

Ph.D. thesis evaluation: *Mathematical models for the dynamics of low-grade gliomas and their response to therapies*

Mrs. Bogdanska Thesis presents a rigorous study of different continuum mathematical models, non – spatial and spatial. It is structured in different chapters approaching the biological processes of cancer growth, chemotherapy treatment and cancer transformation in the context of gliomas. There are two principal elements of interest in the research work. Firstly, the biological problems are interesting as there is not much done yet in the field of low-grade gliomas. And secondly, the mathematical analysis of the models includes different tools that wide from ODEs and PDEs explicit solutions, fixed points analyses, to traveling waves and Turing Instabilities.

Mathematical analysis highlights:

The spatial models are different variations of FKK equations, the principal terms take into account diffusion, proliferation, and spatial constraints. Previous research in the field may be related to Christine Swanson, Angela Stevens, Mark Chaplain or Helen Byrne. Mrs. Bogdanska proves to master a wide set of mathematical tools to analyze non-spatial and spatial models. In general, the theoretical part of the thesis presents a well structured and balanced part of the research.

Biological questions highlights

The biological questions approached in the thesis are sound and well defined. The second and fourth chapters approach the question of therapy from non-spatial and spatial perspectives; including experimental data and computational comparisons.

Of particular interest is chapter 3. It provides, to my knowledge, the first publication in mathematical modeling approaching low grade to high-grade gliomas transformation. The striking part of this chapter is the fact that, albeit some parts of the model may be considered as heuristic (malignant transformation starts at the center of the tumor rather than at the outer rims which may be subjected to debate), clinical data are provided and the model seems to fit very well, what improves considerably the contribution of the research and its applicability. In addition, the simplicity of the model provides an interesting tool for real application in long term therapies. The conclusions of this chapter, suggesting an early treatment are probably in agreement with the current therapies.

In general, I would summarize the striking points of the thesis as the following:

- 1) Mathematical analysis is rigorous and wide enough to describe the behavior of the different systems proposed in the research.
- 2) Comparison to real data is provided. Model fitting is quite accurate and therapy proposals are included so that the thesis provides a potential clinical application.
- 3) A wide set of spatial and non-spatial models are studied, widening the concepts of tumor growth, malignant transformation and therapy.

Taking into account all the previous considerations. Mrs. Bogdanska thesis is sufficient to grant a Ph.D. According to Spanish standards, I propose Mrs. Bogdanska thesis to be granted as CUM LAUDE distinction

Ignacio Ramis Conde



Assistant Prof. Universidad de Castilla la Mancha
PhD Mathematical Biology