An Ontological Analysis of the Electrocardiogram

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Bioinformatics has been a fertile field for the application of the discipline of formal ontology. The principled representation of biomedical entities has increasingly supported biological research, with direct benefits ranging from the reformulation of medical terminologies to the introduction of new perspectives for enhanced models of Electronic Health Records (EHR). This paper introduces an application-independent ontological analysis of the electrocardiogram (ECG) grounded in the Unified Foundational Ontology. With the objective of investigating the phenomena underlying this cardiological exam, we deal with the sub-domains of human heart electrophysiology and anatomy. We then outline an ECG Ontology built upon the OBO Relation Ontology. In addition, the domain ontology sketched here takes inspiration both in the Foundational Model of Anatomy and in the Ontology of Functions proposed under the auspices of the General Formal Ontology (GFO) research program.

Keywords: biomedical ontology, ECG, heart electrophysiology.

Introduction

The field of Bioinformatics is bearing witness of the application of *formal ontology* (the discipline) to the representation of biological entities (e.g., SCHULZ; HAHN, 2007) and (re-)organization of medical terminologies also in view of electronic health records (EHR) (e.g., SCHULZ et al., 2008). The motivation is (basically) to set the ground for: (i) biologists and physicians to store and communicate biomedical information and patient-related data effectively; (ii) gradually integrate these resources in the development of next-generation knowledge-based biomedical computer applications. These applications are meant to provide support in basic science and clinical research, as well as in the delivery of more efficient health care services. As put by ROSSE and MEJINO JR (2003), *"such a widening focus in bioinformatics is inevitable in the post-genomic era, and the process has in fact already begun"*.

A prominent initiative for gathering biomedical ontologies in a principled way is the Open Biomedical Ontologies (OBO) foundry (SMITH et al., 2007). Up this point, it

comprises over 60 ontologies that, although varying a lot in terms of granularity, canonicity and developmental stage, each one aims at representing a clearly bounded subject-matter. Among one of the most referred ontologies kept in OBO, we have the Foundational Model of Anatomy (FMA) (ROSSE; MEJINO JR, 2003). FMA deals with the anatomical structure of the mammalian (especially the human) body. However, despite the fact that the domain of human heart electrophysiology is of significant interest in Biomedicine, an ontology of heart electrophysiology is still missing in OBO as well as in the biomedical ontology literature[1]. Furthermore, although the electrocardiogram (ECG) defines one of the prominent kinds of biomedical data, as far as we know, it has not yet been addressed in the biomedical ontology literature.

The ECG is the most frequently applied test for measuring the heart activity in Cardiology (GESELOWITZ, 1989). In recent years, both the storage and transmission of ECG records have been object of standardization initiatives. Among the reference standards, one might refer to SCP-ECG[2], FDA XML[3] or HL7 ECG Annotation Message v3[4]. However, the focus of such standards is mostly on how *data and information* should be represented in computer and messaging systems (SMITH et al., 2007, p. 1252; YU, 2006, p. 254). On the other hand, there is a need for concentrating on the proper representation of the biomedical reality under scrutiny (SMITH, 2006). Namely, on *what the ECG is*, on both sides of the patient and of the physician. This is clearly relevant, since the ECG, as a vital sign, is an important piece in the composition of the EHR of today, as likely in the EHR of the future.

For the past years, we have been dealing with the ECG as a subject of ontological inquiry. An initial effort of representing ECG data by applying formal ontology techniques resulted in a preliminary ECG domain ontology reported in (GONÇALVES et al., 2007; ZAMBORLINI et al., 2008). Since then, we have been revising the basis underlying this early endeavor. This has led us to reformulate our ECG ontological representation, for the sake of increasing specialization, degree of detail, density and connectivity, to cite the terms conveyed by RECTOR et al. (2006, p. 335).

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[1] We are aware of two ongoing research initiatives which fall roughly in heart electrophysiology. RUBIN et al. (2006) present a symbolic, ontologically-guided methodology for representing a physiological model of the circulation as an alternative to mathematical models commonly employed. In turn, COOK et al. (2004) are putting effort in an extension of the FMA to cover physiology.

[2] Standard Communications Protocol for Computer-Assisted Electrocardiography <http://www.openecg.net/>.

[3] FDA XML Data Format Design Specification <http://xml.coverpages.org/FDA-EGC-XMLDataFormat-C.pdf>.

[4] HL7 ECG Annotation Message v3 <http://www.hl7.org/V3AnnECG>.

This paper introduces an application-independent ontological analysis of the electrocardiogram. Our analysis is grounded on the Unified Foundational Ontology (UFO) (GUIZZARDI; WAGNER, 2009). UFO started as a unification of the GFO (Generalized Formalized Ontology) (HELLER; HERRE, 2004) and the Top-Level ontology of universals underlying OntoClean (http://www.ontoclean.org). However, as shown in (GUIZZARDI; WAGNER, 2009), there are a number of problematic issues related the specific objective of developing general ontological foundations for conceptual modeling which are not covered in a satisfactory manner by existing foundational ontologies such as GFO, DOLCE or OntoClean. For this reason, UFO has been developed into a full-blown reference ontology based on a number of theories from Formal Ontology, Philosophical Logics, Philosophy of Language, Linguistics and Cognitive Psychology. This ontology is presented in depth and formally characterized in (GUIZZARDI, 2005). In this article, we present our formal characterization of this ontological analysis by using standard First-Order Logic (FOL).

By employing the results of this ontological analysis, we outline an ECG domain ontology that embodies both the sub-domains of heart electrophysiology and anatomy. The ECG Ontology also makes use of a number of existing foundational theories, namely: (i) the OBO Relation Ontology, which provides basic relations to be used in biomedical ontologies (SMITH et al., 2005); (ii) the Foundational Model of Anatomy (FMA), when dealing with the human anatomy for the ECG; (iii) the Ontology of Functions (OF) developed under the umbrella of the General Formal Ontology (GFO) research program (BUREK et al., 2007) for tackling heart electrophysiological functions. This outlined ECG ontology is currently implemented in a combination of the representation language OWL DL and its SWRL extension (HORROCKS et al., 2005).

Materials and Methods

Methodological principles for ontology engineering have attracted growing attention in the biomedical ontology literature, cf. (YU, 2006). In our ontological analysis of the ECG, we employ a number of principles from ontology engineering and foundational ontology, which also favor effective automated reasoning and ontology integration.

Ontology engineering

We employ an ontology engineering approach built upon the assumption that fostering a domain ontology (in the AI context) calls for two different ontology artifacts

(GUIZZARDI; HALPIN, 2008), viz., one ontologically well-founded theory of the subject domain meant to be strongly axiomatized for constraining as much as possible the theory's intended meaning; and another meant to be a computable artifact for automated reasoning and information retrieval. In (BITTNER; DONNELLY, 2007), the authors put forward an analogous line of argument and propose the use of First-order Logic (FOL) as a formalism for the former while some sort of Description Logic (DL) could be used for the latter. We follow the same choice of representation languages here, particularly by using for the latter OWL DL (mirrored to a DL) with the SWRL extension for rules (HORROCKS et al., 2005). Moreover, as traditional in Ontology Engineering (YU, 2006, p. 255), we specify a set of competence questions for delimiting the scope and purpose of the domain we have at hand. This methodological technique is also beneficial in the end of the development cycle as a means for evaluating the resulting artifact.

Ontological foundations

We draw attention to the fact that building a (biomedical) domain ontology on the basis of some ontological foundation is beneficial, if not necessary. A top-level ontological framework not only provides us with a support in making ontological decisions, cf. (GUARINO; WELTY, 2002), but also allows us making these decisions as transparent as possible in the resulting domain ontology. Our ECG ontological study is grounded in the top-level framework of the Unified Foundational Ontology (UFO) (GUIZZARDI; WAGNER, 2009). UFO comprises higher-order ontological categories (e.g., endurant, perdurant, kind, role, collective, relator, and so on) that are *instantiated by* the ECG domain universals (e.g., heart, ECG record).

Ensuring effective automated reasoning

One of the main practical objectives of the research discussed here is to use the results of our ECG ontological study to support automated reasoning over universals and particulars of ECG and heart electrophysiology. We have then been (practically) pursuing the sweet spot in expressing as much as possible of the ECG ontological theory we develop here in a combination of OWL DL and its SWRL extension, while keeping computational decidability and tractability. Since higher-order logics jeopardize the goal of practical automated reasoning, UFO categories are expressed in the resulting ECG ontology implementation merely as OWL annotations. In spite of this, we contend that the principled structure of the ontology (e.g. the ontological

soundness of subsumption and parthood taxonomies) is still preserved in the implementation.

Ontology integration

We seek ontology integration, especially towards the OBO foundry and the semantic web effort. The latter has influenced us to select the OWL DL/SWRL combination as an ontology codification language. Regarding the former, firstly, our ECG ontological theory is based on the FMA in what covers human anatomical concepts which are relevant for an ECG theory. Besides that, we apply the Ontology of Functions (OF) proposed in (BUREK et al., 2007) as a top-level ontological framework to model heart electrophysiological functions. Secondly, we borrow relations from the (cross-domain) OBO Relation Ontology (SMITH et al., 2005), which are especially valuable for defining spatial relations over time. We use them in combination with domain-specific relations coined here and complementary relations formally described in UFO.

The OBO Relation Ontology

A fundamental distinction in many foundational ontologies (e.g., DOLCE, GFO, UFO) and, in particular, in the OBO Relation Ontology (RO) is the distinction between *continuants* and *processes*. To put it literally from (SMITH et al., 2005),

> *"Continuants are those entities which endure, or continue to exist, through time while undergoing different sorts of changes, including changes of place. Processes are entities that unfold themselves in successive temporal phases"*

Generally speaking, the notion of continuant can be said similar to what is called *endurant* in UFO, while process can be seen similarly as a *perdurant*. Table 1 presents the RO relations which we employ here. A full discussion on these relations can be found in (SMITH et al., 2005). In this section, for the sake of brevity, we initially maintain the semi-formal syntax employed in that article to later move on to their corresponding First-Order Logic (FOL) counterparts. The following variables and ranges are used in the sequel.

$C, C_1, \ldots$ to range over continuant classes
$P, P_1, \ldots$ to range over process classes
$c, c_1, \ldots$ to range over continuant instances
$p, p_1, \ldots$ to range over process instances
$r, r_1, \ldots$ to range over three-dimensional spatial regions
$t, t_1, \ldots$ to range over instants of time

Table 1. The used relations of the OBO Relation Ontology

Relation	*Definition*
c **instance_of** C **at** t	a primitive relation between a continuant instance and a class which it instantiates at a specific time
p **instance_of** P	a primitive relation between a process instance and a class which it instantiates holding independently of time
c **part_of** c_1 **at** t	a primitive relation between two continuant instances and a time at which the one is part of the other
c **located_in** r **at** t	a primitive relation between a continuant instance, a spatial region which it occupies at a specific time
r_1 **part_of** r_2	a primitive relation of parthood, holding independently of time (i.e., holding constantly) between spatial regions (one a sub-region of the other)
r **adjacent_to** r_1	a primitive relation of proximity between two disjoint spatial regions
t_1 **earlier** t_2	a primitive relation between two times
p **has_participant** c **at** t	a primitive relation between a process, a continuant at a specific time
p **has_agent** c **at** t	a primitive relation between a process, a continuant at a specific time t at which the continuant is causally active in the process
c **exists_at** t	for some p, p **has_participant** c **at** t
p **occurring_at** t	for some c, p **has_participant** c **at** t
t **first_instant** p	p **occurring_at** t and for all t_i, if t_i **earlier** t then not p **ocurring_at** t
t **last_instant** p	p **occurring_at** t and for all t_i, if t **earlier** t_i then not p **ocurring_at** t
c **located_in** c_1 **at** t	for some r, r_1 (c **located_in** r **at** t and c_1 **located_in** r_1 **at** t and r **part-of** r_1)

Results

Anatomy for the ECG

This section is devoted to provide an ontological account of the human body anatomical continuants directly involved to the ECG. We take the FMA as a reference, and then consider continuant universals either with the same terms employed by the FMA or their synonyms. Nonetheless, we have not followed strictly the FMA modeling choices, since they are not fully supported by ontological foundations. For instance, DONNELLY et al. (2005) point to some problems with respect to the conception of part-whole relations in FMA; while KUMAR et al. (2004, p. 505) and RECTOR et al. (2006, p. 345) discuss problems in FMA with respect to granularity.

In consonance with FMA (see Figure 1 for our anatomical parthood taxonomy), we begin from the *human body*, and elaborate on the parts that compose the human *heart*. We include in our model *skin, skin surface* and *skin surface region* because, to anticipate the section dealing with the ECG, the latter is the part of the human body which is object of measurement by a recording device for acquiring the ECG. In our scope, it is worth to say that the heart has as parts the *right* and *left atria*, the *right* and *left ventricles* and the *wall of heart*. While the atria and ventricles are sub-kinds of *organ chamber*, the wall of heart is a sub-kind of *wall of organ*. The wall of heart has as parts the layers of endocardium, epicardium and *myocardium*. The latter is a sub-kind of *muscle layer of organ*, which is further divided (not completely) in *right* and *left atrial myocardium*, and *right* and *left ventricular myocardium*. They are all kinds of *region of myocardium*, and have as parts the conducting systems of right and left atria, and right and left ventricles, respectively.

We consider here only the *conducting system of right atrium*, since it exemplifies a full division into multiple ultimate parts of the heart in our scope. Unlike the FMA curators, we have not included in the main anatomical partonomy universals at *different levels of granularity* (cf. RECTOR et al., 2006), e.g., the *SA node myocyte*. We assume here that such a universal is a *grain of* the *collective* of *SA node myocytes*. This collective of myocytes in turn is a *functional component of* (a specific type of parthood) the *SA node*, which emerges from the collective of cells in addition to an *extracellular fluid*. In our understanding, the grain SA node myocyte is not part of the SA node. The notion of *collective* is contemplated in the UFO ontology (GUIZZARDI, 2005, Chapter 5), and is also discussed in depth in (RECTOR et al., 2006).
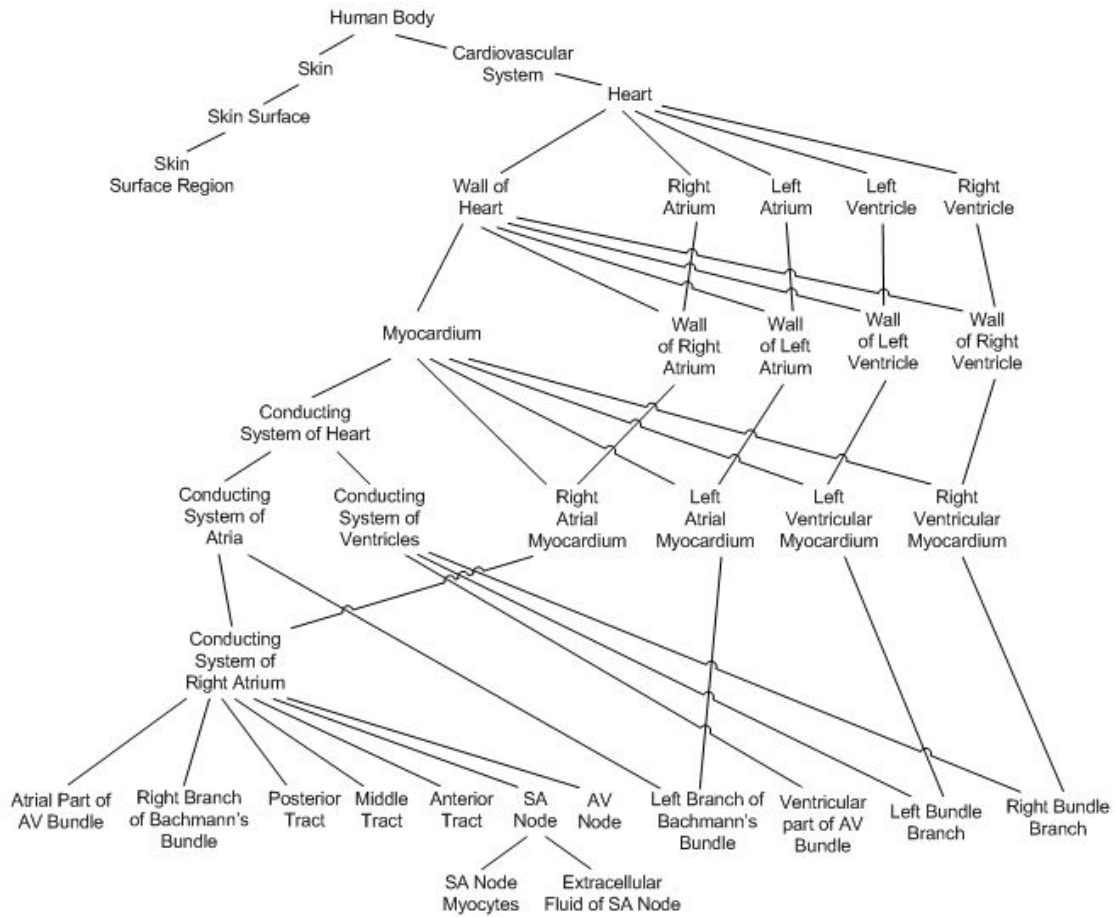
Figure 1. Partonomy of anatomy for the ECG. The lines represent *part-of* relationships (from the bottom to the top) between the anatomical entities.

In the anatomical partonomy of Figure 1, we use the parthood relation by adopting what is known, in Formal Ontology, as *minimal mereology*, cf. (GUIZZARDI, 2005, Chapter 5). The *part_of* links showed in Figure 1 represent a universal-level relation (holding between two universals, e.g. the right atrium is part of the heart) defined from an instance-level *part_of* (holding between two individuals, e.g., my right atrium is part of my particular heart). The universal-level parthood is defined by accounting for the instance-level version. The latter is a primitive relation characterized by the meta-properties of irreflexivity, asymmetry and transitivity. Formally, this means that:

Irreflexivity: $\forall c, t \; \neg \, \textbf{part\_of} \, (c, c, t)$

Asymmetry: $\forall c_1, c_2, t \; \textbf{part\_of} \, (c_1, c_2, t) \rightarrow \neg \, \textbf{part\_of} \, (c_2, c_1, t)$

Transitivity: $\forall c_1, c_2, c_3, t \; \textbf{part\_of} \, (c_1, c_2, t) \wedge \textbf{part\_of} \, (c_2, c_3, t) \rightarrow \textbf{part\_of} \, (c_1, c_3, t)$

The universal-level parthood (the links in Figure 1) can then be obtained as follows:

$$\textbf{part\_of}(C_1, C_2) =_{def} \forall c_1 \exists t_1 \, \textbf{instance\_of} \, (c_1, C_1, t_1) \rightarrow \forall t \, (\textbf{instance\_of} \, (c_1, C_1, t) \rightarrow$$
$$\exists c_2 \, (\textbf{instance\_of} \, (c_2, C_2, t) \wedge \textbf{part\_of} \, (c_1, c_2, t) \,) \,)$$

Notice also in Figure 1 that some entities in the partonomy have only one part. Although this is not a problem when adopting minimal mereology, the real reason here is something else. Those entities do have other universals as parts, but these are not relevant for the representation of the ECG. Finally, it is important to highlight that we have used the relation of part_of here to represent a proper parthood relation. If necessary, an improper parthood relation can be defined as usual:

$$\textbf{improper\_part\_of} \, (c_1, c_2, t) =_{def} \textbf{part\_of}(c_1, c_2, t) \vee (c_1 = c_2 \, \textbf{at} \, t)$$

Human Heart Electrophysiology

Bioelectric sources spontaneously arise in the heart at the cellular level. The heart myocytes (muscle cells) are immersed in an *extracellular fluid* separated from their interior by their membranes, which carry out a control of ions transport. In the resting state, the interior of the myocytes has a negative potential with respect to the exterior, i.e., these cells are electrically polarized. However, particularly in the sinoatrial (SA) and atrioventricular (AV) nodes, parts of the myocardium (cf. Figure 1), the myocytes abruptly depolarize and then return to its resting value. This phenomenon is a result of ions passing in either direction across the cells' membrane (GESELOWITZ, 1989).

Therefore, notably the SA and AV node myocytes give rise to electrical impulses which are propagated to its neighboring myocytes and normally reach the entire heart. That is why the SA and AV nodes are called the heart pacemakers. However, since this kind of electrical impulse arises in the SA node at a faster rate and with a higher intensity, the AV node electrical impulse is said to be overdriven by the SA node impulse (GESELOWITZ, 1989). For conveying the *cardiac electrical impulse* (arisen in the SA node) around the heart, there are myocytes in addition to the SA and AV myocytes (the Purkinje fibers) that constitute the *conducting system of heart* (see Figure 2). The major conducting pathway is so-called His-Purkinje system. It is composed by the atrioventricular bundle (*AV bundle*, or bundle of His), then bifurcated into the *left* and *right bundle branches* (LASKE; IAIZZO, 2005; GUYTON; HALL, 2006). As a response to the cardiac electrical impulse conducted over that system, the myocardium holds contractions in its atrial and ventricular parts for

pushing blood respectively into the ventricles and either into the systemic or pulmonary circulation.
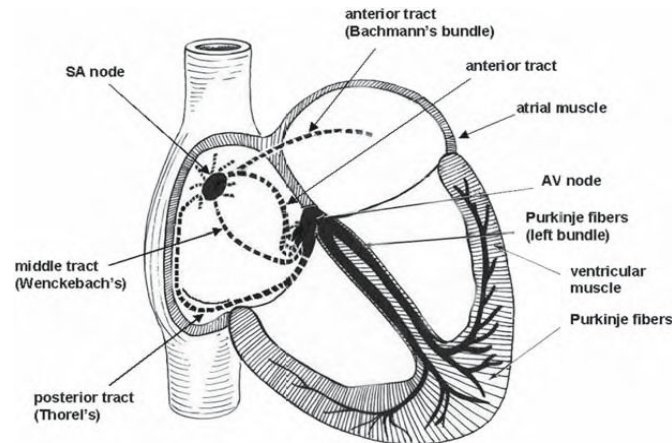

Figure 2. The conduction system of the heart (source: LASKE; IAIZZO, 2005).

Given that overview, we now focus on an ontological representation of human heart electrophysiology meaningful for the representation of the ECG. For this, we build upon the Ontology of Functions (OF) proposed by BUREK et al. (2007). Basically, we aim at providing a clear structure of heart electrophysiological functions (*what* they are), and *how* and by *who* can they be realized. We intend, by these means, to be able to reconstruct those physiological entities from a particular ECG.

The basic structure of a function, as introduced in (BUREK et al., 2007), is a set of labels, a functional item, a set of requirements to be fulfilled in case the function is realizable, and a goal to be satisfied in case the function is in fact realized. A function is connected to a continuant which *has* the function, and can *realize* it by playing a specific *role* (the functional item). This role is exercised by what is named in Philosophy a *qua individual* (GUIZZARDI, 2005, Chapter 7). For instance, if John marries Mary, a number of rights and duties (legally speaking) are to henceforth be satisfied by *John-qua-husband-of-Mary*. Finally, a function is realized by means of a process. This process provides a transition from the state of the world (SOW) in which the requirements of the function are fulfilled, to the SOW in which the goal of the function is satisfied. This process is called the *realization* of the function. A realization can be considered *actual* or *dispositional*. That is, a process can have the disposition of being the realization of the function, even if this disposition is never actualized, e.g., in case of some malfunctioning.
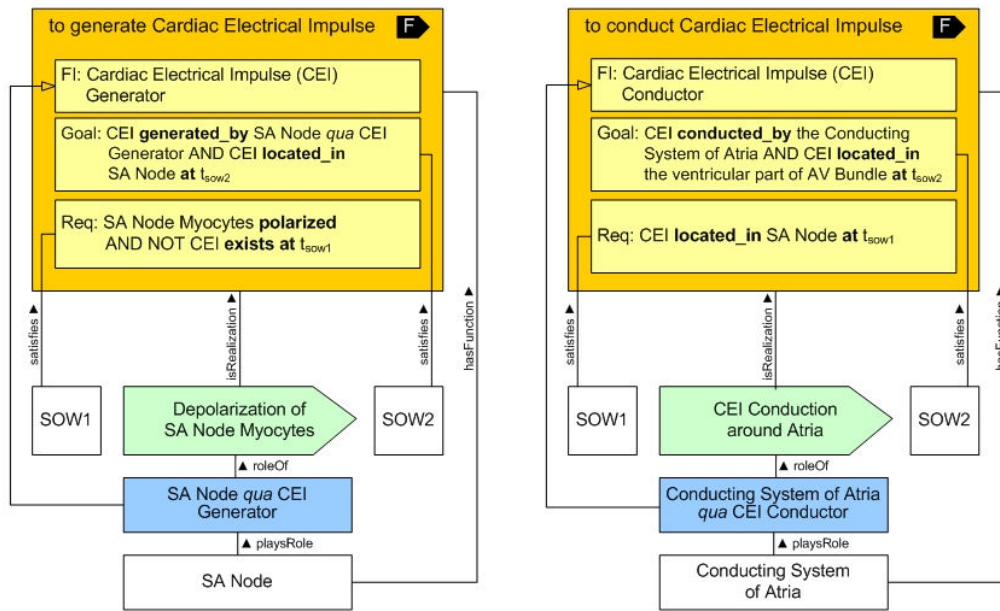
Figure 3. Heart electrophysiological functions represented in the OF framework.

Figure 3 illustrates two examples of heart electrophysiological functions represented by using the OF framework, viz., *to generate cardiac electrical impulse* (CEI) and *to conduct CEI*. While the former is realized by means of the process of *depolarization of the SA node myocytes*, the latter, in its atrial manifestation, is realized by means of the process of *CEI conduction around atria*. The function *to conduct CEI* is manifested by the process of *CEI conduction around ventricles* in a similar fashion. Figure 4 provides an adapted representation of these functions (including the ventricular manifestation of CEI conduction). Their applicability is further clarified in the section about the ECG.
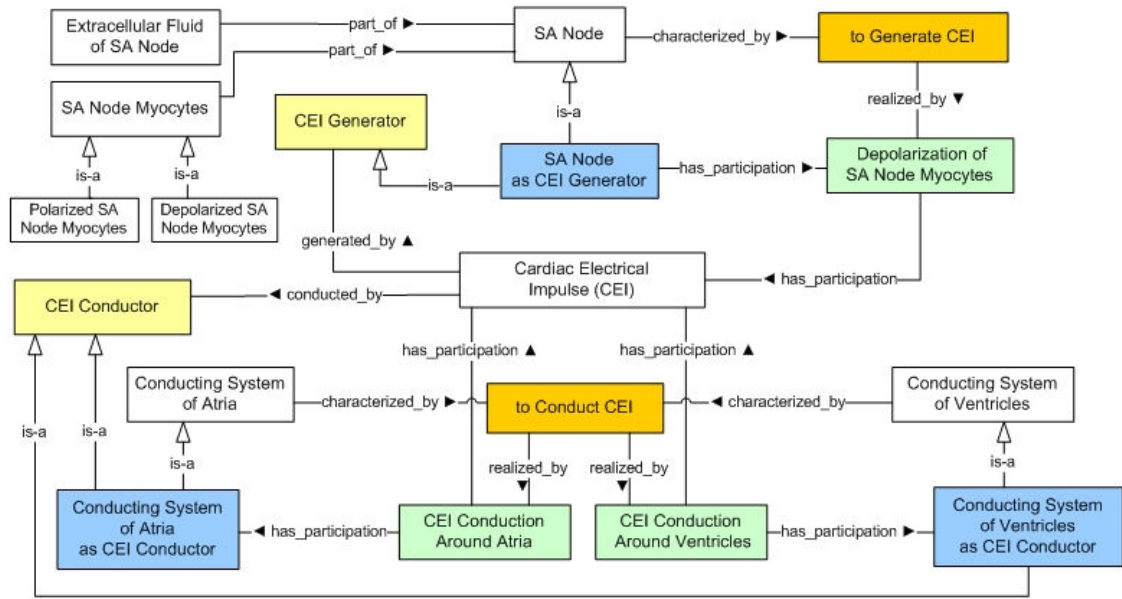
Figure 4. Part of the heart electrophysiology model. The function *to conduct CEI* characterizes both the conducting systems of atria and ventricles. This function can be realized either by the process of CEI conduction around atria or around ventricles. The function *to generate CEI* in turn characterizes the SA node, and can be realized by the process of depolarization of the SA node myocytes.

We use specific relations that are defined as follows. Firstly, before we can define what it means to state that a continuant has been *generated by* another, we need to define the notion of *production*. The instance-level relation *produced_by* holds between a continuant and a process. As formally described below, a continuant c is produced by a process p iff there exists one and only one time instant t_1 such that t_1 is the last instant of p, p has c as participant at t_1, and for all time instants t earlier than t_1 then c does not exist at t. The universal-level relation *produced_by* is defined subsequently.

produced_by(c, p) $=_{def}$
$\exists! t_1$ (**last_instant**(p, t_1) $\wedge$ **has_participant**(p, c, t_1) $\wedge$ $\forall t$ (**earlier**(t, t_1) $\rightarrow$ $\neg$**exists**(c, t)))

produced_by(C,P) $=_{def}$
$\forall c \exists t$ **instance_of** (c, C, t) $\rightarrow$ $\exists p$ **instance_of** (p, P) $\wedge$ **produced_by**(c, p)

Notice that to state that a continuant participates in some process entails it exists during that process, cf. Table 1. We are now able to proceed by giving a definition for the notion of generation. A continuant c is generated by another continuant c_1 iff there exists some process p such that, for all time instants t at which p is occurring

then p has c_1 participating as an agent, and c is produced by p. See also the universal level version.

generated_by (c, c_1) $=_{def}$
$\exists p \; (\; \forall t \; (\; \textbf{occurring\_at}(p, t) \rightarrow \textbf{has\_agent}(p, c_1, t \;) \;) \wedge \textbf{produced\_by}(c, p \;) \;)$

generated_by (C, C_1) $=_{def}$
$\forall c \; \exists t \; (\; \textbf{instance\_of}(c, C, t) \rightarrow \exists c_1, t_1 \; (\; \textbf{instance\_of}(c_1, C_1, t_1) \wedge \textbf{generated\_by}(c, c_1) \;) \;)$

The notion of conduction, in turn, is a bit more complex. First, following UFO we take the category *mode* into account. The reason is that an entity which is object of conduction, like the cardiac electrical impulse (CEI), needs to *inhere* in some conductor to exist (GUIZZARDI, 2005, Chapter 6). Thus, it is existentially dependent on some conductor. The CEI is modeled here as a mode, just as a symptom, which only exists by inhering in some patient. Before providing a definition for conduction, we present below the instance-level primitive relation of inherence, together with its correlated universal-level relation of *characterization*. Inherence is an irreflexive, asymmetric and intransitive type of existential dependence relation; characterization can only be applied if F (see the formulae below) is an instance of the category *moment universal* (from which mode is a specialization). In this case, we add the restriction that the variable F ranges over functions (a specific type of mode).

Irreflexivity: $\forall c, t \; \neg \; \textbf{inheres}(c, c, t)$

Asymmetry: $\forall c, c_1, t \; \textbf{inheres}(c, c_1, t) \rightarrow \neg \; \textbf{inheres}(c_1, c, t)$

Intransitivity: $\forall c_1, c_2, c_3, t \; \textbf{inheres}(c_1, c_2, t) \wedge \textbf{inheres}(c_2, c_3, t) \rightarrow \neg \; \textbf{inheres}(c_1, c_3, t)$

Existential Dependency:
$\forall c_1, c_2, \exists t_1 \; \textbf{inheres}(c_1, c_2, t_1) \rightarrow \forall t \; (\textbf{exists}(c_1, t) \rightarrow \textbf{exists}(c_2, t) \wedge \textbf{inheres}(c_1, c_2, t) \;)$

characterized_by(C, F) $=_{def}$
$\forall c \; \exists t_1 \; \textbf{instance\_of}(c, C, t_1) \rightarrow \forall t \; (\; \textbf{instance\_of}(c, C, t) \rightarrow \exists f \; (\; \textbf{instance\_of}(f, F, t) \wedge \textbf{inheres}(f, c, t) \;) \;)$

We can then proceed to formally describe the relation *conducted by* between two continuants c and c_r. This relation is characterized here using the three formulae below. The first of these formulae states that if c is conducted by c_r then there is a (conduction) process p that eventually occurs and that, in all instants that this process occurs, both c and c_r participate in this process. Moreover, the formula states that c inheres in c_r during this entire process and only during this process. Putting this

formula together with the condition of existential dependence for the inherence relation defined above we have that participating in this conduction process is an essential condition for *c*.

$$\text{conducted\_by}(c,c_r) \rightarrow \exists p,t_1 \; \textbf{occurring\_at} \; (p,t_1) \wedge \forall t \; (\; \textbf{occurring\_at} \; (p,t) \rightarrow \textbf{has\_participant}(p,c,t) \wedge \textbf{has\_participant}(p,c_r,t) \;) \wedge (\forall t_2 \; \textbf{inheres}(c,c_r,t_2) \leftrightarrow \textbf{occurring\_at}(p,t_2) \;)$$

The next formula states that in all instants that *c* inheres in c_r (i.e., all instants that *c* exist), *c* occupies a spatial region r_1 that is a proper part of the spatial region *r* occupied by its bearer (the conductor). Moreover, the formula states that given a time instant *t*, there is only one region occupied by *c* in that instant (analogously for the conductor c_r). Finally, the formula (indirectly) states that during the conduction process *p* (i.e., during the lifetime of *c*), *c* occupies all proper parts of *r* but also that no proper part of *r* is occupied by *c* more than once during the process *p*.

$$\text{conducted\_by}(c,c_r) \rightarrow \forall t \; (\textbf{inheres}(c,c_r,t) \rightarrow \exists r,r_1 \; (\textbf{located\_in}(c_r,r,t) \wedge \textbf{located\_in}(c,r_1,t) \wedge \textbf{part\_of}(r_1,r) \wedge \forall r_2,r_3 \; (\textbf{located\_in}(c_r,r_2,t) \wedge \textbf{located\_in}(c,r_3,t) \rightarrow (r_2 = r) \wedge (r_3 = r_1) \;) \wedge \forall r_4 \; (\textbf{part\_of}(r_4,r) \rightarrow \exists ! t_1 \; \textbf{inheres}(c,c_r,t_1) \wedge \textbf{located\_in}(c,r_4,t_1) \;) \;) \;)$$

Finally, the following formula states that given any two instants t_1 and t_2 such that *c* inheres in c_r both in t_1 and t_2 and that t_1 is the instant immediately earlier t_2 then in each of these instants, *c* occupies regions adjacent to each other.

$$\text{conducted\_by}(c,c_r) \rightarrow \forall t_1,t_2,r_1,r_2 \; (\textbf{inheres}(c,c_r,t_1) \wedge \textbf{inheres}(c,c_r,t_2) \wedge \textbf{located\_in}(c,r_1,t_1) \wedge \textbf{located\_in}(c,r_2,t_2) \wedge \textbf{immediately\_earlier}(t_1,t_2) \rightarrow \textbf{adjacent\_to}(r_1,r_2) \;)$$

Confer below the relation of *immediately_earlier* holding between two time instants.

$$\textbf{immediately-earlier} \; (t_1, t_2) =_{\text{def}} \textbf{earlier}(t_1, t_2) \wedge \neg \exists t \; (\; \textbf{earlier}(t,t_2) \wedge \textbf{earlier}(t_1,t) \;)$$

The universal-level version of the conducted_by relation is the following.

$$\textbf{conducted\_by}(C,C_r) =_{\text{def}}$$
$$\forall c \; \exists t \; \textbf{instance\_of}(c,C,t) \rightarrow \exists c_r \; \textbf{instance\_of}(c_r,C_r,t) \wedge \textbf{conducted\_by}(c,c_r)$$

The Electrocardiogram

Once we have set the ground of anatomy and physiology, we can finally focus our ontological analysis in the ECG itself. The ECG (in German, the electrokardiogram, EKG) was probably the first diagnostic signal to be studied with the purpose of

automatic interpretation by computer programs (GESELOWITZ, 1989). The reason for such an interest in computing ECG records is that the analysis of the ECG waveform can help to identify a wide range of heart illnesses, which are distinguished by specific modifications on the ECG *elementary forms*.

On the side of the *patient*, the ECG is acquired in the context of a *recording session*, in which a *recording device* is used to perform *observations* evenly spaced in time for measuring electrical potential differences (p.d.) around the patient's *skin surface* and with the result of producing *samples*. As discussed in the previous section, these p.d.'s are result of the heart electrical activity. The observations are made at the same time from different *electrode placements* for providing multiple viewpoints of the heart activity (so-called *leads*). Those correlated observations form correlated *observation series*. Each observation series then produces a *sample sequence*.

Now shifting to the physician's perspective, it is worth mentioning that heart beats are mirrored to cardiac cycles that compose the ECG waveform. A canonical cycle, as introduced by W. Einthoven, has *waves* (sub-kinds of elementary forms) named PQRST. They are outlined as *P wave*, the mereological sum of the Q, R and S waves (so-called *QRS complex*), and *T wave* (see Figure 5). The P wave and QRS complex map the *depolarization of atria* and *ventricles*, respectively. The atrial and ventricular myocardial contractions start normally at the peak of these waves. The T wave in turn maps the *repolarization of ventricles*[5] (GESELOWITZ, 1989; GUYTON; HALL, 2006).
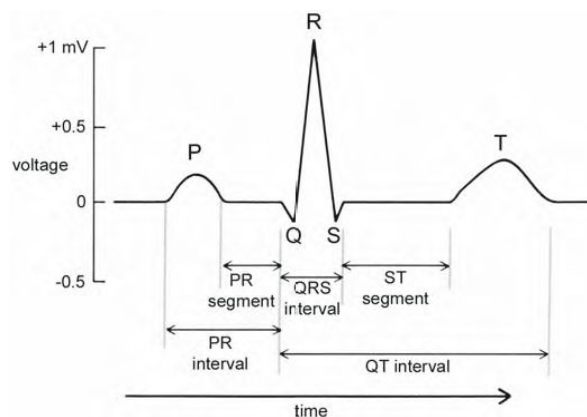

Figure 5. A typical *cycle* (reflecting a heart beat) in the ECG *waveform* (source: LASKE; IAIZZO, 2005). Two cycles are connected by the *baseline*, which reflects the heart resting state.

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[5] The repolarization of atria can not be seen in the ECG waveform since its resulting potentials are small in amplitude and then overridden by the QRS complex. A U wave is also often mentioned, but its origin is still not completely known.

Figures 6 and 7 provide graphical representations of the ECG from the sides of the patient and physician, respectively. In our ontology, these two models are endowed with the corresponding FOL axiomatization, which, for brevity, are omitted here. Here, in these figures, the models are intended uniquely as a visual representation of the ECG domain, without any intention of being complete. These models are based on evidence present in medical textbooks but also synthesize concerns present in current ECG standards (leaving out technological aspects).
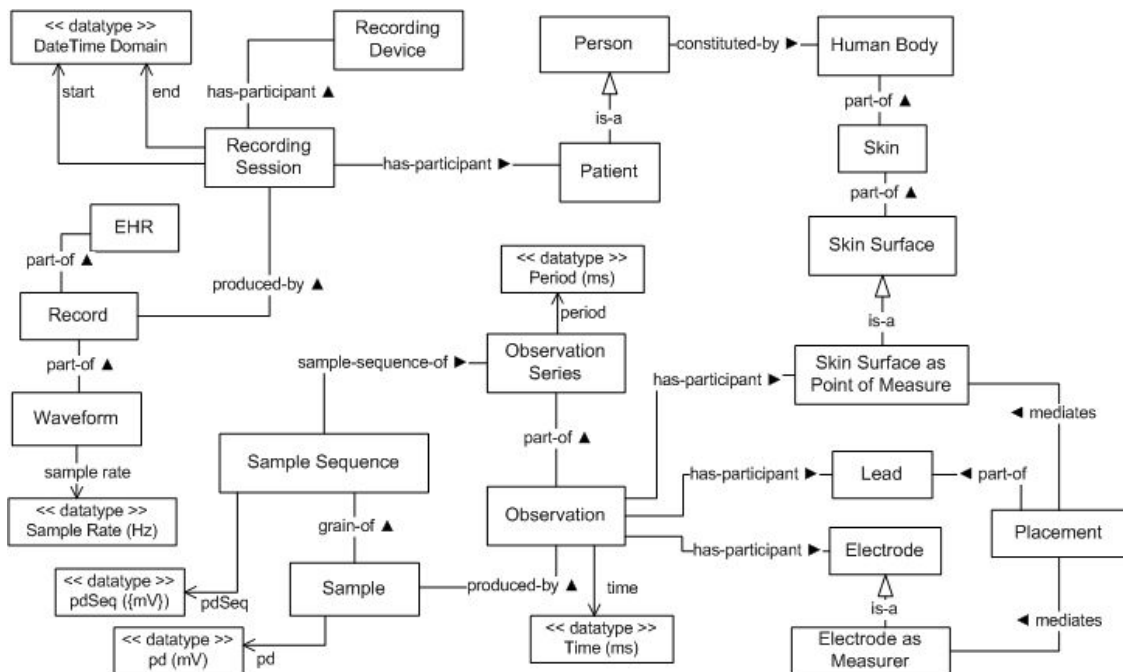
Figure 6. Model of the ECG on the side of the patient. He or she participates in a recording session meant to produce an ECG record. In this session, several observations are made by electrodes placed on the patient's skin surface. Every observation produces a sample, which is a grain of sample sequence (an ordered collective of samples). For brevity, we are omitting here a representation of the several configurations of electrode placements on specific skin surface regions that compose ECG leads (viz., I, II, II, aVL, aVR, aVF, V1, …, V6).
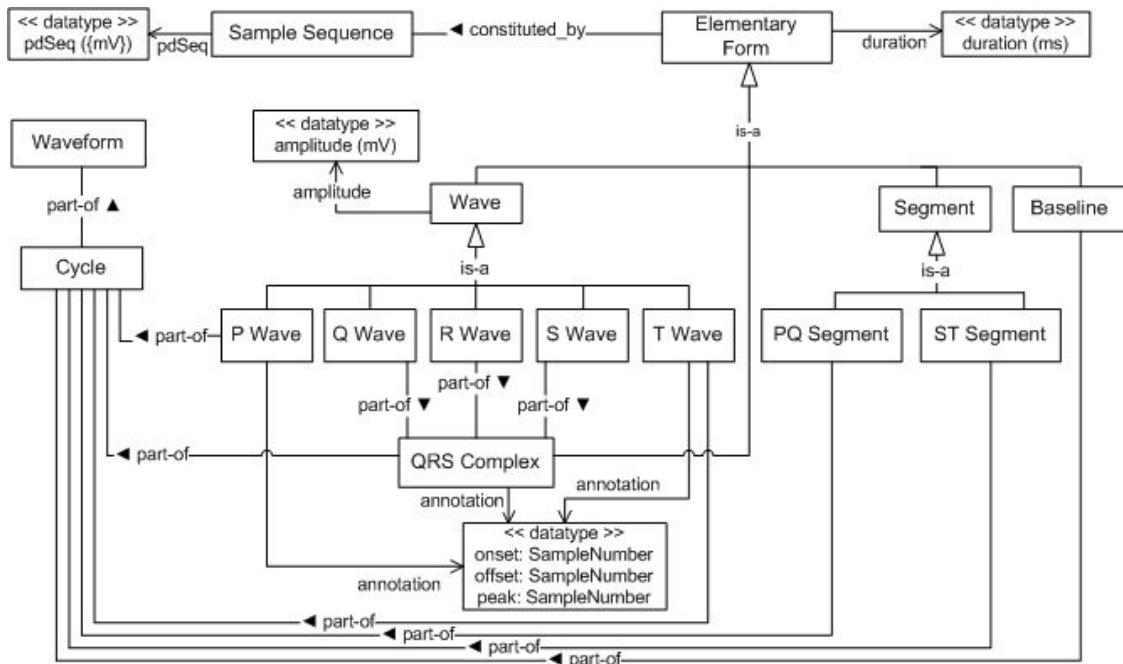
Figure 7. Model of the ECG on the side of the physician. He or she can analyze the ECG waveform, cycle by cycle. Each one represents a heart beat. A cycle has as parts many different elementary forms. An elementary form is constituted by a sample sequence, which is an ordered collective of samples. Notice that this model does not cover any abnormality in the ECG.

The notions of constitution and mediation used in the relations *constituted by* and *mediates* are non-trivial (GUIZZARDI, 2005). For brevity, we refrain from giving their definitions in this text. An in-depth discussion of these relations can be found in (MASOLO et al., 2003) and (GUIZZARDI, 2005, Chapter 6), respectively.

From the ECG to Heart Electrophysiology

We now have material to bridge the domains of ECG and heart electrophysiology. The interpretation of an ECG involves several subtle details that often exist tacitly in the mind of the cardiologist. Our effort here is to provide a method capable of explicitly uncovering, at a first glance, what an ECG maps with respect to canonical heart electrophysiology. We therefore introduce a relation named *maps* meant to associate each of those ECG elementary forms that appears in the ECG to its underlying electrophysiological reality. It can be defined at the instance- and universal-level as follows.

First, we can formally characterize the relation *observation_series_of* between an observation series process *o* and a (conduction) process *p*. The formula below states that if *o* is an observation series of process *p* then every (atomic) observation which is

part of *o* is an observation of a part of *p* (and can only be an observation of a process which is part of *p*).

$$\text{observation\_series\_of}(o,p) \rightarrow \forall o_1 \ (\text{part\_of}(o_1,o) \rightarrow \exists p_1 \ (\text{part\_of}(p_1,p)$$
$$\wedge \ \text{observation\_of}(o_1,p_1)^6\ ) \wedge \forall p_2 \ (\text{observation\_of}(o_1,p_2) \rightarrow \text{part\_of}(p_2,p)\ )\ )$$

In the sequence, we state that if we have two observations o_1 and o_2 which are part of *o* and which are observations of parts p_1 and p_2 (parts of *p*), respectively, such that o_2 *follows* o_1 in the series *o* then their respective observed process parts also follow each other in the same way (i.e., p_2 follows p_1).

$$\text{observation\_series\_of}(o,p) \rightarrow \forall o_1,o_2,p_1,p_2 \ (\text{part\_of}(o_1,o) \wedge \text{part\_of}(p_1,p) \wedge \text{observation\_of}(o_1,p_1)$$
$$\wedge \ \text{part\_of}(o_2,o) \wedge \text{part\_of}(p_2,p) \wedge \text{observation\_of}(o_2,p_2) \wedge \text{follows}(o_2,o_1) \rightarrow \text{follows}(p_2,p_1)\ )$$

The relation *follows* holding between two processes p_2 and p_1 implies that

$$\text{follows}(p_2,\ p_1) \rightarrow \exists t_1,t_2 \ (\text{last\_instant}(t_1,p_1) \wedge \text{first\_instant}(t_2,p_2) \wedge \text{earlier}(t_1,t_2))$$

Now, we can characterize the correspondence between an observation series and a sequence of samples representing this series. The first two of these formulae are analogous to formulae just presented for observation series with two important differences. If *s* is a sample sequence of observation series *o* then: (i) every sample in *s* is produced by exactly one observation in *o*; (ii) there is a direct correspondence between observations in *o* and samples in *s*.

$$\text{sample\_sequence\_of}(s,o) \rightarrow \forall s_1 \ (\text{grain\_of}(s_1,s) \rightarrow \exists o_1 \ (\text{part\_of}(o_1,o) \wedge \text{produced\_by}(s_1,o_1)\ )$$
$$\wedge \ (\ \forall o_2 \ \text{produced\_by}(s_1,o_2) \rightarrow (o_1 = o_2)\ )\ )$$

$$\text{sample\_sequence\_of}(s,o) \rightarrow \forall s_1,s_2,o_1,o_2 \ (\text{grain-of}(s_1,s) \wedge \text{produced\_by}(s_1,o_1) \wedge \text{grain\_of}(s_2,s)$$
$$\wedge \ \text{produced\_by}(s_2,o_2) \wedge \text{successor\_of}(s_2,s_1) \rightarrow \text{directly\_follows}(o_2,o_1))$$

The relation of *successor_of* is defined as usual between an element in a sequence and the (direct) successor of that element in that sequence (following the intrinsic ordering criteria of that sequence). The relation of directly_follows is defined as:

$$\text{directly\_follows}(p_2,\ p_1) =_{\text{def}} \text{follows}(p_2,\ p_1) \wedge \neg \exists p_3 \ (\text{follows}(p_3,\ p_1) \wedge \text{follows}(p_2,\ p_3))$$

Finally, we can define the relation of *maps* between an elementary form *c* and a (conduction) process *p*:

$$\text{maps}(c,p) =_{\text{def}} \exists s,o \ \text{constituted\_by}(c,s) \wedge \text{sample\_sequence\_of}(s,o) \wedge \text{observation\_series\_of}(o,p)$$

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[6] We assume here that if **observation_of**(o,p) then the process *o* occurs either synchronously or after the process *p*. Intuitively, there can be no "observation of the future".

and the corresponding relation at the universal-level.

maps (C, P) $=_{def}$

$\forall c \exists t$ **instance_of** (c, C, t) $\rightarrow \exists p, t_1$ **instance_of** (p, P, t_1) $\wedge$ **maps** (c, p)

By employing the notions just discussed, we give meaning to the ECG elementary forms. We have also specified a set of rules to reconstruct from the ECG waveform the correlated electrophysiological processes occurred over anatomical continuants. These rules make use of our function representations. As an example, consider the rules R1 to R6 given below. They give meaning to the P-wave based on the function of the right hand of Figure 3. So, what are we able to infer once we have a faithfully annotated (thus, recognized) P-wave?

First of all, every P-wave *maps* one and only one electrophysiological process of cardiac electrical impulse (CEI) conduction around atria.

(R1) $\forall c$ **PWave**(c) $\rightarrow \exists p$ (**CEIConductionAroundAtria**(p) $\wedge$ **maps**(c, p) $\wedge$
$\forall p_1$ (**maps**(c,p_1) $\rightarrow$ (p_1 = p)))

Furthermore, every process like this is associated to one and only one CEI and to one and only one conducting system of atria playing the role of CEI conductor. Indeed, they need to participate over the whole process. Formally (cf. R2),

(R2) $\forall p$ (**CEIConductionAroundAtria** (p) $\rightarrow \exists t_1$ (**occurring**(p, t_1) $\wedge \exists! c_1, c_2$ (**CEI** (c_1)
$\wedge$ **ConductingSystemOfAtriaAsCEIConductor**(c_2)
$\wedge \forall t$ (**occurring**(p, t) $\rightarrow$ **has_participant**(p, c_1, t)
$\wedge$ **has_participant**(p, c_2, t))))

In addition, for every such a process, there is one and only one function *to conduct CEI* such that the latter is dispositionally realized by the process. That is to say (cf. R3), they are associated to each other by the disposition the process has to be the realization of the function, even though this disposition may not become actual.

(R3) $\forall p$ (**CEIConductionAroundAtria**(p) $\rightarrow \exists! f$ (**toConductCEI**(f) $\wedge$ **disp_realized_by**(f, p)))

Nevertheless, if we have the process, we are able to infer that (cf. R4) there was one state of the world SOW1 at which its requirements have been fulfilled (see Figure 3).

(R4) $\forall p$ (**CEIConductionAroundAtria**(p) $\rightarrow \exists! c_1, c_2, t_{SOW1}$ (**CEI**(c_1) $\wedge$ **first_instant**(p, t_{SOW1}) $\wedge$
SANode(c_2) $\wedge$ **exists**(c_1, t_{SOW1}) $\wedge$ **located_in**(c_1, c_2, t_{SOW1})))

The recognition of the realization of *to conduct CEI* depends on the annotation whether the P-wave in hand is normal or not. This can be formally described by R5 as follows.

(R5) $\forall p,c,f$ ((**CEIConductionAroundAtria**(p) $\land$ **NormalPWave**(c) $\land$ **toConductCEI**(f)
$\land$ **maps**(c, p) $\land$ **disp_realized_by**(f, p)) $\rightarrow$ **actual_realized_by**(f, p))

In such case, we can then infer that the goals of *to conduct CEI* has been fulfilled by the process of CEI conduction around atria.

(R6) $\forall p,f$ ((**CEIConductionAroundAtria**(p) $\land$ **toConductCEI**(f) $\land$ **actual_realized_by**(f, p))
$\rightarrow \exists c_1,c_2,c_3, t_{SOW2}$ (**CEI**(c_1) $\land$ **ConductingSystemOfAtria**(c_2)
$\land$ **VentricularPartOfAVBundle**(c_3) $\land$ **last_instant**(p, t_{SOW2})
$\land$ **conducted_by**(c_1, c_2) $\land$ **located_in**(c_1, c_3, t_{SOW2})))

Whither: An ECG Ontology

The results of our ontological study of the Electrocardiogram have been the source of domain knowledge in the construction of an ECG ontology. It constitutes a solution-independent theory of the electrocardiogram, which is to be reused across multiple applications. In its essence, the ECG Ontology handles <u>what the ECG is</u> on both sides of the patient and of the physician. As we have seen, that relies on a number of notions related to the heart electrophysiology, which takes place over anatomical entities. The scope of the ECG Ontology can be defined by means of the following competence questions (CQ).

CQ1. What essentially composes the ECG record?

CQ2. How is the ECG record obtained?

CQ3. What in the ECG waveform is object of the physician's analysis for interpreting a correlated heart behavior?

CQ4. For all ECG elementary forms, which heart electrophysiological function(s) does (do) it map?

CQ5. For all heart electrophysiological functions, which anatomical entity(ies) is (are) able to realize it?

CQ6. For all heart electrophysiological functions, which requirements must be satisfied to enable its realization?

CQ7. For all heart electrophysiological functions, which goals must be satisfied to accomplish its realization?

The ECG Ontology is then composed by two extra sub-ontologies, viz., the anatomy for ECG and heart electrophysiology sub-ontologies. It also imports the OBO Relation Ontology (RO), see Figure 8.
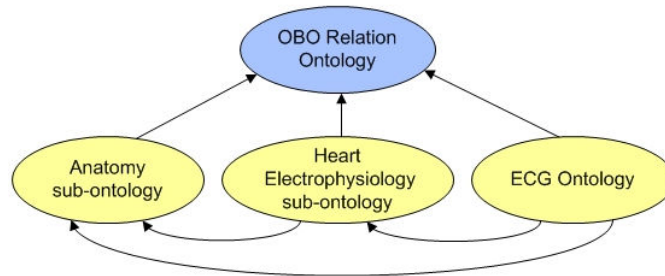

Figure 8. Import relationships of the ECG Ontology. The arrows point towards the ontology being imported. The OBO Relation Ontology is imported here to give us basic relations used in the others.

The ECG Ontology has been implemented in the ontology codification language OWL DL and its SWRL extension. The current version of the implemented ECG Ontology is available for download at the project website[7].

Discussion

Competence

The ECG Ontology's CQs have been axiomatized and also implemented in OWL DL/SWRL. As such, they comprehend a means for evaluation by taking advantage of reasoning services. We give below two examples regarding the axiomatization of the CQ4 and CQ7 (again by taking the P-wave as an example). They are answered by automated reasoning as shown in Figure 9.

CQ4. For all ECG elementary forms, which heart electrophysiological function(s) does (do) it map?

$$\forall c \ (\ \mathbf{Pwave}(c) \rightarrow \exists p \ (\ \mathbf{ImpulseConductionAroundAtria}(p) \land \mathbf{maps}(c, p) \ ) \ )$$

CQ7. For all heart electrophysiological functions, which goals must be satisfied to accomplish its realization?

$$\forall \ f, c, c_1, p, t_{SOW2} \ (\ (\ \mathbf{toConductCEI}(f) \land \mathbf{ConductingSystemOfAtria}(c)$$

$\wedge$ **characterized_by**(c, f) $\wedge$ **CEIConductionAroundAtria**(p)

$\wedge$ **actual_realized_by**(f, p) $\wedge$ **last_instant**(p, t_{SOW2}))

$\wedge$ **CEI**(c_1) $\wedge$ **has_participant**(p, c_1, t_{SOW2})) $\rightarrow$ (**conducted_by**(c_1, c) $\wedge$ $\exists c_2, c_3$

(**VentricularPartOfAVBundle**(c_2) $\wedge$ **ConductingSystemOfHeart**(c_3) $\wedge$ **part-of**(c, c_3) $\wedge$ **part-of**(c_2, c_3) $\wedge$ **located_in**(c_1, c_2, t_{SOW2})))
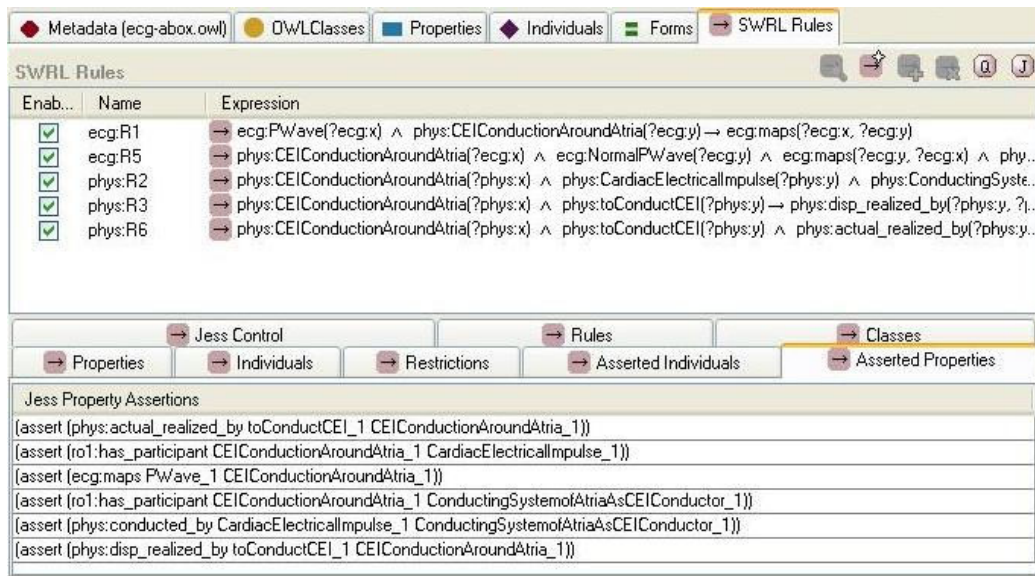
Figure 9. Screenshot of the reasoning service that answers ECG Ontology's CQs by making use of its OWL DL/SWRL implementation.

Applicability

An application-independent domain ontology such as the ECG Ontology can be applied to many different purposes. Examples include the following which are briefly discussed below: (i) managing heterogeneity of information and (ii) reasoning over universals and particulars, similarly as referred to by BURGUN (2006).

Managing heterogeneity of information

Once we assume that the ECG Ontology represents a great deal in representing *what is the ECG* and solely this (e.g., regardless of technology concerns), it can be used to support the design of interoperable versions of ECG data formats like SCP-ECG, FDA XML and HL7. By taking the ECG Ontology as a reference, the entities present in these data formats could be semantically mirrored to the ontology universals, instead of being object of pairwise mappings. Thereby, the ECG data formats should meet CIMINO's desiderata (1998), namely: (i) *non-vagueness*, the entities which form the nodes of the data format must correspond to at least one universal; and (ii) they must

correspond to no more than one universal, i.e., *non-ambiguity*. Since the ECG Ontology axiomatization allows little freedom to both vagueness and ambiguity, this solution would at least force the data formats to make their assumptions explicit. Besides, this proposal is cost-effective, since *n* data formats require *n* mappings to a reference ontology, whereas *n (n - 1) / 2* pairwise mappings would be required (BURGUN, 2006).

Reasoning over universals and particulars

The ECG Ontology outlined here has been fully implemented in an ontology codification language. In our project, we have used OWL DL and its SWRL extension in virtue of its available off-the-shelf reasoning tools, e.g., Pellet (SIRIN et al., 2007). The OWL DL/SWRL file is thus susceptible to be effectively used for automated reasoning, though not keeping all the ontology axiomatization (see Section 'Methods').

The ECG Ontology represents a canonical model of heart anatomy and a canonical model of heart electrophysiology. The ECG model, contrarily, can be filled in by any real ECG record instance. However, a deformed QRS complex (possibly indicating some pathology) would not have a non-canonical cardiac electrical impulse to map to. Given this elucidation, let us put some light of what can be done. By using an instance of a normal ECG record[8] (an artifact for study), we can reconstruct the (canonical) electrophysiology behind it. So, from a normal instance of QRS complex (faithfully annotated), we are able to reconstruct the cardiac electrical impulse behind it and the anatomy on which it has taken place.

A characteristic application for that is a system to support learning in heart electrophysiology and ECG. Indeed, we have built such a system that uses a previous version of the ECG Ontology, cf. (GONÇALVES et al., 2009). In that system, an ECG chart is plotted from an ECG OWL file (with data filled into the ontology individuals). Besides, an illustration of the heart conducting system is able to show animations in response to user clicks either on the latter or on a point in the ECG chart. These clicks call a reasoning procedure that emphasize an elementary form in the ECG waveform and select the correlated conducting phenomena to be animated.

All this could be done with a non-canonical ECG record as well if we had a non-canonical model of physiology to reconstruct. As far as we have investigated, that

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[8] The Physionet (GOLDBERGER, 2000), for example, provides ECG data benchmarks with annotations made either by physicians or computer programs. These annotations are mostly to mark and classify the ECG elementary forms (e.g., the P wave, the QRS complex, and so on).

seems to be possible by extending the sub-ontology of heart electrophysiology to address the fuzziness (vagueness) of the heart electrophysiological functions' realization.

Limitations and Future Work

As exposed in the discussion above, the limitations of our results are mostly due to the complexity in dealing with physiological aspects of the human heart. This is particularly tough when phenotypic issues are to be covered. Therefore, a strong research effort is required to extend the ECG ontological theory presented here with such a purpose.

Among the envisaged directions for future work we include: (i) the release of an updated version of the web reasoning-based system proposed in (GONÇALVES et al., 2009) to put into online use the implemented ECG Ontology; (ii) the investigation of how to capture from the ECG the inherent fuzziness of whether or not a heart electrophysiological function has been actually realized. We believe the latter to be an important starting point to cope with particular pathological cases.

Conclusions

In this article we provide an ontological account of the cardiological exam ECG and its correlation to the human heart electrophysiology. The ECG Ontology outlined here constitutes an axiomatized domain theory grounded in a principled ontological basis. The applicability of this ontology has also been enlightened for two different purposes, viz., managing heterogeneity of ECG data format standards and automated reasoning. With the latter in mind, we have been translated the models and FOL formulae we present here into the ontology codification language OWL DL with its SWRL extension.

As part of an ongoing worldwide research effort to foster ontological representations of biomedical reality, our endeavor is in place. Naturally, our ECG ontological inquiry may be elaborated to increase, say, the *degree of detail*, and even to cover the eventual lacunae. Meanwhile, the challenge of ontology integration is still tough even in this ever more anchored research field of so-called biomedical ontology. However, by striving for keeping compliance with correlated initiatives, we have put an effort forward in this direction. Anyhow, it does is the case that *"The value of any kind of data [or ontology] is greatly enhanced when it exists in a form that allows it to be integrated with other data [or ontology]"* (SMITH et al., 2007). In that spirit, the

ECG Ontology can be understood as a contribution to be aggregated into the biomedical ontology effort.

Acknowledgments

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