



Bridging Epoch: Mapping Two Clinical Trial Ontologies

10th International Protégé Conference
July 17, 2007

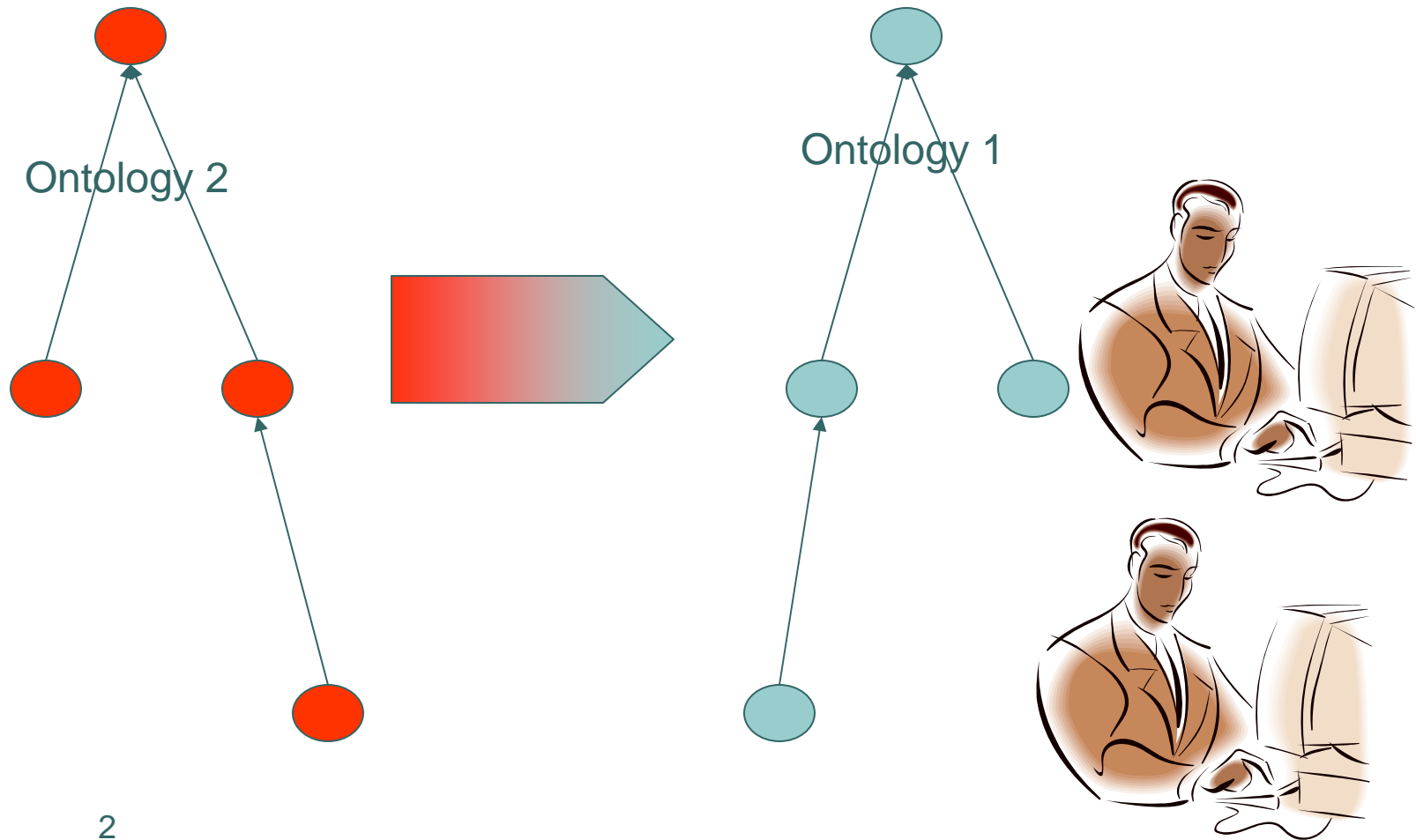
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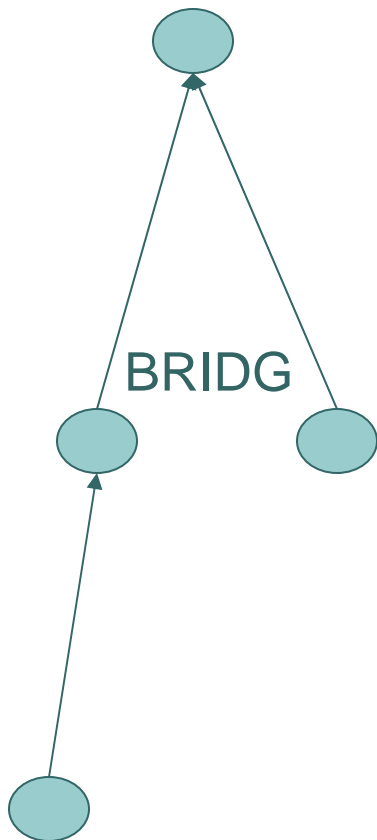
²University of Pittsburgh, USA

³The Immune Tolerance Network, Pittsburgh, PA, USA

Problem: Ontologies and semantic interoperability



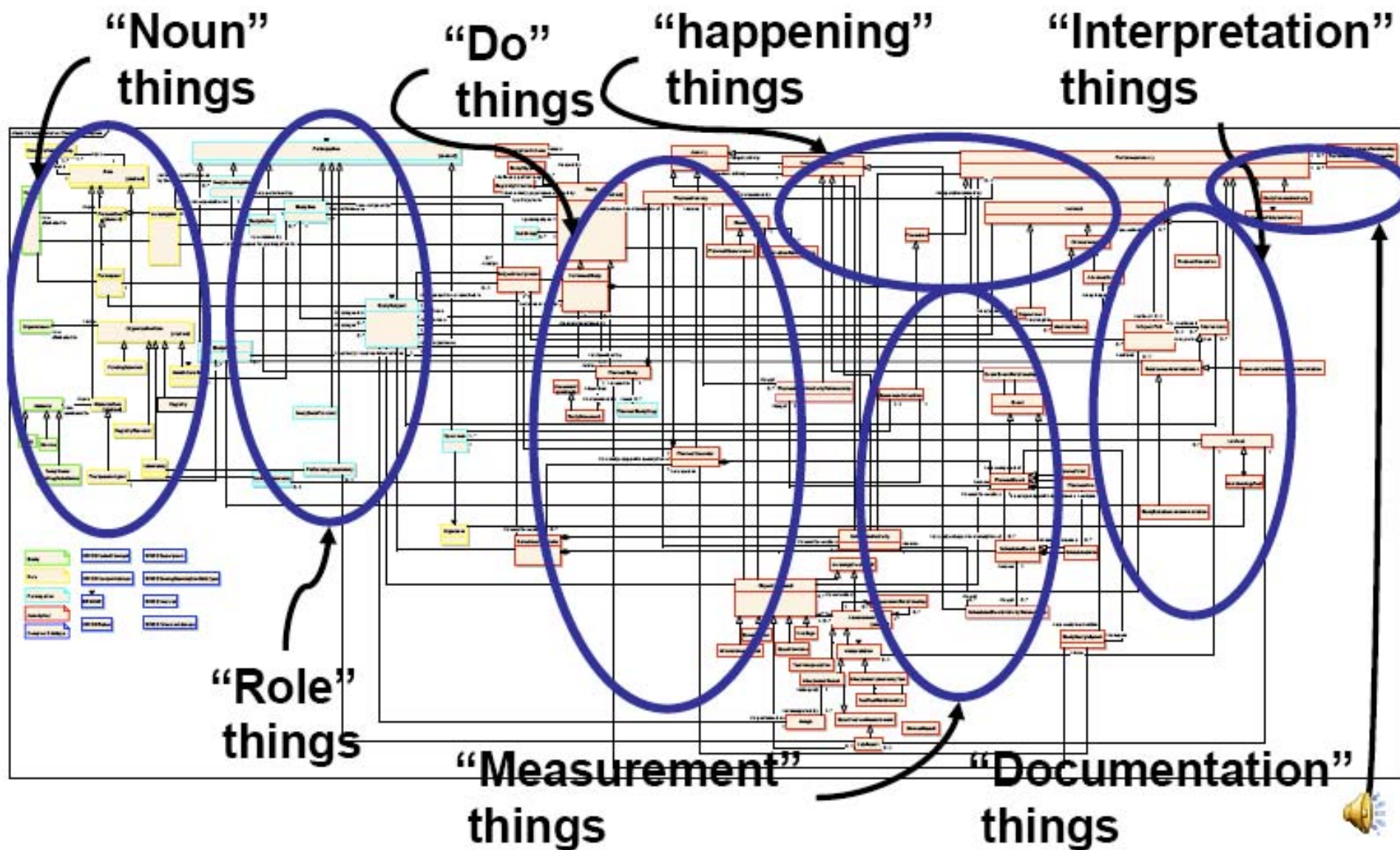
BRIDG: Biomedical Research Integration Group



- 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



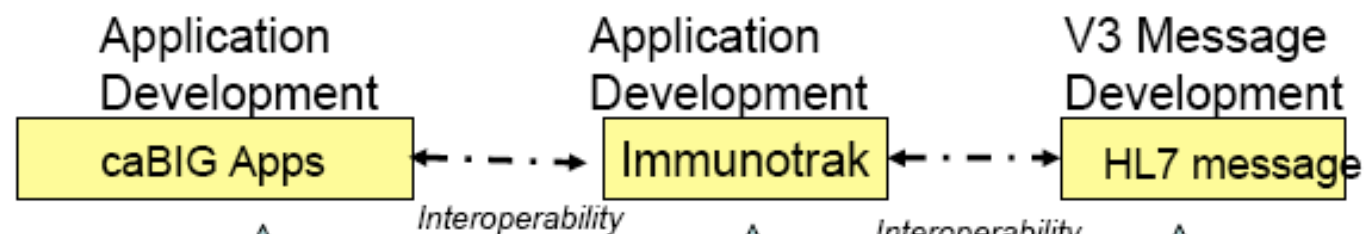
Current Classes in Core Elements



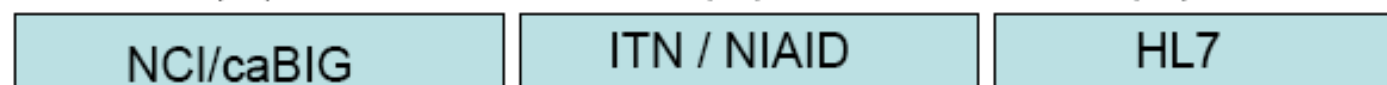


Achieving interoperability from a common semantic foundation

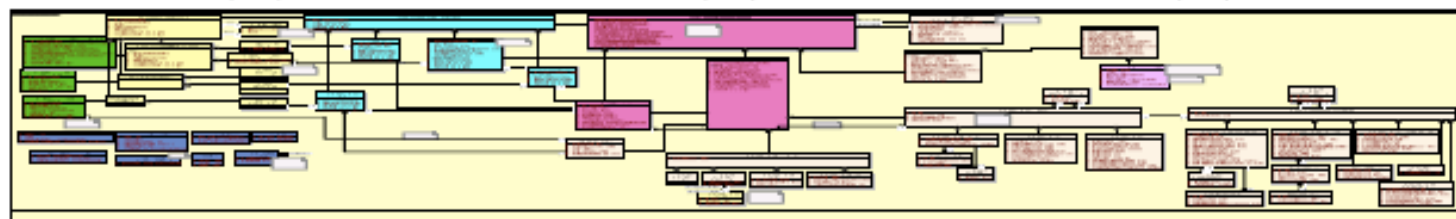
IMPLEMENTATION
SOLUTIONS



STAKEHOLDERS



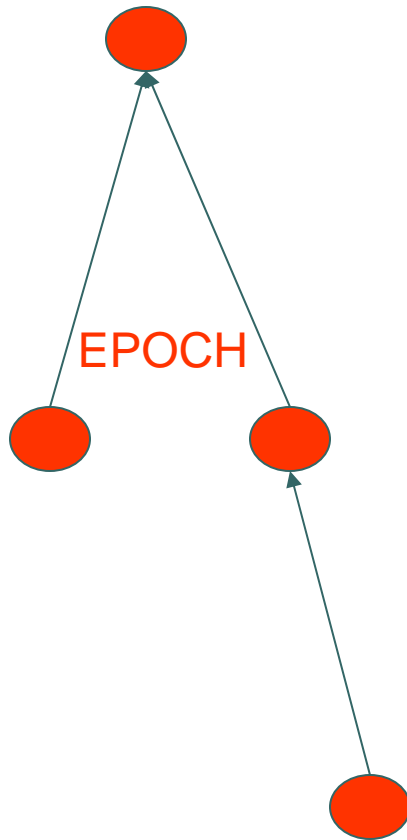
FOUNDATION
MODEL



BRIDG – Domain Analysis Model for Clinical Research

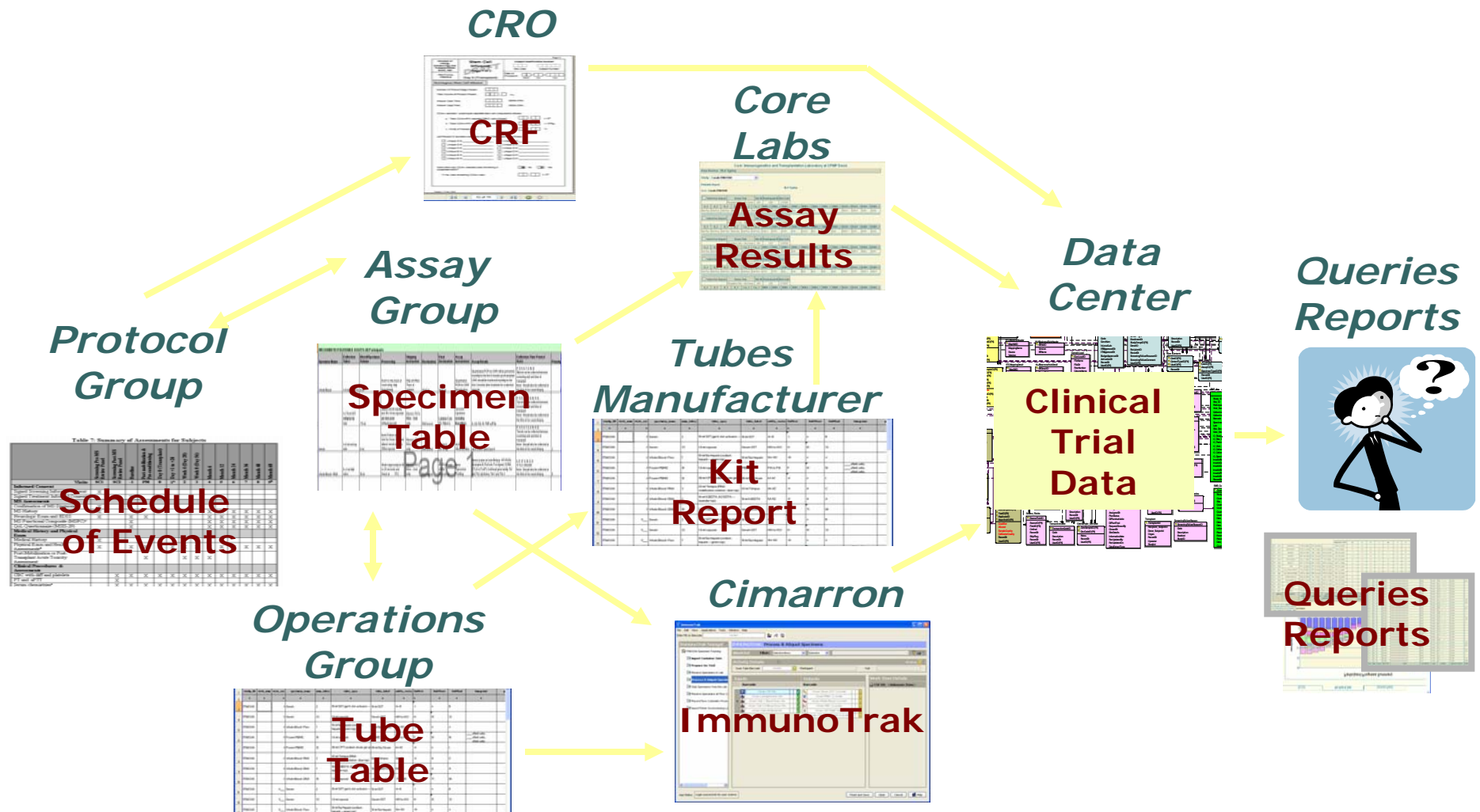


EPOCH: Immune Tolerance Network clinical trial ontologies



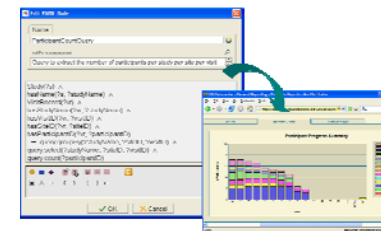
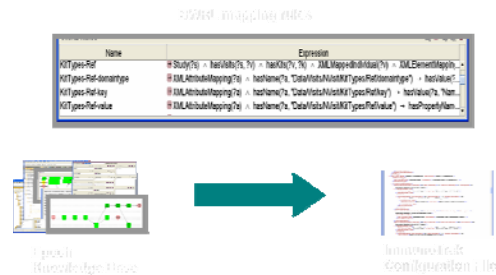
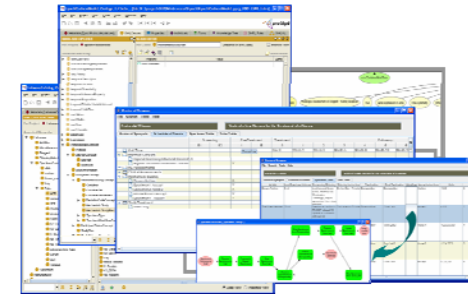
- Immune Tolerance Network (ITN)
 - International collaborative research effort that sponsors clinical trials and mechanistic assays on immune tolerance
- EPOCH clinical trial model
 - Developed at Stanford Medical Informatics
 - Designed to provide **semantic foundation for management of clinical trials**

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

ProtocolOntology Protégé 3.3 beta (file:VC:\projects\ITNI\epoch0.96\ontologies\Epoch\ProtocolOntology.pprj, OWL / RDF Files)

File Edit Project OWL Code Tools Window Help

Metadata (ProtocolOntology.owl) OWLClasses Properties Individuals Forms

SUBCLASS EXPLORER CLASS EDITOR

For Project: ProtocolOntology For Class: Protocol (instance of owl:Class) Inferred View

Asserted Hierarchy

- org:Facility
- assay:Assay
- lab:LabWare
 - lab:PreprocessingCondiitor
 - lab:SpecimenMetaclass_16
 - lab:StorageConditions
- ce:ConstraintExpressi
- mo:Measurement
- mo:Unit
- PROTOCOL EVENT
- ProtocolEntity
 - FacilitiesPlanEntity
 - Protocol
 - ProtocolEventEntity
 - StudyDesignEntity
 - StudyScheduleEntity

Protocol

captures the protocol schema, the events that are planned and their schedule.

Annotations

Lang
t primarily

Properties and Restrictions

- hasFacilitiesPlan (single FacilitiesPlan)
- hasLongTitle (single string)
- hasPrimaryScheduleOfEvents (single ScheduleOfEvents)
- hasProtocolId (single string)
- hasSchedulesOfEvents (multiple ScheduleOfEvents)
- hasSpecimenWorkflow (single SpecimenWorkflow)

Logic view Properties view



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

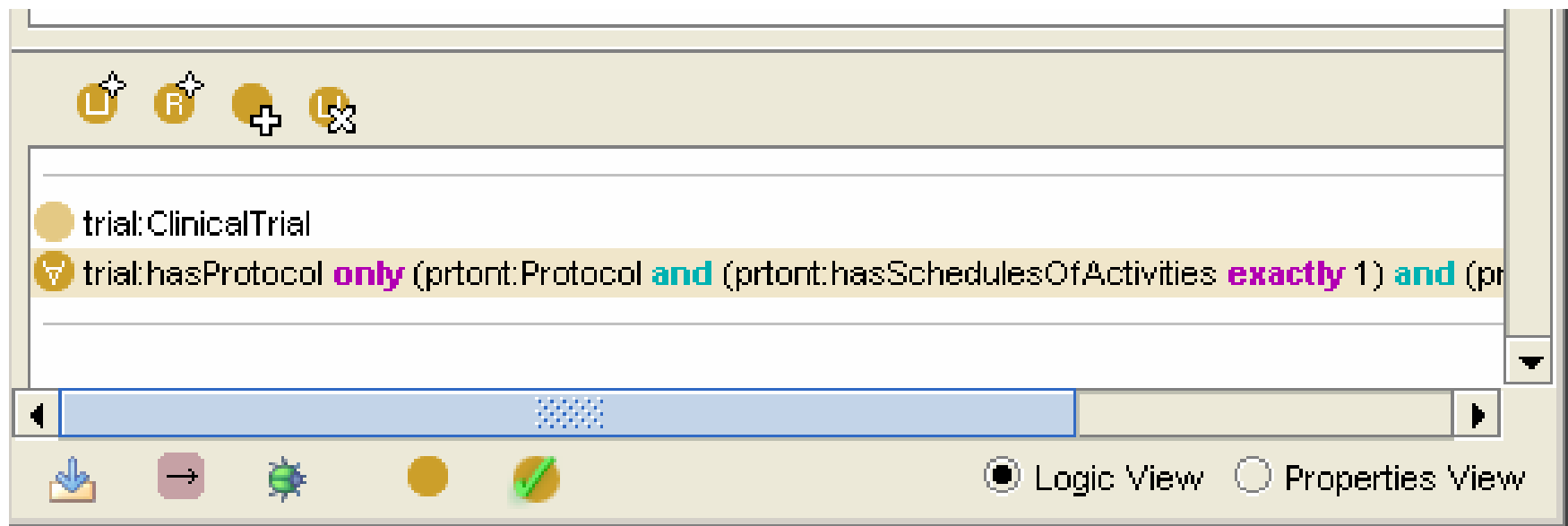
Class	Attribute	Attribute Value or Description	InGreenbaum?	In Scope?	Mappable?	
		The entire protocol is segmented temporally into periods. Each period defines a segment of time that groups protocol activities by their function. For example, the Screening Period defines the protocol timing during which the activities related to protocol	y	y	y	BRIDG.Plan
Period	ClassComment					
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
		a set of sub-periods or encounters that this period is decomposed into	y	y	y	BRIDG.Plan
Period	hasSubTimings					
Period	isPartOfParentTimings	a set of arms that this period is part of	y	y	y	BRIDG.Plan
Period	SubClassOf	#PlannedTiming	y	y	e	epoch-spec
		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	ClassComment					
		annotations that specify instructional or temporal information on the activity	y	y	y	BRIDG.Plan will cover in information between an BRIDG.Cale
PlannedActivity	hasAnnotations					
		a higher-level grouping that the activity belongs to	y	y	y	BRIDG.Conf (allows for c collecting c PlannedAct
PlannedActivity	hasFunctionalGrouping					
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

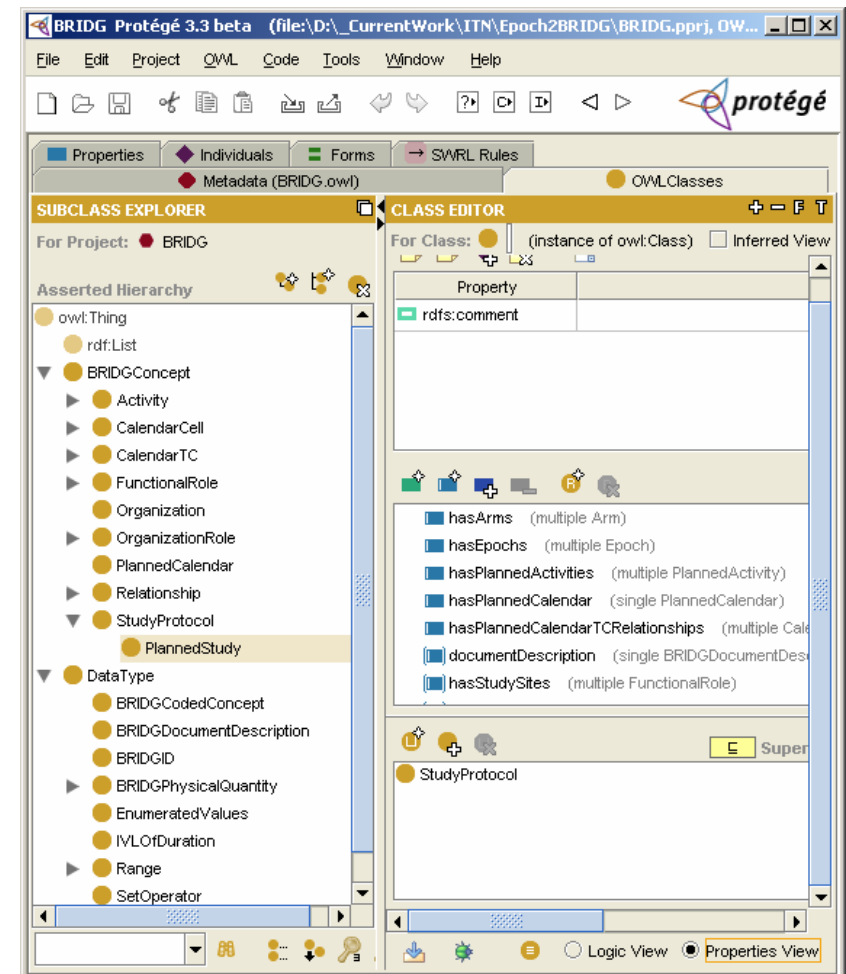
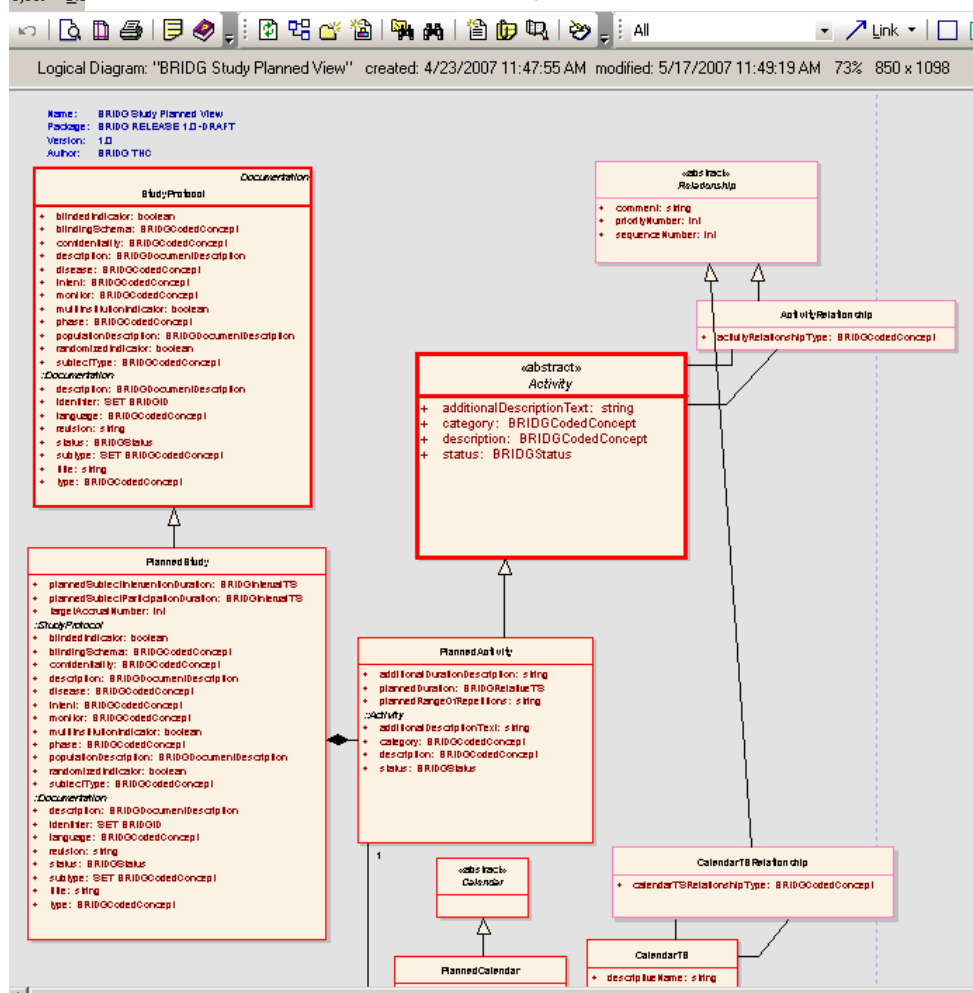


Approach taken

- Semantic alignment
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- Overcoming representation choice mismatches

Overcoming representation language mismatch: BRIDG-in-OWL

Scope: BRIDG Study Planned View + BRIDG Complex Data Types



Example: PlannedStudy

PlannedStudy

- + plannedSubjectInterventionDuration: BRIDGIntervalTS
- + plannedSubjectParticipationDuration: BRIDGIntervalTS
- + targetAccrualNumber: int
- ::StudyProtocol*
 - + blindedIndicator: boolean
 - + blindingSchema: BRIDGCodedConcept
 - + confidentiality: BRIDGCodedConcept
 - + description: BRIDGDocumentDescription
 - + disease: BRIDGCodedConcept
 - + intent: BRIDGCodedConcept
 - + monitor: BRIDGCodedConcept
 - + multiInstitutionIndicator: boolean
 - + phase: BRIDGCodedConcept
 - + populationDescription: BRIDGDocumentDescription
 - + randomizedIndicator: boolean
 - + subjectType: BRIDGCodedConcept
- ::Documentation*
 - + description: BRIDGDocumentDescription
 - + identifier: SET BRIDGID
 - + language: BRIDGCodedConcept
 - + revision: string
 - + status: BRIDGStatus
 - + subtype: SET BRIDGCodedConcept
 - + title: string
 - + type: BRIDGCodedConcept

PlannedStudy (instance of owl:Class)

CLASS EDITOR

For Class: PlannedStudy (instance of owl:Class) ☐ Inferred View

Property	Value
rdfs:comment	

Properties

- hasArms (multiple Arm)
- hasEpochs (multiple Epoch)
- hasPlannedActivities (multiple PlannedActivity)**
- hasPlannedCalendar (single PlannedCalendar)
- hasPlannedCalendarTCRelationships (multiple CalendarTCRelationship)
- documentDescription (single BRIDGDocumentDescription)
- hasStudySites (multiple FunctionalRole)
- identifier (multiple BRIDGID)
- title (single string)

Superclasses

StudyProtocol

Logic View Properties View



Modifications to BRIDG

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



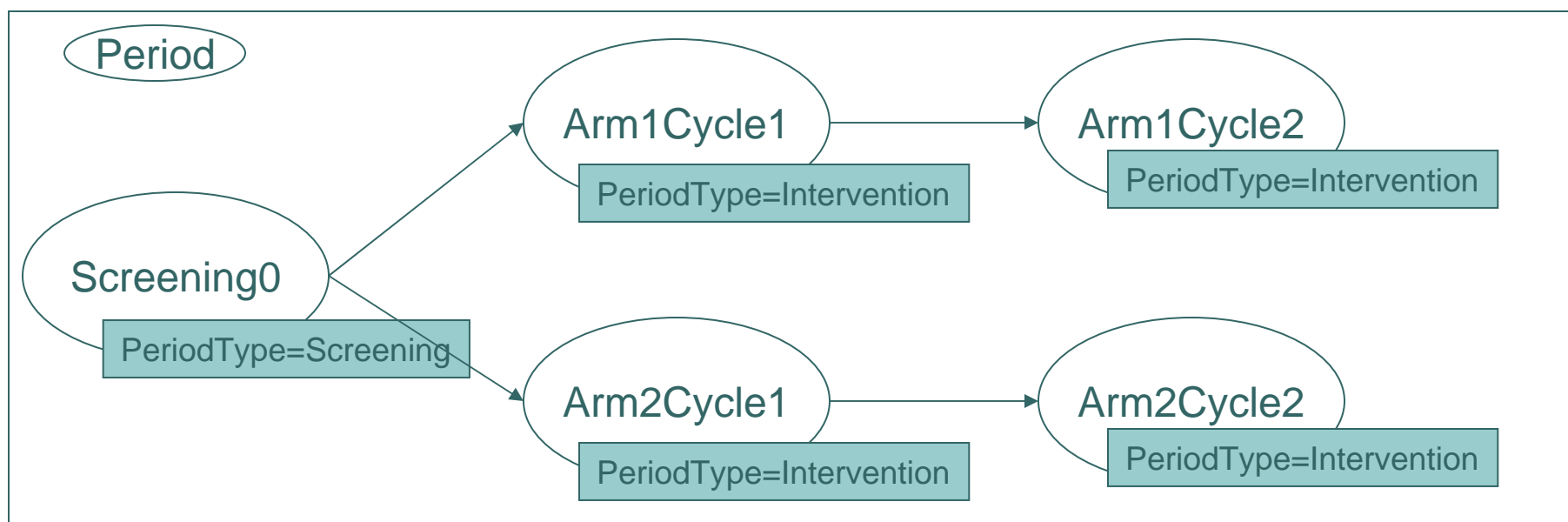
Approach taken

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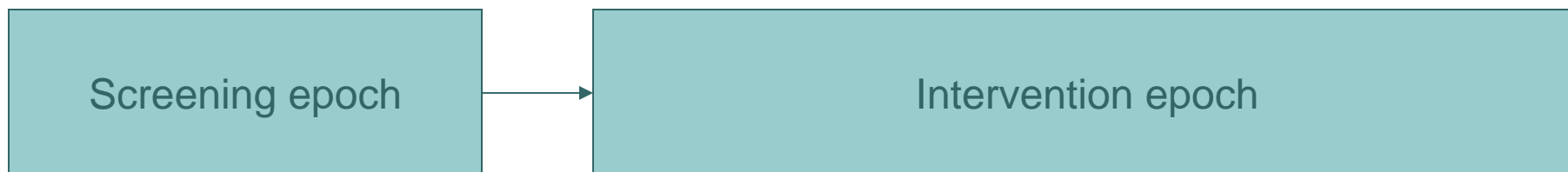


Overcoming representation choice mismatch: *Epoch* example

EPOCH



BRIDG





SWRL rule to map epochs

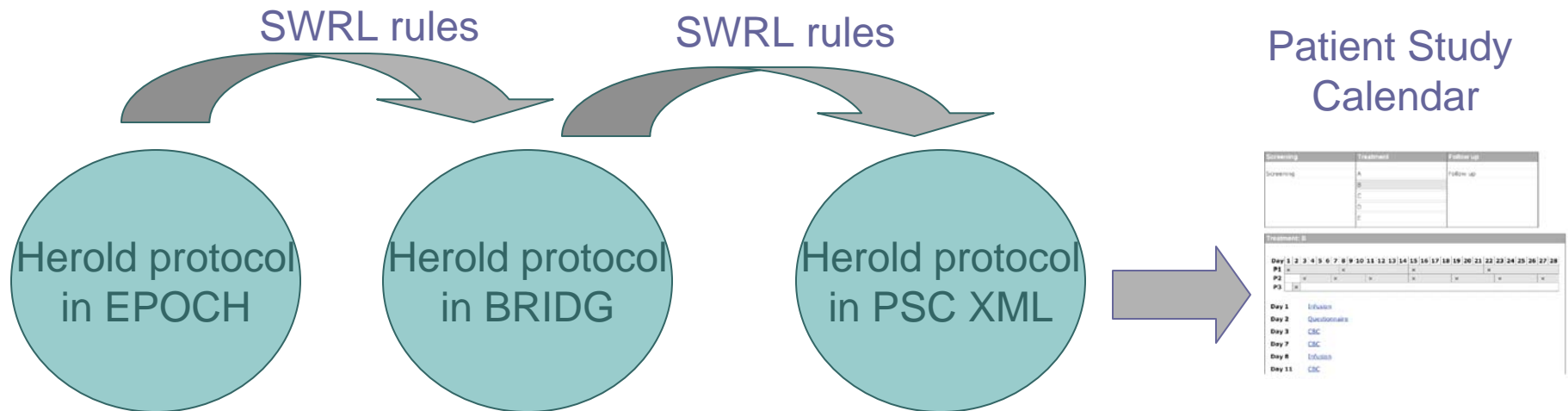
SWRL Rule

```
prontont:Period(?p) ∧  
prontont:hasPeriodType(?p, ?ptype) ∧  
prontont: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?