Agent-Based Distributed Decision Support System for Brain Tumour Diagnosis and Prognosis

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This paper introduces HealthAgents, a research project funded by the European Commission under the FP6 framework. Its main objective is to improve the classification of brain tumours through multi-agent decision support over a distributed network of local databases or Data Marts. HealthAgents will not only develop new pattern recognition methods for a distributed classification and analysis of HRMAS and DNA data, but also define a method to assess the quality and usability of a new candidate local database containing a set of new cases, based on a quality score.

Keywords: Intelligent Agents; Decision-Support Systems; Human Brain Tumours; Magnetic Resonance; eHealth.

1 INTRODUCTION

Brain tumours remain an important cause of morbidity and mortality in a large percentage of the European population. Diagnosis using Magnetic Resonance Imaging (MRI) is non-invasive, but only achieves 60-90% accuracy depending on the tumour type and grade. The current gold standard classification of brain tumours by biopsy and histopathological analysis involves invasive surgical procedure and incurs a risk of 1-2% morbidity.

Nowadays the diagnosis and treatment of brain tumours is typically based on clinical symptoms, radiological appearance and often a histopathological diagnosis of a biopsy. However, treatment response of histologically or radiologically-similar tumours can vary widely, particularly in children. Magnetic Resonance Spectroscopy (MRS) is a non-invasive technique for determining the tissue biochemical composition (metabolomic profile) of a tumour. Additionally, the genomic profile, determined using DNA microarrays, facilitates the classification of tumour grades and types not trivially distinguished by morphologic appearance.

Thus, we propose the definition of decision support system (DSS) which employs MRS and genomic profiles. This DSS will deploy an ad hoc agent-based architecture in order to negotiate a distributed diagnostic tool for brain tumours, implement data mining techniques, transfer clinical data and extract information. The distributed nature of our approach will help the users to observe local centre policies for sharing information whilst allowing them to benefit from the use of the d-DWH. Moreover, it will permit the design of local centres targeting a specific patient population.

We argue that this new information for classifying tumours along with clinical data, should be securely and easy accessible in order to improve the diagnosis and prognosis of tumours. All data will be stored anonymously, and securely through a network of data marts based on all this information acquired and stored at centres throughout Europe. This network will grant bona-fide access to an organisation in return for its contribution of clinical data to a distributed Data Warehouse (d-DWH)/Decision Support System (d-DSS).

This rest of this paper is structured as follows. First, we provide some background on the underlying technologies for this project: brain tumour detection and agent technology. Then we provide the architectural specification. Finally we conclude with our future work.

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2 BACKGROUND

2.1 Brain Tumour Diagnosis

Brain tumours remain an important cause of morbidity and mortality and afflict a large percentage of the European population. In children over 1 year of age, brain tumours are the most common solid malignancies that cause disease-related death.

Diagnosis using Magnetic Resonance Imaging (MRI) is non-invasive, but only achieves 60-90% accuracy depending on the tumour type and grade. The current gold standard classification of a brain tumour by histopathological analysis of biopsy is an invasive surgical procedure and incurs a risk of 1-2% morbidity, in addition to healthcare costs and stress to patients. For tumours that evolve slowly (e.g. pilocytic astrocytoma in children), repeated biopsies may not be advisable or practical. There is a need to improve brain tumour classification, and to provide non-invasive methods for brain tumour diagnosis and prognosis, to aid patient management and treatment. Three techniques are available to address these needs:

1. Magnetic Resonance Spectroscopy (MRS) [6] is a non-invasive technique that provides biochemical information on tissue in vivo.

2. HR-MAS [1,8] is applied to biopsies in vitro in order to improve characterisation and DNA microarray analysis. This can determine tumour phenotype from gene expression profiles and predict better survival than classical histology.

3. MRS, coupled with conventional MRI, provides metabolite profiles of a single voxel (SV) of tumour tissue [6,13] (see Fig. 1). It also produces a molecular image of particular tumour metabolites (see Fig. 2) in 10 minutes using multi-voxel (MV) techniques.

2.2 Agent technology

Several modern complex distributed systems are composed of customisable building blocks, known as agents. Surveys on agent technology enumerate four important characteristics of agent technology [2]. First, agents possess an internal knowledge-based state that can be dynamically altered. Second, they have dynamic reasoning capabilities that determine their internal behaviour through constraints or goals. Third, they sustain a communication status that enables them to interact with agents or human entities. Last, they feature a unique identity that provides roaming and service advertising capabilities.

Extensive research in agent systems has been conducted in Europe, as evidenced by the reach of the AgentLink membership [16]. Data mining agents present human researchers with a set of potential hypotheses deduced from the data sources. Thus, with the information explosion caused by genomics and proteomics research, there is a great need for automated information-gathering agents in order to assist human researchers conducting automated or semi-automated testing of data. Nevertheless, scant multi-disciplinary research has been channelled to the bioinformatics domain, where numerous databases and analysis tools are independently administered in geographically distinct localities, lending themselves almost ideally to the adoption of a multi-agent approach.

Initiatives such as the “Modelling Adult Stem Cells as Multi-agent Systems” [5] in the UK, the ones emanated from the Cesena group in Italy [3], BioAgents [9], and InterLab [12] present some innovative approaches to agent systems in the biological sciences in Europe. Furthermore, GeneWeaver [7], DECAF [4], and MIAKT [10] introduce the use of agents and web services to genome analysis and decision support. In particular MIAKT, provides support for Multi-Disciplinary Meetings (MDMs) between medical practitioners with different expertise, helping them to perform a collaborative diagnosis and plan of action for symptomatic, focal breast diseases.

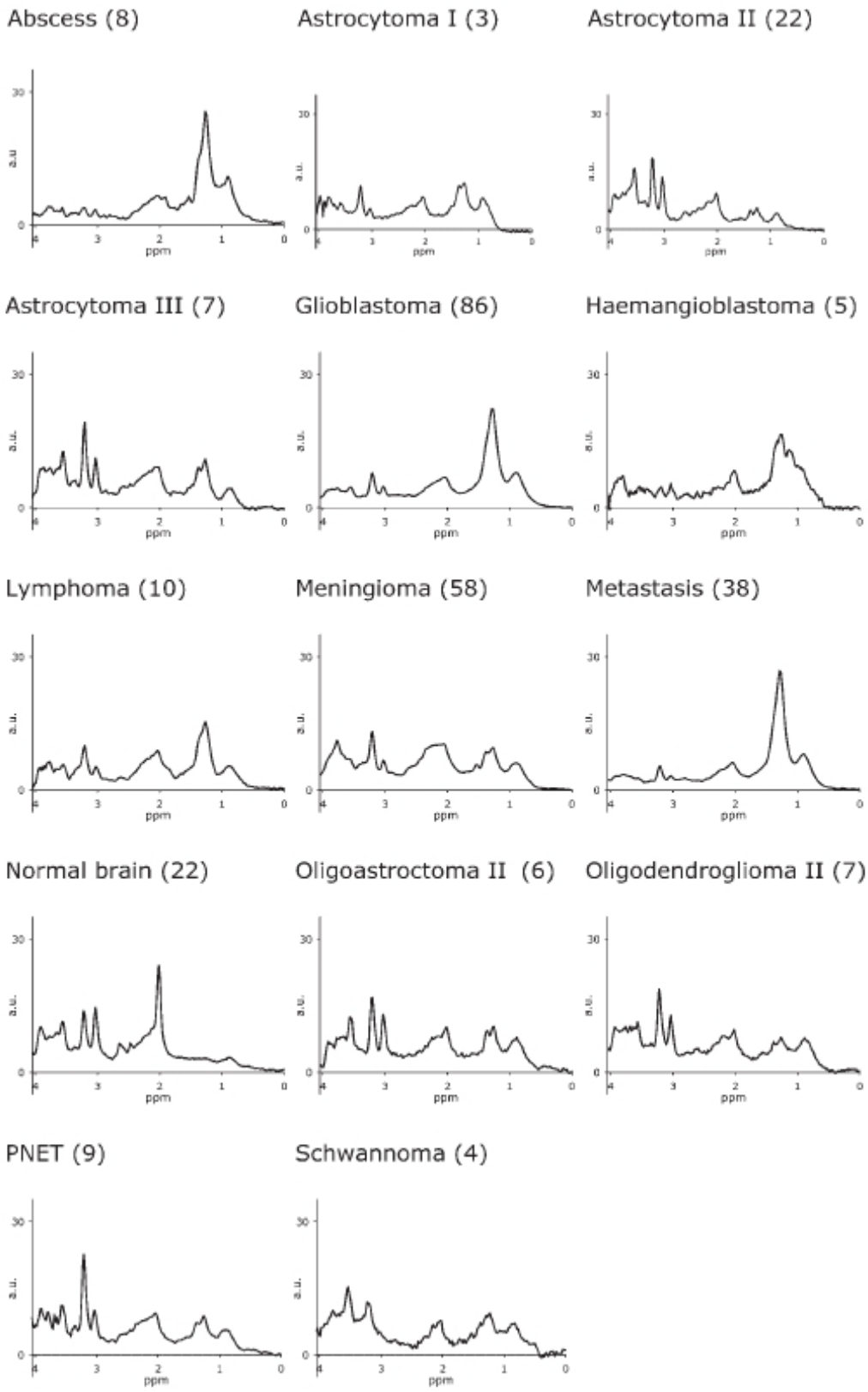
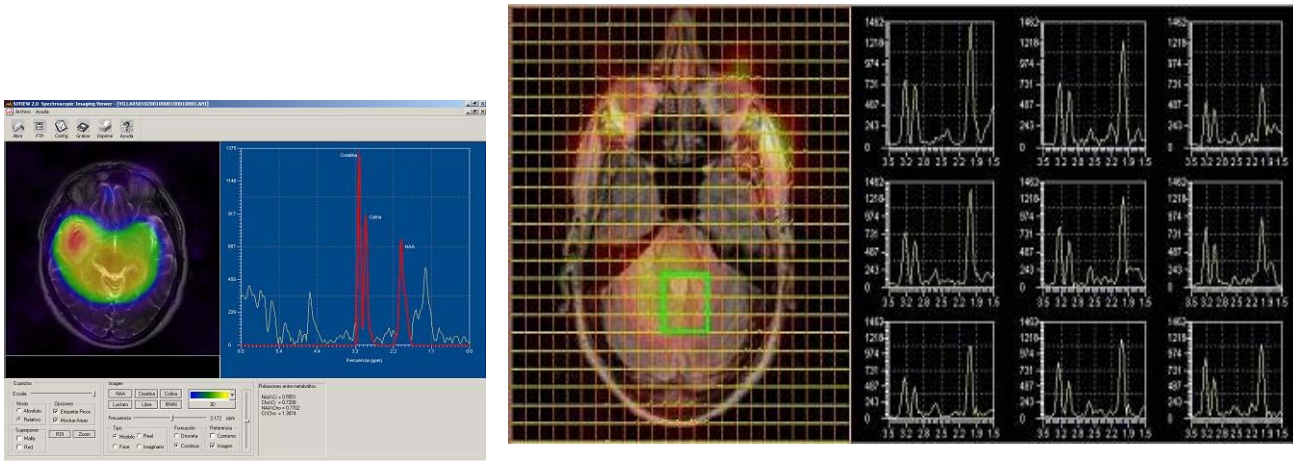


Fig. 1: Mean short echo spectra of representative pathologies in the validated-DB. These were obtained by averaging spectra normalized to the Euclidian norm. The vertical axis is displayed in the same arbitrary units (a.u.) scale for all types. The horizontal axis labels ppm values. Number of cases of each type in parentheses. The most relevant metabolites are: lipids, 0.9 and 1.29 ppm; N-acetyl-containing compounds, 2.03 ppm; acetate, 1.9 ppm; macromolecules and glutamate/glutaminecontaining compounds, 2-2.5 ppm; creatine, 3.03 ppm; choline-containing compounds, 3.21 ppm; myo-inositol and glycine, 3.55 ppm; glutamate/glutamine-containing compounds and alanine, 3.77 ppm. (Adapted from Figure 4 of [13]).



(a) (b)

Fig 2: (a) Molecular image of Cho (cholines) concentration distribution from MV spectra of a patient with a Glioblastoma (red indicates highest Cho levels in the tumour) including the deconvoluted spectrum. (b) MV spectra from the rear cavity with a demyelisation lesion. The nine spectra shown, from the selected green square, present the most abnormal region bottom right.

3 ARCHITECTURAL SPECIFICATION

By focusing on brain tumour diagnosis and prognosis, the project is to apply agent technology to communicate user sites with a central database. It will employ agent negotiation and argumentation mechanisms developed for distributed resource allocations problems. Moreover, HealthAgents intends to build a completely distributed repository with local databases. Grid technologies such as multi-site data partition and distributed data sharing will permit the seamless access to different databases across sites.

A distributed Decision Support System (d-DSS) will furnish a completely new approach to the brain tumour diagnosis. Since inferences from local predictions may well conflict with one another, reasoned argument between intelligent agents, acting on behalf of scientists, in a multi-agent system, will foster consensus.

The HealthAgents project intends to not only apply agent technology into the biomedical field in a multi-disciplinary fashion, but also develop the first distributed repository for brain tumour diagnosis, leading eventually to the formation of a special interest data grid.

A centralized DSS is already available from the INTERPRET project [15] to facilitate the clinical use of MRS in brain tumour diagnosis which uses a classification based on histopathological diagnosis. An evolution of this DSS is currently under construction in the eTUMOUR project [14]. It will incorporate additional MRS data, such as childhood tumours and less common adult tumours, using new classifications based on genetics. The development of this new d-DWH (the “d-DSS”), incorporating concepts of networking, agent technology, and data mining, must increase the number of accessible cases, yielding to an improved classifier, that in turn will achieve the goals described in this proposal.

We proposed a multi-layer system architecture as shown on Fig 3. The database mapping layer is used to map a relational database schema to the HealthAgents ontological schema. The programming API layer abstracts the underlying database interaction from the agent architecture. The business methods layer contributes to the main control flow of an agent such as the new case classification, new classifiers reception, and data retrieval.

The security and trust layer is a crucial system component due to the sensitivity of the data. Its functionalities are access control, data marshalling, track out of on-going data, and the evaluation of reputation and trust of agents. The agent layer is in charge of all the communications and allows their abstraction from the rest of the system to allow flexibility in the underlying framework. The semantic description layer will contain the description of what the agent holds and what is able to do.

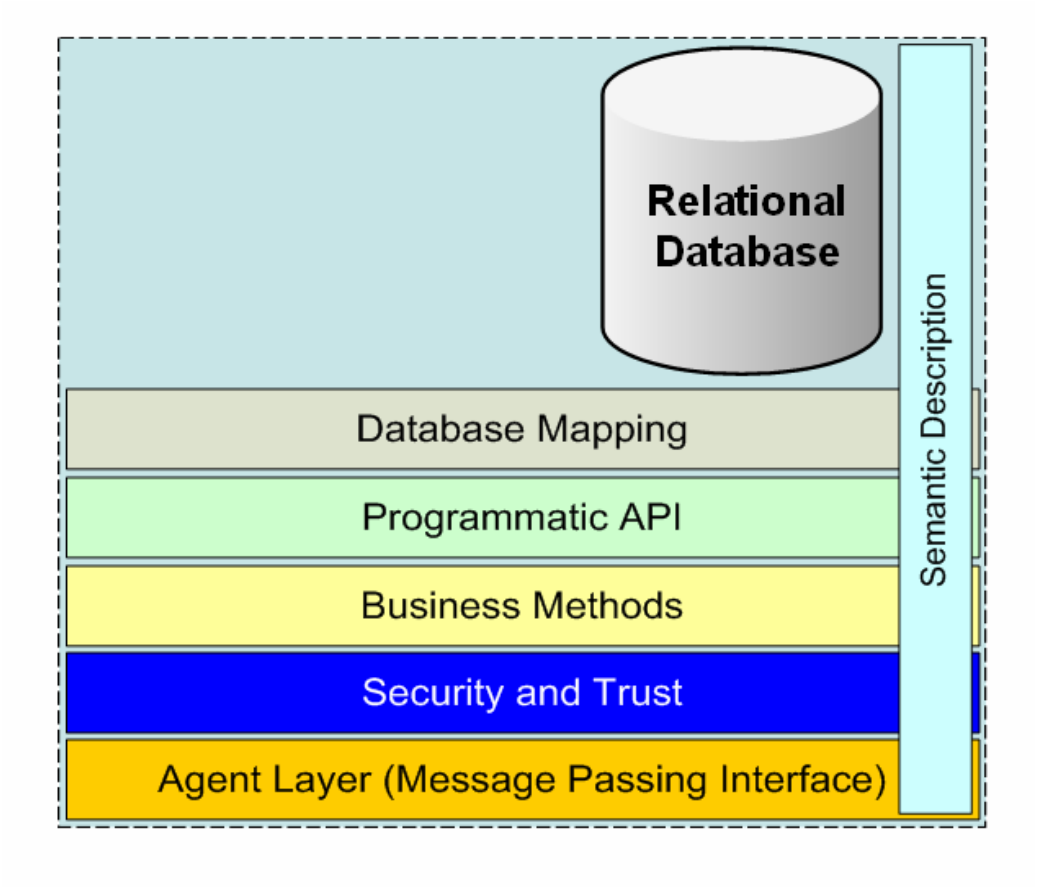


Fig 3: HealthAgents framework.

4 CONCLUSIONS

While the incorporation of multi-voxel MRS techniques provides an important methodology for case analysis, agent-based systems supply a preponderant mechanism for multi-repository management, genomic profiles furnish additional background on individuals, and the pattern recognition techniques allow the rapid case discrimination. As a result, HealthAgents proposes a unique blend of state-of-the-art technologies for the study of brain tumours in living individuals.

We have introduced the HealthAgents project, its objectives, and scope. Although tangible results are to be produced soon, we strongly believe that the conditions are given to produce a cutting edge software system to help in the fight against one of the most pernicious diseases of our time: cancer.

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