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 system 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 the system from reaching failure state. We also define such functional responses as properties of the system. We discuss determinants of the rate of- and measures of systemic failure. We conclude with two assumptions on the principal significance of biological phenomenon.

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, 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 or facilitate events that may occur or may not occur, respectively, in an 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 field 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 are inclined to assume certain state(s) of being than they do others; and if left unaffected by external factors, will tend to occupy such homeostatic state(s). Thus,

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homeostatic state(s) assume the role of the "preferred" state(s). For such systems, deviations from homeostasis can therefore be considered temporary as the system responds in a way that favors re-establishment of said state(s). For simplicity, we shall consider homeostatic state(s) a solitary 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 effects of individual homeostatic variables on other variables of the system in question. Neither does it yield reconciliation of effects of homeostatic variables on the system as a whole. These shortcomings limit both its analytical power and usage as a descriptive tool for processes of biological systems. Thus a revision or addenda is required. Here we introduce a gauge model for biological systems.

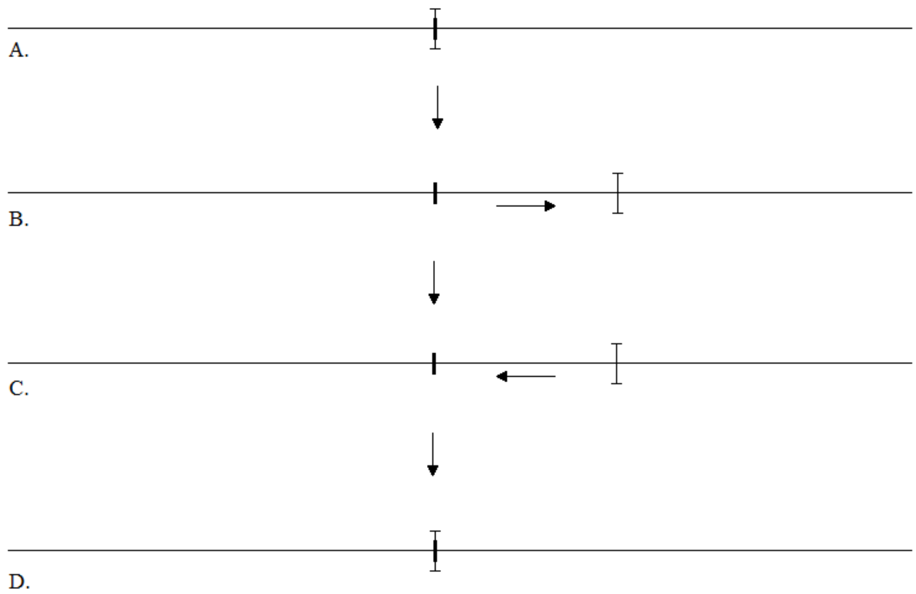

Figure 1.1. Depicts the sequence of changes following disturbance at a single variable of a biological system. (**A**) The variable is shown to initially occupy a preferred state (homeostasis). (**B**) Disturbance at this variable results in change from the initial preferred state to an arbitrary state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

Defining the system and states of its properties

1. We apply two definitions to a biological system: point and set definitions. **Point definition** of a biological system, $\hat{S}$, holds that: system $\hat{S}$ is a defined property of a set that consists of additional properties distinct from $\hat{S}$. In addition, it [system $\hat{S}$] is our primary focus and all occurrences or phenomena outside this focus are considered the surroundings with respect to $\hat{S}$. Also, all observations are made in relation to the

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point ŝ. This definition acknowledges the defined system as a property of a second but undefined larger system, $\hat{\mathbf{S}}_{\mathbf{undefined}}$.

$$\hat{\mathbf{S}}_{\text{undefined}} \equiv \{\dots, \hat{s}, \dots\}$$

Set definition of a biological system, ŝ, holds that the system is a defined set of properties, X, (system-related information), and the set includes only those properties that define ŝ.

$$\hat{s} \equiv \{X_1, \dots, X_{\tilde{N}}\}$$

All phenomena involving these properties are considered to occur with respect to ŝ, and these phenomena are the challenges to- and responses of the system. We suppose the defined system is a collection of all its properties. In addition, we shall consider the total number of properties, $\tilde{N}$, for a system as both a constant value and unique to the system in question. That is, two systems may have completely different values for $\tilde{N}$, but the value for each system remains the same. By so doing, we exclude considerations of emergent properties, as this complicates the intended simplification.

It may seem unreasonable to assign incongruent phenomena into a single set. For example, temperature and hydrogen ion concentration are distinct aspects, but based on the proposed approach, we consider both 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.

2. We suppose that each property can exist in any one state of a number of potential states at any given moment; with most similar states juxtaposed. We suppose that we can quantify the state of a property**,** and we term this quantity the **state value**, x_i of the property (**s-value**). With each state of a property having one and only one value, and that no two or more states of the same property can have the same value. Thus, we shall represent the state of the property in terms of the state value, x_i.

   A suitable measure of s-value is the relative distance, Δx^{o}, between a reference initial state and an arbitrary state; where the distance is the number of intervening states between the states in question. For our interests, we shall consider the reference initial state of a property its **zero-point state**; where 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 that, in its initial state, the property is unaffected by external influences. We designate the s-value of the zero-point state as x_0. Therefore, x_0, represents the *zero* of the range of possible states, and is read: the

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s-value of the property when at zero-point state. The subscript represents the value of the state occupied by the property. Thus the value of the zero-point state is:

$$x_0 = 0$$

Also, since the distance, Δx^{o}, is relative to the zero-point state of the property, it should hold that the s-value of the property equals the distance of the given state from zero-point. That is,

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

We, therefore, can use these interchangeably. We define the minimum distance between states of the property, $\Delta\breve{\mathbf{x}}$, as equivalent to the absolute value of the difference between the s-value of the zero-point state, x_0, and the s-value of the state most proximal to x_0 , x_1.

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

$$= |1 - 0|$$

$$= 1$$

Thus, the s-value of the property when at the 1st most proximal state:

$$\Delta x^{o} = \Delta\breve{\mathbf{x}} = 1$$

The absolute value of the difference between the s-value of the zero-point state, x_0, and the s-value of the state most proximal to x_0 can also be written such that the s-value of the zero-point is taken into account:

$$\Delta x^{o} = x_0 + \Delta\breve{\mathbf{x}} = 1$$

The s-value of the property when at the 2nd most proximal state to x_0 is:

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

The s-value of the property when at the i^{th} most proximal state to x_0 is:

$$\Delta x^{o} = x_0 + i\Delta\breve{\mathbf{x}} = i \qquad (1)$$

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

$$0 \leq i \leq z$$

z is the s-value of the least proximal state to x_0. Note that z can vary for different properties. Thus, the s-value of a property can assume any one of the following contiguous s-values arranged in order from x_0 to least proximal state to x_0.

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

3. The s-value of the property when at an arbitrary state is therefore the sum total of unit distances. Thus, the s-value of the property when at the q^{th} most proximal state to x_0 is,

$$\Delta x^{o} \stackrel{\text{def}}{=} x_0 + \sum_{i=1}^{q} (\Delta \breve{\mathbf{x}})_i \tag{2}$$

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

$$= x_q$$

$$= q$$

Where, q is a specific value within the given interval of possible s-values for the given property.

We define a change in s-value, Δx, of a property as equivalent to the difference between the s-value of the state of the property prior to- and the s-value of the state of the property following disturbance by factors external to the property. As was previously stated, the state of the property prior to challenge presentation is the zero-point state. Thus, the change in s-value, Δx, that follows challenge presentation is the change from zero-point to an arbitrary state which is a function of the intensity of presenting challenge stimulus. Thus for this work, the stated change, Δx, equals the relative distance between states, Δx^{o}, of the property. That is,

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

We therefore determine the change in s-value from zero-point to the state with s-value of x_q by substituiting Δx for Δx^{o} in equation 2.

$$\Delta x = x_0 + \sum_{i=1}^{q} (\Delta \breve{\mathbf{x}})_i \tag{4}$$

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

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

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

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

Where,

$$i \neq 0$$

And

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

4. We suppose that states of a given property can be approximated as either discrete or a continuum of states. However, equations presented above are only for s-values for discrete states. We attempt to present an all inclusive representation for s-values for both discrete and continous states. We express $\Delta\breve{\mathbf{x}}$ as:

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

Substituting unity for κ

$$\Delta\breve{\mathbf{x}} = \sum_{b=1}^{1} \left(x_{\left(b/_{1}\right)} - x_{\left(b-1/_{1}\right)} \right)_b$$

$$= |x_1 - x_0|$$

Therefore, we rewrite equation 4 for a property with discrete states:

$$\Delta x = \lim_{\kappa \to 1} \sum_{i=1}^{q} \sum_{b=1}^{\kappa} \left(x_{\left(b/_{\kappa}\right)} - x_{\left(b-1/_{\kappa}\right)} \right)_{b,i} \tag{5}$$

$$\cong \sum_{i=1}^{q} \sum_{b=1}^{1} \left(x_{\left(b/_{1}\right)} - x_{\left(b-1/_{1}\right)} \right)_{b,i}$$

If, however, we suppose a continuum of states of the property of interest, then

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

Where,

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

We rewrite equation 4 for a property with continuous states:

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

We generalize that:

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

Figure 1.2. Depicts a gauge scale for measure of the extent of change in the s-value of a property. 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 the minimum changes as the absolute value of the difference between the zero-point and most juxtaposed state of a given property.

Overview on challenge stimuli

5. We suppose constant interactions between the system and its surroundings, 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). In the context of this paper, the surroundings are viewed as a single entity consisting of multiple challenges, 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 surroundings. Hence, we can define a challenge from a defined property, and a property from a defined challenge. Henceforth, we shall refer to challenges as stimuli.

We suppose that stimuli are externally derived, and therefore are not properties of the defined system. On the other hand, we suppose the relationship between stimuli and the surrounding is analogous to that of a property and the system to which it is defined. Hence a stimulus, in its own right, is a property of the surrounding environment, and defines the environment. A given stimulus is said to affect a

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change in state of the system by its effect(s) on the state of a property. We term such a property the **primary property**. For this work, we shall consider individual stimulus and therefore individual primary property; where the initial effect of a stimulus on the defined system is a change in state of the primary property from an initial state , x_0, to an arbitrary state which is a nonzero-point state.

Failure state

6. 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 stimuli

We suppose that following presentation of a 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 affected properties. To address the above responses, we assume two hypothetical biological systems based on their response capacities following stimuli. 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 stimuli on obligate conformers: A delta drift hypothesis for deviation response towards failure state

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

$$P_0 \neq P_i$$

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An example is the change in temperature (primary property) of a system following a stimulus –increase in ambient temperature. 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 stimulus, and therefore we suppose that the unadulterated manifestations of a stimulus can be observed.

An increase in ambient temperature would result in change in the s-value of the temperature property of the system, such that the temperature of the system becomes elevated. If ambient temperature is increased further, the internal temperature of the system should also increase in 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 hold 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 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 reactant 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 temperature 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

[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 reactant substrate/product content.

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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 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 stimulus effect–change in state of a primary property–provokes concomitant state changes at other properties of the system. We shall refer to this phenomenon as **delta drift.**

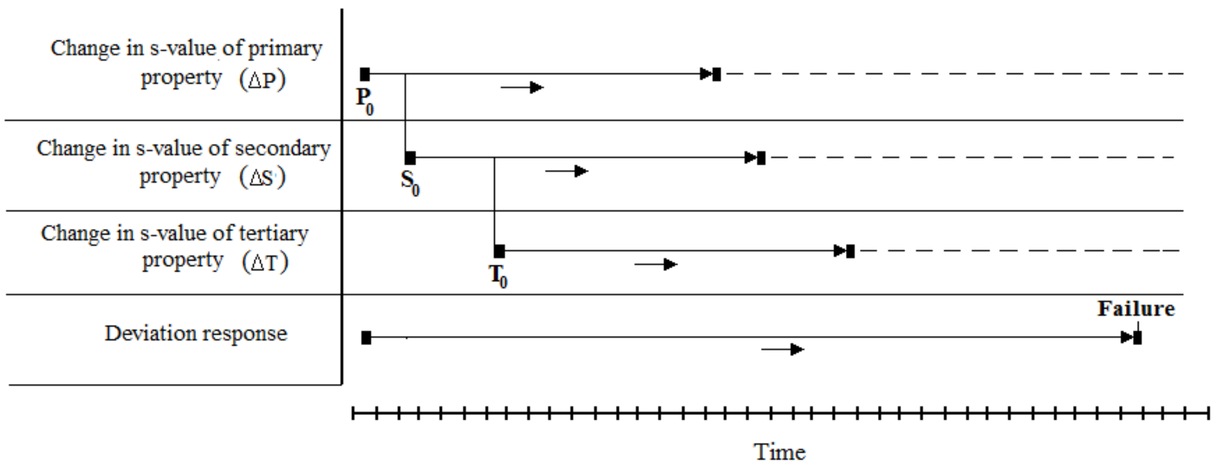

Figure 1.3. Illustrates the delta drift hypothesis. For an obligate conformer, a change in a primary property (ΔP) is shown to incite change in a secondary property (ΔS), and ΔS in turn incites change in a tertiary property (ΔT), up until the entire set of systemic properties are affected. Note that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

Thus, a change in the s-value for a primary property can directly incite changes in s-values of multiple properties (secondary properties). These secondary properties may themselves each incite changes in s-values of 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 involves s-value changes at multiple properties (as a result of a primary change) should result in change in state of the system. Next, we describe in detail the relationship between property and systemic states.

Drift number as a measure of the systemic state:

8. We suppose that, at any given moment, the system can exist in any one state of a number of potential states. We suppose that we can quantify the state of the defined system and we term this quantity the **state value**, N_j, of the system (s-value). With each state of the system having one and only one value, and that no two or more states of the system can have the same value. Thus, we shall represent the state of the system in terms of the s-value, N_j.

According to the delta drift hypothesis, progressive deviation of a system to failure state is related to the number of properties whose states are altered from their respective zero-point states. We define the **drift number, $\boldsymbol{N}$**, as the total number of properties of the defined system whose states are altered from zero-point state. The closer the drift number is to the total number of properties of the system (property number, $\tilde{\mathrm{N}}$), 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. Thus, a reasonable measure of the state of the system is the drift number. That is,

$$\boldsymbol{N} = N_j$$

9. We define the zero-point state of the system, N_0, as the state of the system when all properties are at respective zero-point states. In other words, the zero-point state of the system is the state of the system prior to presentation of stimulus. By assuming this as the state of the system we are supposing that at this initial state, the system is unaffected by external influences. Thus, the concept of zero-point state of the system is tantamount to the concept of homeostatic state. As was for properties, the subscript represents the value of the state occupied by the system. Thus,

$$N_0 = 0$$

10. We define the **standard change,** ΔN^o, in s-value of the system as the difference between the s-value of an initial zero-point state and s-value of an arbitrary state. Also, since ΔN^o is relative to the zero-point state of the system, it should hold that the standard change in s-value of the system equal the s-value of the system. That is,

$$\Delta N^o = N_j$$

We define the **unit difference**, $\Delta\breve{\mathbf{N}}$, between s-values of states of the defined system as equivalent to the absolute value of the difference between the s-value of the zero-point state, N_0, and the s-value of the state of the system when only one property occupies a nonzero-point state. In other words, when the system occupies a state with an s-value of N_1.

$$\Delta\breve{\mathbf{N}} = |N_1 - N_0|$$
$$= |1 - 0|$$
$$= 1$$

The standard change in s-value of the system when at N_1:

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$$\Delta N^{o} = \Delta\breve{\mathbf{N}} = 1$$

The absolute value of the difference between the s-value of the zero-point state, N_0, and the s-value when the system occupies a state with an s-value of N_1 can also be written such that the s-value of the zero-point state is taken into account:

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

The standard change in s-value of the system when two properties have non

zero s-value is:

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

The standard change in s-value of the system when j properties have non

zero s-value is:

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

Where, j is the value for an arbitrary state and is of the given interval of s-values:

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

As noted, Ñ is the property number for the defined system. Thus, the s-value of the system can assume any one of the following contiguous s-values arranged in order from the value at zero-point state of the system to the value of the state when all properties of the system are at nonzero-point states.

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

11. The s-value of an arbitrary state of the system is therefore the sum total of unit differences. Thus, the standard change in s-value of the system to the m^{th} state is,

$$\Delta N^{o} \stackrel{\text{def}}{=} N_0 + \sum_{j=1}^{m} (\Delta\breve{\mathbf{N}})_j$$

$$N_0 + \sum_{j=1}^{m} \left(\Delta\breve{\mathbf{N}}\right)_j = N_0 + (|N_1 - N_0|)_1 + \cdots + (|N_m - N_{m-1}|)_m \tag{8}$$

$$= N_m$$

$$= m$$

Where, m is a specific value within the given interval of possible s-values for the defined system.

12. We define change in s-value of the defined system, ΔN, as equivalent to the difference between the s-value of the state of the defined system prior to- and following disturbance by factors external to the defined system. For this analysis, we suppose that the state of the system prior to stimulus presentation is the zero-point state. Thus, ΔN that follow stimulus presentation is the change from s-value of zero-point to s-value of an arbitrary state which is a function of the intensity of the stimulus. Thus the change in s-value of the system, ΔN, equals the standard change in s-value of the defined system, ΔN^{o}. That is,

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

We, therefore, can determine the change in s-value of the system from zero-point to the N_m state by substituiting ΔN for ΔN^{o} in equation 8.

$$\Delta N = N_0 + \sum_{j=1}^{m} (\Delta \breve{\mathbf{N}})_j \tag{9}$$

Unlike the standard change in s-value, the change in s-value, ΔN, of the defined system can be determined for any two nonzero-point states of the system. For example, the change in s-value of the system from the j^{th} to the $(j+1)^{th}$ state of the system is:

$$\Delta N = N_0 + \big((j+1) - j\big)\Delta N^{o}$$
$$= \Delta N^{o}$$

Where,

$$j \neq 0$$

And

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

Order number and the state of the defined system:

13. We defined the delta drift as involving a series of changes in states of properties; with such changes following change in state(s) of [an] initial property(s). For example, a change in the state of a primary property may directly result in changes in respective states of additional properties (secondary properties). In turn, changes in respective states of secondary properties may directly result in changes in respective states of tertiary properties. Refer to **Figure 1.4** for an illustration. Based on this scheme, it is possible that not all properties of a system are directly affected by change at a primary property. In essence, there is a network structure to the

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relationships between properties of the system. For this reason, we categorize each affected property into an order-based schematic.

14. Assuming a single primary property. We consider the primary property as occurring at the lowest order. In relation to secondary property, we consider the primary property as occurring at a lower order. In relation to the primary property, we consider secondary properties as occurring at a higher order. We can apply the same logic for all other properties: if change in s-value of a property directly affects change in s-value of another property, then the former property can be said to incite the latter. We designate the former a **lower order** property, and latter, a **higher order** property.

We consider the primary property as occupying a 0^{th} order. We consider all secondary properties for a given primary property as occupying a 1^{st} order. We consider all tertiary properties as occupying a 2^{nd} order. The pattern of ordering may continue up to the highest possible order, **η**; where the number of properties for **η** orders is the property number, Ñ. Thus, for **η** orders, the sequence of orders is:

$$\{0, \dots \dots, \boldsymbol{\eta}\}$$

Where **η** is a function of the given primary property. Note that even if the value of **η** differs for different primary properties, the number of properties, Ñ, is a constant for the defined system. Although we suppose that a change in state of a given property can directly affect changes in states 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 the state of only one property. For instance, a given tertiary property can only be affected by state changes of a single secondary property, and state changes of a given quaternary property derives from state changes of a single tertiary property. This, again, is done for simplicity.

15. We define an **ordinal drift number,** u_{ω} as the total number of affected properties, u, of a given order, ω. For example, the ordinal drift number for the first order, u_1, is the sum total number of secondary properties with altered states –from an initial zero-point state – following effects of stimulus at a primary property**.** The ordinal drift number for the second order, u_2, is the total number of tertiary properties whose states are directly affected by changes in states of all secondary properties. Since we assume that the zeroth order consist of a single [primary] property, the ordinal drift number of the zeroth order, u_0, is therefore:

$$u_0 = 1$$

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The drift number, $\boldsymbol{N}$, can therefore be expressed as 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:

$$\boldsymbol{N} = u_0 + \sum_{h=1} u_h = u_0 + \cdots + u_h + \cdots$$

Since,

$$\boldsymbol{N} = N_j = \Delta N$$

We can therefore express the change in s-value of the system from zero-point state as:

$$\Delta N = u_0 + \sum_{h=1} u_h = u_0 + \cdots + u_h + \cdots \qquad (10)$$

Revised definition of failure state:

16. From the information presented above, the change in s-value of the system from zero-point to failure state is:

$$\Delta N = u_0 + \sum_{h=1}^{\eta} u_h = u_0 + \cdots + u_h + \cdots + u_\eta = \tilde{N} - 0$$

Drift segment and path:

17. 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 1.5 for an illustration of drift segment and path.

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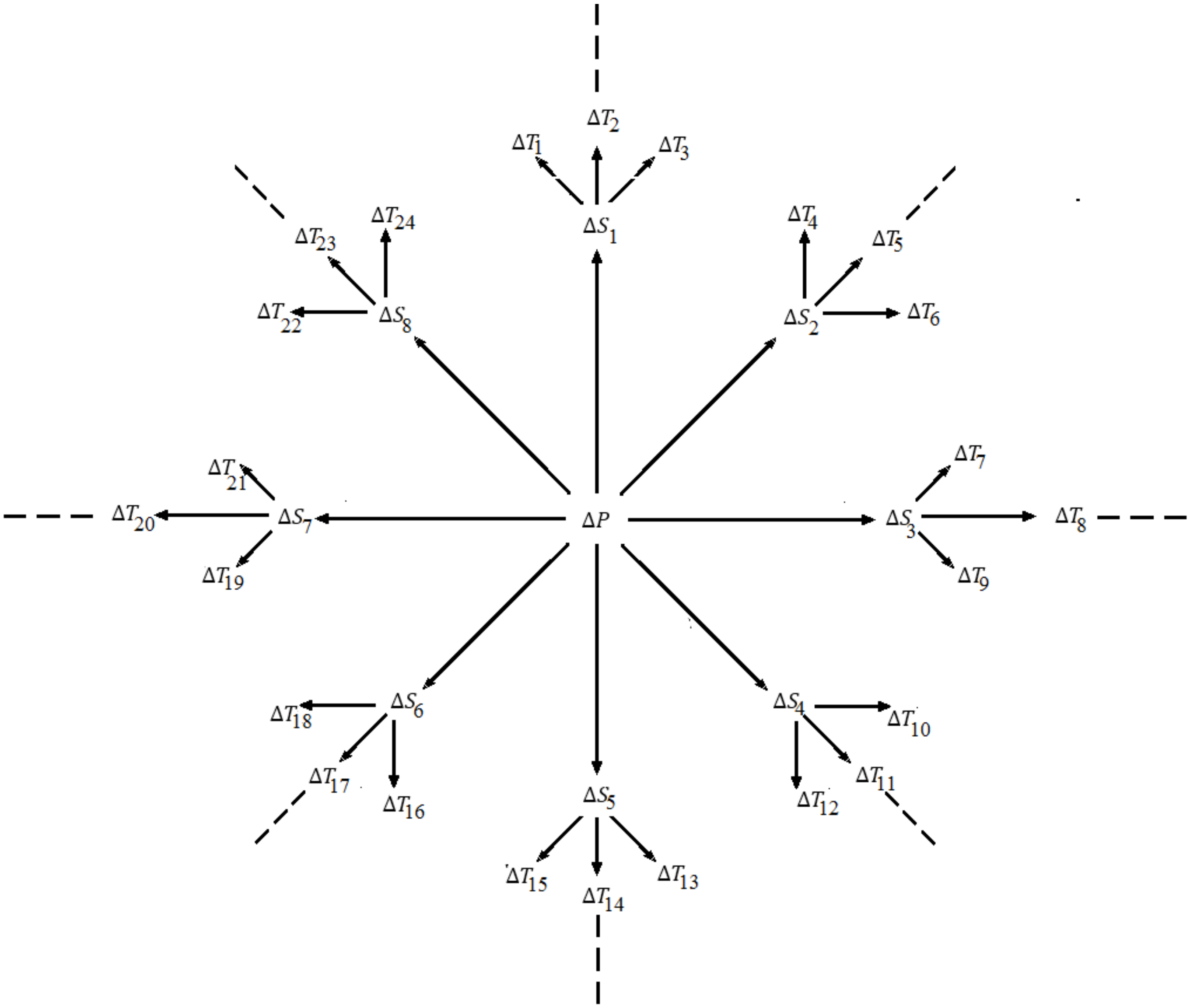

A.

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B.

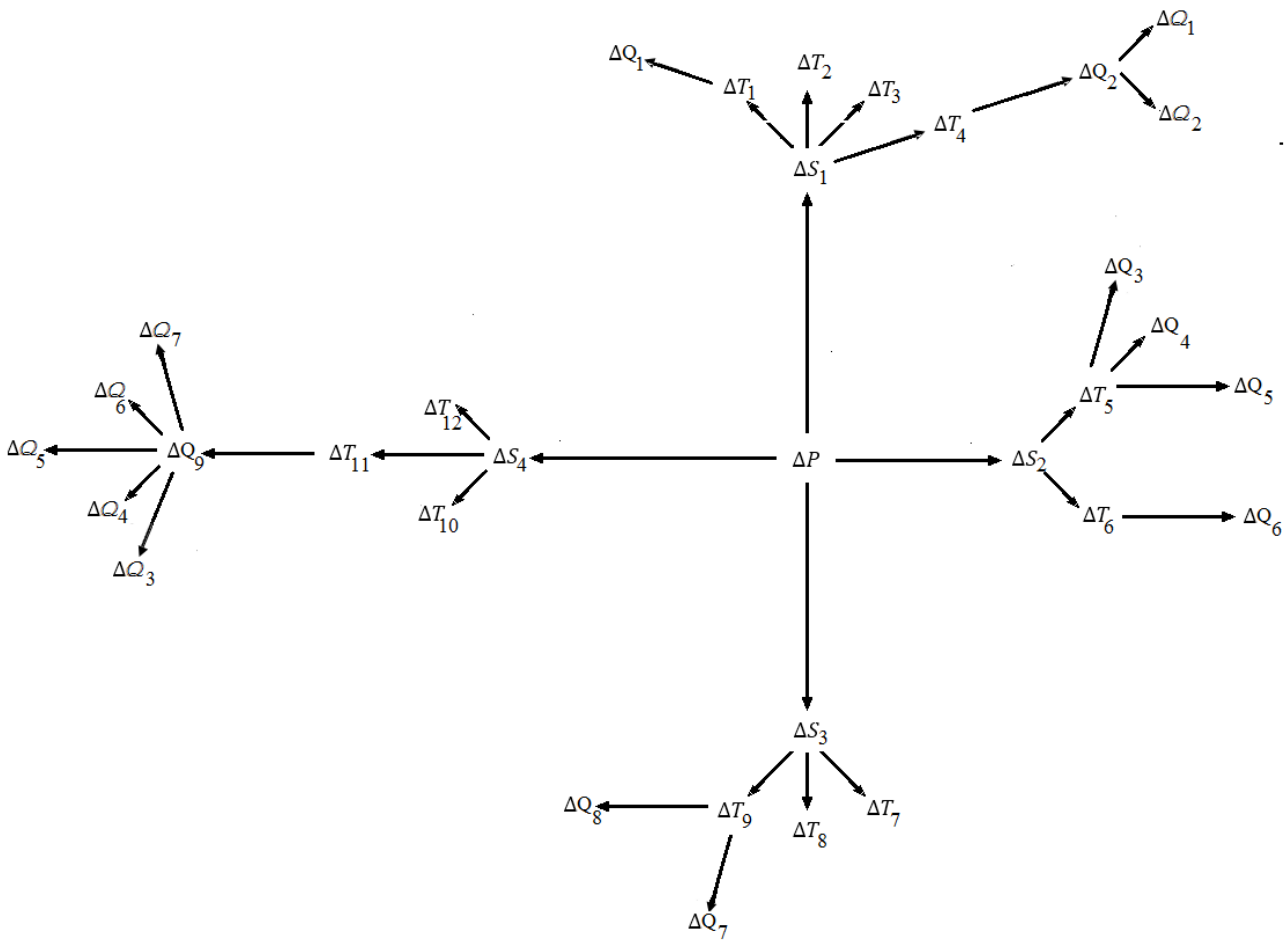

Figure 1.4A. A 2-dimensional rendition of the delta drift hypothesis. Unlike figure 1.3, it shows the series of changes in states of properties that can originate from stimulus presentation at a single [primary] property of the system. It is important to note that although the figure shows symmetric changes at non-primary properties, there is no requirement that this must be the case. That is, changing states of 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 linkage of properties may occur. For both illustrations, observe the number designations given to each affected property, we employ this technique as a means of property “book-keeping”.

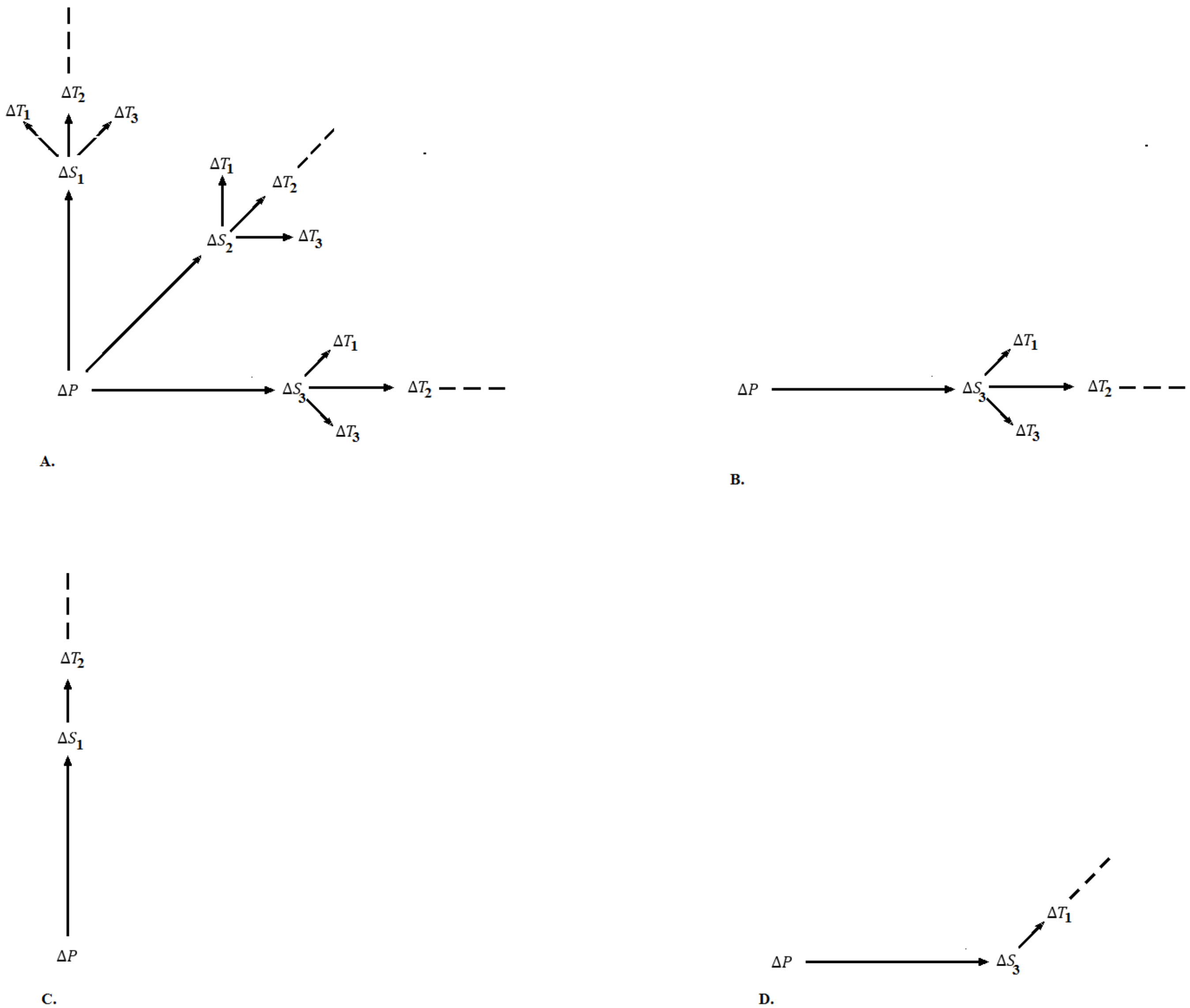

Figure 1.5. An illustration of a drift segment (**A** and **B**), and drift paths (**C** and **D**) for **figure 1.4A**.

Effects of stimuli on obligate regulators: Functional responses:

18. Here we define a counterpart to the obligate conformer, an obligate regulator, as a biological system with a capacity to elicit, at least a single **functional response**, following deviation of both states of properties and defined system. Hence, for the obligate regulator system, all deviation responses are followed by (or occur concurrently with) at least a single concomitant functional response.

    The output of a functional response, its **yield,** attempts at preventing from reaching failure state. Thus, functional response(s) prevent the drift number from reaching the property number. Henceforth we refer to the yield, as the **yield of functional**

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

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

Note,

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

Since functional responses attempt to prevent from reaching 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 towards failure. Thus, we can conclude that YFRs affect a corrected drift change for the system. If the yield is an **appropriate YFR**, then it returns the system to zero-point state. That is, an appropriate YFR results in:

$$N_{\text{po}} = N_0$$

Here we shall define some key features of YFRs:

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

b. 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.

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

d. 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 higher order

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properties with deviation responses that follow from changes in state of said property. Refer to the next section for an explanation of this point.

e. 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 state of a property, x_i, as a mathematical function of the YFR, Y.

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

19. Although we state that deviation in the state of the system can occur following presentation of stimulus, the same does not hold true for reverse changes. That is, a decrease in intensity of stimulus (to conditions prior to stimulus presentation) does not drive the systemic state toward zero-point. Similarly, reversal of deviated states of all other properties does not result from reversal 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 that the system can be returned to its zero-point state. However, as we shall discuss later, functional responses are an exception to this rule.

A functional response at a single (primary) property:

20. For simplicity, we focus on a single functional response and its effect(s) on the system. We shall focus on the property which when affected by a functional response will affect the minimum corrected drift change.

Although a functional response that returns any one property with a non-zero state to zero-point can, in principle, affect the corrected drift change. The degree of such change depends on the number of higher order properties whose respective states are affected following return to zero-point state of the given lower order property.

Thus, if change in state of a property results in deviation (via delta drift) of states of a greater number of systemic properties than a reference, then prevention of further deviation away from zero-point state of this property should result a higher corrected drift change than if change in state of the property results in deviation of states of a smaller number of properties than the reference.

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Of all properties whose states are either directly or indirectly affected by a given stimulus, the primary property affects the maximum number of properties of the system. We arrive at this conclusion from realization that changes in states of all affected properties must have derived from change in state of primary property. Thus, prevention of further deviation from zero-point state of the primary property should prevent further deviation of states of all affected properties. Also, since change in state of primary property incites changes in states of all affected properties, it should also hold that functional responses and appropriate YFRs involving this [primary] property at least result in $\Delta N' = 0$. We shall therefore focus the discourse on presenting stimulus, functional response, and YFR at primary properties.

Functional responses and YFRs as properties of the system:

21. 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 stimulus and change in property state are themselves deviated from their respective zero-point states. These properties can be returned to their respective zero-point states via either one or all of the following means: other functional responses and YFRs; indirect and self-rectifying –by reverting states of properties whose initial state changes incited the functional response; or a combination of these means.

Natural stimulus-functional response pairing:

22. Since a given stimulus affects a system at a single property, and a functional response affects reverse deviation of the state of a single property, it should follow then that for a given property, we can define a stimulus and its functional response(s). By way of their shared relationships to the property, we term these **natural stimulus-functional response pairs**. That is, occurrence of a stimulus is always followed by occurrence of the functional response, as long as the system is an obligate regulator and there is change in state of the given property. If a given stimulus presents, and change in state of a property follows presentation of stimulus, then the natural functional response must also follow in attempts to revert the state of the property to zero-point. If change in s-value of property and functional response, then natural stimulus 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 stimulus and its functional response affect inverse changes in the state of the property. For example, if increase in ambient temperature affects an increase in temperature of the system, and a functional response to the property defined as temperature reduces the s-value of this property, then both increase in ambient temperature and the functional response

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that decreases systemic temperature make up a natural stimulus-functional response pair.

The Rate of delta drift and determinants of the deviation interval

Let presentation of a stimulus at a property of an obligate conformer system occur when drift number of the system is zero, $\boldsymbol{N} = 0$. Let us also suppose that the intensity of the given stimulus is such that it results in deviation from zero-point to failure state. Thus, the rate at which the drift number, $\boldsymbol{N}$, approaches the property number, Ñ, is the ratio of the difference between these measures to the duration of drift. We shall refer to the duration of delta drift toward failure state as the **delay interval**. The delay interval is therefore the interval of time that must elapse for transition from a zero-point state of the system, ($\boldsymbol{N} = 0$), to failure state ($\boldsymbol{N} = \tilde{\text{N}}$), following presentation of stimulus. That is, it is the length of time from the initial change in state of the primary property, t_{d_i} to the moment, t_{d_f}, when a change in states of all properties of the system is affected; with all changes resulting in nonzero-point states at all properties. Thus, the drift rate from zero-point state of the system is:

$$\text{Drift rate} = \frac{(\tilde{\text{N}} - 0)}{(t_{d_f} - t_{d_i})}$$

The drift rate from any given initial state of the system is:

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

Factors that affect the drift rate following presentation of stimulus at a single property are the intensity of presenting stimulus and the number of orders for the primary property.

On the intensity of presenting stimulus:

23. Let us suppose an obligate regulator system, with capacity to rectify systemic state following stimuli. That is, following presentation of stimulus, an appropriate YFR returns both the affected property and system to respective initial zero-point states. It should follow that the corrected drift change, $\Delta N'$, is:

$$\Delta N' < 0$$

We define a **stimulus pulse** as a brief period of stimulus presentation that has the same duration at every presentation. We suppose that presentation of a single pulse is such that it just provokes a quantifiable YFR, albeit indirectly.

We shall quantify the intensity of the presenting stimulus to a primary property

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with respect to the YFR that follows stimulus presentation at the property and attempts reversion of systemic state. Thus, the intensity of a single stimulus pulse can be considered to be equal in magnitude to the resultant YFR that follows the given pulse.

$$Intensity\ of\ stimulus, I, of\ a\ single\ pulse = Y$$

Let us suppose a tandem of n stimulus pulses are presented to an obligate conformer system. Since there are no functional responses for the conformer system, the length of the interval of time between pulses, **pulse interval,** does not determine whether or not the system reaches failure state. That is, following presentation of stimulus pulse(s) 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 stimulus pulses. The intensity of stimulus for n pulses is therefore:

$$Intensity\ of\ stimulus, I, of\ n\ pulses = nY$$

Let us suppose the same tandem of n stimulus pulses are presented to an obligate regulator system. For simplicity, we suppose that following stimulus presentation, sufficient time is allowed for appropriate YFR. In other words, the property must be allowed to return to zero-point state following each pulse and prior to presentation of a subsequent pulse. Hence, the pulse interval must be equal-to or greater-than the lag interval for functional response. We define the **lag interval** as a measure from the moment of initial onset of functional response, t_{L_i}, at the primary property, to the moment at which effects of an appropriate YFR occur, t_{L_f}. Since the system is rectifiable, and thus returned to zero-point state before presentation of a subsequent stimulus pulse, it should follow that effect(s) of each stimulus pulse is isolated from those of subsequent pulses. Thus, the aggregate intensity of such stimulus pulses is equal in magnitude to the intensity of a single pulse.

$$Intensity\ of\ stimulus, I, of\ n\ pulses = Y$$

Let us now suppose gradual reduction in pulse interval, with no change to the length of lag interval. It should hold that with such reductions 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 effect of a preceding pulse is not completely rectified before onset of a subsequent pulse. The degree to which these effects are corrected

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should decrease with decreasing pulse interval. We define a measure, Q_{pL}, as the ratio of pulse interval to lag interval, Q_{pL}.

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

With further reduction in pulse interval, a point at which the pulse interval approaches zero would be reached. When pulse interval equals zero, stimulus pulses would occur simultaneously. Since the pulse interval does not determine whether an obligate conformer system reaches failure state, the intensity of stimulus for n stimulus pulses occurring simultaneously and presented to an obligate conformer system is:

$$Intensity\ of\ stimulus, I, of\ n\ pulses = nY$$

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 stimulus for n pulses occurring simultaneously is:

$$Intensity\ of\ stimulus, I, of\ n\ pulses = nY$$

24. To factor in overlap of stimulus pulses in determination of intensity of stimulus presenting to an obligate regulator system, we define a cumulative factor. The **cumulative factor,** C_f, is a measure of the overlapping effect of stimulus pulses.

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

Since the initial pulse is not preceded by pulse(s), we describe its effect as an initial to which all other effects are added. Thus, for 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:

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

The cumulative intensities of $n\ pulses$ is therefore:

$$Cumulative\ intensity\ of\ n\ pulses = (nY - Y)C_f$$

Substituting for C_f,

$$cumulative\ intensity\ of\ n\ pulses = (nY - Y)e^{-\mathrm{Q}_{pL}}$$

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

Total intensity of n pulses, I, is therefore the sum of intensity of initial pulse and cumulative intensity of n pulses.

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$$I = Y + Y(n-1)e^{-Q_{pL}}$$
$$= Y[1 + (n-1)e^{-Q_{pL}}] \quad (11)$$

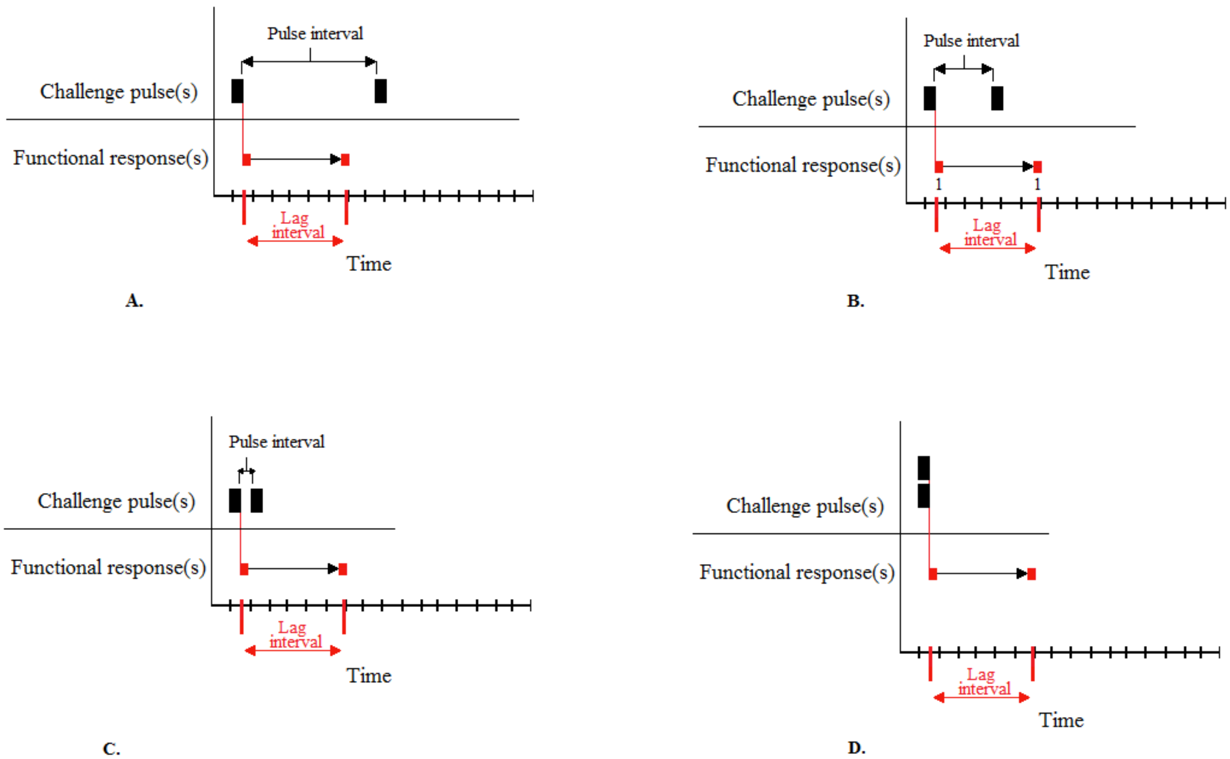

Figure 1.6. Shows the relationship between stimulus pulses and a functional response interval, the pulse interval and lag interval, respectively. Here we suppose a fixed lag interval for a functional response, and a decreasing pulse interval. **(A)** Note that the lag interval is less than the pulse interval, but eventually **(B)**, **(C)** the pulse interval decreases to a value less than the lag interval. **(D)** Simultaneous presentation of two pulses. Note that this illustration is not drawn to scale.

Thus, the drift rate is proportional to the intensity of stimulus:

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

Total number of orders affected by changes in state of primary property:

Let initial changes in respective states of lower order properties occur earlier than those of higher order properties. We can think of this as a wave of changes propagating outwards from the primary property to the highest order which may be η^{th} order for an obligate conformer system. Thus, for the obligate conformer, as η increases so too would the length

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of time required for drift from zeroth to η^{th} order. Thus, the drift rate is proportional to the total number of orders for the given primary property.

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

We refer to those properties that may affect extremely high drift rates, by way of affecting a lower η value, as **critical properties.** The drift rate can therefore be expressed as:

$$\text{Drift rate} = \frac{kI}{\eta} \qquad (12)$$

Where,

k = Proportionality constant

Substituting for I in equation 12

$$\text{Drift rate} = \frac{(\tilde{N} - N)}{(t_{d_f} - t_{d_i})} = \frac{kY[1 + (n-1)e^{-Q_{pL}}]}{\eta}$$

Solving for the delay interval:

$$(t_{d_f} - t_{d_i}) = \frac{\eta(\tilde{N} - N)}{kY[1 + (n-1)e^{-Q_{pL}}]} \qquad (13)$$

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

25. Let us suppose that both a deviation response and at least one functional response follow immediately after presentation of a stimulus. The delay and lag intervals were previously defined. Here we define a measure the quotient of delay and lag interval, Q_{dL}, as the ratio of delay interval 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 reaches failure state, $\mathbf{T}_1$. In other words, $\mathbf{T}_1$ is the **inverse likelihood of systemic failure**:

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$$\mathbf{T}_1 = \begin{cases} 0, & Q_{dL} < 1 \\ 1, & Q_{dL} \geq 1 \end{cases}$$

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

$$\mathbf{T}_1 = 0$$

This is the highest likelihood that the system will reach failure state following a stimulus of a given intensity. Refer to **figure 1.7A** 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, $\mathbf{T}_1$ is:

$$\mathbf{T}_1 = 1$$

This is the least likelihood that the system will reach failure state following stimulus of a given intensity. Refer to **figure 1.7B** 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 full extent of delay interval. In other words, the length of lag interval must be less than or equal the delay interval.

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

26. The measure of inverse likelihood of systemic failure, is a binary measure and therefore 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

$$Q_{dL_1} \gg Q_{dL_2}$$

The inverse likelihood of failure for both quotient values is:

$$\mathbf{T}_1 = 1$$

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However, there is no information about the state of the system following a stimulus presentation and YFR. That $Q_{dL_1}$is greater than Q_{dL_2} is not accounted for. Secondly, in the case of a Q_{dL} value equal to unity, that is:

$$Q_{dL} = 1$$

the inverse likelihood of systemic failure is considered to be the same as for a Q_{dL} value far greater than unity. However, for the Q_{dL} value of unity, an appropriate YFR occurs just at the moment when a change in states of all properties of the system is to be affected. That is, the state of the system has approximated the failure state.

To assess the consequence of such differences on the state of the system, we introduce a second measure, an **inverse predisposition to systemic failure**, $\mathbf{T}_2$ which assesses the state of a system following both stimulus and YFR. In addition, $\mathbf{T}_2$ gives an indication of how well the system can tolerate a subsequent stimulus at its current state. Hence the term "predisposition". We 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 ratio of the difference between property number and drift number to the property number. That is,

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

Note that when:

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

Then, $N = 0$,

And

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

In other words, the system is <u>least</u> likely to reach failure state if a second stimulus is presented. Onthe other hand, when:

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

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

And

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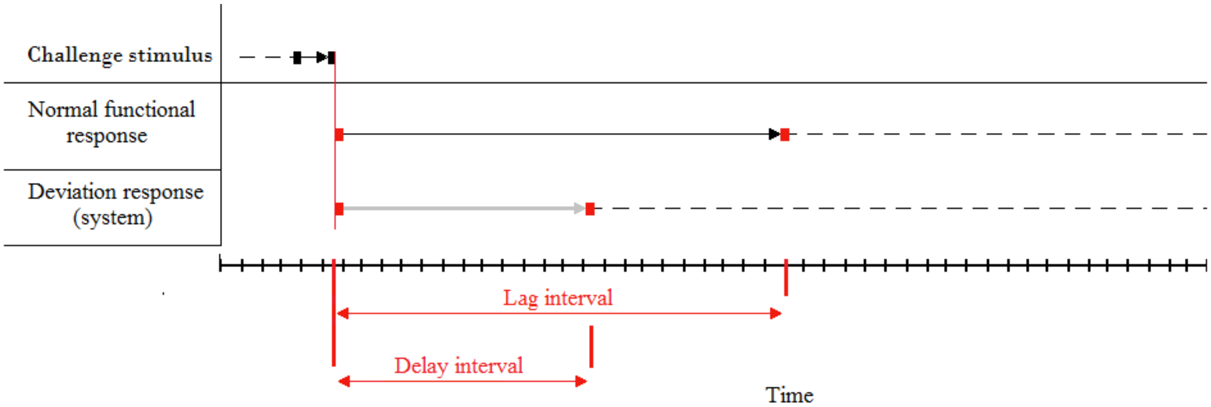
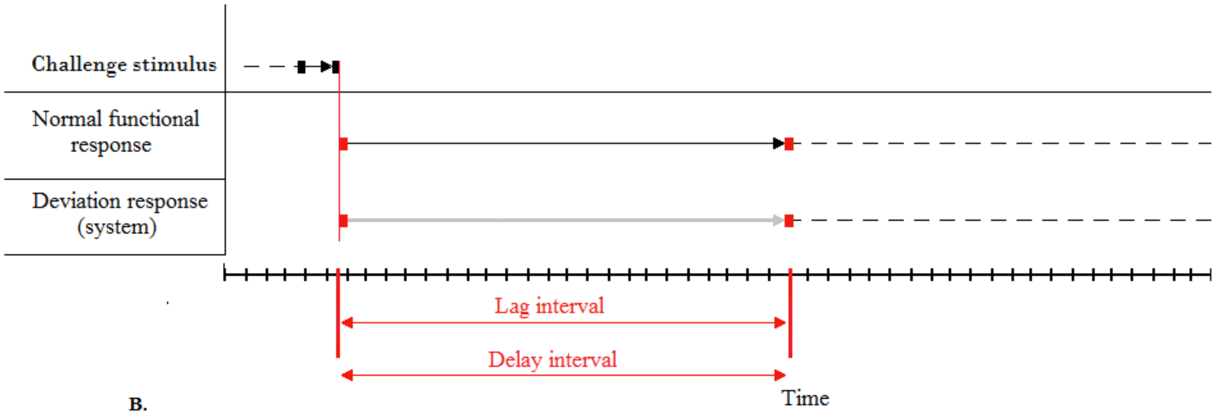
$$1-\frac{N}{\tilde{N}}=0$$



A.



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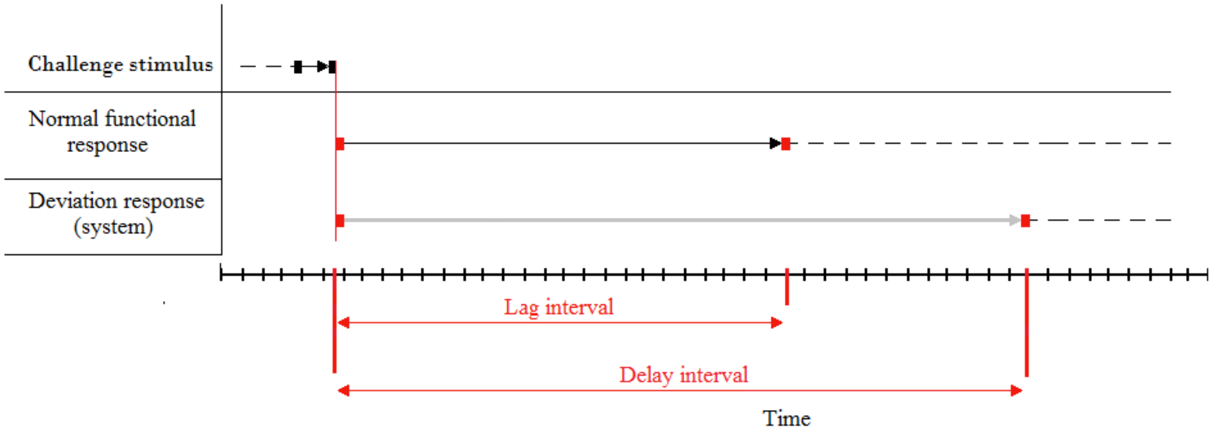

C.

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Figure 1.7. 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.

In other words, the system is most likely to reach failure state if a second stimulus is presented. Note that unlike the first measure, the second measure can take on other values between zero and unity, with the minimum and maximum predisposition values occurring at zero and unity respectively. That is:

$$\mathbf{T}_2 = 0, \quad if\ 1 - \frac{N}{\tilde{\mathrm{N}}} = 0$$

$$\mathbf{T}_2 = 1, \quad if\ 1 - \frac{N}{\tilde{\mathrm{N}}} = 1$$

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:

$$\beth = 1 - \mathbf{T}_1 \mathbf{T}_2 \qquad (14)$$

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 stimulus. On the other hand, the regulator, which only differs from the conformer by its ability to elicit a functional response and YFR, 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 systemic failure.

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 presented stimulus. Thus, the inverse likelihood of failure is always at a maximum for an ideal regulator. Since the

increase in intensity of stimulus 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 hold 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 reduction in delay interval. A second attribute of an ideal regulator is that the inverse predisposition to systemic failure following a subsequent stimulus is at a maximum, since ideal regulators maintain their systemic zero-point state. Thus, the aggregate measure is at a minimum value of zero.

$$ב = 1 - \mathbf{T}_1\mathbf{T}_2 = 0$$

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 states of respective properties. Since a zero-point state is maintained for all properties of an ideal regulator, irrespective of the nature and intensity of presented stimulus, 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

My apologies for any errors that may be present in the mathematical formulations and overall outline. Please notify the corresponding author if such errors are appreciated and limit comprehension of the material.