Current Directions in MIM Development

- MIM specifications - towards the development of a MIM drawing tool
  - Specification
  - Ontology
- Expanding the notation to tackle challenges in signaling pathways (nucleic acids)
  - Cell Cycle. 8:2281-99. 2009
  - Mol Biol Cell 19:1-7. 2008
  - discover.nci.nih.gov/mim
- MIM simulations and validations
  - How two effectors interact to modulate the activity of of the tumor suppressor p53
  - Experimental testing of simulation results

Goals of MIM Ontology and Specification

- Describe an implementation of MIM directed towards software developers
- Facilitate development of an API that will allow interoperability between MIM tools
  - First step - a tool based on Pathvisio
  - A Java-based API in development
- Allow network analysis of MIM diagrams
  - Conversion of diagrams to bipartite (entity/interaction) graphs
  - Meant for feedback loop identification
  - Species enumerators to handle the combinatorial interpretation of MIM

MIM Ontology: Classes

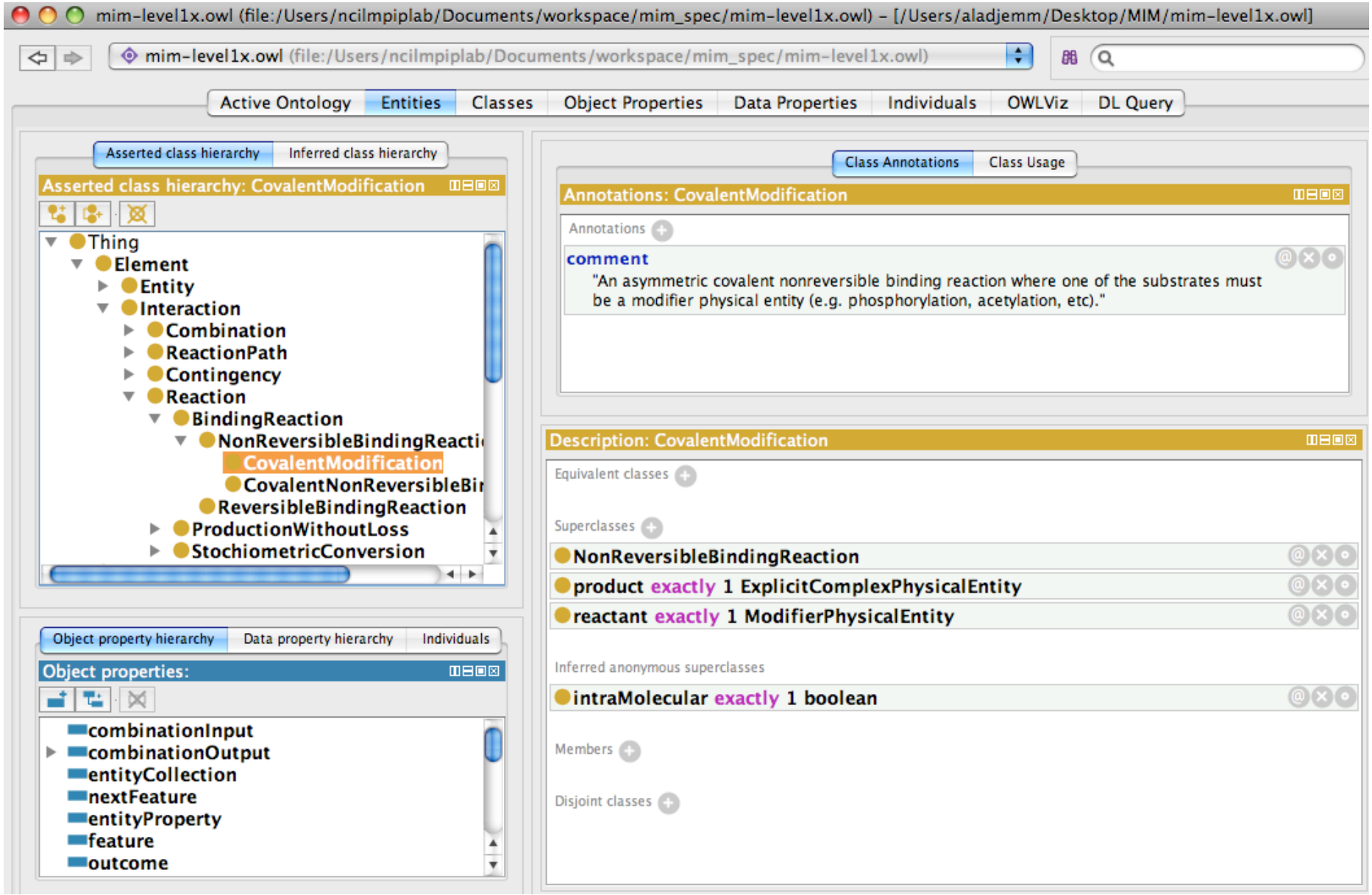
- Entity
  - SourceSinkEntity
  - ConceptualEntity
  - OutcomeEntity
  - PhysicalEntity
    - Feature
    - Modifier
    - RestrictedCopy
    - ComplexPhysicalEntity
    - SimplePhysicalEntity
- Interaction
  - Combination
  - ReactionPath
  - Contingency
  - Reaction
- Utility
  - EntityProperty
  - Annotation
  - ControlledVocabulary
  - Group
  - SequenceLocation
  - XRef

Example: MIM Feature Representation

```
p53 isA SimplePhysicalEntity
p53 hasFeature pxxp
...

pxxp isA EntityFeature
pxxp hasNextFeature od
pxxp hasModificationFeature phos1
pxxp hasModificationFeature phos2
pxxp hasFeatureLocation loc_pxxp
...

od isA EntityFeature
...
```

```
pxxp_binds_od isA CovalentIrreversibleBinding
pxxp_binds_od hasReactant pxxp
pxxp_binds_od hasReactant od
pxxp_binds_od hasProduct pxxp_od
...

phos1 isA ModificationFeature
phos1 hasNextFeature phos2
phos1 hasFeatureLocation loc_phos1
...

loc_phos1 isA SequenceSite
loc_phos1 hasSequencePosition "100"
...

loc_pxxp isA SequenceInterval
loc_pxxp hasSequenceIntervalBegin pxxp_loc_begin
...

pxxp_loc_begin isA SequenceSite
pxxp_loc_begin hasSequencePosition "5"
...
```

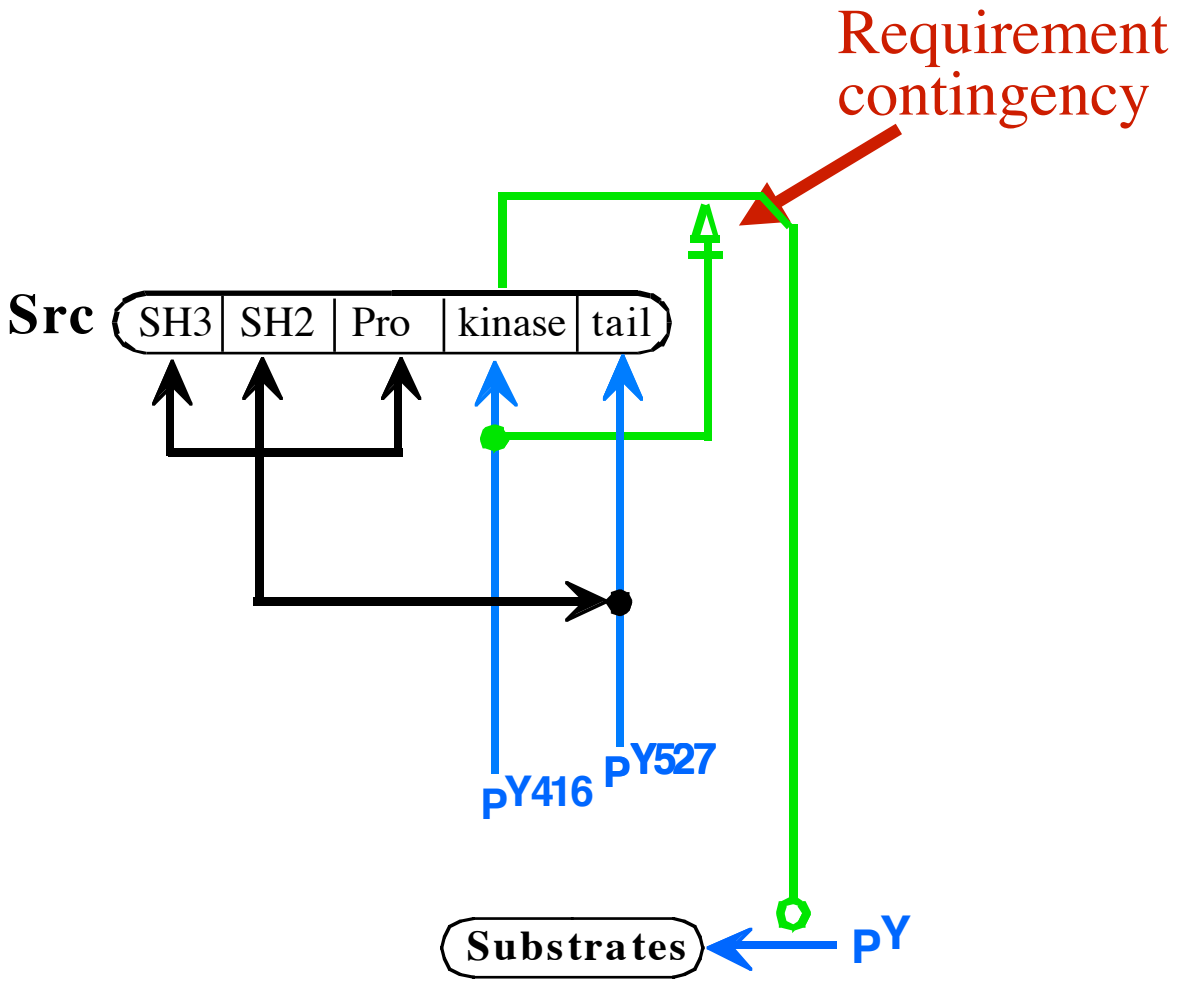
MIM Ontology



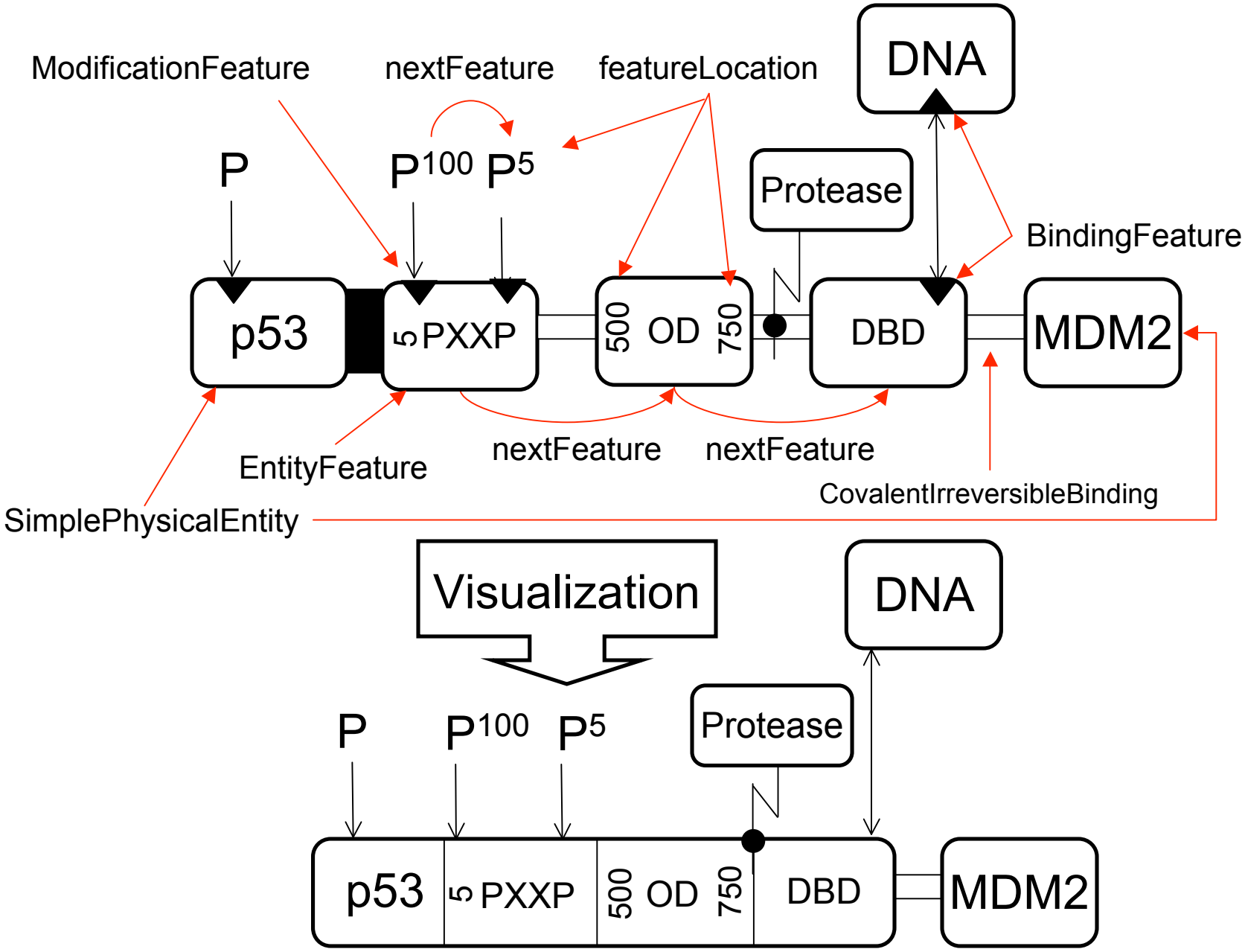
MIM Ontology

- Examples - Feature classes:
  - SimplePhysicalEntity - A physical entity type that can possess features.
  - EntityFeature - A part of a physical entity which can participate in interactions and can have binding or modification features (e.g. domain or motif).
  - BindingFeature - Specifies a feature for covalent or non-covalent binding.
  - ModificationFeature - Specifies a feature for a covalent modification.
- Examples - Object Properties
  - feature - A relationship between a Feature and a SimplePhysicalEntity.
  - nextFeature - The next Feature in a SimplePhysicalEntity.
  - featureLocation - Location of a BindingFeature or ModificationFeature on part of a PhysicalEntity. Features may only have one location along a sequence.
- Object properties form relationships between two classes. For example:
  - SimplePhysicalEntity(“p53”) hasFeature EntityFeature(“DNA Binding Domain”)

Domain Representation in MIM



DOMAINS AS MIM Features



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