Understanding and communicating spatially–oriented ontologies

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Abstract

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Ontologies have become increasingly important for both representation of biomedical knowledge and for using that knowledge to facilitate data integration. However, ontologies are generally not presented in ways that are easy for users to comprehend, which limits their use. In this work I address this problem within the context of two spatially-oriented ontologies: the Foundational Model of Anatomy (FMA) and the Ontology of Craniofacial Development and Malformation (OCDM). I describe an approach to communicating these ontologies that involves (1) identifying content patterns within an ontology, (2) creating a simplified tutorial to explain basic concepts within the ontology, (3) involving potential users in the design of an ontology browser interface, and (4) creating graphics to support the process of building and communicating the ontology. This approach should be

applicable to any spatially-oriented ontology, and should result in visualizations that will enhance understanding of ontologies.

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1 Introduction

The purpose of this work is to develop an approach to communicating the structure and details of spatially-oriented ontologies, specifically ontologies of anatomy. Although it is now recognized that ontologies have great potential for representing and using biomedical knowledge for data integration, it remains difficult to convey the structure and content of an ontology in a way that permits the ontology to be integrated in applications.

In this work I develop an approach to this problem and apply it to two spatially-oriented ontologies describing anatomy.

1.1 Biomedical ontologies

Ontologies provide a method of formally representing a specific domain of knowledge. They consist of terms—formally specified as classes—and relationships between those classes. Ontologies are used as a source of terms for annotating data because they serve as a controlled vocabulary for consistent annotation across different projects and by different groups—which aids later efforts in data integration. But the real value of ontologies comes from structuring knowledge in a way that is not only human readable, but also allows a computer to reason about the domain by using the relationships between classes.

1.2 Communicating anatomy with the aid of an ontology

Traditionally, knowledge about anatomy has been documented within books using a combination of text and illustrations. This book-based approach has served as the basis for medical education and provided references for clinicians and researchers for generations. But to make use of this knowledge in data-intensive research and clinical applications, this anatomical knowledge must be parsed and represented in a way that is accessible to computers. In addition, modern educational resources for teaching anatomy require knowledge of anatomy in digital form.

Representing anatomy through ontologies has the advantage of clarifying ambiguous terms, consolidating multiple terms for the same concept into synonyms, explicitly declaring relationships between structure, and allowing computers to reason across anatomical relationships (for example, tracing the flow of lymph through a region of the lymphatic system). But it also presents challenges, because the traditional use of illustrations to visually communicate structure and clarify concepts is lost by representing anatomical knowledge solely as classes and relationships.

1.3 Two biomedical ontologies: the FMA and the OCDM

The work described in this dissertation focuses on communicating the content and structure of two ontologies: the Foundational Model of Anatomy (FMA) and the Ontology of Craniofacial Development and Malformation (OCDM).

The FMA (Rosse and Mejino, 2003)(Rosse and Mejino Jr., 2008) is a reference ontology for the domain of human anatomy and one of the largest biomedical ontologies in existence. It is considered to be a *reference* ontology because it is not intended for any specific use or user group, but can be used for any application requiring human anatomical knowledge. The OCDM (Brinkley et al., 2013) is a project to model developmental and malformations of the human and mouse head.

Both of these ontologies are projects of the Structural Informatics Group at the University of Washington.

1.4 Overview of the rest of this work

Throughout this thesis I develop an approach to communicating these two ontologies that includes discovering content patterns that can be used for communicating the structure of the ontology and designing an ontology browser based on a user-centered design process.

In Chapter 2, I review two topics to provide a context for this work. First, I present a survey of how anatomy ontologies have been incorporated within model organism atlases and databases to enhance queries or structure the information displayed. Second, I review current approaches to visualizing ontologies.

I describe my work to understand the structure and content of the FMA in Chapter 3. This effort resulted in the development of several "content patterns" that describe how different types of knowledge are modeled within the FMA.

In Chapter 4, I present an ontology I developed, called the Shirt Ontology, that was modeled on the principles of the FMA. The purpose of this ontology is to introduce to users how the FMA models the human body, but using a much simpler object: a button-front shirt.

I present my work to design and implement a browser for the FMA in Chapter 5. The design process involved interviews and feedback on sketches. The final design focuses on the browsing of hierarchies within the FMA, and makes use of simple graphics of anatomical structures as entry points into the ontology.

In Chapter 6, I discuss my work with the OCDM, which requires that I expand the content patterns to include development over time, malformations, and mappings to model organisms, and link these to illustrations of spatial concepts. I conclude the chapter with ideas for further work to design a browser for displaying these additional relationships within the ontology.

In Chapter 7, I summarize how this dissertation contributes to research in the field of biomedical ontologies and the visualization of ontologies.

2 Background

In this chapter I address two topics relevant to the communication to users of spatially-oriented biomedical ontologies. First, I identify how biomedical ontologies have been employed in online anatomy-based atlases and databases for model organisms. Second, I briefly review general methods that have been used to display ontologies in interfaces for viewing ontologies.

2.1 Survey of online atlases and databases for model organisms

I surveyed two types of online resources, anatomical atlases and gene expression databases, for their use of controlled vocabularies and ontologies in queries and structuring information. This survey revealed five types of ways in which ontologies are currently incorporated into web-based information systems for model organisms.

2.1.1 Methods

The anatomical atlases and gene expression databases surveyed in this work were identified through keyword searches of the Science Direct, Scopus, and PubMed databases. The keywords used were *atlas* or *database* in combination with *Arbacia, Caenorhabditis elegans, chick, chicken, Ciona, Danio rerio, Drosophila, fly, frog, Gallus gallus, medaka, mouse, Mus musculus, nematode, Oryzias latipes, rat, Rattus norvegicus, sea squirt, sea urchin, Strongylocentrotus, Xenopus,* or *zebrafish*. Several additional atlases and databases were identified based on Web links within these resources.

Atlases and databases that were included in this survey are described in a peer-reviewed journal article, are publicly available, are provided in English, and are delivered on the web without requiring download. Web availability was tested on July 26, August 4, and September 6, 2014. Resources available on none of these dates were excluded.

These criteria exclude anatomical models to be downloaded and viewed within desktop software. If both online and download components were available, only the online portion is surveyed. Resources structured as textbooks using narrative text with supporting figures are also excluded, as are image collections with little to no annotation of the anatomy represented. Databases consisting solely of microarray data were excluded. This work is limited to model organisms, and therefore resources for human anatomy and development were excluded.

All resources were viewed using operating system Mac OSX 10.9.4 with Java 1.6.0 and the Firefox 31.0 browser. Components provided as self-signed Java applications were excluded from this survey due to security risks.

2.1.2 Results

As described in the following sections, this work resulted in the identification of fourteen anatomical atlases and twenty-one gene expression databases meeting the inclusion criteria. They use a total of twelve controlled vocabularies and ontologies, and I identified five ways ontologies are used to enhance queries for gene expression data or structure information within the interfaces.

2.1.2.1 Anatomical atlases identified

The fourteen anatomical atlases identified for this survey are listed in Table 2-1. The organisms represented are *Caenorhabditis elegans*, *Ciona intestinalis*, *Drosophila*, medaka, mouse, and zebrafish. A brief description of each atlas is provided in Table 2-2. The anatomical scope of these atlases varies from the entire body of the organism to a more narrow topic (such as the brain or vasculature). Most describe a range of embryonic stages, but several are limited to adult anatomy. The anatomical resolution of the atlases also varies. Organisms with the fewest cells (*C. elegans* and *Ciona*) are described at cellular resolution, whereas atlases of other organisms vary in level of resolution from organs to tissues to cells.

The components of each atlas are summarized in Table 2-3. The types of images used in these atlases include confocal micrographs, histological sections, 3D models, and illustrations. The web technologies used to present these atlases varied tremendously, ranging from static HTML pages and embedded movies to Javascript-based image viewers built specifically for the atlases. Six of the fourteen atlases use a controlled vocabulary or ontology that serves as a community standard.

2.1.2.2 Gene expression databases identified

The twenty-one gene expression databases identified for this survey are listed in Table 2-4. The organisms represented are *Caenorhabditis elegans*, chicken, *Ciona intestinalis*, *Drosophila*, medaka, mouse, *Xenopus* and zebrafish. A brief description of each atlas is provided listed in Table 2-5. The spatial scope of most databases is the entire body, although three are specific to only the brain, nervous system, or urogenital system. Eleven of the twenty-one databases use a controlled vocabulary or ontology that is either a community standard or available for download from their website.

2.1.2.3 Controlled vocabularies and ontologies identified

Table 2-6 lists the twelve controlled vocabularies and ontologies used in the atlases and databases. The domain of each vocabulary or ontology and a summary of the modeling is listed in Table 2-7.

Table 2-1. Anatomical atlases surveyed

Atlas	URL, full project name, project leadership	Publication
C. elegans		
WormAtlas	http://wormatlas.org From the laboratory of David Hall at Albert Einstein College of Medicine (Bronx, NY, USA).	(Stephney, 2007)
OpenWorm Browser	http://browser.openworm.org A collaboration between WormBase and OpenWorm (openworm.org).	(Yook et al., 2012)
Ciona intestinalis		
ANISEED (Anatomy section)	http://www.aniseed.cnrs.fr Ascidian Network for In Situ and Embryological Data ANISEED is a collaboration among ascidian researchers led by Patrick Lemaire at the CRM (Montpellier, France).	(Tassy et al., 2010)
FABA	http://tunicate-portal.org/faba/1.4/top.html Four-dimensional Ascidian Body Atlas From the laboratory of Kohji Hotta at Keio University (Yokohama, Japan).	(Hotta et al., 2007)
Drosophila		
Flygut	http://flygut.epfl.ch This atlas complements a publication from Bruno Lemaitre's group at EPFL (Lausanne, Switzerland).	(Buchon et al., 2013)
Virtual Fly Brain	http://www.virtualflybrain.org Members of the Virtual Fly Brain team are from the University of Edinburgh (Edinburgh, Scotland) and the University of Cambridge (Cambridge, England).	(Milyaev et al., 2012)

Medaka		
Medaka Blood Vessel Atlas	http://www.shigen.nig.ac.jp/medaka/medaka_atlas Work by Misato Fujita and Sumio Isogai. Hosted online by the National BioResource Project Medaka (Japan).	(Isogai and Fujita, 2011) (Fujita et al., 2006)
Mouse		
Allen Developing Mouse Brain Reference Atlas	http://developingmouse.brain-map.org/static/atlas Produced by the Allen Institute for Brain Sciences (Seattle, WA, USA).	(Sunkin et al., 2013) (Allen Institute for Brain Science, 2010a)
EMA	http://www.emouseatlas.org/emap/ema/home.html e-Mouse Atlas (also known as the Edinburgh Mouse Atlas) Project led by Duncan Davidson and Richard Baldock within the Medical Research Council Human Genetics Unit and the University of Edinburgh (Edinburgh, Scotland).	(Armit et al., 2012) (Davidson et al., 2001) (Baldock et al., 1999) (Baldock et al., 1992)
Zebrafish		
FishFace	https://www.facebase.org/fishface/home Created by the laboratory of Charles Kimmel at the University of Oregon (Eugene, OR, USA) as part of the FaceBase Consortium (USA).	(Eames et al., 2013)
FishNet	http://www.fishnet.org.au Produced by Robert Bryson-Richardson and Peter Currie at Monash University (Clayton, VIC, Australia).	(Bryson-Richardson et al., 2007)
Interactive Atlas of Zebrafish Vascular Anatomy	http://zfish.nichd.nih.gov/Intro%20Page/intro1.html Produced by Brant Weinstein's group at the National Institutes of Health (Bethesda, MD, USA).	(Isogai et al., 2001)
ZFAP	http://zebrafish.anatomyportal.org Zebrafish Anatomy Portal From Robert Bryson-Richardson's group at Monash University (Clayton, VIC, Australia).	(Salgado et al., 2012)
Zebrafish Atlas	http://zfatlas.psu.edu From the laboratory of Keith Cheng at Penn State College of Medicine (Hershey, PA, USA).	(Cheng, 2004)

Table 2-2. Descriptions of the anatomical atlases

	Description	Spatial scope	Developmental stages	Resolution
C. elegans				
WormAtlas	A collection of resources on the anatomy of *C. elegans.* Includes the SlidableWorm (for viewing annotated electron micrograph sections) and descriptions of individual neurons.	body	adult	cells
OpenWorm Browser	A 3D virtual reconstruction consisting of surface models of 680 cells.	body	adult	cells
Ciona intestinalis				
ANISEED (Anatomy section)	Illustrations of ascidian embryos annotated with cell names.	body	embryos from 16-cell to 112-cell stages	cells
FABA	Confocal micrographs for standardizing developmental stages.	body	zygote through newly hatched larva	cells
Drosophila				
Flygut	Description of the *Drosophila* midgut based on anatomy, histology, and expression patterns of reporter transgenes.	midgut	adult	tissues
Virtual Fly Brain	Virtual sections from a reference brain (with anatomical regions delineated) which supports graphically-driven ontology queries for neurons.	brain	adult	brain regions, neurons
Medaka				
Medaka Blood Vessel Atlas	Annotated illustrations of the vasculature of embryos.	vasculature	embryos at stages 24 to 30, adult	organ
Mouse				
Allen Developing Mouse Brain Reference Atlas	Histological sections of brain with anatomical regions delineated.	brain	embryos at Theiler stages 19, 21, 24, 26; post-natal days 4, 14, and 56	cells
EMA	3D reconstructions of embryos (some with anatomical regions delineated), histological sections, and a guide to embryological stages.	body	embryos at Theiler stages 7 to 26	tissues (in reconstructions), cells (in histological sections)
Zebrafish				
FishFace	Images of fluorescently-labeled chondrocytes, osteoblasts, and bone matrix in the first two pharyngeal arches.	craniofacial skeleton	pharyngula through adult	cells
FishNet	Virtual sections from optical projection tomography (OPT) scans (with selected sections annotated).	body	pharyngula through adult (18 stages)	tissues

Interactive Atlas of Zebrafish Vascular Anatomy	Fluorescent angiograms as movies and annotated diagrams.	vasculature	pharyngula and larva	organ
ZFAP	Images from the FishNet atlas within a viewer that shows three orthogonal planes. Includes a search function for finding images annotated with specific terms.	body	pharyngula through adult (18 stages)	tissues
Zebrafish Atlas	Histological sections and a virtual slide viewer. Slides from two developmental stages are annotated.	body	larva through adult (13 stages)	cells

Table 2-3. Components of the anatomical atlas

	Image types[1]	Web technology and image delivery framework	Controlled vocabulary or ontology
C. elegans			
WormAtlas[2]	• TEMs • illustrations • DIC micrographs • fluorescence micrographs	• Zoomify using Adobe Flash (EM section viewer for the SlidableWorm)	not stated
OpenWorm Browser	• 3D surface models	• WebGL (using the Google Body Browser framework from Google Labs)	not stated
Ciona intestinalis			
ANISEED (Anatomy section)	• illustrations	• Javascript (interactions with illustrations and the ontology)	*Ciona* Developmental Ontology
FABA	• confocal micrographs (as volumes and virtual sections) • brightfield movies	• Adobe Flash (viewer for z-sections, surface reconstructions, movies of development)	not stated[3]
Drosophila			
Flygut	• schematic illustrations • fluorescence micrographs • 3D models	• Javascript (360-degree rotation of models using an image sequence)	not stated
Virtual Fly Brain	• confocal microscopy stack (as virtual sections) • 3D models of neurons	• Javascript with IIP3D (retrieval of arbitrary sections of a 3D volume[4] and ontology information) • WebGL (rotation of 3D models of neurons)	*Drosophila* Anatomy Ontology[4]
Medaka			
Medaka Blood Vessel Atlas	• illustrations • confocal micrographs (as composites)	• Adobe Flash (viewer linking vocabulary terms to illustration labels)	not stated
Mouse			
Allen Developing Mouse Brain Reference Atlas	• histological sections with illustration overlays	• Javascript (retrieval of image tiles and and ontology information)	Developing Mouse Brain Atlas ontology
EMA	• 3D reconstructions of histological sections (as volumes and virtual sections) • histological sections • OPT scans (as volumes) • illustrations of stages	• Javascript with IIP3D (retrieval of arbitrary sections of a 3D volume[5] and ontology information) • Java applet (browser linking sections to ontology terms) • embedded YouTube movies (rotation of 3D models and OPT scans)	EMAP anatomy ontology
Zebrafish			
FishFace	• confocal microscopy stacks (as composites and sections) • OPT scans (as volumes)	• Javascript (movies of OPT scans and confocal sections)	Zebrafish Anatomy Ontology and (Cubbage and Mabee, 1996)

FishNet	• OPT scans (as volumes and virtual sections)	• Adobe Flash (viewer for OPT sections) • QuickTimeVR (free rotation of 3D models)	not stated
Interactive Atlas of Zebrafish Vascular Anatomy	• confocal microscopy stacks (as composites and volumes, and sections) • illustrations	• QuickTime (movies of confocal volumes and sections)	from references at http://zfish.nichd.nih.gov/Intro%20Page/nomenclature.html
ZFAP	• OPT scans (as volumes and virtual sections)	• Javascript (viewer displaying three orthogonal OPT sections) • QuickTimeVR (free rotation of 3D models)	Zebrafish Anatomy Ontology
Zebrafish Atlas	• histological sections	• Javascript (slide previews and virtual slide viewer)	http://zfatlas.psu.edu/reference.php

[1] Acronyms: DIC = differential inference contrast, TEM = transmission electron micrograph, OPT = optical projection tomography

[2] Only the “SlidableWorm” and “Individual Neurons” sections of the WormAtlas are surveyed here.

[3] The FABA established the developmental stages used in the Ciona Developmental Ontology.

[4] The vocabulary from the Insect Brain Name Working Group (Ito et al., 2014) was incorporated into the *Drosophila* Anatomy Ontology as part of the development of the Virtual Fly Brain atlas.

[5] System for retrieving image tiles representing an arbitrary section through a three-dimensional volume described by (Husz et al., 2012).

Table 2-4. Gene expression databases surveyed

Atlas or database	URL, full project name, project leadership	Publication
C. elegans		
Expression patterns for *C. elegans* promoter::GFP fusions	http://gfpweb.aecom.yu.edu/index A project of the British Columbia *C. elegans* Gene Expression Consortium	(Hunt-Newbury et al., 2007)
WormBase (WormMine tool)	http://www.wormbase.org WormBase is an international consortium of researchers and is based at Caltech (Pasadena, CA, USA).	(Harris et al., 2014) (Yook et al., 2012)
Chicken		
GEISHA	http://geisha.arizona.edu/geisha Gallus Expression in Situ Hybridization Analysis Hosted by Parker Antin's group at the University of Arizona (Tuscaon, AZ, USA).	(Antin et al., 2014) (Darnell et al., 2007) (Bell et al., 2004)
Ciona intestinalis		
ANISEED, Expression Data section	http://www.aniseed.cnrs.fr Ascidian Network for In Situ and Embryological Data ANISEED is a collaboration among ascidian researchers led by Patrick Lemaire at the CRM (Montpellier, France).	(Tassy et al., 2010)
Drosophila		
BDGP expression patterns	http://insitu.fruitfly.org/cgi-bin/ex/insitu.pl Berkeley Drosophila Genome Project From the laboratory of Susan Celniker at the Lawrence Berkeley Laboratory (Berkeley, CA, USA).	(Hammonds et al., 2013) (Tomancak et al., 2007) (Tomancak et al., 2002)
FlyBase (QueryBuilder tool)	http://flybase.org FlyBase is an international consortium of *Drosophila* researchers.	(St. Pierre et al., 2014) (McQuilton et al., 2012) (Grumbling et al., 2006)
FlyExpress	http://www.flyexpress.net From the laboratory of Sudhir Kumar at Arizona State University (Tempe, AZ, USA).	(Konikoff et al., 2012) (Kumar et al., 2011)
Fly-FISH	http://fly-fish.ccbr.utoronto.ca From the laboratory of Henry Krause at the University of Toronto (Toronto, Ontario, Canada).	(Lécuyer et al., 2007)
Medaka		
MEPD	http://ani.embl.de:8080/mepd Medaka Expression Pattern Database A project of the Medaka Genome Initiative, an international consortium of researchers.	(Henrich, 2003) (Henrich et al., 2005)
Mouse		

Allen Developing Mouse Brain Atlas (AGEA section)	http://developingmouse.brain-map.org/agea/show Anatomic Gene Expression Atlas of the Allen Developing Mouse Brain Atlas Produced by the Allen Institute for Brain Sciences (Seattle, WA, USA).	(Thompson et al., 2014) (Allen Institute for Brain Science, 2013) (Allen Institute for Brain Science, 2010b) (Lein et al., 2007)
EMBRYS	http://embrys.jp/embrys/html/MainMenu.html From the laboratory of Hiroshi Asahara at the Systems BioMedicine Laboratory of the National Research Institute for Child Health and Development (Tokyo, Japan).	(Shimizu et al., 2013) (Yokoyama et al., 2009)
EMAGE	http://www.emouseatlas.org/emage/home.php e-Mouse Atlas of Gene Expression Project led by Duncan Davidson and Richard Baldock within the Medical Research Council Human Genetics Unit and the University of Edinburgh (Edinburgh, Scotland).	(Richardson et al., 2014a) (Richardson et al., 2014b) (Armit et al., 2012) (Richardson et al., 2010) (Christiansen, 2006)
Eurexpress	http://www.eurexpress.org/ee Eurexpress is a consortium of European researchers.	(Diez-Roux et al., 2011)
GXD	http://www.informatics.jax.org/gxd Mouse Gene Expression Database GXD is a Mouse Genome Informatics resource from Jackson Laboratory (Bar Harbor, ME, USA).	(Smith et al., 2014a) (Smith et al., 2014b) (Finger et al., 2011) (Smith et al., 2007)
GENSAT	http://www.gensat.org/index.html Gene Expression Nervous System Atlas From the laboratory of Nathaniel Heinz at The Rockefeller University (New York, NY, USA).	(Schmidt et al., 2013) (Heintz, 2004)
GenePaint	http://genepaint.org Project led by Gregor Eichele at the Max Planck Institute of Biophysical Chemistry (Göttingen, Germany).	(Visel et al., 2004)
GUDMAP	http://www.gudmap.org GenitoUrinary Molecular Anatomy Project GUDMAP is an international consortium of researchers.	(Harding et al., 2011) (McMahon et al., 2008)
Xenopus		
Xenbase	http://www.xenbase.org Project led by Peter Vize at the University of Calgary (Calgary, Canada).	(James-Zorn et al., 2013) (Bowes et al., 2008)
XenMARK expression patterns	http://genomics.nimr.mrc.ac.uk/apps/XenMARK From the laboratory of Michael Gilchrist at the MRC National Institute for Medical Research (London, UK).	(Gilchrist et al., 2009)
Zebrafish		
GEMS	http://bio-imaging.liacs.nl/liacsgems.html Gene Expression Management System Produced by the Imagery & Media Group at Leiden University (Leiden, Netherlands).	(Belmamoune and Verbeek, 2008)

ZFIN	http://zfin.org Zebrafish Model Organism Database (also known as the Zebrafish Information Network) Based at the University of Oregon (Eugene, OR, USA).	(Howe et al., 2013) (Bradford et al., 2011) (Sprague et al., 2007)

Table 2-5. Descriptions of the gene expression databases surveyed

Atlas or database	Description	Spatial scope	Developmental stages	Controlled vocabulary or ontology[1]
C. elegans				
Expression patterns for *C. elegans* promoter::GFP fusions	Database of expression patterns of transgenic animals with promoter::GFP fusions	body	embryo, larva, adult	site-specific vocabulary
WormBase (WormMine tool)	Community repository of molecular and genetic data from the literature, submissions, and collaborating projects.	body	embryo, larva, adult	*C. elegans* Gross Anatomy Vocabulary *C. elegans* Development Vocabulary
Chicken				
GEISHA	Community repository of in situ hybridization data acquired from high-throughput screens and the literature.	body	embryos at stages X through 35[2]	site-specific vocabulary
Ciona intestinalis				
ANISEED (Expression Data section)	Community repository of gene expression data from the literature, submissions, and collaborating projects.	body	unfertilized egg through mature adult	*Ciona* Developmental Ontology
Drosophila				
BDGP expression patterns	Database of in situ whole mount expression of data	body	(embryos at stages 1 to 16[3]) all embryonic stages	site-specific vocabulary
FlyBase (QuickSearch tool)	Community repository of molecular and genetic data	body	unfertilized egg through adult	*Drosophila* Anatomy Ontology
FlyExpress	A tool for searching in situ expression patterns using image data from BDGP and Fly-FISH	body	all embryonic stages	vocabularies from BDGP and Fly-FISH
Fly-FISH	Database of fluorescent in situ whole mounts showing subcellular localization of mRNA	body	embryos at stages 1 to 9[4] and larva	site-specific vocabulary
Medaka				
MEPD	Database of in situ hybridization data for EST clones	body	stage 15 embryos[5] through young fish	MFO
Mouse				
Allen Developing Mouse Brain Atlas (AGEA section)	Database of in situ hybridization sections	brain	embryos at Theiler stages 19, 21, 24, 26; post-natal days 4, 14, and 28	Allen Developing Mouse Brain Atlas ontology
EMBRYS	Database of whole mount in situ hybridization	body	E 9.5, 10.5, 11.5	site-specific vocabulary

EMAGE	Community repository of molecular and genetic data from the literature and direct submissions.	body	Theiler 6 to 24	EMAP anatomy ontology
Eurexpress	Database of sectional in situ data	body	E14.5	EMAP anatomy ontology
GXD	Community repository of expression data from the literature, direct submissions, and collaborating projects.	body	all and adult	EMAP anatomy ontology ; MA
GENSAT	Database of in situ and transgenic mice with EGFP reporter genes serial sections	nervous system	E10.5 15.5, P7, adult	site-specific vocabulary
GenePaint	Database of in situ serial sections	body	E10.5, 14.5, 15.5, P7, adult	site-specific vocabulary
GUDMAP	Community repository of expression data from the GUDMAP consortium	urogenital system	TS17 through adult	EMAP anatomy ontology
Xenopus				
Xenbase	Community repository of expression data from the literature, submissions, and collaborating projects.	body	all developmental through adult	XAO
XenMARK expression patterns	Database of whole mount in situ data from 21 labs.	body	spanning stages 6 (32 cells) through 45 (premetamorphosing tadpole)	site-specific vocabulary
Zebrafish				
GEMS	Database of expression patterns documented by confocal microscopy	body	Gastrulas	DAOZ
ZFIN	Community repository of molecular and genetic data from literature and direct submissions	body	1-cell through adult	ZAO

[1] Acronyms: DAOZ = Developmental Anatomy Ontology of Zebrafish, MFO = Medaka Fish Anatomy and Development Ontology, XAO = *Xenopus* Anatomy Ontology, ZAO = Zebrafish Anatomy Ontology

[2] Chick stage X is from a freshly laid egg (Eyal-Giladi and Kochav, 1976) ; stage 35 is reached after 8–9 days of incubation (Hamburger and Hamilton, 1992).

[3] Drosophila stages scheme in (1998) consisting of 16 embryonic stages.

[4] Drosophila staging scheme of (Campos-Ortega and Hartenstein, 1985) consisting of 17 embryonic stages.

[5] Medaka stages from (Iwamatsu, 2004).

Table 2-6. Controlled vocabularies and ontologies relevant to this survey

Vocabulary or ontology	URL or OBO ID[1], full name	Publication
C. elegans		
C. elegans Gross Anatomy Vocabulary	id=worm_anatomy also known as the *C. elegans* Cell and Anatomy Ontology	(Lee and Sternberg, 2003)
C. elegans Development Vocabulary	id=worm_development	–
Ciona intestinalis		
Ciona Developmental Ontology	http://www.aniseed.cnrs.fr/aniseed/download/download_data	(Tassy et al., 2010)
Drosophila		
Drosophila Anatomy Ontology	id=fly_anatomy	(Ito et al., 2014) (Costa et al., 2013) (Osumi-Sutherland et al., 2012)
Drosophila Development Ontology	id=fly_development	–
Medaka		
MFO	id=medaka_anatomy_development Medaka Fish Anatomy and Development Ontology	(Henrich et al., 2005)
Mouse		
MA	id=adult_mouse_anatomy Adult Mouse Anatomy	(Hayamizu et al., 2005)
Allen Developing Mouse Brain Atlas ontology	http://help.brain-map.org/display/api/Atlas+Drawings+and+Ontologies	(Allen Institute for Brain Science, 2010a)
EMAP anatomy ontology	id=emap (for stage-specific terms) id=emapa (for “abstract mouse”) e-Mouse Atlas Project anatomy ontology	(Burger et al., 2004) (Hayamizu et al., 2013) (Little et al., 2007)
Xenopus		
XAO	id=xenopus_anatomy *Xenopus* Anatomy Ontology	(Segerdell et al., 2013) (Segerdell et al., 2008)
Zebrafish		
DAOZ	http://bio-imaging.liacs.nl/liacsontology.html Developmental Anatomy Ontology of Zebrafish	(Belmamoune and Verbeek, 2007)
ZFA	id=zebrafish_anatomy Zebrafish Anatomy Ontology	(Van Slyke et al., 2014)

[1] To create a URL using an ID from the Open Biological and Biomedical Ontologies (OBO) Foundry, append the text (such as “id=worm_anatomy”) to “http://www.obofoundry.org/cgi-bin/detail.cgi?”.

Table 2-7. Descriptions of controlled vocabularies and ontologies

Vocaulary or ontology	Domain	Summary of modeling	Atlases using this
C. elegans			
C. elegans Gross Anatomy Vocabulary	• developmental and adult anatomy, including individual cells	• "part of" relationship between a cell and its nucleus	WormBase[1]
C. elegans Development Vocabulary	• developmental stages • time points	• "part_of" relationship between a time point and a stage	WormBase[1]
Ciona intestinalis			
Ciona Developmental Ontology	• developmental and adult anatomy, including individual cells • developmental stages	• "part of" relationship between structures • "develops_from" to model cell and territory lineage • structures related to stages using "start_stage" and "end stage"	ANISEED[1]
Drosophila			
Drosophila Anatomy Ontology	• developmental and adult anatomy • vocabulary from the Insect Brain Name Working Group	• "part of" relationship between structures • several types of relationships between neurons and other structures • "develops from" to model neuron lineage and developmental relationships between structures • "capable of" relationship between structures and biological processes	VFB FlyBase[1]
Drosophila Development Ontology	• developmental stages • cycles of nuclear division	• "part of" relationship cycles of nuclear division and developmental stages	FlyBase[1]
Medaka			
MFO	• developmental and adult anatomy • developmental stages	• "part of" relationship between structures • uses stage-specific terms	MEPD[1]
Mouse			
MA	• adult anatomy	• "part of" relationship between structures	GXD[1]
Allen Developing Mouse Brain Atlas ontology	• developmental anatomy	• "part of" relationship between structures	Allen Developing Mouse Brain Atlas[1]
EMAP anatomy ontology	• developmental anatomy • vocabulary from the GUDMAP consortium (provided as stage-specific and "abstract" versions)	• "part of" relationship between structures • uses stage-specific terms	e-Mouse Atlas[1]
Xenopus			

XAO	• developmental and adult anatomy • developmental stages	• "part of" relationship between structures • "develops from" to model developmental relationships between structures • structures related to stages using "starts during" and "ends during"	Xenbase[1]
Zebrafish			
DAOZ	• developmental anatomy • developmental stages	• "part of" relationship between structures	GEMS[1]
ZFA	• developmental and adult anatomy • developmental stages	• "part of" relationship between structures • "develops from" to model developmental relationships between structures • structures related to stages using "start_stage" and "end stage"	ZFIN[1]

[1] The vocabulary or ontology was developed by the group constructing this atlas.

2.1.2.4 The use of ontologies for querying and information retrieval

The survey revealed five ways ontologies have been used to enhance queries or the information structure within these atlases or databases.

(1) *Partonomy knowledge* w*ithin queries for gene expression data*. Most gene expression databases can be queried using an anatomical term to find gene expression data annotated with that term. These search functions often provide autocomplete suggestions based on characters that have been typed, with the suggestions drawn from a limited set of terms (either a controlled vocabulary or ontology). For example, typing "eye" might produce a list of terms that includes "eye lid". While this autocomplete method is quite helpful, it does not make use of the structure of an ontology.

I identified two ways in which partonomy knowledge ("part of" relationships) contained within ontologies has been applied into queries for gene expression data. The purpose of these methods is to identify gene expression data that have been annotated with a more specific anatomical term than then the term specified by the user. For example, data annotated with “forebrain” will be returned in response to a query for “brain”.

The first method is to provide an option in the query interface for including parts of an anatomical structure. For example, ZFIN (Sprague et al., 2007) provides a checkbox to “include substructures” from the Zebrafish Anatomy Ontology (ZFA) (Van Slyke et al., 2014) when searching for gene expression data using an anatomical term. Similarly, Eurexpress (Diez-Roux et al., 2011) provides an Anatomy Search page that allows a user to select a term from the EMAP anatomy ontology (Hayamizu et al., 2013) for querying, with the option to include children of the selected term.

The second method is to automatically include the substructure classes for a term in a query. This approach is taken by EMAGE (e-Mouse Atlas of Gene Expression) (Richardson et al., 2010), which automatically includes substructures from the EMAP anatomy ontology (Abstract version) in queries, as well as GXD (Smith et al., 2014a), which uses annotations from the EMAP anatomy ontology and Adult Mouse Anatomy (MA) ontology (Hayamizu et al., 2005).

(2) *Developmental relationships within queries for gene expression data.* The gene expression database within Xenbase (James-Zorn et al., 2013) can be searched by typing an anatomical term. This feature has the option to “include successor tissues” and “include predecessor tissues”, which are specified in the Xenopus Anatomy Ontology (XAO) (Segerdell et al., 2013).

(3) *Developmental relationships within information displays and navigation.* The interfaces of several resources use developmental relationships to display and navigate through information. GUDMAP (Harding et al., 2011) organizes information and data on Tissue Summary pages, and developmental relationships are included in these views. For example, the page for “renal distal tubule (TS25-TS28)” indicates that it derives from “early distal tubule”, with a link to the corresponding summary page. ANISEED (Tassy et al., 2010) provides pages that organize information about a single stage, and these are linked by “previous stage” and “next stage” relationships found in the Ciona Developmental Ontology (Tassy et al., 2010).

(4) *Querying across resources.* When ontologies become a standard vocabulary for an organism, they provide a way to move between different resources while querying the same concept. The Zebrafish Anatomy Portal (ZFAP) (Salgado et al., 2012) provides an option to first search the atlas with an anatomical term, then use term to query the external database ZFIN (Howe et al., 2013). Likewise, the e-Mouse Atlas (EMA) (Armit et al., 2012) can be used to query EMAGE and GXD.

(5) *Using terms from an image-based interface to populate queries.* The Virtual Fly Brain (VFB) atlas (Milyaev et al., 2012) displays planes of a 3D fly brain. Clicking on a region displays properties of the region, and also allows that region to serve as the input to a selection of query templates. For example, queries can retrieve the parts of the region or the neurons that terminate in the region. These feature are enabled by the Drosophila Anatomy Ontology (Costa et al., 2013).

2.2 Existing methods of viewing ontologies

Many of the atlases and gene expression databases surveyed in the previous section employ ontologies "behind the scenes", where it is not necessary for users to examine the ontology itself. But the development of these ontologies by content experts requires methods of visualizing and navigating ontologies. This section reviews methods of viewing ontologies. Most have been applied only in the context of tools focused on viewing or authoring ontologies, but at least one method (the folding indented list) has been used to display ontologies within atlases and gene expression databases.

Because ontologies take the form of networks—classes linked by relationships—visualizations of ontologies are based on methods for visualizing networks.

2.2.1 Visualization of hierarchies

The most fundamental structure within ontologies is the class hierarchy formed by the "is a" relationship (for example, "Left kidney" is a "Kidney" is a "Corticomedullary organ"). Therefore, methods of visualizing networks that are structured as hierarchies (known as trees) have been very influential in ontology visualization. Figure 2-1 shows a variety of methods for visualizing trees.

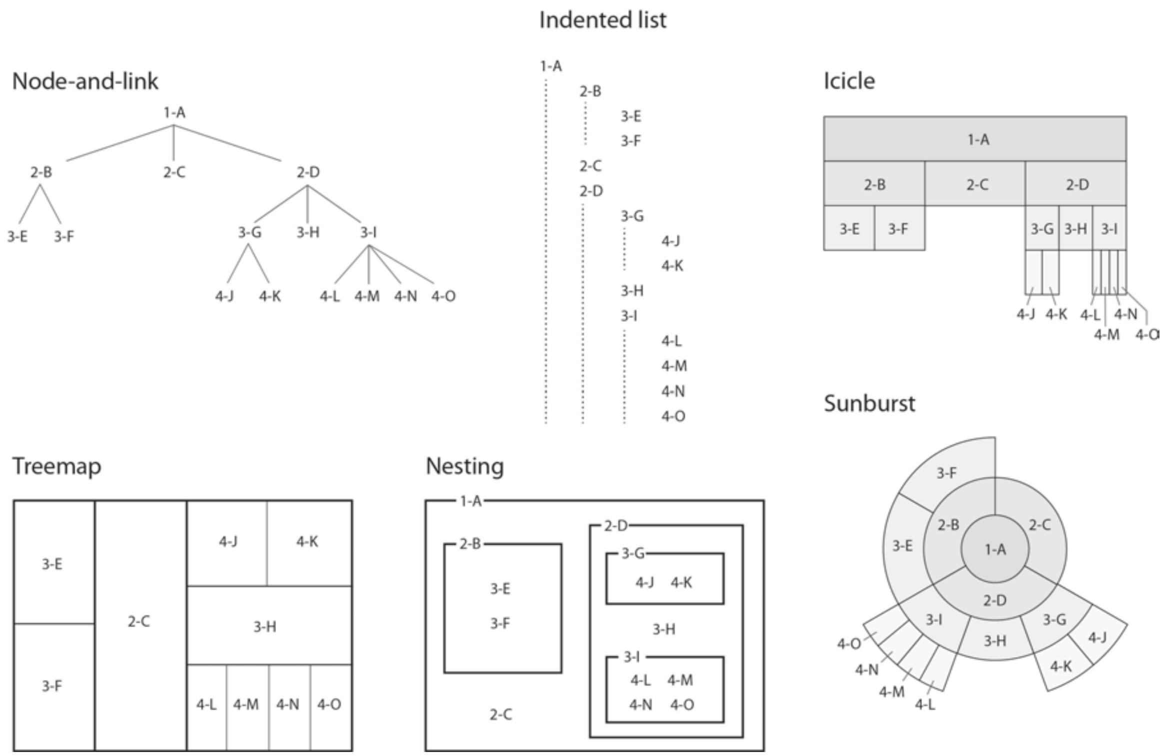


Figure 2-1. The same 15-node tree displayed using methods of node-and-link, indented list, icicle, treemap, nesting, and sunburst.

Surveys of tools for ontology visualization (Katifori et al., 2007)(Lanzenberger et al., 2009)(Sivakuman and Arivoli, 2011) show that most ontology visualizations are based on either the node-and-link or indented list, but researchers have also experimented with the technique of nesting (Storey et al., 2001) and presenting ontology-annotated data in treemaps (Baehrecke et al., 2004).

The indented list has the advantage of being the most compact. A variation known as the "folding indented list" allows the user to hide and reveal nodes at deeper levels of the hierarchy, and is familiar to users because it is widely used within computer operating systems for managing folders and sub-folders.

2.2.2 Visualization of networks

The node-and-link visualization is the only method in Figure 2-1 that can easily be extended to networks that are not of a tree structure. For example, ontologies that allow multiple inheritance (meaning a child class can be linked to more than one parent class through the "is a" relationship), cannot be viewed as a simple hierarchy. In addition, ontologies may include part hierarchies and various relationships between classes, making the true structure of the ontology a network instead of a hierarchy. Therefore, the node-and-link visualization is a popular method for ontology visualization.

Many variations of the node-and-link method have been explored by researchers, including:

- Using a circular layout of nodes with hierarchical edge bundles (Hop et al., 2012) (Figure 2-2A)
- Using a three-dimensional layout (Bosca et al., 2005) (Figure 2-2B)
- Initially displaying only a portion of nodes based on density of surrounding classes in the class hierarchy (Motta et al., 2011) (Figure 2-2C)

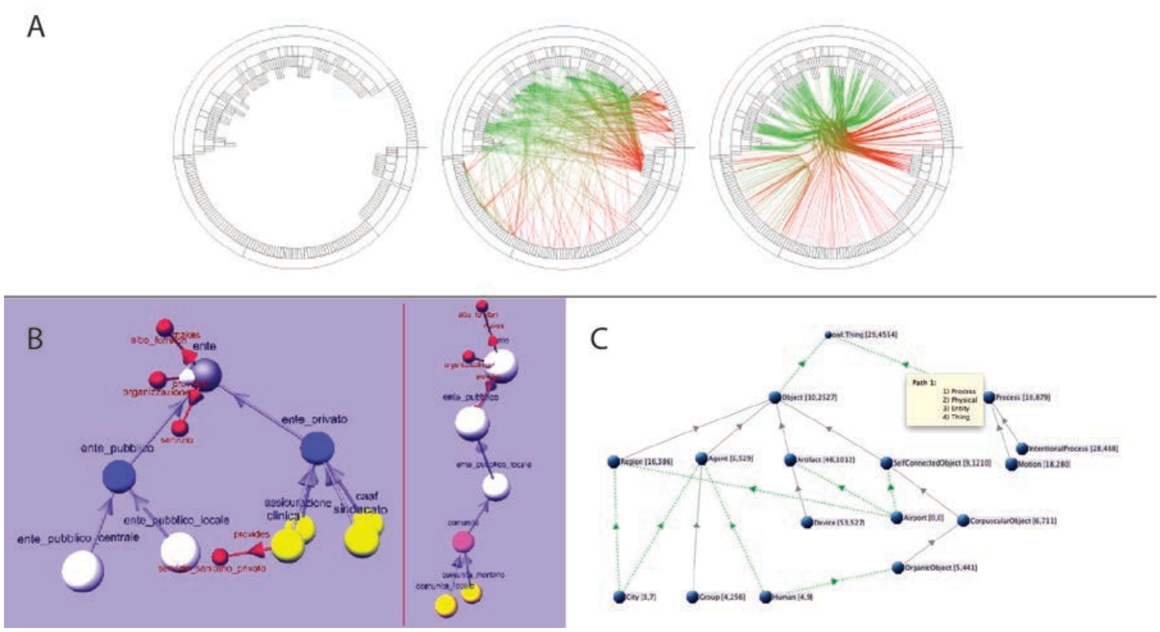


Figure 2-2. Examples of node-and-link network visualizations. A: Circular layout with hierarchical edge bundles from (Hop et al., 2012). B: Three-dimensional layout from (Bosca et al., 2005). C: Initial display of only portion of nodes based on density from (Motta et al., 2011).

2.2.3 Visualization of multiple trees

The visualization of multiple trees has received some attention from the information visualization community, as reviewed in (Graham and Kennedy, 2009). The only tool designed specifically for ontology hierarchies is the work by (Dadzie and Burger, 2005) on 2D and 3D node-and-link visualizations of the EMAP anatomy ontology (this ontology consists of a set of separate class hierarchies for each developmental stage of the mouse) (Burger et al., 2004) (Figure 2-3A).

One group has investigated the visualization of multiple intersecting hierarchies (those that share one or more nodes), which they call “polyarchies” (Robertson et al., 2002). Their tool uses an indented list layout, with each hierarchy occupying a different plane. The user pivots the planes to examine different hierarchies (Figure 2-3B).

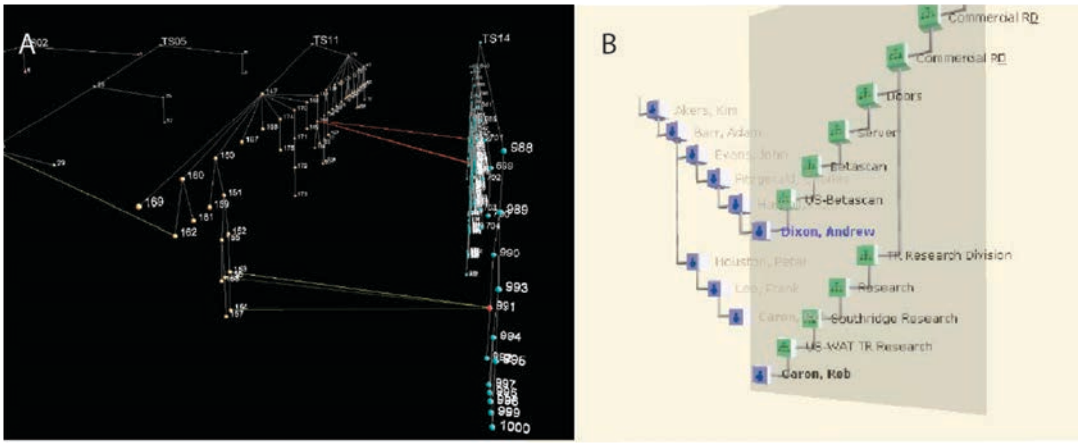


Figure 2-3. Examples of visualizations for hierarchies. A: Multiple hierarchies from (Dadzie and Burger, 2005). B: Multiple intersecting hierarchies from (Robertson et al., 2002).

2.3 Summary

In this chapter I have shown examples of ontologies applied within existing atlases and databases. The development of these ontologies requires visualization and navigation of the ontologies, and I have summarized existing approaches used within tools for authoring and viewing ontologies. In the following chapters I describe my work that resulted in a visualization tool for the FMA I call the FMA Browser.

3 Discovering and implementing content patterns in the FMA

Before I could develop the FMA Browser described in Chapter 5, I needed to understand the overall structure of the FMA. In so doing I discovered patterns by which specific types of anatomical knowledge are modeled with the FMA.

While working to discover these "content" patterns I found a number of inconsistencies in the existing content of the FMA. I have worked with the content author and curator of the FMA (José Mejino) to reconcile a portion of the FMA content with the content patterns. Due to the size and complexity of the FMA, only a portion of the content patterns have been diagramed, and work to reconcile the content is ongoing. The following sections describe this process in more detail.

3.1 Work to understand the FMA

My work began by using the Foundational Model Explorer (FME) (Brinkley et al., 2012) to examine the content of the FMA. This tool presents class and part hierarchies as an indented hierarchical list. In order to more fully understand the content and structure of sections of the FMA, I created overview diagrams for some sections of the FMA. An example of the regional part hierarchy for the class "Upper limb" is shown in Figure 3-1.

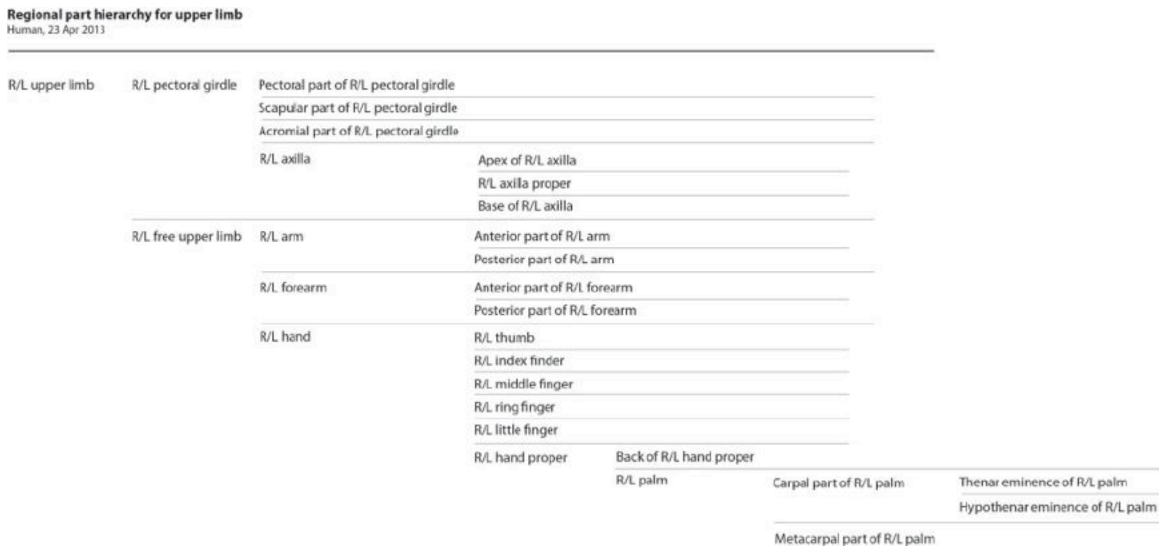


Figure 3-1. Diagram showing regional part hierarchy for the upper limb. Each indented column represents the parts of the class to the left, and the symbol "R/L" indicates that a pair of classes (one for the right structure, one for the left) are present.

As my work progressed, I began to discover content patterns. These are rules that state the allowed class types and relationships for specific types of content in the FMA. I began to develop content patterns as a way to better understand the FMA, but they could be employed for other purposes, such as: (1) establishing a standard for modeling content, (2) communicating the structure of the content to users of the FMA, (3) serving as a guide for constructing queries over the FMA, and (4) devising methods of computationally checking the content for consistency.

3.2 Examples of content patterns

In this section I provide four examples of content patterns in the FMA: four for the musculoskeletal system (Figures 3-2 through 3-5) and one for the lymphatic system (Figure 3-6). All patterns are works-in-progress, and may not reflect the current or future state of the FMA.

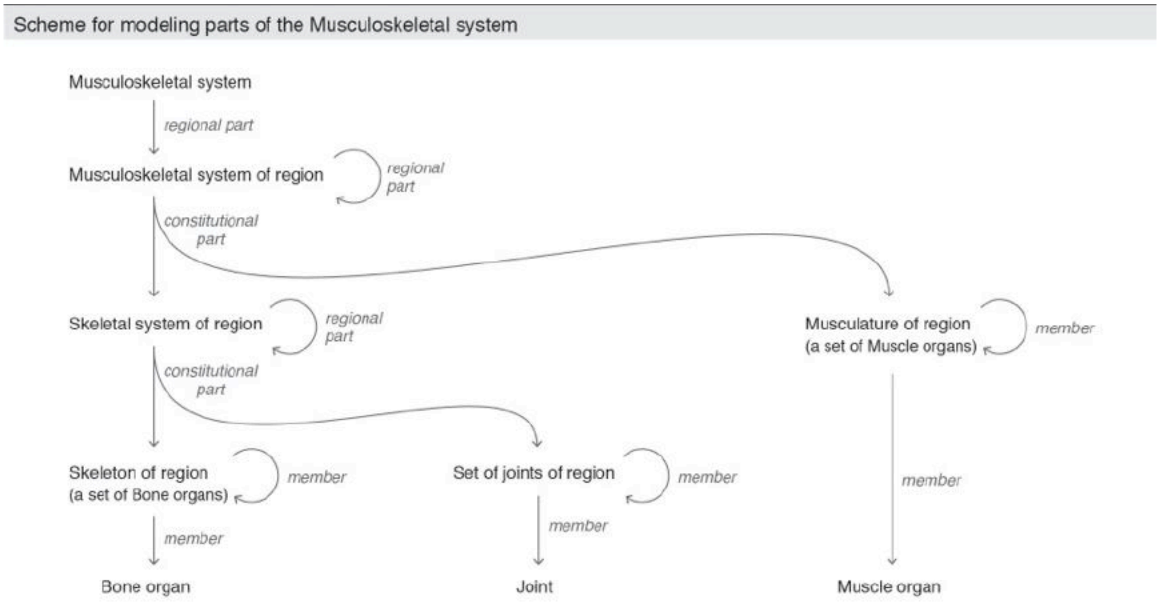


Figure 3-2. Content pattern that relates classes of type "Bone organ", "Joint", and "Muscle organ" to "Musculoskeletal system". The circular arrows indicate that zero or more relationships of that type may be present.

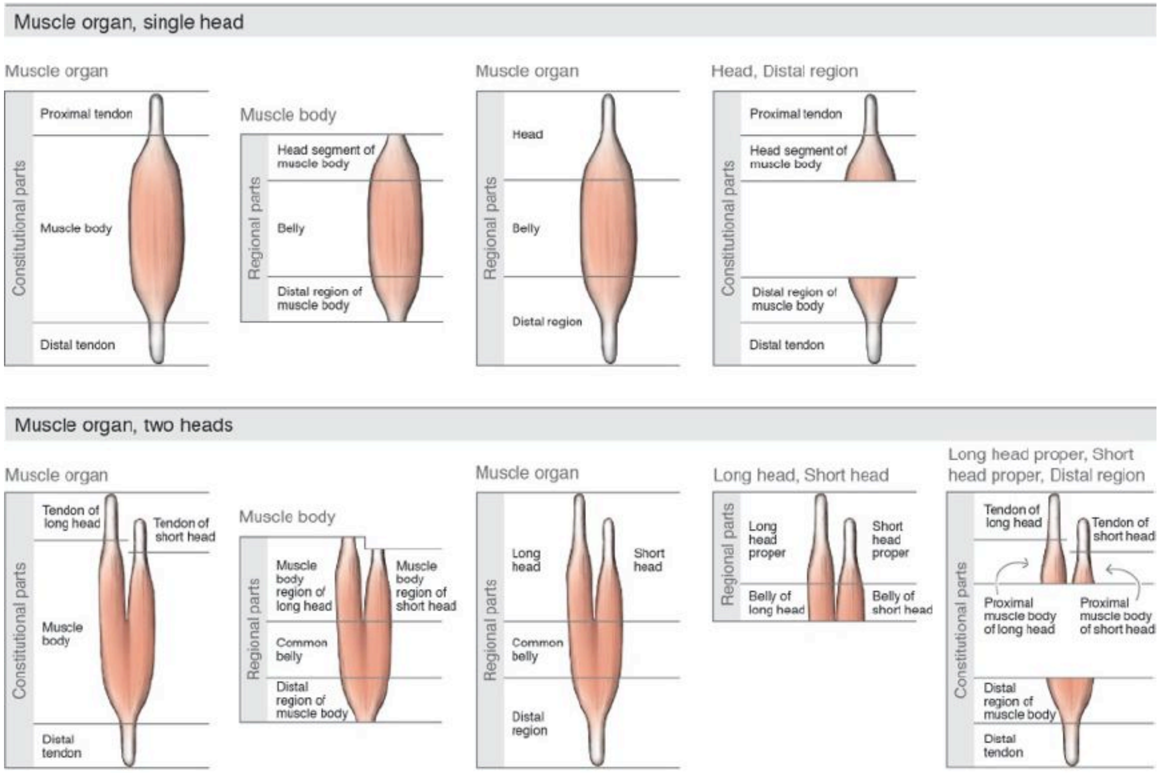


Figure 3-3. Content pattern for constitutional and regional parts of types of muscle organs. Top: Muscle organs with a single head. Bottom: Muscle organs with two heads.

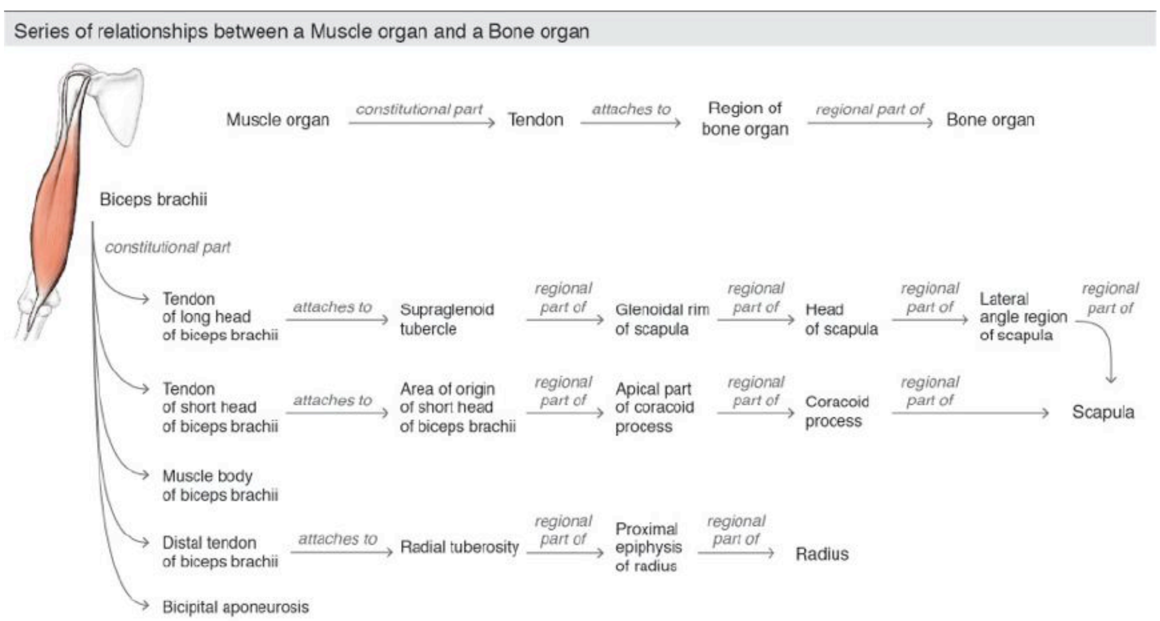


Figure 3-4. Top: Content pattern relating a class of "Muscle organ" to a "Bone organ", with intervening classes of "Tendon" and "Region of bone organ". Bottom: Example showing the pattern between "Biceps brachii" and the bone organs "Scapula" and "Radius".

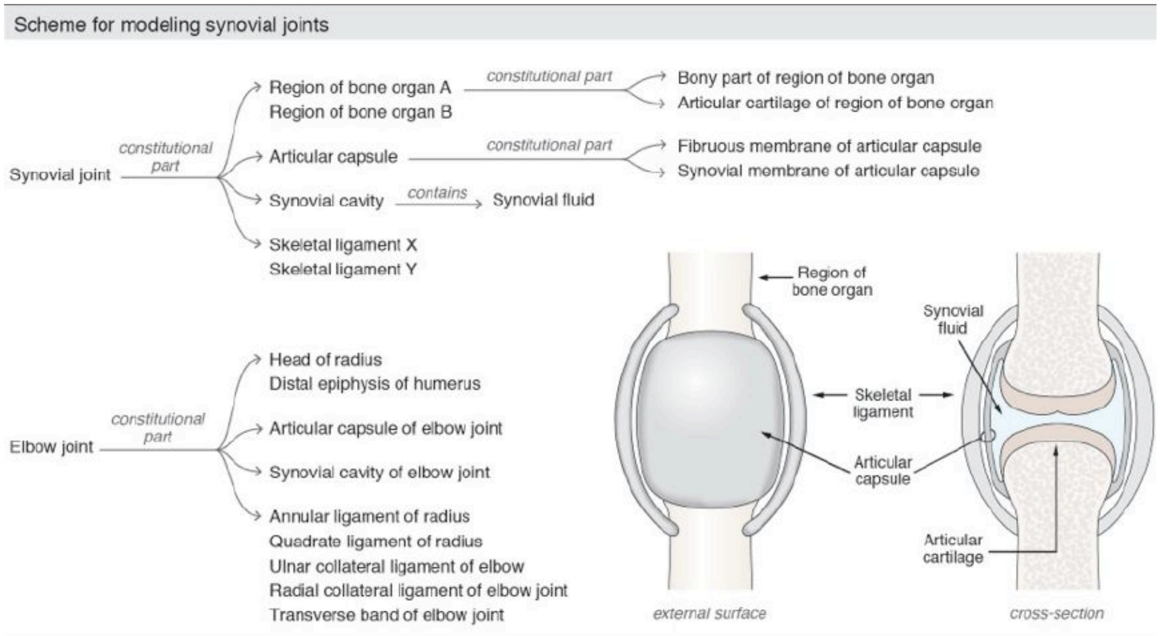


Figure 3-5. Top: Content pattern for synovial joints. Bottom left: Example of the class "Elbow joint". Bottom right: Graphical depiction of anatomy of a synovial joint.

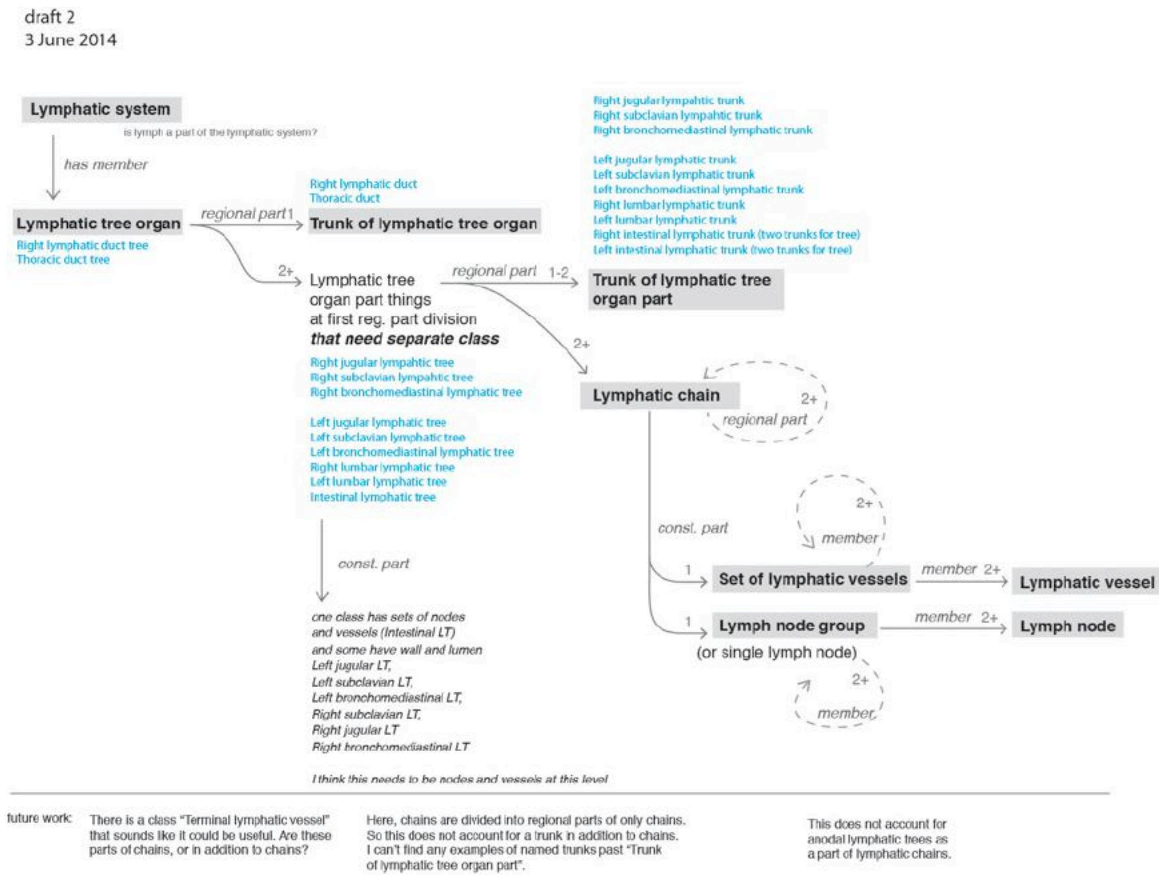


Figure 3-6. Unfinished work on the content pattern for the lymphatic system. The gray boxes represent classes in the FMA that are superclasses of the allowed classes (shown in blue). The numbers ("1", "2+") indicate number of classes required. Further progress on this pattern will require restructuring some of the content in the FMA.

Once these content patterns are further refined, it should possible to write them as path expressions in a graph query language such as SPARQL. This will allow the FMA to be automatically checked for inconsistencies with the patterns, instead of relying on the labor-intensive process of manually checking small portions of the FMA. An example of manually checking part of the content pattern for synovial joints (the relationships between a classes for synovial fluids and synovial joints) is provided within the following section.

3.3 Restructuring FMA content and identifying errors and omissions

My work on the FMA resulted in numerous examples of content in the FMA that was restricted for consistency or corrected for errors or omissions. I also identified issues that may be addressed by the FMA developer (José Mejino) in the future.

My most extensive work was on the musculoskeletal system. The results of this work included (1) redefining regional parts of the musculoskeletal system to correspond to regional parts of the body, and (2) proposing sets of bones that will correspond to regions of the musculoskeletal system. A photo of this work in progress is shown in Figure 3-7.

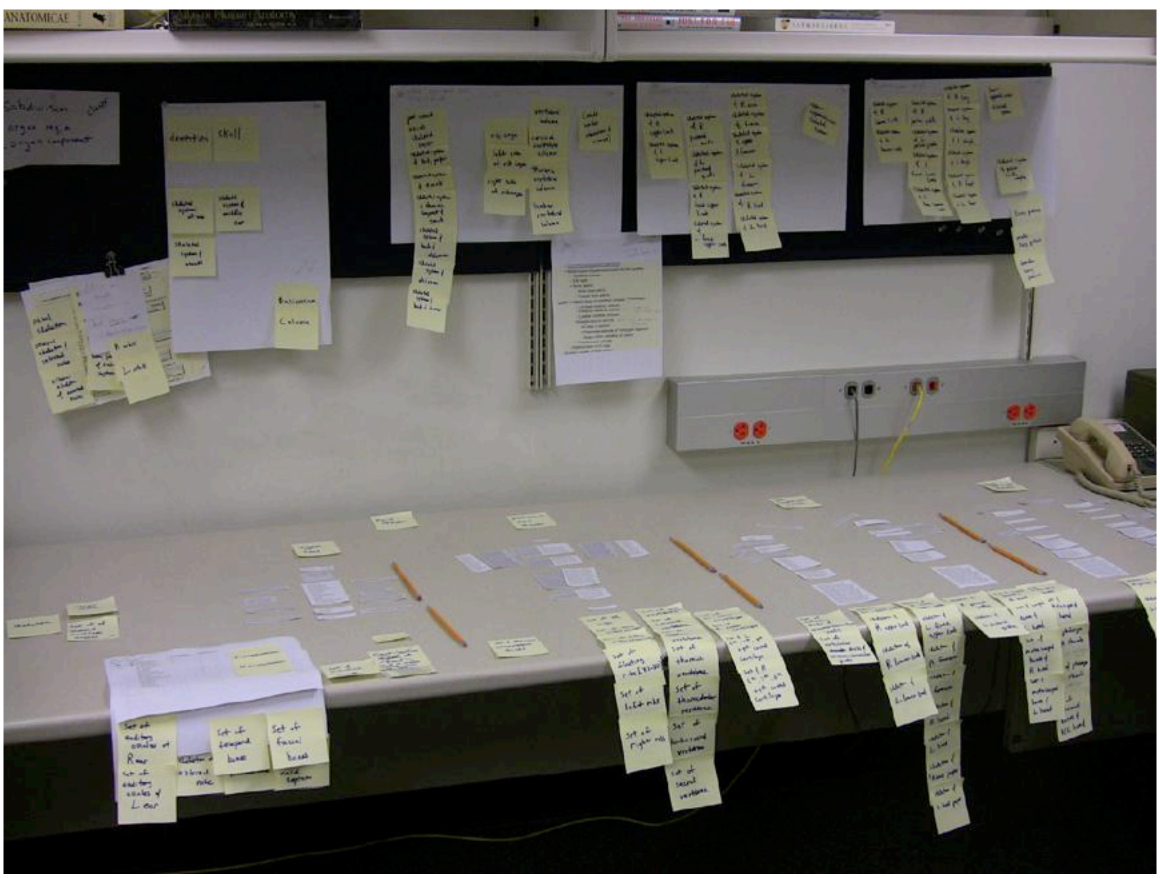


Figure 3-7. Work in progress to group bone organs and skeletal cartilage organs into sets that will correspond to regional partitions of the body. Classes for bone organs and skeletal

cartilage organs are printed on white and gray pieces of paper. Classes for sets are written on adhesive notes on the table. Classes for subdivisions of the skeleton and other related concepts are posted on the wall.

Figure 3-8 shows an example of errors found by manually checking classes of type “Synovial cavity” to determine if they have the relationships “contains” with a class of type “Synovial fluid”, prescribed in the content pattern in Figure 3-5.

Deviations from the pattern of
Synovial fluid of X....contained in....(Synovial) cavity of X

---

no relationships to anything:

Synovial fluid of temporomandibular joint (generic)
Synovial fluid of vertebral arch joint (generic)
Synovial fluid of atlanto-occipital joint (generic)
Synovial fluid of lateral atlanto-axial joint (generic)
Synovial fluid of C4-C5 vertebral arch joint (generic)
Synovial fluid of thoracic vertebral arch joint (generic)
Synovial fluid of T3-T4 vertebral arch joint (generic)
Synovial fluid of lumbar vertebral arch joint (generic)
Synovial fluid of right pisotriquetral joint
Synovial fluid of left pisotriquetral joint
Synovial fluid of subcutaneous trochanteric bursa (generic, R, L)
Synovial fluid of subtendinous bursa of latissimus dorsi (generic)
Synovial fluid of subtendinous bursa of trapezius (generic)
Synovial fluid of elbow joint (generic)
Synovial fluid of synovial tendon sheath of flexor pollicis longus (generic)
Synovial fluid of synovial tendon sheath of flexor carpi radialis (generic)
Synovial fluid of common synovial tendon sheath (generic)
Synovial fluid of synovial tendon sheath of extensores carpi radiales longus and brevis muscles (generic)
Synovial fluid of synovial tendon sheath of abductor pollicis longus and extensor pollicis brevis (generic)
Synovial fluid of synovial tendon sheath of extensor digitorum and extensor indicis (generic)
Synovial fluid of synovial tendon sheath of extensor pollicis longus (generic)
Synovial fluid of synovial tendon sheath of extensor digiti minimi (generic)
Synovial fluid of synovial tendon sheath of extensor carpi ulnaris (generic)

"regional part of" or "constitutional part of":

Synovial fluid of subdeltoid bursa (generic)
Synovial fluid of subscapularis bursa (generic)
Synovial fluid of subtendinous bursa of infraspinatus muscle (generic)
Synovial fluid of subtendinous bursa of teres major (generic)
Synovial fluid of pisotriquetral joint (generic)
Synovial fluid of subacromial bursa (generic)
Synovial fluid of coracobrachialis bursa (generic)
Synovial fluid of subcutaneous acromial bursa (generic)
Synovial fluid of subcutaneous olecranon bursa (generic)
Synovial fluid of bicipitoradial bursa (generic)
Synovial fluid of subtendinous bursa of infraspinatus muscle (generic)
Synovial fluid of subtendinous bursa of teres major (generic)
Synovial fluid of subtendinous bursa of triceps brachii muscle (generic)
Synovial fluid of subcutaneous infrapatellar bursa (generic)

"part-of" and "contained in" both showing in the FME:

Synovial fluid of right atlanto-occipital joint
Synovial fluid of left T2-T3 vertebral arch joint
Synovial fluid of right proximal radioulnar joint

---

has two "contained in" relationships:

Synovial fluid of right C4-C5 vertebral arch joint
Synovial fluid of right T3-T4 vertebral arch joint

Figure 3-8. Example of a document provided to José Mejino that lists errors and omissions for the "contained in" relationships between classes of type "Synovial fluid" and "Synovial cavity". (Note: Most of the classes are identified as "generic", "R", "L". This is our shorthand notation corresponding to classes of the form "Synovial fluid of elbow joint", "Synovial fluid of *right* elbow joint", and "Synovial fluid of *left* elbow joint". The FMA places the "right" and 'left" classes as subclasses of the one without a laterality designation.)

As another example, the regional partitions of the head were revised due to my work. Originally the class “Forehead” was a shared regional part of both the class “Face” and “Head proper”; it is now only a regional part of “Head proper”. Another revision was made to placement of the class “Pharyngotympanic tube” (Eustachian tube), which was originally a regional part of the face. It is now a regional part of “Auricular part of head” (which has “Ear” as another regional part).

I also undertook an extensive audit of the lymphatic system while working on the content pattern in Figure 3-6. This effort identified numerous inconsistencies in modeling the regional partitions, as well as locating disconnected portions of the lymphatic trees. Again, many of these inconsistencies were fixed by the content developer based on the information I provided to him.

4 Communicating the fundamental relationships

Students and researchers who are unfamiliar with biomedical ontologies have the challenge of understanding both 1) the modeling rationale and structure of an ontology and 2) the content of a particular ontology. To address the first challenge I created an ontology—the “Shirt Ontology”—as an analogy to the FMA, as well as an online tutorial that describes the Shirt Ontology and how the concepts within this ontology translate to the FMA.

4.1 The Shirt Ontology

The fundamental relationships that structure the FMA are the class hierarchy and three types of part hierarchies (regional parts, constitutional parts, and membership within sets). In order to explain these relationships, I developed the “Shirt Ontology” as an analogy to the FMA. This ontology describes a standard button shirt, a familiar item that is much more simple in structure than the human body. I choose a shirt as the subject for this ontology because it has several properties that correspond to the human body, including left-and-right symmetry and differences between men’s and women’s shirts (men’s buttons on the right, women’s buttons on the left).

The Shirt Ontology was constructed using the same fundamental relationships as the FMA, except the “constitutional part” relationship is referred to as the “material part” relationship. In addition, the Shirt Ontology represents points, lines, surfaces, and spaces, with definitions similar to those in the FMA.

The Shirt Ontology was developed in Protégé frames. It has thirteen types of relationships, as shown in figure 4-1.

Figure 4-1. Protégé screen capture of relationships in the Shirt Ontology.

As shown in Figure 4-2, the top-level class is “Physical clothing entity”, with subclasses “Immaterial clothing entity” and “Material clothing entity”. Selected subclasses of “Immaterial clothing entity” are shown in Figure 4-3, and selected subclasses of “Material clothing entity” are shown in Figure 4-4. There are a total of 269 classes.

Figure 4-2. Protégé screen capture of the top-level classes of the Shirt Ontology.

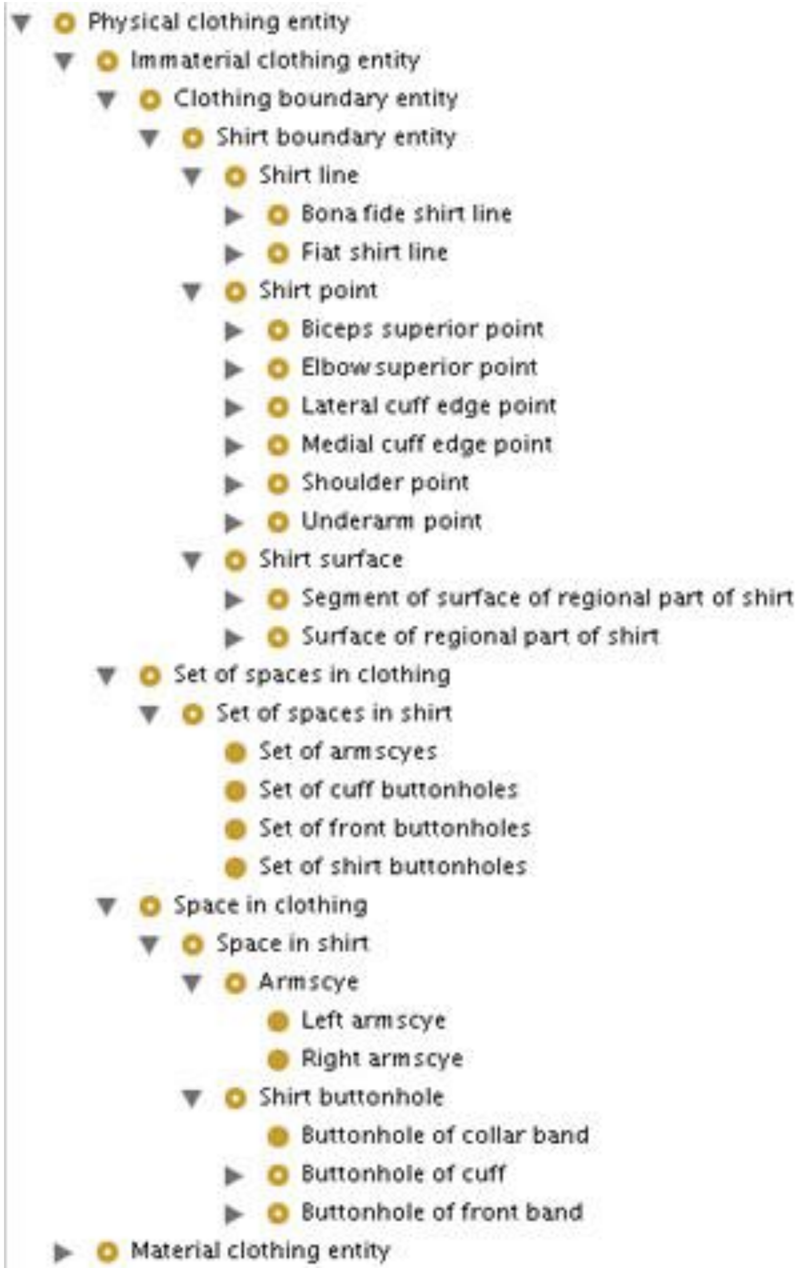


Figure 4-3. Protégé screen capture of selected subclasses of "Immaterial clothing entity".

Figure 4-4. Protégé screen capture of selected subclasses of "Material clothing entity".

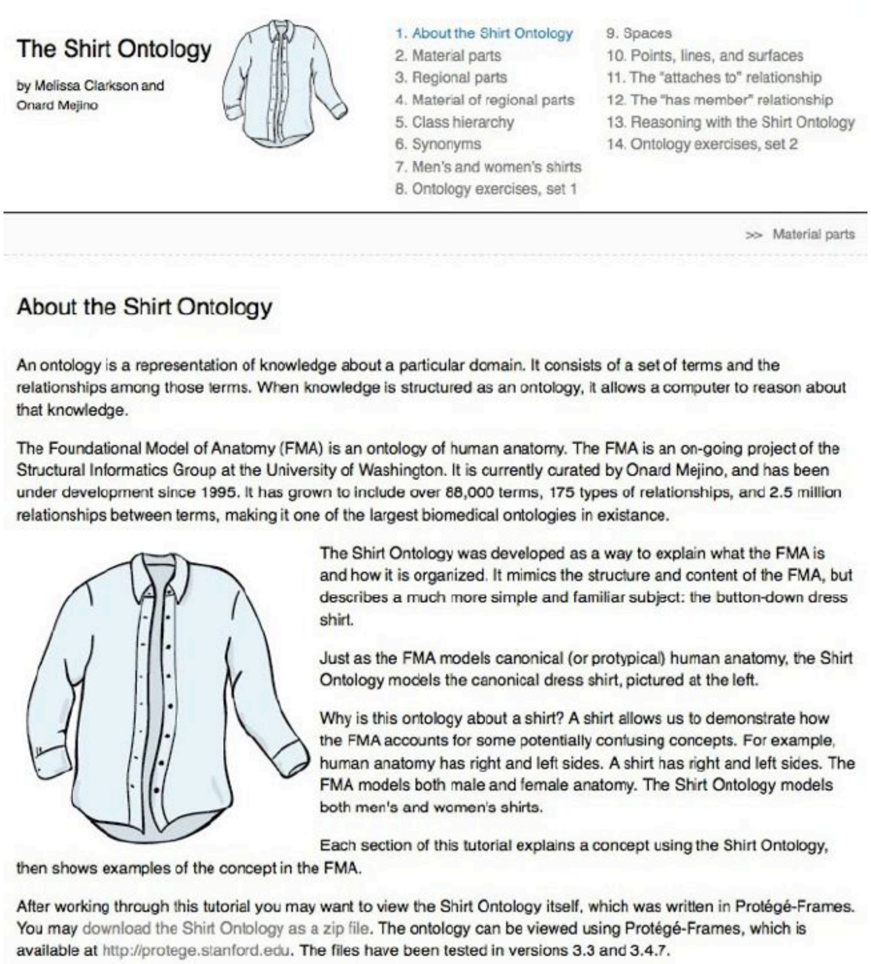
4.2 The Shirt Ontology tutorial

I developed an online tutorial to explain representations within the Shirt Ontology and how they translate to the FMA. The tutorial covers twelve topics:

- Material parts
- Regional parts
- Material of regional parts
- Class hierarchy
- Synonyms
- Men's and women's shirts
- Spaces
- Points, lines, and surfaces
- The "attaches to" relationship
- The "has member" relationship
- Reasoning with the Shirt Ontology

Each section of the tutorial begins by explaining a topic in the Shirt Ontology, then ends with examples of parallel concepts in the FMA. In addition, two sets of exercises (with answers) are provided to assist users in testing their understanding of the concepts presented.

Figures 4-5 and 4-6 show screen captures of the tutorial. The entire tutorial is reproduced in Appendix 1.



The Shirt Ontology

by Melissa Clarkson and Onard Mejino

1. About the Shirt Ontology
2. Material parts
3. Regional parts
4. Material of regional parts
5. Class hierarchy
6. Synonyms
7. Men's and women's shirts
8. Ontology exercises, set 1
9. Spaces
10. Points, lines, and surfaces
11. The "attaches to" relationship
12. The "has member" relationship
13. Reasoning with the Shirt Ontology
14. Ontology exercises, set 2

>> Material parts

About the Shirt Ontology

An ontology is a representation of knowledge about a particular domain. It consists of a set of terms and the relationships among those terms. When knowledge is structured as an ontology, it allows a computer to reason about that knowledge.

The Foundational Model of Anatomy (FMA) is an ontology of human anatomy. The FMA is an on-going project of the Structural Informatics Group at the University of Washington. It is currently curated by Onard Mejino, and has been under development since 1995. It has grown to include over 88,000 terms, 175 types of relationships, and 2.5 million relationships between terms, making it one of the largest biomedical ontologies in existance.

The Shirt Ontology was developed as a way to explain what the FMA is and how it is organized. It mimics the structure and content of the FMA, but describes a much more simple and familiar subject: the button-down dress shirt.

Just as the FMA models canonical (or protypical) human anatomy, the Shirt Ontology models the canonical dress shirt, pictured at the left.

Why is this ontology about a shirt? A shirt allows us to demonstrate how the FMA accounts for some potentially confusing concepts. For example, human anatomy has right and left sides. A shirt has right and left sides. The FMA models both male and female anatomy. The Shirt Ontology models both men's and women's shirts.

Each section of this tutorial explains a concept using the Shirt Ontology, then shows examples of the concept in the FMA.

After working through this tutorial you may want to view the Shirt Ontology itself, which was written in Protégé-Frames. You may download the Shirt Ontology as a zip file. The ontology can be viewed using Protégé-Frames, which is available at http://protege.stanford.edu. The files have been tested in versions 3.3 and 3.4.7.

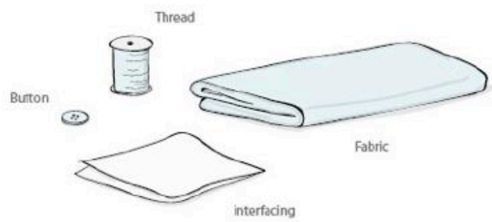
Figure 4-5. Home page of the Shirt Ontology Tutorial. The menu at the top provides a way to navigate to specific sections of the tutorial.

About the Shirt Ontology << >> Regional parts

Material parts

What are the parts of a shirt?

One way to answer this question is to list the types of materials that are used to construct a shirt. The four types of materials are thread, fabric, interfacing, and button.



Each of these is a class in the Shirt Ontology. There is the Thread class, the Fabric class, the Interfacing class, and the Button class. A shirt is made up of these four types of materials, and nothing else. The material parts are essentially the "ingredients" of a shirt.

This part relationship can be represented as:

Shirt $\xrightarrow{\text{has material part}}$ Thread , Fabric , Interfacing , Button

(You may be wondering what interfacing is. It is a fabric-like material that is put inside the collar, cuffs, and front bands to provide stiffness.)

The idea of a class is fundamental to ontologies. A class describes a concept. The class "button" describes the concept of a button. The class "interfacing" describes the concept of interfacing. This is different than talking about a specific button or a specific piece of interfacing. Classes are a way to refer to a category of similar entities, without refering to individual entities.

On the previous page an ontology was defined as a set of terms and the relationships among the terms. A more precise definition of an ontology is that it is a set of classes and the relationships among the classes. In this tutorial, classes will be represented as terms within blue boxes.

In the FMA

In the FMA, the equivalent of material parts are called "constitutional parts". When an anatomical structure is divided into constitutional parts, it is divided into parts that are more simple in composition.

These are the constitutional parts of the class Brain :

Brain $\xrightarrow{\text{has constitutional part}}$ Neural tissue of brain , Ventricular system of brain , Vasculature of brain

The class Ventricular system of brain has its own constitutional parts:

Ventricular system of brain $\xrightarrow{\text{has constitutional part}}$ Wall of ventricular system of brain , Cavity of brain

Figure 4-6. The section of the Shirt Ontology Tutorial describing material parts within the Shirt Ontology and the corresponding concept of constitutional parts within the FMA.

This tutorial is provided as a link from the FMA browser described in Chapter 5. Informal feedback has been positive, with users saying that this helps to clarify the difference between regional parts and constitutional parts in the FMA.

5 Communicating the details

This chapter describes the design and implementation of my FMA browser, which provides access to the entire FMA. This interface is intended to be used by students in biomedical informatics who are studying ontologies, collaborators helping to develop content for the FMA, and software engineers who need to understand the structure and content of the FMA so that they can incorporate the FMA into their own applications as a computable source of anatomical knowledge.

5.1 Existing interfaces for viewing the FMA

The interface for accessing the FMA online for over a decade has been the Foundational Model Explorer (FME) (Detwiler et al., 2003). As shown in Figure 5-1, this interface displays a class or part hierarchy on the left half of the screen, plus selected properties of the selected class on the right half of the screen.

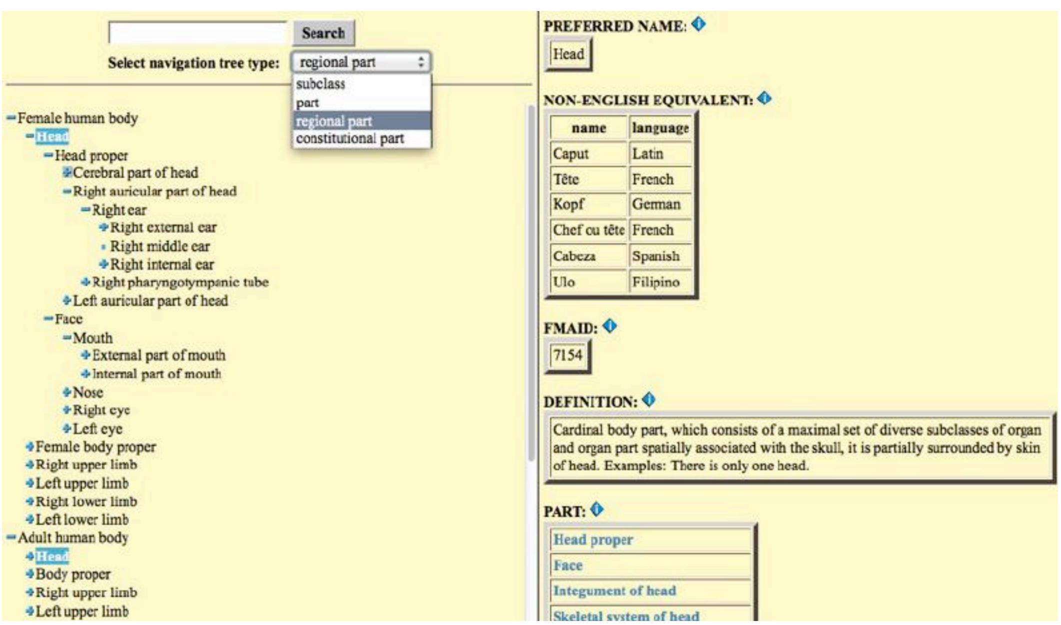


Figure 5-1. Screen capture of the FME, showing a portion of the regional part hierarchy for the class “Head” and a portion of the right panel showing the properties of this class.

One major shortcoming of the FME interface is that a class is viewed within a single hierarchy, even though the class may belong within multiple hierarchies. For example, in Figure 5-1, the class ”Head” (highlighted in blue) is a regional part of “Female human body”, “Adult human body”, and “Male human body” (not shown), and is therefore duplicated on the screen for each hierarchy. In addition, “Head” is also part of a constitutional part hierarchy and the class hierarchy, but this not shown because only a single type of hierarchy can be viewed at a time. The FME does have the option to display a mixed hierarchy of constitutional parts and regional parts (the “part” relationship in the drop-down menu), but this mixing of relationships obscures the structure of the FMA.

It is also possible to view the FMA using node-and-link representations. Figure 5-2 shows two such visualizations. The Ontology Viewer is an application that uses the FMA as a demonstration ontology (Yngve, 2007), and the FlexViz tool is deployed within BioPortal, a repository of biomedical ontologies (Noy et al., 2009).

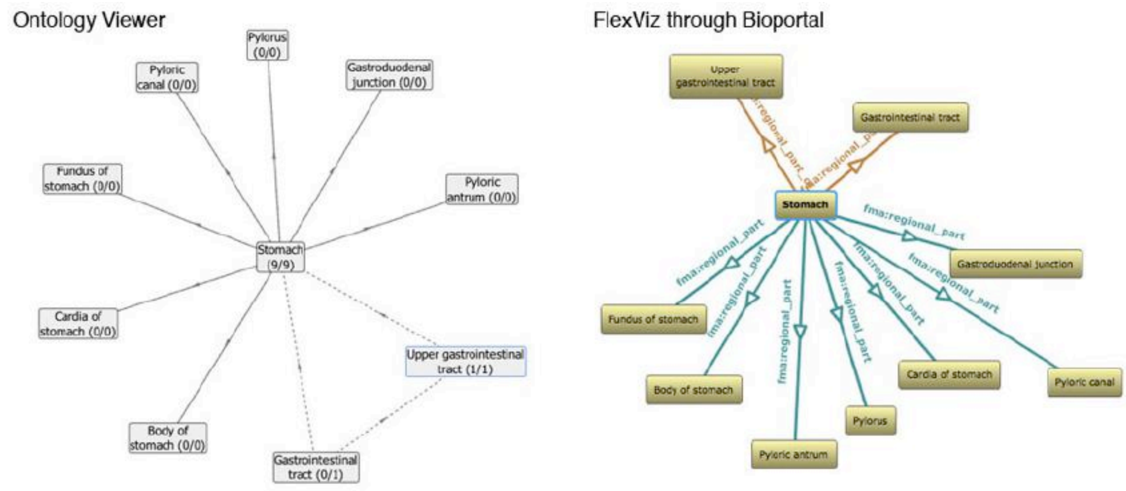


Figure 5-2. Examples of node-and-link representations showing portions of the FMA. From the Ontology Viewer (left) and FlexViz (right).

Node-and link representations have the advantage of accommodating different types of relations in a single view (by using lines of different colors or styles), and they represent an ontology as a network instead of a hierarchical tree. However, these representations quickly become cluttered and difficult to interpret as increasing numbers of classes are displayed.

To better address the need to view the FMA, I designed and developed an online browser. This tool is intended to communicate the structure of the FMA, provide an interface that supports browsing, and to provide intuitive entry points into the ontology.

5.2 Designing the FMA Browser

Note: This section has been published within the conference proceedings of SIGDOC.

Melissa Clarkson (2012). “Understanding conceptualizations of anatomy: Designing a browser for the Foundational Model of Anatomy.” SIGDOC 2012, October 3–5, 2012, Seattle, Washington, USA. Copyright 2012 ACM.

The design process proceeded in two phases: an exploratory phase followed by a design phase.

5.2.1 Exploratory phase

The purposes of the exploratory phase were to understand the structure of the FMA, to identify the users for the browser and the types of tasks they want to perform, and to generate ideas for the design of the browser. Two types of activities were conducted:

(1) Three biomedical researchers who have expert knowledge of the FMA were interviewed individually. During the interview each participant was asked to sketch a map of how they conceptualize the FMA. They were asked how they divide the FMA into "chunks", their entry point(s) when thinking about the FMA, and any important paths through the FMA. The interviews were between 45 and 60 minutes in length. Interviews were recorded, transcribed and then analyzed for themes and methods of visual representation.

(2) An hour-long focus group was conducted with five biomedical researchers who either have expert knowledge of the FMA or have used the FMA in their own research. In order to generate ideas for different styles of visual representation, participants were asked to sketch ideas for visualizing the FMA that were inspired by the wayfinding strategies described by David Gibson (the Landmarks model, Streets model, Connector model, and Districts model) (Gibson, 2009). Architects and graphic designers use these types of strategies when constructing systems to help people navigate through physical spaces.

5.2.1.1 Finding 1

Finding 1: Anatomy and ontologies occupy separate conceptual spaces and have distinct representations.

Participants drew two types of visual representations: outlines of bodies or organs (sometimes divided into regions) and node-and-link diagrams that corresponded to classes and relationships within the FMA. One participant referred to these as the “spatial” and “symbolic” representations (Figure 5-3) and commented, “I think it is very important for me to keep the two sides separate.”

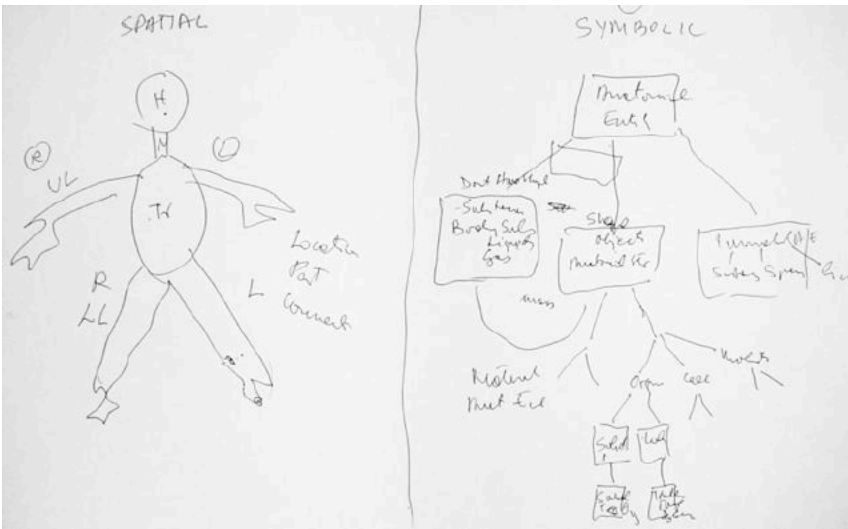


Figure 5-3. Example of a participant’s sketch demonstrating different representations for anatomy and an ontology.

These two styles of representations are products of two different conceptual spaces. The spatial representation reflects an understanding of anatomy as three-dimensional structures and their locations within the body. The symbolic representation is a collection of statements about anatomy, represented by the classes and relationships within the ontology. These two spaces can be described as “What is my understanding of anatomy itself?” and “What is my understanding of how anatomy has been modeled in the FMA?” Participants moved between these two conceptual spaces based on the topic or task of the moment.

Design implication: Provide separate entry points into the FMA to accommodate these different conceptual spaces.

5.2.1.2 Finding 2

Finding 2: The FMA has multiple entry points, and these reflect different purposes and tasks.

The FME uses the class "Human body" as the entry point. When the FMA is displayed in general tools such as the Ontology Viewer or FlexViz, the entry point will be the class "Anatomical entity" at the top of the class hierarchy. But these may not be the most helpful entry points. When participants were asked where they mentally entered the FMA, they responded with several strategies. One strategy was to begin with the class "Human body" and move through the regional parts. Another was to begin with the organ most relevant to the class they wanted. A final strategy was to first decide which subclass of "Anatomical structure" (such as "Organ system", "Organ", or "Portion of tissue") was appropriate.

Design implication: Provide several entry points into the FMA.

5.2.1.3 Finding 3

Finding 3: Three relationships are used for global navigation of the FMA.

During both the interviews and the focus, group participants were asked to describe types of paths they would like to navigate through the FMA. Participants described two types of navigation: global and local. Global navigation relied on class, regional part, and constitutional part relationships to reach a class of interest. Local navigation took place around that class of interest, and could incorporate relationships such as “continuous with” for navigating through arteries or “articulates with” for bones.

Design implication: It is most critical to support navigation through the class, regional part, and constitutional part hierarchies in a browser that is primarily for finding classes of interest and understanding the structure of the FMA.

5.2.2 Design phase

The purposes of the design phase were to identify common sources of confusion about the structure or content of the FMA, to develop methods to represent the content of the FMA and to browse the FMA, and to validate that the emerging design made sense to researchers who are unfamiliar with the FMA.

Four types of activities took place:

(1) Extensive conversations were conducted with José Mejino, who has been working on the development of the FMA for over fifteen years and is currently the sole author and curator.

(2) An informal survey of methods for graphical representation of anatomy was undertaken. This included examining stylized representations of anatomy within collections of clip art on stock image websites and illustrations of organ systems in medical textbooks and on websites.

(3) Graphics and screen layouts for the interface were sketched and refined. These were shown to a total of six biomedical researchers who had some familiarity with the FMA. A feedback session had between one and three participants and lasted between 30 and 60 minutes. These feedback sessions were also repeated at a later stage of the design process. Participants were asked to interpret the graphics I

had drawn to represent FMA classes, to describe what information they would like to see on each screen, and to suggest any alternative designs for the navigation or graphics. Photos from these sessions are shown in Figure 5-4.

(4) The nearly-completed prototypes were shown to two biomedical researchers unfamiliar with the FMA. They were asked for their interpretation and feedback. These sessions lasted between 30 and 45 minutes.

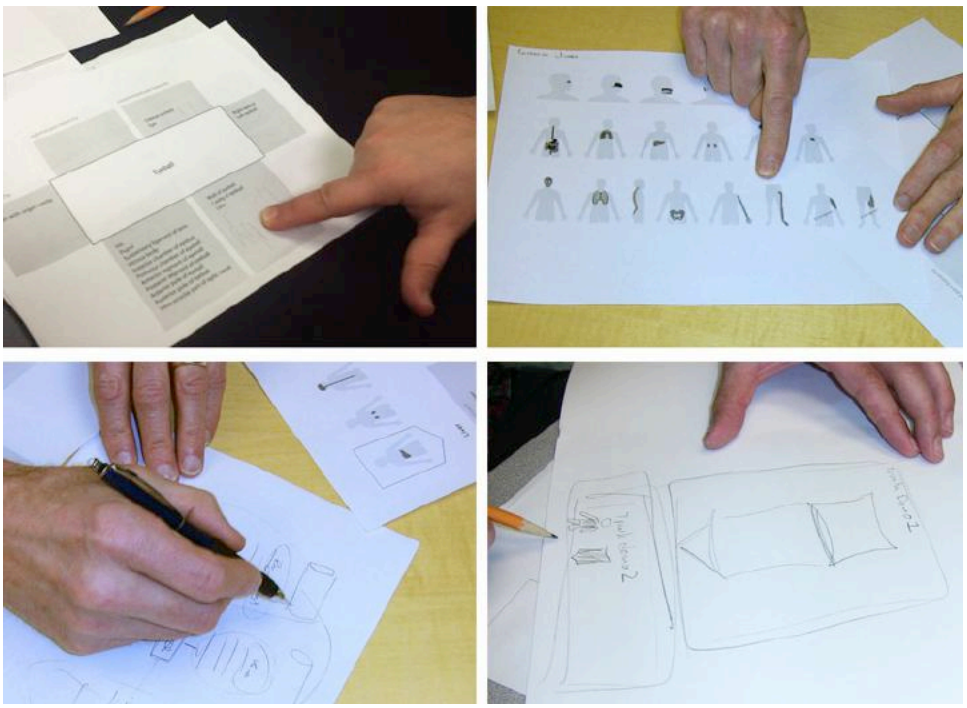


Figure 5-4. Feedback sessions during the iterative design process, showing participants discussing graphics and their ideas.

5.2.2.1 Finding 1

Finding 1: A number of mismatches exist between common conceptual units and FMA classes.

During the survey of methods for graphically representing anatomy a number of "common conceptual units" of anatomy were identified. These are concepts such as “heart”, “kidney”, or “hand” that are widely recognized by a common name and have a fairly standard graphic representation. One of my focus group participants described a similar phenomena as “salient concepts”, explaining that these are “names people recognize as visible structures, and they use these to locate smaller [parts].”

After compiling a set of approximately two dozen common conceptual units, two types of mismatches between some of these common conceptual units and the corresponding class in the FMA were identified (Figure 5-5).

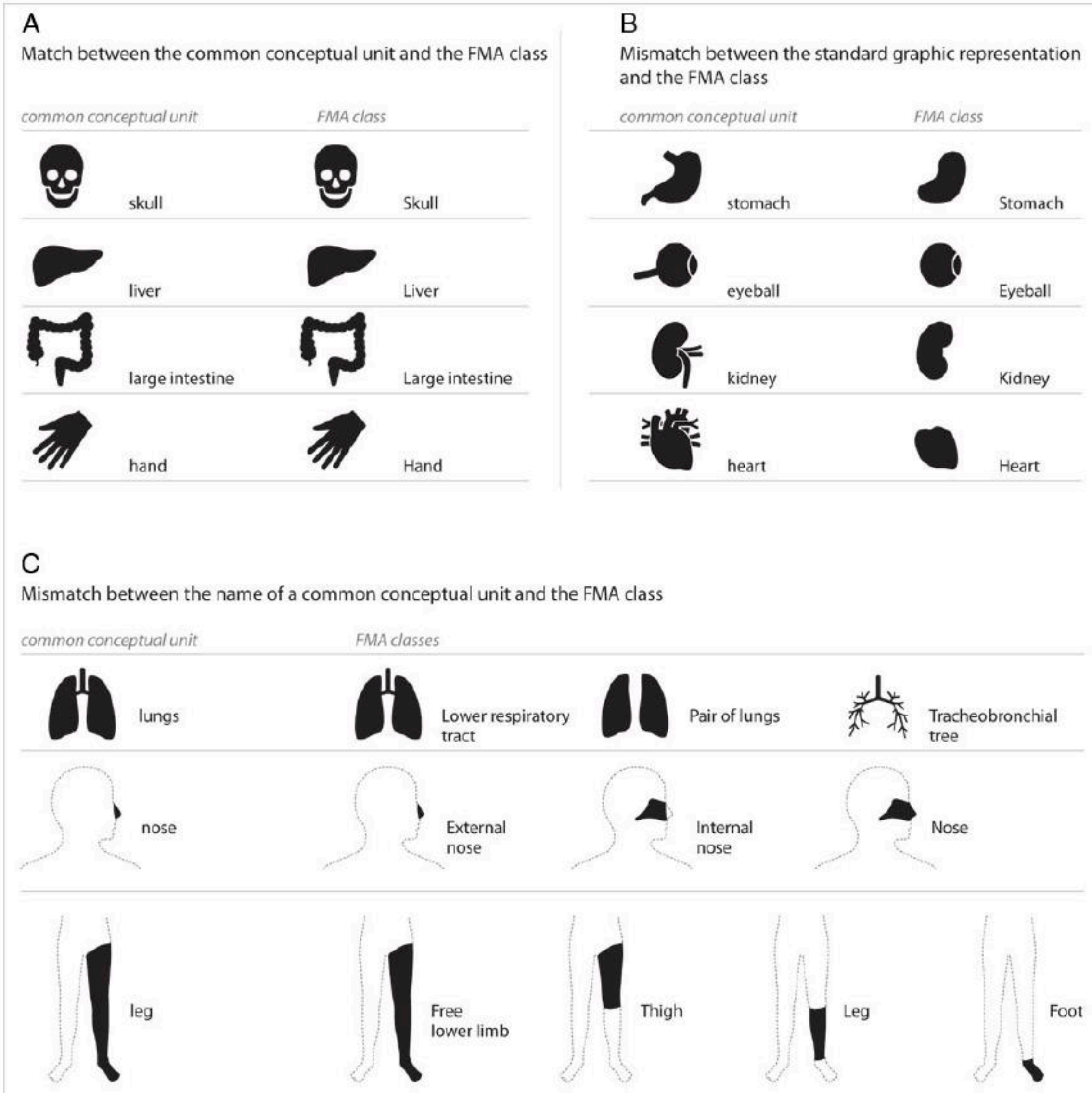


Figure 5-5. Examples of matches and mismatches between common conceptual units of anatomy and classes in the FMA. (A) Matches between common conceptual units and FMA classes. (B) Mismatches between standard graphic representations and FMA classes. (C) Mismatches between the names of a common conceptual units and FMA classes.

The first type of mismatch exists when the standard graphic representation conflicts with the FMA class (Figure 5-5B). For example, the standard graphic of a stomach will show sections of the esophagus and small intestine (Figure 5-5B, first row). Similarly a graphic of a kidney will include not just the kidney, but also sections of the ureter, renal artery, and renal vein (Figure 5-5B, third row).

This type of mismatch could lead to two difficulties. The first is that a user could assume that a class contains a part that it does not. For example, someone could navigate to the class “Heart” with the expectation of finding the class “Aortic arch” as a part of it. The second difficulty arises when designing graphics to accurately represent these classes. Figure 5-6 shows explorations to represent the class “Stomach”. Two approaches are: (a) to add context to the graphic by showing the position within the body or adding dotted lines to show the “missing” parts, and (b) to place the class within a larger, more recognizable class, such as using a graphic for the class “Gastrointestinal tract” instead of “Stomach”.

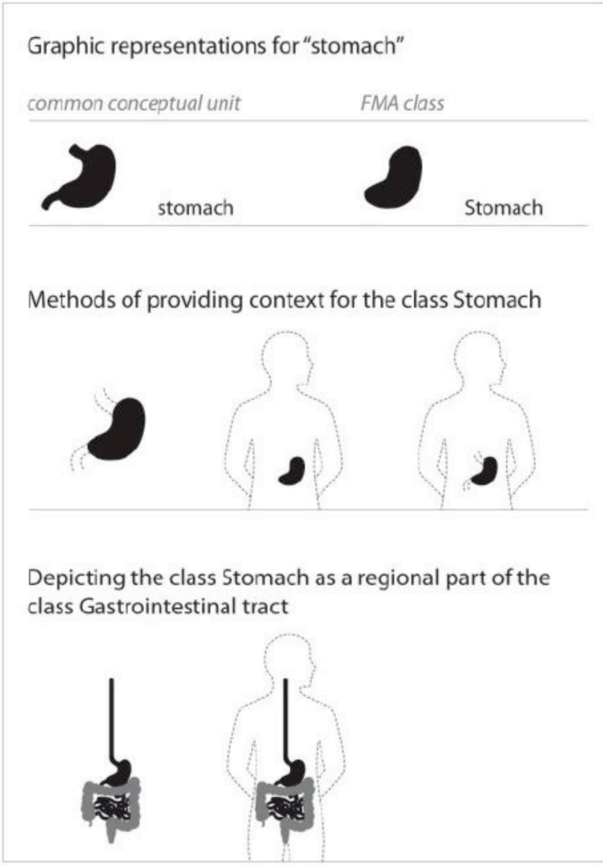


Figure 5-6. Graphical representations of the class "Stomach".

The second type of mismatch exists when the name of a common conceptual unit does not match the corresponding FMA class, but instead refers to a different class (Figure 5-5C). For example, as shown in the third row of Figure 5-5C, the name given to common conceptual unit of "leg" corresponds to the class "Free lower limb" in the FMA. The FMA class "Leg" is the regional part of the class "Free lower limb" between the thigh and foot.

Design implications: (a) There should be a strict correspondence between a graphic and the FMA class it represents, but this can lead to challenges in creating recognizable graphics. (b) Graphics can help people to locate classes within the FMA even if the name of the class is unexpected.

5.2.2.2 Finding 2

Finding 2: The organ systems provide an intuitive way of entering the FMA, and these can be represented graphically.

Anatomy can be taught by two methods: (a) a regional approach in which students learn about all structures within a region of a body (such as the head) before moving to the next region, or (b) a systems approach in which the organ systems (such as the cardiovascular system) are studied one at a time, regardless of their locations within the body. This systems approach has strongly influenced how people conceptualize anatomy. In order to help align the design of the browser with people's existing understanding of anatomy, a series of graphics were designed to represent the organ systems of the FMA (see examples in Figure 5-7). Participants in the feedback sections were generally able to recognize the organ systems represented by the graphics, and small changes were made in response to feedback.

The FMA represents some organ systems separately for males and females. For example, the class "Urinary system" has subclasses "Male urinary system" and "Female urinary system". It is important for the graphics to indicate if the organ system is represented separately for males and females, and this was successfully conveyed by using graphics that show either a single body or side-by-side male and female bodies (Figure 5-7).

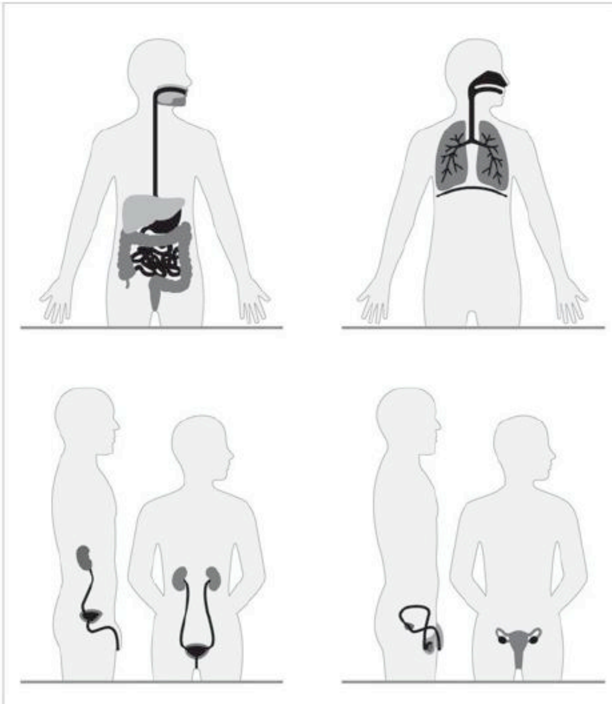


Figure 5-7. Example of graphics developed for the subclasses of "Organ system" (Alimentary system, Respiratory system, Male and female urinary system, Male and female genital system).

Design implication: Graphics representing the subclasses of Organ system provide a good entry point to the FMA, and can be used to convey that some organ systems are modeled separately for males and females.

5.2.2.3 Finding 3

Finding 3: Several levels of the regional parts hierarchy can be successfully navigated using graphics if the graphics maintain context

Many participants wanted an option to select regional parts using a graphic of a human body. Therefore, several methods were explored to allow users to graphically navigate the first few levels of the regional part hierarchy. The final scheme is shown in Figure 5-8. Each selection reveals an additional graphic presenting the regional parts of the previous. This allows the user to return to the previous graphic and make a new selection, and it also helps to give context to the new graphic. If a series of graphics would require more screen space than is available, showing only the last two graphics (with an option to scroll to earlier graphics) was acceptable to participants.

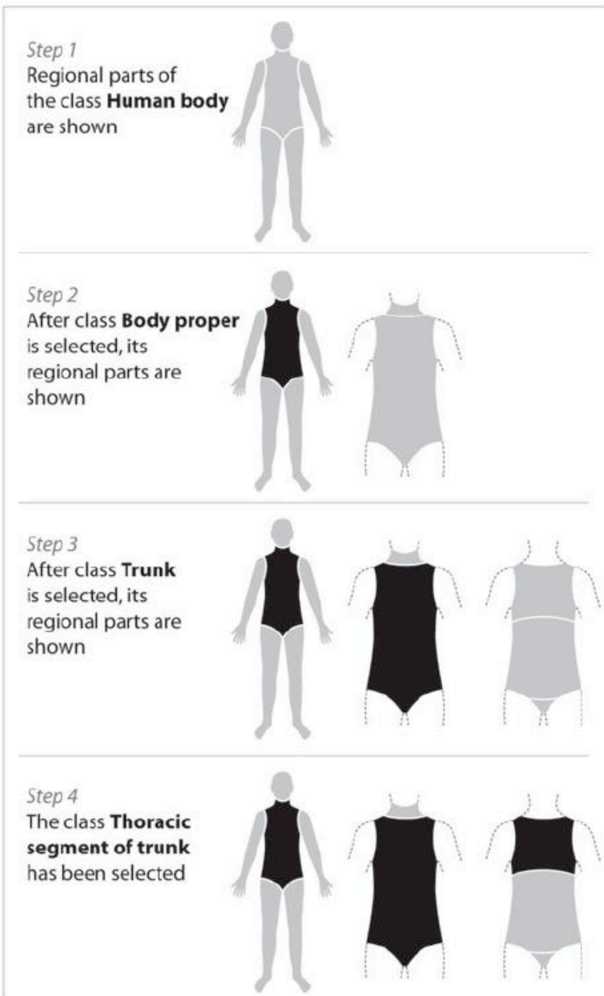


Figure 5-8. A scheme for selecting regional parts of the class "Human body".

With the exception of the initial graphic, the entire body is not shown. Each new graphic is an enlargement of the region of interest in order to prevent regions from becoming too small to display and select.

Design implication: Several levels of the regional part hierarchy can be successfully navigated using graphics.

5.2.2.4 Finding 4

Finding 4: By centering on a single class, a browser can simultaneously display the position of that class within the three hierarchies of class, regional part, and constitutional part relationships in a way that is intuitive to users.

To address the task of global navigation, participants were shown a sketch of a hierarchy browser similar to Figure 5-9. Participants responded favorably to this design. For participants unfamiliar with the FMA, this layout not only clarified how a single class can exist within these three hierarchies, but also helped them to understand the differences between the three hierarchies.

Design implication: The layout shown in Figure 5-9 will support navigation through the class, regional part, and constitutional part hierarchies and help users to understand the structure of the FMA.

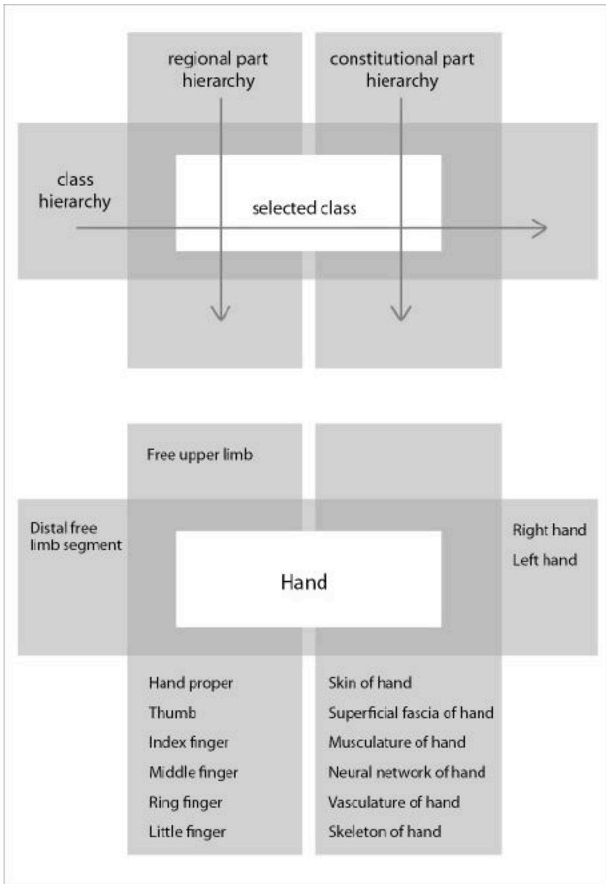


Figure 5-9. General layout of the hierarchy browser (top) and an example with the class "Hand" selected (bottom).

5.2.3 The preliminary design

The preliminary design for the FMA browser is shown in Figure 5-10. The initial screen will present the user with four entry points:

(1) *A collection of selected classes (including "Heart", "Liver", "Eyeball").* These classes are intended to reflect common conceptual units, particularly the major organs. Selecting a graphic will reveal the regional and constitutional parts of that class, and may also provide an explanation of that class and short list of related

classes. This entry point is provided so that users can quickly compare their understanding of common conceptual units to the way they are modeled in the FMA.

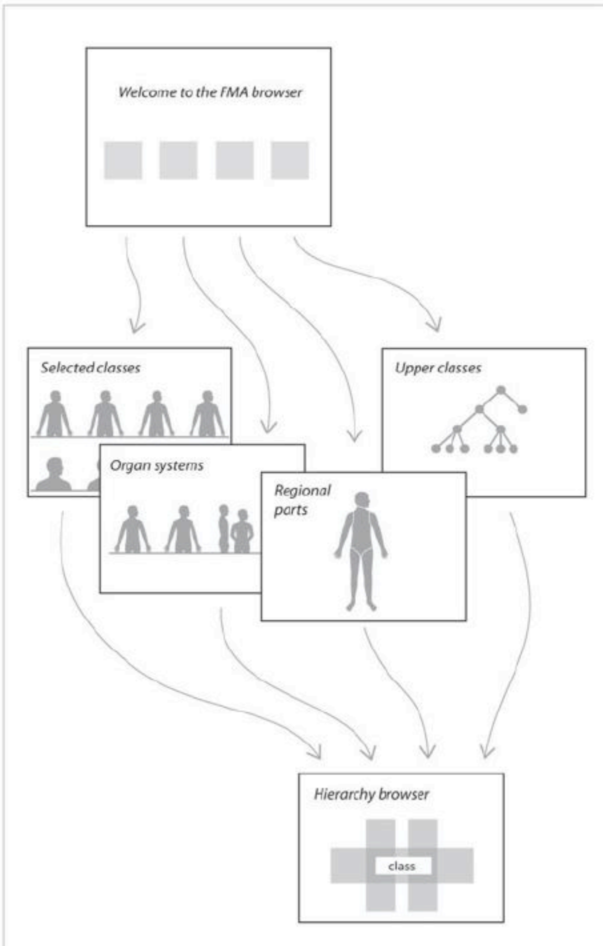


Figure 5-10. Summary of the preliminary design for the FMA browser.

(2) *The organ systems.* The FMA defines nine classes as subclasses of “Organ system” (including the “Alimentary system”, “Respiratory system”, and “Musculoskeletal system”). Selecting one of these graphics will reveal the names of the regional and constitutional parts of that class. For those systems modeled separately for males and females, the user must select either the male or female class for that organ system before viewing regional and constitutional parts. The

Musculoskeletal system will include a graphical selector for regional parts, allowing users to navigate to classes for muscles, bones, and joints.

(3) *Regional parts of class Human body.* A graphic of the human body divided into regional parts will be presented. The user will navigate two to four levels into the regional part hierarchy by selecting a sequence of regions (such as "Upper limb", "Free upper limb", "Hand").

(4) *The upper classes of the ontology.* For users entering from an ontology conceptual space, an option to view the upper classes as a node-and-link tree will be provided. This view will display the top five levels of the class hierarchy (from the class "Anatomical entity" through classes at the level of "Body", "Cardinal body part", "Organ system", and "Organ"). Once the user has navigated through a set of entry point screens with graphical displays, navigation deeper into the FMA will be done through the hierarchy browser (Figure 5-9). The name of a class will be displayed in the center of the hierarchy browser, and the placement of that class within the three hierarchies of class, regional part, and constitutional part relationships will be shown (Figure 5-9). Selecting the name of a class within one of those hierarchies will move that class to the center of the screen and the hierarchies will be updated.

5.3 Final design and implementation of the FMA browser

Once the preliminary design was established, I began to develop a coded prototype. During this phase four notable changes were made to the design.

5.3.1 Changes to the final design

My preliminary design work arrived at the general layout for the browser shown in Figure 5-9, with a class displayed within the class hierarchy, regional part hierarchy, and constitutional part hierarchy. A third type of part hierarchy—the membership hierarchy—is critical to understanding some classes. For example, the class “Set of carpal bones” has eight members (including “Hamate”, “Capitate”, and “Trapezoid”). Upon discussions with José Mejino, we decided to include the membership hierarchy, using the layout show in Figure 5-10.

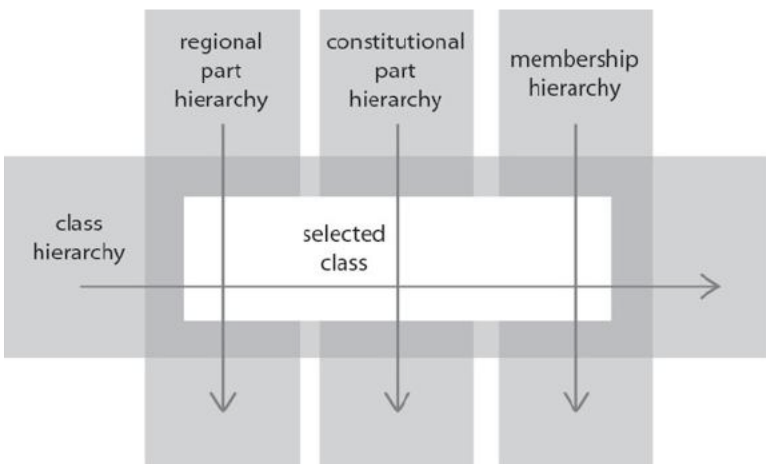


Figure 5-10. General layout of the FMA browser showing a single class positioned within four hierarchies.

My earliest prototype had six pages, as shown in Figure 5-10. The user began at the home page, moved to one of the four entry point pages, and then upon selecting a graphic was sent to the browsing page displaying the hierarchies. While developing this prototype it became clear that moving between these pages had the potential to disorient the user. Therefore, I eliminated the pages for the four entry points and replaced them with sliding panels on the browsing page.

In my preliminary design, the user browsed regional parts of the body by selecting successively smaller regions of a responsive graphic. My final implementation uses a series of static graphics in order to simplify implementation and to maintain consistency with the presentation of graphics at the other entry points.

Finally, the preliminary design included a graphical selector to help the user to navigate classes for muscles, bones, and joints. This idea was eliminated after my work revealed inconsistencies in how the musculoskeletal system was modeled in the FMA, and time did not permit these inconsistencies to be addressed by restructuring that portion of the ontology.

5.3.2 Method of implementation

The browser interface was developed using the Prototype and script.aculo.us JavaScript libraries. Graphics are rendered as SVGs using the Raphaël JavaScript library.

Queries over the FMA are preformed using the Query Integrator (Brinkley et al., 2012), which allows templates for SPARQL queries to be stored and then later accessed as a web service. Appendix 2 lists the templates for the queries used in the browser and composed with the assistance of Todd Detwiler. For example, query #274 returns all classes that the query class is a regional part of. Therefore, submitting query #274 with the class “Nose” returns the classes “Face” and “Midface”. “The Query Integrator returns results as XML, which is parsed using JavaScript and displayed within the interface.

The interface of the Query Integrator can be accessed at http://xiphoid.biostr.washington.edu:8080/QueryManager/QueryManager.html. Requests are submitted to the Query Integrator using a URL such as http://xiphoid.biostr.washington.edu:8080/QueryManager/TemplateQueryResults?qid=274&args=Nose

Because web browsers do not allow pages to make requests to web services from a different domain than the web page as a security measure, I access the Query Integrator using the Simple PHP Proxy (version 1.6), made available by Ben Alman.

5.3.3 Final interface and graphics

The major features of the interface, and well as the final graphics, are presented in Figures 5-11 through 5-21.

Figure 5-11. Home page of the FMA browser. The four square graphics are buttons representing the four entry points. These send the user to specific panels on the browsing page.

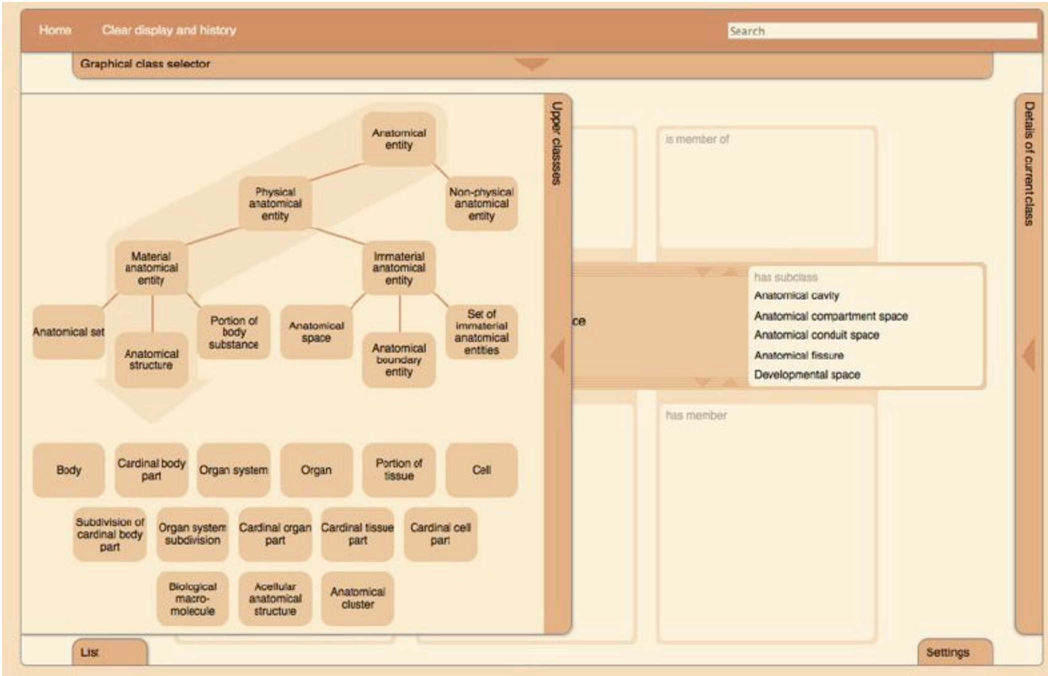


Figure 5-12. Browsing page showing the left panel that opens when the user selects the entry point of *Upper classes*. Clicking a term in the graphic initiates a query. Clicking the panel tab closes the panel.

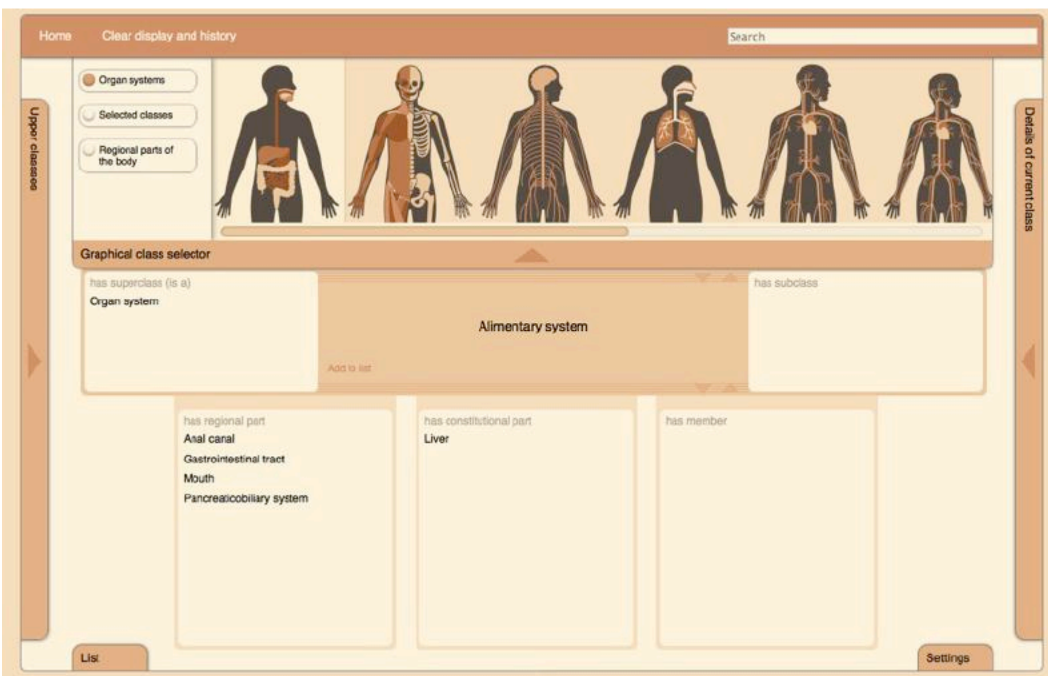


Figure 5-13. Browsing page showing the top panel that opens when the user selects the entry point of *Organ systems*. A total of twelve classes are represented graphically. Clicking a graphic initiates a query. Clicking the panel tab closes the panel.

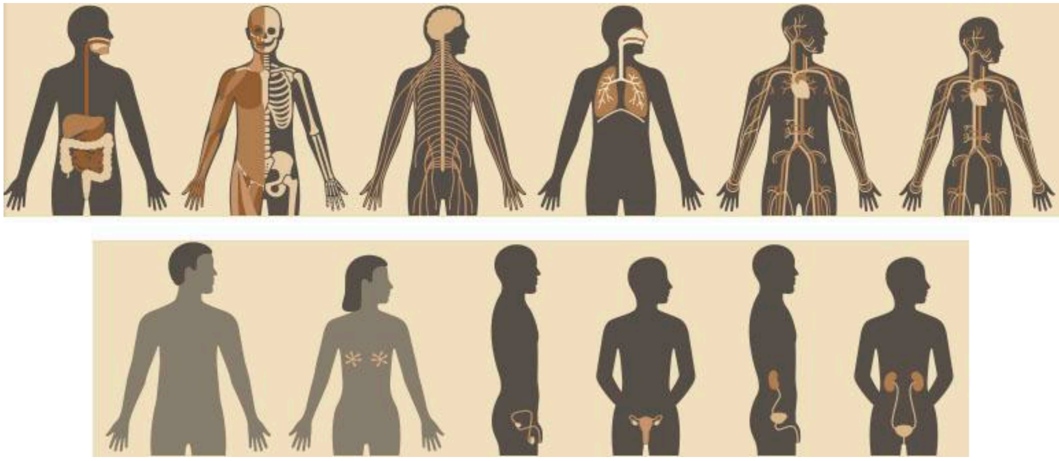


Figure 5-14. Set of graphics for the entry point *Organ systems*. They represent the classes (top row) “Alimentary system”, “Musculoskeletal system”, “Nervous system”, “Respiratory system”, “Cardiovascular system of male human body”, “Cardiovascular system of female human body”, (bottom row) “Integumentary system of male human body”, “Integumentary system of female human body”, “Genital system of male human body”, “Genital system of female human body”, “Urinary system of male human body”, and “Urinary system of female human body”.

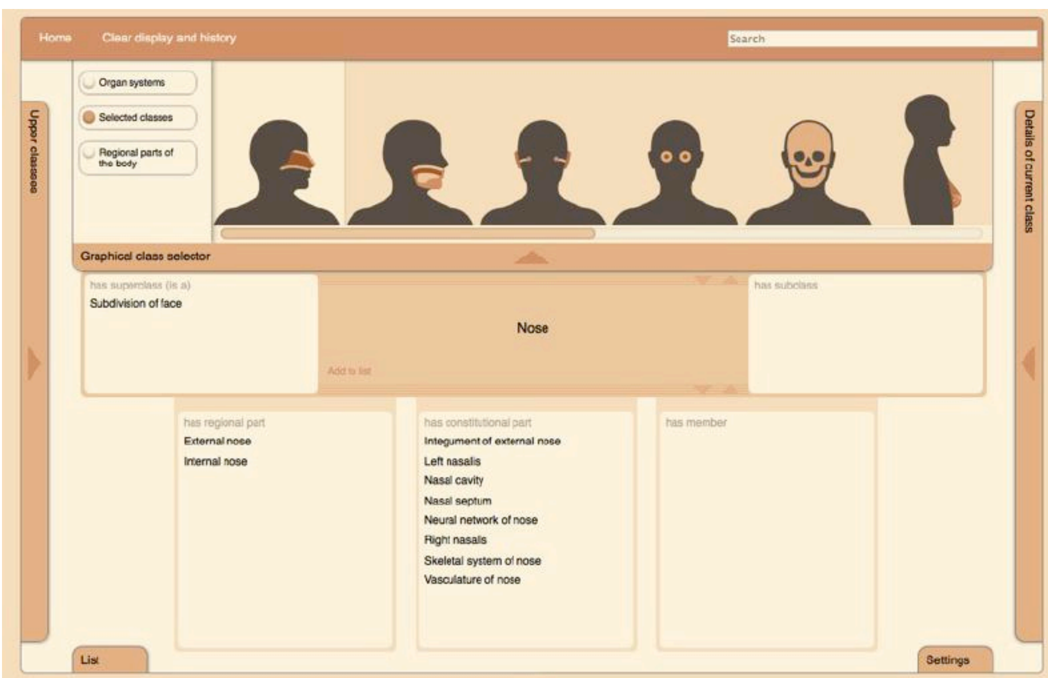


Figure 5-15. Browsing page showing the top panel that opens when the user selects the entry point of *Selected classes*. A total of eleven classes are represented graphically. Clicking a graphic initiates a query. Clicking the panel tab closes the panel.

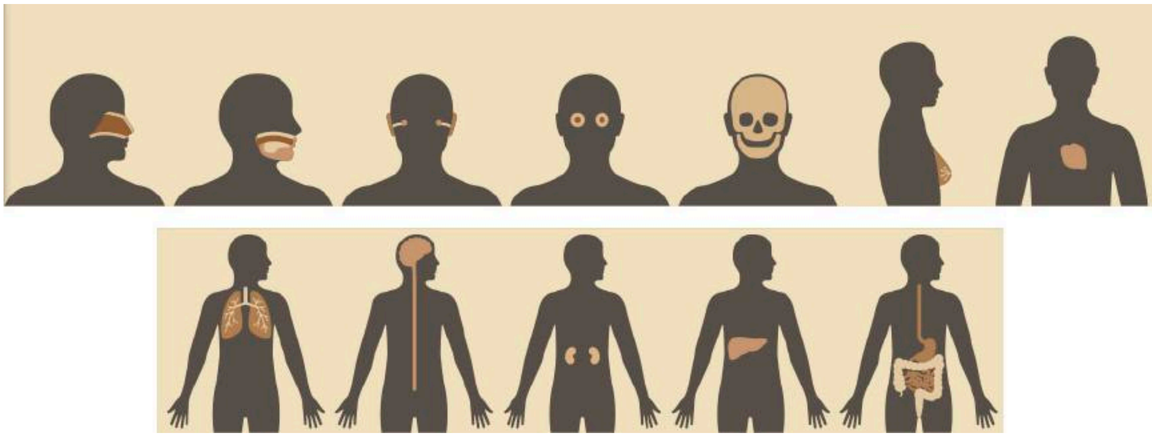


Figure 5-16. Set of graphics for the entry point S*elected classes*. They represent the classes (top row) "Mouth", "Set of ears", "Set of eyeballs", "Skull", "Female breast", "Heart", (bottom row) "Lower respiratory tract", "Neuraxis", "Set of kidneys", "Liver", and "Gastrointestinal tract".

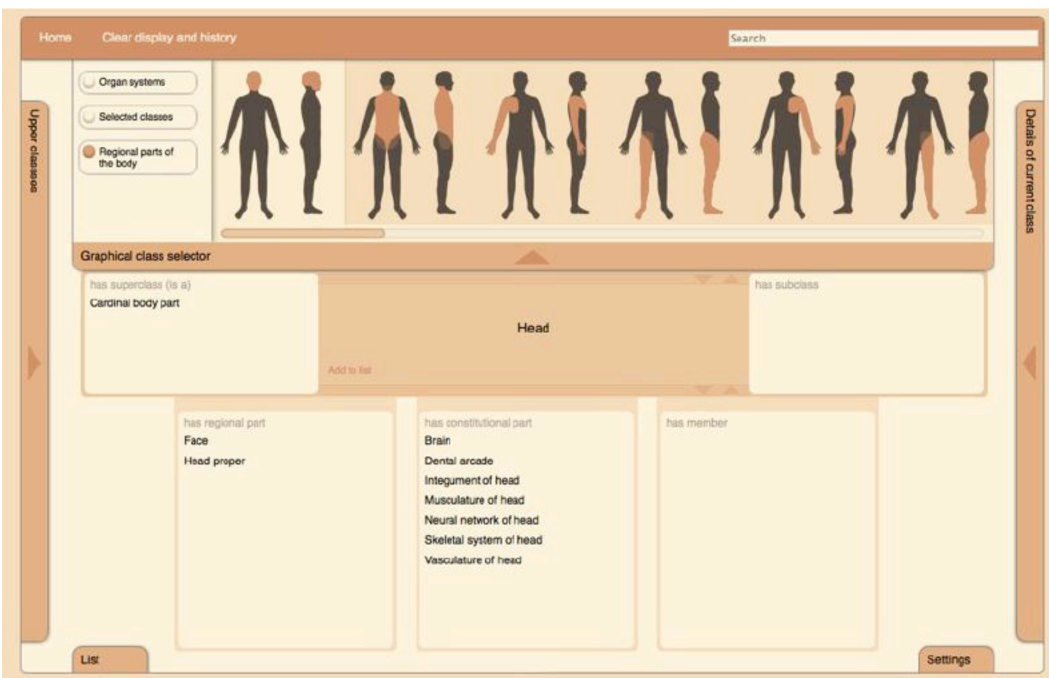


Figure 5-17. Browsing page showing the top panel that opens when the user selects the entry point of *Regional part of body*. A total of 23 classes are represented graphically. Clicking a graphic initiates a query. Clicking the panel tab closes the panel.

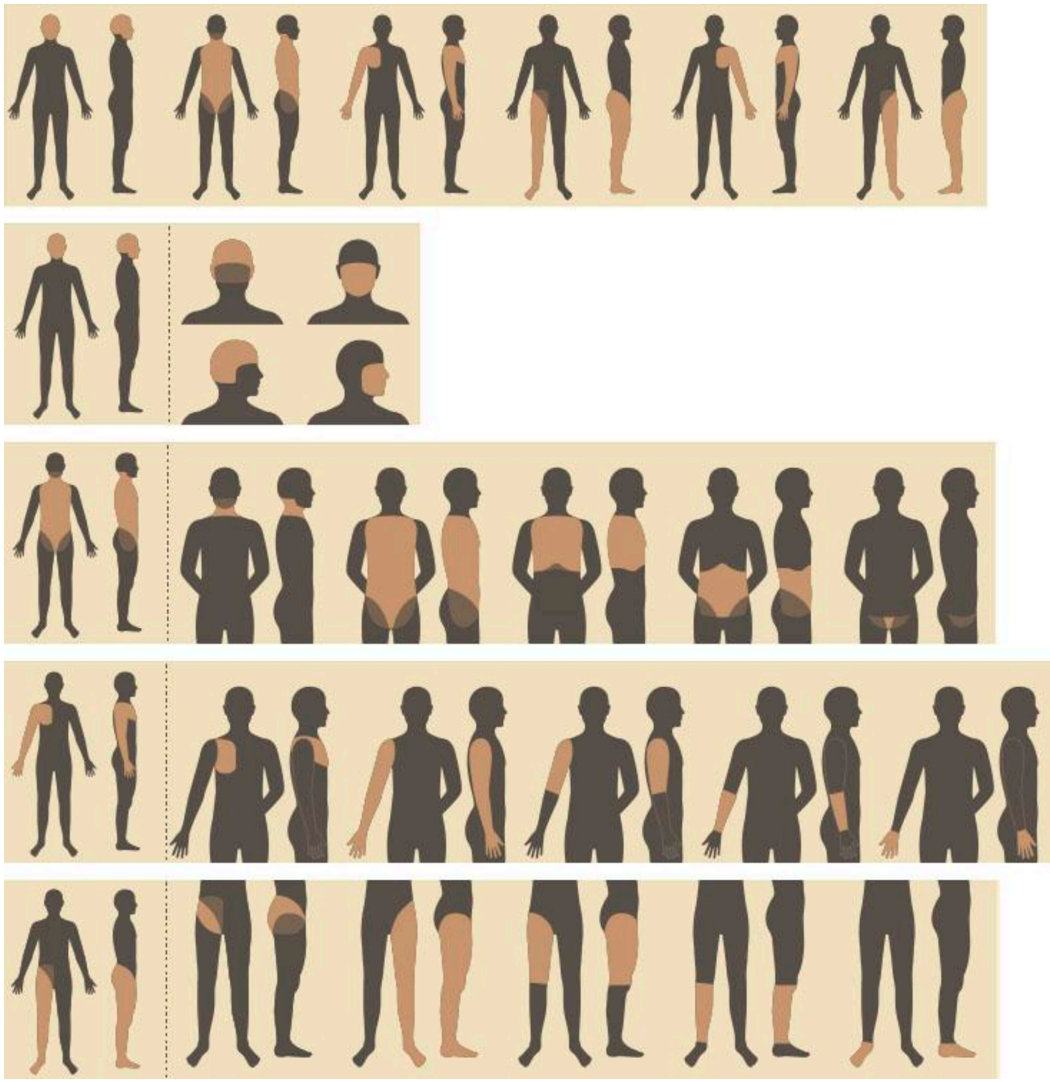


Figure 5-18. Set of graphics for the entry point *Regional parts of the body*. The scrolling panel of graphics is divided into five sections, with the first section showing the six top-level regional parts of the body and each of the last four sections showing further divisions. Transparency indicates regions that are not on the surface of the body. The graphics represent the classes (top row) "Head", "Body proper", "Right upper limb", "Right lower limb", "Left upper limb", "Left lower limb", (second row) "Head", "Head proper", "Face", (third row) "Body proper", "Neck", "Trunk", "Thoracic segment of trunk", "Abdominal segment of trunk", "Perineum", (fourth row) "Right upper limb", "Right pectoral girdle", "Right free upper limb", "Right arm", "Right forearm", "Right hand", (last row) "Right lower limb", "Right pelvic girdle", "Right free lower limb", "Right thigh", "Right leg", and "Right foot".

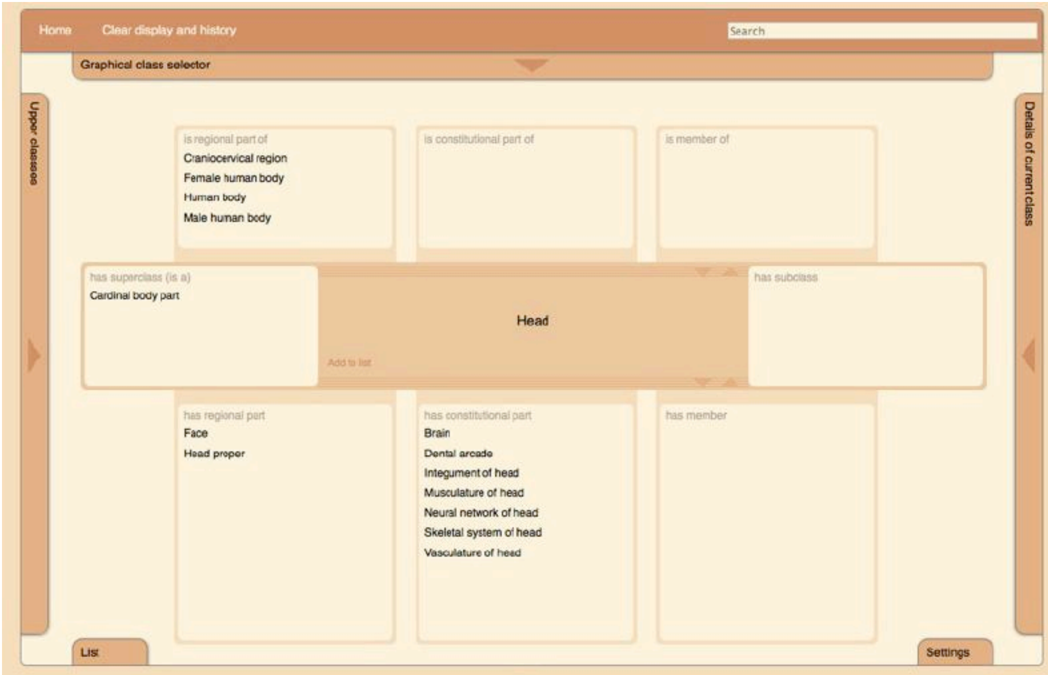


Figure 5-19. Browsing page showing the query results for the class "Head", with all panels closed. Clicking on a class in one of the relationship boxes initiates a new query for that class.

Because this design process emphasized displaying the relationships most fundamental to the FMA (the class and three types of part hierarchies), other types of relationships are not as easily accessible. As shown in Figure 5-20, any additional relationships for a class are displayed in a sliding panel on the right. Other options for accommodating these relationships would be to place them on the main window or to design pages for different anatomical themes that display relevant relationships (for example, pages for browsing the lymphatic system, musculoskeletal system, or nervous system that prominently display the relationships critical to these systems).

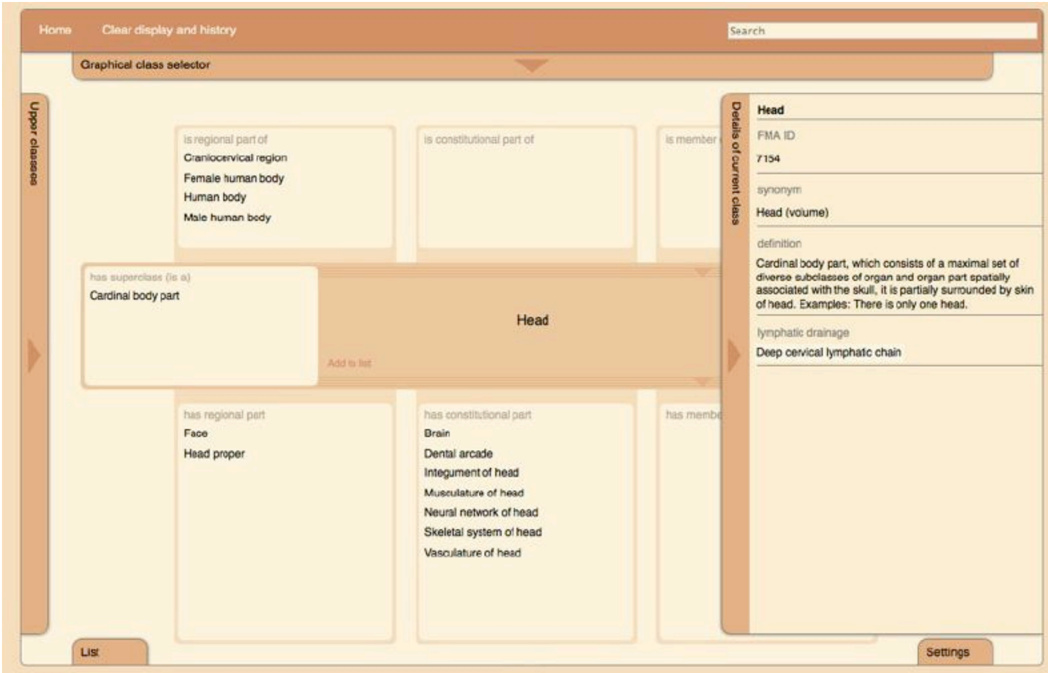


Figure 5-20. Browsing page showing the detail panel for the class "Head". This panel will show any additional relationships for a class. Queries can also be initiated from classes displayed this panel. For example, clicking on the class "Deep cervical lymphatic chain" displayed beneath the "lymphatic drainage" relationships in this panel will initiate a query for that class.

During conversations about my paper prototypes, several participants expressed a desire to view an additional level in a hierarchy without changing the current view of the interface. (For example, querying for the class "Head" shows that it has regional parts "Face" and "Head proper". But to determine the regional parts of "Face", a new query would need to be performed, removing the information about the class "Head".) I addressed this problem by implementing folding indented hierarchies for each relationships on the main window, as shown in Figure 5-21. Moving "down" a hierarchy with a folding indented hierarchy is a well-established visualization method. I modified this technique for moving "up" a hierarchy. A comparison is shown in Figure 5-22. The interface provides an option to enable this "extended hierarchy".

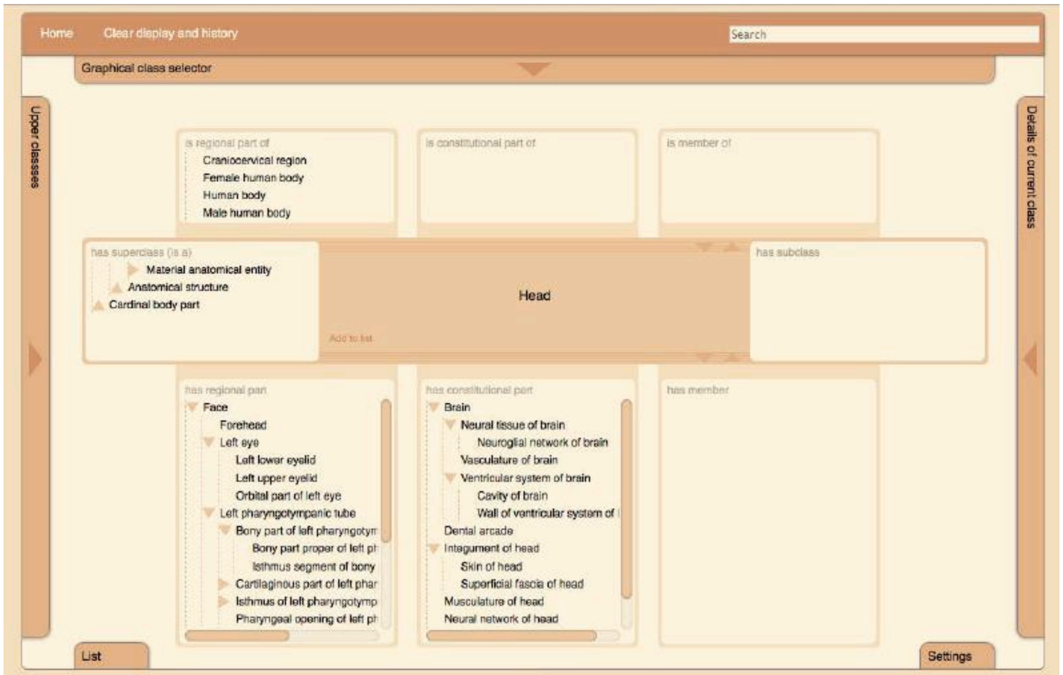


Figure 5-21. Browsing page showing the display for the class "Head" with the extended hierarchy option. This option displays class or part hierarchies within the eight relationship boxes surrounding the query term. This allows the user to walk "up" hierarchies within the "has superclass", "is regional part of", "is constitutional part of", and "is member of" relationships boxes, and walk "down" hierarchies within the "has subclass", "has regional part", "has constitutional part", and "has member" relationship boxes. In this screen capture, the "has superclass" box displays two additional levels of the class hierarchy above "Cardinal body part". In the "has regional part" box, the hierarchy below "Face" is shown. In the "has constitutional part" box, the hierarchies below "Brain" and "Integument of head" are shown.

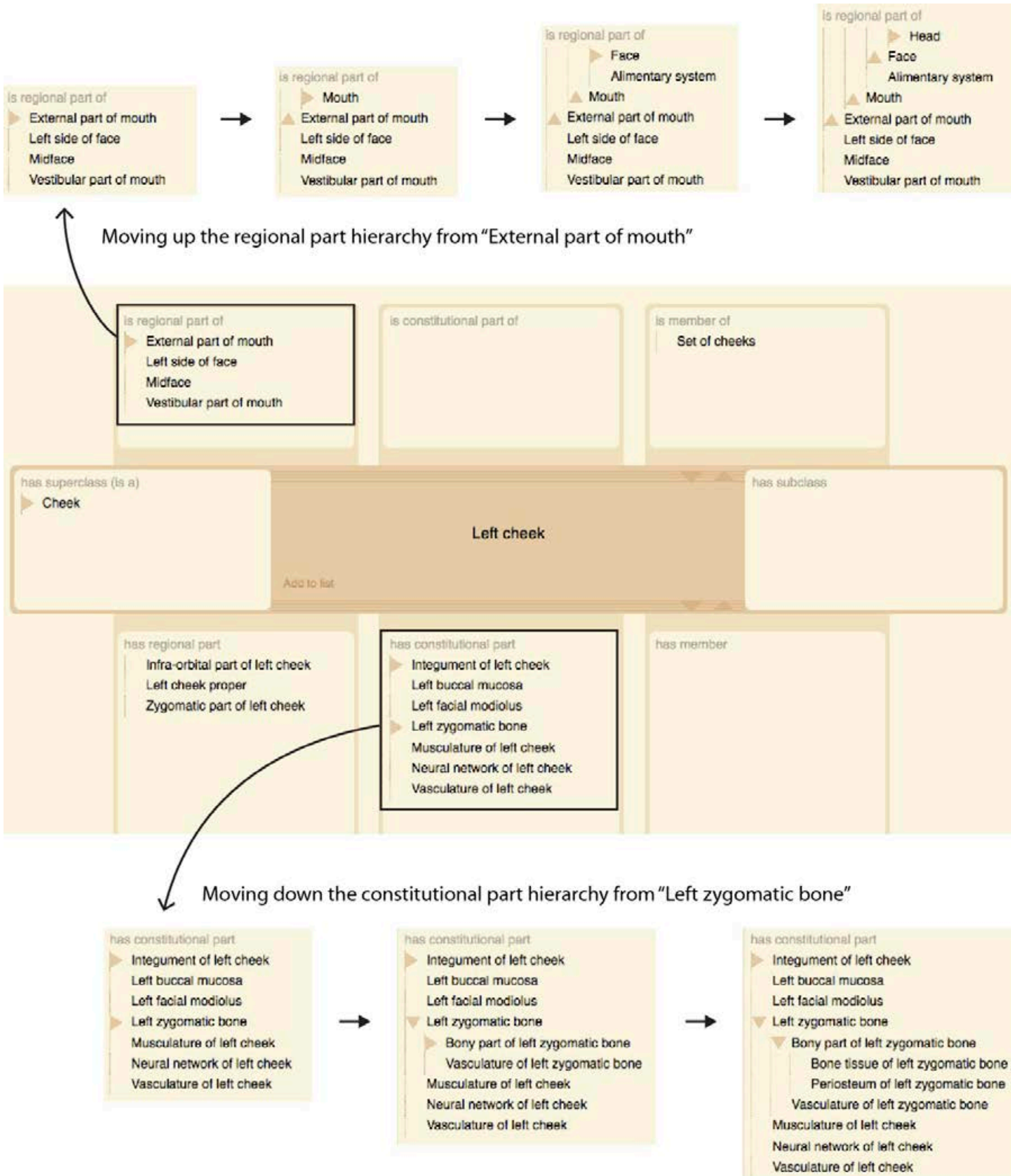


Figure 5-22. Comparison of methods for displaying hierarchies. The traditional method of using a folding indented list for showing a hierarchy below a term is demonstrated at the bottom. My modification of this method for moving up a hierarchy is displayed at the top.

5.4 Availability and use

The FMA Browser was made available at http://purl.org/sig/fma/browser in March 2014. In response to feedback from several users, I made a number of adjustments to the code, including (1) correcting an error in the code for initially loading the graphs within the panels, (2) adding an error message for failed responses from the Query Integrator, (3) making the contrast of the color of the arrows on the panel tabs more distinct, and (4) having the top panel open more slowly when the user is sent from the home page to the browser page (in order to communicates that the panel is not a static element, but can be opened and closed).

5.5 Summary and conclusions

In this chapter I have described the design and implementation of the FMA Browser, which emphasizes hierarchical relationships within the FMA and was designed using an iterative user-centered design principles. The resulting browser has been well received, and the Structural Informatics Group is currently considering adopting and extending it as the primary means for visualizing the FMA.

6 Adding additional relations

The FMA has over 200 different types of relationships, and until recently all described adult human structures. In this chapter I extend the methods used for the FMA to relationships for describing development, malformation, and mappings between organisms, as well as ideas for visualizing these relationships. This work takes place in the context of the Ontology for Craniofacial Development and Malformation (OCDM).

6.1 The Ontology of Craniofacial Development and Malformation (OCDM)

The OCDM is being developed by the Structural Informatics Group as part of the FaceBase consortium. The FaceBase consortium was established in 2009 as a collection of biological research and technology projects with the goal of acquiring craniofacial data and making this available to researchers (Hochheiser et al., 2011). The Structural Informatics Group was funded to develop an ontology to support annotation and semantic integration of the data.

The OCDM consists of a set of sub-ontologies. One of these sub-ontologies describes adult canonical anatomy, and it duplicates the classes of the FMA describing the head (but excluding the brain). The use cases for FaceBase focus on the nose and mouth, and therefore these areas of the FMA/OCDM were refined and extended by José Mejino. As described in the sections below, additional sub-ontologies are under development to describe developmental anatomy and malformations. In addition, sub-ontologies for mouse canonical adult anatomy, developmental anatomy, and malformations are being developed, as well as mappings between classes of human and mouse anatomy. Figure 6-1 shows an overview of the sub-ontologies.

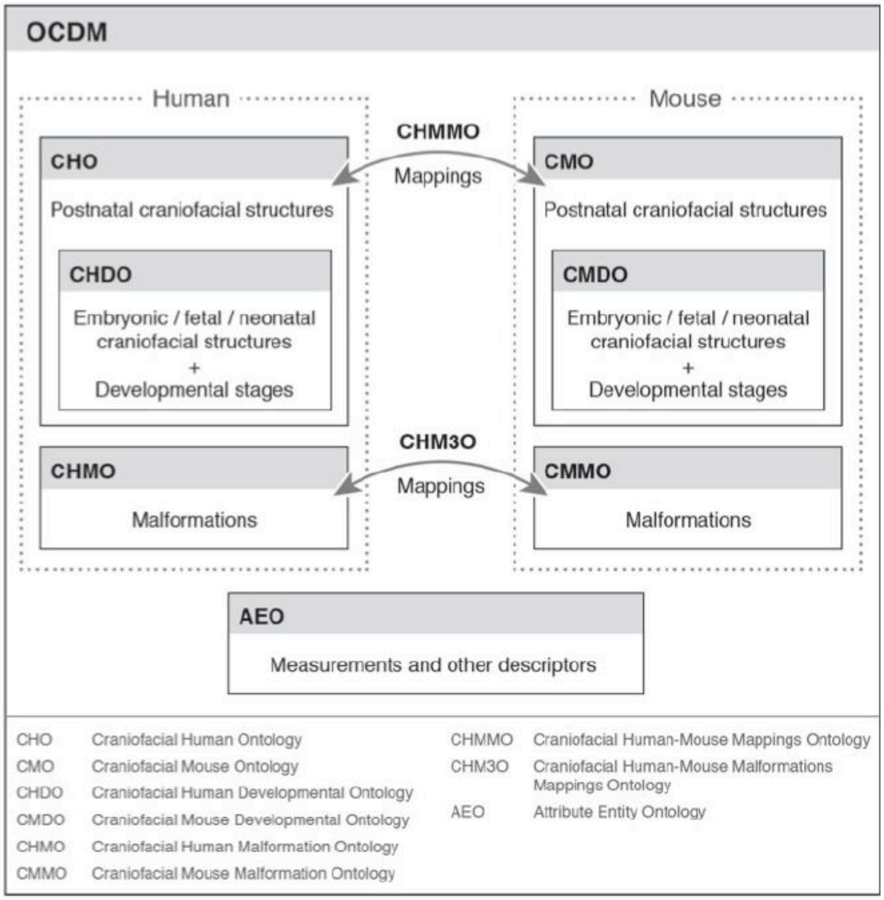


Figure 6-1. Overview of the sub-ontologies of the OCDM.

Previously published in J. F. Brinkley et al. (2013) "The Ontology of Craniofacial Development and Malformation for translational craniofacial research." ***American Journal of Medical Genetics Part C (Seminars in Medical Genetics)*****. 163C:232–245. Copyright 2013 Wiley Periodicals, Inc.**

6.1.1 Developmental anatomy and developmental relationships

One of the purposes of the OCDM is to represent knowledge of development (from the zygote, to embryo, to fetus, to adult), in a way that can be computationally accessed to display and reason about developmental lineages. Therefore, it is necessary to not only create classes to represent developmental anatomical structures, but to specify relationships that logically connect those classes into developmental lineages. José Mejino, in consultation with Timothy Cox from Seattle Children's Research Institute, developed a set of four relationships for modeling development. These are shown in Figure 6-2. The "transforms into" relationship connects two classes that describe the same entity, but at earlier and later stages of development. The "derives" relationship is used when an entity of a single class is described as two separate classes at the next stage. Both the "merges" and "fuses" relationships refer to processes in which two (connected) regions become a single region. Merging describes a displacement of the epithelial cell layer, while fusing describes a process in which the folded epithelial cell layer is dispersed into vesicles and degraded.

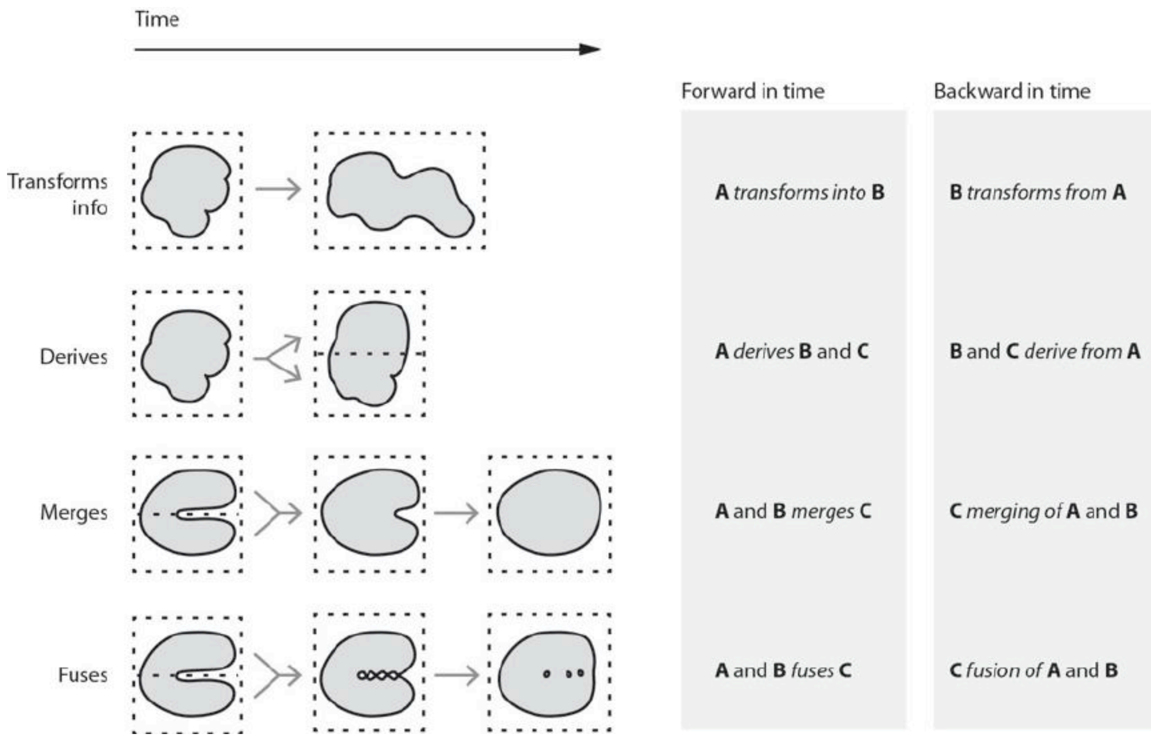


Figure 6-2. The four relationships used to model development.

Preliminary graphics that use these relations to show development of selected regions of the face are presented in Figure 6-3, accompanied by examples of developmental relationships applied to classes of the OCDM.

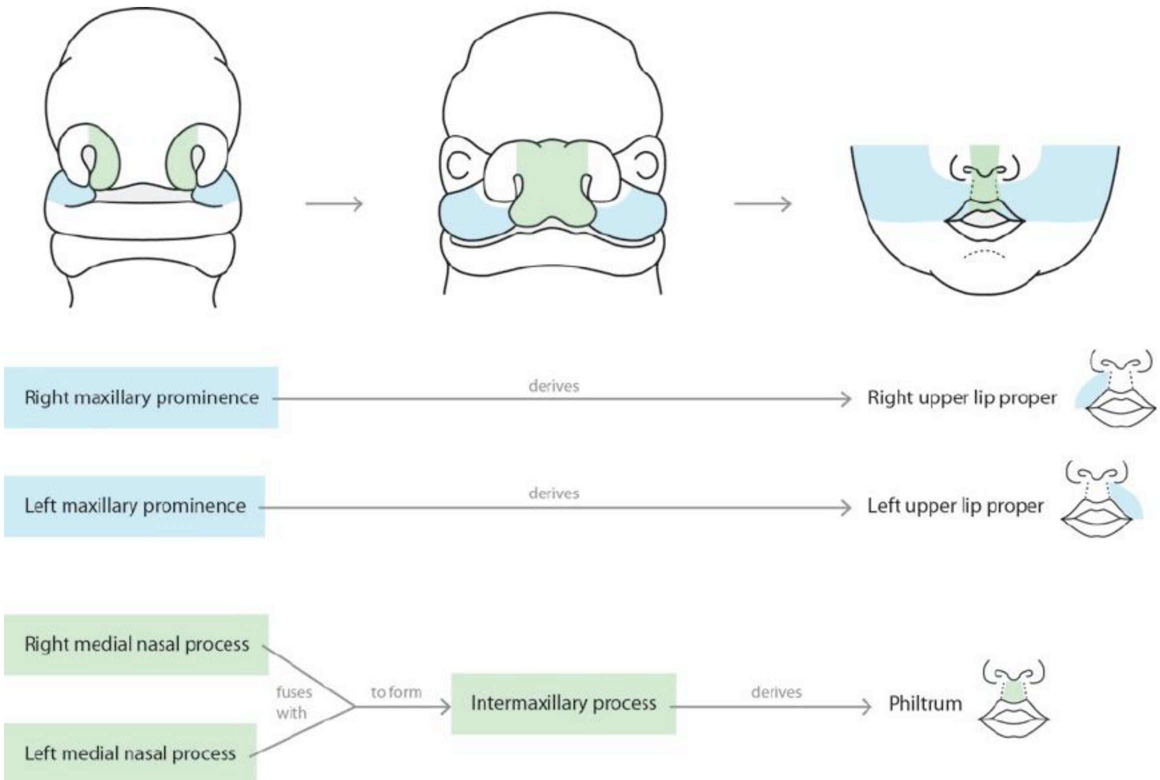


Figure 6-3. Graphics of face development. Blue regions represent the right and left maxillary prominences and the post-natal regions they develop into. Green regions represent the right and left nasal processes and the post-natal regions they develop into. (Note: Regions and graphics are preliminary and have yet to be refined based on embryological evidence.)

6.1.2 Malformations

Because data from experimental studies and clinical applications often refer to malformations, the OCDM must represent malformations. The initial emphasis of FaceBase was the mouth and nose, and therefore clefts of these structures have been described in the OCDM. Figure 6-4 uses graphics to contrast normal face development and development that results in cleft lip.

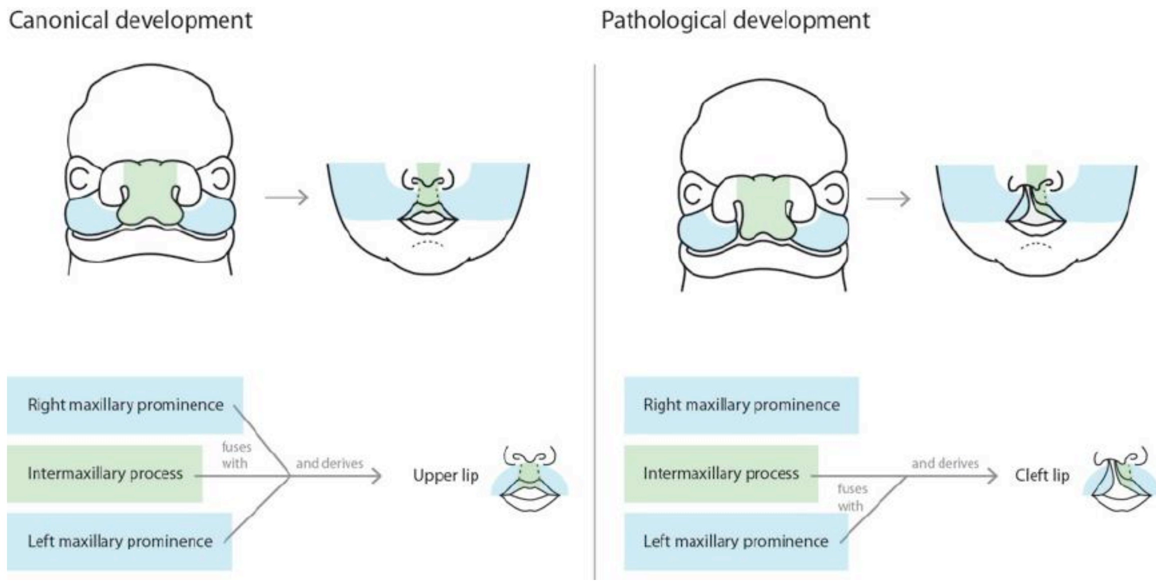


Figure 6-4. Comparison of canonical development of the upper lip and pathological development of cleft upper lip.

6.1.3 Mappings to model organisms

Experimental work is performed on laboratory organisms such as mice, but the goal of the translational research enabled by FaceBase is clinical applications in humans. Therefore, mappings must be established between classes describing human anatomy and those describing non-human anatomy. The OCDM currently contains mappings between a number of homologous human and mouse anatomical structures. Future work will add zebrafish as an additional model organism.

6.2 Understanding and organizing the content

As in the FMA my roles in understanding and assisting with content development have included creating illustrations and diagrams to support discussions with content experts and to gather descriptions of development from textbooks and published literature. In addition, I helped to clarify how terms are currently used by clinicians and researchers. For example, a search of the literature and the Web revealed that the term "premaxilla" has at least two distinct uses: (1) an embryological bone that forms part of the adult maxillae, and (2) the portion of soft tissue and bone beneath the nose of an individual with an unrepaired bilateral cleft lip/palate.

6.2.1 Content patterns

If the OCDM is to be used for queries involving developmental lineages, then it is necessary to develop a content pattern for modeling lineages, a more complex task than the content patterns for the static structures of the FMA. My preliminary work to develop this pattern is shown in Figure 6-3, with an example of a lineage of interest in Figure 6-4. One issue that complicates this work is that the developmental relationships ("transforms into", "merges", "fuses", "derives") will typically apply to larger regions of anatomy than a specific anatomical structure of interest (such as the upper lip). Therefore, a series a regional part and constitutional part relationships may need to be incorporated into these developmental lineages for them to incorporate anatomical structures of interest. For example, Figure 6-4 uses a series of three part relationships to link the class "Os incisivum segment of right maxilla" to "Hard palate".

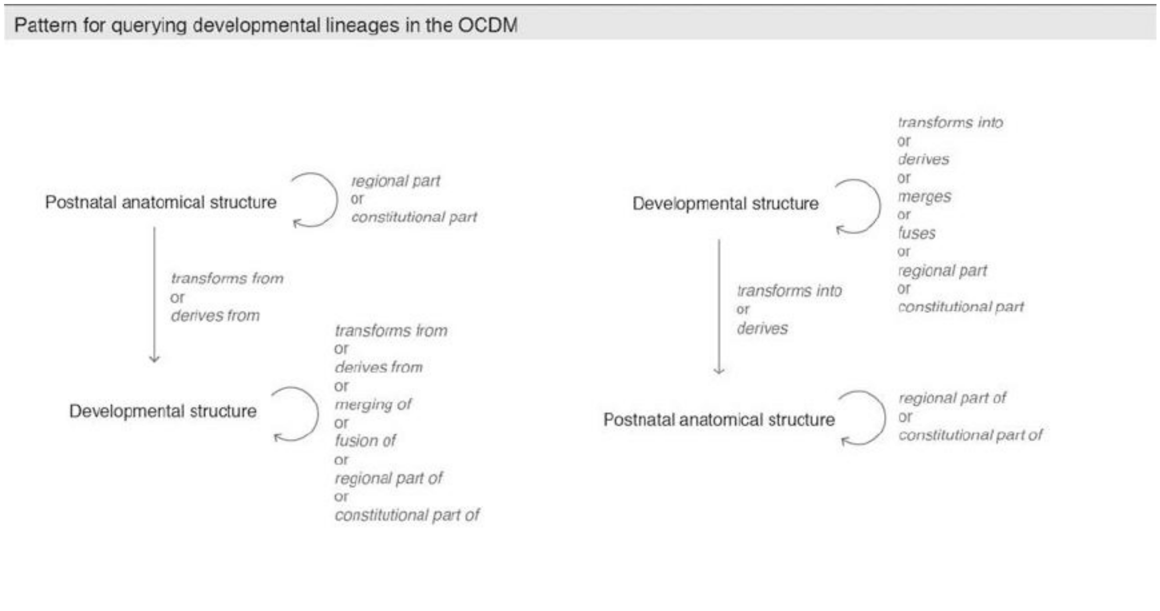


Figure 6-3. Preliminary content pattern for tracing developmental lineages in the OCDM. Left: Pattern for tracing developmental lineages backward in time. Subclasses of "Postnatal anatomical structure" are related to each other through the "regional part" and "constitutional part" relationships. Moving from a subclass of "Postnatal anatomical structure" to "Developmental structure" makes use of either the "transforms from" or "derives from" relationship. Subclasses of "Developmental structure" are related to each other using one of six relationships: "transforms from", "derives from", "merging of", "fusion of", "regional part of", and "constitutional part of". Right: Pattern for tracing developmental lineages forward in time. This pattern is the inverse of that shown on the left.

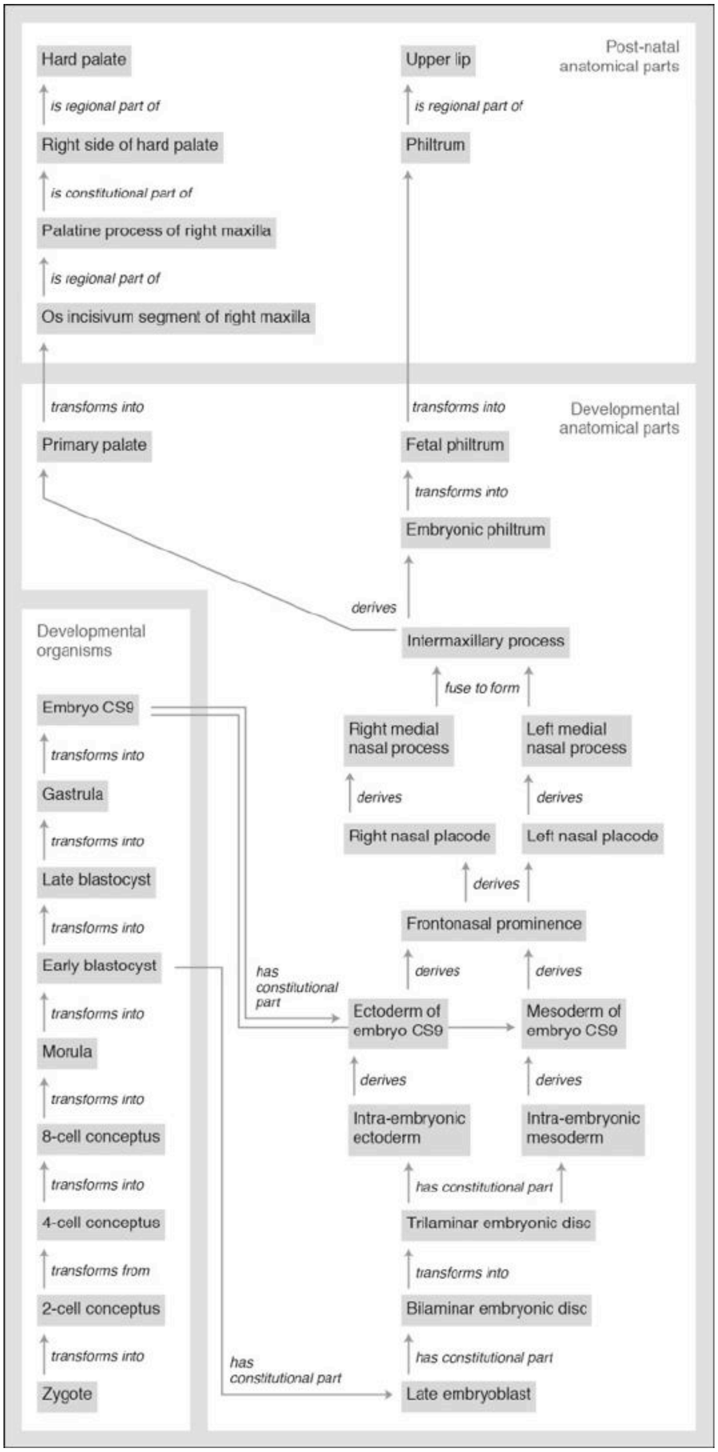


Figure 6-4. Example of developmental lineage within the OCDM connecting the zygote to the hard palate and upper lip. This follows the content patterns shown in Figure 6-3.

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6.2.2 Illustrations of cleft lip and palate as examples of malformations

I developed a series of illustrations of cleft lip and palate in order to support discussions about how to model these malformations in the OCDM and to standardize visual representations of these malformations. The reference photographs the illustrations are based on were from the Web (cleft lip and palate) and clinical photographs provided by collaborators at Seattle Children's Research Institute (cleft lip).

6.2.2.1 Illustrations of Cleft lip

Illustrations I created for cleft lip include unilateral cleft lip (Figure 6-5), bilateral cleft lip (Figure 6-6) , complete bilateral cleft lip (Figure 6-7), and midline cleft lip (Figure 6-8). These were developed first as vector-based line drawings in Adobe Illustrator, then rendered using carbon dust and carbon pencil on Mylar drafting film.

The illustrations are intended to represent an infant at approximately six months of age. Although choosing an age is not critical for the set of isolated mouths and noses I have described here, if the image set was extended to include the entire face, having a consistent age would become more critical. In countries where surgery is available, surgery to address cleft lip is generally performed between three and six months of age and procedures for cleft palate generally begin closer to 1 year of age. Therefore, I choose six months for these illustrations because it is the latest age when it is reasonable to see "unrepaired" cleft lips; in addition, six months is the age at which teeth generally erupt, so the illustrations do not need to depict teeth.

The vector line drawings are constructed from a set of lines that are reused from image to image when possible. For example, the lower lip is the same in all illustrations of cleft upper lip, and the lateral extent of the ala is depicted with one of three lines (reflecting extent of displacement of the ala due to severity of cleft).

The carbon dust illustrations depict the alveolar arch (consisting of the bony alveolar arch and gingiva), which is not included in the vector line drawings. This is necessary for constructing a naturalistic drawing. However, clefts of the lip and clefts of the alveolar arch are classified as separate malformations in the OCDM, and the appearance of the clefted alveolar arch can vary between very similar instances of cleft lips. Because clefted alveolar arch has not been extensively modeled in the OCDM, I illustrated a typical alveolar arch or clefted alveolar arch (based on my reference photos) for each cleft lip illustration where the alveolar arch is visible.

Figure 6-5. Illustrations of unilateral cleft lip as (top) vector line drawings and (bottom) carbon dust renderings, showing diversity of severity of clefts.

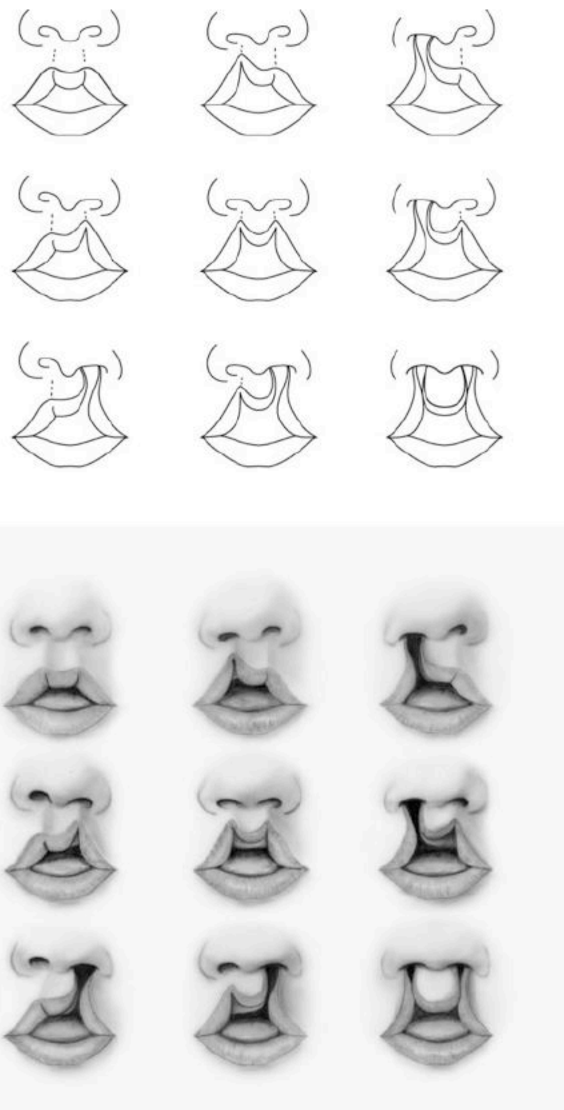


Figure 6-6. Illustrations of bilateral cleft lip as (top) vector line drawings and (bottom) carbon dust renderings, showing diversity of extent of clefts.

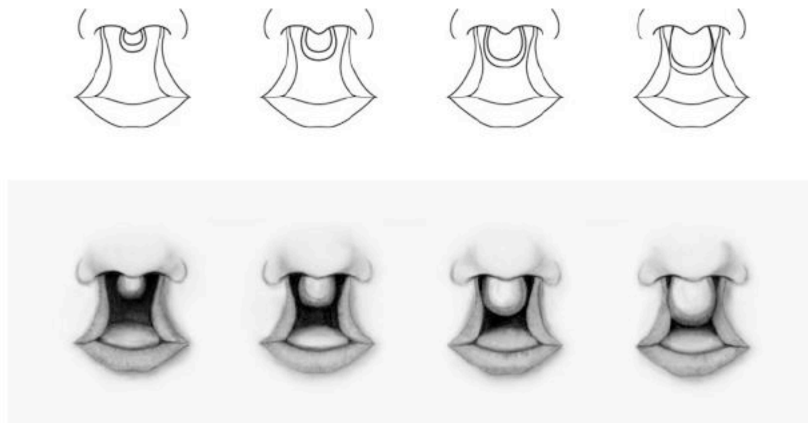


Figure 6-7. Illustrations of complete bilateral cleft lip as (top) vector line drawings and (bottom) carbon dust renderings, showing varying size of philtrum.

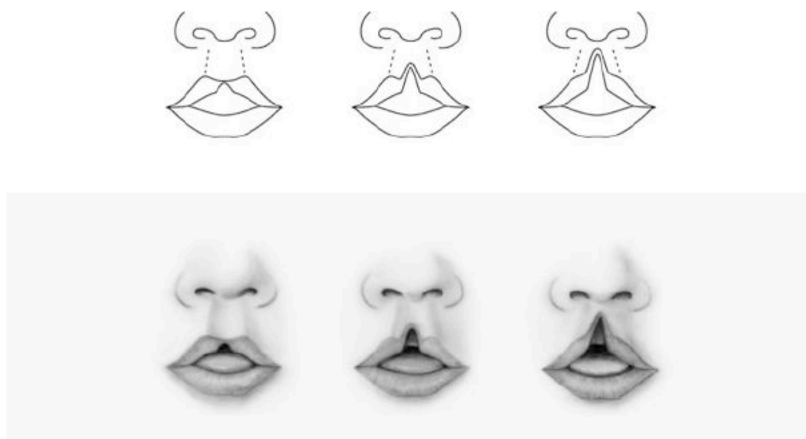


Figure 6-8. Illustrations of midline cleft lip as (top) vector line drawings and (bottom) carbon dust renderings, showing diversity of extent of clefts.

There is not a one-to-one correspondence between these illustrations and classes in the OCDM because each class represents a small range of phenotypes. The relationship between the illustrations and classes is shown in Figure 6-9. If the OCDM were to be implemented in a clinical information system, clefts within each class could be characterized by measurements. For example, a left unilateral incomplete cleft could be further characterized by associating it with a class for length within the Attribute entity hierarchy of the OCDM, and a data value could be entered as a property of this class.

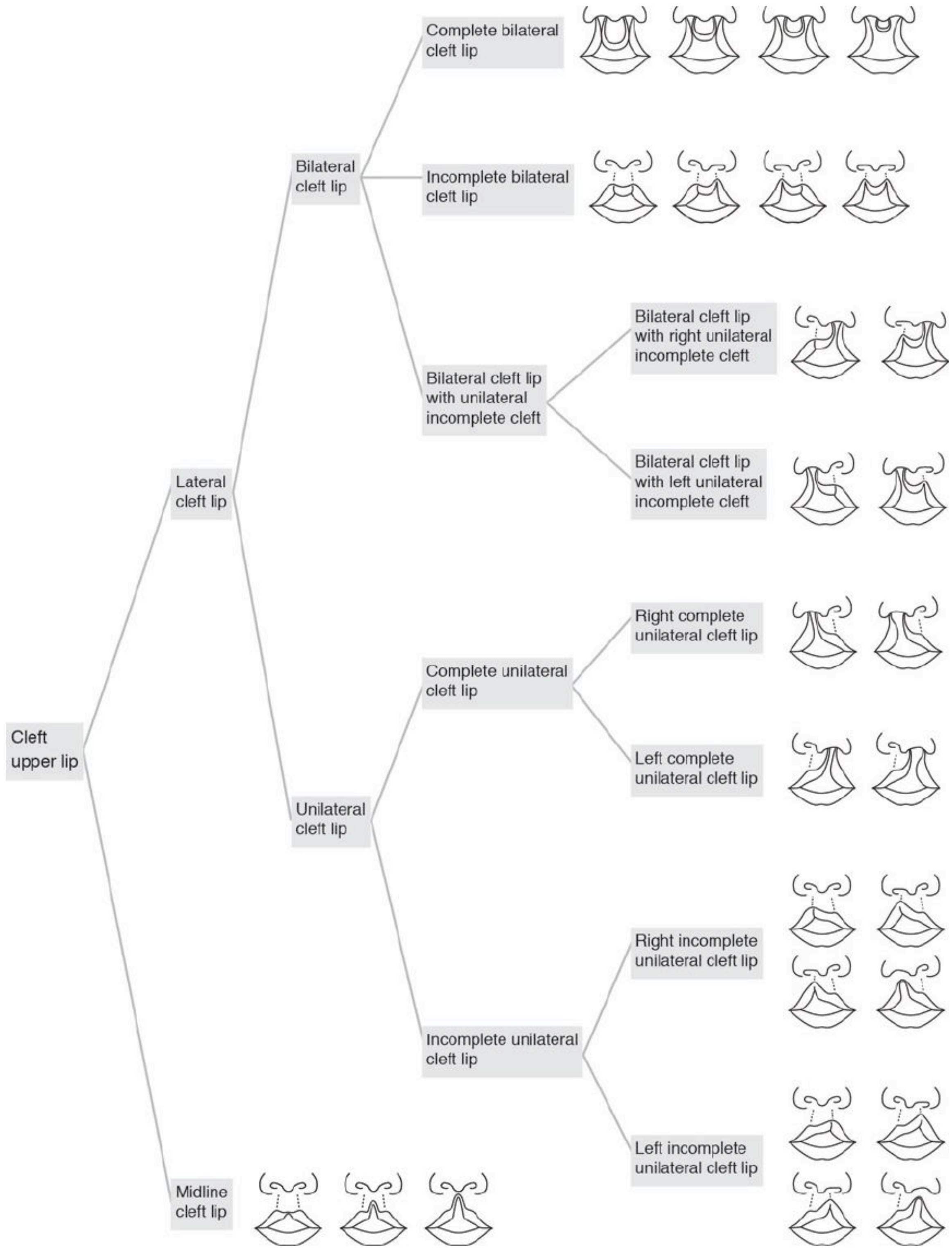


Figure 6-9. Correspondence between the class hierarchy for cleft lip in the OCDM and my illustrations of cleft lip.

As a demonstration of how the set of vector graphics can be extended, Figure 6-10 shows phenotypes of lip pits and cleft lower lip. An overlay of all lines for the graphics is shown in Figure 6-11, suggesting that in future work these kinds of illustrations could be dynamically displayed with the aid of the ontology.

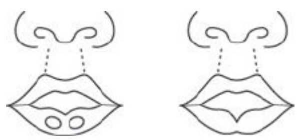


Figure 6-10. Vector line drawings for malformations of lip pits and cleft lower lip.

Figure 6-11. Complete set of lines in the set of vector line drawings for lip malformations.

6.2.2.2 Illustrations of cleft palate

The OCDM has much less content developed for the classes representing cleft palate than cleft lip. Figure 6-12 shows preliminary graphics I created to support discussions with content experts about cleft palate and as ideas for illustrations to be part of a browser for the OCDM. Cleft palate phenotypes include clefts of both the soft tissue and bone of the palate, as well as "submucous" clefts in which the soft tissue is intact and the cleft is present in only the bone. The purpose of the graphics was to begin to establish typical shapes of clefts and to explore ways to depict the bone structure without the overlying soft tissue.

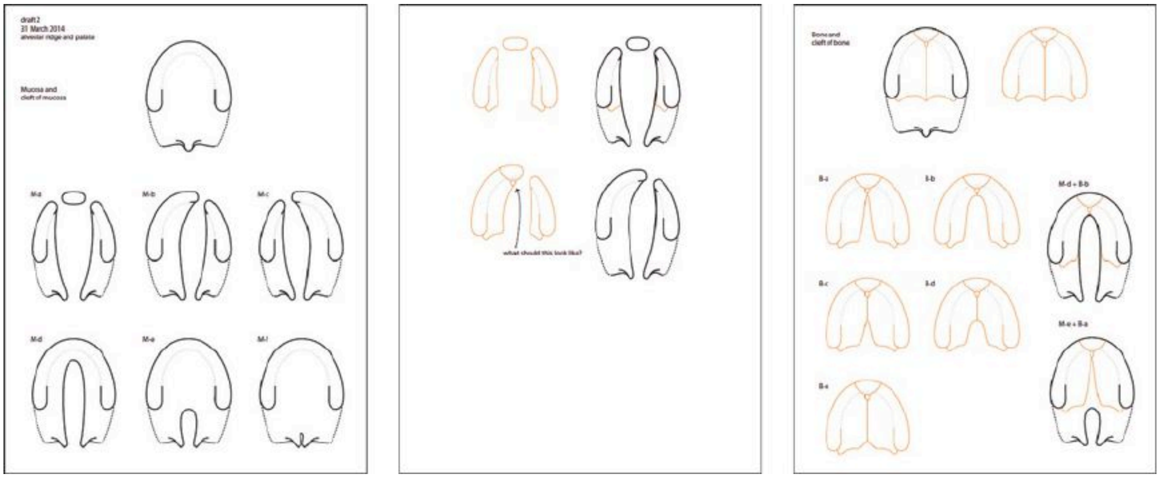


Figure 6-12. Preliminary graphics to represent cleft palate.

6.3 Current OCDM viewer

I developed a class hierarchy viewer for the OCDM, which has been available at http://purl.org/sig/ocdm/viewer since February 2013. This viewer was developed to allow members of the development team and the content experts to view the OCDM, and not intended for use by outside researchers. It is constructed as a set of stand-alone pages, one for each type of hierarchy OCDM plus a page for mappings.

The interface was developed using the Prototype JavaScript library. Queries over the OCDM are preformed using the Query Integrator (Brinkley et al., 2012), which returns results as XML.

6.3.1 Screen captures

Figure 6-13 is the home page of the viewer. Figures 6-14 through 6-20 show how the hierarchies are presented on the left side of the screen and class properties for a selected class are listed on the right.

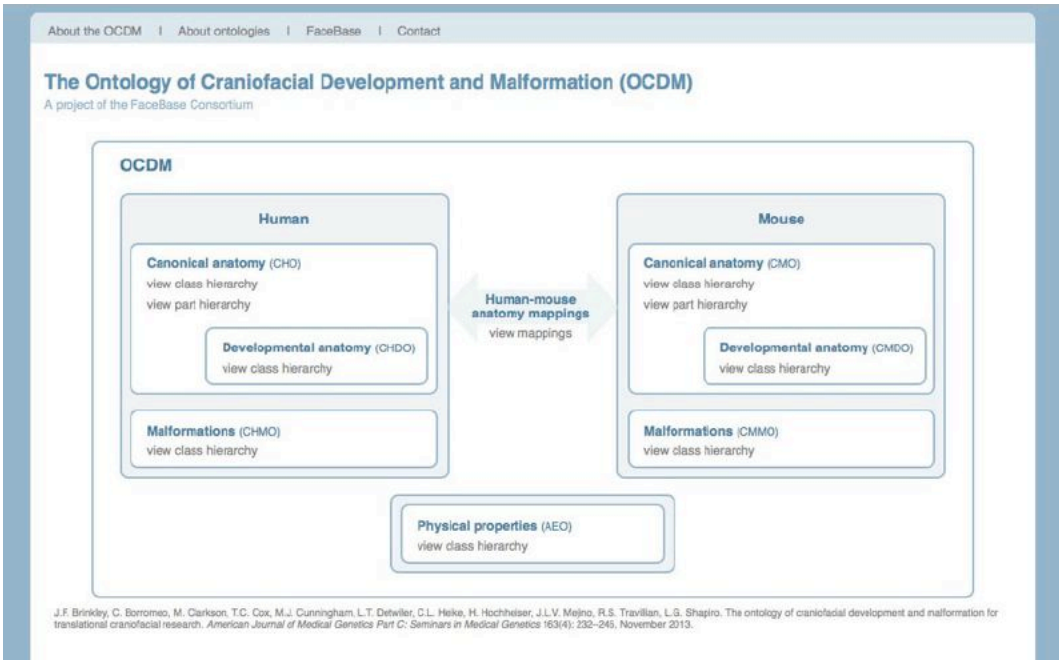


Figure 6-13. Home page of the OCDM viewer, showing the relationships of the sub-ontology components.

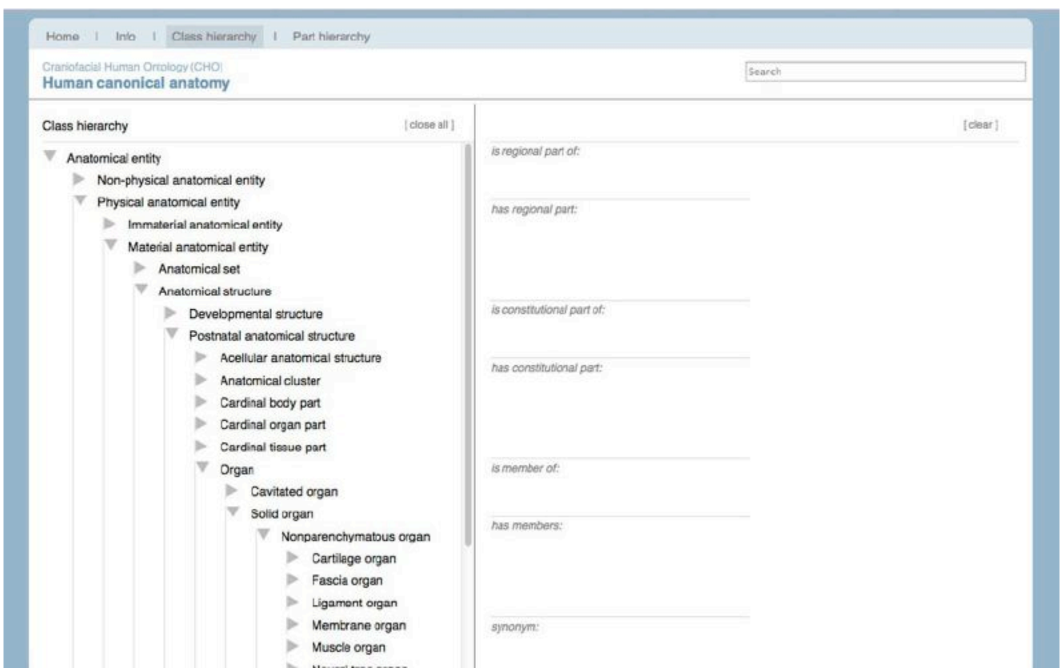


Figure 6-14. Human canonical anatomy classes within the OCDM, displayed as a class hierarchy. The hierarchy has been opened to show the class structure between "Physical anatomical entity" and the subclasses of "Nonparenchymatous organ". This sub-ontology is known as the Craniofacial Human Ontology (CHO).

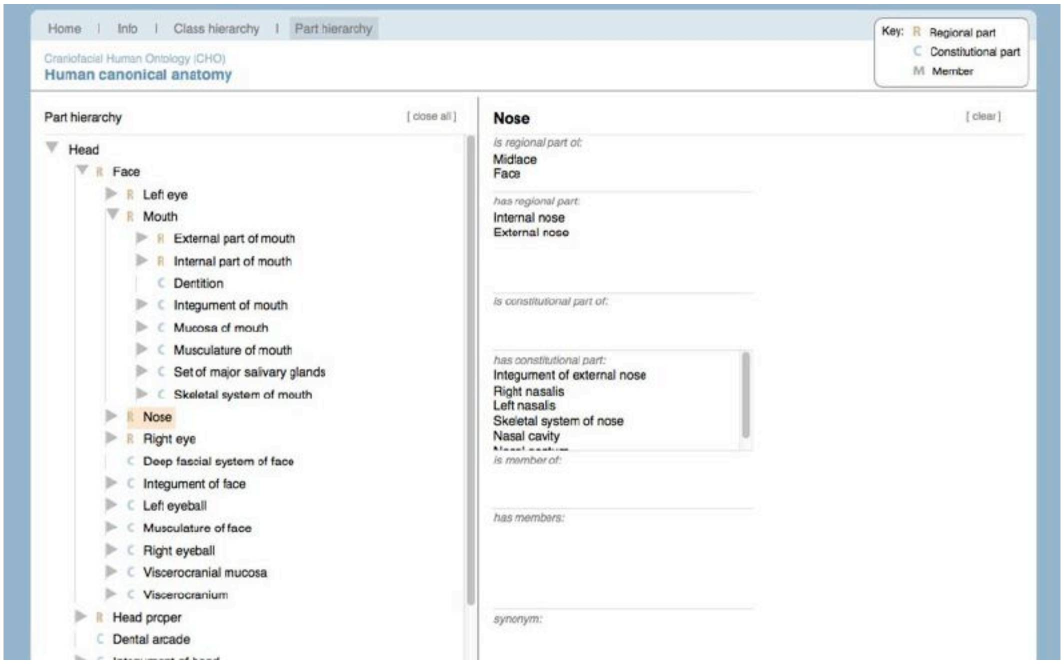


Figure 6-15. Human canonical anatomy classes within the OCDM, displayed as a part hierarchy. The "R" icons indicate regional parts and the "C" icons constitutional parts. The class "Nose" has been selected, and its properties are displayed in the right panel.

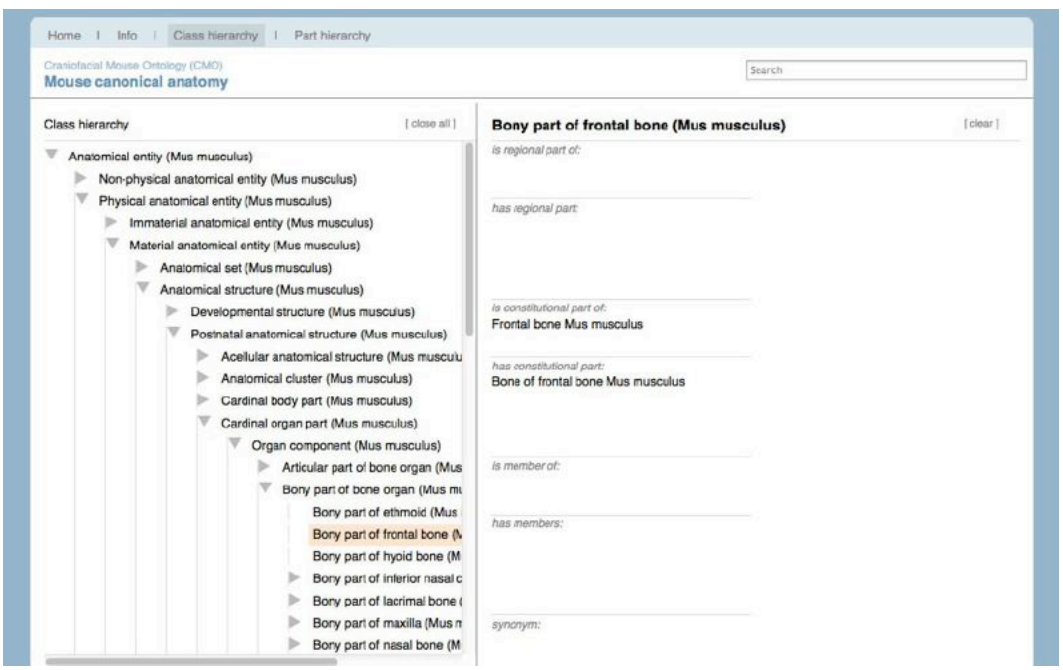


Figure 6-16. Mouse canonical anatomy classes within the OCDM, displayed as a class hierarchy. The class "Bony part of frontal bone (Mus musculus)" has been selected, and its properties are displayed in the right panel. This sub-ontology is known as the Craniofacial Mouse Ontology (CMO).

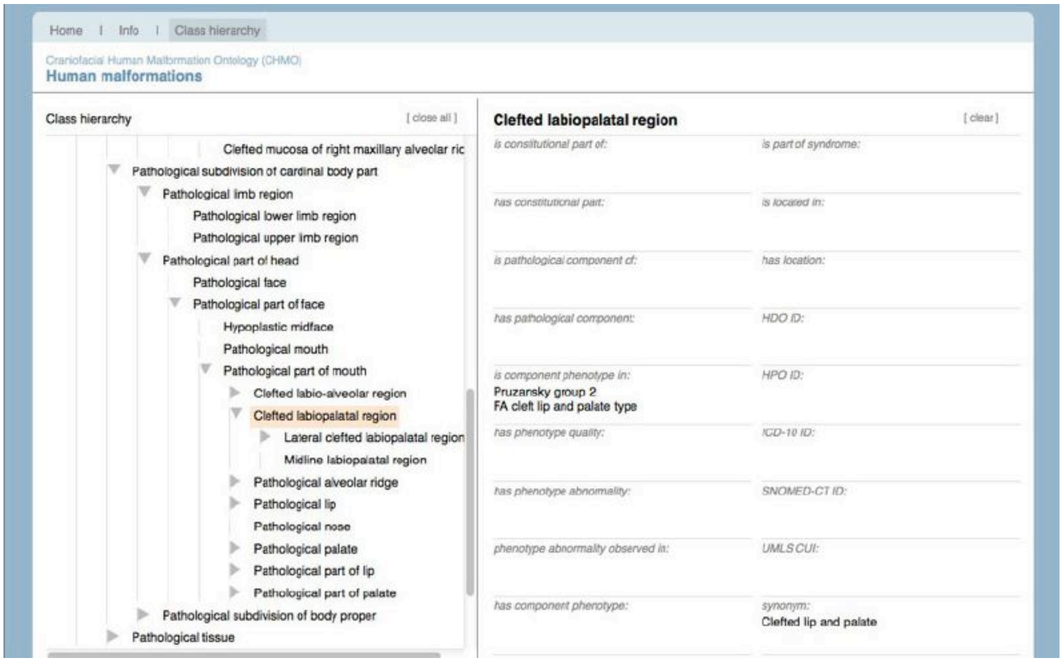


Figure 6-17. A portion of the human malformation classes within the OCDM, displayed as a class hierarchy. The class "Clefted labiopaletal region" has been selected, and its properties are displayed in the right panel. This sub-ontology is known as the Craniofacial Human Malformation Ontology (CHMO).

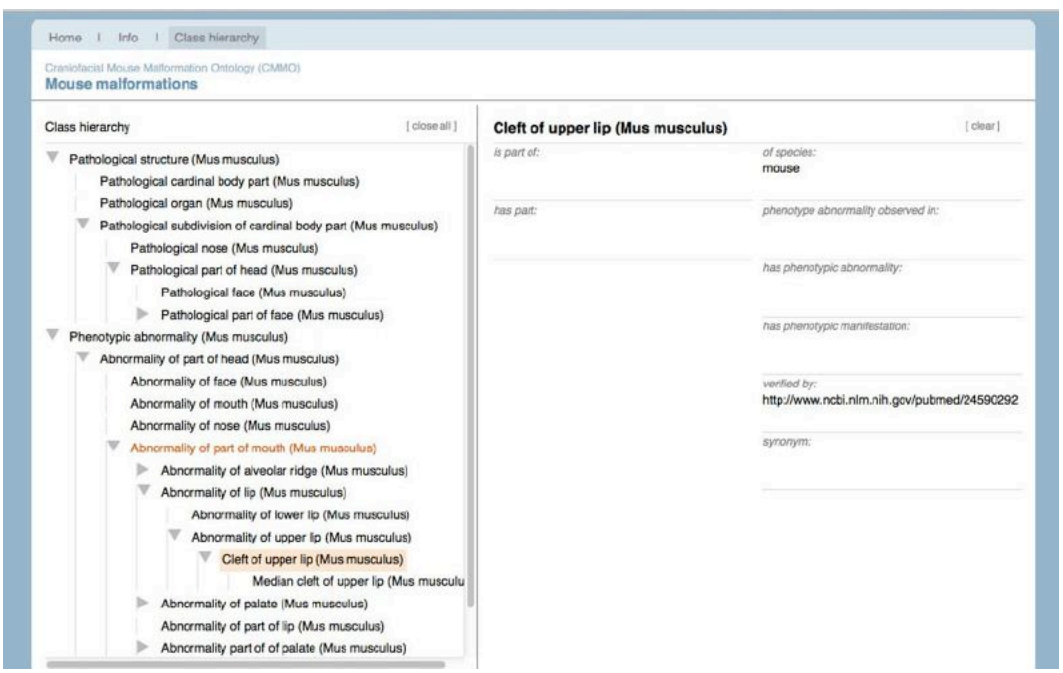


Figure 6-18. Mouse malformation classes within the OCDM, displayed as a class hierarchy. The class "Cleft of upper lip (Mus musculus)" has been selected, and its properties are displayed on the right panel. One class name is displayed in orange type because a cursor is positioned over it. This sub-ontology is known as the Craniofacial Mouse Malformation Ontology (CMMO).

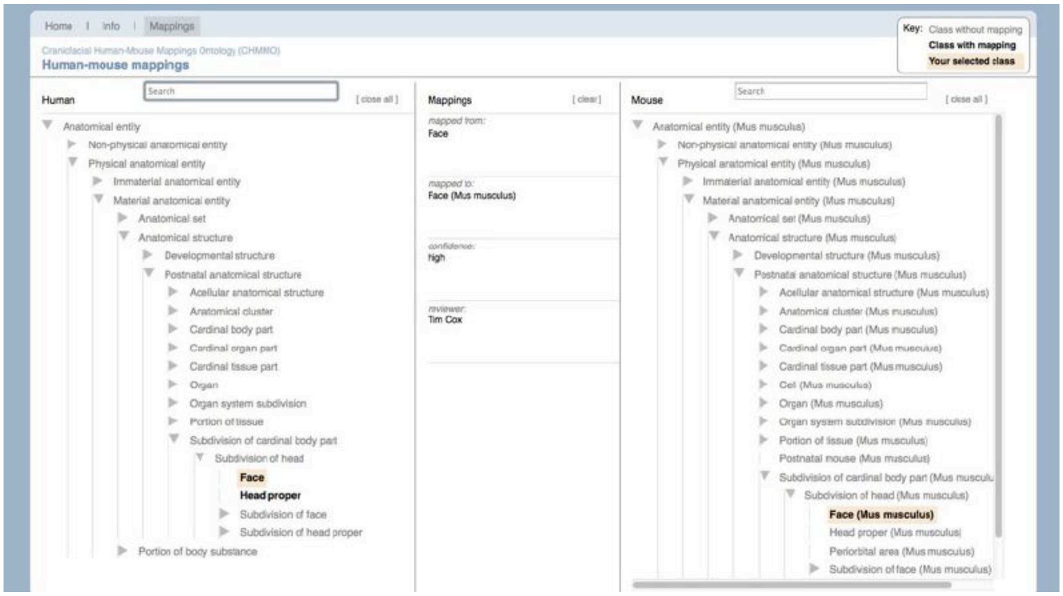


Figure 6-19. Screen layout for displaying mappings within the OCDM. The left and right panels are class hierarchies, with human on the left and mouse on the right. Classes with mappings are shown in bold ("Face" and "Head proper" in the human panel in this screen capture. The class "Face" has been selected in the human hierarchy, and its mapping properties are shown in the middle panel and the mapped class for mouse is highlighted in the left panel.

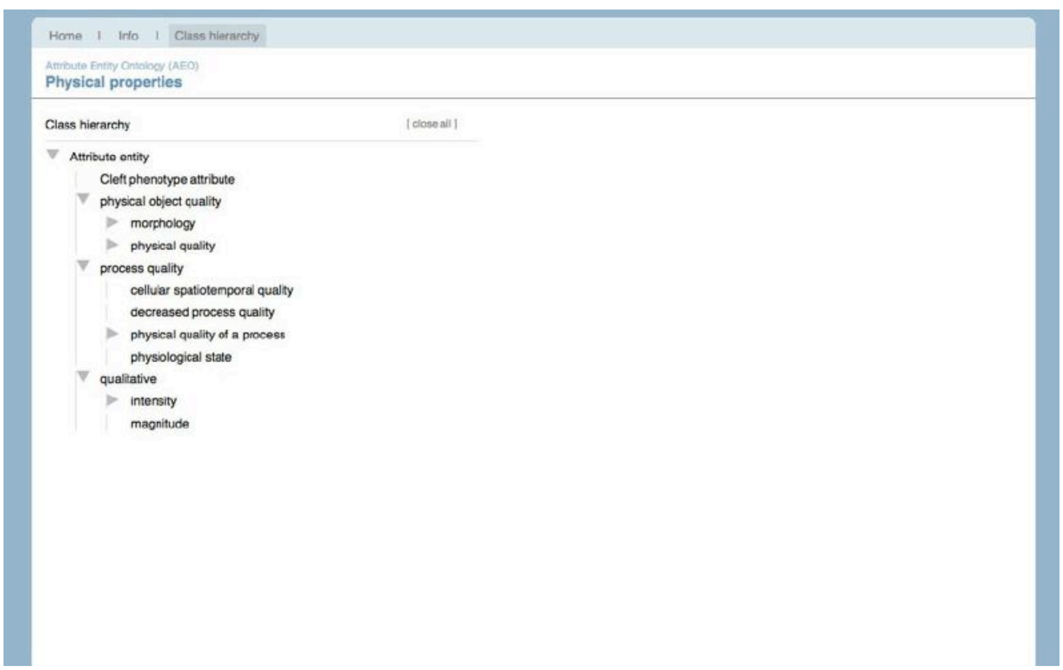


Figure 6-20. Hierarchy of classes describing physical properties within the OCDM. This sub-ontology is known as the Attribute Entity Ontology (AEO).

6.3.2 Strengths and limitations

The OCDM viewer shows how the OCDM has been developed as a set of sub-ontologies, and it also demonstrates use of the Query Integrator as a web service for querying ontologies. Because the OCDM sub-ontologies are presented solely as hierarchies (and the user is required to open each level of the hierarchy), the current viewer is not an appropriate end-user tool for finding classes of interest or understanding the structure of the sub-ontologies. The mappings page is particularly frustrating to use because there are relatively few mappings, and there is no mechanism for locating the mappings that do exist except by opening each level of the hierarchy to find terms in bold. In addition there are no illustrations like those presented earlier in this chapter.

6.4 Ideas for an improved OCDM browser

This section contains ideas for the design of an OCDM browser. Like the FMA browser, the initial purpose of this OCDM browser would not be to support specific tasks such as annotation of data, but rather to help users understand the structure and content of the OCDM. In future work the browser could be extended to support these tasks within applications like anatomy atlases and databases.

These ideas are based on (1) my experience designing the FMA browser, (2) the existing structure and content of the OCDM (which is still largely under development), and (3) formal and informal discussions with collaborators and FaceBase participants about the OCDM and how a browser might display portions of the OCDM.

6.4.1 Ideas and insights from discussions

During the national FaceBase meeting in 2013 I conducted interviews with two researchers from other groups. The ideas and insights from those interviews are:

- One participant who had experience annotating images of mice heads using terms from another ontology described uncertainty as to when to use a general term and when to use a more specific term. (Therefore, providing textual or visual definitions of these more specific terms may help users to understand how and when they should be applied.)
- There is a need for a resource that explains embryologic development of the mouse within the context of the ontology.
- It was suggested by a researcher with clinical experience that clinicians think in terms of regional parts, but laboratory researchers may be more likely to also consider constitutional parts.
- Diagrams should provide sufficient anatomical context, because line drawings that are over-simplified may not be readily recognizable for some anatomical regions and views.
- When asked how they might envision navigating the ontology to find anatomical structures, both participants expressed a preference for beginning with a graphic of the head (or face), and then selecting

regions from this graphic and seeing information appear next to the graphic.

During an additional discussion with two other researchers, it was stated that most developmental biologists who would use the OCDM are not familiar with the course of embryological development because they focus on a much more specific time period and anatomical region in their work. Therefore, the browser should not expect users to have knowledge of development in order to locate classes for developmental anatomical structures.

Another suggestion was made concerning the display of cross-species mappings. The current OCDM viewer displays the human and mouse hierarchies on the left and right sides of the screen, respectively (Figure 6-19). It was suggested that because researchers will be primarily interested in one hierarchy, there is no need to display both. Instead, the existence of a mapping can be indicated by placing an indicator next to a class within a single hierarchy.

6.4.2 Suggestions for the design

Further design work for an OCDM browser should begin with paper prototypes and more discussions with José Mejino about the content (particularly the relationships that could be used to navigate between the sub-ontologies). In this section I present suggestions for beginning the process of paper prototyping and further development of graphics.

6.4.2.1 Entry points

My discussions with researchers suggest that the most intuitive way to enter the ontology is to use a graphic of a head to locate regional parts of interest. This technique could be applied to both the human and mouse sub-ontologies, and may require a set of two to three graphics that depict the head from different angles.

6.4.2.2 Development

Based on the need for the browser to explain development within the context of the ontology—but the lack of familiarity with development by most users—this suggests that navigation should allow the user to first locate the relevant post-natal structures then move to the developmental structure(s) of interest. Once a developmental structure is reached, it should be then possible to follow developmental pathways.

It may be possible to adapt the layout of the FMA browser (Figure 5-10) to display developmental relationships. By removing the class hierarchy (displayed horizontally) and replacing it with a box on the left for the structure(s) earlier in development and a box on the right for the structure(s) later in development, the traditional left-to-right display of time would be preserved. The particular relationships involved ("transforms into", "derives from", "merges with [some class] to form", and "fuses with [some class] to form") would need to be dynamically displayed for each query. This approach has the advantage of retaining information about regional parts, constitutional parts, and membership relationships. Therefore, a browser of this layout could be used to browse through the path shown in Figure

6-4. The disadvantage of this approach is that only three steps in a developmental pathway could be viewed at once.

6.4.2.3 Malformations

The approach to initially navigating post-natal structures could also apply to locating classes for malformations. For example, the interface could offer a regional part hierarchy with links to malformation classes. The relationship that can be used to navigate from canonical anatomical structures to the corresponding pathological structures is "has variation" (for example, "Upper lip" has variation "Overt clefted upper lip"). Alternatively, malformations grouped by region ("mouth", "ear", "nose", etc.) could serve as entry points for browsing malformations.

However, one complication to displaying and communicating how malformations are modeled in the OCDM is that pathological structures and pathological phenotypes (conditions) are distinct concepts within their own class hierarchies. For example, "Overt clefted upper lip" is a subclass of "Pathological structure", while "Overt cleft of upper lip" is a subclass of "Phenotypic abnormality". Subclasses of "Pathological structure" are appropriate for use in annotating regions of clinical images, while subclasses of "Phenotypic abnormality" are appropriate to assign as a diagnosis or to describe a mutant phenotype. It is unrealistic to expect most users to understand the subtle difference between these classes. If the OCDM is deployed through a software application, that application could direct the user to the appropriate class based on the intended use of the tool. But for the design of a general browser for examining the ontology, an explanation of the differences between pathological structures and phenotypic abnormalities will be needed.

Because very little of the OCDM has been developed in these areas, it is unclear if there is a strong one-to-one correspondence between classes of pathological structures and those of phenotypic abnormalities. If there is, one option would be to design an interface that incorporates illustrations for the pathological structures, then provide links to corresponding classes of phenotypic abnormalities.

There are a quite a number of relationships relevant to malformations that will need to be accommodated to display the full structure of the malformation sub-ontologies and link to other sub-ontologies. These relationships are still under development, but currently include “is pathological component of”, “has phenotype quality”, “has phenotype abnormality”, “phenotype abnormality observed in”, “has component phenotype”, “is part of syndrome”, and “has location”.

6.4.2.4 Mappings across species

Although ontology developers may prefer the view of two complete hierarchies shown in Figure 6-19, other options need to be explored. Because the ideas presented in this section are intended to support browsing (not comparison across hierarchies), it may be sufficient to display a mapping across species as simply a piece of information about a specific class. This could be as simple as displaying the corresponding class name (or an icon) when a mapping is available. Clicking the class name (or icon) would redirect the browser to the class within the other species. However, to allow users to examine the properties of the mapping instances (such as the confidence level and reviewer), a more complex interface would be needed.

6.4.2.5 Graphics

The graphics in the FMA browser serve only as navigational icons, referring to general anatomical concepts that should not be new to users. Therefore, these graphics are drawn in a very stylized manner.

Graphics within a browser for the OCDM could play a similar role as navigational icons at the high-level entry points (such as “ear”, “mouth”, “nose”). But any graphics intended to represent (or visually define) classes within the OCDM have a different type of role: providing information about how knowledge is modeled in the OCDM, which may or may not match a user’s previous understanding. Therefore graphics of this type need to more closely depict the form of anatomical structures. They also must have sufficient detail.

In this chapter I have presented both vector-based line drawings and illustrations rendered in carbon dust. Both types have the potential to convey the anatomical information required, and further testing would be required to recommend one over the other. The advantage of the line drawings is that they can be displayed as SVGs within an interface and they require less time to prepare. The carbon dust illustrations have the advantage of more easily communicating three-dimensional anatomy, and I have learned through discussions that they are more engaging to view.

6.5 6.5 Summary and Conclusions

In this chapter I have applied the methods developed for the FMA and FMA Browser to the discovery of content patterns in the OCDM, implementation of a prototype OCDM viewer, and user-inspired design suggestions for a next generation OCDM browser that combines illustrations with text to visualize complex relations such as development over time, malformations, and mappings between species.

7 Discussion and conclusions

7.1 Summary

This work has demonstrated an approach to understanding and communicating biomedical ontologies that involves identifying content patterns within an ontology, explaining fundamental relationships through a tutorial, designing an interface using an iterative design process, and developing graphics to both assist in both developing and communicating the ontology content. This work has used two ontologies, the FMA and OCDM, but it should be possible to apply this approach to any spatially-oriented ontology.

7.2 Additional work

The work presented in this dissertation could be continued or extended in five ways, as described below.

7.2.1 Testing the FMA browser with users

The FMA browser presented in this work (Section 5.3) is the result of an iterative design process relying on the input of potential users. However, the final design has not been formally tested with users. This testing could involve a series of tasks, and perhaps compare to performance using the Foundational Model Explorer interface. It would be helpful to also conduct a "think aloud" exercise to verify whether the graphical icons and layout of the main window are communicating as intended.

7.2.2 Accommodating additional relationships within the FMA browser

Because the design process for the FMA browser focused on only the fundamental relationships (the class hierarchy and the three types of part hierarchies), other relationships are not as easy to browse. Future work could address this need by incorporating these relationships into the main window or by creating additional windows for specific themes (such as focusing on branching relationships within the cardiovascular system or the relationships between muscles, bones, and ligaments in the musculoskeletal system).

7.2.3 Designing and developing a OCDM browser

Section 6.4 describes my efforts to begin designing a browser for the OCDM. Based on my discussions with researchers and ideas for general organization, the next step is to develop paper prototypes for sections of the interface, create additional graphics, and solicit feedback from potential users.

7.2.4 Refining, expanding, and implementing the content patterns

In Chapter 3 I described my work to identify content patterns in the FMA. Further work on content patterns needs to proceed in three ways. First, the inconsistencies and omissions in the FMA that were identified need to be reviewed and brought into alignment with the content pattern. Second, my preliminary content patterns need to be reviewed and refined, and then content patterns should be extended to other sections of the FMA and OCDM. Third, methods to express the content patterns in a query language need to be explored, so that computational checking of the ontologies against the patterns can eventually be implemented.

7.2.5 Generalizing to ontologies in other domains

This work has taken place within the context of two spatially-oriented ontologies. An extension of this work would be to apply the principles and approaches to other ontologies. These could be ontologies outside the realm of biomedicine—as I demonstrated how the relationships in the FMA can apply to a shirt. An ontology would be a candidate for this approach if it has a set of well-defined and consistently implemented relationships, uses an extensive hierarchical structure, and describes a domain of objects with spatial properties.

7.3 Contributions

In addition to my overall approach this dissertation makes three specific contributions to research in the field of biomedical ontologies and the visualization of ontologies.

7.3.1 Content patterns for describing ontologies

As described in Section 3.2, I have introduced the idea of "content patterns" as a method to record and diagram the modeling logic used in ontologies. These content patterns have four purposes: (1) establishing a standard for modeling content, (2) communicating the structure of the ontology, (3) serving as a guide for constructing queries, and (4) devising methods of computationally checking the ontology for consistency.

7.3.2 Visual design patterns for browsing ontology hierarchies

I have introduced two visual design patterns useful in browsing ontology hierarchies.

The first is a method for viewing the position of a class within multiple hierarchies, as shown in Figure 5-19. Unlike other ontology-viewing tools which are concerned with providing a view of many classes and large sections of an ontology, my approach takes the opposite approach: it focuses on a single class. This design enables browsing of an ontology with a focus on details of each class.

My second visual design pattern is a modification of the folding indented list for displaying hierarchies. As shown in Figure 5-22, this method has been used for moving "down" a hierarchy, and I modified it for moving "up" a hierarchy. Therefore, this modification allows hierarchies to be opened from anywhere in the hierarchy—rather than requiring the user to begin opening the hierarchy at the root.

7.3.3 Using graphics to visually define ontology classes

The discipline of anatomy relies heavily on visuals for communication. My experience with both the OCDM and the FMA provides evidence that illustrations may have an equally critical role in biomedical ontologies, and that textual definitions are not sufficient for defining many types of classes.

7.4 Conclusions

This work demonstrates that building biomedical ontologies that will be useful in research and clinical applications requires efforts beyond the traditional work of authoring content. I have demonstrated the value of (1) identifying content patterns within an ontology, (2) creating a tutorial to explain basic concepts within an ontology, (3) involving potential users in the design of a browser interface, and

(4) creating graphics to support the process of building and communicating an ontology.

This approach should apply to any spatially-oriented ontology. By first improving the internal consistency of an ontology through the use of content patterns, visualizations can be developed that will not only help users to understand the structure of the ontology, but also permit more sophisticated use of the ontologies in digital atlases, databases and other scientific and clinical applications.

Appendix 1

The Shirt Ontology

by Melissa Clarkson and Onard Mejino

>> Material parts

About the Shirt Ontology

An ontology is a representation of knowledge about a particular domain. It consists of a set of terms and the relationships among those terms. When knowledge is structured as an ontology, it allows a computer to reason about that knowledge.

The Foundational Model of Anatomy (FMA) is an ontology of human anatomy. The FMA is an on-going project of the Structural Informatics Group at the University of Washington. It is currently curated by Onard Mejino, and has been under development since 1995. It has grown to include over 88,000 terms, 175 types of relationships, and 2.5 million relationships between terms, making it one of the largest biomedical ontologies in existance.

The Shirt Ontology was developed as a way to explain what the FMA is and how it is organized. It mimics the structure and content of the FMA, but describes a much more simple and familiar subject: the button-down dress shirt.

Just as the FMA models canonical (or protypical) human anatomy, the Shirt Ontology models the canonical dress shirt, pictured at the left.

Why is this ontology about a shirt? A shirt allows us to demonstrate how the FMA accounts for some potentially confusing concepts. For example, human anatomy has right and left sides. A shirt has right and left sides. The FMA models both male and female anatomy. The Shirt Ontology models both men's and women's shirts.

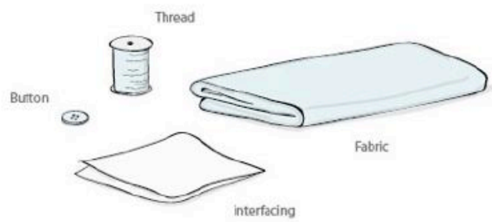
Each section of this tutorial explains a concept using the Shirt Ontology, then shows examples of the concept in the FMA.

After working through this tutorial you may want to view the Shirt Ontology itself, which was written in Protégé-Frames. You may download the Shirt Ontology as a zip file. The ontology can be viewed using Protégé-Frames, which is available at http://protege.stanford.edu. The files have been tested in versions 3.3 and 3.4.7.

Material parts

What are the parts of a shirt?

One way to answer this question is to list the types of materials that are used to construct a shirt. The four types of materials are thread, fabric, interfacing, and button.



Each of these is a class in the Shirt Ontology. There is the Thread class, the Fabric class, the Interfacing class, and the Button class. A shirt is made up of these four types of materials, and nothing else. The material parts are essentially the "ingredients" of a shirt.

This part relationship can be represented as:

Shirt $\xrightarrow{\text{has material part}}$ Thread , Fabric , Interfacing , Button

(You may be wondering what interfacing is. It is a fabric-like material that is put inside the collar, cuffs, and front bands to provide stiffness.)

The idea of a class is fundamental to ontologies. A class describes a concept. The class "button" describes the concept of a button. The class "interfacing" describes the concept of interfacing. This is different than talking about a specific button or a specific piece of interfacing. Classes are a way to refer to a category of similar entities, without refering to individual entities.

On the previous page an ontology was defined as a set of terms and the relationships among the terms. A more precise definition of an ontology is that it is a set of classes and the relationships among the classes. In this tutorial, classes will be represented as terms within blue boxes.

In the FMA

In the FMA, the equivalent of material parts are called "constitutional parts". When an anatomical structure is divided into constitutional parts, it is divided into parts that are more simple in composition.

These are the constitutional parts of the class Brain :

Brain $\xrightarrow{\text{has constitutional part}}$ Neural tissue of brain , Ventricular system of brain , Vasculature of brain

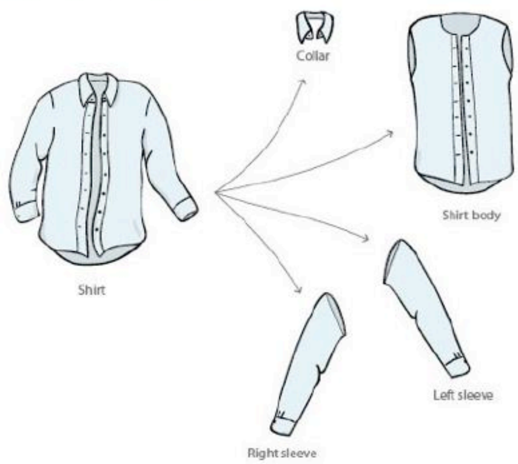
The class Ventricular system of brain has its own constitutional parts:

Ventricular system of brain $\xrightarrow{\text{has constitutional part}}$ Wall of ventricular system of brain , Cavity of brain

Regional parts

What are the parts of a shirt?

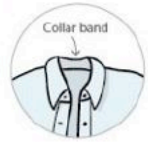
The second way to answer this question is to divide a shirt into spatial regions. The Shirt Ontology divides Shirt into Collar , Shirt body , Left sleeve , and Right sleeve .



This part relationship can be represented as:

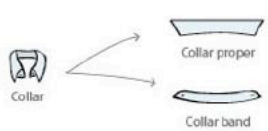
Shirt $\xrightarrow{\text{has regional part}}$ Collar , Shirt body , Left sleeve , Right sleeve

Each of these regional parts has its own regional parts. We will begin with the regional parts of the class Collar .



If you examine a shirt, you will see that the collar consists of two pieces: the collar band (which fits around the neck and stands up) and a part that folds down. The part that folds down is commonly known as a "collar". This presents a problem in the ontology, because there is already a class named Collar .

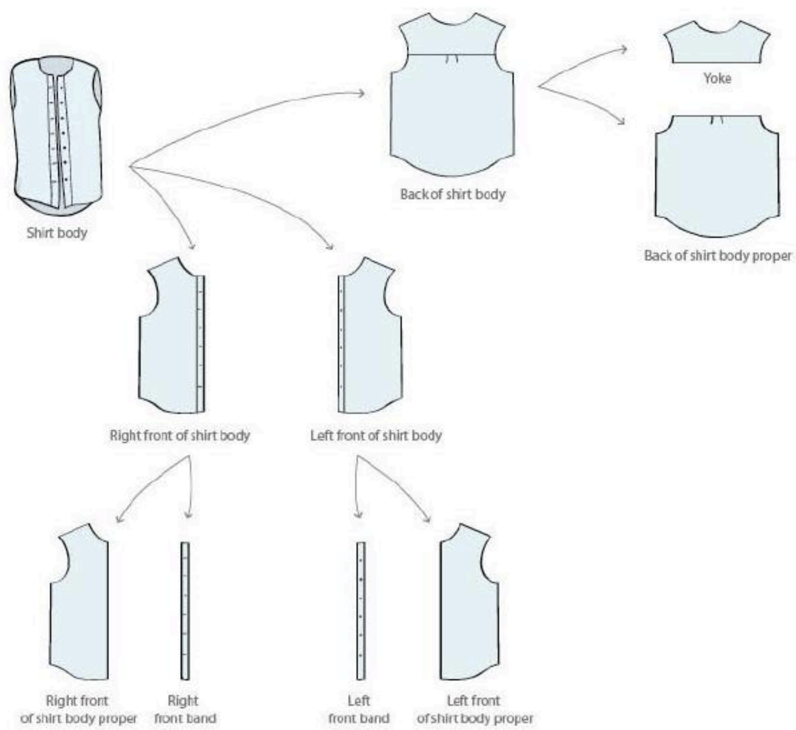
We solve this problem by using a simple strategy: add the word "proper" to the region that remains once the region that already has a unique name is accounted for. In this case, we name the classes Collar proper and Collar band



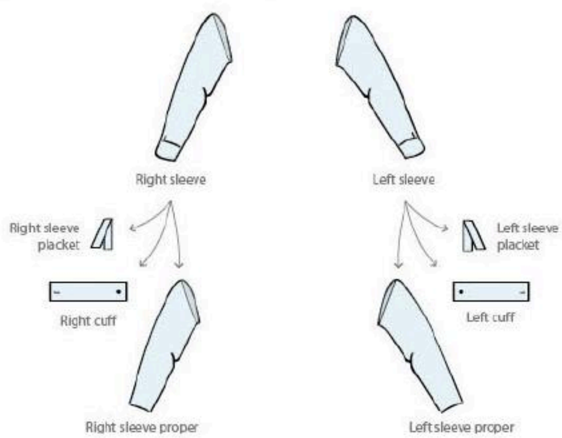
This relationship can be represented as:

Collar $\xrightarrow{\text{has regional part}}$ Collar proper , Collar band

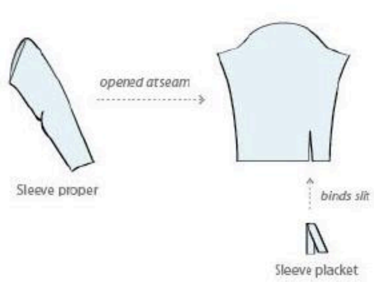
The Shirt body is divided into these regional parts:



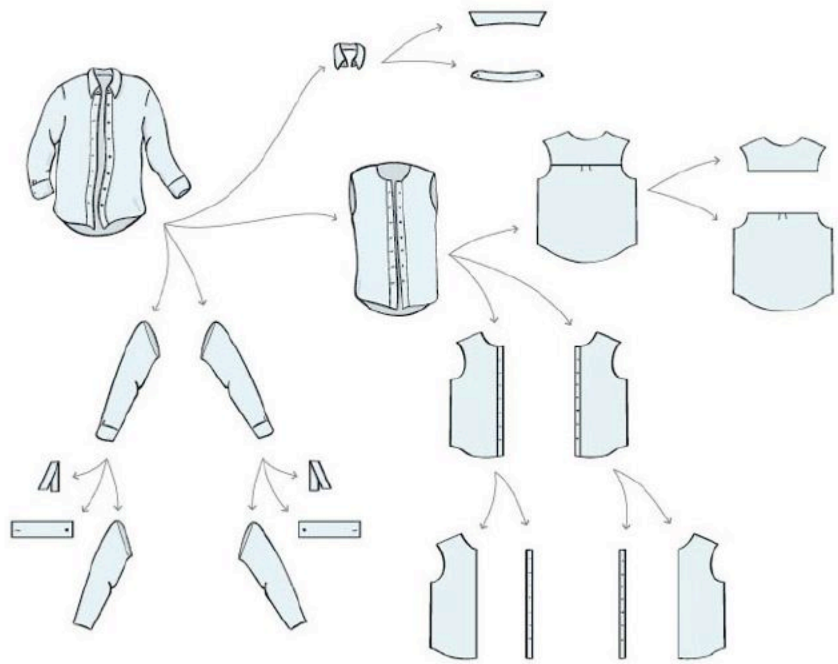
The Right sleeve and Left sleeve are also divided into regional parts:



(You may not know what a "sleeve placket" is. There is a slit in the sleeve where the cuff opens. The binding of that slit is the sleeve placket.)



This diagram summarizes all of these regional part relationships for the shirt:



So in summary, there are two ways of defining the parts of a shirt: (1) the **material parts** (the types of "ingredients" present), and (2) the **regional parts** (the spatial divisions of the shirt).

In the FMA

The FMA also defines regional parts. These are the regional parts of the class `Brain`:

`Brain` $\xrightarrow{\text{has regional part}}$ `Forebrain`, `Midbrain`, `Hindbrain`

The class `Hindbrain` has its own regional parts:

`Hindbrain` $\xrightarrow{\text{has regional part}}$ `Medulla oblongata`, `Metencephalon`

So in summary, there are two ways of defining the parts of the human body: (1) the **constitutional parts** (divisions of compositionally distinct elements), and (2) the **regional parts** (the spatial divisions of the body).

Material of regional parts

The Shirt Ontology has the class Fabric (a material part) and the class Collar band (a regional part). But what if we want to refer to the fabric of the collar band?

There are also classes for material parts of a regional parts. One of these is Fabric of collar band .

This example shows the material parts of the Collar band :

Collar band $\xrightarrow{\text{has material part}}$

Fabric of collar band , Interfacing of collar band , Button of collar band , Thread

If you are curious why Thread —and not Thread of collar band —is given as a material part of Collar band , it is because the authors of the Shirt Ontology decided that thread is not interesting enough to be divided into regions.

In the FMA

The FMA has classes representing constitutional parts of regional parts. For example, these are the constitutional parts of Hand :

Hand $\xrightarrow{\text{has constitutional part}}$

Skin of hand , Superficial fascia of hand , Musculature of hand , Neural network of hand , Vasculature of hand ,

Skeleton of hand

Material of regional parts <<

>> Synonyms

Class hierarchy

All ontologies are structured by using hierarchical class relationships. Moving down the hierarchy (following the subclass relationship) leads to more specific classes.

Shirt part $\xrightarrow{\text{has subclass}}$ Regional shirt part $\xrightarrow{\text{has subclass}}$ Sleeve

Moving up the hierarchy (following the superclass relationship) leads to more general classes.

Shirt part $\xleftarrow{\text{has superclass}}$ Regional shirt part $\xleftarrow{\text{has superclass}}$ Sleeve

The superclass relationship is also known as an "is a" relationship.

Shirt part $\xleftarrow{\text{is a}}$ Regional shirt part $\xleftarrow{\text{is a}}$ Sleeve

This next example shows the sequence of classes from the most general class in the Shirt Ontology (Physical clothing entity) down to the class Interfacing of collar band :

Physical clothing entity $\xrightarrow{\text{has subclass}}$ Material clothing entity $\xrightarrow{\text{has subclass}}$ Clothing part
$\xrightarrow{\text{has subclass}}$ Shirt part $\xrightarrow{\text{has subclass}}$ Material of regional shirt part $\xrightarrow{\text{has subclass}}$
Interfacing of regional shirt part $\xrightarrow{\text{has subclass}}$ Interfacing of collar $\xrightarrow{\text{has subclass}}$ Interfacing of collar band

The position of every class within the Shirt Ontology could be traced in a similar way, beginning from Physical clothing entity . (You may be wondering why the most general category in this ontology refers to clothing, instead of a shirt. The ontology has been constructed so that it can be expanded to describe other types of clothing, such as pants. We leave this as an exercise for the reader.)

A shirt has right and left sides. Some parts of the shirt are present in pairs—once on the right side and once on the left side. Classes provide a way to account for this. For example, we can refer to a sleeve in general, or specifically to the right sleeve or the left sleeve.

Regional shirt part $\xrightarrow{\text{has subclass}}$ Sleeve $\xrightarrow{\text{has subclass}}$ Right sleeve , Left sleeve

In the FMA

The FMA has a very extensive hierarchy of classes. This example shows the sequence of classes from the most general class, called Physical anatomical entity, down to the class Heart :

Physical anatomical entity $\xrightarrow{\text{has subclass}}$ Material anatomical entity $\xrightarrow{\text{has subclass}}$

Anatomical structure $\xrightarrow{\text{has subclass}}$ Organ $\xrightarrow{\text{has subclass}}$ Cavitated organ $\xrightarrow{\text{has subclass}}$

Organ with cavitated organ parts $\xrightarrow{\text{has subclass}}$ Heart

The FMA uses classes to account for right and left anatomical structures.

Long bone $\xrightarrow{\text{has subclass}}$ Femur $\xrightarrow{\text{has subclass}}$ Right femur , Left femur

Class hierarchy << >> Men's and women's shirts

Synonyms

Each class is assigned a term that serves as the name of that class. But what if there is more than one term that could be used to name a class? In that situation, one term is selected as the preferred term, and the others are associated as synonyms.

Collar band $\xrightarrow{\text{has synonym}}$ Collar stand

Front band $\xrightarrow{\text{has synonym}}$ Front placket

In the FMA

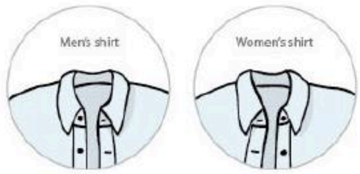
The FMA has many synonyms, including:

Limb $\xrightarrow{\text{has synonym}}$ Extremity

Uterine tube $\xrightarrow{\text{has synonym}}$ Fallopian tube , Oviduct

Men's and women's shirts

There is one difference between men's and women's shirts: the placement of the buttons and buttonholes. Men's shirts have buttons on the right. Women's shirts have buttons on the left.



Therefore, the class Shirt has two subclasses:

Shirt $\xrightarrow{\text{has subclass}}$ Men's shirt , Women's shirt

The difference in button and buttonhole placement means that some of the regional parts of men's and women's shirts are different:

Men's shirt $\xrightarrow{\text{has regional part}}$ Men's shirt body , Men's collar , Right sleeve , Left sleeve

Women's shirt $\xrightarrow{\text{has regional part}}$ Women' shirt body , Women's collar , Right sleeve , Left sleeve

Some of the material parts are also different. Here are the material parts of the right front bands:

Men's right front band $\xrightarrow{\text{has material part}}$
Fabric of right front band , Interfacing of right front band , Thread , Set of front buttons

Women's right front band $\xrightarrow{\text{has material part}}$
Fabric of right front band , Interfacing of right front band , Thread

In the FMA

The class Human body has two subclasses:

Human body $\xrightarrow{\text{has subclass}}$ Male human body , Female human body

These are the regional parts of male and female bodies:

Male human body $\xrightarrow{\text{has regional part}}$
Head , Male body proper , Right upper limb , Left upper limb , Right lower limb , Left lower limb

Female human body $\xrightarrow{\text{has regional part}}$
Head , Female body proper , Right upper limb , Left upper limb , Right lower limb , Left lower limb

Ontology exercises, set 1

Exercises for class and part relationships

One of the fundamental tasks in constructing an ontology is the identify the class, regional part, and constitutional / material part relationships in a collection of terms. So grab a piece of paper and test yourself on these questions before continuing with the rest of the tutorial.

Each question has one class that is related to each of the other two classes by one of these relationships: "has subclass", "has regional part", or "has constitutional / material part" (Answers are below, but don't peek yet.)

1) Car $\xrightarrow{???}$ Plastic , Metal

2) Car $\xrightarrow{???}$ Trunk , Passenger compartment

3) Car $\xrightarrow{???}$ Sedan , Station wagon

4) Tooth $\xrightarrow{???}$ Crown of tooth , Root of tooth

5) Tooth $\xrightarrow{???}$ Enamel , Dental pulp

6) Bird $\xrightarrow{???}$ Chicken , Dove

7) Chicken $\xrightarrow{???}$ Wing , Leg

8) Chicken egg $\xrightarrow{???}$ Shell , Yolk

9) Hat $\xrightarrow{???}$ Brim , Crown

10) Latte $\xrightarrow{???}$ Expresso , Milk

11) Transmission $\xrightarrow{???}$ Manual transmission , Automatic transmission

12) Cookie $\xrightarrow{???}$ Chocolate chip cookie , Ginger snap

13) Chocolate chip cookie $\xrightarrow{???}$ Chocolate chip , Butter

14) Book $\xrightarrow{???}$ Autobiography , Novel

15) Glove $\xrightarrow{???}$ Right glove , Left glove

Answers...

1) Car **has constitutional parts (or material parts)** Plastic and Metal , because plastic and metal are each more simple in composition than the entire car.

2) Car **has regional parts** Trunk and Passenger compartment , because the trunk and passenger compartments are spatially distinct regions of the car.

3) Car **has subclasses** Sedan and Station wagon , because sedans and station wagons are types of cars.

4) Tooth **has regional parts** Crown (above the gum line) and Root (below the gum line).

5) Tooth **has constitutional parts** Enamel and Dental pulp , because enamel and dental pulp are more simple in composition than the entire tooth.

6) Bird **has subclasses** Chicken and Dove , because chickens and doves are types of birds.

7) Chicken **has regional parts** Wing and Leg , because the wing and the leg are spatially distinct regions of a chicken's body.

8) Chicken egg **has constitutional parts** Shell and Yolk , because the shell and yolk are each more simple in composition than the entire egg.

9) Hat **has regional parts** Brim (the projecting edge) and Crown (the region above the brim that covers the head).

10) Latte **has constitutional parts (or ingredients)** Expresso and Milk .

11) Transmission **has subclasses** Manual transmission and Automatic transmission , because manual transmissions and automatic transmissions are types of transmissions.

12) Cookie **has subclass** Chocolate chip cookie and Ginger snap , because chocolate chip cookies and ginger snaps are are types of cookies.

13) Chocolate chip cookie **has constitutional parts (or ingredients)** Chocolate chip and Butter , because chocolate chips and butter are each more simple in composition than the entire chocolate chip cookie.

14) Book **has subclasses** Autobiography and Novel , because an autobiography and a novel are each a type of book.

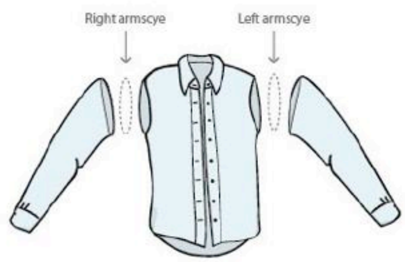
15) Glove **has subclasses** Right glove and Left glove , because a right glove and a left glove are each types of gloves.

Spaces

So far we have discussed subclasses of the Material clothing entity class. But some classes are not material entities. If we want to describe spaces, we need to account for immaterial entities.

Physical clothing entity $\xrightarrow{\text{has subclass}}$ Immaterial clothing entity $\xrightarrow{\text{has subclass}}$ Space in clothing $\xrightarrow{\text{has subclass}}$ Space in shirt

One type of space in a shirt is the armhole, technically known as the Armscye . This is the opening between the Shirt body and the Sleeve .



Buttonholes are another type of space described by the Shirt Ontology. Each buttonhole is a class.

Space in shirt $\xrightarrow{\text{has subclass}}$ Shirt buttonhole $\xrightarrow{\text{has subclass}}$ Buttonhole of collar band

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In the FMA

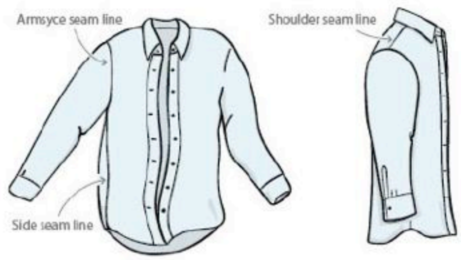
The FMA contains classes for a large number of spaces. One of these is the Uterotubal orifice , which is the opening between the Uterus and Uterine tube .

Points, lines, and surfaces

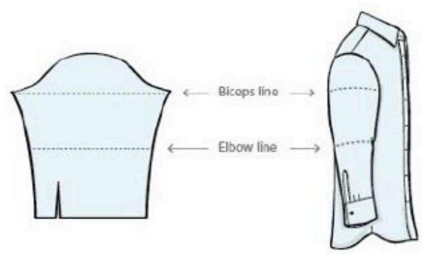
Points, lines, and surfaces are also subclasses of Immaterial clothing entity .

Lines

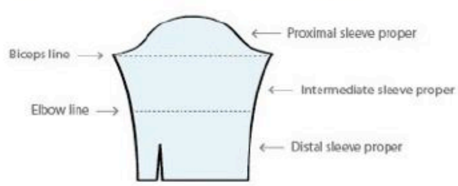
If you look at a shirt, you will see some lines. The Shirt Ontology contains the classes Armsyce seam line , Side seam line , and Shoulder seam line .



These visible lines are called "bona fide" lines. There is another category of lines, called "fiat lines", which are not visible. Two of these are the Biceps line and the Elbow line of the Sleeve proper .



In the Shirt Ontology, these lines have been used to divide the Sleeve proper into regional parts.

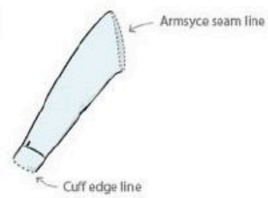


Sleeve proper $\xrightarrow{\text{has regional part}}$ Proximal sleeve proper , Intermediate sleeve proper , Distal sleeve proper

Surfaces

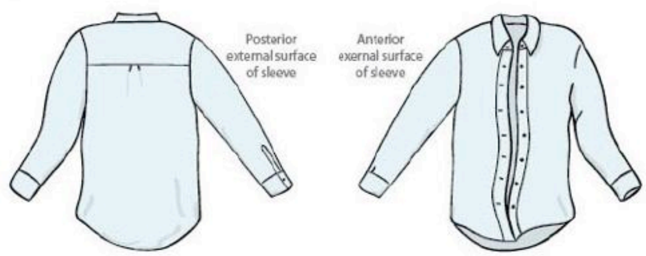
We can also refer to two-dimensional surfaces of the shirt, such as the external surface of a sleeve. Surfaces are bounded by lines. In the case of a sleeve, the surface is a tube, bounded at one end by the Armsyce seam line and at the other by the Cuff edge line .

The surface and the lines are related by an "is bounded by" relationship.

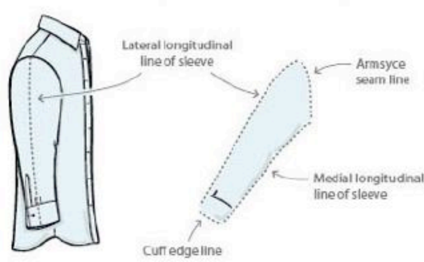


External surface of sleeve $\xrightarrow{\text{is bounded by}}$ Armsyce seam line , Cuff edge line

Surfaces can be divided into regions. External surface of sleeve has been divided into Posterior external surface of sleeve and Anterior external surface of sleeve .



In order to define these regions, two additional classes of lines have been created: Lateral longitudinal line of sleeve (on the top of the sleeve, from shoulder to cuff) and the Medial longitudinal line of sleeve (on the bottom of the sleeve, from underarm to cuff). If you think that those terms might have been made up just for the Shirt Ontology, you are correct. One task in making an ontology is to come up with names for concepts that don't already have names.

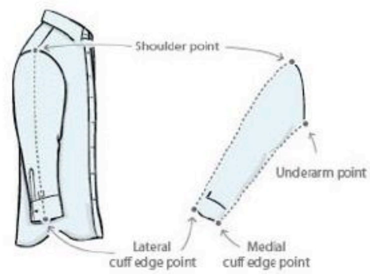


Anterior external surface of sleeve $\xrightarrow{\text{is bounded by}}$

Armsyce seam line , Cuff edge line , Lateral longitudinal line of sleeve , Medial longitudinal line of sleeve

Points

In order to more precisely describe Lateral longitudinal line of sleeve , we can refer to its endpoints. Therefore we must create classes for those points.



Lateral longitudinal line of sleeve $\xrightarrow{\text{is bounded by}}$ Shoulder point , Lateral cuff edge point

Medial longitudinal line of sleeve $\xrightarrow{\text{is bounded by}}$ Underarm point , Medial cuff edge point

---

In the FMA

The FMA follows this scheme for points, lines, surfaces, and volumes:

- Volumes (3D) are bounded by surfaces (2D)
- Surfaces (2D) are bounded lines (1D)
- Lines (1D) are bounded by points (0D)

A few examples are:

Heart (3D) $\xrightarrow{\text{is bounded by}}$ Surface of heart (2D)

Mediastinal surface layer of upper lobe of lung (3D) $\xrightarrow{\text{is bounded by}}$

Mediastinal surface of upper lobe of lung (2D)

Mediastinal surface of upper lobe of lung (2D) $\xrightarrow{\text{is bounded by}}$

Anterior margin of upper lobe of lobe (1D), Posterior margin of upper lobe of lobe (1D), Fissural margin of upper lobe of lobe (1D)

Anterior margin of upper lobe of lobe (1D) $\xrightarrow{\text{is bounded by}}$

Anterior mediastinal point of upper lobe of lung (0D), Apex of lung (0D)

The FMA contains classes for both bona fide and fiat lines. Bona fide lines include Vermilion border of upper lip and Vermilion border of lower lip . An example of a fiat line is the Midclavicular line , which is a vertical line extending from the middle of the clavicle (or collar bone) down to the hip bone.

The “attaches to” relationship

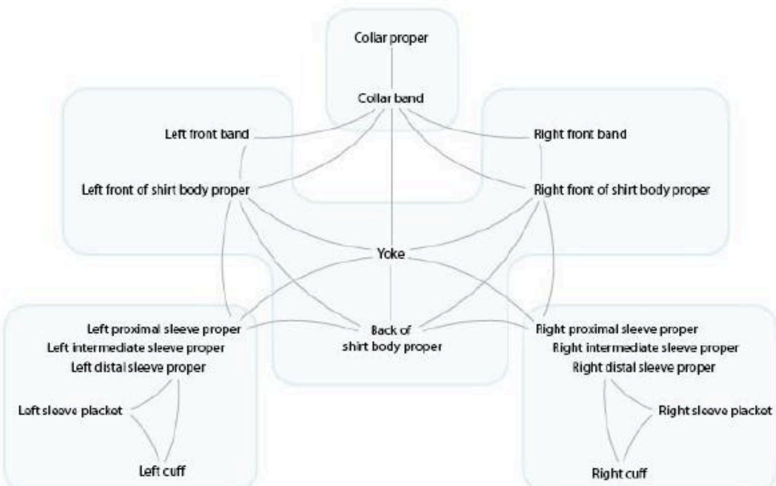
The Shirt Ontology is structured by the part relationships and hierarchical class relationships. But other types of relationships can also be defined. One of these is the "attaches to" relationship.

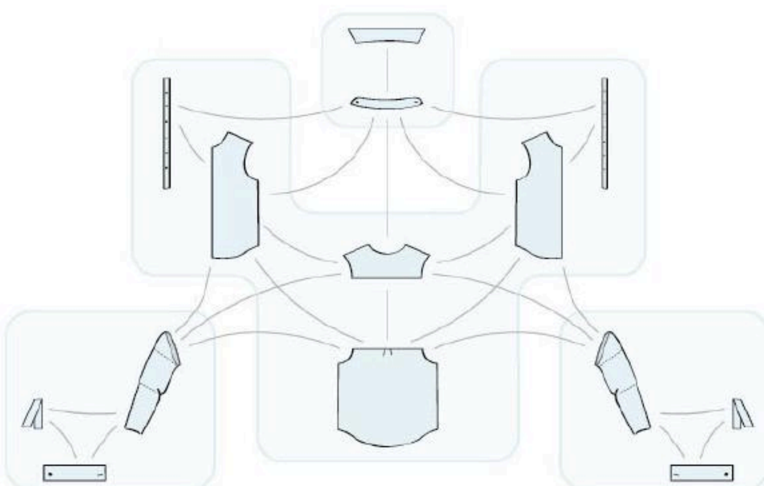
The "attaches to" relationship describes two regional parts that are connected by a seam. An example of this relationship is:

Collar proper — attaches to — Collar band

Notice that this is a bidirectional relationship (and therefore the arrowhead has been omitted).

The two diagrams below display all the "attaches to" relationships for the shirt. The first diagram uses the names of the classes and the second uses pictures. The blue shapes group together the classes that are regional parts of the classes Collar , Shirt body , Left sleeve , and Right sleeve .





Recall that Sleeve proper has been divided into three regions (proximal, intermediate, and distal). These regions are related by a "is continuous with" with relationship.

This is the series of relationships from Left front of shirt body proper to Left Cuff :

Left front of shirt body proper — attaches to — Left proximal sleeve proper — is continuous with —

Left intermediate sleeve proper — is continuous with — Left distal sleeve proper — attaches to — Left cuff

In the FMA

The FMA contains a number of relationships that describe how anatomical structures are connected.

Pharynx — is continuous with — Esophagus — is continuous with — Stomach

Right hip bone — articulates with — Right femur — articulates with — Right tibia

Short head of biceps brachii — attaches to — Apical part of coracoid process

Right lymphatic duct $\xrightarrow{\text{efferent to}}$ Right brachiocephalic vein

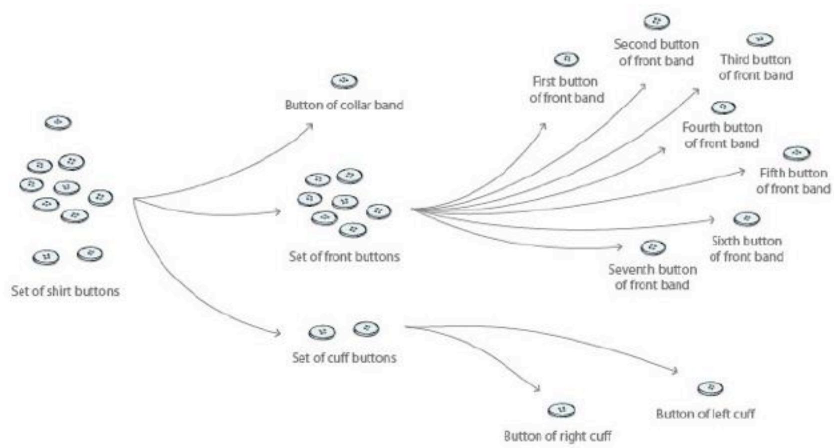
The "has member" relationship

We may want to refer to all the buttons of the shirt. Each of the ten buttons is itself a class. In order to refer to a set of buttons, we must define a new class that represents the set. The "has member" relationship specifies the members of the set.

The class Set of shirt buttons has been defined as:

Set of shirt buttons $\xrightarrow{\text{has member}}$ Button of collar band , Set of front buttons , Set of cuff buttons

This diagram shows all the "has member" relationships for the buttons.



In the FMA

The FMA also has sets. One example is the vertebrae:

Set of all vertebrae $\xrightarrow{\text{has member}}$

Set of cervical vertebrae , Set of thoracic vertebrae , Set of lumbar vertebrae , Set of sacral vertebrae , Coccyx

Each of these sets of vertebrae is composed of individual vertebrae. For example:

Set of sacral vertebrae $\xrightarrow{\text{has member}}$

First sacral vertebrae , Second sacral vertebrae , Third sacral vertebrae , Fourth sacral vertebrae , Fifth sacral vertebrae

Reasoning with the Shirt Ontology

Ontologies are the most useful when they are developed within in applications that allow for reasoning over the ontology. Reasoning is not covered in this tutorial, but here are examples of questions that could potentially be answered using the Shirt Ontology and the FMA:

Question: What part of a men's shirt has the set of front buttons?

Men's shirt $\xrightarrow{\text{has regional part}}$ Men's shirt body

Men's shirt body $\xrightarrow{\text{has regional part}}$ Men's right front of shirt body

Men's right front of shirt body $\xrightarrow{\text{has regional part}}$ Men's right front band

Men's right front band $\xrightarrow{\text{has material part}}$ Set of front buttons.

Answer: The right front band.

Question: Which part of the brachial nerve plexus supplies the deltoid muscle?

Deltoid muscle $\xrightarrow{\text{has nerve supply}}$ Deltoid branch of anterior branch of axillary nerve

Deltoid branch of anterior branch of axillary nerve $\xrightarrow{\text{is branch of}}$ Anterior branch of axillary nerve

Anterior branch of axillary nerve $\xrightarrow{\text{is branch of}}$ Axillary nerve

Axillary nerve $\xrightarrow{\text{is branch of}}$ Posterior cord of brachial nerve plexus

Posterior cord of brachial nerve plexus $\xrightarrow{\text{is regional part of}}$ Brachial nerve plexus

Answer: The posterior cord of brachial nerve plexus.

Ontology exercises, set 2

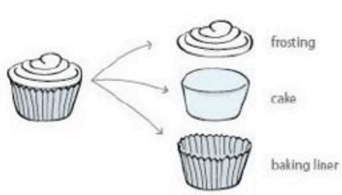
Exercises for membership relationships

Each of the examples below has three terms that represent classes. Identify the "has member" and "has subclass" relationships among the three terms. (Answers are below.)

1) Index finger , Set of fingers , Finger
2) Football player , Quarterback , Football team
3) Blue crayon , Crayon , Set of crayons
4) Fork , Set of silverware , Piece of silverware

The Cupcake Ontology

Imagine that you have been asked to create an ontology for the domain of cupcakes. The users of the ontology need to be able to describe what your clients call the "components" of a cupcake (cake, frosting, and baking liner) as well as the "ingredients" that make up the cake and frosting.



Cupcakes

cake	frosting
$2\frac{1}{4}$ cups flour	1 cup butter
$1\frac{1}{3}$ cups sugar	$2\frac{1}{3}$ cups powdered sugar
3 teaspoons baking powder	1 teaspoon vanilla
$\frac{1}{4}$ teaspoon salt	
$\frac{1}{2}$ cup shortening	
1 cup milk	
1 teaspoon vanilla	
2 eggs	

1) Create the class hierarchy. It should account for the components (cake, frosting, baking liner) as well as the ingredients (eggs, four, butter...).

2) Add relationships to the ontology that describe the relationships between the components and the ingredients.

3) Once you have a basic structure for your ontology, think about how you could expand it. Can you account for edible vs. non-edible components? How would a class for the uncooked batter fit into the ontology, and what would be its relationship to the cake? Could an ontology describe items such as sprinkles or candles?

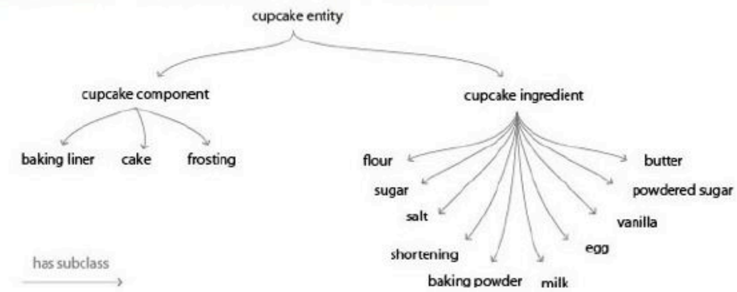
Answers...

Exercises for membership relationships

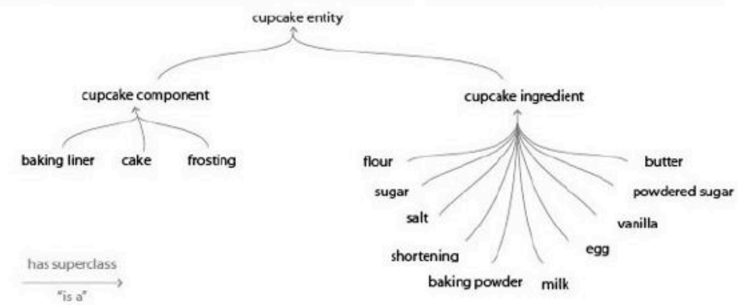
1) Set of fingers $\xrightarrow{\text{has member}}$ Index finger $\xleftarrow{\text{has subclass}}$ Finger
2) Football team $\xrightarrow{\text{has member}}$ Quarterback $\xleftarrow{\text{has subclass}}$ Football player
3) Set of crayons $\xrightarrow{\text{has member}}$ Blue crayon $\xleftarrow{\text{has subclass}}$ Crayon
4) Set of silverware $\xrightarrow{\text{has member}}$ Fork $\xleftarrow{\text{has subclass}}$ Piece of silverware

Exercises for the cupcake ontology

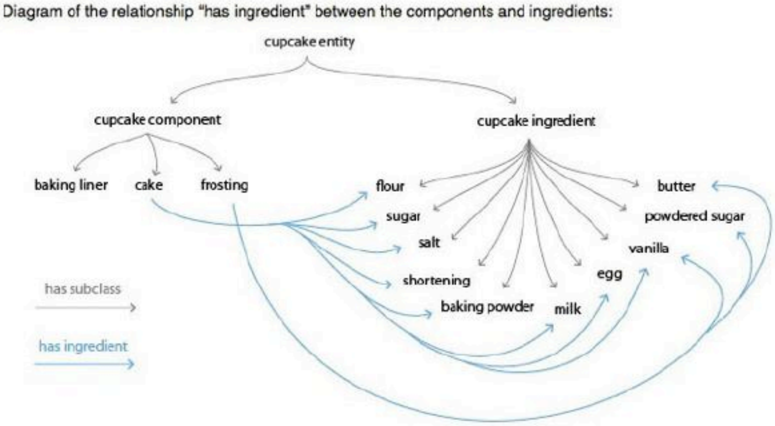
1) Diagram of the class hierarchy, showing the relationship "has subclass":



The same diagram of the class hierarchy, but showing the opposite relationship "has superclass" (or "is a"):



2) Diagram of the relationship "has ingredient" between the components and ingredients:



3a) To account for edible and non-edible components, you could add Edible component and Non-edible component as subclasses of Component .

3b) To account for uncooked batter, you could use a relationship such as Batter $\xrightarrow{\text{upon baking becomes}}$ Cake .

3c) You could model sprinkles and candles in several ways. For example, one approach is to create new subclasses of Cupcake component called Sprinkles and Candle . Or you could create a class Topping as a subclass of Cupcake component , and place Frosting , Candle , and Sprinkles as subclasses of Topping .

Appendix 2

Query #274 for the FMA
[Queried class] *is a regional part of* [some class], submitted and returned as labels of the classes.

```
PREFIX rdfs:<http://www.w3.org/2000/01/rdf-schema#>
PREFIX fma:<http://purl.org/sig/fma#>

CONSTRUCT {?b rdfs:label ?val}
FROM <http://purl.org/sig/fma>
WHERE{    ?a rdfs:label "<#0>"@en.    ?a fma:regional_part_of ?b .    ?b rdfs:label ?val .}
```

Query #166 for the FMA
[Queried class] *has regional part* [some class], submitted and returned as labels of the classes.

```
PREFIX rdfs:<http://www.w3.org/2000/01/rdf-schema#>
PREFIX fma:<http://purl.org/sig/fma#>

CONSTRUCT {?b rdfs:label ?val}
FROM <http://purl.org/sig/fma>
WHERE{    ?a rdfs:label "<#0>"@en.    ?a fma:regional_part ?b .    ?b rdfs:label ?val .}
```

Query #275 for the FMA
[Queried class] *is a constitutional part of* [some class], submitted and returned as labels of the classes.

```
PREFIX rdfs:<http://www.w3.org/2000/01/rdf-schema#>
PREFIX fma:<http://purl.org/sig/fma#>

CONSTRUCT {?b rdfs:label ?val}
FROM <http://purl.org/sig/fma>
WHERE{    ?a rdfs:label "<#0>"@en.    ?a fma:constitutional_part_of ?b .    ?b rdfs:label ?val .}
```

Query #167 for the FMA
[Queried class] *has constitutional part* [some class], submitted and returned as labels of the classes.

```
PREFIX rdfs:<http://www.w3.org/2000/01/rdf-schema#>
PREFIX fma:<http://purl.org/sig/fma#>

CONSTRUCT {?b rdfs:label ?val}
FROM <http://purl.org/sig/fma>
WHERE{    ?a rdfs:label "<#0>"@en.    ?a fma:constitutional_part ?b .    ?b rdfs:label ?val .}
```

Query #273 for the FMA
[Queried class] i*s member of* [some class], submitted and returned as labels of the classes.

```
PREFIX rdfs:<http://www.w3.org/2000/01/rdf-schema#>
PREFIX fma:<http://purl.org/sig/fma#>
```

```
CONSTRUCT {?b rdfs:label ?val}
FROM <http://purl.org/sig/fma>
WHERE{    ?a rdfs:label "<#0>"@en.    ?a fma:member_of ?b .    ?b rdfs:label ?val .}
```

Query #272 for the FMA
[Queried class] *has member* [some class], submitted and returned as labels of the classes.

```
PREFIX rdfs:<http://www.w3.org/2000/01/rdf-schema#>
PREFIX fma:<http://purl.org/sig/fma#>

CONSTRUCT {?b rdfs:label ?val}
FROM <http://purl.org/sig/fma>
WHERE{    ?a rdfs:label "<#0>"@en.    ?a fma:member ?b .    ?b rdfs:label ?val .}
```

Query #271 for the FMA
[Some class] *is subclass of* [query class]. Returns subclasses of the query class, submitted and returned as labels of the classes.

```
PREFIX rdfs:<http://www.w3.org/2000/01/rdf-schema#>
PREFIX fma:<http://purl.org/sig/fma#>

CONSTRUCT {?b rdfs:label ?val}
FROM <http://purl.org/sig/fma>
WHERE{    ?a rdfs:label "<#0>"@en.    ?b rdfs:subClassOf ?a .    ?b  rdfs:label ?val.}
```

Query #276 for the FMA
[Queried class] *is subclass of* [some class]. Returns super classes of the query class, submitted and returned as labels of the classes.

```
PREFIX rdfs:<http://www.w3.org/2000/01/rdf-schema#>
PREFIX fma:<http://purl.org/sig/fma#>

CONSTRUCT {?b rdfs:label ?val}
FROM <http://purl.org/sig/fma>
WHERE{    ?a rdfs:label "<#0>"@en.    ?a rdfs:subClassOf ?b .    ?b rdfs:label ?val .}
```

Query #385 for the FMA
[Queried class] [some relationship] [some class]. Returns all properties and associated classes, submitted and returned as labels of the classes.

```
PREFIX rdfs:<http://www.w3.org/2000/01/rdf-schema#>
PREFIX fma:<http://purl.org/sig/fma#>

CONSTRUCT {?a ?b ?c.}
FROM <http://purl.org/sig/fma>
WHERE{

   ?a rdfs:label "<#0>"@en.
   {
```

```
    ?a ?b ?test . ?test rdfs:label ?c.
  } UNION
  {
    ?a ?b ?c.
    OPTIONAL {?c rdfs:label ?c_label.}
    FILTER(!bound(?c_label)).
  }
}
```

Query #304 for the FMA

Determines if queried term corresponds to an FMA class, either as a preferred name, synonym, or non-English equivalent. If so, the preferred name of that class is returned.

```
PREFIX rdfs:<http://www.w3.org/2000/01/rdf-schema#>
PREFIX fma:<http://purl.org/sig/fma#>
PREFIX temp:<http://sig.uw.edu/temp#>

CONSTRUCT {?a temp:matches_search_term "<#0>". ?a rdfs:label ?label.}
FROM <http://purl.org/sig/fma>
WHERE{
  ?name_inst fma:name "<#0>"^^<http://www.w3.org/2001/XMLSchema#string> .
  ?a fma:Preferred_name|fma:Synonym|fma:Non-English_equivalent ?name_inst.
  ?a rdfs:label ?label.
}
```

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