

SCUOLA GALILEIANA DI STUDI SUPERIORI
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Lesson I

Models of Tumor Growth *in vivo*

Models of tumor growth *in vivo* are analyzed. The models describe proliferating and quiescent compartments of tumor cells, and cells indexed by successively mutated cell phenotypes of increasingly proliferative aggressiveness. The models incorporate spatial dependence due to both random motility and directed movement chemotaxis and haptotaxis. Models of tumor cell population growth that distinguish tumor cells by variables such as cell age and cell size are investigated. The models consist of systems of nonlinear partial differential equations for the classes of cells. The existence, uniqueness, positivity, regularity, and growth characteristics of the solutions are investigated.

Lesson II

Models of Tumor Growth *in vitro*

Models are developed to investigate *in vitro* experimental cell cultures. Models are used to analyze experimental oncogene-expressing human mammary epithelial cells *in vitro* under transforming growth factor TGF- β . The models separate the TGF- β properties of tumor suppressor and tumor promoter, which simultaneously both inhibit cell proliferation and enhance cell motility. The models are based on the Fisher-Komolgorov nonlinear partial differential equation. The properties of existence, uniqueness, and stability of the equations are investigated.

Lesson III

Models of Tumor Chemotherapy

Models are developed to quantify the cytostatic and cytotoxic effects of an experimental drug lapatinib that blocks the proto-oncogene HER2. The models describe the effects of lapatinib in experiments using human mammary epithelial cells that over-express HER2. The models indicate that lapatinib acts by slowing the transition through cell cycle G1 phase and also indicate a late cell cycle cytotoxic effect.

Models are also developed of the intercellular transfer of the drug efflux P-glycoprotein Pgp from resistant donor cells to sensitive recipient cells. The models combine the processes of cell proliferation, Pgp induction and degradation, and cell-to-cell Pgp transfer for *in vitro* experimental cultures of BE(2)-C human neuroblastoma and MCF-7 human breast adenocarcinoma. The objective of the models is the investigation of tumor intrinsic factors, such as Pgp transfer rates, and treatment management parameters, such as cycles of drug administration.

Lesson IV

Models of Antibiotic Therapy Resistance in Hospitals

Infections caused by antibiotic-resistant pathogens are a global public health problem. Numerous individual-level and population-level factors contribute to the emergence and spread of these pathogens. An individual based model, formulated as a system of stochastically determined events, is developed to describe the complexities of the transmission dynamics of antibiotic-resistant bacteria. To simplify the interpretation and application of the model's conclusions, a corresponding deterministic model is created, which describes the average behavior of the individual based model over a large number of simulations. The integration of these two model systems provides a quantitative analysis of the emergence and spread of antibiotic-resistant bacteria, and demonstrates that early initiation of treatment and minimization of its duration mitigates antibiotic resistance epidemics in hospitals.

