

(RESEARCH ARTICLE)



## Matrix mechanics of pharmacology, nonlinear biomechanics, three principles of self-cultivation and health, and epidemic equations of COVID-19

Yi-Fang Chang \*

*Department of Physics, Yunnan University, Kunming, 650091, China.*

GSC Biological and Pharmaceutical Sciences, 2023, 25(01), 031–040

Publication history: Received on 29 August 2023; revised on 05 October 2023; accepted on 7 October 2023

Article DOI: <https://doi.org/10.30574/gscbps.2023.25.1.0412>

### Abstract

First, we introduce the diagnostic space, treatment space and some medicinal vectors, and propose the matrix mechanics of pharmacology, and corresponding linear algebra and quantum medicine. Second, we discuss nonlinear biomechanics, which includes chaos, fractal and soliton, etc. It is related to entropy decrease. Lorenz model may be applied to describe the model of brain. Third, based on the Chinese traditional culture, we propose three principles of self-cultivation and health: health must first nourish self-heart, life should be a combination of movement and peace, and the body-mind-spirit union. Finally, we research the preliminary epidemic equations of COVID-19, and discuss their meaning.

**Keywords:** Biomechanics; Pharmacology; Matrix Mechanics; Health; Self-Cultivation; Epidemic Equations; COVID-19.

### 1. Introduction

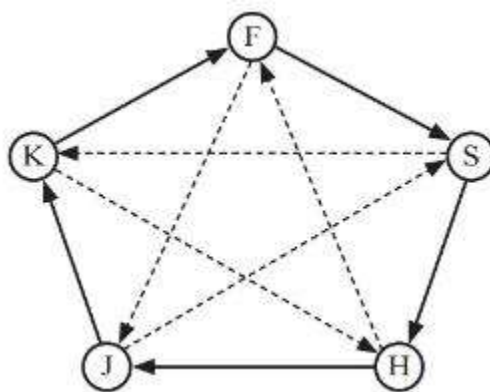
Based on the inseparability and correlativity of the biological systems, we proposed the nonlinear whole biology and its basic hypotheses [1]. This may unify reductionism and holism, structuralism and functionalism on biology, and is consistent with systems biology [2,3], which integrates multiple different levels in biological systems, from multiple molecules, cells, individuals, to populations, communities, ecosystems [4]. Further, based on the same character of human body, we proposed the nonlinear whole medicine and its three hypotheses and mathematics [5]. The propagation of COVID-19 is a typical nonlinear process with fractals and chaos. Based on human physiological indicators and the extensive quantum biology, we discussed the extensive quantum medicine [5]. It may quantitatively simulate the biological structure and physiological function from gene, cell to whole organ and system [6]. In this paper, we propose the matrix mechanics of pharmacology, and discuss nonlinear biomechanics, and three principles of self-cultivation and health, and the epidemic equations of COVID-19.

### 2. Matrix Mechanics of Pharmacology and Quantum Medicine

Basic method of Chinese traditional medicine is treatment based on an overall analysis of the illness and the patient's condition. It is applied by the wholeness of the human body and the relevance of its parts.

In 1989 we proposed that the theory of Chinese traditional medicine is based on strict mathematical symmetry group, in which the Yin-Yang theory is the simplest binary symmetry group, and the Five-Elements theory (Fig. 1) is the five element rotation group [7], which is completely determined by the angle of rotation.

\* Corresponding author: Yi-Fang Chang.



**Figure 1** The Five-Elements Promotion-Restraint theory

Here the solid lines represent promotion relations, and the dotted lines represent restraint relations.

We discussed some mathematical and physical developments of biology and medicine, which include biofield and biological electromagnetics. We researched nonlinear biology and biotopology in which some knots may describe the protein folding, and symbolic dynamics of biology and the extensive quantum biology, and the biothermodynamics and entropy. In thermodynamics of pharmacology, the main effects of various drugs are to promote internal interactions in body, and entropy decrease. Further, we introduced the diagnostic space, treatment space and some medicinal vectors, and propose the matrix mechanics of pharmacology. We searched biology, medicine and pharmacology with time sequences. If we master the medication time, this will be able to get the minimum amount of medication, and the drugs can play the maximum treatment effect. If period is accurate, it can determine the time of play, negotiations, attack, etc. But, period of each individual should be change follow age, etc. This is a very valuable research [8].

Pharmacology studies interaction principles and mechanism between drugs and organism, which includes pharmacodynamics and pharmacokinetics. Drugs include chemical drugs and biological drugs in modern medicine, and natural drugs in traditional medicine.

The Chinese traditional medicine is related to the space of Five Elements and Eight Diagrams [9]. Yin-Yang, Five Elements and Eight Diagrams as the corresponding basic vectors in n-dimensional space form a diagnostic space. A person's state of illness as a vector is projected in this space. At the same time, i type of the drugs used constitute a set of agents, and the characteristics of each drug are also quantitatively projected in the diagnostic and treatment space. From this we obtain the equilibrium relations and a set of equations, and corresponding matrices. Such it can solve the amount of the drug used according to the vector value of this human.

More specifically, we list several equations corresponding to n dimensional diagnostic space, let  $(b_1, b_2, b_3, \dots, b_n)$  is the projection of a person's state of illness in n dimensional space, which forms a vector B with n row and i column on state of illness. Let  $(a_{1i}, a_{2i}, a_{3i}, \dots, a_{ni})$  is the projection of i type of drug in n dimensional space, so that the set of agents used forms a matrix A with n rows and i columns. So the equations can be simplified as matrix equations:

$$BX = \begin{pmatrix} b_1 \\ b_2 \\ \dots \\ b_n \end{pmatrix} X = \begin{pmatrix} a_{11} & a_{12} & \dots & a_{1i} \\ a_{21} & a_{22} & \dots & a_{2i} \\ \dots & \dots & \dots & \dots \\ a_{n1} & a_{n2} & \dots & a_{ni} \end{pmatrix} = A. \quad (1)$$

Its solution is:

$$X = B^{-1}A = (x_1, x_2, x_3, \dots, x_i). \quad (2)$$

It is a row vector with 1 row and i column, and its value is namely the amount of each i type drug used to treat this person.

Further, the matrix mechanics of pharmacology may be related to the matrix form in quantum mechanics, and Heisenberg equation:

$$\frac{dF}{dt} = \frac{1}{i\hbar}[F, H]. \quad (3)$$

It may form the quantum medicine and its some characters. Different individuals have different matrices, which correspond to the dosage of the different agents. The change of the matrix is related to time and meridian flow(子午流注), and corresponds to the different effects of different treatment steps with visualization.

For equations the initial condition is age, and the boundary conditions are four seasons and environments. The dimension of diagnosis and treatment space is different, the number and elements of agents collection are also different, the corresponding equation can have multiple solutions, which corresponds to a variety of treatment can be used prescriptions. This set of linear equations may have multiple solutions, unique solutions, or even no solutions. The latter is namely that for this illness there was no cure in the circumstances. It can be related to different quantum path integrals with different probabilities and efficacy, or even theoretical treatments with multi-world. Different processes combined with nonlinear theory can correspond to cure if homing, or to chaos and death. This again corresponds to destiny.

In pharmacokinetics the processes of drug in the body, including absorption, distribution, biotransformation and transport, etc., are all internal interactions. In particular, in compartment model of pharmacokinetics the body acts as a system of multiple rooms must be an isolated system, in which the concentration change rate is described by the nonlinear Michaelis-Menten equation.

Cell dynamics studies the changing rules of cell growth, reproduction, differentiation and death. The basic pharmacological action of antineoplastic agents affects mainly the biochemical process of biomacromolecules, and derives important genetic substances and protein metabolism disorders in cells, and prevents the division and reproduction of cell disorder. Gene therapy is a medical intervention based on modification of genetic material of living cells. It includes gene correction and gene replacement. Antisense drugs are a class of synthetic drugs carrying biological information, and are called as information drugs.

The same drugs, i.e., input the same energy and entropy, will produce different effects for various factors, which include age, sex, genetic factors, etc. Here emotional factors, pathological states, etc., all are some internal factors. In a word, we believe that the treatment is mainly based on internal interactions, including gene interactions, self-healing. Drugs enter the body, which form also an isolated system. Drug effect mainly depends on the reaction process between drug and the target site of organism.

In modern medicine selectivity and specificity of drugs are all the directional internal interactions. For the human body they must derive entropy decrease [10], whether for the etiological treatment or the symptomatic treatment. This cannot consider that phenotype of drug effect, excitation and inhibition, central stimulants and sedative drugs, immunosuppressive agents and immunostimulants all are entropy increase. Only various adverse reactions are entropy increase. Therefore, except trauma and surgery, in the final analysis, almost all treatments are mainly based on the internal interaction in body as isolated system. Disease and death are entropy increase. Conversely, disease recovery and growth are entropy decrease, and are mainly internal interactions. Treatments are mainly internal conditioning.

The mechanism of drug actions, whether acting on the enzyme or receptor or carrier or gene, especially as the relations between the receptor and the ligand, the dynamics of drug and receptor reactions must be internal interactions.

It is known that matrix is the non-commutative, which corresponds to drugs applied must be considered in a sequential order. Matrix has addition, multiplication, and the inverse matrix, etc. Different operations correspond to different combinations of drugs. There have symmetric or anti-symmetric matrix. By chemical-biological methods drugs can often be turned into a diagonal matrix with a single index. Further, we should study various linear space, linear transformation and linear algebra, etc., and their meaning in pharmacology. Linear equations may derive the discrimination theorem and structure of solutions.

In fact, this approach is universal method in any pharmacology, and can be extended to general medicine. The specific method is: first find out a number of indicators of the treatment of some diseases, such as the circulatory diseases are heart rhythm, blood pressure, blood lipid, heart tone and so on. They as a group of linear independent base vector

constitute a space for diagnosis and treatment. Other diagnostics can be used as boundary and initial conditions for the equation. Secondly, the patient's conditions and the performances of each drug are quantitatively projected in this space. Third, list the equations and their solutions. If a drug  $k$  is not effective to treat the disease, it will be a zero vector in the diagnosis space, and its dose must be  $x_k = 0$ . This is the most basic approach of drug matrix mechanics. Various formulas and methods of linear algebra can be applied in medicine and pharmacology. Since the quantification of the diagnosis of modern medicine, this method is probably more suitable.

The foundation of quantum medicine is DNA, various cells and biological individuals are all quantized. It corresponds to the extensive quantum biology [11]. Further, it may develop to the quantum S-matrix of reaction theory, which may describe possible reactions with conservation laws. This may probably develop into the momentum representation, and derive the momentum spectra that may correspond to the sick ranks.

### 3. Nonlinear Biomechanics and Entropy Decrease

Generally, biomechanics should be nonlinear. In nonlinear mechanics there are strange attractors and chaos. In biology and physiology there are widely various chaos and fractals [12] and the nonlinear dynamics. They include the excited or stimulated state of neuron and whose Hodgkin-Huxley equation [13], and the heart beats rhythmically and whose Bonhoeffer-Van der Pol equation [14], and the exudation of hormone, and the dynamical disease and epidemic, and the complex structure of living systems [15], etc. Hartline equation in the inhibitory neural network may add the nonlinear terms, and then chaos will appear.

Goldberger et al., [16,17] proposed the fractal hypothesis on a mechanism of cardiac electrical stability, and some observations on the question as ventricular fibrillation 'chaos'. The fractal in biology may be dependent on gene, DNA and their structural formations. They are continuously embedded by some self-similarity, and form various organism. A self-similarity may construct the same new cells, synapses and so on. The blood, breathing and neural systems possess the fractal characters and the fractal dimensions.

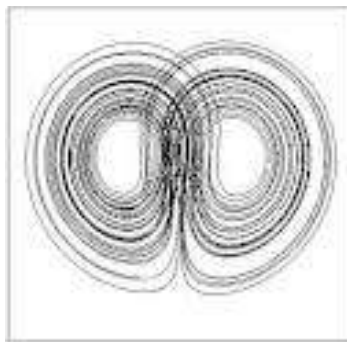
The nonlinear mechanics includes hydrodynamics and Lorenz model, whose equations are:

$$dx/dt = -vx + ky, \quad (4)$$

$$dy/dt = ax - by - xz, \quad (5)$$

$$dz/dt = -cz + xy. \quad (6)$$

This result is a spatial mode. If various parameters in Eqs.(4)(5)(6) take suitable values, a beautiful Lorenz strange attractor (Fig.2) will be obtained.



**Figure 2** X-Z view of Lorenz model

The neural meaning of the Lorenz model should be a phenomenological model of brain, whose two wings correspond to two hemispheres of brain, and two hemispheres jump about, which may describe thinking [18]. It shows that life lies in cooperation in chaos. Moreover, we discussed the fractal, chaos and soliton in nonlinear biology and neurobiology, in which soliton may keep the integrality and veracity of information in neural transfer. The nonlinear mechanism of memory is researched [19].

The soliton and exciton of energy transfer in biological macromolecules are the typical nonlinear phenomena. Davydov investigated the soliton model of the vibrational energy transported along the biological macromolecules [20]. The known neural conduction may use Davydov soliton and its extension. For the Davydov model of a one-dimensional protein, Lomdahl and Kerr added the fluctuation and dispersion terms, and the lifetime of Davydov soliton is only the order ns [21]. Cottingham and Schweitzer calculated that the lifetime of a Davydov soliton at finite temperature is still 1ns for the  $\alpha$ -helical protein molecule using a first-order perturbation theory [22]. This is too short to be useful in biological processes. Using the quantum Monte Carlo technique, Wang, et al., investigated the one-dimensional Davydov model in the  $\alpha$  helix, and found that Davydov soliton at 310K is instable [23].

Generally, the fractal, chaos and soliton will appear in the nonlinear biology, in particular, for in which there are soliton-chaos double solutions [18]. We discussed biofield and some nonlinear theories in biology. They include chaos in biology and its application to cancer, and fractal and complex dimension in biology, etc. We proposed the matrix representations of hypercycle theory, which can be defined by a degree of connectivity. Its fuzzy element corresponds to that each element is fractal [12].

In biology the quasispecies equation is:

$$\dot{x}_i = \sum_{j=0}^n x_j f_j Q_{ji} - \phi x_i, \quad (i=0,1,\dots,n) \quad (7)$$

The replication equation is:

$$\dot{x}_i = x_i [f_j(\bar{x}) - \phi(\bar{x})], \quad (i=0,1,\dots,n). \quad (8)$$

They and Lotka-Volterra equations are all some nonlinear biological equations.

In the neurobiology Hodgkin-Huxley equations, FitzHugh-Nagumo equations and much interactions are all nonlinear. FitzHugh-Nagumo dynamical equations of a single neuron are:

$$c \frac{dV(t)}{dt} = V(t) - V^3(t) - y(t), \quad (9)$$

$$\frac{dy(t)}{dt} = \gamma W(t) - y(t) + b + \sqrt{2D} \xi(t). \quad (10)$$

Here b is a constant, and  $\xi(t)$  represents Gauss white noise. We apply the qualitative analysis theory of the nonlinear equations, the characteristic matrix of Eqs.(9) and (10) is:

$$\begin{pmatrix} 1-3V^2 & -1 \\ \gamma & -1 \end{pmatrix}. \quad (11)$$

Its eigen-equation is:

$$\lambda^2 + 3V^2 \lambda + (3V^2 - 1 + \gamma) = 0. \quad (12)$$

The eigen-solutions are:

$$\lambda = \frac{1}{2} (-3V^2 \pm \sqrt{9V^4 - 12V^2 + 4 - 4\gamma}). \quad (13)$$

This result of the qualitative analysis is independent of b and random term  $\xi(t)$ . It is also a fractal structure.

Life forms a nonlinear, multi-level, complex and complete system during long-term evolution. Generally, biological evolutions are increases of complexity and bioinformation. They correspond to entropy decrease. In an evolutionary process with long time, life forms a nonlinear complex and complete system with multi-levels: gene, cell, tissue, organ, system, individual, population, community, ecosystem, bio-sphere. If the biosystem is isolated at a certain time, the second law of thermodynamics will be violated [24].

Different sensation systems are usually independent each other. Our collective opened out the potential of blind children, and found through a period training of time, some children by touch or nose or ear can distinguish different colors, even simple figure and numbers. From this and other research, we proposed a hypothesis: The neural excitable cell is continuously induced and excited, then grow out new synapse and dendrite, and the feeling system, hearing system, smell system, etc., may joint to visual system, and form a new neural network, and achieve finally a transformation among vision and other sensations. Further, we proposed some possible tests, for example, for trained mammal, etc., and researched possible theories. It is a testable application of the nonlinear whole neurobiology. This may build a bridge between modern science and traditional culture, religion [25].

The molecular motors play a very important role in maintaining high levels of order in biological systems. We think, the molecular motor corresponds to  $dS < 0$ , in which the chemical energy of cell translates into mechanical energy. In the microtubule the motor proteins have kinesin and dynein. Their moving way is hand-over-hand [26]. The kinesin moves matter of cell nucleus to cell membrane, and dynein moves matter of cell membrane to cell nucleus. Their transport direction is just opposite, but, both are not competition [27]. Moreover, many motors may work together, and produce speed with 10 time unit motor. It is namely order cooperative action [28].

Molecular motor transforms chemical energy to mechanical energy [28-31]. Motor protein general scale is 10nm, which is called Brownian motor [32]. It is also an extensive quantum.

The rotary motor is composed of biologic macromolecule, whose volume is small, and efficiency is very high almost 100%, and they may converse rotate. Its typical model is ATPase, which is a core enzyme for biologic energy translation in organism. The entire process of cell upgrowth and metabolism need energy, which is obtained from the chemical energy hydrolyzed by ATP under the most cases, and ATP is synthesized from ATPase. The molecular motor of ATPase may hydrolyze ATP, and may also synthesize ATP. This is similar with membrane and Maxwell demon.

Brownian motor may apply stochastic differential equation [33,34]:

$$\frac{dx}{dt} = \frac{\partial V(x(t), f(t))}{\partial x} + y(t) + F + D\xi(t). \quad (14)$$

Here  $V(x, f)$  is the asymmetric potential of spatial period,  $y(t)$  is periodic force, or random force;  $F$  is load as study motor efficiency;  $\xi(t)$  is Gauss white noise.

For Brownian motor, nonequilibrium and some breaking of the system symmetry are two necessary conditions to achieve directional motion in system [31,35]. For a simplified motor system:

$$\frac{dx}{dt} = \frac{\partial V(x(t), f(t))}{\partial x} + A \sin \Omega t + D\xi(t). \quad (15)$$

If  $A=0$ , it will an equilibrium system.

Except Brownian motor motion induced by thermal noise, temporal or spatial symmetry breaking of a deterministic unbiased external force can also lead to directional motion of particles, called deterministic directional transport. Further, considering the mass and damping, the inertia of the particles will have a great impact, correspondingly called the inertial motor [36,37,31]. Inertial motors have very complex dynamical manifestations with regular transport orbits, chaotic transport phenomena, and the reversal phenomena of flows. And the direction of the flow depends on the mass and damping of the motor particles [38].

Directed motion at thermodynamic equilibrium implies the conversion of heat absorption from a single heat source into useful work, which is contrary to the second law of thermodynamics.

If changes of particle conformations are considered, the different moving states of motor particles can be described by coupled diffusion models [39]:

$$\frac{dx}{dt} = \frac{\partial V_i(x)}{\partial x} + D_i \xi_i(t), i = 1, 2, \dots, N. \quad (16)$$

Here  $x = x(t, \omega)$ .

Consider the stochastic differential equations for the coupled diffusion processes:

$$\frac{dx}{dt} = \left[ F + \frac{\partial V_i(x)}{\partial x} \right] + D_i \frac{dB_i(t)}{dt}, i = 1, 2, \dots, N. \quad (17)$$

Symmetry breaking, such as the asymmetric periodic potential, can obtain the directional transport of Brownian motor [40,41,39]. Spatial asymmetry is parity non-conserved, and the momentum is not uniform.

#### 4. Three Principles of Self-cultivation and Health

Chinese traditional medicine and culture have rich health care contents: such as martial arts, Taijiquan, Qigong, meditation, heart nourishing, etc. Based on these traditions, we propose three principles of self-cultivation and health:

The first principle: health must first nourish self-heart, to achieve body-life double repair.

A good attitude is not only beneficial to disease prevention, but also easy to heal when sick. Children are angels, and their bodies grow strong. But, we ordinary people, especially in the face of the changeable external world were a series of mind-body diseases. It disturbed the calm nature of mind, so lost the living order and life purpose and meaning. We use the Buddhism way, for example, by *The Sutra of Hui Neng*. Buddhism is the best and five-star psychology. We can achieve the real understanding of the three different stages of life: after wind moves, the heart is still empty. Then “our body is the Bodhi-tree, and our mind is a mirror bright, carefully we wipe them hour by hour, and let no dust alight.” Finally tend to “there is not Bodhi-tree, nor stand of a mirror bright. Since all is void, where can dust alight.” In short, the heart wide disease less, more like less angry.

The second principle: life is not only about movement, it should be a combination of movement and peace.

The traditional concept that “life lies in movement” is a one-sided view. Big and strenuous movements are not good for health. This exercise is a heroic feat that pushes the limit, but it hurts the body. Only “life lies in the combination of movement and peace”, “life lies in the balance of Yin and Yang” is a comprehensive and conducive to health [42].

Breathing-meditation, proper exercise, timely exercise with different four seasons, different ages, different time sequence are necessary. Special meditation is the good way of the human body. Zen is the spiritual effect of the instruction heart to focus but not scattered. It the unity of the body and mind, and prevents the both scattered. At meditation you can adjust the physiological state, cultivation of body-mind, and free trouble. Zen is the basis of opening wisdom, and is a kind of heart and body synergy, spirit and flesh synergy. Now it has swept the world, former US President Bill Clinton also invited special guidance for meditation after retirement and illness. This kind of cultivation has a close relation with the Qigong of strengthening physical health. Mencius said, “I am good at cultivating my noble spirit”, which deeply reflects the interaction and relation among cultivating one's body, mind and morality.

The third principle: the body-mind-spirit union. It is based and combined on psychology and parapsychology, religions, etc.

Disease and health involve various causes, which include the three aspects: body, mind and spirit. We proposed three dimensional body-mind-spirit worlds on human society and parapsychology. Some observed results imply “ghosts” are probably the existences of some biological or non-biological objects that can not be detected usual methods, but can be detected by infrared light, etc. It will be a great contribution for world, and is the discovery of a new class of substances. Any observations and detections on mind and spirit worlds and on relations between both and matter are all valuable [43,44].

In a word, for the sake of the health of all mankind, we must abandon stereotypes, and combine the related traditional culture-medicine and modern medicine, parapsychology and religion, etc.

### 5. Preliminary Epidemic Equations of COVID-19

The propagation of COVID-19 is a typical nonlinear process with fractals and chaos. A key of controlling COVID-19 prevents propagation from reaching an irreversible chaos point. From corresponding nonlinear equations and their solutions, we may obtain three basic origins of disease, and corresponding therapeutic methods may be applied to COVID-19 [5]. This testifies that research on infectious diseases must apply the nonlinear whole medicine.

Liu, et al., developed two differential equations on COVID-19 epidemic model [45]. Beira, et al., discussed differential equations model-fitting analysis of COVID-19 epidemiological data to explain multi-wave dynamics [46]. Hall, et al., researched a mathematical modelling of the COVID-19 epidemic in Northern Ireland in 2020 [47].

By similar infectious disease epidemic equations [48,49], let  $x(t)$  is the number of people exposed, and  $y(t)$  is the number of those potentially infected, we propose the preliminary epidemic equations of COVID-19:

$$\frac{dx}{dt} = \alpha xy - (\varepsilon + \delta)x - ky, \quad (18)$$

$$\frac{dy}{dt} = -\alpha xy + \delta x + ky. \quad (19)$$

Here  $\alpha$  is infection rate,  $\varepsilon$  is mortality rate,  $\delta$  is cure rate, and  $k$  is prevention rate. Their characteristic matrix is:

$$\begin{pmatrix} \alpha y - \varepsilon - \delta & \alpha x - k \\ -\alpha y + \delta & -\alpha x + k \end{pmatrix}. \quad (20)$$

Its eigen-equation is:

$$\lambda^2 + [\alpha(x - y) - k + \varepsilon + \delta]\lambda + \varepsilon(\alpha x - k) = 0. \quad (21)$$

$$\frac{d(x + y)}{dt} = -\varepsilon x, \quad (22)$$

For Eq.(18) if  $k=0$ ,

$$x = C \exp[\alpha y - (\varepsilon + \delta)t]. \quad (23)$$

As long as  $\alpha y > \varepsilon + \delta$ , it will increase exponentially. If  $\alpha y = \varepsilon + \delta$ ,  $dx/dt=0$ . Eq.(23) replaces into Eq.(19) with  $k=0$ , and derives

$$\frac{dy}{dt} = C' e^{\alpha y} (-\alpha y + \delta). \quad (24)$$

Integral of Eq.(24) is:

$$C_0 + \ln |y| - y + \frac{\alpha y^2}{2 \cdot 2!} - \frac{\alpha^2 y^3}{3 \cdot 3!} + \dots = -C' \alpha t. \quad (25)$$

Its first approximant is:



$$y = C'' e^{-\alpha t}. \quad (26)$$

It will decrease exponentially.

For COVID-19 we edited the Special Issue in EC Neurology in January 2021. We believe that science will surely defeat the epidemic, and mankind will greet a bright future.

## Compliance with ethical standards

### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

## References

- [1] Chang YF. Nonlinear whole biology and loop quantum theory applied to biology. *NeuroQuantology*. 2012; 10(2):190-197.
- [2] Weston AD, Hood L. Systems biology, proteomics, and the future of health care: toward predictive, preventative, and personalized medicine. *Journal of Proteome Research*. 2004; 3(3): 179-196.
- [3] Bonneau R, Baliga NS, Deutsch EW, Shannon P, Hood L. Comprehensive de novo structure prediction in a systems-biology context for the archaea Halobacterium sp. NRC-1. *Genome Biology*. 2004; 5(8): R52.
- [4] Vidal, M. A biological atlas of functional maps. *Cell*. 2001, 104(1): 333-339.
- [5] Chang YF. Nonlinear whole medicine, extensive quantum medicine and three basic origins of disease. *EC Neurology*. 2021; SI.02:187-194.
- [6] Noble D. Modeling the heart from genes to cells to the whole organ. *Science*. 2002; 295: 1678-1682.
- [7] Chang YF. Theoretical base of traditional Chinese medicine is symmetrical groups. *Exploration of Nature (China)*. 1989; 8(1):49-50.
- [8] Chang YF. Developments of mathematical-physical biology, matrix mechanics in pharmacology, and medicine with time sequences. *Sumerianz Journal of Scientific Research*. 2021; 4(4):85-94.
- [9] Chang YF. Space of Five Elements-Eight Diagrams and pharmacologic matrix mechanics. *Culture & Application of I Ching & Traditional Chinese Medicine*. Hua Xia Press. 1995. p75-79.
- [10] Chang YF. Possible entropy decrease in biology and some new research of biothermodynamics. *NeuroQuantology*. 2013; 11(2):189-196.
- [11] Chang YF. Extensive quantum biology, applications of nonlinear biology and nonlinear mechanism of memory. *NeuroQuantology*. 2012; 10(2):183-189.
- [12] Chang YF. Chaos, fractal in biology, biothermodynamics and matrix representation on hypercycle". *NeuroQuantology*. 2013; 11(4):527-536.
- [13] Aihara K, Matsumoto G, Ikegaya Y. Periodic and non-periodic responses of a periodically forced Hodgkin-Huxley oscillator. *J.Theor.Bio*. 1984; 109:249-269.
- [14] Fitzhugh R. *Biological Engineering* (H.P.Schwan ed.). McGraw Hill. 1969.
- [15] Cramer F. *Chaos and Order: The Complex Structure of Living Systems*. Verlags-Anstalt. 1988.
- [16] Goldberger AL. Some observations on the question: Is ventricular fibrillation 'chaos'. *Physica*. 1986; 19D:282-289.
- [17] Goldberger AL, Bhargava V, West BJ, et al. On a mechanism of cardiac electrical stability: The fractal hypothesis. *Biophys.J*. 1985; 48:525-528.
- [18] Chang YF. Neural synergetics, Lorenz model of brain, soliton-chaos double solutions and physical neurobiology. *NeuroQuantology*. 2013; 11(1):56-62.
- [19] Chang YF. Extensive quantum biology, applications of nonlinear biology and nonlinear mechanism of memory. *NeuroQuantology*. 2012; 10(2):183-189.
- [20] Davydov AS. *Biology and Quantum Mechanics*. Pergammon. 1982.

- [21] Lomdahl PS, Kerr WC. Do Davydov solitons exist at 300K? *Phys.Rev.Lett.* 1985; 55(11): 1235-1238.
- [22] Cottingham JP, Schweitzer JW. Calculation of the lifetime of a Davydov soliton at finite temperature. *Phys.Rev.Lett.* 1989; 62(15):1792-1795.
- [23] Wang X, Brown DW, Lindenberg K. Quantum Monte Carlo simulation of the Davydov model. *Phys.Rev.Lett.* 1989; 62(15):1796-1799.
- [24] Chang YF. Possible entropy decrease in biology and some new research of biothermodynamics. *NeuroQuantology.* 2013; 11(2):189-196.
- [25] Chang YF. A testable application of nonlinear whole neurobiology: Possible transformation among vision and other sensations. *NeuroQuantology.* 2013; 11(3):399-404.
- [26] Yildiz A, Forkey JN, McKinney SA, et al. Myosin V walks hand-over-hand: single fluorophore imaging with 1.5nm localization. *Science.* 2003; 300: 2061-2065.
- [27] Karp G. *Cell and Molecular Biology* (3th ed.). New York: John & Whley Sons, Inc. 2002.
- [28] Julicher F, Ajdari A, Prost J. Modeling molecular motors. *Rev.Mod.Phys.* 1997; 69:1269-1281.
- [29] Hill TL. *Free Energy Transduction in Biology.* Academic Press. 1977.
- [30] Hill TL. *Free Energy Transduction and Biochemical Cycle Kinetics.* Springer-Verlag. 1995.
- [31] Reimann P. Brownian motor: noisy transport far from equilibrium. *Phys.Rep.* 2002; 361:57-265.
- [32] Astumian RD. Thermodynamics and kinetics of Brownian motor. *Science.* 1997; 276:917-922.
- [33] Magnasco MO. Forced thermal ratchets. *Phys.Rev.Lett.* 1993; 71:1477-1479.
- [34] Astumian RD, Bier M. Fluctuation driven ratchets: molecular motor. *Phys.Rev.Lett.* 1994; 72:2652-2654.
- [35] Qian, M.; Qian, M.P.; Zhang, X.J. Fundamental facts concerning reversible master equations. *Phys.Lett.* 2003, A309:371-376.
- [36] Mateos, J. Chaotic transport and current reversal in deterministic ratchets. *Phys.Rev.Lett.* 2000, 84:258-260.
- [37] Barbi M, Salerno M. Phase locking effect and current reversal in deterministic under damped ratchets. *Phys.Rev. E.* 2000; 62:1988.
- [38] Jung P, Kissner JG, Hanggi P. Regular and chaotic transport in asymmetric periodic potentials: Inertia. *Phys.Rev.Lett.* 1996; 76(18):3436-3439.
- [39] Zhou HX, Chen YD. Chemically driven motility of Brownian particles. *Phys.Rev.Lett.* 1996; 77:194-196.
- [40] Parmeggiani A, Julicher F, Ajdari A, Prost J. Energy transduction of isothermal ratchets: generic aspects and specific examples close to and far from equilibrium. *Phys.Rev.* 1990; E60: 2127.
- [41] Bartussek R, Hanggi P, Kissner JG. Periodically rocked thermal ratchets. *Europhys.Lett.* 1994; 28:459-464.
- [42] Chang YF. Examination of the Channels parenchyma, and geometric symmetry therapy. *Journal of Chinese Traditional Medicine (Supp).* 2003;10:56-57.
- [43] Chang YF. Three dimensional body-mind-spirit worlds on human society, social fields and Chinese cultural-social ecology. *Sumerianz Journal of Scientific Research.* 2020; 3(12): 156-165.
- [44] Chang YF. Three dimensional body-mind-spirit worlds on parapsychology and human society, and preliminary classification. *World Institute for Scientific Exploration (WISE) Journal.* 2021;9 (2):32-40.
- [45] Liu Z, Magal P, Seydi O, Webb G. A COVID-19 epidemic model with latency period. *Infect Dis Model.* 2020; 5:323-337.
- [46] Beira MJ, Sebastião PJ. A differential equations model-fitting analysis of COVID-19 epidemiological data to explain multi-wave dynamics. *Scientific Reports.* 2021; 11: 16312.
- [47] Hall PA, Kiss G, Kuhn T, Moutari S, Patterson E, Smith E. Mathematical modelling of the COVID-19 epidemic in Northern Ireland in 2020. *Open Journal of Modelling and Simulation.* 2021; 9(2):91-110.
- [48] Bailey NTJ. *The Mathematical Theory of Infections Diseases and Its Applications.* New York: Hafner Press. 1975.
- [49] Anderson RM, May RM., *Infections Diseases of Humans.* Oxford University Press. 1991.