Structural Bioinformatics Training Workshop & Hackathon 2017

Basic Spark

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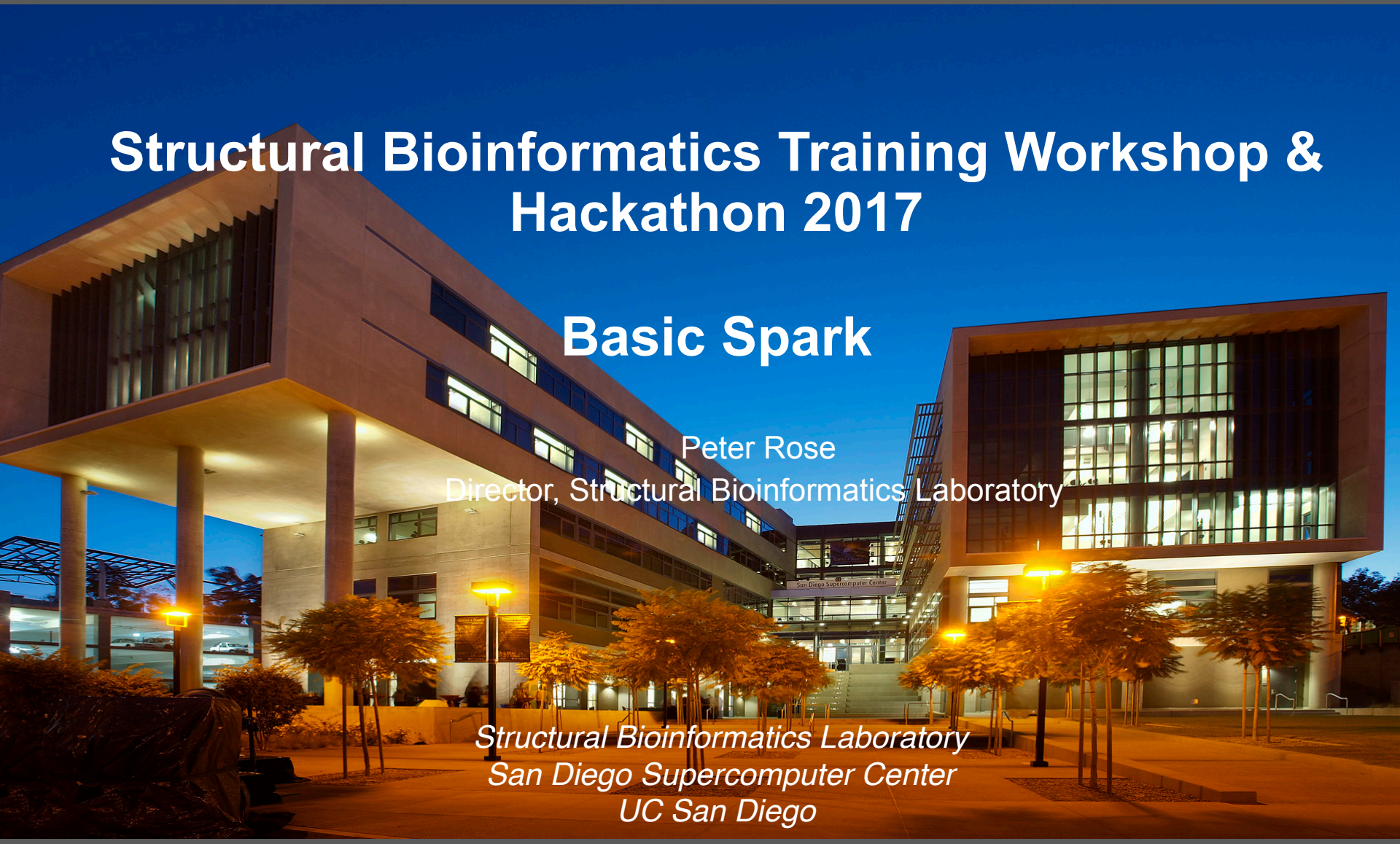


SDSC SAN DIEGO SUPERCOMPUTER CENTER RCSB PDB UC San Diego

mmtf-spark

- **Framework for parallel distributed analysis and mining of the PDB in MMTF file format with Apache Spark**
- **MMTF data sources**
  - Single <pdbId>.mmtf.gz files downloaded using RESTful web services
    - analyze a few PDB entries
  - Locally downloaded Hadoop Sequence file with MMTF records
    - analyze many or all PDB entries
  - See: http://mmtf.rcsb.org/download.html

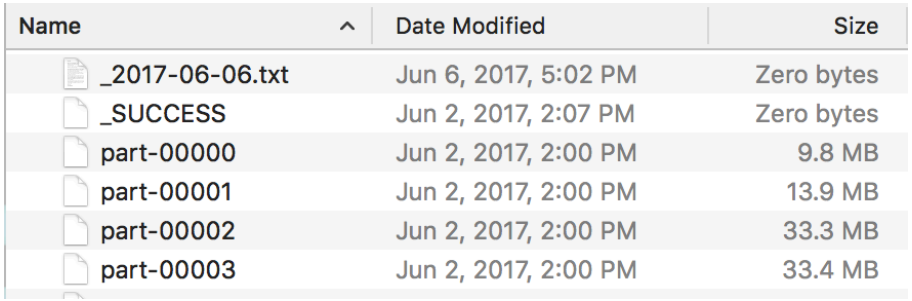
Hadoop “Sequence” Files

- **A flat file of binary key/value pairs**
- **Used by Big Data Frameworks (Hadoop, Spark)**
  - File systems need few big files for efficient processing
- **Files are splittable**
  - Can be processed in parallel
- **Often consists of a directory of Sequence files**
- **See** https://wiki.apache.org/hadoop/SequenceFile

MMTF-Hadoop Sequence Files

- **Two representations**
  - **full**
    - all atoms
    - full data precision
  - **reduced**
    - polymers
      - polypeptides: C-alpha
      - polynucleotides: P
      - 1st model only (e.g., NMR)
      - no alternative locations
      - except polysaccharides
        - » all atom
    - non-polymers
      - all atoms
    - water
      - excluded
    - Reduced precision (0.1): coordinates, temperature-factor, occupancy

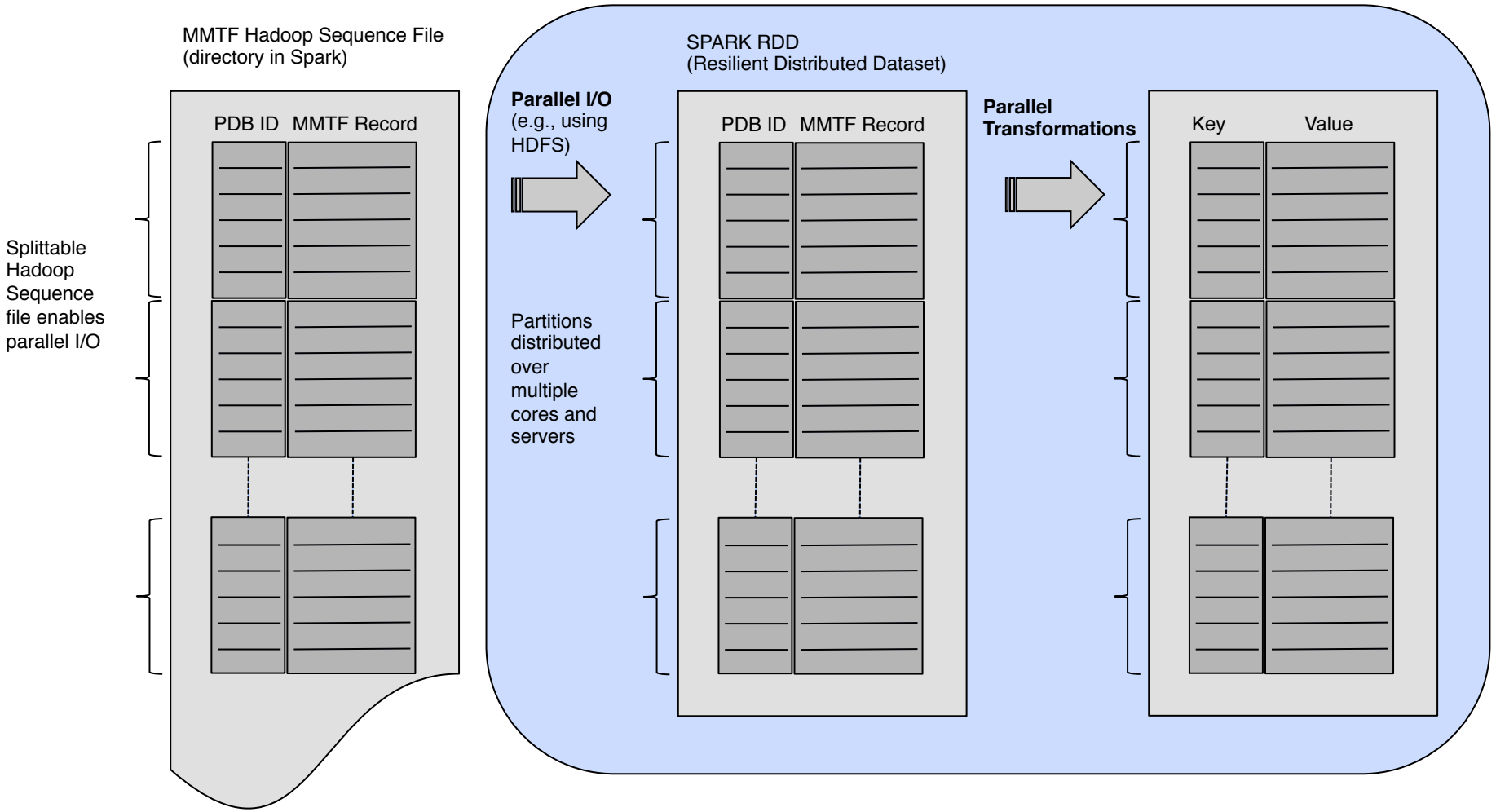
- **Example: full directory structure**



Name	Date Modified	Size
_2017-06-06.txt	Jun 6, 2017, 5:02 PM	Zero bytes
_SUCCESS	Jun 2, 2017, 2:07 PM	Zero bytes
part-00000	Jun 2, 2017, 2:00 PM	9.8 MB
part-00001	Jun 2, 2017, 2:00 PM	13.9 MB
part-00002	Jun 2, 2017, 2:00 PM	33.3 MB
part-00003	Jun 2, 2017, 2:00 PM	33.4 MB

- **Timestamp file (release date)**
  - _yyyy-mm-dd.txt
- **Updated every Wed. ~00:00 UTC**
- **Multiple sequence files**
  - part-00000 …
- **Download**
  - http://mmtf.rcsb.org/download.html

MMTF-Spark Data Pipeline



Basic MMTF-Spark Operations

- Reading MMTF Files & Hadoop Sequence files
- Filtering PDB structures
- FlatMapping PDB structures
- Filtering with RCSB PDB web services
- Using Map/Reduce with Lambda Expressions
- Writing custom Hadoop Sequence files

Downloading mmtf.gz files

```
 // spark setup
JavaSparkContext sc = …

// download a list of PDB entries from http://mmtf.rcsb.org
List<String> pdbIds = Arrays.asList("1AQ1","1B38","1B39","1BUH");

JavaPairRDD<String, StructureDataInterface> pdb = MmtfReader
                                    .downloadMmtfFiles(pdbIds, sc);
```

JavaPairRDD is a resilient distributed dataset of key/value pairs

key : String – structureId, e.g., pdbId (4HHB)
value: StructureDataInterface - structure representation in uncompressed form

Reading from a Sequence File

```
 // get path to full Sequence file
String path = System.getProperty("MMTF_FULL");

 // spark setup
JavaSparkContext sc = …

// read a list of PDB entries
List<String> pdbIds = Arrays.asList("1AQ1","1B38","1B39","1BUH");

JavaPairRDD<String, StructureDataInterface> pdb = MmtfReader
                                    .readSequenceFile(path, pdbIds, sc);

// or read all PDB entries
JavaPairRDD<String, StructureDataInterface> pdb = MmtfReader
                                    .readSequenceFile(path, sc);
```

Problem 0

- **Reading Files**
  - Navigate to project: 3-basic-spark in Eclipse
  - Find and and open Problem00.java (src/main/java)
  - Look at // TODO for the problem description
  - Insert your code after the // TODO and run it

Filtering by Quality Metrics

```
// read all PDB entries
JavaPairRDD<String, StructureDataInterface> pdb = MmtfReader
                                    .readSequenceFile(path, sc);

// keep PDB entries with a resolution in the inclusive range [0, 2]
pdb = pdb.filter(new Resolution(0.0, 2.0));


// or more concisely with method chaining
JavaPairRDD<String, StructureDataInterface> pdb = MmtfReader
                                    .readSequenceFile(path, sc)
                                    .filter(new Resolution(0.0, 2.0));
```

Related filters: Rfree and Rwork

Note, these filters will eliminate any entries that do not have these metrics, e.g., NMR structures.

See http://pdb101.rcsb.org/learn/guide-to-understanding-pdb-data/introduction

Filtering by Polymer Chain Types

```
// keep PDB entries that contain at least one L-protein chain
JavaPairRDD<String, StructureDataInterface> pdb = MmtfReader
                                .readSequenceFile(path, sc)
                                .filter(new ContainsLProteinChain());
```

```
// keep PDB entries that contain exclusively L-protein chains
boolean exclusive = true;

JavaPairRDD<String, StructureDataInterface> pdb = MmtfReader
                                .readSequenceFile(path, sc)
                                .filter(new ContainsLProteinChain(exclusive));
```

Related filters:
ContainsDProteinChain
ContainsDnaChain
ContainsRnaChain
ContainsDSaccharideChain
ContainsPolymerChainType
PolymerComposition

Filtering by Heterogeneous Polymer Chain Types

```
// keep PDB that contain DNA, RNA, or both (DNA/RNA hybrid)
JavaPairRDD<String, StructureDataInterface> pdb = MmtfReader
        .readSequenceFile(path, sc)
        .filter(new ContainsPolymerChainType("DNA LINKING","RNA LINKING"));
```

Monomer types (most frequent types in bold)
PEPTIDE_LINKING (achiral, e.g., GLY)

D_PEPTIDE_LINKING
D_PEPTIDE_COOH_CARBOXY_TERMINUS
D_PEPTIDE_NH3_AMINO_TERMINUS

L_PEPTIDE_LINKING
L_PEPTIDE_COOH_CARBOXY_TERMINUS
L_PEPTIDE_NH3_AMINO_TERMINUS

DNA_LINKING
DNA_OH_3_PRIME_TERMINUS
DNA_OH_5_PRIME_TERMINUS

NON_POLYMER
SACCHARIDE (achiral)

D_SACCHARIDE
D_SACCHARIDE_14_and_14_LINKING
D_SACCHARIDE_14_and_16_LINKING

L_SACCHARIDE
L_SACCHARIDE_14_AND_14_LINKING
L_SACCHARIDE_14_AND_16_LINKING

RNA_LINKING
RNA_OH_3_PRIME_TERMINUS
RNA_OH_5_PRIME_TERMINUS

See http://mmcif.wwpdb.org/dictionaries/mmcif_mdb.dic/Items/_chem_comp.type.html

Problem 1

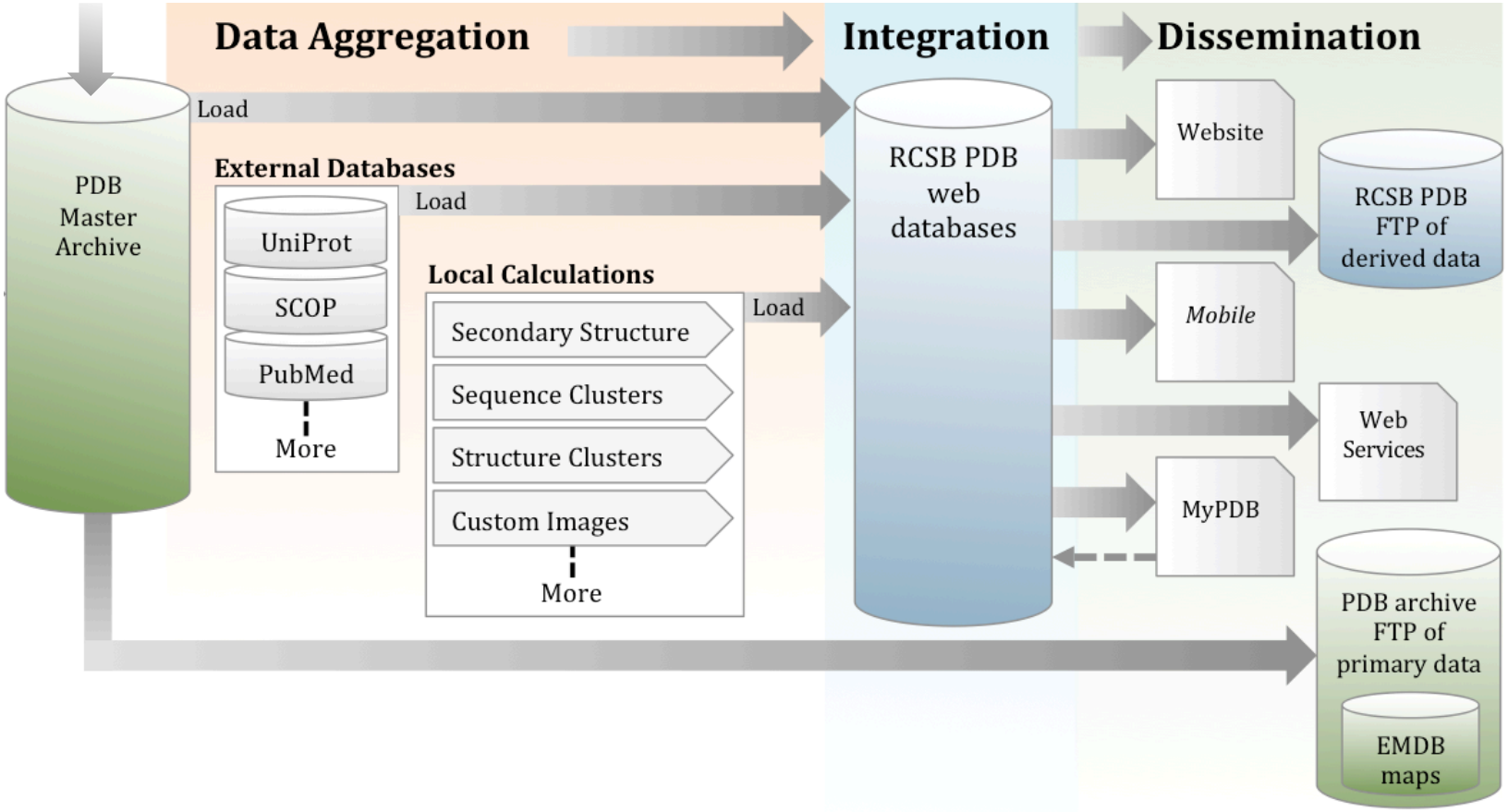
- **Filtering**
  - Navigate to project: 3-basic-spark in Eclipse
  - Find and and open Problem01.java (src/main/java)
  - Look at the // TODO for the problem description
  - Insert your code after the // TODO and run it

Filtering with RCSB PDB Web Services

- **MMTF file content focused on structural data**
- **Additional data and annotations from RCSB PDB**
  - Ids and keywords, structure annotation, structure features, sequence features, chemical components, biological info, methods info, deposition info, publications
  - http://www.rcsb.org/pdb/staticHelp.do?p=help/advancedsearch/index.html
- **Any advanced query from the RCSB PDB website can be run through RESTful web services**
  - http://www.rcsb.org/pdb/search/advSearch.do?search=new
  - The RCSB Protein Data Bank: redesigned web site and web services (2011) Nucleic Acids Res. 39: D392-D401 doi:10.1093/nar/gkq1021

RCSB PDB Data Pipeline

Data In

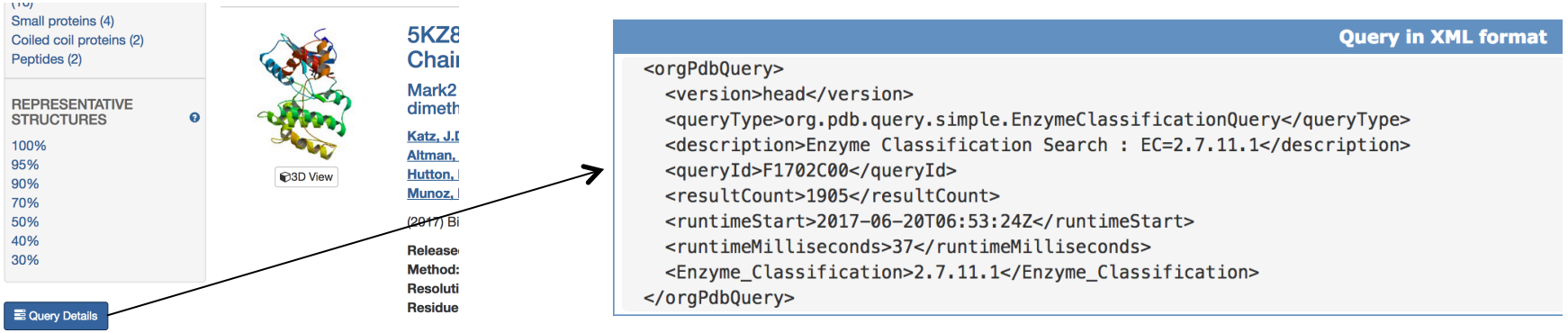


Demo

RCSB PDB Advanced Query

Filtering by Advanced Search XML

- Run any advanced query at http://www.rcsb.org
- Go to results page and click Query Details



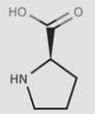
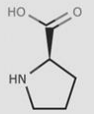
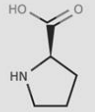
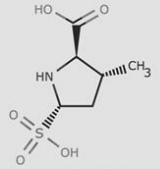
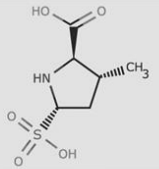
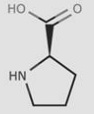
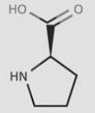
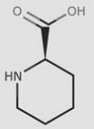

```
String query =
"<orgPdbQuery>" +
    "<queryType>org.pdb.query.simple.EnzymeClassificationQuery</queryType>”+
    "<Enzyme_Classification>2.7.11.1</Enzyme_Classification>" +
"</orgPdbQuery>”;

pdb = pdb.filter(new AdvancedQuery(query));
```

Filtering by SMILES

```
// keep structures that contain a chemical component
// with this substructure
pdb = pdb.filter(new
    ChemicalStructureQuery("OC(=O)CCCC[C@@H]1SC[C@@H]2N
    C(=O)N[C@H]12”,
    ChemicalStructureQuery.SUBSTRUCTURE, 0));
```

```
// keep structures that contain a chemical component
// that is >= 70% similar to the query structure
int similarity = 70;
pdb = pdb.filter(new
    ChemicalStructureQuery("OC(=O)CCCC[C@@H]1SC[C@@H]2N
    C(=O)N[C@H]12”,
    ChemicalStructureQuery.SIMILAR, similarity));
```

Query Types:
EXACT
SUBSTRUCTURE
SUPERSTRUCTURE
SIMILAR

Search type	Query	Result
Exact		
Substructure		
Superstructure		
Similar		

Problem 3

- **Filtering with RCSB PDB Web Services**
  - Open Problem03.java
  - Insert the code after the // TODO and run your code
  - Pick one of the result PDB Ids and check the http://www.rcsb.org website to see if the result matches the expected result.

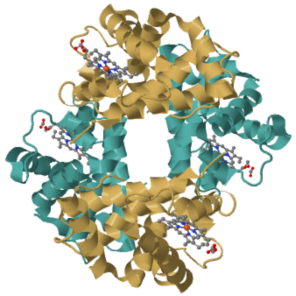
FlatMapping

- Maps one data record to zero or more data records
- Flatmap a PDB entry (quaternary structure) to its polymer chains (tertiary structure)

```
// Extract polymer chains out of PDB entries
JavaPairRDD<String, StructureDataInterface> pdb = MmtfReader
                                .readSequenceFile(path, sc)
                                .flatMapToPair(new StructureToPolymerChains());
```

FlatMapping Effect on Keys

```
List<String> pdbId = Arrays.asList("4HHB");
JavaPairRDD<String, StructureDataInterface> pdb = MmtfReader
                                    .downloadMmtfFiles(pdbId, sc);
```



```
pdb.keys().foreach(k -> System.out.println(k));
```

=> 4HHB (4HHB is a tetramer or dimer of dimers)

```
pdb.flatMapToPair(new StructureToPolymerChains())
   .keys().foreach(k -> System.out.println(k));
```

=> 4HHB.A 4HHB.B 4HHB.C 4HHB.D (4HHB contains 4 protein chains)
Chain name is appended to PDB Id

```
// exclude chains with identical sequences
boolean excludeDuplicates = true;
pdb.flatMapToPair(new StructureToPolymerChains(false, excludeDuplicates))
   .keys().foreach(k -> System.out.println(k));
```

=> 4HHB.A 4HHB.B (4HHB contains two unique protein chains: hemoglobin alpha and beta)

Map and Reduce

Count number of atoms in the PDB

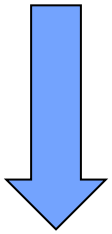
JavaPairRDD<String, StructureDataInterface>

PDB ID	Structure
1ABC	…
2BCD	…
3CDE	…
4DEF	…
5EFG	…

map (getNumAtoms())

JavaRDD<Integer>

NumAtoms
1,000
2,000
3,000
4,000
5,000



reduce (sum)

15,000

Map and Reduce Using Lambda Expressions

```
// count total number of atoms in PDB
long numAtoms = pdb
                    .map(t -> t._2.getNumAtoms())
                    .reduce((a,b) -> a+b);
```

Problem 3

- Open Problem02.java
- Insert the code after the // TODO and run your code
- Look up one of the result PDB Ids on the http://www.rcsb.org website and check if the query result matches your expectation.

Writing Hadoop Sequence Files

```
// read all PDB entries
JavaPairRDD<String, StructureDataInterface> pdb = MmtfReader
                                    .readSequenceFile(path, sc);

// keep PDB entries with a resolution in the inclusive range [0, 2]
pdb = pdb.filter(new Resolution(0.0, 2.0));

MmtfWriter.writeSequenceFile(path + ”_highResolution", sc, chains);
```

Use MmtfWriter.writeMmtfFiles(path, sc, structure)
to write (a small subset) to individual mmtf.gz files

Summary

- **mmtf-spark: Framework for parallel distributed mining of the PDB with Apache Spark**
- **Hadoop Sequence file is an efficient container format to process large number of structures**
- **PDB structures represented as key/value pairs**
- **Spark transformations**
  - filter, keys, map, flatMap
- **Spark actions**
  - count, foreach, reduce, collect

Resources

- **MMTF Website**
  - http://mmtf.rcsb.org
- **GitHub Repository**
  - https://github.com/sbl-sdsc/mmtf-spark
- **MMTF File Format**
  - Bradley AR, et al. (2017) MMTF—An efficient file format for the transmission, visualization, and analysis of macromolecular structures. PLOS Computational Biology 13(6): e1005575. https://doi.org/10.1371/journal.pcbi.1005575
  - Valasatava Y, et al. (2017) Towards an efficient compression of 3D coordinates of macromolecular structures. PLOS ONE 12(3): e0174846. https://doi.org/10.1371/journal.pone.0174846
- **RCSB PDB Web Services and Query System**
  - Rose, PW, et al. (2013) The RCSB Protein Data Bank: new resources for research and education, Nucleic Acids Res 41: D475-D482. https://doi.org/10.1093/nar/gks1200
  - Rose, PW, et al. (2011) The RCSB Protein Data Bank: redesigned web site and web services, Nucleic Acids Res 39: D392-D401. https://doi.org/10.1093/nar/gkq1021