Bridging Epoch: Mapping Two Clinical Trial Ontologies

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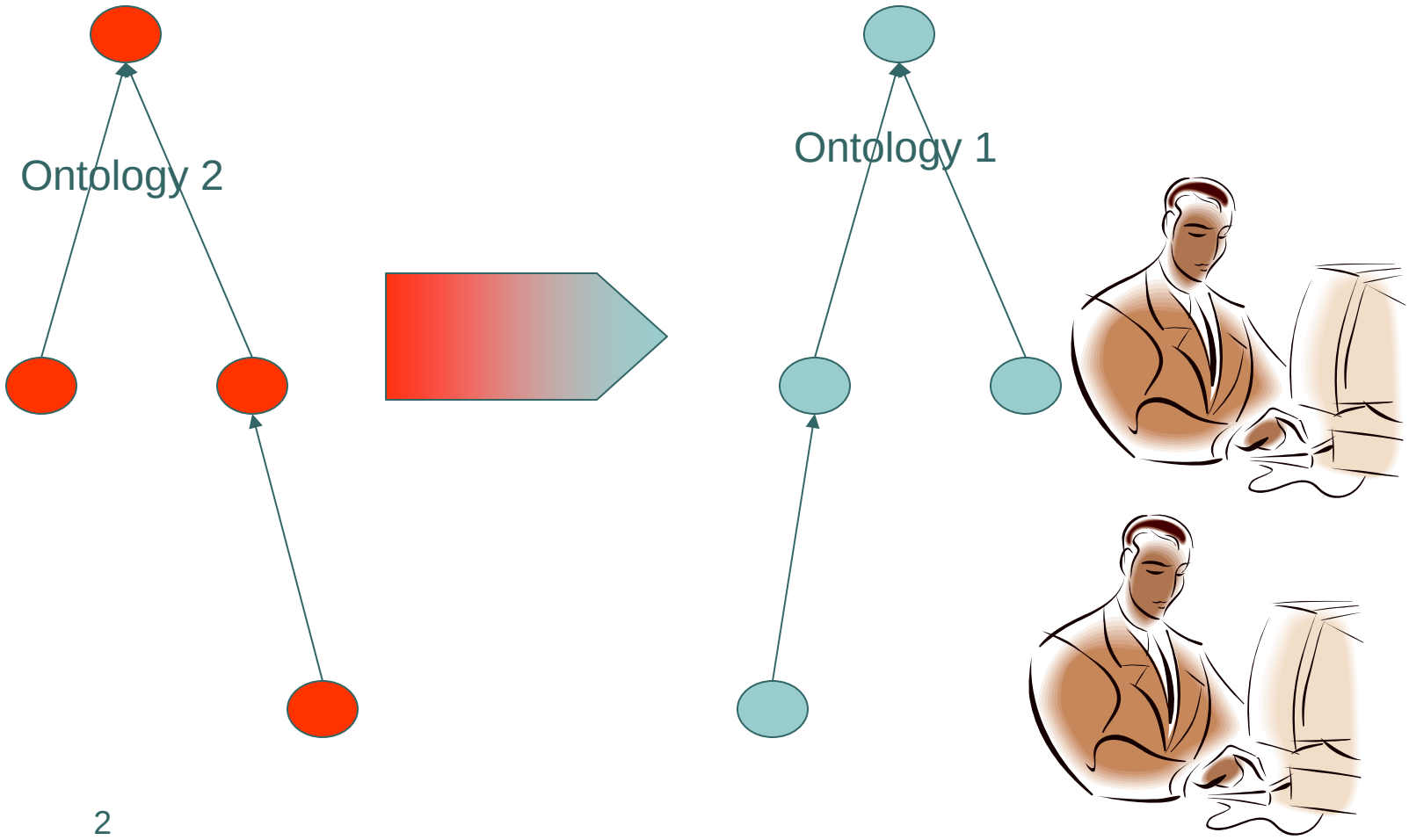
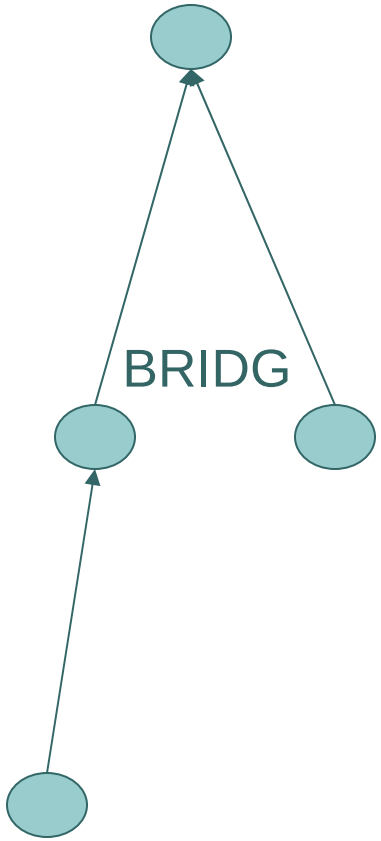
Problem: Ontologies and semantic interoperability

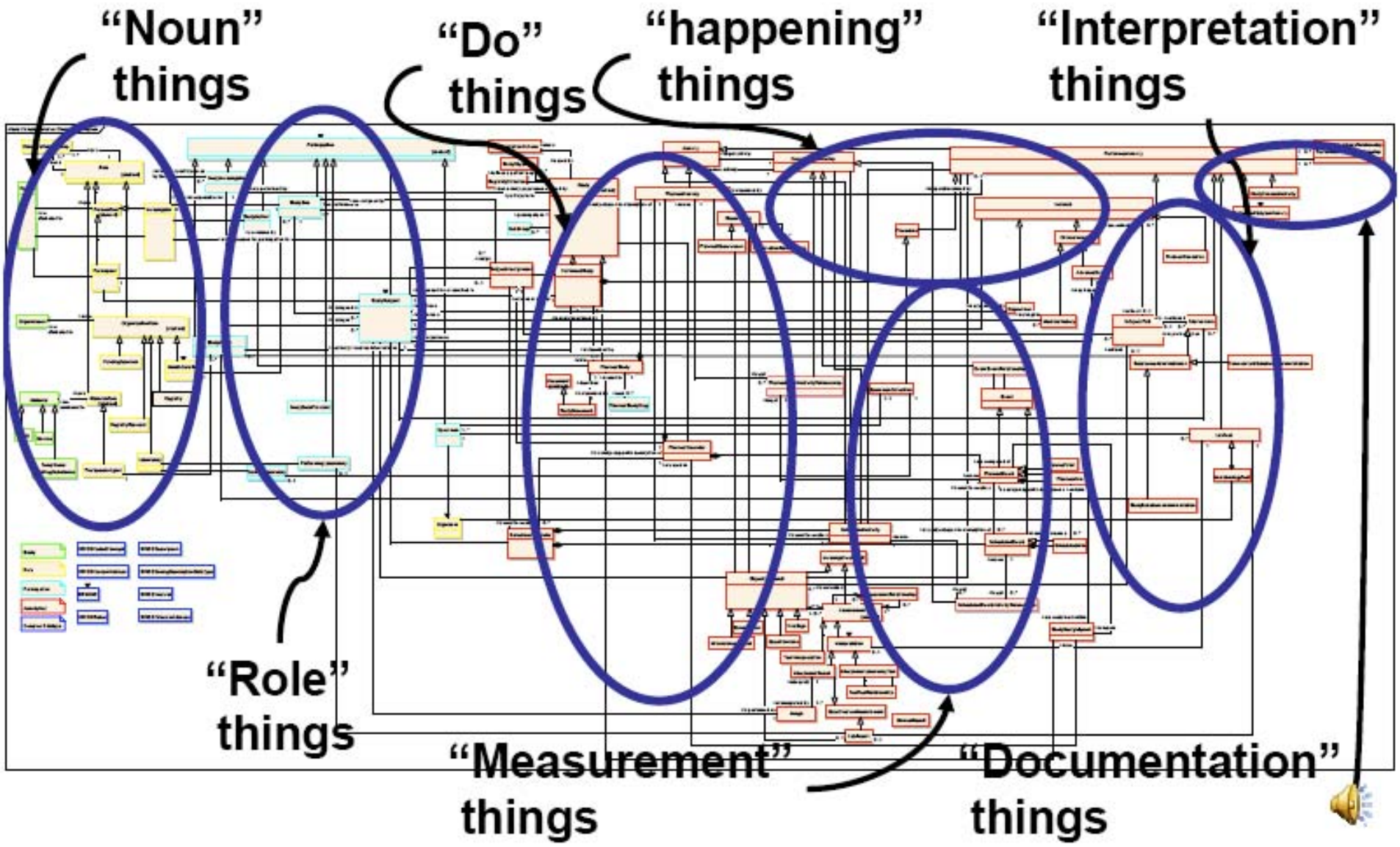


BRIDG: Biomedical Research Integration Group



- Part of US NCI Cancer Biomedical Informatics Grid (caBIG)
- Stakeholders include US FDA, HL7, CDISC
- Create shared domain model for protocol-driven clinical research
  - Comprehensive
  - Consensus-based
  - Abstract and context neutral

Current Classes in Core Elements



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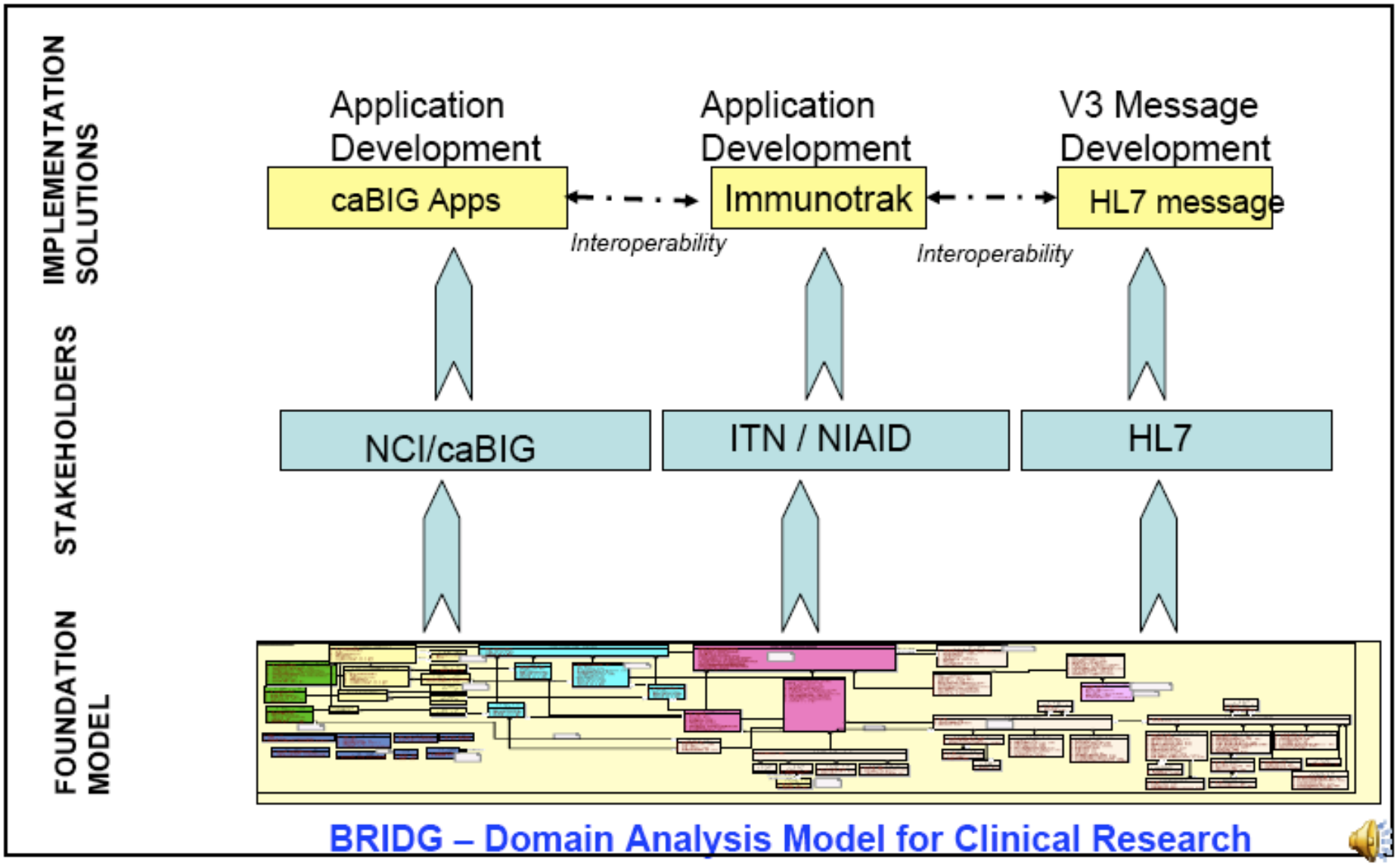
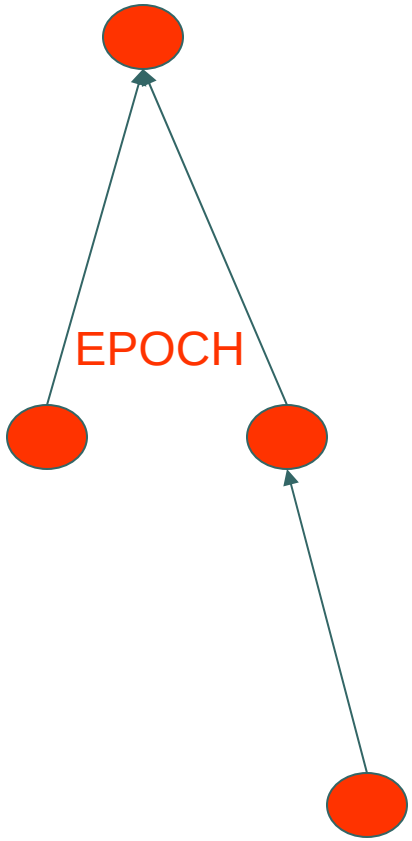
Achieving interoperability from a common semantic foundation

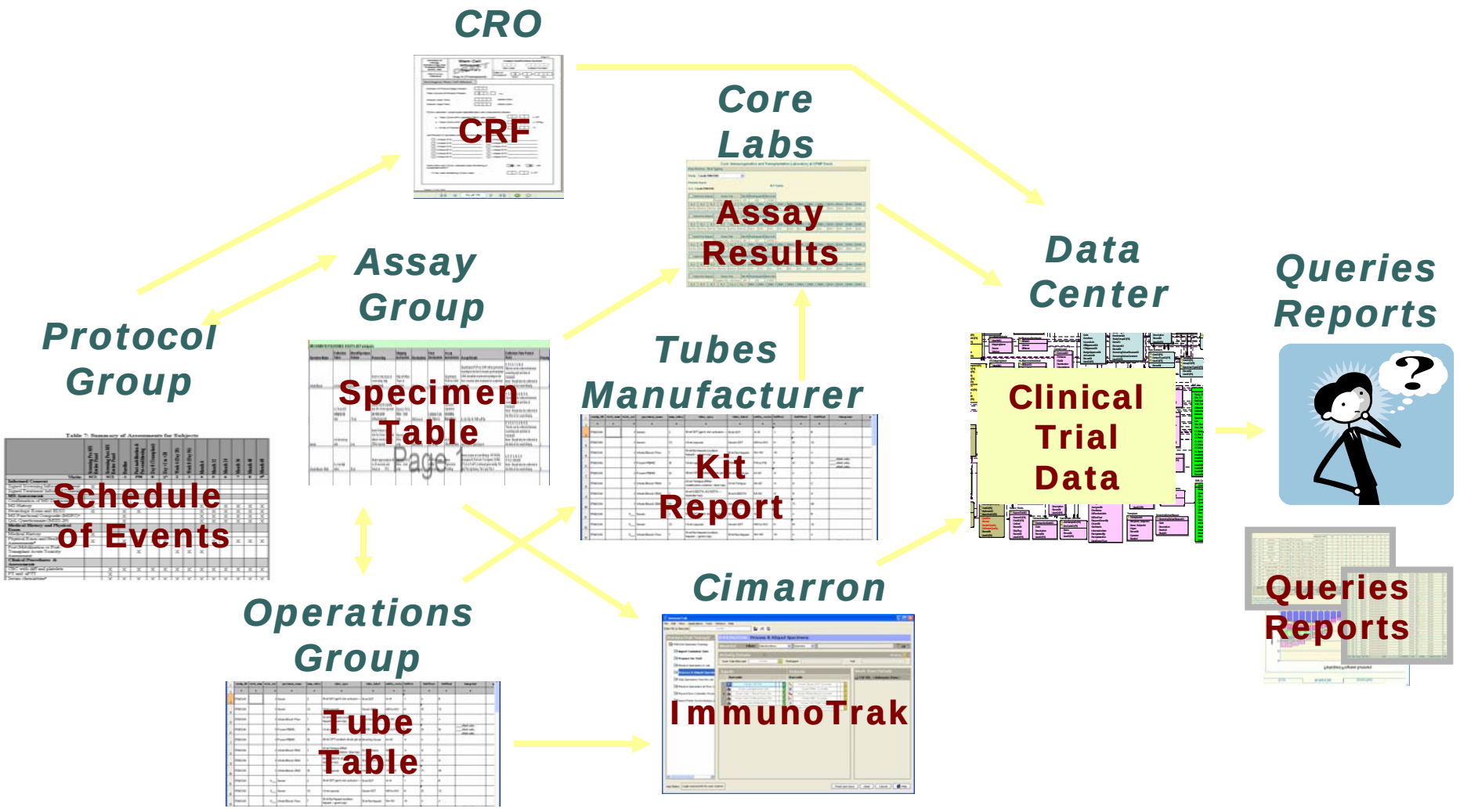


EPOCH: Immune Tolerance Network clinical trial ontologies



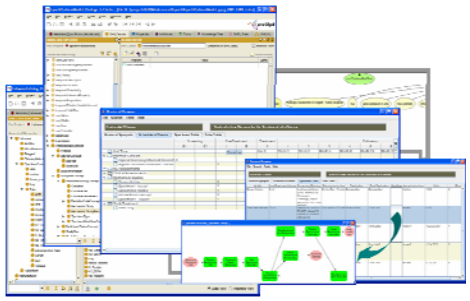
- Immune Tolerance Network (ITN)
  - International collaborative research effort that sponsors clinical trials and mechanistic assays on immune tolerance
- EPOCH clinical trial model
  - Developed at Stanford Medical Informatics
  - Designed to provide semantic foundation for management of clinical trials

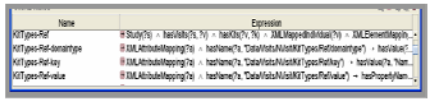
Management of clinical trials involves complex data and multiple groups

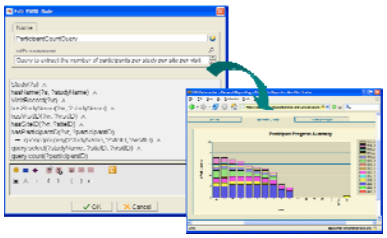


Three goals of EPOCH ontologies

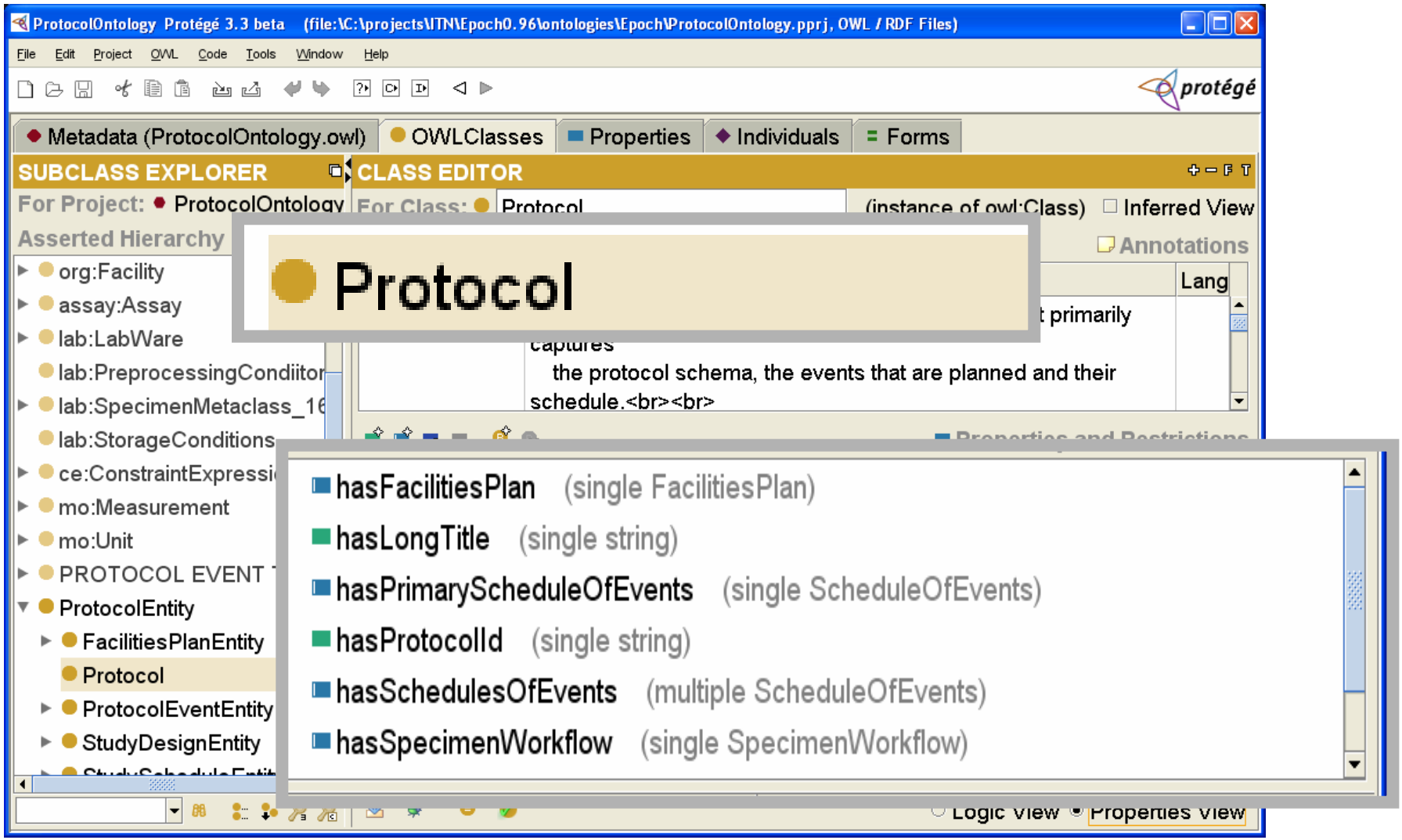
- Design tools to help acquire and maintain knowledge about protocol and assay designs
- Use this knowledge to drive data collection during a trial
- Implement querying methods to support trial management, and ad hoc data analysis







EPOCH ontologies created in Protégé OWL



ITN wants to use BRIDG-compliant applications

- ITN protocols encoded as EPOCH knowledge bases to drive caBIG applications (e.g., Patient Study Calendar)
- Challenge: Develop methods to
  - Harmonize common subset of BRIDG & EPOCH: shared semantics
  - Overcome representational mismatch
    - Representation languages
    - Representation choices
    - (Terminological mismatch not consider here)

Approach taken

- Semantic alignment
- Overcoming representation language mismatch
- Overcoming representation choice mismatches

Approach taken

- Semantic alignment
  - Use Excel spreadsheet to systematically review and document possible mappings
  - Define necessary preconditions for mapping
- Overcoming representation language mismatch
- Overcoming representation choice mismatches

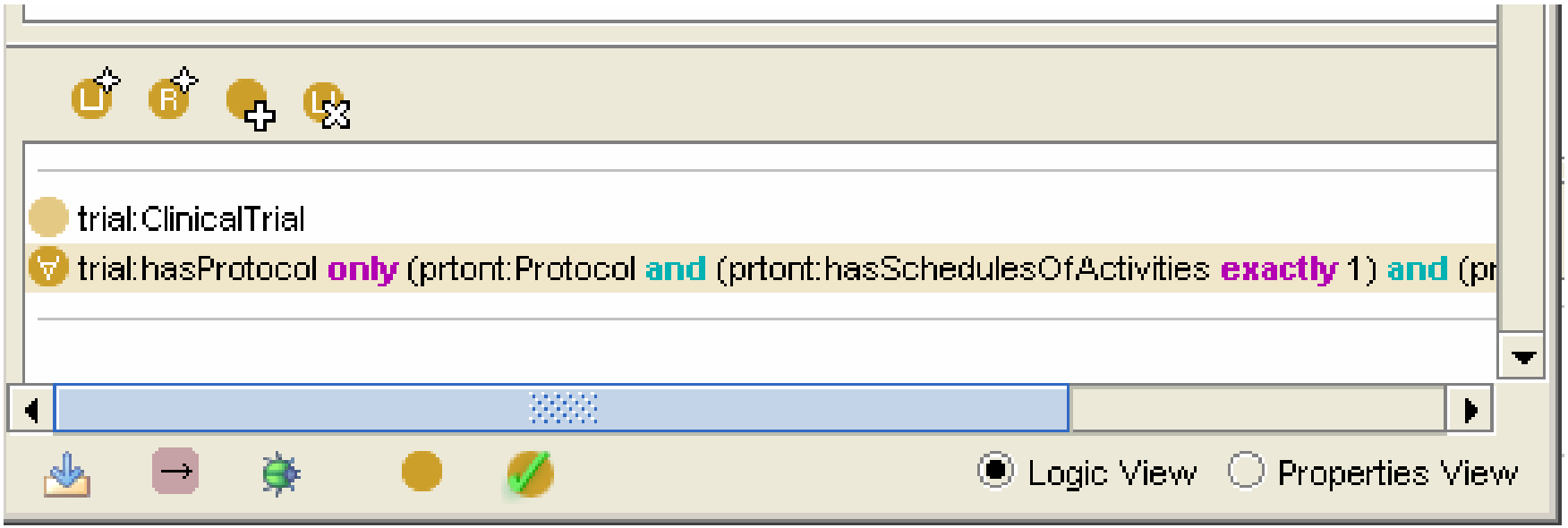
Semantic Alignment: Excel spreadsheet

Class	Attribute	AttributeValue or Description	InGreenbaum?	In Scope?	Mappable?	
Period	ClassComment	The entire protocol is segmented temporally into periods. Each period defines a segment of time that groups proctocol activites by their function. For example, the Screening Period defines the protocol timing during which the activites related to protocol	y	y	y	BRIDG.Plan
Period	hasName	name of the period	y	y	y	BRIDG.Plan
Period	hasPeriodType	a generic label assigned to the period	y	y	n	<<no type ir
Period	hasSubTimings	a set of sub-periods or encounters that this period is de-composed into	y	y	y	BRIDG.Plan
Period	isPartOfParentTimings	a set of arms that this period is part of	y	y	y	BRIDG.Plan
Period	SubClassOf	#PlannedTiming	y	y	e	epoch-speci
PlannedActivity	ClassComment	Protocol-related activity such as a clinical assessment, a treatment or a mechanistic study, which involves participants and study site personnel.	y	y	y	BRIDG.Plan
PlannedActivity	hasAnnotations	annotations that specify instructional or temporal information on the activity	y	y	y	BRIDG.Plan will cover in information between an BRIDG.Cale
PlannedActivity	hasFunctionalGrouping	a higher-level grouping that the activity belongs to	y	y	y	BRIDG.Con (allows for c collecting c PlannedAct
PlannedActivity	hasName	name of the activity	y	y	y	BRIDG.Plan in the BRID

Semantic Alignment: Restrictions on EPOCH

- Mapping from EPOCH to BRDG => Place restrictions on EPOCH
  - Only one schedule of activities
  - Period has no subperiods
  - Limited temporal annotations
  - …
- Define necessary conditions for mapping
  - Formulate as DL definition of “BRIDGClinicalTrial” subclass of epoch:ClinicalTrial

BRIDGClinicalTrial in EPOCH



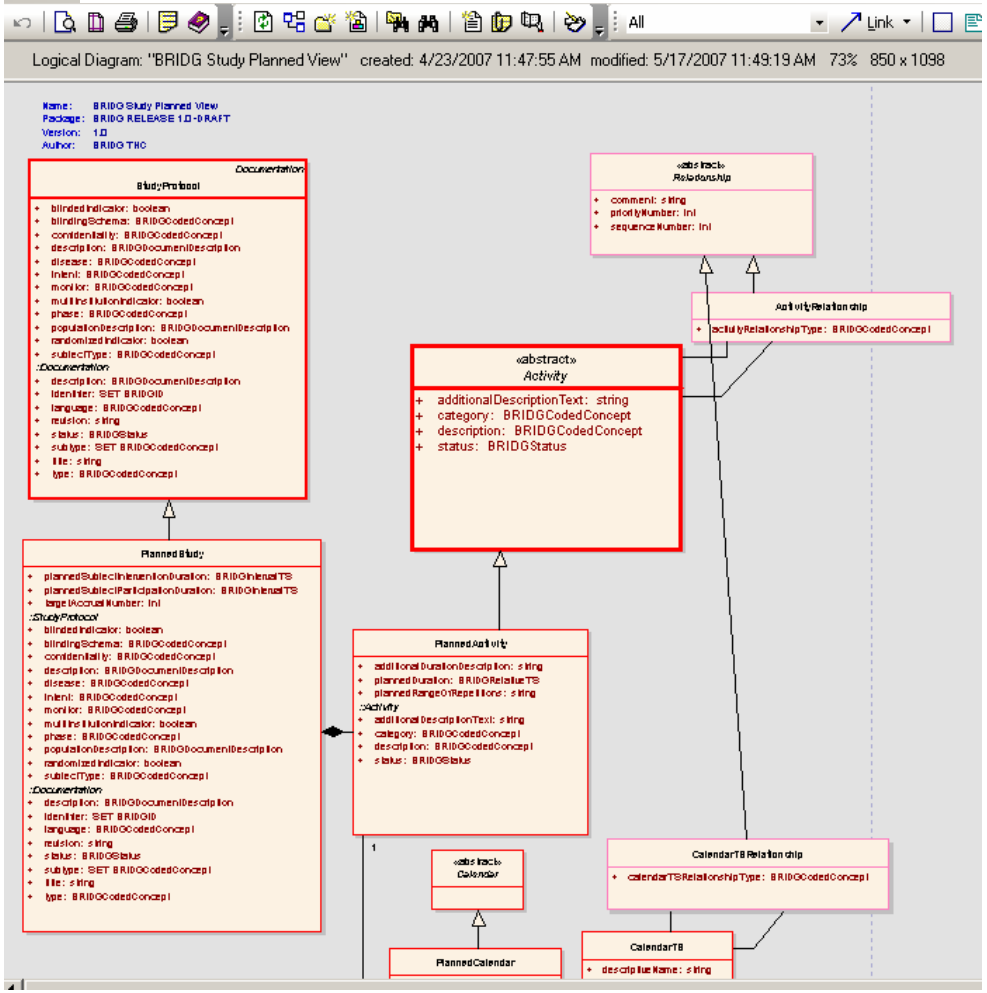
- Need trial-specific closure axioms to do automated classification of EPOCH trials that can be mapped to BRIDG

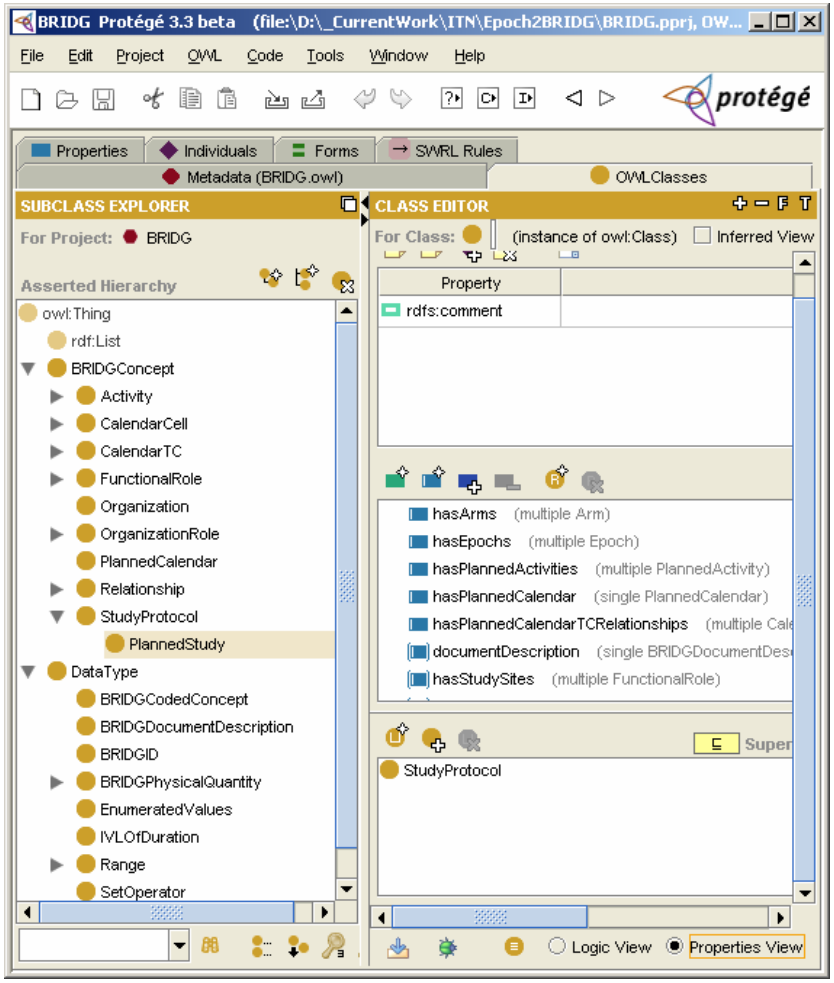
Approach taken

- Semantic alignment
- Overcoming representation language mismatch
- Overcoming representation choice mismatches

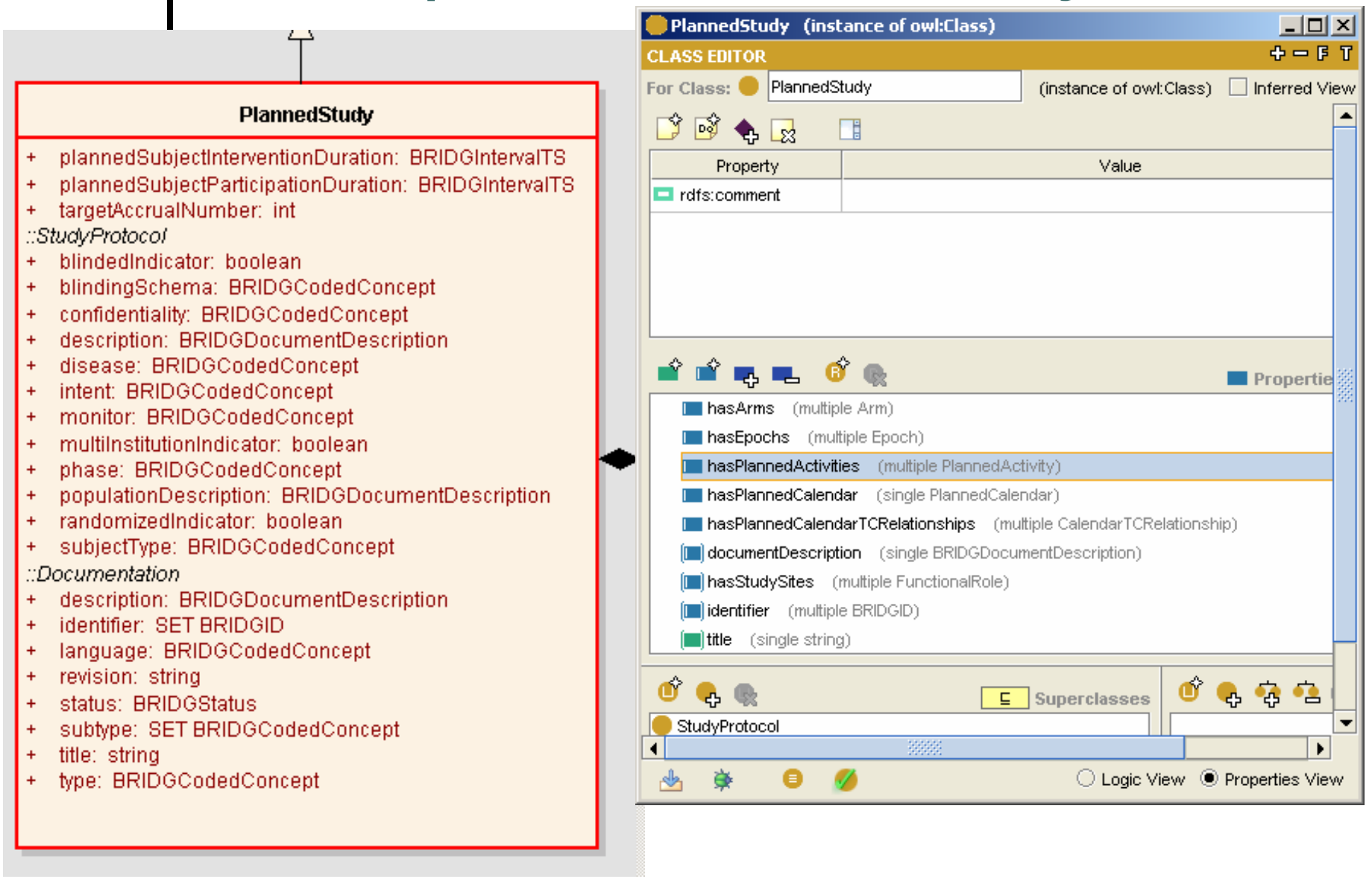
Overcoming representation language mismatch: BRIDG-in-OWL

Scope: BRIDG Study Planned View + BRIDG Complex Data Types





Example: PlannedStudy



Modifications to BRIDG

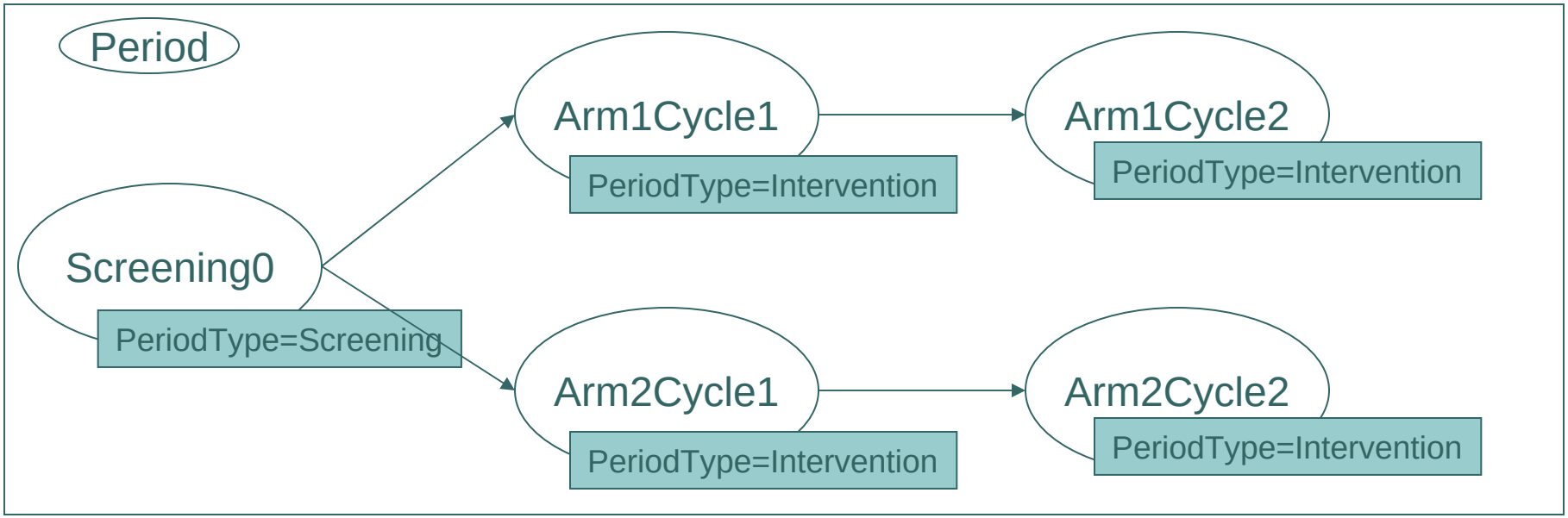
- Driven by Patient Study Calendar application requirements
- Added several associational relationships
- Modified some subsumption relations

Approach taken

- Semantic alignment
- Overcoming representation language mismatch
- Overcoming representation choice mismatches

Overcoming representation choice mismatch: *Epoch* example

EPOCH



BRIDG

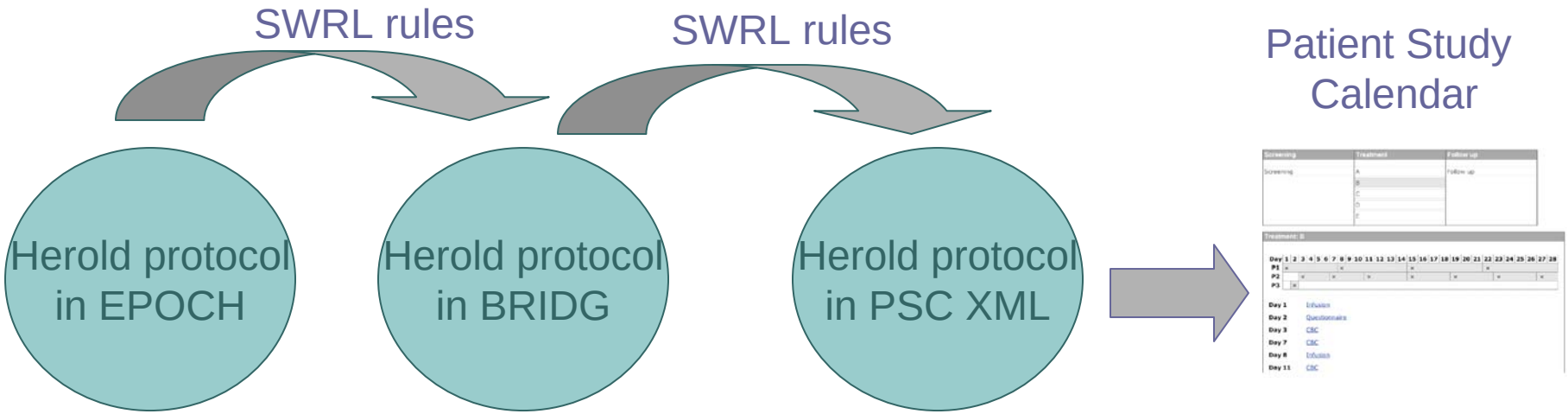
SWRL rule to map epochs

SWRL Rule

```
prtont:Period(?p) ∧
prtont:hasPeriodType(?p, ?ptype) ∧
prtont:label(?ptype, ?epochLabel) ∧
swrlx:createOWLThing(?epoch, ?ptype) ∧
swrlx:createOWLThing(?code, ?epoch) ∧
bridg:PlannedStudy(?pstudy)
  → bridg:Epoch(?epoch) ∧
bridg:BRIDGCodedConcept(?code) ∧
bridg:epochName(?epoch, ?code) ∧
bridg:displayName(?code, ?epochLabel) ∧
bridg:descriptiveName(?epoch, ?epochLabel) ∧
bridg:hasEpochs(?pstudy, ?epoch)
```

- EPOCH:periodTypes of periods correspond to BRIDG:epochs
- EPOCH :periodType.label corresponds to BRIDG:epoch.code. displayName

Successfully used an EPOCH clinical trial to configure BRIDG Patient Study Calendar application



- Automated mappings except for one relationship
  - Because of OWL/SWRL's open-world assumption, *First epoch* cannot be derived as *an epoch that has no predecessor*

Conclusions

- Semantic interoperability requires
  - Harmonization of subsets of ontologies/models
  - Overcoming mismatches in representation languages and representation choices
- OWL restrictions and SWRL rules help to overcome semantic and syntactic mismatches
- Possible future work
  - Continued harmonization of BRIDG/EPOCH
  - Scalability and (semi-)automation of method

Thank you!

- Questions?
- Comments?
- Suggestions?