Medical Ontology Maintenance: A Multiple Sclerosis Case Study

Mariam Gawich, Marco Alfonse, Mostafa Aref and Abdel-Badeeh M. Salem

***Abstract*—** The medical ontology is used to represent and reorganize the medical knowledge that can be shared by medical information systems. In order to ensure the reliability and the novelty of the medical knowledge (new treatments and tests) provided by the ontology, it should be maintained in a consistent way. This paper presents the maintenance of the Multiple Sclerosis (MS) disease ontology. The treatments of this disease evolve regularly. The maintenance of MS is realized by the use of a medical ontology maintenance system. The maintenance of MS ontology is done through evolution and pruning. The evolution focuses on the addition of the new treatments applied for the MS and the pruning focuses on removing the ontology elements that are irrelevant to the MS disease. Three additional classes are added to the maintained ontology during the evolution process while 68 terms (classes and individuals) are removed from it during the pruning process.

***Keywords*—** Ontology Maintenance, Ontology Engineering, Medical informatics, Knowledge Discovery, Multiple Sclerosis.

I. Introduction

THE ontology maintenance have several definitions; Madeche and Volz [1] have defined it as a complex process that consists of two subprocesses; the ontology evolution and the ontology pruning. They consider the ontology evolution as the refinement of the ontology elements, whereas the ontology pruning is the verification of the relevance of the ontology elements according to the domain of interest. Luczak-Rosh [2] has defined the ontology maintenance as the evolution of the ontology that is used by an application. Shaban-Nejad and Harrslev [3] assumed the ontology maintenance focuses on the detection of changes that are occurred on the ontology. Finally, Doing-Harris and colleagues [4] have defined the ontology maintenance as the extension of the current ontology. Almost all the researchers assumed the ontology maintenance as the evolution of the ontology.

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Haase and Stojanovic [5] and Plessers et al [6] have defined the ontology evolution as the adaptation and the updating of the ontology depending on the changes that are occurred in the domain of interest.

Various ontology evolution systems are implemented to evolve the medical and biomedical ontologies such as SemCado [7], DyKosMap [8], subontology evolution [9], SEAM [4] and a medical ontology evolution system [10]. All the previous systems focus on the maintenance of the medical ontology according to the evolution notion except the medical ontology maintenance system that implements both of the ontology evolution process as well as the pruning process.

The objective of this article is the use of the ontology evolution system which is developed by the authors of this article [10] and an ontology pruning subsystem to maintain the MS ontology [11] that is provided by Bioportal [12]. This ontology is released at the end of 2014. It involves 1174 classes that reflect the treatments, pathology and clinical finding terms of the MS disease. The other ontology elements are classified as follows: 13 object properties, 9 individuals and 3 data properties. This paper is organized as follows; section 2 provides the medical background of the MS disease, section 3 provides the application of the ontology maintenance system on the MS ontology along with its validation and section 4 contains the conclusions and future work.

II. Medical Background

The statistics of the MS disease [13] that are provided by the atlas of MS [14] (A common project between World Health Organization (WHO) [15] and the Multiple Sclerosis International Federation (MSIF) [16] indicate that the number of patients who suffer from MS is 2.3 million in 2013, while there are only 2.1 million MS cases in 2008. As figure 1 demonstrates, both of north America continent and the north Europe regions have the highest prevalence of MS (140 and 108 per 100000 respectively). In contrast, the east Asia regions and Sub-Saharan Africa recorded the lowest prevalence of MS (2.1 and 2.2 per 100000 respectively). The MS is an autoimmune disease [17] that belongs to the neurological autoimmune diseases group [18]. It attacks usually people whom their age starts from 15 to 60. It affects the female more than males with a ratio 2:1.

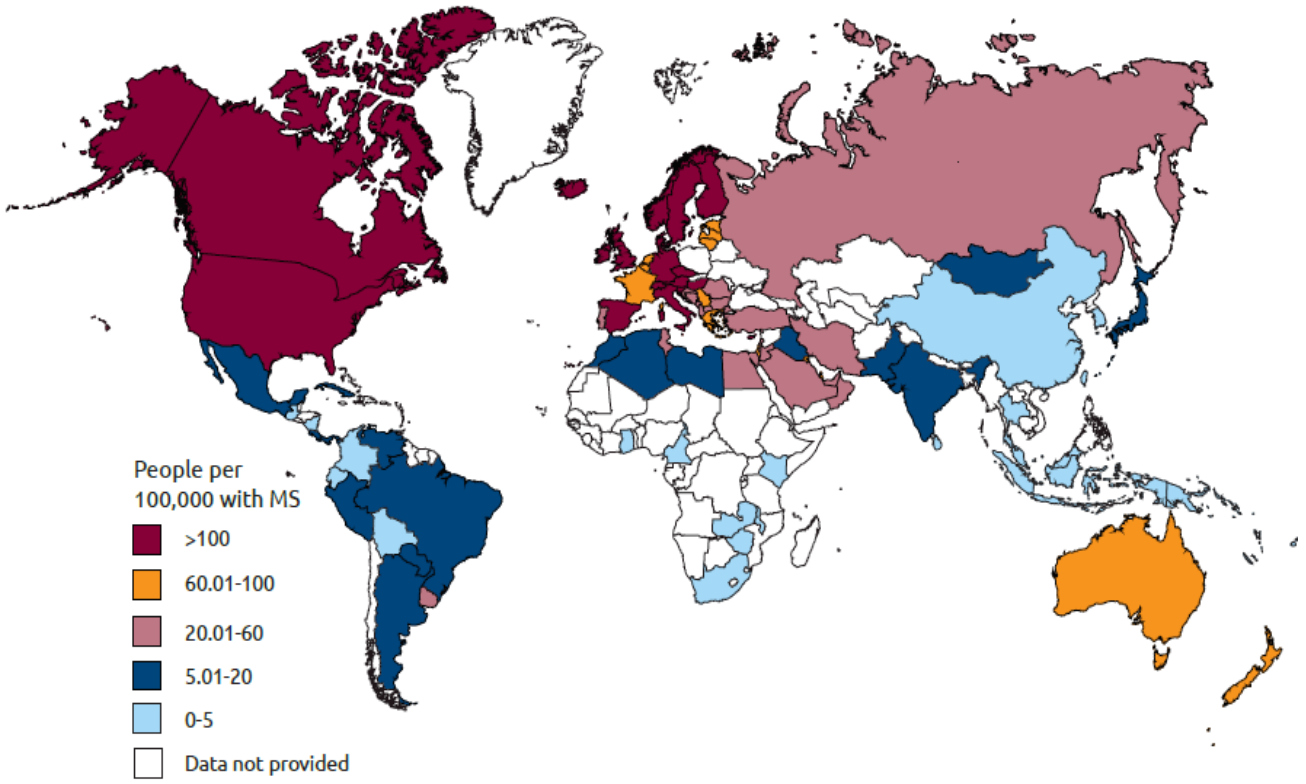

Fig.1 The Prevalence of MS by Country [13]

The MS damages the myelin sheath that surrounds the nerve fibers. The myelin communicates the brain with the other body parts. The symptoms of the MS [17] differs from person to another but the common symptoms involve fatigue, vision problems, numbness and tingling, muscle stiffness, muscle spasms, muscle weakness, mobility problem, bladder problems, thinking problems, learning problems and speech difficulties

The MS patients take a set of treatments to manage the previous symptoms. The MS treatments [19] are classified into two main sets of corticoids medication and disease modifying drugs. Examples of these treatments are; Daclizumab, Fingolinod, Interferon beta 1-a, Mitoxantrone and Teriflunomide. There are a set of laboratory tests to diagnose the MS such as the Magnetic Resonance Imaging (MRI), spinal tap and evoked potential tests (tests used to measure the electrical activity in parts of the brain). The evoked potential tests involve the Visual Evoked Potentials (VEP), Brainstem Auditory Evoked Potentials (BAEP) and Sensory Evoked Potentials (SEP). The urinary tract test is applied to verify the existence of bladder problems. There are biomarkers tests, under development, that can be used for the diagnosis.

III. Applying the Ontology Maintenance System to the Multiple Sclerosis Ontology

As figure 2 demonstrates, the ontology maintenance system is composed of two subsystems; the ontology evolution subsystem and the ontology pruning subsystem. Both of them depend on the use of trusted medical data sources such as the UMLS metathesaurus [20], Rxterms [21] and a MS corpus.

The goal of the ontology evolution subsystem is to update an existing medical ontology in a consistent way. It enables the user to implement basic and complex changes to the ontology.

The basic changes involve the addition / removal / modification of ontology elements (classes, individuals, object properties and data properties) and the complex changes involve the split, merge and move operations. In addition, the evolution subsystem discovers the new treatments that are applied in a particular disease. The evolution subsystem compares the ontology elements (classes and individuals names) with the UMLS concepts that belong to a specific disease. If an UMLS concept doesn't exist in the current ontology, the evolution subsystem adds it to the ontology. The goal of the pruning subsystem is to verify the evolved ontology in order to keep its elements relevant to the domain of interest.

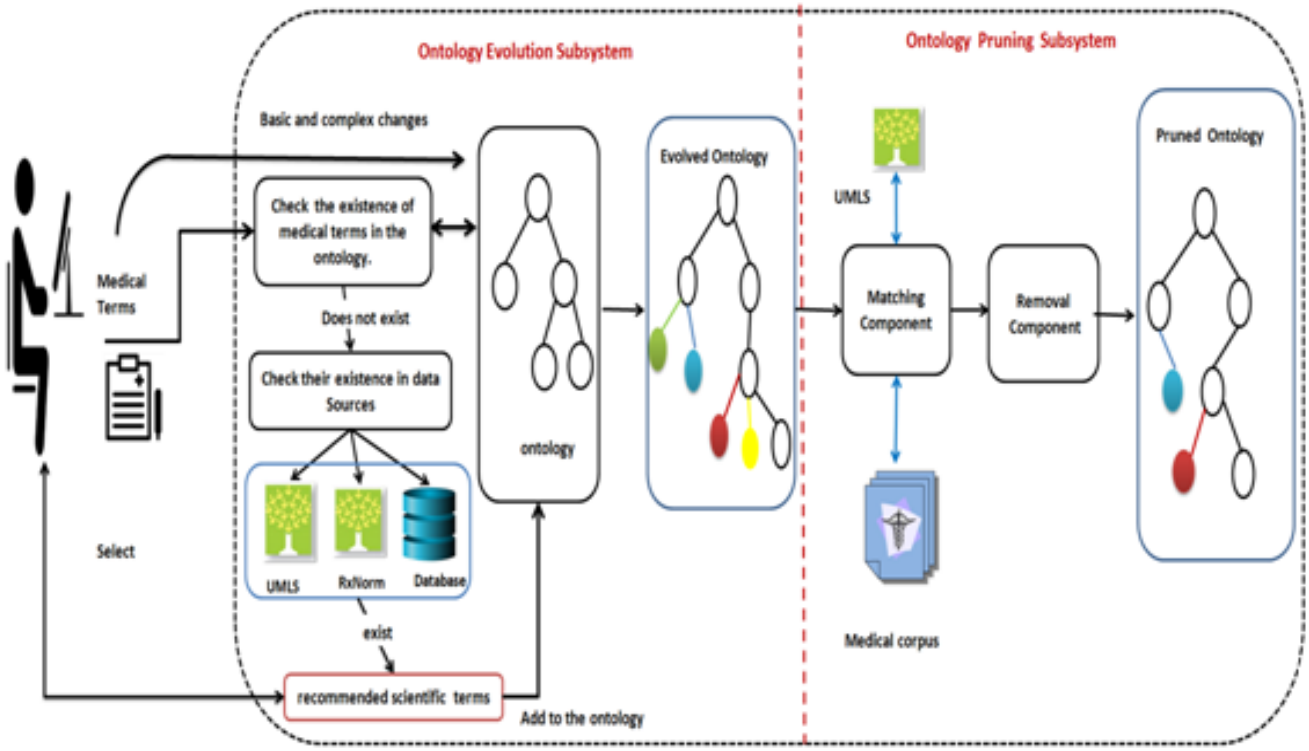

Fig.2 The Ontology Maintenance System Architecture

A detailed description of the proposed maintenance system along with a comparison between this system and other evolution systems/approaches is presented in [10].

A. MS Ontology Evolution

The evolution is implemented on the MS ontology by two ways; automatic and semi-automatic. For the automatic evolution, the system takes the MS ontology as input and extracts all the ontology classes and individuals to compare them with the UMLS metathesaurus (only the concepts that belong to the MS disease are considered). The comparison takes into consideration the synonyms of each class and individual through the use of a treatment database, the UMLS metathesaurus and the Rxterms. If the evolution subsystem detects new treatments that their synonyms do not exist in the current MS ontology, it adds them to the MS ontology. For the semi-automatic evolution, the system takes the current MS ontology and enables the user (physician, patient, health care personnel…etc) to implement the basic and complex changes on the MS ontology taking into account the ontology consistency; for example:

- If the user decides to delete a class, all its subclasses will be deleted too.
- If the user decides to split a particular class, the evolution subsystem ensures that the new classes inserted by the user do not exist in the current MS ontology.

Concerning the automatic evolution of MS ontology, it focuses on the discovery of new treatments. The ontology evolution subsystem compares the MS ontology elements (classes and individuals names) to the UMLS drugs that belong to the MS disease and immunosuppressive drugs and discovered three new treatments; two of them belong to immunosuppressive drugs (Mercaputorine and Azaserine) and one term (baclofen) is a drug used for the management of Multiple Sclerosis.

Since the MS disease belongs to the autoimmune diseases, three experts who work in the immunology domain are consulted to validate the recommended treatments. The first expert works in Hotel Dieu de France, Lebanon. The other two experts work in the World Health Organization. A set of treatments and their synonyms recommended by the automatic evolution process are presented to the experts. All of them suggest eliminating the synonyms of the treatments specially the Mercaptopurine treatment, which involve 19 synonyms provided by the UMLS. In addition, two experts suggest classifying the treatments into three sets:

- Treatments that are used in the MS disease.
- Treatments that belong to the immunosuppressive drugs used in general for the autoimmune diseases (some of them can be used for the MS disease therefore they should be taken into consideration).

- Treatments that belong to the immunosuppressive drugs and can be used in the MS disease.

The ontology evolution subsystem suggests three treatments Baclofen, Mercaputorine and Azaserine. The three experts confirm that the terms Baclofen and Mercaputorine are used for MS while they exclude the term Azaserine.

In addition, one of the experts recommends to add a treatment called Tecfidera to the MS ontology, the evolution subsystem discovers its existence in the ontology with its scientific name; dimethyl fumarate. Therefore, the evolution subsystem did not add it to the MS ontology in order to keep its consistency.

B. MS Ontology Pruning

The pruning of MS ontology is implemented through two phases; the matching phase and the removal phase. In the matching phase, the evolved MS ontology is imported to the pruning subsystem as an input. All the MS ontology classes and individuals are matched with the UMLS concepts that belong to the MS disease and the medical corpus. The medical corpus is determined by two experts of immunity diseases who work in the WHO. The medical corpus involves the following corpora:

- Multiple Sclerosis medication provided by drugs.com [22, 23, 24].
- Multiple Sclerosis medication provided by the National Multiple Sclerosis Society [25].
- Multiple Sclerosis medication provided by Medscape [26].
- Multiple Sclerosis treatment provided by the National Health Service (NHS) in England [27].
- "Making The Diagnosis Of Multiple Sclerosis" article [28].
- Pubmed articles which are:
    - Multiple Sclerosis: diagnosis, management and prognosis [29].
    - Evolving concepts in the treatment of relapsing Multiple Sclerosis [30].
    - Treatment of Multiple Sclerosis relapses with high-dose methylprednisolone reduces the evolution of contrast-enhancing lesions into persistent black holes [31].
    - Oligodendrocyte cell death in pathogenesis of Multiple Sclerosis: Protection of oligodendrocytes from apoptosis by complement [32].
    - Enolase autoantibodies and retinal function in Multiple Sclerosis patients [33].

The output of this phase is a list of unmatched classes and individuals that are not relevant to the MS disease. The total number of the unmatched classes and individuals are 68 terms that are not found in the UMLS and the medical corpus. In the removal phase, the pruning subsystem deletes the unmatched classes and individuals from the MS ontology.

IV. Conclusion and Future Work

This paper presents an ontology maintenance system that is applied to the MS disease. It recommends to the user both of new terms which belong directly to the MS disease and the new terms which belong to the autoimmune diseases. The ontology maintenance system enables the user to accept or reject those terms. In addition, it allows the user to perform basic and complex changes on the MS ontology taking into account its consistency. The use of the UMLS and the medical corpus is a way to validate the terms that exist before and after the evolution. Three human experts validate the output of the system. In future work, the ontology maintenance system will be applied to other diseases.

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