Unison Tutorial

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2006-05-12

Tutorial Outline

- Introduction
  - data sources, algorithms, update scheme
- Schema
  - overview, design themes, critical tables
- Access
  - web pages, command line tools, perl API, psql
- Example Queries
  - Finding sequences
  - Finding parameters
  - Getting predictions for a sequence
  - Mining for sequence based on predictions
  - Tips
- Future Plans

What Can I Do With Unison?

- Retrieve sequence analysis for a single sequence.
- Mine for sequences based on predicted features, sequence origins, taxonomy, patents, orthology, and structure.
- Find all sources of a single sequence.
- Find patents for a sequence.
- Locate sequence variations relative to domains and in structure.
- Build new tools.

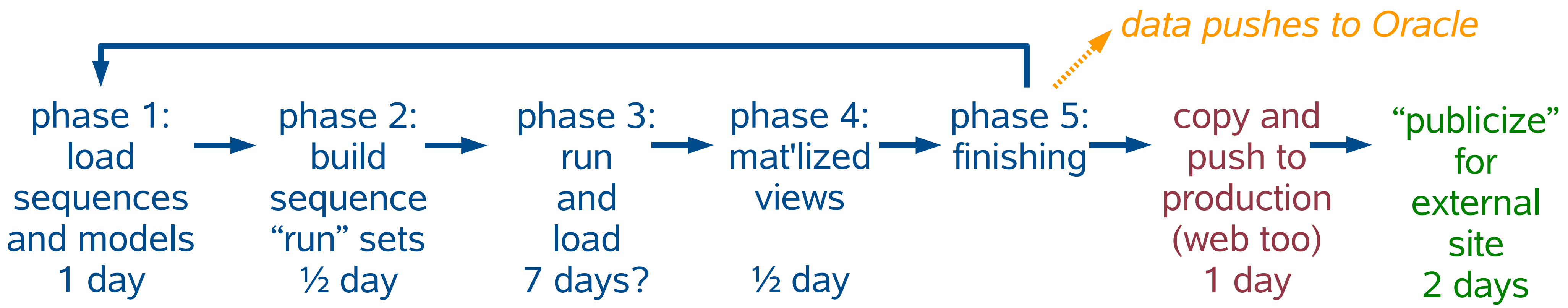
Design Goals

- Sequences are stored non-redundantly.
  - eliminates redundant computation and analysis
  - Results are keyed to sequences, parameters, and optionally a model.
  - Sequences are immutable and therefore results are never stale.
  - Sequences are linked to their origins and aliases.
- Fast, reliable, differential updates.
- Multiple result sets for different invocations
- Make no assumptions and provide no interpretations.
- Synopses of prediction results only, but and enable regeneration of results.

Unison Contents

- Non-redundant Sequences
  - UniProtKB/Swiss-Prot, IPI, Genengenes, Genehub representative sequences, RefSeq, Curagen, Incyte, ..., Ensembl *ab initio*, miscellaneous fragments
- Non-redundant Results
  - Pfam, TMHMM, SignalP, protcomp
  - BIG-PI, PSI-PRED, RegExp motifs
  - disprot, dispro, pmap
- Lots of other Data
  - patents, PDB, SCOP, GO, GOng, NCBI tax, HomoloGene, MINT, ...
- Statistics
  - 75 tables, 108 views, 120 functions
  - ~6 CPU-years' worth of data, >440M protein features
  - 14GB of compressed data, 130GB on disk w/indexes

Update Procedure and Run Sets


data pushes to Oracle
phase 1: load sequences and models 1 day
phase 2: build sequence "run" sets ½ day
phase 3: run and load 7 days?
phase 4: mat'lized views ½ day
phase 5: finishing
copy and push to production (web too) 1 day
"publicize" for external site 2 days

Set	Criteria	Algorithms
runA	human 100-1000 AA reliable origins	prospect antigenic BLAST†
runB	human, mouse, rat 100-1500 AA reliable origins	Pfam (fs & ls) BIG-PI RegExp PSIPRED
runC	human, mouse, rat, cow, zebrafish 100-3000 AA all sequence sources	pepcoil SignalP TMHMM antigenic pmap protcomp
	ad hoc	disprot† disprot†

† these methods are currently unsupported

Implementation

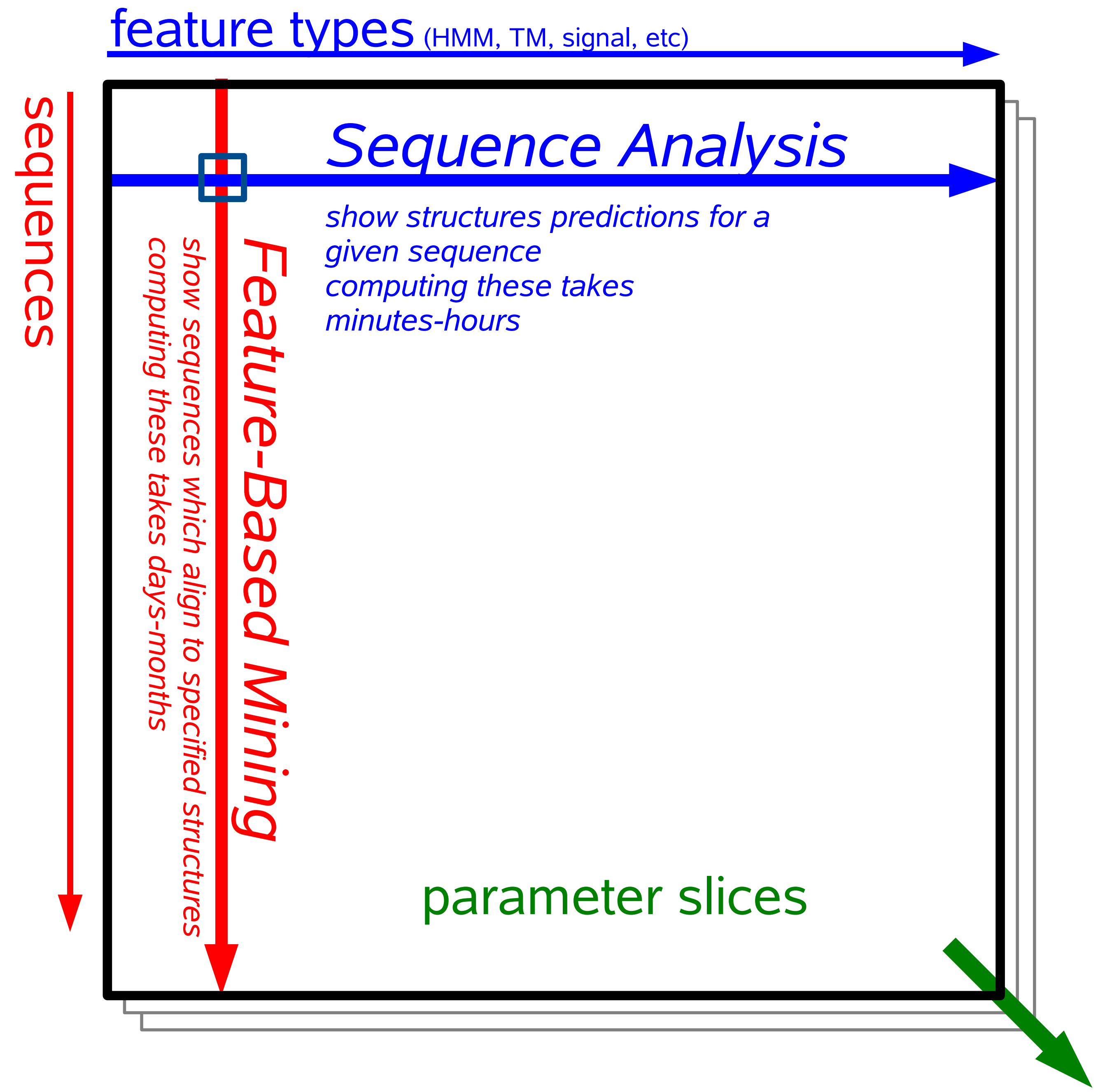
- Hardware
  - hostname `csb`
  - 4 dual-core Opterons, 2.4 GHz
  - 32GB RAM
  - 500GB FC-RAID
- Linux
  - SuSE 10.0, kernel 2.6
- PostgreSQL 8.1.3
  - 3 databases: `csb`, `csb-stage`, `csb-dev`
  - unison is a schema within each
- Perl 5.8
- Apache 2.0 web pages

Unison Schema

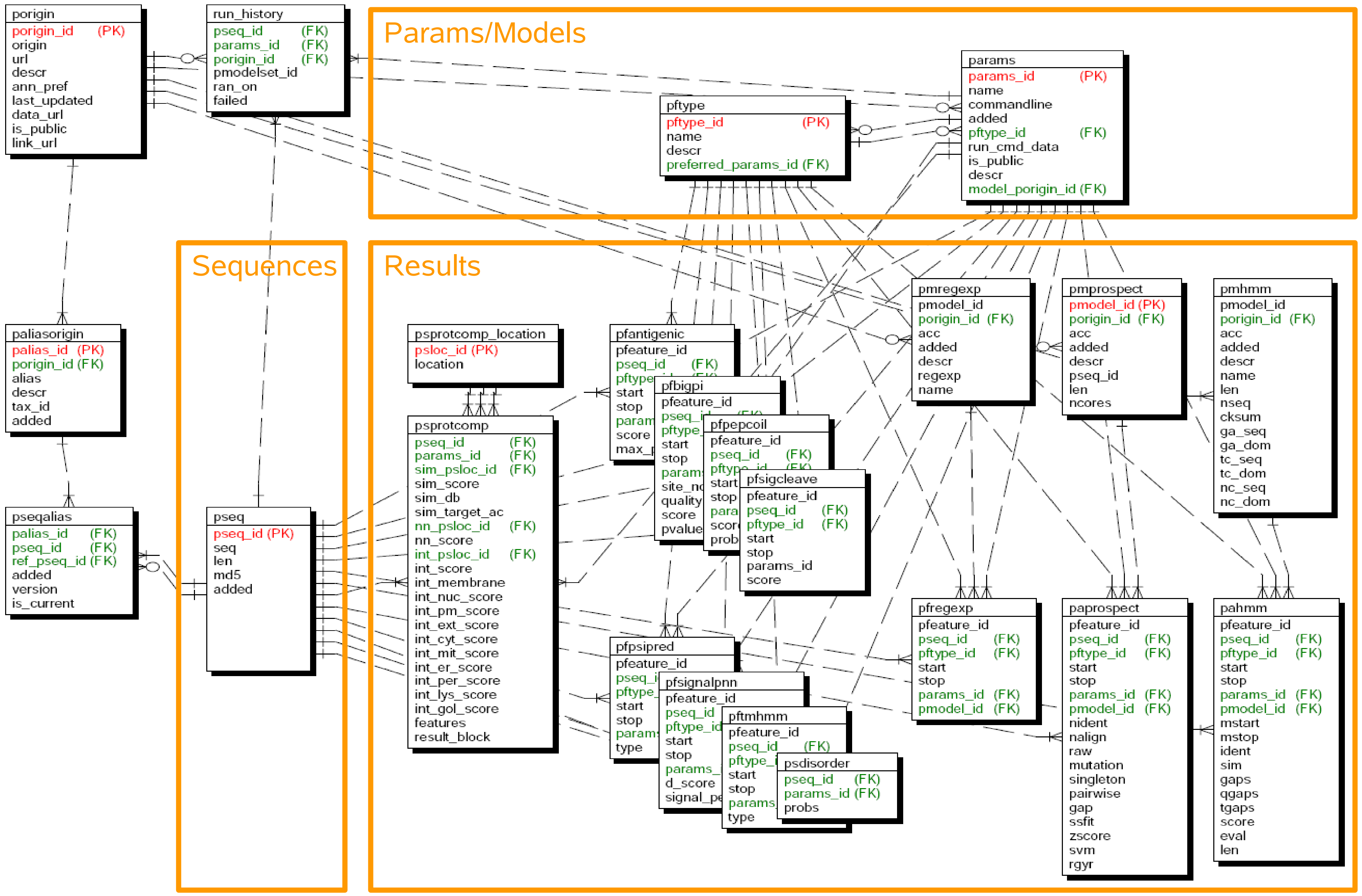
Design Themes

- Abstraction and Normalization
  - most tables are essentially data types
  - expect a lot of joins, but views exist for common queries
  - facilitates updates of new params, etc
- Rely on database for correctness
  - pedantic and paranoid use of triggers and constraints
- Selective incorporation of external databases
  - schemas: unison, ncbi, tax, dali, go, pdb

Results Cube


feature types (HMM, TM, signal, etc)
sequences
Sequence Analysis
show structures predictions for a given sequence
computing these takes minutes-hours
Feature-Based Mining
show sequences which align to specified structures
computing these takes days-months
parameter slices

Schema Overview



Critical Tables, Views, Functions

- Tables and views
  - porigin, pseq, pftype, params
  - palias (view) and current_annotations_v
  - pahmm + pmhmm => pahmm_v
  - pfbigpi => pfbigpi_v
  - pfsignalpnn
  - psprotcomp + psprotcomp_locations => psprotcomp_v
  - pfregexp + pmregexp => pfregexp_v
  - run_history => run_history_v
- Functions
  - pseq_id_from_sequence()
  - params_id() and preferred_params_id_by_pftype()
  - porigin_id()

Table and Column Names

- `X_id` is always a primary or foreign key
  - foreign and primary keys always have the same name
  - except for pairwise sequence comparisons which use q_pseq_id and t_pseq_id
- `psX` – protein sequence property
  - e.g., psprotcomp
- `pfX` – protein feature
  - e.g., pfsignalpnn
- `paX` and `pmX` – protein alignments to models
  - e.g., pmhmm and pahmm

View Name Suffixes

- `_mv` – materialized view
- `_dv` – “defining view”
  - mostly for internal use
  - not optimized, often slow
  - look for a corresponding `_mv`
- `_cv` – “canned view”
  - views for complex data mining
  - exposed to public
  - see canned_views table
- `_v` – ye olde standard view

Accessing Unison

- How:
  - native protocol
  - *psql interactive shell (akin to sqlplus)*
  - perl DBI
  - *perl API*
  - ODBC/JDBC
  - *web pages (and linking to them)*
  - *command line tools*
  - Oracle snapshot in biodev1 and bioprd1
- Details:
  - host `csb`
  - database `csb` or `csb-dev`
  - as self with Kerberos (user `PUBLIC`, no password is deprecated)

☞ *Use Kerberos authentication wherever possible. Be prepared to change logins which use `PUBLIC`.*

Web Page Linking

- http://csb/unison/cgi/pseq_summary.pl?q=<query>
  - query may be pseq_id, alias, md5, or sequence itself
  - all links use GET method (*i.e.*, params in URL)
- Sequence analysis pages
  - summary page
  - aliases
  - patents
  - protein features
  - protein structure and variant mapping
  - HomoloGene homologs
  - pmap and blat genome maps
- Other pages
  - feature-based mining
  - browse “canned views”

unison-get-seq

- Fetch sequences by pseq_id or alias, from stdin or args
- Useful flags:
  - `-A` select by alias
  - `-b` “best alias” in defline
  - `-B` “best annotation” in deflne
  - `-u` Unison:pseq_id in defline (-bu may be used together)
  - `--iupac20` select only sequences with standard AA
  - `-v` verbose – prints progress to stderr
- Example:
  - `kinit`
  - `unison-get-seq -Abu TNFA_HUMAN`

```
>Unison:98 UniProtKB/Swiss-Prot:TNFA_HUMAN (Tumor necrosis factor precursor (TNF-alpha)
   (Tumor necrosis factor ligand superfamily member 2) (TNF-a) (Cachectin))
MSTESMIRDVELAEEALPKKTGGPQGSRRCLFLSLFSFLIVAGATTLFCLLHFGVIGPQR
EEFPRDLSLISPLAQAVRSSSRTPSDKPVAHVVANPQAEGQLQWLNRRANALLANGVELR
DNQLVVPSEGLYLIYSQVLFKGQGCPSTHVLLTHTISRIAVSYQTKVNLLSAIKSPCQRE
TPEGAEAKPWYEPIYLGGVFQLEKGDRLSAEINRPDYLDFAESGQVYFGIIAL
```

unison-annotation

- Provides features and other information for sequences specified by pseq_id, alias, or fasta

```
$ unison-annotation -S <myseqs.fa
*Unison:98:UniProtKB/Swiss-Prot:TNFA_HUMAN (Tumor necrosis fac...
*signalp (SignalP 3.0 (euk), ran on 2005-11-03 16:40)

*tm (TMHMM 2.0c, ran on 2005-11-16 14:05)
#start stop
35  57

*regexp (regexp, ran on 2005-11-16 11:26)
#start stop   feature
133 138 ITIM

*pfam (Pfam 19.0 ls, ran on 2006-01-13 21:30)
#start stop   score  eval   acc feature   descr
102 233 210 4.8e-60   PF00229.8  TNF TNF(Tumour Necrosis Factor) family

*protcomp (protcomp default, ran on 2005-08-10 05:40)
#loc
Plasma membrane

*alia#alias  origin  descr
NP_000585       RefSeq  tumor necrosis factor alpha [Homo sapiens].
PRO34403        GenenGenes      Human TNF-a
PRO21907        GenenGenes      Human TNF-a
PRO6    GenenGenes      Human TNF-a
IPI00001671.1   IPI     Tumor necrosis factor precursor; SWISS-PROT:P01375|
...
```

Unison perl API

- Unison perl modeule
  - acts like a subclass of DBI
  - adds many utility methods
  - is stable but homely
- The module is available to all users of `/usr/local/tools/bin/perl` by default
- more info:
  - `perldoc Unison`
  - `/gne/research/apps/unison/examples/`

```
use Unison;
my $u = new Unison;
my $q = $u->pseq_id_by_sequence('YGGFM');
my $np = $u->selectrow_array(<<EOSQL,undef,$q);
  SELECT count(*) FROM patents_v WHERE pseq_id=?
EOSQL
print(“$q\t$np\t”, $u->best_annotation($q), “\n”);
my $sth = $u->prepare('select * from run_history_v where pseq_id=?');
$sth->execute($q);
$sth->dump_results();
```

psql

PostgreSQL's command-line interface

psql intro

- Do this:
  - `kinit`
  - `psql -h csb -d csb`
- The most important commands
  - `\?` – help
  - `\d+` [selection] – describe object
  - `\dv+` [selection] – view summary
  - `\dt+` [selection] – table summary
  - `\df+` [selection] – function summary
  - selection may be:
    - a table, view, or function name, optionally schema-qualified
      - e.g., pseq, unison.palias
    - a shell-style glob
  - `explain` [query]

Browsing Tables and Views

```
unison@csb=> \dt+ unison.
                                  List of relations
 Schema |                 Name                 | Type  | Owner  |          Description
--------+------------------------------------+-------+--------+-------------------------
 unison | _readme                              | table | unison | READ THIS FIRST -- Unison
 unison | best_annotation_mv                   | table | unison | materialized view of best
 unison | canned_views                         | table | unison | curated data mining views
 unison | ensembl_coordinates_mv               | table | unison |
 unison | ensembl_unambiguous_coordinates_mv   | table | unison |
 unison | ensembl_unambiguous_overlaps_mv      | table | unison |
 unison | genasm                               | table | unison | genome and assembly


unison@csb=> \dv+ unison.*pmap*
                                             List of relations
 Schema |               Name               | Type | Owner  |                    Description
--------+--------------------------------+------+--------+-------------------------------
 unison | pmap_aln_unambiguous_overlaps_v | view | unison |
 unison | pmap_aln_unambiguous_v          | view | unison |
 unison | pmap_v                          | view | unison | view of pmap alignments ...
```

Viewing a Table Definition

```
unison@csb=> \d+ pahmm
                                         Table "unison.pahmm"
   Column    |     |      Description
------------+-//--+---------------------------------------------------
 pfeature_id | //  | unique feature id
 pseq_id     | //  | unique protein sequence identifier -- see pseq(pseq_id)
 pftype_id   | //  | protein feature type identifier -- see pftype(pftype_id)
 start       | //  | start of prediction in protein sequence
 stop        | //  | stop of prediction in protein sequence
 params_id   | //  | parameter set identifier -- see params(params_id)
 pmodel_id   | //  | unique protein model identifier
 mstart      | //  | start of match /in model/
 mstop       | //  | stop of match /in model/
 ident       | //  |
 sim         | //  |
 gaps        | //  |
 qgaps       | //  | number of gaps in query sequence
 tgaps       | //  | number of gaps in target sequence
 score       | //  | algorithm-specific score
 eval        | //  | expectation value
 len         | //  |
Indexes:
    "pahmm_redundant_feature" UNIQUE, btree (pseq_id, "start", stop, pmodel_id,
params_id, mstart, mstop) CLUSTER
    "pahmm_search1" btree (pmodel_id, eval, params_id)
    "pahmm_search2" btree (params_id, eval, pmodel_id)
    "pahmm_search3" btree (params_id, score, pmodel_id)
Foreign-key constraints:
    "pahmm_params_id_exists" FOREIGN KEY (params_id) REFERENCES params(params_id) ON
UPDATE CASCADE ON DELETE CASCADE
```

Viewing a View Definition

```
unison@csb=> \d+ pmap_v
                                      View "unison.pmap_v"
   Column    |     Type     | Modifiers |                     Description
------------+--------------+-----------+----------------------------------------------------
 params_id  | integer      |           | parameter set identifier -- see params
 genasm_id  | integer      |           | genome assembly identifier -- see genasm
 pseq_id    | integer      |           | unique protein sequence identifier -- see pseq
 aln_id     | integer      |           | pmap_aln alignment identifier
 pstart     | integer      |           | start of alignment in protein sequence
 pstop      | integer      |           | stop of alignment in protein sequence
 exons      | bigint       |           | number of exons
 aln_length | bigint       |           | length of alignment
 pct_cov    | integer      |           | percent coverage
 ident      | integer      |           |
 pct_ident  | integer      |           | percent identity
 chr        | text         |           | chromosome
 strand     | character(1) |           | genomic strand ('+' or '-')
 gstart     | integer      |           | genomic start position on chromosome
 gstop      | integer      |           | genomic stop position on chromosome
View definition:
 SELECT a.params_id, a.genasm_id, h.pseq_id, ah.aln_id, min(h.pstart) AS pstart, ...
   FROM pmap_hsp h
   JOIN pmap_alnhsp ah ON h.hsp_id = ah.hsp_id
   JOIN pmap_aln a ON ah.aln_id = a.aln_id
   JOIN pseq q ON h.pseq_id = q.pseq_id
  GROUP BY a.params_id, a.genasm_id, h.pseq_id, ah.aln_id, h.chr, h.strand, ...
  ORDER BY h.pseq_id, (sum(h.pstop - h.pstart + 1)::double precision / ...
```

Reality Queries

(using psql,
but applies to all access modes)

Finding A Sequence

- By sequence
  - `select pseq_id_from_sequence('MYSEQ')`
- By md5
  - `select pseq_id from pseq where md5='f9e8d7...';`
- By alias
  - `select pseq_id from palias where alias='PRO54321'`
    - *or* `alias LIKE 'NP_00123%'`
    - *or* `alias ~ '^NP_0123'`
  - `AND porigin_id=porigin_id('RefSeq')`
  - `AND porigin_id=porigin_id('GenenGenes')`
  - `AND tax_id=gs2tax_id('BRARE')`
- By NCBI gene
  - `select pseq_id from palias where porigin_id=porigin_id('RefSeq gi') and alias=73967277;`

Finding Parameters

- select params_id,name,descr from params;

```
 params_id |             name              |             descr              |          commandline
-----------+-------------------------------+--------------------------------+------------------------------
        19 | BIG-PI default                | BIG-PI GPI prediction; http:// | bigpi metazoa %s short
         3 | BLAST                         | UNSUPPORTED! Unison internal u | blastall -FF -z2829482 -p blas
        36 | Bcl-2 ls                      | Bcl-2 homology domains custom  | ldhmmpfam --acc -E10 -Z8183
         4 | EMBOSS/antigenic              | antigenicity predictions; http | antigenic -minlen 6 -rformat s
        37 | EMBOSS/pepcoil                | EMBOSS pepcoil coiled-coil pre | pepcoil -noother -window 28 -f
         5 | EMBOSS/sigcleave              | signal cleavage prediction; ht | sigcleave -minweight 3.5 -rfor
        11 | Genome BLAT                   | genomic localization of protei | gfClient -t=dnax -q=prot trp 1
        38 | PMAP 2006-03-20               | genomic localization of protei | pmap.2006-03-20 -d NHGD_R35 -B
         8 | PSSM default                  |                                |
        33 | Pfam 19.0 fs                  | Pfam 19.0 /f/ragmentary models | ldhmmpfam --acc -E10 -Z8183
        34 | Pfam 19.0 ls                  | Pfam 19.0 local models         | ldhmmpfam --acc -E10 -Z8183
        14 | Prospect2 SCOP default        | Prospect protein threading; ht | -scop
         1 | Prospect2 default             | Prospect protein threading; ht | -global
         2 | Prospect2 global_local        | Prospect protein threading; ht | -global_local
        23 | Prospect2 ssp_psipred default | Prospect protein threading; ht | -global
        17 | Psipred v2.45                 | PSIPRED secondary structure pr | runpsipred -j 3 -h 0.001 -a 2
        28 | SignalP 3.0 (euk)             | Signal sequence prediction per | /gne/compbio/i686-linux-2.6/bi
        29 | TMHMM 2.0c                    | TMHMM 2.0c, http://www.cbs.dtu | /gne/compbio/i686-linux-2.6/op
        41 | dispro                        | http://www.ics.uci.edu/~baldig | MANUAL
        39 | disprot VL3H                  | disprot protein disorder predi | MANUAL: temple-disprot.pl
        31 | gne_prospect                  | Prospect protein threading; ht | gne_prospect -a 2 -p -b
         0 | no args                       |                                |
        20 | protcomp default              | ProtComp protein localization  | protcomp
        12 | regexp                        |                                |
         9 | tmdetect default              | Genentech in-house TM detectio | tmdetect
```

- commandline in params
- Consider using:
  - `select params_id('Pfam 19.0 ls')`
  - `select preferred_params_id_by_pftype('HMM')`

What's Been Run?

- Always consult `run_history_v` to see whether Unison contains the results you seek.

```
unison@csb=> select * from run_history_v where pseq_id=76;
 pseq_id | params_id |       params        | // |      ran_on      | failed
---------+-----------+---------------------+-//-+------------------+--------
      76 |        19 | BIG-PI default      | // | 2005-02-06 01:50 | f
      76 |         3 | BLAST               | // | 2003-08-18 14:36 | f
      76 |        36 | Bcl-2 ls            | // | 2006-02-01 19:50 | f
      76 |         4 | EMBOSS/antigenic    | // | 2003-10-07 20:56 | f
      76 |        37 | EMBOSS/pepcoil      | // | 2006-05-03 18:37 | f
      76 |         5 | EMBOSS/sigcleave    | // | 2003-10-13 16:30 | f
      76 |        11 | Genome BLAT         | // | 2004-02-11 10:48 | f
      76 |        38 | PMAP 2006-03-20     | // | 2006-03-23 14:53 | f
      76 |        33 | Pfam 19.0 fs        | // | 2006-01-12 03:05 | f
      76 |        34 | Pfam 19.0 ls        | // | 2006-01-13 21:20 | f
      76 |         1 | Prospect2 default   | // | 2004-02-25 15:14 | f
      76 |         1 | Prospect2 default   | // | 2004-02-20 08:03 | f
      76 |        17 | Psipred v2.45       | // | 2005-06-11 07:51 | f
      76 |        28 | SignalP 3.0 (euk)   | // | 2005-11-03 16:22 | f
      76 |        29 | TMHMM 2.0c          | // | 2005-11-16 08:34 | f
      76 |        41 | dispro              | // | 2006-05-04 22:42 | f
      76 |        39 | disprot VL3H        | // | 2006-05-04 17:42 | f
      76 |        20 | protcomp default    | // | 2005-08-10 03:11 | f
      76 |        12 | regexp              | // | 2005-11-16 11:26 | f
      76 |        12 | regexp              | // | 2006-04-13 04:47 | f
      76 |         9 | tmdetect default    | // | 2006-02-21 17:38 | f
```

Fetching Pfam Domains

- The hard way
-

```
unison@csb-dev=> SELECT A.pseq_id,M.name,M.acc,A.eval,A.score,M.descr
FROM pahmm A
JOIN pmhmm M on A.pmodel_id=M.pmodel_id
WHERE A.params_id=34 AND A.eval<1e-10 AND pseq_id=15;

 pseq_id |  name   |    acc    |  eval   | score |                  descr
---------+---------+-----------+---------+-------+--------------------------------------
      15 | Insulin | PF00049.8 |   6e-23 |    86 | Insulin/IGF/Relaxin family
      15 | IGF2_C  | PF08365.1 | 2.2e-35 |   128 | Insulin-like growth factor II E-
(2 rows)

Time: 1.900 ms
```

Fetching Pfam Domains 2

- A better way
  - use the pahmm_v view
  - for queries you want to rerun, use preferred_params_id_by_pftype

```
unison@csb-dev=> SELECT pseq_id,name,acc,eval,score,descr
 FROM pahmm_v
 WHERE params_id=preferred_params_id_by_pftype('HMM') AND eval<1e-10 AND pseq_id=15;
 pseq_id |  name    |    acc     |  eval    | score | ends |              descr
---------+---------+-----------+---------+-------+------+------------------------------
      15 | IGF2_C  | PF08365.1 | 2.2e-35 |   128 |   [] | Insulin-like growth factor...
      15 | Insulin | PF00049.8 |   6e-23 |    86 |   [] | Insulin/IGF/Relaxin family...
(2 rows)

Time: 2.574 ms
```

Fetching "All" Features

- pseq_features_v provides *current* results for *common* feature

```
unison@csb-dev=> SELECT feature,start,stop,score,eval,descr FROM pseq_features_v WHERE
pseq_id=82;
 feature | start | stop | score |  eval   |                   descr
---------+-------+------+-------+---------+------------------------------------------
 SS      |     1 |   31 | 0.884 |         | signal sequence
 TM      |     7 |   29 |       |         | transmembrane domain
 PAN_1   |    34 |  124 |    64 | 3.9e-16 | PAN domain
 Kringle |   128 |  206 |   178 |   2e-50 | Kringle domain
 Kringle |   211 |  288 |   178 | 1.6e-50 | Kringle domain
 Kringle |   305 |  383 |   181 |   2e-51 | Kringle domain
 Kringle |   391 |  469 |   155 | 1.3e-43 | Kringle domain
 Trypsin |   495 |  716 |   223 | 4.3e-64 | Trypsin
 Y-ITIM  |   619 |  628 |       |         | ITIM motif with second upstream Y; more ...
 ITIM    |   623 |  628 |       |         | Immunotyrosine Inhibition Motif
(10 rows)

Time: 8.624 ms
```

Wrap Up

Dos and Don'ts

(Not *"Dos and Donuts"*)

- Do
  - specify params_id in all queries for results.
  - consult the run_history_v view, especially when your query returns no results.
  - use the helper functions params_id, params_id_by_pftype, porigin_id, etc.
  - experiment with Unison.
  - provide feedback and suggestions.

- Don't
  - hesitate to ask questions.
  - rely on PUBLIC user.

Developer Resources

- Unison
  - http://csb/unison/tour/
  - /gne/research/apps/unison/examples/
  - `perldoc Unison`
- PostgreSQL
  - psql \d commands
  - http://www.postgresql.org/docs/
- cvs -d :ext:csb/srv/cvs unison
  - contains code examples
- cvs -d :ext:csb/srv/cvs unison-web

The Future

- Kiran will assume a greater role for Unison
  - nearly all data loading and maintenance
  - user help
  - API maintenance
  - Oracle data pushes
- I will continue to be involved in
  - mining efforts using Unison
  - added new data types
  - schema, API, and web oversight

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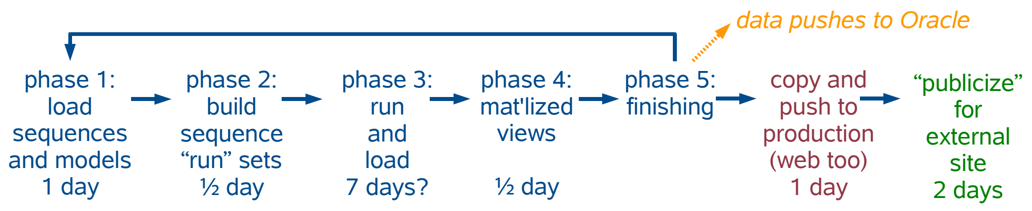
  - 14GB of compressed data, 130GB on disk w/indexes

Update Procedure and Run Sets


data pushes to Oracle
phase 1: load sequences and models 1 day
phase 2: build sequence “run” sets ½ day
phase 3: run and load 7 days?
phase 4: mat'lized views ½ day
phase 5: finishing
copy and push to production (web too) 1 day
“publicize” for external site 2 days

Set	Criteria	Algorithms
runA	human 100-1000 AA reliable origins	prospect antigenic BLAST†
runB	human, mouse, rat 100-1500 AA reliable origins	Pfam (fs & ls) BIG-PI RegExp PSIPRED
runC	human, mouse, rat, cow, zebrafish 100-3000 AA all sequence sources	pepcoil SignalP TMHMM antigenic pmap protcomp
	ad hoc	disprot† dispro†

† these methods are currently unsupported

Implementation

- Hardware
  - hostname `csb`
  - 4 dual-core Opterons, 2.4 GHz
  - 32GB RAM
  - 500GB FC-RAID
- Linux
  - SuSE 10.0, kernel 2.6
- PostgreSQL 8.1.3
  - 3 databases: `csb`, `csb-stage`, `csb-dev`
  - unison is a schema within each
- Perl 5.8
- Apache 2.0 web pages

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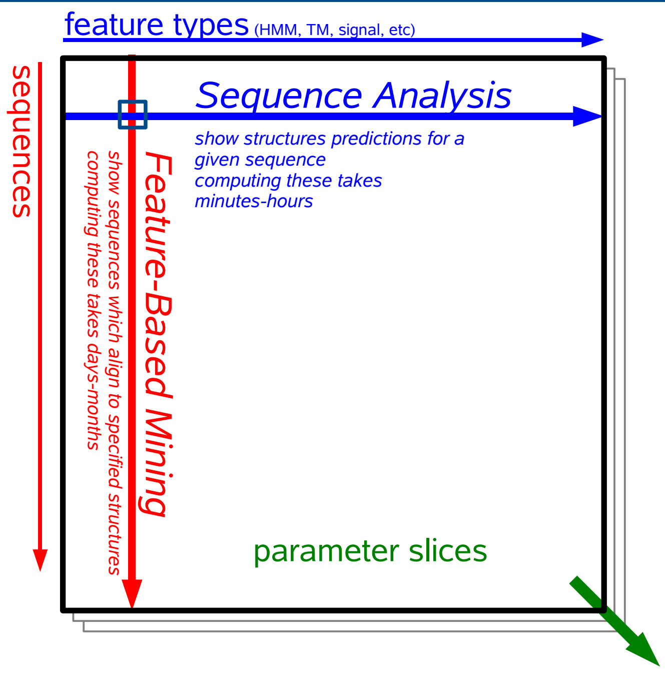
Unison Schema

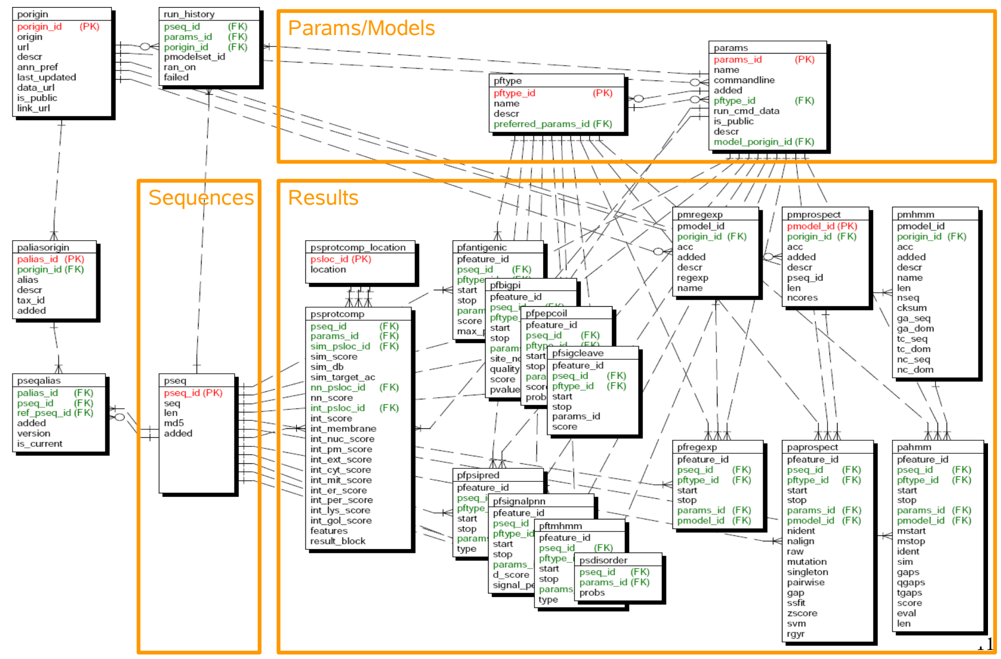
Design Themes

- Abstraction and Normalization
  - most tables are essentially data types
  - expect a lot of joins, but views exist for common queries
  - facilitates updates of new params, etc
- Rely on database for correctness
  - pedantic and paranoid use of triggers and constraints
- Selective incorporation of external databases
  - schemas: unison, ncbi, tax, dali, go, pdb

Results Cube


feature types (HMM, TM, signal, etc)
sequences
Sequence Analysis
show structures predictions for a given sequence
computing these takes minutes-hours
Feature-Based Mining
show sequences which align to specified structures
computing these takes days-months
parameter slices

Schema Overview



Critical Tables, Views, Functions

- Tables and views
  - porigin, pseq, pftype, params
  - palias (view) and current_annotations_v
  - pahmm + pmhmm => pahmm_v
  - pfbigpi => pfbigpi_v
  - pfsignalpnn
  - psprotcomp + psprotcomp_locations => psprotcomp_v
  - pfregexp + pmregexp => pfregexp_v
  - run_history => run_history_v
- Functions
  - pseq_id_from_sequence()
  - params_id() and preferred_params_id_by_pftype()
  - porigin_id()

Table and Column Names

- `X_id` is always a primary or foreign key
  - foreign and primary keys always have the same name
  - except for pairwise sequence comparisons which use q_pseq_id and t_pseq_id
- `psX` – protein sequence property
  - e.g., psprotcomp
- `pfX` – protein feature
  - e.g., pfsignalpnn
- `paX` and `pmX` – protein alignments to models
  - e.g., pmhmm and pahmm

View Name Suffixes

- `_mv` – materialized view
- `_dv` – "defining view"
  - mostly for internal use
  - not optimized, often slow
  - look for a corresponding `_mv`
- `_cv` – "canned view"
  - views for complex data mining
  - exposed to public
  - see canned_views table
- `_v` – ye olde standard view

Accessing Unison

- How:
  - native protocol
  - *psql interactive shell (akin to sqlplus)*
  - perl DBI
  - *perl API*
  - ODBC/JDBC
  - *web pages (and linking to them)*
  - *command line tools*
  - Oracle snapshot in biodev1 and bioprd1
- Details:
  - host `csb`
  - database `csb` or `csb-dev`
  - as self with Kerberos (user `PUBLIC`, no password is deprecated)

☞ *Use Kerberos authentication wherever possible. Be prepared to change logins which use `PUBLIC`.*

Web Page Linking

- http://csb/unison/cgi/pseq_summary.pl?q=<query>
  - query may be pseq_id, alias, md5, or sequence itself
  - all links use GET method (*i.e.*, params in URL)
- Sequence analysis pages
  - summary page
  - aliases
  - patents
  - protein features
  - protein structure and variant mapping
  - HomoloGene homologs
  - pmap and blat genome maps
- Other pages
  - feature-based mining
  - browse “canned views”

unison-get-seq

- Fetch sequences by pseq_id or alias, from stdin or args
- Useful flags:
  - `-A` select by alias
  - `-b` “best alias” in defline
  - `-B` “best annotation” in deflne
  - `-u` Unison:pseq_id in defline (-bu may be used together)
  - `--iupac20` select only sequences with standard AA
  - `-v` verbose – prints progress to stderr
- Example:
  - `kinit`
  - `unison-get-seq -Abu TNFA_HUMAN`

```
>Unison:98 UniProtKB/Swiss-Prot:TNFA_HUMAN (Tumor necrosis factor precursor (TNF-alpha)
   (Tumor necrosis factor ligand superfamily member 2) (TNF-a) (Cachectin))
MSTESMIRDVELAEEALPKKTGGPQGSRRCLFLSLFSFLIVAGATTLFCLLHFGVIGPQR
EEFPRDLSLISPLAQAVRSSSRTPSDKPVAHVVANPQAEGQLQWLNRRANALLANGVELR
DNQLVVPSEGLYLIYSQVLFKGQGCPSTHVLLTHTISRIAVSYQTKVNLLSAIKSPCQRE
TPEGAEAKPWYEPIYLGGVFQLEKGDRLSAEINRPDYLDFAESGQVYFGIIAL
```

unison-annotation

- Provides features and other information for sequences specified by pseq_id, alias, or fasta

```
$ unison-annotation -S <myseqs.fa
*Unison:98:UniProtKB/Swiss-Prot:TNFA_HUMAN (Tumor necrosis fac...
*signalp (SignalP 3.0 (euk), ran on 2005-11-03 16:40)

*tm (TMHMM 2.0c, ran on 2005-11-16 14:05)
#start stop
35  57

*regexp (regexp, ran on 2005-11-16 11:26)
#start stop   feature
133 138 ITIM

*pfam (Pfam 19.0 ls, ran on 2006-01-13 21:30)
#start stop   score  eval   acc feature   descr
102 233 210 4.8e-60   PF00229.8  TNF TNF(Tumour Necrosis Factor) family

*protcomp (protcomp default, ran on 2005-08-10 05:40)
#loc
Plasma membrane

*alia#alias  origin  descr
NP_000585       RefSeq  tumor necrosis factor alpha [Homo sapiens].
PRO34403        GenenGenes      Human TNF-a
PRO21907        GenenGenes      Human TNF-a
PRO6    GenenGenes      Human TNF-a
IPI00001671.1   IPI     Tumor necrosis factor precursor; SWISS-PROT:P01375|
...
```

- Provides features and other information for sequences specified by pseq_id, alias, or fasta
- unison-annotation <myseqs.fa
- *Unison:98:UniProtKB/Swiss-Prot:TNFA_HUMAN (Tumor necrosis factor precursor (TNF-alpha) (Tumor necrosis factor ligand superfamily member 2) (TNF-a) (Cachectin) [Contains: Tumor necrosis factor, membrane form; Tumor necrosis factor, soluble form])
- *signalp (SignalP 3.0 (euk), ran on 2005-11-03 16:40)
-
- *tm (TMHMM 2.0c, ran on 2005-11-16 14:05)
- #start stop
- 35   57
-
- *regexp (regexp, ran on 2005-11-16 11:26)
- #start stop   feature
- 133   138   ITIM
-

Unison perl API

- Unison perl modeule
  - acts like a subclass of DBI
  - adds many utility methods
  - is stable but homely
- The module is available to all users of `/usr/local/tools/bin/perl` by default
- more info:
  - `perldoc Unison`
  - `/gne/research/apps/unison/examples/`

```
use Unison;
my $u = new Unison;
my $q = $u->pseq_id_by_sequence('YGGFM');
my $np = $u->selectrow_array(<<EOSQL,undef,$q);
  SELECT count(*) FROM patents_v WHERE pseq_id=?
EOSQL
print("$q\t$np\t", $u->best_annotation($q), "\n");
my $sth = $u->prepare('select * from run_history_v where pseq_id=?');
$sth->execute($q);
$sth->dump_results();
```

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psql

PostgreSQL's command-line interface

psql intro

- Do this:
  - `kinit`
  - `psql -h csb -d csb`
- The most important commands
  - `\?` – help
  - `\d+` [selection] – describe object
  - `\dv+` [selection] – view summary
  - `\dt+` [selection] – table summary
  - `\df+` [selection] – function summary
  - selection may be:
    - a table, view, or function name, optionally schema-qualified
      - e.g., pseq, unison.palias
    - a shell-style glob
  - `explain` [query]

Browsing Tables and Views

```
unison@csb=> \dt+ unison.
                                  List of relations
 Schema |                Name                | Type  | Owner  |          Description
--------+------------------------------------+-------+--------+--------------------------
 unison | _readme                            | table | unison | READ THIS FIRST -- Unison
 unison | best_annotation_mv                 | table | unison | materialized view of best
 unison | canned_views                       | table | unison | curated data mining views
 unison | ensembl_coordinates_mv             | table | unison |
 unison | ensembl_unambiguous_coordinates_mv | table | unison |
 unison | ensembl_unambiguous_overlaps_mv    | table | unison |
 unison | genasm                             | table | unison | genome and assembly


unison@csb=> \dv+ unison.*pmap*
                                               List of relations
 Schema |              Name               | Type | Owner  |                  Description
--------+---------------------------------+------+--------+------------------------------
 unison | pmap_aln_unambiguous_overlaps_v | view | unison |
 unison | pmap_aln_unambiguous_v          | view | unison |
 unison | pmap_v                          | view | unison | view of pmap alignments ...
```

Viewing a Table Definition

```
unison@csb=> \d+ pahmm
                                        Table "unison.pahmm"
   Column    |     |      Description
-------------+-//--+-----------------------------------------------------------
 pfeature_id | //  | unique feature id
 pseq_id     | //  | unique protein sequence identifier -- see pseq(pseq_id)
 pftype_id   | //  | protein feature type identifier -- see pftype(pftype_id)
 start       | //  | start of prediction in protein sequence
 stop        | //  | stop of prediction in protein sequence
 params_id   | //  | parameter set identifier -- see params(params_id)
 pmodel_id   | //  | unique protein model identifier
 mstart      | //  | start of match /in model/
 mstop       | //  | stop of match /in model/
 ident       | //  |
 sim         | //  |
 gaps        | //  |
 qgaps       | //  | number of gaps in query sequence
 tgaps       | //  | number of gaps in target sequence
 score       | //  | algorithm-specific score
 eval        | //  | expectation value
 len         | //  |
Indexes:
    "pahmm_redundant_feature" UNIQUE, btree (pseq_id, "start", stop, pmodel_id,
params_id, mstart, mstop) CLUSTER
    "pahmm_search1" btree (pmodel_id, eval, params_id)
    "pahmm_search2" btree (params_id, eval, pmodel_id)
    "pahmm_search3" btree (params_id, score, pmodel_id)
Foreign-key constraints:
    "pahmm_params_id_exists" FOREIGN KEY (params_id) REFERENCES params(params_id) ON
UPDATE CASCADE ON DELETE CASCADE
```

Viewing a View Definition

```
unison@csb=> \d+ pmap_v
                                      View "unison.pmap_v"
   Column   |     Type     | Modifiers |                    Description
------------+--------------+-----------+------------------------------------------------
 params_id  | integer      |           | parameter set identifier -- see params
 genasm_id  | integer      |           | genome assembly identifier -- see genasm
 pseq_id    | integer      |           | unique protein sequence identifier -- see pseq
 aln_id     | integer      |           | pmap_aln alignment identifier
 pstart     | integer      |           | start of alignment in protein sequence
 pstop      | integer      |           | stop of alignment in protein sequence
 exons      | bigint       |           | number of exons
 aln_length | bigint       |           | length of alignment
 pct_cov    | integer      |           | percent coverage
 ident      | integer      |           |
 pct_ident  | integer      |           | percent identity
 chr        | text         |           | chromosome
 strand     | character(1) |           | genomic strand ('+' or '-')
 gstart     | integer      |           | genomic start position on chromosome
 gstop      | integer      |           | genomic stop position on chromosome
View definition:
 SELECT a.params_id, a.genasm_id, h.pseq_id, ah.aln_id, min(h.pstart) AS pstart, ...
   FROM pmap_hsp h
   JOIN pmap_alnhsp ah ON h.hsp_id = ah.hsp_id
   JOIN pmap_aln a ON ah.aln_id = a.aln_id
   JOIN pseq q ON h.pseq_id = q.pseq_id
  GROUP BY a.params_id, a.genasm_id, h.pseq_id, ah.aln_id, h.chr, h.strand, ...
  ORDER BY h.pseq_id, (sum(h.pstop - h.pstart + 1)::double precision / ...
```

Reality Queries

(using psql,
but applies to all access modes)

Finding A Sequence

- By sequence
  - `select pseq_id_from_sequence('MYSEQ')`
- By md5
  - `select pseq_id from pseq where md5='f9e8d7...';`
- By alias
  - `select pseq_id from palias where alias='PRO54321'`
    - *or* `alias LIKE 'NP_00123%'`
    - *or* `alias ~ '^NP_0123'`
  - `AND porigin_id=porigin_id('RefSeq')`
  - `AND porigin_id=porigin_id('GenenGenes')`
  - `AND tax_id=gs2tax_id('BRARE')`
- By NCBI gene
  - `select pseq_id from palias where porigin_id=porigin_id('RefSeq gi') and alias=73967277;`

Finding Parameters

- select params_id,name,descr from params;

```
 params_id |             name              |             descr              |          commandline
-----------+-------------------------------+--------------------------------+--------------------------------
        19 | BIG-PI default                | BIG-PI GPI prediction; http:// | bigpi metazoa %s short
         3 | BLAST                         | UNSUPPORTED! Unison internal u | blastall -FF -z2829482 -p blas
        36 | Bcl-2 ls                      | Bcl-2 homology domains custom  | ldhmmpfam --acc -E10 -Z8183
         4 | EMBOSS/antigenic              | antigenicity predictions; http | antigenic -minlen 6 -rformat s
        37 | EMBOSS/pepcoil                | EMBOSS pepcoil coiled-coil pre | pepcoil -noother -window 28 -f
         5 | EMBOSS/sigcleave              | signal cleavage prediction; ht | sigcleave -minweight 3.5 -rfor
        11 | Genome BLAT                   | genomic localization of protei | gfClient -t=dnax -q=prot trp 1
        38 | PMAP 2006-03-20               | genomic localization of protei | pmap.2006-03-20 -d NHGD_R35 -B
         8 | PSSM default                  |                                |
        33 | Pfam 19.0 fs                  | Pfam 19.0 /f/ragmentary models | ldhmmpfam --acc -E10 -Z8183
        34 | Pfam 19.0 ls                  | Pfam 19.0 local models         | ldhmmpfam --acc -E10 -Z8183
        14 | Prospect2 SCOP default        | Prospect protein threading; ht | -scop
         1 | Prospect2 default             | Prospect protein threading; ht | -global
         2 | Prospect2 global_local        | Prospect protein threading; ht | -global_local
        23 | Prospect2 ssp_psipred default | Prospect protein threading; ht | -global
        17 | Psipred v2.45                 | PSIPRED secondary structure pr | runpsipred -j 3 -h 0.001 -a 2
        28 | SignalP 3.0 (euk)             | Signal sequence prediction per | /gne/compbio/i686-linux-2.6/bi
        29 | TMHMM 2.0c                    | TMHMM 2.0c, http://www.cbs.dtu | /gne/compbio/i686-linux-2.6/op
        41 | dispro                        | http://www.ics.uci.edu/~baldig | MANUAL
        39 | disprot VL3H                  | disprot protein disorder predi | MANUAL: temple-disprot.pl
        31 | gne_prospect                  | Prospect protein threading; ht | gne_prospect -a 2 -p -b
         0 | no args                       |                                |
        20 | protcomp default              | ProtComp protein localization  | protcomp
        12 | regexp                        |                                |
         9 | tmdetect default              | Genentech in-house TM detectio | tmdetect
```

- commandline in params
- Consider using:
  - `select params_id('Pfam 19.0 ls')`
  - `select preferred_params_id_by_pftype('HMM')`

What's Been Run?

- Always consult `run_history_v` to see whether Unison contains the results you seek.

```
unison@csb=> select * from run_history_v where pseq_id=76;
 pseq_id | params_id |       params       | // |      ran_on      | failed
---------+-----------+--------------------+-//-+------------------+--------
      76 |        19 | BIG-PI default     | // | 2005-02-06 01:50 | f
      76 |         3 | BLAST              | // | 2003-08-18 14:36 | f
      76 |        36 | Bcl-2 ls           | // | 2006-02-01 19:50 | f
      76 |         4 | EMBOSS/antigenic   | // | 2003-10-07 20:56 | f
      76 |        37 | EMBOSS/pepcoil     | // | 2006-05-03 18:37 | f
      76 |         5 | EMBOSS/sigcleave   | // | 2003-10-13 16:30 | f
      76 |        11 | Genome BLAT        | // | 2004-02-11 10:48 | f
      76 |        38 | PMAP 2006-03-20    | // | 2006-03-23 14:53 | f
      76 |        33 | Pfam 19.0 fs       | // | 2006-01-12 03:05 | f
      76 |        34 | Pfam 19.0 ls       | // | 2006-01-13 21:20 | f
      76 |         1 | Prospect2 default  | // | 2004-02-25 15:14 | f
      76 |         1 | Prospect2 default  | // | 2004-02-20 08:03 | f
      76 |        17 | Psipred v2.45      | // | 2005-06-11 07:51 | f
      76 |        28 | SignalP 3.0 (euk)  | // | 2005-11-03 16:22 | f
      76 |        29 | TMHMM 2.0c         | // | 2005-11-16 08:34 | f
      76 |        41 | dispro             | // | 2006-05-04 22:42 | f
      76 |        39 | disprot VL3H       | // | 2006-05-04 17:42 | f
      76 |        20 | protcomp default   | // | 2005-08-10 03:11 | f
      76 |        12 | regexp             | // | 2005-11-16 11:26 | f
      76 |        12 | regexp             | // | 2006-04-13 04:47 | f
      76 |         9 | tmdetect default   | // | 2006-02-21 17:38 | f
```

Fetching Pfam Domains

- The hard way
-

```
unison@csb-dev=> SELECT A.pseq_id,M.name,M.acc,A.eval,A.score,M.descr
FROM pahmm A
JOIN pmhmm M on A.pmodel_id=M.pmodel_id
WHERE A.params_id=34 AND A.eval<1e-10 AND pseq_id=15;

 pseq_id |  name   |    acc    |  eval   | score |                  descr
---------+---------+-----------+---------+-------+-------------------------------------
      15 | Insulin | PF00049.8 |   6e-23 |    86 | Insulin/IGF/Relaxin family
      15 | IGF2_C  | PF08365.1 | 2.2e-35 |   128 | Insulin-like growth factor II E-
(2 rows)

Time: 1.900 ms
```

Fetching Pfam Domains 2

- A better way
  - use the pahmm_v view
  - for queries you want to rerun, use preferred_params_id_by_pftype

```
unison@csb-dev=> SELECT pseq_id,name,acc,eval,score,descr
 FROM pahmm_v
 WHERE params_id=preferred_params_id_by_pftype('HMM') AND eval<1e-10 AND pseq_id=15;
 pseq_id |  name   |    acc     |  eval    | score | ends |             descr
---------+---------+-----------+---------+-------+------+------------------------------
      15 | IGF2_C  | PF08365.1 | 2.2e-35 |   128 |   [] | Insulin-like growth factor...
      15 | Insulin | PF00049.8 |   6e-23 |    86 |   [] | Insulin/IGF/Relaxin family...
(2 rows)

Time: 2.574 ms
```

Fetching “All” Features

- pseq_features_v provides *current* results for *common* feature

```
unison@csb-dev=> SELECT feature,start,stop,score,eval,descr FROM pseq_features_v WHERE
pseq_id=82;
 feature | start | stop | score |  eval   |                    descr
---------+-------+------+-------+---------+---------------------------------------------
 SS      |     1 |   31 | 0.884 |         | signal sequence
 TM      |     7 |   29 |       |         | transmembrane domain
 PAN_1   |    34 |  124 |    64 | 3.9e-16 | PAN domain
 Kringle |   128 |  206 |   178 |   2e-50 | Kringle domain
 Kringle |   211 |  288 |   178 | 1.6e-50 | Kringle domain
 Kringle |   305 |  383 |   181 |   2e-51 | Kringle domain
 Kringle |   391 |  469 |   155 | 1.3e-43 | Kringle domain
 Trypsin |   495 |  716 |   223 | 4.3e-64 | Trypsin
 Y-ITIM  |   619 |  628 |       |         | ITIM motif with second upstream Y; more ...
 ITIM    |   623 |  628 |       |         | Immunotyrosine Inhibition Motif
(10 rows)

Time: 8.624 ms
```

Wrap Up

Dos and Don'ts

(Not *"Dos and Donuts"*)

- Do
  - specify params_id in all queries for results.
  - consult the run_history_v view, especially when your query returns no results.
  - use the helper functions params_id, params_id_by_pftype, porigin_id, etc.
  - experiment with Unison.
  - provide feedback and suggestions.

- Don't
  - hesitate to ask questions.
  - rely on PUBLIC user.

Developer Resources

- Unison
  - http://csb/unison/tour/
  - /gne/research/apps/unison/examples/
  - `perldoc Unison`
- PostgreSQL
  - psql \d commands
  - http://www.postgresql.org/docs/
- cvs -d :ext:csb/srv/cvs unison
  - contains code examples
- cvs -d :ext:csb/srv/cvs unison-web

The Future

- Kiran will assume a greater role for Unison
  - nearly all data loading and maintenance
  - user help
  - API maintenance
  - Oracle data pushes
- I will continue to be involved in
  - mining efforts using Unison
  - added new data types
  - schema, API, and web oversight