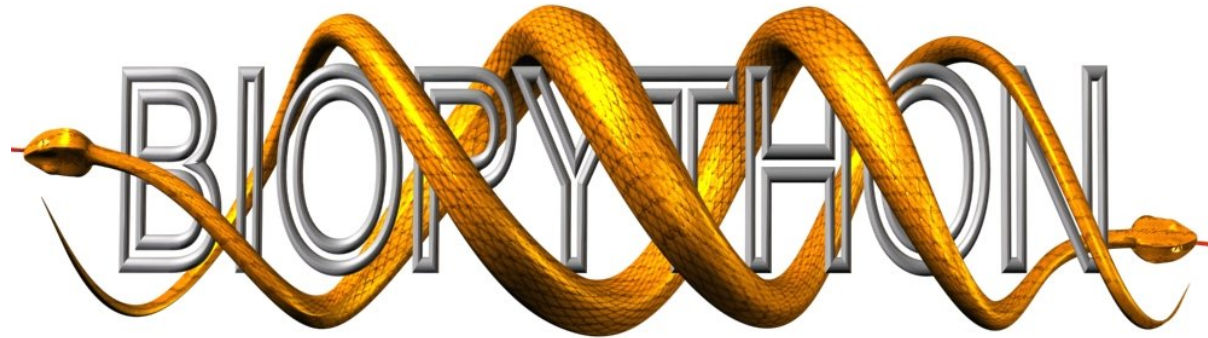


# The Biopython Project: Philosophy, functionality and facts

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## 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 pycopg; 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** – EUtills 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;  
MLTKPLQGPPAPPGTPTPPPGGKDREAFAEYRLGPLLGKGGFGTVFAGHRLTDRLQVAIKVIPRNRVLG  
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](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 < biosqlldb-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    | MLTKPLQGPPAPPGTPTPPPGGKDREAFAEYRLGP  |
| 370    | MARATNLNAAPSAGASGPPDSLPSTLAPPSPGSPAA |
| 326    | MLLSKFGSLAHLCPGGVDHLPVKILQPAKADKESF  |



## 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

