

Title: Dynamics of prion proliferation under combined treatment of pharmacological chaperones and interferons

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Abstract: Prions are proteins that cause fatal neurodegenerative diseases. The misfolded conformation adopted by prions can be transmitted to other normally folded proteins. Therapeutics to stop prion proliferation have been studied experimentally; however, it is not clear how the combination of different types of treatments can decrease the growth rate of prions in the brain. In this article, we combine the implementation of pharmacological chaperones and interferons to develop a novel model using a non-linear system of ordinary differential equations and study the quantitative effects of these two treatments on the growth rate of prions. This study aims to identify how the two treatments affect prion proliferation, both individually and in tandem. We analyze the model, and qualitative global results on the disease-free and disease equilibria are proved analytically. Numerical simulations, using parameter values from in vivo experiments that provide a pharmaceutically important demonstration of the effects of these two treatments, are presented here. This mathematical model can be used to identify and optimize the best combination of the treatments within their safe ranges