Fluctuations Hypothesize the New Explanation of Meridians in Living Systems

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Abstract

Biosystems are complex. Their physiology is well-controlled with various negative feedback signals and processes, it describes by opposite interfering effects which are characterized in the Eastern philosophy by Yin-Yang (Y-Y) pairs. Y-Y pairs could be described by the promoter-suppressor pairs in a wide range of physiologic signals creating the homeostasis of the complex system. This type of control appears as fluctuations from the average (mean) value of the signal. The mean carries an ineluctable fluctuation (called pink-noise or $1/f$ noise). All signals in homeostasis have equal entropy (S_E = 1.8), which is the character of the complex equilibrium. The various controlling opposite signals (Y-Y) have different time-scales which change by aging. The processes with smaller time-scale are degraded by aging, but the pink-noise ensures that the deviations of the signals of the healthy homeostatic system remain constant. Meridians are connected to the general transport systems that combined the material and the information transport with the considerable transport networks, like blood, lymph, nerve, cell-junctions, mesenchymal "ground substance" cytoskeletons. The meridians in this meaning only virtual line averaged from multiple realized paths to connect two acupuncture points by the material, energy and information transport processes. The meridian network is designed by various coupling points (acupoints), which could be perturbed by actuating stimulus. Our objective is to describe the meridian system from complexity point of view.

Keywords

Pink-Noise, Complexity, Living System, Meridians, Acupoints, Homeostasis

1. Introduction

There are numerous questions related to Traditional Chinese Medicine (TCM),

especially to acupuncture and the existence of meridians [1]. Is it an ancient cure or modern therapy? Is it art (psychology) or a treatment (physiology)? Is it a natural philosophy or an experimental medical practice? Answers are not formed yet [2].

When the importance of the dissipative processes was recognized, and the general system theory was established [3], we started to examine living systems differently from before [4]. It was discovered how environmental impact affected living systems and we started to examine the complexity of life. We understood the problem of complexity in physiologic processes and had more and more complications to explain the interference of the signals while studying the complete system as one. We face difficult challenges to examine individual physiologic changes in isolation from the body; but discovered specific general mechanisms (universalities) which do not depend on the details of the system with the same scales through few orders of magnitudes in spatiotemporal descriptions. The hallmarks of complexity give us new insights into the description and understanding of the general integrity of living objects. Non-stationarity (time-dynamics), non-linearity (cross-talks of signals, complicated interactions), multiscale organization (spatiotemporal fractal behavior), time irreversibility (non-equilibrium dynamics and fluctuations) are all giving surprising news when studying living objects. Non-equilibrium thermodynamics started to be connected to explanations and the equilibrium became a dynamic fluctuation with unique noises.

The dialectic dynamics of life had connections to philosophy (from Lao-Zi through Heraclitus of Ephesus to Hegel GWF), understanding the strict negative feedback connections by the thesis ↔ antithesis ↔ synthesis triad.

The ancient knowledge was based on long-term and much extended observations and experimental trials which of course were mixed with the ancient beliefs, philosophy and explanation of the environmental structures. In this paper, we would like to show some consequences of the complex physiology, some hypothesized effects which could explain the existence of acupoints and meridians without using any formulation or philosophical points from the ancient explanations.

2. Method

Multiple solutions were developed for the calculation of entropy of the data-row with finite length (like a representative sampling of physiological signals). These solutions are coherent with Shannon's entropy formulation. The Richman-Moorman entropy [5] was applied to the analysis of multiscale entropy (MSE) of physiological signals [6].

Following the calculation of [6], let us denote a time-series containing N samples by $\{X_l\} = \{X_1, \cdots, X_l, \cdots, X_N\}$. Choose from this vector with m-dimension:

$$u_m(i) = \{x_i, x_{i+1}, \cdots, x_{i+m-1}\}, \quad 1 \le i \le N - m + 1 \tag{1}$$

We use the maximum of the absolute deviation of components to characterize

the distances between the vectors, so

$$d\left[u_m(i),u_m(j)\right]=\max\left[\left|x(i+k)-x(j+k)\right|\right],\quad 0\le k\le m-1 \tag{2}$$

The $u_m(i)$ and $u_m(j)$ vectors are r-neighbors when their distance is less than *r*. The negative logarithm of that conditional probability when the vectors remain *r*-neighbors is when an additional sampling is given to the time-series increasing, the length of the vectors too. Consequently, by applying this definition, Richman-Moorman-entropy is:

$$S_E=-\ln P\left(\left|x_i-x_j\right|\le r,\left|x_{i-1}-x_{j-1}\right|\le r\right) \tag{3}$$

where S_E is the Richman-Moorman-entropy. Denote $n_i^m(r)$, the number of $u_m(j)$ $(i\neq j)$ vectors which have a distance from the vector $u_m(i)$ is smaller than *r*. The probability that the vector $u_m(j)$ is located in the distance of *r*-radius from a vector $u_m(i)$ is:

$$P_i^m(r)=\frac{n_i^m(r)}{N-m+1} \tag{4}$$

where the $P_i^m(r)$ is the probability of the distance of $u_m(j)$ form $u_m(i)$ is smaller than *r*; while the probability that the vector $u_{m+1}(j)$ is found in the *r*-radius neighborhood of $u_{m+1}(i)$ is:

$$P_i^{m+1}(r)=\frac{n_i^{m+1}(r)}{N-m+2} \tag{5}$$

The conditional probability from these would be:

$$\frac{P_i^m(r)}{P_i^{m+1}(r)}\cong\frac{n_i^m(r)}{n_i^{m+1}(r)} \tag{6}$$

with these notations the Richman-Moorman-entropy could be interpreted in this form:

$$S_E=-\ln\frac{P_i^m(r)}{P_i^{m+1}(r)}\cong-\ln\frac{n_i^m(r)}{n_i^{m+1}(r)} \tag{7}$$

The $n_i^m(r)$ and $n_i^{m+1}(r)$ values could be determined to know the probability density function. We may suppose that Gaussian pink noise [6] is allowed by the central limit theorem in physiological signals [7]. To characterize the multidimensional Gaussian distribution, the covariance matrix must be given too. The power-spectrum defines the covariance matrix, and from that the entropy could be derived.

The definition of the covariance matrix containing N-number of random variables:

$$\bar{\bar{C}}\left(X_i,X_j\right):=E\left[\left(X_i-\bar{X}_i\right)\left(X_j-\bar{X}_j\right)\right] \tag{8}$$

The diagonal of the covariance matrix represents the deviations of the individual random variables. Due to the symmetry and real-elements of the hermitic matrix it could be transformed to the principal axis. The eigenvalues for this transformation:

$$\bar{\bar{C}}\bar{U}_i = \lambda_i \bar{U}_i \tag{9}$$

Therefore:

$$\bar{U}_j \bar{\bar{C}} \bar{U}_i = \lambda_i \bar{U}_j \bar{U}_i = \lambda_i \delta_{ij} \tag{10}$$

Consequently, when we form a $\bar{U}$ matrix from the eigenvectors like its columns, then:

$$\bar{\bar{U}}^{\mathrm{T}} \bar{\bar{C}} \bar{\bar{U}} = diag\left(\lambda_1, \cdots, \lambda_i, \cdots, \lambda_N\right) = \bar{\bar{\Lambda}} \tag{11}$$

is a diagonal matrix. The covariance matrix transformed random variable is:

$$\bar{Y} = \bar{\bar{U}}^{\mathrm{T}} \bar{X} \tag{12}$$

because

$$\begin{aligned}
\bar{\bar{U}}^{\mathrm{T}} \bar{\bar{C}} \bar{\bar{U}} &= \bar{\bar{U}}^{\mathrm{T}} E\left[\left(\bar{X} - \bar{\bar{X}}\right)\left(\bar{X} - \bar{\bar{X}}\right)^{\mathrm{T}}\right] \bar{\bar{U}} \\
&= E\left[\bar{\bar{U}}^{\mathrm{T}}\left(\bar{X} - \bar{\bar{X}}\right)\left(\bar{X} - \bar{\bar{X}}\right)^{\mathrm{T}} \bar{\bar{U}}\right] \\
&= E\left[\left(\bar{\bar{U}}^{\mathrm{T}} \bar{X} - \bar{\bar{U}}^{\mathrm{T}} \bar{\bar{X}}\right)\left(\bar{X}^{\mathrm{T}} \bar{\bar{U}} - \bar{\bar{X}}^{\mathrm{T}} \bar{\bar{U}}\right)\right] \\
&= E\left[\left(\bar{\bar{U}}^{\mathrm{T}} \bar{X} - \bar{\bar{U}}^{\mathrm{T}} \bar{\bar{X}}\right)\left(\bar{\bar{U}}^{\mathrm{T}} \bar{X} - \bar{\bar{U}}^{\mathrm{T}} \bar{\bar{X}}\right)^{\mathrm{T}}\right] \\
&= E\left[\left(\bar{Y} - \bar{\bar{Y}}\right)\left(\bar{Y} - \bar{\bar{Y}}\right)^{\mathrm{T}}\right]
\end{aligned} \tag{13}$$

Consequently, the deviation of the transformed random variable Y_j is:

$$\sigma_j' = \sqrt{\lambda_j} \tag{14}$$

On the other hand, the probability density function of an N-dimensional Gaussian noise is:

$$p\left(\bar{X}\right) = \frac{1}{\sqrt{(2\pi)^N \det \bar{\bar{C}}}} e^{\left[-\frac{1}{2}\left(\bar{X} - \bar{\bar{X}}\right)\bar{\bar{C}}^{-1}\left(\bar{X} - \bar{\bar{X}}\right)\right]} \tag{15}$$

Moreover, from this the distribution function of the transformed random variable is:

$$\begin{aligned}
p\left(\bar{Y}\right) &= \frac{1}{\sqrt{(2\pi)^N \det \bar{\bar{\Lambda}}}} e\left[-\frac{1}{2}\left(\bar{Y} - \bar{\bar{Y}}\right)\bar{\bar{\Lambda}}^{-1}\left(\bar{Y} - \bar{\bar{Y}}\right)\right] \\
&= \prod_{i=1}^{N} \frac{1}{\sqrt{2\pi\lambda_i}} e^{-\frac{\left(Y_i - \bar{\bar{Y}}_i\right)^2}{2\lambda_i}} = \prod_{i=1}^{N} p\left(Y_i\right) \\
p\left(Y_i\right) &= \frac{1}{\sqrt{2\pi\lambda_i}} e^{-\frac{\left(Y_i - \bar{\bar{Y}}_i\right)^2}{2\lambda_i}}
\end{aligned} \tag{16}$$

To calculate the covariance matrix starting from the power-density of the pink-noise:

$$S(\omega) = \begin{cases} \dfrac{K}{\omega}, & \omega_1 \le \omega \le \omega_2 \\ 0, & \text{otherwise} \end{cases} \tag{17}$$

The autocorrelation function could be determined from this by the Wiener-Khinchin-theorem [8]:

$$\Phi(\tau)=\frac{K}{2\pi}\int_{\omega_1}^{\omega_2}\frac{\cos\omega\tau}{|\omega|}\mathrm{d}\omega=\frac{K}{2\pi}\left[Ci(\omega_2\tau)-Ci(\omega_1\tau)\right],$$
$$Ci(\tau)=\gamma+\ln(\tau)+\sum_{k=1}^{\infty}\frac{(-1)^k\tau^{2k}}{(2k)!2k} \tag{18}$$

where $Ci(\tau)$ is the function of integral-cosine, and $\gamma=0.5772$ is the Euler's constant. Consequently:

$$\Phi(\tau)=\frac{K}{2\pi}\left\{\ln\frac{\omega_2\tau}{\omega_1\tau}+\sum_{k=1}^{\infty}\frac{(-1)^k}{(2k)!2k}\left[(\omega_2\tau)^{2k}-(\omega_1\tau)^{2k}\right]\right\} \tag{19}$$

3. Results

The connection of the autocorrelation function and covariance matrix for such ergodic processes like the pink-noise is 6:

$$\overline{\overline{C}}=\begin{bmatrix}\Phi(0) & \Phi(\tau) & \Phi(2\tau) & \cdots & \Phi(N\tau)\\ \Phi(\tau) & \Phi(0) & \Phi(\tau) & \cdots & \Phi((N-1)\tau)\\ \Phi(2\tau) & \Phi(\tau) & \Phi(0) & \cdots & \Phi((N-2)\tau)\\ \vdots & \vdots & \vdots & \ddots & \vdots\\ \Phi(N\tau) & \Phi((N-1)\tau) & \Phi((N-2)\tau) & \cdots & \Phi(0)\end{bmatrix} \tag{20}$$

with these conditions the MSE entropy of pink-noise [6]:

$$S_E=1.8 \tag{21}$$

To determine the homeostatic equilibrium, we make a multi-scale entropy analysis, where the $\{x_1,\cdots,x_j,\cdots,x_N\}$ is a one-dimensional discrete time-series. From this, a consecutive coarse-grained $\left\{y_r^{(\tau)}\right\}$ time-series can be constructed with τ scale-factor, as shown in Figure 1.

According to Figure 1, the members of the τ scale series are:

$$y_j^{(\tau)}=\frac{1}{\tau}\sum_{i=(j-1)\tau+1}^{j\tau}x_i,\quad 1\le j\le N/\tau \tag{22}$$

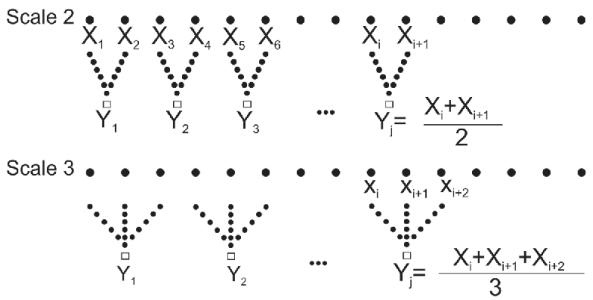


Figure 1. Illustration of the coarse-graining process in the 2nd and 3rd scale (after [9]).

MSE method is used to calculate the entropy of all the coarse-grained time-series. This was made for pink and white noises 6, and the results are shown in Figure 2. (The scale-factor is the number of terms in the average.) The $1/f$ noise does not change by the smoothing (cutting of high frequencies) of the function, and the Rich-man-Moorman entropy of pink-noise is scale-independent in a definite interval, it is constant and could characterize the homeostasis. The results are in perfect harmony with the others obtained by the other methods [10] [11], and applied to living systems [12].

The correlation of the white noise is small, so the entropy of the white noise decreases by series of higher time-factors, while in case of the pink noise the complex internal structure remains constant on the large time-scales due to its long correlation length. The short correlation length of the white noise causes high entropy on the small scales (<4), while the weaker correlation for long-scale ensures the constant entropy for pink noise in the wide range of scales.

4. Discussion

From a physical point of view, the scaling of discrete time series is a filtering process of some of the high-frequency components of the noise. We may construct a series of scales by bandwidths. The highest bandwidth is at the 1st scale, and by averaging more and more high-frequency components, higher scales have gradually narrower band-gaps. The highest frequency in the signal is well approximated by Shannon's sampling theorem [13], declaring that the highest frequency in the sampled noise is the half of the sampled frequency. Consequently, in the scale of the 2nd factor, the upper frequency is half of the half of sampled frequency, in the nth the nth-part of the bandwidth, and a similar one is valid on the low-frequency limit as well. The length of the data-series characterizes the time-length of the registering of the noise; when the sampling time is ΔT, and N is the size of the data-series then the length of the registration is $N\Delta T$. The reciprocal value of $N\Delta T$ is the smallest frequency in the sampled signal, so is the low limit of the bandwidth. Due to the decreasing length of the data series the low-frequency limit of the bandwidth grows. The scaling of the power-function $S(\omega)$ is shown in Figure 3.

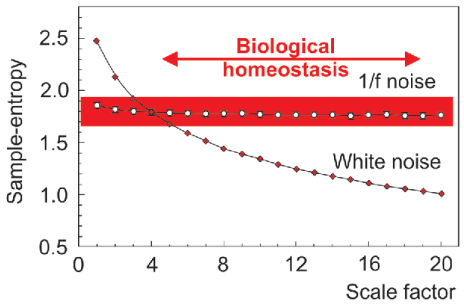


Figure 2. The result of MSE analysis of pink and white noises [6].

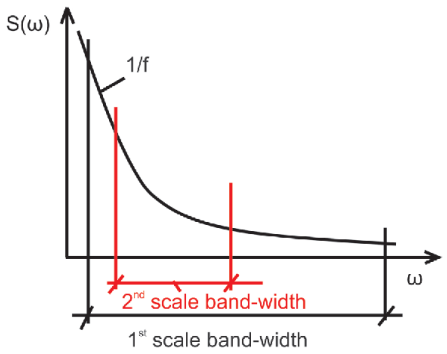


Figure 3. The shortening of bandwidth in the scaling, using the Shannon's sampling theorem. The upper limit is cutting the half of the maximal sampling frequency, while the lower limit is the double of the minimal sampling frequency. This process is continued to the 3rd, 4th, etc. scaling steps, using the n-th bandwidth determining the $(n + 1)$-th by the same procedure.

In this meaning, the Richman-Moorman-entropy of time-series shows some kind of a holographic behavior of the pink-noise, namely the entropy does not change by the truncating of the registering of the pink-noise.

The Richman-Moorman-entropy has a natural physical meaning too, (like the Shannon entropy also [14]), from its multiplication with Boltzmann constant ($kB \approx 1.38 \times 10^{-23}$ [$m^2 \cdot kgs^{-2} \cdot K^{-1}$]) we get the physical entropy of the sample. We know from thermodynamics that the entropy is a function of the state of a system, so it is a function of the state-variables, like the internal decisional energy. The internal energy in our case is the sum of the energy content of the Fourier components. Consequently, the physical entropy of the signals from pink-noise does not change by decreasing its energy, similarly to the thermodynamical entropy that has extremum in the function of energy. This allows energy exchange between the sub-systems in the thermodynamic equilibrium in the form of fluctuations without its entropy changing.

A similar attribute could exist in case of stochastic processes when a system emits pink-noise. Subsystems could change energy without changing their entropy in this fluctuation analogy. However, in this case, the entropy is not extensive. The energy is an additive magnitude but the entropy, which is constant in the homeostasis, is not an additive parameter. Consequently, on the grounds of experience, the entropy is intensive in systems of homeostasis.

In the realization of homeostasis of a living system the "ground substance", which is a considerable part of the whole weight of the system, [15], has a central role. This ground state is a gel-like mesenchymal tissue, a soft connection material. The basic information transport goes through this connective tissue, which structure contains a large amount of the extracellular matrix too. The mesenchyme ensures the alimentation and excretion of cells, it is a transmitter and filter between the capillaries and cells containing highly polymerized carbo-

hydrates glucosaminoglycans, protein associated ologasacharid chains, proteoglycans and structural glycoproteins, glycolipids in the ordered set, networked with dendrites and extracellular matrix of glycocalyx. The mesenchyme is active in three communication levels on the regulation of the system: cellular, humoral and nervous. The cellular level ensures the chemical equilibrium of the connective tissue with the system of reticuloendothelial cells. It locally controls the capillary transported materials, like oxygen, metabolites and enzymes cell-life signals. Through the humoral transports, it communicates over a long distance with subsystems by electrolyte transports (lymph, blood-stream). The nervous network functionally connects the distant parts of the system. The humoral level of systemic transport processes is slow, while the nervous communications are transported fast. All the controls have negative feedback regulating the equilibrium with action signal-pairs promoting or suppressing the actual process. We could note the balancing signal pairs as Y-Y pairs taking the notation from Ying-Yang introduced by Traditional Chinese Medicine (TCM). This feedback mechanism is the smart solution to fixing the actual expected values. A simple example for the negative feedback control in non-living systems is the weight hanging on a spring. Gravitation attracts the weight in the direction of the Earth-center, while the spring suppresses the gravitation, always works against it with the same force as gravitation acts and forms equilibrium position somewhere. During any external perturbation, the opposite effects compensate the deviations, and the weight is in its equilibrium place in the time-average. In the physiological signals, a large number of controlling pairs form the average value (equilibrium value) of the physiological signal. All the three action levels are connected in the mesenchyme; which gives "stage" to form an equilibrium.

The controlled parameters of the regulation system of homeostasis (like the actual value of a physiological signal) are realized with dialectic determination. This means that the controlled value of the physiological process is formed by the dynamical equilibrium of a large number of interfering controlling signal pairs (Y-Y). Let us study the proliferation homeostasis to elucidate this process. The essence of proliferation homeostasis is the exchange of the old or damaged to new ones, fixing the size of the organs and parts of the system. The two acting opposite regulation signals (Y-Y) generate the annihilation (Yin) and creation (Yang). Programmed cell death (apoptosis) is on the Yin side while cellular division generated by the growth-factors has a leading role on the Yang side. The healthy arrangement is a dynamic equilibrium turning to disease when it comes apart. When the Yin is dominant, apoptosis overrides the situation and an autoimmune disease is formed. In case the Yang is the dominant, creation has a central role; tumorous diseases are shaped by switching-off of the programmed cell death. The complete accommodation of the system is better when it has more Y-Y pairs which interact and form subsystems too. The homeostatic equilibrium stabilizes the energy-intake of the subsystem and the whole system as well which is described by the allometry of the living systems [16].

Their board equilibrium governs multiple other effects. The Y-Y pairs could interfere with the same proliferation process controlling hypoxia or many other factors in the microenvironment of the cell by coupling like the humoral control. When oxygen delivery is not satisfactory (hypoxia, Yin-dominance), as it can happen at an excessive muscle activity, blood-perfusion becomes more active to compensate with increased permeability of the vessel walls, or even angiogenesis can begin (Yang-effects). In case of a further load (like regular sport activity) protocol enzymes will solute the extracellular matrix helping the mobility of the cells, and due to the effect of vascular endothelial growth factor (VEGF) they will start a higher proliferation activity and chemomechanical migration by the gradient of VEGF, building up a primitive blood-vessel network. The network is controlled by not only VEGF but the gradient of electric potential like a morphogenetic factor [17]. Potential gradient is formed by the more negative newborn daughter cells rather than by the matured neighbors (**Figure 4**).

The 4th period of angiogenesis is the maturation when the extracellular matrix is fixed; the appropriate cells are coupled and form the vessel-wall; angiopoietins complete the existing capillary network with the new one and make the vessel-system ready for proper physiological operation. Angiogenesis itself is not enough, the direction of the forming vessel is also important which is governed by the potential gradient. The final stage of angiogenesis is the optimizing stage, when the dialectic determination of Y-Y recovers its dynamic equilibrium from the alimentation point of view.

The above regulation process is rather simplified but shows a very complex adjustment of the parameters and is only one of the large number of cooperation processes forming homeostatic control. This must not be deterministic, because neither the appropriate accuracy nor the adequate stability could be ensured with quick signal-exchange. The non-deterministic process emphasizes the accidental processes determining the homeostasis on the way when the regulation is flexible and "economic", therefore it is no more accurate than it is necessary for the actual function.

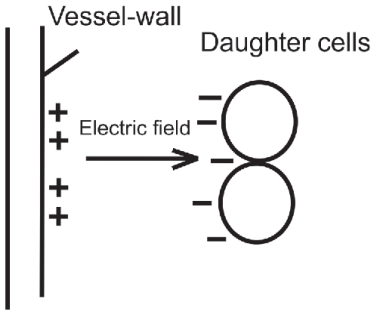


Figure 4. The forming of electric potential at angiogenesis. The electric field is an effector of the epithelial transition producing cellular joints and cytoskeletal polymerization [17].

The optimal accuracy governed by the goals of homeostasis is to provide constant environmental conditions for the living cells and their collective development. These requests are keeping the parameters within tolerance limit without the environmental conditions remaining for a longer period, assuring the mean and the deviation of a constant value. The constant mean allows fluctuations, noises when their deviation remains under the predefined limits.

We would like to show that the time-fractal fluctuation is a perfect error-signal satisfying the homeostatic requirements. We consider the mean $\left(\langle x(t)\rangle\right)$ of the n number of $x_i(t)$ signals in time t in the homeostatic controlled environment as basic signal:

$$\langle x(t)\rangle = \frac{1}{n}\sum_{i=1}^{n} x_i(t) \tag{23}$$

where the sign $\langle\ \rangle$ denotes the averaging in time. The error is the deviation from this mean, so the controlling error is the noise due to the accidental processes in the homeostatic regulation, Figure 5.

The noise $\left(z(t)\right)$ is the deviation of the actual signal $\left(x(t)\right)$ from the mean $\langle x(t)\rangle$:

$$z(t) = x(t) - \langle x(t)\rangle \tag{24}$$

Let us study the $\langle z^2(t)\rangle$ variance (square of the standard deviation) of the $x(t)$ as a function of time:

$$\langle z^2(t)\rangle = f(t) \tag{25}$$

Due to the self-similarity of the biological processes [18], the deviation of the signal must be a power function:

$$\langle z^2(t)\rangle = t^{H'} \tag{26}$$

where $H > 0$ in every case. When $H = 1$ the $\langle z^2(t)\rangle$ of the controlling error is a linear function of the time:

$$\langle z^2(t)\rangle = ct \tag{27}$$

where c is a constant. Form (26) we obtain the scaling conditions:

$$\langle z^2(rt)\rangle = r^{H'}\langle z^2(t)\rangle \tag{28}$$

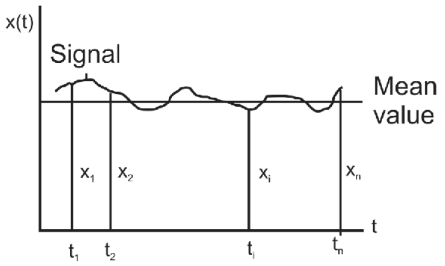


Figure 5. The noise around the mean value of a signal.

The error-signal could be characterized by its spectral power-density ($S(f)$) [19] too:

$$S(f)=F\left[G(\Delta t)\right] \tag{29}$$

where $G(\Delta t)$ is the autocorrelation function [20] of the error-signal:

$$G(\Delta t)=\left\langle z(t)z(t+\Delta t)\right\rangle-\left\langle z(t)^2\right\rangle \tag{30}$$

The power density of the noises like (28), is [21]:

$$S(f)\propto\frac{1}{f^{H'+1}} \tag{31}$$

If the error signal is a pink ($1/f$) noise, then $H'=0$. Considering (28), when the signal is pink-noise, the deviation does not depend on any r-value, so the deviation is constant in time. Consequently, there are definite limits which are never taken over by the error signal; because based on the Chebyshev inequality [22] the probability that the signal is in an interval $(\bar{x}-k\sigma,\bar{x}+k\sigma)$ is:

$$P\left(|x-\bar{x}|<k\sigma\right)>1-\frac{1}{k^2} \tag{32}$$

Therefore, when k is appropriately large for the tolerance, the signal is practically always in the requested interval.

If the power-spectrum of the error-signal is not pink-noise, its exponent is larger than [11], then according to (28), the error-signal will be increased by time and the homeostatic equilibrium will be overset. This is a failure of the balancing, it leads to a jumble of control forming irregular processes, developing the disease. The character of the noise changes, it becomes "colored noise", having $H'>0$ in (31).

The above discussion proves the fact that the physiologic signals have a pink-noise deviation from their averages keeping the limits of the homeostatic control, which in thermodynamical meaning keeps the sample entropy constant in a broad scale, $S_E=1.8$. The famous quotation formulates this dynamic request by A. Einstein: "Life is like riding a bicycle. To keep your balance, you must keep moving.", [23]. Showing it in a simple sketch, representing the instability with a double-well potential, life is somewhere at the breaking point: it has no excess energy to lose but has enough energy to not be trapped in one fixed position, so it is always fluctuating at the breaking-point, energy means the E_{breaking}, and the fluctuation is time-fractal ($1/f$ pink noise). Energy keeps the system in this point pumped from the environment, **Figure 6**.

Life is on the edge of chaos, [24], as the quote from A. Szentgyorgyi, a Nobel laureate said: "Life is nothing but an electron looking for a place to rest.", [25].

The complex properties emphasize the request for change of paradigm of physiological evaluation, [26]. The problem is that in most of the medical diagnostics organ function is examined by its own structural or functional failure, and sometimes connects with a network view. However, even networking is not enough to get the realistic picture; a complex fractal view is necessarily taking

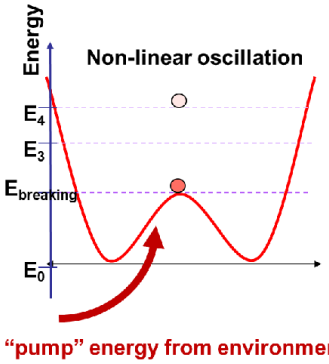


Figure 6. When the incoming energy is too high, the electron occupies a high energy level (noted by E_4 in the figure), which does not fit the homeostatic equilibrium. The electron start loosing its energy, and reaches the breaking point ($E_{breaking}$). When it looses too much energy, it will be "frozen" in one energy-well, which is again out from the homeostatic regulation. Consequently, energy keeps the electron in a "frustrated" position, at "edge of chaos" to fulfill the homeostatic equilibrium. The energy-fluctuations in this position are parts of the $1/f$-noise.

self-organized structural and dynamical (time) fractal behavior of the system into account. The mean of the physiological values does not give enough information; even its deviation could be unsatisfactory to compose a realistic diagnosis. Pink noise decides about the homeostatic equilibrium, so noise structure carries important information about the actual status of the living system.

We have to note that healthy, the healthy cell-division is also governed by fractal noise, [27]. It is shown that the relative error in the generation of the cells rapidly grows in a classical (non-fractal) model, while it remains constant (almost errorless) in case of pink-noise [28].

Aging decreases the complexity of the system, the dialectic formation of the Y-Y pairs degrades. On this way the Y-Y pairs act different time-scales, and the high frequencies gradually vanish in the noise. Consequently, aging has MSE scaling, the system develops higher scaling factors, but during the aging the entropy of physiologic signals does not change, it remains constant when the system is healthy. Thus, healthy aging is well distinguished from the disease on the level of homeostatic control, the deviation from the Y-Y determination is a character of the disease only.

The meridians are introduced by TCM to visualize the channels where the Y-Y pair acts. It is of course, a considerable simplification of the actual homeostatic balance due to the large number of active networks in the system (blood-, lymph-, nerve-networks completed with cell-junctions, cellular adherent connections, cytoskeletons, mesenchymal tissue, soft connective tissue, polymer-formations, etc.). These are interconnected and act in promoter suppressor (Y-Y) balancing as regulators. This is a controlling negative feedback loop from the initial product to the final one by interaction promoters and suppressors,

Figure 7.

The regulation network of the homeostasis is complex, having various levels of Y-Y actions, which are genuinely in interaction grouping and making new sets of actions on all levels of complexity, Figure 8.

This massive regrouping over the complete system has a well-defined regulation network based on the same negative feedback principles as the details of where this huge complexity built up, Figure 9. Life is developed as an open system, its exchange with the environment with materials, energy and other parameters essentially keep life stable. The openness is completed with energy dissipation [29], limiting the efficacy according to the entropy law of thermodynamics [30]. Of course, the inputs are noisy, as well as the outputs and all the feedback mechanisms have specific homeostatic noises as it is discussed above. The stability of this regulation is based on the constant dissipation in the open living system in a very broad scaling measured by MSE entropy ($S_E = 1.8$) keeping the entropy in the $1/f$ noise range in a very broad scaling interval.

There is a further crucial structural point of the complete organizing process. The feedback mechanisms are connected to the actual "hardcovers", so are the large networks (blood, lymph, nerve, junctions, adherents, mesenchyme, polymers, etc.). This hardware carries the "software", the regulation mechanisms, like the internet, a global network of interconnected computers, the world-wide-web (WWW), and information exchange place is based on the internet as "hardware". While WWW builds up a fractal structure, the internet does not [31]. The internet hardware has "hubs", which attract each other by the better communication possibilities guided by the economic optimizing. These systems are vulnerable due to the strong and large number of links in hubs forming strong characteristically assortative clusters. The WWW follows the user's optimization having a wide range of "weak links" meaning the connection of users outside the hub; weakens the connections to the hubs. These weak-links connect hubs with non-hubs, they make repulsion-like structures between hubs, and stabilize the system well; thus they are less vulnerable than the internet "hardware".

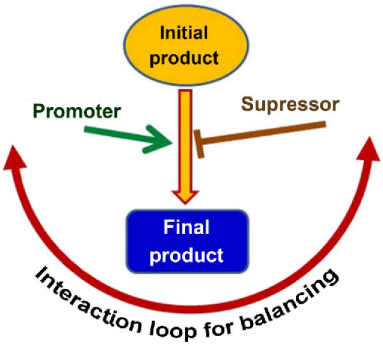


Figure 7. The balance of promoters and suppressors (Y-Y pairs) make an interaction negative feedback loop regulating each other, keeping the final product controlled.

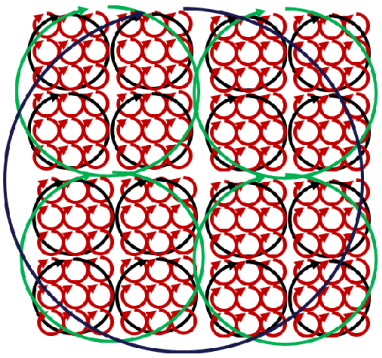


Figure 8. The regulation Y-Y loops are grouped, forming new regulation levels, and re-grouping again and so on subsequently.

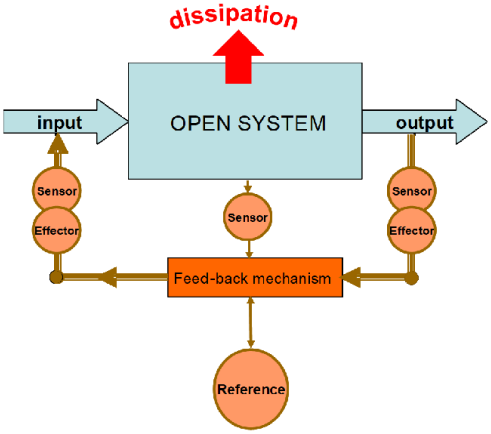


Figure 9. The complexity after all looks like one single Y-Y interaction which is regarded in TCM as the unified negative feedback Yin-Yang balance. It is a well-known negative feedback regulating principle in engineering, including dissipation due to the open system.

Living objects are built in the same way, Figure 10. The metabolic networks, the neural information exchange, the long-range correlated structures of information exchange in the living organisms work on WWW style (WS), while the large hubs as organs of the body structure are internet-like (IL). The information short-cuts (small-worlds [32]) optimize the integration of the systems as shown in the functional brain networks [33].

Meridians are probably structures that partly include large networks ("hardware", like blood, lymph, nerve), but also contain "software" components for communication between the organs ("hubs") and having intermediate points (probably the acupoints), on which we may modify the broken homeostatic equilibrium. Since the "ground substance" is the central place of the information

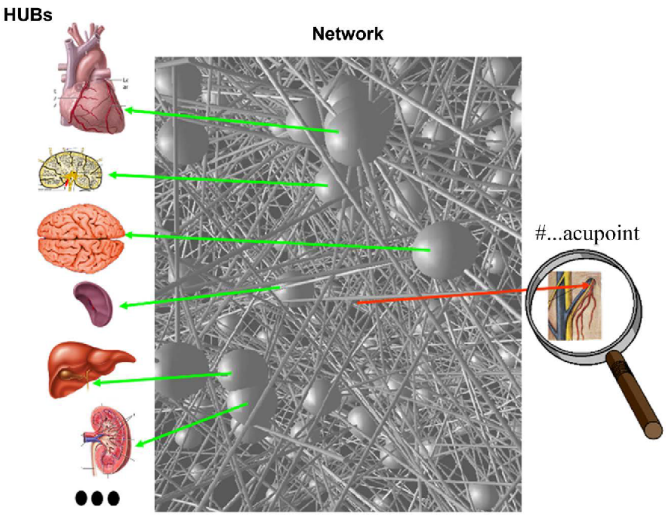


Figure 10. The schematic organizing network of the human living system. The large hubs collecting many connections and some connections are concentrated in the intermediate places (acupoints).

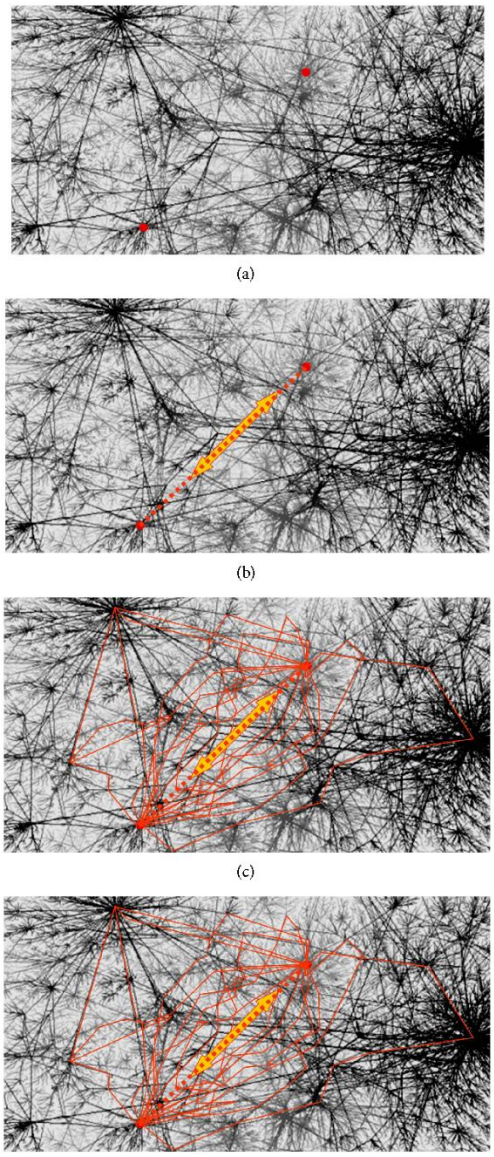
exchanges, the meridian network is probably tightly connected to the mesenchymal tissues in all over the body. However, the meridians as independent structures are not observable even by the most developed autopsy investigations. There are two reasons for this. The first is that the information exchange for homeostasis is valid only in living state. The second reason is more crucial than the first one. According to our hypothesis the meridians are information exchange lines, so they are part of the informational networks. It means that between two points (acupoints) they are not necessarily a hard connection, but the information is exchanged by the multiple connections between the points, Figure 11. The picture is similar to the traffic situation in a town. The two points could virtually be linked by a straight line (bee-line), but this line is not a real direct connection between the points. However, many routes exist, even in case we are forced to detour. The two chosen points are connected without a straight line connection between them.

The ground substance is not only a "meeting volume" of the signals but also a place for the action of interference. The links for these from the body surface are probably the acupuncture points, which connect the internal balance with the environment too. In this line, it is trivial that there is a possibility to step-in to the regulation process of homeostasis.

There are three possibilities of the effects, [34]:

1) The ground substance over-regulates. In this case, the decrease of the regulator-signal is desired;

2) The ground substance under-regulates. Toning is applied to increase the signal;



(a)

(b)

(c)

(d)

Figure 11. The forming of meridians as an information exchange virtual channel. (a) Two acupoints denoted by dots (chosen from the same meridians according to TCM); (b) The expected line of meridian according to TCM; (c) Multiple ways of information exchange connecting the two chosen points; (d) Due to the extremely large number of the possible ways for information exchange, the meridian virtually builds up. Due to the almost homogenous continue of the info-channels, the picture is very similar to the dipole forming an electric field between two opposite electric charges.

3) The deviation of the signal is too large. The error-noise is not $1/f$ pink noise. In this case, the homeostatic balance must be reconstructed by multiple acupuncture points.

5. Conclusion

We used the complexity of biosystems to study the acupuncture and meridian transports. We showed that physiology is well controlled by a complete interacting network or various negative feedback signals and processes, described by opposite interfering effects which are characterized in Traditional Chinese Medicine (TCM) by Yin-Yang (Y-Y) pairs. These regulatory pairs have a meaning in modern biology through the regulatory signals, transports, and interactions, and have a decisional role in the homeostasis of the complex system. The mean of fluctuations is used as a basis carrying a time-fractal fluctuation (called pink-noise or $1/f$ noise) of it. All signals in homeostasis have equal MSE entropy ($S_E = 1.8$). The various controlling opposite signals (Y-Y) have different time-scales and compose the pink-noise. The processes with smaller time-scale degrade by aging but pink-noise ensure that the deviations of the signals of the healthy homeostatic system remain constant by aging. The meridians are connected to the general material and information transport systems of the body completed as a meridian network by various coupling points. The coupling points which are near the skin-surface are called acupunctural points. These could be perturbed by actuating stimulus. We described the meridian system designated by the surface acupoints explaining why no structural appearance could be shown on these channels.

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Conflicts of Interest

The authors declare that there is no conflict of interest.

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