Role-based representation and inference of biochemical processes

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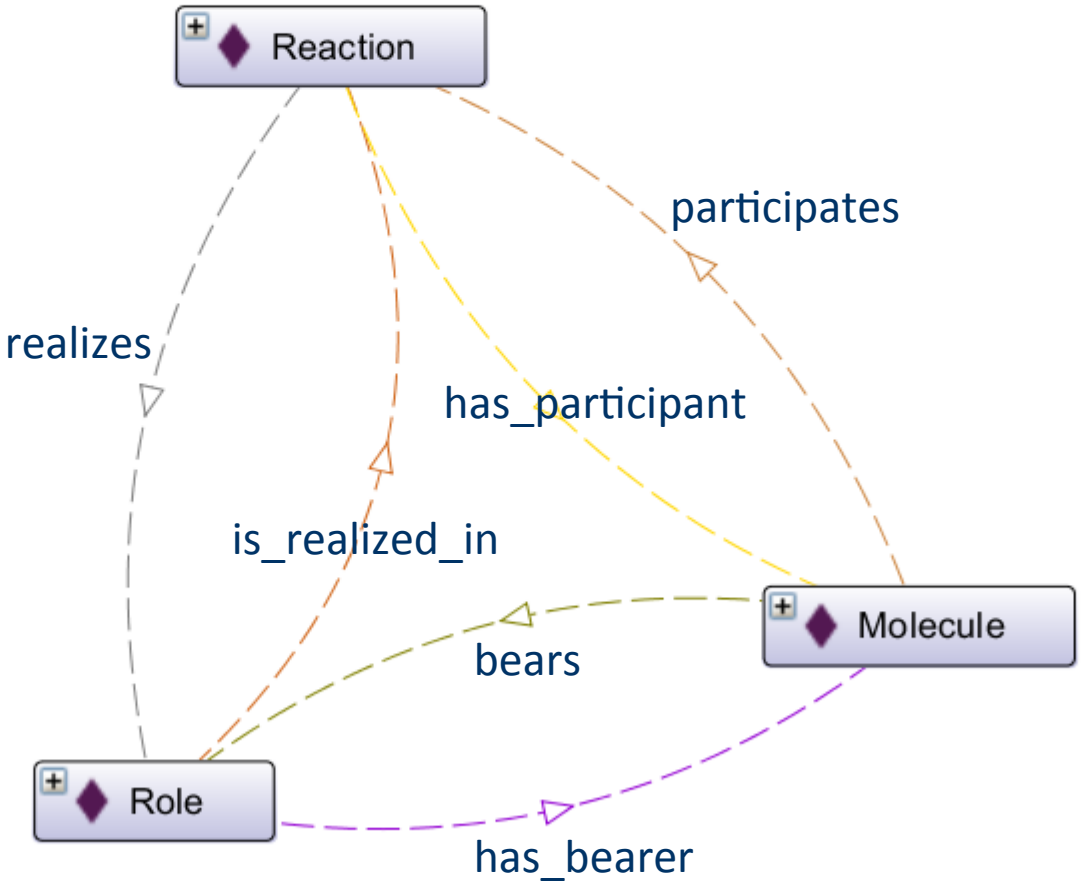
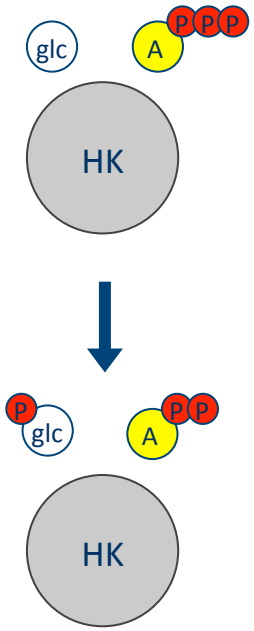
motivation

- computational approaches to study biochemistry require machine accessible representations of biochemical knowledge
- existing representations adopt formal semantics to varying degrees
- limited expressivity and ability for reasoning

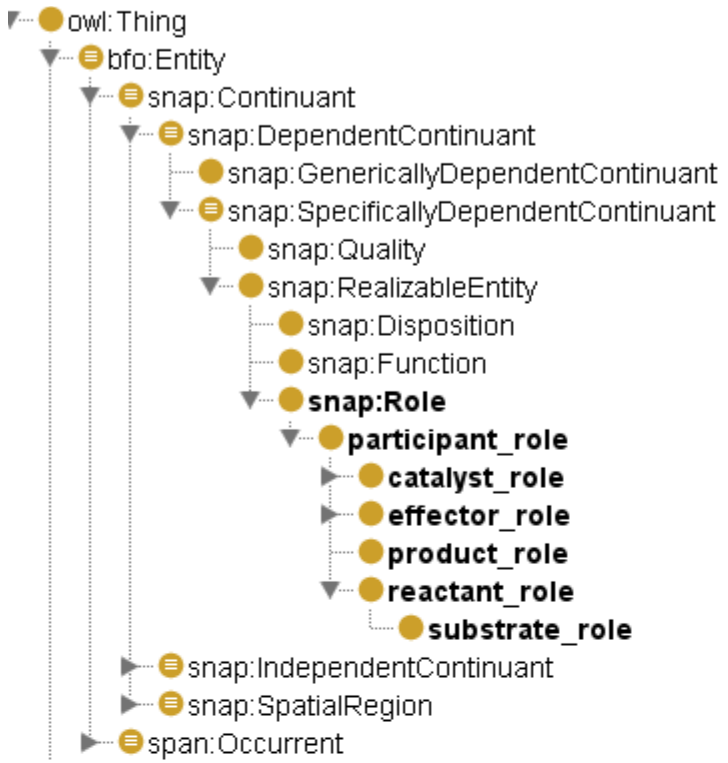


Dumontier (2008) Proc. 5th OWLED Workshop on OWL: Experiences and Directions



- biochemical processes viewed as ***microscopic molecular events***
- individuals of classes describing chemical species represent ***single molecules***
- individuals of classes describing biochemical processes represent single molecular events, i.e. ***directed transitions of a chemical system from an initial to a terminal state*** involving individual molecules

Roles


owl:Thing
bfo:Entity
snap:Continuant
snap:DependentContinuant
snap:GenericallyDependentContinuant
snap:SpecificallyDependentContinuant
snap:Quality
snap:RealizableEntity
snap:Disposition
snap:Function
snap:Role
participant_role
catalyst_role
effector_role
product_role
reactant_role
substrate_role
snap:IndependentContinuant
snap:SpatialRegion
span:Occurrent


role
participant_role
catalyst_role
enzyme_role
effector_role
activator_role
enzyme_activator_role
allosteric_activator_role
allosteric_effector_role
allosteric_inhibitor_role
inhibitor_role
enzyme_inhibitor_role
allosteric_inhibitor_role
irreversible_inhibitor_role
reversible_inhibitor_role
competitive_inhibitor_role
mixed_inhibition_inhibitor_role
non-competitive_inhibitor_role
uncompetitive_inhibitor_role
product_role
reactant_role
substrate_role

main axis of classification: stoichiometry

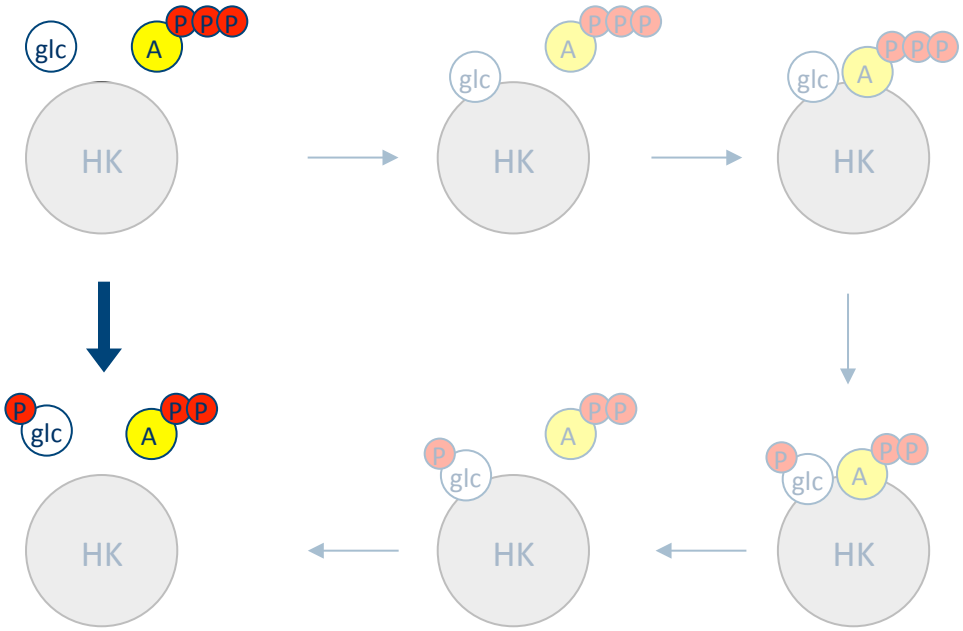
aA + bB → xX + yY

EquivalentTo:
(*realizes* exactly a (reactant_role and (*has_bearer* some A))) and
(*realizes* exactly b (reactant_role and (*has_bearer* some B))) and
(*realizes* exactly x (product_role and (*has_bearer* some X))) and
(*realizes* exactly y (product_role and (*has_bearer* some Y))) and
realizes exactly (a+b) reactant_role and
realizes exactly (x+y) product_role

glc + atp → g6p + adp

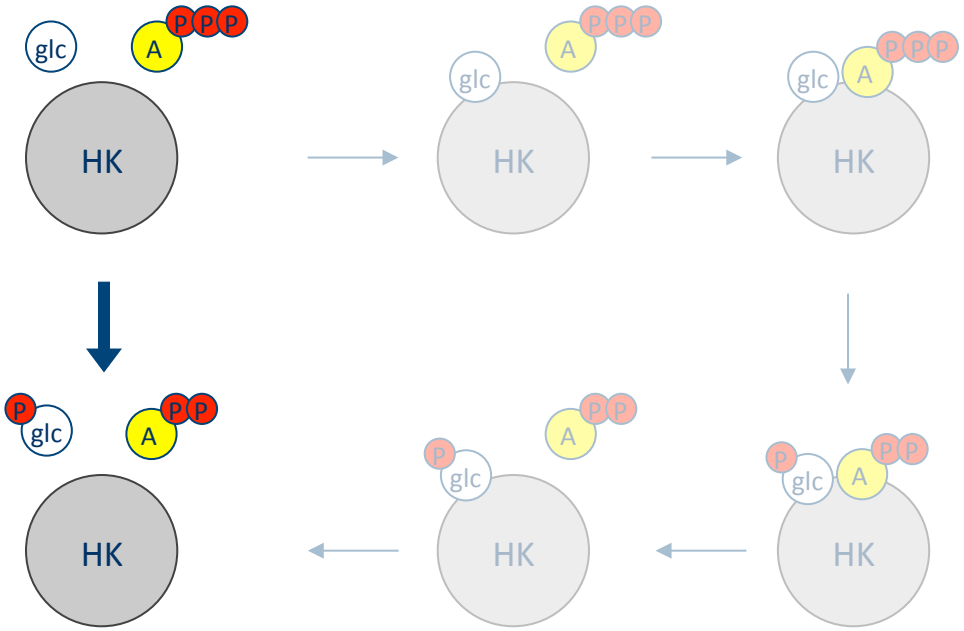
EquivalentTo:
(*realizes* exactly 1 (reactant_role and (*has_bearer* some glc))) and
(*realizes* exactly 1 (reactant_role and (*has_bearer* some atp))) and
(*realizes* exactly 1 (product_role and (*has_bearer* some g6p))) and
(*realizes* exactly 1 (product_role and (*has_bearer* some adp))) and
realizes exactly 2 reactant_role and
realizes exactly 2 product_role

classification by overall stoichiometry



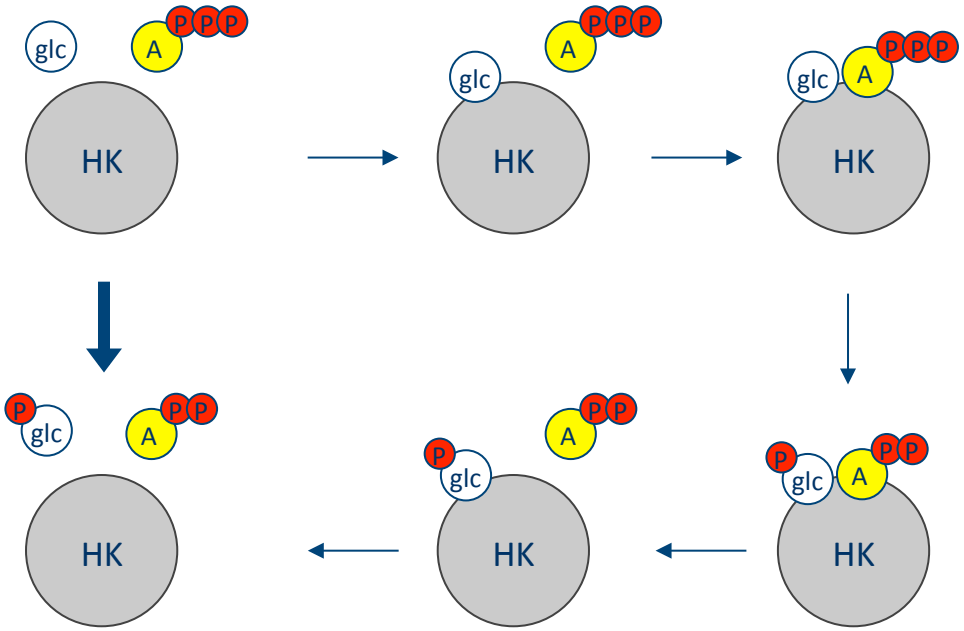
EquivalentTo:
(*realizes* exactly 1 (reactant_role and
(*has_bearer* some glc))) and
(*realizes* exactly 1 (reactant_role and
(*has_bearer* some atp))) and
(*realizes* exactly 1 (product_role and
(*has_bearer* some g6p))) and
(*realizes* exactly 1 (product_role and
(*has_bearer* some adp))) and
realizes exactly 2 reactant_role and
realizes exactly 2 product_role

… and catalysis



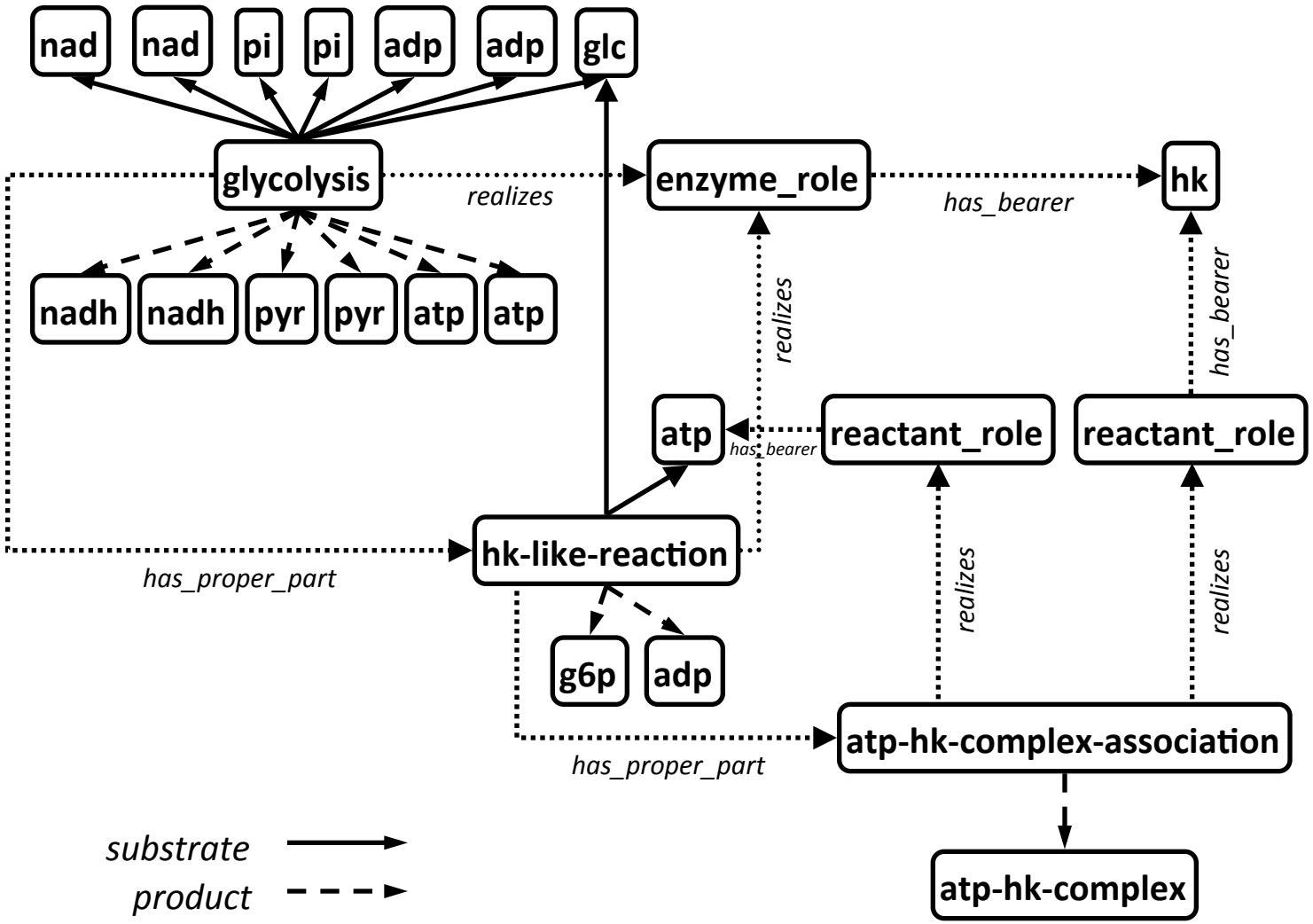
EquivalentTo:
(*realizes* exactly 1 (reactant_role and
(*has_bearer* some glc))) and
(*realizes* exactly 1 (reactant_role and
(*has_bearer* some atp))) and
(*realizes* exactly 1 (product_role and
(*has_bearer* some g6p))) and
(*realizes* exactly 1 (product_role and
(*has_bearer* some adp))) and
realizes exactly 2 reactant_role and
realizes exactly 2 product_role and
**(*realizes* exactly 1 (enzyme_role and
(*has_bearer* some hk)))**

… and mechanism

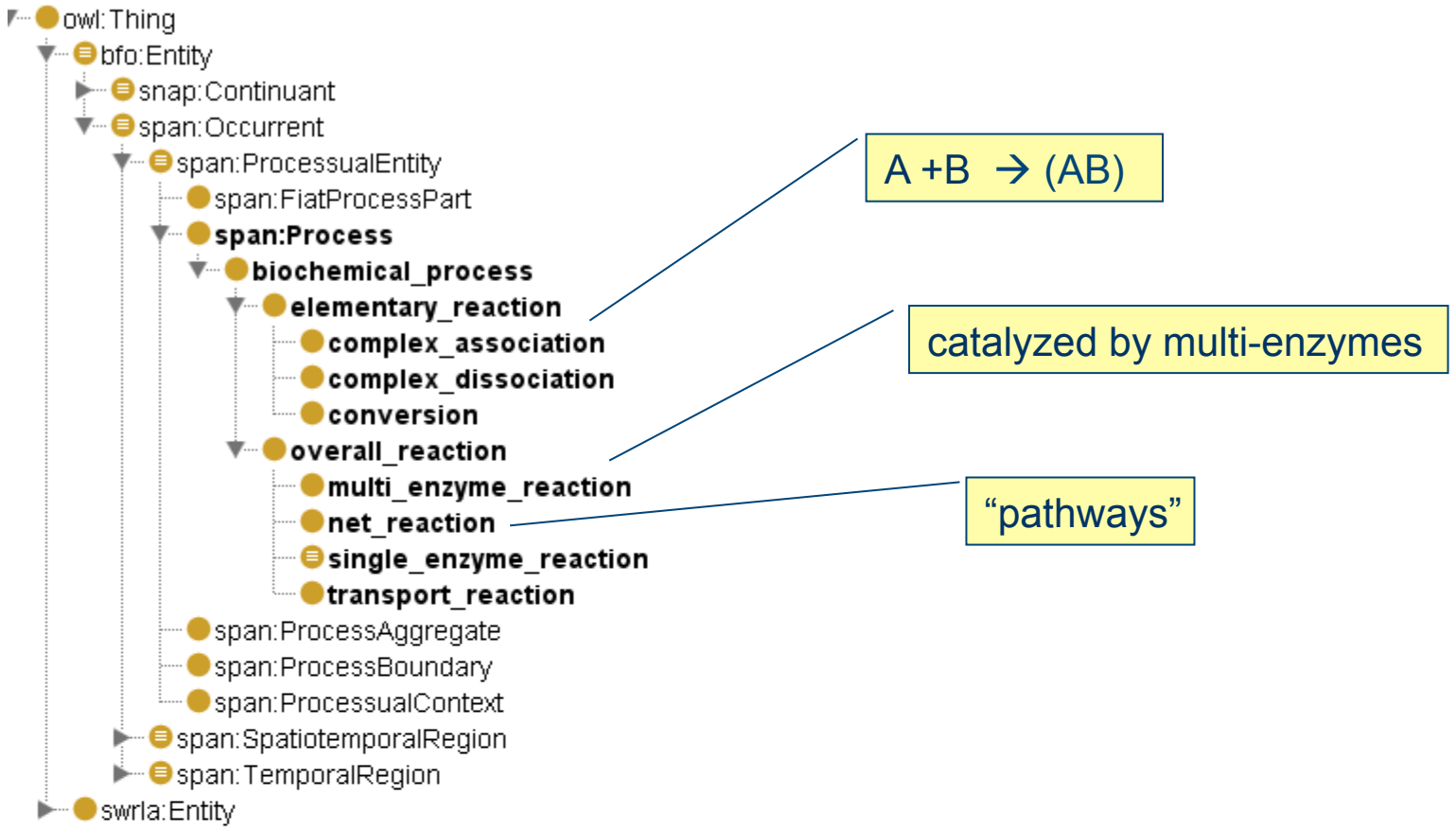


EquivalentTo:
(*realizes* exactly 1 (reactant_role and
(*has_bearer* some glc))) and
(*realizes* exactly 1 (reactant_role and
(*has_bearer* some atp))) and
(*realizes* exactly 1 (product_role and
(*has_bearer* some g6p))) and
(*realizes* exactly 1 (product_role and
(*has_bearer* some adp))) and
realizes exactly 2 reactant_role and
realizes exactly 2 product_role and
(*realizes* exactly 1 (enzyme_role and
(*has_bearer* some hk))) and
(has_proper_part …)

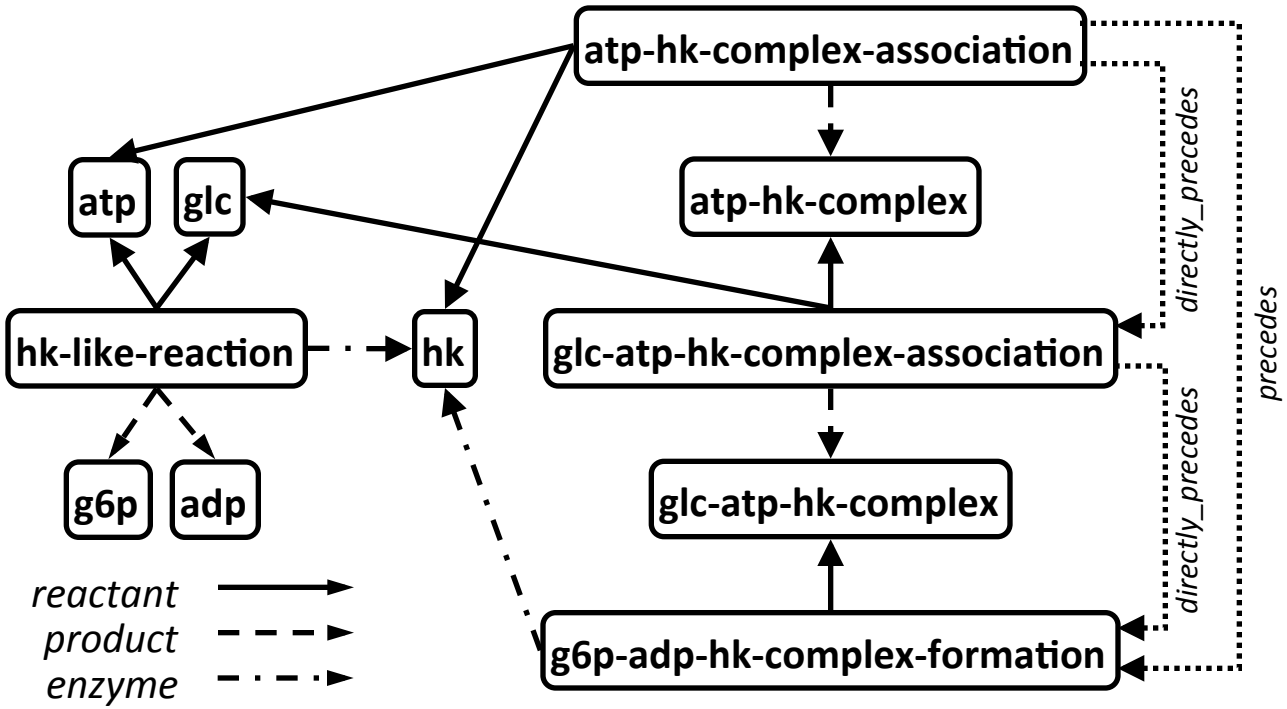
partonomy of processes



process types



shared reactants & products: sequence of processes

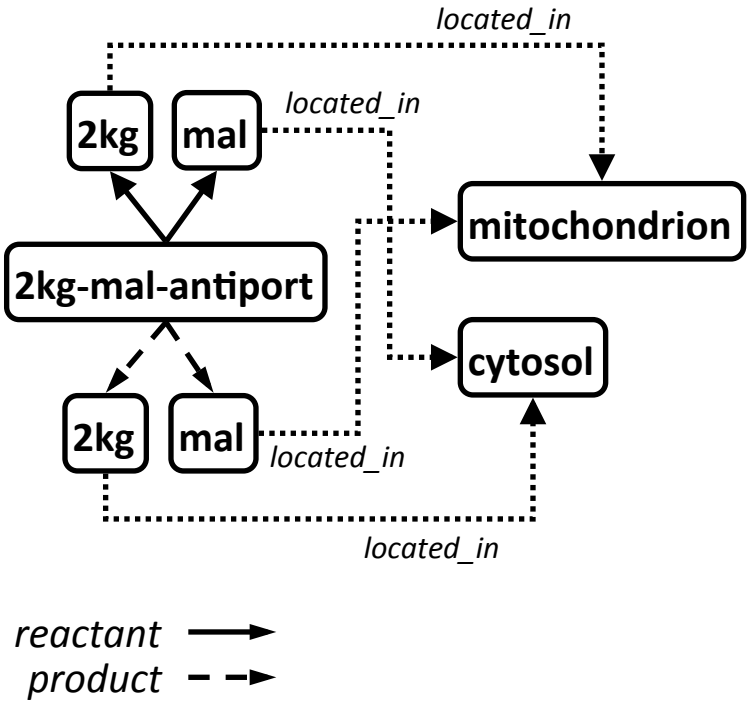


location of processes and transport

glc + atp → g6p + adp in the cytosol of human liver cells

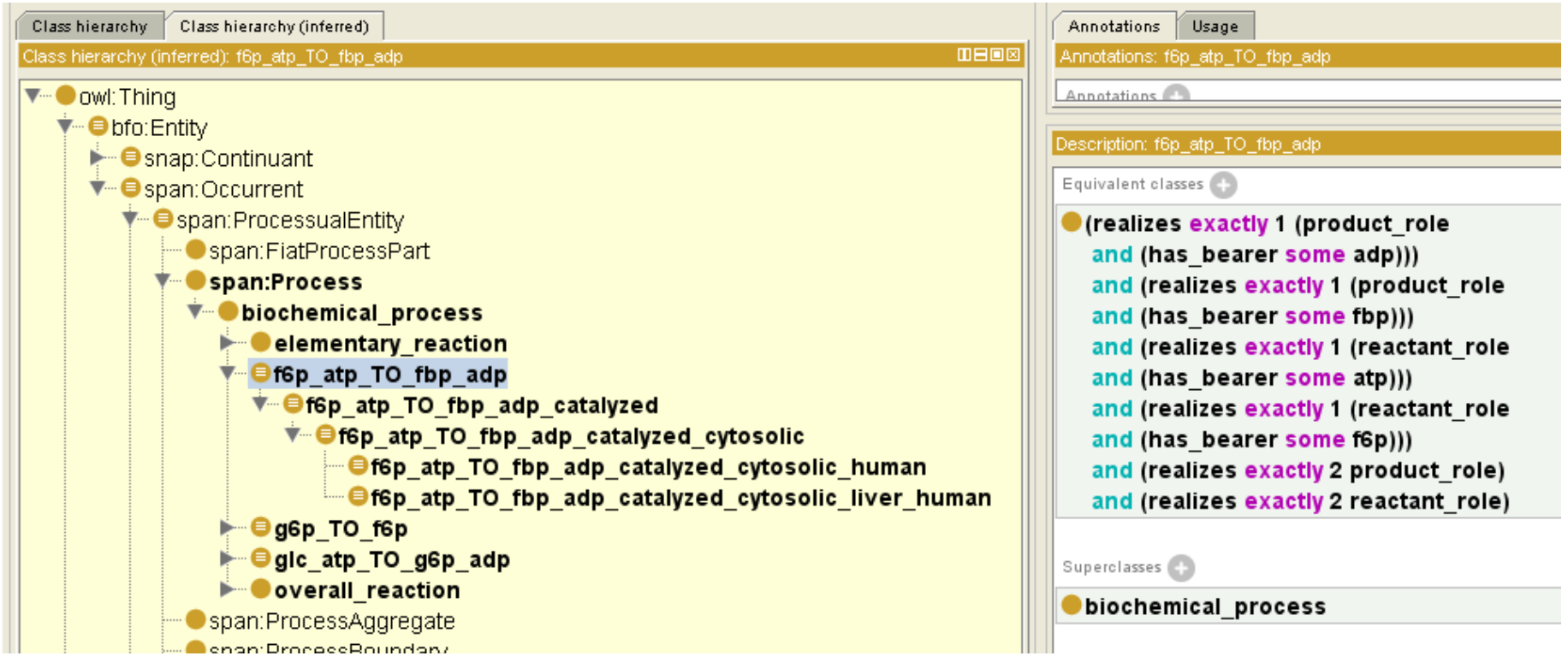
EquivalentTo:
(*realizes* exactly 1 (reactant_role and (*has_bearer* some glc))) and
(*realizes* exactly 1 (reactant_role and (*has_bearer* some atp))) and
(*realizes* exactly 1 (product_role and (*has_bearer* some g6p))) and
(*realizes* exactly 1 (product_role and (*has_bearer* some adp))) and
(*realizes* exactly 2 reactant_role) and
(*realizes* exactly 2 product_role) and
(*occurs_in* some (cytosol and (*part_of* some (cell and (*part_of* some (liver and (*part_of* some Homo_sapiens))))))

location of processes and transport



EquivalentTo:
(*realizes* exactly 1 (reactant_role and
(*has_bearer* some (2kg and (*located_in*
some mitochondrion)))) and
(*realizes* exactly 1 (reactant_role and
(*has_bearer* some (mal and (*located_in*
some cytosol)))) and
(*realizes* exactly 1 (product_role and
(*has_bearer* some (2kg and (*located_in*
some cytosol)))) and
(*realizes* exactly 1 (product_role and
(*has_bearer* some (mal and (*located_in*
some mitochondrion)))) and
realizes exactly 2 reactant_role and
realizes exactly 2 product_role

inference of process and entity characteristics



inference of process and entity characteristics

- location of reaction participants:
  biochemical_process(?p), occurs_in(?p,?l), has_participant(?p,?o) -> located_in(?o,?l)
- sequence of processes within same location:
  product_role(?r1), reactant_role(?r2), has_bearer(?r1,?o), has_bearer(?r2,?o), realizes(?p1,?r1), realizes(?p2,?r2), occurs_in(?p1,?l), occurs_in(?p2,?l) -> directly_precedes(?p1,?p2)

outlook

- integrate with ontological descriptions of chemical entities, cell-types, tissues
- implement design patterns / rules for classification according to taxonomies of chemicals, locations, reaction mechanisms,…
- add support for quantitative description of reactions / participants
- expand on other molecular interactions
- use for biochemical network reconstruction, integration of pathway datasets, inference of molecular associations…

Acknowledgments

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