sensory Conflict hypothesis, and presents a revised model for the dynamic coupling between the putative conflict signals and nausea magnitude estimates. The use of quantitative models for sensory conflict offers a possible new approach to improving the design of visual and motion systems for flight simulators and other "virtual environment" display systems.

**STIMULI CAUSING MOTION SICKNESS: EXOGENOUS MOTION
AND "SENSORY REARRANGEMENT"**

Motion sickness is a syndrome characterized in humans by signs such as vomiting and retching, pallor, cold sweating, yawning, belching, flatulence, decreased gastric tonus; and by symptoms such as stomach discomfort, nausea, headache, feeling of warmth, and drowsiness. It has a significant incidence in civil and military transportation, and is a common consequence of vestibular disease. Virtually everyone is susceptible to some degree, provided the stimulus is appropriate and lasts long enough. Many other animal species also exhibit susceptibility.

A century ago, physicians commonly attributed motion sickness to acceleration-induced cerebral ischemia, or to mechanical stimulation of abdominal afferents (Reason and Brand, 1975). These theories were largely discounted when the role of the inner ear vestibular organs in body movement control was appreciated, and when James (1882) noted that individuals who lack

vestibular function were apparently immune. As a result, it was commonly thought that motion sickness results simply from vestibular overstimulation.

Certainly the most common physical stimulus for motion sickness is exogenous (i.e., non-volitional) motion, particularly at low frequencies. However, when individuals are able to (motorically) anticipate incoming sensory cues, motion stimuli are relatively benign. For example, drivers of cars and pilots of aircraft are usually not susceptible to motion sickness, even though they experience the same motion as their passengers. In daily life, we all run, jump, and dance. Such endogenous (volitional) motions never make us sick. Thus, it is now recognized that motion sickness cannot not result simply from vestibular overstimulation.

Many forms of motion sickness consistently occur when people are exposed to conditions of "sensory rearrangement"—when the rules which define the normal relationship between body movements and the resulting neural inflow to the central nervous system have been systematically changed (Reason, 1978). Whenever the central nervous system receives sensory information concerning the orientation and movement of the body which is unexpected or unfamiliar in the context of motor intentions and previous sensory-motor experience—and this condition occurs for long enough—motion sickness typically results. Thus, sickness occurs when a person moves about while wearing a new pair of glasses (spectacle sickness) or when a subject in laboratory experiments walks around wearing goggles which cause left-right or up-down reverse vision. Similarly, sickness is also encountered in flight simulators equipped with compelling visual displays (simulator sickness) and in wide-screen movie theaters (Cinerama sickness), since visual cues to motion are not matched by the usual pattern of vestibular and proprioceptive cues to body acceleration. Space sickness among astronauts is believed to result in part because the sensory cues provided by the inner ear otolith organs in weightlessness do not correspond to those experienced on Earth. Astronauts also commonly experience visual spatial reorientation episodes which are provocative. When one floats in an inverted position in the spacecraft, a true ceiling can seem somehow like a floor. Visual cues to static orientation can be ambiguous, often because of symmetries inherent in the visual scene. Cognitive reinterpretation of ambiguous visual orientation cues results in a sudden change in perceived orientation, which astronauts have found can be nauseogenic (Oman, 1988). These various forms of sickness illustrate that the actual stimulus for sickness cannot always be adequately quantified simply by quantifying the physical stimulus. The trigger for sickness is a signal inside the central nervous system (CNS) which also depends on the subject's previous sensory motor experience.

PHYSIOLOGICAL BASIS OF MOTION SICKNESS

Despite the ubiquity of motion sickness in modern society and significant research (well reviewed, collectively, by Tyler and Bard, 1949; Chinn and Smith, 1955; Money, 1970; Reason and Brand, 1975; Graybiel, 1975; and Miller, 1988), the physiological mechanisms underlying motion sickness remain poorly defined. Classic studies of canine susceptibility to swing sickness (Wang and Chinn, 1956; Bard et al. 1947) indicated that the cerebellar nodulus and uvula—portions of the central vestibular system—are required for susceptibility. Many neurons in the central vestibular system which subserve postural and oculomotor control are now known to respond to a variety of spatial orientation cues, as reviewed by Henn et al. (1980). A brain stem vomiting center was identified by Wang and Borison (1950) and Wang and Chinn (1954), which initiates emesis in dogs in response to various stimuli, including motion. Nausea sensation in humans is

commonly assumed to be associated with activity in the vomiting center (Money, 1970). The integrity of an adjacent chemoreceptive trigger zone (CTZ), localized in area postrema on the floor of the fourth ventricle, was also believed to be required for motion sickness (Wang and Chinn, 1954; Brizzee and Neal, 1954). It was generally assumed that signals originating somewhere in the central vestibular system somehow traverse to the chemoreceptive trigger zone, which in turn activates the vomiting center. Wang and Chinn (1953) and Crampton and Daunton (1983) have found evidence suggestive of a possible humoral agent in cerebrospinal fluid (CSF) transported between the third and fourth ventricle. However, an emetic linkage via CSF transport does not easily account for the very short latency vomiting which is occasionally observed experimentally. The vomiting center receives convergent inputs from a variety of other central and peripheral sources, including the diencephalon and gastrointestinal tract. The possibility of multiple emetic pathways and significant interspecies differences in mechanism must be considered. Also, more recent experiments have led workers to question the notion that medullary emetic centers are discretely localizable. Attempts to verify the earlier findings by demonstrating motion sickness immunity in area postrema ablated and cerebellar nodulectomized and uvulectomized animals have not been successful (Miller and Wilson, 1983a,b; Borison and Borison, 1986; Wilpizeski, Lowry, and Goldman, 1986).

The act of emesis itself involves the somatic musculature. However, many other signs of motion sickness as listed earlier and associated with vasomotor, gastric, and respiratory function suggest that areas in the reticular core of the brain stem and limbic system, which are associated with autonomic regulation are also coactivated. The limbic system and associated hypothalamus-pituitary-adrenal cortex (H-P-A) neuroendocrine outflow pathway is involved. Increases in circulating levels of such stress-related hormones as epinephrine and norepinephrine, ADH, ACTH, cortisol, growth hormone, and prolactin have been found during sickness (e.g., Eversmann et al., 1978; La Rochelle et al., 1982). Whether the limbic system and H-P-A axis simply mediate a generalized stress response, or are also involved in motion-sickness adaptation by somehow triggering stimulus-specific sensory/motor learning is unknown. The question of the site of action of antimotion-sickness drugs is also far from resolved. There is no substantial evidence that effective drugs act on the vestibular end organs. Their primary effect is probably simply to raise the threshold for sickness. Antimotion-sickness drugs could be acting on brain-stem emetic centers. Alternatively, they may shift the fundamental adrenergic-cholinergic balance in the limbic system (e.g., Janowsky et al., 1984).

DEVELOPMENT OF THE SENSORY CONFLICT THEORY

Although our physiological understanding of motion sickness is thus incomplete, analyses of the wide variety of physical stimuli which produce the same syndrome of symptoms and signs and the dynamic pattern of these responses have nonetheless given us some insight concerning possible etiologic mechanisms. Recognition that motion sickness could occur not only under exogenous motion stimulation, but also as a result of sensory rearrangement, as defined above, has led to the development of a succession of sensory conflict theories for the disorder.

The sensory conflict hypothesis for motion sickness was originally proposed by Claremont (1931), and has since been revised and extended by several authors. Implicit is the idea that a neural or humoral sensory conflict-related signal originates somewhere in the brain and somehow couples to brain centers mediating sickness symptoms. In early statements of the theory, conflict

signals were assumed to somehow result from a direct comparison of signals provided by different sensory modalities (e.g., "the signals from the eye and ear do not agree"; canal-otolith, and visual-inertial conflicts). However, Reason (1978) emphasized that a direct intermodality comparison of afferent signals is simply not appropriate, because signals from the various sense organs have different "normal" behavior (in terms of dynamic response and coding type), and whether they can be said to conflict or not actually depends upon context and previous sensory-motor experience. Hence the conflict is more likely between actual and anticipated sensory signals. Extrapolating from earlier interrelated work by von Holst and Held, Reason argued that the brain probably evaluates incoming sensory signals for consistency using an "efference copy" based scheme. As motor actions are commanded, the brain is postulated to continuously predict the corresponding sensory inputs, based on a neural store (memory bank or dictionary) of paired sensory and motor memory traces learned from previous experience interacting with the physical environment. Sensory conflict signals result from a continuing comparison between actual sensory input and this retrieved sensory memory trace. Any situation which changed the rules relating motor outflow to sensory return (sensory rearrangement, a term coined by Held) would therefore be expected to produce prolonged sensory conflict and result in motion sickness. Adaptation to sensory rearrangement was hypothesized to involve updating of the neural store with new sensory and motor memory-trace pairs. Reason proposed a formal Neural Mismatch model which incorporated these concepts. However, the model was only qualitative, making simulation and quantitative prediction beyond its reach. Key structural elements such as the Neural Store and memory traces were only intuitively defined. The model did not really address the question of why the CNS should have to compute a sensory conflict signal, other than to make one sick. Reason's model dealt with sensory conflict only and did not incorporate emetic brain output pathway elements which must be present to account for the latency and order of appearance of specific symptoms.

A MATHEMATICAL DEFINITION OF SENSORY CONFLICT

In order to address these difficulties, the author proposed a model for motion sickness (Oman, 1978; 1982) in a mathematical form, shown in block diagram format in figures 1-3. This new model contained a statement of the conflict theory which was congruent with Reason's view, and also the emetic linkage output pathway dynamics missing from Reason's model. The conflict theory portion of the model was formally developed by application of Observer Theory concepts from control engineering to the neural information processing task faced by the CNS in actively controlling body movement using a limited set of noisy sensory signals. The conflict model formulation can be considered an extension of the optimal control model in the field of Manual Control (Baron and Kleinman, 1968) and in the field of spatial orientation research, an extension of Kalman filter models (Young, 1970; Borah, Young, and Curry, 1978). The latter have been used to predict orientation perception in passive observers with some success. In these previous models, however, sensory conflict was not defined in the same sense as that used by Reason and me.

In the guidance, control, and navigation systems, engineers are often faced with the problem of controlling a vehicle's state vector (e.g., angular and linear position, velocity, and acceleration) when information from sensors which measure these states is noisy or is even not directly measured at all. To deal with this problem, engineers now routinely incorporate into the control system design a computational element known as an "observer," whose function is to provide an optimal estimate of the actual states of the vehicle (or other system) being controlled. Control loops are closed using the state estimate provided by the observer in lieu of direct feedback sensor

measurements in the traditional way. Analytical techniques have been developed (Kalman, 1960; Wonham, 1968) for mathematically linear systems which allow designers to choose observer and control-loop parameters so that the observer state estimate is always converging with reality, and which optimizes the closed-loop performance of the entire system. In control engineering parlance, such systems are formally called "output feedback" optimal-control systems.

Of particular importance in the present context is the way in which the observer state estimate is calculated in these engineering systems. The observer contains an internal dynamic model of the controlled system and of the sensors being used. The observer element uses these models to calculate what the available feedback sensor measurements should be, assuming the vehicle state estimate of the observer is correct. The difference between the expected and the actual feedback measurements is then computed, because it is an indirect measure of the error in the observer state estimate. The difference signals play an important role in the observer. They are used to continuously steer the observer vehicle state estimate toward reality, using a method described in more detail below.

There is a direct analogy between the "expected" feedback sensor measurement and "internal dynamic model" concepts in control engineering Observer Theory, and the "efference copy" and "neural store" concepts which have emerged in physiology and psychology. From the perspective of control engineering, the "orientation" brain must "know" the natural behavior of the body, i.e., have an internal model of the dynamics of the body, and maintain a continuous estimate of the spatial orientation of all of its parts. Incoming sensory inputs would be evaluated by subtraction of an efference copy signal, and the resulting sensory conflict signal used to maintain a correct spatial orientation estimate.

The mathematical model for sensory conflict and movement control in the orientation brain is shown schematically in figure 2, and mathematically in figure 3. (Arrows in the diagrams represent vector quantities. For example, the actual state of the body might consist of the angular and/or linear displacement of all the parts of the body, and higher derivatives.) The model function can be summarized as follows: the internal CNS models are represented by differential equations describing body and sense organ dynamics. Based on knowledge of current muscle commands, the internal model equations derive an estimated orientation state vector, which is used to determine new muscle commands based on control strategy rules. Simultaneously, the estimated orientation state is used by the CNS sense organ model to compute an efference copy"vector. If the internal models are correct, and there are no exogenous motion disturbances, the efference copy vector nearly cancels polysensory afference. If not, the difference—the sensory-conflict vector—is used to steer the model predictions toward reality, to trigger corrective muscle commands, and to indicate a need for reidentification of the internal model differential equations and steering factors.

How a sensory conflict vector might be used to correct internal model predictions is shown explicitly in figure 3. Here, the physical body and sense organ dynamic characteristics are expressed in linearized state variable notation as a set of matrix equations of the form:

$$1) \quad \dot{\mathbf{x}} = \mathbf{A} \mathbf{x} + \mathbf{B} \mathbf{u}$$

$$2) \quad \mathbf{a} = \mathbf{S} \mathbf{x} + \mathbf{n}_s$$

$$3) \quad \mathbf{u} = \mathbf{m} + \mathbf{n}_c$$

The coefficients of the state differential equations for body and sense organ characteristics are thus embodied in the matrices A, B, and S. These equations are shown graphically in the upper half of figure 3. The internal CNS dynamic model is represented by an analogous state differential equation using hatted variables in the bottom half of the figure. This state estimator (the observer) with its matrices \hat{A} , \hat{B} , and \hat{S} corresponds to the Neural Store of Reason's (1978) model. The sensory conflict vector \mathbf{c} is obtained by subtracting actual sensory input \mathbf{a} from expected sensory input $\hat{S} \hat{\mathbf{x}}$. Sensory conflict normally originates only from exogenous motion cue inputs \mathbf{n}_e , and noise \mathbf{n}_a . The conflict vector is multiplied by a matrix K calculated using an optimization technique defined by Kalman and Bucy (1961) which lightly weights noisy modalities. When the result is added to the derivative of the estimated state, the estimated state vector is driven toward the actual state, and the component of the conflict vector magnitude due to noise is reduced. However, when exogenous motion cues inputs \mathbf{n}_e are present, or under conditions of sensory rearrangement, such that matrices A, B, and/or S are changed, and no longer correspond to the matrices of the internal model, actual sensory input \mathbf{a} will be large, and will not be cancelled by the efference copy vector. Sensory-motor learning takes place via reidentification by analysis of the new relationship between muscle commands and polysensory afference (reidentification of \hat{A} , \hat{B} , and \hat{S}), and internal model updating. Additional details are available in Oman (1982).

This model for sensory conflict overcomes many of the limitations of Reason's Mismatch approach outlined earlier. The Neural Store is replaced by an internal mathematical dynamic model, so that efference copy and sensory conflict signals are quantitatively defined. Increased sensory conflict is noted to result not only from sensory rearrangement, but also from exogenous disturbance forces acting on the body. The role of active movement in creating motion sickness in some circumstances, and in alleviating them in others is clarified.

A REVISED MODEL FOR SYMPTOM DYNAMICS

The author's 1982 motion-sickness model included dynamic elements in the path between sensory conflict and overall discomfort and nausea in motion sickness. This model has since been altered in some important details; the current version is shown in figures 4 and 5.

The input to the model is a sensory conflict vector. Because of the bandwidth requirements imposed on signals involved in orientation perception and posture control, it seems likely that the components of the conflict vector are neurally coded. In the nausea model, the various conflict vector components (describing the visual, vestibular, proprioceptive modalities) are rectified, and then weighted and added together. Rectification is required because sensory conflict components, as Reason and I have defined them, are signed quantities. The information carried in the sign is

presumably useful in correcting orientation perception and posture control errors. However, stimuli which presumably produce sensory conflicts of opposite signs produce the same type and intensity of nausea, as far as we can tell. Hence rectification is appropriate here. In weighting the various conflict components, vestibular conflicts (i.e., semicircular canal and otolith modalities) must be weighted relatively heavily in the model, since people without vestibular function seem to be functionally immune. Visual motion inputs (as in Cinerama and simulator sickness) may thus exert their major sick-making effects indirectly: Visual inputs would create illusory movement and thus expected vestibular signals, so sensory conflicts would be produced in the heavily weighted vestibular modality. However, to be consistent with our experimental evidence that visual and proprioceptive conflicts under prism goggle sensory rearrangement (Oman, 1987; Eagon, 1988) eventually become provocative while writing or when building can structures on a desktop, absent concomitant head motion or vestibular conflict, visual and proprioceptive modality model weighting factors are not zero.

As shown in figures 4 and 5, rectified, weighted conflict signals then pass along two parallel, interacting dynamic pathways (fast and slow paths) before reaching a threshold/power law element and resulting in a nausea-magnitude estimate model output. Magnitude estimates are assumed to be governed by a power law relationship (Stevens, 1957) with an exponent of about 2. Susceptibility to motion sickness is determined in the model not only by the amount of sensory conflict produced, but also by the fast and slow pathway gains, time constants, and the nausea threshold. The transfer of a generalized adaptation from one different nauseogenic stimulus situation to another might result from adaptation in these output pathways.

The parallel arrangement of the fast and slow pathways and their relationship to the threshold element requires some explanation. In the past, many authors have therefore assumed that sensory conflict coupling to symptom pathways is a temporary (facultative) phenomenon. However, I have argued (Oman, 1982) that some level of subliminal sensory conflict coupling must be present in normal daily life because conflict signals seem to be continuously functionally averaged at subliminal levels, probably by the same mechanisms or processes which determine the intrinsic dynamics (latency, avalanching tendency, recovery time, etc.) of symptoms and signs when conflict exceeds normal levels. The output pathways probably consist functionally of dynamic elements followed by a threshold, and not the reverse, as would be the case if the linkage were temporary.

In the model, information flows along two paths prior to reaching the threshold. Both paths incorporate dynamic blocks which act to continuously accumulate (i.e., low pass filter or "leaky" integrate) the weighted, rectified conflict signal. One block (the fast path) has a relatively short characteristic response time, and the other (the slow path) has a relatively long one. (In the model simulations shown in the insets of figure 5, the fast path is a second low-pass filter with 1-min time constants; the slow path is a similar filter with 10-min time constants. Second-order or higher block dynamics are required so that model predictions show characteristic overshoot when the conflict stimulus is turned off.) The slow path block normally has a higher gain (by a factor of about 5) than the fast path, and at the beginning of stimulation is functionally the more important element. Slow path output acts together with other classes of fast-acting nauseogenic inputs (e.g., vagal afference from the gut, or emetic drug stimulation) to bias the threshold of nausea response. In the present model, the slow path block output also acts as a multiplicative factor on fast path response gain. When prolonged stimulation has raised the slow path output, the response of the fast path becomes much larger, as shown in the figure 5 simulation. Thus, the revised model mimics the much magnified response to incremental stimulation which we observe experimentally

in long-duration sickness. (In the 1982 version of this model, increased response sensitivity at high symptom levels was a consequence only of the time-invariant, power-law, magnitude-estimation characteristic at the output of the model. This earlier model failed to adequately simulate the rapid rise and fall of sensation at high sickness levels).

Physically, the fast and slow dynamic elements in the model could correspond to physiological mechanisms responsible for conveying conflict-related information from the orientation brain to the emetic brain. Since conflict signals must be rectified, and the dynamics of the fast and slow pathways are qualitatively those of a leaky integration process, it is tempting to think that at least the slow dynamics might involve a humoral mediator and/or a second messenger agent. Alternatively, the dynamics might reflect the action of some diffusion or active transport process, or instead be the intrinsic dynamics exhibited by a network of vomiting center neurons to direct neural or humoral conflict signal stimulation.

CONCLUSIONS

Over the past decade, the sensory conflict theory for motion sickness has become the generally accepted explanation for motion sickness, because it provides a comprehensive etiologic perspective of the disorder across the variety of its known forms. Motion sickness is now defined as a syndrome of symptoms and signs occurring under conditions of real or apparent motion creating sensory conflict. Symptoms and signs (e.g., nausea, vomiting) are not pathognomonic of the motion sickness syndrome unless conditions of sensory conflict are also judged to be present, since the same symptoms and signs also occur in many other nausea related conditions. Thus, the definition of sensory conflict is implicit in any formal definition of the syndrome. It is essential to define as precisely as possible what is meant by the term sensory conflict. Mathematical models for sensory conflict have sharpened our definitions considerably.

The models presented here capture many of the known characteristics of motion sickness in semi-quantitative fashion. However, they have certain limitations, e.g., the sensory conflict model posits a mathematically linear observer. Although recent experimental data are consistent with the notion that the CNS functions as an observer, there is some evidence that sensory conflict is evaluated in nonlinear ways. Also, the model can only mimic, but not predict, the adaptation process. The model for symptom dynamics does not (yet) incorporate elements which account for observed autogenous waves of nausea at high symptom levels, nor the "dumping" of the fast and slow process pathways when emesis occurs. Models for response pathways mediating other physiologic responses such as pallor, skin temperature, and EGG changes have not yet been attempted.

Do the sensory conflict pathways postulated in the models really exist? Unfortunately, to date no such sensory conflict neuron has been found which satisfies the functional criteria imposed by the current theory. The strongest evidence for the existence of a neural or humoral entity which codes sensory conflict is the ability of the conflict theory to account for and predict the many different known forms of motion sickness. One possibility is that conflict pathways or processes do not exist, but in view of the strong circumstantial evidence, this seems unlikely. There are several alternative explanations:

1. Until recently, there has been surprisingly little discussion of exactly what one meant by the term sensory conflict, so that a physiologist would be able to recognize a "conflict" neuron experimentally. The availability of mathematical models has now changed this situation, and provided a formal definition. However, such models must be presented in ways which physiologists can understand.

2. So far, relatively few animal experiments have been conducted with the specific objective of identifying a conflict neuron. The search has been largely limited to the vestibulo-ocular pathways in the brain stem and cerebellum. Recent evidence suggests that cortex and limbic system are major sites for spatial orientation information processing. Real progress may be limited until orientation research focuses on these areas.

3. Although sensory conflict signals are arguably neurally coded, the conflict linkage mechanisms may have a significant humoral component. If so, a search for the emetic link using classical anatomical or microelectrode techniques will be unsuccessful.

Mathematical characterization of the dynamic characteristics of symptom pathways is a difficult black-box, system-identification problem. The model described above was based only on the character of responses to exogenous motion and sensory rearrangements. Much can potentially be learned from the study of dynamic responses to other classes of emetic inputs, and from studying the influence of behavioral (e.g., biofeedback) and pharmacological therapies.

In other areas of systems physiology and psychology, mathematical models have proven their value by providing a conceptual framework for understanding, for interpreting and interrelating the results of previous experiments, and for planning new ones. Mathematical models can become a useful new tool in motion-sickness research. In the fields of flight simulation and virtual environment displays, simulator sickness is an important practical problem. Models for sensory conflict and motion sickness may become useful tools in the design of these systems.

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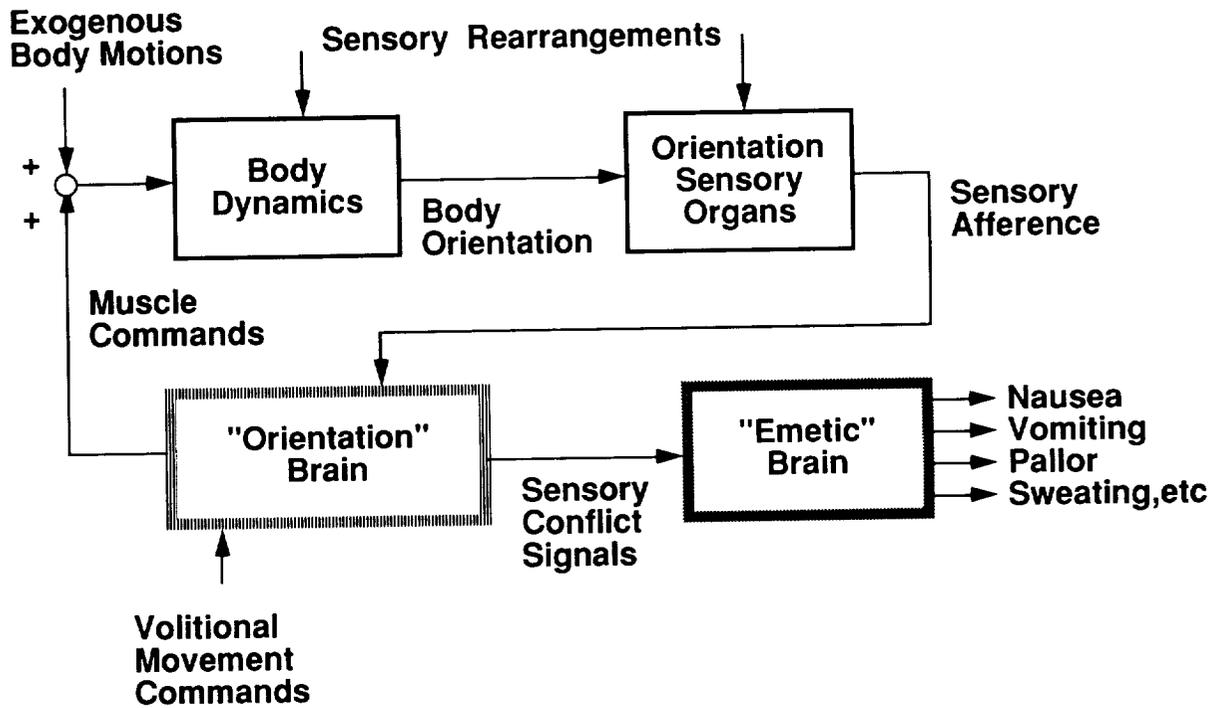


Figure 1.— Schematic diagram of model for movement control, sensory conflict, and motion-sickness symptom dynamics (Oman, 1982). Under conditions of sensory rearrangement, the rules which relate muscle commands to sensory afference are systematically changed. Sensory conflict signals used spatial orientation perception and movement control in the orientation brain couple to the emetic brain.

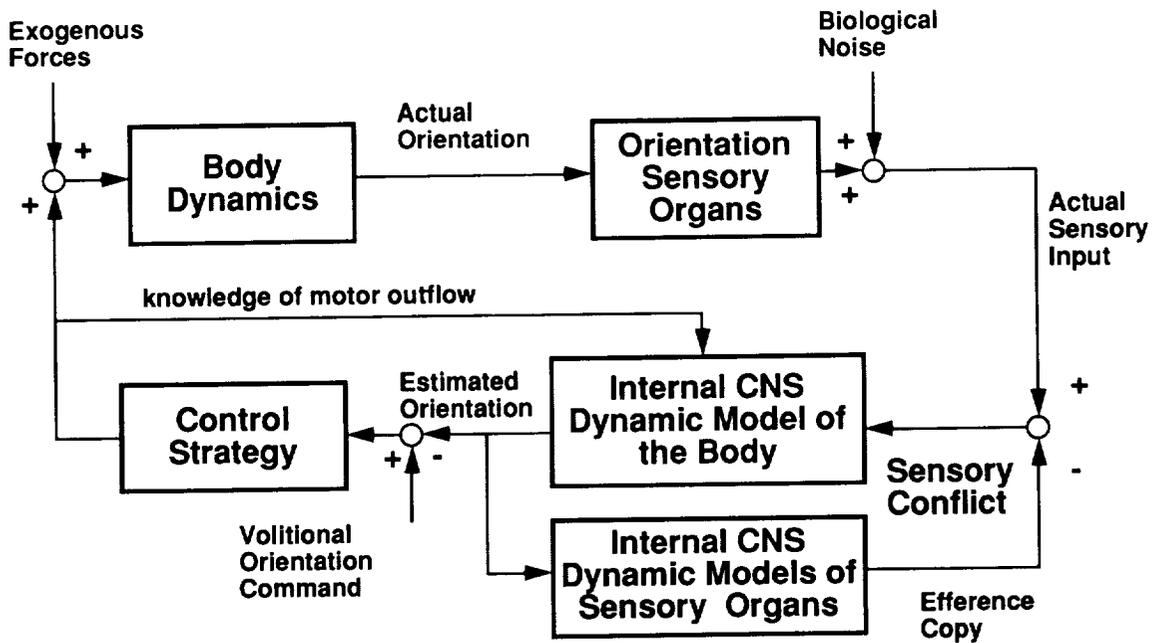


Figure 2.— Observer theory model for movement control (Oman, 1982).

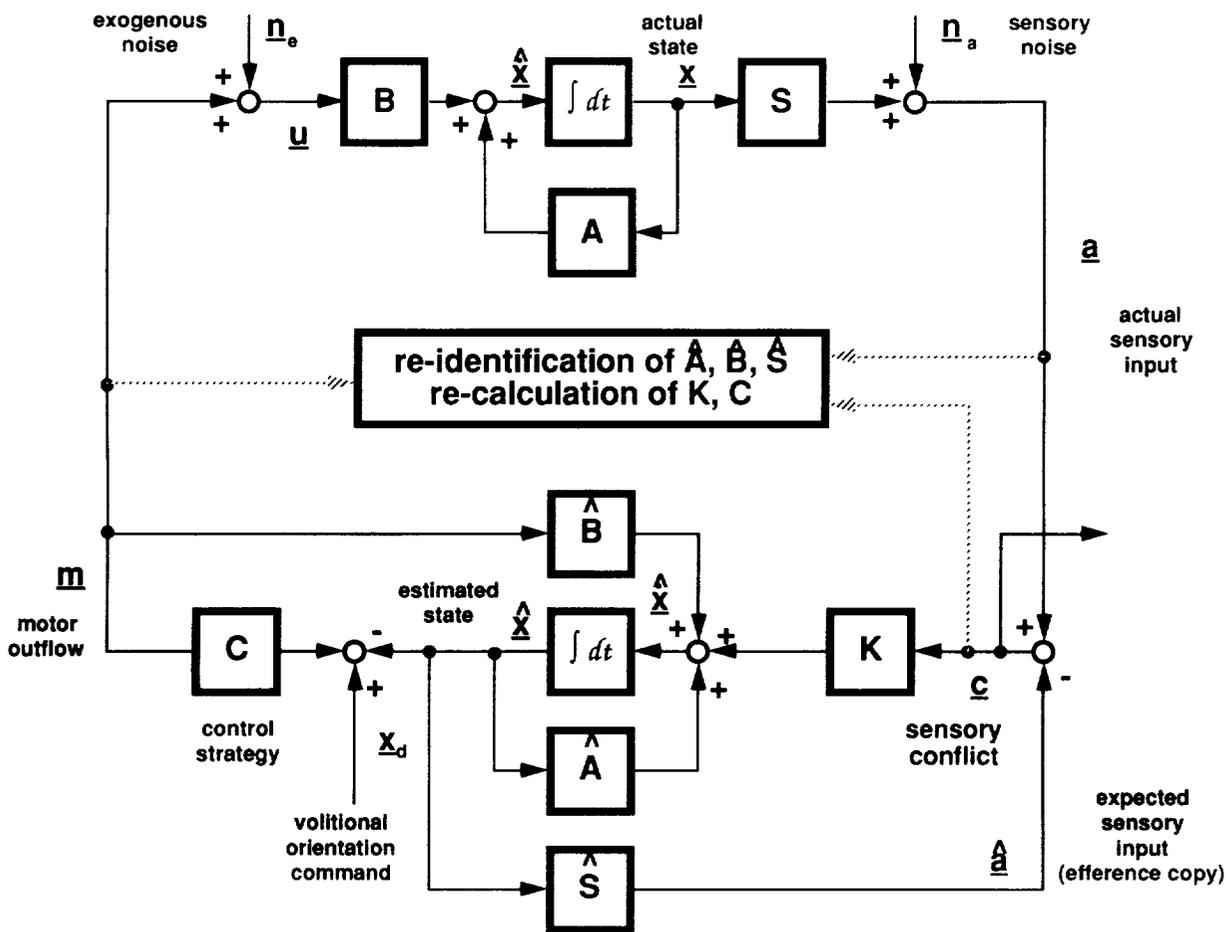
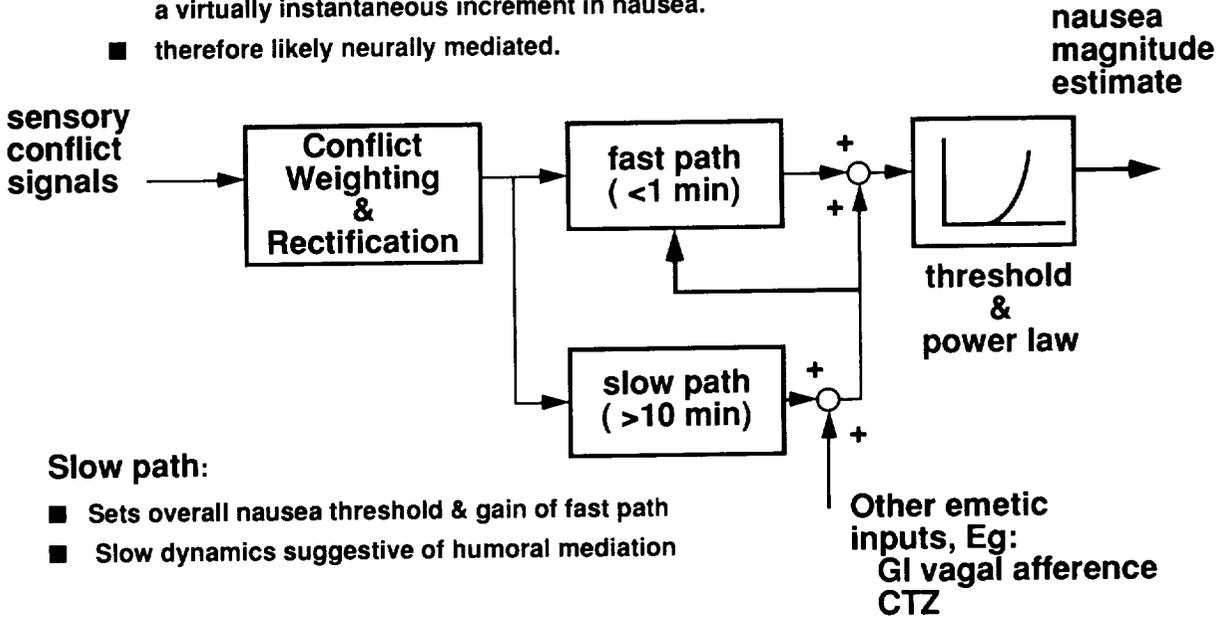


Figure 3.- Mathematical formulation of model shown in figure 2 (Oman, 1982).

Fast path:

- At high nausea levels, a single conflict stimulus produces a virtually instantaneous increment in nausea.
- therefore likely neurally mediated.



Slow path:

- Sets overall nausea threshold & gain of fast path
- Slow dynamics suggestive of humoral mediation

Figure 4.- Schematic diagram of revised model for nausea-path symptom dynamics.

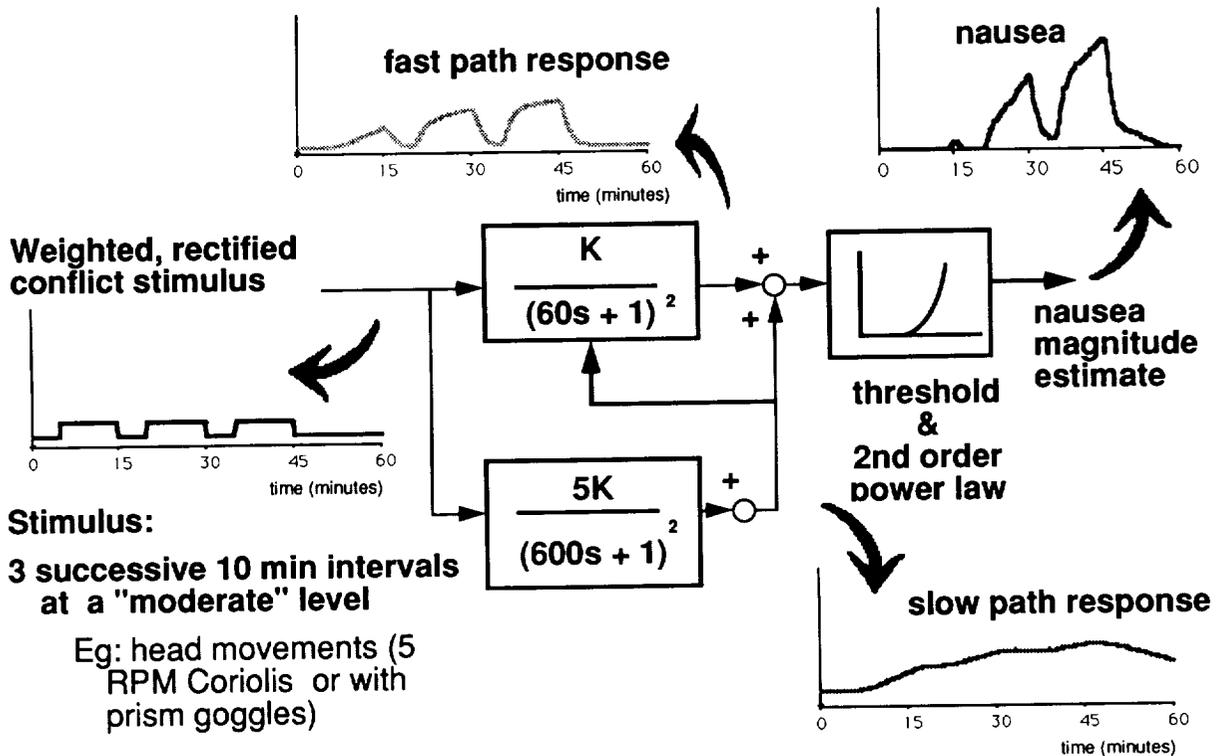


Figure 5.- Mathematical model for nausea-path symptom dynamics. Insets show results of computer simulation.

