FOIS 2004
International Conference on Formal Ontology in Information Systems

Ontological Foundations of Biological Continuants

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Representation of Continuants in Bio-ontologies

- Human Anatomy
  - Foundational Model of Anatomy (FMA)
  - Portions of SNOMED, OpenGalen, MeSH
- Other Organisms
  - Open Biological Ontologies (OBO)
    - Mouse (developmental stages), Zebrafish, Drosophila,…
- Species-Independent
  - Gene Ontology: Cellular Component branch

Size: 10^3 (Adult Mouse) – 10^5 (FMA)

Mouse (embryonal stage TS11, source: MGI)

- cardiovascular system
- - heart
- - - cardiogenic plate

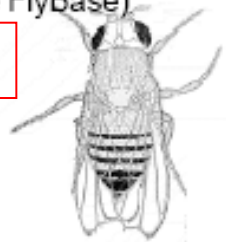
Mouse (embryonal stage TS18 , source: MGI)

- cardiovascular system
- - heart
- - - atrio-ventricular canal
- - - atrium
- - - bulboventricular groove
- - - bulbus cordis
- - - endocardial cushion tissue
- - - mesentery
- - - outflow tract
- - - pericardium
- - - primitive ventricle
- - - sinus venosus

Mouse (embryonal stage TS26 , source: MGI)

- cardiovascular system
- - heart
- - - aortic sinus
- - - atrio-ventricular canal
- - - atrio-ventricular cushion tissue
- - - atrium
- - - bulbar cushion
- - - endocardial cushion tissue
- - - endocardial tissue
- - - mesentery
- - - pericardium
- - - trabeculae carneae
- - - valve
- - - ventricle

Drosophila (adult, source FlyBase)

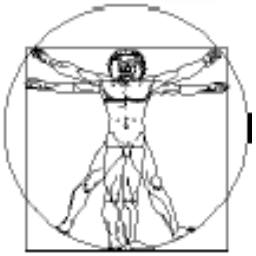


- circulatory system
- - heart
- - - heart muscle
- - - adult aortic funnel
- - - adult ostia
- - - dorsal diaphragm
- - - heart chamber
- - - terminal opening

Zebrafish (adult, source: ZFIN)

- cardiovascular system
- - heart
- - - atrium
- - - bulbus arteriosus
- - - hypobranchial vessels
- - - sinus venosus
- - - ventricle

Human, Adult, (source: FMA)



- cardiovascular system
- - heart
- - - wall of heart
- - - right atrium
- - - left atrium
- - - right ventricle
- - - left ventricle

} is-a organ chamber

- - - right side of heart
- - - left side of heart
- - - fibrous skeleton of heart
- - - papillary muscle
- - - cardiac valve
- - - tricuspid valve
- - - mitral valve
- - - aortic valve
- - - pulmonary valve

} is-a cardiac valve

- - - interatrial septum
- - - (...)

Semantic framework for biological structure…

- Foundational Relations
- General Attributes
- Theories

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Some Foundational Relations between Biological Continuants

Rel(x,y) — y / x	**Classes**	**Individuals**
Classes	*Is-A*	
Individuals	*Instance-of*	*part-of, has-location has-branch, bounds, connects has-developmental-form*

Some Foundational Relations between Biological Continuants

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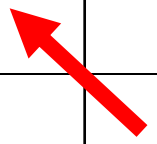
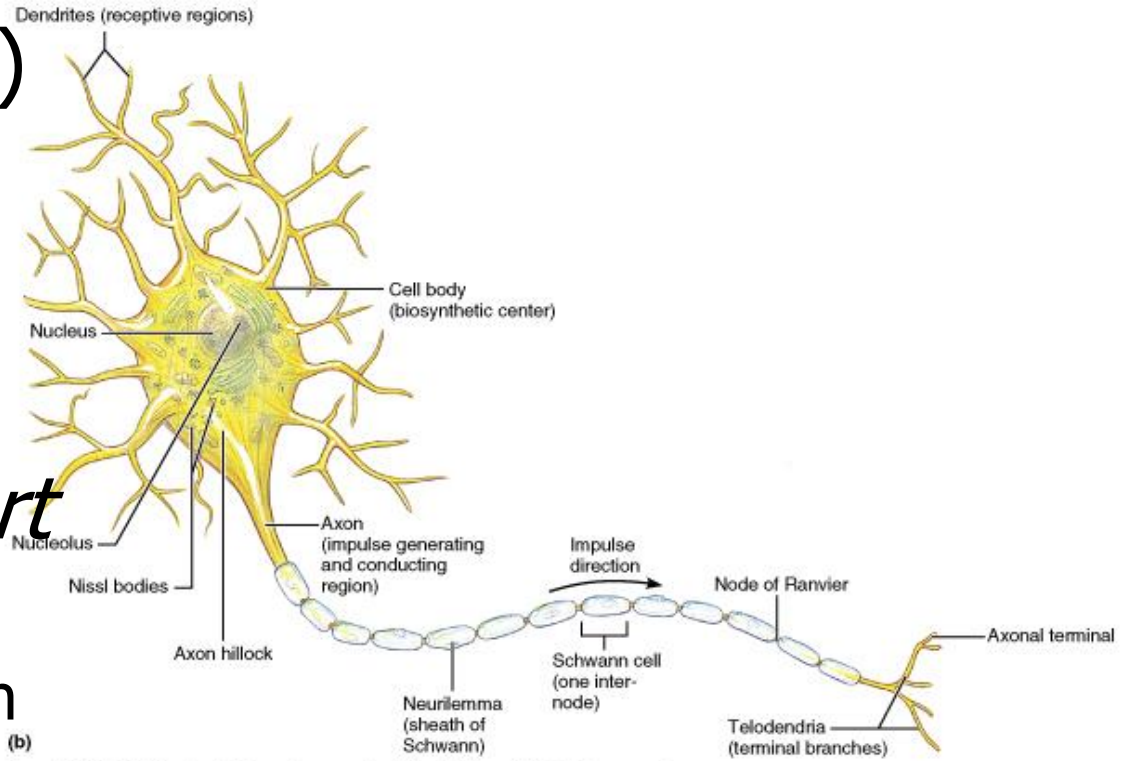


Some Foundational Relations between Biological Continuants

Rel(x,y) y / x	**Classes**	**Individuals**
Classes	*Is-A, Part-Of, Has-Location Bounds, Has-Branch, Connects Has-Developmental-Form*	
Individuals	*Instance-of*	*part-of, has-location has-branch, bounds, connects has-developmental-form*

Class-Level Relations (I)

- "*Cell has-part Axon*" (Gene Ontology)
  - Do cells without axons exist ?
  - Do axons without cells exist ?
- "*Neuron has-part Axon*" (FMA)
  - Does every neuron has an axon?



Class-Level Relations (II)

- "*Cell has-part Axon*" (Gene Ontology)
  - Do cells without axons exist ?
  - Do axons without cells exist ?
- "*Neuron has-part Axon*" (FMA)
  - Does every neuron has an axon?

"Keep in mind that part_of means can be a part of, not is always a part of "
GO Editorial Style Guide, Oct 2003

***"The part_of relationship (…) is usually necessarily* is_part"**
GO Editorial Style Guide, Jan 2004

"A part_of B if and only if: for any instance x of A there is some instance y of B which is such that x stands to y in the instance-level part relation, and vice versa".

Rosse & Smith MEDINFO 2004

Class-Level Relations (III)

A, B: classes,
inst-of: class membership
rel: relation between instances
Rel: relation between classes

$$Rel\ (A, B) =_{def}$$

$$\forall x: inst\text{-}of(x, A) \rightarrow \exists y: inst\text{-}of\ (y, B) \wedge rel\ (x, y)$$

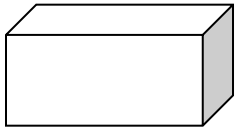
cf.
Schulz (AMIA 2001)
Schulz & Hahn (KR 2004, ECAI 2004)
Rosse & Smith (MEDINFO 2004)

Semantic framework for biological structure…

- Foundational Relations
- General Attributes
- Theories

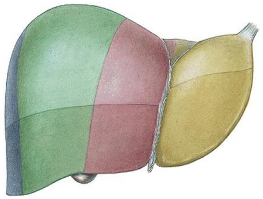
General Attributes (top level categories)

- Point
- 1-D
- 2-D
- 3-D

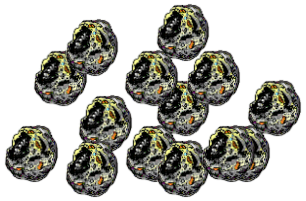
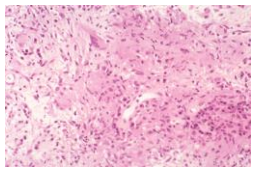



- Solids
- Holes
- Boundaries





- Pluralities
- Masses
- Count Objects


cf. Schulz & Hahn, FOIS 01

Semantic framework for biological structure…

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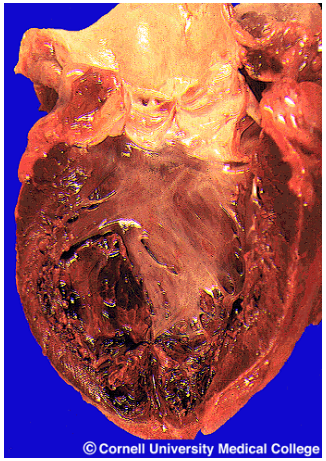
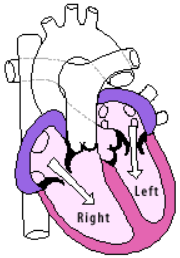
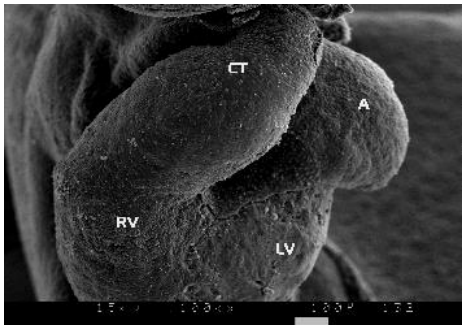
“Heart”


© Cornell University Medical College


V
BA


Left
Right


CT
A
RV
LV

Theories

- A set of formal axioms which describe a restricted (local) domain.
- Four orthogonal theories for Biological Structure
  - **Granularity**
  - **Species**
  - **Development**
  - **Canonicity**

Theories

- A set of formal axioms which describe a restricted (local) domain.
- Four orthogonal theories for Biological Structure

Granularity	**epistemiological**
Species	
Development	**ontological**
Canonicity	

Theories

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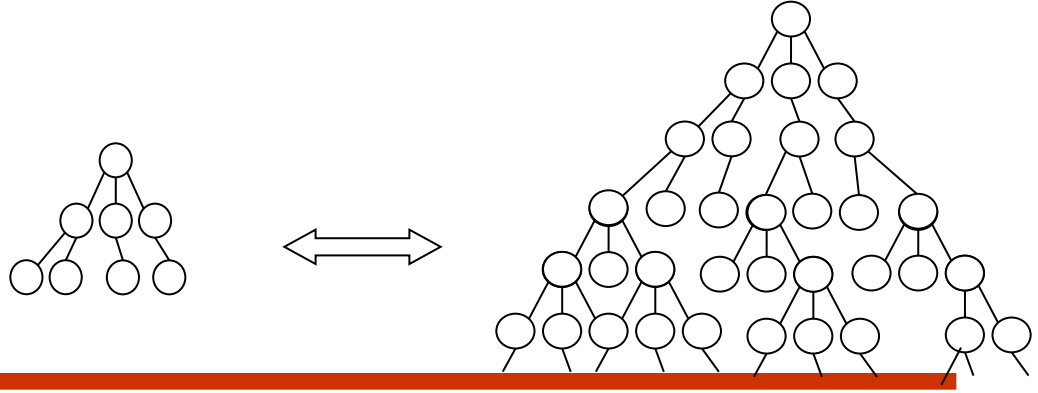
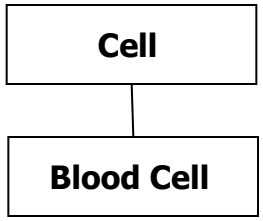
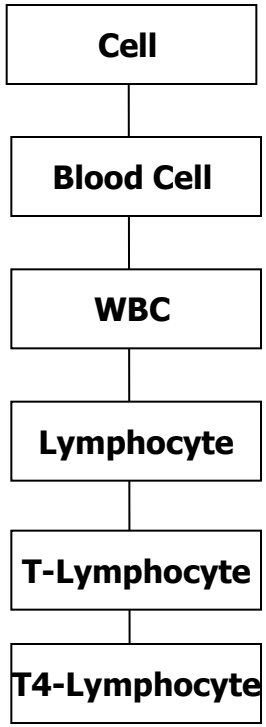
Granularity



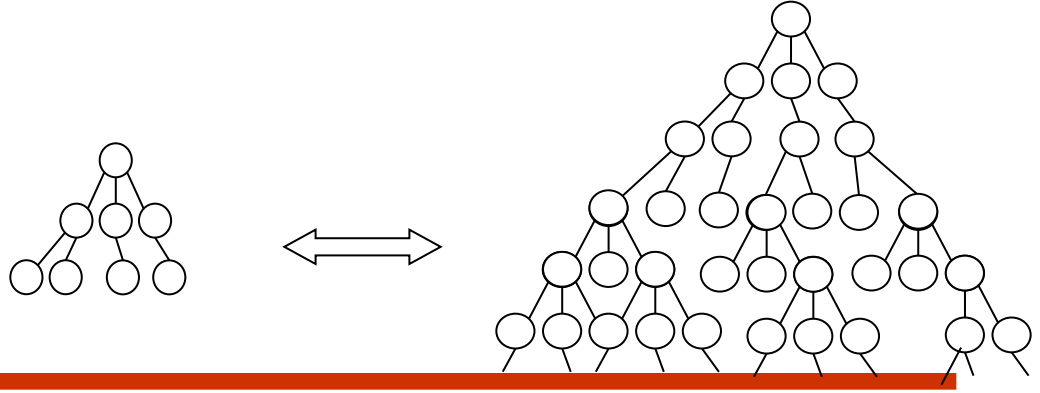
- Classification (level of detail of class distinction)



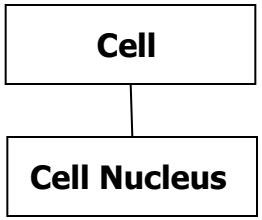


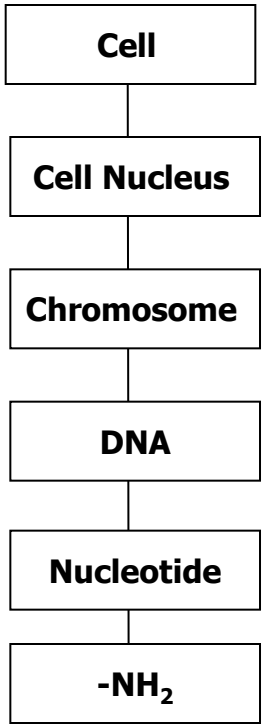
(taxonomy)

Granularity



- Classification (level of detail of class distinction)
- Dissection (focus on organism, tissue, cell, molecule)



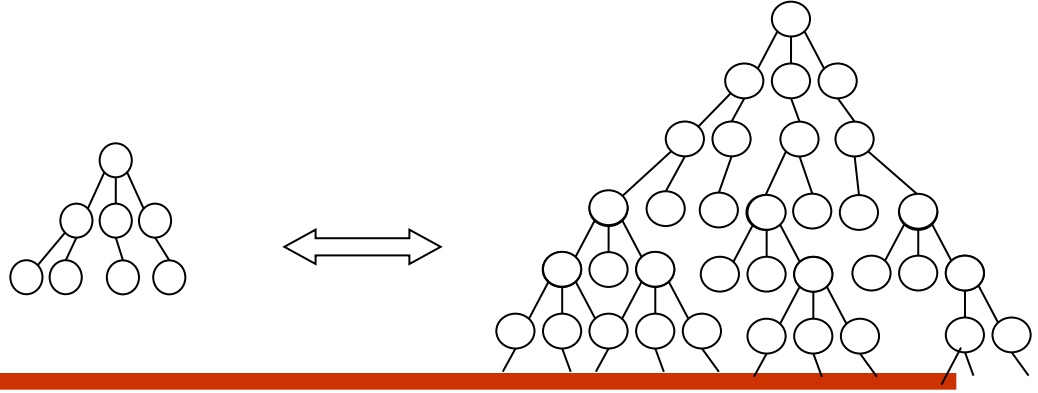


(partonomy)

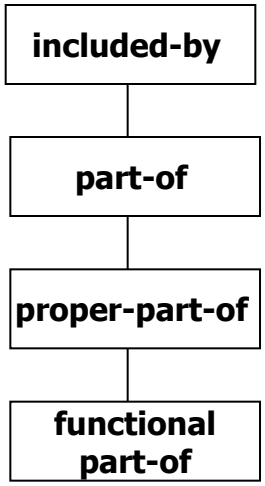
Granularity of Dissection

- Change in Granularity level may be non-monotonous
  - Change of sortal restrictions:
    - 3-D $\rightarrow$ 2-D boundary
    - Plurality $\rightarrow$ Mass object
  - Change of relational attributions:
    - disconnected $\rightarrow$ connected

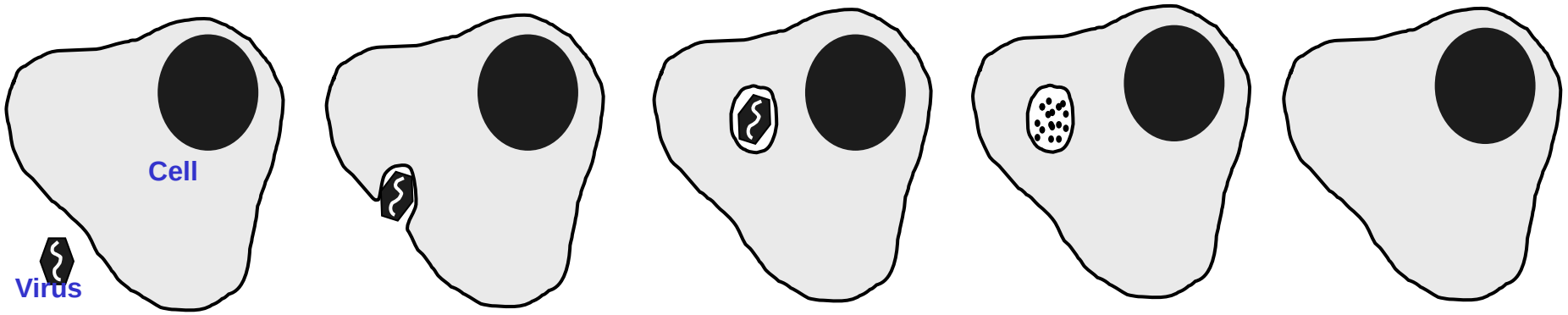
Granularity



- Classification (level of detail of class distinction)
- Dissection (focus on organism, tissue, cell, molecule)
- Relations (relation hierarchy vs. few foundational relations)



Granularity of Relations



included-by(CellNucleus, Cell)

part-of(CellNucleus, Cell)

included-by(VirusProtein, Cell)

part-of(VirusProtein, Cell) ??

Theories

- A set of formal axioms which describe a restricted (local) domain.
- Four orthogonal theories for Biological Structure
  - **Granularity**
  - **Species**
  - **Development**
  - **Canonicity**

Linnean Taxonomy of Species

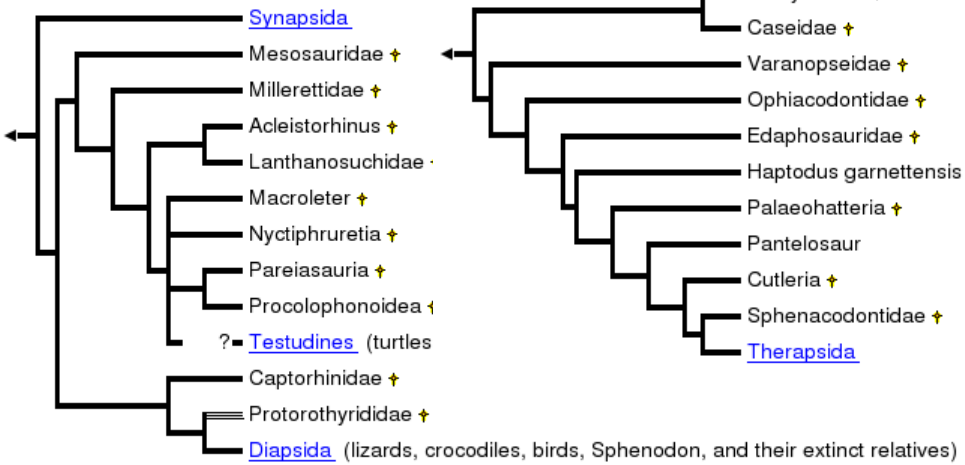
Deuterostomia
- Echinodermata
- Hemichord
- Chordata
  - ?– Calcichordata †
  - Urochordata (tunicates)
  - Cephalochordata (a
  - Yunnanozoon †
  - Craniata — Hyperotreti, Vertebrata
    - Hyperoartia (lampreys)
    - ?– Euconodonta †
    - Pteraspidomorphi †
    - ?≡ Thelodonti †
    - ?– Anaspida †
    - Galeaspida †
    - ?– Pituriaspida †
    - Osteostraci †
    - Gnathostomata
      - Sarcopterygii
      - Actinopterygii
      - Acanthodii †
      - Chondrich
      - Placoderm
        - ?– Onychodontiformes †
        - Coelacanthimorpha
        - Porolepimorpha †
        - Dipr taxon links
        - Rhizodontimorpha †
        - Osteolepimorpha †
        - Terrestrial Vertebrates

Ecdysozoa
- Arthropoda
- Onychophora (velvet worms)
- Tardigrada (water bears)
- Nematoda (roundworms)
- Nematomorpha (horsehair worms)
- Kinorhyncha
- Loricifera
- Priapulida (penis worms)

Lophotrochozoa
- ?– Platyhelminthes (flatworms, tapeworms, flukes)
- ?– Chaetognatha (arrow worms)
- ?– Gastrotricha
- ?– Rotifera (rotifers)
- ?– Gnathostomulida (jaw worms)
- ?– Micrognathozoa
- ?– Cycliophora
- ?– Mesozoa
- Annelida (bristleworms, ragworms, earthworms, leeches and their allies)
- Sipuncula (peanut worms)
- Mollusca (snails, clams, squids, etc.)
- Nemertea (ribbon worms)
- Bryozoa (moss animals)
- Entoprocta (kamptozoans)

THE TREE OF LIFE WEB PROJECT
http://tolweb.org

Linnean Taxonomy of Species



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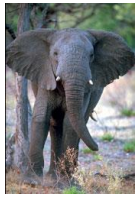
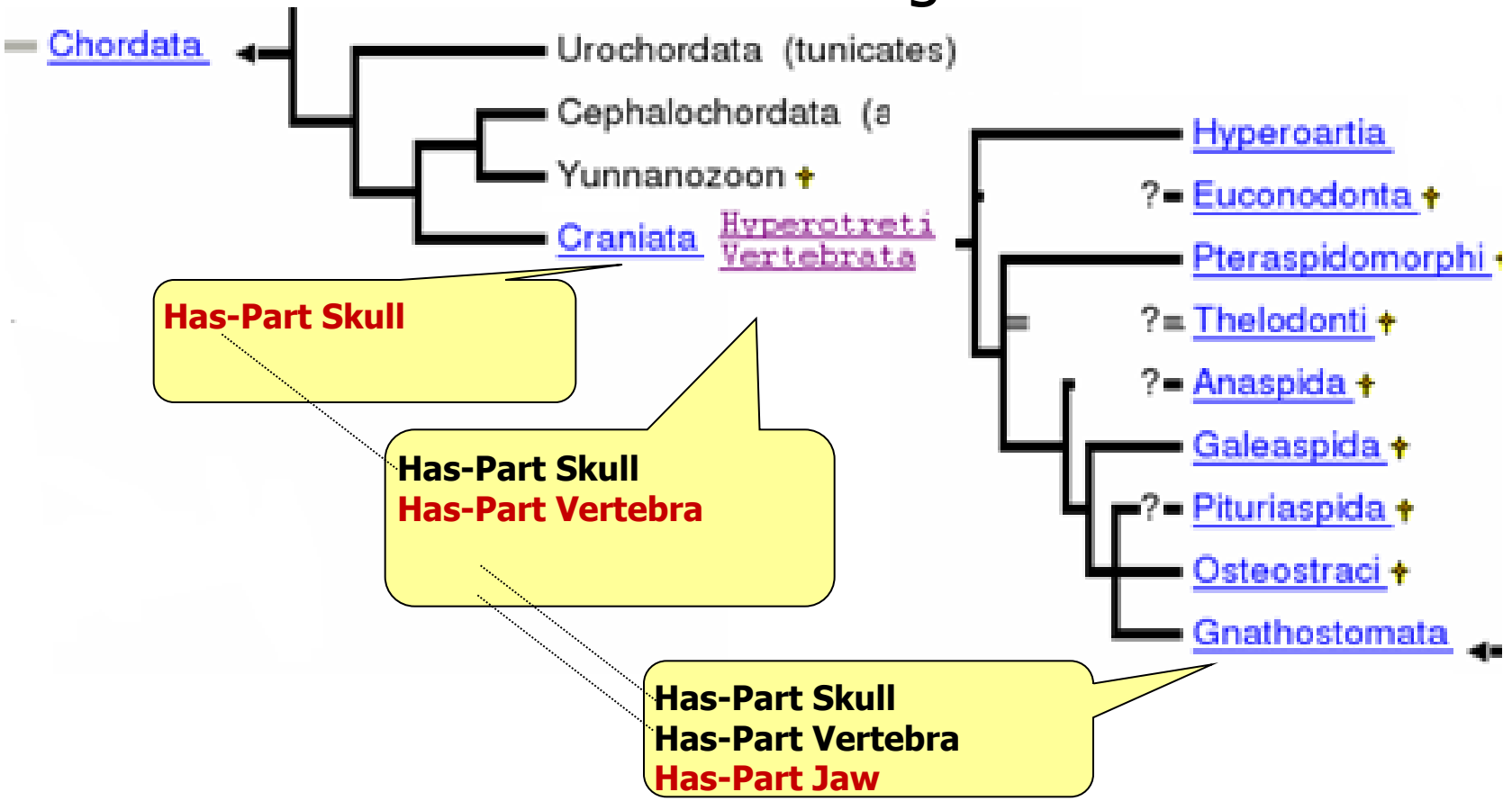


- Triconodonts †
- Monotremata
- taxon links
- Multituberculata
- Marsupialia
- Palaeoryctoids †
- Eutheria
  - Edentata (anteaters, sloths, armadillos)
  - Pholidota (pangolins)
  - Glires
    - Lagomorpha (rabbits, hares, and pikas)
    - Rodentia (mice)
    - Macroscelidea
  - Primates
    - Platyrrhini
    - Catarrhini
      - Cercopithecidae
      - Hominidae
        - Pongo (orangutan)
        - Pan (chimpanzee and bonobo)
        - Ardipithecus †
        - Australopithecus †
        - Homo (humans)
        - Gorilla
      - Hylobatidae
    - Tarsii
    - Strepsirhini
  - Scandentia
  - Chiroptera (bats)
  - Dermoptera (colugos or flying lemurs)
  - Insectivora (shrews, moles, hedgehogs, etc.)
  - Creodonta †
  - Carnivora (dogs, cats, bears, raccoons, weasels, mongooses, hyenas, seals, walruses)
  - Condylarthra †
  - Artiodactyla (pigs, deer, cattle, goats, sheep, hippopotamuses, camels, etc.)
  - Cetacea (whales, dolphins, porpoises)
  - Tubulidentata (aardvark)
  - Perissodactyla (horses, tapirs, rhinoceroses)
  - Hyracoidea (hyraxes, dassies)
  - Sirenia (manatees, dugong, sea cow)
  - Desmostylia †
  - Embrythopoda †
  - Proboscidea (elephants, mammoths, mastodons, etc.)

Species

Introduction of axioms at the highest common level

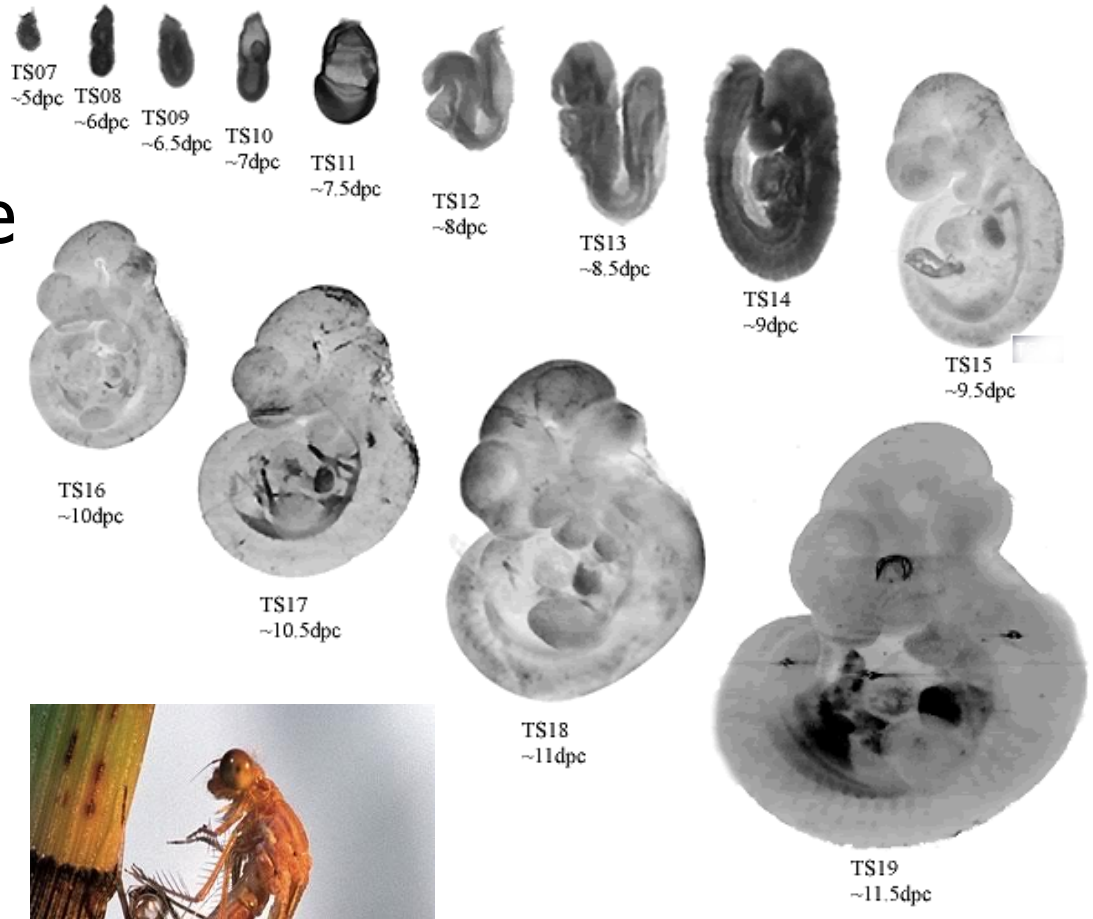


Theories

- A set of formal axioms which describe a restricted (local) domain.
- Four orthogonal theories for Biological Structure
  - **Granularity**
  - **Species**
  - **Development**
  - **Canonicity**

Development

- Represents time-dependent "snapshots" from the life cycle of an organism, e.g., zygote, embryo, fetus, child, adult
- Development stages are species-dependent e.g. metamorphosis



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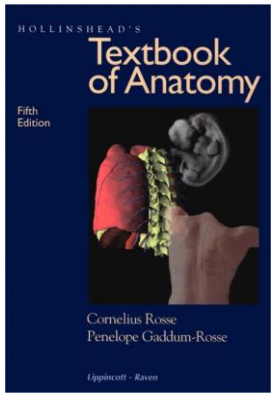
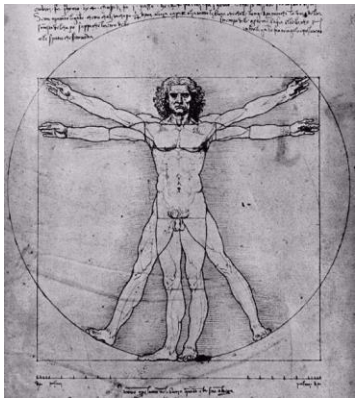
Canonicity

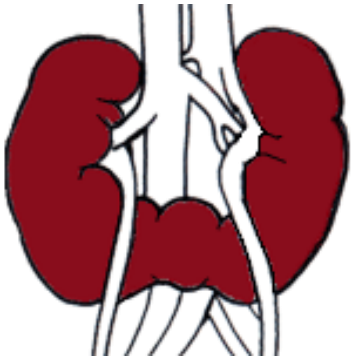
- Degrees of "Wellformedness" of Biological Structure:
  - Canonic structure





Canonicity

- Degrees of "Wellformedness" of Biological Structure:
  - Canonic structure
  - Structural Variations



Canonicity

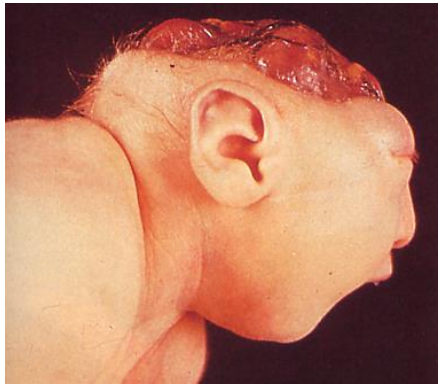
- Degrees of "Wellformedness" of Biological Structure:
  - Canonic structure
  - Structural Variations
  - Pathological Structure

acquired

congenital

Canonicity

- Degrees of "Wellformedness" of Biological Structure:
  - Canonic structure
  - Structural Variations
  - Pathological Structure
  - Lethal Structure



Canonicity

- Degrees of "Wellformedness" of Biological Structure:
  - Canonic structure
  - Structural Variations
  - Pathological Structure
  - Lethal Structure
  - Derivates of biological structure

Canonicity

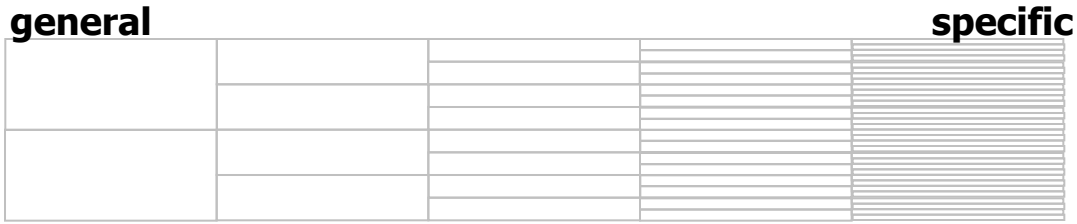
- Five canonicity levels: each level introduces axioms valid for higher levels

Level	1	2	3	4	5
Theory	any amount of matter, if of biological origin	any living or dead organism	any living organism	living organism without pathologic modifications	ideal organism
Set of Axioms	n_1	n_2 $n_1 \subset n_2$	n_3 $n_2 \subset n_3$	n_4 $n_3 \subset n_4$	n_5 $n_4 \subset n_5$

Examples

Granularity

Species



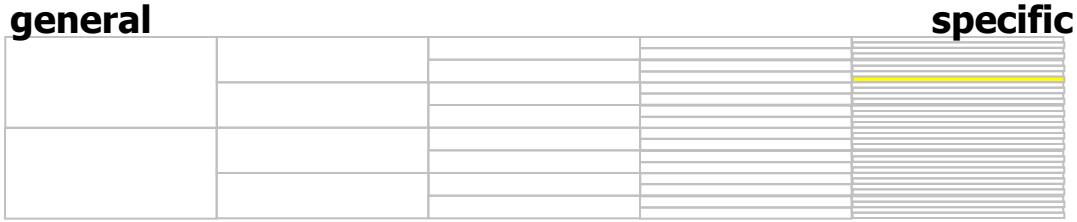
Development

Canonicity

Coverage: Foundational Model of Anatomy

Granularity

Species



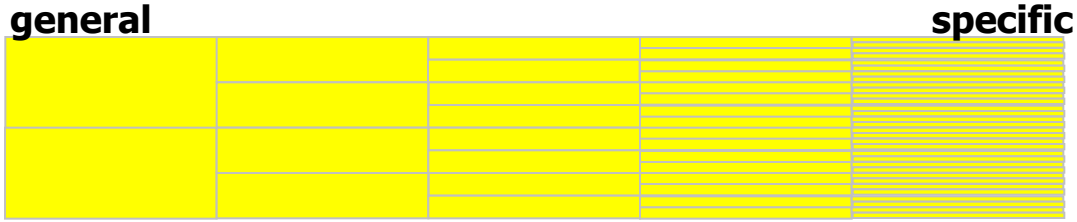
Development

Canonicity

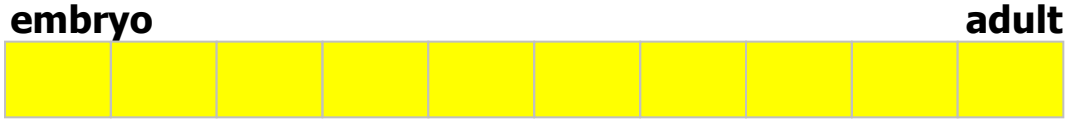
Coverage:
Gene Ontology

Granularity

Species



Development

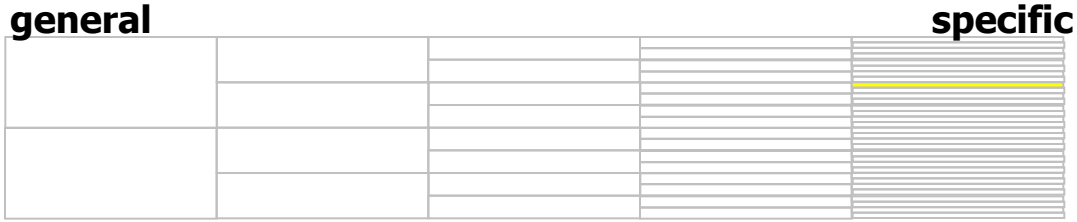


Canonicity

Coverage:
Mouse Anatomy

Granularity

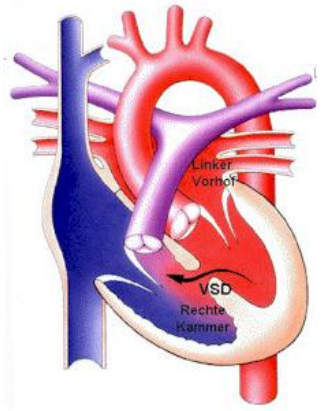
Species



Development

Canonicity

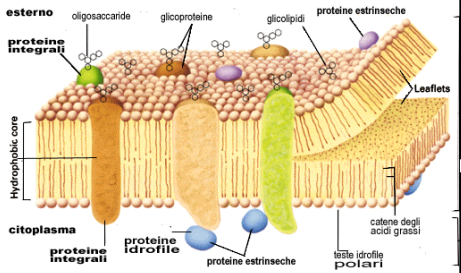
Examples



Connects (RightVentricle, Left Ventricle)

Granularity	**= normal**	**false**
Species	**= mammal**	
Development	**= adult**	
Canonicity	**= 4-5**	

Granularity	**= any**	**true**
Species	**= vertebrate**	
Development	**= early embryo**	
Canonicity	**= any**	



Is-A (Membrane, 3-D object)

Granularity	**= normal**	**true**
Species	**= any**	
Development	**= any**	
Canonicity	**= any**	

Granularity	**= lowest**	**false**
Species	**= any**	
Development	**= any**	
Canonicity	**= any**	

Conclusion

- Integration of bio-ontologies requires
  - Uncontroversial semantics of relations and attributes
  - Clear commitment to theories, such as granularity, species, development and canonicity
- Redundancy can be avoided
  - Encoding axioms at the highest common level in the species taxonomy (e.g. vertebrates, arthropods, primates) and benefit from inheritance in subsumption hierarchies

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