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Left- and Right-Regulating Systems

A Steady-State Analysis of Function and Structure of Simple Feedback Systems

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Abstract. Two aspects of real systems — unidirectional corrector activity and non-negative signals — are analysed with regard to the steady state function and structure of negative feedback systems. Two classes of simple systems are distinguished: left-regulating systems (LRS) correcting decreases of the regulated variable, and right-regulating systems (RRS) acting against increases. The RRS-comparator differs in structure from the (classical) LRS-comparator: the signs of its inputs are reversed and the feedback path is positive. Opening the feedback path — which leads to maximal activity of a LRS — switches a RRS off.

Introduction

The classical blueprint for a simple feedback system (Fig. 1) needs further elaboration with regard to the properties and the limitations of (models for) biological feedback systems. This is of special importance for pathophysiology. Many diseases are of a semi-stationary nature. The level of the regulated variable is and stays either too high or too low. A detailed "zero order", i.e. steady state, analysis of the structure and function of simple feedback systems is, therefore, necessary. In this paper an analysis is presented of the function and the structure of systems working either against increases or against decreases of the regulated variable.

The Classical Diagram

An elaboration of the classical diagram for a simple negative feedback system is given in Fig. 1. The effects of multiple elements and of the combination of elements into lumped elements (cf. Verveen, 1978) are not included, since it is the basic structure that needs to be treated here. The diagram explicitly contains the *system environment.* We may not neglect the environment in the consideration of biological systems, since it

a) may control the regulating system (dashed arrows in Fig. 1),

b) "disturbs" the level of the regulated variable (influences $x_{d,\,i}$ in Fig. 1),

c) determines the behaviour of the organism, which depends upon the state of the regulated variable: it *functions* within the organism.

For biological feedback systems these aspects always have to be kept in mind. A pathological decrease of body temperature, for example (which occurs during long-term overload, such as "freezing" to death in a cold winter), reduces the maximal heat output of the corrector. A vicious cycle ensues and the organism may die as a result.

Input Variables

There are at least two sets of functional input variables into the system.

1. Controlling variables [cf. (13)]:

a) the reference signal x_i. It may be generated within the system environment or in the system itself, where it may exist as a hidden variable [within lumped elements such as sensor-reference-comparator elements, Verveen (1978)].

b) An additional controlling input variable exists in some feedback systems. Here the sensor gain K_f is separately controlled (like in the gamma control of muscle length).

2. "Disturbing" variables $x_{d,\,i}$ which cause the value of the output variable (here the regulated variable y_r) to deviate from the ideal state y_i . The usage to directly write a "disturbing" variable input into the regulated system is disadvantageous. It may have come about by a confusion with electronic feedback amplifiers, where all variables are of the same nature.

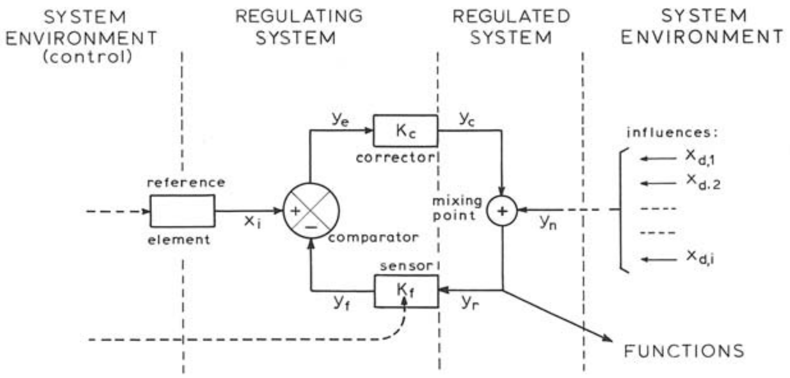

Fig. 1. Basic diagram for simple feedback systems within organisms. Gains *K*, independent variables *x*, dependent variables *y*, indices after the first letter(s) (italics) of the name, except for the reference signal x_i (symbolizing the ideal state y_i), regulated variable y_r, feedback gain (sensor gain) K_f, error signal y_e, corrector gain K_c, correction y_c, nonregulated state y_n. Dashed arrows: possible external control of the reference signal and/or sensor gain

For biological systems (and many technical ones) one has to consider the following points.

a) The properties of the regulated system with regard to a given "disturbing" influence have to be taken into account.

b) One often finds a combination of "disturbing" influences from different sources.

In thermoregulation, for instance, conduction, convection and radiation are different mechanisms, related to different thermal sinks and sources (the "disturbances" $x_{d,\ i}$), while nonregulatory metabolic heat production forms still another source.

c) The nature of the deviation is unspecified. Is it the remaining error y_{re} (= y_i — y_r), or the pending deviation (the threat y_i — y_n), or does it make no sense to try to specify the deviation? One may tend to equate deviation with disturbance, which gives rise to conceptual problems.

d) The term "disturbance" suggests an unwanted influence. For many biological systems the presence of "disturbing" variables is, however, a matter of life or death. These influences *must* be there, since their existence is essential for survival of the organism.

In thermoregulation the effective environmental temperature is a primary *condition:* it must lie within a given range (some tens of degrees around 290 K), in order for the system to regulate the body temperature at all. Outside this range the organism dies, regulation or no regulation. In glucose homeotasis the glucose level is stabilized for the organism to *use* it. Disuse means death.

The Nonregulated Variable y_n

For the theoretical analysis of the steady state behaviour of simple biological feedback systems, the problems generated by the collection of environmental influences upon the regulated system can be avoided by a simple method: the use of the nonregulated variable y_n as the input variable into the regulated system. The nonregulated variable y_n is then *defined* as the end-result of all external influences upon the regulated system when the correction y_c is *not* taken into account. The symbol *y* (index *n* for *nonregulated)* indicates its dependence upon the collection of independent external influences $x_{d,\ i}$. Hence

$$y_r = y_n \underset{\text{def}}{=} f\,(x_{d,i}) \quad \text{with} \quad i = 1,\,2,\,3 \ldots \text{for}\ y_c = 0\,, \qquad (1)$$

where the influence of time is discarded.

In a graphical analysis the first step now becomes quite easy, since a comparison of the effects of regulation with the nonregulated state y_n starts with relationship (1): $y_r = y_n$, a line with unity slope through the origin (Fig. 2).

In order to discuss the properties of simple biological (and technical) systems, the diagram of Fig. 1 represents too high a level of abstraction. Real systems impose at least two essential restrictions: one-sided corrector activity and non-negative signals.

One-Sided Corrector Action

A single corrector organ works into one direction only. It either increases the level of the regulated variable (a heat-producing corrector, such as a stove) or it decreases it (by a corrector which takes heat out of the regulated system, like a correctly mounted air-conditioner). The first type of corrector works against decreases of the regulated state y_r, the second acts against increases only. For both corrector types the regulated state y_r is given by

$$y_r = y_n + y_c\,, \qquad (2)$$

where the sign of the correction y_c depends upon the type of corrector. The differences in properties between the two kinds of correctors lead to different regulation characteristics in plots of the regulated variable y_r against the nonregulated variable y_n (Fig. 2).

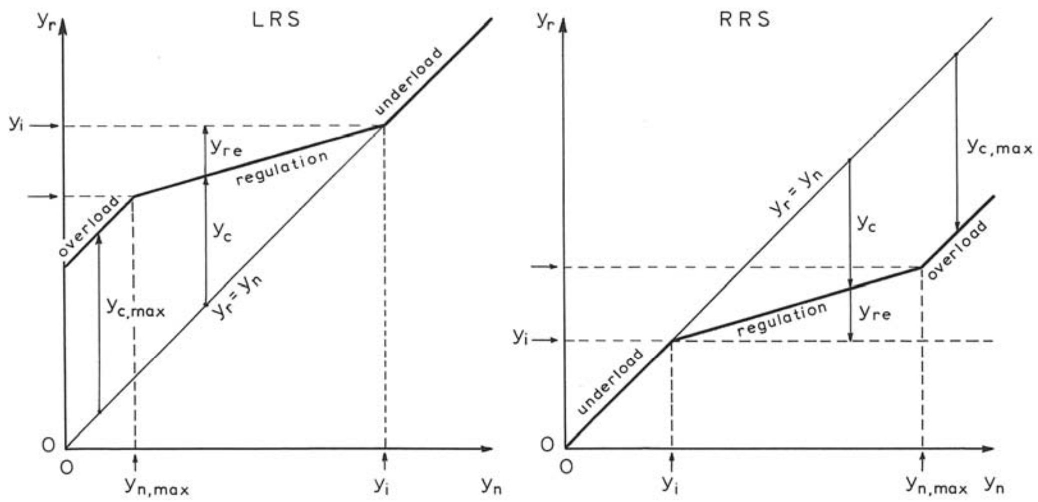

Fig. 2. Piece-wise linearized steady state characteristics. LRS: left-regulating system, RRS: right-regulating system. Remaining error y_{re} , maximal correction $y_{c\,,\,max}$, unmarked arrows: $y_r = y_n + y_{e\,,max}$. For other symbols: see Fig. 1; see text for explanation

Regulation Characteristics: Underload, Regulation, and Overload

For a feedback system with a corrector working against decreases of the regulated state y_r the correction y_c is positive (upward pointing arrow in Fig. 2: LRS). Correction occurs, however, when and only when the regulated state y_r drops *below* a certain value, the ideal state y_i. *Above* this value no correction takes place and

$$y_r = y_n \quad \text{for} \quad y_n \geq yi\ . \tag{3}$$

The system is *not* switched off, since correction comes into play as soon as y_r drops below y_i , it senses y_r all the time, whether it corrects or not. This situation is the opposite of overload. To describe it a new term need to be coined, which can not be misunderstood. Hence the name *underload* for the situation in which no correction is possible.

Saturation of corrective action (in which the correction is maximal: $y_{c,\ \max}$ with index *c,* max from *maximal correction)* occurs in the states of *overload,* where y_n falls below a value $y_{n,\ \max}$:

$$y_r = y_n + y_{c,\ \max} \qquad \text{for} \quad y_n \leq y_{n,\ \max}\ . \tag{4}$$

Note that these descriptions are piece-wise linearized, for non-linearities in real systems create rounded corners.

In between the two corners (the critical points y_i , y_i and $y_{n,\ \max} + y_{c,\ \max}$, $y_{n,\ \max}$) lies the working range where the system regulates (for y_n also called the "range of proportionality"). Here both the correction y_c and the remaining error y_{re} increase proportional to the deviation of y_n from y_i towards the left.

For feedback systems with a corrector working against raised levels of y_r (downward pointing arrow y_c in Fig. 2: RRS) correction y_c only occurs when the regulated state rises *above* the ideal state y_i . Here

$$y_r = \begin{cases} y_n & \text{for} \quad y_n \leq y_i \\ y_n + y_c & \text{for} \quad y_i \leq y_n \leq y_{n,\ \max} \\ y_n + y_{c,\ \max} & \text{for} \quad y_{n,\ \max} \leq y_n\ , \end{cases} \tag{5}$$

where y_c and $y_{c,\ \max}$ are negative. For this kind of system the ranges of overload and underload are reversed with respect to the former type [(2)–(4) and Fig. 2].

Left- and Right-Regulating Systems

The line $y_r = y_n$ divides the y_r, y_n -plane into two segments (Fig. 2). The characteristic for the feedback system regulating against decreases lies completely within the left segment, while the right segment contains the relationship for a system correcting increases of the regulated variable. This property nicely enables the classification of the two types of feedback systems. Simple feedback systems which correct decreases of the regulated state will be named *left-regulating systems* (abbreviated to *LRS),* while those that counteract increases are, hence, called *right-regulating systems (RRS).* With the use of these terms we avoid:

a) ambiguity, since terms related to the behaviour of the regulated variable (such as "decrease", "loss", "down" or "negative") may be thought to apply to the *opposite* behaviour of the corrective action and vice versa,

b) confusion, for a term like "downward regulation" is used for the decrease in cell membrane receptors upon prolonged exposure to a raised concentration of their ligands: the term "positive regulation" is in use for the opposite effect (cf. Catt et al., 1979).

An additional advantage is, that they do not suggest unrelated usage and are grasped quickly from the steady state graphs. Comparator behaviour also falls within these terms (Fig. 4).

Basic Equation: Graphical Derivation

Within the working range (Fig. 2) the remaining error y_{re} is equal to the difference between the ideal state y_i and the regulated state y_r:

$$y_{re} = y_i - y_r \,. \tag{6}$$

The size of the correction is equal to the difference between the regulated state y_r and the nonregulated state y_n :

$$y_c = y_r - y_n \,. \tag{7}$$

For a LRS y_{re} and y_c are positive, while they are negative for a RRS. This follows from (6) and (7) and accounts for the convention used in (2) and (5). Both increase proportional to the pending deviation from the ideal state [yi, which can be read from the graphs (after linearization) as the critical point upon the $y_r = y_n$ line] (Fig. 2). The quotient of y_c and y_{re} is by definition the (open loop) gain K:

$$K \underset{\text{def}}{=} \frac{y_c}{y_{re}}$$

The expression for the regulated state y_r follows after insertion of (6) and (7) into (8) and rearrangement:

$$y_r = \frac{K}{1+K} y_i + \frac{1}{1+K} y_n \tag{9}$$

Note that (9) applies to both left- and right-regulating systems. Insertion of (9) into type (5) equations (instead of $y_i = y_n + y_c$) includes the whole range of y_n and preserves the differences between LRS and RRS.

Corrector Organ: Block Diagram

For a LRS the effect of corrective action results in an addition of the correction to the nonregulated state [(2) and Fig. 3A]. For a RRS the correction amounts to a subtraction (Fig. 2: RRS and Fig. 3B). With the mentioned convention: for y_c to include its sign (7), Fig. 3C is the result. The corrector *type* is now specified by the placement of a negative sign in front of the corrector gain in a RRS. This also avoids possible confusion between the mixing point symbol for the regulated system of Fig. 3B and the comparator symbol. The two diagrams (Fig. 3 B and C) are, of course, mathematically identical.

Non-Negative Signals

In real systems the signals y_f, x_i and y_e (feedback, reference and error signal, respectively) are either positive or zero, since they are modulations of a non-negative carrier in a one-to-one relationship. Negative signals do not exist (the possibility of a spontaneously active element, signaling both negative and positive values of its inputs, is not considered here). The *effect* of a signal hence indicates its sign: one type of signal excites the following element (plus sign), another inhibits it (minus sign), both are *measured* and plotted in terms of non-negative units.

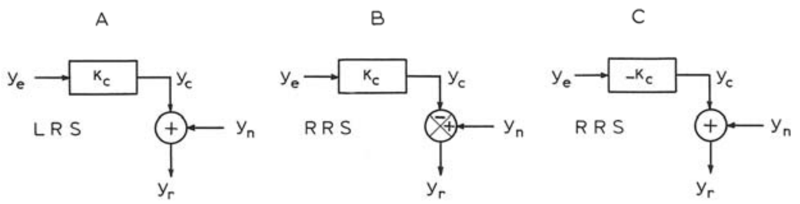

Fig. 3A–C. Block diagrams of corrector action and regulated system. **A** LRS, **B** and **C** RRS. The negative sign within the mixing point in **B** has been carried over into the corrector in **C**

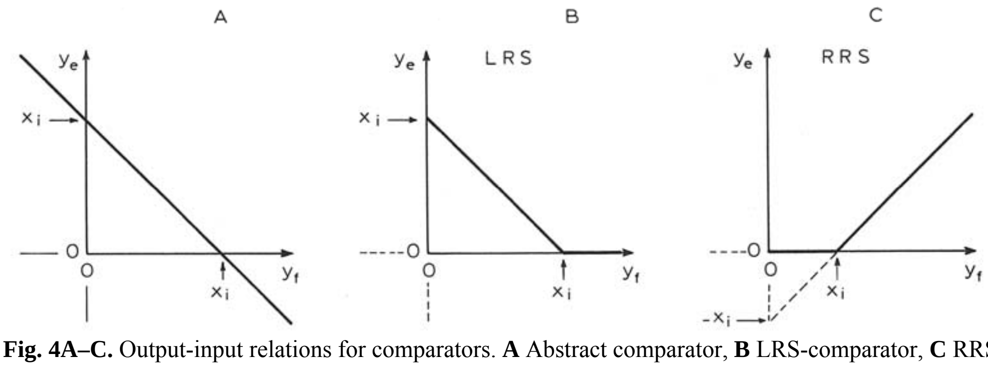

Fig. 4A–C. Output-input relations for comparators. **A** Abstract comparator, **B** LRS-comparator, **C** RRS-comparator. Dashed lines: nonexisting ranges

For the abstract comparator of Fig. 1 this implies that the y_e vs. y_f diagram of Fig. 4A is unrealistic. The conditions imposed upon our representations are

$$y_f \geq 0, \quad x_i \geq 0, \quad \text{and} \quad y_e \geq 0\,. \tag{10}$$

In terms of y_e, y_f —diagrams the conditions lead to two kinds of comparators (Fig. 4B and C, piece-wise linearized).

The output of the comparator of Fig. 4B goes down with y_f (slope — 1):

$$y_e = \begin{cases} x_i - y_f & \text{for} \quad 0 \leq y_f \leq x_i \\ 0 & \text{otherwise}\,. \end{cases} \tag{11}$$

It only signals decreases of the regulated state y_r, since the first expression of (11) is equal to

$$y_e = x_i - K_f y_r\,.$$

This comparator, therefore, forms part of a LRS. Note that its working range lies to the left of the point
$y_f = x_i$.

The other type of comparator (Fig. 4C) has a threshold at $y_f = x_i$, from where the (linearized) line rises with slope plus one:

$$y_e = \begin{cases} y_f - x_i & \text{for} \quad y_f \geq x_i \\ 0 & \text{otherwise}\,. \end{cases} \tag{12}$$

This one only works against increases of the regulated variable:

$$y_e = K_f y_r - xi$$

and is, therefore, the comparator element of a RRS. Its working range lies at the right side of the point $y_f = x_i$. Note that the terms "left-" and "right-regulation" also apply to the actions of the comparators.

The corresponding block diagrams for these comparators, following from the restriction to positive signals, are given in Fig. 5. The LRS-comparator is pictorially identical with the abstract comparator of Fig. 1, while the RRS-comparator has the signs of its inputs reversed.

Complete Block Diagrams

The results from the analyses of corrector action and of comparator action (Figs. 3A and 5A; Figs. 3C and 5B) can now be assembled into the complete diagrams for a LRS and a RRS (Fig. 6). Calculation of the regulated variable y_r from both diagrams results into (9), with the ideal state

$$y_i = \frac{x_i}{K_f} \tag{13}$$

and the (open loop) gain

$$K = K_f K_c. \tag{14}$$

A LRS has the classical structure, but for a RRS the feedback signal y_f *excites* the comparator, while the reference signal x_i *inhibits* it. Although the feedback as such is *positive* indeed, the system is not a positive feedback system. This is directly visible when the negative sign for the gain K_c is carried over into the comparator. The diagram of Fig. 6B then changes into that of Fig. 1.

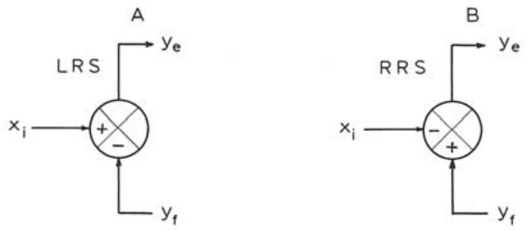

Fig. 5A and B. Block diagrams for the comparator elements of a LRS (**A**) and a RRS (**B**)

Implications

The differences in structure and function of left- and right-regulating systems are essential and clear our insight into their behaviour in health and disease.

1. The nature of the action of the feedback *signal* (negative or positive feedback) does not enable us to classify the corresponding system into a negative or positive feedback *system.* The *whole* system has to be taken into account. The isolated terms "negative feedback" and "positive feedback" do not convey any information whatsoever; unless they are restricted either to the actual structure of the feedback path, or to effector action, which is quite confusing.

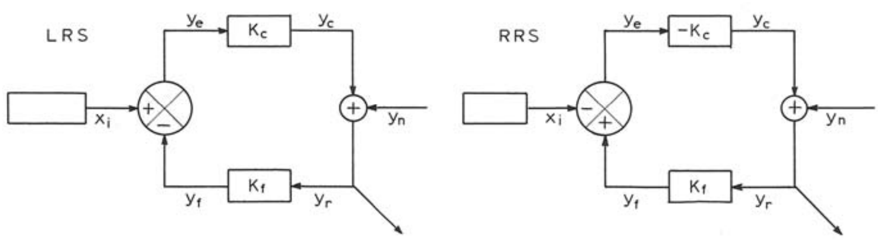

Fig. 6. Block diagrams for a LRS and a RRS

2. The practice to diagram negative feedback systems according to the blueprint of Fig. 1 carries the danger of neglect of the structure and properties of right-regulating systems.

3. One phenomenon (opening the feedback path) serves to illustrate a difference in behaviour. From Fig. 1 follows that such a situation leads to

$$y_r = K_c \, x_i \tag{15}$$

which cannot occur. For a LRS the corrector saturates and

$$y_r = y_n + y_{c,\,\max} \,. \tag{16}$$

The system is and stays maximally active. Damage results from the increased level and, especially, from the continuous expenditure of energy, which leads to exhaustion.

For a RRS the situation is different, since it ceases corrector action. Here

$$y_r = y_n \tag{17}$$

and the system is switched of. A biological application of this property of right-regulating systems is found in gamma control of muscle length. The sensors are “set” by gamma neuron activity. During sleep (and sometimes during strong emotions) gamma neuron activity ceases, sensor activity disappears ($K_f = 0$) and the muscles slacken: the system has been switched off via the feedback. This sometimes happens via an intial gamma control of muscle length overshoot (the jolt before one falls asleep). Others experience a differential awakening at night. They are paralysed for a few moments, unable to move their limbs since the system for the regulation of muscle length is still switched off.

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Note added in proof: For a RRS the error signal is positive. It excites (actuates) the corrector. The steady state *effect* of corrector action is described by a negative sign placed before its gain.

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