The Biopython Project: Philosophy, functionality and facts

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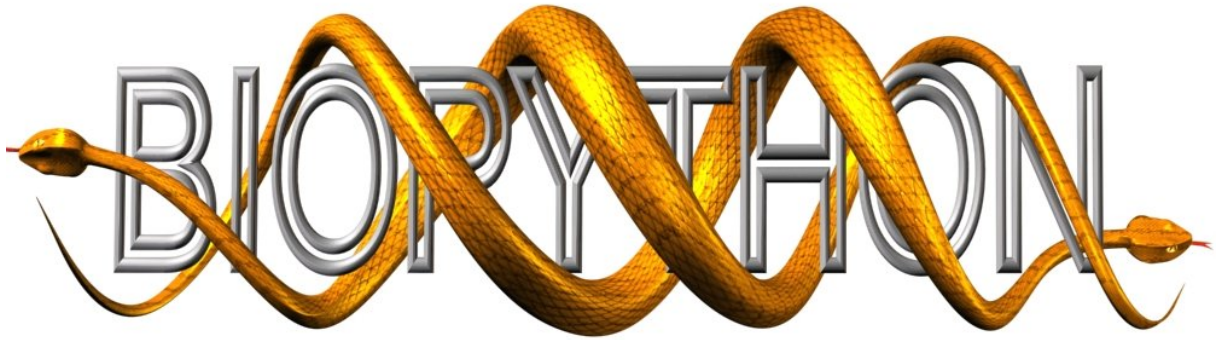
11 March 2004



Biopython – one minute overview

- The Biopython Project is an international association of developers of freely available Python tools for computational molecular biology.
  - History of Biopython
  - Organization and makeup of the Biopython community
  - What Biopython contains and why you'd want to use it
  - Detailed examples of Biopython, for use and development

- http://biopython.org

Who Am I?

- Molecular biologist who drifted to programming during graduate school
- Graduating in August of this year
- Starting programming in Python in 1999
- Starting doing Biopython work in 2000
- Coordinating the project since November of 2003

Biopython history

- Biopython began in August of 1999
  - The brainchild of Jeff Chang and Andrew Dalke
  - Significant push from Ewan Birney, of BioPerl and Ensembl fame
- February 2000 – started having CVS and project essentials (stop talking, start coding)
- July 2000 – First release
- March 2001 – First 1.00-type "semi-complete" release
- December 2002 – First "semi-stable" release

Biopython and the Open-Bio Foundation

- Open Bioinformatics Foundation
  - Non profit, volunteer run organization focused on supporting open source programming in bioinformatics.
  - Grew out of initial Bio-project – BioPerl
  - http://www.open-bio.org/
- Main things Open-Bio does:
  - Support annual Bioinformatics Open Source (BOSC) conferences
  - Organize "hackathon" events
  - Obtain and support hardware for projects

Biopython and other Bio* projects

- Basically a sibling project with BioPerl, BioJava and BioRuby
- Work together, both informally and during organized "hackathon" events
  - BioCORBA (now mostly defunct)
  - BioSQL – standard set of SQL for storing sequences plus annotations
  - File indexing – Flat-files (FASTA, GenBank, Swissprot. . .)
  - Retrieval from web databases
  - Managing access to biological resources

Biopython developer community

Founders – Andrew and Jeff; building framework of Biopython

Coordinator – currently me;

- Benevolent dictator style organization, like Python itself (except I'm not much of a dictator)
- Development handles switches in leadership roles

Module contributors

- Requiring specialized knowledge of an area
- Create and maintain; code, tests, documentation
- Recent examples – Clustering, Structural Bioinformatics, NMR data, Sequencing related files, Wise alignments

How many total users are there?

Web site views – Since May of 2003

- 15,020 unique IP views, 52,580 total
- About 51 unique views and 178 total views a day

Release downloads

Release	Date	Unique Downloads	Per Day
1.20	July 27, 2003	67	*67*
1.21	July 28, 2003	759	10.4
1.22	October 9, 2003	121	13.5
1.23	October 18, 2003	1114	9.2
1.24	February 16, 2004	347	15.3

Project organization – philosophy

Contributing

- Fairly relaxed attitude; whoever codes it wins
- Maintain some "standard" ways to develop parsers and iterators, as well as coding conventions; to ease use and bug fixing
- Just want generally good coding practices in modules

License

- Short and open as possible
- Basically, keep copyright (don't pretend it's yours) and we aren't responsible if it messes something up (cover ourselves)

Project organization – what we have

CVS

- Write access: 12 active developers with access
- Anonymous CVS access: `http://cvs.biopython.org`

Mailing Lists

- Active discussion list
- Development list (patches, attachments, arguing over code details. . .)

Documentation

- Long tutorial-style doc
- Docs for specific parts (installation, BioSQL, Cluster)
- On-line courses with Biopython content

Project organization – the code

Bugs

- On-line Bugzilla tracker plus quick-fixes from mailing list
- Bug assignment normally done by module owner or others with time

Releases

- No standard schedule
- Try to work from a stable CVS base to simplify the release cycle and encourage people to work directly from CVS

Tests

- Testing framework based on unittest from standard library

Required and useful libraries

Try to keep pre-install requirements to a minimum

Python – works with 2.2 and higher

mxTextTools – Fast text manipulation library; underlies parser framework

Numerical Python – fast array manipulation; used for Cluster code, PDB, NaiveBayes and Markov Model code

Database modules – either MySQLdb or psycopg; relational database storage and access

What does Biopython provide? – Sequence-based

Sequences themselves – Sequence classes, manipulations (translation, codon usage, melting temperature. . .)

Dealing with sequence formats – FASTA, GenBank, Swissprot, GFF

Parsers for output from bioinformatics programs – BLAST, Clustalw

Access to on-line resources – EUtils at NCBI, ExPASy, SCOP

Running bioinformatics programs – BLAST, Clustalw, EMBOSS

Alignments – Clustalw, Wise, NBRF/PIR

What does Biopython provide? – Others

Microarray data – Clustering, reading and writing Tree-View type files

Structure data – PDB parsing, representation and analysis

Structure calculation – NMR, predicting NOE coordinates, nmrview style files

Sequence data – Ace and PHD files

Journal data – Medline

What does Biopython provide? – Tools

Relational databases – BioSQL: standard amongst all open-bio projects SQL for storing sequences plus annotations

Parser development

- Martel: parser generator using mxTextTools
- ParserSupport: python-only based parser development using a Event/Consumer parsing model

File indexing – Mindy: flat-file indexing supported by all open-bio projects (flat-file only and BerkeleyDB)

Biopython usage example

Goal – Retrieve and store in a relational database GenBank records identified by BLAST searches of a given FASTA sequence

1. BLAST sequence against Swissprot database
2. Parse BLAST results, get hit IDs
3. Retrieve GenBank sequences from NCBI
4. Store in a relational database

Standard Biopython parser setup

Parsers

RecordParser – Parse a file into a format specific record object
FeatureParser – Parse into a generic class of sequence plus features

Iterator – Go over a file one record at a time

- Use any of the parser objects
- Also return raw text
- Works like both traditional and Python 2.2 iterators

FASTA sequence

```
>gi|42821112|ref|NP_006866.2| pim-2 oncogene;
MLTKPLQGPPAPPGTPTPPPGGKDREAFEAEYRLGPLLGKGGFGTVFAGHRLTDRLQVAIKVIPRNRVLG
WSPLSDSVTCPLEVALLWKVGAGGGHPGVIRLLDWFETQEGFMLVLERPLPAQDLFDYITEKGPLGEGPS
```

```
input_handle = open("input.fasta")

from Bio import Fasta
parser = Fasta.RecordParser()
iterator = Fasta.Iterator(input_handle, parser)
rec = iterator.next()
```

BLASTing FASTA

```
from Bio.Blast import NCBIWWW
results_handle = NCBIWWW.blast('blastp', 'swissprot',
                               str(rec), expect=1e-10)
```

- Do a remote BLAST against NCBI
- Calling `str` on a Fasta Record returns a nicely formatted Fasta sequence, for writing to files or printing
- Parser can be used on HTML results to retrieve IDs from the description lines

Parsing BLAST results

```
<HTML>
<b>BLASTP 2.2.8 [Jan-05-2004]</b>
<a href="http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&
   db=Protein&list_uids=20139243&dopt=GenPept" >
   gi|20139243|sp|Q9P1W9|PIM2_HUMAN</a>  Serine/threonine-protein k...
   <a href = #20139243>614</a>   e-176
```

```
blast_parser = NCBIWWW.BlastParser()
record = blast_parser.parse(results_handle)

swissprot_ids = []
for description in record.descriptions:
    swissprot_id = description.title.split("|")[1]
    swissprot_ids.append(swissprot_id)
```

Retrieving GenBank from NCBI

- Interface to the EUtils interface for batch retrieval of Entrez queries
- http://www.ncbi.nlm.nih.gov/entrez/query/static/eutils_help.html

```
from Bio.EUtils import DBIds
from Bio.EUtils import DBIdsClient

db_ids = DBIds("protein", swissprot_ids)
eutils_client = DBIdsClient.from_dbids(db_ids)
genbank_handle = eutils_client.efetch(retmode="text", rettype="gp")
```

Standard sequence objects

SeqRecord – main interface for sequences plus features

- **Seq** – a sequence object, acts like a string
  - **data** – the sequence itself (a string)
  - **alphabet** – a class describing the type of sequence and which letters are allowed in it
- **Id information** – id, name, description for the sequence
- **Annotations** – annotations about the whole sequence (organism, references. . .)
- **Features** – information about particular part of the sequence (exons, binding sites. . .)

Parsing GenBank into sequence objects

```
LOCUS       Q9P1W9                  311 aa            linear   PRI 15-SEP-2003
DEFINITION  Serine/threonine-protein kinase Pim-2 (Pim-2h).
ACCESSION   Q9P1W9
VERSION     Q9P1W9  GI:20139243
DBSOURCE    swissprot: locus PIM2_HUMAN, accession Q9P1W9;
```

```
from Bio import GenBank
parser = GenBank.FeatureParser()
iterator = GenBank.Iterator(genbank_handle, parser)
```

BioSQL

Standard set of SQL tables for storing sequences plus features and annotations

- Supported by all of the Bio projects (BioPerl, BioJava, BioRuby)
- Works on MySQL and Postgresql in Biopython
- Basic use case is to store something like a GenBank record, but extensible for individualized data
- Biopython interface which makes reading sequences exactly like dealing with a `SeqRecord` object
- Can also use raw SQL queries

Storing in a SQL database

```
> mysqladmin -u chapmanb -p create oncogene
> mysql -u chapmanb -p oncogene < biosqldb-mysql.sql
```

```
from BioSQL import BioSeqDatabase
server = BioSeqDatabase.open_database(driver = "MySQLdb", user = "chapmanb",
            passwd = "biopython", host = "localhost", db = "oncogene")
db = server.new_database("swissprot_hits")

db.load(iterator)
```

Final results

```
> mysql -u chapmanb -p oncogene
mysql> select accession, identifier, division, description from bioentry;
+----------+------------+----------+-----------------------------------+
| accession | identifier | division | description                       |
+----------+------------+----------+-----------------------------------+
| Q9P1W9    | 20139243   | PRI      | Serine/threonine-protein kinase Pim-2.
| Q62070    | 20138972   | ROD      | Serine/threonine-protein kinase Pim-2.
| Q86V86    | 38502964   | PRI      | Serine/threonine-protein kinase pim-3.
mysql> select length, seq from biosequence;
+--------+-----------------------------------+
| length | seq                               |
+--------+-----------------------------------+
|    311 |MLTKPLQGPPAPPGTPTPPPGGKDREAFEAEYRLGP
|    370 |MARATNLNAAPSAGASGPPDSLPSTLAPPSPGSPAA
|    326 |MLLSKFGSLAHLCGPGGVDHLPVKILQPAKADKESF
```

Useful Biopython development tools – parsing

Biopython also includes tools, in addition to ready to go code

- Martel – provides a basis for developing parsers
- Uses regular expression format definitions to make parsers
- Parses into XML which can be dealt with through a SAX interface
- Fast, uses mxTextTools C code for the work
- Provides standardized indexing of files, through Mindy

Building a parser with Martel – example

Goal – Parse output from BLAT; sequence search tool from Jim Kent

1. Build a Martel Regular Expression grammar to deal with BLAT psl-style files

2. Demonstrate how this file can be used to build a parser

3. Show XML based output of the parser

4. Describe utilities to simplify dealing with the XML output

BLAT simplified input

```
psLayout version 3

Q             Q      Q     T              T       T
name          start  end   name           start   end
-----------------------------------------------------
sequence_10   0      1775  sequence_12    10      1675
sequence_10   840    1244  sequence_13    940     1344
```

- Tab delimited hits – not the hardest to parse but nice for an example
- Many columns removed from normal BLAT psl output

Understanding Martel – basics

Provides a regular expressions on steroids interface for parsing

- Classes to match particular items, some examples:

  Str – match an exact string
  Spaces – match whitespace (not newlines) – `[\\t\\v\\f\\r ]+`
  Integer – digits with optional + or - sign – `[+-]?\d+`
  AnyEol – Match any type of newline: `\n`, `\r` or `\r\n`
  ToEol – Match the rest of a line including the newline

- Classes to repeat matches:

  Rep – Repeat 0 or more times
  Rep1 – Repeat 1 or more times
  RepN – Specify N times to repeat

Martel grammar – header

```
psLayout version 3

Q             Q      Q     T              T       T
name          start  end   name           start   end
-----------------------------------------------------
```

```
import Martel

title = Martel.Str("psLayout version") + Martel.Spaces() + \
        Martel.Integer("blat_version") + Martel.Rep(Martel.AnyEol())

header_lines = Martel.RepN(Martel.ToEol(), 3)
```

Understand Martel – more information

- Individual items of interest in a file are designated with names
  - Martel emits XML
  - These names will be the XML tags surrounding the information
- Can group different items together under a mega-group – like nested XML tags

```
<hit_line>
  <query_name>The Name</query_name>
</hit_line>
```

- Utilities to parse files with standard separators (tabs)

Martel grammar – hit lines

```
sequence_10  0      1775  sequence_12   10      1675
```

```
hit_line = Martel.Group("hit_line",
  # read the query information
  Martel.UntilSep("query_name", "\t") + Martel.Str("\t") +
  Martel.Integer("query_start") + Martel.ToSep(sep = "\t") +
  Martel.Integer("query_end") + Martel.ToSep(sep = "\t") +

  # read the target information
  Martel.UntilSep("target_name", "\t") + Martel.Str("\t") +
  Martel.Integer("target_start") + Martel.ToSep(sep = "\t") +
  Martel.Integer("target_end"))
```

Using Martel grammars

- All of the regular expressions combine together to create larger regular expressions which handle records in a file and the whole file

- We use standard tags (`Std`) for things which occur regularly in files
  - records
  - identifiers, descriptions, database cross references
  - sequences, alphabets
  - features
  - homology searches – headers, application names

Martel grammar – putting it all together

```
from Martel import RecordReader
from Bio import Std

record = Std.record(hit_line + Martel.AnyEol())

format = Martel.HeaderFooter("blat", {"format" : "blat"},
            title + header_lines, RecordReader.CountLines, (5,),
            record, RecordReader.CountLines, (1,),
            None, None, None)
```

- Can build formats in other ways

  StartsWith – Fasta Records >
  EndsWith – GenBank Records //

Using the parser – creating an iterator

```
import blat

input_handle = open("blat_ex.psl")
iterator_builder = blat.format.make_iterator("record")
```

- Standard Python 2.2 style iterator
- Since Martel emits XML – can connect different handlers to the iterator
  - `XMLGenerator` – just print out the XML
  - `LAX` – convert the XML to a dictionary
  - Custom handlers

Using the parser – XML output

```
from xml.sax import saxutils
handler = saxutils.XMLGenerator()
iterator = iterator_builder.iterateFile(input_handle, handler)
iterator.next()
```

```
<?xml version="1.0" encoding="iso-8859-1"?>
<record xmlns:bioformat="http://biopython.org/bioformat">
  <hit_line>
    <query_name>sequence_10</query_name>
    <query_start>0</query_start><query_end>1775</query_end>
    <target_name>sequence_12</target_name>
    <target_start>10</target_start><target_end>1675</target_end>
  </hit_line>
</record>
```

Using the parser – LAX handler

```
from Martel.LAX import LAX
handler = LAX(fields = ["query_name", "query_start", "query_end",
                        "target_name", "target_start", "target_end"])
iterator = iterator_builder.iterateFile(input_handle, handler)
for result in iterator:
    print result
```

```
{'target_name': ['sequence_12'], 'query_start': ['0'],
 'query_end': ['1775'],  'target_start': ['10'],
 'query_name': ['sequence_10'], 'target_end': ['1675']}

{'target_name': ['sequence_13'], 'query_start': ['840'],
 'query_end': ['1244'], 'target_start': ['940'],
 'query_name': ['sequence_10'], 'target_end': ['1344']}
```

Translating into a Biopython-style parser

- For something simpler like FASTA – use the LAX handler and write wrapper classes for Iterators and Parsers around it

- More complicated cases like GenBank
  - Derive from standard `xml.sax.handler` class
  - Helpful class in Biopython to turn Martel XML tags into Events (`EventGenerator`) so you can use an Event/Consumer framework for organizing the parser

Ease of developing parsers without starting from scratch

Future Biopython goals

- More modules; always more formats and programs to support
- Improved documentation; cookbook-style documentation
- Bug fixing – keeping up with changes to bioinformatics formats
- New/developmental items:
  - Standardized mechanism for running applications
  - Standardized access to bioinformatics resources
  - More reliance on Martel for parsing – conversions between formats