Enabling Part-Whole Reasoning in Biomedical Terminologies

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Objectives

- Understand the ontological disctinction between taxonomic (*is-a*) and partonomic (*part-of*, *has-part*) hierarchies in the biomedical domain.
- Understand the peculiarities of partonomic reasoning in comparison to taxonomic reasoning
- Appreciate a formal ontology engineering approach that emulates partonomic reasoning by classification-based taxonomic reasoning
- Discuss these findings in the light of the requirements of knowledge engineering in medicine and biology

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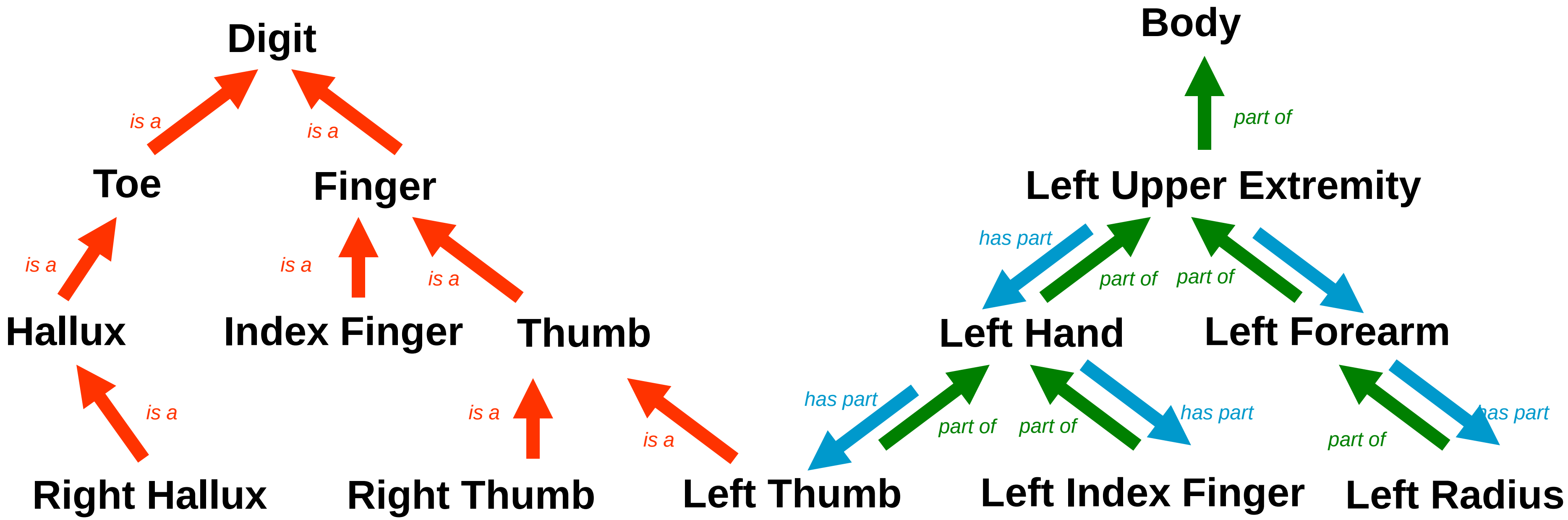
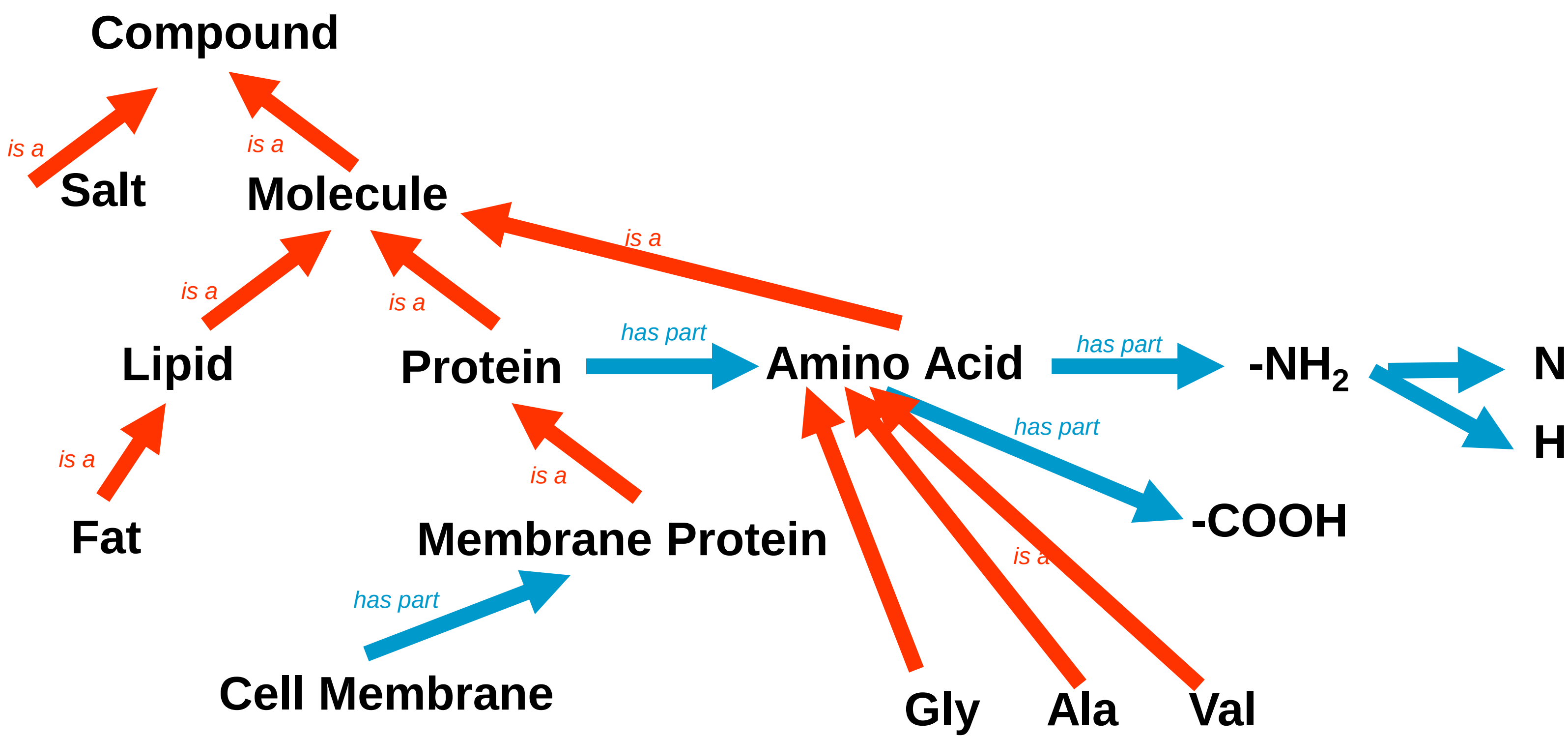
Double Hierarchical Structure: Anatomy

Taxonomic Order	*(is a)*
Mereologic Order	*(part of, has part)*



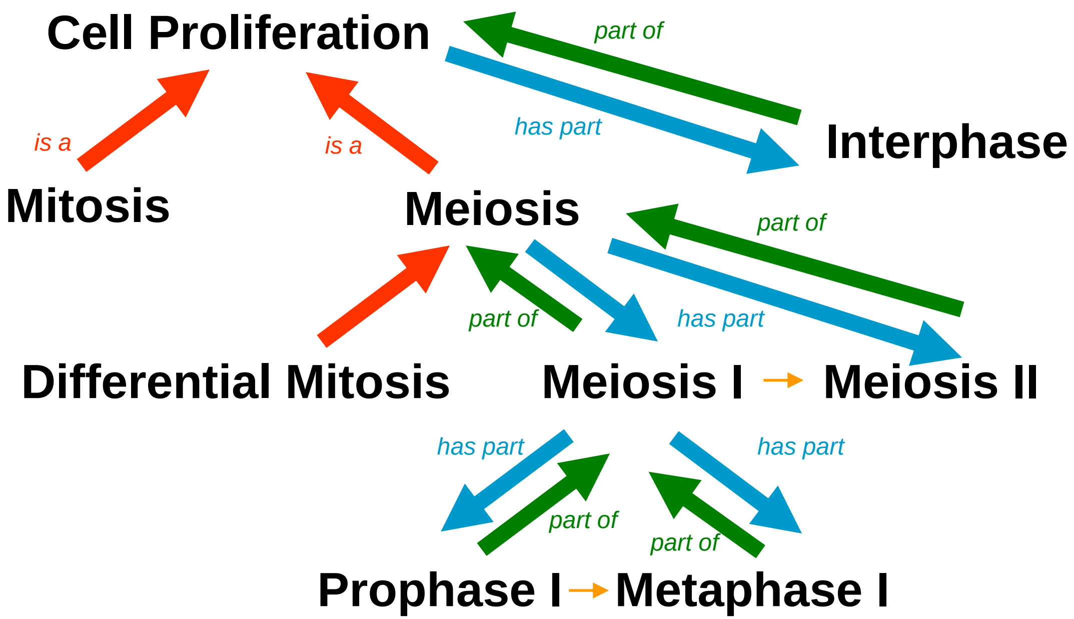
Double Hierarchical Structure: Biochemistry

Taxonomic Order	*(is a)*
Partonomic Order	*(part of, has part)*



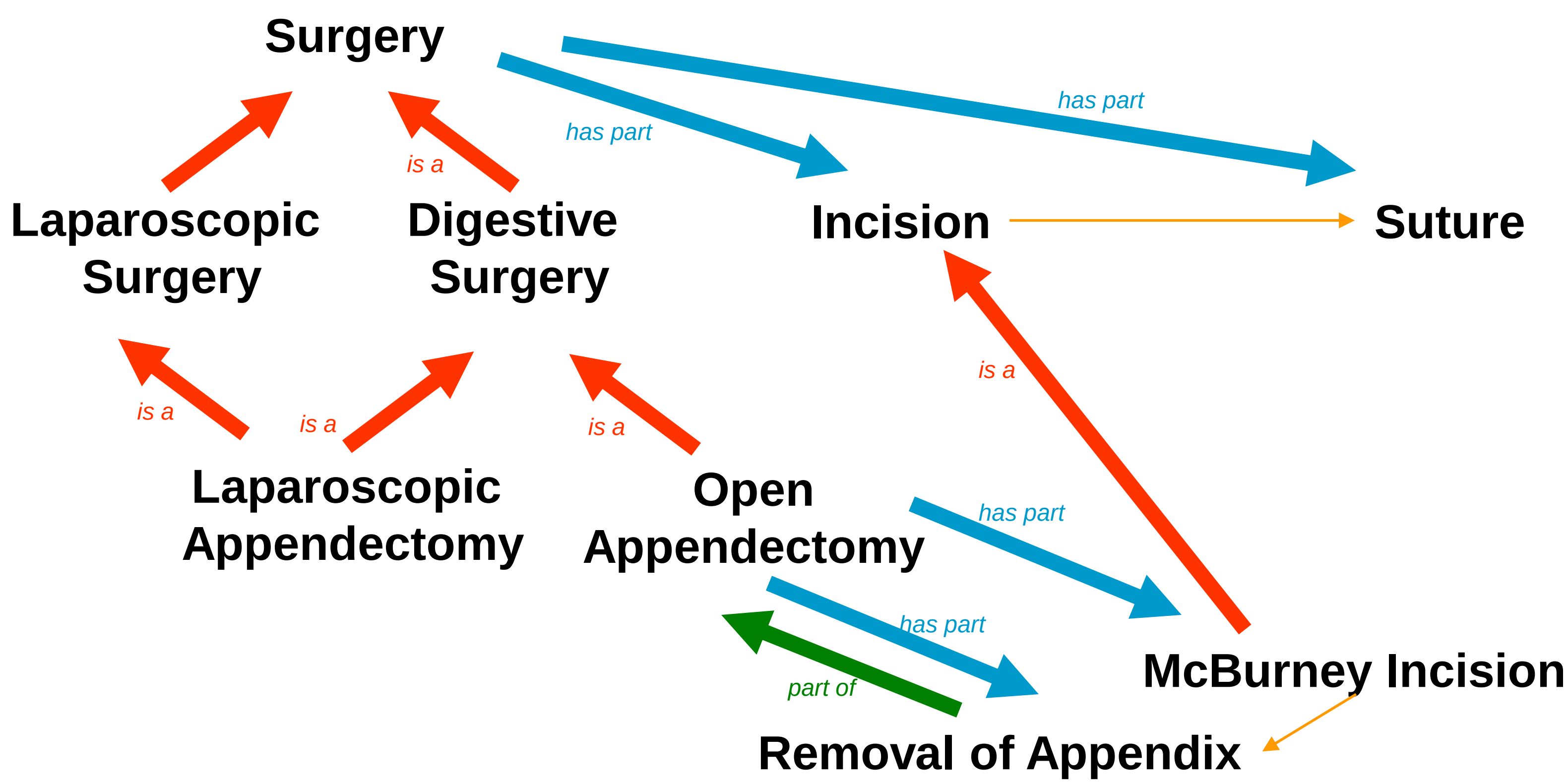
Double Hierarchical Structure: Events

Taxonomic Order	*(is a)*
Partonomic Order	*(part of, has part)*
Temporal Order	*(follows)*



Double Hierarchical Structure: Actions

Taxonomic Order	*(is a)*
Partonomic Order	*(part of, has part)*
Temporal Order	*(follows)*



Conclusion

- Ubiquity of partonomies in the ordering of biomedically relevant knowledge
- Part-of and has-part relation capture notions of
  - physical parts (components) and wholes
  - constituents of substances
  - events and subevents
  - actions and parts of actions

Partonomies in Medical Terminologies (I)

- ICD: only taxonomic structure
- Terminologia Anatomica: no explicit hierarchical relations
- MeSH: broader/narrower hierarchy regardless of taxonomic or partonomic meaning
- Read Codes, SNOMED CT: „Structure“ concepts subsume both an anatomical entity and its parts

Partonomies in Medical Terminologies (II)

- Digital anatomist: clear distinction between part-of/has-part and is-a. Recently sub-relations of part-of/has-part
- GeneOntology: clear distinction between part-of and is-a.
- OpenGalen: clear distinction between part-of and is-a. Formal reasoning across part-of
- UMLS: mostly broader/narrower hierarchies, part-of/is-a restricted to anatomy (comes from Digital Anatomist)

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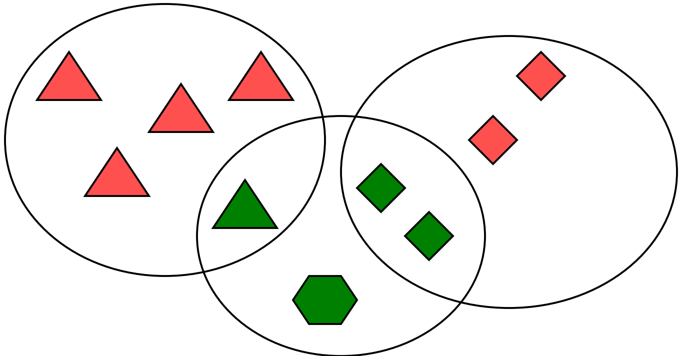
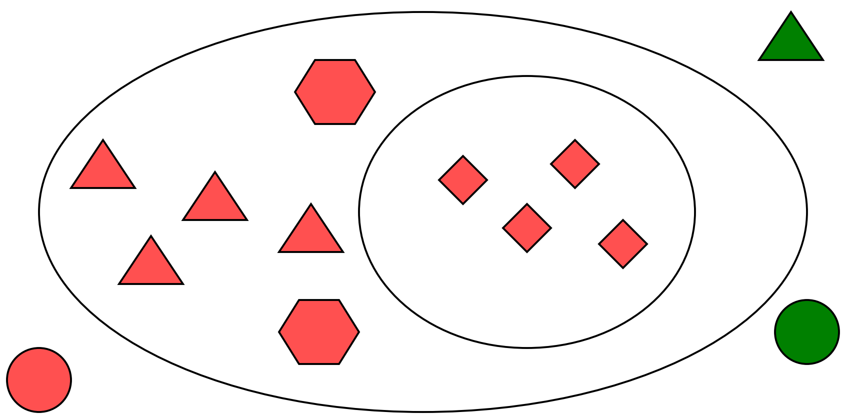
Commonalites of Taxonomic Reasoning (I)

- Classes vs. Instances:
  - Instances are concrete objects in the world, e.g. *my left thumb*, *Peter‘s cat*, *Mr X‘s diabetes*, ...
  - Classes denote abstract entities, e.g. all fingers, all cats, all occurrences of diabetes
  - The assignment of individuals to a class normally obeys defined *properties*.



Commonalites of Taxonomic Reasoning (II)

- Class subsumption & Inheritance:
  - One class C_1 subsumes an other one C_2 if each of the instances of C_2 is an instance of C_1, too.
  - All properties of C_2 are inherited by C_1 . Example: Birds can fly → eagles can fly
  - Multiple inheritance



Commonalites of Taxonomic Reasoning (III)

- Transitivity & Roles:
  - *C_1 subsumes $C_{2,,}$ and subsumes C_3* → *C_1 subsumes C_3*
    Example: lymphocyte is a leukocyte is a cell → lymphocyte is a cell
  - Roles: attributes containing links to another concept, e.g.
    ∃has-location Liver is a role for *Liver disease,* and is therefore inherited by all subsumees, e.g. *Hepatitis, Hepatitis A* etc.

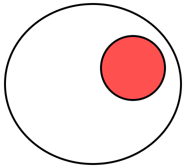
Commonalites of Partonomic reasoning (I)

- Mereology: reasoning about individuals, not abstract entities
- *part-of* relation in its broadest sense
  - transitive: I_1 *part-of* I_2, I_2 *part-of* I_3, → I_1 *part-of* I_3
  - reflexive: I_1 *part-of* I_2 → I_2 *part-of* I_1
- Subrelations of *part-of*
  - non-reflexive: proper-part-of (common notion when describing the physical world)
  - non-transitive: combinations of subrelations (hand *part-of* musician *part-of* orchestra)

Commonalites of Partonomic reasoning (II)

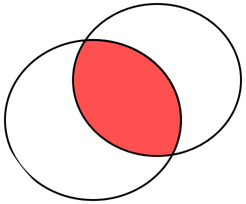
- Inverse relation: *has-part*

  I_1 *part-of* $I_2 \leftrightarrow I_2$ *has-part* I_1

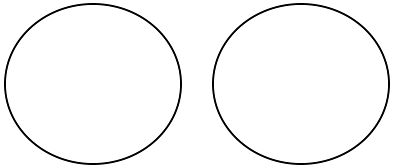
  MyBrain part-of MyHead ↔ *MyHead has-part MyBrain*

- Overlap: I_1 *part-of* I_2 , I_1 *part-of* I_3 → I_2 *overlaps* with I_3

  MyBrain part-of MyHead, MyBrain part-of MyCNS → *MyHead overlaps MyCNS*

- Disconnected: I_2 *disconnected* from I_3 if they do not share any parts

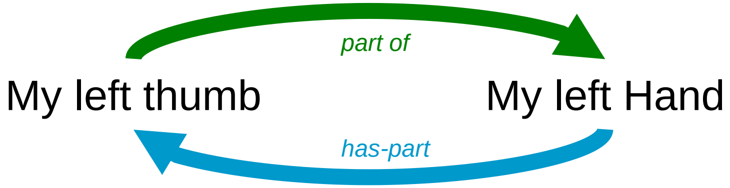
  MyHead disconnected from MyFoot, but also *MyHead disconnected from X's CNS*

Taxonomies (*is-a*) vs. Partonomies (*part-of*, *has-part*)

- Main difference:
  - The *is-a* relation relates <u>concepts</u> (classes of individuals)
  - *part-of* and *has-part* relate <u>individuals</u> (concepts don‘t have parts !)
- How to use the part-of relation in conceptual systems ?
  - Additional semantics needed !

Partonomic Relations between Individuals and Concepts

- between individuals:



$\forall(x,y)$: *x part-of y* ⇔ *y has-part x*

- between concepts:

UMLS

CUI1	RELA	CUI2
HEART	has part	MITRAL-VALVE
MITRAL-VALVE	part of	HEART
HEART	has part	HEART-SEPTUM
HEART-SEPTUM	part of	HEART
HEART	has part	MYOCARDIUM
MYOCARDIUM	part of	HEART
HEART	has part	CAVITY-OF-HEART

„Heart *has-part* Mitral Valve“

- Possible Meanings:
  - $\exists x,y$: *Heart(x)* $\wedge$ *Mitral-Valve(y)* $\wedge$ *x has-part y*
    “a heart can have a mitral valve”
  - $\forall x{:}\exists y$: Heart(*x*) $\wedge$ *Mitral-Valve(y)* $\wedge$ *x has-part y*
    “every heart has a mitral valve as part”
  - $\forall x{:}\exists y$: *x has-part y* $\Leftrightarrow$ $\forall y{:}\exists x$: *y part-of x*
    “If for every x there is a part y, then for every y there is an x it is part of

Semantics for Partonomies in Concept Systems (I)

hnw

- *A has-necessary-whole B*: All instances of a concept *A* have the role *part-of* filled by an instance of *B (necessary condition)*

  $A \sqsubseteq \exists part\text{-}of.B$

hnp

- *B has-necessary-part A*: All instances of a concept *B* have the role *has-part* filled by an instance of *A (necessary condition)*

  $B \sqsubseteq \exists has\text{-}part.A$

- *A has-necessary-whole B* does not necessarily imply B *has-neceesary-part* A

Semantics for Partonomies in Concept Systems (II)

hpw

- *A* *has-possible-whole* *B*: Instances of *A* and *B* are in the extension of the relation *part-of*

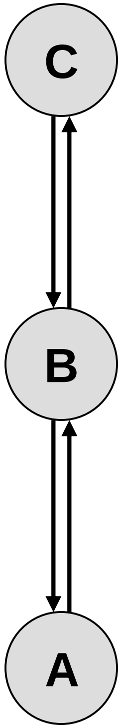
hpp

- *B* *has-possible-part* *A*: Instances of *A* and *B* are in the extension of the relation *has-part* .

- *A* *has-necessary-whole* *B* implies *B* *has-possible-part* *A*
- *A* *has-possible-whole* *B* implies *B* *has-possible-part* *A*
- B *has-necessary-part* A *implies A* *has-possible-whole* *B*
- B *has-possible-part* A *implies A* *has-possible-whole* *B*
- *A disconnected from B:* nothing can be part of both and instance of *A* and of *B*

Stipulations for Part/Whole Combinations

	A *hnw* B	B *hnp* A	*pw*(A,B)	*dc*(A,B)
B *hnw* C	A *hnw* C	*pw*(A,B)	*pw*(A,B)	*pw*(A,B)
C *hnp* B	*pw*(A,B)	C *hnp* A	*pw*(A,B)	*pw*(A,B)
pw(B,C)	*pw*(A,B)	*pw*(A,B)	*pw*(A,B)	*pw*(A,B)
dc(B,C)	*dc*(A,C)	*pw*(A,B)	*pw*(A,B)	*pw*(A,B)



hnw = has necessary whole
hnp = has necessary part

hpw = has possible whole
hpp = has possible part
} *pw* = can be related by part-whole

dc = disconnected (cannot have common parts)

Examples for part-of / has-part Asymmetry

- Every *thumb* is part of a *hand*, but not every *hand* has a *thumb*
- Every *spleen* has *lymph follicles*, but not all *lymph follicles* are part of a *spleen*
- Every *cell nucleus* is part of a *cell* but not every *cell* has a *nucleus*
- Every *amino acid* has a *-NH2 group*, but not every *-NH2 group* is part of an *amino acid*
- Every *meiosis* has a *prophase*, but not every *prophase* is part of a *meiosis*
- Every *defibrillation* is part of a *CPR*, but not in every *CPR* there is a *defibrillation*

Reasons for part-of / has-part Asymmetry

has-necessary-whole
has-necessary-part

- Anatomical Variations
  - Azygos Lobe → Lung (has-necessary-whole holds; has-necessary-part negated)
- Congenital Malformations
  - Mitral valve → Heart (has-necessary-whole holds; has-necessary-part negated)
- Pathological Anatomy
  - Glioblastoma → Brain (has-necessary-whole holds; has-necessary-part negated)
- „Iatrogenic Anatomy“
  - Appendix → Intestine (has-necessary-whole holds; has-necessary-part negated)
- Mass concepts
  - Connective Tissue → Liver (has-necessary-whole negated; has-necessary-part holds)
- Multiple objects
  - Goblet cell → Gastric Mucosa (has-necessary-whole negated; has-necessary-part holds)
- Unspecific subevents
  - Suture → Append-ectomy (has-necessary-whole negated; has-necessary-part holds)

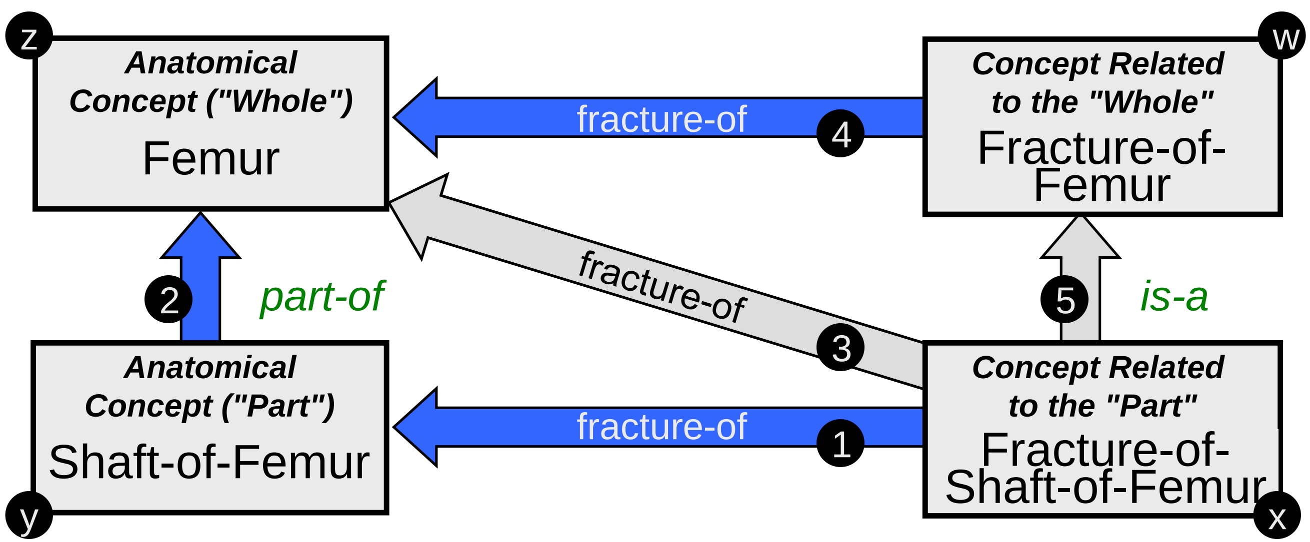
Role Propagation & Concept Specialization

Let *R* be an arbitrary relation

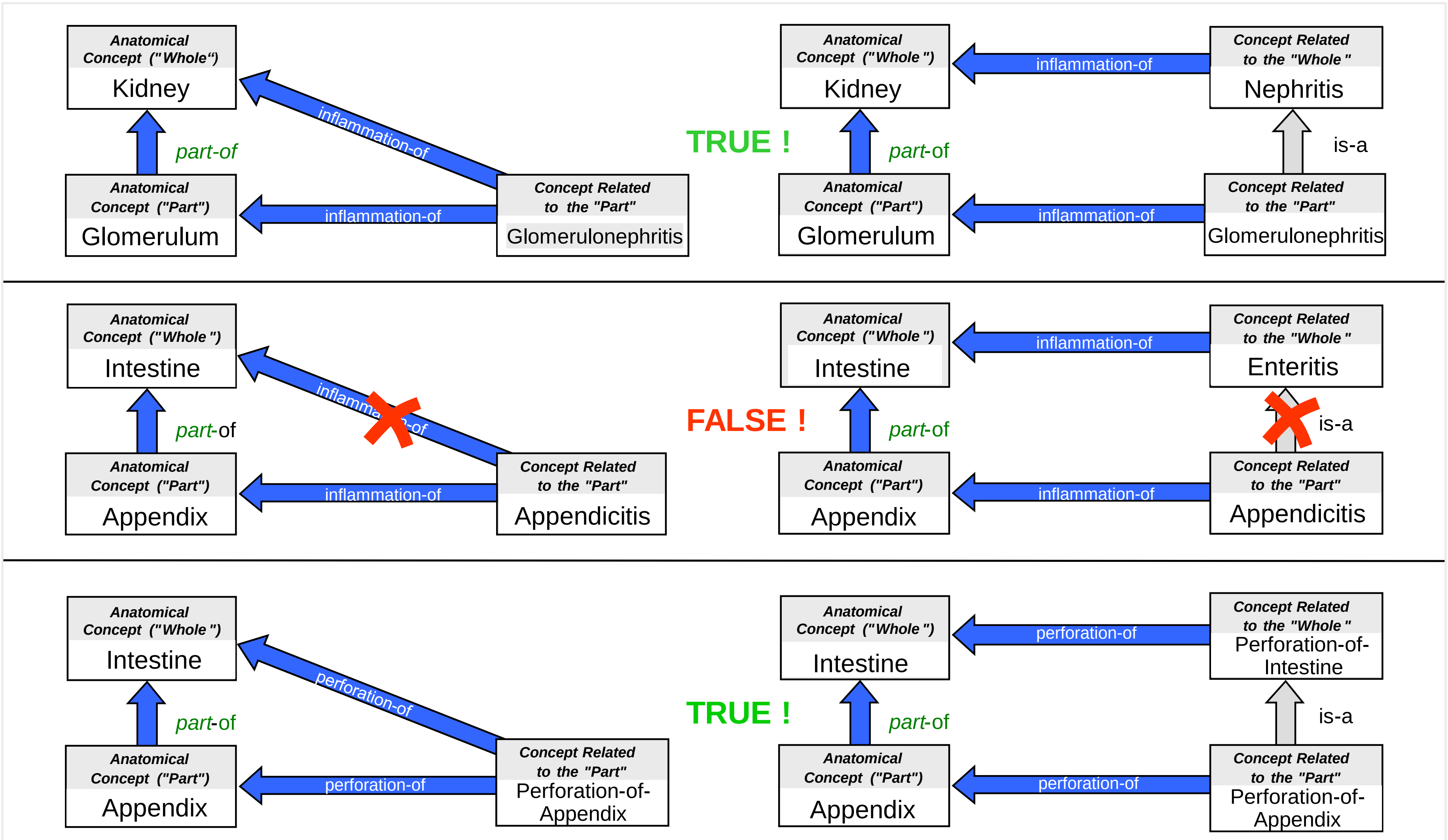
Role Propagation: $y \sqsubseteq \exists \text{part-of}.z \wedge x \sqsubseteq \exists R.y \Rightarrow x \; \exists r.z$

Concept Specialization: $y \sqsubseteq \exists \text{part-of}.z \wedge w \sqsubseteq \exists R.z \wedge x \sqsubseteq \exists R.y \Rightarrow x \sqsubseteq w$

$$xRy \wedge wRz \wedge ySz \Rightarrow xIsAw$$



Reasoning Anomalies within Partonomies



Other examples

insulin synthetase *produce* insulin
beta cells *has-part* insulin synthetase

→ beta cells *produce* insulin
Langerhans islets *has-part* beta cells

→ Langerhans islets *produce* insulin
pancreas *has-part* Langerhans islets

→ pancreas *produce* insulin

amputation of toe *has-target* toe
toe *part-of* foot

→ amputation of toe *has-target* foot
foot *part-of* leg

→ amputation of toe *has-target* leg

amputation of toe *las-location* toe
toe *part-of* foot

→ amputation of toe *las-location* foot

Backbone Fracture *fracture-of* Backbone
Vertebral Fracture *fracture-of* Vertebra
Vertebra *part-of* Backbone

→ Vertebral Fracture *fracture-of* Backbone

Spinous Process Fracture *fracture-of* Vertebra
Backbone Fracture *fracture-of* Backbone
Spinous Process *part-of* Vertebra
Vertebra *part-of* Backbone

→ Spinous Process Fracture *fracture-of* Backbone

Pancreatectomy *removal-of* Pancreas
Pancreas *has-part* Beta Cells
Vertebra *part-of* Backbone

→ Pancreatectomy *removal-of* Beta Cells

Analysis of Reasoning Patterns

- Propagation „downstream“: „*removal-of*“, „*loss-of*“, „*death-of*“
- Propagation „upstream“: „*location-of*“
- No propagation: „*has-target*“
- Uncertain propagation: „*inflammation-of*“, „*fracture-of*“, „*excision-of*“

Important: Most relations have shallow semantics: generalization of propagation behavior is difficult !

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Requirements for a Formal Approach

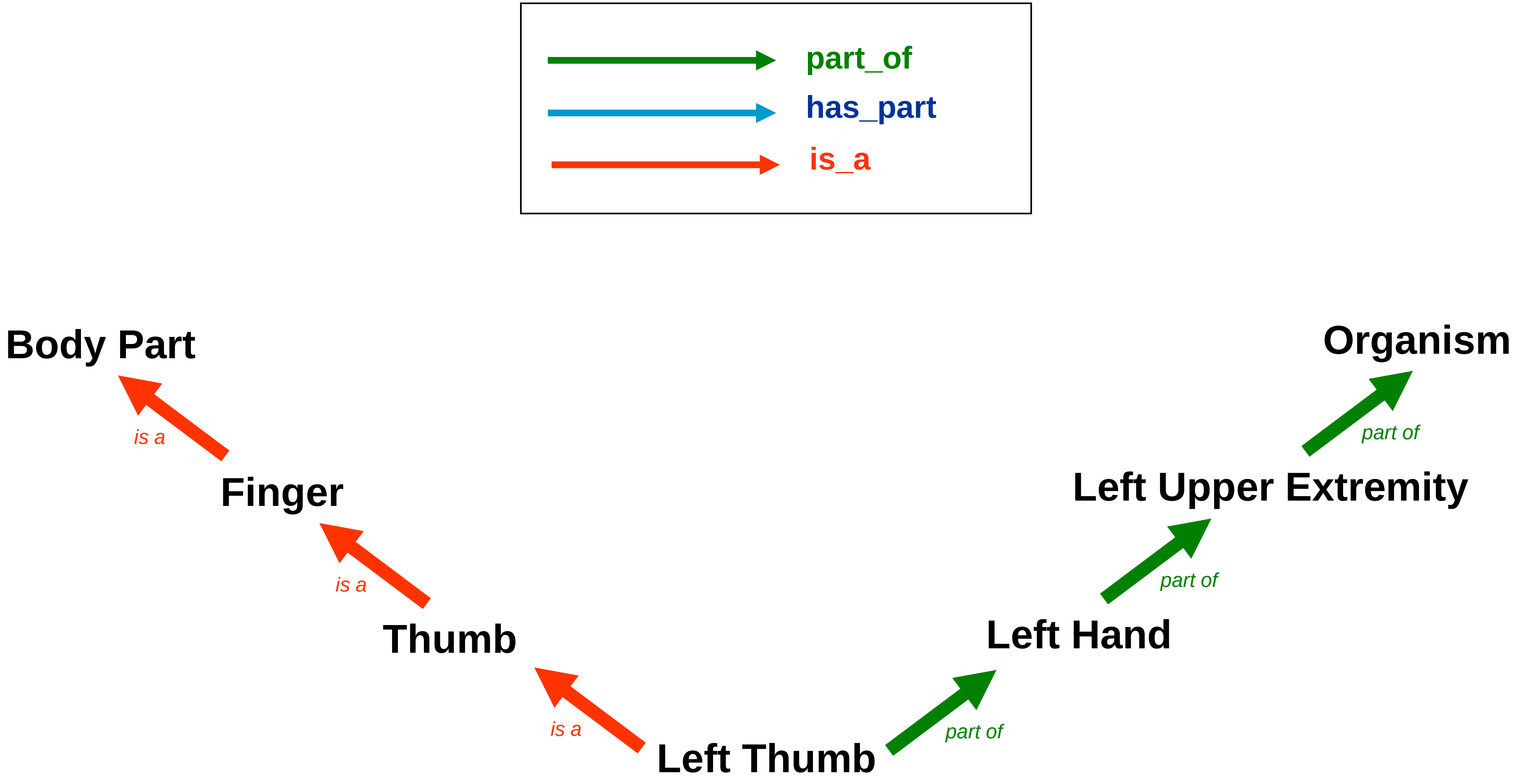
- Retrieve all necessary parts (of necessary parts)* of a concept
  - Blood has-part Erythrocytes
    Erythrocytes has-part Erythrocyte
    Erythrocyte has-part Hemoglobin
    Blood has-part Hemoglobin
- Retrieve all necessary wholes (of necessary wholes)* of a concept
  - Nucleolus part-of Cell-Nucleus
    Cell-Nucleus part-of Eucaryotic-Cell
    Nucleolus part-of Eucaryotic-Cell
- Control propagation of properties along part/whole hierarchies
  - Gas-Exchange function-of Alveolus
    Alveoli has-part Alveolus
    Lung has-part Alveoli
    Gas-Exchange function-of Lung

Mitosis function-of Eucaryotic-Cell
Human-Body has-part Eucaryotic-Cell
Mitosis function-of Human-Body ???

Proposed Solution

- Introduction of "reificator concepts" for each concept and each mereological role
- Mereological reasoning via concept subsumption
- Parsimonious language: concept subsumption, existential quantification, conjunction

Part-Of Hierarchies as Taxonomies



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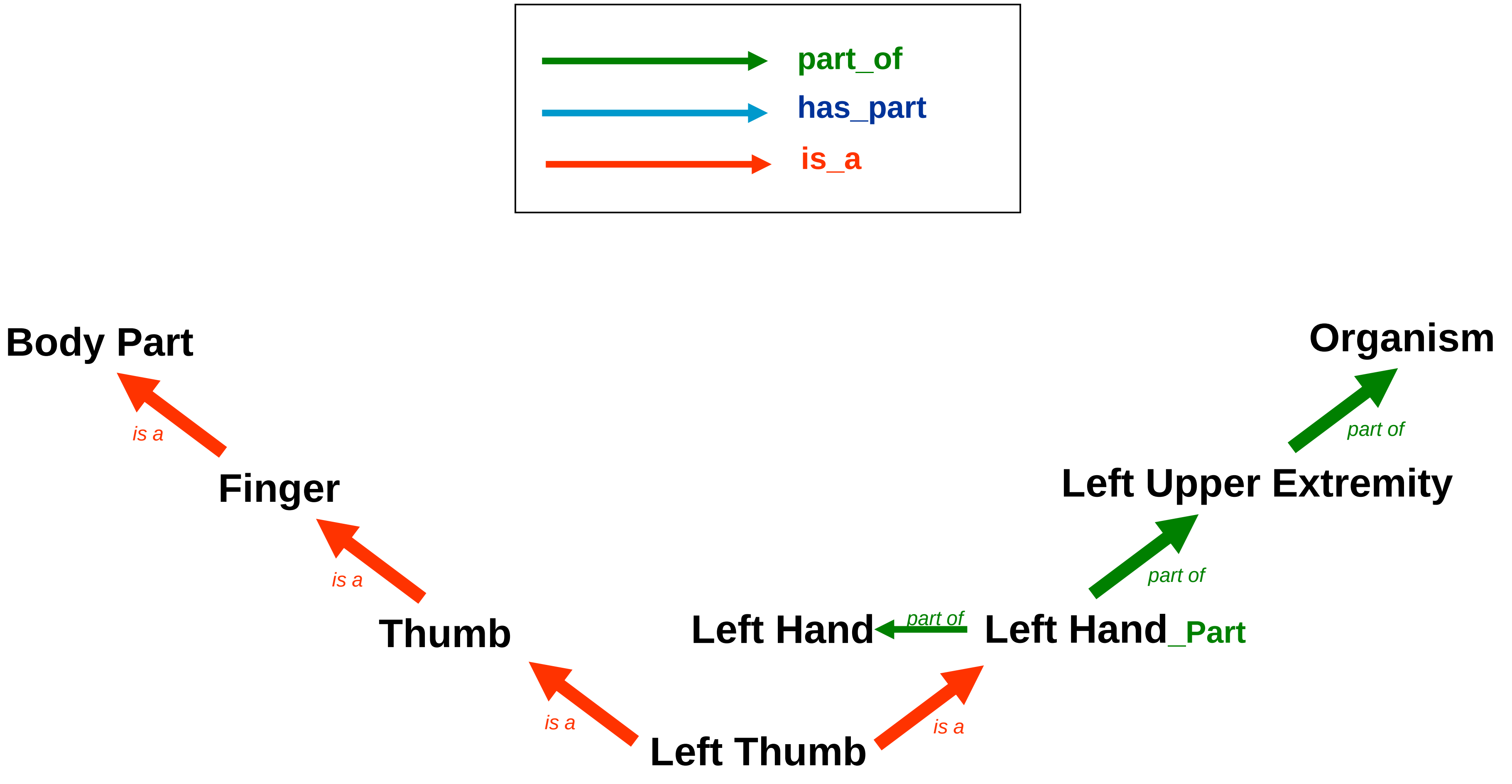

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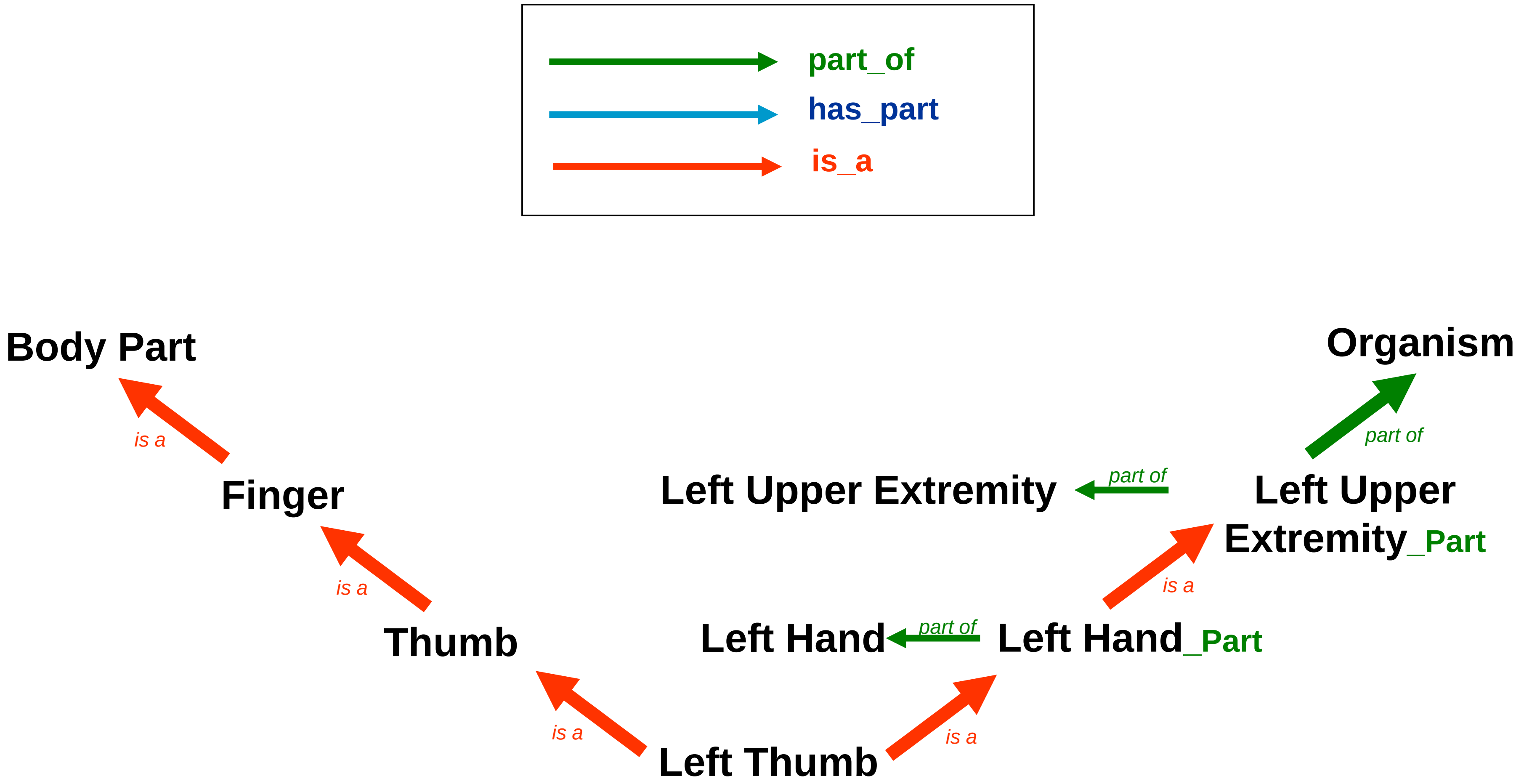

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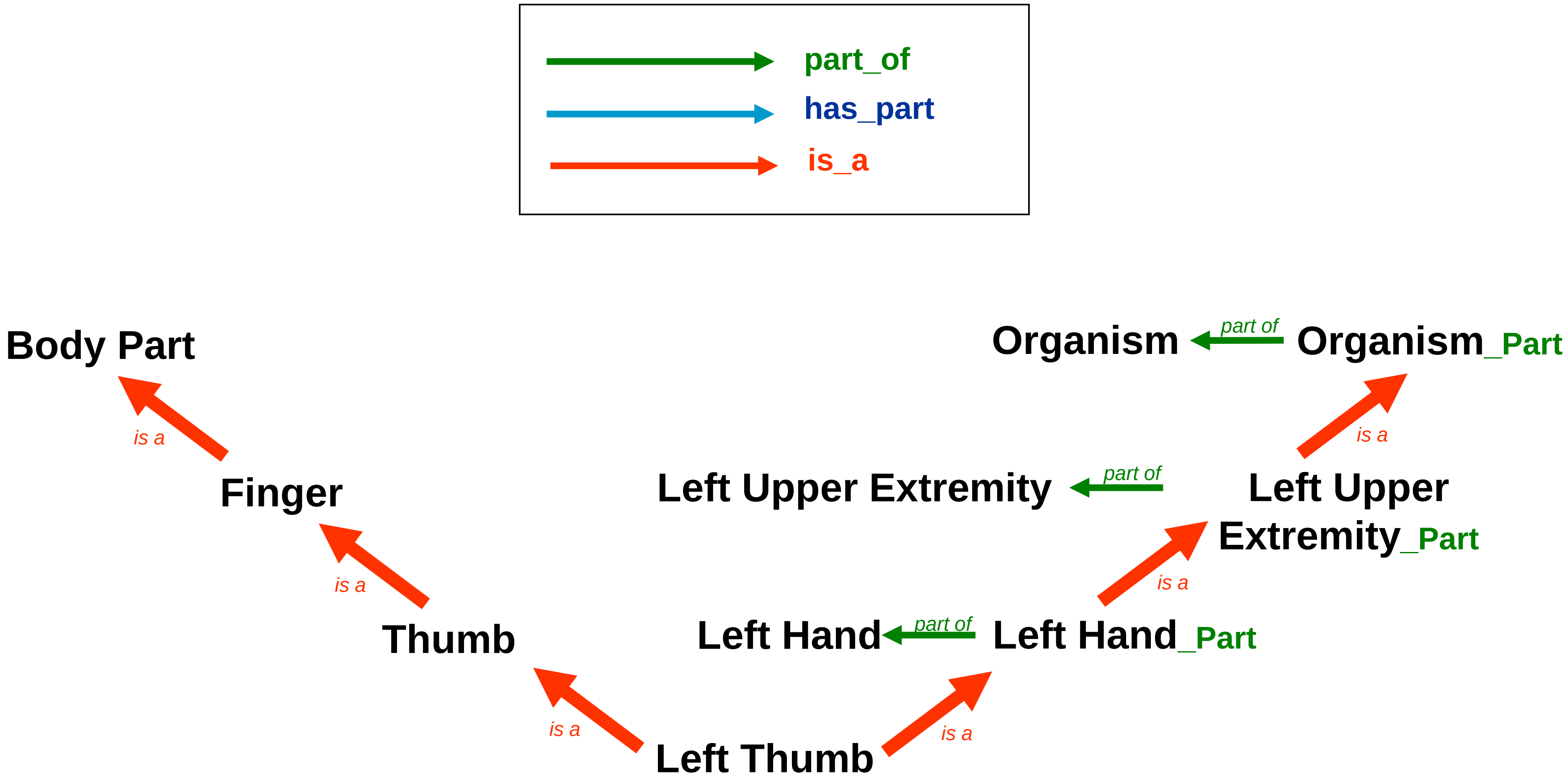
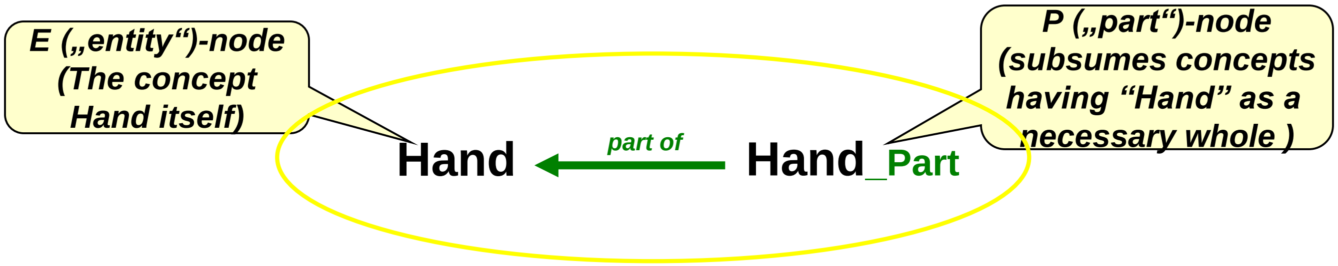
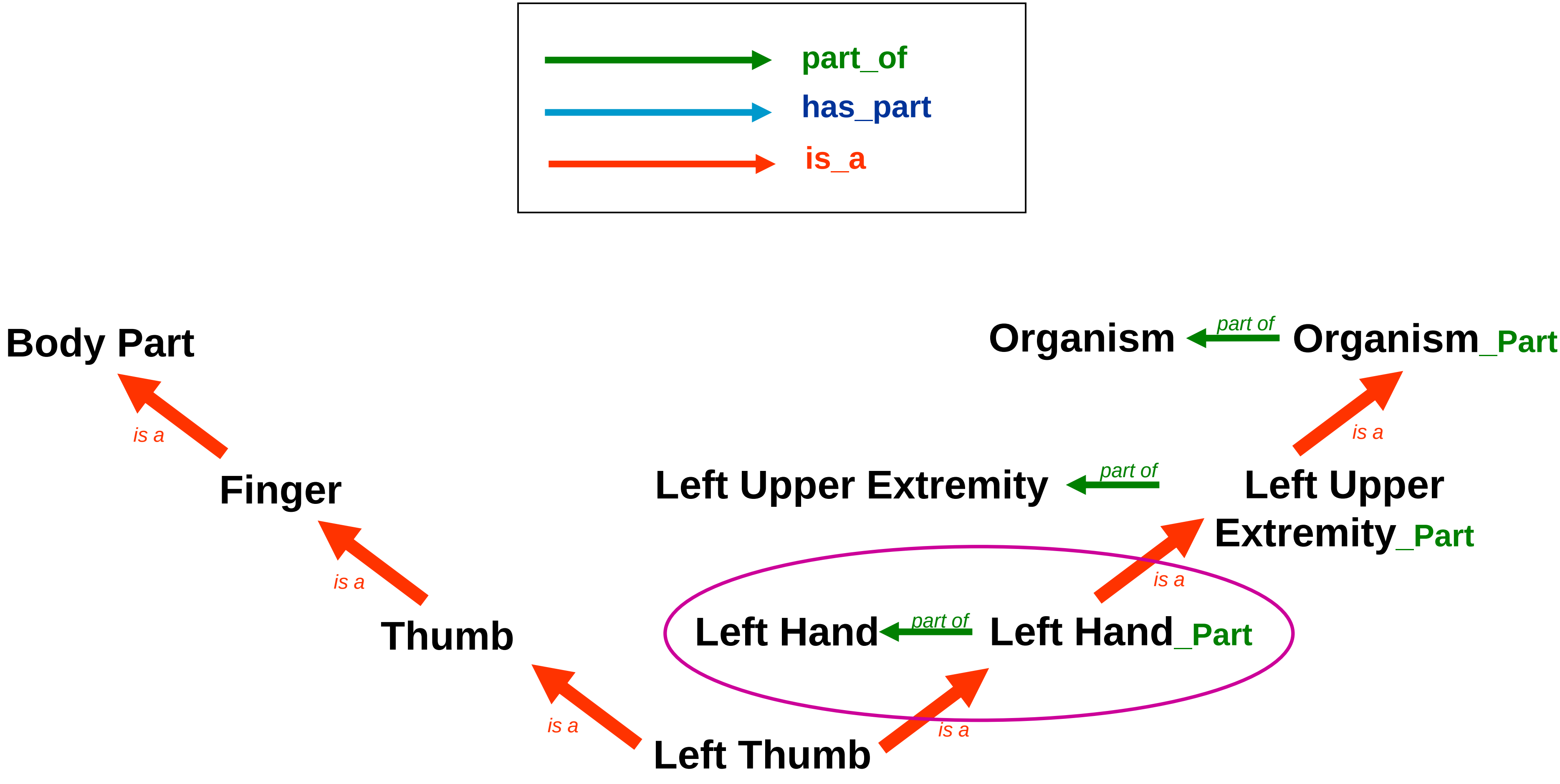


Part-Of Hierarchies by SEP triplets

Schulz et al. AMIA 98; Hahn et al. AAAI 99

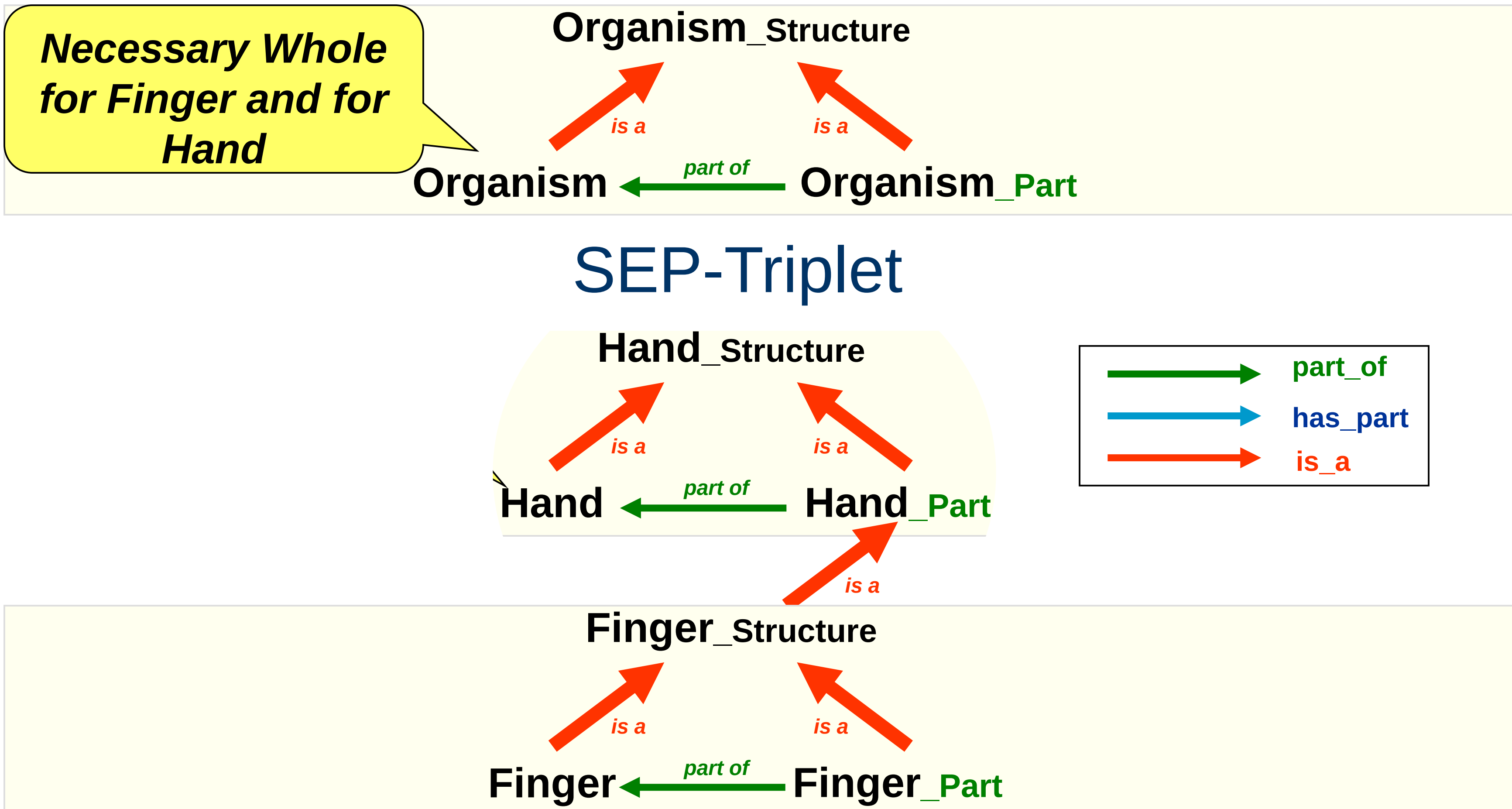


Part-Of Hierarchies as Taxonomies



Part-Of Reification by SEP triplets

Schulz et al. AMIA 98; Hahn et al. AAAI 99



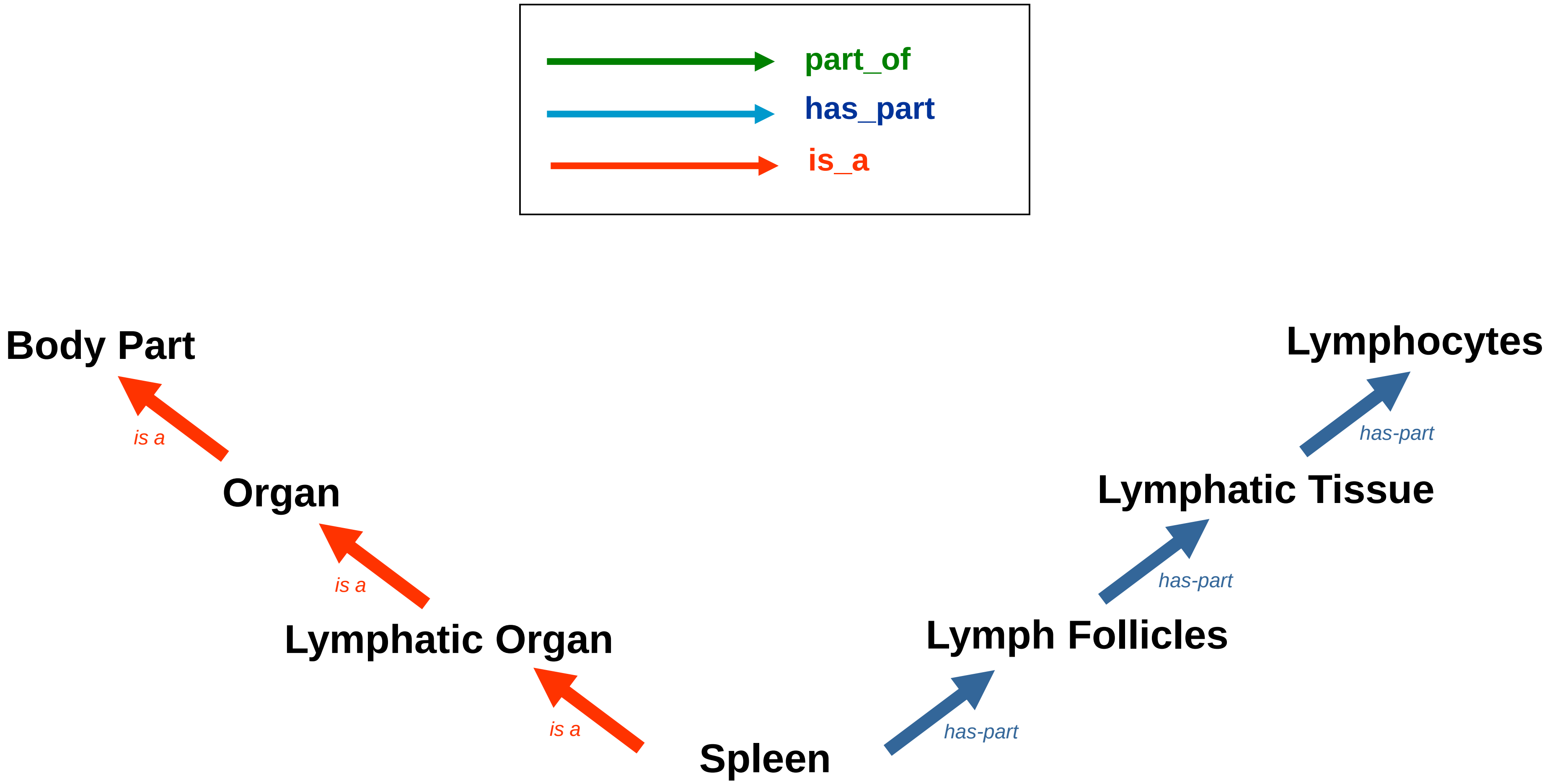
SEP Triplets

- Emulate part-of-hierarchies by taxonomies
- Emulate transitivity of concepts

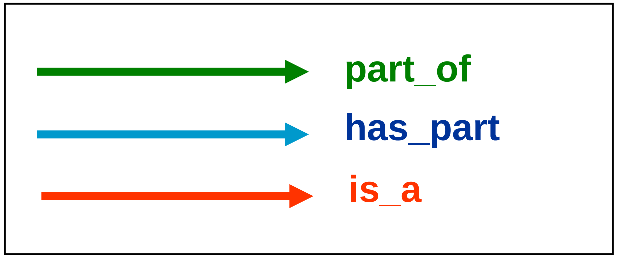
  Finger *is a* Hand_Part, Hand_Part *is a* Arm_Part ⇒

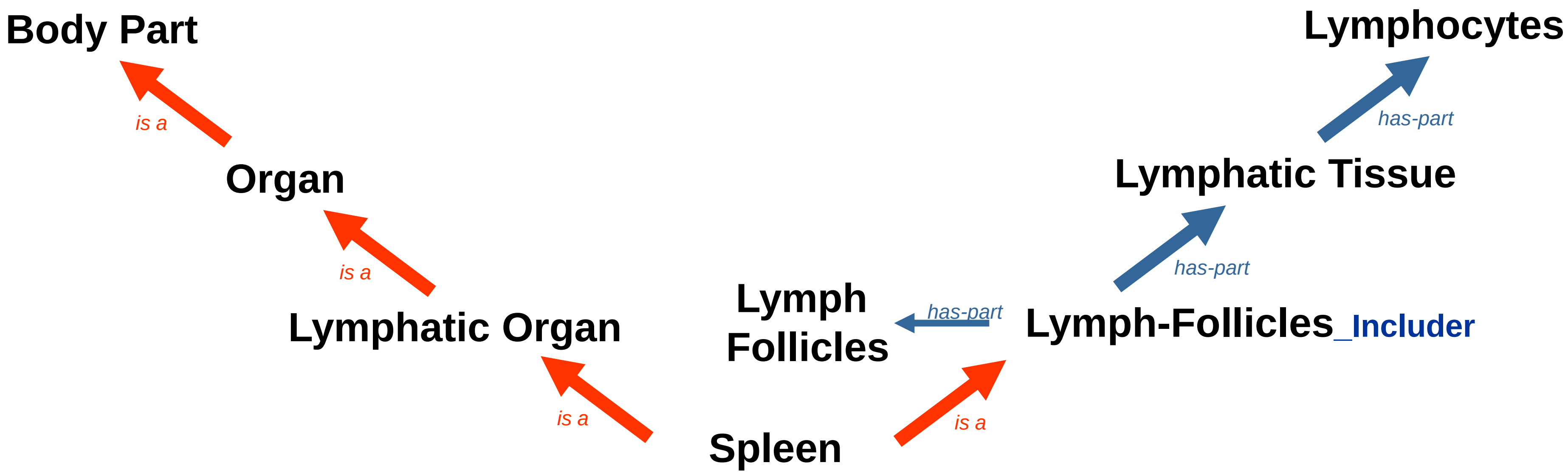
  Finger *is a* Arm_Part
- Necessary wholes can be inferred by taxonomic subsumption
- What about necessary parts ?

Has-Part Hierarchies as Taxonomies



Has-Part Hierarchies as Taxonomies





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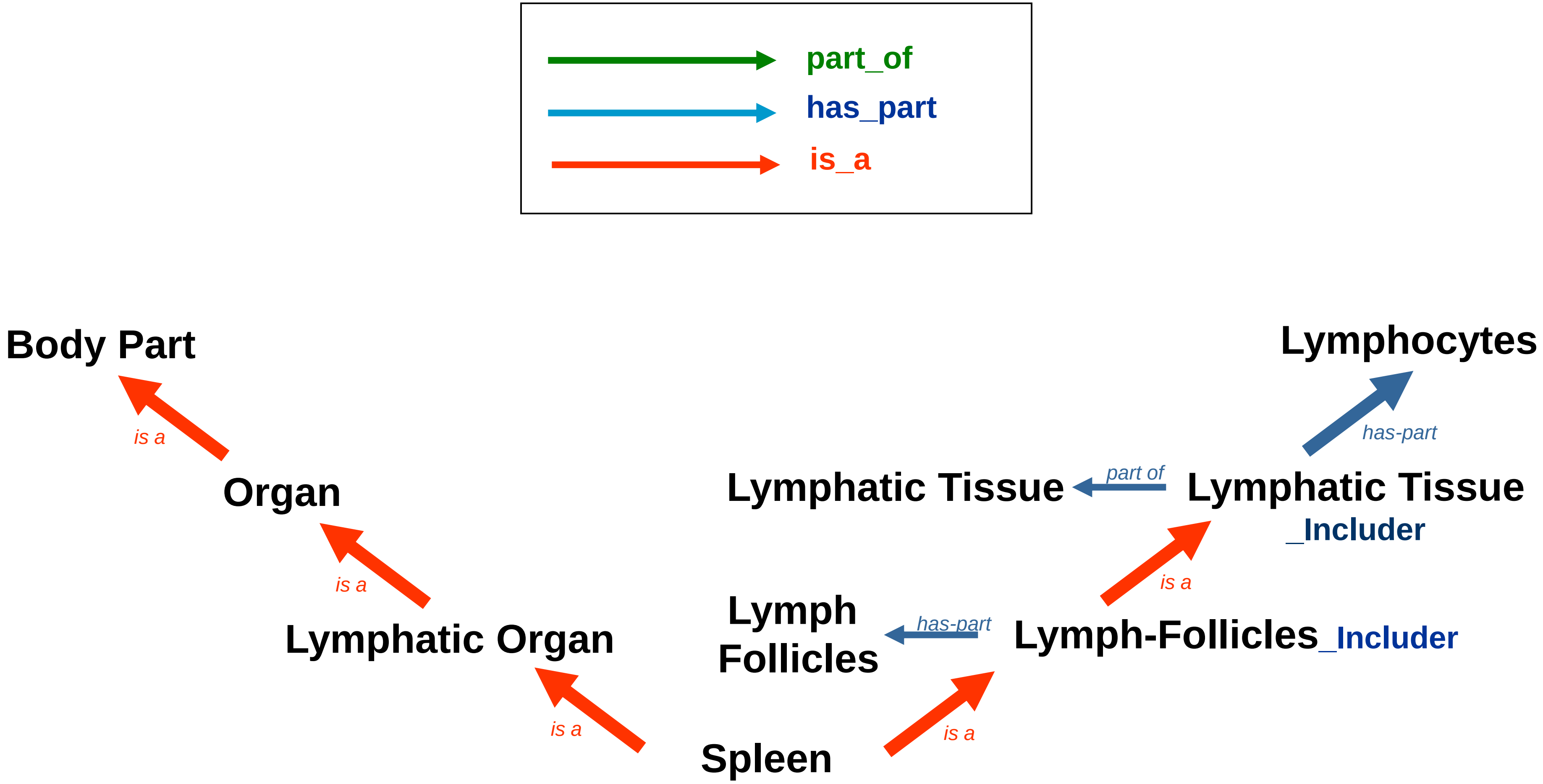

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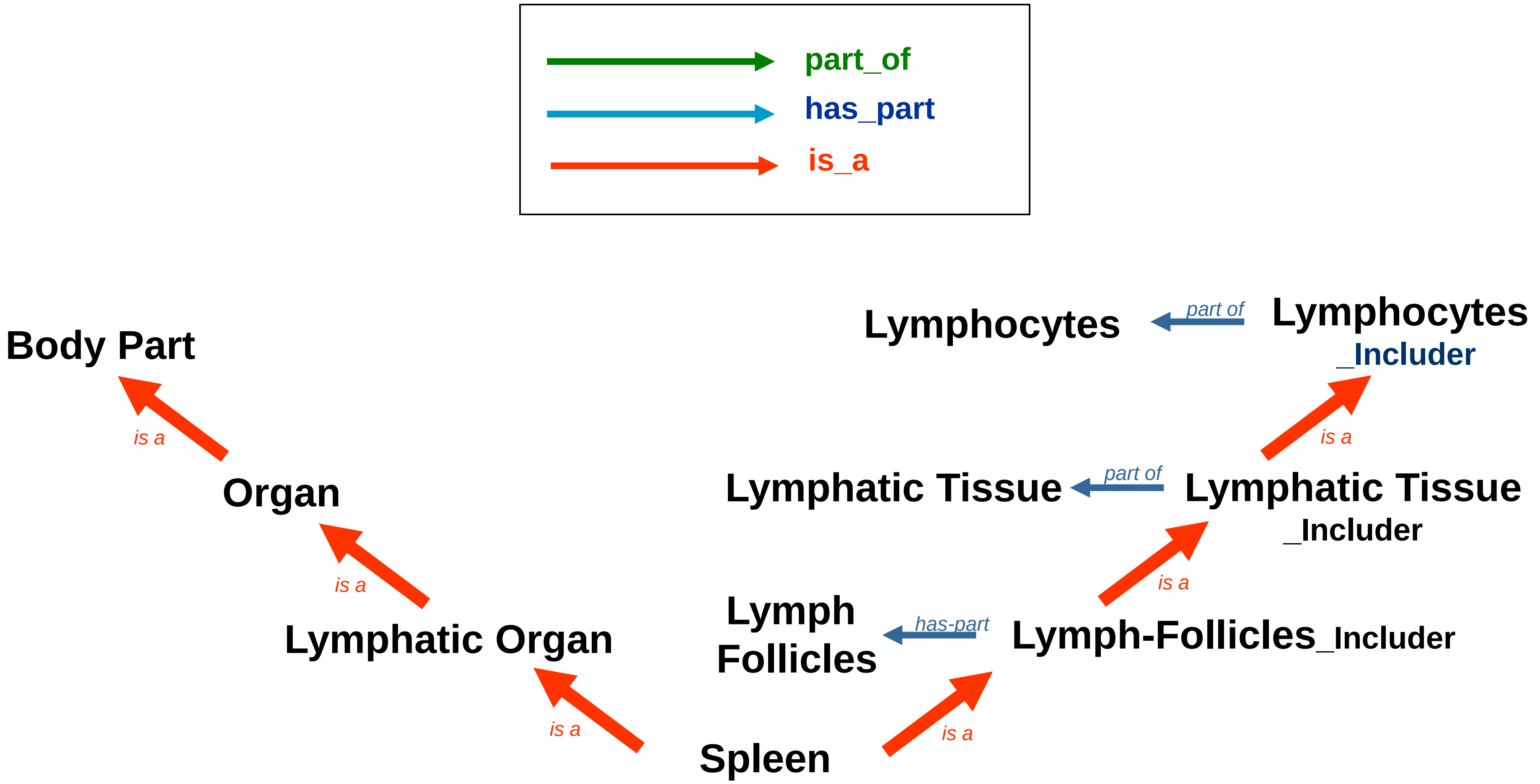
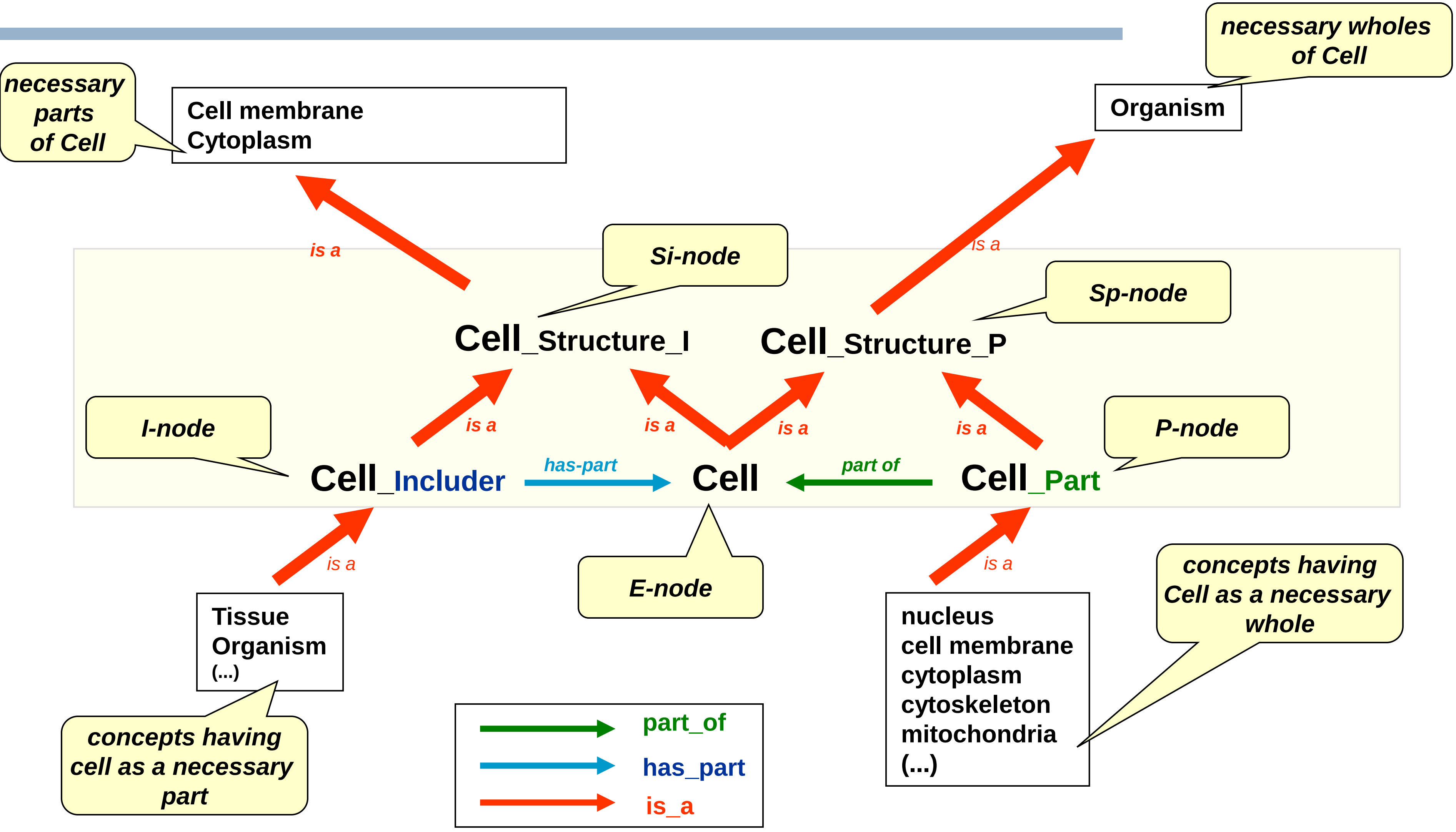
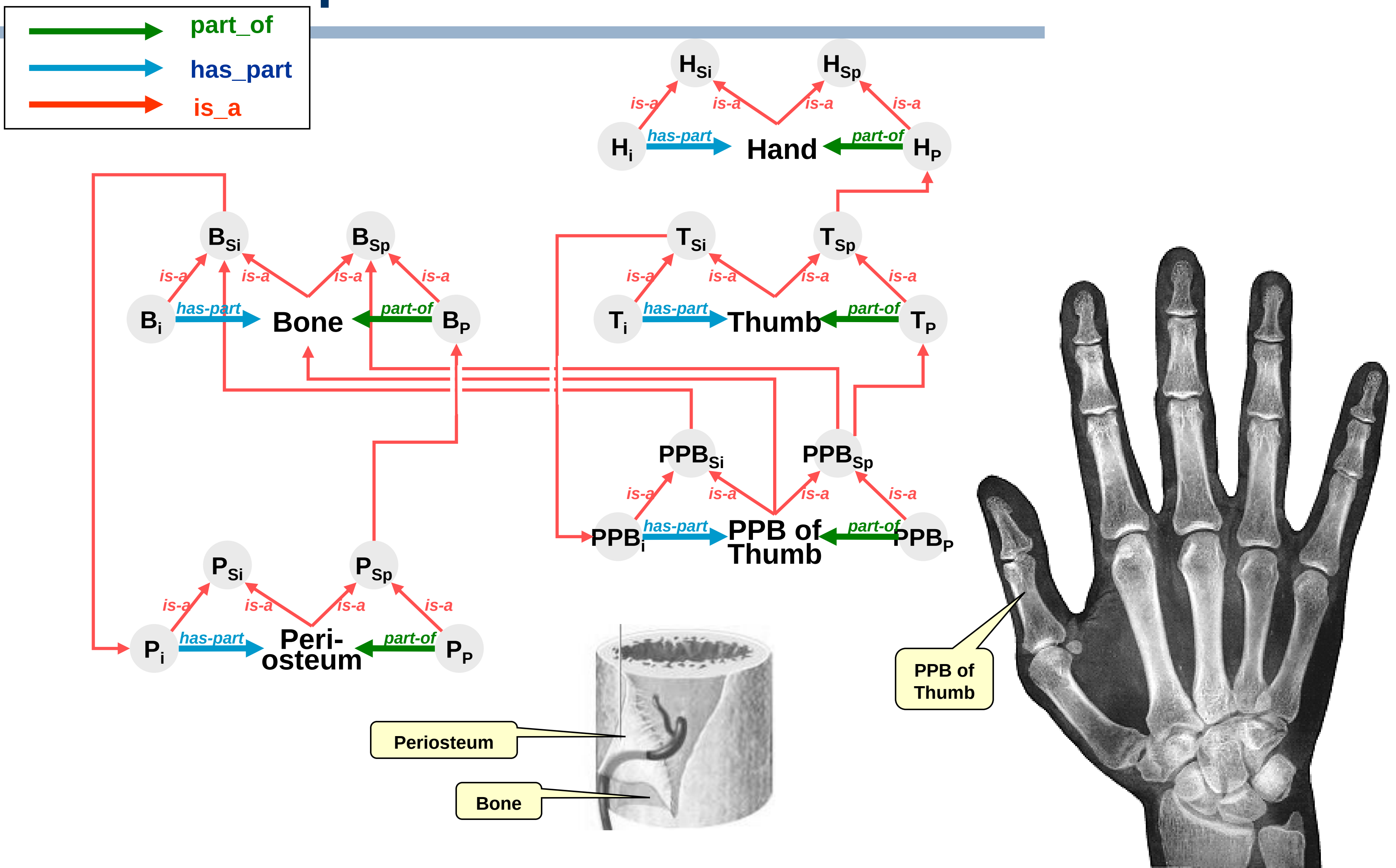


Extended SEP

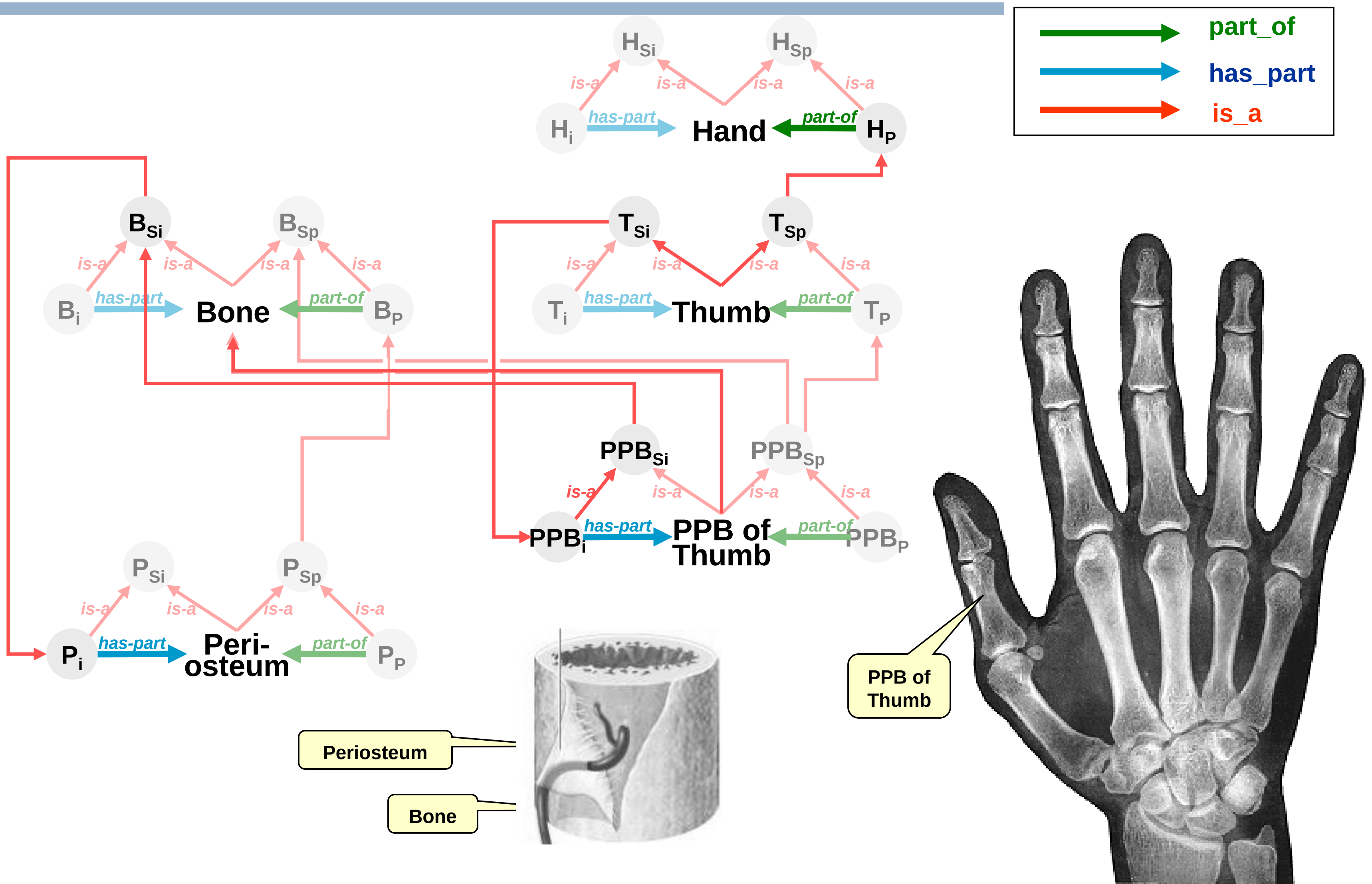


Example 1



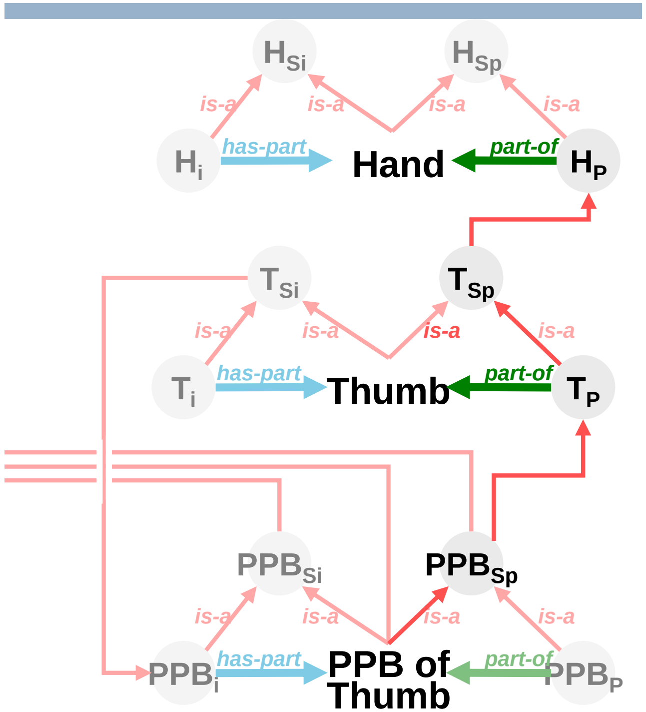
part_of
has_part
is_a
H_{Si}
H_{Sp}
H_i
Hand
H_P
B_{Si}
B_{Sp}
B_i
Bone
B_P
T_{Si}
T_{Sp}
T_i
Thumb
T_P
PPB_{Si}
PPB_{Sp}
PPB_i
PPB of Thumb
PPB_P
P_{Si}
P_{Sp}
P_i
Peri-osteum
P_P
is-a
has-part
part-of
Periosteum
Bone
PPB of Thumb

Example 1



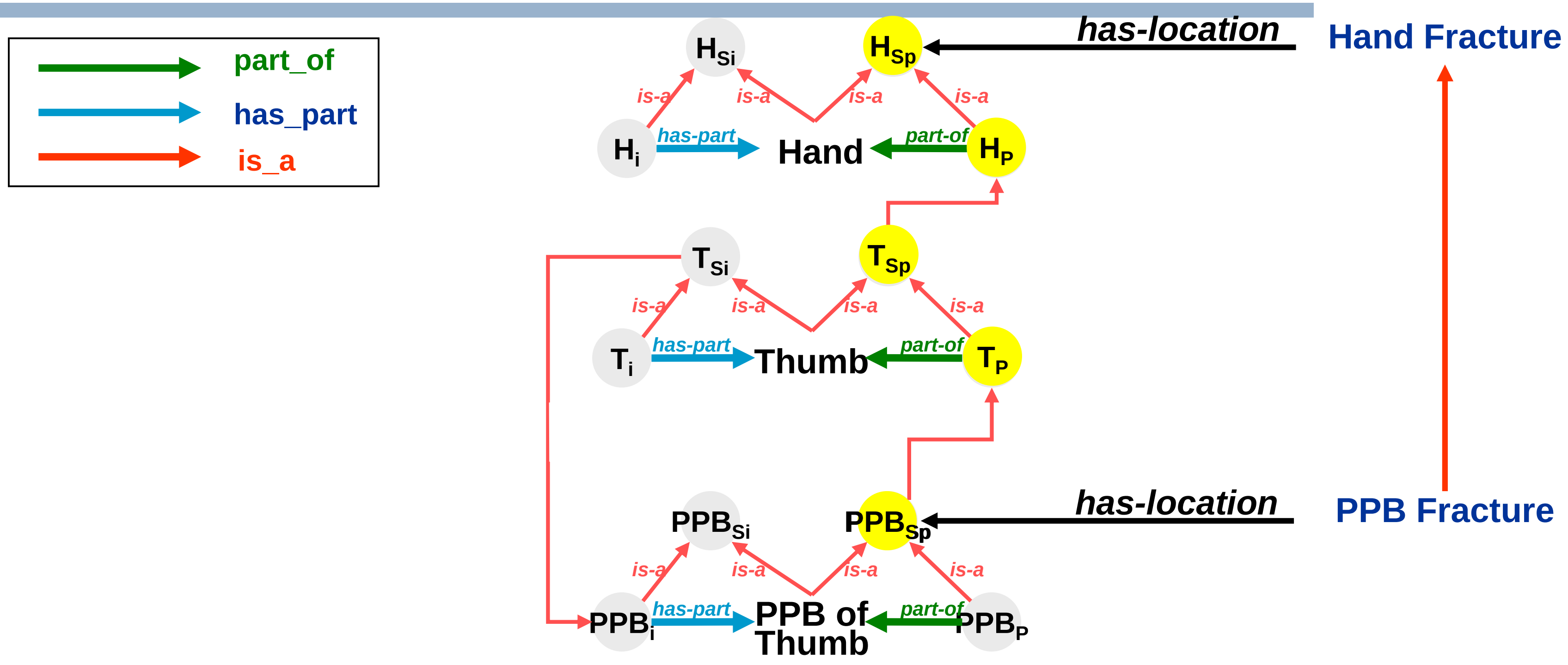
part_of
has_part
is_a
H_{Si}
H_{Sp}
H_i
has-part
Hand
part-of
H_P
is-a
B_{Si}
B_{Sp}
B_i
Bone
B_P
T_{Si}
T_{Sp}
T_i
Thumb
T_P
PPB_{Si}
PPB_{Sp}
PPB_i
PPB of Thumb
PPB_P
P_{Si}
P_{Sp}
P_i
Peri-osteum
P_P
Periosteum
Bone
PPB of Thumb

Example 1



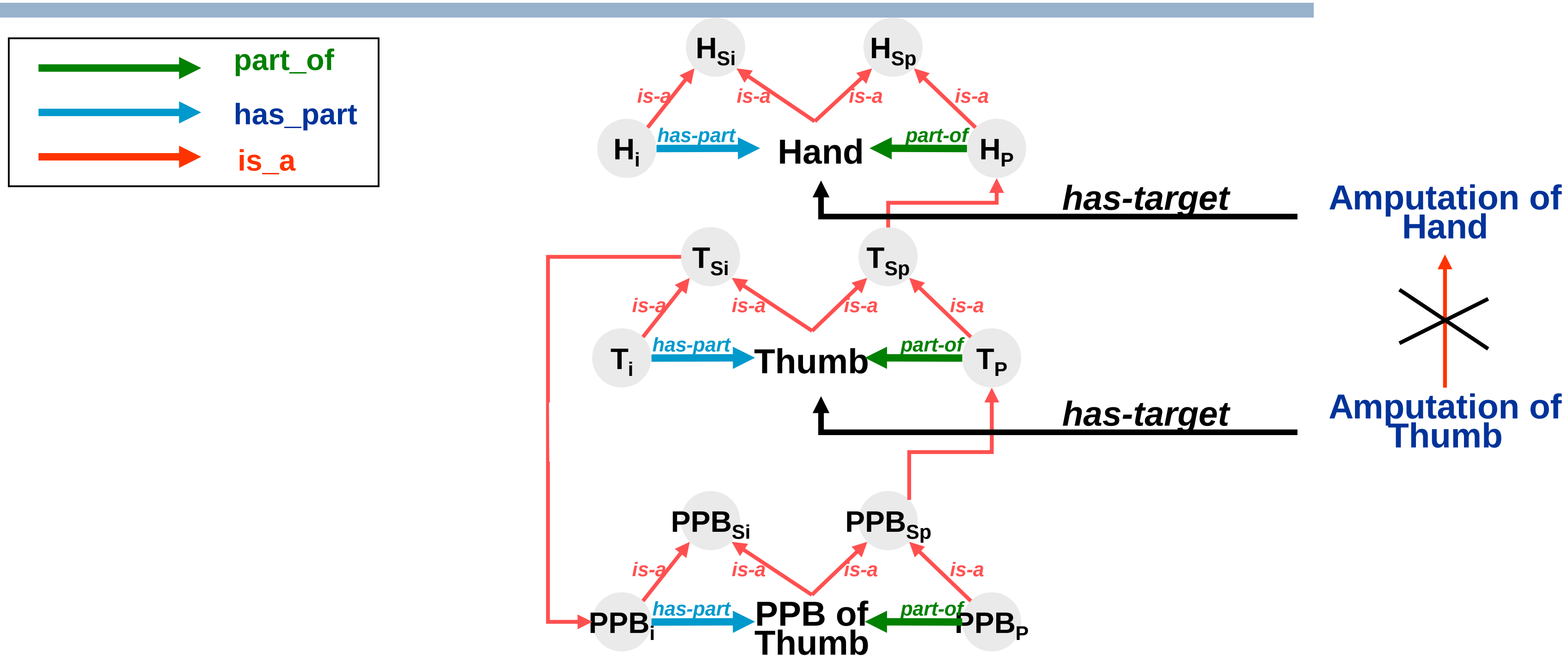
H_{Si}
H_{Sp}
is-a
is-a
is-a
is-a
H_i
has-part
Hand
part-of
H_P
T_{Si}
T_{Sp}
is-a
is-a
is-a
is-a
T_i
has-part
Thumb
part-of
T_P
PPB_{Si}
PPB_{Sp}
is-a
is-a
is-a
is-a
PPB_i
has-part
PPB of Thumb
part-of
PPB_P

Example 2
(role propagation enabled)



Role Propagation enabled

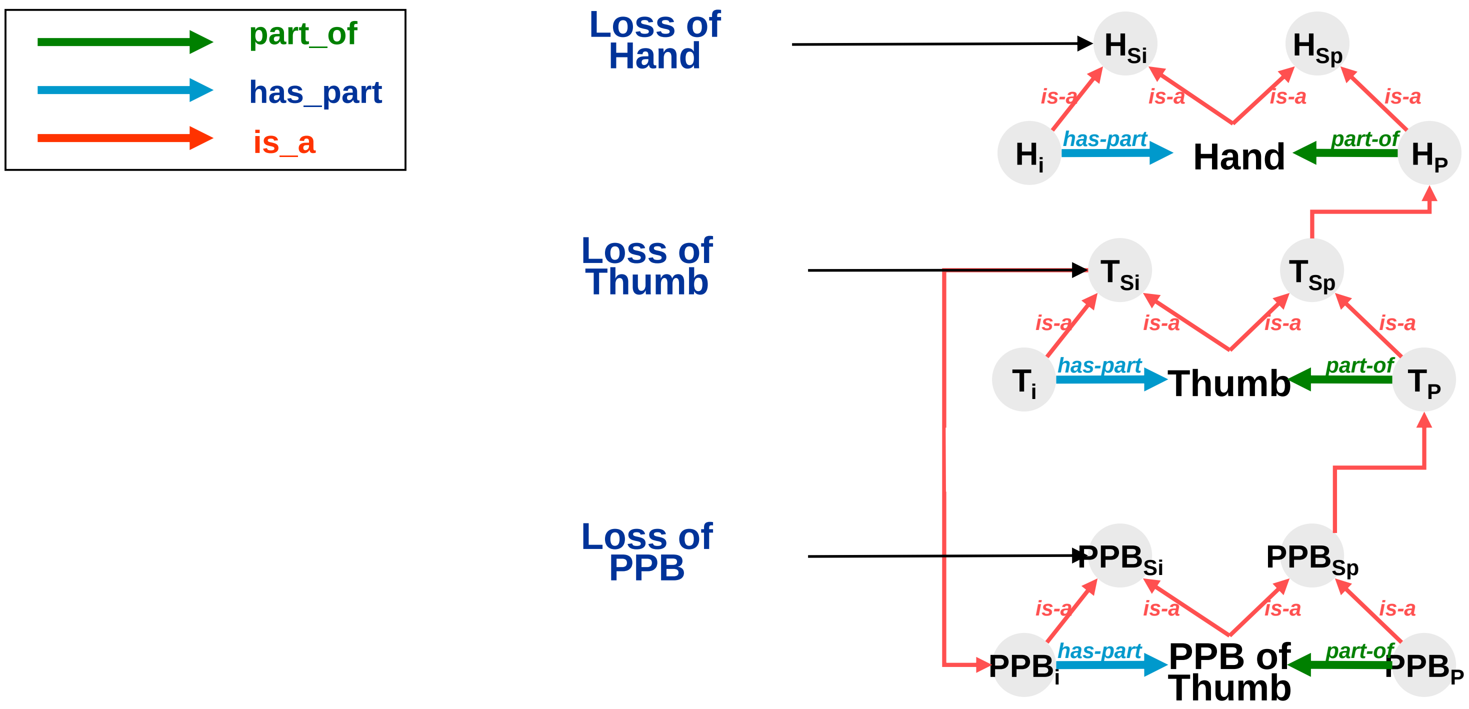
Example 3
(role propagation disabled)



Amputation of a body part targets the body part itself, not a part of it

Amputation of Thumb = *Amputation* $\wedge$ $\exists$*has-target.Thumb* $\wedge$ $\forall$*has-target.Thumb*

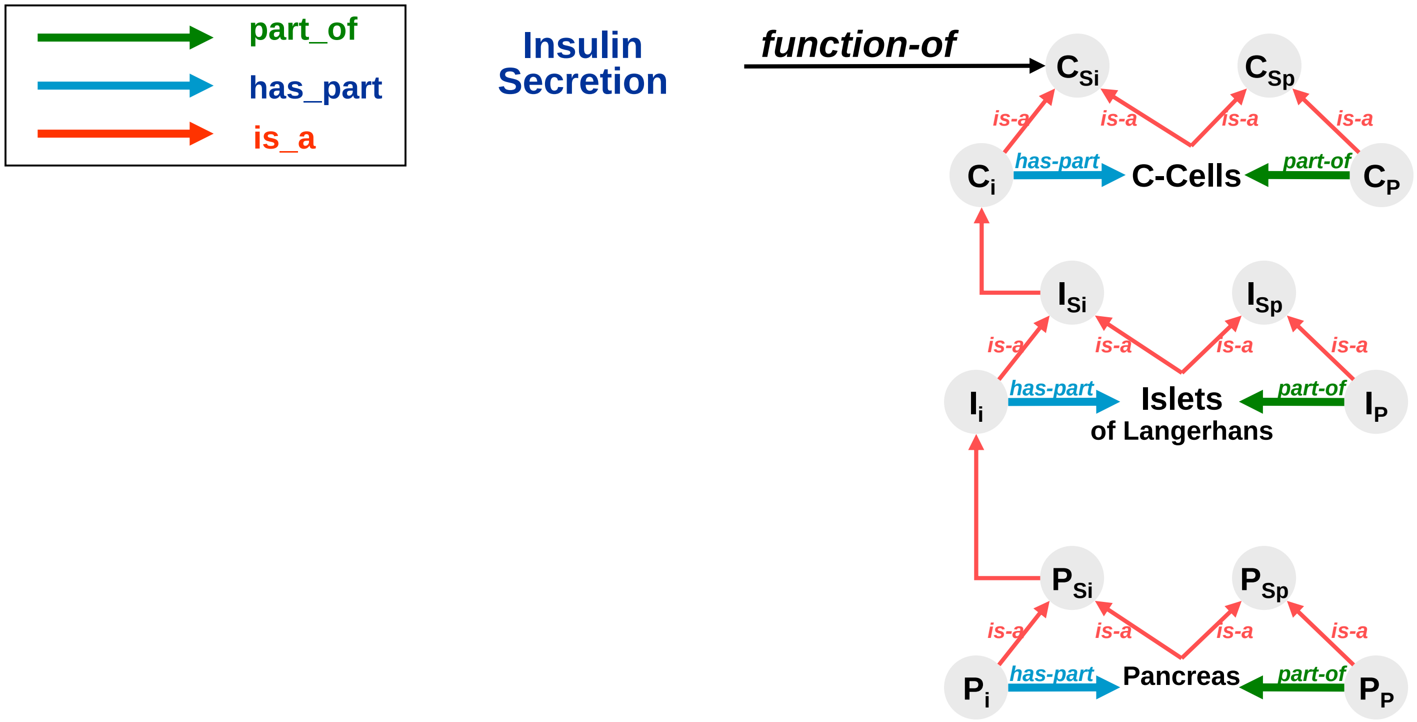
Example 4 (role propagation enabled)



Loss of a body implies the loss of all necessary parts

Loss of Thumb = Loss of BodyPart $\wedge$ $\exists$*loss-of.Thumb*$_{Si}$ $\wedge$ $\forall$*loss-of.Thumb*$_{Si}$

Example 4
(role propagation enabled)



Insulin secretion is a function of the pancreatic c-cells and anything which necessarily includes them.

$InsulinSecretion = \exists function\text{-}of.C_{Si} \wedge \forall function\text{-}of.C_{Si}$

Conclusion

- Clarification of the meaning of mereological relationships in the biomedical domain
- Expressing mereological relationships (necessary wholes / necessary parts) and constraints by complex taxonomies
- Mereological reasoning is reduced to taxonomic reasoning
- Benefits:
  - parsimonious language
  - expressivity WRT transitivity, flexible role propagation
  - massive knowledge acquisition & engineering (KR00)