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Antagonistic Redundancy – A Theory of Error-Correcting Information Transfer in Organisms

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Abstract

Living organisms are exposed to numerous influencing factors. This holds also true for their infrastructures that are processing and transducing information like endocrine networks or nerval channels. Therefore, the ability to compensate for noise is crucial for survival. An efficient mechanism to neutralise disturbances is instantiated in form of parallel complementary communication channels exerting antagonistic effects at their common receivers. Different signal processing types share the ability to suppress noise, to widen the system's regulation capacity, and to provide for variable gains while leaving the transferred signal to a large extent unchanged.

1. Introduction

Redundancy is a common phenomenon in living systems. Its high costs in terms of energy, space consumption and ontogenetic complexity are balanced by a significant gain of robustness against damages [Kitano 2001, Krakauer and Plotkin 2002]. Redundant structures can also be found at the level of processing circuits. While they obviously contribute to fault tolerance it is also conceivable that this kind of parallelity has some impact on the quality of transmitted signals.

The large number of variables that are able to irritate processing and transduction structures has its origin both outside and inside the organism. While known load factors can be compensated for by means of feedforward mechanisms and efference copies [von Holst and Mittelstaedt, 1950], the situation is different for unknown influences like noise signals.

The following study aims to evaluate how complementary antagonistic processing structures influence the impact of noise on the quality of signal transfer.

As a starting point the control of plasma glucose by the two polar hormones glucagon and insulin – a fragment of a more complex network – may be considered. Both hormones are antidromicly controlled by the plasma glucose level and act mutually oppositionally on the production and degradation of glucose (Fig. 1).

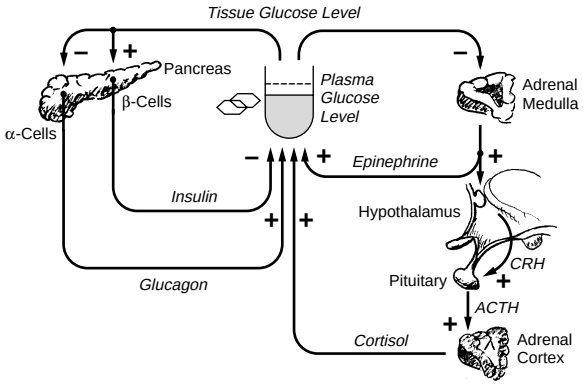

Figure 1: Control of plasma glucose level by several complementary hormones. Mutual influences of insulin on glucagon secretion and *vice versa* and of epinephrine on insulin and glucagon secretion are not shown.

2. Models

2.1 Simplified models

A first very plain model (Figure 2) may start with an original signal a encoded in the subtractively complementary channels b_1 and b_2 that are given with

$$b_1 = a \tag{1}$$

and

$$b_2 = -a\,. \tag{2}$$

Then the output signal c is defined with

$$c = \frac{b_1 - b_2}{2} = a\,. \tag{3}$$

The two channels b_1 and b_2 can be subsumed as mediation vector $\vec{b}$ with

$$\vec{b} = G_{ij}\, a \tag{4}$$

and

$$c = H_{ij}\,\vec{b}\,, \tag{5}$$

where G_{ij} denotes a dispatcher matrix and H_{ij} a collector matrix performing a summation of the mediation vector's components. In the example depicted above the assumption is

$$i = 1; j = 2, \tag{6}$$

but the vector form allows for the formulation of even multiple transmission channels.

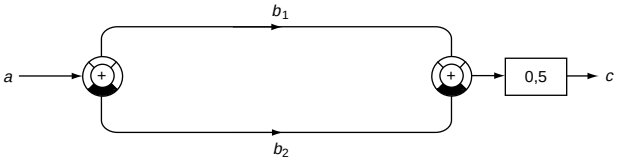

Figure 2: Subtractive antagonistic redundancy. See the appendix for an explanation of symbols.

Similarly, in a divisive model from eqn. (1) and

$$b_2 = \frac{1}{a} \tag{7}$$

the output follows with

$$c = \sqrt{\frac{b_1}{b_2}} = a\,. \tag{8}$$

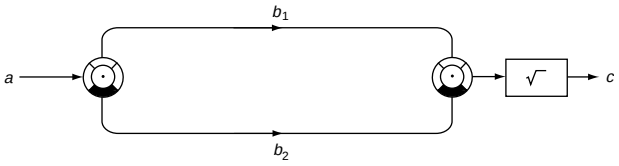

Figure 3: Divisive antagonistic redundancy

Logarithmic transformation of the mediation variables b_i allows for using the dispatcher and collector matrices of equations (4) and (5) for the divisive model, too.

2.2 Michaelis-Menten-Hill Kinetics

In organisms signal transduction is usually implemented as Michaelis-Menten-Hill (MMH) kinetics

$$y_a = \frac{Gx_e}{D + x_e}\,. \tag{9}$$

According to this Langmuir-equation we get the agonistic channel b_1 with

$$b_1 = \frac{G_{b1}a}{D_{b1} + a} \tag{10}$$

and the antagonistic channel as result of a non-competitive inhibition process [Zech and Domagk 1986, Dietrich 2002, Dietrich et al. 2002] with

$$b_2 = \frac{1}{1 + \frac{G_{b2}a}{D_{b2} + a}} \tag{11}$$

(Figure 4).

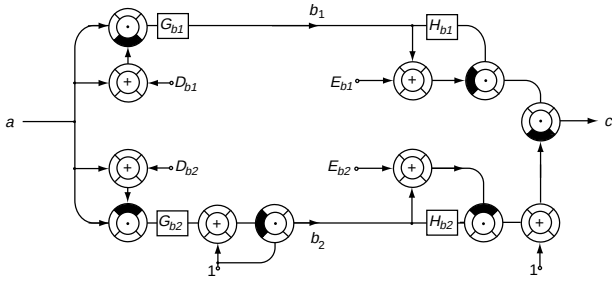

Figure 4: Antagonistic Redundancy with Michaelis-Menten-Hill kinetics and non-competitive inhibition.

From

$$c = \frac{H_{b1}b_1}{(E_{b1} + b_1)(1 + \frac{H_{b2}b_2}{E_{b2} + b_2})} \tag{12}$$

the output signal follows as a function of a with

$$c = G_{b1}H_{b1}a \,/\, [(D_{b1} + a)(E_{b1} + \frac{G_{b1}\,a}{D_{b1} + a})\,(1 + \frac{H_{b2}(D_{b2} + a)}{D_{b2} + a + E_{b2}a + D_{b2}E_{b2} + E_{b2}G_{b2}a})]\,. \tag{13}$$

2.3 Inhibiting subsystems

Subsystems with inhibiting effect have generally the same formal structure as depicted above, except for an inverted output stage (Figure 5). Especially in endocrine intercausal networks MMH kinetics with inverted structure are frequently to be found as components of feedback control circuits.

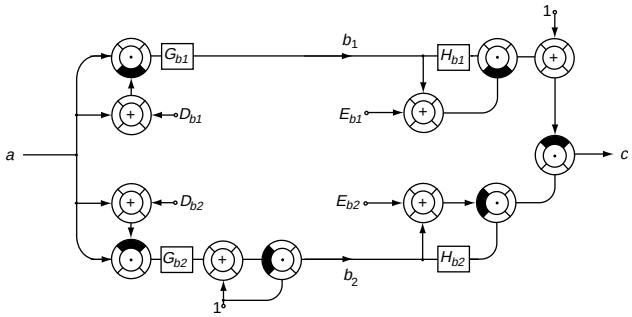

Figure 5: Antagonistic Redundancy using Michaelis-Menten-Hill kinetics with inverting characteristics.

Similar to equation (12) c is defined by

$$c = \frac{H_{b2} b_2}{(E_{b2} + b_2)(1 + \frac{H_{b1} b_1}{E_{b1} + b_1})} . \quad (14)$$

Then in dependence of a c is given with

$$c = H_{b2} / \left(1 + \frac{G_{b2} a}{D_{b2} + a}\right) \left(E_{b2} + \frac{1}{1 + \frac{G_{b2} a}{D_{b2} + a}}\right) \left(1 + \frac{H_{b1} G_{b1} a}{(D_{b1} + a)\left(E_{b1} + \frac{G_{b1} a}{D_{b1} + a}\right)}\right) \quad (15)$$

3. Results

Assuming that in the simple subtractive model exactly one channel is disturbed with an additively superimposed noise signal z with

$$b_1 = a + z \quad (16)$$

then in the resulting signal

$$c = a + \frac{z}{2} \quad (17)$$

the noise influence is halved. In the case of both channels being disturbed with the same interfering signal the perturbation will be entirely eliminated.

With the additive noise signal of eqn (16) c is in the divisive model given with

$$c = \sqrt{a\,(a + z)} . \quad (18)$$

If both signals are simultaneously disturbed with eqn (16) and

$$b_2 = \frac{1}{a} + z \quad (19)$$

then c follows with

$$c = \sqrt{\frac{a\,(a + z)}{1 + az}} \quad (20)$$

As shown in Figs. 6 and 7 in the cases of both one and two channels being additively disturbed the influence of erroneous signals is significantly diminished in a system with Antagonistic Redundancy (AR) compared to transmission with single channels.

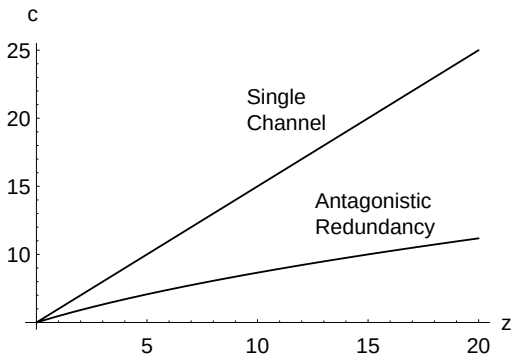

Figure 6: Comparison of the effects of additive noise (z) impacting one channel only on the output signal of unichannel transmission and on a system with divisive antagonistic redundancy.

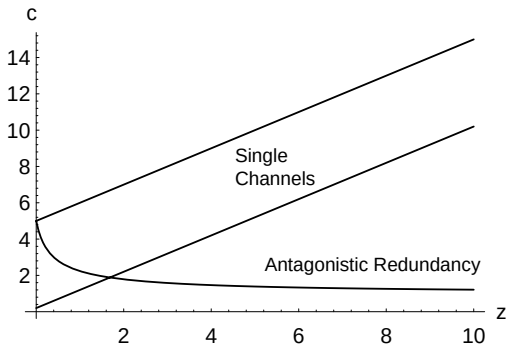

Figure 7: The two additively disturbed channels b_1 and b_2 and the resulting signal c in divisive antagonistic redundancy.

If both signals are disturbed in a multiplicative manner then with

$$c = \sqrt{\frac{a\,z}{\frac{z}{a}}} = a \quad (21)$$

the noise is completely eliminated.

Models with Michaelis-Menten-Hill Kinetics show a more complex behaviour. Nevertheless, they are also capable of reducing the dependency of c from the error signal z significantly (Figure 8 and Figure 9).

In a similar way, in inverted MMH kinetics AR is able to reduce the influence of noise signals on the output signal, too (Figs. 10 and 11).

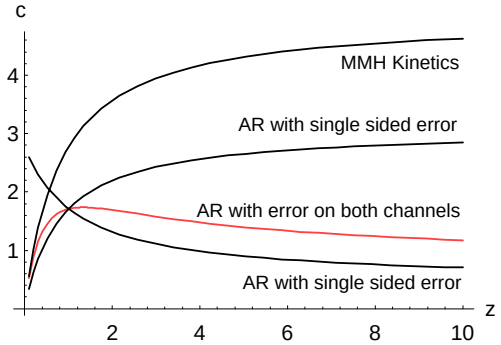

Figure 8: Dependency between z and c for a single channel with Michaelis-Menten-Hill kinetics and for AR with the disturbance signal influencing only the agonistic or the antagonistic channel, respectively, and for AR with both channels disturbed.

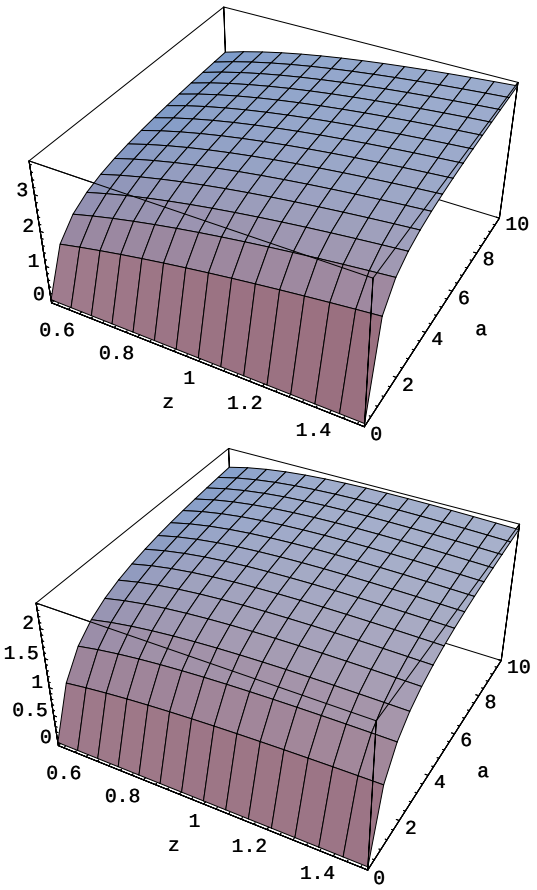

Figure 9: The relation between *a*, *z* and *c* in transfer systems with MMH kinetics shows the reduction of the influence of *z* on *c* by antagonistic redundance (bottom) when compared to a single channel (top). Note the different scales of the vertical axis.

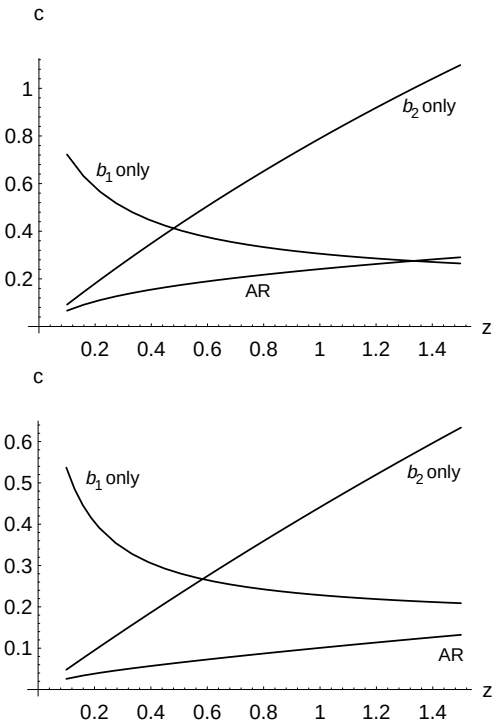

Figure 10: Inhibiting MMH kinetics with AR: Relation between *z* and *c* for *a*=1 (top) and *a*=10 (bottom).

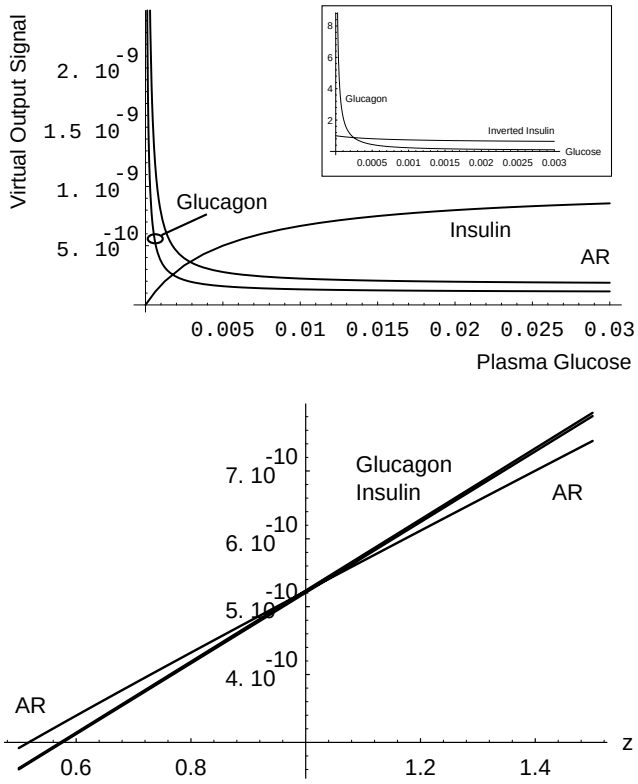

Figure 12: Dependency of insulin, glucagon and a unified output from glucose (top) and an error signal (bottom). Inset in the upper panel: Comparison of glucagon and a virtual signal derived from inverted insulin. Note that the glucagon concentration has been multiplied with 10^{13} to make its curves visible.

The extent of error extinction in coupled MMH kinetics depends from the parameters of the respective network. As shown in Figure 12 the subsystem of glucagon and insulin controlling the glucose level in blood plasma shows only a slight error reduction [Parameters from Cascieri et al. 1999, Cypess et al. 1999, Hjorth et al. 1998, Hoefig et al. 1996, Kruszynska et al. 1998, Kurstjens et al. 1990, Lundquist and Panagiotidis 1992, Lynch et al. 1996, Marks and Botelho 1986 and Rizza et al. 1981]. This restriction is a consequence of the high nonlinear amplification G_{b2} of the input stage of the glucagon path resulting in very low glucagon concentrations (see Figures 5 and 12, where the glucagon concentration had to be multiplied with the factor 10^{13} to be visible). *In vivo*, this asymmetry is adjusted by the fact that insulin has multiple additional antagonists like catecholamines and glucocorticoids. In any case, each hormone compensates for the limitations in the effect of the respective other hormone. Where the glucagon-level is very small near the threshold of undetectability insulin is in the range of high concentrations. Conversely, in the situation of low plasma glucose glucagon shows an intense response (inset of Figure 12).

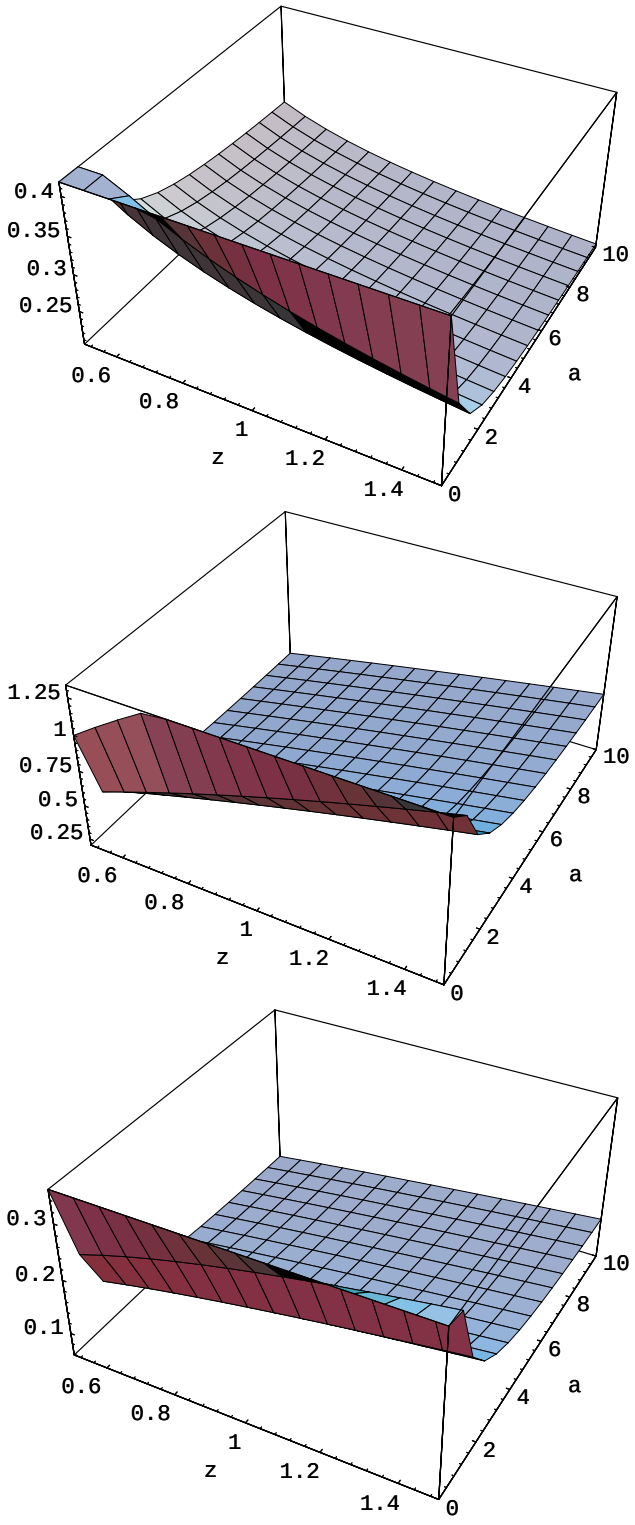

Figure 11: Effect of input *a* and error *z* on the output signal *c* in single channel transfer with b_1 (top) or b_2 (middle), respectively, compared to antagonistic redundancy (bottom) in a system with inverting MMH kinetics.

4. Discussion

Information processing structures with antagonistic redundance – e. g. in the autonomous nervous system – have been known for decades without being described mathematically. In 1969 Manfred Clynes reported on an organizational principle compensating for unidirectional rate sensitivity in neural signal transmission [Clynes 1969] which he called rein control. A functional – albeit not quantitative – description has been formulated in the early 1970s when Sachsse [1971] described bipolar control structures in the autonomous and central nervous system. A special case of antagonistic organization in integral feedback control systems has been illustrated by Saunders et al. [1998 and 2000].

These models have significantly contributed to our understanding of parallel complementary signal-transduction even though they abstained from systematically analysing the influence of error signals on the quality of the transmitted information.

AR can be found in different types of biological information transfer. Besides the autonomous nervous system where centrifugal control signals are transmitted via the two complementary sympathetic and parasympathetic systems antagonistic redundance is common in the somatic nervous system, too. Due to mechanical necessity scelettal muscles are arranged in an antagonistic manner. This finds its reflection in the information processing structure of the corresponding nerval organization. Other examples of nerval encoded AR are the implementation of temperature perception with different receptor types for cold and warm stimuli and the joint control system for respiration and acid-base balance which is not only equipped with distinct receptors for e.g. O_2 and acidity but that is also antagonistically organised on the level of control in the medulla oblongata.

Numerous endocrine transfer systems share antagonistic organization. Important examples to be mentioned are the complementary effects (and regulation) of growth-hormone RH and somatostatin, TRH and somatostatin, leptin and ghrelin, and parathyroid hormone and calcitonin. Apart from glucagon insulin has multiple other antagonists like catecholamines and cortisol.

Endocrine control systems are easily disturbed by exogenous and endogenous interfering factors, first of all variations in the body fluid balance. Intake of water after fluid restriction rapidly decreases the concentrations of all hormones. However, its impact on the controlled system is considerably reduced, as all antagonistic channels are disturbed in the same extent.

In pathological situations the function of one channel can be impaired or delayed. As seen from the examples this results in higher sensitivity to interference and, depending from the affected information processing structure, narrowed control range.

For decades feedback control systems have been known as universal compensation mechanisms for various interference factors in organisms, and their characterisation has been one of the classic objects of biological cybernetics. The reafference principle [von Holst and Mittelstaedt, 1950] has been described as a first adjustment circuit in form of feedforward control. Reafferences balance the efferent output of the nervous system that would otherwise disturbe the interpretation of sensory perception. Unlike efference copies compensating for pre-known disturbance factors antagonistic redundancy provides for elimination or at least attenuation of *a priori* unknown interfering

signals like the effect of blood plasma's dilution on the concentration of hormones.
It may be expected that further examples of antagonistic redundancy will be found in the hormonal and the nervous system and even in the cell. To evaluate this structure's consequences on physiology and pathology of several information processing systems is a task that remains for the future.

5. References

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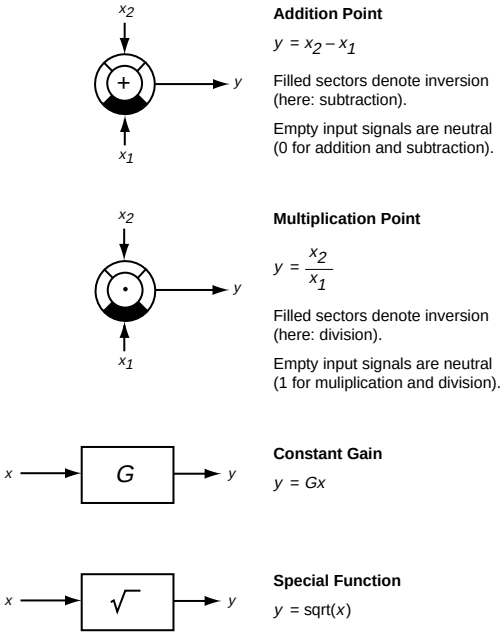
Appendix

Legend for IPS symbols:



Symbols used (see the OEP-site http://open-site.org/Science/Mathematics/Applied/Cybernetics/K1_and_K2_-_General_Cybernetics/Systems_Science/Information_Processing_Structures/)