Lua for Molecular Biology

Yutaka Ueno

Neuroscience,

AIST Tsukuba, Japan

Lua is good in Molecular biology for:

1. programming tasks
2. database management tasks
3. development of algorithms

Current Projects

1. sequence annotation
2. molecular simulation
3. image processing

Processing Sequence Annotation Data using the Lua Programming Language

Yutaka Ueno, Masanori Arita, Toshitaka Kumagai, Kiyoshi Asai

Computational Biology Research Center (CBRC) AIST

Genome Informatics 14 (2003) 164-175.

`http://www.jsbi.org/journal/GIW03/GIW03F016.html`

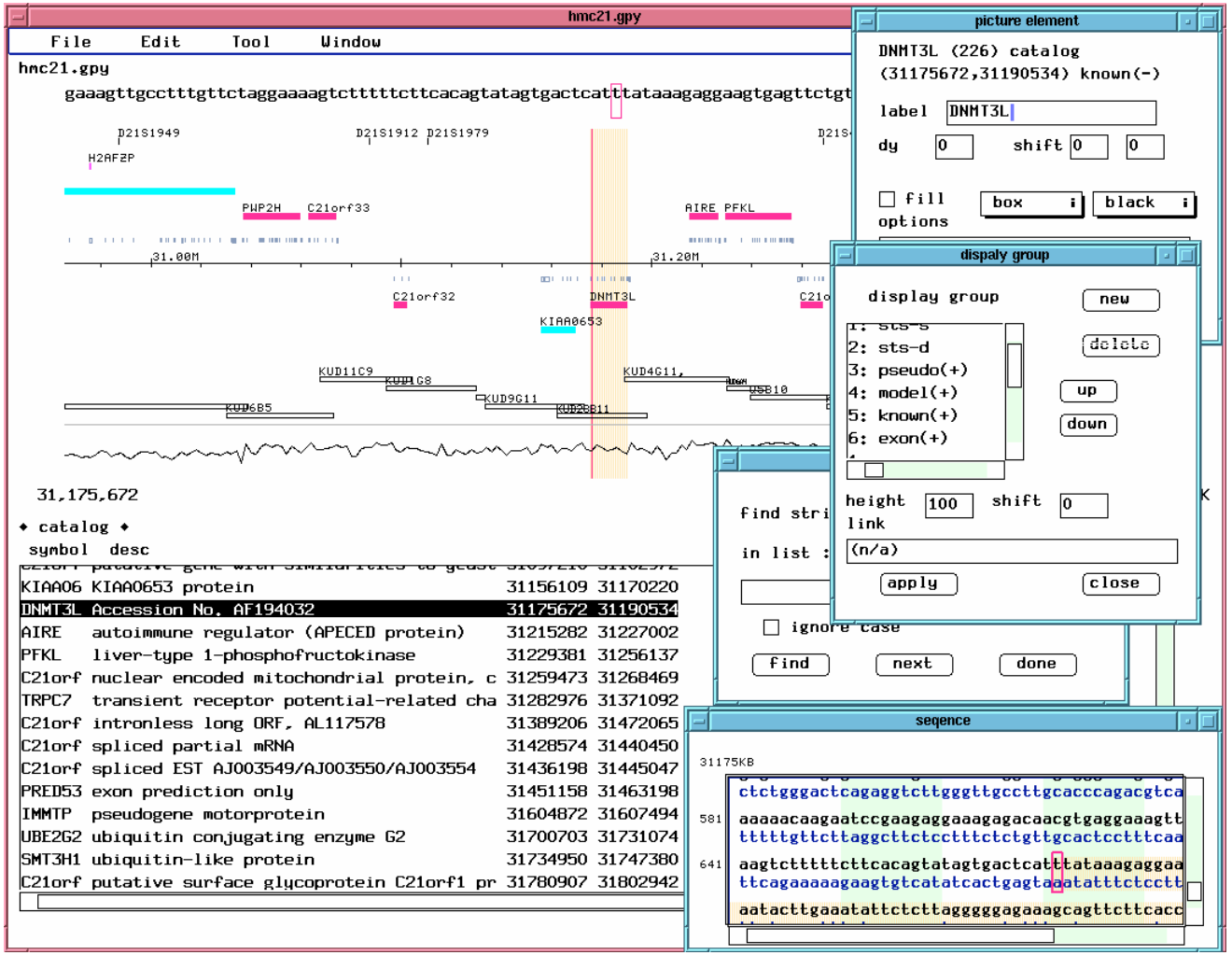
GUPPY : Genetic Understanding Perspective Preview sYstem

- An sequence map viewer program

GUPPY home page

Methods and GUPPY script files are provided

`http://staff.aist.go.jp/yutaka.ueno/guppy`



GUPPY Catalog Data

The basic annotation data format in Lua

```
one={
      {symbol="orfD", pos1=18, pos2= 48, category=1},
      {symbol="orfE", pos1=58, pos2= 78, category=3},
      {symbol="gene1",pos1=88, pos2=188;
        {symbol="5'utr",pos1=88,pos2=94},
      }
    }   .......
}
```

A Lua program to list subsidary annotations

```
num=getn(one)
print(" total", num)

for idx=1,num do
    cnt=one[idx]
    if(cnt[1]) then
        print(idx,cnt[1].symbol)
    end
end

  ---- print(one[3][1].symbol)
```

In Perl Language

```
@one=(
          {symbol=>"orfD", pos1=>18, pos2=> 48, category=>1},
          {symbol=>"orfE", pos1=>58, pos2=> 78, category=>3},
          {symbol=>"gene1",pos1=>88, pos2=>188,
            child=> [
            {symbol=>"5'utr",pos1=>88,pos2=>94},
            ]
          },
);

$num = $#one+1;

print "total    $num\n";

for( $idx=0; $idx<$num ; $idx++ ) {
        $cnt=$one[$idx];
        if( $cnt->{child}[0] ) {
                print "$idx child $cnt->{child}[0]{symbol} \n";
        };
};
        ### $one[2]{child}[0]{symbol}
```

PRO : Widely accepted

CON : Difficulties in hierarchical data with a notion of "reference"

In Python Language

```
one = [
          {'symbol': "orfD", 'pos1': 18, 'pos2':  48, 'category': 1},
          {'symbol': "orfE", 'pos1': 58, 'pos2':  78, 'category': 3},
          {'symbol': "gene1",'pos1': 88, 'pos2': 188,
           'child':  [
                  {'symbol': "5'utr",'pos1': 88,'pos2': 94},
            ],
          },
]

num=len(one)                    ## 3

print "total",num

for idx in range(num):          ## 0,1,2
    cnt=one[idx]
    if cnt.get('child'):
        print idx,"  ",
            cnt['child'][0]['symbol'],"\n"

  ### one[2]['child'][0]['symbol']
```

PRO : Rappidly growing community in scientific applications

CON : Unusal indentation rule

In Ruby Language

```
one = [
          {'symbol'=>"orfD", 'pos1'=>18, 'pos2'=> 48, 'category'=>1},
          {'symbol'=>"orfE", 'pos1'=>58, 'pos2'=> 78, 'category'=>3},
          {'symbol'=>"gene1",'pos1'=>88, 'pos2'=>188,
           'child'=> [
                  {'symbol'=>"5'utr",'pos1'=>88,'pos2'=>94},
            ],
          },
]

num=one.size

print("total ",num,"\n")

for idx in 0..num-1
    cnt=one[idx]
    if( cnt['child'] )
        print(idx,"  ",
            cnt['child'][0]['symbol'], "\n")
    end
end
      ### one[2]['child'][0]['symbol']
```

PRO : Modern programming technology

CON : Involving tricky object oriented programming topics

Comparison of Languages

	C	Java	Lisp	Basic	Perl	Tcl	Python	Ruby	Lua
1.dynamic data			○		○	○	○	○	◎
.auto memory		○	○		○	○	○	○	○
2.variables	○	○	○	○	○	○	○	○	○
.numericals	○	○	○	○	○		○	○	○
3.syntax	○	○		○			○	○	◎
.ease of use				○	○	○	○	○	○

SIZE is another issue in the implementation for a

High speed interactive computer graphics

```
LOCUS       HUMHA2WC     2226 bp    DNA             PRI       09-NOV-1994
DEFINITION  Human gene for aquaporin-2 water channel.
ACCESSION   D31846
NID         g567249
KEYWORDS    aquaporin-2 water channel.
SOURCE      Homo sapiens DNA.
  ORGANISM  Homo sapiens
            Eukaryotae; mitochondrial eukaryotes; Metazoa; Chordata;
            Vertebrata; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 2226)
  AUTHORS   Uchida,S., Sasaki,S., Fushimi,K. and Marumo,F.
  TITLE     Isolation of human aquaporin-CD gene
  JOURNAL   J. Biol. Chem. 269 (38), 23451-23455 (1994)
  MEDLINE   94375443
COMMENT     Submitted (17-Jun-1994) to DDBJ by:
            Shinichi Uchida
FEATURES             Location/Qualifiers
     source          1..2226
                     /organism="Homo sapiens"
     TATA_signal     545
     exon            574..1027
                     /number=1
     CDS             join(668..1027,1095..1259,1327..1407,1465..1674)
                     /codon_start=1
                     /product="human aquaporin-2 water channel"
                     /db_xref="PID:g567250"
                     /translation="MWELRSIAFSRAVFAEFLATLLFVFFGLGSL
                     AMAFGLGIGTLVQALGHISGAHINPAVTVACLVGCHVSVL
                     YNYVLFPPAKSLSERTHISISNOTCORRECT"
     intron          1028..1094
                     /number=1
     exon            1095..1259
                     /number=2
     polyA_signal    2221
BASE COUNT      412 a    686 c    666 g    462 t
ORIGIN      Chromosome 12.
        1 aagcttaatg atttatgggt gattagctgc aagaatgcaa
        2 cacaaacctt tatgc
```

```
HUMHA2WC={
LOCUS     ="HUMHA2WC", bp=2226,     DNA=           "PRI", date="09-NOV-1994",
DEFINITION="Human gene for aquaporin-2 water channel.",
ACCESSION ="D31846",
NID       ="g567249",
KEYWORDS  ="aquaporin-2 water channel.",
SOURCE    ="Homo sapiens DNA.",
  ORGANISM="Homo sapiens", taxon =
           "Eukaryotae; mitochondrial eukaryotes; Metazoa; Chordata;"
         .. "Vertebrata; Eutheria; Primates; Catarrhini; Hominidae; Homo.",
REFERENCE ={ [ 1] = { loc= "(bases 1 to 2226)",
  AUTHORS ="Uchida,S., Sasaki,S., Fushimi,K. and Marumo,F.",
  TITLE   ="Isolation of human aquaporin-CD gene",
  JOURNAL ="J. Biol. Chem. 269 (38), 23451-23455 (1994)",
  MEDLINE ="94375443",  }, },
COMMENT   ="Submitted (17-Jun-1994) to DDBJ by:"
         .. "Shinichi Uchida"
FEATURES={
 {k="source",         loc= {1,2226} ,
                      organism="Homo sapiens"},
 {k="TATA_signal",    loc= {545}},
 {k="exon",           loc= {574,1027} ,
                      number=1},
 {k="CDS",            loc={tpg="join";{{668,1027},{1095,1259},{1327,1407},{1465,1674}}},
                      codon_start=1,
                      product="human aquaporin-2 water channel",
                      db_xref="PID:g567250",
                      translation="MWELRSIAFSRAVFAEFLATLLFVFFGLGS"
                  .."AMAFGLGIGTLVQALGHISGAHINPAVTVACLVGCHVSVL"
                  .. "YNYVLFPPAKSLSERLAVLKTHISISNOTCORRECT"},
 {k="intron",         loc= {1028,1094} ,
                      number=1},
 {k="exon",           loc= {1095,1259} ,
                      number=2},
 {k="polyA_signal",   loc={2221}},  },
COUNT={ a=   412 , c=   686 , g=   666 , t=   462  },
ORIGIN =   " Choromosome 12."
seqence= "aagcttaatgatttatgggtgattagctgcaagaatgcaagcacagaaga"
       .."cacaaacctttatgc"
}
```

Processing annotations

Suppose if we need to marge two annotation data differently formatted...

1. Data Rearrangement:

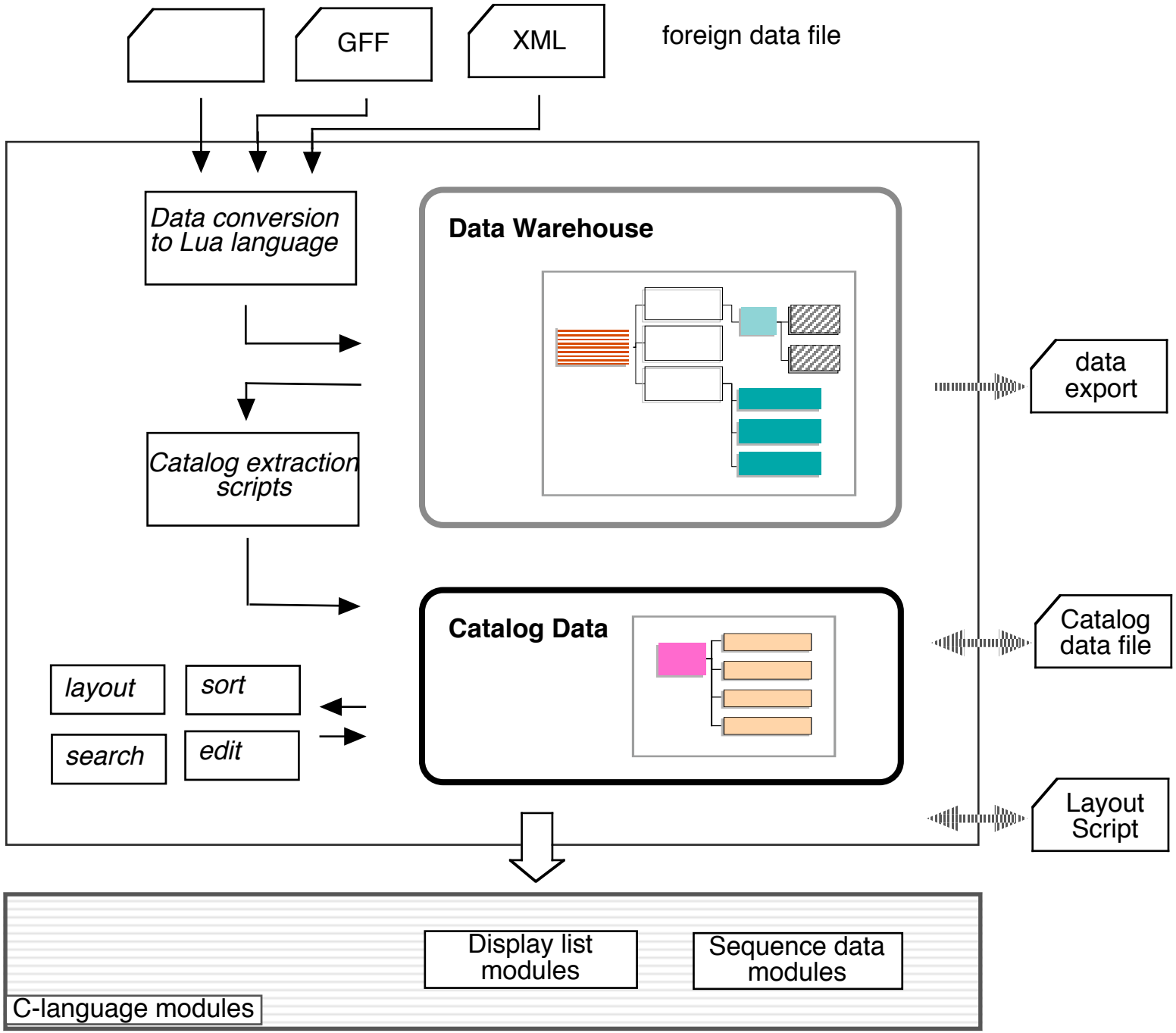
Picking-up, grouping, sorting, comparing, ...

2. Coordinate Translation:

GenBank data are annotated by its 'locus' coordinate starting from 1 ...

3. On-Demand Editing:

Adding, or modifying annotation is the biological objective


GFF
XML
foreign data file
Data conversion to Lua language
Data Warehouse
data export
Catalog extraction scripts
Catalog Data
Catalog data file
layout
sort
search
edit
Layout Script
Display list modules
Sequence data modules
C-language modules

Implementation

An in-house Graphics ang GUI library (ASHLEY)

- ANSI-C : 33,000 lines
- Linux/X-Window, Windows, MacOS Classic & Carbon

Lua 4.0.1

- patch for fgets() to support foreign CR LF.
- support $endinput

Lua code 6,400 lines

ANSI C 4,900 lines

- - - source code is available

Bermuda Principles for Human Genome

- 1996 - Bermuda international meeting for the genome project agreed to formalize the conditions of data access :
  - Primary genomic sequence should be in the public domain
  - Sequence data should be released as soon as possible (24 hour)
  - Annotation should be submitted immediately to public databases
- URLs:
  - Heritage of Humanity (by Dr. John Salston)
    - **http://mondediplo.com/2002/12/15genome**
  - Bermuda Principles
    - **http://www.gene.ucl.ac.uk/hugo/bermuda.htm**

A Persistent Large Table on Disk

A virtual memory based large table

A huge table of lua whose part is in the disk

- several GB of data
- read only access (DVD-ROM)
- update journal would be nice

A Simple implementation in Lua by swapping out unused table data does work fine.

Conclusion

- Computational tasks to visualize annotation data for genetic sequences involve :
  - (1) data rearrangement,(2) coordinate translation (3)local editing.
- Those tasks are greatly aided by a programming language that provides the necessary functions:
  - (1) handling of data containers,(2) symbolic references,(3) a simple programming syntax.
- Lua language was successfuly applied to GUPPY, a sequence visualization program with arrangement of annotation data and a flexible layout.