# Theory of Diseases of Steady-State Proportional Control Systems

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**Abstract**. In many diseases of a semi-stationary nature (chronical diseases) the level of the regulated variable of the diseased system either is too high (a hyper-state disease) or too low (a hypo-state disease). In this paper the steady-state behavior of proportional control systems is, hence, analysed with regard to a longterm pathological change of each single variable or parameter. Each pathological change has its own pattern of changes of the system variables, which also depends upon the system class (left- or right-regulating). Both the block diagram and the regulation characteristic, when used together, allow one to easily derive the pathological behaviour of the system in the steady-state.

## The Steady-State

To investigate diseases of the steady-state of a regulating system we use both the regulation characteristic and the block diagram (Figs. 1 and 2), (Verveen, 1979). Given a diseased variable ($x_j$ or $y_j$ see Fig. 1) or parameter ($K_j$) we investigate the regulation characteristic for its steady-state effects. The block diagram gives us the steady-state changes of the variables. With the use of the block diagram we derive the changes of the variables as follows: start with the diseased variable or parameter and work through the diagram *following* the arrows until the starting point is again encountered. Since the process itself is dynamical, "paradoxes" may occur upon repassage through the loop. The regulation characteristic helps us, however, to evaluate the end result.

Suppose, for example, that the reference $x_i$ of a left-regulating system (LRS) is pathologically increased. The block diagram of Fig. 1 gives us the following sequence of events after a stepwise increase of $x_i$:

high $x_i$ $\rightarrow$ high $y_d$ $\rightarrow$ high $y_c$ $\rightarrow$ high $y_r$ $\rightarrow$ high $y_f$

while $K_c$, $y_n$, and $K_f$ are not changed at the end of our first passage through the loop. This result also is our diagnostic series of *final qualitative* changes for the steady-state.

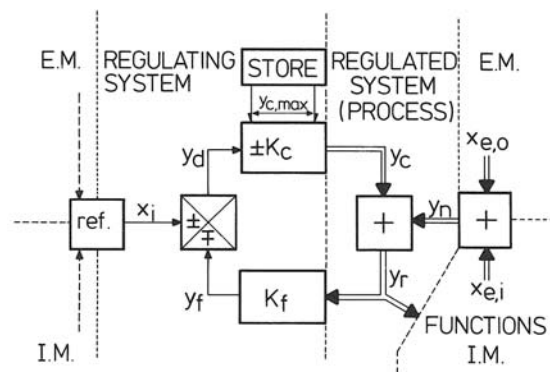Repeating the passage through the loop may give us difficulties, since the increased value of $y_f$ suggests a



Fig. 1. Elementary block diagram for a regulating system. LRS: left-regulating system, control by addition: upper parts of combined symbols: + for ± and — for ∓ and for a right-regulating system RRS: control by removal: lower parts of combined symbols: — of ± and + of ∓. Abbreviations (indexes refer to corresponding names with the use of italics): External milieu E.M., internal milieu I.M.: external influences $x_e$ from outside the organism ($x_{e,o}$) and from within ($x_{e,i}$), non-regulated state $y_n$, regulated variable $y_r$, feedback gain factor $K_f$, feedback signal $y_f$, reference input $x_i$, difference signal $y_d$, effector (corrector) gain factor $K_c$, correction $y_c$ and maximal correction $y_{c,\,max}$. Controlling influences are indicated by the dashed arrows
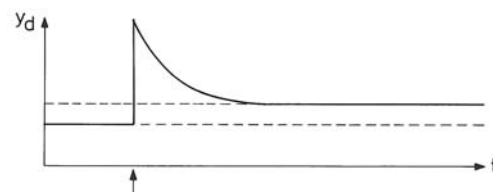


Fig. 2. Time dependent behaviour of difference signal $y_d$ after a step change of $x_i$ (arrow)

decrease of the subtractor output $y_d$, with decreases of all subsequent variables. This does indeed occur upon a sudden stepwise increase of $x_i$. The decrease is relative, however. The transient shows a decrease of an increase, while the final effect (the steady-state effect) is still an increase. For a first-order process the behaviour of the difference signal $y_d$ as a function of time after the change of the reference signal $x_i$ is pictured in Fig. 2. The transient behavior shows an overshoot, going down to a still increased value in the steady state.

The steady-state situation follows from the regulation characteristic

$$y_r = \begin{cases} y_n & \text{(1a)} \\ \dfrac{K}{1+K}\, y_i + \dfrac{1}{1+K}\, y_n & \text{(1b)} \\ y_n + y_{c,\,max} & \text{(1c)} \end{cases}$$

(Fig. 3), with Central critical point $C_c$ coordinates $y_i$ both equal to

$$y_i = x_i/K_f, \tag{2}$$

and with the open loop gain factor $K$ given by

$$K = K_f K_c. \tag{3}$$

After a step-wise increase of the reference $x_i$ the central critical point

$$C_c = (y_i, y_i) = (x_i/K_f,\ x_i/K_f) \tag{4}$$

shifts upwards along the "line for non-regulation"

$$y_r = y_n\,.$$

The Peripheral intersection point

$$P_i = (y_n = -K_c x_i;\ y_r = 0) \tag{5}$$

shifted towards the left. The gain factors do not change, neither does the distribution of the non-regulated variable $y_n$. The line for regulation hence moves up in parallel to the original line.

It follows that the regulated variable $y_r$ has been raised definitively. The disease is of the *hyper-$y_r$* type. The feedback signal $y_f$ shows a definite increase [block diagram and (9)]. The regulation characteristic also shows a definite raise of the correction $y_c$ *(6)*. Hence the difference signal $y_d$ also is increased [block diagram and (7)].

This is in accordance with our "first passage through the diagram" result. Those who still doubt the validity of the reasoning used here may calculate the steady-state expressions for $y_c$, $y_d$, and $y_f$ as functions of $x_i$ and $y_n$ [start with the chosen variable and work back *against* the direction of the arrows ; cf. Verveen (1978)]. Insertion of the increase of $x_i$ leads to the
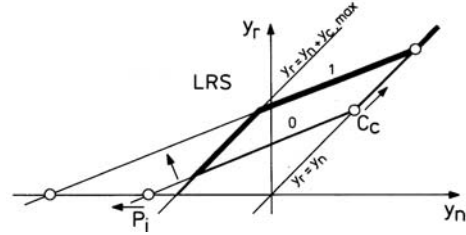


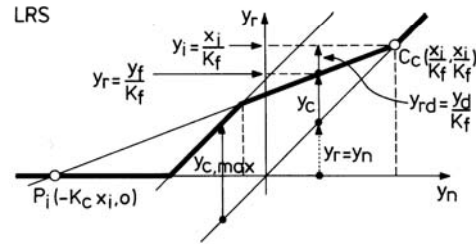**Fig. 3.** Regulation characteristic for a LRS with an increase of $x_i$



**Fig. 4**. Regulation characteristic for LRS with block diagram variables and parameters

results presented above. The expressions are :

$$y_c = \frac{K}{1+K}\,(y_i - y_n) \quad \text{(LRS and RRS),} \tag{6}$$

$$y_d = \frac{1}{1+K} \cdot x_i - \frac{K}{1+K} \cdot \frac{y_n}{K_c} \quad \text{(LRS),} \tag{7}$$

$$y_d = \frac{-1}{1+K} \cdot x_i + \frac{K}{1+K} \cdot \frac{y_n}{K_c} \quad \text{(RRS),} \tag{8}$$

$$y_f = \frac{K}{1+K}\left(x_i + \frac{y_n}{K_c}\right) \quad \text{(LRS and RRS),} \tag{9}$$

We even may, apart from changes of $K_f$, refrain from the use of the block diagram altogether (Figs. 3 and 4). The expressions :

$$y_{rd} = y_i - y_r \quad \text{(LRS)} \quad \text{and} \quad y_{rd} = y_r - y_i \quad \text{(RRS)}.$$

when multiplied by the sensor gain factor $K_f$ become:

$$K_f \cdot y_{rd} = K_f \cdot y_i - K_f \cdot y_r \quad \text{(LRS)} \tag{10}$$

and

$$K_f \cdot y_{rd} = K_f \cdot y_r - K_f \cdot y_i \ \text{(R RS)}\,. \tag{11}$$

The left terms of (10) and (11) are also equal to

$$y_f = K_f \cdot y_i \tag{12}$$

(see Fig. 1) and the expressions (10) and (11) are identical with the steady-state-difference equations (see Fig. 1) :

$$y_d = x_i - y_f \quad \text{(LRS)} \tag{13}$$

and

$$y_d = y_f - x_i \quad \text{(RRS)}\,. \tag{14}$$

Hence our "graph-to-block" transformation equations (written into Fig. 4) :

$$y_d = K_f \cdot y_{rd} \rightarrow y_{rd} = y_d / K_f , \tag{15}$$

$$y_i = K_f \cdot x_i \rightarrow x_i = y_i / K_f , \tag{16}$$

and

$$y_f = K_f \cdot y_r \rightarrow y_r = y_f / K_f . \tag{17}$$

### Derivation of the Diseases

The effect of a change of a block diagram variable or parameter can now be read off from the regulation characteristic of Fig. 4 (apart from the effects of a change of $K_f$) keeping in mind whether we deal with a LRS or with a RRS.

It is, however, much more easy to refer to the original drawing of the regulation characteristic *plus* the block diagram, especially for the derivation of the changes of the variables.

In the regulation characteristic all external variables ($y_n$ and $x_i$) and parameters ($K_f$, $K_c$, and $y_{c, max}$) are visible (Fig. 4). The steady-state result of a definite change of one of these can be easily drawn into the corresponding (LRS or RRS) regulation characteristic (cf. Figs. 5 through 9) :

a) A shift of the distribution of $y_n$ (of its average value $<y_n>$) merely shifts the $y_r$ distribution into partial or total over- or underload (Fig. 5).

b) A change of $y_{c, max}$ shifts the medial critical point $C_m$ towards the left or the right, which increases or decreases the working range of the system (Fig. 6).

c) A change of the forward gain $K_c$ shifts the peripheral intersection point along the $y_n$-axis, while the central critical point stays in its original position (Fig. 7). The line of regulation hence turns through $C_c$: upwards toward (but not reaching) $y_r = y_i$ upon an increase of $K_c$, and down to $y_r = y_n$ for a decrease of $K_c$. $y_r = y_n$ when $K_c = 0$ (opening of the forward path of the loop).

Note that the changes will be very small for systems for which $K_c$ originally is large, unless $K_c$ decreases towards very small values.

d) A change of the reference $x_i$ shifts both $C_c$ and $P_i$ (Fig. 8). The line for regulation moves in parallel with its original: upwards for an increase of $x_i$ and downwards for a decrease.

e) A change of the feedback (sensor) gain factor $K_f$ shifts $C_c$ along $y_r = y_n$ while $P_i$ does not move (Fig. 9). Here the line for regulation turns through $P_i$ : upwards towards infinity (in parallel with $y_r = y_n$) for a *decrease* of $K_f$ and down to $y_r = 0$ for an *increase* of $K_f$. The system is now forcibly clamped onto a low level of $y_r$, while the reference signal $x_i$ does not change.

Proceeding along these lines we may classify the theoretically possible diseases according to the nature of the original diseasing change. In the following examples secondary effects (due to induced hyper- or hypo-trophia by the long-term changes of excitatory or inhibitory drives) will not be mentioned.

### Classification of Diseases

*A. Load Diseases* are caused by a long-term change of the average $<y_n>$ of the distribution of the non-regulated variable $y_n$ , which either generates (partial) overload or underload (Fig. 5) dependent upon the new position of $<y_n>$: partial, when $<y_n>$ still lies within the working range; total after a shift out of this range.

The four possibilities are :

For *increases* of $<y_n>$:

1. A hyper-$y_r$ disease for a LRS, with underload. From the block diagram follows that $y_f$ is increased, while $y_d$ is zero. There is no energy production involved ($y_c = 0$).

2. A hyper-$y_r$ disease with overload for a RRS. The feedback signal $y_f$ is maximal, as is the difference signal $y_d$ and the use of energy ($y_c = y_{c, max}$).

For *decreases* of $<y_n>$ :

3. A hypo-$y_r$ disease with overload for a LRS, where $y_f$ is small and $y_d$ is increased, with maximal energy dissipation ($y_c = y_{c, max}$).

4. A hypo-$y_r$ disease for a RRS, with underload. $y_f$ is decreased, while $y_d$ is zero, with no energy expenditure ($y_c = 0$).

For les extreme shifts of the average of $y_n$ the direction of the changes is as indicated, but the over- or underload is partial only.

There are no changes of the other variables and parameters.

Continuous production of thyroid hormones by a TSH-independent tumor forms an example of under-load, as is the regular ingestion of large doses of thyroid hormones in the wrongly applied "treatment" of adipositas (a *iatrogenic* disease, i.e. caused by the physician).

"Freezing" to death in the snow or in mountains forms an example of a thermal overload disease.

The (rare) case of nephrotic loss of thyroid hormones generates overload of the thyroid hormone regulation system.
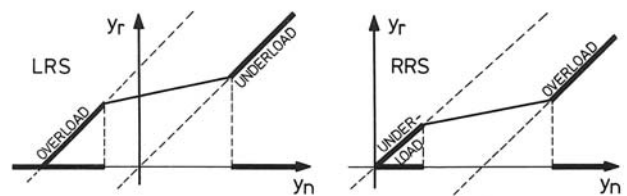


**Fig. 5.** Regulation characteristics for LRS and RRS for longterm changes of $y_n$ (heavy segments)
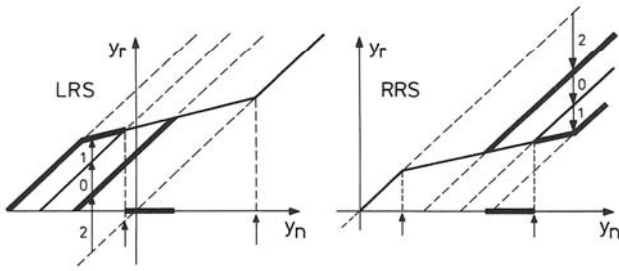
**Fig. 6**. Regulation characteristics for LRS and RRS after definite changes of $y_{c, max}$ (heavy segments). Arrows for $y_n$ indicate the original working range. Vertical arrows: $y_{c, max}$ is normal (0), increased (1) or decreased (2). The heavy segments of $y_n$ indicate the overload ranges in cases of decreased $y_{c, max}$

*B. Store Diseases* are caused by a definite change of the maximal capacity for correction, indicated by the size of $y_{c, max}$ (Fig. 6).

An increase of the maximal correction does *not* influence the system itself – the working range *expands* – and it has to be diagnosed by other means: we might call it a para-$y_r$-disease.

A decrease changes the working range only: it *shrinks* and the organism more easily experiences overload.

The four possibilities are :

For *increases* of $y_{c, max}$ :

1 and 2. For LRS and RRS no changes within the system itself. The disease might manifest itself, but in such a situation by means other than those directly associated with the system. One may think of the effects of, for instance, growth as such. Here we have a para-$y_r$-disease.

For *decreases* of $y_{c, max}$ :

*3.* for LRS partial overload with decreased $\langle y_r \rangle$ – a hypo-$y_r$ disease – and $\langle y_f \rangle$, while $\langle y_d \rangle$ is increased and energy expenditure is maximal for some $y_n$ .

*4.* for RRS partial overload occurs, with increases of $\langle y_r \rangle$ – a hyper-$y_r$ disease – of $\langle y_f \rangle$ and of $\langle y_d \rangle$, with smaller but in part maximal energy expenditure.

A disease which results in an hyper- or hypo-state for a (regulated) variable which forms the *store* for the next regulating system affects the maximal correction for that system.

In caloric undernourishment, for instance, the glycogen store in the liver may become insufficient to cope with large quests for glycogen, while the bloodglucose level in the resting state is not affected. The patient is in a state of partial overload, which manifests itself during exercise or during another intermittent disease.

Overeating, on the other hand, overincreases the caloric stores without an effect upon bloodglucose levels as such.

Note that the properties of the system are unchanged as long as $y_n$ stays within the (changed) range of regulation.
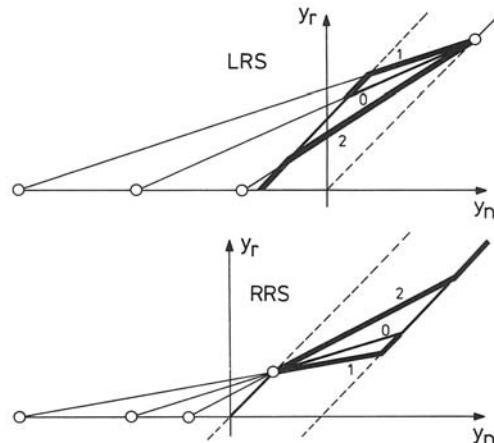


**Fig. 7.** Steady-state characteristics for LRS and RRS and the effects of changes of $K_c$ (low-gain systems). The line pivots through $C_c$. Original situation: 0; increase of Kc: 1; decrease: 2. Note the occurrence of partial overload in situations 1, but with higher or lower $y_r$ values for all $y_n$ of the original working range

*C. Forward Gain Diseases* have effects which depend on the direction of the change and upon the initial size of the forward gain factor, i.e. whether the system has a large gain factor (15 or larger) or if the gain is low (5 or smaller; these numbers are indicative only, for the effect also depends on the range of $y_r$-variability tolerated by the organism and is not necessarily identical with the working range).

C-1. For *high-gain-systems* an increase of the gain factor (which may for instance be the result of a growth of the effector) does not affect the system significantly, while a decrease (by atrophy, operation or intoxication) also does not influence it. This is due to the property of regulating systems not to be dependent upon the size of the forward gain, since the *closed loop gain* (lb) is equal to :

$$\frac{K}{1 + K} = 1 \text{ for large } K . \tag{18}$$

For drastic decreases of $K_c$ the system will reach a hypo-$y_r$ state, which will be discussed in the following part.

C-2. For *low-gain systems* (such as the control of the prolactin level) changes of the forward gain do affect the regulated variable $y_r$ (the line for regulation turns through $C_c$, Fig. 7).

An increase of $K_c$ increases the closed loop gain (18) significantly. The system becomes more powerful, which generates a hyper-$y_r$ disease, while a decrease causes a hypo-$y_r$ disease (Fig. 7).

There are, hence, six possibilities :

For *increases* of $K_c$ either

*1.* nothing with regard to the system itself (but growth, for instance, might lead to effects on other tissues), or

*2.* for a LRS a hyper-$y_r$ disease with increased $y_f$ and decreased $y_d$ values ;

*3.* for a RRS a hypo-$y_r$ disease with a decrease of $y_f$ and a decrease of $y_d$.

For *decreases* of $K_c$ also either

*4.* nothing (perhaps a smaller effector organ or organs), or

*5.* for LRS a hypo-$y_f$ disease with a decrease of $y_f$ and an increase of $y_d$ ;

*6.* for RRS a hypo-$y_r$ disease with an increase of $y_f$ and an increase of $y$ ..

Other variables and parameters are not directly affected.

The weak prolactine control system shows an increase of forward gain upon proliferation of the prolactine producing cells in the anterior hypothalamus (micro-adenoma). The resulting gain increase generates a hyperprolactinemia (with sterility as a result).

Stronger systems do not change considerably upon a decrease of the effector. Removal of one adrenal gland does not affect the corticosteroid levels, while removal of one renal similarly does not change the levels of variables which it controls.

Hypertrophy or the development of dependent adenoma of such systems increases without changes of the closed loop gain and, hence, of $y_r$. Such adenome are, therefore, often called (clinically) *silent adenoma.*

*D. Reference Diseases* are caused by changes of the reference signal or value $x_i$. Here the line shifts up for an increase of $x_i$ and down for a decrease (Fig. 8).

There are four possibilities:

Upon an *increase* of $x_i$:

1. A hyper-$y_r$ disease for a LRS, with partial overload. $y_f$ is increased as is $y_d$ and energy expenditure;

2. A hyper-$y_r$ disease for a RRS, with partial underload. $y_f$ is increased, while $y_d$ is decreased as is the energy expenditure.

After a *decrease* of $x_i$:

3. For LRS a hypo-$y_r$ disease with lowered $y_f$ and decreased $y_d$. Energy expenditure decreases.

4. For RRS a hypo-$y_r$ disease with lowered value of $y_f$, a larger one for $y_d$. Larger energy dissipation.

Hypothalamically induced increases or decreases of TRH or other releasing hormones form examples of such diseases.

*E. Sensor Diseases* are those for which the feedback gain factor $K_f$ has been changed (caused for instance by an increase or decrease of the number of receptors for $y_r$).

Now the line for regulation pivots through $P_i$, with a raise when $K_f$ decreases and vice versa (Fig. 9).

Again four situations are possible :

With *increased* $K_f$:

1. A hypo-$y_r$ disease for LRS, where $y_r$ is forcefully clamped onto the lower value. $y_f$ is increased, while $y_d$ and energy dissipation are decreased. The reference $x_i$ does not change. Partial underload is present at the right side of the working range.

2. For RRS also a clamped hypo-$y_r$ disease but with a large $y_d$ and energy expenditure. $y_f$ is increased.

For a *decreased* $K_f$:

3. For LRS a hyper-$y_r$ disease with lowered open loop gain factor (which results in larger fluctuations with variations of $y_n$). $y_f$ is decreased while $y_d$ is increased and also the energy expenditure. Note partial underload at the left.

4. For RRS also a hyper-$y_r$ disease, but with partial underload. $y_f$ is larger, while $y_d$ and energy expenditure are lowered.
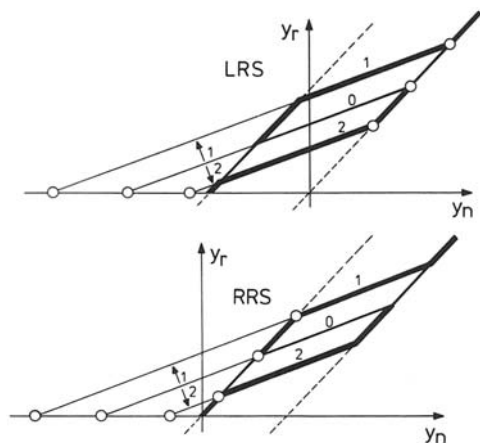


**Fig. 8.** Steady-state characteristics for LRS and RRS upon changes of $x_i$. Original situation: 0; increases of $x_i$: 1; decreases: 2. Note the occurrence of partial under- or overload (compare with working range indicated by original situation: 0)
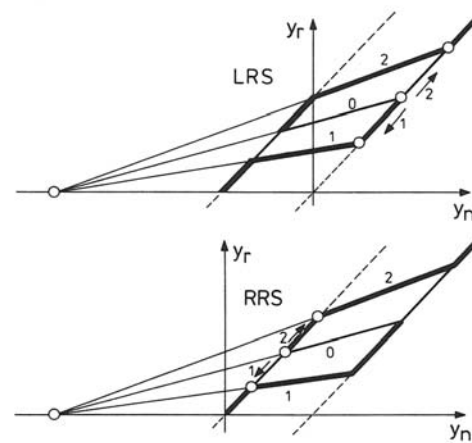


**Fig. 9.** Steady-state characteristics for LRS and RRS upon changes of $K_f$. Original situation: 0; increases of $K_f$: 1; decreases: 2. Note partial under- and overload (as compared with the original working range given by 0)
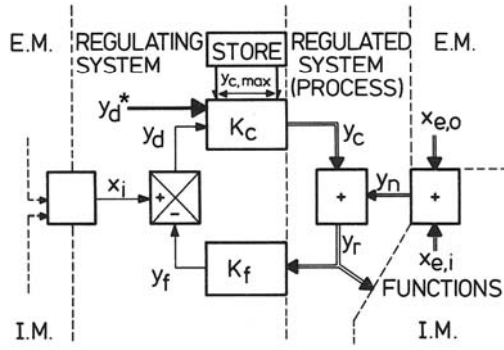
**Fig. 10.** LRS with false difference signal $y_d$*

Fever is thought to be caused by a decrease of the sensitivity of the central heat-sensitive receptors for thermoregulation.

Similarly a decrease of peripheral baroreceptor sensitivity may cause a (passing) hypertension.

Another example is given by "hyperthyroidy without hyperthyroidy" — i.e. without apparent hypermetabolism (Werner, 1971) — which is caused by a decreased sensitivity of *all* body cells to the thyroid hormones, including the thyrotropic hypothalamic cells, which translates into a decrease of $K_f$. This quite nicely compensates the decrease of responsiveness, which leads to clinical euthyroidy (with theoretically larger fluctuations of the bloodlevel upon changes of $y_n$ ).

Well documented cases of clamping on lower levels by increases of receptor feedback gain $K_f$ are not known (to me), but some cases of dwarfism may be due to such a phenomenon in growth hormone regulation. Nature has prevented the occurrence of these grave diseases upon proliferation of sensor organs by the neat trick of combination of elementary functions (Verveen, 1978).

*F. False Signal Diseases* are caused by the generation of $y_f$ — , $x_i$ — or $y_d$ —like substances with different chemical structure but similar action, generated by extraneous non-regulatory sources.

Graves-Basedow hyperthyroidy is a case in point. Here TSH-like substances such as LATS (long acting thyroid stimulator) are developed as a result of the autoimmune attack upon the thyroid. The false "difference signal" in effect is a (somewhat overeffective) defence mechanism of the thyroid.

Let us indicate a false signal with the use of an asterisk (Fig. 10). Calculation of its effect with the use of the block diagram of Fig. 10 gives us for a false difference signal $y_d$* :

$$y_r = \frac{K}{1+K} \cdot \frac{A}{K_f} + \frac{1}{1+K} \cdot y_n. \qquad (19)$$

Here the term $A$ is given by :

$$A = x_i + y_d* \text{ for LRS} \qquad (20)$$

while

$$A = x_i - y_d* \text{ for RRS.} \qquad (21)$$

For a false reference (signal) $x_i$* or a false feedback signal $y_f$* we obtain (19) again, but with for LRS and

**Table 1**. Pattern of changes for a LRS

| | | | $y_r$ | $y_f$ | $x_i$ | $y_d$ | $y_c$ | $y_n$ | $y_i$ | $K$ | Clinical disease |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Load diseases | $y_n$ | ↑ | ↑ | ↑ | = | ↓ | ↓ | ↑ | = | = | Hyper |
| | $y_n$ | ↓ | ↓ | ↓ | = | ↑ | ↑ | ↑ | = | = | Hypo |
| Store diseases | $y_{n, max}$ | ↑ | = | = | = | = | = | = | = | = | Normo (no disease) |
| | $y_{n, max}$ | ↓ | ↓ | ↓ | = | ↑ | ↓ | = | = | = | Hypo |
| Forward gain diseases | $K_c$ | ↑ | ↑ | ↑ | = | ↓ | ↑ | = | = | ↑ | Hyper |
| | $K_c$ | ↓ | ↓ | ↓ | = | ↑ | ↓ | = | = | ↓ | Hypo |
| Reference diseases | $x_i$ | ↑ | ↑ | ↑ | ↑ | ↑ | ↑ | = | ↑ | = | Hyper |
| | $x_i$* | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | = | ↓ | = | Hypo |
| Sensor gain diseases | $K_f$ | ↑ | ↓ | ↑ | = | ↓ | ↓ | = | = | ↑ | Hypo |
| | $K_f$ | ↓ | ↑ | ↓ | = | ↑ | ↑ | = | = | ↓ | Hyper |
| False signal diseases | $y_d$* | | ↑ | ↑ | = | ↓ | ↑ | = | ↑ | = | Hyper |
| | $x_i$* | | ↑ | ↑ | = | ↑ | ↑ | = | ↑ | = | Hyper |
| | $y_f$* | | ↓ | ↓ | = | ↓ | ↓ | = | ↓ | = | Hypo |
| Target diseases No sensor change | t. sens. | ↑ | = | = | = | = | = | = | = | = | Hyper |
| | t. sens. | ↓ | = | = | = | = | = | = | = | = | Hypo |
| With sensor change | t. sens. | ↑ | ↓ | ↑ | = | ↓ | ↓ | = | = | ↑ | Normo (no disease) |
| | t. sens. | ↓ | ↑ | ↓ | = | ↑ | ↑ | = | = | ↓ | Normo (no disease) |

Symbols: ↑ increase; ↓ decrease; = no change; t. sens.: target sensitivity

**Table 2**. Pattern of changes for a RRS

| | | $y_r$ | $y_f$ | $x_i$ | $y_d$ | $y_c$ | $y_n$ | $y_i$ | $K$ | Clinical disease |
|---|---|---|---|---|---|---|---|---|---|---|
| Load diseases | $y_n$ ↑ | ↑ | ↑ | = | ↑ | ↑ | ↑ | = | = | Hyper |
| | $y_n$ ↓ | ↓ | ↓ | = | ↓ | ↓ | ↑ | = | = | Hypo |
| Store diseases | $y_{n,max}$ ↑ | = | = | = | = | = | = | = | = | Normo (no disease) |
| | $y_{n,max}$ ↓ | ↑ | ↑ | = | ↑ | ↓ | = | = | = | Hyper |
| Forward gain diseases | $K_c$ ↑ | ↓ | ↓ | = | ↓ | ↑ | = | = | ↑ | Hypo |
| | $K_c$ ↓ | ↑ | ↑ | = | ↑ | ↓ | = | = | ↓ | Hyper |
| Reference diseases | $x_i$ ↑ | ↑ | ↑ | ↑ | ↓ | ↓ | = | ↑ | = | Hyper |
| | $x_i^*$ ↓ | ↓ | ↓ | ↓ | ↑ | ↑ | = | ↓ | = | Hypo |
| Sensor gain diseases | $K_f$ ↑ | ↓ | ↑ | = | ↑ | ↑ | = | ↓ | ↑ | Hypo |
| | $K_f$ ↓ | ↑ | ↓ | = | ↓ | ↓ | = | ↑ | ↓ | Hyper |
| False signal diseases | $y_d^*$ | ↓ | ↓ | = | ↓ | ↑ | = | ↓ | = | Hypo |
| | $x_i^*$ | ↓ | ↓ | = | ↑ | ↑ | = | ↑ | = | Hypo |
| | $y_f^*$ | ↓ | ↓ | = | ↑ | ↑ | = | ↓ | = | Hypo |
| Target diseases No sensor change | t. sens. ↑ | = | = | = | = | = | = | = | = | Hyper |
| | t. sens. ↓ | = | = | = | = | = | = | = | = | Hypo |
| With sensor change | t. sens. ↑ | ↓ | ↑ | = | ↑ | ↑ | = | ↓ | ↑ | Normo (no disease) |
| | t. sens. ↓ | ↑ | ↓ | = | ↓ | ↓ | = | ↑ | ↓ | Normo (no disease) |

Symbols: ↑ increase; ↓ decrease; = no change; t. sens.: target sensitivity

RRS both :

$$A = x_i + x_i^* \qquad \text{LRS and RRS} \tag{22}$$

and

$$A = x_i - y_f^* \qquad \text{LRS and RRS ,} \tag{23}$$

from which we learn that the *effect* of a false signal is *in all cases* equal to a change of the reference!

For a false reference signal $y_d^*$ in a LRS the block diagrams shows us that $y_r$ and $y_f$ are increased, while $y_d$ itself is decreased. The disease is of the hyper-$y_r$ kind with increased energy expenditure.

For a RRS a hypo-$y_r$ disease exists, with decreased levels of $y_r$, $y_f$, and $y_d$, but also with an increase of energy dissipation ($y_c$ is increased).

In a similar way the effects of other false signals ($x_i^*$ or $y_f^*$) can be derived, as well as the effects of

*G. Extraneous Signals* which are identical with the original ones (caused by cancerous growth, for instance), and

*H. Signal Counteracting Substances.*

The reader may now also derive the effects of the existence of

*I. Thresholds or Spontaneous Activity* of elements of these feedback systems, as well as the effects of a change of threshold or spontaneous activity.

It similarly is of interest to derive the effects of

*J. Changes in the Sensitivity of the Targets of $y_r$.* Here a decrease of the sensitivity causes a clinical hypo-$y_r$ disease with a *normal* $y_r$ level and normal values of all other variables while an increase of the sensitivity generates a clinical hyper-$y_r$ disease with normal levels of all variables.

But when the sensor sensitivity is similarly affected than the "patient" is clinically healthy but his $y_r$-level is too high or too low, respectively, while the other variables are also changed (see sensor-diseases). Such a "disease without a disease" is found, for instance in the mentioned "hyperthyroidy without hyperthyroidy", which of necessity will be a chance finding (cf. Werner, 1971).

The patterns of changes are tabulated in Tables 1 for a LRS and 2 for a RRS. A study of the results (presented above) learns us that all different diseases have their own pattern of changes, different from each other.

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