Maximizing Epilepsy Data Usage for Better Outcomes: Informatics and Common Language

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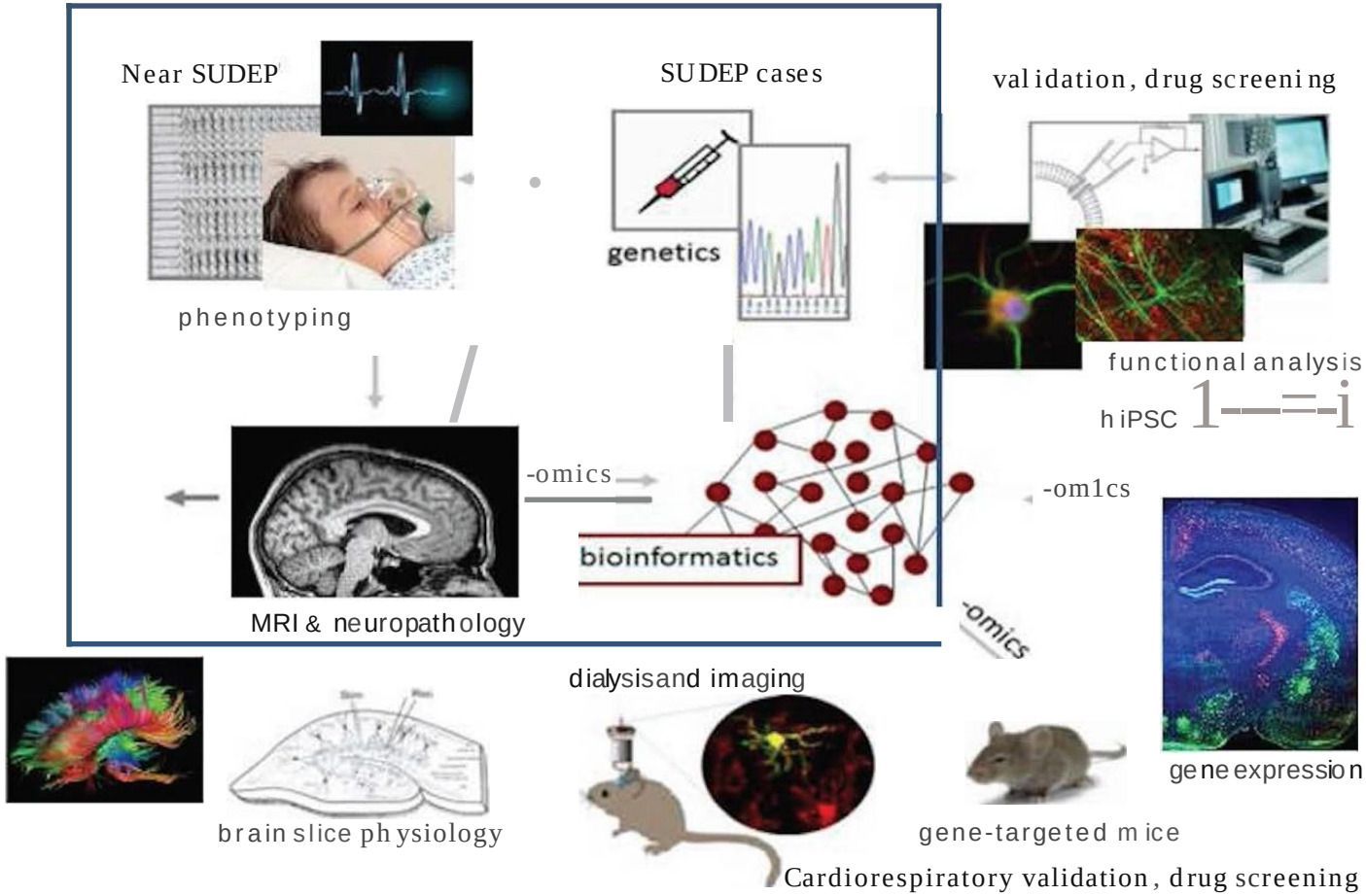
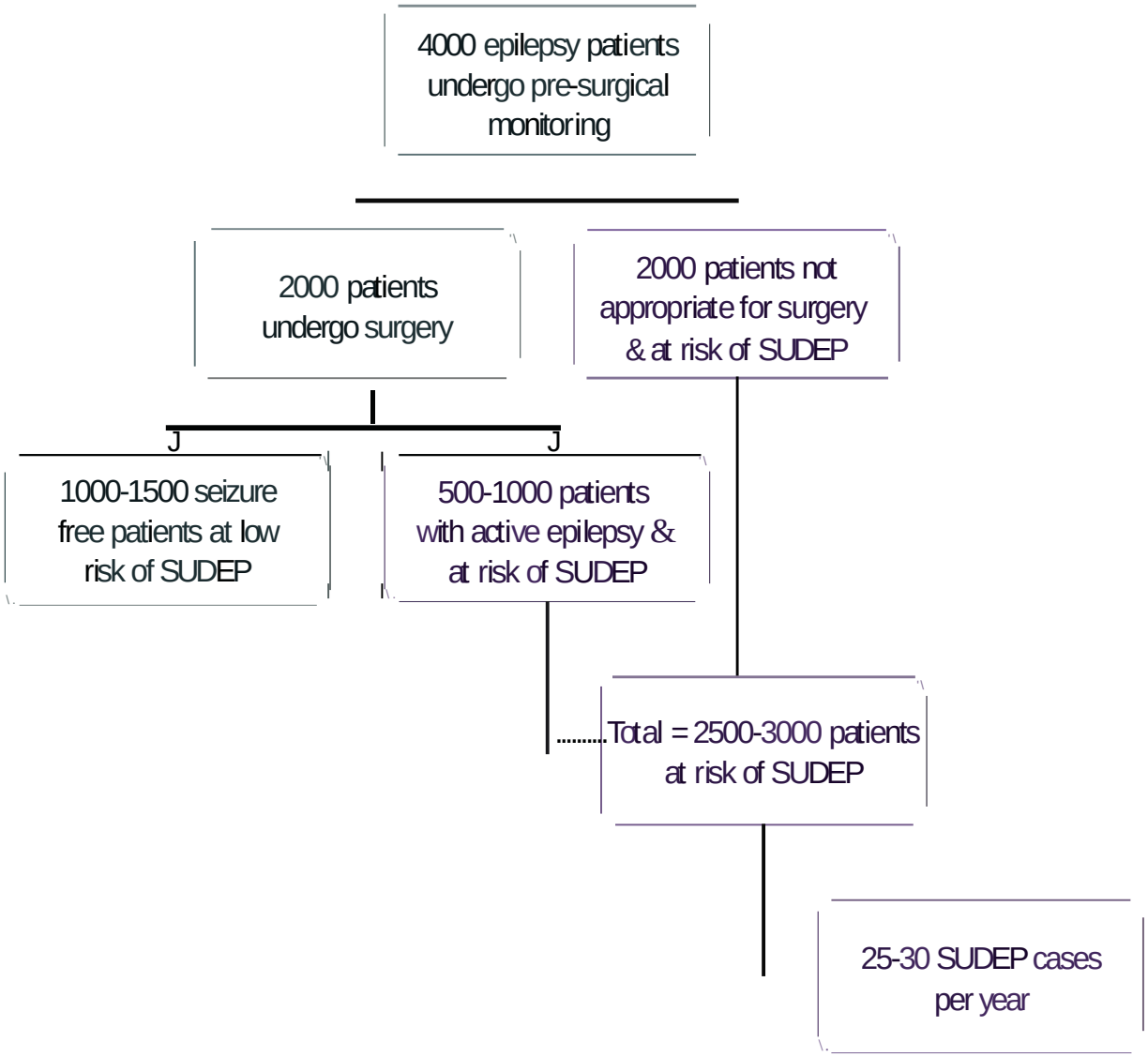
ICARE: Interagency Collaborative to Advance Research in Epilepsy

NIH Center for SUDEP Research {CSR)

Predictive genes, clinical biomarkers and basic mechanisms of SUDEP

BCM
Case
Columbia
Harvard
Jefferson
MIT
Northwestern
NYU
UC London
UCLA
UCSF
U Iowa
U Michigan

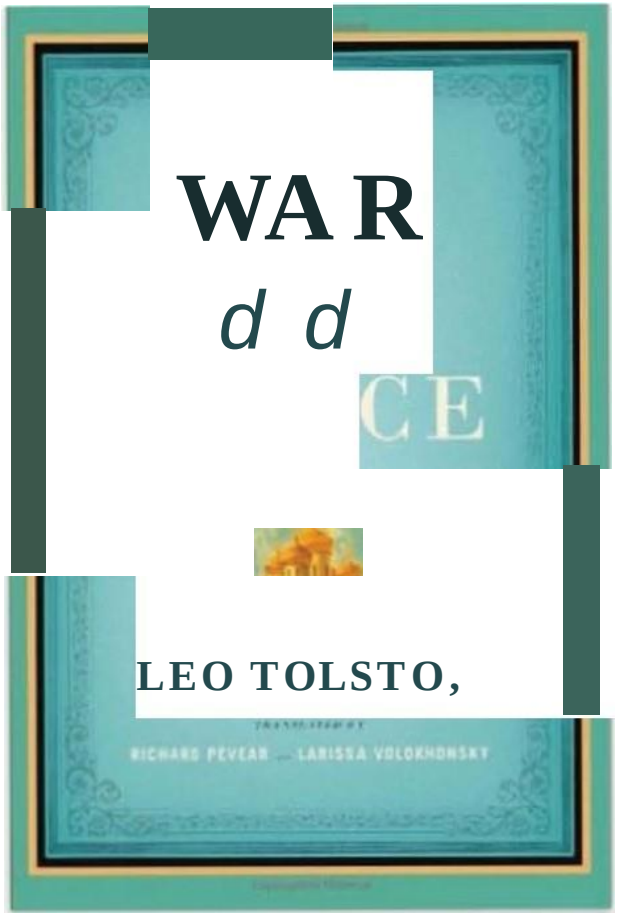



4000 epilepsy patients undergo pre-surgical monitoring
2000 patients undergo surgery
2000 patients not appropriate for surgery & at risk of SUDEP
1000-1500 seizure free patients at low risk of SUDEP
500-1000 patients with active epilepsy & at risk of SUDEP
Total = 2500-3000 patients at risk of SUDEP
25-30 SUDEP cases per year

The Challenges

- Multi-center – each center follows different approaches
  - Disparate terminology
  - Paper based, Electronic documents
  - Distinct form structure
- Difficulty in post collection data analysis:
  - Patient cohort identification across centers
  - Uncovering disease association
  - Correlating signal data (EEG) across centers
- Data quality – without increasing workload or cost

- Focal dyscognitive seizure
- Complex partial seizure
- Dialeptic seizure



Classic Literature & Fiction (6 055)

Literature & Fiction (32,940)

Historical {3,698)

Family Saga (357)

Literary (4,319)

War (1,176)

Military Historical Fiction (453)

History & Criticism (7,436)

Russian Literary Criticism (202)

Politics & Social Sciences c 405)

Romance 935)

Author

Louise Shanks Maude

Richard Pevear

Larissa Volokhonsky

A. N. Wilson

Pat Conroy

Andrew Davies

Fyodor Dostoyevsky

Leo Tolstoy

Mona Simpson

Nina Nikolaevna Berberova

Alice Walker

Gore Vidal

Richard Tuck

Jimmy Carter

David Grossman

- The Requirements
  - Consistent terminology – facilitates interoperability, data sharing
  - Real-time data curation – range check, auto-completion
  - Optimized data entry – skip patterns to dynamically change form structure
  - Structured data stored in patient database – easy to query and analyze
  - Shared resource – develop once, deploy at multiple locations
  - Easy maintenance – changes are easily propagated

Informatics Highway: Interoperability and Integration

- Common Terminology System – upfront or backend
- Common Data Elements (CDE): NINDS CDEs
- Shared Meaning for Data Integration
- Accurate and Consistent Interpretation of Data

What Can Common Terminology Achieve?

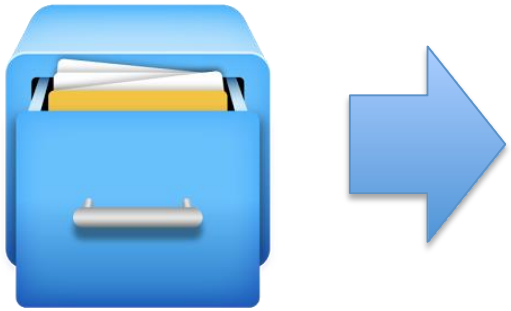
- Reconcile different categories of heterogeneity:
  - syntactic heterogeneity: Slow Spike and Wave complex vs. Slow Spike-and-Wave complex
  - structural heterogeneity: ADNFLE vs Autosomal Dominant Nocturnal Frontal Lobe Epilepsy
  - semantic heterogeneity: Focal dyscognitive seizure vs. Dialeptic seizure vs. Complex partial seizure

Managing Epilepsy Well (MEW) Network Informatics

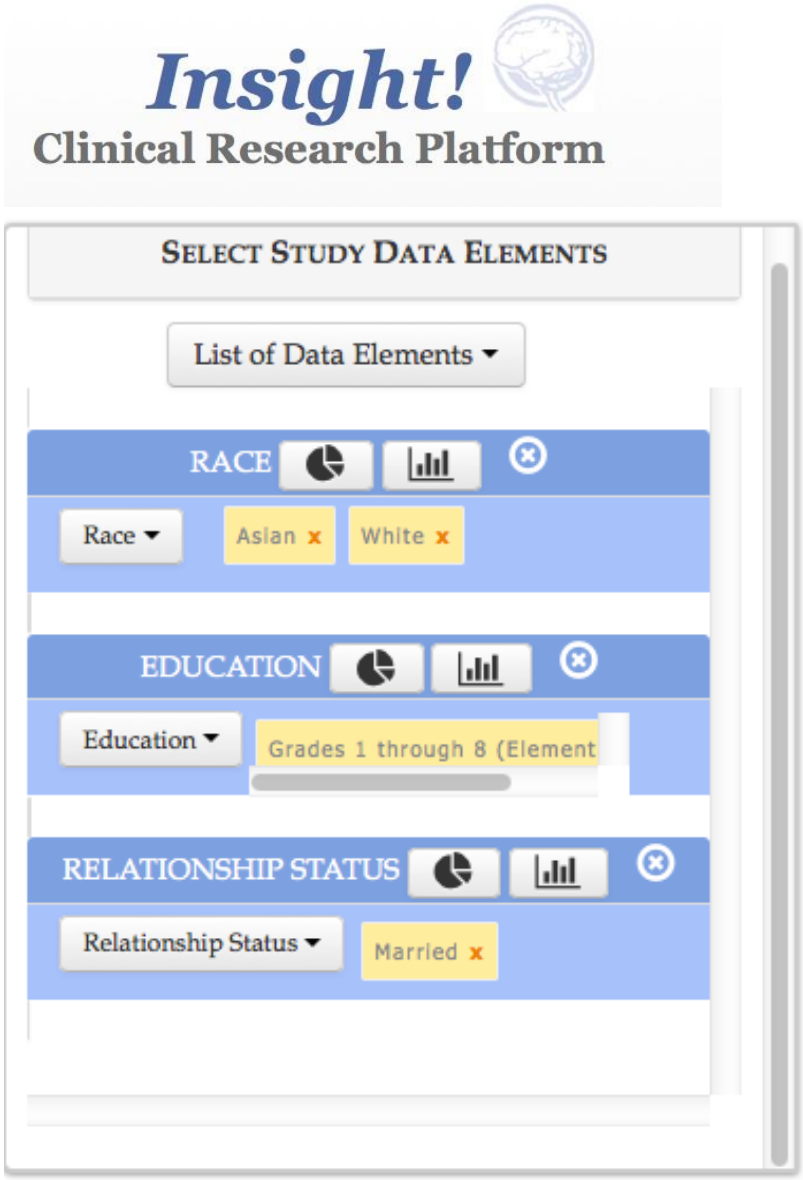
- 8 centers across US
- Multiple approaches for self management of epilepsy
- Integrated data from different studies for cohort studies and comparative analysis

Multi-Center Epilepsy Cohort Identification

- Integrate Multiple Studies



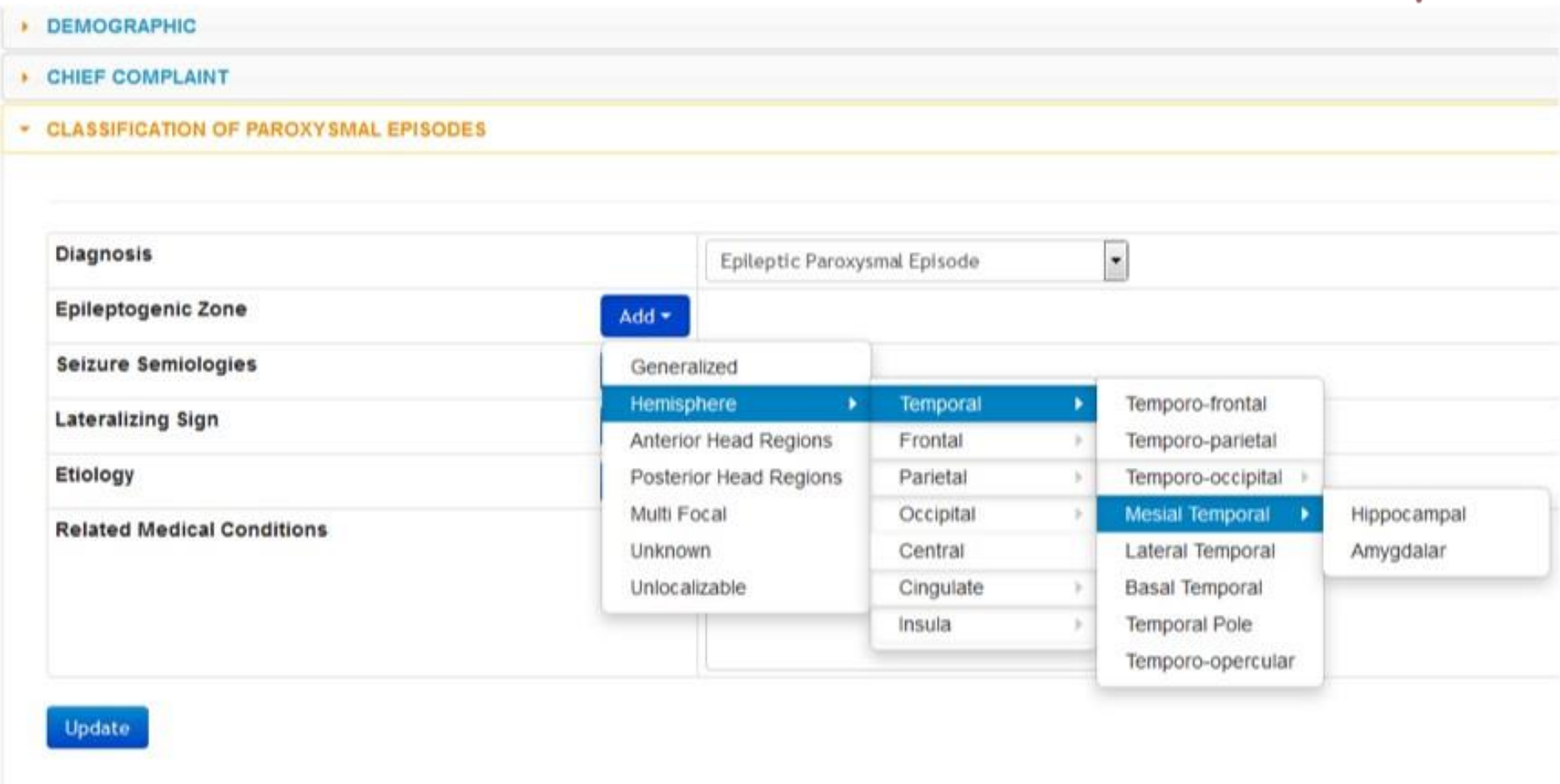
- Common Vocabulary



Multi-Center Epilepsy Cohort Identification

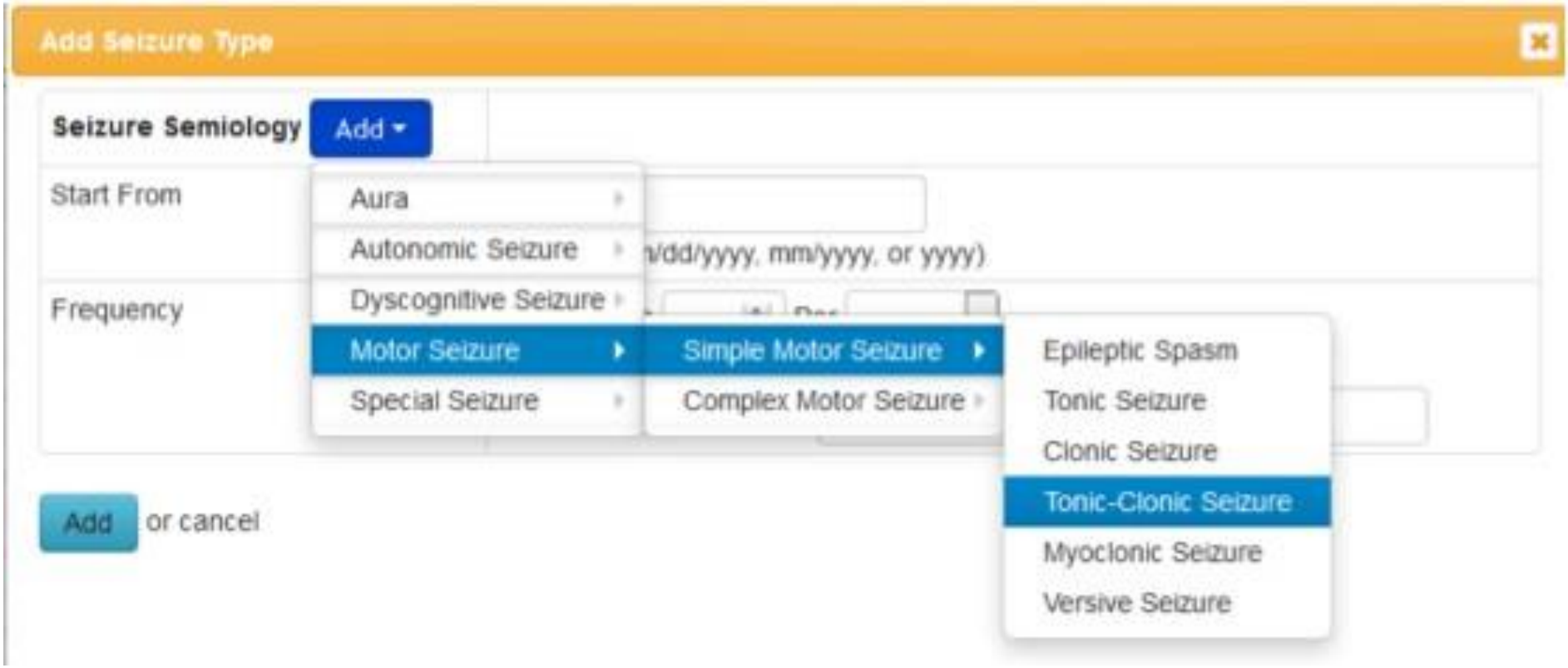
Ontology-driven Patient Information Capture (OPIC)

- Structured data entry

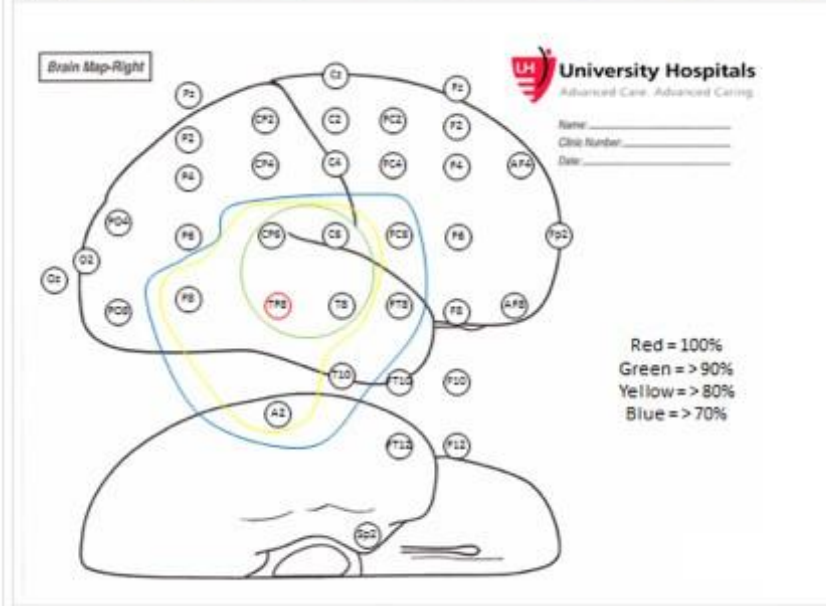


Ontology-driven Patient Information Capture (OPIC)

- High level of granularity



Ontology-driven Patient Information Capture (OPIC)



- Support embedding of multi-media images
- Data entered can be immediately queries
- Important for both care and clinical research
- Easier sharing across multiple collaborators

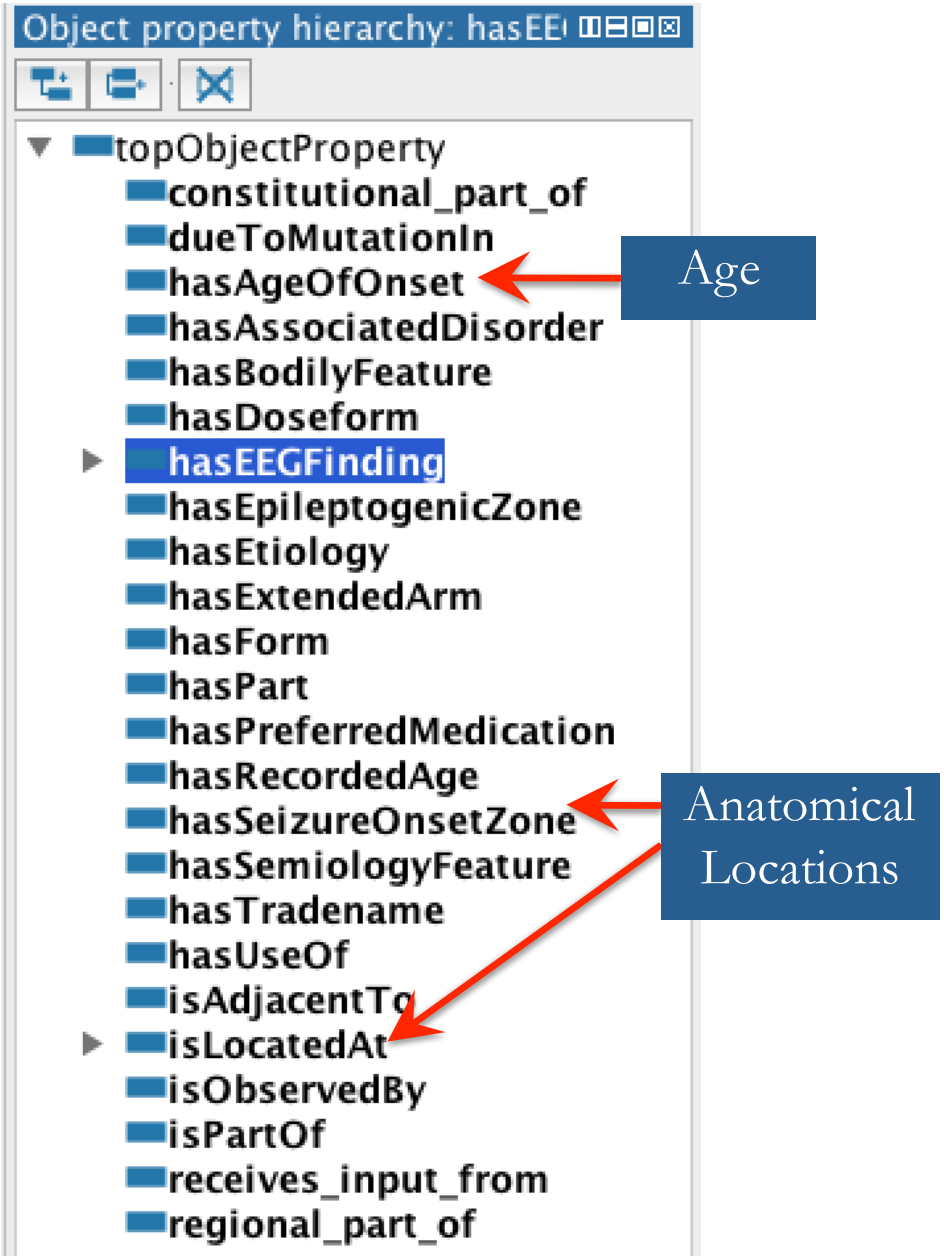
Epilepsy and Seizure Ontology

- Etiology
  - GeneticDefect
    - ChromosomalAbnormality
    - GeneticMutation
      - MitochondrialEncephalomyopathy
  - MetabolicCause
    - SubstanceAbuse
  - StructuralCause
    - BifocalEncephalomalacia
    - BirthInjury
    - BrainTumor
    - CerebralPalsy
    - CerebrovascularDisease
    - CorticalDevelopmentMalformation
    - HypoxicIschemicInjury
    - Infection
    - Inflammation
    - LeftFrontalAstrocytoma
    - LeftHemisphereTumorResection
    - LeftMesialTemporalLesion
    - Neoplastic
    - PrenatalBirthInjury
    - RightFrontalEncephalomalacia
    - RightFrontoParietalAbcess
    - RightFrontoTemporalGlioma
    - RightHemisphericStroke
    - RightMesialLesion
    - Sclerosis
    - TraumaticBrainInjury
    - VascularMalformation
  - UnknownCause

- Follows four-dimensional classification approach
  - Etiology
  - Seizures
  - Anatomical Location
  - Related Medical Conditions
- Uses Web Ontology Language (OWL2)
- Description Logic allows consistent and accurate interpretation of terms

Sahoo et al., JAMIA 2014

Epilepsy and Seizure Ontology: Multi-axial Structuring



- OWL2 Object Properties: Allows classification of ontology terms along multiple dimensions
  - Etiology
  - Anatomical Location
  - Genetics
  - Others…
- Objects properties link terms together: Networked terminological system

Epilepsy and Seizure Ontology: Links to Existing Terminological Systems

- RxNorm: Developed by the NLM
- Gene Ontology
- Foundational Model of Anatomy (FMA) Ontology

Epilepsy and Seizure Ontology: Formal Model and Multi-Dimensional

- Epilepsy
  - BiLobarEpilepsy
  - FocalEpilepsy
    - MultiFocalEpilepsy
    - SingleFocalEpilepsy
      - AutosomalDominantNocturnalFrontalLobeEpilepsy
      - AutosomalDominantPartialEpilepsyWithAuditoryFeatures
      - BenignChildhoodEpilepsyWithCentrotemporalSpikes
      - ChildhoodEpilepsyWithOccipitalParoxysms
      - ChildhoodRolandicEpilepsy
      - ChronicProgressiveEpilepsiaPartialisContinuaofChildhood
      - CingulateEpilepsy
      - FrontalLobeEpilepsy
      - HypothalamicEpilepsy
      - InsularEpilepsy
      - OccipitalLobeEpilepsy
      - ParietalLobeEpilepsy
      - TemporalLobeEpilepsy
  - GeneralizedEpilepsy
- GeneralLearningDisability
- NeuropsychiatricProblem
- SleepDisorder
- EEGPattern
- ElectrodePlacementSystem
- Etiology
- Gender
- HealthCareEncounter
- MeasurementUnit
- Person
- PhysiologicalData
- SomatotopicArrangement
- IndependentContinuant
- SpatialRegion
- Occurrent

ADNFLE

Description: AutosomalDominantNocturnalFrontalL

Equivalent classes

Superclasses

- SingleFocalEpilepsy
- dueToMutationIn some (CHRNA2 or CHRNA4 or CHRNB2) — Genes
- hasAgeOfOnset some Child
- hasAssociatedDisorder some GeneralLearningDisability — Etiology
- hasEtiology some GeneticMutation
- hasIctalEpileptiformAbnormality some SeizurePattern
- hasInterIctalEpileptiformAbnormality some (PolySpike or SharpWave or Spike) — Signal Features
- hasPreferredMedication some Zonisamide
- hasSemiologyFeature some HypermotorSeizure — Semiology

Inherited anonymous classes

- hasPreferredMedication some Carbamazepine

Sahoo et al., JAMIA 2014

Community Participation: Epilepsy Ontology Consortium

Epilepsy Ontology Consortium

Logged in as Admin. Log out

1. Add Name of Syndrome

+ Add New Syndrome

Edit Syndrome label

2. Add Details of the Syndrome

List of Syndromes

- Childhood Epilepsy with Occcipital paroxysms
- Primary Reading Epilepsy
- Parietal Lobe Epilepsy
- Generalized Epilepsy with Febrile Seizures Plus (GEFS+)
- Autosomal Dominant Nocturnal Frontal Lobe Epilepsy (ADNFLE)
- Autosomal Dominant Partial Epilepsy With Auditory Features (ADPEAF)

Community Participation: Epilepsy Ontology Consortium

Epilepsy Ontology Consortium

Logged in as Admin. Log out

Home

Primary Reading Epilepsy

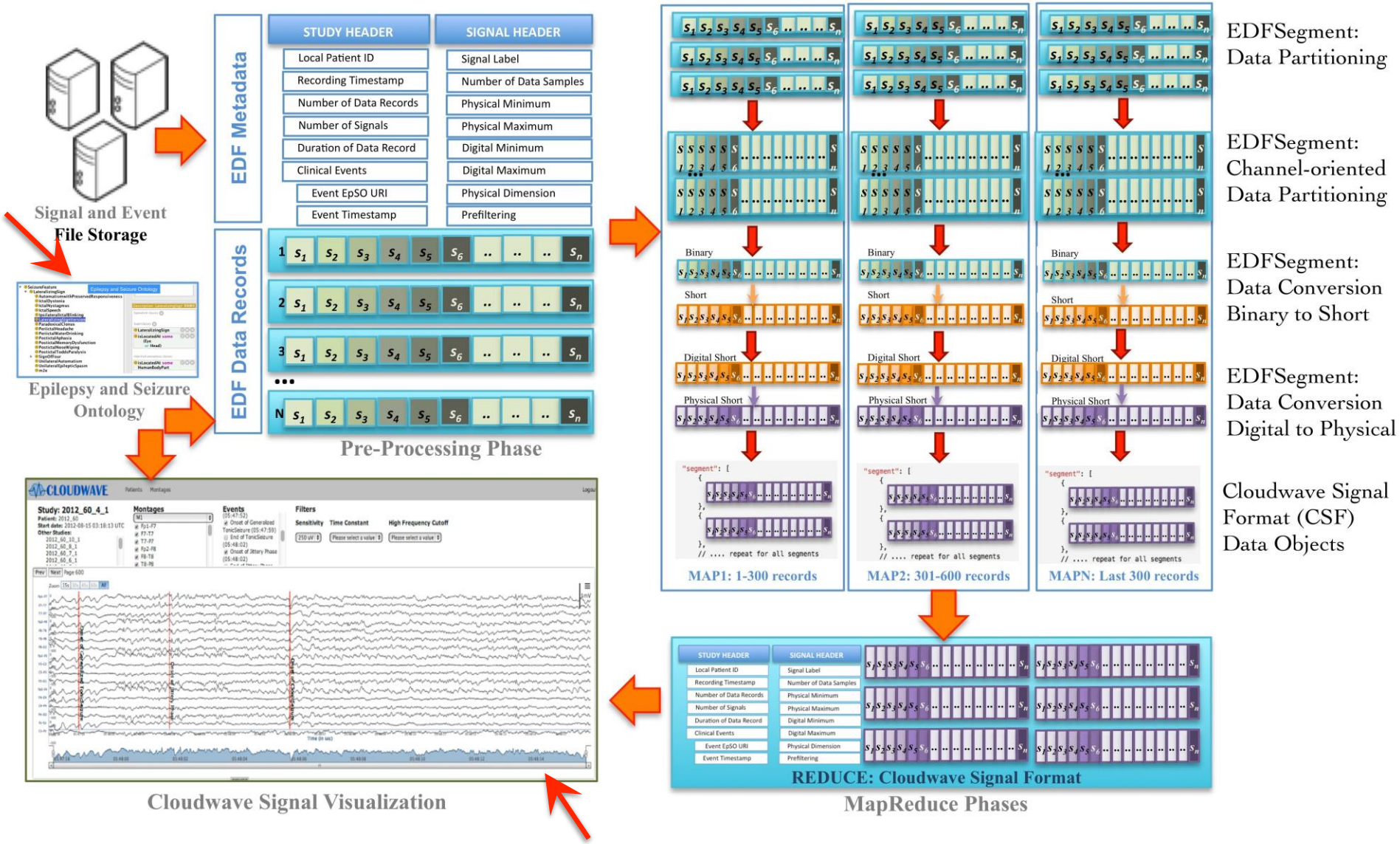
Existing User Entries

USER ID	CLINICAL FINDINGS				ETIOLOGY	MEDICATIONS OF CHOICE	EEG				MRI	GENES
	Age of Onset	Unique Clinical Features	Mental Retardation	Physical Findings			Ictal Onset Zone	Interictal Epileptiform Abnormalities	Interictal Non-Epileptiform Abnormalities	Ictal Epileptiform Abnormalities		
Admin Entry Date April 13th, 2015 17:12	8 to 20 Years	Myoclonic Seizure			Genetic	Lamotrigine,Levetiracetam,Topiramate,Valproate,Zonisamide		PolySpikes,Spike-and-slow-wave Complex		Polyspike, Spike Slowwave Complex		CACNB4,CLCN2,EFHC1,GABRA1,GABRD

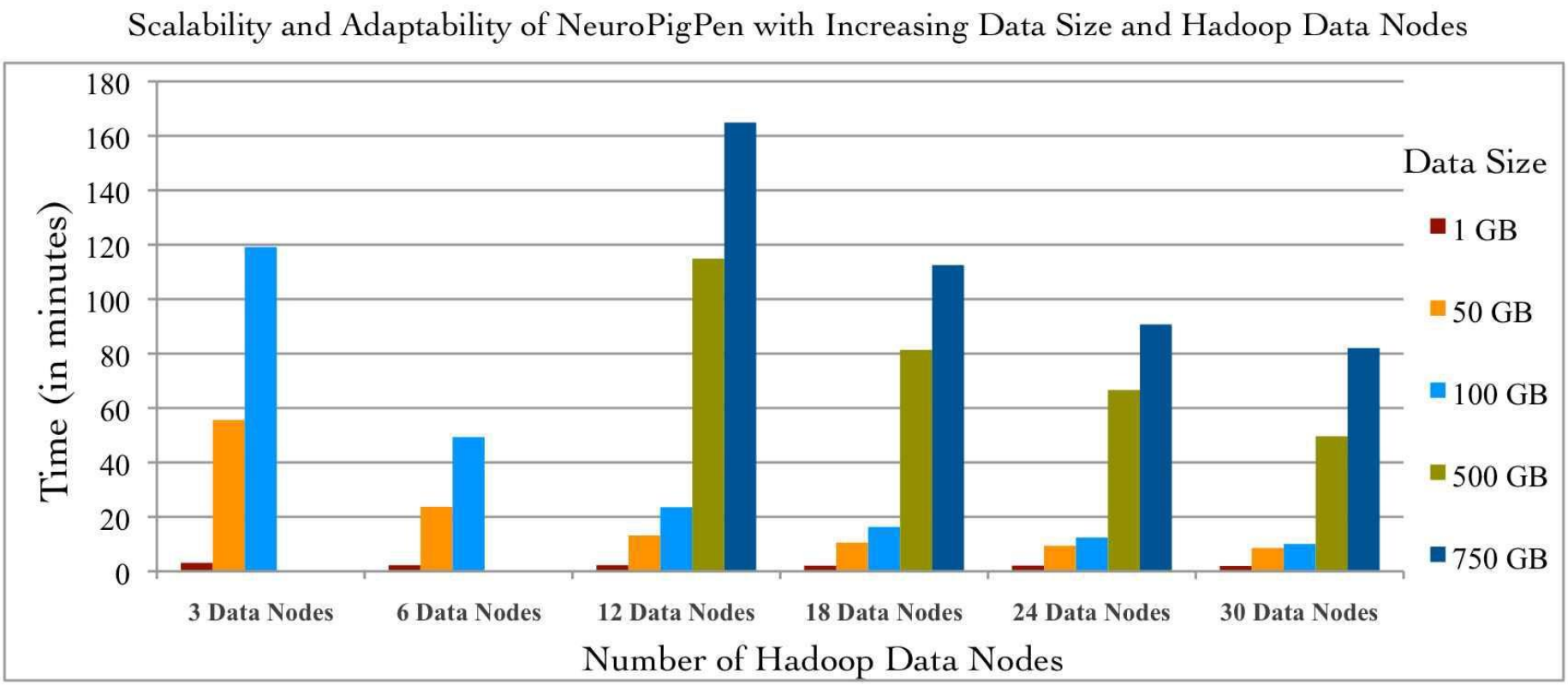
- Community participation through wiki-based features
- Interactive discussions and threads
- Community agreement towards a common epilepsy terminology

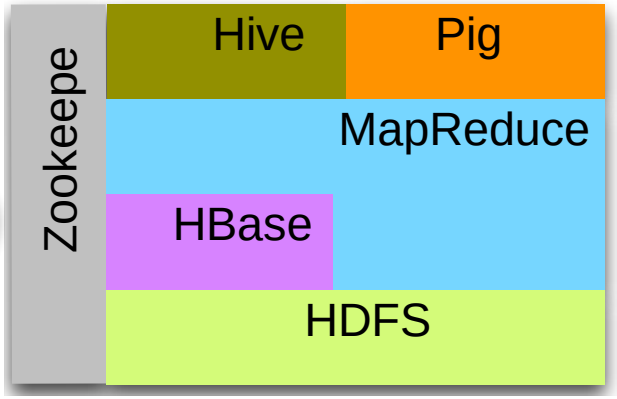
Ongoing and Future Directions: Neuroscience Big Data

- High performance computational pipeline for electrophysiological data



Ongoing and Future Directions: Neuroscience Big Data





Acknowledgements

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CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

BD2K NIH BIG DATA TO KNOWLEDGE