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NASH EQUILIBRIUM OF DRUGS CONTROL IN THE MATHEMATICAL MODEL OF ALZHEIMER AND MATHEMATICAL ANALYSIS OF PET

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ABSTRACT

Alzheimer is mainly an aging disease characterized by dementia, where symptoms include cognitive decline, memory loss, and impairment of daily functioning. The main hallmarks of the disease are aggregation of plaques of amyloid- β ($A\beta$) and neurofibrillary tangles of tau proteins (τ). They can be detected in PET scans of the brain. The disease can remain asymptomatic for decades, while the densities of $A\beta$ and τ continue to grow. Drugs are urgently needed for the treatment of AD and unfortunately almost all clinical trials of AD drug candidates have failed or been discontinued to date. Mathematical, computational and statistical tools were employed in the construction of clinical trial simulators to assist in the improvement of trial design and enhance the chances of success of potential new therapies. In [1] was developed a mathematical model that can produce simulated patterns of ($A\beta$ and τ) seen in PET scans of AD patients. The model is based on the assumption that early inflammations R and $\bar{R}$ drive the growth of $A\beta$ and τ , respectively. The essential point is that in these equations are not included explicitly exterior drugs. One of the objectives of this article is to include to some of these equations injection of drugs and to optimize the choice of drugs according to some rules. The rules means a kind of functional that should measure the behavior of interesting result with respect to these injections. By an interesting result, we mean loss of plaques amyloid- β and τ as well growth of the number of microglia cells and astrocytes glial cells. Next, we formulate a differential game problem. One of the aim of the paper is to formulate a sufficient conditions in a form of verification theorem for the existence of a feedback Nash equilibrium. As a result, based on the verification theorem, we state an algorithm that allows efficient calculation to find optimal treatment of drugs in the given time. Next for given treatment (calculated from the first problem), a maximum surface of reactive oxygen species (ROS) with which, during the treatment, plaques amyloid- β and τ is still losing to a healthy stage. The last study concerns the problem of the amyloid hypothesis vs the tau hypothesis. This is a continuation of the talk from the former (XXX) conference.

REFERENCES

- [1] Lee C, Friedman A (2024) Generating PET scan patterns in Alzheimer's by a mathematical model. PLoS ONE 19(4): e0299637. <https://doi.org/10.1371/journal.pone.0299637>