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The Representational Challenge for Designing and Managing 5P Medicine Ecosystems

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Abstract. Health and social care systems around the globe currently undergo a transformation towards personalized, preventive, predictive, participative precision medicine (5PM), considering the individual health status, conditions, genetic and genomic dispositions, etc., in personal, social, occupational, environmental and behavioral context. This transformation is strongly supported by technologies such as micro- and nanotechnologies, advanced computing, artificial intelligence, edge computing, etc. For enabling communication and cooperation between actors from different domains using different methodologies, languages and ontologies based on different education, experiences, etc., we have to understand the transformed health ecosystems and all its components in structure, function and relationships in the necessary detail ranging from elementary particles up to the universe. That way, we advance design and management of the complex and highly dynamic ecosystem from data to knowledge level. The challenge is the consistent, correct and formalized representation of the transformed health ecosystem from the perspectives of all domains involved, representing and managing them based on related ontologies. The resulting business view of the real-world ecosystem must be interrelated using the ISO/IEC 21838 Top Level Ontologies standard. Thereafter, the outcome can be transformed into implementable solutions using the ISO/IEC 10746 Open Distributed Processing Reference Model. Model and framework for this system-oriented, architecture-centric, ontology-based, policy-driven approach have been developed by the first author and meanwhile standardized as ISO 23903 Interoperability and Integration Reference Architecture.

Keywords. Health and social care transformation, Ecosystems, Systems architecture, Knowledge representation and management, Information modelling, Language types, Ontologies

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Introduction

Over many years, healthcare systems around the globe evolved from empiric medicine, locally providing domain-specific general services through evidence-based medicine, providing domain-specific group-specific services to person-centered medicine, providing coordinated multiple domain services to the subject of care, also called managed care.

Traditionally, own observations and conclusions, in evidence-based medicine also observations and conclusions from other domain experts available in related databases, have been re-used. The paradigm, what work yesterday should work today as well, dominated the practice despite the long-term development of anatomy, toxicology, histology, and pathology up to the cellular level. In the 1990s, it became more and more evident that individuals differentiate in their molecular, physiological and behavioral characteristics, accompanied by different environmental and occupational exposure, etc. but also regarding their individual health history. This lead to the development of personalized medicine by providing multiple domain services to the subject of care including telemedicine. Thereby, the clinically justified individual status and context of the subject of care must be considered and understood.

So far, medicine is just understood as service on diseased subjects, managed by care professionals. The ongoing healthcare systems transformation aims at personalized, preventive, predictive, participative precision medicine (P5M). It considers individual health status, conditions, genetic and genomic dispositions in personal social, occupational, environmental and behavioral context, thus turning health and social care from reactive to proactive. Table 1 summarizes the described health transformation. Further aspects, such as presentational challenges, standards, etc., will be discussed later on.

Table 1. Health and social care transformation towards 5P medicine including related representation styles and standards

Care Paradigm	Services	Way of Practicing	Justification	Representation Style	Electronic Comm./ Coop.	Standard
Phenomeno-logical Medicine	Domain-specific general services – one solution fits all	Observation	Pattern recognition	Data	Local data repository; Inside the unit	Data standards
Evidence-Based Medicine	Domain-specific, group specific services	Observation with objective evaluation	Statistical justification of group-specific treatment outcome	Information	Central data repositories	Information standards
Person-Centered Medicine	Multiple domains' services	Managed care	Process mgmt., Best medical practice guidelines	Agreed terminology, DMP Best Practice Guidelines	Cross-organizational Business Process	Terminology standards; Process standards
Personalized Medicine	Multiple domains' services - Telemedicine	Considering the translational pathology of disease	Clinically justified individual status and context	Disciplinary concepts in situational context	Knowledge management	Domain ontology standards
P5 Medicine	Cross-domain services - Consumerism, Telemedicine	Understanding the pathology of disease from elementary particle up to society	Scientifically justified individual status	Multidisciplinary concepts in comprehensive context	Knowledge Space management	Multiple ontologies guided by Top-Level Ontologies standards

In the P5M approach, we cannot consider the health and social care system in isolation, but must incorporate its political, legal, ethical, economic and ecological framework. Therefore, we must consider all those domains and their actors as well. In other words, we have to manage the 5PM ecosystem. Thereby, an ecosystem is defined as a structural and functional unit of ecology where the living organisms interact with each other and the surrounding environment. It is the community of living organisms in conjunction with non-living components of their environment, interacting as a system [1].

1. Foundations for Designing and Managing Transformed Health and Social Care Ecosystems

It is impossible to represent the highly complex, highly dynamic, multidisciplinary/ multi-domain healthcare system by one domain‘s terminology or even by using ‘simple’ ICT ontologies. There are approaches for representing multi-domain concepts in a hierarchical set of ontologies. An ontology is a formal explicit specification of a shared conceptualization of a domain of interest, providing an ordering system of entities of a domain and their relations [2]. A concept is a knowledge component the expert community has agreed on. A concept must be uniquely identifiable, and independently accepted by experts and users. For enabling consistent communication and cooperation, we have to guarantee that all actors refer to the same real world component. For that reason, an abstract and generic reference architecture able to represent any viewpoint or domain of interest for any ecosystem in question is inevitable. Starting point could be an abstract mathematical representation based on universal type theory and universal logics such as the Barendregt Cube [3] to formally and consistently represent any system in the universe. More details can be found in [4].

For managing systems and systems engineering, a system-theoretical approach is more practical. However, for managing systems in their structure and function, a black box approach just considering the relations of the system and its environment is not sufficient. Instead, we must understand all systems elements, their composition and decomposition as well as their internal and external relations by using a white box approach. Moreover, this must be done from the perspectives of all domains and their actors involved in the ecosystem. The granularity level considered depends on the domain experts’ objectives in the context of the actual use case of the business system, thereby reaching from elementary particles up to the universe. The resulting generic component model (GCM), introduced by the first author in the early nineties of the last century, consists of the following three perspectives or dimensions [5]:

- System’s Architectural Perspective,
- System’s Evolutionary or Development Perspective,
- System’s Domain Perspective.

Meanwhile, the approach has been standardized as ISO 23903:2021 Interoperability and integration reference architecture – Model and framework [6]. Figure 1 presents the GCM reference architecture.

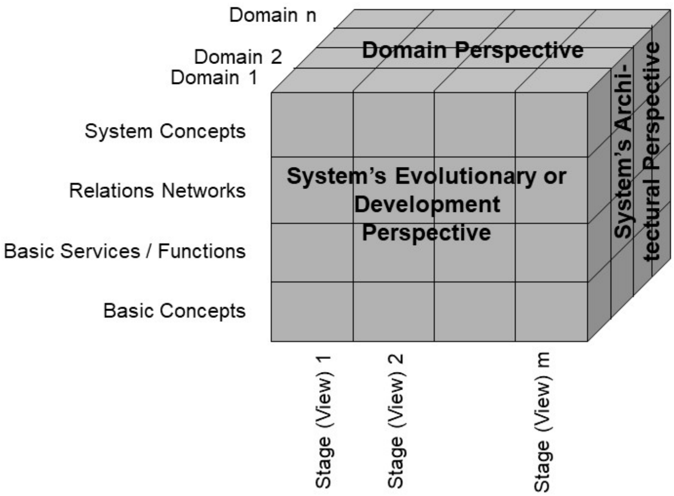

Figure 1. Generic Component Model Reference Architecture

Regarding the dimension of the system's evolution or development process from an architectural perspective, there are different standards to manage this process:

- The Object Management Group (OMG) Model Driven Architecture (MDA) [7]
- ISO/IEC 10746 Reference Model for Open Distributed Processing (RM-ODP) [8]
- ISO 23903 Integration and Interoperability Reference Architecture

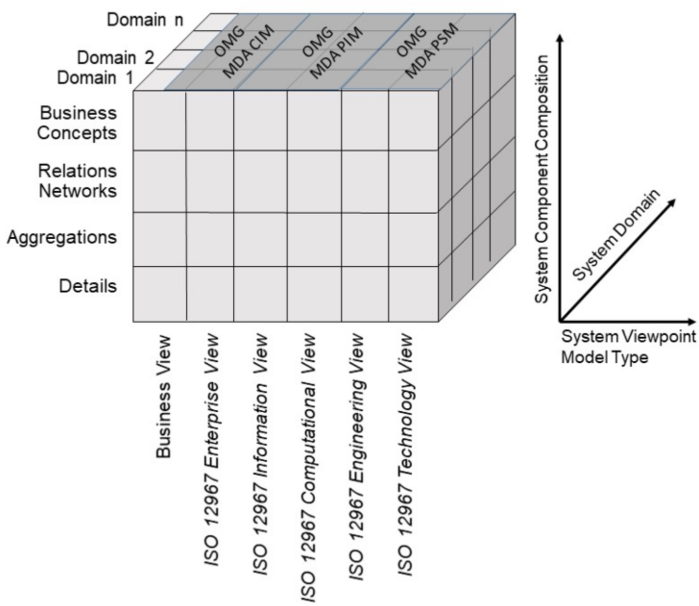

Figure 2. Generic Reference Architecture

The OMG MDA starts with the Computation Independent Model (CIM) as primary model. On that basis, a Platform Independent Model (PIM) is defined, which contains enough information to derive one or more Platform Specific Models (PSMs). The ISO/IEC 10746 Reference Model for Open Distributed Processing provides a methodology for describing and building widely distributed ICT systems and applications. Thereby it defines the following view: Enterprise view, information view, computational view, engineering view and technology view.

ISO 23903 Integration and Interoperability Reference Architecture allows the formal representation, design and management of any ecosystem. Therefore, it must extend the RM-ODP by the real world system viewpoint, called business view. That way, it also provides a methodology for integration and interoperability of any specifications and work products according to the aforementioned standards families. Figure 2 defines it's development process dimension, thereby integrating the two other standards.

2. Modeling Transformed Health Ecosystems

In scientific modeling, we distinguish four dimensions of data modelling: Data, Information, Knowledge, and Knowledge Space [9]. Thereby, the transformation from data to information considers interpretation, meaning and semantics, the transformation from information to knowledge considers action, structure and pragmatics, and the transformation from knowledge to knowledge spaces supports reflection, innovation and collaboration across domains [10]. Another way of classifying models is the data model level [11], ranging from very high data model representing the ISO 23903 Business View, the high level data model according to the ISO/IEC 10746 Enterprise View, the logical data model level corresponding to the ISO/IEC 10746 Information View and Computational View, and finally the physical data model level corresponding to the ISO/IEC 10746 Engineering view [12]. Furthermore, we can classify data models according to the related information model level [13]. Hereby, we distinguish between external (Business View), conceptual (Enterprise View), logical (Information View and Computational View) and physical (Engineering View). Table 2 summarizes those model classifications.

2.1. Knowledge Representation

From the modeling perspective, three levels of knowledge representation are distinguished and must be consecutively processed:

a) epistemological level (domain-specific modeling)
b) notation level (formalization, concept representation)
c) processing level (computational, implementations)

A model is thereby defined as a representation of objects, properties, relations and interactions of a domain, enabling rational and active business in the represented domain.

The generalization of domain-specific epistemological models requires their transformation into a universal KR notation. The outcome must be validated on the real world system and thereafter adopted if needed. [14]

Table 2. Classification of models

Data Model Level	Dimension of Modeling	Data Models at Different Information Levels	Modeling Actors	Model Scope	ISO 23903 Interop. & Integration RA	Examples		
Very-high-level data model	Knowledge space	External	Business domains stakeholders	Scope, requirements and related basic concepts of business case	Business View			ISO 23903 Interoperability and Integration Reference Architecture
High-level data model	Knowledge	Conceptual	Business domains stakeholders	Relevant information and representation & relationships of basic concepts	Enterprise View	DCM, CSO	ISO 10746 ODP-RM	
Logical data model	Information	Logical	Data modelers and analysts	Layout & types of data and object relationships	Information View	HL7 V3 (CMETs), HL7 CIMI, openEHR Archetypes, FHIM		
					Computational View	HL7 FHIR		
Physical data model	Data	Physical	Data modelers and developers	Implementation-related and platform-specific aspects	Engineering View			
					Technology View	HL7 V2/V3 ITS, SQL, OHDSI, OMOP		

Following, we will consider the described aspects in more detail.

2.2. Language Aspect of Knowledge Representation

Symbols, operators, and interpretation theory give sequences of symbols *meaning* within a KR.

A key parameter in choosing or creating a KR is its *expressivity*. The more expressive a KR, the easier and more compact it is to express a fact or element of knowledge within the semantics and grammar of that KR. However, more expressive languages are likely to require more complex logic and algorithms to construct equivalent inferences. A highly expressive KR is also less likely to be complete and decidable. Less expressive KRs may be both complete and decidable. [15]

Any business system can be represented using ICT data ontologies. However, the justification of correctness and completeness of structure and behavior of the represented ecosystem can only be provided at the ecosystem's business view using the involved domains' ontologies. Justification of structure and behavior representation includes the representational components, their underlying concepts, their relations, but also the related constraints.

Therefore, natural languages are not only efficient in representing meaning, shared knowledge, skills, and experiences assumed. They also provide an optimum between *restriction to special structure* and *generative power* according to the Chomsky grammar hierarchy (regular, context-free, context-sensitive, recursively enumerable) enabling the rich and nevertheless decidable representation of real-world concepts, supported of course by common sense knowledge (Figure 3) [16].

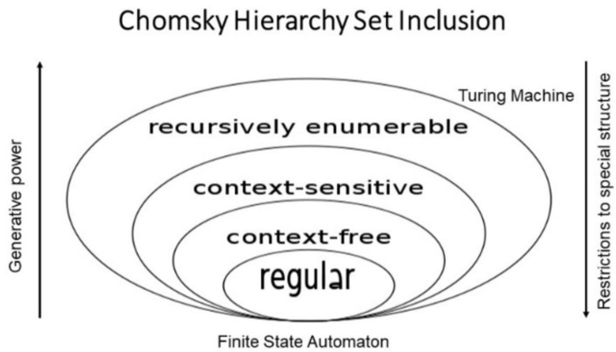

Figure 3. Chomsky Hierarchy [16]

Knowledge can be represented at different levels of abstraction and expressivity, ranging from implicit knowledge (tacit knowledge) up to fully explicit knowledge representation, i.e. from natural language up to universal logic. Figure 4 presents the Different types of ontologies. In case that an ontology is not available, we can deploy as first step the adopted Top-Level Ontology framework according to ISO/IEC 21838 instead (Figure 5) [17].

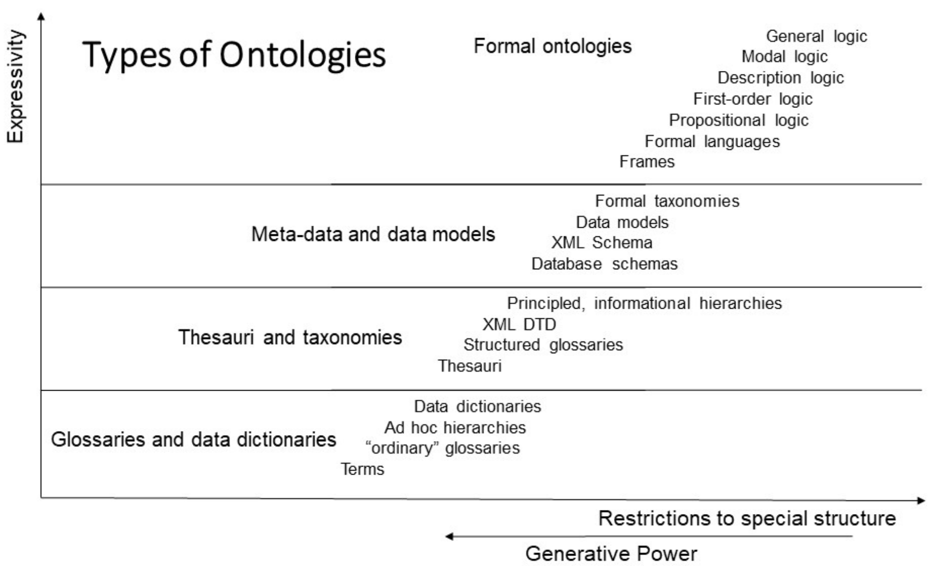

Figure 4. Types of ontologies (after [15])

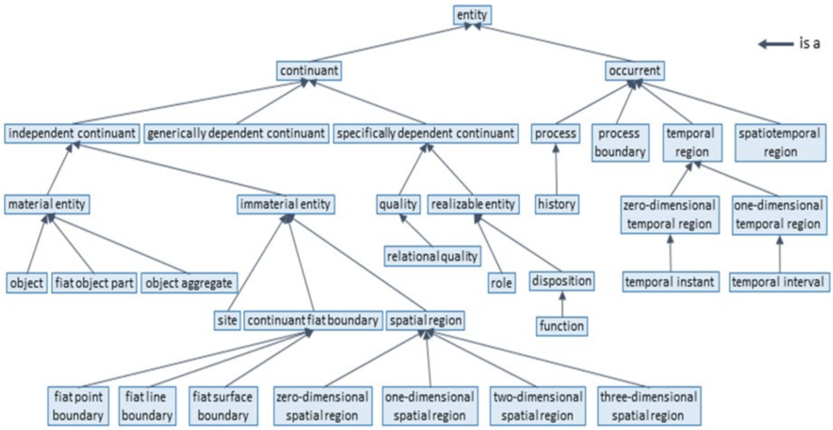

Figure 5. BFO 2020 is_a Hierarchy (after ISO/IEC 21838:2020 [17])

2.3. Good Modeling Practice

A model is an unambiguous, abstract conception of some parts or aspects of the real world corresponding to the modeling goals. Hereby, the domain of discourse, the business objectives, and the stakeholders involved have to be defined. The relevant stakeholders define the provided view of the model as well as the way of structuring and naming the concepts of the problem space. [13]

Data modeling covers the domains' concept space, refined to the business concepts, followed by the logical and finally physical models.

First capturing key concepts and key relations at a high level of abstraction, different abstraction levels should be used iteratively, where the first iteration is performed in a top-down manner to guarantee the conceptual integrity of the model. This requires meeting design principles such as orthogonality, generality, parsimony, and propriety. Figure 6 represents the ISO 23903 Framework in the Light of Good Modeling Best Practices [13].

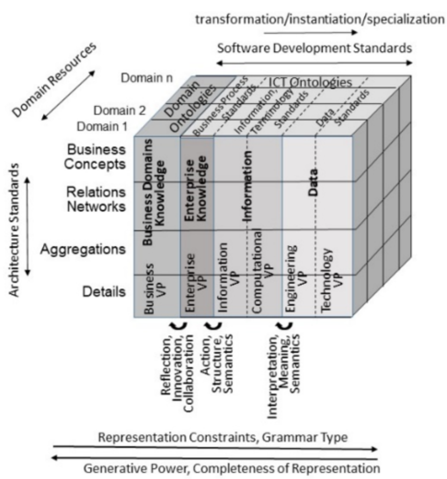

Figure 6. ISO 23903 Framework in the Light of Good Modeling Best Practices

All views are represented through the related ontologies. Facts as outcome of observations are represented by data. The interpretation of facts requires information. Understanding the system requires domain concepts (knowledge), and the integration of systems requires external (non-IT) knowledge represented by knowledge spaces. Fact-based practices are realized through observations resulting in physical data models. Logical data models enable the interpretation of data, while the understanding the system requires the conceptual data model representation. Managing a real-life system requires external model representation. Figure 7 shows the domain ontologies developed by the Open Biological and Biomedical Ontologies Foundry [18]

RELATION TO TIME / GRANULARITY	CONTINUANT				OCCURRENT
	INDEPENDENT		DEPENDENT		
ORGAN AND ORGANISM	Organism (NCBI Taxonomy)	Anatomical Entity (FMA, CARO)	Organ Function (FMP, CPRO)	Phenotypic Quality (PaTO)	Biological Process (GO)
CELL AND CELLULAR COMPONENT	Cell (CL)	Cellular Component (FMA, GO)	Cellular Function (GO)		
MOLECULE	Molecule (ChEBI, SO, RnaO, PrO)		Molecular Function (GO)		Molecular Process (GO)

Figure 7. OBO Foundry Ontologies (after [18])

For correctly designing and managing the transformed health ecosystem, we have to start with the Business view represented by domain experts using their terminologies/ontologies. Thereafter, the resulting model must be use case per use case as well as context/constraints per context/constraints transformed in a strict top-down approach into the different views according to the development process. Thereby, the instantiation of the views must be re-engineered according to the knowledge defining the correct and consistent instances, e.g. information and data from studies or repositories, EHRs, biobanks, etc.

3. Discussion

5PM ecosystems are characterized by the advancement from an empirical data-focused to a knowledge-driven concept-focused approach. This requires starting the design and management process with the real-world system by representing multidisciplinary concepts in comprehensive context, that way reflecting the knowledge spaces of all domains and actors involved in the specific use case. As different actors from different domains may use the same low level models (physical and/or logical) to represent different domain concepts and vice versa, integration and interoperability at this representational level are not decidable. For considering external knowledge spaces and contexts in very high level models domain experts or ecosystem actors deploy, the traditional and still widely practiced interoperability and integration focus on low-level representation style is even more critical.

Starting with data or low level models does not allow a correct decision on the components, their structures, functions and relations. First we have to understand the real-world business system's use case, to correctly represent the different views in the development process to implement and use the correct solution. This makes ISO 23903 to a universal standard enabling the design and management of any system from any domain in any context, covering living and non-living systems, plants, technologies, etc., at any level of granularity from elementary particles up to the universe.

The presented approach provides integration and interoperability between any ecosystem components including the actors by facilitating ontology-based translation within the individual educational background and skills, but also any components of the different viewpoints to re-use existing artifacts such as standards, specifications, information models and data.

4. Conclusions

Being based on a sophisticated, foundational, system-theoretical, architecture-centric, ontology-based, policy-driven approach, ISO 23903

- Enables representation and management of multiple domains' knowledge → Understanding the pathology of diseases and sharing that knowledge
- Enables the integration of different domains
- Enables interoperability and integration of existing specifications and artifacts, so supporting sustainability
- Enables interoperability between any ecosystem components including the involved actors
- Serves as Methodology for Developing Advanced 5P Medicine Solutions

Blindly defining, managing and using data spaces as currently performed in the context of the European Health Data Space (EHDS) are not really helpful, but could even become dangerous, automating killing the patient.

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