

# DYNAMICS OF RESOURCE ALLOCATION IN BIOLOGICAL SYSTEMS

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## Abstract

Here we present a single working model that attempts at reconciliation of biological systems. To do this we recognize and emphasize a universal theme of all biological systems: a need for resources. That is, we consider the dynamics of resource allocation as a requirement for actuation of responses to stimuli. In addition, all contemplations are founded on four postulates that are motivated by the homeostatic principle as conceived of by Claude Bernard and Walter Cannon: biological systems exhaust attempts to prevent from reaching the absolute maximum failure potential; biological systems tend in the direction toward the absolute minimum failure potential; biological systems attempt to assume the failure potential of an ideal regulator system; and all biological systems attempt to be in agreement with all four postulates. Finally, we attempt to determine biological manifestations of the stated model.

## Introduction

The following statements are motivated by Claude Bernard's and Walter Cannon's conceptions of homeostasis. Both for the sake of brevity and considering that there are no platforms on which extensively rigorous evaluations can be made as to the validity of these statements, we shall endorse these [statements] as postulates. Thus, in the tradition of axiomatic systems as applied in other areas of study, we shall consider these as starting points on which all contemplations shall be based. Although implicit in scientific practices, I believe it noteworthy to also add that all conclusions arrived at in this work must only be considered substantial following experimental validation.

### 1st postulate:

Biological systems exhaust attempts to prevent from reaching the absolute maximum failure potential.

### 2nd postulate:

Biological systems tend in the direction toward the absolute minimum failure potential.

### 3rd postulate:

Biological systems attempt to assume the failure potential of an ideal regulator system.

### 4th postulate:

All biological systems attempt to be in agreement with all four postulates.

An **ideal regulator system**, as used here, is a hypothetical biological system that maintains a constant absolute minimum failure potential irrespective of nature, intensity, or spontaneity of presenting stimuli. **Failure**, as used here, is in reference to cell death. However, since we shall be considering the cell as a system, it is only fitting that a far more technical term (failure) be applied instead.

Note that agreement with the 3<sup>rd</sup> postulate when faced with presenting stimuli, requires and therefore implies agreement with the 2<sup>nd</sup> postulate. That is, in order to assume or attempt reaching

the absolute minimum failure potential, the system must tend in the direction toward the absolute minimum failure potential.

## Context of focus

1. Suppose that a transient noxious (offensive) stimulus presents to a cell. Let us call this **stimulus- $i$** , and the cell, we shall consider as the biological system of interest. Let the net effect of stimulus- $i$  on the cell be an increase in potential for cell injury and/or death. The given potential can be considered a spectrum bounded by the lowest potential for injury which represents a non-injurious state of the cell, and a highest potential for injury which represents cell death. Henceforth, we shall refer to the potential for cell injury and/or death as the **failure potential**. Thus the lowest and highest potentials for injury can be considered the absolute minimum and absolute maximum failure potentials, respectively. Also consider the noted potential to increase with the intensity of the presenting stimulus.
2. Suppose that the cell response that follows after presentation of stimulus- $i$  is an attempt at termination of noxious effects of stimulus- $i$  on the cell; either by elimination of the given stimulus at its source and/or by dampening effects of stimulus- $i$  on the cell. We shall call this **response- $i$** ,  $Y_{Ri}$ . Irrespective of which, the net effect of response- $i$  on the cell is an attempt at reduction in the failure potential.
3. Suppose that if response- $i$  is not elicited, then the failure potential increases in proportion to the intensity of presented stimulus- $i$ ,  $I_{Ri}$ ; such that increase in intensity of stimulus- $i$  is followed by a proportional increase in failure potential. Henceforth, we shall refer to the intensity of presented stimulus- $i$  that affects the absolute maximum failure potential as the **failure threshold**,  $I_{Fi}$ . In other words, the failure threshold of a given stimulus is the intensity of stimulus such that when presented to an obligate conformer system, results in the absolute maximum failure potential and thus failure of the conformer system.
4. Obligate conformer and obligate regulator systems are applied here as hypothetical systems. An **obligate conformer system** lacks the capacity to elicit responses. Thus, as intensities of stimuli presented to such systems increase, so too do their failure potentials. Thus, the conformer system can be considered a reflection of the unperturbed effects of intensities of stimuli on the failure potential of a cell. An **obligate regulator system**, on the other hand, has the capacity to elicit responses. Thus, the failure potential of an obligate regulator system does not follow the patterns of an obligate conformer system.
5. Let us suppose that the extent of response- $i$  occurs in proportion to intensity of presented stimulus- $i$ ,  $I_{Ri}$ , such that increase in the extent of response- $i$  follows increase in the intensity of stimulus- $i$ .

$$f(I_{Ri}) = Y_{Ri}$$

6. In addition, suppose that actuation of response- $i$  requires investment of resources: such as organic carbon skeletons (amino acids, sugars, lipids, energy substrates, etc. in their respective monomeric or polymeric forms). These resources are invested in the production of effectors of the given response and for response actuation. Let the given required resource be considered the **required resource content** for response- $i$ ,  $R_{Ri}$ .

7. Let us suppose that the required resource content occurs in proportion to the extent of response- $i$  such that increase in the extent of response- $i$  necessitates an increase in required resource content; and that the increase in required resource content must occur so as to allow for the increase in the extent of response- $i$ . Thus the required resource content for a response- $i$ :

$$h(f(I_{Ri})) = h \circ f(I_{Ri}) = R_{Ri}$$

8. Thus, under the stated condition and context, increments in intensity of presented stimulus- $i$  strongly correlate with increments in required resource content for response- $i$ .

$$H(I_{Ri}) = h \circ f(I_{Ri}) = R_{Ri}$$

9. Also of relevance to this work is the required resource content when intensity of presented stimulus- $i$  corresponds to the failure threshold. We shall refer to given required resource content as the **required resource content at failure threshold**,  $R_{Fi}$ .

$$H(I_{Fi}) = R_{Fi}$$

10. Let us also suppose that the **total available resource content**,  $\dot{R}$ , of the given biological system is partitioned between responses of the system. In other words, each response has available for consumption, a portion of the total available resource content. Henceforth, we shall refer to the portion available for a response- $i$  as: the **resource partition** for response- $i$ ,  $R_{Ai}$ .

$$\sum_{i=1} R_{Ai} = R_{A1} + R_{A2} + \dots = \dot{R}$$

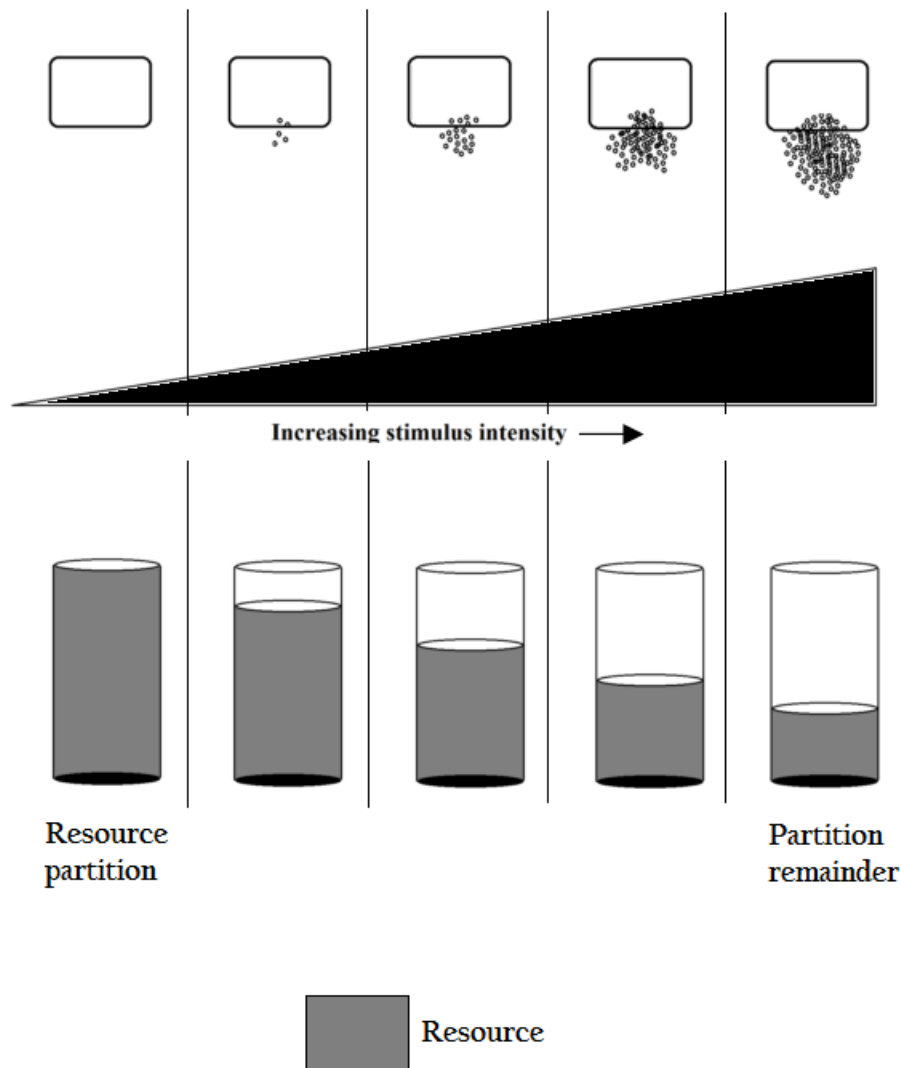
11. Consider that, at least in theory, there exist an intensity level of the given stimulus- $i$  such that when reached, the response that follows requires utilization of cell resources up to the limit of available resource partition for the given response- $i$ . In other words, the required resource content,  $R_{Ri}$ , equals the resource partition for response- $i$ ,  $R_{Ai}$ . It should hold that if the intensity of stimulus- $i$  is increased past this threshold, then the required resource content exceeds the resource partition for response- $i$ . That is,

$$R_{Ai} < R_{Ri}$$

We consider the system to undergo failure from insufficient resources if actuation of responses is attempted when past this stimulus intensity. Henceforth, we shall refer to such an intensity level as the **lethal threshold**,  $I_{Li}$ .

$$H^{-1}(R_{Ai}) = I_{Li}$$

Thus, actualization of a cell response that may be of significance to the cell at intensities below the lethal threshold, can become deleterious to the cell, at- and above the lethal threshold.



**Diagram 1:** The above is an illustration of the relationship between stimulus intensity, response to stimulus, and resource utilization. Cell (rounded rectangles) response (secretion of discrete quantities) following presentation of stimulus at varied intensities; with the given extent of response (as gauged by amount of secreted discrete quantities) occurring as a function of the stimulus intensity. On the other hand, the resource partition for the given response decreases with increasing stimulus intensity, as the given resource is invested in the response yield.

## Definitions for conditional conformers and conditional regulators

12. Under conditions of zero resource input and therefore limited total available resource content: If the required resource content at failure threshold for response- $i$ ,  $R_{Fi}$ , is an excess of resource partition for response- $i$ , then in order to prevent failure (in agreement with the first postulate) following presentation of stimulus- $i$  at intensities that fall between failure threshold and lethal threshold, the cell must not elicit response- $i$ . That is, if:

$$R_{Ai} < R_{Ri} < R_{Fi}$$

then, in order to be in agreement with 1<sup>st</sup> postulate, response- $i$  must not be elicited. To understand the rationale, consider that if response- $i$  is to be elicited in proportion to stimulus intensities that fall between the given range and if the required resource content is greater than the resource partition for response- $i$ ,  $R_{Ai} < R_{Ri}$ , then the resource partition for response- $i$  will be insufficient for actuation of full extent of response- $i$ . Thus, if response- $i$  is elicited, then absolute maximum failure potential and thus failure will result from insufficient resource partition for the given response<sup>1</sup>. However, being that the required resource content is less than the failure threshold,  $R_{Ri} < R_{Fi}$ , it should hold that presentation of stimulus at intensity  $I_{Ri}$  and in an absence of response- $i$  will not result in the absolute maximum failure potential and thus will not result in failure. Thus, the outcome that is most likely in agreement with the 1<sup>st</sup> postulate is that response- $i$  is not elicited.

13. Also note that if response does not occur, then by definition the system can be considered a conformer with respect to effects of the given stimulus- $i$ . Since the conformer character arises under such conditions, we consider this a **conditional conformer**. Thus, we state that: The system is a conditional conformer with respect to effects of a given stimulus- $i$  if:

$$\begin{cases} R_{Ai} < R_{Ri} < R_{Fi} \\ \sum_{i=1} R_{Ai} = \dot{R} \end{cases}$$

14. Under conditions of no resource input and thus limited total available resource content: If the resource partition for response- $i$  is in excess of the required resource content at failure threshold for response- $i$ ,  $R_{Fi} < R_{Ai}$ , then in order to prevent failure following presentation

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<sup>1</sup> Although stated otherwise, for the conditional conformer, failure does not result from resource insufficiency that occur with actuation of the given response. Instead, being that resources are required in order to elicit response, it should therefore hold that the given response cannot be elicited if resources are depleted. This is a limitation imposed by the laws of conservation (of mass and energy). However, in order to allow for consistency in definitions for conditional conformers and regulators, we instead consider responses to be elicited even if resources are depleted. In other words, to get a similar outcome as imposed by the physical limitation, a biological implication is applied; with this being that if response is elicited under the stated condition, the system reaches the absolute maximum failure potential.

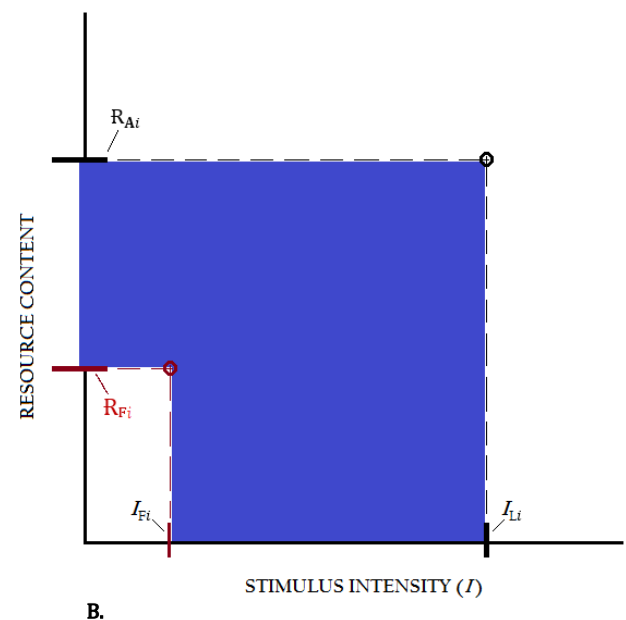
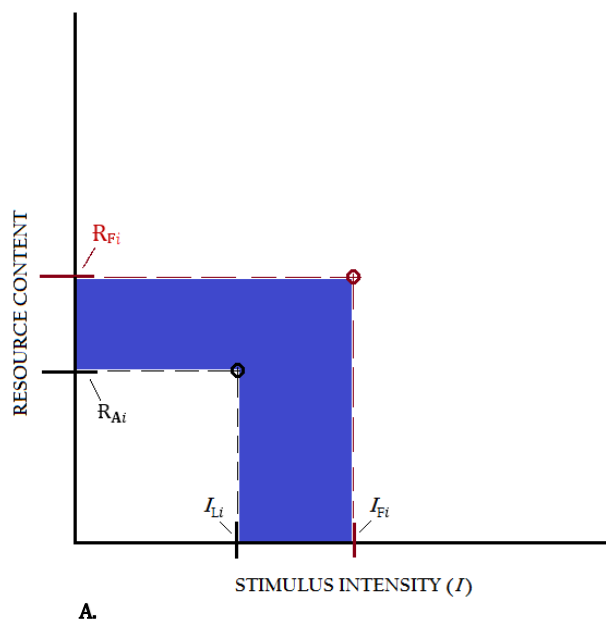
of stimulus at intensities that fall between failure and lethal thresholds, the cell must elicit response. That is, if

$$R_{Fi} < R_{Ri} < R_{Ai}$$

then, in order to be in agreement with 1<sup>st</sup> postulate, response-1 must be elicited. Consider that if response-*i* is to be elicited in proportion to stimulus intensities that fall between the given range and if the required resource content is less than the resource partition for response-*i*,  $R_{Ri} < R_{Ai}$ , then the resource partition for response-*i* will be sufficient for actuation of full extent of response-*i*. Thus an inability to elicit a response-*i* will not result from insufficient resources. However, since the given intensity is greater than the failure threshold,  $I_{Fi} < I_{Li}$ , an absence of a response-*i* in proportion to the given stimulus intensity will result in failure from effects of stimulus-*i*. Thus in order to prevent failure under such conditions, the given response must be elicited in proportion to the presented stimulus.

15. If response occurs, then under such conditions the system can be considered a regulator with respect to the given stimulus effect. More specifically, we consider this a **conditional regulator**. Thus, we state that: The system is a conditional regulator with respect to effects of a given stimulus-*i* if:

$$\begin{cases} R_{Fi} < R_{Ri} < R_{Ai} \\ \sum_{i=1} R_{Ai} = \dot{R} \end{cases}$$



**Figure 1:** Plot of resource content versus stimulus intensity. The point of intersection between horizontal and vertical black dashed lines represent the stimulus intensity (lethal threshold) at which the resource partition for response-*i* is totally consumed in actuation of the given response. The point of intersection between horizontal and vertical red dashed lines represent the required resource content for response-*i* as a function of the stimulus intensity that results in failure of an obligate conformer (failure threshold). **Figure 1A.** The resource partition is less than the required resource content when at failure threshold. Thus, a presenting stimulus-*i* at intensities that fall between lethal threshold and failure threshold (blue-colored region on stimulus intensity axis) would have a required resource content that falls between the required resource content for lethal and failure thresholds. This relationship is represented by the blue-colored area. Thus, the system is a conditional conformer with respect to effects of a stimulus-*i*. **Figure 1B.** The resource partition is greater than the required resource content when at failure threshold. Thus, a presenting stimulus-*i* at intensities that fall between lethal threshold and failure threshold (blue-colored region on stimulus intensity axis) would have a required resource content that falls between the required resource content for lethal and failure thresholds. This relationship is represented by the blue-colored area. Thus, the system is a conditional regulator with respect to effects of a stimulus-*i*.

## Extension of definition of conditional regulators

16. Consider a conditional regulator with respect to effects of a stimulus-*i*,

$$R_{Fi} < R_{Ri} < R_{Ai}$$

$$R_{ri} = R_{Ai} - R_{Ri} > 0$$

That is, the resource partition for the given response-*i* is in excess of the resource requirements, and thus the resource remainder,  $R_{ri}$ , can be considered a surplus. As stated for a conditional regulator, if all else remain the same, presentation of stimulus at an intensity,  $I_{Ri}$ , should elicit a response-*i*. To put it another way, an inability to elicit a response-*i* will not result from insufficient resources. Thus, even if systemic failure may occur, it will not occur as a result of insufficient resources.

Where,

$$I_{Ri} = H^{-1}(R_{Ri})$$

Let us now consider a second situation involving a limited total available resource content,  $\bar{R}$ . For the given situation we consider resource depletion following actuation of response. Presentation of stimulus at lethal threshold,  $I_{Ri} = I_{Li}$  should yield the noted situation,

$$R_{ri} = R_{Ai} - R_{Ri} = 0$$

Although the resource partition is depleted, depletion occurs after actuation of the given response. In other words, the required resource content matches the resource partition for the given response-*i*. Thus, based on the above line of reasoning, if a response-*i* is elicited following presentation of stimulus at an intensity,  $I_{Ri} = I_{Li}$ , and if the resource partition is  $R_{Ai} = R_{Ri}$ , then systemic failure does not result from insufficient resources. Such a system can therefore be considered a conditional regulator with respect to effects of the given stimulus-*i*.

17. Let us now suppose a third situation involving a limited total available resource content,  $\bar{R}$ . For the given situation, we consider the required resource content,  $'R_{Ri}$ , is less than both the required resource content for failure threshold,  $'R_{Fi}$ , and the resource partition for the given response- $i$ ,  $'R_{Ai}$ .

$$'R_{Ri} < 'R_{Fi} < 'R_{Ai}$$

Where, the resource parameters as compared to the first situation:

$$'R_{Ai} = R_{Ai}$$

$$'R_{Fi} = R_{Fi}$$

We question whether or not the given system can be considered a conditional regulator, especially since the required resource content falls outside the defined interval bounded by  $'R_{Fi}$  and  $'R_{Ai}$ .

Since,

$$'R_{Fi} = R_{Fi}$$

Therefore,

$$'R_{Ri} < 'R_{Fi} < R_{Ri} < R_{Ai}$$

And

$$'R_{Ri} < R_{Ri}$$

Also, since

$$'R_{Ai} = R_{Ai}$$

$$'R_{ri} = 'R_{Ai} - 'R_{Ri}$$

Thus, substituting  $R_{Ai}$  for  $'R_{Ai}$

$$'R_{ri} = R_{Ai} - 'R_{Ri}$$

Since  $'R_{Ri} < R_{Ri}$ ,

$$R_{Ai} - R_{Ri} < R_{Ai} - 'R_{Ri}$$

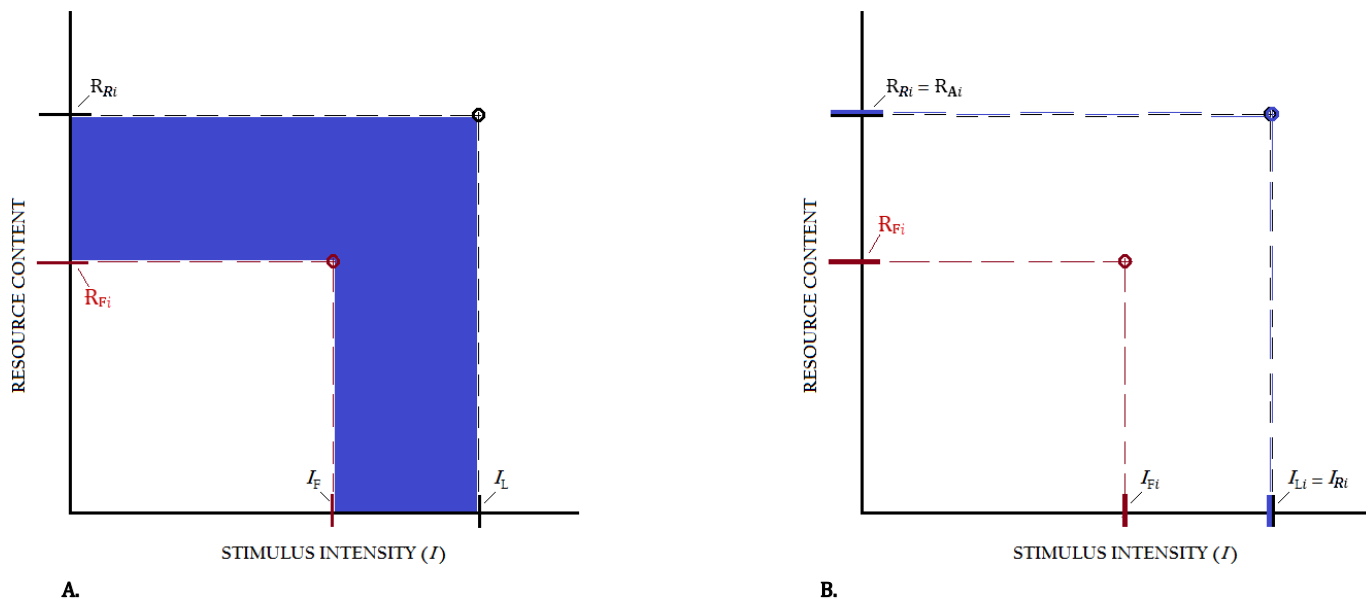
$$R_{ri} < 'R_{ri}$$



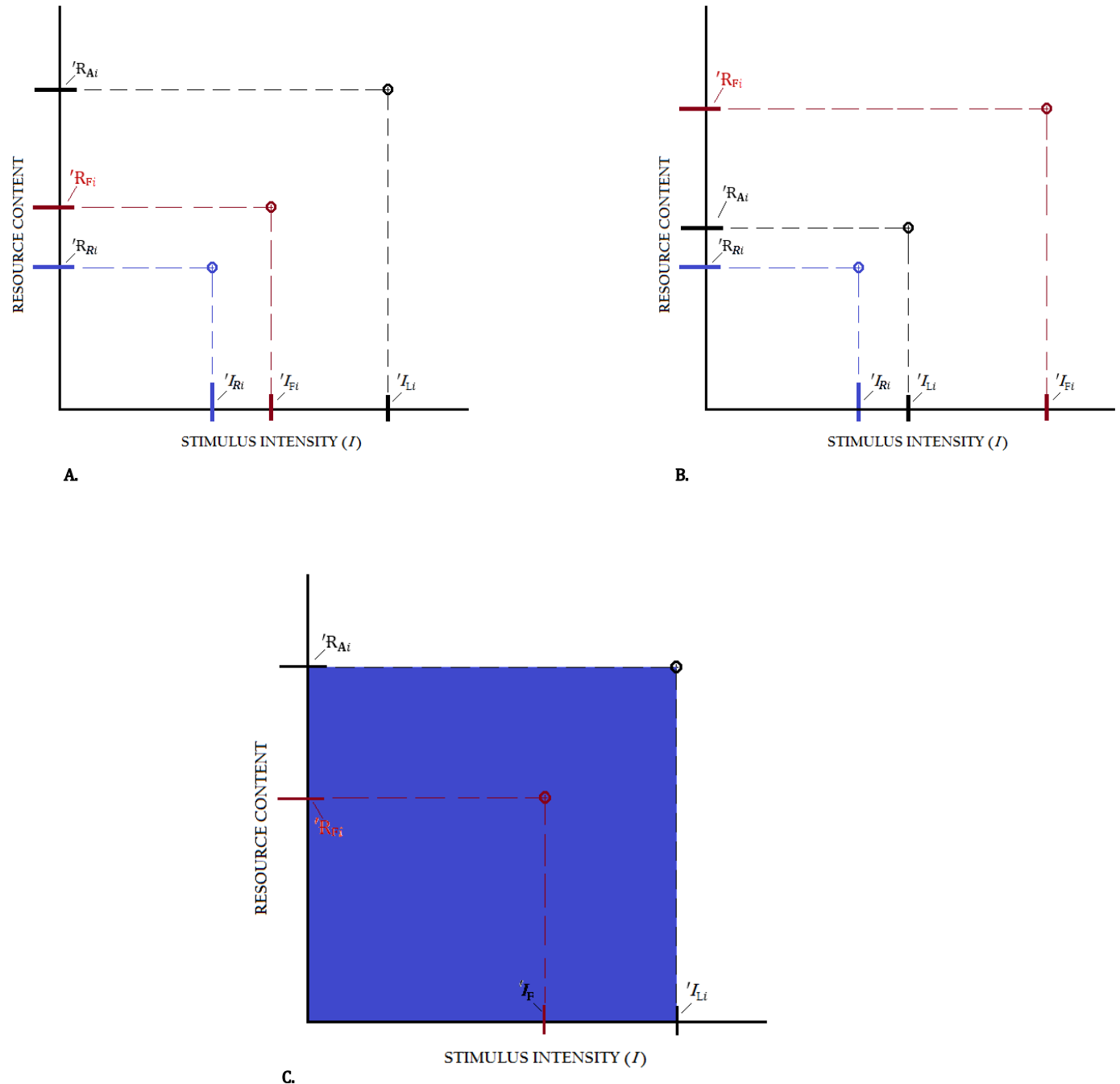
Since it was shown for the first situation, that  $R_{ri} > 0$ , and therefore systemic failure from an inability to elicit response- $i$  will not occur as a result of an insufficient resource partition for response- $i$ , the same must hold for the third situation where  $R_{ri} < R_{ri}$ , and therefore  $R_{ri} > 0$ . Thus, the system can be considered a conditional regulator with respect to response- $i$  even for required resource contents that fall below the defined interval bounded by  $R_{Fi}$  and  $R_{Ai}$ .

18. Thus we can extend the definition of a conditional regulator: The system is a conditional regulator with respect to effects of a given stimulus- $i$  if:

$$\begin{cases} 0 \leq R_{Ri} \leq R_{Ai} \\ \sum_{i=1} R_{Ai} = \dot{R} \end{cases}$$



**Figure 2.** Plot of resource content versus stimulus intensity. **Figure 2A.** is a plot for a conditional regulator with respect to effects of the given stimulus- $i$ . The resource partition for the given response- $i$ ,  $R_{Ai}$ , is in excess of required resource content,  $R_{Ri}$ , for all intensity values  $I_{Fi} < I_{Ri} < I_{Ai}$ . That is,  $R_{Ri} < R_{Ai}$ . Thus the resource remainder,  $R_{ri}$ , can be considered a surplus. If all else remain the same, then presentation of stimulus at an intensity,  $I_{Ri}$ , does not result in systemic failure from insufficient resource partition. **Figure 2B.** The resource partition for the given response- $i$ ,  $R_{Ai}$ , is equal in magnitude to the required resource content,  $R_{Ri}$ . That is,  $R_{Ri} = R_{Ai}$ . If a response- $i$  is elicited following presentation of stimulus at an intensity,  $I_{Ri} = I_{Li}$ , and if the resource partition is  $R_{Ai} = R_{Ri}$ , then systemic failure does not result from insufficient resources. Thus, by definition, the system can be considered a conditional regulator when  $R_{Ai} = R_{Ri}$ .



**Figure 3.** Plot of resource content versus stimulus intensity. **Figure 3A.** the required resource content,  $R_{Ri}$ , is less than both the required resource content for failure threshold,  $R_{Fi}$ , and the resource partition for the given response- $i$ ,  $R_{Ai}$ . That is,  $R_{Ri} < R_{Fi} < R_{Ai}$ . Since  $R_{Ri} < R_{Ai}$ , systemic failure from an inability to elicit response- $i$  will not occur as a result of insufficient resources. Thus, the system can be considered a conditional regulator with respect to effects of stimulus- $i$ . **Figure 3B.** the required resource content,  $R_{Ri}$ , is less than both the required resource content for failure threshold,  $R_{Fi}$ , and the resource partition for the given response- $i$ ,  $R_{Ai}$ . However, unlike figure A,  $R_{Ai} < R_{Fi}$ . That is,  $R_{Ri} < R_{Ai} < R_{Fi}$ . Since  $R_{Ri} < R_{Ai}$ , systemic failure from an inability to elicit response- $i$  will not occur as a result of insufficient resources. Thus, irrespective of the relationship between the resource partition and required resource content at failure threshold, the system can be considered to be a

conditional regulator if  $'R_{Ri} < 'R_{Ai}$ . **Figure 3C.** Thus, the system can be considered a conditional regulator with respect to effects of stimulus- $i$  for all required resource contents such that  $0 \leq 'R_{Ri} \leq 'R_{Ai}$ .

### Transformation of conditional conformers to conditional regulators.

19. Consider two biological systems, one an obligate conformer and the other an obligate regulator. Suppose that these systems are identical with respect to their initial failure potentials. Also, let us suppose that the initial failure potential is neither the absolute minimum nor absolute maximum failure potential. In order to be in agreement with the 2<sup>nd</sup> and 3<sup>rd</sup> postulates, it will require that change in the failure potential from this initial must occur such that the final potential is closer to the absolute minimum failure potential. This would require that one or more response(s) attempt rectification of the given failure potential. By definition, systems that can initiate such response(s) are considered regulator systems. The same cannot be stated for a conformer, since by definition an elicited response does not follow presentation of stimulus for such a system. Thus, of the two, the obligate conformer system cannot be in agreement with said postulates. In order to be in agreement with the 2<sup>nd</sup> and 3<sup>rd</sup> postulates, the given conformer system must have a capacity for transformation from a conformer to a regulator system. We noted such a capacity for conditional conformers and conditional regulator systems. As the given conformer or regulator character is based on the given resource condition (available vs. unavailable resources). Thus, we shall restrict analysis to such systems.

20. In order for transformation of a conditional conformer to conditional regulator, the given relationships between aforementioned metrics must be achieved. One can intuitively appreciate that this can be achieved through any one of three means:

- I. Reduction of required resource content for a fixed resource partition, such that  $'R_{Ri} \leq 'R_{Ai}$ . Figure 4A and 4B.
- II. Increase in resource partition for a fixed required resource content, such that  $'R_{Ri} \leq 'R_{Ai}$ . Figure 4C.
- III. Reduction of the required resource content and increase in resource partition for stimulus-1. Such that  $'R_{Ri} \leq 'R_{Ai}$ . Figure 5A and 5B.

21. In addition, there are at least two possible ways to yield reduction in required resource content for a given response- $i$  from a value prior to transformation,  $R_{Ri}$ , to the value following transformation,  $'R_{Ri}$ ; where both  $R_{Ri}$  and  $'R_{Ri}$  are functions of stimulus intensity,  $I$ . The first (refer to Figure 4A) involves change in required resource content for a fixed stimulus intensity,  $I_{Ri}$ , such that:

$$'R_{Ri} < R_{Ri}$$

$$R_{Ri} = H(I_{Ri})$$

$$'R_{Ri} = G(I_{Ri})$$

$$G(I_{Ri}) < H(I_{Ri})$$

The second (refer to Figure 4B) involves changes in both required resource content and stimulus intensity such that initial and final intensity values are inverse functions of  $R_{Ri}$  and  $'R_{Ri}$ , respectively:

$$'R_{Ri} < R_{Ri}$$

$$R_{Ri} = H(H^{-1}(R_{Ri})) = H(I_{Ri})$$

$$'R_{Ri} = H(H^{-1}('R_{Ri})) = H('I_{Ri})$$

$$H('I_{Ri}) < H(I_{Ri})$$

For this work, all changes in the required resource content as occurs with transformations will be considered in the context of the latter approach. In addition, changes involving all resource metric will be considered in the context of the latter approach. Thus:

$$R_{Ri} = H(I_{Ri}) \quad 'R_{Ri} = H('I_{Ri}) \quad ''R_{Ri} = H(''I_{Ri})$$

$$R_{Ai} = H(I_{Li}) \quad 'R_{Ai} = H('I_{Li}) \quad ''R_{Ai} = H(''I_{Li})$$

Also consider that

$$|G(I_{Fi}) - H(I_{Fi})| \rightarrow |G(I_{Ri}) - H(I_{Ri})|$$

$$|H('I_{Fi}) - H(I_{Fi})| \rightarrow |H('I_{Ri}) - H(I_{Ri})|$$

Thus, the equivalent relationship should hold

$$| 'R_{Fi} - R_{Fi} | \rightarrow | 'R_{Ri} - R_{Ri} |$$

And if,

$$'R_{Fi} < R_{Fi}$$

Then,

$$'R_{Ri} < R_{Ri}$$

22. However, we shall rely on a comparatively rigorous approach as opposed to an intuitive appreciation as to plausible approaches to transformation. Let us suppose that the total available resource content,  $\mathbf{\bar{R}}$ , is a constant, and therefore remains unchanged with transformation. Let us suppose that systemic transformation occurs with respect to effects of stimulus-1. Also, suppose that prior-to and following transformation,  $\mathbf{\bar{R}}$  is partitioned

between two response(s) only: response-1 and response-2. All resource parameters following transformation will be given a prime followed by the given parameter. For example,  $'R_{Ai}$ ,  $'R_{Ri}$ , and  $'R_{ri}$ .

$$\begin{aligned}\dot{\mathbf{R}} &= R_{A1} + R_{A2} \\ \dot{\mathbf{R}} &= 'R_{A1} + 'R_{A2}\end{aligned}$$

Consider that the resource partition for response- $i$  is the sum of the required resource content and a partition remainder.

$$\begin{aligned}R_{Ai} &= R_{Ri} + R_{ri} \\ 'R_{Ai} &= 'R_{Ri} + 'R_{ri}\end{aligned}$$

Thus, the partition remainder is the difference between the resource partition and required resource content.

$$\begin{aligned}R_{ri} &= R_{Ai} - R_{Ri} \\ 'R_{ri} &= 'R_{Ai} - 'R_{Ri}\end{aligned}$$

The partition remainder for the untransformed and transformed system can be considered to each be **balanced** if  $R_{ri} = 0$  and  $'R_{ri} = 0$ , respectively. The partition remainder for the untransformed and transformed system can be considered to each be a **deficit** if  $R_{ri} < 0$  and  $'R_{ri} < 0$ , respectively. The partition remainder for the untransformed and transformed system can be considered to each be a **surplus** if  $R_{ri} > 0$  and  $'R_{ri} > 0$ , respectively. The change in partition remainder for response- $i$  that occurs with transformation is the sum of the change in resource partition and change in required resource content for the given stimulus.

$$\begin{aligned}'R_{ri} - R_{ri} &= 'R_{Ai} - 'R_{Ri} - R_{Ai} + R_{Ri} \\ &= 'R_{Ai} - R_{Ai} + R_{Ri} - 'R_{Ri}\end{aligned}$$

Thus for the given response-1

$$\begin{aligned}R_{r1} &= R_{A1} - R_{R1} \\ 'R_{r1} &= 'R_{A1} - 'R_{R1} \\ 'R_{r1} - R_{r1} &= 'R_{A1} - 'R_{R1} - R_{A1} + R_{R1} \\ &= R_{R1} - 'R_{R1} + 'R_{A1} - R_{A1}\end{aligned}$$

where,

$$R_{r1} < 'R_{r1}$$

**Proposition 1:** If, following systemic transformation with respect to effects of stimulus-1, there is no change in resource partition for response-1 only,

$${}'R_{A1} - R_{A1} = 0$$

then,

$${}'R_{r1} - R_{r1} = R_{R1} - {}'R_{R1} + 0$$

Also, since  $R_{r1} < {}'R_{r1}$ ,

$${}'R_{R1} < R_{R1}$$

If, following systemic transformation with respect to effects of stimulus-1, there is no change in required resource content for response-1 only,

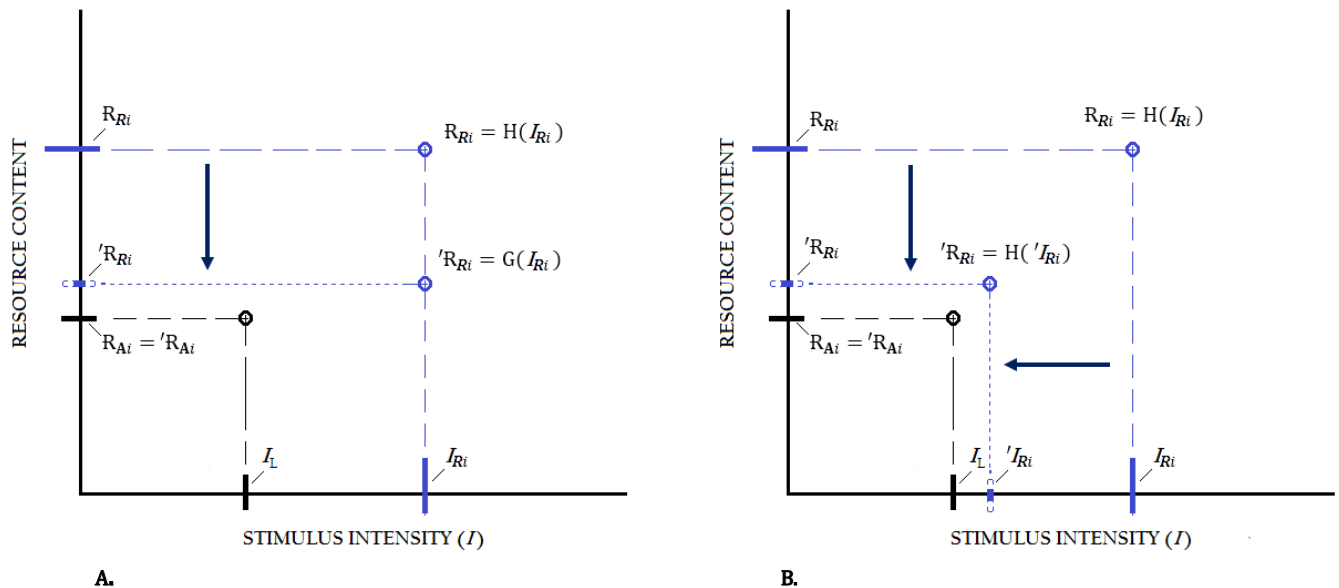
$${}'R_{R1} - R_{R1} = 0$$

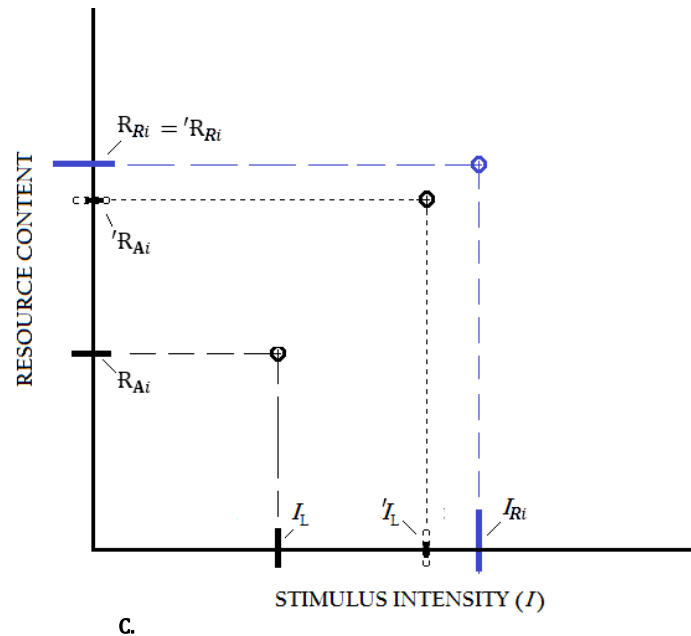
then,

$${}'R_{r1} - R_{r1} = 0 + {}'R_{A1} - R_{A1}$$

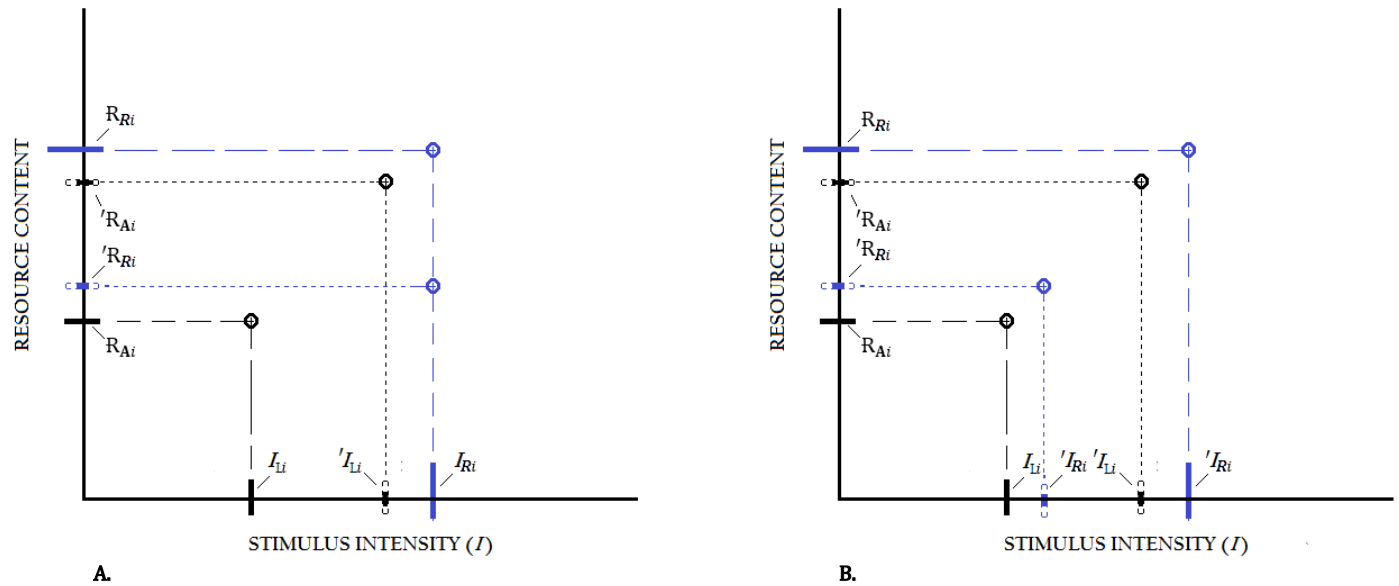
Also, since  $R_{r1} < {}'R_{r1}$ ,

$$R_{A1} < {}'R_{A1}$$





**Figure 4.** Plot of resource content versus stimulus intensity. **Figure 4A.** Depicts, for a fixed resource partition, reduction in required resource content from  $R_{Ri}$  (blue dashed horizontal lines) to  $'R_{Ri}$  (blue dotted horizontal lines) such that  $'R_{Ri} < R_{Ri}$ . Also note that the change in required resource content occurs for a fixed stimulus intensity,  $I_{Ri}$ . Since for the same stimulus intensity, there are different requirements for resources, it should hold that the relationship between the stimulus intensity and the required resource content differs. **Figure 4B.** Depicts, for a fixed resource partition, reduction in required resource content from  $R_{Ri}$  (blue dashed horizontal lines) to  $'R_{Ri}$  (blue dotted horizontal lines) such that  $'R_{Ri} < R_{Ri}$ . Also note changes occur for both required resource content and stimulus intensity such that initial and final intensity values are inverse functions of  $R_{Ri}$  and  $'R_{Ri}$ , respectively. That is,  $H^{-1}(R_{Ri}) = I_{Ri}$ , and  $H^{-1}('R_{Ri}) = 'I_{Ri}$ . Note that unlike for Figure 4A, the relationship between the stimulus intensity and the required resource content remains the same. Differences in required resource content arise from differences in intensity of presenting stimulus. **Figure 4C.** Depicts, for a fixed required resource content, an increase in resource partition from  $R_{Ai}$  (black dashed horizontal lines) to  $'R_{Ai}$  (black dotted horizontal lines) such that  $R_{Ai} < 'R_{Ai}$ .



**Figure 5.** Plot of resource content versus stimulus intensity. Depicts reduction of the required resource content and increase in resource partition for stimulus-1 such that  $'R_{Ri} < R_{Ri}$ . **Figure 5A**, transformation resulting from change in required resource content for a fixed stimulus intensity,  $I_{Ri}$ , such that  $'R_{Ri} < R_{Ri}$  and an increase in resource partition such that  $R_{Ai} < 'R_{Ai}$ . **Figure 5B**, transformation resulting from change in both required resource content and stimulus intensity such that  $'R_{Ri} < R_{Ri}$  and an increase in resource partition such that  $R_{Ai} < 'R_{Ai}$ .

23. Let us now consider response-2 as affected by transformation with respect to effects of stimulus-1. We begin by first considering how changes in metrics for response-1 affect those for response-2. Let the change in resource partition for a response- $i$  be the difference between the resource partitions for the given response for the transformed,  $'R_{Ai}$  and untransformed system,  $R_{Ai}$ . That is,  $'R_{Ai} - R_{Ai}$ . We show that the change in resource partition for response-1,  $'R_{A1} - R_{A1}$ , equals the negative of the change in resource partition for response-2,  $R_{A2} - 'R_{A2}$ .

$$\dot{R} = R_{A1} + R_{A2}$$

$$\dot{R} = 'R_{A1} + 'R_{A2}$$

$$R_{A1} + R_{A2} = 'R_{A1} + 'R_{A2}$$

$$'R_{A1} - R_{A1} = R_{A2} - 'R_{A2}$$

If, following systemic transformation with respect to effects of stimulus-1, there is no change in required resource content for response-1 only,

$$'R_{R1} - R_{R1} = 0$$

then,

$$'R_{r1} - R_{r1} = 0 + 'R_{A1} - R_{A1}$$



Also, since  $R_{r1} < 'R_{r1}$ ,

$$R_{A1} < 'R_{A1}$$

From the above relationship

$$\begin{aligned} 'R_{r1} - R_{r1} &= 0 + R_{A2} - 'R_{A2} \\ &= 0 + R_{R2} + R_{r2} - 'R_{R2} - 'R_{r2} \\ &= 0 + R_{R2} - 'R_{R2} + R_{r2} - 'R_{r2} \end{aligned}$$

**Proposition 2:** If, following systemic transformation with respect to effects of stimulus-1, there is no change both in required resource contents for response-1 and response-2 only,

$$\begin{aligned} 'R_{R1} - R_{R1} &= 0 \\ 'R_{R2} - R_{R2} &= 0 \end{aligned}$$

then,

$$'R_{r1} - R_{r1} = 0 + 0 + R_{r2} - 'R_{r2}$$

Also: since  $R_{r1} < 'R_{r1}$ ,

$$'R_{r2} < R_{r2}$$

**Proposition 3:** If, following systemic transformation with respect to effects of stimulus-1, there is no change both in required resource contents for response-1 and the partition remainder for response-2 only,

$$\begin{aligned} 'R_{R1} - R_{R1} &= 0 \\ R_{r2} - 'R_{r2} &= 0 \end{aligned}$$

then,

$$'R_{r1} - R_{r1} = 0 + R_{R2} - 'R_{R2} + 0$$

Also:

since  $R_{r1} < 'R_{r1}$ ,

$$'R_{R2} < R_{R2}$$

Based on all three propositions, we can conclude that systemic transformation with respect to effects of stimulus-1 occurs at the expense of resources for response-2.

24. Now consider that the following is in agreement with the 1<sup>st</sup> postulate: prior to transformation with respect to effects of stimulus-1, the system is a conditional regulator with respect to effects of stimulus-2, and following the stated transformation the system is a conditional conformer with respect to effects of stimulus-2. We can symbolize this using the following two representations **Table 1**.

	R	'R
1	$R_{A1} < R_{R1}$	$'R_{R1} \leq 'R_{A1}$
2	$R_{R2} \leq R_{A2}$	$'R_{A2} < 'R_{R2}$

A.

	R	'R
1	-	+
2	+	-

B.

**Table 1:** Both representations reflect the same concepts. All  $R_{Ai} < R_{Ri}$  in table 1A are represented in table 1B using a minus sign (-), and all  $R_{Ri} \leq R_{Ai}$  in table 1A are represented in table 1B using a plus sign (+). The yellow highlights represent the given stimulus effect for which the system is to undergo the given transformation event. Prior to transformation, the system can be considered a conditional conformer (-) with respect to the effect of stimulus-1, whereas a conditional regulator (+) with respect to effects of stimulus-2. Systemic transformation with respect to effects of stimulus-1 and at an expense of resources for response-2 yields a conditional regulator and conditional conformer with respects to effects of stimulus-1 and stimulus-2, respectively. Thus, with transformation, the system is not in agreement with the second postulate.

25. It is, however, not in agreement with the 2<sup>nd</sup> postulate since the system is considered a conditional conformer, with respect to stimulus-2 and thus does not tend toward the absolute minimum failure potential. Being that agreement with the 3<sup>rd</sup> postulate requires agreement with the 2<sup>nd</sup> postulate, we can conclude that the system is also not in agreement with the 3<sup>rd</sup> postulate. We can therefore consider that transformation of a conditional conformer to a conditional regulator with respect to a given stimulus must not result in a conditional conformer with respect to effects of a different stimulus.

26. In order to be in agreements with all postulates, either: the stated transformation that yields the conditional conformer system, with respect to effects of stimulus-2, does not occur or subsequent transformation(s) occur, with the final transformation resulting in a conditional regulator system with respect to effects of stimulus-2. In other words, the final transformation is with respect to effects of stimulus-2 and therefore at an expense of resources for response-1. For brevity, we restrict the maximum number of transformations to two. Thus, the second transformation is with respect to effects of stimulus-2 and the outcome must be  $''R_{R2} \leq ''R_{A2}$ .

	R	'R
1	-	+
2	+	+

A.

	R	'R	"R
1	-	+	+
2	+	-	+

B.

**Table 2.** Consider both table 2A and table 2B. For both tables, the system can be considered a conditional conformer (-) with respect to the effect of stimulus-1, whereas a conditional regulator (+) with respect to effects of stimulus-2 prior to transformation. **Table 2A**, following transformation with respect to effects of stimulus-1 and at the expense of resources for response-2, the system can be considered to be a conditional regulator with respect to effects of both stimulus-1 and stimulus-2. Thus, the system is in agreements with all four postulates and no further transformation is required. **Table 2B**, following transformation with respect to effects of stimulus-1 and at the expense of resources for response-2, the system can be considered to be a conditional regulator with respect to effects of stimulus-1 only and a conditional conformer with respect to effects of stimulus-2. Thus, the system is not in agreements with all four postulates. In order to be in agreements with all postulates, the system must undergo, at least, a second transformation event. However, the second transformation event (green highlight) is with respect to effects of stimulus-2 and at an expense of resources for response-1. Following transformation with respect to effects of stimulus-2, the system can be considered to be a conditional regulator with respect to effects of both stimulus-1 and stimulus-2. Thus, the system is in agreements with all four postulates and no further transformation is required.

27. As was previously stated for response-1, in order for transformation of a conditional conformer to conditional regulator, the given relationships between resource parameters must be achieved. This may involve either:

- IV. Reduction in required resource content for a fixed resource partition, such that  $''R_{Ri} \leq ''R_{Ai}$ .
- V. Increase in resource partition for a fixed required resource content, such that  $''R_{Ri} \leq ''R_{Ai}$ .
- VI. Reduction in the required resource content and increase in resource partition for stimulus-1. Such that  $''R_{Ri} \leq ''R_{Ai}$ .

Transformation with respect to effects of stimulus-2 would require that the above statements also hold for the given response-2.

28. Let the change in resource partition for a response- $i$  be the difference between the resource partitions for the given response for the transformed,  $''R_{Ai}$ , and untransformed system,  $'R_{Ai}$ . That is,  $''R_{Ai} - 'R_{Ai}$ . We show that the change in resource partition for response-2,  $''R_{A2} - 'R_{A2}$ , equals the negative of the change in resource partition for response-1.

$$\dot{R} = 'R_{A1} + 'R_{A2}$$

$$\dot{R} = ''R_{A1} + ''R_{A2}$$

$$'R_{A1} + 'R_{A2} = ''R_{A1} + ''R_{A2}$$

$$''R_{A2} - 'R_{A2} = 'R_{A1} - ''R_{A1}$$

Consider that the resource partition for response-*i* is the sum of the required resource content and a partition remainder.

$$'R_{Ai} = 'R_{Ri} + 'R_{ri}$$

$$''R_{Ai} = ''R_{Ri} + ''R_{ri}$$

Thus, the partition remainder is the difference between the resource partition and required resource content.

$$'R_{ri} = 'R_{Ai} - 'R_{Ri}$$

$$''R_{ri} = ''R_{Ai} - ''R_{Ri}$$

The change in partition remainder for response-*i* that occurs with transformation is the sum of the change in resource partition and change in required resource content for the given stimulus.

$$\begin{aligned} ''R_{ri} - 'R_{ri} &= ''R_{Ai} - ''R_{Ri} - 'R_{Ai} + 'R_{Ri} \\ &= ''R_{Ai} - 'R_{Ai} + 'R_{Ri} - ''R_{Ri} \end{aligned}$$

Thus for the given response-2

$$'R_{r2} = 'R_{A2} - 'R_{R2}$$

$$''R_{r2} = ''R_{A2} - ''R_{R2}$$

$$\begin{aligned} ''R_{r2} - 'R_{r2} &= ''R_{A2} - ''R_{R2} - 'R_{A2} + 'R_{R2} \\ &= 'R_{R2} - ''R_{R2} + ''R_{A2} - 'R_{A2} \end{aligned}$$

where,

$$'R_{r2} < ''R_{r2}$$

Thus, based on proposition 1, we declare that: If, following systemic transformation with respect to effects of stimulus-2, there is no change in resource partition for response-2 only,

$$''R_{A2} - 'R_{A2} = 0$$

then,

$$''R_{r2} - 'R_{r2} = 'R_{R2} - ''R_{R2} + 0$$

Also, since  $'R_{r2} < ''R_{r2}$ ,

$$''R_{R2} < 'R_{R2}$$

If, following systemic transformation with respect to effects of stimulus-2, there is no change in required resource content for response-2 only,

$$''R_{R2} - 'R_{R2} = 0$$

then,

$$''R_{r2} - 'R_{r2} = 0 + ''R_{A2} - 'R_{A2}$$

From the above relationship;  $''R_{A2} - 'R_{A2} = 'R_{A1} - ''R_{A1}$

$$\begin{aligned} ''R_{r2} - 'R_{r2} &= 0 + 'R_{A1} - ''R_{A1} \\ &= 0 + 'R_{R1} + 'R_{r1} - ''R_{R1} - ''R_{r1} \\ &= 0 + 'R_{R1} - ''R_{R1} + 'R_{r1} - ''R_{r1} \end{aligned}$$

Thus, based on proposition 2, we declare that: If, following systemic transformation with respect to effects of stimulus-2, there is no change in both required resource contents for response-1 and response-2 only,

$$''R_{R1} - 'R_{R1} = 0$$

$$''R_{R2} - 'R_{R2} = 0$$

then,

$$''R_{r2} - 'R_{r2} = 0 + 0 + 'R_{r1} - ''R_{r1}$$

Also:

Since  $'R_{r2} < ''R_{r2}$ ,

$$''R_{r1} < 'R_{r1}$$

Thus, based on proposition 3, we declare that: If, following systemic transformation with respect to effects of stimulus-2, there are no changes in partition remainder for response-1 and required resource content for response-2 only,

$$'R_{r1} - ''R_{r1} = 0$$

$$''R_{R2} - 'R_{R2} = 0$$

then,

$$''R_{r2} - 'R_{r2} = 0 + 'R_{R1} - ''R_{R1} + 0$$

Also:

Since  $'R_{r2} < ''R_{r2}$ ,

$$''R_{R1} < 'R_{R1}$$

## **Translation of propositions to biological outcomes (manifestations).**

Here we attempt interpretation of the above positions into biological manifestations and whether we can reconcile these with known biological processes. We expect in future works that we can attempt prediction of unknown processes from information outlined in this paper. It is important to consider the possibility that these biological outcomes occur in a combinatorial manner.

### **1. Reduction in the required resource content for response processes.**

- I. Reduction in required resource content for response processes may *directly or indirectly* result from reduction in elicited responses. That is, since response actuation requires consumption of resources, reduction in the extent of the actuated response would also imply a reduction in the resource requirement for actuation of given response process. Thus, factors that decrease the extent of an elicited response should also decrease the required resource content for the given response. In its own right, the given reduction in elicited responses may have derived from any one of the following, or a combination of these:
  - i. **Reduction in intensity of presented stimulus:** This may directly or indirectly result from reduction in stimulus output at source, and thus a reduction in intensity of the presenting stimulus. Thus, the extent of the given response elicited should be decreased as compared to a situation where stimulus output is not interrupted. Refer to Figure 4B.
  - ii. **Reduction in intensity of [perceived] stimulus:** This involves a discrepancy between the actual stimulus intensity and the stimulus intensity, as determined from stimulus effect on the given system. That is, stimulus effect is dampened such that the resultant elicited response that occurs in proportion to presenting stimulus is less than if presented to an obligate conformer replica of the given system. Refer to Figure 4A. Some examples of such manifestations are: receptor/sensor modification and/or degradation; receptor/sensor gene suppression and silencing.
  - iii. **Change in proportionality between intensity of presented stimulus and resource requirement:** The given change in proportionality is such that: for a fixed quantity of effectors of the given response, there is reduction in resource requirement. Refer to Figure 4A. This could result from a change in the efficacy of effectors (as may occur with covalent/non-covalent modulation of effectors, mRNA splicing, isoform switching etc.).

### **2. Changes to the partition remainder:**

- I. **Changes to the partition remainder: Increase in the partition remainder with transformation.** For a constant total available resource content, and in keeping with the conservation laws for energy and mass, the given surplus must derive from reallocation of resources from other response processes. This occurs such that the given response is afforded resource partition in excess of or exactly the required resource content.

- i. **Increase in the partition remainder following transformation.** This involves a deficit in partition remainder that occurs prior to transformation, with subsequent increase in partition remainder with transformation. The resultant partition remainder is either balanced or at a surplus.

$$R_{ri} < 0; \quad 'R_{ri} \geq 0; \quad R_{ri} < 'R_{ri}$$

- ii. **Increase in the partition remainder with surplus following transformation.** This involves a balanced or deficient partition remainder that occurs prior to transformation, with subsequent increase in partition remainder following transformation. The resultant partition remainder is at a surplus.

$$R_{ri} \leq 0; \quad 'R_{ri} > 0; \quad R_{ri} < 'R_{ri}$$

- iii. **Increase in the partition remainder with increased surplus following transformation.** This involves a surplus in partition remainder that occurs prior to transformation, with subsequent increase in partition remainder following transformation. Thus an increase in surplus.

$$R_{ri} > 0; \quad 'R_{ri} > 0; \quad R_{ri} < 'R_{ri}$$

- II. **Changes to the partition remainder: Decrease in the partition remainder with transformation.** For a constant total available resource content, and in keeping with the conservation laws for energy and mass, the given deficit must derive from resources not considered as part of the resource partition for the given response.

- i. **Decrease in the partition remainder with deficit following transformation.** This involves either a balanced or surplus of partition remainder that occurs prior to transformation, with subsequent decrease in partition remainder following transformation. The resultant partition remainder is at a deficit.

$$R_{ri} \geq 0; \quad 'R_{ri} < 0; \quad 'R_{ri} < R_{ri}$$

- ii. **Decrease in the partition remainder with decreased surplus following transformation.** This involves a surplus in partition remainder that occurs prior to transformation, with subsequent decrease in partition remainder following transformation. However, a surplus still occurs even with such reductions, albeit less.

$$R_{ri} > 0; \quad 'R_{ri} > 0; \quad 'R_{ri} < R_{ri}$$

- iii. **Decrease in the partition remainder with increased deficit following transformation.** This involves a deficit in partition remainder that occurs prior to transformation, with further increase in deficit following transformation.

$$R_{ri} < 0; \quad 'R_{ri} < 0; \quad 'R_{ri} < R_{ri}$$