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Development and adaptation of a web enabled *in silico* oncology application in grid environment

A. Menychtas, G. Kousiouris, D. Kyriazis, T. Athanaileas, D. Dionysiou, G. Stamatakos, D.Varvarigou, D. Kaklamani and N. Uzunoglu
National Technical University of Athens
School of Electrical and Computer Engineering
9 Heroon Polytechneioy Str, Zografou, Athens, Greece
E-mail: {a_menychtas, gkousiou, dkyr}@telecom.ntua.gr, {thathan, dimdio}@esd.ntua.gr, gestam@central.ntua.gr, dora@telecom.ntua.gr, dkaklam@mail.ntua.gr, nuzu@cc.ece.ntua.gr

1. Introduction

In silico **oncology is an emerging interdisciplinary field aiming at mathematically describing and computationally simulating the multiscale biological mechanisms that constitute the phenomenon of cancer and its response to therapeutic techniques. Within this framework, the *In Silico* Oncology Group, National Technical University of Athens, has already developed a four-dimensional simulation model of glioblastoma multiform (GBM) response to radiotherapy and chemotherapy. The simulation algorithms have been ported to the EGEE infrastructure and a web based interface has been implemented for providing a user-friendly environment.**

2. Grid Enabling the *In Silico* Oncology Simulation and Grid Added Value

Exploitation of grid technologies is imperative for *In Silico* Oncology for the following reasons:

- **exponential increase of required computational resources when considering a more dense discretization of the space-time (4D) grid of the biological problem**
- **heterogeneity of required data (imaging, histopathologic, genetic) with different preprocessing requirements**
- **large number of involved patients**

The simulation models of imageable GBM response to radiotherapy and chemotherapy have been successfully ported to the grid environment. The model is based on the clinical, imaging, histopathologic, and molecular data of the patient and numerous fundamental biological mechanisms are incorporated and explicitly described. The clinician delineates the tumour and its metabolic subregions on the available imaging data by using a dedicated computer tool. A prototype system of quantizing cell clusters included within each geometrical cell of a discretizing mesh covering the anatomic area of interest lies at the heart of the proposed simulation approach.

For more details please refer to:

Stamatakos G.S. et al.: In silico radiation oncology: combining novel simulation algorithms with current visualization techniques. IEEE Proceedings: Special Issue on "Bioinformatics: Advances and Chalenges 90 (2002) 1764-1777,

Dionysiou D.D. et al.: A Four Dimensional In Vivo Model of Tumour Response to Radiotherapy: Parametric Validation Considering Radiosensitivity, Genetic Profile and Fractionation. J. theor. Biol. 230 (2004) 1-20.

In order for *in silico* Oncology to be efficiently transferred to the HellaGrid infrastructure, certain aspects were addressed regarding its adaptation to the grid programming model:

- **mechanisms for automatic simulation submission and monitoring**
- **data management and result aggregation**
- **provide some basic QoS to the user (e.g. provide an optimal response time for various simulation models – always taking into consideration the characteristics of the model)**

3. Architecture – Implementation

The first step towards grid-enabling of the application was to bring it to a form appropriate for execution on the grid. This involved adapting source code in order to be externally parameterizable and also creating the required scripts and description files which are used by the grid workload management system for job execution on the grid.

On the other hand, the *in silico* oncology simulation application targets specific user groups. These groups consist mainly of doctors and researchers; people that are not computer experts and are not familiar with grid technologies. The important user requirement for usability was addressed with the design and the development of a web portal. Web portals are considered as cutting edge technology for user interfaces providing advanced services to the end users in a friendly and efficient way. The role of the portal in the application is of major importance since it offers grid services to the research community eliminating any usability issues. Additionally, the portal adds new features in the application beyond the job submission and file management, such as user management and usage statistics services.

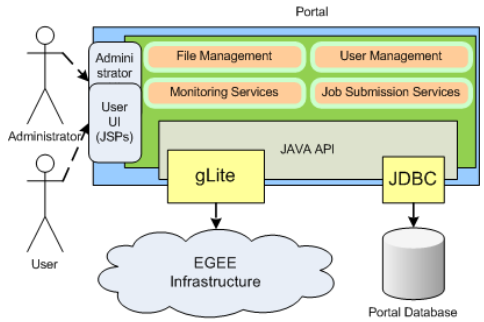

Fig. 1: The application Architecture
The simulation application consists of four layers: ***presentation (UI), portal services, gLite and database.***

The in silico oncology grid portal has all the characteristics of an enterprise simulation toolkit. The portal communicates continuously with the underling glite services and the database to provide the core grid functionality and adds new business features and respective interfaces for them. Additionally the application supports different users types, the common users and the administrators.

The portal has several advantages for the end users:

- ✓ **Usability**
- ✓ **Efficiency**
- ✓ **Operating System independence**
- ✓ **Application extension**

The web version of the simulation application can be easily accessed from an increased number of end users since it instantly enables access to the advanced computational resources of grid infrastructures through user friendly processes.

4. Indicative Simulation Results

The following simulations have been submitted for execution on the resources provided by the South Eastern Europe Virtual Organization (SEE-VO) using the application framework. Each therapeutic scheme has been treated as a different parameter sweep simulation.

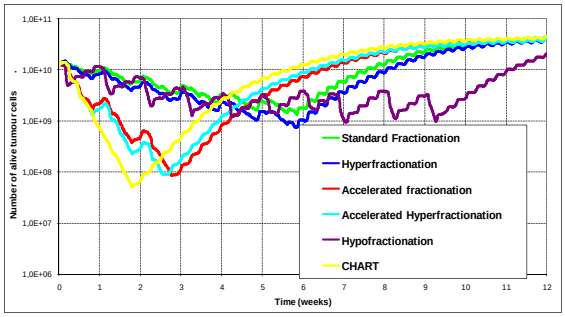

Fig 2. Indicative simulation results: Comparing the relative merits of dose fractionation schemes commonly used for the radiation therapy of solid tumours.

The accelerated fractionation and the accelerated hyperfractionation schemes seem to be particularly efficient in terms of tumour cell kill. They achieve maximum cell kill at specific instants compared to the other schedules. Nevertheless, their duration is smaller and as a result, if they fail in eradicating "all" tumour cells, tumour repopulation begins earlier. At the other extreme, hypofractionation is advantageous in terms of the duration of tumour control, but achieves less tumour cell kill. Of course, in clinical practice the choice of the appropriate radiotherapy schedule depends both on the expected tumour cell kill and the expected normal tissue complications.

5. Ongoing and Future Work

Exploitation of the vast resources provided by a grid may lead to a better understanding of the biological and clinical behavior of cancer and especially solid tumours. Furthermore, computer simulation may be employed in order to optimize treatment of cancer, by conducting a number of simulations for different therapeutic schemes based on the individual data of a patient. A restraining factor is that simulations need to be conducted in clinically accepted computational time. As the number of possible therapeutic schemes and consequently the number of simulations increases, the time required for evaluating and comparing the effects of the different schemes may become forbiddingly high. Exploiting grid computing is a very attractive solution, as the resources provided in a grid infrastructure may be efficiently used to reduce overall required execution time in a cost-effective and efficient manner.

Within the plans for future work is to exploit any parallelization patterns that may apply to the In Silico Oncology simulation models and develop a simulation-level parallelization scheme that may be executed on massively parallel processors (e.g. using MPICH)

Additionally, we plan to port additional therapeutic methods to the grid-enabled toolkit and use the grid in order to perform similar comparative simulations.

Moreover the simulation application will be extended in order to address the user requirements for Quality of Service (QoS). New mechanisms are under development to provide advanced job scheduling based on the user needs, the grid resources capabilities and the experience of the previous job executions.

This work has been performed in the context of the research project "Development and adaptation of an *in silico* oncology application in grid environment" (GRID-APP). The project is funded by the General Secretariat for Research and Technology, Ministry of Development, Greece (75%) and the European Regional Participation Fund (25%).