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A Semantic Clinical Decision Support System: conceptual architecture and implementation guidelines

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Abstract. Clinical Decision Support Systems (CDSS) are computer applications that focus on assisting medical decisions required during clinical tasks. Although CDSS have been extensively studied for more than 30 years, their use is not broadly extended yet in daily clinical practice. Identified challenges of CDSS include (*i*) automating decision support, (*ii*) clinical workflow integration, (*iii*) ability of the system to be maintained and extended, (*iv*) timely advice and (*v*) evaluation of decisions effects and costs. In this paper, we hypothesize that Knowledge Engineering techniques and semantic technologies could be applied to CDSS in order to overcome the current identified challenges. We present a generic architecture for a Semantic CDSS, which we call SCDSS, and implementation guidelines for the breast cancer domain. Our approach follows a cyclic-federated paradigm allowing the reutilization of knowledge gathered at every stage of the clinical cycle.

Keywords: Decision support system, architecture, implementation, breast cancer

1 Introduction

Clinical Decision Support Systems (CDSS) are active knowledge resources that use patient clinical data to generate case specific advice [1]. Such advice is aimed at assisting clinicians during decision making about individual patients, in the following aspects: (*i*) to manage the huge quantity of knowledge involved, (*ii*) to focus attention on relevant aspects of their treatment, (*iii*) to provide patient-specific recommendations and (*iv*) to reduce avoidable medical errors [2,3].

CDSS are reportedly not completely integrated in daily clinical environments [2,4,6]. The reasons for this lack of success have been studied by some authors [2,3,5], who have identified the main challenges that CDSS have to face: (*a*) computerizing decision support, for which improvements in reasoning capabilities are still in need; (*b*) clinical workflow integration, needing efforts in order to integrate CDSS with clinical systems already present in hospitals and medical centers; (*c*) maintaina-

bility and extensibility of CDSS [3], which requires the development of mechanisms for the evolution of the knowledge bases and the criteria of CDSS; (*d*) timely advice, for which solutions providing (quasi) real time answers are needed, and (*e*) evaluation of the effects and costs of the CDSS itself, which leads to a need of mechanisms for the quantitative and qualitative evaluation of the performance of the system and the knowledge embodied in it [3]. Additionally, the creation of an architecture for sharing executable clinical decision support modules and services is identified a grand challenge in [5].

In particular, clinical workflow integration is only achieved if reutilization of knowledge between the different stages of clinical tasks, such as diagnosis, prognosis, treatment, monitoring and prevention, is provided [6,7]. Approaches covering only the knowledge involved during one of the stages are not enough, as decisions in stages carried out later could be influenced on decisions of previous stages [7].

To overcome the reported gaps, we propose a clinical tasks model that is both, cyclic and federated. This twofold view of the model is achieved by the use of semantic technologies. For this reasons, in this paper we also propose a novel idea of Semantic CDSS (SCDSS). We present a general architecture for SCDSS, which is aimed at covering as well the rest of the aforementioned challenges. Additionally, a case study of this architecture is also presented, oriented at a CDSS for diagnosis and treatment of breast cancer.

This paper is arranged as follows: in section two the related work which is relevant for our approach is presented; in section three the cyclic and federated model for clinical tasks is introduced and a generic architecture for SCDSS is proposed; in section four implementation guidelines for the breast cancer domain are presented, and lastly in section five, the conclusions and future work are summarized.

2 Related concepts

The generic architecture of CDSS presented in this paper is based on (*i*) the proposed clinical task model, (*ii*) semantic technologies and (*iii*) multi-agent systems. In this section we present a short overview of the previous work mentioning briefly concepts related to these three aspects.

2.1 Clinical tasks and decision support

During daily clinical practice, clinicians need to perform different clinical tasks oriented to provide the best care for their patients. The key stages of clinical tasks include [6,7]: (*a*) **diagnosis**, the process that identifies the syndrome or the disease of the patient; (*b*) **prognosis**, the process of generation of a set of previsions about the pathologic process that affects the patient, such as life expectancy and future complications; (*c*) **treatment**, the process of understanding the global effects of a diagnosed disease on a patient and prescribing an appropriate therapy or pre-established medicament; (*d*) **monitoring**, the follow up of patients during the evolution of the disease,

the treatment or once the patient has been recovered, and (*e*) **prevention**, the process aimed at avoiding a disease.

During clinical decision making clinicians apply knowledge and experience acquired during some stages in decisions of other stages. Hence, decision support must handle this knowledge reutilization. In section three, we will propose a cyclic and federated clinical task model that reflects these ideas and permits the seamless integration of decision support techniques during the clinical workflow.

2.2 Knowledge-based clinical decision support

Knowledge Engineering (KE) techniques and semantic technologies have been described in the literature as a promising approach to solve knowledge handling and decision support in the medical domain [8,9]. With the application of semantics in CDSS, the reutilization of the knowledge generated during the different clinical tasks is possible [9]. In particular, the use of ontologies for the modeling of domain knowledge in medical applications has been broadly studied [8]. Ontologies are defined by Gruber [10] for the computer science domain as the explicit specification of a conceptualization. Among others, they also deliver interesting benefits when used for reasoning and inferring of new knowledge [9].

Semantic CDSS have been previously reported, such as the semantic web framework for CDSS presented by Hussain et *Al.* [12], which is focused at computerizing clinical guidelines. Nevertheless, the reutilization of knowledge among different stages of clinical tasks is not covered. We intend to bridge this aspect with the use of multi-agent systems, as we describe in Section 3.2. Colantonio et *Al.* [11] present an interoperable and standardized CDSS based on ontologies and a rule-based reasoner. However, evolution of concepts and their maintainability is not covered in their work. Additionally, and even if the proposed CDSS is intended to be integrated in the whole clinical workflow, the different stages are proposed as separate tasks, and no direct reutilization of knowledge between the stages is supported. We argue that a cyclic and federated approach is needed in order to provide the required knowledge reutilization for the complete integration in the clinical workflow.

We propose in this paper the evolution of the approach presented by Sanchez et *Al.* in [9] where a generic architecture for the semantic enhancement of CDSS was presented. In our former work, the integration of CDSS in the whole clinical workflow was not supported. In addition, system maintainability and extensibility tasks relied on domain experts. The current approach proposes the use of user experience modeling and acquisition technologies, such as Set Of Experience Knowledge Structure (SOEKS) and Decisional DNA (DDNA) [13], in order to allow the evolution of the knowledge bases and the criteria embedded in the system, based on the clinician's previous experience.

2.3 Multi-agent based CDSS

Reutilization of knowledge between different stages of the clinical workflow is needed in CDSS, for which (*i*) each stage needs to be partially independent, and (*ii*) at the

same time connected to a central entity that handles the generated knowledge. These requirements can be correctly approached by Multi-Agent Systems (MAS).

MAS are applications in which many autonomous software agents are combined to solve large problems [14]. In particular, different MAS have been already proposed for medical applications in general, and for clinical decision support in particular [14,15]. They are mainly oriented at the reutilization of medical resources distributed in different health centers, and not to the reutilization of knowledge during the different stages of the clinical workflow.

The work presented by Shirabad et *Al.* in [16] shares some ideas with our approach, such as the focus on supporting the entire clinical decision making process and the use of MAS. Nevertheless no knowledge reutilization is supported between the different stages, as separate decision systems are proposed for each stage. Also, in our approach we provide evolution mechanisms based on user experience, for the knowledge and criteria embedded in the system, which is not covered in [16].

3 Proposed architecture for a Semantic CDSS

In this section we propose (*i*) a clinical task model that allows the reutilization of knowledge among the different stages of clinical tasks, and (*ii*) a generic architecture for multi-agent SCDSS that follows this model.

3.1 Proposed Clinical Task Model

Some authors have modeled clinical tasks as cyclic, such as in the work of Ramaswamy et *Al.* [17]. For instance, after the application of a treatment to a patient, the evolution could not be as expected and a different diagnosis would need to be made. With this new diagnosis the cycle would start again with a new prognosis, treatment, (and when applicable) monitoring and prevention plans. Actually, in clinical practice, conclusions obtained during the different stages are not definite [7] and new results coming from next stages may change conclusions that were obtained in previous ones.

We share this view partially, in which clinical tasks are defined as cycles consisting of diagnosis, prognosis, treatment, monitoring and prevention stages. Nevertheless, with a cyclic model, clinical tasks are not completely defined. Actually, the stages performed in every cycle could vary. Moreover, the different stages do not necessarily need to form part of the cycle and could also act independently.

On the other hand, decision support must handle the knowledge involved during the whole clinical workflow, as medical professionals need to handle the decisions and the experience generated among all the different stages [7]. For this reason, reutilization of knowledge among different stages is necessary.

This reutilization of knowledge can be achieved if each stage is both (*i*) independent, but (*ii*) at the same time is related to a central entity that controls the generated knowledge for its reutilization.

This idea is similar to a federation in the political domain, which is a type of sovereign state characterized by a union of partially self-governing states or regions united by a central government [18]. In the CDSS domain, the same concept can be applied, if the clinical stages are partially independent entities united to a central one that controls the knowledge generated by each of the stages, for its reutilization within the whole clinical workflow.

Thus, we propose the combination of a cyclic and federated model for clinical task, as is depicted in Fig. 1. In our model diagnosis, prognosis, treatment, monitoring and prevention are partially independent stages, which (*i*) follow a cyclic paradigm and (*ii*) are united to a central SCDSS. This SCDSS handles the knowledge and experiences acquired in each stage and reuses them on following ones. In this way, knowledge sharing between stages is supported, with no semantic loss. In fact, the use of semantic technologies allows the system to be federated as well as cyclic.

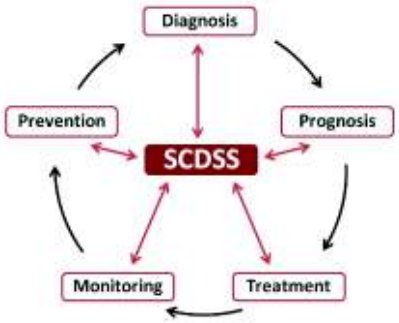

Fig. 1. Proposed lifecycle for clinical decision support

3.2 Proposed semantic multi-agent based generic architecture

The approach proposed in the previous section imposes some requirements to the SCDSS from the architectural aspect: (*i*) each stage needs to be independent, but (*ii*) at the same time connected to a central entity that handles the generated knowledge. In fact, our system should provide specialization, to cover the different tasks performed during the stages, and control, to handle the knowledge and the performance of the system.

Both specialization and control capabilities are adequately approached by multi-agent systems, where each agent can be oriented at specific tasks. These tasks also cover inter-agent communication and synchronization.

Therefore a generic multi-agent based architecture for SCDSS is proposed in this Section. In particular, 8 agents are proposed in the architecture: (*i*) information agent, (*ii*) data translation agent, (*iii*) standards and interoperability agent, (*iv*) reasoning and model agent, (*v*) experience acquisition agent, (*vi*) application agent, (*vii*) user profiling agent and (*viii*) the majordomo agent.

The use of the agents-based paradigm provides the system with modularity, so that scalability and reutilization in other domains is supported. New agents could be im-

plemented and added to the system to enrich it, and the rest could be reused. For instance, agents for different diseases or domain models could be implemented, as well as agents communicating with local data repositories or clinical systems from different hospitals. Thereby, this architecture could be integrated in the whole clinical workflow and decision support could be offered as a service for different domains and different hospitals. Furthermore, this architecture is based on a cloud paradigm, where more resources for a specific agent are allocated when more resources are needed. Fig. 2 depicts an overview of our architecture.

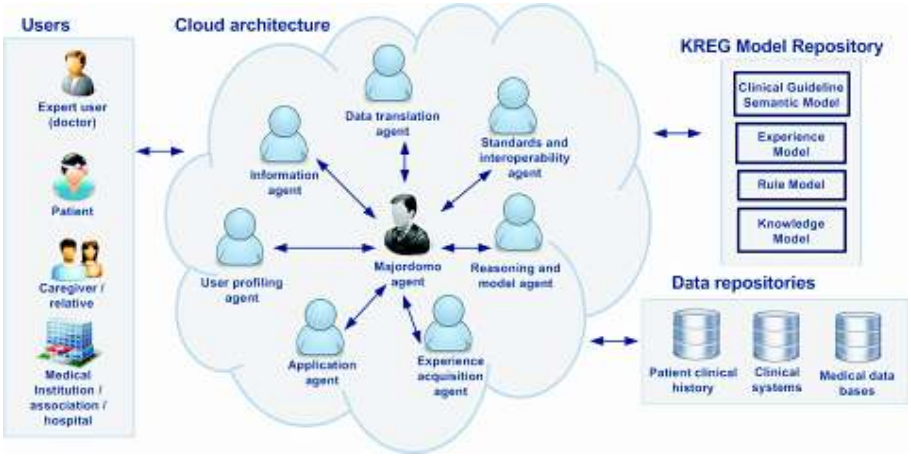

Fig. 2. Proposed architecture for Semantic Clinical Decision Support Systems

The **information agent** gets information from the different accessible data bases, medical image repositories and clinical systems. It is common to find that these DB are heterogeneous, as well as spatially disperse.

The **data translation agent** translates the data structure in each data base to the knowledge model stored in the ontologies of the Knowledge-Rule-Experience-Guideline (KREG) Model Repository. The KREG Model is a four-layered model containing the knowledge model (aligned domain ontologies), set of production rules containing the criteria for the reasoning, user experience model and computerized clinical guideline semantic model.

In order to provide interoperability to the system the **standards and interoperability agent** is in charge of aligning the knowledge model with standards such as HL7 and ISO 13606, and standardized ontologies such as SNOMED CT and ICD-10.

The **reasoning and model agent** interacts with the KREG Model, a semantic reasoner and the query engine in between, in order to obtain the inferred responses that will aid clinicians during decision making.

During these reasoning processes, with regard to face the aforementioned timely advice challenge and provide quasi-real time performance, the use of fast query systems such as Reflexive Ontologies (RO) [13] is proposed.

The **experience acquisition agent** gathers user experience and stores it in the aforementioned Experience Model. With this experience, the system is able to evolve

the knowledge and rule models, in the same way as clinicians evolve the criteria for making decisions from the conclusions obtained during daily experiences. In this way, the maintainability and updating of the KREG Model is supported by an upper experience layer.

The **application agent** is in charge of the interaction between the user and the system, that will be held by graphical user interfaces (GUI) oriented at different purposes: (*i*) decision support, (*ii*) authoring tools for the edition or visualization of the underlying models, and (*iii*) patient interface for accessing clinical results, non-clinical results and biosignals coming from user medical devices. Visual analytic techniques will be presented to facilitate the visualization of patient data, criteria for decision, next steps on the process, and most probable diagnosis or suitable treatments for a specific patient, among others.

The **user profiling agent** detects different users of the system, characterizes them, and provides them the corresponding user interfaces they can access. The different users could be doctors (or domain expert users), patients, relatives/caregivers, and/or medical institutions, associations and hospitals.

Finally, **the majordomo agent** synchronizes and controls the other agents. It is in charge of the communication between agents, so that each one only communicates with it. Thereby, security issues are reduced and inconsistencies due to simultaneous communications between different agents are avoided. Whereas the rest of the agents are specialized in different task, the majordomo agent controls the knowledge and performance of the rest of the system.

4 Implementation guidelines: SCDSS for breast cancer

We will use as an example the case of breast cancer, in order to present a domain that can be easily understood by most of the readers. Let us assume that a given patient visits a clinician after having discovered by palpation a lump in the breast.

During the first visit, the clinician starts with the diagnosis phase. It consists of gathering the relevant clinical history of the patient, the results of physical explorations as well as the required complementary explorations. Then, the clinician analyzes these patient data and makes the diagnosis of the patient, as well as the prognosis and the treatment plans, based on his prior experience. Once the treatment has started, patient's follow-up plans and prevention actions are also decided by the clinician. It could happen that during the follow-up of this patient, some new symptoms reveal a variation on the diagnosis of the patient, for which a different treatment procedure is required. During the whole process the clinician follows clinical guidelines on breast cancer domain.

Let us assume that the clinician has a SCDSS during the aforesaid process. When the clinician logs in the system, the **majordomo agent** takes control of the tasks to be performed by the rest of the agents, and it is in charge of the communication between them. This communication must be encoded, due to the confident character of medical data.

The next step is the user characterization. In order to do so, the **user profiling agent** starts working by request of the majordomo agent. A good user characterization is provided by a user profiling tool that uses the minimum number of parameters that could characterize user behavior and user attributes. There exist some user characterization modules such as GOMS [20], that present implementation and logic modules for user characterization.

Once a user is characterized, the **application agent** deals with the interaction between the user and SCDSS. The application agent should follow dialog based recommendations and should be visually appealing, easy to handle and, when possible, web based. Having in mind the nowadays tendency to use handheld devices, tablets and multi-touch computerized environments, Graphical User Interface (GUI) implementation should move towards connectivity and easy interaction. In other words, classical point-and-click GUI should be avoided in favor of more natural ways of interaction that include voice recognition, gesture based and behavioral GUI.

The clinician is then able to introduce the gathered results in the system, which should be stored in the **Patient DB** of the SCDSS. Optionally, these data could be stored in an external clinical system that offers standard communication interfaces with the SCDSS. In this case, **the standards and interoperability agent** should manage the access to these data, by dealing with HL7 and ISO 13606 standards. The **Information agent** deals with the access to data in the Patient DB, in both directions. In order to provide a quasi-real time response, the information agent should implement fast data accessing protocols.

The reasoner modules used by the SCDSS needs the data to be translated to upper (more complex) knowledge models, with which the semantic reasoning processes are possible. The **Data translation agent** translates the data structure in the aforementioned Patient DB to the KREG model. This translation process should be consistent. In [9] we developed a flexible translation module, based on an xml paradigm. Everytime data is created or modified in the DB, two xml documents are created in real-time, containing both, (*i*) the new data structure and (*ii*) the query calls.

The reasoning process to infer the corresponding diagnoses, prognoses, treatment plans, monitoring plans and prevention actions is handled by the **Reasoning and model agent**. All output should be shown to the clinician as recommendations with their attached prove. We recommend the use of semantic reasoner tools such as Pellet or FaCT++. In order to speed up the reasoning process, fast query engine techniques, such as Reflexive Ontologies (RO) [13] could be applied.

For the **Knowledge model** we recommend the use of OWL DL for the formalization of the domain ontologies. Nevertheless, depending on the semantic load of the system, OWL 2.0 could also be interesting, as range assignation is supported. Mappings to standard domain ontologies are suggested, as proposed in the work of Toro et *Al.* [19]. In particular, and following the work by Sanchez et *Al.* [9] we argue that three ontologies are sufficient for the modeling of the breast cancer domain: (*i*) SNOMED CT, for clinical description of the patient, the disease and the procedures involved; (*ii*) SWAN, for bibliographic endorsement of clinical criteria, and (*iii*) a domain ontology of breast cancer, containing the results of the specific clinical tests carried out to patients.

The **Rule model** should consist of an initial set of production rules given by domain experts. We suggest the use of an easy to use and implement rule system in order to facilitate rule handling (i.e. deprecation, extension, etc). We recommend the use of a rule syntax that follows an IF-THEN-ELSE structure and that is both, (*i*) weighted within an importance hierarchy of rules, and (*ii*) endorsed by the corresponding bibliographic source. Also an easy serialization language should be supported by the model, such as xml. We proposed in [9] a rule model that follows these requirements. The rule syntax in [9] is similar to Rule ML, but with a twist as Rule ML does not support neither rule weighting nor bibliographic endorsement. Our format is not public yet, although we are working to offer it in the near future.

In the **Clinical Guideline Semantic model** an implementation of a Breast Cancer clinical guideline should be developed. For reutilization purposes, we suggest using only computerized clinical guidelines, like the ones presented by ten Teije et *Al.* [21].

We suggest implementing the **Experience model** using DDNA and SOEKS technologies for experience modeling [13]. We recommend the implementation of DDNA following the ontology form, where an OWL DL DDNA/SOEKS Ontology stores the decisional events acquired by the **Experience acquisition agent**. The Experience model should be formed by a collection of Decisional Chromosomes [13] storing the experience of medical institutions or hospitals in different regions. In this way decisions could be regionalized giving a population characteristics aware knowledge system.

5 Conclusions and future work

In this paper we have presented a cyclic and federated clinical task model, which permits the integration and reutilization of decision support systems along the whole clinical workflow. A generic architecture for SCDSS supporting our task model has been also presented. Our architecture overcomes the main challenges of CDSS introduced in Section 1. Implementation guidelines of such architecture for the breast cancer domain have been introduced. Our architecture is based on a multi-agent approach, which provides system modularity, scalability and reutilization.

Regarding lines of future work, we will explore methodologies and tools for the evaluation of the quality and quantity of knowledge and experience in the system.

Also, we will work in the development of new visualization paradigms (e.g. visual analytics), for facilitating better comprehension of the results and gathered data for decision making.

6 References

1. Joseph, L., Wyatt, J.C., Altman, D.G.: Decision tools in health care: focus on the problem, not the solution. In: BMC Medical Informatics and Decision Making 6(4), 2006.
2. Berner, E.S.: Clinical Decision Support Systems, Theory and Practice. Second Edition. Springer, New York, 2007.

3. Peleg, M., Tu, S.: Decision support, knowledge representation and management in medicine. In: Yearbook of Medical Informatics, 2006, pp 72-80.
4. Garg AX, Adhikari NKJ, McDonald H, Rosas-Arellano MP, Devereaux PJ, Beyene J, et *Al.* Effects of Computerized Clinical Decision Support Systems on Practitioner Performance and Patient Outcomes: A Systematic Review. JAMA 293(10), 2005, pp 1223-1238.
5. Sittig, D.F., Wright, A., Osheroff, J.A., Middleton, B., Teich, J.M., Ash, J.S., Campbell, E. and Bates, D.W: Grand challenges in clinical decision support. In: Journal of biomedical in-formatics, 41(2), 2008, pp. 387-392.
6. De Castro, S.: Manual de Patología General. Ed: Pérez Arellano, J.L. 6th edition, ELSEVIER-MASSON, Barcelona, Spain, 2006. (Spanish)
7. Rozman, C.: Compendio de Medicina Interna. ELSEVIER, 3rd edition, Madrid, Spain, 2006 (Spanish).
8. Gnanambal, S., Thangaraj, M.: Research Directions in Semantic Web on Healthcare. In: Jour-nal of Computer Science 1, 2010, pp 449-453.
9. Sanchez, E., Toro, C., Carrasco, E., Bueno, G., Parra, C., Bonachela, P., Graña, M. and Guijarro, F.: An Architecture for the Semantic Enhancement of Clinical Decision Support Systems. A. König et *Al.* (Eds.): Knowledge-Based and Intelligent Information & Engineering Systems, Part II, LNAI 6882, 2011, pp. 611–620
10. Gruber, T.R.: Toward principles for the design of ontologies used for knowledge sharing. In: International Journal of Human-Computer Studies 43(5–6), 1995, pp. 907–928.
11. Colantonio, S., Martinelli, M., Moroni, D., Salvetti, O., Chiarugi, F., Emmanouilidou, D.: A Decision Support System for Aiding Heart Failure Management. In: Proceedings of the Ninth International Conference on Intelligent Systems Design and Applications, Pisa, Italy, 2009, pp 351-356.
12. Hussain, S., Raza Abidi, S., Raza Abidi S.S.: Semantic Web Framework for Knowledge-Centric Clinical Decision Support Systems. In: Bellazzi, R., Abu-Hanna, A., Hunter, J. (eds.) Artificial Intelligence in Medicine. LNCS 4594, 2007, pp. 451-455.
13. Toro, C., Sanín, C., Szczerbicki, E., Posada, J.: Reflexive Ontologies: Enhancing Ontologies with self-contained queries. In: Cybernetics and Systems 39, 2008, pp 171-189.
14. Isern, D., Sanchez, D., Moreno, A.: Agents applied in health care: A review. In: International Journal of Medical Informatics 79, 2010, pp. 145-166.
15. Paranjape, R., Sadanand, A.: Multi-Agent Systems for Healthcare Simulation and Modeling: Applications for System Improvement. IGI Global, Hershey, PA, USA, 2010.
16. Shirabad, JS., Wilk, S., Michalowski, W., Farion, K.: Implementing an Integrative Multiagent Clinical Decision Support System with Open Source Software. In: Journal of Medical Systems 36(1), 2012, pp 123-137.
17. Ramaswamy, M., Ortiz-Fournier, L.: Healthcare knowledge collection for clinical decision support systems. In Issues in Information Systems 11(1), 2010, pp. 538-546.
18. Xing, L., Shengjun, Z.: One mountain with two tigers – China and the United States in East Asian Regionalism. In: Perspectives of federalism 2(3), 2010, pp. 110-129.
19. Toro, C., Graña, M., Posada, J., Vaquero, J., Szczerbicki, E.: Domain Modeling Based on Engineering Standards. In: Knowledge-Based and Intelligent Information and Engineering Systems LNCS 5711, pp 95-102, 2009.
20. Gray, W. D., John, B. E., & Atwood, M. E.: Project Ernestine: Validating a GOMS analysis for predicting and explaining real-world performance. In: Human-Computer Interaction, 8(3), 1993, pp 237-309.
21. ten Teije, A., Marcos, M., Balser, M., van Croonenborg, J., Duelli, C., van Harmelen, F., Lucas, P., Miksch, S., Reif, W., Rosenbrand, K., Seyfang, A.: Improving medical protocols by formal methods. In: Artif. Intell. Med. 36(3), 2005, pp 193-209.