

Mathematical Models for Tangle's Formation in Alzheimer's Disease.

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Alzheimer's disease (AD) is characterized by the presence of two specific structures in brain of patients: senile plaques (SP) and neurofibrillary tangles (NTFs). Oligomers of beta amyloid protein are the main component of SP, while NTFs are constituted by oligomers of aberrantly phosphorylated tau protein. The aim of this talk is to present two studies concerning the process of diffusion and agglomeration of tau protein first into fibrils and eventually up to neurofibrillary tangles. The aforesaid researches share the use of Smoluchowski-type equations (including diffusion and monomers production) on a finite weighted graph, which is conceived as a theoretical approximation of the human brain, where each vertex represents a cerebral area of interest, while the connections between them are described by the edges.

The first model, that we present, concerns the processes of aggregation and diffusion of hyperphosphorylated tau and is based on a finite dimensional Smoluchowski-type system on a finite graph. The aim of the model is to reproduce tau patterns in human brain obtained through suitable *in vivo* measurements. In such model, clusters whose length exceeds an *a priori* established critical threshold are defined to be tangles. Statistical analysis is performed, comparing the model-predicted tau concentrations (in monomeric, oligomeric form and in tangles) with cortical atrophy data and empirical tau measurements in AD patients provided by *in vivo* neuroimaging.

The second research considers the process of aggregation in tangles of hyperphosphorylated tau protein as a result of a coagulation process of this protein. The formation of neurofibrillary tangles is mathematically characterized in terms of a sol-gel phase transition for a polymerization problem, modelled by means of infinite dimensional Smoluchowski-type system on a finite graph. From a biological point of view, the process of formation of gel is a suitable tool for the description of the process of formation of neurofibrillary tangles, since it allows one to formulate conjectures and to provide insights on the nature of this phenomenon in AD scenario. This could open new interesting perspectives concerning the role of NTFs in neurodegenerative disorders.