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Adding Cognition to the Semanticscience Integrated Ontology

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Abstract

The goal of the NIMH RDoC initiative is to establish a biological basis for mental illness that includes linking cognition to molecular biology. A key challenge lies in how to represent such large, complex, and multi-scale knowledge in a manner that can support computational analysis, including query answering. Formal ontologies, such as the Semanticscience Integrated Ontology (SIO), offer a scaffold in which complex domain knowledge such as neurological and cognitive functions can be represented and linked to knowledge of molecular biology. In this article, we explore the use of SIO to represent concepts in molecular biology and in cognition. We extend SIO to traditional cognitive topics by illustrating axioms for both an information-processing and a neuroscience perspective on reading. We next discuss the NIMH RDoC taxonomy and include SIO axioms for the units-of-analysis and functions-of-behavior dimensions. An example demonstrates its use of deductive reasoning to establish causal relations across RDoC dimensions. From a broader perspective this article demonstrates how informatics can assist in integrating work in clinical psychology, cognitive psychology, cognitive neuroscience, computer science, molecular biology, and philosophy.

Keywords: Cognition, Molecular biology, Neuroscience, Reasoning, Research Domain Criteria, Semanticscience Integrated Ontology.

Abbreviations: RDoC- Research Domain Criteria, SIO- Semanticscience Integrated Ontology, SUMO- Suggested Upper Merged Ontology, OWL- Ontology Web Language.

Introduction

The use of computers to organize information, often labeled informatics, is becoming increasingly necessary to impose some structure on a large and diverse array of data [1]. The fields of biology and medicine are leading the way as revealed by the frequent use of the term bioinformatics. A search of Google Scholar in 2012 returned over 1 million hits for bioinformatics compared to only 18 hits for the term psychoinformatics [2]. The extensive work in the field of bioinformatics and the increasing emphasis on the biological basis of behavior creates an opportunity to include more cognitive processes to enhance informatics.

For example, new insights into the neural basis of normal and abnormal behavior have resulted in reconsideration of syndromes, once considered exclusively mental, as brain disorders that can disrupt neural, cognitive, and behavioral systems [3]. The NIMH Research Domain Criteria (RDoC) initiative organizes research according to a taxonomy that relates units of analysis (such as genes, molecules, cells, and circuits) to functional dimensions of behavior (negative affect, positive affect, cognitive systems, social processes, and arousal/regulatory systems). Although taxonomies provide a plan for organizing knowledge, formal ontologies such as the Suggested Upper Merged Ontology (SUMO) provide a detailed theoretical framework for organizing knowledge [4-5].

Formal ontologies consist of both a hierarchy that decomposes knowledge from the general to the specific and a logic that allows deductive reasoning. Leaders in the fields of neuroscience and informatics suggest that the use of upper-level ontologies and the assignment of semantic relations between terms in mental ontologies will enhance knowledge integration [1]. Articles on the application of Information Science tools (ontologies, WordNet, FrameNet) to Psychology [3] and on distinctions among Psychology ontologies [6] discuss progress in meeting this objective.

The purpose of this article is to introduce and then expand the application of a more specialized ontology for bioinformatics. The Semanticscience Integrated Ontology (SIO) builds on the Ontology Web Language (OWL), which has a less powerful logic than SUMO but is easier to learn. OWL is a formal knowledge representation language with a vocabulary for expressing knowledge of types, relations, individuals, and data values. It uses a (RDF) format to describe entities in terms of their types, attributes and relations to other entities such as ‘nucleus’ ‘part of’ ‘cell’ [7].

SIO is a practical ontology consisting of a broad set of upper- and mid-level terms that can be coupled with a minimal set of domain-independent relations to richly represent knowledge through a set of simple design patterns [8]. Its framework is believed to be sufficiently flexible to accommodate a wide range of data. Our objective in this article is therefore to extend SIO's application from its current focus on molecular biology to include cognitive processes. We are particularly motivated by the RDoC initiative of establishing a biological basis for cognitive behavior that links cognition to molecular biology. SIO could provide a common language for this integration.

The next section provides an overview of SIO and shows how it organizes knowledge in the life sciences [8]. Section 3 extends its application to cognition to represent both an information-processing and a neuroscience perspective on reading. Section 4 discusses the NIMH RDoC taxonomy and then illustrates SIO descriptions for the units of analysis and the functions-of-behavior dimensions. All of these extensions include SIO axioms to demonstrate their capability to formalize statements about cognitive processing. The theoretical content of these axioms, however, would need to be qualified by combining them with other axioms for large-scale applications. Section 5 illustrates the use of these axioms to answer an RDoC query. Section 6 compares SIO with related work and Section 7 makes several concluding remarks.

The Semanticscience Integrated Ontology

Foundational model

Figure 1 shows selected portions of the SIO hierarchy. An advantage of using SIO as a biomedical ontology for cognition is that the four top-level categories in SIO ('object', 'process', 'attribute', 'relation') correspond to fundamental components of knowledge in cognitive science [9-11]. We will explain SIO terms in the text by highlighting them in single quotes to distinguish them from other terms. In addition, **Table 1** lists definitions of some key terms in SIO that are relevant to this article.

An **agent** is a relation between a process and an entity, where the entity is present throughout the process and is a causal participant in the process.
An **attribute** is a characteristic of some entity.
A **description** is a language entity in which elements of a language (formal or natural) are used to characterize an entity.
A **disposition** is the tendency of a capability to be exhibited under certain conditions or in response to a certain stimulus (trigger).
Encode is a relation between two objects, in which the first object contains information that is used to produce the second object.
Everything is an **entity**.
A **morpheme** is the smallest semantically meaningful unit in a language.
An **object** is an entity that is wholly identifiable at any instant of time during which it exists.
A **phrase** is a group of words functioning as a single unit in the syntax of a sentence.
A **process** is an entity that is identifiable only through the unfolding of time, has temporal parts, and unless otherwise specified/predicted, cannot be identified from any instant of time in which it exists.
A **proposition** is a sentence expressing something true or false.
In **relation** to is a comparative relation to indicate that the instance of the class holding the relation exists in relation to another entity.
A **representation** is an entity that in some way represents another entity (or attribute thereof).
A **textual entity** is a language entity that is manifested as a sequence of one or more distinct characters.
Transcribed is a relation between two information content entities in which one is transcribed into (an exact or similar kind) another through some process. DNA is transcribed into RNA.
Translated is a relation between two information content entities in which one is translated into (a completely different kind of entity) another through some process. RNA is translated into Protein.
A **verbal language entity** is a language entity that is manifested through sound.

Table 1: Some Key SIO Definitions.

An 'object' is an 'entity' that occupies space and is fully identifiable by its attributes at any moment in time. For example, a person is a kind of object because they have mass and can occupy space; and we can recognize a person even though they gain (e.g. a benign growth) or lose parts (e.g. an arm) over their lifetime. In contrast, a 'process' is an 'entity' that unfolds in time and has temporal parts. It includes 'behavior', broadly defined in SIO as "the set of actions and mannerisms made by systems (biological or otherwise) in response to stimuli or inputs, whether internal or external, conscious or subconscious, overt or covert, and voluntary or involuntary". An 'attribute' is either an intrinsic 'quality' or 'realizable' through a 'capability' or 'role' (Figure 1A). Examples are the "brown" color of hair as an intrinsic physical quality, the capability "to breathe air", and the extrinsic social role of being a "judge". The basis for a capability lies in one or more parts and/or qualities, and reflects possibility of an entity to act in a specified way under certain conditions. The ability to act (agency) only requires that a particular entity has the physical basis to behave in the way specified. SIO's objects and capabilities are not necessarily driven by elements of consciousness.

'Relations', shown in Figure 1B, include 'has attribute', 'is located in', and 'represents'. While all SIO entities (object, processes, attributes) 'exist at' and are 'located in' some time and space, these are not necessarily real space or real time. Thus, SIO supports the description of objects, processes and attributes arising from a mental representation using any part of terminology that also describes real world objects. One limitation of this approach is that SIO is constructed with axioms to describe the attributes and relations of "real world" objects and processes, which may not hold in fictional, mental, or virtual environments.

- entity
  - attribute
    - quality
      - informational quality
      - normality
    - realizable entity
      - capability
      - role
  - object
    - information content entity
      - language entity
        - description
          - proposition
          - specification
        - visual language entity
          - textual entity
        - verbal language entity
      - representation
        - model
          - object model
          - process model
        - symbol
    - material entity
  - process
    - behavior
      - emotion
        - negative emotion
        - indifference
        - positive emotion
    - interacting
      - communicating
      - comparing
      - creating
      - regulating
    - procedure

Figure 1a: Selected portions of class hierarchies in SIO.

- is related to
  - has attribute
  - is spatiotemporally related to
    - is connected to
    - is location of
    - is participant in
  - refers to
    - describes
      - specifies
        - encodes
          - is transcribed into
          - is translated into

Figure 1b: Selected portions of object-property hierarchies in SIO.

Some key objects and relations are diagrammed in Figure 2A. Processes have objects as participants that can realize specific 'roles' and 'capabilities'. SIO's representation allows for the 'capability' or 'role' of an 'object' to become realized as a 'process' that has value 'quality' or 'measurement value' and can result in new processes, objects, or their attributes. For instance, anxiety could be represented as: A student ('object) has an anxiety trait ('disposition') that is realized in taking a test ('process') of a particular duration ('measurement value') and resulting in poor performance ('measurement value'). A 'disposition' is the tendency of a 'capability' to be exhibited under certain conditions (taking a test) or in response to a certain stimulus (encountering a difficult question). Therefore, a 'capability' in SIO is about the mere possibility while a 'disposition' focuses on the likelihood.

Other key entities in SIO are 'space', 'time' (Figure 2B), and 'information' (Figure 2C), which we discuss later. Space and time are considered objects in SIO and can occupy some portion of space and exist in some portion of time. Information content entities focus on symbolic representations that convey some meaning. For instance, the composition and topology of a protein or class of proteins can be represented by a protein sequence-a ordered list in which each letter in the string denotes a specific type of amino acid.

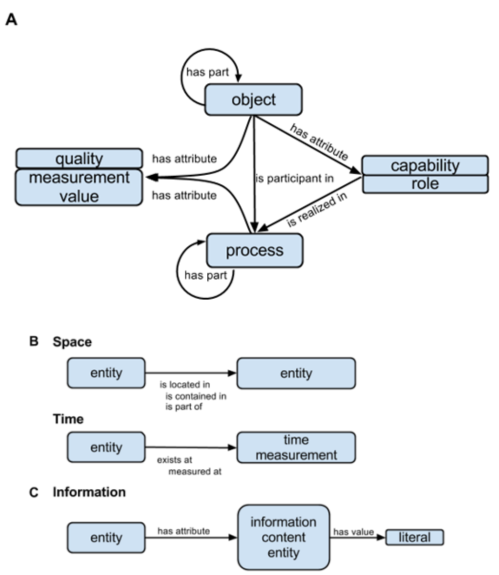
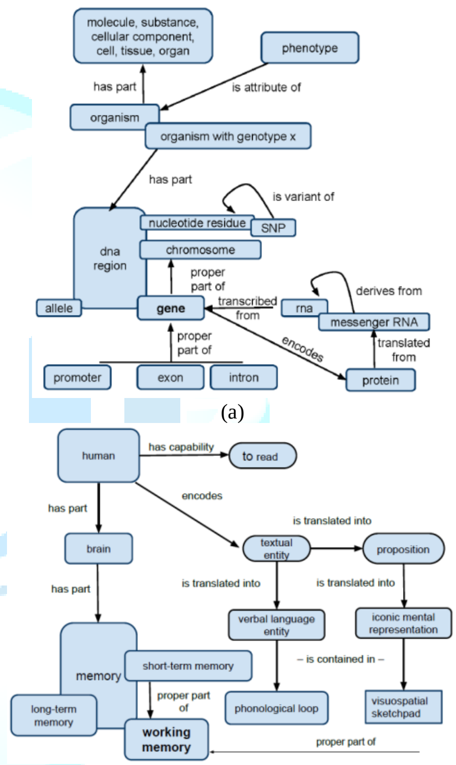


Figure 2: Key entities and relations in SIO.

Application to molecular biology

The design of the Semanticscience Integrated Ontology was motivated by the need to integrate knowledge in biomedical research for the domains of biology, chemistry, biochemistry, and bioinformatics. Examples of its application therefore focused on genetics and molecular biology [8].

Figure 3a shows an application of SIO entities and relations to molecular biology including that organs, cells, and molecules are parts of an organism and a phenotype is an attribute of an organism. The overlap of one concept on another indicates a subclass relation, such as a gene is a subclass of a DNA region. Many other relations, such as 'is attribute of' and 'has part', are also frequently used to organize knowledge. Figure 3a shows that a phenotype 'is attribute of' an organism and an organism 'has part' cells.



(b)

Figure 3: Conceptual map of SIO entities and their relations as applied to molecular biology (a) and an information-processing model of reading (b).

An important relation in molecular biology is 'encodes', defined by SIO as a relation between two objects in which the first object contains information that is used to produce the second object. Figure 1b and 3a distinguish between two types of encoding used in genetics – 'translated from' and 'transcribed from'. 'is transcribed into' is a relation in which the information encoded in one object produces an exact or similar kind of object. For instance, in classical molecular biology RNA molecules are assembled by molecular machines capable of reading and interpreting DNA-based genes. DNA and RNA are structurally quite similar in terms of their nucleotide composition, but have different roles in the cell regarding information storage and transfer. 'Is translated into' describes a relation in which a completely different kind of entity is generated as a result of a process that uses the information from the source object. For instance, RNA molecules are interpreted by molecular machines to produce proteins.

Adding Cognition to SIO

The theme of this article is that SIO can be extended from molecular biology to cognition and therefore serve as a foundation for establishing closer connections across the biological and cognitive sciences. Section 3.1 summarizes how SIO represents information for subsequent application to how people encode and store it. The next two sections show an application to reading text from a traditional information-processing perspective (Section 3.2) and from a more recent neuroscience perspective (Section 3.3). This comparison enables us to demonstrate SIO's flexibility in describing cognition from different perspectives.

Information

In its most basic sense, information in SIO is an interpretable sequence of symbols. Information arises from the interpretation of the symbols by some 'agent' using a decoding procedure. Decoding involves the parsing of the sequence and the subsequent assignment of meaning.

Informational entities exist independently of any particular physical manifestation, although there must have been at least one manifestation (a physical embodiment in the past or present). 'Information content entities' are informational entities that can be concretized as characteristics (ink pattern, electromagnetic pattern, and neuronal pattern) of physical entities (a page, a hard drive, a brain).

Figure 1a shows that an 'information content entity' includes a 'language entity' consisting of a 'visual language entity' and a 'verbal language entity' that will be used in our discussion of reading. A 'verbal language entity' is manifested through sound. A 'visual language entity' is manifested through light and can be perceived and processed by a visual system. Our intention is both to apply current SIO terminology and create new terminology that can facilitate the comparison of information across the various grain sizes of genes, molecules, cells, brain circuits and behavior. Such a language should be useful not only for comparisons across the RDoC units of analysis but for the description of traditional topics such as the cognitive processes involved in reading. The next two sections describe these processes from an information-processing and a neuroscience perspective.

Application to an information-processing model of reading

Figure 3b shows the encoding and storing of information while reading a text. The diagram is based on an information-processing perspective that emphasizes different types of encoding and memory structures. As in Figure 3a, overlap of one concept on another indicates a subclass relationship. Long-term memory, short-term memory, and working memory are all types of memory.

Reading requires using background knowledge to decode a 'textual entity' into a representation that is mentally accessible. The generation of a verbal representation requires encoding this representation into a speech-based, phonological code ('verbal language entity') and as a meaning-based semantic code based on morphemes. A 'morpheme' is a basic unit of meaning that is used to construct the meaning of words. Morphemes consist of stem words, prefixes and suffixes. The word unfriendly consists of the stem word friend, the suffix ly and the prefix un. Notice how each morpheme changes the meaning of the word. The first axiom in **Figure 4** states that a textual entity is translated into words consisting of morphemes.

In addition to representing meaning as morphemes readers sometimes create visual simulations of the semantic information [12]. For instance, Stanfield and Zwaan [13] found supporting evidence for visual simulations in statements such as "She pounded the nail into the floor" and "She pounded the nail into the wall".

1. A textual entity is translated into words consisting of morphemes.
'textual entity'
subClassOf
'is translated into' some
(**'words'** that **'has proper part'** some **'morpheme'**)

2. An iconic mental representation is a visual sensory representation in memory that has been either perceived or created.
'iconic mental representation'
subClassOf
'visual sensory representation'
and **'represents'** some
(**'sensory process'** that **'is preceded by'** some (**'perception'** or **'creation'**))

3. Memory is a store for recording and retrieving information.
'memory' subClassOf
'behaviour'
that **'has capability'** some **'to record'**
and **'has capability'** some **'to retrieve'**

Figure 4: SIO description of representations for an information-processing model of reading shown in Figure 3b.

When participants had to verify whether a picture of an object was mentioned in the sentence, their verification times were faster for a picture of a vertical nail if given the first sentence and a horizontal nail if given the second sentence. There is now extensive evidence that these simulations are highly flexible and, like sensory-motor interactions, can focus on specific modalities, change according to context, and take perspective into account [14].

Although all encodings in Figure 3b are examples of 'translations', they differ in whether the input is sensory or mental. The encoding of text into either a phonological or a semantic code begins with a sensory input. In contrast, forming a visual simulation of an event in a text begins with a mental (semantic) input [15]. Representing visual simulations in SIO was previously not possible because its definition of 'image' (as an affine projection of a visual entity to a two dimensional surface) does not fit use of the term 'image' by cognitive scientists such as Kosslyn [16]. We therefore added the term 'iconic mental representation' to SIO to represent a visual experience that was either perceived or created, see the second axiom in Figure 4 for its formal description.

Figure 3b shows that working memory also plays a major role in reading [17]. The phonological loop and the visuospatial sketchpad are two components of a working memory model proposed by Baddeley [18]. The phonological loop is responsible for maintaining and manipulating speech-based information. The visuospatial sketchpad is responsible for maintaining and manipulating visual and spatial information. The term 'memory' typically refers to a store for preserving information. The concept of a store is consistent with the extended definition of a container that can hold information as well as physical objects [19]. A SIO description of memory as a store that has 'has capability' 'to record' and 'to retrieve' is included as the third axiom in Figure 4. This definition is consistent with the APA Dictionary [20] definition of memory as the hypothesized part of the brain where traces of information and past experiences are stored.

Application to a neuroscience model of reading

A potential problem with Baddeley's [18] working memory model is that it incorporates only phonological and visuospatial information. Postle [21] proposed that, instead of adding more modalities to the model, working memory directs attention to the many different types of memory codes stored in LTM. According this view working memory functions through the coordinated recruitment of brain systems that have evolved to accomplish sensory-, semantic- and action-related functions.

A model consistent with this approach is based on the concept of a hierarchical process memory [22]. The term "process memory" distinguishes this perspective from the traditional perspective of encapsulated memory systems such as working memory. A motivation for proposing this model is that online processing and memory are interwoven for many everyday situations such as reading a book or conversing with a friend [23]. For spoken sentences the brain must recognize sounds and integrate them with prior sounds to recognize words while at the same time integrating newly recognized words with previous words.

Processes are hierarchical in the sense that the timescale gradually increases from sensory areas to higher-order semantic areas [22]. **Figure 5A** shows a temporal sequence for reading in which grain size increases from phonemes to words to sentences to paragraphs to the entire narrative. Larger grain sizes require more processing time, which is represented in Figure 5A by a temporal receptive window-the window of time that an ongoing stimulus can influence the processing of subsequent stimuli. Phonemes have a short temporal window that supports their integration for word recognition. The integration of words in a sentence occurs over a longer temporal window of several seconds.

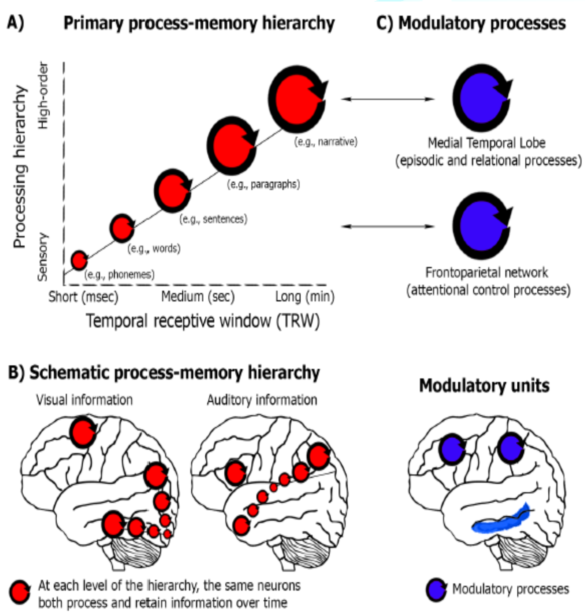


Figure 5: A Neuroscience model of reading. From Hasson, Chen, and Honey (2015).

The first axiom in **Figure 6** is a formal statement of the process for combining words into a sentence. The different durations of the temporal windows can be represented within SIO by 'maintenance of duration of process', which regulates a target process to maintain its duration within an expected interval. For instance, each incoming word in the sentence "The boy took the ball and he kicked it into the goal" has to be integrated with preceding words [22]. Attentional control processes regulate the maintenance of words across a delay period, as described by the second axiom in Figure 6.

Another characteristic of the hierarchical-process model shown in Figure 5B is that the same neurons both encode and maintain information at each level of the hierarchy. For instance, functional MRI evidence indicates that goal-related variables in the lateral prefrontal cortex maintain persistent neural activity in the sensory regions during a short delay task [24]. The third axiom in Figure 6 is a SIO-formulated statement of this occurrence.

1. Sentences are constructed from words.
'sentence construction'
subClassOf
'process'
that **'has input'** some **'word'**
and **'has output'** some **'sentence'**

2. Attentional control processes regulate word maintenance.
'Attentional control process'
subClassOf
'regulates' some '**word maintenance**'
'**word maintenance**'
subClassOf
'process'

3. The same neurons are used to encode and maintain information.
'neuron'
subClassOf
'has capability' some **'to encode information'**
and **'has capability'** some **'to maintain information'**

Figure 6: SIO description of processes for a hierarchical-process model of reading shown in Figure 5.

To summarize, Section 3 distinguished among different types of 'information content entities' within an information-processing framework. It also distinguished among different types of 'processes' within a neurologically-inspired hierarchical process model. Both applications included descriptions to extend SIO to the cognitive domain. Section 4 continues this extension by providing SIO descriptions for the units-of-analysis and the functions-of-behavior dimensions of the NIMH RDoC taxonomy.

NIMH Research Domain Criteria

Overview

Perhaps the most important taxonomy to organize psychological knowledge is the ongoing development of the NIMH Research Domain Criteria (RDoC) described on the NIMH website http://www.nimh.nih.gov/research-priorities/rdoc/index.shtml.

As stated by Insel and Cuthbert (2015) in their Science article: Recently psychiatry has undergone a tectonic shift as the intellectual foundation of the discipline begins to incorporate the concepts of modern biology, especially contemporary cognitive, affective, and social neurosciences. As these rapidly evolving sciences yield new insights into the neural basis of normal and abnormal behavior, syndromes once considered exclusively as "mental" are being reconsidered as "brain" disorders or, to be more precise, as syndromes of disrupted neural, cognitive, and behavioral systems (p. 499). The goal of RDoC is to deconstruct current diagnostic groups to identify subgroups that have biological validity.

Table 2 shows the RDoC framework. The rows of the matrix are concepts representing functional dimensions of behavior. These consist of Negative Valence Systems such as Fear and Anxiety, Positive Valence Systems such as Reward Seeking and Consummatory Behavior, Cognitive Systems such as Attention and Working Memory, Systems for Social Processes such as Understanding the Self and the Mental States of Others, and Arousal/Regulatory Systems such as Arousal and Circadian Rhythms. Current constructs in the Cognitive Systems domain are Attention, Perception, Declarative Memory, Language, Cognitive Control, and Working Memory.

	Genes	Molecules	Cells	Circuits	Physiology	Behavior	Reports	Paradigms
Negative Valence								
Positive Valence								
Cognitive Systems								
Social Processes								
Arousal/Regulatory								

Table 2: RDoC Framework.

The columns of the matrix are units of analysis. These consist of Genes, Molecules, Cells, Circuits, Physiology, Behavior, Self-reports and Paradigms. The two criteria for including a construct in the matrix are [18] there has to be data to support the construct as a valid functional dimension of behavior or cognition and [25] there has to be data specifying a neural circuit or system that accounts for a preponderant amount of the variance in implementing the particular function. The next section discusses relations among cognitive constructs and the RDoC units of analysis.

Relations among units of analysis

There is a growing interest in establishing and organizing a biological basis of behavior [26] such as displayed in the columns of Table 2. In 2008 a group of investigators argued that although biological knowledge at the genomic level was progressing rapidly, informatics could help advance this research by developing multi-level models [27]. They advocated a neuropsychiatric phenomics strategy that progressed upward from genes, proteins, signaling (dopamine signaling, synaptic development), neural symptoms (prefrontal function, hippocampal function), cognitive constructs (working memory, response inhibition), symptoms (psychotic, impulsive), and syndromes (schizophrenic, ADHD).

As a step toward developing a structured knowledge base Sabb and his collaborators focused on findings regarding Cognitive Control, a construct considered important to multiple neuropsychiatric syndromes. An examination of the co-occurrence of 83 terms in the PubMed database with the term ‘Cognitive Control’ resulted in Response Inhibition, Response Selection, Task Switching and Working Memory as the four terms that co-occurred most frequently. The next step was to use the BrainMap database to determine whether these constructs map onto independent neural systems [28]. Some classifications (Response Selection versus Cognitive Control, Response Inhibition, and Working Memory) could be based on the patterns of brain activity; others were either more ambiguous (Cognitive Control, Response Inhibition, and Working Memory) or inconsistent (Task Switching).

In July 2010 a group of experts assembled for an NIMH-sponsored workshop to formulate a definition of working memory (WM) and determine its relation to genes, molecules, cells, circuits, and behavioral tasks in the RDoC matrix (http://www.nimh.nih.gov/research-priorities/rdoc/working-memory-workshop-proceedings.shtml). The discussion of these units of analysis resulted in an agreement that WM consists of four inter-related components, which are sufficiently different to require their own set of entries in the units of analysis. The four components are the active maintenance of information, flexible updating, interference control, and limited capacity. Three of these components active maintenance, flexible updating, and interference control are ‘processes’ in the SIO ontology. The other component- limited capacity is the quality arising from a measure of ‘information’ (Figure 2C). The group decided that some entries within an analysis unit, such as dopamine for molecule, affected all four components of working memory.

The first axiom in **Figure** 7 includes a SIO description of increasing dopamine level. The direction of influence, however, can differ across the four components. Increasing dopamine level increases learning by updating task-relevant information but at the cost of making learners more susceptible to distracting information [29]. Other units, such as some inhibitory cells, applied to only a single component (interference control). Classification of circuits linked the dorsal/lateral prefrontal cortex to flexible updating, interference control, and limited capacity. The ventral/lateral prefrontal cortex was considered influential for active maintenance and limited capacity. The second axiom in Figure 7 is a SIO description of the prefrontal cortex’s role in maintaining information.

1. Description of the phenomenon of increasing levels of the quantity of dopamine as a process.
'increasing dopamine level'
subClassOf
'regulation of molecular quantity'
that **'has quality'** some **'increased'**
and **'in relation to'** some 'dopamine'

2. One function of the prefontal cortex is to maintain information.
'prefrontal cortex'
subClassOf
'is agent in' some **'information maintenance'**

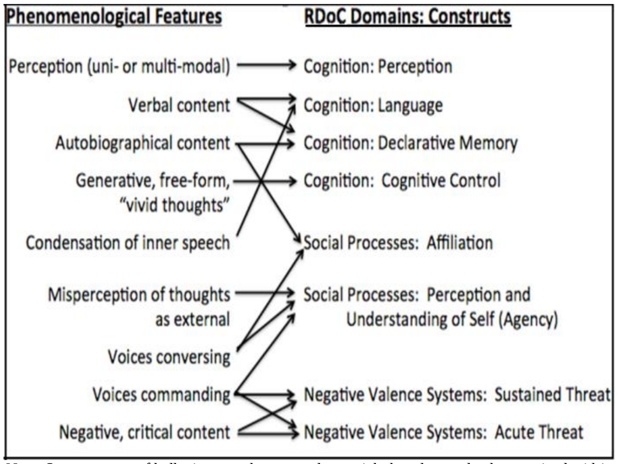
3. Stress reduces a molecule known to enhance cell survival.
'stress'
subClassOf
'results in' some **'reduced quantity of cell survival enhancing molecule'**
'reduced quantity of cell survival enhancing molecule'
subClassOf
'reduced quantity'
and **'has participant'** some 'cell survival enhancing molecule'
and **'results in'** some 'reduced cell survival'

Figure 7: SIO description of relations among RDoC units of analysis.

Progress in understanding the biological basis of behavior is also occurring for topics such as stress [30]. Stressful experiences such as restraint, social defeat, and sleep deprivation, have been shown to decrease the number of new neurons in the dentate gyrus region of the brain. Stress also reduces a molecule (brain-derived neurotrophic factor) known to enhance cell survival, as described in Figure 7 by the third axiom. Encountering environments in which exploration is rewarding results in a brain primed for improved cognition rather than a brain primed to prioritize safety and avoidant behavior. The influence of affect on cognition is an example of formulating relations across the RDoC dimensions of behavior- the topic of the next section on auditory hallucinations.

Relations among Dimensions of Behavior

Dimensions of behavior include negative affect, positive affect, cognitive systems, social processes, and arousal/regulatory systems as displayed in the rows of **Table 2**. Auditory Verbal Hallucinations (AVH) are relevant to the RDoC framework because, as illustrated in **Figure 8**, they involve several functional dimensions of behavior such as negative affect, cognitive systems, and social processes.



Note: Some aspects of hallucinatory phenomenology might be adequately characterized within one construct and others might reflect the interactive contributions of multiple constructs.

Figure 8: Functional Dimensions of Auditory Hallucinations. From Ford, et al (2014).

Such hallucinations are imagined but nonetheless attributed to an external source, as stated by the first axiom in **Figure 9**. Auditory hallucinations contain perceived speech (the second axiom in Figure 9) that distinguishes them from hallucinations in other sensory modalities.

People who do not require treatment typically attribute their voices to spiritual sources such as deceased people or guardian angels. They hear voices with neutral or pleasant content and experience low distress. People who need care typically attribute their voices to real people such as the secret police, drug gangs, or malevolent neighbors [31]. This misperception of thoughts to others involves Social Processes (Figure 8). A relevant Cognitive construct is memory. A significant proportion of schizophrenics report voices that are either identical or similar to memory of previously heard speech [32]. These voices often follow consistent themes with unpleasant content that results in high distress.

The distress that occurs in clinical patients is captured by Negative Valence Systems within the RDoC taxonomy (Figure 8). Negative Valence Systems are responsible for emotions such as fear, anxiety and loss that result from aversive situations. SIO partitions the 'emotion' category into 'positive emotion', 'negative emotion', and 'indifference' (Figure 1). There are many examples of specific emotions including 'guilt', 'hostility', 'hysteria', 'sadness', and 'shame' for 'negative emotion'. The third axiom in Figure 9 states that negative emotions are an attribute of abnormal AVH. The next section discusses the usefulness of SIO axioms for answering queries within the RDoC framework.

Applications

Answering RDoC queries

One of the primary purposes of a formal representation of ontology is to use deductive reasoning to answer queries. Answering queries becomes challenging when the answer depends on a sequence of deductions based on different stages of a disease. An example is a stage model that links stressful life events to increased risk of disease [33]. The stages are [18] life events [25] that are appraised as stressful, which result in [6] a negative emotional response causing [34] disease related physiological changes.

Consider the question 'Do abnormal auditory hallucinations reduce cell survival?' The three axioms on auditory hallucinations in Figure 9 are insufficient for answering this question because none mentions cell survival. Axiom 3 in Figure 7 states that stress reduces a molecule known to enhance cell survival [30] but does not mention abnormal auditory hallucinations. In order to establish a relation between abnormal auditory hallucinations and cell survival it is therefore necessary to add at least one additional axiom.

1. Hallucinations are attributed to an external source.
'**hallucination**'
subClassOf
and **'has source'** some '**material entity'**

2. Auditory hallucinations contain perceived speech.
'auditory hallucinations contain perceived speech'
subClassOf
'**hallucination**'
and **'has part'** some **'perceived speech'**

3. An attribute of abnormal auditory hallucinations is negative affect.
'abnormal auditory hallucination'
subClassOf
'**hallucination**'
'results in' some **'negative emotion'**

Figure 9: SIO description of relations between auditory hallucinations and RDoC functional dimensions.

The three axioms in **Figure 10** result in the conclusion that abnormal auditory hallucinations do influence cell survival. The first axiom taken from Figure 9 states that an attribute of abnormal auditory hallucination is negative emotion [32]. The second (added) axiom states that negative emotion causes stress [33], resulting in the deduction from axioms 1 and 2 that abnormal auditory hallucinations cause stress. The third axiom taken from Figure 7 states that stress reduces a molecule that enhances cell survival, resulting in the deduction from axioms 2 and 3 that abnormal auditory hallucinations reduce a molecule that enhances cell survival.

1. An attribute of abnormal auditory hallucinations is negative affect.
'abnormal auditory hallucination'
subClassOf
'**hallucination**'
that **'results in'** some **'negative emotion'**

2. Negative emotion causes stress.
'**negative emotion**'
subClassOf
'**emotion**'
that '**results in**' some 'stress'

3. Stress reduces a molecule known to enhance cell survival.
'**stress'**
subClassOf
'**results in**' some 'reduced quantity of cell survival enhancing molecule'
'reduced quantity of cell survival enhancing molecule'
subClassOf
'**reduced quantity'**
that '**has participant**' some 'cell survival enhancing molecule'
and '**results in**' some ('**reduced quantity'** that '**is quality of**' some 'cell survival enhancing molecule')
that '**results in**' some 'reduced cell survival'

Figure 10: Axioms that are relevant for answering the question 'Do abnormal auditory hallucinations influence cell survival?'

By encoding these axioms in SIO and using the deductive reasoning afforded by an OWL reasoner such as Hermit [35] we can ask about the relationships between auditory hallucinations and cell survival. Figure 11 shows the results of a query in Protégé 5.0.0 [36], a computer program designed to construct, view, and interact with OWL ontologies such as SIO.

We can then ask 'Which entities result in reduced cell survival?' The answer to the query reveals multiple causes- abnormal auditory hallucination, negative emotion, reduced quantities of cell survival enhancing molecule, and stress - that are components of the causal change established by the axioms in Figure 10. Abnormal auditory hallucinations cause a negative emotion that causes stress that causes a reduction in the cells that enhance cell survival. The three axioms show the interrelationships among entities at the molecular and behavioral levels in the RDoC taxonomy. Additional detailed axioms would provide greater specification of these interrelationships.

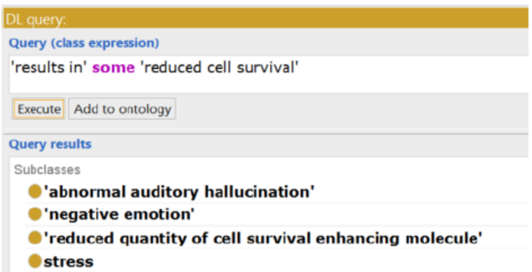


Figure 11: Screenshot from Protégé 5.0.0 over an application ontology to answer the question 'Which entities result in reduced cell survival?".

Reasoning from uncertain knowledge

A limitation of the axioms in Figure 10 of this article is that they are based on the assumption that each of the causes has a probability of 1.0 of producing the effect. A more realistic approach- WatsonPaths- expands on the Watson question-answering system that became famous on Jeopardy [37]. The project in collaboration with the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University presents a patient summary and asks for the most likely diagnosis or most appropriate treatment. Guiding the diagnosis is a model of entity types and relations. An application of these ontological relations occurs in an assertion graph that connects input symptoms to hypotheses. For instance, data that the patient exhibits a resting tremor suggests that the patient has Parkinson's disease, which suggests that the patient's Substantia Nigra area of the brain is affected.

Probabilistic-driven deductive inferences connect input symptoms to hypotheses. In the WatsonPaths example a resting tremor indicates Parkinson's disease with probability 0.8 [37]. A probabilistic reasoning system would attach probabilities to the axioms in Figure 10 such as 'An attribute of abnormal auditory hallucinations is negative affect'. Laroi and his collaborators [38] found that although all groups experiencing hallucinations reported hearing positive voices, 100% of the schizophrenics, 93% of the dissociative patients, and 53% of the nonpatients reported hearing negative voices [39]. The big data revolution [40] should provide large amounts of data that can serve as a basis for estimating probabilities for probabilistic deductive reasoning.

Formulating hypotheses and research questions

The development of accurate, personalized, and predictive models of cognition that synchronize with our understanding of biology is crucial to the advancement of cognitive science. A key aspect of this is to not only represent general knowledge of cognitive processing, but also to integrate this in the context of experimental results. For instance, reasoning over OWL ontologies generated from computational models of systems biology revealed errors in human curation as well as misuse of the model language. Complete formalization of experimental knowledge, model, and simulation results not only enables queries across all three, but also enables researchers to assess whether these are consistent with one another [7]. By employing more sophisticated hypothesis testing systems such as HyQue [25] it becomes possible to automatically retrieve evidence from multiple databases that may support or dispute a hypothesis or its associated claims. Of course, all of this becomes substantially easier when communities come together to build shared vocabularies for their research.

Related Work

Several cognitively focused ontologies have recently been developed and include the Mental Functioning Ontology, the Cognitive Paradigm Ontology, the Neural ElectroMagnetic Ontology, the Neuroscience Information Framework, the Neurological Disease Ontology, and the NeuroPsychological Testing Ontology [1]. Many of these ontologies use the Basic Formal Ontology [41] as an upper level ontology. However, the Basic Formal Ontology is founded on a brand of realism that is insufficiently flexible for the needs of scientists [41-43] For instance, Ceusters and Smith (2010) define a cognitive representation within BFO as a representation that specifically depends on an anatomical structure in the cognitive system of an organism. We propose that cognitive representations exist independently as theoretical constructs, and have their own attributes. Although mental representations are implemented by the brain, their importance as theoretical constructs does not require neuroscientific explanations. Indeed, cognitive theories have typically guided neuroscience research. As expressed by two neuroscientists [29].

Neuroscience is rapidly accumulating a wealth of data at multiple levels ranging from molecules to cells to circuits to systems. However, in the absence of cognitive theory, this effort runs the risk of mere "stamp collecting", or the tendency to catalog the phenomena of the brain without gaining understanding or explanation. It follows, then, that many of the most influential findings in neuroscience have been understood within the functional context of cognitive theory (p. 14).

The importance of visual imagery as a theoretical construct was initially based on the difficulty of explaining many research findings without a theory that incorporated visual imagery [44]. Subsequent research by cognitive neuroscientists added additional anatomical evidence for the theory [45]. Another example is the theoretical construct of Cognitive Control. A search of the PubMed database revealed its frequent co-occurrence with the terms Response Inhibition, Response Selection, Task Switching, and Working Memory [27]. This discovery was followed by a search of the BrainMap database to determine the neurological basis of these constructs [28]. Participants in the NIMH workshop on Working Memory decided that the four inter-related cognitive components of working memory were sufficiently different to merit their separate inclusion in the RDoC matrix. The distinction between these theoretical components of Working Memory continues to be a productive one [46]. This perspective of representing knowledge at multiple levels aligns with the flexible underpinnings of the Semanticscience Integrated Ontology. It makes it possible to connect knowledge across levels in the RDoC taxonomy.

A challenge for the development of upper ontologies is to adopt standardized definitions of cognitive processes and then integrate these processes within the framework of the ontology [1]. An advantage of using SIO as an ontology for cognition is that its top-level categories ('object', 'process', 'attribute', 'relation') correspond to fundamental components of knowledge in cognitive science [9-11]. In contrast, the Basic Formal Ontology has two top-level categories: Occurrents and Continuants [1]. Occurrents are entities that unfold over time and have temporal parts; Continuants are entities that endure through time. These words seldom occur in Cognitive Science and therefore introduce unnecessary terminology.

There is also reason to believe that the categorization in use by the BFO is difficult to understand and incorrectly applied in ontology projects. BFO includes concepts such as occurrent, continuant, independent continuant, specifically dependent continuant, generically dependent continuant, and process profile. Parts of the BFO do map to SIO- an occurrent simply corresponds to a 'process', an independent continuant is simply an 'object', a generically dependent continuant is ignored in favor of a correspondence to its sole subclass information content entity to 'information content entity', a type of 'object'. A specifically dependent continuant is an 'attribute' and a process profile corresponds to a 'process quality', which is a kind of 'attribute'. Ontologies such as SIO that are based on the Web Ontology Language OWL offer terminology that is helpful for both theoretical and practical extensions to work in Psychology.

Our arguments for the use of SIO should not overshadow the tremendous contributions of the Basic Formal Ontology. BFO has established an ontological foothold for cognitive science such as its use in the Cognitive Paradigm Ontology [47]. As a proposal for a biological basis of mental illness [41] BFO foreshadowed the RDoC initiative. Users now have a wider range of choices in selecting an upper level ontology to meet their representational needs [48], a range that has expanded with the creation of new ontologies.

Concluding Remarks

Our goal in this article has been to demonstrate a proof-of-concept that SIO can provide a general language for integrating knowledge across a wide range of domains related to Cognitive Science. Additional development is required to formulate definitions and axioms for a more extensive application. Although scaling up requires extensive effort, constructing formal ontologies for psychology has numerous advantages [25]. To convert databases to knowledge bases requires tools that are capable of operating on data to identify extract and visualize regularities and inconsistencies. Seeing how specific results fit into a broader picture also supports evaluation of how much a particular set of results impacts a theory.

Poldrack and Yarkoni [49] document numerous challenges for organizing data within ontologies but conclude with a hopeful outlook: Optimistically, we predict that within a few years, researchers will be able to easily (i.e., without requiring advanced technical skills) upload raw data they have acquired and annotated to centralized patterns that run state-of-the-art cloud-based processing and analysis pipelines; interactively explore the results of such analyses via rich, user-friendly web interfaces that include extensive literature-based quantitative interpretation and allow easy piping to other third-party services; and use ontology-driven inference engines to conduct sophisticated, highly customized meta-analyses that draw on thousands of datasets acquired and deposited using similar platforms (p. 608).

Our article attempts to contribute to that objective by equipping readers with an overview of the organization of the Semanticscience Integrated Ontology and its extension to cognition.

Compliance with Ethical Standards

The authors have no potential conflict of interests with information reported in this article. In addition, the article is a review rather than original research involving human participants or animals.

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