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A core ontology of instruments used for neurological, behavioral and cognitive assessments

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Abstract. Neurosciences are progressively moving into a mass computational intensive era with the fusion of numerous large heterogeneous data sets from cellular to system level. To process and share this mass of information in a consistent and computational amenable form, computerized techniques – among them, ontologies - are currently designed to store, analyze and access this information. Recently, we proposed a multi-layered and multi-components ontology to deal with MR images and regions-of-interest that can be represented onto the images. In the present paper, we extend our initial ontology by adding a core ontology of subject data acquisition instruments modeling neuroclinical, neuropsychological and neurobehavioral tests used for neurological, behavioral and cognitive skills assessment. This ontology deals with instruments \textit{per se} as specific artefacts, their variables and measured scores, and actions performed using instruments. In the paper, we underline the major aspects of our approach and emphasize its potential interest as a semantic reference for various neuroscience applications.

Keywords. Biomedical ontology, Artefact ontology, Knowledge Representation, Neuroscience, Brain

Introduction

Similarly to other biomedical scientists, neuroscientists collect facts, use knowledge (what they currently know about these facts) and then make inferences to produce new knowledge and facts [4]. As a consequence, there is a crucial need for computerized techniques to store, manage, analyze and share this information [1][36]. Alike bioinformatics with \textit{in silico} experiments [33], neuroscience is progressively moving into a mass computational intensive era with fusion of various large heterogeneous data sets from cellular to system level [23]. These datasets are often disseminated in various medical centers and carried out in highly distributed environments such as grids [31][36]. Many research groups in various institutions make strong efforts to develop
federated and distributed infrastructures for biomedical imaging data [2][14][18]. To process the mass of information in a consistent and computational amenable form, ontologies have become recently very important in neurosciences [19][34]. The prominent effort in this direction is currently done via the Biomedical Informatics Research Network (BIRN) which proposes, based on an ontology-based vocabulary called BIRNLex a unified representation of the biomedical domains typically used to describe neuroscience data [5]. This ontological effort is driven by the OBO (Open Biomedical Ontologies) initiative that promotes shared biomedical ontologies[32].

In Neuroscience, imaging plays a central role providing information about brain structure and function. Among the different imaging modalities, Magnetic Resonance Imaging (MRI) strongly contributes to studying the healthy and the pathological brain, from both anatomical and functional perspectives and appears as the cornerstone of most cognitive studies [22]. In parallel with MRI images, questionnaires and batteries of tests are currently used to assess the neurological state of the subjects as well as their cognitive and behavioural performances. All these instruments focus on specific brain functions, which rely on specific anatomical structures or pathways, so they can be used in diagnosing brain dysfunction or damage and measuring intensity/severity of a subject’s trait (e.g. behavioral, personality, psychological, psychopathological) [21]. Such tests and questionnaire-based interviews are complementary to MR images to investigate the correlation between measures of brain structure and function, derived from MR image analysis, and neurological, cognitive and behavioural traits, highlighted by test- and questionnaire-based assessments [9].

Recently, we proposed a multi-layered ontology (named OntoNeuroLOG) to deal with MR images and regions-of-interest that can be represented onto the images [34]. In the present paper, we extend our initial ontology by adding a new component to model the general characteristics of the neuroclinical, neuropsychological and behavioral tests and scores mostly used. To our knowledge, this significant effort represents the first attempt to model this kind of data. This core ontology is currently specialized for sharing data between four French neuroimaging centres through the federated NeuroLOG architecture², leading to the conceptualization of specific classes of instruments.

The paper is organized as follows: in the next section we remind of the most generic modules of OntoNeuroLOG onto which our Instrument ontology relies, especially the foundational ontology DOLCE³ and a formal ontology of artefacts recently designed [17]. We then detail our main contribution, an ontology of subject data acquisition instruments, including instruments per se as specific technical artefacts, with their variables and scores associated, and actions performed using an instrument. In the Discussion section we underline the major aspects of our approach and emphasize in Conclusion its potential interest as a semantic reference for various neurosciences applications.

1. Methods: Our ontological reference framework

To define the OntoNeuroLOG ontology, we adopted a multi-layer and multi-components approach [35]. OntoNeuroLOG is organized into sub-ontologies (modules)

² see http://neurolog.polytech.unice.fr/doku.php
³ http://www.loa-cnr.it/DOLCE.html
with different levels of abstraction. Schematically, three levels can be identified: at the
most abstract level, the foundational DOLCE ontology [24] provides a set of abstract
corcepts (e.g. physical object, event, quality) and relations (e.g. parthood, constitution)
for structuring (by specialization) any type of domain. At this level, DOLCE is
supplemented by a few ontologies such as a formal ontology of artefacts [17]. At an
intermediate level, “core” domain ontologies [12] define generic and central concepts
in various domains such as medical images [34] or programs and software [20]. Lastly,
at the most specific level, the previously mentioned ontologies are then specialized to
define more specific concepts in the field of neuroimaging and image processing tools,
respectively.

We adopt two different modeling languages for specifying our ontologies. At a
developmental stage, modeling choices are specified – in the context of OntoSpec
methodology [16] – by means of a semi-informal language which is semantically rich
and includes temporally-indexed relations and meta-properties of the OntoClean
methodology [13]. At run-time, the ontologies are encoded in a dialect of OWL –
OWL-Lite augmented with rules – which is semantically much poorer than the former
but allows for effective automatic inferences (the semantic search engine Corese [8] is
currently used within the NeuroLOG project).

The new ontology of subject data acquisition instruments is situated at the
intermediate level of core ontologies. Its definition relies on abstract primitives
provided by generic ontologies (a list of these modules is presented in Table 1).
Furthermore, it is used to model classes of specialized instruments (e.g. neuroclinical
and neuropsychological instruments) which correspond to “domain” ontologies.

In the following part of this section, we remind of the main structuring principles
and concepts provided by the modules of Table 1.

Table 1. Domains covered by most generic modules composing OntoNeuroLOG, along with the location of
their OntoSpec manifestation (prefix=http://www.laria.u-picardie.fr/IC/Site/IMG/pdf)

<table>
<thead>
<tr>
<th>Module</th>
<th>domains</th>
<th>Location of OntoSpec manifestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Particular</td>
<td>Endurant, perdurant, quality, abstract</td>
<td>prefix/Particular-OS.pdf</td>
</tr>
<tr>
<td>Action</td>
<td>Deliberate action, intentional action, physical action, conceptual action</td>
<td>prefix/Action-OS.pdf</td>
</tr>
<tr>
<td>Participant role</td>
<td>Agent, substrate, consequent, result, instrument</td>
<td>prefix/Participant-role-OS.pdf</td>
</tr>
<tr>
<td>Function &amp; artefact</td>
<td>Artificial object, functional object, artefact, technical artifact, social artefact</td>
<td>prefix/Function-artefact-OS.pdf</td>
</tr>
<tr>
<td>Inscription &amp; Expression &amp; Conceptualization</td>
<td>Support, inscription, Linguistic expression, concept, proposition</td>
<td>prefix/Inscription-OS.pdf</td>
</tr>
</tbody>
</table>

1.1 DOLCE

DOLCE’s domain is that of Particulars⁴, that is to say entities that cannot be
instantiated (e.g. “my car”) rather than universals (e.g. “being a car”). Four sub-
domains of Particulars are distinguished (see Fig. 1):

⁴ With respect to our notation, the informal labels on DOLCE’s categories appear in the text in the
Courrier new font with First Capital Letters for the concepts and a javaLikeNotation
for relations. The same conventions apply for all the ontologies presented in the paper.
Endurants are entities “enduring in time”\(^5\). Within Endurants, Physical Objects (e.g. a printed copy of an article) are distinguished from Non-Physical Objects (e.g. the contents of this article), this distinction corresponding to a difference between two realities or modes of existence for the entities. Basically, Non-Physical Objects exist insofar as agents speak about them. The domain of Non-Physical Objects covers entities whose existence depends on either an individual (for Mental Objects) or a community of agents (for Social Objects).

Perdurants are entities “occurring in time” (e.g. your reading of this article) in which Endurants temporarily participate.

Endurants and Perdurants have Qualities that we perceive and/or measure (e.g. the weight of the printed copy of an article, the time it takes for you to read this article). Note that these Qualities are inherent to the entity that bears them, since they are characteristic for it and they are present throughout the course of the entity’s existence.

Qualities take “values”, called Qual� (e.g. 25 grams, 20 minutes) within quality region spaces.

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\(^5\) Due to space limitations, we are only able to provide a very brief characterization of DOLCE’s categories and we limit ourselves to categories of use in our ontology of instruments.
Searle’s terms – which differ according to their temporality, role and content [27]. A prior intention consists in planning an action (prior to the realization of the action) and then rationally controlling the action. It relies on a conceptual representation of the type of action to be performed, comprising an objective (i.e. a goal) and, optionally, a means of achieving it (i.e. a plan). Once the action has been initiated, the intention-in-action consists in the continuous guidance and control of the initiated action by relying on a descriptive, context-sensitive representation of the said action.

Taking into account current knowledge on the phenomenology of actions [28], we first assimilate Actions to processes controlled by an intention (intention-in-action and/or prior intention); these contrast with Happenings which lack an intentional cause. We then introduce two specializations of Actions. Firstly, Deliberate Actions are initiated by a prior intention comprising a conceptual representation of the intended goal. Secondly, within Deliberate Actions, Successful Actions are carried out to completion and lead to their intended result.

1.2 I&DA

I&DA is a core ontology in the domain of information content entities and their physical materialization that was initially built for classifying documents by their contents [11]. I&DA extends DOLCE by introducing three main types of entities (see Fig. 2):

- Inscriptions (e.g. printed texts) are knowledge forms materialized by a substance (e.g. ink) and inscribed on a physical support (e.g. a sheet of paper, a hard disk). The peculiarity of these Physical Endurants lies in their intentional nature: Inscriptions count as other entities, Expressions.

- Expressions (e.g. texts, logical formulae) are non-physical knowledge forms ordered by a communication language. Inscriptions realize Expressions and, like Inscriptions, Expressions are intentional entities conveying contents for agents.

- Conceptualizations consist of the ultimate means by which agents can reason about a world. Two kinds of Conceptualizations are distinguished: Propositions, as a means of describing a state of affairs; and Concepts, as a means to classify entities. Note that, as for the practical semiotics introduced in the ontology SUMO [29], Propositions may encompass the content expressed by sentences, theories, books, and even libraries.

Figure 2. An excerpt of I&DA’s hierarchy of concepts
We are going to see (in Section 3) that Propositions and Concepts correspond to the intrinsic nature of our instruments. Before that, we extend DOLCE in another way to account for the intentional nature of these instruments and their function.

1.3 Artefacts

The notion of artefact that we adopt elaborates on the common philosophical notion of an “entity intentionally made or produced for some reason” [15]. Analyzing the notions of intention and reason, this leads us to identify different classes of entities we find important to clearly distinguish and define [17] (see Fig. 3):

- Firstly, we contrast entities resulting from an action of production (Producing Consequents) with entities that are not intentionally produced (Happening Consequents). Among the latter figure Experimental Artefacts (which are unwanted results).
- Secondly, according to whether the intention of production is a prior intention or not, Artefacts are distinguished from Non-Targeted Objects (the latter result from Non-Deliberate Actions of production, e.g. routines).
- Thirdly, different kinds of reasons for producing Artefacts (hence different kinds of Artefacts) are considered: (i) conveying an emotion and being of aesthetic interest, for works of art, (ii) enabling their author (or another agent) to do something, for “functional” or Technical Artefacts. The latter are Artefacts to which a Function is ascribed, taking a Function to be an “acknowledged capacity to enable the realization of a kind of action” [17].

It is important to note that DOLCE’s distinction between Physical and Non-Physical Objects transcends the domain of Artefacts. Indeed, the latter are defined by the origin of their existence (i.e. their intentional production) rather than a mode of existence. This difference explains why we are able to distinguish between physical artefacts (e.g. an oscilloscope, an image acquisition equipment) and non-physical artefacts (e.g. the content of an article, a subject data acquisition instrument).

To sum up, Technical Artefacts have – at least – a triple nature as entities (i) possessing an internal essence (be it physical, social or cognitive), (ii) having been intentionally (and successfully) produced, and (iii) having necessarily a Function.
With the modules presented in this section in hand, we now have at our disposal a minimal set of conceptual primitives which enables us to tackle the modeling of the domain of neurological, neuropsychological and behavioral instruments.

2. Our core ontology of instruments

In the core ontology we propose, instruments *per se* are considered as specific technical artefacts, with their own variables and scores associated, and actions performed using an instrument as specific conceptual actions.

2.1. Instrument-based assessments

An *Instrument-Based Assessment* action corresponds to an administration of an instrument or a ‘testing’ (to use the term recommended by [7]). The conceptualization of this action plays a pivotal role, linking together a large number of entities (cf. Fig. 4): a Healthcare Professional (for instance clinical neuropsychologist or neurologist), as Agent; the Subject about whom data are acquired and, more widely, the context in which this acquisition is performed (i.e. an Examination within a Study); the used instrument prescribing which data are to be acquired and how; results obtained following questions raised and/or tests performed.

These actions commonly take two forms according to whether they solicit an authentic production from the Subject (e.g., a reflex, a performance such as drawing, or a 500-meter walk), for Test-Based Assessments, or they consist in an interview, an inventory, for Questionnaire-Based Assessments. Assessments are then specialized according to the type of acquired data (e.g., psychological, behavioral, neuroclinical), mirroring in part the instruments taxonomy (cf. Fig. 5). The raison d’être of this specialization is to take into account specifications of the evidence of competence (knowledge, skills, abilities, specialties) that would be expected from someone seeking qualification as a test user.

![Figure 4. Taxonomy of Instrument-based assessments.](image)
2.2. Subject data acquisition instruments

The instruments used to evaluate the state of subjects clearly are technical artefacts. For their conceptualization, we follow our theory of the threefold nature of technical artefacts [17]. This prompts to describe them as being:

- Intangible artefacts, i.e. propositional contents including “clearly defined methods and instructions for administration or responding, a standard format for data collection, and well-documented methods for scoring, analysis, and interpretation of results” [6].
- Technical artefacts allowing to explore entities related to the state of the subject – these categories of entities correspond to the Domain(s) of the instrument.
- Social artefacts intentionally created, adopted for use, then adapted and maintained by a community ascribing them the status of standard.

As the definition adopted from [6] indicates, we are faced to complex propositional contents. As an illustration of this complexity, some Instruments are explicitly composed of Sub-instruments exploring sub- or related domains (see Fig. 5). For example, to explore the multidimensional aspect of memory, the General Memory Index of the Wechsler Memory Scale-III (WMS-III) - a composite instrument designed to explore several memory abilities - is based on the delayed recall performances of several core “memory” tests, like the Visual Memory Test or the Verbal Memory Test [37]. Such a composition is also found for Instruments which assess a restricted set of cognitive functions. For example, the Mini-Mental State (MMS) [10], which is probably the most widely used instrument for dementia [21], is structured according to a set of several items such as the MMS Orientation Test, the MMS Registration Test or the MMS Language Tests. Moreover the MMS Language Tests consist of several items such as the MMS Oral Order Language Test or the MMS Written Order Language Test. This indicates that even an Instrument which addresses a relatively small domain may be structurally complex. Such a structure is important to model because, according to the context, only some parts of an instrument may be administrated.

The effects of brain disorders being rarely confined to a single behavioral dimension or functional system [21], Instrument-Based Assessments focus on different issues: neurological disorders (e.g. weakness, stiffness or visual impairments), cognitive impairments (e.g. aphasia, failure of judgment, lapse of memory), and other behavioral disorders (e.g. personality change, reduced mental efficiency or depression). Functionally, Instruments explore entities (their Domain(s)) which are of different ontological nature (e.g., states, abilities, cognitive functions, behaviors). For instance the memory is a cognitive function, while the depression is a Subject's pathological state. Moreover, an Instrument can be designed to explore one or several domains (Mono-domain vs Multi-domain Instrument). Generally, the goal with a Multi-domain Instrument is to integrate into one index the scores obtained by the patient while exploring different dimensions or functional systems. For instance, the MMS, which addresses the Global Cognitive efficiency, tries to obtain a global measure while exploring a whole set of domains: orientation, calculation, language, memory, praxia. Formally, a Domain is modeled as an individual concept which classifies classes of entities.
2.3. Instrument variables

Instrument variables are themselves Subject data acquisition artefacts. They carry two fundamental characteristics of the related instrument. First, they define what is being explored and measured using this instrument, represented by an explored Domain and a measured Quality, respectively. A distinction is introduced between Main variables, which explore the same Domain as the related instrument (i.e. same cognitive function or trait of the subject), and Secondary variables, which provide complementary information. Variables may also be categorized as Sex dependent variables, Age dependent variables, and Cultural skill dependent variables. When, for a variable, a typical value from a population of reference is available, the measured value can be standardized and stored in the corresponding score associated to the variable.

Second, Instrument variables define the range of allowed score values, with a basic distinction between Coded variables, which register Coded scores, and Numerical variables that register Numerical scores. The former are associated to a set of allowed Coded variable values, which are parts of the definition of the instrument. The latter, Numerical variables, can take any value in a certain range (which may be specified using min and max values). For instance, the MMS Calculation variable is a Numerical variable belonging to the range [0;5]. The Pessimistic thoughts variable of the Montgomery-Asberg Depression Rating Scale (MADRS) [26] is a Coded variable with the following Coded variable values \{0 = ‘No pessimistic thoughts’, 2 = ‘Fluctuating ideas of failure, self-reproach or self-depreciation’, 3 = ‘Persistent self-accusation, or definite but still rational ideas of guilt or sin. Increasingly pessimistic about the future’, 6 = ‘Delusions of ruin, remorse or irredeemable sin. Self-accusations, which are absurd and unshakable’\}. Values are Propositions denoting, e.g., that “the subject has no pessimistic thoughts as measured by the MADRS Pessimistic thoughts variable”. In the latter proposition, the term ‘subject’ does not refer to a particular individual, but to an abstract Subject.
2.4. Scores

Scores are Propositions that result from the recording of a particular Subject’s cognitive performance (e.g. calculation performance) or a particular Subject’s trait intensity (e.g. pessimistic thoughts intensity) during a particular Instrument-based assessment, in relation to a particular Instrument Variable. For instance a Score may correspond to the following propositions: "During one MMS Calculation assessment, Patient X’s Calculation performance is equal to 4 as measured by such MMS Calculation variable" or "During one MADRS assessment, Patient X has no pessimistic thoughts as measured by the MADRS Pessimistic thoughts variable".

Scores are divided into Coded scores and Numerical scores. Coded scores specialize the Coded variable values allowed for a particular Coded variable by referring to a particular Subject.

Numerical scores are further categorized as Raw scores, Corrected scores and Standardized scores depending whether they result of the direct registering of the subject’s performance, or result of some correction or standardization of such raw scores. One also distinguishes between Scores with (respectively without) unit of measure.
2.5. Codes

We have seen that Variable values and Scores are Propositions. To help synthesize these values and offer calculus facilities, these Propositions are usually coded. Let’s take, for instance, the Beck Depression Inventory (BDI-III) [3], one of the most widely used instruments for measuring the severity of depression. One of its variables measures the sleeping dimension with values such as: “The patient sleeps somewhat more than usual” or “The patient sleeps most of the day”. These Propositions are both qualitatively coded (by the respective Qualitative Score codes: ‘Minimal’ and ‘Severe’) and quantitatively coded (by the respective Quantitative Score codes: ‘1a’ and ‘3a’). The latter Codes refer to a number (resp. 1 and 3), therefore enabling applying order relationships.

Figure 8. Taxonomy of Score codes.

3. Discussion

A central quest in current neuroscience is the understanding of relations, under normal or pathological conditions, between brain anatomy and brain function. Brain functions can be mainly explored by neuroimaging, such as functional MRI, and neuropsychology, when concerned with the behavioral expression of brain functions [19]. One of our goal, with the construction of the proposed core ontology, was to define a model supporting the investigation of correlations between MRI based findings and neuroclinical, behavioural and neuropsychological based findings. The latter can be assessed by scores, which register the subject’s task ability, cognitive performance or trait intensity. These correlations will be investigated in mining a large collection of data via a federation of heterogeneous and distributed databases (NeuroLOG project). For instance in Alzheimer’s disease (AD), Gray Matter (GM) loss in the temporal regions lobes seems correlated with a decrease in Global Cognitive Efficiency (GCE) score. The two widely used instruments to examine the cognitive changes that characterize AD are the Mini Mental State (MMS) and the Mattis Dementia Rating Scale (MDRS) [25]. Indeed, MMS and MDRS are multi-domains instruments because their sub-instruments screen a large set of cognitive skills: attention, orientation, calculation, language, memory, praxia. The MMS and MDRS main variables register a total score which is based on the scores obtained during each of their sub-instrument assessments. Depending on the clinicians habits or the context of the assessment, MMS or MDRS is considered to define the subject’s GCE. NeuroLOG’s platform allows to search for: “all patients with a low GCE and with T1-weighted images presenting a GM loss temporal lobes ”. Firstly, our core ontology allows (i) to retrieve all the Instruments (and their Main variables) that explore the Domain: Global Cognitive Efficiency, and (ii) to scan the entire set of related
Scores, while filtering those which have a value less than a cut-off value (the latter is provided by the user and is Instrument and research study dependent). Secondly, images of the patient are retrieved and a specific computational anatomy pipeline is processed to quantify the possible GM volume loss in temporal lobes in the selected images.

The definition of the present core ontology was based on the detailed examination of the common instruments routinely used in three neurology hospital departments in France. We consider this set of instruments as representative of the minimal core that core ontology should support via dedicated sub-ontologies.

Two important modeling choices should be emphasized. The first one concerns the conceptualization of Instruments and the fact that we chose to model specific standard Instruments (e.g. MMS, WMS-III) as classes and not instances. The reason is that, in some centers, administered Instruments do not strictly conform to the defined standard. To account for these variations, local Instruments are modeled as instances of classes, with the latter representing shared properties of standard Instruments. Such properties correspond to structural and functional properties presented in Section 2.2. As a consequence, our core ontology is specialized by sub-ontologies, each accounting for a specific Instrument. In some cases, however, variations become so important that this modeling is no longer adequate. A new standard is then built as a version of a previous one. Such a versioning relation is introduced between the two standards so that we can maintain the class/instances representation. The second modeling choice concerns the distinction between Variable values and Scores. As we have seen, the former are modeled as Propositions (referring to an abstract Subject) which pertain to the definition of Instrument, whereas the latter (referring to a particular Subject) are the result of an Assessment. We therefore have two different propositional contents which are linked by a specialization relation (thanks to this relation, information about Score codes is only attached to Variable values). It is important to note that Scores are moreover characteristic of Assessments (i.e. two Assessments do not share the same Score). This choice enlarges our model with a greater number of instances. However, when requesting to a given a Score, we directly obtain its specific context (Subject, Examination and Study).

4. Conclusion and perspectives

In this paper, we have proposed a core ontology of instruments which builds upon a conceptual framework comprising the foundational ontology DOLCE and a recently designed ontology of artefacts. Thanks to this building approach and the possibilities of mapping it offers with other biomedical ontologies (such as those based on BFO6), we would like to stress its potential interest as a semantic reference for various neurosciences applications.

Before it can be used, our core ontology must be complemented with ontologies modeling the actually shared Instruments (more precisely the common properties of shared Instruments, as stressed earlier). This work is in progress. Once these ontologies available, the next step will consist in aligning the different Instruments’

6 http://www.ifomis.org/bfo
instantiations (at the different clinical sites) to a common reference, thanks to the mediator used in the NeuroLOG system (Data Federator, SAP). This will enable to query the actual Subjects’ Scores and to correlate such Scores with image findings, which is what the end-users are primarily interested in. A current limitation of our conceptualization of Instruments lies in our preliminary description of the Domains and Qualities respectively explored and measured by Instrument variables. Such Domains and Qualities are modeled as independent concepts, which strongly limits the kind of reasoning that can applied. Our intention is to define ontologies of brain functions and states, as well as ontologies of the Qualities that may be measured during Instrument-based assessments, that will certainly lead to enhanced querying and reasoning capabilities.

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