ΙΤΕ/ΕΙΧΗΜΥΘ

OMIΛHTHΣ: **Dr. Antonios Armaou**, Associate Professor
Department of Chemical Engineering, The Pennsylvania State University
USA

ΘΕΜΑ: **Multi-scale modeling of tumor progression and chemotherapy response.**

ΤΟΠΟΣ: Αίθουσα Σεμιναρίων ΙΤΕ/ΕΙΧΗΜΥΘ

ΗΜΕΡΟΜΗΝΙΑ: **Τετάρτη, 22 Φεβρουαρίου 2012**

ΩΡΑ: **12:00**

ΠΕΡΙΛΗΨΗ:

The American Cancer Society estimated that 22,070 patients would be diagnosed with brain and other central nervous system cancers and 12,970 patients with this disease would die in the US during 2009. Glioblastomas, the most common and lethal of these diseases, are intracranial neoplasms with uncontrolled proliferation, generally with a necrotic core, marked angiogenesis, a diffuse infiltration and highly resistance to radio/chemotherapy. Median survival for patients receiving treatment (which includes surgical resection, radiation, and chemotherapy) is only about 12 months, with a low chance of long term survival. The dismal prognosis for patients diagnosed with glioblastoma has sparked considerable efforts, clinically and otherwise, to understand the progression of this disease. Mathematical models and computational tools are increasingly being accepted in cancer research as aids for visualizing and integrating information, testing different mechanism hypotheses and suggesting optimal treatment strategies. \The degree of complexity of these modeling approaches depends on the biological processes that are included in the model and the depth of integration. A key limiting factor in the detail of current modeling descriptions is the very high computational resources needed for modeling processes spanning multiple length scales.

Οδός Σταδίου, Ρίο, Τ.Θ. 1414, 265 04 Πάτρα
Τηλ.: 2610 965 300 & 3, Fax: 2610 990 987
www.iceht.forth.gr

Tumor progression is the ultimate outcome of several time and space dependent interacting processes which entail the combined intracellular and extracellular events that govern cell survival, proliferation, and migration, as well as angiogenic, inflammatory, and immune responses. In the present talk I'll discuss our efforts on developing a mathematical agent-based model that describes the progression of a brain tumor by capturing the interplay between processes occurring at the intracellular and tissue levels [1]. The usual efforts to address this issue focus on developing lattice-based models. A major shortcoming of lattice-based models is the difficulty to incorporate mechanical interactions. In addition, proliferation and migration in these models are commonly restricted to cells that have free lattice sites in their neighborhood (i.e., contact inhibition), even though these events can occur in the internal regions of the tumors. In this talk we discuss an alternative, lattice-free, approach to alleviate these shortcomings. This is achieved by formulating a large-scale optimization problem as a surrogate of the tumor mechanics, during the evolution of the tumor. The proposed method enables us to account for mechanical interactions determining tumor cell location and allows the proliferation and migration of tumor cells to occur at any location in the tumor. Including a realistic vessel topology, the same approach is also used for vessel-tumor interactions thus enabling us to describe vasculature remodeling through vessel occlusion, vessel dilation, and angiogenesis. In addition, we included intracellular model signaling pathways regulating tumor cell migration (i.e., PLC pathway), resistance to apoptosis (i.e., PI3K/Akt pathway) and response to hypoxia (i.e., HIF-1 signaling). The current model describes tumor growth, invasion, and vasculature remodeling as well as the distribution of temozolomide (TMZ; an FDA-approved chemotherapeutic agent). Based on in vitro and in vivo experiments for TMZ pharmacokinetics and pharmacodynamics, we simulate the effect of TMZ on tumor progression under various treatment strategies (e.g., different drug dosing and/or scheduling). The goal of this modeling base is to establish an in silico approach to explore the effect of possible migration mechanisms on the growth and invasion properties of the tumor and provide insight regarding tumor suppression mechanisms of various therapeutics, ultimately to develop more efficacious treatment regimes for this devastating disease.