MATHEMATICS

PARTIAL DIFFERENTIAL EQUATION MODELS FOR INTRANUCLEAR DIFFUSION, INVERSE PROBLEMS IN NANOBIOLOGY AND CELL CYCLE SPECIFIC EFFECTS OF ANTICANCER DRUGS

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In this dissertation we have applied partial differential equation models to various problems arising in biology.

We investigated the diffusional motility of p53, a key tumor suppressor protein, in living cells using fluorescence recovery after photobleaching (FRAP). In the case of p53, we found that diffusion of p53–GFP within the cell nucleus is well described by a mathematical model for diffusion of particles that bind temporarily to a spatially homogeneous immobile structure. On the other hand, the inert protein GFP was found to diffuse freely and therefore provided a negative control.

The work that forms chapter III is likewise rooted in biophysics. An open problem is to understand how DNA–binding proteins (such as p53) find their specific target sequences in the genome. We argue that inverse problems for wave equations in elastic media can be directly applied to biophysical problems of fiber-ligand association.

We have used age–structured models of population dynamics to understand the cytostatic and cytotoxic effects of the anticancer drug lapatinib. Our mathematical model is fully continuous with respect to time and maturity (the position of a cell in its cell cycle) and contains only a small number of parameters. These parameters have a straightforward biological interpretation and can be determined experimentally. The

model can be applied to a variety of drugs that have cell cycle specific cytostatic and cytotoxic effects.

Finally, we analyze mathematically two age–structured models of population dynamics. A characteristic of many growth processes is that as the number of individuals reaches a certain threshold, the population growth slows. The Gompertzian growth model has been widely applied to such populations. In the case of a tumor cell mass, cells can belong to two distinct subpopulations, namely those of proliferating respectively nonproliferating cells. We show that a nonlinear population dynamic model based on chronological age must have a nontrivial equilibrium solution.

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