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Biophysical and Biochemical Mechanisms of Developments in Mental Activity During Life of a Human Organism in Norm and Pathology

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Abstract

The article studies development of human organism in condition interactions between organisms and environment activity. There were described mechanism maintenance stability of an open non equilibrium non linear thermodynamic system of an organim after his birth and first breath of an eukaryotic genetics of an organism according to famous Glandsdorff and Prigogine theory as well as Prigogine theorem. Also there were described further development through lifetime of mechanisms maintenance stability of an open non equilibrium non linear thermodynamic system of human organism according famous Glandsdorff and Prigogine theory. All described processes are supported by inherited energy of Basic Internal Energy (E_{bas}) in exerting genomic processes. Also the mental activity of humen organisms are exerted by inherited energy of Basic Internal Energy (E_{bas}) which driving mechanisms are shared into Basic Internal Energy of Molecular Bonds (E_{bas}MolBonds) builded bonds of atoms into molecule and bonds among compound biologic substances, into Basic Internal Energy of Trophic Processes (E_{bas}TroPr) creating trophic processes of open thermodynamic system of an organism and into Basic Internal Energy of Mental-Soul Processes (E_{bas}MenPr) of forming human mental activities. Thus the article studies biophysical and biochemical mechanisms of the pathologic mental states of the different mental diseases. On the one hand, the all pathologic processes of mental activities are touched on inherited energy of genomic processes. All these processes are subjected to environmental influences which are resisted by defensive processes of an organism. On the other hand, the inherited energy of Basic Internal Energy (E_{bas}) and energy obtaining from environment from Receptors through nerves how transmitters to brain neurons' cells with the metabolic energy of feed exert mechanisms of an organism's actovities leading to consumption Basic Internal Energy (E_{bas}) during lifetime for development of an organism that results in elderly of an organism according Glandsdorff and Prigogine theory. However the consumption Basic Internal Energy (E_{bas}) during lifetime of an organism can shift normal Stationary State of an organism into Quasi-stationary State of an organism pathology, including its mental diseases according Glandsdorff and Prigogine theory. All these mechanisms are considered in the article.

Keywords: Internal Energy of an Organism, Stem Cells, Basic Internal Energy in Neurons, Trophic Processes, Molecular Bonds Processes, Mental-Soul Processes

Introduction

Development activity of an open thermodynamic system of a human organism is subjected to thermodynamic laws that give possibility to study developments of human mental activities during life of an organism in norm causing by exchanges with substances and energy between open thermodynamic system of an organism and Environment. Just these exchanges substances and energy between open thermodynamic systems of both an organism and Environment are engaging as internal works (W_{int}) of an organism through metabolic mechanisms with mental activities through Receptors↔nerves (how transmitters)↔neurons' cells of an organism as well as external works (W_{ext}) of an organism supporting by immune and hormonal defensive processes that cause maintenance stability Internal Energy (U) of an organism according to first law of thermodynamics. Also the mental activity is exerted by genetical inherited energy of Basic internal energy (E_{bas}) [1-3]. Thus all these mechanisms create normal mental activity of Stationary States of an organism [1-3]. Besides there were explained mechanisms of transiting normal Stationary State of an organism's mental activities

into pathologic mental activities of Quasi-Stationary State of an organism. The all pathologic processes of mental activities are touched on inherited energy of genomic processes. The some pathologic states of Schizophrenia disease are arisen from early age of human life. However the pathologic states of the Dementia Bipolar Disorder (BD) are arisen because of different reasons in different age of the human life. Therefore the Dementia diseases are shared forming different Dementia diseases or different the stage of Dementia. Thus there are the Dementia which are arisen by different reasons: the paralytic dementia, pseudoparalytic dementia, terminal dementia, posttraumatic dementia, miltiinfart (or vascular) dementia, sclerotic dementia, toxic dementia, postinsult dementia, syphilitic dementia (or syphilitic meningoencephalites). Besides there are the Dementia which are arisen by different age of the elderly human life forming different Dementia diseases or the different stages of Dementia: the senile dementia, presenile dementia, pseudosenile dementia, sclerotic dementia, amnestic dementia, hebephrenic dementia, which form as the different stages of Dementia how the catatonic dementia, lacunare dementia, acute dementia, primary dementia, secondary dementia, as well as different deep Dementia diseases how Parkinson disease and Alzheimer disease.

The Forming Mental Activity in open Non Equilibrium Non Linear Thermodynamic System of an Organism

1. Development Metabolism During Life of an open Non Equilibrium Non Linear Thermodynamic System of an Organism

The birth of an organism after first breath forms catabolic aerobic oxidative processes which are joined to catabolic anaerobic processes of oxidative phosphorilation creating through interaction with the Environment of the open thermodynamic system of an organism. Thus the open thermodynamic system of an organism exchanges substances and energy with Environment through inner metabolic processes including oxidative processes and biosynthetic processes that forms balance catabolic oxidative systems and anabolic biosynthetic system causing mechanism maintenance stability of Internal Energy (U) of an open non equilibrium thermodynamic system according famous Prigogine theorem (Figure 1 and Figure 2) [3-6].

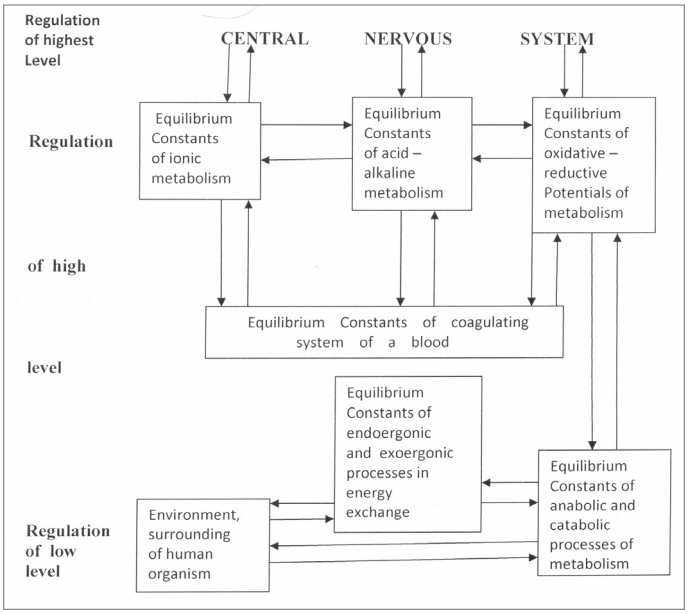


Figure 1: The mechanism of maintenance stability of Internal Energy and Internal Medium an organism.

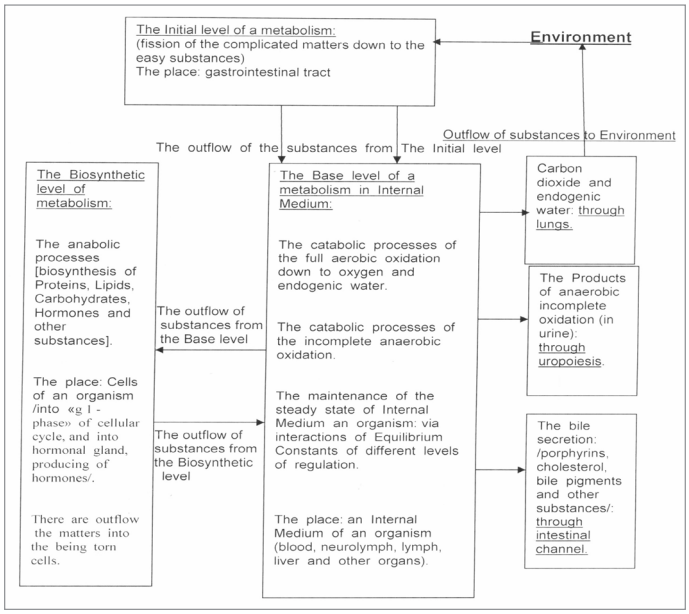


Figure 2: Three levels of Metabolism causing excretion waste substances into environment.

There is the Theorem Prigogine:

[The symbols: Entropy – S; Stream of Substances – Js; Stream of Energy – Je; Force of Substances – Fs; Force of Energy – Fe; Phenomenological Streams of Combination Substances with Energy – Zse or Zes, of separate Substances and Energy – Zss and Zee] $dS = JsFs + JeFe > 0$. Conjugated flows: $Js = ZssFs + ZseFe$ and $Je = ZeeFe + ZesFs$. $dS = (ZssFs + ZseFe)Fs + (ZeeFe + ZesFs)Fe = ZssFs^2 + ZseFsFe + ZesFsFe + ZeeFe^2 = \underline{ZssFs^2 + 2ZseFsFe + ZeeFe^2 > 0}$, corresponding to the Onsager concept: $Zse = Zes$. However there are $Zss > 0$; $Zee > 0$; $Zse > 0$ in Stationary State.

It is known that there is not changed <u>flow of Substances</u> in Stationary State, i.e. inflows Substances are equal outflows Substances in Stationary State of an organism: $Js = 0$. The concentrations of Substances in Internal Medium of an organism (in blood and in neurolymph) are constants, i.e. the quantity inflow Substances into an organism are equal quantity outflow Substances from an organism. Hence there is the derivative dS from Fs, if it's Fe = constant (the constant production calories for maintenance temperature 36,0ºC – 37,5ºC by which all enzymes operate). That leads to following formula:

$dS/dFs = 2\,ZseFe + 2\,ZssFs = 2\,(ZseFe + ZssFs)$, $2\,Js = 0$.

The second derivative (flexon) from S is peer: $d^2S / dFs^2 = 2Zss > 0$

It corresponds to extreme point. It means that dS min.

Footnotes: Metabolic and Energy "Equilibrium Constants" regulate interactions of intracellular and extracellular chemical potentials ($\mu_{int.} \leftrightarrow \mu_{ext.}$) for maintenance stability of Internal Energy and Internal Medium an organism. The intracellular and extracellular chemical potentials ($\mu_{int.}$ and $\mu_{ext.}$) cause the formations of the positive/negative charges on internal and external membranes of cellular wall, promoting operation of remote cellular reactions via cellular capacitors operation.

Footnote: Basal metabolic rates (BMR) or Basal Work (Wbasal) promotes stable state of Internal Energy (ΔU) of an organism stimulating metabolism and causing excretion waste substances into environmet.

So the minimization increment of dissipation energy via minimization of gain entropy causes the stability of the open non equilibrium thermodynamic system of an organism's beginning life [3, 4].

Also stability of an open non equilibrium thermodynamic system of an organism is supported by mechanisms corresponding to the first law of thermodynamics. There is the formula of first law of an open thermodynamic system of an organism: $H = U + W_{int} + W_{ext}$, [symbols: H – enthalpy (general energy), U – internal energy of an organism, W_{int} – internal work of an organism, W_{ext} – external work of an organism] [3, 4].

Just internal energy of an organism (U) contains, on the one side, of the partial obtained energy from environment for metabolic processes creating activity of an organism and its inner organs due to biochemical processes both anabolic biosynthetic processes and catabolic oxidative processes and, on the other side, of inherited from the parents genetic energy as the Basic internal energy (E_{bas}) in the neurons (basic stem cells) for exerting cellular cycle of the cells development through basic stem cells (neurons) → totipotent stem cells → pluripotent stem cells → multipotent stem cells → oligopotent stem cells → unipotent stem cells → then type cells. causing trophic processes, molecular bonds processes and mental processes (Figure 1 and Figure 2) [1-6]. Furthermore the formed stability of an open thermodynamic system of a born organism after first breath has not prepared yet to share of Basic internal energy (E_{bas}) among different stem cells, that compel an organism to obtain energy for neurons' cells from environment through different Receptors of an organism's transmitters to different brain's places of basic stem cells [neurons] [7, 8]. Only mutual interactions via exchanges with energy and substances /according Prigogine theorem/ between this birth organism and its surrounding medium promote to share right Basic internal energy (E_{bas}) among them learning different functions of the birth organism in Babyhood age through learning memory manager of Birth organism's Software (see below Part 2.2) [7-10]. Thus stability of open non equilibrium thermodynamic system of an organism occurs through non linear development of an organism according famous Glansdorff and Prigogine theory.

There is the Glansdorff and Prigogine Theory:

They divided the local production of entropy into two datasets and explained the stability in the non-linear development of the open thermodynamic system of the human organism with the following formula:

$$d\beta / dt = d/dt \left(\sum_k J_k X_k\right) = \sum_k J_k dX_k/dt + \sum_k X_k dJ_k/dt$$

(β – entropy; t – time; X – force; and J - stream).

The Stability of the System is Displayed by the following Formula:

$d\beta/dt = \sum_k dJ_k dX_k/dt = d_x\beta/dt$, if $dJ_k/dt = 0$. Hence, the stability of the thermodynamic system defines force (X). Thus, the minimization of gain increased entropy is: $d_x\beta/dt \leq 0$, i.e. a negative fluctuation in entropy. This means that the thermodynamic system is far from equilibrium, although the sign of equality defines its stationary state.

Stability of the stationary state arises if $d_x\beta = \sum_k dJ_k dX_k /dt > 0$ (or If $dJ_k/dt = 0$), corresponding to positive fluctuations in entropy ($+\Delta_x\beta$). However, positive fluctuations in entropy ($d_x\beta > 0$) rapidly disappear in the case of the thermodynamic system being in a stationary state due to the principle of minimization of gain in entropy and so the thermodynamic system must return to its initial state. However, negative fluctuations in entropy ($d_x\beta < 0$) ($-\Delta_x\beta$) arise, which transite the thermodynamic system to a new stationary state of decreased entropy $\Delta Sx < 0$ (ΔS_x is the gain in entropy). Thus, Glansdorff and Prigogine's theory explains the mechanism of the maintenance of internal energy stability of development an open non equilibrium of the human organism's thermodynamic system through its life **as an open non equilibrim non-linear** of the normal Stationary State of themodynamic system of an organism. The organism's metabolism develops via fluctuations in the local production of positive and negative entropy ($\Delta x\beta > 0$ and $\Delta x\beta < 0$) from its birth right up and down to its death (Figure 3) [1, 3, 4, 7-10].

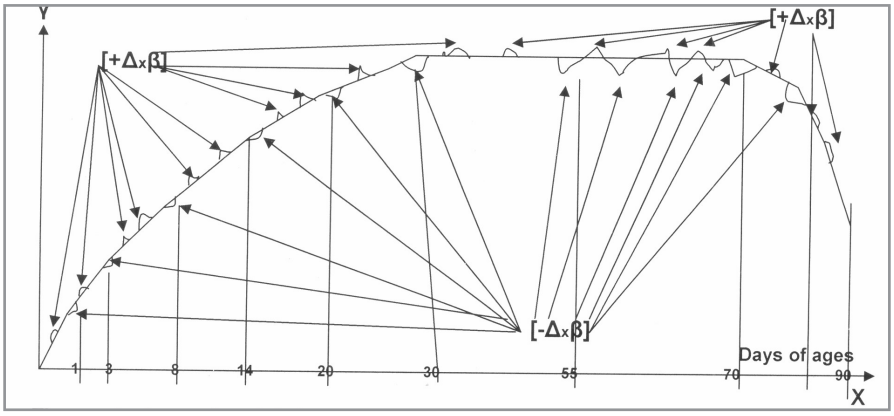


Figure 3: The changes of metabolism during a life of an organism.

The organism's ages: from 0 till 3years – babyhood; from 3 till 14 years - young age; from 14 till 20 - juvenile age; from 20 till 30 years - middle age; from 30 till 55 years - full age; from 55 till 70 years – elderly age; after 70 years - old age.

2. Development Mental Activities During Life of an open Non Equilibrium Non Linear Thermodynamic System of an Organism

Taking into account the changes of metabolism during the life of an organism, it occurs the interactions between development of an open non equilibrium non linear thermodinamic system of a human organism's mental activities and its Environment. Thus the aging of an organism occurs from the birth of an organism into babyhood (0 till 3 years) then into young age (3 till 14 years) then into juvenile age (14 till 20 years) then into middle age (20 till 30 years) then into full age (30 till 55 years) then into elderly age (55 till 70 years) then into old age (after 70 years) leading to death of an organism (Figure 3) [1, 3, 7]. Hence the mechanism of the aging of an organism is supplied by energy of inherited Basic Internal Energy (E_{bas}) of the organism's manager of Software (see below) which is engaged by Hardware of organism's metabolism development via fluctuations in the production of positive and negative entropy ($\Delta x\beta > 0$ and $\Delta x\beta < 0$) from its birth showing Graph beginning of the line up in young ages and finishing of the line down right in old age to its death (see above Clandsdorff and Prigogine theory) (Figure 3) [1-3, 9, 10]. Just the changed metabolism in cytoplasms of the neurons' cells creates the identical some changes of the cellular chemical potential (μ_{neur}) in Software of the semiconductor features of cytoplasms' of the neurons' cells causing corresponding changes in memory of mental activities Software of an open non equilibrium non linear thermodinamic system of a human organism.

Thus the each neuron's wall and neuron's wall receptors are provided as by the different capacitors as well as by different variable capacitors [1, 3, 4]. Hence neurons' walls are possessed by capacitors which produce resonance waves of different characteristics creating connections between all neurons of human brain's Software.

Basic Internal Energy (E_{bas}) of different neurons of Central Nervous System is distributed energy among Trophic Processes (E_{bas}TroPr), Molecular Bonds Processes (E_{bas}MolBondsPr) and Mental-Soul Processes Software (E_{bas}MenPr Software). Neuron's cell contains cellular nucleus having double helix of nucleic acids DNA which double-stranded molecules has chemical potential (μ_{nucl}). Thus DNA double helix has electrical charge (q_{DNA}). Therefore this structure can be identified as inductor for its inductive feature (L). Thus neuron's cells' nuclei showing inductive features interacts with many capacitors on cellular walls showing capacitive features which completed energy forms oscyllating electromagnetic waves. The oscillating electromagnetic waves with the semiconductor features of the neurons' cells cytoplasms are supplied as by bioelectric energy through peripheral Receptors with nerves /as transmitters/ as well as by energy from Basic Internal Energy (E_{bas}) and external energy from metabolic processes of substances delivered from environment through gastrointestinal tract (Figure 2). Thus the energy of inductor forms Inductance (L) feature and energy of capacitors forms Capacitance (C) feature. Besides cytoplasms of neuron-cells possess of two inverse features electric conductance and electric resistance because of containing as ions and ionic molecules as well as dielectric molecules [some proteins and even some non-electroconductive hydrofobic lipids etc.] which interactions form semiconductance feature of neurons' cytoplasms. Thus interaction between neurons three features Inductance (L) with Capacitance (C) and Resistance (R) forms Oscillating Circuit (LC) of neurons' cells how Software of the neurons functions (Figure 4) [1, 3, 4]. The neurons' activities are exerted electric Current (I) through electric charge (qDNA) of neuron nucleus Inductor (L) that creates magnetic field with energy (E_L) which is the electromotive force (emf) of Inductor:

$$E_L = \frac{LI^2}{2}$$

The electric Current (I) through electric charge ($q_{capacitor}$) of neuron wall's Capacitor (C) creates electric tension of voltage (U) with Capacitance energy (E_c) which is the electromotive force (emf) of Capacitor:

$$E_C = \frac{CU^2}{2}$$

There are occurred to exchange ratio electromotive forces of Capacitance (emf_C) and electromotive force of Induction (emf_L) in following sequences of Oscillating Circuit: Increased current charge in capacitors results in stream for discharge of capacitors and increased magnetic field of Inductor. However magnetic flux creates emf in direction contrary to electric current in Inductor that cause resistance via slowdown discharge for increased current charge of capacitors in electric circuit. Therefore the capacitors are discharged through certain time (t_1) which is determined by inductance of inductor and total capacitance of capacitors via formula:

$$t_1 = \frac{\pi\sqrt{LC}}{2}$$

Thus electric energy of capacitors transits into magnetic energy of inductor after t_1 time. Then it is occurred decreased magnetc flux in inductor from maximum to zero because reduced magnetic flux causes change magnetic emf and increase capacitor emf and charge of capacitors from zero to maximum which occurs during t_2 time. Further it is occurred the opposite direction during t_3 time and so on t_4, t_5 etc times causing oscillation. Just all times are equal: $t_1 = t_2 = t_3 = t_4$ and so on through binary calculations (math.). Thus magnetic energy of inductor (L) transits into electric energy of capacitors (C) and then vice-versa: from electric energy of capacitors (C) into magnetic energy of inductor (L). Each two intervals [t_1 and t_2; t_3 and t_4; and so on] will put together two halves of one complete oscillation in oscillating circuit. Besides it is occurred the change direction of electric stream and magnetic streams after each time interval (t_1, t_2 etc) which create changes positive and negative charges on membranes of capacitors (Figure 4) [1, 3]. Thus the stream of electic energy is coupled with stream of magnetic energy creating electromagnetic energy (CL) which have following parameters.

The period oscillation (T): $T = 2\pi\sqrt{LC}$

The frequency of oscillations (f): $$f = 1 / T = \frac{1}{2\pi\sqrt{LC}}$$

The resistance in Oscillating Circuit (R_e): (R_{L+C} - total resistor) $$R_e = \frac{L}{CR_{L+C}}$$

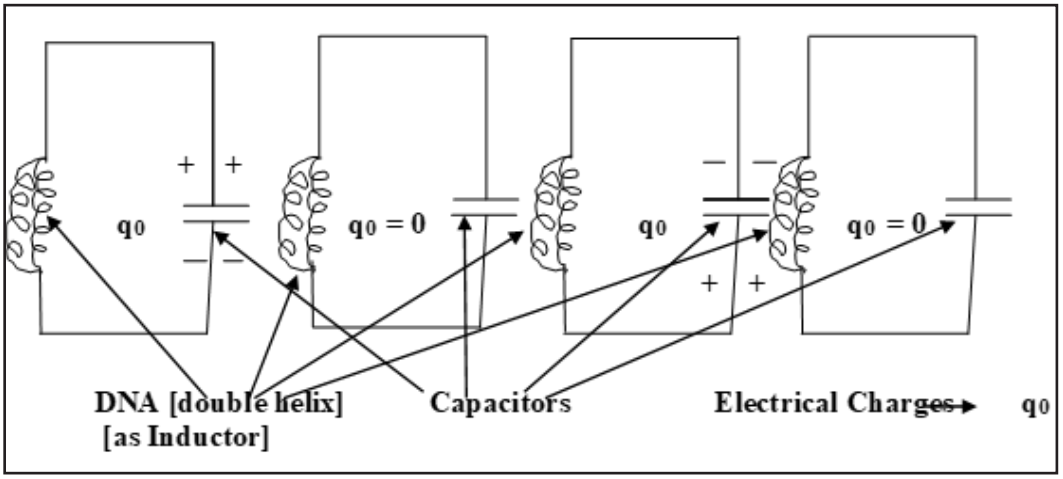


Figure 4: The neuron-cell's oscillating circuit of Central Nervous System.

Just the parameters of period oscillations, frequency of oscillations and resistance in Oscillating Circuit of different neurons determine as different common electromagnetic waves of each neuron. Also being supplied by energy from different Receptors (via electric sygnals), single each neuron's Oscillating Circuit creates different electromagnetic waves which have different length waves with different frequencies and different forces as voltages. Thus the energy from Basic Internal Energy (E_{bas}) of Basic stem cells [neurons] in the different areas of the brain is transformed into oscillating energy of electromagnetic waves of corresponding wave-lengths creating by Oscillating Circuits of corresponding neurons. Contrariwise the different corresponding Receptors of the different organs of an organism obtain the electrical energy of the different wavelengths [light energy, sound energy, mechanical energy, painful energy etc.] from Environment which are transmitted through nerves Transmitters to the corresponding neurons-cells' Oscillating Circuits of the corresponding areas of the brain. The corresponding neurons-cells' Oscillating Circuits transform the received electrical energy into electromagnetic energy of the corresponding wavelengths of different quanta energy for converting this energy into either Trophic Processes (E_{bas}TroPr) energy, or Molecular Bonds Processes (E_{bas}MolBondsPr) enargy, or Mental-Soul Processes Software (EbasMenPr Software) energy (see below) [1, 3, 4]. Besides the Oscillating Circuits of energy (LC) are exchanged by corresponding neurons reciprocally which bioelectrical signals are obtained by different neurons in Central Nervous System from the corresponding Transmitters of the corresponding Receptors of the nerve to visceral organs and skin of a human organism which is shared into Receptors of the Locomotion System, Lung Mechanoreceptors in Ventilation, Receptors of regulation of the Heartbeat, Pain Receptors, Vision in the Eye through Special Receptors, Hearing in the Ears through Special Receptors, Sensory Receptors Contribute to Proprioception and the other Receptors. Just the completed bioelectric signal from these Recepters is exerted as by environmental influence as well as by people communications in human community. Also these electrical signals from the corresponding Transmitters and Receptors of the nerves form energy Molecular Bonds (E_{bas}MolBonds) from Basic Internal Energy which exert cellular proliferative processes via cellular cycle and induce cells' development through sequence of stem cells to type cells [Basic stem cells → Totipotent stem cells → Pluripotent stem cells → Multipotent stem cells → Oligopotent stem cells → Unipotent stem cells → type cells]. The obtained from receptors' outer electrical charges (q_{out}) by receptivity of neurons' Basic Internal Energy (E_{bas}), it is occurred transformed different quanta energy causing by oscillating circuit's electromagnetic waves of interactions between different neuron-cells in different places of brain in Central Nervous System. These exchanges with electromagnetic waves of different quanta energy between some different neurons form spatial notion about surroundings of environment and even about the changes in motion of environment. These exchanges with electromagnetic waves of different quanta energy between some different neurons create common electromagnetic wave of certain rate quantum energy that involves the semiconductive properties of cytoplasms in these different neurons which carry out two functions simultaneously as function of half resistor as well as function of half conductor of electric current for forming memory function into semiconductive function of cytoplasms. Also the exchanges with spatial notion about surroundings and with memories between different human persons learn each human organism to compare and even to think.

All these processes are supported by Basic Internal Energy (E_{bas}) of all neurons of brain in Central Nervous System which influence on Ostillating Circuits of all neurons of brain in Central Nervous System especially on inductors of all neurons, i.e. DNA of neurons, and on semiconductive features of all neurons' cytoplasms [1, 3, 4]. All these processes use energy Mental-Soul Processes (E_{bas}MenPr) from Basic Internal Energy (E_{bas}) creating human mental activity of thoughts, comparisons, jokes, fantasy, inventions, discovery and ever trickery and so on [1, 3, 4, 6, 7]. Also it is occurred corresponding generating and then changes memory, thoughts, comparisons, jokes, fantasy, inventions, discoveries etc during life of an open non equilibrium non linear thermodynamic systems of human organisms [1, 3].

Just, on the one hand, the mechanism development of maintenance stability Internal Energy of non linear thermodynamic

systems causing disordered cells via creating change fluctuations of an entropy via transition from normal Stationary State into pathologic Quasi-stationary State which is characterized by shift positive fluctuations in entropy ($+\Delta_x\beta$) with transiting shift into strong negative fluctuations in entropy ($-\Delta_x\beta$) that results in shift of transition normal graph line into pathologic other directed line of graph positive fluctuations in entropy ($+\Delta_x\beta$) according Glansdorff and Prigogine theory (Figure 5). Thus the eminent Glansdorff and Prigogine theory elucidates mechanism transition normal neurons activity into pathologic neuron activities (Figure 5) [1, 2].

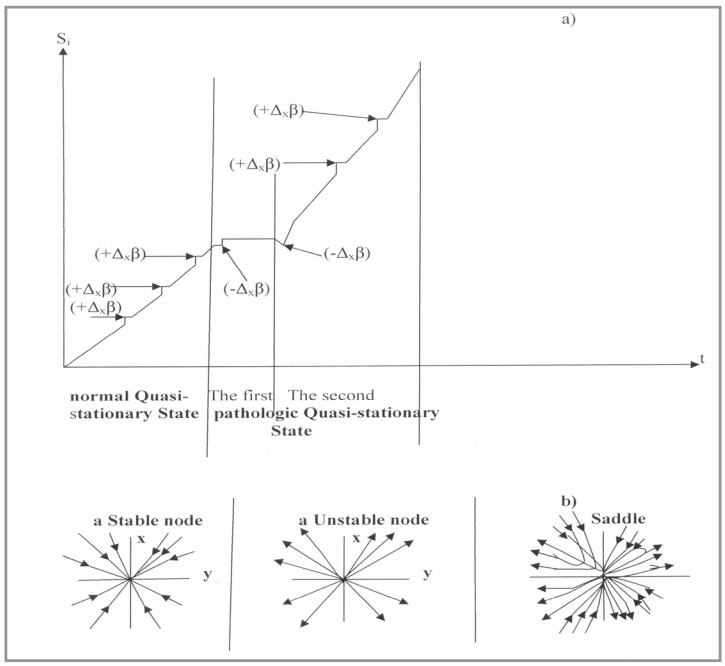
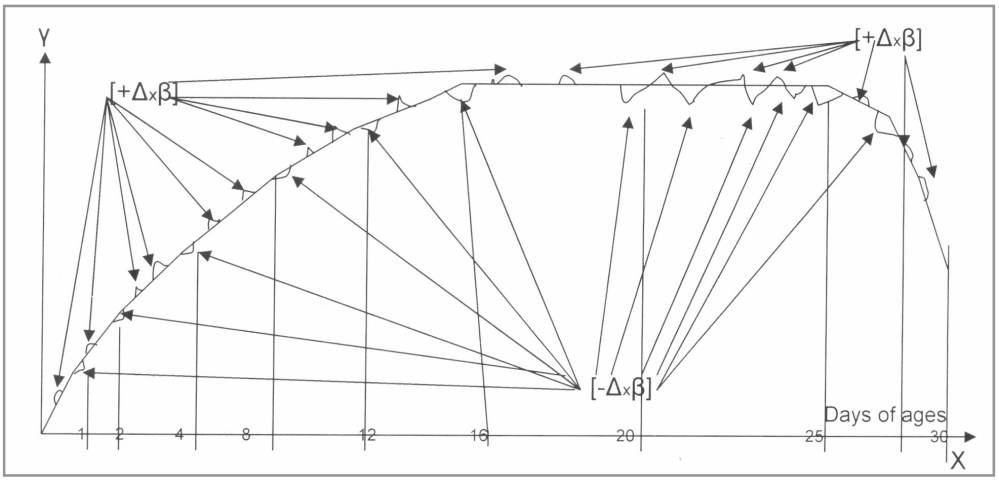


Figure 5: Change fluctuations of an entropy at transition from normal Quasi-stationary State into pathologic Quasi-stationary State.

However, on the other hand, the mechanism development of maintenance normal stability Internal Energy of non linear thermodynamic systems of cells via cells‘ lifetimes is characterized by positive fluctuations in entropy ($+\Delta_x\beta$) with temporary shift into negative fluctuations in entropy ($-\Delta_x\beta$) according Glansdorff and Prigogine theory (Figure 6) [1, 3-6, 8]. Hence the mechanism development of maintenance normal stability Internal Energy of non linear thermodynamic systems of cells via cells‘ lifetimes are characterized by fluctuations normal positive fluctuations in entropy ($+\Delta_x\beta$) into temporary negative fluctuations in entropy ($-\Delta_x\beta$) that transiting graph into new state of entropy ($+\Delta_x\beta$), which is meant that the normal stability Internal Energy of cells‘ lifetimes are characterized develipment cells during their lifetimes according to famous Glansdorff and Prigogine theory (Figure 6) [1, 3-6, 8].



Cellular ages: from 0 till 16 – the young age; from 16 till 25 - the middle age; from 25 till 30 - the old age; after 30 – cell death.

Figure 6: The changes of cell metabolism during a life of a cell.

2.1 The Role of the Organism's Processes Creating Stable Internal Energy of an Organism Exerts the Mechanisms of Mental Activities for Cognitive Functions, thinks, Memory and the other Mental Activities of a Human Organisms

The open non equilibrium non linear thermodynamic system of human organism is subjected to first law of thermpdynamics: $H = U + W_{int} + W_{ext}$ [H – Enthalpy, U – Internal Energy of an organism, W_{int} – Internal Works of organism, W_{ext} – External Works of an organism]. The energy of Basic Internal Energy (E_{bas}) with surrounding feeding energy for metabolic processes support stability Internal Energy (U) of an organism's open thermodynamic system and stability Internal Energy (U) of open thermodynamic systems of its cells forming balance anabolic processes and catabolic prosesses (Figure 2).

The stability Internar Energy (U) of open thermodynamic systems both an organism and its cells are supported by Basic Internal Energy (E_{bas}) in Neurons' Basic stem cells which form balance anabolic biosynthetic processes and catabolic oxidative processes in an organisn and in each cell of an organism. The normal quantities of both 8-dihydroguanosine (8-oxo-Guo), 8-hydroxy-2-deoxyguanosine (8-oxo-2G) and brain erythropoietin (EPO) was found in healthy cerebrospinal fluid as well as very small quantity in urine [2, 11-19]. It is meant that normal quality of 8-dihydroguanosine (8-oxo-Guo) and 8-hydroxy-2-deoxyguanosine (8-oxo-2G) are the marks of catabolic oxidative processes, and normal quality of brain erythropoietin (EPO) is the mark of anabolic biosynthetic processes. Therefore the balance anabolic biosynthetic processes and catabolic oxidative processes reflects balance catabolic oxidative processes of concentrations both 8-dihydroguanosine (8-oxo-Guo) with 8-hydroxy-2-deoxyguanosine (8-oxo-2G) and anabolic biosynthetic processes of concentration erythropoietin (EPO) as in the cerebrospinal fluid as well as in neurons' cytoplasms' which create stability of Intertnal Energy (U) as in the normal neurons' cells as well as in all cells of an organism [2, 11-19]. Just the normal concentrations of substances in neurons cells' cytoplasms are depended on the concentration of substances in their external medium, i.e. in cerebrospinal fluid. Hence dependance between concentrations of substances in neurons cells' cytoplasms and concentration of substances in cerebrospinal fluid is created by interactions between internal cytoplasms' chemical potentials (μ_{cytopl}) and external cerebrospinal fluid's chemical potential ($\mu_{cerebflu}$) according famous Theorell formula.

There is the Theorell's Formula: $dn/dt = -UcA\, d\mu/dx$ [dn /dt – quantity of molecules diffusing in a unit of time, U – substances mobility, c – substance concentration, A – membrane area, μ - chemical potential, x – distance of the molecules from the membrane].

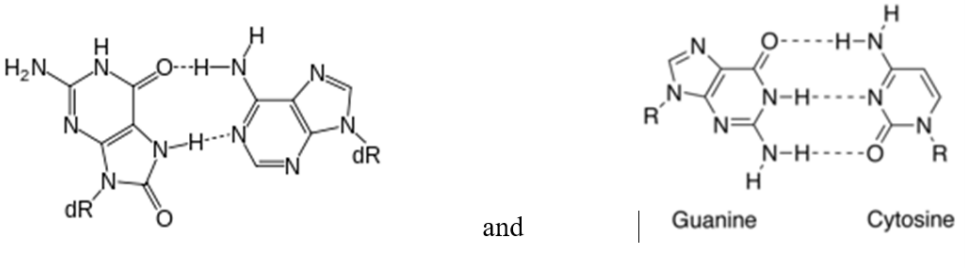
The interactions between neurons cytoplasms' chemical potentials (μ_{cytopl}) and cerebrospinal fluid's chemical potential ($\mu_{cerebflu}$) determine electroconductive feature of the neurons cells' cytoplasms. Therefore the normal balance of catabolic oxidative processes 8-dihydroguanosine (8-oxo-Guo), 8-hydroxy-2-deoxyguanosine (8-oxo-2G) and anabolic biosynthetic processes of erythropoietin (EPO) determines the normal concentrations both 8-dihydroguanosine (8-oxo-Guo), 8-hydroxy-2-deoxyguanosine (8-oxo-2G) and brain erythropoietin (EPO) that creates the neurons cytoplasms' chemical potentials (μ_{cytopl}) forming the semiconductive feature of the normal neurons' cytoplasms. Thus the normal semiconductive feature of the neurons' cytoplasms are supported by inteactions between inner cytoplasm's chemical potential (μ_{inchem}) of neuron's cytoplasm and outer chemical potential (μoutchem) of cerebrospinal fluid. It is meant the following interactions that Oscillating Circuits of neusons' nuclei are used inner inherited energy of Basic Internal Energy (E_{bac}) which is interacted with semiconductive feature of the neurons' cytoplasms being supporting with outer energy through Transmitters /Receptors with nerves/ from Environment. Thus the energy of Mental-Soul Processes Software (E_{bas}MenPr Software) is arising the normal neurons' mental activities of memory, thoughts, cognition, comparisons, jokes, fantasy, inventions, discoveries etc.

3. The Mechanisms of Development Mental Activity During Organism's Lifetime from Birth to Death

The dependence of mental activities from development of an open thermodynamic system of an organism is occurred through learning Softwares of cytoplasm's semiconductive features together with Oscillating Circuit of brain's neurons' nuclei during lifetime from birth to death of an organism. There are shared both Basic Internal Energy [E_{bas}] and External Energy from foods [E_{food}] via exerting metabolic processes which promote mechanisms of learning Software of cytoplasm's semiconductive properties through fluctuating electromagnetic waves of Oscillating Circuit in neurons's nuclei that causes arising both mental memory and cognitive capabilities (Figure 2) [1, 3]. Just both mental memory and cognitive capabilities exert development of all functions of an organism via linking up Hardwares, i.e. Internal Energy (U) with Internal Works (W_{int}) and External Works (W_{ext}) of an organism. Thus using total 100% Basic Internal Energy (E_{bas}), the child from birth organism into babyhood (0 till 3 years) learns whole surrounding world using all Receptors of nerves which share received the corresponding bioelectric signals from the corresponding Receptors through nerves as Transmitters into the corresponding area of a brain [3, 7-9]. Thus the child in babyhood age (0 till 3 years) learns the corresponding Softwares of cytoplasm's semiconductive features for maintaining stability of balance catabolic oxidative processes of normal concentrations both 8-dihydroguanosine (8-oxo-Guo), 8-hydroxy-2-deoxyguanosine (8-oxo-2G) and anabolic biosynthesis processes of normal concentration erythropoietin (EPO). The forming electromagnetic waves of Oscillating Circuit with semiconductive function in the corresponding places of brain's neurons share electively to learn more of Lung Mechanoreceptors in Ventilation in the beginning of the bioelectric signals and then to learn more of Receptors of the Locomotion System for walking (Figure 3 and Figure 6). The obtaining almost 85% quantity Basic Internal Energy (E_{bas}) for intensive metabolic processes, the child of young age (3 till 14 years) learns more electively bioelectric signals of Vision in the Eyes through Special Receptors, Hearing in the Ears Through Special Receptors and Sensory Receptors Contribute to Proprioception from Software development both mental memory and cognitive capabilities for obtaining initial school knowledges (Figure 3 and Figure 6) [3, 7-9]. Then there are formed the men of juvenile age (14 till 20 years) obtaining 75% quantity energy from Basic Internal Energy (E_{bas}) whose mental activities are learnt by distributing interests among different spheres of human activities [3, 7-9]. Just obtaining

sufficient quantity energy of Basic Internal Energy (E_{bas}) for mental activity with intensive metabolic processes in the age from birth to 20 years, the normal fluctuations balance anabolic biosyntetic process with Erythropoietin (EPO) & catabolic oxidative process with 8-hydroxy-2-deoxyguanosine (8-oxo-2G) is caused ascending graph of mental activity according to Glandsdorff and Prigogine theory (Figure 6 and Figure 7). Then it's begun middle age (20 till 40 years) who learn further electively more bioelectric signals of Vision in the Eyes through Special Receptors, Hearing in the Ears through Special Receptors and Sensory Receptors Contribute to Proprioception for further development both mental memory and cognitive capabilities for obtaining whole school and institute knowledges and either academic knowledges or professional knowledges (Figure 6) [3, 7-9]. Just using energy of inherited Basic Internal Energy [E_{bas}] in middle age, the mental activities with organism's metabolism develops the normal fluctuations balance anabolic biosyntetic process with Erythropoietin (EPO) & catabolic oxidative process with 8-hydroxy-2-deoxyguanosine (8-oxo-2G) that is caused ascending graph of mental activity according to Glandsdorff and Prigogine theory (Figure 6 and Figure 7). Then men of full age (39 till 55 years) use energy from some decreased Basic Internal Energy (E_{bas}) with External Energy of foods (E_{food}) and through Sensory Receptors Contribute to Proprioception for Software development both mental memory and cognitive capabilities with development metabolic processes [3, 7-9]. Further elderly age (55 till 70 years) is occurred by normal balance anabolic biosyntetic process with Erythropoietin (EPO) & catabolic oxidative process with 8-hydroxy-2-deoxyguanosine (8-oxo-2G) which shows horizontal graph of metabolic processes in these years corresponding to Glandsdorff and Prigogine theory (Figure 6 and Figure 7) [3, 7-9]. Therefore the mental activities of both full and elderly ages (40 till 70 years) give possibility to use the memory and cognitive capability for learning remembering the passed events in comparison with the current events [3, 7-9]. At last, it is occurred old men of old age (after 70 years) whose exhausted Basic Internal Energy (E_{bas}) does not ensure the support of mental activities with unsufficient metabolic processes of the fluctuations normal balance anabolic biosyntetic process with Erythropoietin (EPO) & catabolic oxidative process with 8-hydroxy-2-deoxyguanosine (8-oxo-2G) that shows the movement of the graph line down corresponding to Glandsdorff and Prigogine theory (see above) (Figure 6 and Figure 7) [3, 7-9]. Also the men of old age (after 70 years) are subjected to some senile diseases how atherosclerosis, violating hearing and vision, forgetfullness as well as unsufficient defensive mechanisms against environmental influences and so on. That cause also some decreased metabolic processes and mental activities of an organism's memory and cognitive capability. Just the exhausted Basic Internal Energy (E_{bas}) and violations of metabolic processes with decreased mental activities lead gradually to death of the organism.

8-dihydroguanosine [8-oxo-Guo] of oxidative products.



The brain erythropoietin (EPO) is Glykoprotein-Hormon for stimulation of erythropoietic processes.

Erythropoietin (EPO) for biosynthetic products

Figure 7: Balance catabolic oxidative processes & anabolic biosynthetic processes

The Violation of Development Mental Activity Via Bipolar Disorder (BD) of an open Non Equilibrium Non Linear Thermodynamic System of an Organism

1. The Mechanisms of the Worsening of Development Mental Activity Causing Mental Diseases of an open Non Equilibrium Non Linear Thermodynamic System of an Organism

The Glansdorff and Prigogine theory (see above) shows normal alternations in the fluctuation of positive production entropy ($\Delta x\beta > 0$) and temporarily of negative production entropy ($\Delta x\beta < 0$) causing mechanism of development through the transition an open thermodynamic system of an organism from one state of normal Stationary State into other state of normal Stationary State, i.e. mechanusm of non linear normal development of an open non equilibrium non linear thermodynamic system of an organisn through its lifetime which is shown in graph (Figure 3) [3, 9]. The normal state of fluctuations in positive production of entropy ($\Delta x\beta > 0$) and in negative production of entropy ($\Delta x\beta < 0$) cause stability of Stationary State of an open non equilibrium non linear thermodynamic systems both of an organism and cells of an organism which are shown with the stable Internal Energy (U) as an organism's thermodynamic system as well as cells' thermodynamic systems [3, 5, 6, 9]. The stable Internal Energy (U) of an organism's thermodynamic system and its cells' termodynamic systems are the marks of stable balance anabolic biosynthetic processes & catabolic oxidative processes which is supported by normal quantity of inherited energy from genetic Basic Internal Energy (E_{bas}) [3, 9, 10]. Besides mechanism stability of Internal Energy (U) of a normal open thermo-

dynamic system of an organism's cells are formed by stable balance anabolic biosynthetic processes & catabolic oxidative processes [3, 9, 10]. Hence it is meant that normal fluctuations balance anabolic biosyntetic process with Erythropoietin (EPO) & catabolic oxidative process with 8-hydroxy-2-deoxyguanosine (8-oxo-2G) are carried out the alternations sequentially into some increased anabolic biosyntetic process with Erythropoietin (EPO) and then into some increased catabolic oxidative process with 8-hydroxy-2-deoxyguanosine (8-oxo-2G) resulting in maintenance stability Internal Energy (U) of an open non equilibrium non linear thermodynamic systems of an organism's cells including neurons (Figure 6 and Figure 7) [1, 3-6, 8-10]. Thus being supported by normal quantity inherited energy from genetic Basic Internal Energy (E_{bas}), the such normal fluctuations balance anabolic biosyntetic process with Erythropoietin (EPO) & catabolic oxidative process with 8-hydroxy-2-deoxyguanosine (8-oxo-2G) is the driving mechanism of development thermodynamic systems of cells including neurons through their lifetimes (Figure 6 and Figure 7) [1, 3-6, 8-10]. Therefore the normal alternations in the fluctuations of balance in positive production entropy ($\Delta x\beta > 0$) and in temporary negative production entropy ($\Delta x\beta < 0$) cause development of neurons cells' thermodynamic systems through their lifetime which are corresponded to alternations of normal fluctuations balance anabolic biosyntetic process with Erythropoietin (EPO) & catabolic oxidative process with 8-hydroxy-2-deoxyguanosine (8-oxo-2G). The matter is that normal fluctuations balance anabolic biosyntetic process with Erythropoietin (EPO) & catabolic oxidative process with 8-hydroxy-2-deoxyguanosine (8-oxo-2G) is supported by normal quantity inherited energy from genetic Basic Internal Energy (E_{bas}) during the lifetimes of cells via determining of development in their lifetimes [1, 3, 7-10]. Also such normal development thermodynamic systems both an organism and cells of an organism through their lifetimes don't change stability of Internal Energy (U) of an open thermodynamic systems both of an organism and cells of an organism according Prigogine theorem as well as Glansdorff and Prigogine theory (see above) [3]. However the stability Internal Energy (U) of an organism can be violated as by insufficient inherited from parents genetic energyof Basic Internal Energy (E_{bas}) as well as by power of strong influentions of negative energy from environment (Figure 2) [1, 3]. The Basic Internal Energy (E_{bas}) supply with parents inherited genetic energy of all live processes of an organism which energy is shared among stem cells for cellular cycles of cells' development [1, 3, 7-10]. If the inherited genetic energy of Basic Internal Energy (E_{bas}) is distributed through either insufficient energy of Basic Internal Energy for Molecular Bonds Processes (E_{bas}MolBondsPr), or unsufficient energy of Basic Internal Energy for Trophic Processes (E_{bas}TroPr), or unsufficient energy of Basic Internal Energy for Mental-Soul Processes (E_{bas}MenPr) that results in the violating stability of corresponding Internal Energy (U) an organism [1, 3, 7-10]. Sometimes it is come about that balance fluctuations in the positive production of entropy ($\Delta x\beta > 0$) and then in the negative production of entropy ($\Delta x\beta < 0$) that transits through considerably increased the negative production of entropy ($\Delta x\beta < 0$) leading to disbalance of fluctuations in the positive production of entropy ($\Delta x\beta > 0$) and in the negative production of entropy ($\Delta x\beta < 0$). Hence the pathologic alternations in the fluctuation of positive production entropy ($\Delta x\beta > 0$) and in negative production entropy ($\Delta x\beta < 0$) cause the transition from normal Stationary State of a normal open thermodynamic system of an organism's neurons into pathologic Quasi-stationary State of an ill open thermodynamic system of an organism's neurons. This pathologic disbalance alternations the fluctuation of positive production entropy ($\Delta x\beta > 0$) and negative production entropy ($\Delta x\beta < 0$) induces the transition from normal Stationary State into pathologic Quasistationary State of an ill open thermodynamic system of an organism's neurons (Figure 5). Therefore mechanism stability of Internal Energy of an ill open thermodynamic system of neurons cells are formed by disbalance anabolic biosynthetic processes & catabolic oxidative processes. It's meant that disbalance of considerably increased anabolic biosynthetic process with increased quantity Erythropoietin (EPO) & considerablx increased catabolic oxidative process with increased quantity 8-hydroxy-2-deoxyguanosine (8-oxo-2G) reflects either increased quantity of both 8-dihydroguanosine (8-oxo-Guo) and 8-hydroxy-2-deoxyguanosine (8-oxo-2G) or increased quantity of brain erythropoietin (EPO) creating Bipolar Disorder (BD) of pathologic Internal Energy (U) of Quasi-stationary State of pathologic neurons cells (Figure 5) [2, 3, 11-19]. Hence Glansdorff and Prigogine theory (see above) explains pathologic transiting in fluctuations positive production of entropy ($\Delta x\beta > 0$) through increased negative production of entropy ($\Delta x\beta < 0$) that leads to the other pathologic positive production of entropy ($\Delta x\beta > 0$) resulting in transition pathologic state of disbalance anabolic biosynthetic processes & catabolic oxidative processes via shifting either into increased anabolic biosynthetic processes or into increased catabolic oxidative processes (Figure 5) [2, 3, 11-19]. Hence, on the one hand, the fluctuations of disbalance anabolic biosyntetic process with Erythropoietin (EPO) & catabolic oxidative process with 8-hydroxy-2-deoxyguanosine (8-oxo-2G) via shift into considerably increased catabolic oxidative processes with 8-hydroxy-2-deoxyguanosine (8-oxo-2G) results in the considerably increased quantity of 8-hydroxy-2-deoxyguanosine (8-oxo-2G) in neurons cytoplasms causing electroconducting feature of some neurons' cytoplasms versus semiconductive feature. Also shift into considerably increased catabolic oxidative processes with 8-hydroxy-2-deoxyguanosine (8-oxo-2G) in neurons' cytoplasms oxidate DNA of Neurons' nuclei resulting in DNA demethylation that leads to violating of the Oscillating Circuit of neurons' nuclei [20-25]. Thus some neurons lose mental activity features forming bipolar disorder (BD) of neurons cellular metabolic processes that leads to the loss of the some mental activity in some neurons cells showing flows down of graph line mental activities in old age of an organism's metabolism (Figure 5). Also, on the other hand, it can be occurred that fluctuating disbalance anabolic biosyntetic process with Erythropoietin (EPO) & catabolic oxidative process with 8-hydroxy-2-deoxyguanosine (8-oxo-2G) via shift into considerably increased quantity of anabolic biosyntetic process with Erythropoietin (EPO) causing decreasing semiconductive feature of neurons' cytolasms because of the approaching their features nearer to dielectric feature of the neurons' cytoplasms that destruct mental functions of these neurons causing neurodegenerative diseases and amyotrophic lateral sclerosis of chronic progressive multiple sclerosis in elderly age of an organism (Figure 3, Figure 5) [26-39]. Thus these elderly age of bipolar disorder (BD) diseases of mental pathologic states are arisen due to the decreased quantity obtained energy from the Basic Internal Energy for Mental-Soul Processes (E_{bas}MenPr) activities that re-

sults in violated semiconductive feature of some neurons‘ cytoplasms leading to all of these changes of an elderly aged organisms because of the worsening of the bipolar disorder (BD) of memory activity of a human organism. Besides it can be occurred that the some Receptors‘ functions are weakened which are reflected on the corresponding neurons‘ cells causing in the corresponding places of a brain that leads to absent or insufficient of the corresponding bioelectric signals to the Oscillating Circuit from the corresponding neurons' cytoplasms resulting in complete bipolar disorder (BD) disease for the function of these neurons [40-50]. The loss of the function of these neurons releases the some energy of the Basic Internal Energy of Mental-Soul Processes (E_{bas}MenPr) which are redirected to the functions of other neurons by an organism’s mechanisms of the learning into the losed functions [40-50]. Thus these supplemental functions of the other neurons are made more strong. For example, the strong eye’s pressure by glaucoma disease destructs Vision in the Eyes‘ Special Eyes Receptors through destruction of the eyes‘ neurons that increases force of the Receptors of the Locomotion System and Sensory Receptors which increased force of corresponding Sensory Neurons‘ Cytoplasms of Oscillating Circuit mechanisms for increasing Sensitivity Functions of hands [40-50].

2. The Mechanism of Violation of Development Mental Activity Causing Pathologic Mental Activity of an open Non Equilibrium Non Linear Non Equilibrium Thermodynamic System of an Organism

According to Glansdorff and Prigogine’s theory fluctuations in entropy can promote transition the development of an open non equilibrium non linear Stationary State of tharmodynamic system of an organism into an open non equilibrium non linear pathologic Quasi-stationary pathologic State of thermodynamic system of an organism [1-5]. The pathologic fluctuations of positive fluctuations in the local production of entropy ($\Delta x\beta > 0$) through considerably increased negative fluctuations in the local production of entropy ($\Delta x\beta < 0$) shift into other positive fluctuations in the local production of entropy ($\Delta x\beta > 0$) that shows an elevating graph describing the Quasi-stationary state of an open non equilibrium non linear thermodynamic system of an organism, according to Clansdorff and Prigogine theory (Figure 5) [1-3]. What of the life events lead to the cardinal shift of Stationary State of the normal mental activities into Quasi-stationary pathologic State of an open non equilibrium non linear thermodynamic system of an organism? The insufficient inherited energy from Basic Internal Energy (E_{bas}) either of elderly organism, or injured organism, or weaked organosm after serious disease and the other reasons are the inner causes leading to bipolar disorders of an organism which become apparent as considerably weakended memory, violation of Cognitive function etc, i.e. forming Parkinson disease or Altzheimer disease [51-63]. Therefore the mental bipolar disorders are become apparent deeds which are differed from inner terrestrial surroundings. However there are mental diseases which don’t depend from only inner terrestrial surroundings. For example, hallucinations, unexpected aggressions connected with hallucinations, soliloquizer of lose one’s marbles and the other syndromes of schizophrenia ever suicidal action. The sources of the mechanisms of these syndromes are impossibly to explain using viewpoints of genetics or the other inner terrestrial reasons, but only outer Environmental surrounding reasons which affect mental processes through Receptors and nerves as transmitters of surrounding influences. Matter is that mental activities are forming permanently even during sleep how dreams which are occurred the following processes:

1. The certain specialized neurons obtained from certain Receptors through nerves how transmitters of bioelectrical signals from environment [55-68].
2. These bioelectrical signals are converted into electromagnetic waves in Oscillating Circuit of neurons‘ cells which are fixed in the memories of semiconductive features of cytoplasms of neurons cells.
3. The different memories of different neurons‘ cells are jointed of following: optical memories, auditive memories, locomotive memories, and the other memories. Thus these different memories use of interactions between electromagnetic waves of neurons‘ nuclei Oscillating Circuit for forming common mental thoughts and opinions. The violation either of Oscillation Circuit of neurons cells‘ nuclei or semiconguctive features of cytoplasms of different neurons cells create disordered either of Oscillation Circuit of neurons cells‘ nuclei or semiconguctive features of cytoplasms of neurons cells causing Bipolar Disorder (BD) of interactions between electromagnetic waves of neurons’ nuclei Oscillating Circuit for forming disordered common mental violating as thoughts as well as opinions and so on [66-68].

References

1. Ponizovskiy, M. R. (2022). Interactions Environmental Processes and development of Human organisms’ activity via mechanisms of Mental Activity from point of view of Biophysics, Biochemistry and Thermodynamics. Journal of Psychiatry Research Reviews & Reports, 4, 1-15.
2. Miskowiak, K. W., Simonsen, A. H., Meyer, M., Poulsen, H. E., Wilkan, M., et al. (2023). Cerebrospinal fluid erythropoietin, oxidative stress, and cognitive functions in patients with bipolar disorder and healthy control participants: A longitudinal case-control study. Journal of Psychiatric Research, 163, 240-246.
3. Ponizovskiy, M. R. (2023). Biophysical and Biochemical Mechanisms of Organism Development in Norm and Pathology. House Publishing Cambridge Scholars Publishing.
4. Ponisovskiy, M. R. (2011). Driving mechanisms of passive and active transport across cellular membranes as the mechanisms of cell metabolism and development as well as the mechanisms of cellular distance reaction on hormonal expression and the immune response. Critical Reviews in Eukaryotic Gene Expression, 21, 267-290.
5. Ponizovskiy, M. R. (2013). The Central Regulation of all Biophysical and Biochemical Processes as the Mechanism of Maintenance Stability of Internal Energy and Internal Medium both in a Human Organism and in cells of an Organism. Modern Chemistry & Application, 1, 1-2.
6. Ponizovskiy, M. R. (2013). The mechanisms maintenance stability Internal Energy and Internal Medium an organism in norm and in quasi-stationary pathologic states. Biochemistry & Physiology, 2, 1-11.
7. Ponizovskiy, M. R. (2017). Biophysical and biochemical mechanisms of forming and development a human eukaryotic organism from single pluripotent cell into multicellular Embrio and a living organism in norm. Journal of Genetics and DNA research, 1, 1-12.

8. Ponizovskiy, M. R. (2015). Biophysical and Biochemical Mechanisms of Interactions Cytoplasm Processes with Nucleus Processes and Mitochondria Processes in Norm and in Pathology. Journal of Molecular and Genetic Medicine, 9, 1-13.
9. Ponizovskiy, M. R. (2018). Genetic mechanisms an open thermodynamic system of an organism in norm and pathology. Journal of Molecular and Genetic Medicine, 12, 1-15.
10. Ponizovskiy, M. R. (2021). Driving mechanisms of different tissues cellular cycle in norm and in cancer pathology from the point of view of thermodynamics, biophysics and biochemistry. Journal of cancer research review & report, 3, 1-21.
11. Kim, Y., Vadodaria, K. C., Lenkei, Z., Kato, T., Gage, F. H., et al. (2019). Mitochondria, metabolism, and redox mechanisms in psychiatric disorders. Antioxidants & Redox Signaling, 31, 275-317.
12. Sargin, D., Friedrichs, H., El-Kordi, A., & Ehrenreich, H. (2010). Erythropoietin as neuroprotective and neuroregenerative treatment strategy: comprehensive overview of 12 years of preclinical and clinical research. Best Practice Research Clinical Anaesthesiology, 24, 573-594.
13. Miskowiak, K. W., Vinberg, M., Harmer, C. J., Ehrenreich, H., & Kessing, L. V. (2012). Erythropoietin: a candidate treatment for mood symptoms and memory dysfunction in depression. Psychopharmacology, 219, 687-698.
14. Tian, M., Liu, S., Liu, L., Zhang, E. K., Wang, H. W., et al. (2019). Correlations of the severity of diabetic retinopathy with EPO, Caspase-3 expression ans oxidative stress. European Review for Medical and Pharmacological Sciences, 23, 9707-9713.
15. Brettschneider, J., Widl, K., Ehrenreich, H., Riepe, M., & Tumani, H. (2006). Erythropoietin in the cerebrospinal-fluid in neurodegenerative diseases. Neuroscience Letters, 404, 347-351.
16.
17. Brettschneider, J., Widl, K., Schattauer, D., Ludolph, A. C., & Tumani, H. (2007). Cerebrospinal fluid Erythropoietin (EPO) in amyotrophic lateral sclerosis. Neuroscience Letters, 416, 257-260.
18. Janik, P., Kwiecinski, H., Sokolowska, B., & Niebroj-Dobosz, I. (2010). Erythropoietin concentration in serum and cerebrospinal fluid of patients with amyotrophic lateral sclerosis. Journal of Neural Transmission, 117, 343-347.
19. Widl, K., Brettschneider, J., Schattauer, D., Süssmuth, S., Huber, R., et al. (2007). Erythropoietin in cerebrospinal fluid: age-related reference values and relevance in neurological disease. Neurochemical Research, 32, 1163-1168.
20. Ehrenreich, H., Fischer, B., Norra, C., Schellenberger, F., Stender, N., et al. (2007). Exploring recombinant human erythropoietin in chronic progressive multiple sclerosis. Brain, 130, 2577-2588.
21. Massaad, C. A., & Klann, E. (2011). Reactive oxygen species in the regulation of synaptic plasticity and memory. Antioxidants & Redox Signaling, 14, 2013-2054.
22. Beckhauser, T. F., Francis-Oliveira, J., & De Pasquale, R. (2016). Reactive Oxygen Species: Physiological and Physiopathological Effects on Synaptic Plasticity. Journal of Experimental Neuroscience, 10, 23-48.
23. Zhou, X., Zhuang, Z., Wang, W., He, L., Wu, H., et al. (2016). OGG1 is essential in oxidative stress induced DNA demethylation. Cellular Signalling, 28, 1163-1171.
24. Ba, X., & Boldogh, I. (2018). 8-Oxoguanine DNA glycosylase 1. Beyond repair of the oxidatively modified base lesions. Redox Biology, 14, 669-678.
25. Seifermann, M., & Epe, B. (2017). Oxidatively generated base modifications in DNA: Not only carcinogenic risk factor but also regulatory mark?. Free Radical Biology and Medicine, 107, 258-265.
26. Bayraktar, G., & Kreutz, M. R. (2018). The Role of Activity-Dependent DNA Demethylation in the Adult Brain and in Neurological Disorders. Frontiers in Molecular Neuroscience, 11, 169.
27. Mead, R. J., Shan, N., Reiser, H. J., Marshall, F., & Shaw, P. J. (2023). Amyotrophic lateral sclerosis: a neurodegenerative disorder poised for successful therapeutic translation. Nature Reviews Drug Discovery, 22, 185-212.
28. Kato, S., Sumi-Akamaru, H., Fujimura, H., Sakoda, S., Kato, M., et al. (2001). Copper chaperone for superoxide dismutase co-aggregates with superoxide dismutase 1 (SOD1) in neuronal Lewy body-like hyaline inclusions: an immunohistochemical study on familial amyotrophic lateral sclerosis with SOD1 gene mutation. Acta Neuropathologica, 102, 233-238.
29. Ling, S.-C., Polymenidou, M., & Cleveland, D. W. (2013). Converging mechanisms in ALS and FTD: disrupted RNA and protein homeostasis. Neuron, 79, 416-438.
30. Tan, R. H., Ke, Y. D., Ittner, L. M., & Halliday, G. M. (2017). ALS/FTLD: experimental models and reality. Acta Neuropathologica, 133, 177-196.
31. Mackenzie, I. R. A., Bigio, E. H., Ince, P. G., Geser, F., Neumann, M., et al. (2007). Pathological TDP-43 distinguishes sporadic amyotrophic lateral sclerosis from amyotrophic lateral sclerosis with SOD1 mutations. Annals of Neurology, 61, 427-434.
32. Vance, C., Rogelj, B., Hortobágyi, T., De Vos, K. J., Nishimura, A. L., et al. (2009). Mutations in FUS, an RNA processing protein, cause familial amyotrophic lateral sclerosis type 6. Science, 323, 1208-1211.
33. van Rheenen, W., van der Spek, R. A. A., Bakker, M. K., van Vugt, J. J. F. A., Hop, P. J., et al. (2021). Common and rare variant association analyses in amyotrophic lateral sclerosis identify 15 risk loci with distinct genetic architectures and neuron-specific biology. Nature Genetics, 53, 1636-1648.
34. Shepheard, S. R., Parker, M. D., Cooper-Knock, J., Verber, N. S., Tuddenham, L., et al. (2021). Value of systematic genetic screening of patients with amyotrophic lateral sclerosis. Journal of Neurology, Neurosurgery & Psychiatry, 92, 510-518.
35. Zhang, S., Cooper-Knock, J., Weimer, A. K., Shi, M., Moll, T., et al. (2022). Genome-wide identification of the genetic basis of amyotrophic lateral sclerosis. Neuron, 110, 992-1008.
36. Barber, S. C., & Shaw, P. J. (2010). Oxidative stress in ALS: key role in motor neuron injury and therapeutic target. Free Radical Biology and Medicine, 48, 629-641.
37. Ferraiuolo, L., Kirby, J., Grierson, A. J., Sendtner, M., & Shaw, P. J. (2011). Molecular pathways of motor neuron injury in amyotrophic lateral sclerosis. Nature Reviews Neurology, 7, 616-630.
38. Goh, C. W., Lee, I. C., Sundaram, J. R., George, S. E.,

Yusoff, P., et al. (2018). Chronic oxidative stress promotes GADD34-mediated phosphorylation of the TAR DNA-binding protein TDP-43, a modification linked to neurodegeneration. Journal of Biological Chemistry, 293, 163-176.
39. Zuo, X., Zhou, J., Li, Y., Wu, K., Chen, Z., et al. (2021). TDP-43 aggregation induced by oxidative stress causes global mitochondrial imbalance in ALS. Nature Structural & Molecular Biology, 28, 132-142.
40. Jhanji, R., Behl, T., Sehgal, A., & Bungau, S. (2021). Mitochondrial dysfunction and traffic jams in amyotrophic lateral sclerosis. Mitochondrion, 58, 102-110.
41. Proske, U., & Gandevia, S. C. (2012). The proprioceptive senses; their roles in signaling body shape, body position and movement, and muscle force. Physiological Reviews, 92, 1665-1697.
42. Grillner, S., Cangiano, L., Hu, G., Thompson, R., Hill, R., et al. (2000). The intrinsic function of a motor system – from ion channels to networks and behavior. Brain Research, 886, 224-236.
43. Myslivecek, J., Farrar, V., & Valuskova, P. (2017). M (4) muscarinic receptors and locomotor activity regulation. Physiological Research, 66, 443-445.
44. Proske, U., Wise, A. K., & Gregory, J. E. (2000). The role of muscle receptors in detection of movements. Progress in Neurobiology, 60, 85-96.
45. Feldman, J., MacCrimmon, D. R., & Morrison, S. F. (2013). Pulmonary Stretch Receptors. In Neural Control of Respiratory and Cardiovascular Function (pp. 749-766).
46. Fahim, M. (2003). Cardiovascular sensory receptors and their regulatory mechanisms. Indian Journal of Pharmacology, 35, 124-146.
47. Woolf, C. J., & Thompson, S. W. N. (1991). The induction and maintenance of central sensitization is dependent on N-methyl-D-aspartic acid receptor activation; implications treatment of post-injury pain hypersensitivity states. Pain, 44, 293-299.
48. Schiller, P. H. (2010). Parallel information processing channels created in the retina. Proceedings of the National Academy of Sciences of the United States of America, 107, 17087-17094.
49. Westheimer, G. (2007). The ON-OFF dichotomy in visual processing: from receptors to perception. Progress in Retinal and Eye Research, 26, 636-648.
50. Brownell, W. E. (1997). How the ear work – Nature's solutions for listening. Volta Review, 99, 9-28.
51. Graham, C. E., Basappa, J., Turcan, S., & Vetter, D. E. (2011). The cochlear CRF signaling systems and their mechanisms of action in modulating cochlear sensitivity and protection against trauma. Molecular Neurobiology, 44, 383-406.
52. Day, J. J., & Sweatt, J. D. (2011). Epigenetic modifications in neurons are essential for formation and storage of behavioral memory. Neuropsychopharmacology, 36, 357-358.
53. Martínez-Arán, A., Vieta, E., Reinares, M., Colom, F., Torrent, C., et al. (2004). Cognitive function across manic or hypomanic, depressed, and euthymic states in bipolar disorder. American Journal of Psychiatry, 161, 262-270.
54. Robinson, L. J., & Ferrier, I. N. (2006). Evolution of cognitive impairment in bipolar disorder; a systematic review of cross-sectional evidence. Bipolar Disorders, 8, 103-116.
55. Kjærstad, H. L., Mistarz, N., Coello, K., Stanislaus, S., Melbye, S. A., et al. (2019). Aberrant cognition in newly diagnosed patients with bipolar disorder and their unaffected relatives. Psychological Medicine, 50, 1808-1819.
56. Bernard-Marissal, N., Chrast, R., & Schneider, B. L. (2018). Endoplasmic reticulum and mitochondria in diseases of motor and sensory neurons: a broken relationship?. Cell Death & Disease, 9, 333.
57. Montagnese, M., Leptourgos, P., Fernyhough, C., Waters, F., Larøi, F., et al. (2021). A Review of Multimodal Hallucinations: Categorization, Assessment, Theoretical Perspectives, and Clinical Recommendations. Schizophrenia Bulletin, 47, 237-248.
58. Ehrenreich, H., Hinze-Selch, D., Stawicki, S., Aust, C., Knolle-Veentjer, S., et al. (2007). Improvement of cognitive function in chronic schizophrenic patients by recombinant human erythropoietin. Molecular Psychiatry, 12, 206-220.
59. Császár, N., Kapócs, G., & Bókkon, I. (2019). A possible key role of vision in the development of schizophrenia. Reviews in the Neurosciences, 30, 359-379.