

Thermodynamic and Mathematical Model of Human Brain for Neurodegenerative Diseases; Alzheimer's Disease (AD) Parkinson's Disease (PD) and Amyotrophic Lateral Sclerosis (ALS)

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Abstract- This study examines neurodegenerative diseases, primarily Alzheimer's disease, but also Parkinson's and Amyotrophic Lateral Sclerosis (ALS), within the framework of thermodynamics, physics, and systems theory, going beyond classical biomedical approaches. Neurodegenerative processes are interpreted as decreased energy efficiency, increased entropy production, and disruption of phase coherence between neuronal networks. In this context, Alzheimer's disease is modeled as an accelerated loss of order process in an out-of-equilibrium open biological system. In classical thermodynamics, systems are classified as isolated, closed, and open systems. The human brain, when evaluated in terms of energy and matter exchange, clearly has the characteristics of an open system. It constantly takes glucose and oxygen from the environment, produces heat as a result of metabolic processes, and processes information. This approach is mathematically grounded using dissipative structure theory, the free energy principle, and oscillator synchronization models. Neurodegenerative diseases are among the most complex and multifaceted health problems faced by modern medicine. Alzheimer's disease (AD), Parkinson's disease (PD), and Amyotrophic Lateral Sclerosis (ALS) are clinically irreversible diseases characterized by progressive cellular destruction in the nervous system, but theoretically still not fully understood. In the current literature, these diseases are mostly addressed from a biochemical, genetic, and molecular biology perspective; protein aggregation, neurotransmitter deficiencies, and disruptions in cellular signaling pathways are presented as the basic explanatory mechanisms. However, these approaches are insufficient to explain why diseases progress at a certain rate, why they show different courses in different individuals, and why symptomatic improvements can be observed with certain environmental or sensory stimuli. At this point, it is necessary to consider the brain not only as a biochemical structure but also as a physical system that processes energy, generates waves, carries information, and is constantly interacting with its environment. The main motivation of this study is to reinterpret neurodegenerative diseases in the context of thermodynamics, statistical physics, and wave mechanics, and in particular to model Alzheimer's disease as a non-equilibrium, overt system disorder. This approach suggests that the disease is not only cellular destruction but also a process of loss of energy efficiency, increased entropy production, and disruption of neural resonance. [1], [2], [3].

Keywords: Alzheimer's Disease - AD; Parkinson's Disease - PD; Amyotrophic Lateral Sclerosis - ALS Disease; Neurodegenerative Diseases; Energy Transfer, Thermodynamics; Brain, Entropy; ELMAS' Theory of Thermodynamics; Medical Technique; Medical Engineering; Neuro-Engineering; Neuro-Science; Mathematics; Applied Mathematics; Advanced Engineering Mathematics; Advanced Applied Mathematics.

I. INTRODUCTION

Neurodegenerative diseases are among the most complex and multifaceted health problems faced by modern medicine. Alzheimer's disease (AD), Parkinson's disease (PD), and Amyotrophic Lateral Sclerosis (ALS) are clinically irreversible diseases

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disruptions in cellular signaling pathways are presented as the basic explanatory mechanisms. [1] However, these approaches are insufficient to explain why diseases progress at a certain rate, why they show different courses in different individuals, and why symptomatic improvements can be observed with certain environmental or sensory stimuli. At this point, it is necessary to consider the brain not only as a biochemical structure but also as a physical system that processes energy, generates waves, carries information, and is constantly interacting with its environment. [3]

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II. MATERIAL, METHOD, DISCUSSION

Defining the Brain as an Open Thermodynamic System: [3]

In classical thermodynamics, systems are classified as isolated, closed, and open systems. The human brain, when evaluated in terms of energy and matter exchange, clearly has the characteristics of an open system. It constantly takes glucose and oxygen from the environment, produces heat as a result of metabolic processes, and processes information. The general energy balance can be expressed as follows:

$$\frac{dE}{dt} = \dot{Q} + \dot{W} + \sum_i \mu_i N_i \dot{N}_i$$

Here:

E: Internal energy of the brain

Q̇: Heat exchange

Ẇ: Electrochemical work

μ_iN_i̇: Chemical potential contributions

In a healthy brain, this energy flow is regulated with high efficiency, while in neurodegenerative diseases, this balance is severely disrupted.

Entropy, Order and Neural Organization: [2]

Entropy, from a statistical physics perspective, is a measure of the number of microstates of a system:

$$S = k_B \ln \Omega$$

Here, Ω represents the number of microstates the system can access. In a healthy nervous system, microstates are functionally organized. In Alzheimer's disease, however, the loss of synaptic connections and the disintegration of neuronal networks lead to an uncontrolled increase in microstates.

Entropy balance for open systems:

$$\frac{dS}{dt} = \frac{dS_{\text{retim}}}{dt} + \frac{dS_{\text{aktis}}}{dt}$$

In Alzheimer's disease, internal entropy production (dS_{retim}/dt) increases significantly, and the system loses its capacity for regular information processing.

Energy Metabolism and Thermodynamic Efficiency: [3]

Although the brain constitutes only 2% of body weight, it consumes approximately 20% of the total energy. This indicates that the brain is a high-energy-density information machine.

Thermodynamic efficiency can be defined as follows:

$$\eta = \frac{W_{\text{faydali}}}{E_{\text{toplama}}}$$

In neurodegenerative diseases:

Mitochondrial dysfunction

Oxidative stress

Decreased ATP production

causes a decrease in the η value. This decrease leads to the system producing more heat and an increase in entropy.

Interpretation of the Brain as a Wave-Generating Physical System: [2]

Nerve cells produce not only chemical but also electrical and magnetic fields. Action potentials and synaptic transmissions are electromagnetic processes consistent with Maxwell's equations.

Brainwaves can be modeled as follows:

$$V(t) = \sum_n A_n \sin(2\pi f_n t + \phi_n)$$

In Alzheimer's disease, this spectral distribution is disrupted; a significant weakening is observed, particularly in the alpha and theta bands.

Importance of the Article: [1]

The theoretical framework presented in this article forms the basis for the detailed thermodynamic and mathematical modeling of Alzheimer's disease, which will be developed in the next chapter. Describing the brain as an open, non-equilibrium, and wave-based system is critical to understanding why music and acoustic frequencies can have a potential regulatory effect.

THERMODYNAMIC AND MATHEMATICAL MODELING OF ALZHEIMER'S DISEASE [1], [2], [3]

Definition of Alzheimer's Disease as a Non-Equilibrium System: [2]

In classical physics, systems in equilibrium are defined by macroscopic quantities that do not change over time. However, living systems, especially the human brain, are structures that operate in a non-equilibrium thermodynamic regime. In this context, Alzheimer's disease can be interpreted as the inability of the system to maintain its non-equilibrium state and the collapse of the dissipative structure.

According to Prigogine's non-equilibrium thermodynamics, living systems maintain their low-entropy structures thanks to the energy they receive from the environment. In Alzheimer's disease, although this energy flow continues, the system begins to use this energy to produce disorder instead of order. This situation can be expressed mathematically as follows:

$$\frac{dS_{iç}}{dt} > \left| \frac{dS_{çevre}}{dt} \right|$$

In other words, the system's internal entropy production exceeds the entropy it can release into the environment. This imbalance forms the physical basis of cognitive decline.

Free Energy Principle and Alzheimer's: [2]

The Free Energy Principle, put forward by Friston, describes the brain as a probabilistic inference machine. According to this principle, a healthy brain minimizes its free energy in order to minimize uncertainty about the environment.

Free energy is defined as follows:

$$F = \langle E \rangle - TS$$

Here:

$\langle E \rangle$: Average internal energy

T: Absolute temperature

S: Entropy

In Alzheimer's disease, both entropy increases and energy distribution becomes irregular. Therefore:

$$\frac{dF}{dt} > 0$$

This happens. This condition is directly related to the brain losing its ability to interpret and predict environmental stimuli.

Statistical Mechanics Model of Synaptic Networks: [3]

Synaptic networks in the brain can be likened to interacting particle systems in statistical mechanics. Each neuron can be modeled as a node, and synapses as interaction links.

The total system energy can be expressed as follows:

$$H = -\sum_{i,j} J_{ij} s_i s_j$$

Here:

J_{ij} : Synaptic bond strength

s_i : Neuron activation state

In Alzheimer's disease:

$J_{ij} \rightarrow 0$

Network connections weaken

Energy minimum is lost

This causes the system to become trapped in multiple local minima and unable to process information.

Entropy Production Rate and Disease Progression: [2]

Entropy production rate is a critical parameter for defining the rate of progression of Alzheimer's:

$$\sigma = \frac{dS}{dt}$$

In the early stages of the disease:
σearly < σadvanced

This increase is the mathematical equivalent of the rate of neuronal loss. Clinically observed "sudden deteriorations" correspond physically to phase transitions in entropy production.

Cognitive Decay Equation: [2]

Cognitive capacity C(t) can be related to energy efficiency and entropy:

$$\frac{dC}{dt} = -\alpha\sigma(t)C(t)$$

Here:

α: System sensitivity coefficient

When this differential equation is solved:

$$C(t) = C_0 e^{-\alpha \int_0^t \sigma(\tau) d\tau}$$

This statement mathematically explains the exponential cognitive decline in Alzheimer's disease.

Heat, Energy Density and Local Thermodynamic Imbalances: [3]

Hypometabolic regions observed in PET and fMRI studies of Alzheimer's disease are physically local energy pits. They can be expressed by the heat equation:

$$\rho c \frac{\partial T}{\partial t} = k \nabla^2 T + Q_{met}$$

Here, metabolic heat production (Q_{met}) is dysregulated in Alzheimer's disease and distorts spatial temperature gradients.

Thermodynamic Feedback Loop: [3]

Alzheimer's disease creates a self-reinforcing cycle:

Energy efficiency decreases

Entropy increases

Synaptic network deteriorates

Information processing decreases

Energy is used even more inefficiently

This cycle has a mathematically unstable fixed point:

$$\frac{dE}{dt} < 0, \quad \frac{dS}{dt} > 0$$

III. COMPARATIVE THERMODYNAMIC ANALYSIS OF PARKINSON'S AND ALS [1], [2], [3]

Common Physical Denominator of Neurodegenerative Diseases: [2]

Although Alzheimer's disease, Parkinson's disease, and Amyotrophic Lateral Sclerosis (ALS) present with clinically different symptoms, they share a common ground on the physical plane: impaired energy transfer, increased entropy production, and loss of system stability. In this context, all three diseases can be interpreted as different manifestations of a living system losing its ability to remain in an out-of-equilibrium regime. In this section, the thermodynamic model developed for Alzheimer's is discussed comparatively with Parkinson's and ALS; the energy-entropy signatures of the diseases are differentiated.

Thermodynamic Characteristics of Parkinson's Disease: [2]

Parkinson's disease (PD) is primarily associated with the loss of dopaminergic neurons in the substantia nigra pars compacta region. Dopamine can be considered not only a chemical neurotransmitter but also a modulator that regulates energy transfer in motor networks.

Energy Flow and Efficiency Loss: [3]

Useful work in motor control system:

$$W_{motor} = \int F \cdot dx$$

This is expressed as follows: In Parkinson's disease, dopamine deficiency creates a friction-like effect in the transmission of motor commands. This leads to a decrease in thermodynamic efficiency.

$$\eta_{PH} = \frac{W_{motor}}{E_{no}ral} \downarrow$$

Energy is still entering the system, but it is dissipating as heat and disorder instead of being converted into ordered motion.

Entropy Production in Parkinson's Disease: [3]

Entropy production in Parkinson's disease has a more localized structure compared to Alzheimer's. While dysregulation in motor circuits increases,

cognitive networks are relatively preserved in the early stages.

$$\sigma_{PH}(t) = \sigma_{motor}(t) + \varepsilon$$

Here, ε represents a small term compared to the widespread entropy increase in Alzheimer's. Therefore, Parkinson's can be classified as a disease with a high local entropy – low global entropy profile.

Thermodynamic and Time Scale Analysis of ALS: [2]

ALS is the neurodegenerative disease with the most aggressive energy-entropy disruption. The rapid destruction of motor neurons causes the system to transition to a high-entropy state in a very short time.

Maximizing Entropy Production Rate: [3]

Entropy production rate for ALS:

$$\sigma_{ALS} = \frac{dS}{dt}_{ALS}$$

It is quite high, and the following inequality generally applies:

$$\sigma_{ALS} \gg \sigma_{PH} > \sigma_{AD}$$

This provides a physical explanation for why ALS progresses with rapid clinical deterioration.

Time Constant and Decay Dynamics: [3]

In ALS, the characteristic decay time τ is quite small:

$$C(t) = C_0 e^{-t/\tau}_{ALS}, \quad \tau_{ALS} \ll \tau_{AD}$$

This indicates that the system veered into instability before it had a chance to return to equilibrium.

Comparative Energy-Entropy Map: [2]

Disease	Entropy Production Rate	Spatial Expansion	Time Scale
Alzheimer's	Medium – High	Widespread (cortical)	Long
Parkinson's	Medium	Local (motor circuits)	Medium

This table shows that each disease has its own unique thermodynamic signature.

Mathematical Representation of Brainwaves: [2]

Brainwaves observed with EEG measurements are classified into different frequency bands:

Delta (0.5–4 Hz)

Theta (4–8 Hz)

Alpha (8–12 Hz)

Beta (13–30 Hz)

Gamma (>30 Hz)

Mathematically, the brain signal can be expressed as follows:

$$V(t) = \sum_{n=1}^N N A_n(t) \sin(2\pi f_n t + \phi_n(t))$$

In Alzheimer's disease, within this spectrum:

Alpha and beta bands weaken

Low-frequency oscillations become dominant

Phase coherence decreases

This indicates that the system has lost its ability to synchronize.

IV. CONCLUSION

Limitations of the Mathematical Model: [3]

The differential equations and oscillator models provided: Represent linearized methodologies, Include parameters that differ among individuals, Do not fully capture the complexity of the actual biological system. Specifically, coefficients like α , K , and γ need to be individually calibrated.

Lack of Experimental Data and Scale Problems: [3]

The current body of literature reveals certain limitations, including small sample sizes, short-term applications, and a lack of standardization. These issues result in challenges such as reduced statistical power. To address these concerns, the recommended minimum experimental design should include at least 60 patients, a duration of application spanning no less than 12 weeks, the incorporation of a control group, and evaluations conducted in a blinded manner. The vectorial energy and substance transfers outlined here enable drug-cell interactions, ultimately paving the way for achieving effective drug therapies. In this context,

the emphasized "ELMAS's Thermodynamic Theory" serves as a foundational framework for Medical Thermodynamics. [3]

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