

Extending Inner-Ear Anatomical concepts in the Foundational Model of Anatomy (FMA) Ontology

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Abstract—The inner ear is physically inaccessible in living humans, which leads to unique difficulties in studying its normal function and pathology as in other human organs. Recently, biosimulation model has gained a significant attention to understand the exact causative factors that give rise to impairment in human organs. However, to build a biosimulation model for human organ concepts and their topological relationships from multiple and semantically overlapping domains such as biology, anatomy, geometrical, mathematical, physical models are required. In this paper, we focus on modelling the inner-ear macro anatomical concepts and their topological relationships. We extended the Foundational Model of Anatomy (FMA) ontology to cover micro-level version of human inner-ear anatomy where connection between simulating tissues, liquids, soft tissues and connecting adjacent (e.g. hair cells, perilymph) parts studied in detail, included and implemented.

Keywords-Biosimulation; Healthcare and Life Sciences; Inner-Ear; Semantic Web; Ontology Building;

I. INTRODUCTION

The creation of a realistic model to understand the inner-ear function and behaviour is a complex scientific task to achieve, depends on the understanding of different structures from multi-domain expertise. Orchestration between anatomical structures governed by different physical principles and having different scales is integral part of the hearing process. The physical models describing distinct structures within the inner-ear follow different physical descriptions which are intrinsically interdependent. The vibration model of the *basilar membrane* originated from *organ of corti*, differs from hair cell both mechanically and electrically. The creation of a multi-scale model for the cochlea mechanics depends on the composition of different physical models with supporting clinical data and combining efforts from groups with different domains of expertise.

In this paper we target on the representation aspect of biosimulation models, more specifically on modelling the inner-ear macro anatomical concepts and their topological relationships by extending the Foundational Model of Anatomy (FMA) Ontology [1] to represent the anatomical structures which influence the inner-ear physiological performance. It covers concepts and relationships related to the geometric and mechanical modelling of the inner-ear. Figure

1 represents a schematic drawing of the cochlea. It contains two separated and chemically distinct fluid compartments, the endolymphatic compartment (scala media), and the perilymphatic compartment (comprised of the scala vestibuli and the scala tympani), which are connected at the helicotrema. The Organ of Corti resides on the basilar membrane in the scala media and is responsible for the transduction of vibrational energy of the middle ear ossicular system to electrical energy by depolarization of the cochlear hair cells and the subsequent production of auditory nerve impulses that are conducted to specialized areas in the brain.

The work presented in this article is developed as part of the SIFEM EU project¹. The SIFEM project results in the delivery of an infrastructure, which will semantically integrate finite element simulation data with experimental and clinical data, aiming towards the delivery of a robust multi-scale model of the inner-ear. SIFEM aims at developing a linked data platform [2] for finite element biosimulation of the sensorineural hearing loss.

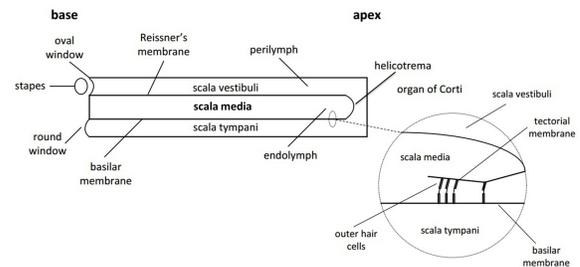


Figure 1: Schematic representation of the human cochlea

II. MOTIVATION SCENARIO

Our work is motivated by rapid demand from clinical organisations and labs conducting biosimulation experiments to understand the pathophysiological consequences and risk factors of hearing impairment in humans. This scenario can be very well observed by basic anatomy of ear where, there are three major parts to the ear, with distinct functions; The outer ear collects sound waves and funnels them towards the middle ear. The middle ear ossicular chain oscillates in

¹<http://www.sifem-project.eu>

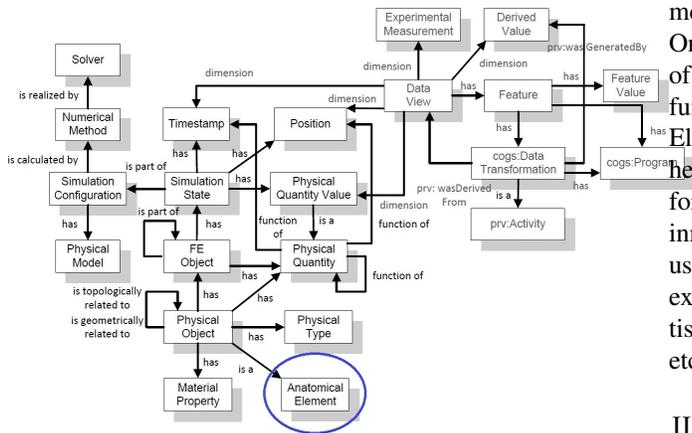


Figure 2: Excerpt of SIFEM multi-scale conceptual model

response to the airborne pressure waves, generating pressure waves in the inner ear fluid chambers. The inner-ear turns pressure waves into electrical signals that our brain can understand. The hearing impairments, which could lead to hearing loss, are mainly caused by cochlear and cochlear nerve pathology and are classified as sensorineural hearing loss [3].

Being an internal organ the inner ear is physically inaccessible in living humans, which leads to unique difficulties in studying its normal function and pathology as in other human organs. Thus biopsy, surgical excision and other conventional techniques of pathological studies are not feasible, without further impairing function [3]. Therefore mathematical modelling is particularly attractive as a tool in researching the *cochlea* and its pathology. Mathematical models were introduced into the study of cochlear pathology and physiology, providing a useful tool in order to observe the system’s behaviour, which was difficult in previous human *in-vivo*, *in-vitro* studies [4][5]. The **Finite Elements Method (FEM)** – a mathematical framework – is assisting researchers in studying the structure-function relationship in normal and pathological cochlear.

Figure 2 shows a SIFEM conceptual model which is designed to support simulation of hearing processes and the biological system of the inner-ear. The simulation of any biological system, in our case inner-ear, requires two types of models; e.g., models for conceptual representation of the studied phenomenon, and mathematical/numerical models for describing the behaviour of the system. Hearing models gives us the conceptual representation of inner-ear system from different perspectives: (i) geometric modelling specifies the physical structures and their relations; (ii) mechanical modelling defines the characteristics of sound vibrations, and (iii) electrical modelling describes the electrical responses which in turn refers to behaviour of the *hair cells* connected to the *organ of corti*. These three models provide comple-

mentary views for understanding the inner ear mechanism. On the other hand, numerical model describes the behaviour of a system by mathematical representations of input/output functions under various conditions. In SIFEM we use Finite Element Method (FEM) technique to simulate the modelled hearing system. Figure 2 shows the concepts and relations for geometric and mechanical multi-scale modelling of inner-ear. The “Anatomical Element” (in circle) is defined using the FMA Ontology (shown in Figure 4) and further extended to include the simulating tissues, liquids, soft tissues and connecting adjacent (e.g. hair cells, perilymph etc.).

III. CONSTRUCTION METHODOLOGY OF THE SEMANTIC MODEL

This section describes the methodology used to develop the semantic model for human inner-ear macro anatomy. The approach followed to develop the semantic model in many aspects mirrors the METHONTOLOGY approach - a systematic methodology for ontology engineering [6], with the ontology life cycle being viewed as an evolving prototype in both approaches. Since there is no ‘one size fits all’, we have adapted and modified METHONTOLOGY in accordance with our usecase, with steps being carried out in a different order or not being deemed necessary at all. Also we followed an incremental approach with steps being repeated when necessary. The systematic methodologies used to develop the semantic model are listed below:

- 1) Specification of the high-level requirements for the ontology, e.g. components need to be covered to have meaningful and anatomically relevant modelling.
- 2) Definition of end users of the application platform of the semantic model, e.g. researchers in the domain of cochlear physiology who develop and/or use the finite element models of cochlea etc.
- 3) To ground the specifications, primary use cases were defined.
- 4) In parallel with requirements analysis and specification, a knowledge acquisition phase was carried out by means of a literature review. This stage also involved exploring for, and examination of, relevant existing ontologies that could be re-used.
- 5) A first draft of the overall semantic model to structure the domain knowledge was developed.
- 6) A glossary of terms for key domain concepts (many of which were identified during the requirements specification and literature review steps) was formalized and extended at this point and related terms were categorised.
- 7) Triples (Subject, Predicate, Object) linking classes to classes and classes to data values via object and data properties respectively were written in natural language.

- 8) A validation for correctness and completeness of these triples was performed by the end users (domain experts) and their feedback was used to correct errors. This step was done in part. The final semantic model can only be fully evaluated in combination with the semantic infrastructure.
- 9) The first T-boxes for human inner-ear anatomy model were formalised by implementing it in Protege (version 4.3) with the main classes and object and data properties specified.
- 10) Use cases identified in step 3 were implemented in A-boxes. It was necessary to add/amend T-box classes and properties at this stage to model items that previously had been overlooked or were ill-considered.

IV. HUMAN INNER-EAR ANATOMY MODEL

The macro-anatomy of the inner-ear is detailed in the semantic model. Since SIFEM is mainly concerned with *sensorineural* (or inner-ear) hearing loss, rather than *conductive* (or middle-ear) hearing loss, more emphasis is given here to inner-ear anatomical structures and their topological relations rather than to those of the middle- and outer-ear. In the semantic model classes describe anatomical structures (e.g. *cochlea*, *organ of corti* and *reissner's membrane*) and object properties describe their topological relationships (e.g. *contains*, *bounds*, *separated_from*, *separated_by*, *connects_to* and *connects_at*).

A key class of the semantic model is the *cochlea*, which is the snail shaped spiral structure of the inner-ear and for the *lower turn of the cochlea* the class *basal turn of cochlea* is used. Another core anatomical structure in SIFEM is the *basilar membrane of cochlea*. This is because incident sound waves cause a mechanical disturbance (in the form of a travelling wave) along the *basilar membrane* and modelling which is fundamental to many biosimulation models of hearing.

The *cochlea* contains three *scalae* (or chambers) called the *scala vestibuli*, the *scala media* (or cochlear duct) and the *scala tympani*. The latter two are separated by the *basilar membrane*. This is modelled in the semantic model by using the following restriction on the *scala tympani* class: (*separated_by* exactly 1 *basilar membrane of cochlea*) and (*separated_from* exactly 1 *cochlear duct of membranous labyrinth*). A similar form of restriction is used to convey the fact that the *scala vestibuli* is separated from the *scala media* by the *vestibular membrane* (or *reissners membrane*). The *scala vestibuli* meets the *scala tympani* at the *helicotrema*. This is also modelled in the semantic model using a restriction class and is depicted in Figure 3.

Micro study of *cochlea* led us to further examine the components which helps simulation to cover adjacent tissues, fluids and defines cause and effect of the covered inner-ear part. Examples mentioned below gives a deep insight about

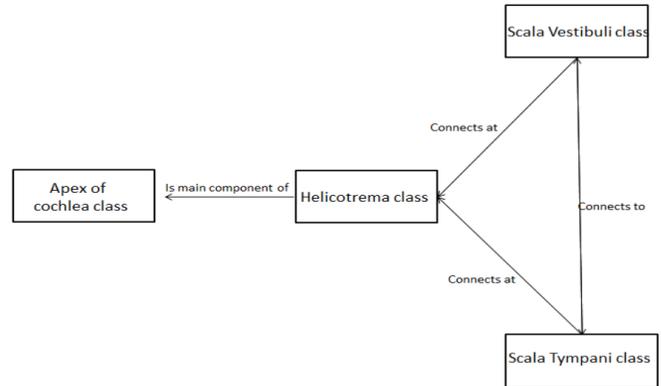


Figure 3: Classes and object properties showing that the scala vestibuli and scala tympani meet at the helicotrema which is the main component of the cochlear apex

these with exhaustive micro connections. This study could be understood by the following two examples.

The first example talks about *hair cells* accompanied by *stereocilia* bathing in the surrounding *endolymph*, as mentioned in Listing 1. Technically both *inner and outer hair cells* differed by their pattern of *stereocillia*. *Stereocillia* plays a crucial role in electromechanical transduction of *inner and outer cells*. This study will help to understand communication between IHC and OHC and their causes and effects. *Stereocilia* are mechanosensor organelles located at the apex of hair cells and form bundles. It is also closely adjoined with *reticular lamina* and canal based separation. Another diversion from *hair cell body* here clarifies that whole dimension in *cochlea* could be its extended relation with *stereocillia* which help to connect both *cochlea* and *vestibular sensory*. *Stereocilia* bathing surrounding *endolymph* performs this action of connection and gives an identity to both *inner hair cells* (IHC) and *outer hair cells* (OHC) by electromechanical transduction. This simulation not only exposes the connection but will also help to understand causes and effects of IHC and OHC.

```

Class: ieam:Stereocilia
SubClassOf:
  ieam:Macro_anatomical_entity,
  ieam:is_projected_from some fma:Cochlear_hair_cell,
  ieam:contains some fma:Stereocillum,
  ieam:separated_from some ieam:Hair_cell_body,
  ieam:adjoins exactly 1 fma:Reticular_lamina,
  ieam:is_part_of some fma:Cochlear_hair_cell
  
```

Listing 1: Stereocilia

As mentioned in Listing 2 inner most part of *cochlea* connection arises from *cochlea* called *basilar membrane*. It also acts as host tissue for the placement of *organ of corti* and later surrounded by *hair cells* to provide a mechanical mechanism for auditory functions. This concludes the mechanism for perception of sound which describes the

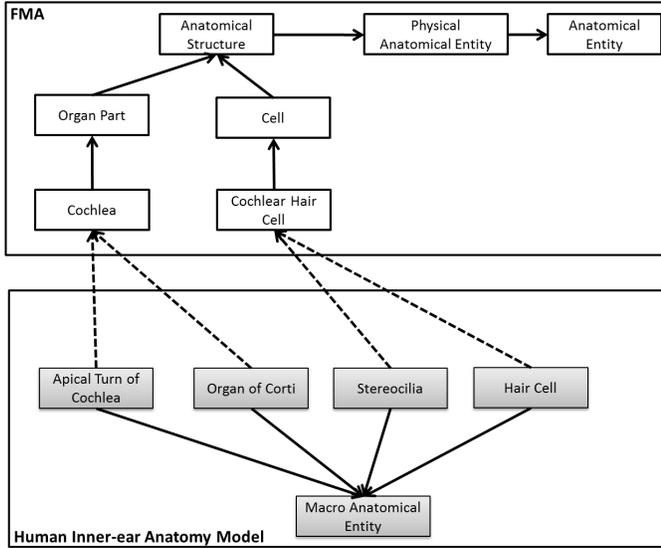


Figure 4: Human Inner-ear Anatomy Model alignment with FMA

role of *organ of corti* in mechano-electrical transduction as described above.

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Class: ieam:Organ_of_Corti
EquivalentTo:
  fma:Spiral_organ_of_cochlea
SubClassOf:
  ieam:Macro_anatomical_entity,
  ieam:contains exactly 1 ieam:Inner_hair_cell_row,
  ieam:adjoins exactly 1 fma:Basilar_membrane_of_cochlea,
  ieam:contains exactly 3 ieam:Outer_hair_cell_row,
  ieam:contains exactly 1 ieam:Tunnel_of_Corti,
  ieam:separates exactly 1 fma:
    Basilar_membrane_of_cochlea,
  ieam:lined_by some fma:Cochlear_inner_hair_cell,
  ieam:lined_by some fma:Cochlear_outer_hair_cell,
  ieam:contains some fma:Cochlear_hair_cell,
  ieam:is_above exactly 1 fma:
    Basilar_membrane_of_cochlea,

```

Listing 2: Organ of Corti

As the inner-ear interacts and functionally affected by other anatomical structures external to it, external anatomical elements are also described in the semantic model. For example *middle-ear*, *stapes* and *modiolus* of the *cochlea* are classes in the semantic model. URIs from the Foundational Model of Anatomy (FMA) [1] has been reused for most of the classes in the semantic model e.g. it has classes for such detailed inner-ear structures as *afferent neurons*, *actin filaments* and *cochlear inner hair cells*. It was only necessary to define SIFEM specific URIs for extremely detailed structures such as for *inner hair cell rows* and *Hensen's stripe*.

Foundational Model of Anatomy: The Foundational Model of Anatomy (FMA) is the essential ontology reused

in the semantic model for describing anatomical elements. FMA is a reference ontology for anatomy, which satisfies fundamental requirements for ontological representation of human anatomy according to independent evaluations. Figure 4 depicts the alignment of concepts from our local ontology, i.e. our extension to FMA with the concepts from global ontology of the anatomy domain. FMA is considered as a foundation model in the domain of human anatomy [7]. Selected portion of the class taxonomical hierarchy in the semantic model is depicted in Figures 5.

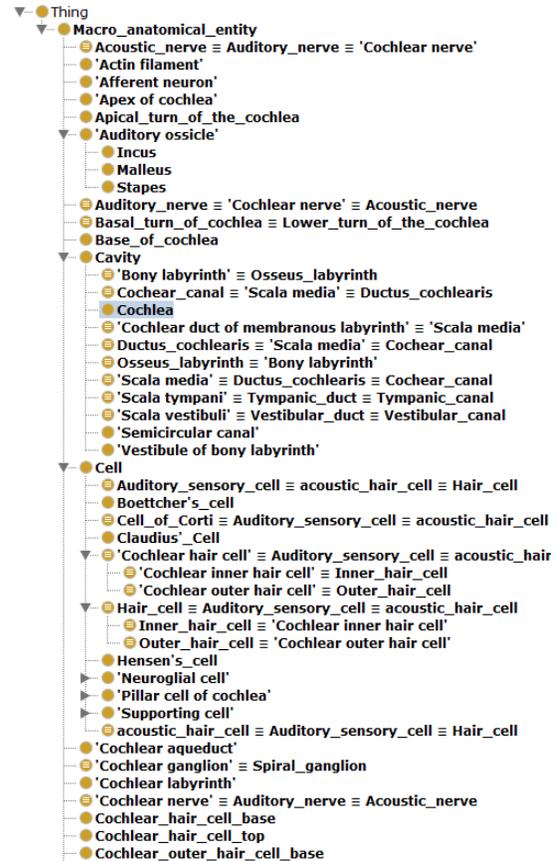


Figure 5: Class Hierarchy of the Inner-Ear Model

V. IMPLEMENTATION

The proposed version of the semantic model (extension to FMA ontology) having fine grained level anatomical concepts and their relationships has been practically modelled in Protege². We decided to use the "Human assessment and conformity with requirements" method of evaluation [8], carried out by the domain experts who seek to verify the adherence of the semantic model to certain criteria and patterns. Firstly, the semantic model got evaluated syntactically to check any syntactic inconsistencies. We used the OOPS! tool [9], a Web-based tool intended to detect

²<http://protege.stanford.edu/>

potential syntactic errors in formal ontologies. The initial evaluation concluded with minor pitfalls (e.g., missing annotations, domain and/or range in properties). OOPS! helped us to prepare a syntactically clean version of the semantic model. The model has been shared with the domain experts involved in the SIFEM project to get feedback from domain experts and to evaluate the semantic aspects of the model to evaluate the correctness and completeness in the modelling of concepts and their hierarchical relationships. As discussed in Section III, several iterations of this step performed and captured to accumulate feedback from domain experts till the completion of final semantic model.

The final stage of evaluation of the semantic model relates to its application in the associated use case. The semantic model has been integrated and instantiated along with the other models in the context of SIFEM project which provides an infrastructure on top of these conceptual models which semantically integrates finite element simulation data with experimental and clinical data to deliver a robust multi-scale model of the inner-ear. The principled semantic representation of the biosimulation and experimental data in the form of the semantic model, its associated models and their instantiations enabled the reproducibility, integration and reusability of different experiments and the automation of experimental analysis.

VI. RELATED WORK

Here [10] an ontology-based framework proposed for finite element analysis in a product development environment, uses a three-stage automated finite element modelling (FEM) method to identify and classify structural configurations and analysis. Modelling knowledge into a set of formal ontologies described in OWL. Gennari et. al. [11], [12] integrates three different biosimulation models of the heart, with three distinguish scales: (i) a cardiovascular fluid dynamics model; (ii) a model of heart regulation; and (iii) a sub-cellular model of the arteriolar smooth muscle. Gennari et al built a lightweight ontological framework, called Application Model Ontology (AMO), using small subsets of the reference ontologies, to annotate these biosimulation models semantically and to map between matching concepts. Further, to merge computational models of biological processes into reusable, multi-scale models, two reference ontologies were used, namely the Foundational Model of Anatomy (FMA) [1] and the Ontology of Physics for Biology (OPB). Researchers addressed the question of how heart rate and blood pressure depend on calcium uptake into arteriolar smooth muscle cells, a question that could be difficult to answer using single biosimulation model alone. The representation of biosimulation models has been steadily developed in the literature (Sauro & Bergmann [13]), including CellML[14] and SBML [15]. Ontologies such as the Systems Biology Ontology (SBO) [16] and Terminology for the Description of Dynamics (TEDDY) [16]

have been used to conceptualize biosimulation and results. In this paper, we extended the Foundational Model of Anatomy (FMA) ontology [1] to cover detail level version of human inner-ear anatomy where connection between simulating tissues, liquids, soft tissues and connecting adjacent (e.g. *hair cells, perilymph* etc.) parts studied in detail, included and implemented.

VII. CONCLUSION

In order to cover detailed concepts and relationships related to the geometric and mechanical modelling of the inner-ear, we have extended the Foundational Model of Anatomy (FMA) ontology. The proposed extension is specifically targeted towards inner-ear anatomy relating connection between simulating tissues, liquids, soft tissues and connecting adjacent (e.g. *hair cells, perilymph* etc.). The extended Foundational Model of Anatomy (FMA) ontology has been applied within the SIFEM project to improve the automation in integration, analysis and visualisation of biosimulation models for the inner-ear (cochlea) mechanics.

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