A Gauge Model for Analysis of Biological Systems

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Abstract

For this initial work, we shall focus on introducing a biological model for utilization [mainly] as a descriptive framework on which future analyses will be based. The model includes a definition of a biological systems as a composite of properties that occupy defined states. We also introduce a concept of failure; in addition to a hypothetical mechanism by which failure occurs. We then define a functional response as a means of preventing attainment of failure state. We also define such functional responses as properties of the system, in addition to interactions between these systemic properties. We discuss determinants of the rate of- and measures of systemic failure. We conclude with two assumptions on the principal significance of systemic phenomena.

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Introduction

An essential feature of a computable biological model with universal application is that it negates intention, thus it can be applied to biological systems devoid of all perceptual experiences (e.g. cells, non-neuronal tissues, and etcetera). Perception, as used here, refers to a conscious appreciation that can eventually lead to a goal-directed outcome. The misguided use of intention in describing biological systems, irrespective of level of organization, can affect conclusions that derive from them. For example, to state that a mediator is secreted from cells in order to…, implies that the cell has an objective to prevent events that may occur in the absence of such a mediator. Instead, for the gauge model, we shall apply the term *significance* when describing biological responses. For the following analyses, we repeatedly use the word *attempt*, when describing biological phenomena. However, attempt as used here, refers to initiation of phenomena that may or may not affect a defined outcome.

We begin by reintroducing a well-known concept in the realm of physiology: the **homeostatic principle**. A revolutionary idea by Claude Bernard, to whom discovery of the concept is credited, and Walter Cannon who is arguably its greatest contributor. The principle holds that organisms favor certain states of being than they do others, and if left unaffected by external factors, will tend to occupy these states [homeostatic states]. As such, deviations from homeostasis are temporary as the system responds in a way that favors re-establishment of the homeostatic state. An essential part of this concept is the acknowledgement of a steady state. **Steady state** refers to a range of states, for which the system is inclined to assume. For simplicity we consider them, a solitary state. In the context of homeostasis, it [steady state] assumes the role of the "preferred" state. Due to the success of this principle in applications across diverse fields of biological sciences, we suppose that it stands as a general principle governing the patterns of biological systems. However, it does not give a quantifiable working mechanism for reconciliation of the effect(s) of individual variables on other variables of the system in question, and/or on the system as a whole. These shortcomings limit both its analytical power and usage as a descriptive tool for biological processes. Thus a revision or addenda is required. Here we introduce a gauge model for biological systems.

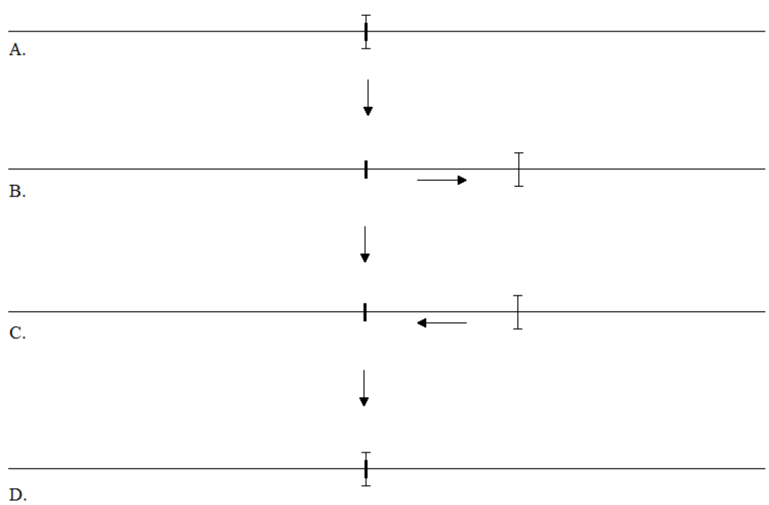

Figure 1.1. Depicts the sequence of changes following disturbance at a single variable of a biological system. (**A**) The variable is shown to initially occupy a steady state. (**B**) Disturbance at this variable affects a change from the initial steady state, (**C**) followed by return of the variable toward steady state,(**D**) and eventual attainment of steady state (homeostasis).

Defining the system and states of its properties

We apply two definitions to a biological system: point and set definition. Each gives the system attributes that allow for proper analysis under varying contexts. **Point definition** of a biological system, **s**, holds that: system **s** is a defined property of a set that consists of additional properties distinct from **s**. In addition, it [system **s**] is our primary focus and all occurrences or phenomena outside this focus are considered the surrounding with respect to **s**. Also, all observations are made in relation to the point **s**. This definition acknowledges the defined system as a property of a second but undefined larger system. **Set definition** of a biological system, **s**, defines the system as a defined set of properties (system-related information), and the set includes only those properties that define, **s**. All phenomena involving these properties are considered to occur with respect to **s**, and these phenomena are the challenges to**-** and responses of the system. We suppose the defined system is a conglomerate of all its properties. The total number of properties **Ñ**, for a system is both a constant value, and unique to the system in question. That is, two systems may have completely different values for **Ñ,** but the value for each system remains the same.

It may seem unreasonable to assign incongruent phenomena into a single set. For example, the temperature and hydrogen ion concentration, are distinct phenomena but both are classified as similar irrespective of these differences. The rationale rests in simplifying analyses, by way of generalizing these phenomena, and grouping them merely as measurable attributes of the system. Thus, the property can be likened to a homeostatic variable.

We suppose that, at any given moment, each property can exist in any one state, $\boldsymbol{x_i}$, of a potential number of discrete or continuous states. We suppose that most similar states are juxtaposed. Hence, within the context of this primary work, the states of a given property can be approximated as either a discrete or continuum of states.

We suppose that we can quantify the state of a property, $\boldsymbol{x_i}$**,** and we term this quantity the state value of the property (**s-value**). A suitable measure is the relative distance, $\Delta\boldsymbol{x}^{\mathbf{o}}$, between a reference initial state and an arbitrary state. The distance is the number of intervening states between the states in question. We shall term the reference initial state of a property its **zero-point state**, $\boldsymbol{x}_0$. The zero point state is the state of the property prior to presentation of challenge. Thus, by assuming this as the state of the property, we are supposing this occurs in the absence of**-** and prior to presentation of external influences on the property in question. Therefore, $\boldsymbol{x_0}$, represents the *zero* of the range of possible states, and is read: the value of the state of the property when at zero point state. The subscript represents the value of the state occupied by the property. Thus,

$$x_0 = 0$$

Also, since the distance, $\Delta\boldsymbol{x}^{\mathbf{o}}$, is relative to zero point state of the property, it should follow that the state of the property equals the distance from zero point. That is,

$$\Delta x^{\mathrm{o}} = x_i$$

We can therefore use these interchangeably. We define the minimum distance between states of the property, $\breve{\Delta}\boldsymbol{x}$**,** as: equivalent to the absolute value of the difference between the state of the property at zero-point state, $\boldsymbol{x}_0$, and the most juxtaposed state, $\boldsymbol{x}_1$. Thus, the s-value, $\Delta\boldsymbol{x}^{\mathbf{o}}$ for the state most proximal to $\boldsymbol{x}_0$ is:

$$\Delta x^{\mathrm{o}} = \breve{\Delta}x$$

With,

$$\breve{\Delta}x = (x_1 - x_0)$$

$$\breve{\Delta}x = |x_1 - x_0|$$

$$= |1 - 0|$$

$$= 1$$

Thus, the absolute value of the difference between the state of the property at zero-point, $\boldsymbol{x}_0$ and the most juxtaposed state can also be written such that the zero-point state value is taken into account:

$$\breve{\Delta x} = x_0 + \breve{\Delta x} = 1$$

The s-value for the second most juxtaposed state is:

$$\Delta x^{\text{o}} = x_0 + 2\breve{\Delta x} = 2$$

The s-value for the i^{th} most juxtaposed state is:

$$\Delta x^{\text{o}} = x_0 + i\breve{\Delta x} = i \tag{1}$$

Where, i is an arbitrary value of the given interval of values:

$$0 \leq i \leq z$$

and $\boldsymbol{z}$ is the maximum possible state for a property. Note that $\boldsymbol{z}$ can vary for different properties. The s-value of a property can assume the following contiguous states:

$$\{0, \dots \dots z\}$$

The s-value of an arbitrary state of the property is therefore the sum total of unit distances. Thus, the s-value of a q^{th} state for z number of states is:

$$\begin{aligned} \Delta x^{\text{o}} &= x_0 + \sum_{i=1}^{q} (\breve{\Delta x})_i \\ &= x_0 + (x_1 - x_0)_1 + (x_2 - x_1)_2 + (x_3 - x_2)_3 + \cdots + \left(x_q - x_{q-1}\right)_q \\ &= x_q \\ &= q \end{aligned} \tag{2}$$

Where, $\boldsymbol{q}$ is a specific value within the given interval of values. Also, a change in s-value of a property, $\Delta \boldsymbol{x}$ is equivalent to the difference between the state of the property prior to disturbance, and the state of the property following disturbance. For this analysis, we suppose that the state of the property prior to challenge presentation is its zero-point state. Thus, the change in s-value from zero-point to an arbitrary state equals the s-value of the property. That is,

$$\Delta x = \Delta x^{\text{o}}$$

We can therefore determine the change in s-value from zero-point to the q^{th} state for z number of states by substituiting Δx for Δx^{o} in equation 2.

$$\Delta x = x_0 + \sum_{i=1}^{q} (\breve{\Delta x})_i = x_0 + (x_1 - x_0)_1 + (x_2 - x_1)_2 + (x_3 - x_2)_3 + \cdots + \left(x_q - x_{q-1}\right)_q \tag{3}$$

We must reiterate that the choice of initiating challenge when the property is at zero-point state is for the convenience of simplicity. Unlike the s-value (of a property) which is defined with respect to the zero-point state of the property, the change in s-value can be determined for any two non-zero-point states of the system. For example, the change in s-value of a property from the i^{th} to the $(i+1)^{th}$ state of the property is:

$$\Delta x = x_0 + \big((i+1) - i\big)\Delta x^{\text{o}}$$

$$= \Delta x^{o}$$

Where,

$$i \neq 0$$

And

$$(i+1) \neq 0$$

For this reason, we choose to represent equation 3 without acknowledgement of a zero-point origin. Thus equation 3 becomes:

$$\begin{aligned} \Delta x &= \sum_{i=1}^{q} (\widetilde{\Delta x})_i \\ &= (x_1 - x_0)_1 + (x_2 - x_1)_2 + (x_3 - x_2)_3 + \cdots + (x_q - x_{q-1})_q \end{aligned} \quad (4)$$

Note that the set of equations presented above are not expressions for properties with continous changes in their s-values. Instead, they are representions for those properties with discrete changes in s-values. We now attempt to present an all inclusive representation for both continous and discrete properties. Note that we can express the absolute value of the minimum distance between states of the property, $\widetilde{\boldsymbol{\Delta x}}$, as

$$\widetilde{\Delta x} = \lim_{\kappa \to 1} \sum_{b=1}^{\kappa} \left(x_{(b/\kappa)} - x_{(b-1/\kappa)} \right)_b$$

Substituting unity for κ

$$\begin{aligned} \widetilde{\Delta x} &= \sum_{b=1}^{1} \left(x_{(b/1)} - x_{(b-1/1)} \right)_b \\ &= (x_1 - x_0) \end{aligned}$$

We can therefore rewrite equation 4 in the form:

$$\begin{aligned} \Delta x &= \sum_{i=1}^{q} \left(\lim_{\kappa \to 1} \sum_{b=1}^{\kappa} \left(x_{(b/\kappa)} - x_{(b-1/\kappa)} \right)_b \right)_i \\ &= \sum_{i=1}^{q} \left(\sum_{b=1}^{1} \left(x_{(b/1)} - x_{(b-1/1)} \right)_b \right)_i \end{aligned} \quad (5)$$

If however, we suppose the change in s-value of the property of interest occurs along a continuum, then

$$\widetilde{\Delta x} = (x_1 - x_0) = \lim_{\kappa \to \infty} \sum_{b=1}^{\kappa} \left(x_{(b/\kappa)} - x_{(b-1/\kappa)} \right)_b$$

Where,

$$x_0 = x_{(0/\kappa)} < x_{(1/\kappa)} < x_{(2/\kappa)} < \cdots < x_{(\kappa-1/\kappa)} < x_{(\kappa/\kappa)} = x_1$$

Thus we can express Δx for a continuous property as:

$$\Delta x = \sum_{i=1}^{q} \left(\lim_{\kappa \to \infty} \sum_{b=1}^{\kappa} \left(x_{(b/\kappa)} - x_{(b-1/\kappa)} \right)_b \right)_i$$

We can therefore generalize that:

$$\Delta x = x_0 + \sum_{i=1}^{q} \left(\lim_{\kappa \to \mu} \sum_{b=1}^{\kappa} \left(x_{(b/\kappa)} - x_{(b-1/\kappa)} \right)_b \right)_i ; \quad \begin{matrix} if, \mu = 1, then\ discrete\ changes \\ if, \mu = \infty, then\ continous\ changes \end{matrix} \qquad (6)$$

Figure 1.2. Depicts a gauge scale for measure of the extent of change in the state of a property (s-value). The zero value represents the initial point of the system prior to presentation of a challenging stimulus. ***i*** is an arbitrary s-value along the series of possible s-values. ***z*** is the maximum possible s-value for the given property. Note that unlike figure 1.1 the scale is unidirectional, which is important since we define a quanta of change as the absolute value of the difference between the zero-point and most juxtaposed states of a given property.

We therefore define an initial change in state of the system as a change in state of one or more properties. In addition, we suppose that the system and its surroundings are constantly interacting, hence the system is not in isolation. This is in agreement with Bertalanffy's *The theory on open systems in Physics and Biology*, (Bertalanffy, 1950).We shall build on this notion in subsequent sections.

Overview on challenge stimuli

In the context of this paper, the surrounding is viewed as an entity consisting of multiple challenge stimuli, with each challenge bearing an identity or uniqueness defined by its ability to directly affect (change the state of) a single property of the system. That is, every property of the defined system has a complimentary challenge within the surrounding. Hence, we can define a challenge from a defined property, and a property from a defined challenge.

We suppose that challenge stimuli are externally derived, and therefore are not properties of the defined system. On the other hand, we suppose the relationship between challenge stimuli and the surrounding is analogous to that of a property and the system to which it is defined. Hence a challenge stimulus, in its own right, is a property of the surrounding environment, and defines the environment. A given challenge is said to affect a change in state of the system by its effect(s) on the state of a property. We term such a property the **primary property**.

The initial effect of a challenging stimulus on a system is deviation of a primary property from an initial state , x_0 to an arbitrary state. Again, we consider the initial state of a property to occur at zero point. Also note that all interactions between the system and its surroundings occur as challenge presentations by the surroundings.

Failure state

Before we describe responses of biological systems, we must introduce the concept of failure. Failure is a technical term that describes an ultimate, detrimental fate of a biological system. As an example, we describe a unicellular organism as a biological system. Let us suppose such a cell is subjected to high osmotic conditions such that cellular rupture occur, with concomitant dissolution of intracellular components. It should follow therefore that cellular processes can no longer occur. We term such a state of the organism a **failure state**. Also, it is important to note that such a phenomenon is irreversible. That is, the cellular organism cannot spontaneously return to its unaffected state. Hence we conclude that attainment of a failure state is an irreversible event.

Biological systems and their response(s) to challenge

We suppose that following presentation of a challenge stimulus are two responses that affect the state of the system: a **deviation response** which affects deviation of both primary and non-primary properties in the direction away from their respective zero-point states; and **functional responses** which attempt to prevent further deviation of their respective properties. To address the above responses, we assume two hypothetical biological systems based on their responses to challenges. These are obligate conformers and obligate regulators. Although both systems are assumed to have respective potentials for deviation response, we suppose that only **obligate regulators** elicit functional responses. Thus, **obligate conformers** are devoid of such [functional] responses. Regulators and conformers are useful categorizations with principal usage in physiology as applied by Hill et al, 2004a.

Effects of challenge stimuli on obligate conformers: A delta drift hypothesis for deviation response towards failure state

Let us suppose that following presentation of a challenge stimulus, the state of a primary property of a defined system undergoes a change from an initial zero-point state, $\boldsymbol{P_0}$ to a non-zero-point state at $\boldsymbol{P_i}$. Where,

$$P_0 \neq P_i$$

An example is the change in the temperature of a system (primary property) following a challenge by the ambient thermal condition. To demonstrate how such a change affects the system, let us examine a hypothetical obligate conformer system. The supposed advantage of observing an obligate conformer, as opposed to an obligate regulator, is that it does not possess any intrinsic means or active mechanisms to counteract the effect of the challenge, and therefore we suppose that the unadulterated manifestations of a challenge stimulus can be observed.

An increase in the ambient temperature, surrounding a conformer system, would result in a change in the state value of the temperature property of the system, such that the temperature of the system becomes elevated in complementarity with the inciting challenge. If the ambient temperature is increased further, the internal temperature of the system should also increase in direct proportion.

If we assume that systemic properties are independent of one another –meaning that changes to the state of the primary property has negligible (if any) effect on other properties of the defined system– then, it should follow that changes to a primary property would occur in isolation. However, we suppose these properties are instead interwoven such that a change in s-value of one property affects others; which is in agreement with Bertalanffy's

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position(s) on the connectedness of systemic parts, (Trewavas, 2006)[1]. Thus, we suppose that continuous increments in ambient temperature will affect changes in s-values of additional properties.

To illustrate this, let us define an enzyme and its activity as two separate properties of a defined system. Where the activity of an enzyme is a measure of the amount of substrates converted by the enzyme into products over a given interval of time. It is known that this activity depends (in part) on the temperature of the system, which we have previously defined as the primary property. Hence, changes in the temperature value of the system should affect a change in the activity of the enzyme (secondary property). The working explanation is that the temperature of the surroundings wherein an enzyme is located is one of multiple determinants of its [enzyme] structural conformation (Hill et al, 2004b). We can suppose therefore that if an enzyme activity is initially at its possible maximum, a continuum of miniscule deviations in s-value of temperature would affect a proportional deviation in enzymatic activity. Since we already assumed an initial maximum, such shifts must therefore be in a direction away from maximum enzyme activity.

To appreciate the impact of such changes in the state of temperature property, let us imagine what happens when multiple enzymatic activities are affected. Loss of enzymatic activities should yield an accumulation and/or depletion of metabolites (substrates and products), and such changes can affect the state of the system. For example, let us suppose a decline in the activity of an enzyme whose function can be ascribed to that of a polymerase, and whose monomeric substrates are osmolytes. It should follow that such a decline would therefore produce an increased osmolarity (tertiary property) if the rate of occurrence of monomers is in excess of enzyme activity. One can begin to appreciate how this can have an impact on a cellular organism. Note how an initial challenge and change in the s-value of a primary property provokes concomitant changes in s-values at other properties of the system. We'll call this phenomenon **delta drift**.

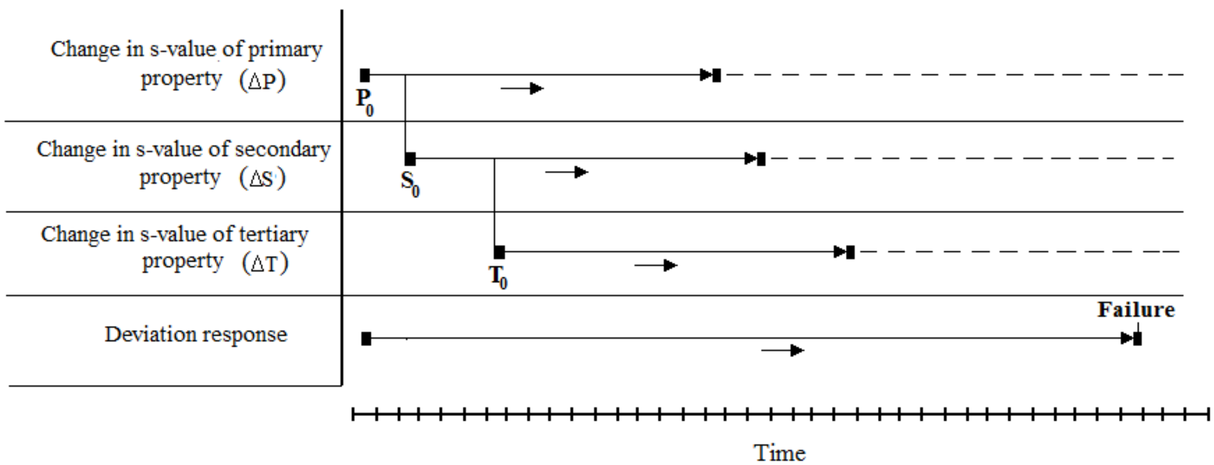

Figure 1.3. Illustrates the delta drift hypothesis. For an obligate conformer, a change in a primary property (ΔP) is shown to affect a change in a secondary property (ΔS), and ΔS in turn affects a change in a tertiary property (ΔT), up until the entire set of systemic properties are affected. Note that this illustration is not drawn to scale.

Thus, a change in the s-value for a primary property can directly affect changes in s-values of multiple properties (secondary properties). These secondary properties may themselves each affect additional properties (tertiary properties). Since the state of the system is said to be a composite of the states of its properties a delta drift which

[1] The cited position and work had negligible influence on the assumptions that properties are connected. The citation merely reflects acknowledgement of precedence of the related works of Ludwig Von Bertalanffy as the initial mention of such connectedness; and Trewavas, 2006 as the initial source of this finding. The assumptions, as used here, derive from inferences on already established phenomena such as the stated example on effects of temperature on enzyme activity, and loss of enzyme activity on substrate/product content.

involves s-value changes at multiple properties (as a result of a primary change) should affect changes in the state of the system with respect to all deviated properties. Next, we describe in detail the relationship between property and systemic states.

Drift and order numbers as a measure of the systemic state:

Based on the delta drift hypothesis, the progressive deviation of a system to failure state is related to the number of properties whose s-values are altered from their respective zero-point states. The **drift number,** $\boldsymbol{N}$ is the total number of properties whose states are affected by change in state of a primary property. The closer the drift number is to the total number of properties of the system (property number, Ñ), the greater extent of deviation in the direction toward failure. The system reaches failure state when the drift number equals the property number for the system. Using the drift number, we therefore can gauge the state of the system. Thus, the drift number for the system is analogous to the s-value of a property. We can apply the same set of assumptions used in defining states of properties for the systemic state. In this case, the gauge would be based on the drift number.

We define the zero-point state of the system as the state of the system prior to presentation of challenge. The extent of deviation from zero-point state increases as the drift number approaches Ñ. Using a drift-number-based gauge, the systemic zero-point state, $\boldsymbol{N_0}$ can be considered the state of the system when the drift number is zero. The subscript represents the drift value for the system

$$N_0 = 0$$

We use the notation, $\boldsymbol{N_j}$ for the j^{th} state of the system. Where, $\boldsymbol{j}$ is an arbitrary value for the drift number of the system. Similar to the case for properties, the systemic gauge is a representation of most similar states juxtaposed along the spectrum of possible systemic states. Also, we can quantify the state value of the system. We define such a measure as the relative distance, $\Delta\boldsymbol{N^o}$ between the zero-point and an arbitrary state of the system. Since this distance, $\Delta\boldsymbol{N^o}$ is relative to systemic zero-point, we suppose then that the systemic state equals the distance from zero point. That is,

$$\Delta N^o = N_j$$

We formally define a **unit state value** of the system, $\breve{\Delta}\boldsymbol{N}$ as: equivalent to the absolute value of the difference in drift numbers between the state of the system at zero-point and the most juxtaposed state. The state value, ΔN^o for the systemic state most proximal to zero-point is therefore the absolute value of the difference between the drift numbers at zero point and most proximal state:

$$\Delta N^o = \breve{\Delta} N$$

With,

$$\breve{\Delta} N = (\mathrm{N}_1 - \mathrm{N}_0)$$

$$\breve{\Delta} N = |N_1 - N_0|$$

$$= |1 - 0|$$

$$= 1$$

Thus, the absolute value of the difference between drift numbers at zero-point, $\boldsymbol{N}_0$ and the most juxtaposed state, $\boldsymbol{N}_1$, can also be written such that the zero-point value is taken into account:

$$N_0 + \breve{\Delta} N = 1$$

The state value for the 2nd most juxtaposed systemic state is:

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$$\Delta N^{o} = N_0 + 2\widetilde{\Delta N} = 2$$

The state value for the j^{th} most juxtaposed systemic system is:

$$\Delta N^{o} = N_0 + j\widetilde{\Delta N} = j \tag{7}$$

As stated above, j is an arbitrary value of the given interval of values:

$$0 \leq j \leq \tilde{N}$$

Therefore, the state value of the system can assume the following contiguous states:

$$\{0,1, \dots \dots \tilde{N}\}$$

The s-value of an arbitrary state of the system is therefore the sum total of unit state values. Thus, the s-value of an m^{th} state is:

$$\begin{aligned} \Delta N^{o} = N_0 + \sum_{j=1}^{m} (\widetilde{\Delta N})_j \\ = N_0 + (N_1 - N_0)_1 + (N_2 - N_1)_2 + (N_3 - N_2)_3 + \cdots + (N_m - N_{m-1})_m \\ = N_m \\ = m \end{aligned} \tag{8}$$

Where, $\boldsymbol{m}$ is a specific value within the given interval of values. Just as the number of states of a property, $\boldsymbol{z}$ can vary from one property to another, so too can the property number, Ñ vary for different systems. A change in state value of the system, $\Delta\boldsymbol{N}$ is equivalent to the difference between the state of the system prior to disturbance, and the systemic state following disturbance. For simplicity, we suppose the systemic state prior to challenge presentation is its zero-point state. Thus, the change in state value from zero-point to an arbitrary state equals the state value of the system. That is,

$$\Delta N = \Delta N^{o}$$

We can therefore determine the change in state value from zero-point to an m^{th} state by substituiting ΔN for ΔN^{o} in equation 8.

$$\begin{aligned} \Delta N = N_0 + \sum_{j=1}^{m} (\widetilde{\Delta N})_j \\ = N_0 + (N_1 - N_0)_1 + (N_2 - N_1)_2 + (N_3 - N_2)_3 + \cdots + (N_m - N_{m-1})_m \end{aligned} \tag{9}$$

Since the change in state value of the system is not defined in relation to the systemic zero point state, it should follow that we can express equation 9 as:

$$\Delta N = \sum_{j=1}^{m} (\widetilde{\Delta N})_j = (N_1 - N_0)_1 + (N_2 - N_1)_2 + (N_3 - N_2)_3 + \cdots + (N_m - N_{m-1})_m \tag{10}$$

Thereby neglecting the zero –point reference.

A weakness of the drift number-based gauge for systemic states, is that unlike those properties whose s-values undergo change along well-defined, constant, discrete states, $\widetilde{\Delta x}$, the discreteness of the unit state value of the system, $\widetilde{\Delta N}$, can vary. To explain this variation, let us suppose that following a challenge, only the s-value of a single property is altered. It should follow that the change in state value, ΔN, which is equal in magnitude to the drift number, is:

$$\Delta N = N_1$$

Where

$$N_1 = 1$$

If we now suppose that s-values of $\boldsymbol{u}$ number of secondary properties are altered following change in s-value at primary property (that is, when system is at N_1) then it should follow that the number of properties affected, and therefore the state value is:

$$sum\ of\ secondary\ properties + primary\ property = (u + 1)$$

We previously stated that a change in the s-value at a property can directly affect changes in s-values at multiple properties. Thus:

$$u \geq 1$$

If,

$$u = 1$$

Then

$$(u + 1) = 2$$

And the system can assume drift values of the following contiguous states:

$$\{0,1,2 \ldots \ldots \tilde{N}\}$$

If,

$$u > 1$$

Then

$$(u + 1) \neq 2$$

And the system assumes the following drift values:

$$\{0,1,(u + 1) \ldots \ldots \tilde{N}\}$$

Thus the drift number cannot assume a value of 2.

The consequential effect is that: if using the drift number as a gauge of systemic states, the system can assume differentially quantized states. Thus, a drift-number-based gauge fails in this regard, and is inadequate if used alone. A supplementary gauge is the number of orders affected by changes to a given property.

We previously stated that change in s-value of a primary property can directly affect s-values of secondary properties, and change in s-values of secondary properties affect the s-values of tertiary properties. **Figure 1.4** illustrates such multi-property shift. Also, note that although change in s-value of a property affects changes in s-values at other properties of the system, not all properties of a system are directly affected by change at a single property. For this reason, we categorize each affected property into an order-based schematic.

We describe the primary property as occurring at a lower order with respect to secondary properties and secondary properties occurring at a higher order with respect to the primary property. We can apply the same logic for all other properties as will be done in a later section. All secondary properties for a given primary property are said to occupy a 1^{st} order. On the other hand, the primary and tertiary properties occur at 0^{th} and 2^{nd} order, respectively. Thus, we can apply orders to each grouping of properties. The beauty of using number of orders, $\boldsymbol{\omega}$ as a gauge of the systemic state is that we can quantify, using a constant integer value, the state of the system. For $\boldsymbol{\eta}$ orders, the sequence of orders is:

$$\{0, \ldots\ldots\ \eta\}$$

Where η is specific to the given primary property affected. We define the fundamental change in order, $\breve{\Delta\boldsymbol{\omega}}$, as: equivalent to the absolute value of the difference between the 0^{th} and 1^{st} orders:

$$\breve{\Delta\omega} = (1-0)$$

$$\breve{\Delta\omega} = |1-0|$$

$$\breve{\Delta\omega} = 1$$

We can also focus on a specific order, and similar to the methods used for properties and drift number, we define the order of a system relative to its distance from zeroth order. In other words, the order of the system, $\Delta\boldsymbol{\omega}^{\mathbf{o}}$ is the product of an integer multiple and the fundamental change. Thus a change from the zeroth to first order is:

$$\Delta\omega^{o} = \breve{\Delta\omega}$$

and from the zeroth to the second order is:

$$\Delta\omega^{o} = 2\breve{\Delta\omega}$$

The change in state of the system from zero-point to the h^{th} order of the system is:

$$\Delta\omega^{o} = h\breve{\Delta\omega}$$

Our approach to quantifying systemic states is integration of both gauge schemes.

Before we introduce the comprehensive gauge model for systemic states, let us add a brief but important point regarding interactions between properties. Although we suppose that a change in s-value of a given property can directly affect changes in s-values of one or multiple properties, this one property effect on many does not hold true for multiple property effects on one. That is, we assume that a given non-primary property can be directly affected by change in s-value of only one property. For instance, a given tertiary property can only be affected by change in s-value of a single secondary property, and a change in s-value of a given quaternary property derives from change in s-value of a single tertiary property. This, again, is done for simplicity.

A comprehensive gauge model for systemic states:

We define an **ordinal drift number,** $\boldsymbol{u_{\omega}}$ as the total number of affected properties, $\boldsymbol{u}$, of a given order, $\boldsymbol{\omega}$. For example, the ordinal drift number for the first order, $\boldsymbol{u_1}$, is the sum total number of all secondary properties whose s-values are altered from zero-point state following challenge at a given primary property**.** The ordinal drift number for the second order, $\boldsymbol{u_2}$, is the sum of all tertiary properties whose states are directly affected by changes in states of all secondary properties. It is important to mention that since the zeroth order consist of a single [primary] property, the ordinal drift number of the zeroth order, $\boldsymbol{u_0}$, is:

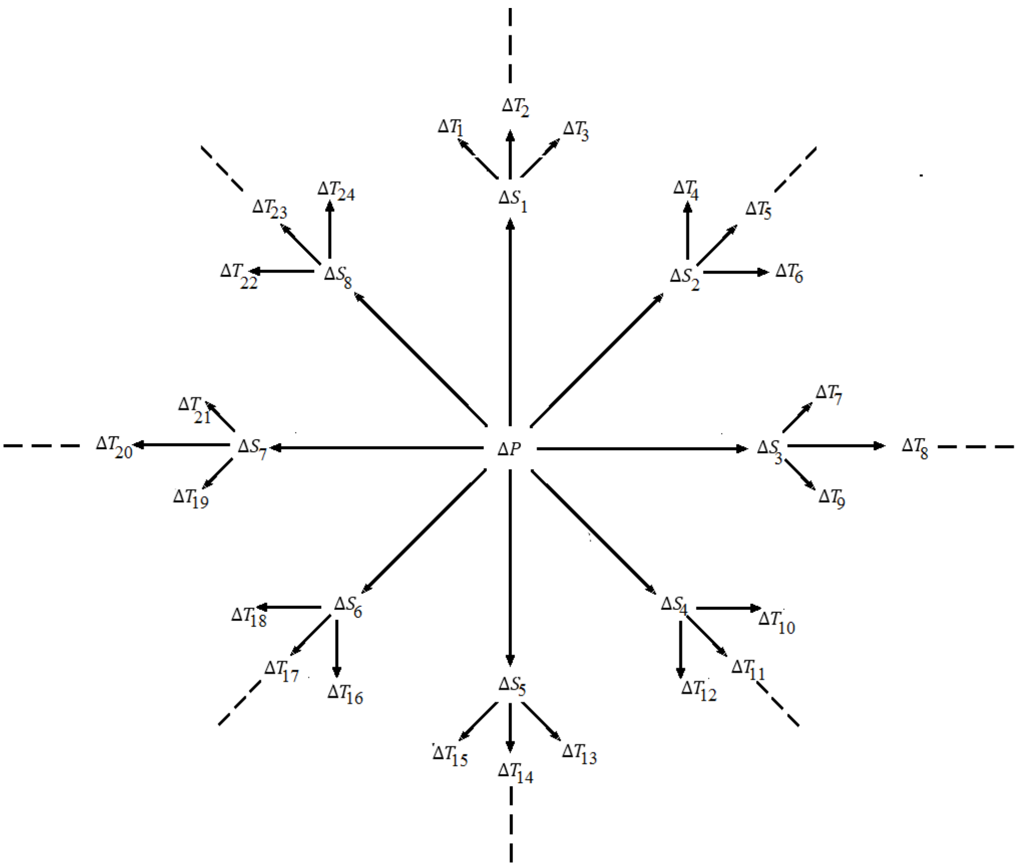
$$u_0 = 1$$

The drift number, N is the sum of ordinal drift numbers from all orders of deviation. That is for a primary property and system, the drift number when properties of the h^{th} order are affected is:

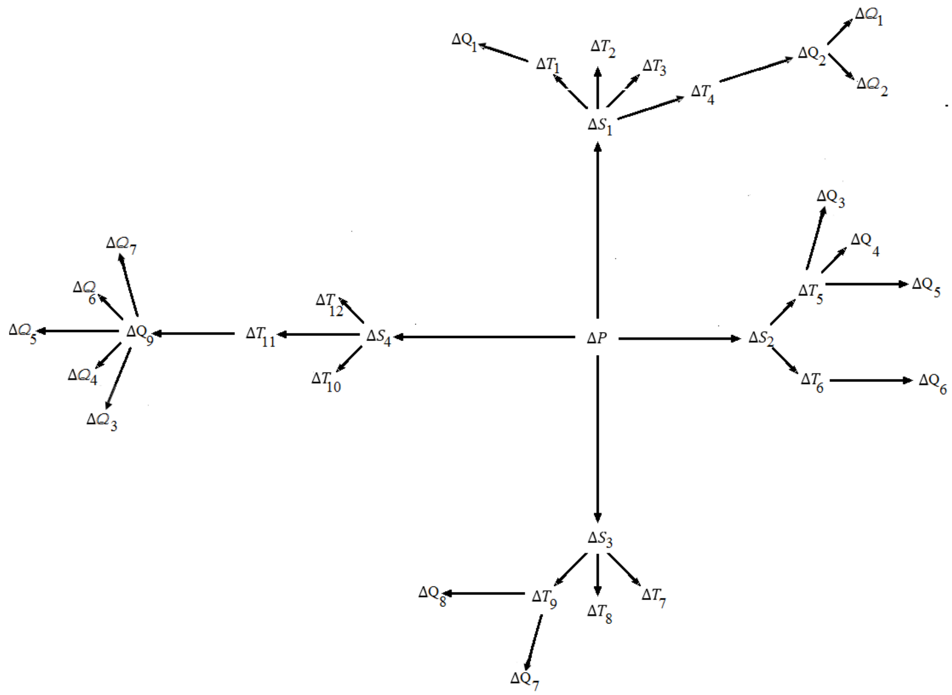
$$N = \sum_{h=1}^{\eta}(u_h) + 1 = (u_1 + \cdots + u_\eta) + 1; \quad \eta \neq 1 \tag{11}$$

Note that the range of possible values for which $\boldsymbol{h}$ can assume is:

$$1 \leq h \leq \eta$$



A.



B.

Figure 1.4A. A 2-dimensional rendition of the drift hypothesis, and unlike figure 1.3, it shows the spread of changes that can originate from challenge presentation at a single [primary] property of the system. It is important to note that although the figure shows symmetric changes at non-primary properties, there is no requirement that this must be the case. That is, changing properties that follow directly (secondary properties) or indirectly (higher order properties) from the primary property can occur in an asymmetric fashion (refer to **Figure 1.4B**). In addition, each property may have varied effects or, two or more properties have, convergent effects on other properties of the system. Thus, a much more complicated picture may result. For both illustrations, observe the number designations given to each affected property, we employ this technique as a means of property "book-keeping".

Let us suppose that the change in s-value of a given secondary property, S_1, affects changes in s-values of some but not all tertiary properties. We denote the total number of tertiary properties whose s-values are altered by change in s-value of S_1 as u_{2_1}. We term this the **component-of-ordinal drift number**. The component-of-ordinal drift number values resulting from changes in s-values of S_2 and S_3 are u_{2_2} and u_{2_3}, respectively. We can also apply this same characterization to other orders. For example, the component-of-ordinal drift number values resulting from changes in s-values of T_1 and T_2 are u_{3_1} and u_{3_2}, respectively. Thus we can apply a general form to the expression of component-of-ordinal drift number for any value as $(u_h)_l$; where h is the order of interest, and l is the specific designation for the lower order whose s-value changes directly affect changes in the order of interest. The ordinal drift number value can be expressed in terms of component-of-ordinal drift number values. For example, let us suppose all properties whose s-values are affected at a lower order affect [at least] a property of each order of interest, then the ordinal drift number would be:

The ordinal drift number for a 0th order property, u_0

$$u_0 = 1$$

The ordinal drift number for a 1st order, u_1

$$u_1 = \sum_{l=1}^{a_1} (u_1)_l \ ; \quad a_1 = 1 \qquad (12)$$

$$= \sum_{l=1}^{1} (u_1)_l$$

$$= u_{1_1}$$

The ordinal drift number for a 2nd order, u_2

$$u_2 = \sum_{l=1}^{a_2} (u_2)_l = \left(u_{2_1} + \cdots + u_{2_{a_2}}\right); \quad a_2 \neq 1 \tag{13}$$

The ordinal drift number for a 3rd order, u_3

$$u_3 = \sum_{l=1}^{a_3} (u_3)_l = \left(u_{3_1} + \cdots + u_{3_{a_3}}\right); \quad a_3 \neq 1 \tag{14}$$

Thus, we can generalize that: The ordinal drift number for an h^{th} order, u_h

$$u_h = \sum_{l=1}^{a_h} (u_h)_l = \left(u_{h_1} + \cdots + u_{h_{a_h}}\right); \quad a_h \neq 1 \tag{15}$$

Note that the ${a_h}^{th}$ term is the component-of-ordinal drift number value of the ${u_{(h-1)}}^{th}$ property. For instance, the ${a_2}^{th}$ term is the component-of-ordinal drift number value for the ${u_1}^{th}$ term; and the ${a_3}^{th}$ term is of the component-of-ordinal drift number value for the ${u_2}^{th}$property. Thus, we can substitute $u_{(h-1)}$ for a_h in equation 15:

$$u_h = \sum_{l=1}^{u_{(h-1)}} (u_h)_l = (u_{h_1} + \cdots + u_{h_{u_{(h-1)}}})$$

The drift number value can also be expressed in terms of component-of-ordinal drift number values.

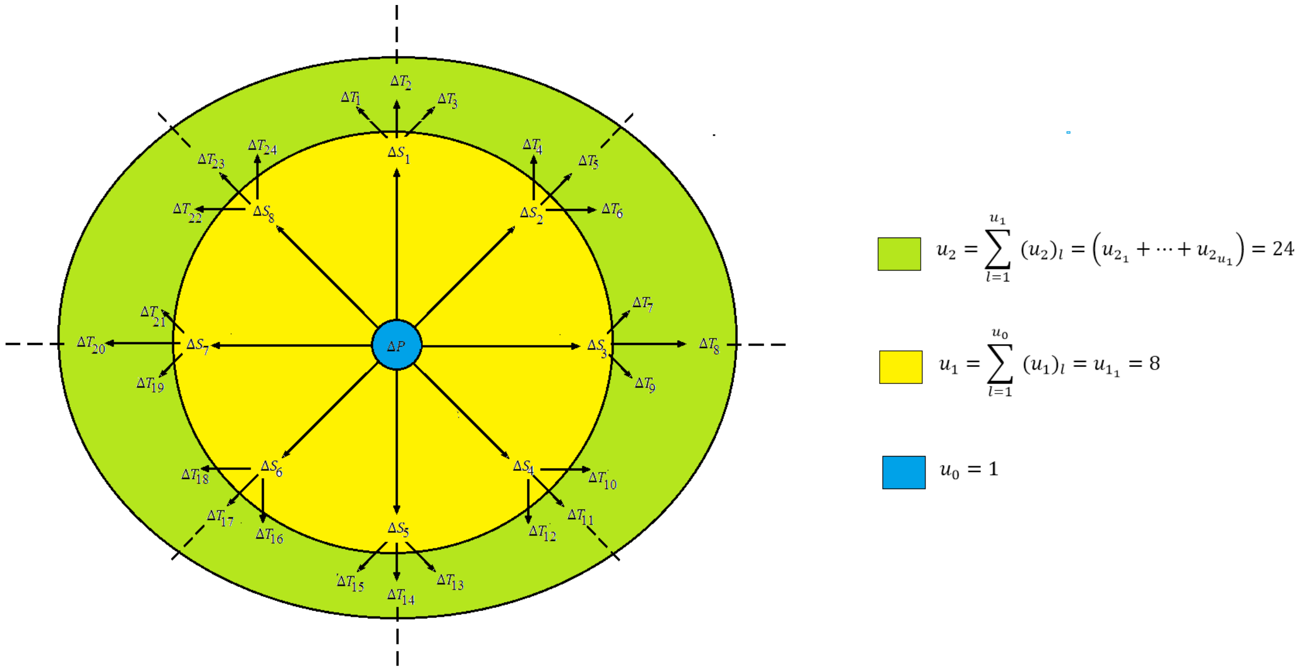
Substituting for u_h in equation 11:

$$N = \sum_{h=1}^{\eta} \sum_{l=1}^{u_{(h-1)}} (u_h)_l + 1; \quad \eta \neq 1$$

$$= \left(\sum_{l=1}^{u_0} (u_1)_l + \cdots + \sum_{l=1}^{u_{(\eta-1)}} (u_\eta)_l \right) + 1; \quad \eta \neq 1$$

$$= \left(\sum_{l=1}^{1} (u_1)_l + \cdots + \sum_{l=1}^{u_{(\eta-1)}} (u_\eta)_l \right) + 1; \quad \eta \neq 1$$

$$= \left(\sum_{l=1}^{1} (u_1)_l + \sum_{h=2}^{\eta} \sum_{l=1}^{u_{(h-1)}} (u_h)_l \right) + 1 \tag{16}$$



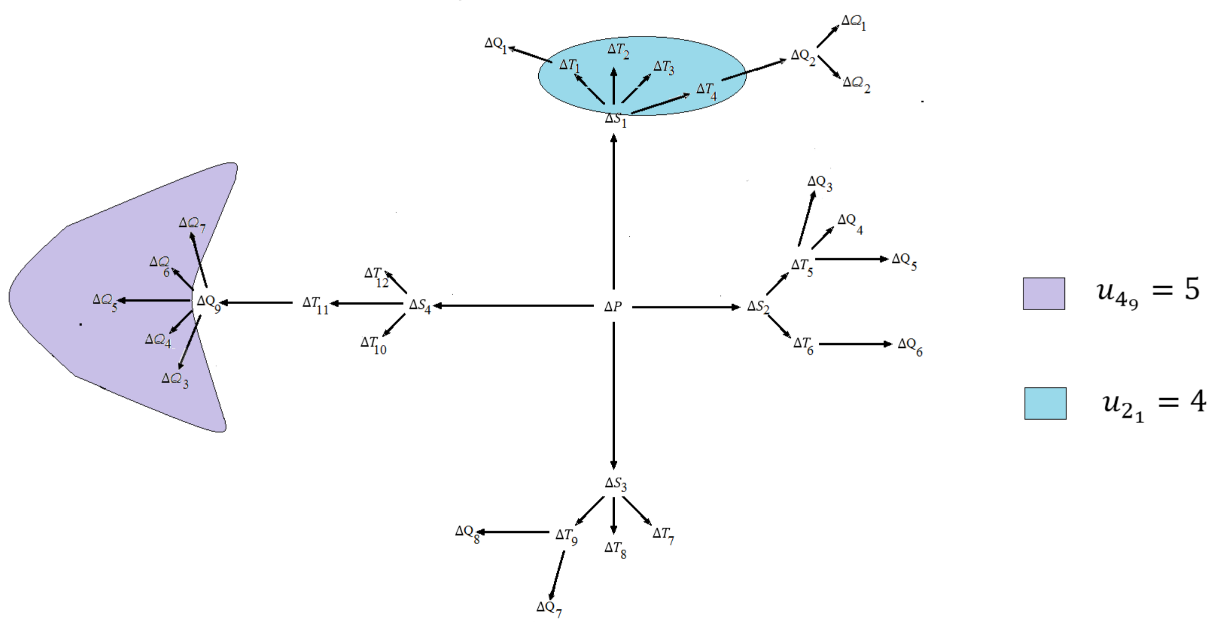


Figure 1.5A highlights the order structure for characterization of properties whose s-values are altered by a challenge at a single primary property (blue area). Note that the ordinal drift numbers for: 0^{th} order, 1^{st} order (yellow area), and 2^{nd} order (green area) are 1, 8, and 24, respectively. Thus, $N = 33$. **Figure 1.5B** highlights the component-of-ordinal drift number structures. Note that the component-of-ordinal drift number values for properties Q_9 (lavender) and S_1 (light turquoise) are u_{4_9} and u_{2_1}, respectively. Since a change in Q_9 directly affects s-values of five properties within the 4^{th} order, it should follow that u_{4_9} has a value of 5. Also, since a change in S_1 directly affects s-values of four properties within the 2^{nd} order, it should follow that u_{2_1} has a value of 4.

Revised definition of failure state:

We define failure state as the state of the system when the drift number, ***N***, equals the property number, Ñ, for the given system. From the information above, it should follow that the drift number when at failure is:

$$N = \left(\sum_{l=1}^{1} (u_1)_l + \sum_{h=2}^{\eta} \sum_{l=1}^{u_{(h-1)}} (u_h)_l \right) + 1$$

Since the drift number and property number are the same when the system is at failure state, it should follow then that:

$$Ñ = \left(\sum_{l=1}^{1} (u_1)_l + \sum_{h=2}^{\eta} \sum_{l=1}^{u_{(h-1)}} (u_h)_l \right) + 1$$

Note that even if the value of η differs for different primary properties, the property number remains a constant for the given system. It must follow then that as η decreases, for a fixed property number and drift number, the **average ordinal drift number** increases. We define a measure of the distance to failure as the difference between the property number and the drift number, $(Ñ - N)$.

We can therefore define two extremes for the state of the system (that is, the zero point and failure states, respectively). Since at zero point state of the system

$$N = 0$$

It should follow that at this state,

$$Ñ - N = Ñ$$

$$= \left(\sum_{l=1}^{1} (u_1)_l + \sum_{h=2}^{\eta} \sum_{l=1}^{u_{(h-1)}} (u_h)_l \right) + 1$$

On the other hand, at failure state,

$$N = Ñ$$

Hence, at this state,

$$Ñ - N = 0$$

Information on the distance from failure following change in s-value at a single primary property can be attained from the difference between property and drift number of the system.

Drift segment and path:

In some instances, we may want to consider some, but not all properties affected by delta drift. Thus, it is important we discuss some of the terminologies that we will apply to this end. A **drift segment** is a component of the total number of properties affected by change in s-value of a single property. The **drift path** is a sequence of affected properties along contiguous orders and consists of a single property per order. Refer to figure 1.6 for an illustration of drift segment and path.

Relationship between the intensity of challenge and the change in s-value of primary property:

Let us suppose that two identical challenge stimuli, $\boldsymbol{I}_1$ and $\boldsymbol{I}_2$ affect distinct degrees of change in s-value of a given primary property. Of the two, the stimulus intensity that affects the greater magnitude of change can be said to have the greater intensity. Thus, the magnitude of change of a primary property is a parameter for measurement of the intensity of challenge at the given property. The change in state of a primary property can therefore be considered a [mathematical] function of the intensity of challenge presented.

$$x(I) = \begin{cases} x_i, & i \neq 0, \quad I > 0 \\ x_0, & \quad\quad\quad I = 0 \end{cases}$$

In general, we suppose that this relationship applies to all stimuli and their incited properties. That is, the intensity of a stimulus (be it a challenge or change in s-value of a property) is directly proportional to the magnitude of change in s-value of the property affected. As previously defined, Δx is the degree of change to the state of the property following stimulus presentation. The degree of change is a measure of how far off the state of a property is altered from its zero point state.

Relationship between s-value changes at different properties:

We previously stated that a change in the s-value of a primary property can directly affect the s-values of secondary properties, and changes in s-values of secondary properties affect s-values of tertiary properties. Thus, we can consider the primary property an ***inciting stimulus*** of secondary properties, and secondary properties inciting stimuli of tertiary properties. We therefore generalize this inciting stimulus and altered s-value relationship as: if a change in s-value of a property directly affects a change in s-value of a second property, then the former property is considered an inciting stimulus of the latter. We designate the former a **lower order** property, and latter, a **higher order** property.

A change in the s-value of a lower order property may or may not affect the same magnitude of change in s-value at a higher order property. For instance, a change in the s-value of a primary property need not affect the same magnitude of s-value change at a secondary property. Also, a change in the s-value of a lower order property need not affect equal magnitude of changes in s-values of properties at the same higher order. For example, changes in s-values at two or more secondary properties need not be the equal, even if such changes result from a change at a single primary property. Lastly, since properties are not identical, their state values differ and cannot be compared in that account. Thus if two primary properties, defined as temperature and pH are said to have identical s-values or magnitude of change in s-values, this does not mean that they affect equal changes in drift number of the system.

We define an altered s-value ratio as the ratio of change in s-value of one property to that of another. For conventional purposes, we shall apply the change in higher order s-value as the numerator and that of the lower order as the denominator. For example, the change in s-value at a secondary property to the change in s-value at the primary property is:

$$S - value\ ratio = \frac{\Delta S}{\Delta P}$$

$$= \frac{\sum_{i=1}(\breve{\Delta S})_i}{\sum_{i=1}(\breve{\Delta P})_i}$$

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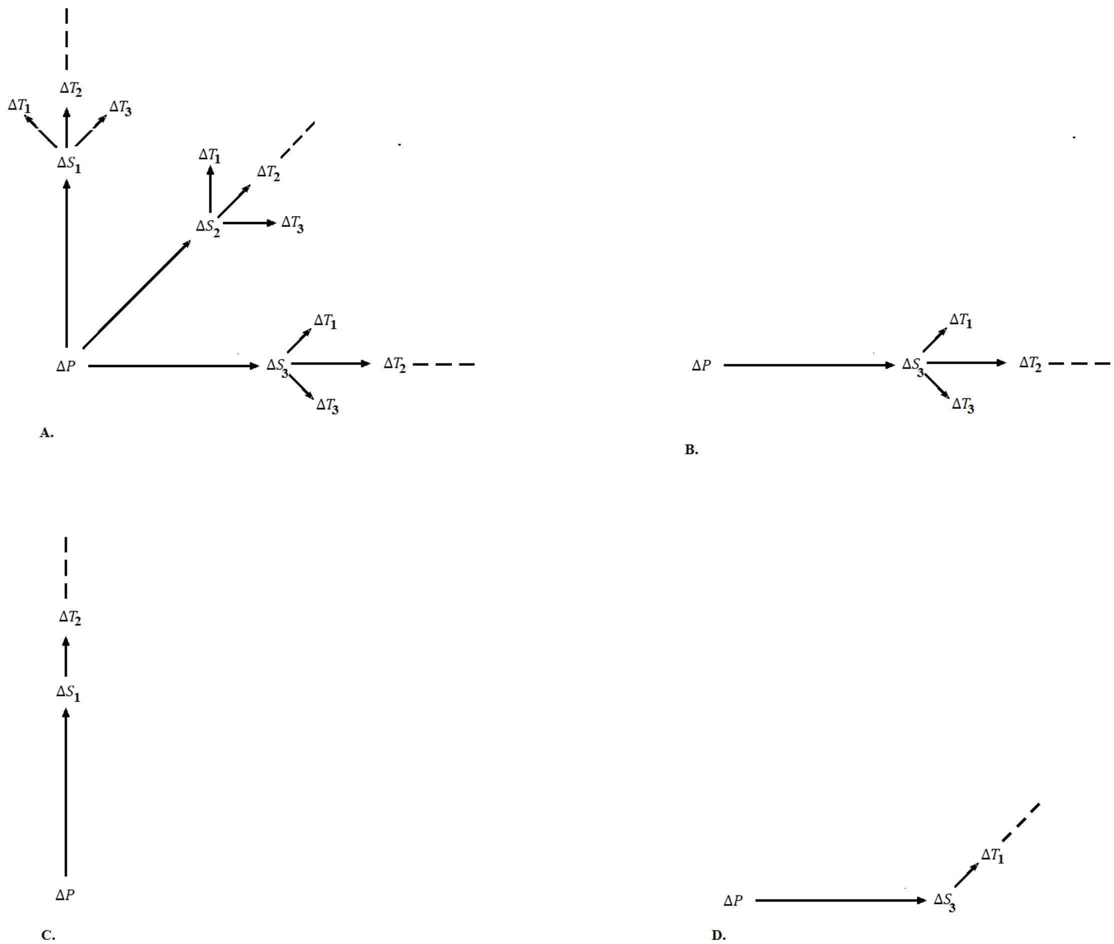

Figure 1.6. An illustration of a drift segment (**A** and **B**), and drift paths (**C** and **D**) for **figure 1.4A**.

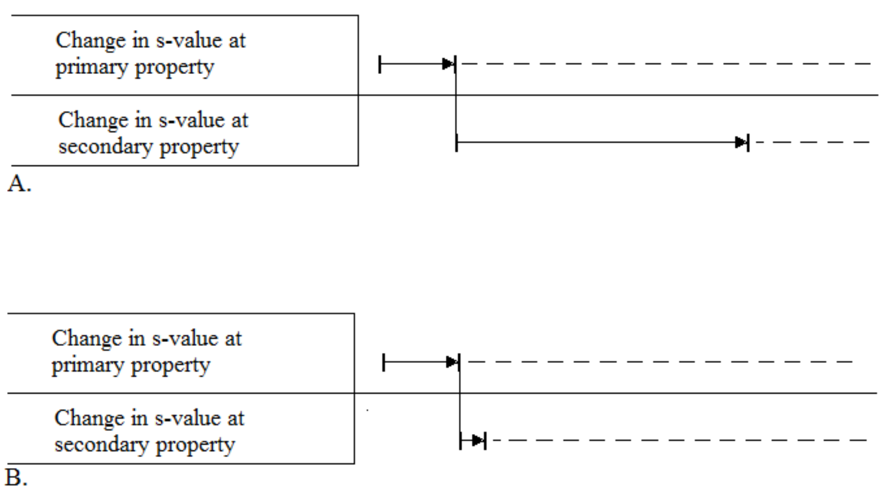

Figure 1.7. The above representations highlight differences between extents of deviation both at a primary and secondary property. **(A)** A change in the s-value of a primary property affects a greater extent of change in the s-value of a secondary property. **(B)** A change in the s-value of a primary property affects a smaller extent of change in the secondary property. Thus, there is no requirement that a higher order property change by the same extent as the inciting lower order property. In addition, there are no requirements that two higher order properties change by the same extent following deviation at a common lower order property.

Effects of challenge stimuli on obligate regulators: Functional responses:

We gather from physiology that there must exist a means by which the system is returned to homeostasis. In addition, it should follow that the effects of such means can only be appreciated if it follows a challenge stimulus. Thus, we suppose that such effects occur after the challenge is presented. Here we define a counterpart to the obligate conformer, an obligate regulator, as a biological system with a capability such that following deviation of both states of property and system, as results from a challenge, at least a single **functional response** occur for the system. Hence, all deviation responses are followed by (or occur concurrently with) at least a single concomitant functional response. The effect(s) of a functional response, its **yield,** attempts to prevent attainment of failure state. Henceforth we refer to the yield, as the **yield of functional response** (**YFR**). Specifically, if an *appropriate YFR* is available, then the tendency that the system reaches failure is minimal. Since functional responses affect failure, it should follow that these responses also affect the tendency that the drift number equals the property number. Such an effect must occur in such a way that YFRs prevent the drift number from approaching the property number.

We define a second measure, the **corrected drift change**, $\boldsymbol{\Delta N'}$**,** as the difference between the drift number post-YFR, $\boldsymbol{N_{\mathrm{po}}}$, and the drift number value **prior**-to-YFR, $\boldsymbol{N_{\mathrm{pr}}}$. While the latter drift number represents the drift number following challenge of a given intensity (but not the required YFR), the former represents the drift number following both the challenge and YFR.

$$\Delta N' = N_{\mathrm{po}} - N_{\mathrm{pr}}$$

Note,

1) if $\Delta N' > 0$, then $N_{\mathrm{po}} > N_{\mathrm{pr}}$;
2) if $\Delta N' < 0$, then $N_{\mathrm{po}} < N_{\mathrm{pr}}$;
3) if $\Delta N' = 0$, then $N_{\mathrm{po}} = N_{\mathrm{pr}}$.

Since functional responses attempt to prevent failure, we suppose that: the effect of YFRs on the system is such that:

$$\Delta N' \leq 0$$

Of the conditions listed above, only 2 and 3 satisfy the requirement. Condition **(2)** by reverting the state of the system in the direction away from failure state in the presence or absence of an inciting factor; or **(3)** stabilizing the state of the system so as not to allow for further deviation. Thus, we can conclude that YFRs affect changes to the corrected drift change value, $\boldsymbol{\Delta N'}$, for the system. For simplicity, we suppose that an *appropriate YFR* can only stabilize the state of the system so as not to allow for further deviation toward failure. In other words, an *appropriate YFR* can only affect:

$$\Delta N' = 0$$

Thus, the system is non-rectifiable.

Other features of YFRs include:

1. YFRs affect change in drift number via their effects on the system at the property level.

2. No two or more properties are affected by the same functional response and/or YFRs. That is, a YFR can directly affect only the change in s-value of a single property.

3. On the other hand, two or more functional responses and their YFRs may affect the same property.

4. Effects of YFR on an affected property is an attempt at returning the property to its zero-point state. This can only prevent further changes in its [affected property] component-of-ordinal drift number value, but does not return its higher order properties to their respective zero-point states. Refer to the next section for an explanation of this point. By preventing further changes to states of affected properties, YFRs can indirectly affect multiple properties of the system.

5. YFRs affect s-values of properties such that further changes, and thus the degree of change from property zero point state is diminished. Hence we can define the s-value of a property, $\boldsymbol{x}$, as a mathematical function of the response yield, $\boldsymbol{Y}$.

6. For a functional response, one can define: the function of the response, mechanisms of the function, and processes that follow these mechanisms. We shall discuss this in a subsequent work.

States of both the system and of higher order properties are non-rectifiable by means of reverse changes to challenge intensity and/or lower order properties:

Although we state that deviation in the state of the system can occur following presentation of challenge, the same does not hold true for reverse changes. That is, a decrease in challenge intensity (to pre-challenge conditions) does not drive the systemic state toward zero point.

Similarly, reverse-deviation in the state of all other properties does not result from correction of the s-value for the inciting lower order property. For example, reestablishment of zero-point state of the primary property does not affect return of other deviated properties to their zero-point states. Thus, these properties are non-rectifiable by such means. In order for such properties to return to zero-point state, each property must instead be affected by one or more functional responses defined for the specific property. It is by such means of correction that the system can be returned to its zero-point state. However, as we shall discuss later, there is a group of properties that is an exception to this rule.

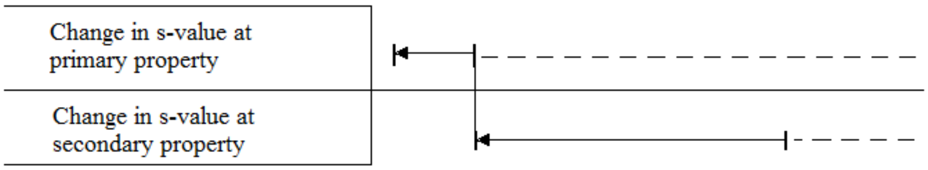

Figure 1.8. Shows two properties of a system undergoing rectification in the direction towards their respective initial zero-point states. We suppose for the sake of simplicity that the model system does not undergo such rectification.

A functional response at a single (primary) property:

For simplicity, we focus on a sole functional response and its effects on the system. Since we stated that a solitary functional response can only affect a single property, it is important that we find the property which when affected by the functional response, will affect the minimum corrected drift change. Thus, maximally prevents attainment of failure state. Note that since negative values for $\Delta N'$ are assumed to be unattainable, this minimum is restricted to $\Delta N' = 0$.

Although a functional response that affects any one of the altered properties can, in principle, affect the corrected drift change, the degree of such change depends on the number of properties whose s-values are affected following a change in the s-value of the property in question. Thus, if the s-value of a property affects a small proportion of properties, prevention of further deviation to the state of this property, would affect a higher corrected drift change than if the property s-value affected a greater proportion of properties. To illustrate this point, consider figure 1.5B. Whereas reversion of Q_9 to its zero-point state prevents further changes in s-values of those properties highlighted in lavender (i.e, properties Q_3, Q_4, Q_5, Q_6, and Q_7) reversion of S_4 should prevent further deviation of properties $T_{10}, T_{11}, T_{12}, Q_9$, Q_3, Q_4, Q_5, Q_6, and Q_7. Note that properties Q_9, Q_3, Q_4, Q_5, Q_6, and Q_7 are indirectly affected, but are along the drift path that results from changes in S_4. Since reversion of S_4 affects s-values of more properties than does Q_9 we suppose that functional responses at S_4 would have a greater impact in preventing failure, than would functional responses at Q_9. Hence, functional response and YFR at a property whose altered s-value affects the greatest number of properties should affect the lowest possible corrected drift change. Thus, a functional response that affects this property is the most likely to prevent failure of the system.

Of all properties whose s-values are either directly or indirectly affected by a challenge stimulus, the primary property affects the maximum number of properties of the system. Hence, we focus our discussion on a challenge, functional response, and YFR at primary properties.

The state of the system is non-rectifiable:

As stated previously, we suppose that, following a challenge stimulus, the state of the system cannot be reversed towards zero-point state, and that an appropriate YFR at a property can only affect the corrected drift value such that:

$$\Delta N' = 0$$

Thus, a model of the effects of a functional response and its YFR at a single (primary) property, post-challenge, would mean that the observed system is non-rectifiable. That is, cannot tend toward zero-point state.

Functional responses and YFRs as properties of the system:

Since Functional responses and their YFRs are derived from the system, it should follow then that these are themselves properties of the system, and thus have defined zero point states. Functional responses following after a challenge stimulus and s-value change (at a property), are themselves deviated from their zero point states. We suppose that, as a group, functional responses and YFRs are rectifiable properties, and are thus exceptions to the general rule. These properties can be rectified via either one or all of the following means: other functional responses and YFRs; indirect and self-rectifying, by affecting reverse changes in s-values at properties whose initial s-value changes incited the functional response; or a combination of these means. We can also consider steps for a functional response as a drift path for the property whose s-value change affects its [functional response] occurrence.

Natural stimulus-response pairing:

Since a given challenge affects a system at a single property, and a functional response affects a reverse deviation of the state of a single property, it should follow then that for a given property, we can define a challenge stimulus and its functional response(s). By way of their shared relationships to the property, we term these **natural stimulus-response pairs**. That is, occurrence of a challenge stimulus is always followed by occurrence of the functional response, as long as the system is an obligate regulator and a deviation response occurs at the given property. If challenge with change in s-value of property, then the natural response to the challenge follows. If change in s-value of property and functional response, then natural challenge for the functional response must have occurred. We shall discuss variations to these pairings in a different work. It must also be stated that a natural challenge stimulus and its functional response affect inverse changes in the s-value of the property. For example, if an increase in ambient temperature affects an increase in temperature of the system and a functional response to the property defined as temperature affects a decrease in the s-value of this property, then both increase in ambient temperature and the functional response that decreases systemic temperature make up a natural stimulus-response pair.

The Rate of delta drift and determinants of the deviation interval

If we suppose that challenge presentation at a property occurs when drift number of the system is zero ($\boldsymbol{N} = 0$), then the rate at which the drift number, $\boldsymbol{N}$ approaches the property number, Ñ is the ratio of the difference in these measures to the duration of drift. Where the duration of drift or delay interval, is the interval of time that must elapse for transition from a zero point state of the system, ($\boldsymbol{N} = 0$), to failure state ($\boldsymbol{N}$ = Ñ), following challenge. That is, it is the length of time from the initial change in s-value of the primary property, $\boldsymbol{t_{d_i}}$ to the moment, $\boldsymbol{t_{d_f}}$, when a change in the last property is affected.

$$\text{Drift rate} = \frac{(\tilde{N} - N)}{(t_{d_f} - t_{d_i})}$$

This is the drift rate of the system. Factors that affect the drift rate following a challenge at a single property are the challenge intensity and the number of orders for the primary property.

Challenge intensity: Relative lengths of pulse and lag intervals

For the following analysis, we suppose a rectifying system. That is, following challenge presentation, an appropriate YFR returns both the affected property and system to their initial zero-point s-values. Since we assume a rectifiable system, it should follow then that the corrected drift change is:

$$\Delta N' \leq 0$$

We define a challenge pulse as a brief period of challenge presentation that has the same duration at every presentation. We suppose that presentation of a single pulse is such that it just affects a quantifiable yield of functional response. Since we stated that the yield is a reversal of changes to the property state, and that changes to the property state correspond to the given challenge, we can surmise that the yield is also an inverse of the challenge. Hence the natural stimulus-response pairing. A challenge to a property can therefore be quantified with respect to a YFR, $\boldsymbol{Y}$ affecting the property. Thus, $\boldsymbol{Y}$, can be considered to be equal in magnitude to the intensity of challenge from a single pulse.

$$\textit{Challenge intensity } (I) \textit{ from a single pulse} = Y$$

Let us suppose a tandem of $\boldsymbol{n}$ challenge pulses are presented to an obligate conformer system. Since there are no functional responses (hence no lag intervals) for the conformer system, the length of the interval of time between pulses, **pulse interval,** is an irrelevant piece of information. That is, following challenge pulse the drift number of the system increases and remains at the given value. Thus, no matter the pulse interval chosen, there is an aggregate effect of challenge pulses. The intensity of challenge for $\boldsymbol{n}$ pulses is therefore:

$$Challenge\ intensity\ (I)\ of\ \boldsymbol{n}\ pulses = n \cdot Y$$

On the other hand, let us suppose the same tandem of $\boldsymbol{n}$ challenge pulses are presented to an obligate regulator system. For simplicity, we suppose that following challenge presentation, sufficient time is allowed for availability of appropriate YFR. In other words the property must be allowed to return to zero point state before onset of a subsequent challenge pulse. Hence, the pulse interval must be equal to or greater than the **lag interval** for functional response. The lag interval is a measure from the moment of initial onset of functional response, $\boldsymbol{t_{L_i}}$, at the primary property, to the moment during which an appropriate YFR occurs, $\boldsymbol{t_{L_f}}$. Since the system is returned to zero point state before presentation of subsequent challenges, it should follow that the effect(s) of each challenge pulse is isolated from that of subsequent pulses. Thus, the aggregate intensity of such challenge pulses is equal in magnitude to the intensity, $\boldsymbol{Y}$, of a single pulse.

$$Challenge\ intensity\ (I)\ of\ n\ pulses = Y$$

If we now suppose gradual decrement in pulse interval, with no change to the length of lag interval. It should follow that a point would be reached at which the pulse interval is just less than lag interval. At this point the system no longer returns to a zero-point state before onset of subsequent pulses. That is, the effects of a preceding pulse is not completely corrected before onset of a subsequent pulse. The degree to which these effects are corrected decreases with decreasing pulse interval, and increasing lag interval. We define the relative length of pulse and lag intervals as a measure of the ratio of pulse to lag interval, $\mathbf{Q}_{\boldsymbol{pL}}$.

$$\mathrm{Q}_{pL} = \frac{(t_{p_f} - t_{p_i})}{(t_{L_f} - t_{L_i})}$$

With further decrements in pulse interval, a point is reached at which pulses begin to overlap within the interval. Pulses occur simultaneously when pulse interval equals zero. For an obligate conformer system, there are no differences between the effects of such simultaneity and the increasing pulse interval stated above. Thus, for the obligate conformer the intensity of challenge for $\boldsymbol{n}$ pulses occurring simultaneously is:

$$Challenge\ intensity\ (I)\ of\ n\ pulses = n \cdot Y$$

Similarly, since presentation of simultaneous pulses to an obligate regulator precede initiation of functional responses, the obligate regulator system would be no different from the obligate conformer. Thus, for the obligate regulator, the intensity of challenge for $\boldsymbol{n}$ pulses occurring simultaneously is:

$$Challenge\ intensity\ (I)\ of\ n\ pulses = n \cdot Y$$

In order to factor in this overlap of pulses in determination of challenge intensity, we define a cumulative factor. The **cumulative factor,** $\boldsymbol{C_f}$ is a measure of the overlapping effect of challenge pulses following initiation of pulse presentation. Since the initial pulse is not preceded by pulse(s), we describe its effects as an initial to which all other effects are added. Thus, for $\boldsymbol{n}$ pulses, the number of pulses which have a potential cumulative effect must be the difference between the total number of pulses and the initial pulse. That is:

$$number\ of\ pulses\ with\ potential\ cummulative\ effects = nY - Y$$

The cumulative intensities of $\boldsymbol{n}\ pulses$ is therefore:

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$$Cummulative\ intensity = (nY - Y) \times\ C_f$$

Moreover, we previously stated that when the pulse interval equals or is greater than the lag interval, the cumulative intensity of such challenge pulses is equal in magnitude to the intensity of a single challenge, $\boldsymbol{Y}$.Under such conditions, the stimulus intensity is therefore independent of the number of pulses presented. Thus, for $\boldsymbol{n}$ pulses, the stimulus intensity is $\boldsymbol{Y}$**,** if the pulse interval is greater than lag interval. The cumulative factor must therefore be at a minimum, negligible value when $\mathbf{Q}_{\boldsymbol{pL}}$ is greater than 1.

On the other hand, when the pulse interval is nil for a given lag interval, the cumulative intensity of such challenge pulses is equal in magnitude to the sum of all pulse intensities. Thus, the cumulative factor must be at a maximum value when Q_{pL} equal 0.

We define the cumulative factor as**:**

$$C_f = e^{-\mathrm{Q}_{pL}}$$

Substituting for C_f,

$$Cummulative\ intensity = \frac{(nY - Y)}{e^{\mathrm{Q}_{pL}}}$$

$$= \frac{Y(n-1)}{e^{\mathrm{Q}_{pL}}}$$

Total intensity of n pulses, I, is therefore;

$$I = Y + \left(\frac{Y(n-1)}{e^{\mathrm{Q}_{pL}}}\right) \qquad (17)$$

Note that when Q_{pL} is 0, C_f is 1 and the total intensity equals:

$$\lim_{\mathrm{Q}_{pl} \to 0} \left[Y + \left(\frac{Y(n-1)}{e^{\mathrm{Q}_{pL}}}\right)\right] = Y +\ Y(n-1)$$

$$= Y + Yn - Y$$

$$= n \cdot Y$$

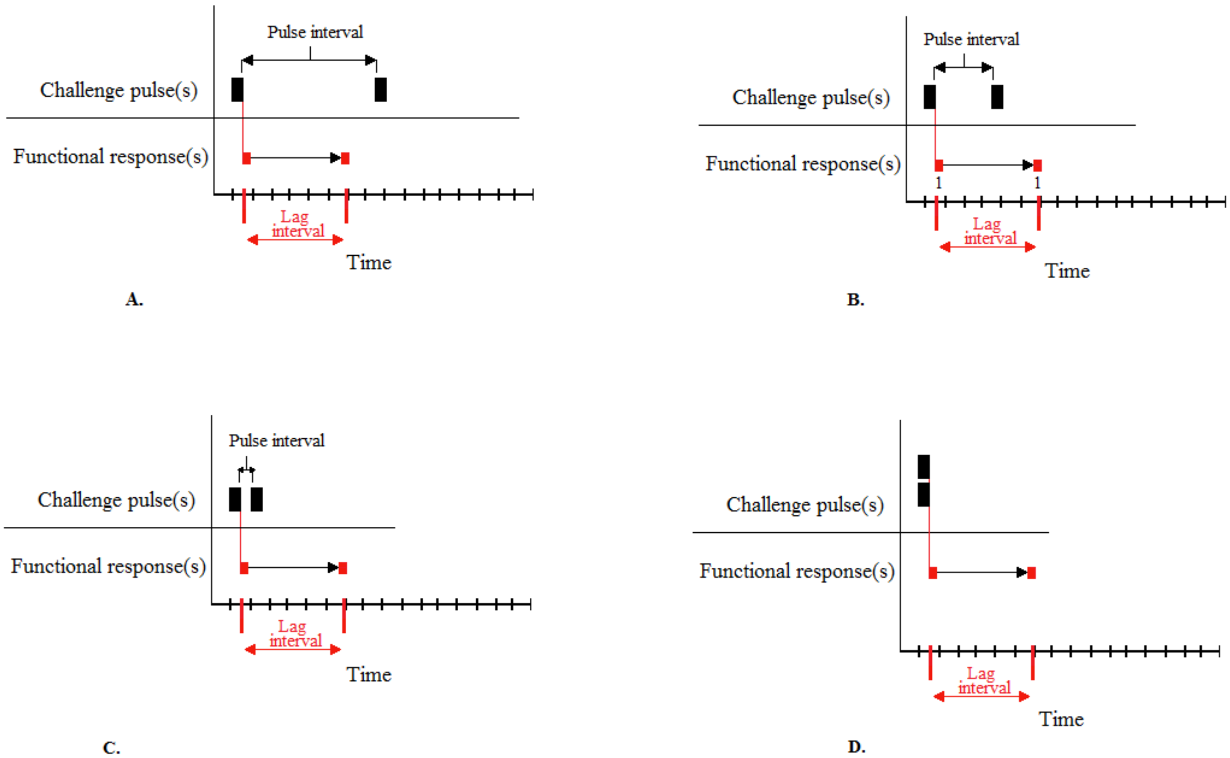

Figure 1.9. Shows the relationship between challenge pulses and a functional response interval, the pulse interval and lag interval, respectively. Here we suppose a fixed lag interval for a functional response, and a decreasing pulse interval. **(A)** Note that the lag interval is less than the pulse interval, but eventually **(B)**, **(C)** the pulse interval decreases to a value less than the lag interval. **(D)** Concurrent occurrence of two pulses. Note that this illustration is not drawn to scale.

Thus, the drift rate is directly proportional to the intensity of challenge:

$$\text{Drift rate} \propto I$$

Total number of orders, η affected by changes in s-value of primary property:

We suppose that all properties of a given order undergo identical rates of change in their respective s-values. On the contrary, properties of different orders undergo differing rates of changes in their respective s-values. With changes to s-values of those properties most proximal to primary property (lower order), occurring earlier than those of more distal, higher order properties, along the drift path. We can think of this as a wave of changes propagating outwards from the primary property to the η^{th} order. With, **η** being the number of orders for the given system.

Since, for a given system, each property shares unique relationships with other properties, direct effects of changes in the state of one property may not be the same as that affecting another. That is, the nature and number of the most directly affected properties may differ from property to property. Whereas a change in s-value of one property may directly affect a larger quantity of properties, a change in s-value of another may directly affect a smaller quantity of properties. We can conclude that the former has a greater **component ordinal number** than does the latter.

In the same way, if we suppose that the **average component ordinal number** for all properties within a given order is greater than that of a second property, then we can suppose that the ordinal drift number of the given order is also greater for the former. Suppose the average component ordinal number is the same for all orders of the system, we can conclude that for a given property number, the former would have fewer orders than the latter. Since the s-values of lower order properties are altered before those of higher order properties, it should follow that the property that affects the fewest number of orders affects the same number of properties at a shorter time interval. Thus, the rate of drift from challenge at the former property would be greater than that of the latter. Thus, the drift rate is inversely proportional to the number of orders for the property.

$$\text{Drift rate} \propto \frac{1}{\eta}$$

Note that η is specific for the affected primary property. We refer to those properties that affect extremely high drift rates, by way of affecting the fewest number of orders, as **critical properties**.

The drift rate can therefore be expressed as:

$$\text{Drift rate} = k \cdot \left(I \cdot \frac{1}{\eta}\right) \tag{18}$$

Where,

k = Proportionality constant

Substituting for I in equation 18

$$\text{Drift rate} = \frac{(\tilde{N} - N)}{(t_{d_f} - t_{d_i})} = \frac{k \cdot \left[Y + \left(\frac{Y(n-1)}{e^{Q_{pL}}}\right)\right]}{\eta} \tag{19}$$

Solving for the delay interval:

$$(t_{d_f} - t_{d_i}) = \frac{\eta \cdot (\tilde{N} - N)}{k \cdot \left[Y + \left(\frac{Y(n-1)}{e^{Q_{pL}}}\right)\right]} \tag{20}$$

First measure of systemic failure: Delay-lag interval quotient, Q_{dL} as a measure of the inverse likelihood of failure.

Let us suppose that both deviation and functional responses follow immediately after presentation of a challenge stimulus. The delay and lag interval were previously defined. Here we define a measure of the relative length of time between these intervals, the quotient of delay and lag interval, $\boldsymbol{Q_{dL}}$, as the ratio of delay to lag interval:

$$Q_{dL} = \frac{(t_{d_f} - t_{d_i})}{(t_{L_f} - t_{L_i})}$$

We use this as a measure of the likelihood that a regulator system does ***not*** reach failure state, $\boldsymbol{T_1}$. In other words, $\boldsymbol{T_1}$ is the **inverse likelihood of systemic failure**:

$$T_1 = \begin{cases} 0, & Q_{dL} < 1 \\ 1, & Q_{dL} \geq 1 \end{cases}$$

If the length of lag interval is **greater than** the delay interval, then the inverse likelihood of failure, $\boldsymbol{T_1}$ is:

$$T_1 = 0$$

This is the least likelihood that the system will *not* reach failure state following a challenge with a given intensity. In other words, this is the greatest likelihood that the system will reach a failure state. Refer to **figure 1.0A** for illustration. On the other hand, if the length of lag interval is **less than** or **equal to** the delay interval, then the inverse likelihood of failure, $\boldsymbol{T_1}$ is:

$$T_1 = 1$$

This is the greatest likelihood that the system will *not* reach failure state following challenge of a given intensity. In other words, this is the least likelihood that the system will fail following challenge presentation. Refer to **figure 1.0B** and **C** for illustration.

We can conclude then that in order to prevent a regulator system from reaching failure state, the required functional response(s) must affect the appropriate YFR before the delay interval elapses. In other words, the length of lag interval must be less than or equal the delay interval. The likelihood of failure is therefore determined by the relative rates of deviation and functional responses.

Second measure of systemic failure: A measure of the inverse predisposition to failure.

The reason for two measures stems from ambiguity of a measure of likelihood ($\boldsymbol{T_1}$). This is a binary measure, and thus fails to appropriately differentiate between two Q_{dL} values greater than 1. For example, suppose we aim to compare the rates of two Q_{dL} values: Q_{dL_1} and $Q_{dL_2}$with:

$$Q_{dL_1} > 1$$

and

$$Q_{dL_2} > 1$$

but

$$Q_{dL_1} \ggg Q_{dL_2}$$

The inverse likelihood of failure for both quotient values is:

$$T_1 = 1$$

However, there is no information given on the state of the system following a challenge and YFR. The effect of Q_{dL_1}being greater than Q_{dL_2} is therefore not accounted for. Secondly, in the case of a Q_{dL} value equal to unity, that is:

$$Q_{dL} = 1$$

the inverse likelihood of failure is considered to be the same as for a Q_{dL} value far greater than unity, even in lieu of the fact that, for the Q_{dL} value of unity, an appropriate YFR occurs just at the moment when a change in the last property is to be affected. That is, the system has approached the point of failure.

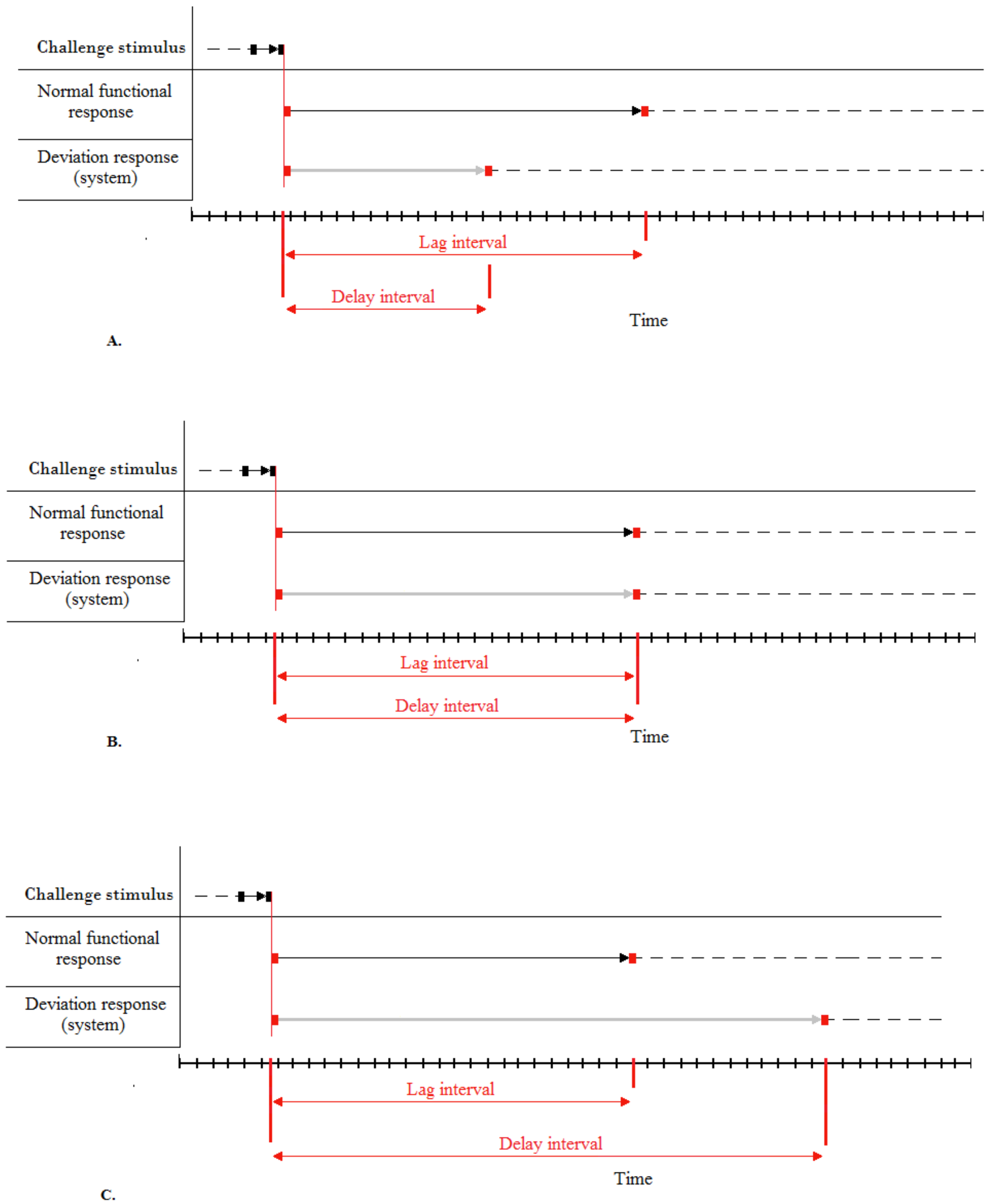

Figure 1.10. Compares interval lengths between delay interval (gray arrow bounded by red boxes) and lag interval (black arrow bounded by red boxes). **(A)** Depicts a situation wherein the lag interval is greater than the delay interval, thus the rate of drift (and therefore deviation response) is greater than the rate of functional response and availability of appropriate YFR. **(B)** Depicts a situation wherein the lag interval equals the delay interval, thus the deviation response occurs at the same rate as functional response and availability of appropriate YFR. **(C)** Depicts a situation wherein the lag interval is less than the delay interval, thus the rate of deviation response is less than the rate of functional response and availability of appropriate YFR. Note that this illustration is not drawn to scale.

To assess the consequence of such differences on the state of the system, we introduce a second measure, an **inverse predisposition to failure**, $\boldsymbol{T_2}$ which assesses the state of a system following both initial challenge and functional response. We previously defined a measure of the distance to failure as the difference between the property number and the drift number. We can gauge the distance to failure as the ratios of the difference between property and drift number to the drift number. That is,

$$\left(\frac{\tilde{N} - N}{\tilde{N}}\right) = \left(1 - \frac{N}{\tilde{N}}\right)$$

Note that when

$$\frac{N}{\tilde{N}} = 0$$

Then, $N = 0$,

And

$$\left(1 - \frac{N}{\tilde{N}}\right) = 1$$

Thus the system has the highest inverse predisposition to failure. On the other hand, when

$$\frac{N}{\tilde{N}} = 1$$

Then, $N = \tilde{N}$,

And

$$\left(1 - \frac{N}{\tilde{N}}\right) = 0$$

Thus the system is of the least inverse predisposition to failure. Note that unlike the first measure, the second measure can range from zero to unity, with the minimum and maximum predisposition values occurring at zero and unity respectively. That is:

$$T_2 = 0, \quad if \ \left(1 - \frac{N}{\tilde{N}}\right) = 0$$

$$T_2 = 1, \quad if \ \left(1 - \frac{N}{\tilde{N}}\right) = 1$$

If used alone, this measure gives no information on the delay interval, which carries information on the intensity of the inciting stimulus. Thus, we resolve the issue by taking an **aggregate measure of failure**, ב:

$$ב = 1 - (T_1 \cdot T_2) \tag{21}$$

Conclusion

From the above discussions, we introduce a set of assumptions that would guide how we approach future work(s).

1. **The ultimate significance of biological functions is prevention of failure of the system:**
   To demonstrate this, we have repeatedly compared two hypothetical systems, obligate conformers and regulators, with the former described as a system without functional responses, and thus no YFRs. Therefore, for such a system, the aggregate measure of failure depends on the nature and intensity of challenge. On the other hand, the regulator, which only differs from the conformer by its functional response and YFR capabilities, would have a lower aggregate measure, than its conformer counterpart. Thus, the significance of these biological functions to the systems that possess them are their ability to prevent failure of these systems.

2. **Real biological systems attempt the functionality of ideal regulator systems:**
   An **ideal regulator system** is a system that is constantly at zero-point state: irrespective of nature, intensity, or spontaneity of challenge presented. Thus, the inverse likelihood of failure is always at a maximum for an ideal regulator. Since the increase in intensity of challenge results in a decrease in delay interval, it should follow that for a constant lag interval, the Q_{dL} ratio decreases, hence a decrease in inverse likelihood of failure. It must follow then that for an ideal regulator to maintain systemic zero point state, even with such varying delay intervals, it must affect functional responses with lag intervals always less than delay intervals. Thus, Q_{dL} is always greater than unity irrespective of the extent of decrement in delay interval. A second attribute of an ideal regulator is that the inverse predisposition to failure following a subsequent challenge is at a maximum, since ideal regulators maintain their systemic zero-point state. Thus, the aggregate measure is at a minimum value:

$$\beth = 1 - (T_1 \cdot T_2) = 0$$

   As stated in the opening, attempt refers to initiation of phenomena that may or may not affect a defined outcome. Functionality refers to the effectiveness of all functional responses; which is the extent to which all functional responses prevent changes in s-values of their respective properties. Since a zero-point state is maintained for all properties of an ideal regulator, irrespective of the nature of challenge and intensity presented, it should follow that this is the maximum functionality that can be attained. It is obvious that real systems do not attain such functionality, however we assume that functional responses of real systems approach, but do not reach, this maximum.

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Author’s comments

The use of mathematics was to serve three ends: For formality; a supplement to the limits of the English language (as a descriptive tool); and most of all, for the intended quantification schematic. My apologies in arrears for any errors that may be present in the mathematical formulations and overall outline: for I am not thoroughly versed in the conventions of the field (mathematics). Please notify the corresponding author if such errors are appreciated and limit comprehension of the material.