UT Southwestern Medical Center

Infectious Disease Ontology

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GOALS

- Coverage of the entire infectious disease domain
  - domain-specific entities (*e.g.*, infection)
  - generally relevant entities (*e.g.*, lung)
  - basic biological as well as clinical entities (*e.g.*, genes and clinical tests)
  - spanning:
    - different diseases, hosts, and pathogens
    - biological scales (molecule, cell, organism, population)
    - entities in the chain of infection (host, pathogen, vector, reservoir)

GOALS

- Interoperability with other disease/health domains
- Support for computation
- Application independence

Building IDO

- Import terms from OBO Foundry ontologies
- Define new terms as needed, adhering to OBO Foundry principles
- Assert relations between terms
- Take a core-extension approach

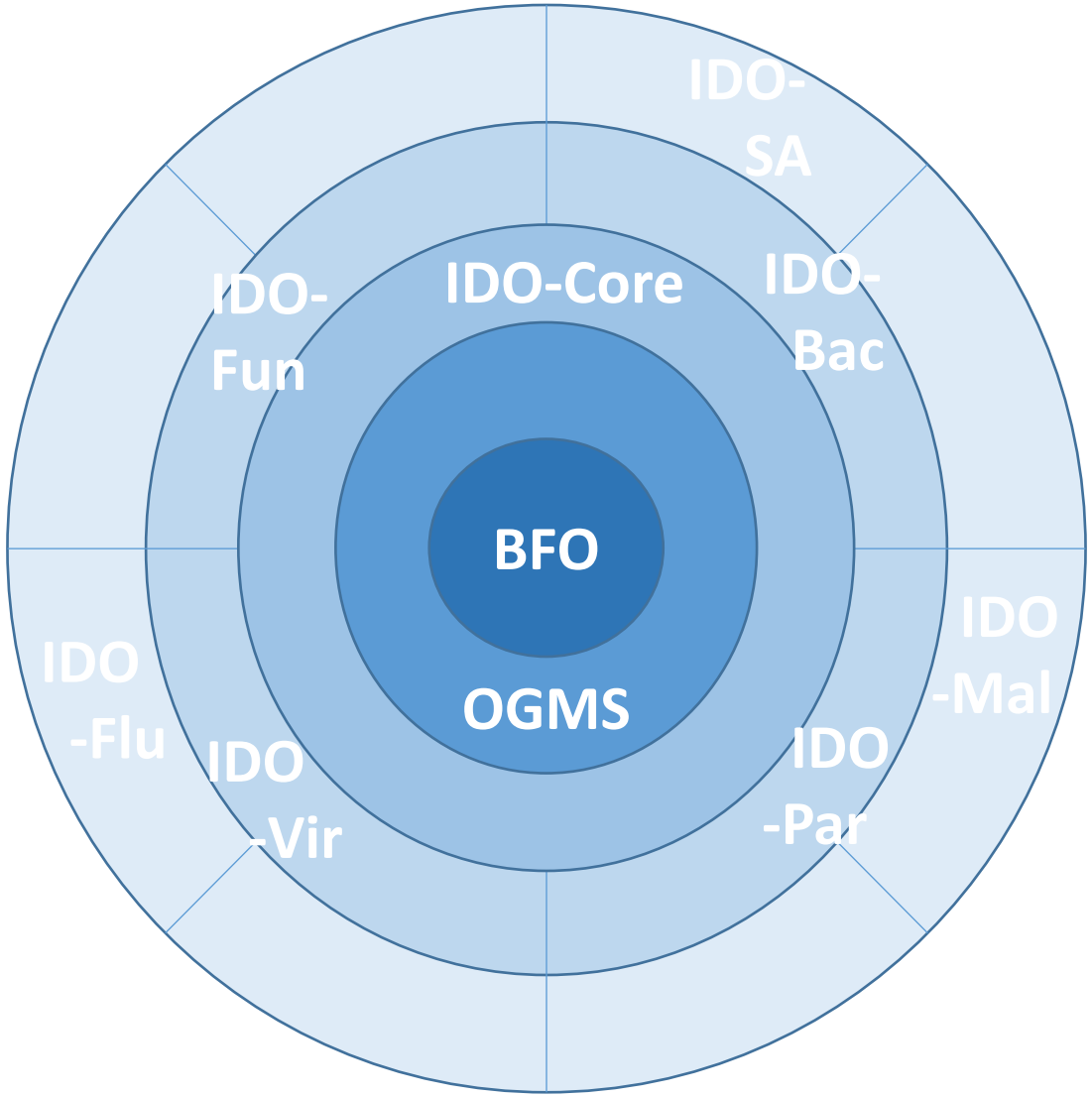
Characterization of an Infectious Disease

disease	signs and symptoms	diagnostic criteria	disease course stages
host organism type	relevant polymorphisms	host niches	endemic areas
pathogen organism type	pathogen classification	virulence traits	drug susceptibilities
host-pathogen interaction	infection process	host response	epidemiological characteristics
routes of transmission	vector organism types	reservoirs	prevention measures

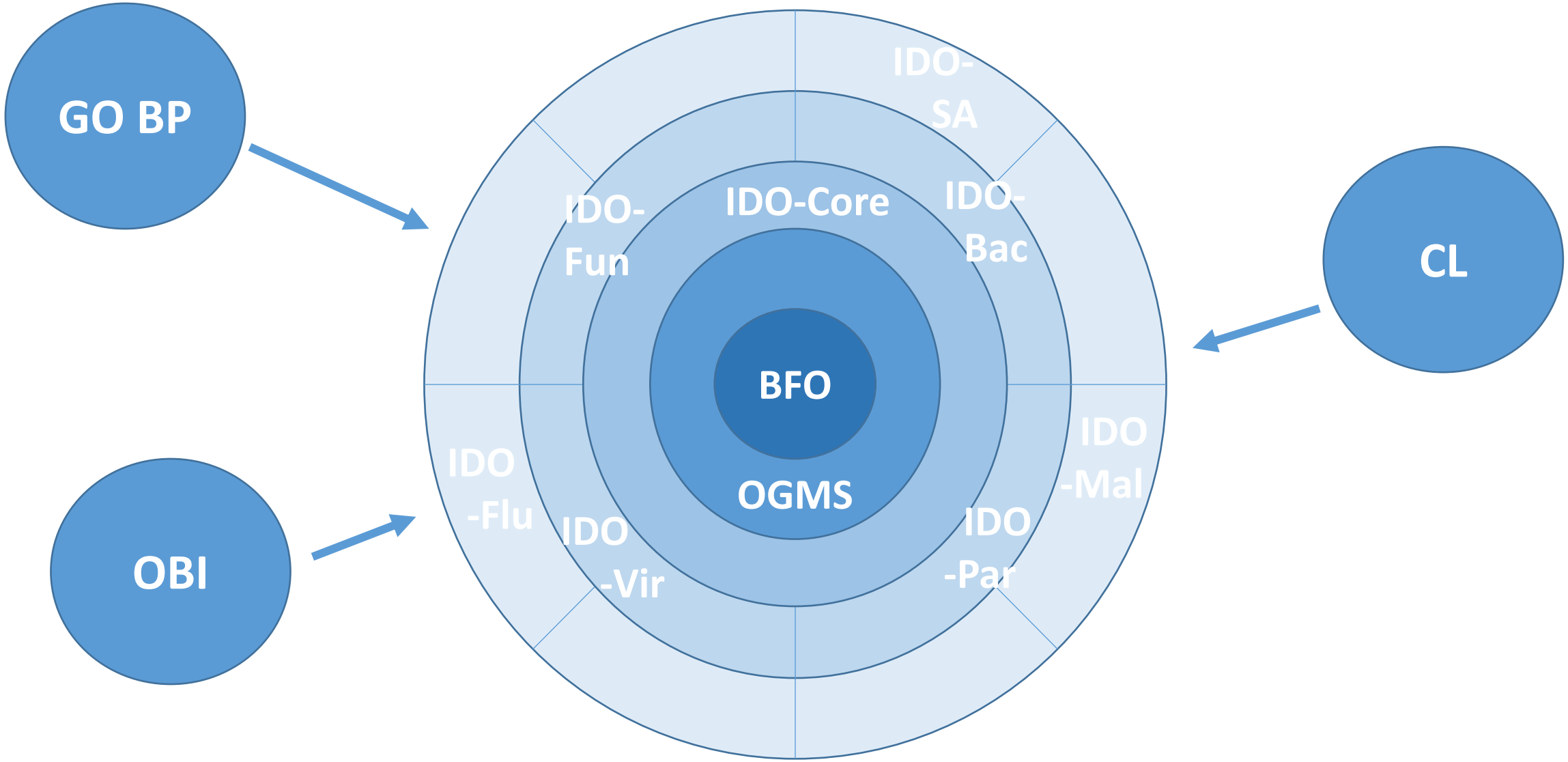
Ontologies used by IDO

Clinical Entities	Biological Entities	Investigational Entities
Ontology of General Medical Science	NCBI Taxonomy	Ontology of Biomedical Investigation
Vital Signs Ontology	Common Anatomy Reference Ontology	
Symptom Ontology	Cell Ontology	
Disease Ontology	Gene Ontology Cellular Component Ontology	
Transmission Ontology	Protein Ontology	
	Chemical Entities of Biological Interest	
	Phenotype and Trait Ontology	
	Environment Ontology	
	Gene Ontology Biological Process Ontology	Sequence Ontology

Core-Extension Approach



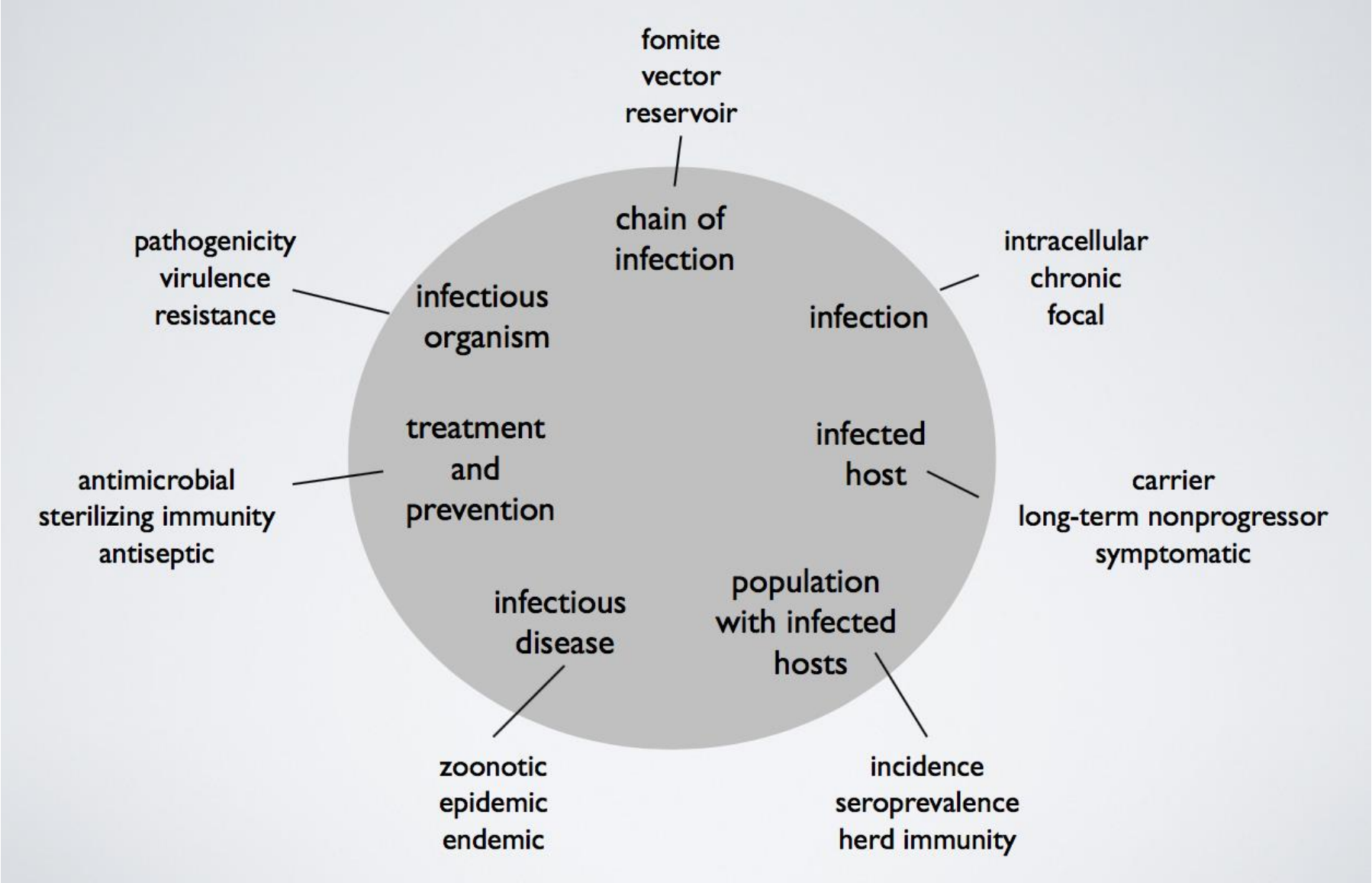
Core-Extension Approach



Purpose of IDO Core

- Provide terms relevant to infectious diseases generally (*e.g.*, infection, host, pathogen, vector)
  - reducing duplication of effort
- Ensure interoperability between IDO extensions
  - terminological consistency (term names and meanings)
  - definition templates
  - consistent approach to classification
  - consistent approach to asserting relations
- Allows parallel development by domain experts
  - prevent common mistakes
  - ensure utility for computational applications

Scope of IDO Core



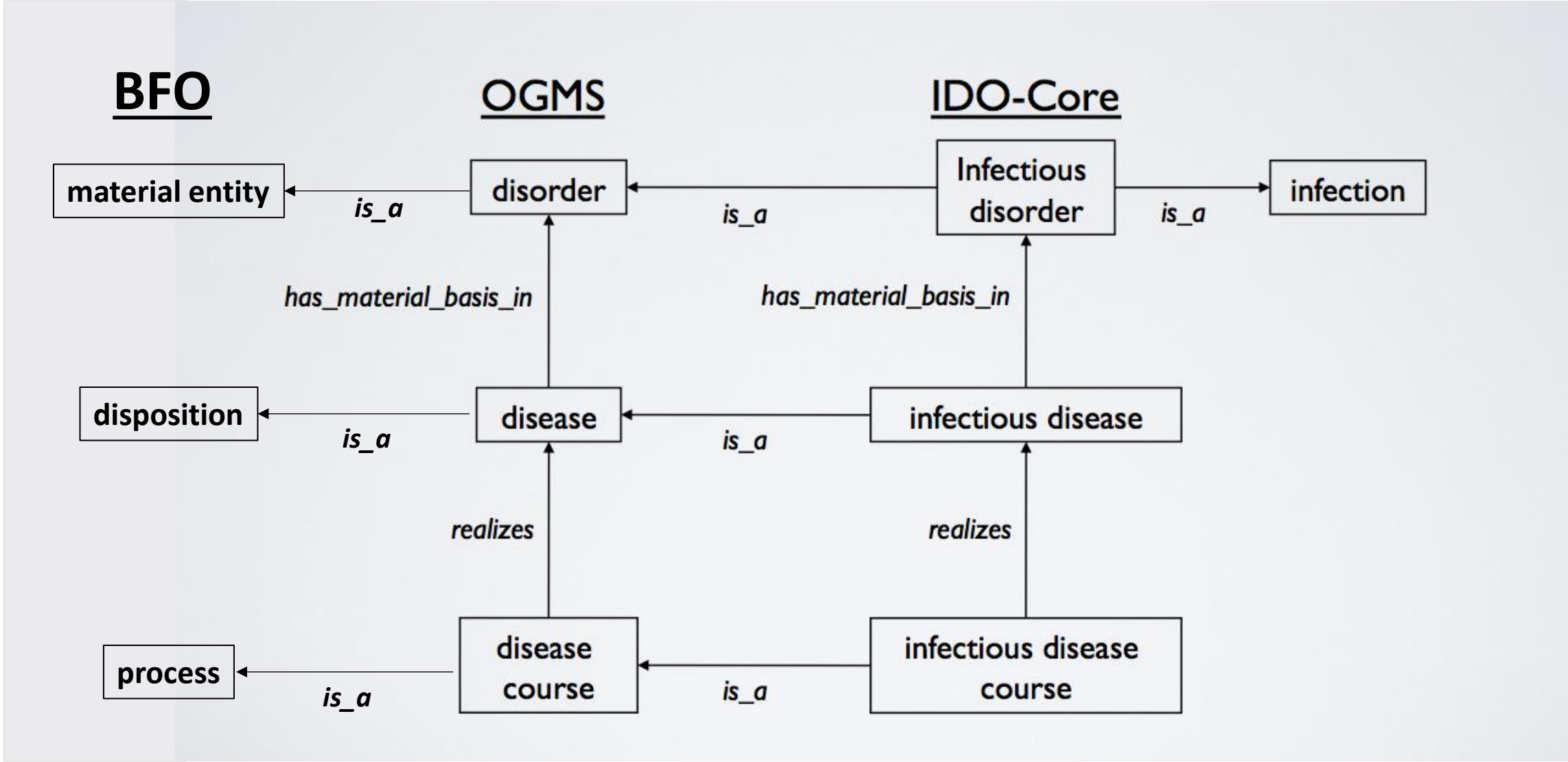
IDO Core Development Timeline

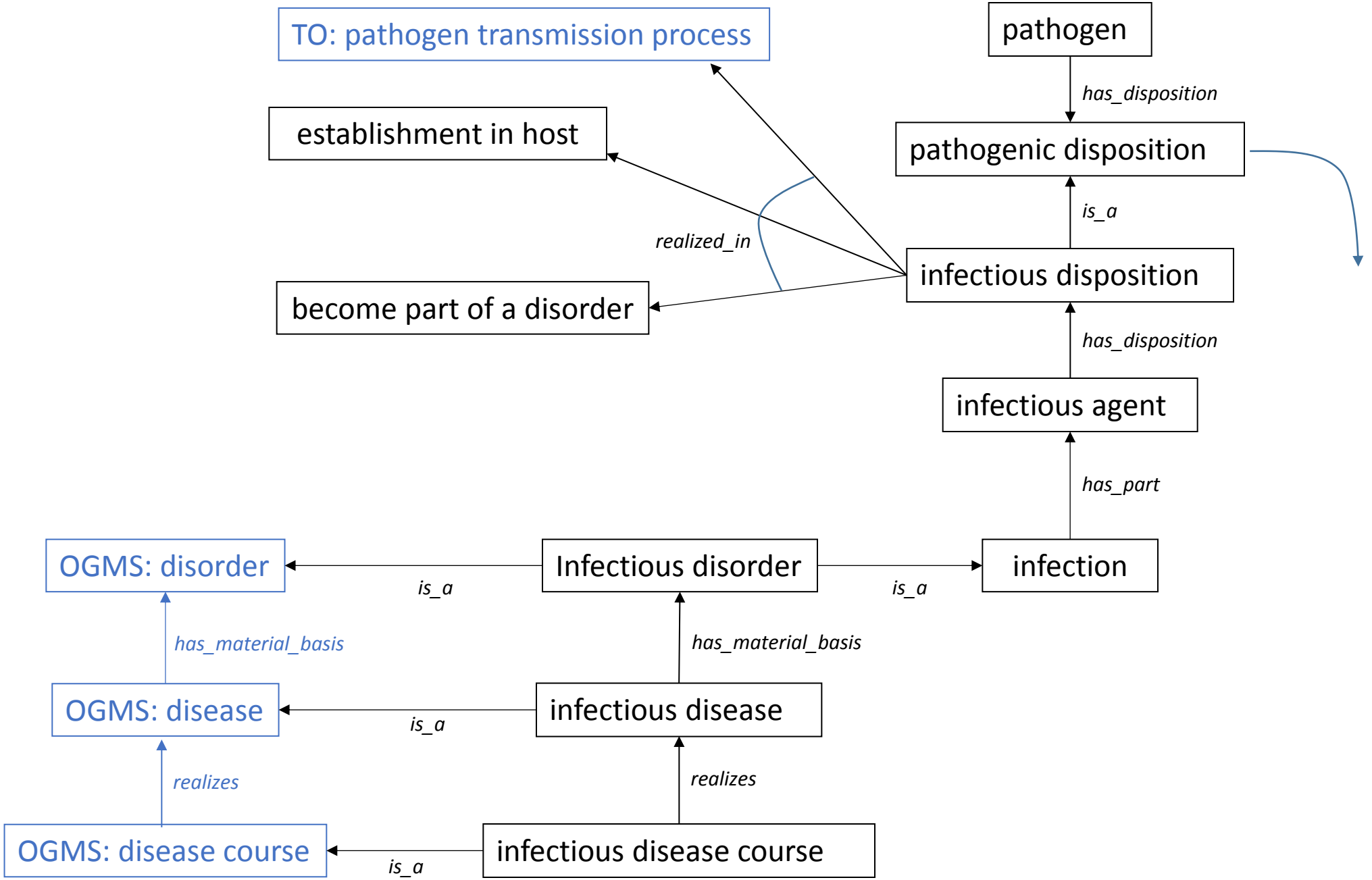
- September, 2007
  - term list
- September, 2008
  - draft hierarchy
- February - July, 2009
  - revise term list and hierarchy
  - write structured natural language definitions
- September - December, 2009
  - write simplified natural language definitions
  - revise definitions to include prions
- January - June, 2009
  - write OBO cross-product definitions
  - write DL expressions
- December 2010
  - Last release

Definition Strategy

- Avoid circular definitions
- Dependent Continuants
  - Bearer
  - Process in which realized
  - Roles - Circumstances that confer the role
  - Dispositions - Categorical basis
  - Qualities
- Processes
  - Structure in time (*e.g.,* boundaries, ordering)
- Aggregates
  - Criteria for membership

IDO Core Representation of Infectious Disease




TO: pathogen transmission process
pathogen
has_disposition
establishment in host
pathogenic disposition
is_a
realized_in
infectious disposition
become part of a disorder
has_disposition
infectious agent
has_part
OGMS: disorder
is_a
Infectious disorder
is_a
infection
has_material_basis
has_material_basis
OGMS: disease
is_a
infectious disease
realizes
realizes
OGMS: disease course
is_a
infectious disease course

IDO Core Central Dispositions

pathogenic disposition	A disposition to initiate processes that result in a disorder.
pathogen	A material entity with a pathogenic disposition.
infectious disposition	A pathogenic disposition that inheres in an organism and is a disposition for that organism (1) to be transmitted to a host, (2) to establish itself in the host, (3) to initiate processes that result in a disorder in the host, and (4) to become part of that disorder.
infectious agent	An organism that has an infectious disposition.

IDO Core Central Definitions

- infection $=_{def}$ A part of an extended organism that itself has as part a population of one or more infectious agents and that
  - (1) exists as a result of processes initiated by members of the infectious agent population and is
  - (2) clinically abnormal in virtue of the presence of this infectious agent population, or
  - (3) has a disposition to bring clinical abnormality to immunocompetent organisms of the same Species as the host through transmission of a member or offspring of a member of the infectious agent population.

IDO Core Central Dispositions

infectious disorder	An infection that is clinically abnormal.
infectious disease	A disease whose physical basis is an infectious disorder.
infectious disease course	A disease course that is a realization of an infectious disease.

IDO Extension: terms and definitions

- *Staphylococcus aureus* infection $=_{def}$ An infection that has as part organisms of type *Staphylococcus aureus*.

- *Staphylococcus aureus* bacteremia $=_{def}$ An infection that has as part organisms of type *Staphylococcus aureus* located in the blood.

IDO Extension: terms and definitions

- drug resistance $=_{def}$ A protective resistance that mitigates the damaging effects of a drug.

- antibiotic resistance $=_{def}$ A drug resistance that mitigates the damaging effects of an antibiotic.

- resistance to beta-lactam antibiotic $=_{def}$ An antibiotic resistance that mitigates the damaging effects of a beta-lactam antibiotic.

IDO Extension: terms and definitions

- methicillin-resistant *Staphylococcus aureus* $=_{def}$ An organism of type *Staphylococcus aureus* that has resistance to beta-lactam antibiotics.

What's Notable?

- What's notable:
  - Our treatment of dispositions:
    - Blocking dispositions
    - Complementary dispositions
    - Object aggregates and collective dispositions
  - High level of generality (reusability)
  - Inference of host-pathogen-(vector)-disease-etc lattice

What's Notable?

- **Our treatment of dispositions – Blocking Dispositions**

  - Blocking Disposition: A disposition the manifestation of which prevents the manifestation of another disposition.
    - If D_1 is a disposition and D_2 is a blocking disposition for D_1, then it must be the case that the manifestation of D_2 prevents the manifestation of D_1.

  - **Protective Resistance**=*def* A disposition that inheres in a material entity in virtue of the fact that the entity has a part (*e.g.,* a gene product), which itself has a disposition to mitigate damage to the entity.
    - The disposition is realized in a process that mitigates damage to the bearer and has the part as a participant.
    - Examples include the following: CCR5 mutations protect T cells from HIV invasion. A tumor cell's resistance to chemotherapy protects the cell from damage by the drug (although this harms the patient). An insect's resistance to insecticide protects it from the insecticide.

What's Notable?

- **Our treatment of dispositions – Complementary Dispositions**

  - Complementary Dispositions: two dispositions oriented "towards" each other with a potential for mutual manifestation

  - The **infectious disposition** has a complementary disposition that inheres in an organism and is the **capability to be host to an organism with an infectious disposition and to undergo processes initiated by that infectious organism that result in a disorder**.

  - **Opportunistic infectious disposition** =def An infectious disposition to become part of a disorder only in organisms whose defenses are compromised.

  - **Immunodeficient Organism** =def An organism that has an immunodeficiency.
  - **Immunodeficiency** =def A disorder of an immune system component that results in defective functioning of the immune system.

What's Notable?

- **Our treatment of dispositions – Object Aggregates and Collective Dispositions**

  - Extended Organism
  - Infection
    - Simple Infection
    - Complex Infection
  - Organism Population
    - Infectious Agent Population
    - Susceptible Population
    - Infected Population
    - Immune Population
    - Diseased Population
    - Normal Resident Microbiota

What's Notable?

- **Our treatment of dispositions – Object Aggregates and Collective Dispositions**

  - Collective Dispositions =def A disposition inhering in an object aggregate *OA* in virtue of the individual dispositions of the constituents of *OA* and that does not itself inhere in any part of *OA* or in any larger aggregate in which *OA* is a part.

  - Collective pathogenic disposition =def A collective disposition to initiate processes that result in a disorder.

  - Collective resistance disposition =def A collective disposition the realization of which mitigates the damaging effects of some entity on members of the collection.

  - Herd Immunity =def A collective resistance disposition that inheres in an organism population in virtue of the fact that the proportion of the population with immunity to an infectious agent is high resulting in a low number of transmissions from hosts in the population to susceptible individuals in the population and thereby mitigating the damaging effects of the infectious agent on the population.

What's Notable?

- **High level of generality**

  - **Protective Resistance**=*def* A disposition that inheres in a material entity in virtue of the fact that the entity has a part (*e.g.,* a gene product), which itself has a disposition to mitigate damage to the entity.
  - Resistance to Drug
  - Resistance to Infectious Agent
    - Genetic Resistance to Infectious Agent
    - Immunity to Infectious Agent
      - Acquired
      - Innate
      - Humoral
      - Leukocyte-mediated
      - Passive
      - Sterilizing
  - Resistance to Insecticide

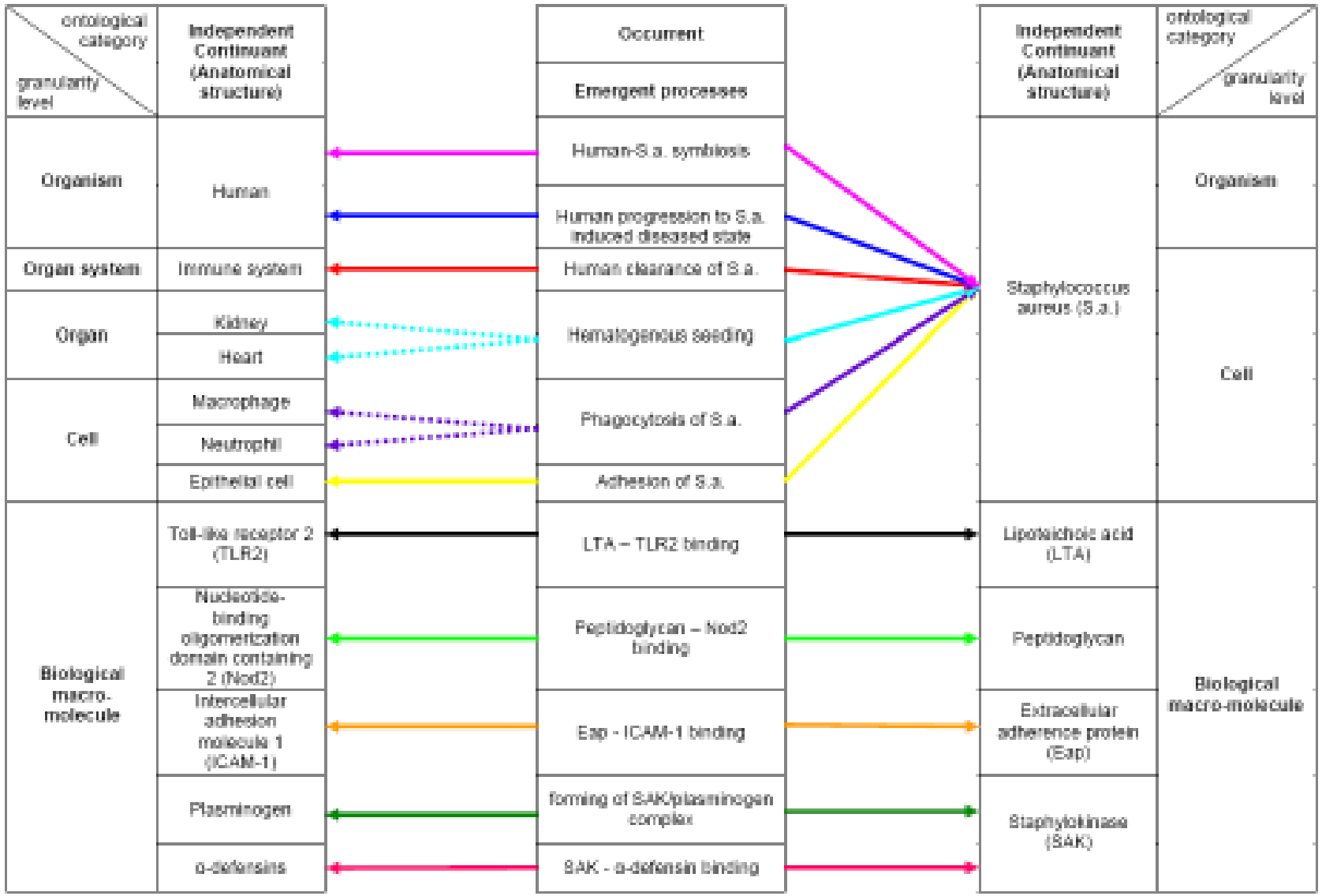
What's Notable?

- **Inference of lattice**

- Given future network visions of disease classification, how can we provide views of disease relationships?
  - Including molecular information about host and pathogen
  - Including clinical manifestations

- IDO provides computable, logical representations of genus-differentia definitions from which we can infer a network of infectious diseases based on selected differentia.

Ontology of S.a. - Human Interaction



Ways of differentiating infectious diseases

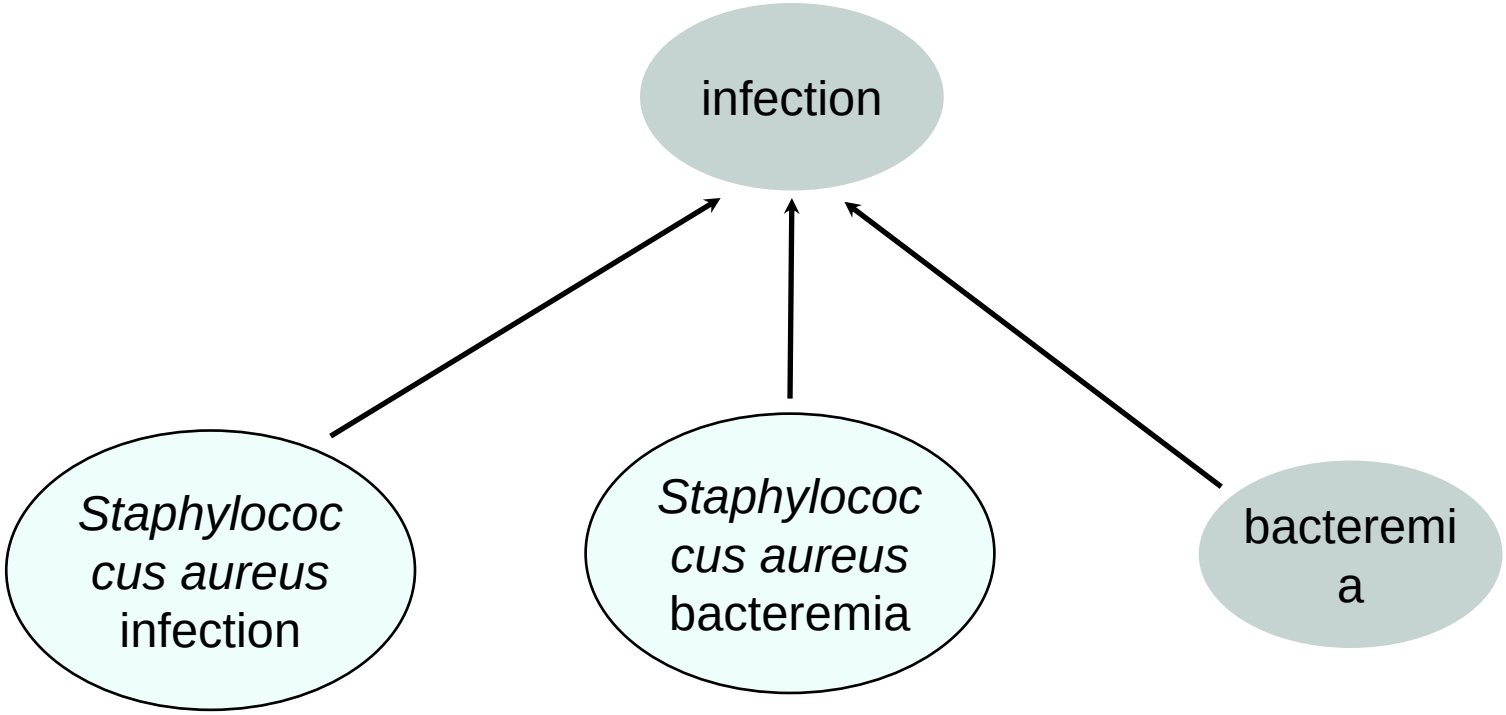
- High-level types
  - By host type (species)
  - By anatomical site of infection
  - By signs and symptoms
  - By mode of transmission
  - By (sub-)species of pathogen

- Differentiation based on host features
  - Clinical phenotype
  - Strain (*e.g.,* A/J)
  - Gene types (*e.g.,* C5-deficient)
  - SNP alleles

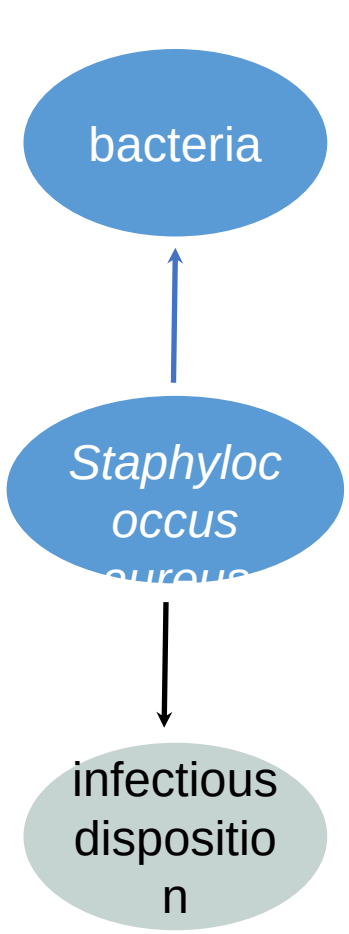
- Differentiation based on pathogen features
  - By phenotype (*e.g.,* drug resistance)
  - By genotype
    - By banding patterns (*e.g.,* PFGE)
    - By typing of house-keeping genes (*e.g.,* MLST)
    - By virulence factor typing (*e.g.,* spa, SCC*mec*)
    - By whole genome?

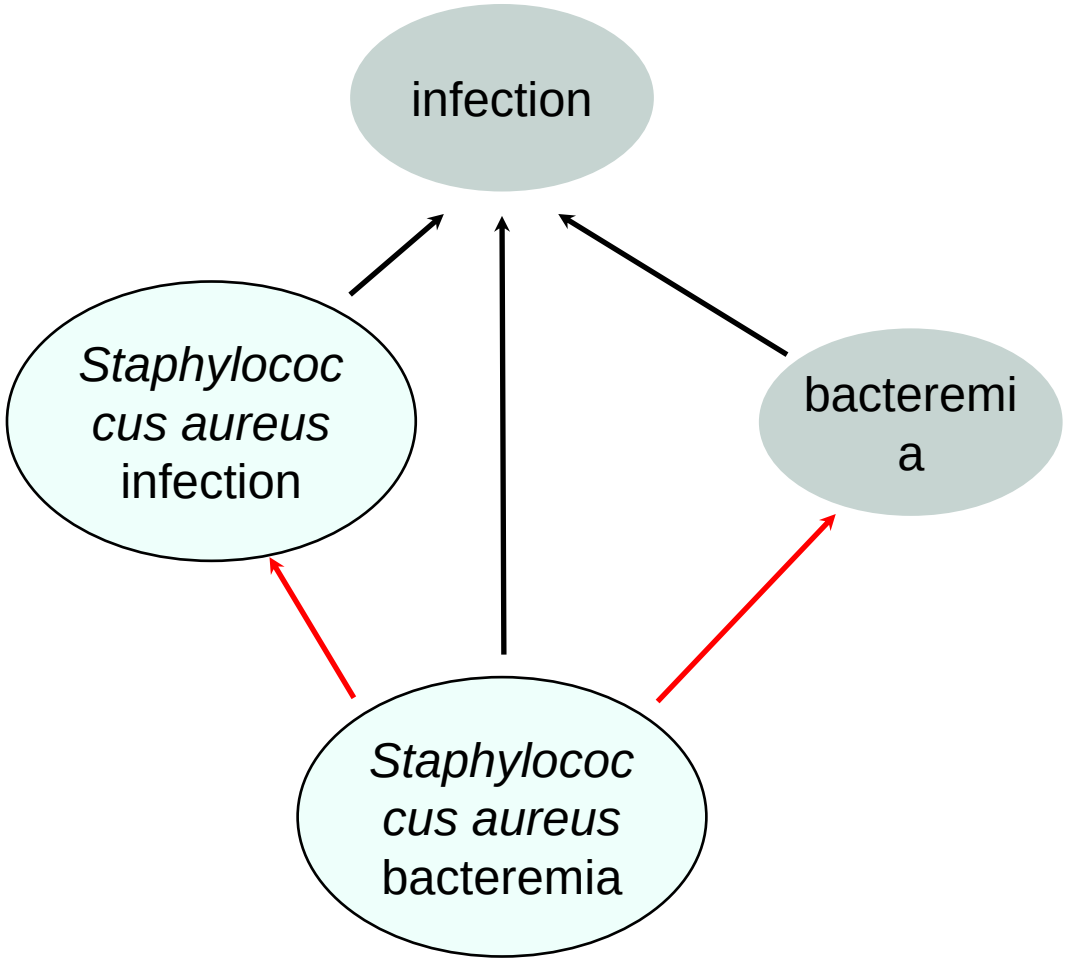
- *Staphylococcus aureus* bacteremia equivalentClass
  - infection AND
  - has_part SOME [
    - *Staphylococcus aureus* AND
    - located_in SOME blood]

IDO-core and Extensions: asserted hierarchy

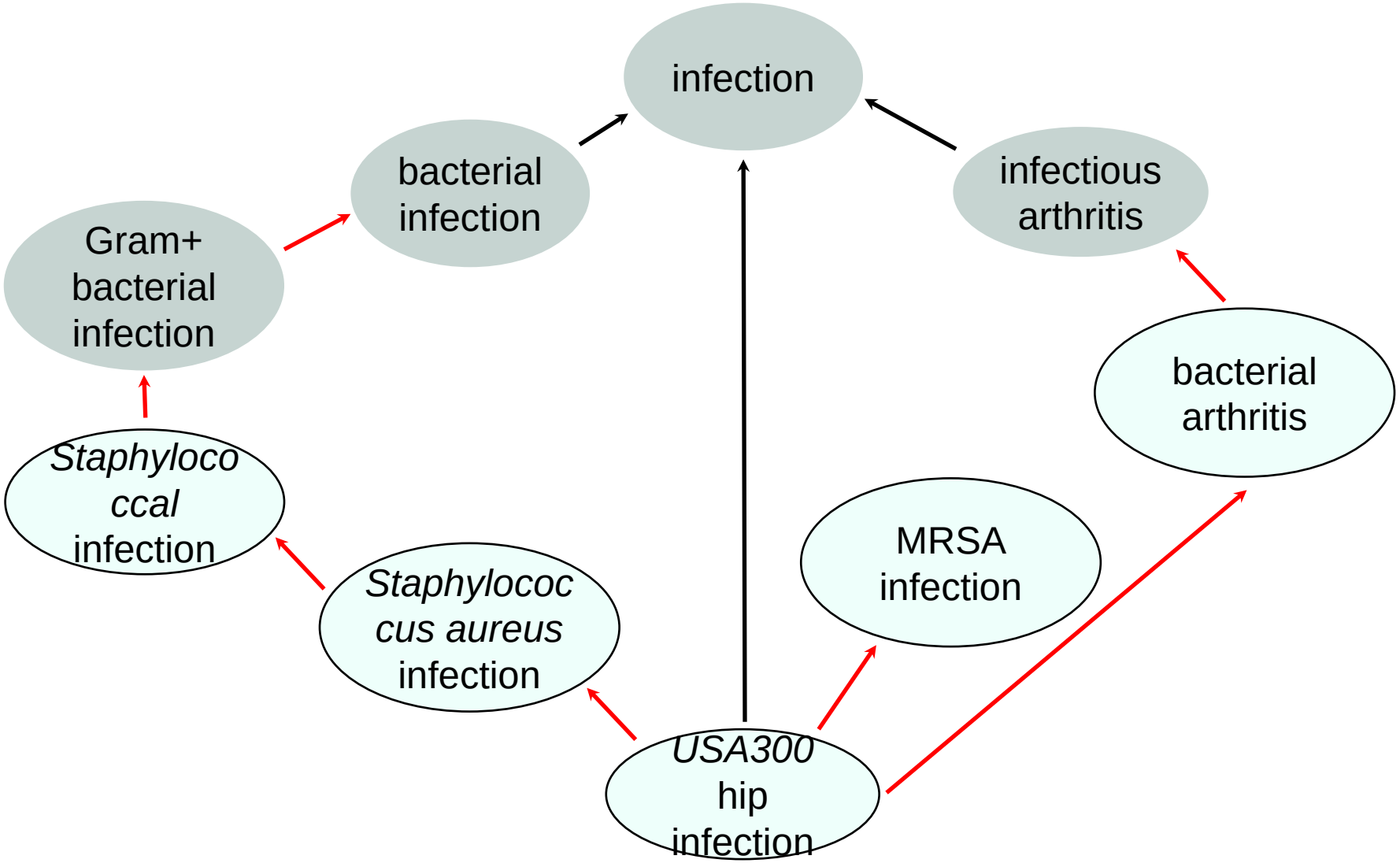


IDO-core and Extensions: asserted hierarchy

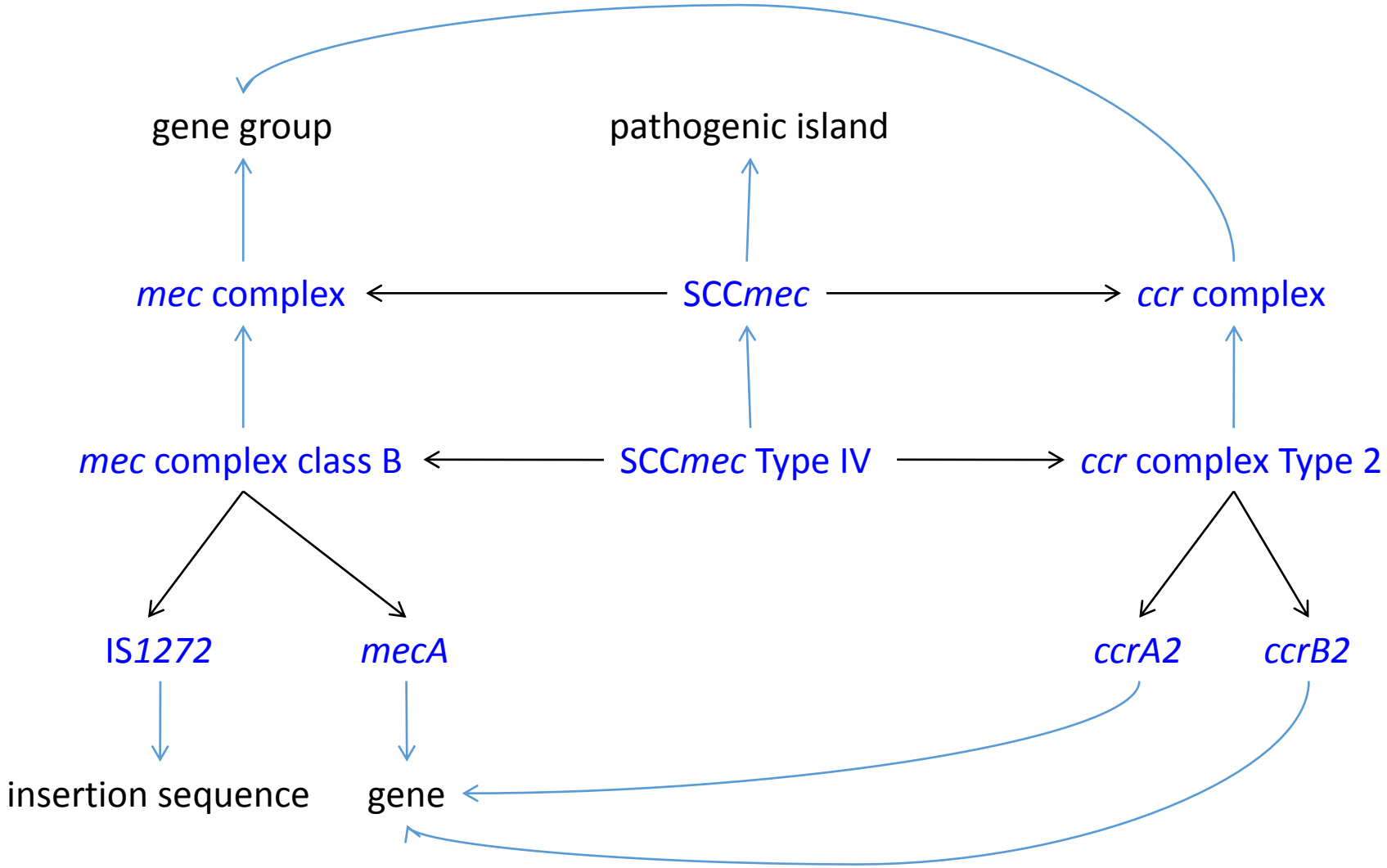




IDO-core and Extensions: asserted hierarchy



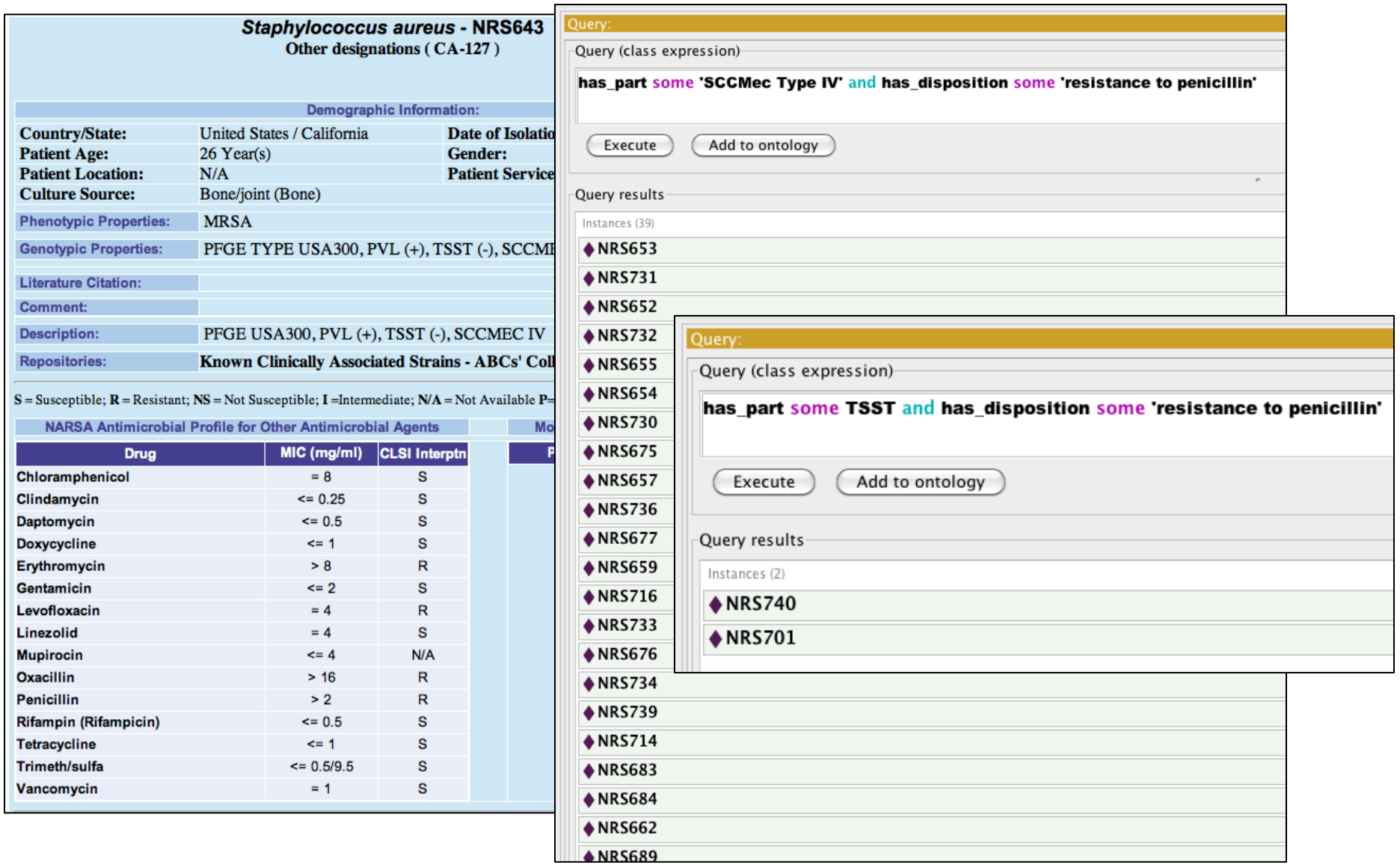
Genomic Typing Data



Sequence Ontology

IDO-SA

Assert Instances for Data Annotation



***Staphylococcus aureus* - NRS643**
Other designations (CA-127)

Demographic Information:		
Country/State:	United States / California	**Date of Isolatio**
Patient Age:	26 Year(s)	**Gender:**
Patient Location:	N/A	**Patient Service**
Culture Source:	Bone/joint (Bone)	
Phenotypic Properties:	MRSA	
Genotypic Properties:	PFGE TYPE USA300, PVL (+), TSST (-), SCCME	
Literature Citation:		
Comment:		
Description:	PFGE USA300, PVL (+), TSST (-), SCCMEC IV	
Repositories:	**Known Clinically Associated Strains - ABCs' Coll**	

S = Susceptible; **R** = Resistant; **NS** = Not Susceptible; **I** =Intermediate; **N/A** = Not Available **P**=

NARSA Antimicrobial Profile for Other Antimicrobial Agents | **Mo**

Drug	MIC (mg/ml)	CLSI Interptn
Chloramphenicol	= 8	S
Clindamycin	<= 0.25	S
Daptomycin	<= 0.5	S
Doxycycline	<= 1	S
Erythromycin	> 8	R
Gentamicin	<= 2	S
Levofloxacin	= 4	R
Linezolid	= 4	S
Mupirocin	<= 4	N/A
Oxacillin	> 16	R
Penicillin	> 2	R
Rifampin (Rifampicin)	<= 0.5	S
Tetracycline	<= 1	S
Trimeth/sulfa	<= 0.5/9.5	S
Vancomycin	= 1	S

Query:

Query (class expression)

```
has_part some 'SCCMec Type IV' and has_disposition some 'resistance to penicillin'
```

Execute | Add to ontology

Query results

Instances (39)

- NRS653
- NRS731
- NRS652
- NRS732
- NRS655
- NRS654
- NRS730
- NRS675
- NRS657
- NRS736
- NRS677
- NRS659
- NRS716
- NRS733
- NRS676
- NRS734
- NRS739
- NRS714
- NRS683
- NRS684
- NRS662
- NRS689

Query:

Query (class expression)

```
has_part some TSST and has_disposition some 'resistance to penicillin'
```

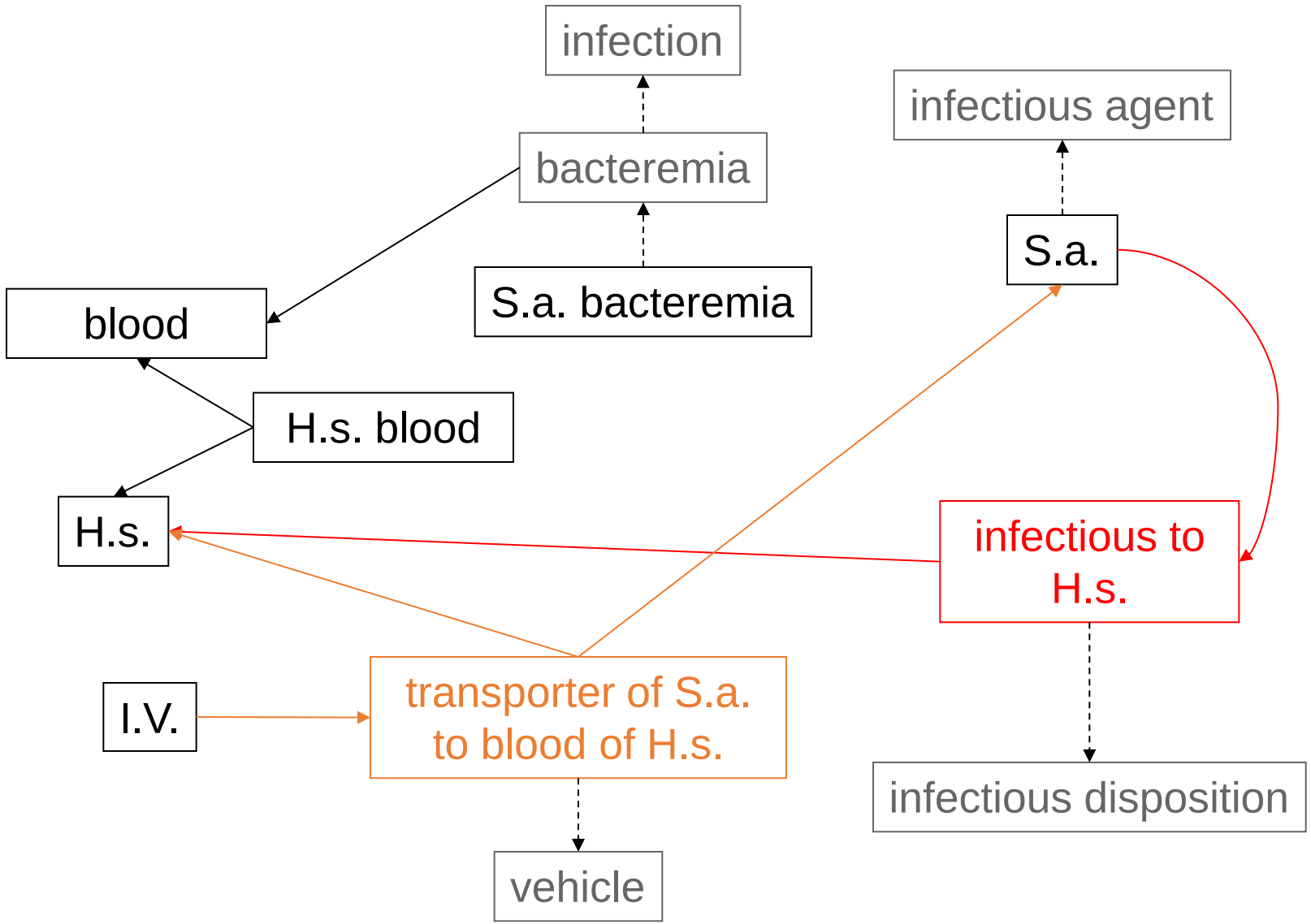
Execute | Add to ontology

Query results

Instances (2)

- NRS740
- NRS701

Integration across three dimensions



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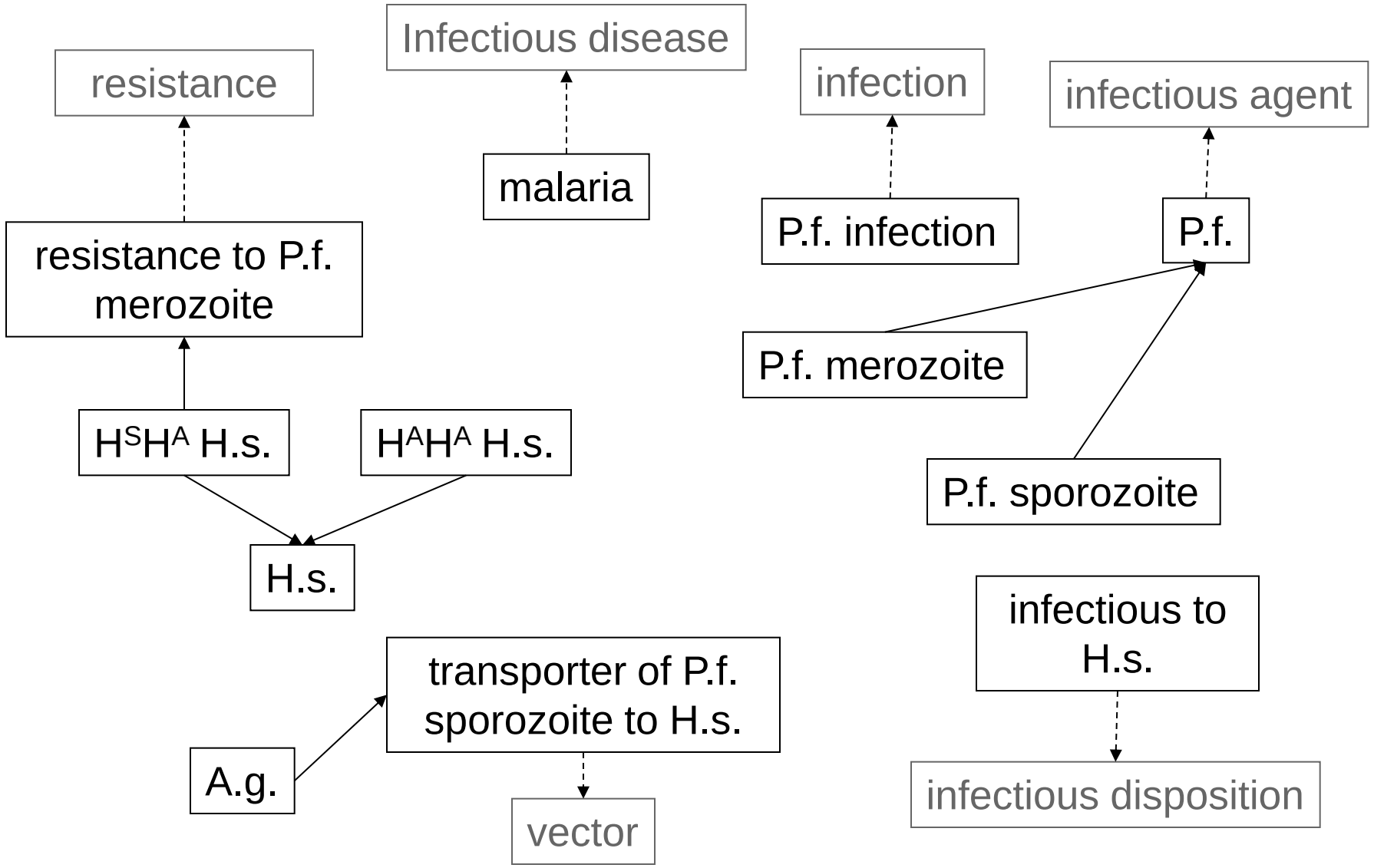

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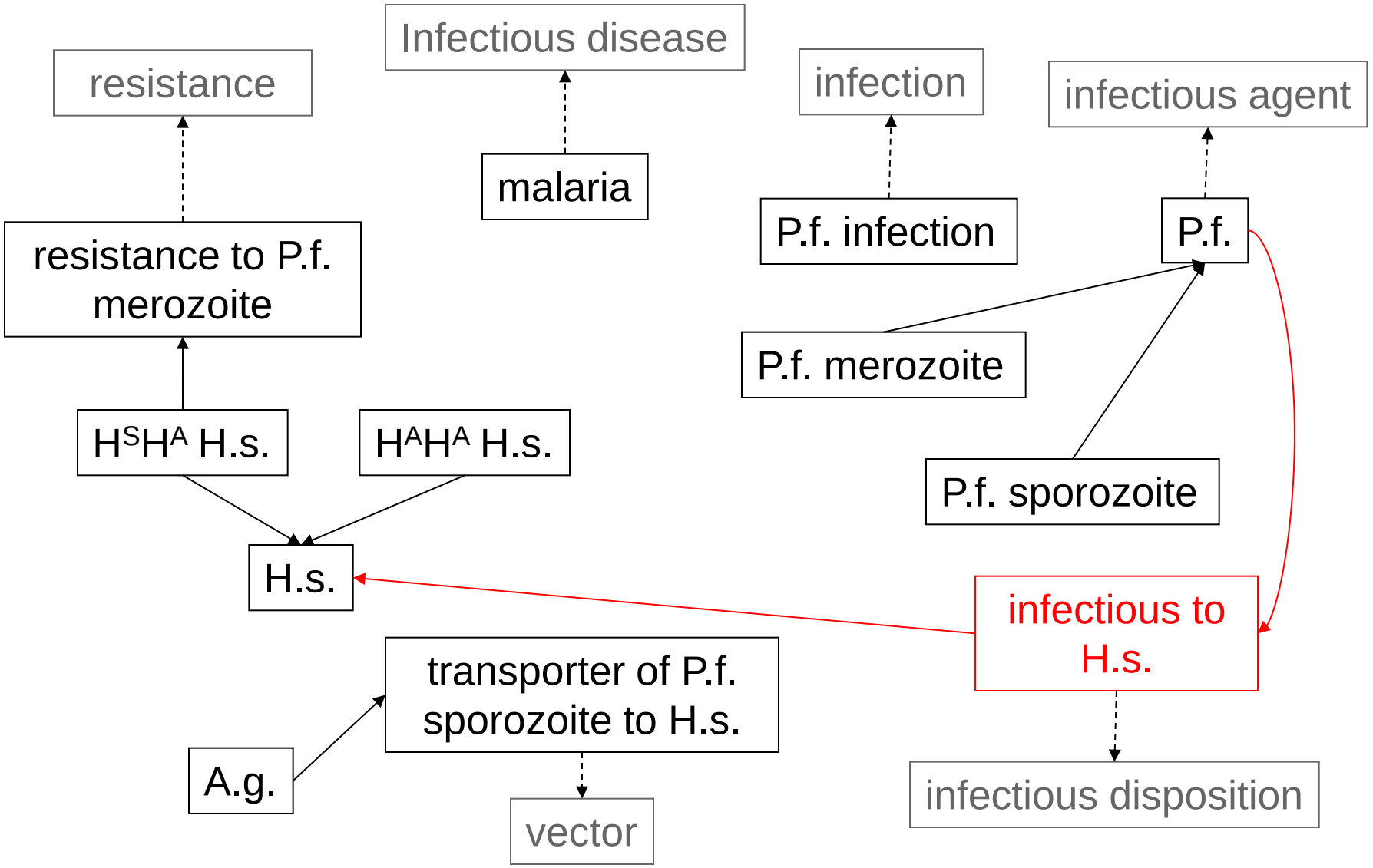

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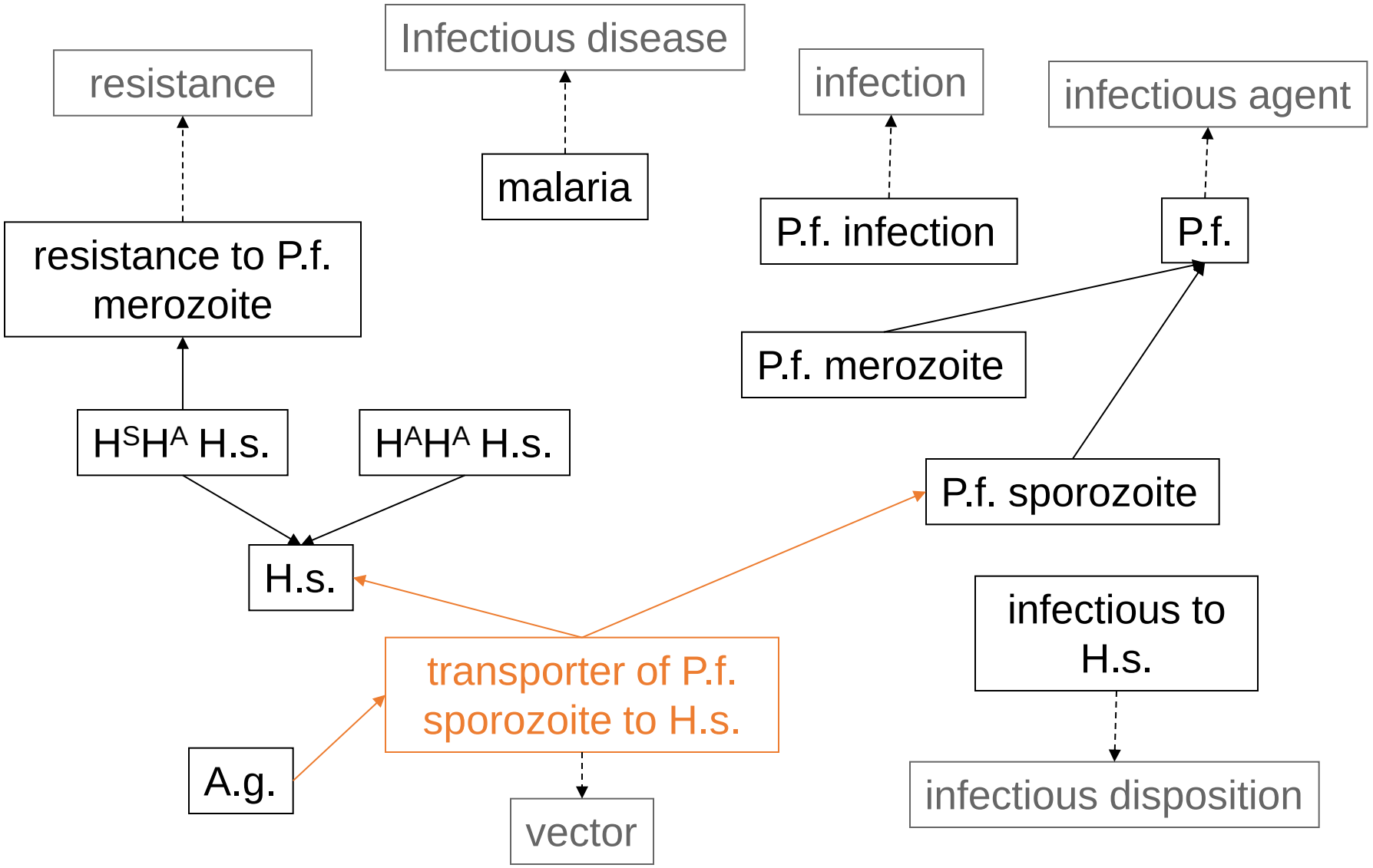
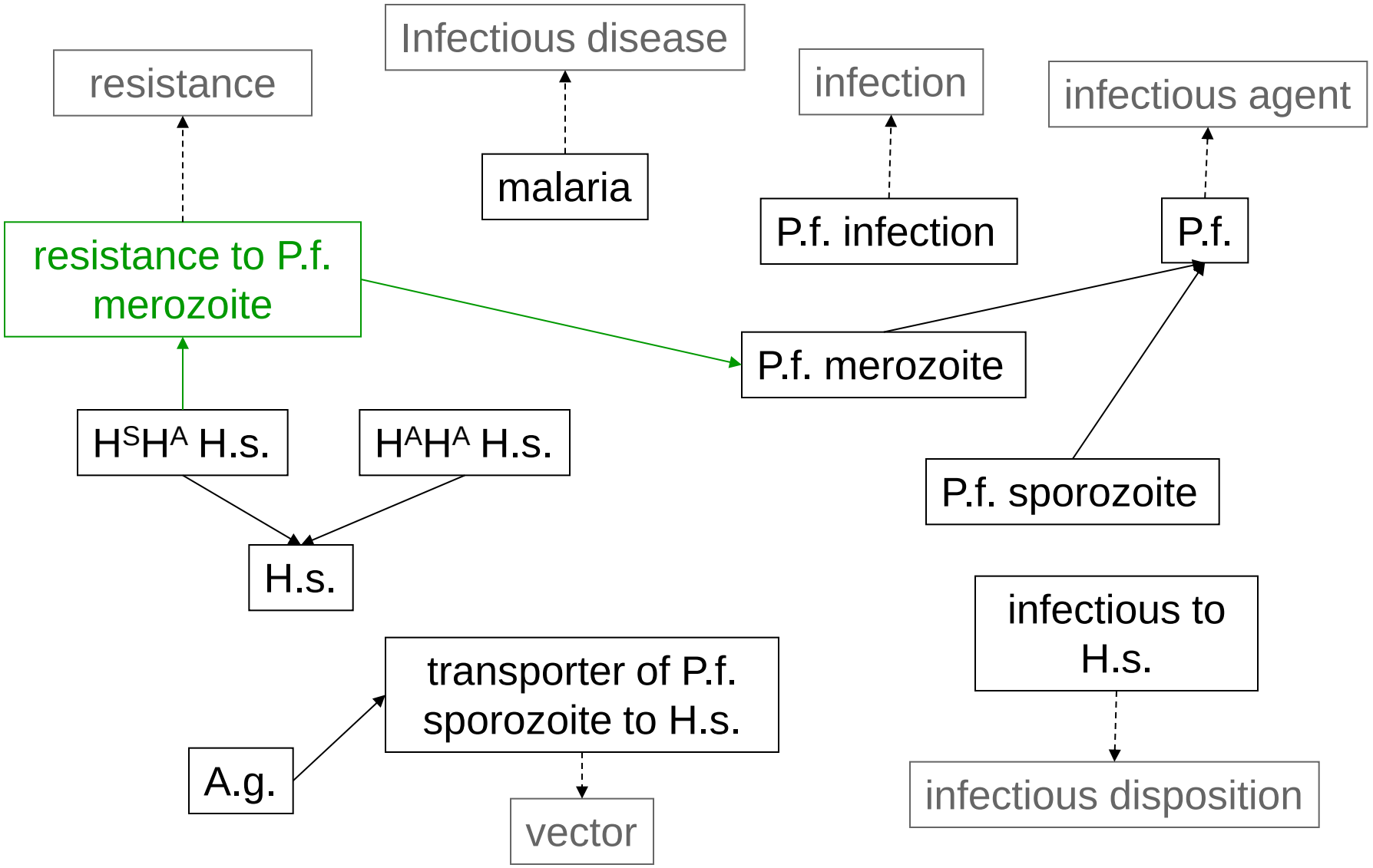


Integration across three dimensions



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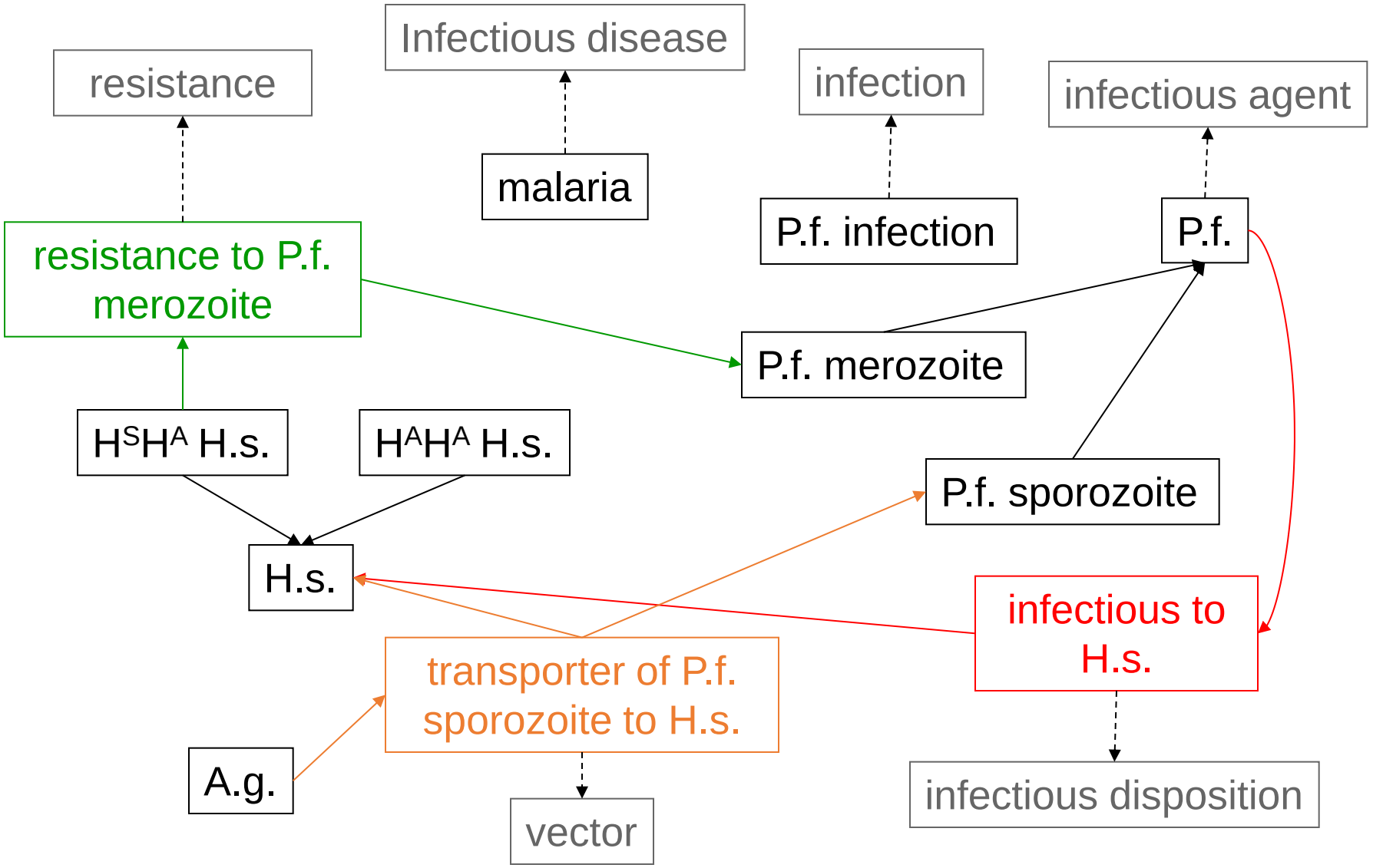

USERS

- Staphylococcus aureus
  - Vance Fowler - Duke University Medical Center
- Brucellosis
  - Oliver He - University of Michigan
- Salmonella
  - Ina Hulsegge - Animal Breeding and Genomics Centre
- Influenza
  - Richard Scheuermann – JCVI
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