Persistent Bioperl

BOSC 2003

Hilmar Lapp

Genomics Institute

Of The Novartis Research Foundation

San Diego, USA

Acknowledgements

- Bio* contributors and core developers
  - Aaron, Ewan, ThomasD, Matthew, Mark, Elia, ChrisM, BradC, Jeff Chang, Toshiaki Katayama
  - And many others
- Sponsors of Biohackathons
  - Apple (Singapore 2003)
  - O’Reilly (Tucson 2002)
  - Electric Genetics (Cape Town 2002)
- GNF for its generous support of OSS development

Overview

- Use cases
- BioSQL Schema
- Bioperl-DB
    - Key features and design goals
    - Examples
- Status & Plans
- Summary

Use cases (I)

- ‘Local GenBank with random access’
  - Local cache or replication of public databanks
  - Indexed random access, easy retrieval
  - Preserves annotation (features, dbxrefs,…), possibly even format
- ‘GenBank in relational format’
  - Normalized schema, predictably populated
  - Allows arbitrary queries
  - Allows tables to be added to support my data/question/…

Use Cases (II)

- ‘Integrate GenBank, Swiss-Prot, LocusLink, …’
  - Unifying relational schema
  - Provide common (abstracted) view on different sources of annotated genes
- ‘Database for my lab sequences and my annotation’
  - Store FASTA-formatted sequences
  - Add, update, modify, remove various types of annotation

Use Cases (III)

- Persistent storage for my favorite Bio* toolkit
  - Relational model accommodates object model
  - Persistence API with transparent insert, update, delete

Persistent Bio*

- Normalized relational schema designed for Bio* interoperability

BioSQL

- Toolkit-specific persistence API

Biojava
Bioperl-DB
Biopython
Bioruby

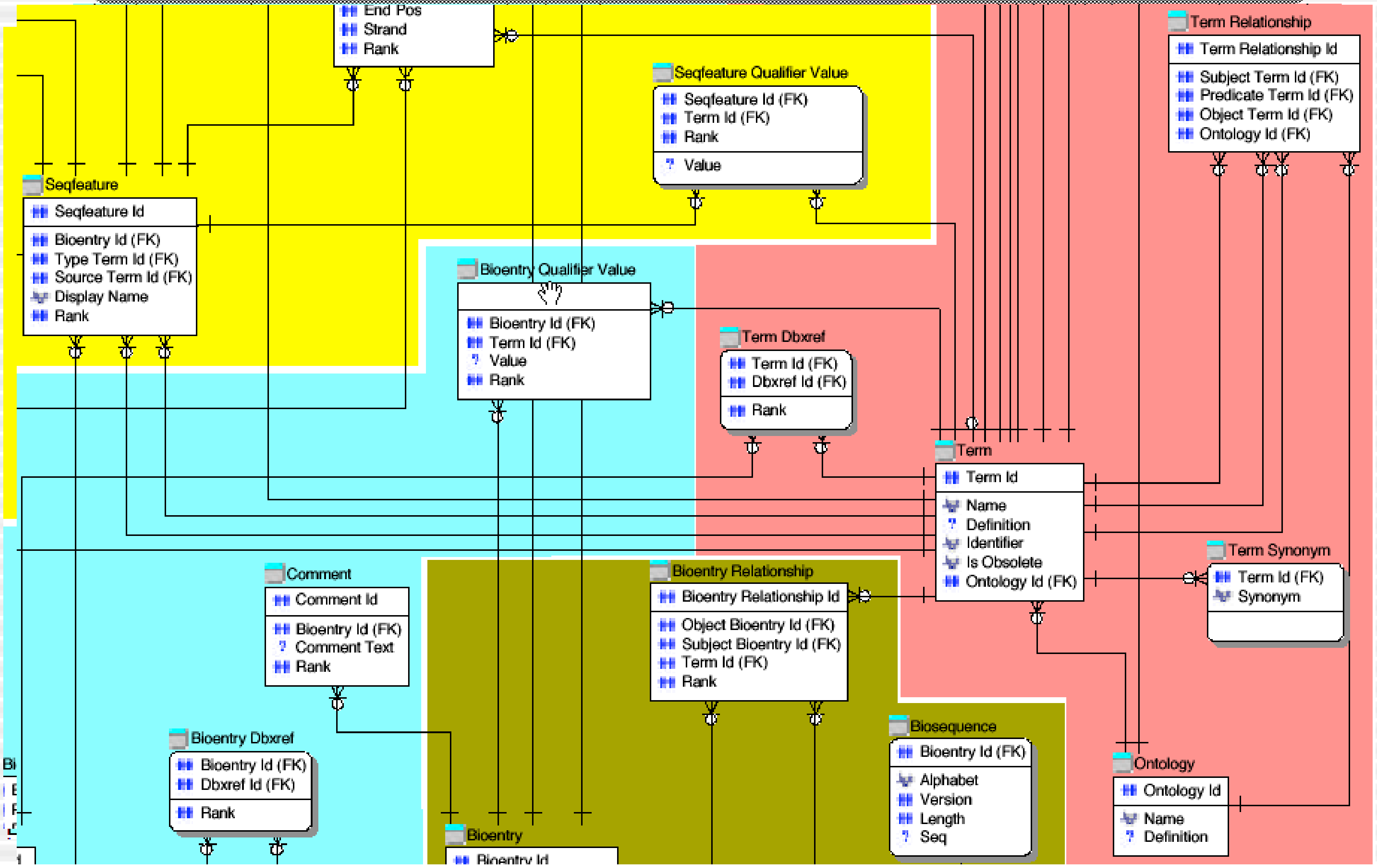
BioSQL

- Interoperable relational data store for Bio*
  - Language bindings presently for Bioperl, Biojava, Biopython, Bioruby
- Very flexible, normalized, ontology-driven schema
  - Focal entities are Bioentry, Seqfeature, Term (and Dbxref)
- Schema instantiation scripts for different RDBMSs
  - MySQL, PostgreSQL, Oracle
- Release of v1.0 imminent
  - Schema has been stable for the last 3 months
  - Relatively well documented (installation, how-to, ERD)
- Mailing list (biosql-l@open-bio.org), CVS (biosql-schema), links at http://obda.open-bio.org

BioSQL: Some History

- Ewan Birney started BioSQL and Bioperl-db in Nov 2001
  - Initial use-case was to serialize/de-serialize Bio::Seq objects to/from a local sequence store (as a replacement for SRS)
- Schema redesigned at the 2002 Biohackathons in Tucson and Cape Town
  - Series of incremental changes later in 2002
- Full review at the 2003 Biohackathon in Singapore
  - Changed Taxon model to follow NCBI's
  - Full ontology model, resembles GO's model
  - Features can have dbxrefs
  - Consistent naming

BioSQL ERD



End Pos
Strand
Rank
Seqfeature Qualifier Value
Seqfeature Id (FK)
Term Id (FK)
Rank
Value
Term Relationship
Term Relationship Id
Subject Term Id (FK)
Predicate Term Id (FK)
Object Term Id (FK)
Ontology Id (FK)
Seqfeature
Seqfeature Id
Bioentry Id (FK)
Type Term Id (FK)
Source Term Id (FK)
Display Name
Rank
Bioentry Qualifier Value
Bioentry Id (FK)
Term Id (FK)
Value
Rank
Term Dbxref
Term Id (FK)
Dbxref Id (FK)
Rank
Term
Term Id
Name
Definition
Identifier
Is Obsolete
Ontology Id (FK)
Term Synonym
Term Id (FK)
Synonym
Comment
Comment Id
Bioentry Id (FK)
Comment Text
Rank
Bioentry Relationship
Bioentry Relationship Id
Object Bioentry Id (FK)
Subject Bioentry Id (FK)
Term Id (FK)
Rank
Biosequence
Bioentry Id (FK)
Alphabet
Version
Length
Seq
Ontology
Ontology Id
Name
Definition
Bioentry Dbxref
Bioentry Id (FK)
Dbxref Id (FK)
Rank
Bioentry
Bioentry Id

Language Binding: OR Mapping

- Object-Relational Mapping connects two worlds
  - Object model (Bioperl) Relational model (Biosql)
  - Object and relational models are orthogonal (though ‘correlated’)
    - E.g., inheritance, n:n associations, navigability of associations, joins
- General goals of the OR mapping are
  - Bi-directional map between objects and entities
  - Transparent persistence interface reflecting all of INSERT, UPDATE, DELETE, SELECT
- Generic approaches exist, most of which are commercial
  - TopLink, CMP (e.g., Jboss), JDO, Tangram

Bioperl-db Is An OR-Mapper

```
# get persistence adaptor factory for database
my $db = Bio::DB::BioDB->new(-database  => 'biosql',
                             -dbcontext => $dbc);
# open stream of objects parsed from flatfile
my $stream = Bio::SeqIO->new(-fh     => \*STDIN,
                             -format => 'genbank');
while(my $seq = $stream->next_seq()) {
      # convert to persistent object
      $pobj = $db->create_persistent($seq);
      # insert into datastore
      $pobj->create();
}
```

Where can I get Bioperl-db?

- Bioperl-db is a sub-project of Bioperl
  - Links and news at http://www.bioperl.org/
  - Email to bioperl-l@bioperl.org
    - but biosql-l@open-bio.org will often work, too
  - CVS repository is bioperl-db under bioperl (/home/repository/bioperl/bioperl-db)
- No release of the current codebase yet
  - But v0.2 is imminent

Bioperl-db: Key Features (I)

- Transparent persistence API on top of object API
  - Persistent objects know their primary keys, can update, insert, and delete themselves
    - Full API in Bio::DB::PersistentObjectI
  - Peristent objects speak both the persistence API and their native tongue
- Several retrieval methods on the persistence adaptor API:
  - find_by_primary_key(), find_by_unique_key(), find_by_query(), find_by_association()
  - Full API in Bio::DB::PersistenceAdaptorI

Bioperl-db: Key Features (II)

- Extensible framework separating object adaptor logic from schema logic
  - Central factory loads and instantiates a datastore-specific adaptor factory at runtime.
  - Adaptor factory loads and instantiates persistence adaptor at runtime - no hard-coded adaptor names
  - Queries are constructed in object space and translated to SQL at run-time by schema driver
  - Designed with adding bindings to other schemas than BioSQL in mind (e.g., Chado, Ensembl, MyBioSQL, …)

Bioperl-db: Examples (I)

- Step 1: connect and obtain adaptor factory

```
use Bio::DB::BioDB;
# create the database-specific adaptor factory
# (implements Bio::DB::DBAdaptorI)
$db = Bio::DB::BioDB->new(-database  =>”biosql”,
                          # user, pwd, driver, host …
                          -dbcontext => $dbc);
```

Bioperl-db: Examples (II)

- Step 2: depends on use case
  - Load sequences:

```
use Bio::SeqIO;
# open stream of objects parsed from flatfile
my $stream = Bio::SeqIO->new(-fh     => \*STDIN,
                             -format => 'genbank');
while(my $seq = $stream->next_seq()) {
   # convert to persistent object
   $pseq = $db->create_persistent($seq);
   # $pseq now implements Bio::DB::PersistentObjectI
   # in addition to what $seq implemented before
   # insert into datastore
   $pseq->create();
}
```

Bioperl-db: Examples (III)

- Step 2: depends on use case
  - Retrieve sequences by alternative key:

```
use Bio::Seq; use Bio::Seq::SeqFactory;
# set up Seq object as query template
$seq = Bio::Seq->new(-accession_number => “NM_000149”,
                     -namespace        => “RefSeq”);
# pass a factory to leave the template object untouched
$seqfact = Bio::Seq::SeqFactory->new(-type=>“Bio::Seq”);
# obtain object adaptor to query (class name works too)
# adaptors implement Bio::DB::PersistenceAdaptorI
$adp = $db->get_object_adaptor($seq);
# execute query
$dbseq = $adp->find_by_unique_key(
                        $seq, -obj_factory => $seqfact);
warn $seq->accession_number(),
     ” not found in namespace RefSeq\n“ unless $dbseq;
```

Bioperl-db: Examples (IV)

- Step 2: depends on use case
  - Retrieve sequences by query:

```
use Bio::DB::Query::BioQuery;
# set up query object as query template
$query = Bio::DB::Query::BioQuery->new(
    -datacollections => [“Bio::Seq s”,
                         “Bio::Species=>Bio::Seq sp”],
    -where           => [“s.description like ‘%kinase%’”,
                         “sp.binomial = ?”]);
# obtain object adaptor to query
$adp = $db->get_object_adaptor(“Bio::SeqI”);
# execute query
$qres = $adp->find_by_query($query, -name => “bosc03”,
                            -values => [“Homo sapiens”]);
# loop over result set
while(my $pseq = $qres->next_object()) {
    print $pseq->accession_number,”\n”;
}
```

Bioperl-db: Examples (V)

- Step 2: depends on use case
  - Retrieve sequence, add annotation, update in the db

```
use Bio::Seq; use Bio::SeqFeature::Generic;
# retrieve the sequence object somehow …
$adp = $db->get_object_adaptor(“Bio::SeqI”);
$dbseq = $adp->find_by_unique_key(
          Bio::Seq->new(-accession_number => “NM_000149”,
                        -namespace        => “RefSeq”));
# create a feature as new annotation
$feat = Bio::SeqFeature::Generic->new(
                        -primary_tag => “TFBS”,
                        -source_tag  => “My Lab”,
                        -start=>23,-end=>27,-strand=>-1);
# add new annotation to the sequence
$dbseq->add_SeqFeature($feat);
# update in the database
$dbseq->store();
```

Bioperl-db: Examples (VIa)

- Extensibility: handle my own object by adding my own adaptor. A) Custom sequence class

```
package MyLab::Y2HSeq;
@ISA = qw(Bio::Seq);
sub get_interactors{
    my $self = shift;
    return @{$self->{'_interactors'}};
}
sub add_interactor{
    my $self = shift;
    push(@{$self->{'_interactors'}}, @_);
}
sub remove_interactors{
    my $self = shift;
    my @arr = $self->get_interactors();
    $self->{'_interactors'} = [];
    return @arr;
}
```

Bioperl-db: Examples (VIb)

- Extensibility: handle my own object by adding my own adaptor. B) Custom adaptor class

```
package Bio::DB::BioSQL::Y2HSeqAdaptor;
@ISA = qw(Bio::DB::BioSQL::SeqAdaptor);
sub store_children{
  my ($self,$obj) = @_;
  # call inherited method
  $self->SUPER::store_children(@_);
  # obtain persistent term object for the rel.ship type
  my $term = Bio::Ontology::Term->new(
                   -name => “interacts-with”,
                   -ontology => “Relationship Types”);
  my $termadp = $self->db->get_object_adaptor($term);
  my $reltype = $termadp->find_by_unique_key($term) or
    $self->db->create_persistent($term)->create();
  # continued on the next page …
```

Bioperl-db: Examples (VIb)

- Extensibility: handle my own object by adding my own adaptor. B) Custom adaptor class (cont’d)

```
   # store the interacting sequences
   foreach my $seq ($obj->get_interactors()) {
     # each interactor needs to be persistent object
     $seq = $self->db->create_persistent($seq)
       unless $seq->isa("Bio::DB::PersistentObjectI");
     # each interactor also needs to have a primary key
     $seq = $seq->adaptor->find_by_unique_key() or
       $seq->create();
     # associate the interactor with this object
     $seq->adaptor->add_association(
               -objs => [$obj, $seq, $reltype],
               -contexts => [“object”,”subject”,undef]);
   }
   return 1; # done
 }
```

Ready-To-Use Scripts (I)

- load_seqdatabase.pl (bioperl-db/scripts/biosql)
  - Use for loading and updating bioentries and their annotation
  - Supports all Bio::SeqIO supported formats
    - genbank, embl, swiss, locuslink, fasta, gcg, ace, …
  - Supports all Bio::ClusterIO supported formats
    - Unigene
- Many command line options
  - For flexible handling of updates
    - --lookup, --noupdate, --remove, --mergeobjs
  - For filtering and post-processing sequences
    - --seqfilter, --pipeline

Ready-To-Use Scripts (II)

- load_ontology.pl (bioperl-db/scripts/biosql)
  - Use for loading and updating ontologies and terms
  - Supports all Bio::OntologyIO supported formats
    - dagflat (incl. soflat, goflat), InterPro, simplehierarchy
  - Tested for GO and SOFA
- Many command-line options
  - For handling updates and obsoleted terms
    - --lookup, --noupdate, --remove
    - --noobsolete, --updobsolete, --delobsolete, --mergeobjs
  - For (re-)computing the transitive closure
    - --computetc

Ready-To-Use Scripts (III)

- load_ncbi_taxonomy.pl (biosql-schema/scripts)
  - Use for loading and updating the taxon tables with the NCBI Taxonomy database
  - Downloads the database from NCBI automatically if desired
  - Some options to configure and tune load and update
  - Automatically updates the Nested Set values in the taxon table

Current Status

- BioSQL is stable and release-ready
  - Imminent release of v1.0
  - Well-documented ;-) , ER-diagram
  - Supports MySQL, PostgreSQL, and Oracle
  - Toolkit-independent script for populating taxa
- Bioperl-db is stable but documentation is patchy
  - Core APIs stable and documented, but no How-To's
  - All tests pass on all 3 RDBMS platforms
  - Head revision wants Bioperl >= 1.2.2 (but for RichSeqI attributes you need Bioperl main trunk)
  - Fuzzy locations get transformed to simple locations
- BioSQL & Bioperl-db are used in production and at multiple places

Plans For The Future (I)

- Persistence Adaptors for more object types
  - Phenotypes (OMIM)
  - Markers (SNPs, STSs, …)
- Increased support for lazy loading
  - Features and annotations for a sequence (sequence itself is already lazy-loaded)
- Write adaptors for other applications to run off of BioSQL
  - Genome browsers: GBrowse, Apollo
  - Ontology editors: DAG-edit

Plans For The Future (II)

- Proof-of-Concept for interoperability
  - Load through Bioperl/Bioperl-db, retrieve through Biojava
- Proof-of-Concept of the architecture’s flexibility
  - Map to schemas different from BioSQL: Chado, Ensembl

Summary

- BioSQL is a very flexible, ontology-driven, stable relational schema to capture richly annotated databank entries
- BioSQL is supported as the persistent storage across the Bio* projects
- Bioperl-db is the object-relational mapping for Bioperl objects to BioSQL
- Bioperl-db adds a transparent persistence API on top of all supported Bioperl objects
- Presently supported areas of the object model are sequences, features, annotations, clusters, ontologies