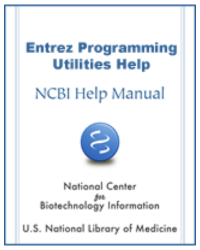
NLM Citation: Kans J. Entrez Direct: E-utilities on the UNIX Command Line. 2013 Apr 23 [Updated 2020 Apr 17]. In: Entrez Programming Utilities Help [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2010-.
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/



Entrez Direct: E-utilities on the UNIX Command Line

Jonathan Kans, PhD[1]

Created: April 23, 2013; Updated: April 17, 2020.

Getting Started

Introduction

Entrez Direct (EDirect) provides access to the NCBI's suite of interconnected databases (publication, sequence, structure, gene, variation, expression, etc.) from a UNIX terminal window. Functions take search terms from command-line arguments. Individual operations are combined to build multi-step queries. Record retrieval and formatting normally complete the process.

EDirect also includes an argument-driven function that simplifies the extraction of data from document summaries or other results that are returned in structured XML format. This can eliminate the need for writing custom software to answer ad hoc questions. Queries can move seamlessly between EDirect commands and UNIX utilities or scripts to perform actions that cannot be accomplished entirely within Entrez.

Installation

EDirect will run on UNIX and Macintosh computers that have the Perl language installed, and under the Cygwin UNIX-emulation environment on Windows PCs. To install the EDirect software, click on the download EDirect installer link to obtain the install-edirect.sh script, then execute it by running:

```
  source ./install-edirect.sh
```

Alternatively, open a terminal window and execute one of the following two commands:

```
  sh -c "$(curl -fsSL ftp://ftp.ncbi.nlm.nih.gov/entrez/entrezdirect/install-edirect.sh)"

  sh -c "$(wget -q ftp://ftp.ncbi.nlm.nih.gov/entrez/entrezdirect/install-edirect.sh -O -)"
```

or if neither curl nor wget are available, copy the following commands and paste them into a terminal window:

```
  cd ~
  /bin/bash
  perl -MNet::FTP -e \
    '$ftp = new Net::FTP("ftp.ncbi.nlm.nih.gov", Passive => 1);
     $ftp->login; $ftp->binary;
     $ftp->get("/entrez/entrezdirect/edirect.tar.gz");'
```

Author Affiliation: 1 NCBI; Email: kans@ncbi.nlm.nih.gov.

Corresponding author.

```
gunzip -c edirect.tar.gz | tar xf -
rm edirect.tar.gz
builtin exit
export PATH=${PATH}:$HOME/edirect >& /dev/null || setenv PATH "${PATH}:$HOME/edirect"
./edirect/setup.sh
```

Any of these methods will download several programs into an "edirect" folder in the user's home directory. The setup.sh script then downloads any missing Perl modules, and may print an additional command for updating the PATH environment variable in the user's configuration file. The editing instructions will look something like:

```
echo "export PATH=\$PATH:\$HOME/edirect" >> $HOME/.bash_profile
```

As a convenience, the installation process now ends by offering to run the PATH update command for you. Answer "y" and press the Return key if you want it run. If the PATH is already set correctly, or if you prefer to make any editing changes manually, just press Return.

Entrez Direct Functions

Navigation functions support exploration within the Entrez databases:

- **esearch** performs a new Entrez search using terms in indexed fields.
- **elink** looks up neighbors (within a database) or links (between databases).
- **efilter** filters or restricts the results of a previous query.

Records can be retrieved in specified formats or as document summaries:

- **efetch** downloads records or reports in a designated format.

Desired fields from XML results can be extracted without writing a program:

- **xtract** converts EDirect XML output into a table of data values.

Several additional functions are also provided:

- **einfo** obtains information on indexed fields in an Entrez database.
- **epost** uploads unique identifiers (UIDs) or sequence accession numbers.
- **nquire** sends a URL request to a web page or CGI service.

Entering Query Commands

UNIX programs are run by typing the name of the program and then supplying any required or optional arguments on the command line. Argument names are letters or words that start with a dash ("-") character.

In order to begin an Entrez search, the user types "esearch" and then enters the required -db (database) and -query arguments. A query on unqualified search terms:

```
esearch -db pubmed -query "opsin gene conversion"
```

constructs the appropriate Entrez Utilities (E-utilities) URL from the query terms and executes the search. EDirect handles many technical details behind the scenes (avoiding the learning curve normally required for E-utilities programming), and saves the results on the Entrez history server.

Constructing Multi-Step Queries

EDirect allows individual operations to be described separately, combining them into a multi-step query by using the vertical bar ("|") UNIX pipe symbol. Piping esearch to elink:

```
  esearch -db pubmed -query "opsin gene conversion" | elink -related
```

will look up related articles (precomputed PubMed neighbors) of the initial results.

Writing Commands on Multiple Lines

A query can be continued on the next line by typing the backslash ("\") UNIX escape character immediately before pressing the Return key. Continuing the query links to all protein sequences published in the neighbor articles:

```
  esearch -db pubmed -query "opsin gene conversion" | \
  elink -related | \
  elink -target protein
```

The vertical bar pipe symbol also allows the query to continue on the next line.

Retrieving PubMed Reports

Piping PubMed query results to efetch and specifying the "abstract" format:

```
  esearch -db pubmed -query "lycopene cyclase" |
  efetch -format abstract
```

returns a set of reports that can be read by a person:

```
  ...
  10. PLoS One. 2013;8(3):e58144. doi: 10.1371/journal.pone.0058144. Epub ...

  Levels of lycopene β-cyclase 1 modulate carotenoid gene expression and
  accumulation in Daucus carota.

  Moreno JC(1), Pizarro L, Fuentes P, Handford M, Cifuentes V, Stange C.

  Author information:
  (1)Departamento de Biología, Facultad de Ciencias, Universidad de Chile,
  Santiago, Chile.

  Plant carotenoids are synthesized and accumulated in plastids through a
  highly regulated pathway. Lycopene β-cyclase (LCYB) is a key enzyme
  involved directly in the synthesis of α-carotene and β-carotene through
  ...
```

Using efetch -format "medline" instead produces a report that can be entered into common bibliographic management software packages:

```
  ...
  PMID- 23555569
  OWN - NLM
  STAT- MEDLINE
  DA  - 20130404
  DCOM- 20130930
  LR  - 20131121
  IS  - 1932-6203 (Electronic)
  IS  - 1932-6203 (Linking)
```

```
VI  - 8
IP  - 3
DP  - 2013
TI  - Levels of lycopene beta-cyclase 1 modulate carotenoid gene expression
      and accumulation in Daucus carota.
PG  - e58144
LID - 10.1371/journal.pone.0058144 [doi]
AB  - Plant carotenoids are synthesized and accumulated in plastids
      through a highly regulated pathway. Lycopene beta-cyclase (LCYB) is a
      key enzyme involved directly in the synthesis of alpha-carotene and
      ...
```

Retrieving Sequence Reports

Nucleotide and protein records can be downloaded in FASTA format:

```
esearch -db protein -query "lycopene cyclase" |
efetch -format fasta
```

which consists of a definition line followed by the sequence:

```
...
>gi|735882|gb|AAA81880.1| lycopene cyclase [Arabidopsis thaliana]
MDTLLKTPNKLDFFIPQFHGFERLCSNNPYPSRVRLGVKKRAIKIVSSVVSGSAALLDLVPETKKENLDF
ELPLYDTSKSQVVDLAIVGGGPAGLAVAQQVSEAGLSVCSIDPSPKLIWPNNYGVWVDEFEAMDLLDCLD
TTWSGAVVYVDEGVKKDLSRPYGRVNRKQLKSKMLQKCITNGVKFHQSKVTNVVHEEANSTVVCSDGVKI
QASVVLDATGFSRCLVQYDKPYNPGYQVAYGIIAEVDGHPFDVDKMVFMDWRDKHLDSYPELKERNSKIP
TFLYAMPFSSNRIFLEETSLVARPGLRMEDIQERMAARLKHLGINVKRIEEDERCVIPMGGPLPVLPQRV
VGIGGTAGMVHPSTGYMVARTLAAAPIVANAIVRYLGSPSSNSLRGDQLSAEVWRDLWPIERRRQREFFC
FGMDILLKLDLDATRRFFDAFFDLQPHYWHGFLSSRLFLPELLVFGLSLFSHASNTSRLEIMTKGTVPLA
KMINNLVQDRD
...
```

Additional FASTA -format variants are fasta_cds_na, fasta_cds_aa, and gene_fasta.

Sequence records can also be obtained as GenBank (-format gb) or GenPept (-format gp) flatfiles, which have features annotating particular regions of the sequence:

```
...
LOCUS       AAA81880                 501 aa            linear   PLN ...
DEFINITION  lycopene cyclase [Arabidopsis thaliana].
ACCESSION   AAA81880
VERSION     AAA81880.1  GI:735882
DBSOURCE    locus ATHLYC accession L40176.1
KEYWORDS    .
SOURCE      Arabidopsis thaliana (thale cress)
  ORGANISM  Arabidopsis thaliana
            Eukaryota; Viridiplantae; Streptophyta; Embryophyta;
            Tracheophyta; Spermatophyta; Magnoliophyta; eudicotyledons;
            Brassicales; Brassicaceae; Camelineae; Arabidopsis.
REFERENCE   1  (residues 1 to 501)
  AUTHORS   Scolnik,P.A. and Bartley,G.E.
  TITLE     Nucleotide sequence of lycopene cyclase (GenBank L40176) from
            Arabidopsis (PGR95-019)
  JOURNAL   Plant Physiol. 108 (3), 1343 (1995)
...
FEATURES             Location/Qualifiers
     source          1..501
                     /organism="Arabidopsis thaliana"
                     /db_xref="taxon:3702"
     Protein         1..501
                     /product="lycopene cyclase"
     transit_peptide 1..80
     mat_peptide     81..501
                     /product="lycopene cyclase"
     CDS             1..501
                     /gene="LYC"
                     /coded_by="L40176.1:2..1507"
ORIGIN
        1 mdtllktpnk ldffipqfhg ferlcsnnpy psrvrlgvkk raikivssvv sgsaalldlv
       61 petkkenldf elplydtsks qvvdlaivgg gpaglavaqq vseaglsvcs idpspkliwp
      121 nnygvwvdef eamdlldcld ttwsgavvyv degvkkdlsr pygrvnrkql kskmlqkcit
      181 ngvkfhqskv tnvvheeans tvvcsdgvki qasvvldatg fsrclvqydk pynpgyqvay
      241 giiaevdghp fdvdkmvfmd wrdkhldsyp elkernskip tflyampfss nrifleetsl
      301 varpglrmed iqermaarlk hlginvkrie edercvipmg gplpvlpqrv vgiggtagmv
      361 hpstgymvar tlaaapivan aivrylgsps snslrgdqls aevwrdlwpi errrqreffc
      421 fgmdillkld ldatrrffda ffdlqphywh gflssrlflp ellvfglslf shasntsrle
      481 imtkgtvpla kminnlvqdr d
//
...
```

Searching and Filtering

Restricting Query Results

The current results can be refined by further term searching in Entrez (useful in the protein database for limiting BLAST neighbors to a taxonomic subset):

```
esearch -db pubmed -query "opsin gene conversion" |
elink -related |
efilter -query "tetrachromacy"
```

Results can also be filtered by time. For example, the following statements:

```
efilter -days 60 -datetype PDAT
efilter -mindate 1990 -maxdate 1999 -datetype PDAT
```

restrict results to articles published in the previous two months or in the 1990s, respectively.

Qualifying Queries by Indexed Field

Query terms in esearch or efilter can be qualified by entering an indexed field abbreviation in brackets. Boolean operators and parentheses can also be used in the query expression for more complex searches.

Commonly-used fields for PubMed queries include:

```
[AFFL]    Affiliation
[ALL]     All Fields
[AUTH]    Author
[FAUT]    Author - First
[LAUT]    Author - Last
[PDAT]    Date - Publication
[FILT]    Filter
[JOUR]    Journal
[LANG]    Language
[MAJR]    MeSH Major Topic
[SUBH]    MeSH Subheading
[MESH]    MeSH Terms
[PTYP]    Publication Type
```

[WORD]	Text Word
[TITL]	Title
[TIAB]	Title/Abstract
[UID]	UID

and a qualified query looks like:

```
"Tager HS [AUTH] AND glucagon [TIAB]"
```

Filters that limit search results to subsets of PubMed include:

```
humans [MESH]
pharmacokinetics [MESH]
chemically induced [SUBH]
all child [FILT]
english [FILT]
freetext [FILT]
has abstract [FILT]
historical article [FILT]
randomized controlled trial [FILT]
clinical trial, phase ii [PTYP]
review [PTYP]
```

Sequence databases are indexed with a different set of search fields, including:

[ACCN]	Accession
[ALL]	All Fields
[AUTH]	Author
[GPRJ]	BioProject
[ECNO]	EC/RN Number
[FKEY]	Feature key
[FILT]	Filter
[GENE]	Gene Name
[JOUR]	Journal
[KYWD]	Keyword
[MLWT]	Molecular Weight
[ORGN]	Organism
[PACC]	Primary Accession
[PROP]	Properties
[PROT]	Protein Name
[SQID]	SeqID String
[SLEN]	Sequence Length
[SUBS]	Substance Name
[WORD]	Text Word
[TITL]	Title
[UID]	UID

and a sample query in the protein database is:

```
"alcohol dehydrogenase [PROT] NOT (bacteria [ORGN] OR fungi [ORGN])"
```

Additional examples of subset filters in sequence databases are:

```
mammalia [ORGN]
mammalia [ORGN:noexp]
cds [FKEY]
lacz [GENE]
beta galactosidase [PROT]
protein snp [FILT]
reviewed [FILT]
country united kingdom glasgow [TEXT]
```

```
biomol genomic [PROP]
dbxref flybase [PROP]
gbdiv phg [PROP]
phylogenetic study [PROP]
sequence from mitochondrion [PROP]
src cultivar [PROP]
srcdb refseq validated [PROP]
150:200 [SLEN]
```

(The calculated molecular weight (MLWT) field is only indexed for proteins (and structures), not nucleotides.)

Examining Intermediate Results

EDirect stores intermediate results on the Entrez history server. EDirect navigation functions produce a custom XML message with the relevant fields (database, web environment, query key, and record count) that can be read the next command in the pipeline.

The results of each step in a query can be examined to confirm expected behavior before adding the next step. The Count field in the ENTREZ_DIRECT object contains the number of records returned by the previous step. A good measure of query success is a reasonable (non-zero) count value. For example:

```
esearch -db protein -query "NP_567004 [ACCN]" |
elink -related |
efilter -query "28000:30000 [MLWT]" |
elink -target structure |
efilter -query "0:2 [RESO]"
```

produces:

```
<ENTREZ_DIRECT>
  <Db>structure</Db>
  <WebEnv>NCID_1_545606712_172.16.22.25_5555_1348089299_358182861</WebEnv>
  <QueryKey>7</QueryKey>
  <Count>39</Count>
  <Step>5</Step>
</ENTREZ_DIRECT>
```

with 39 protein structures being within the specified molecular weight range and having the desired (X-ray crystallographic) atomic position resolution.

(The QueryKey value is 7 instead of 5 because each elink command obtains the record count by running a separate ESearch query immediately after the ELink operation.)

Combining Independent Queries

Independent esearch, elink, and efilter operations can be performed and then combined at the end by using the history server's "#" convention to indicate query key numbers. (The steps to be combined must be in the same database.) Subsequent esearch commands can take a -db argument to override the database piped in from the previous step. (Piping the queries together is necessary for sharing the same history thread.) For example, the query:

```
esearch -db protein -query "amyloid* [PROT]" |
elink -target pubmed |
esearch -db gene -query "apo* [GENE]" |
elink -target pubmed |
esearch -query "(#3) AND (#6)" |
efetch -format docsum |
xtract -pattern DocumentSummary -element Id Title
```

uses truncation searching (entering the beginning of a word followed by an asterisk) to return titles of papers with links to amyloid protein sequence and apolipoprotein gene records:

```
23962925    Genome analysis reveals insights into physiology and ...
23959870    Low levels of copper disrupt brain amyloid-β homeostasis ...
23371554    Genomic diversity and evolution of the head crest in the ...
23251661    Novel genetic loci identified for the pathophysiology of ...
...
```

The use of (#3) AND (#6) instead of (#2) AND (#4) above reflects the need for each elink command to execute a separate ESearch query, which increments the QueryKey, in order to obtain the record count. The -label argument can be used to get around this artifact. The label value is prefixed by a "#" symbol and placed in parentheses in the final search. Thus:

```
esearch -db structure -query "insulin [TITL]" |
elink -target pubmed -label struc_cit |
esearch -db protein -query "insulin [PROT]" |
elink -target pubmed -label prot_cit |
esearch -query "(#struc_cit) AND (#prot_cit)" |
efetch -format uid
```

will return:

```
15299880
9235985
9141131
8421693
...
```

without the need to keep track of the internal QueryKey values.

Structured Data

Advantages of XML Format

The ability to obtain Entrez records in structured XML format, and to easily extract the underlying data, allows the user to ask novel questions that are not addressed by existing analysis software.

The advantage of XML is that many pieces of information are in specific locations in a well-defined data hierarchy. Accessing individual units of data that are fielded by name, such as:

```
<PubDate>2013</PubDate>
<Source>PLoS One</Source>
<Volume>8</Volume>
<Issue>3</Issue>
<Pages>e58144</Pages>
```

requires matching the same general pattern, differing only by the element name. This is much simpler than parsing the units from a long, complex string:

```
1. PLoS One. 2013;8(3):e58144 ...
```

The disadvantage of XML is that data extraction usually requires programming. But EDirect relies on the common pattern of XML value representation to provide a simplified approach to interpreting XML data.

Conversion of XML Data into Tabular Form

The xtract function uses command-line arguments to direct the selective conversion of XML data into a tab-delimited table. The -pattern argument divides the results into rows, while placement of data into columns is controlled by -element. A trivial example:

```
  xtract -pattern ENTREZ_DIRECT -element Count
```

will print the number of records in the current query.

Xtract provides control over data conversion with a divide-and-conquer strategy using separate arguments for element selection, path exploration, conditional processing, and report formatting.

Element selection finds every occurrence of each indicated item, printing values as they are encountered. Exploration control limits selection by context, presenting specified objects one at a time. Conditional processing filters by content, requiring presence (or absence) of a particular data value in order to continue. Finally, custom formatting can override the normal tabular layout of the default output.

The details and ramifications of this flexible approach are discussed in the remainder of this section.

Extraction Arguments

Selection arguments (-element, -first, and -last) extract and print data values from the indicated element names:

```
  -element Id -first Name Title
```

Exploration arguments (-pattern, -group, -block, and -subset) limit data extraction to specified regions of the XML, visiting all relevant objects one at a time. This sets a context for data collection, eliminates the need to provide the full path to a data element, and uncouples the concept of "what to look for" from "where to find it":

```
  -pattern DocumentSummary
    -block Author
```

Each pattern can have multiple groups, each group can have multiple blocks, and each block can have multiple subsets. This design allows nested exploration of complex, hierarchical data to be controlled by a linear chain of command-line argument statements.

Conditional processing arguments restrict exploration statements by object name and value (-if and -unless) or item location (-position):

```
  -if Source -equals "J Bacteriol"
  -position first
```

These commands are issued immediately after an exploration argument.

Formatting arguments (-ret, -tab, -sep, -pfx, -sfx, and -def) allow extensive customization of the default row/column table presentation:

```
  -pfx "\n[" -sfx "]\t" -sep " " -tab "" -ret "\n\n" -def "-"
```

and apply to subsequent selection statements.

(The "\n" escape sequence indicates a line break, while "\t" specifies a tab character.)

XML Document Summaries

Entrez provides a document summary in structured XML format for every record. Piping a query to "efetch -format docsum":

```
esearch -db pubmed -query "Garber ED [AUTH] AND PNAS [JOUR]" |
elink -related |
efilter -query "mouse" |
efetch -format docsum
```

will generate an XML document summary set:

```
<DocumentSummarySet status="OK">
  <DbBuild>Build150407-2207m.3</DbBuild>
  <DocumentSummary>
    <Id>19650888</Id>
    <PubDate>2009 Aug 3</PubDate>
    <EPubDate>2009 Aug 3</EPubDate>
    <Source>BMC Microbiol</Source>
    <Authors>
      <Author>
        <Name>Cano V</Name>
        <AuthType>Author</AuthType>
        <ClusterID></ClusterID>
      </Author>
      <Author>
        <Name>Moranta D</Name>
        <AuthType>Author</AuthType>
        ...
```

Piping the document summary output to:

```
xtract -outline
```

will give an indented overview of the XML structure hierarchy:

```
DbBuild
DocumentSummary
  Id
  PubDate
  EPubDate
  Source
  Authors
    Author
      Name
      AuthType
      ClusterID
    Author
      Name
      ...
```

The outline view presents a clear, uncluttered picture of the XML hierarchy that is useful in designing the appropriate command for actual data extraction. Copy and paste from the -outline output to xtract arguments can help avoid typographical errors. Thus:

```
esearch -db pubmed -query "Garber ED [AUTH] AND PNAS [JOUR]" |
elink -related |
efilter -query "mouse" |
efetch -format docsum |
xtract -pattern DocumentSummary -element Id SortFirstAuthor Title
```

returns the PubMed identifier (PMID), first author name, and article title:

```
19650888    Cano V        Klebsiella pneumoniae triggers a cytotoxic ...
19262028    Suto J        Metabolic consequence of congenital asplenia ...
```

```
19248821    Fukumoto N    Hypoalgesic behaviors of P/Q-type voltage- ...
18822497    Trishin AV    [Protective activity of secreted proteins of ...
18582214    Singh A       Generation and characterization of monoclonal ...
...
```

Using xtract "-synopsis" instead of -outline show the full path to each element. Piping those results to "sort-uniq-count" (see below) produces a table of unique path counts.

Processing Results with UNIX Utilities

A tab-delimited table can be processed by many UNIX utilities. For example:

```
esearch -db pubmed -query "Garber ED [AUTH] AND PNAS [JOUR]" |
elink -related |
efilter -query "mouse" |
efetch -format docsum |
xtract -pattern DocumentSummary -element Id SortFirstAuthor Title |
sort -t $'\t' -k 2,2f -k 3,3f
```

sorts the results of the previous example by author name and then (if there are multiple publications by the same author) alphabetically by title:

```
17474906    Benghezal M     Inhibitors of bacterial virulence ...
19650888    Cano V          Klebsiella pneumoniae triggers a cytotoxic ...
17102561    Chatterjee S    How reliable are models for malaria vaccine ...
17371870    Clements A      Secondary acylation of Klebsiella ...
17142396    Fresno S        A second galacturonic acid transferase is ...
16735743    Fresno S        The ionic interaction of Klebsiella ...
...
```

Rather than always having to retype a series of common post-processing instructions, frequently used combinations of UNIX commands can be placed in a function, stored in an alias file (e.g., the user's .bash_profile), and executed by name. (The following two functions are now included as scripts with the EDirect software.) For example:

```
WordAtATime() {
  sed 's/[^a-zA-Z0-9]/ /g; s/^ *//' |
  tr 'A-Z' 'a-z' |
  fmt -w 1
}
alias word-at-a-time='WordAtATime'

SortUniqCountRank() {
  sort -f |
  uniq -i -c |
  perl -pe 's/\s*(\d+)\s(.+)/$1\t$2/' |
  sort -t $'\t' -k 1,1nr -k 2f
}
alias sort-uniq-count-rank='SortUniqCountRank'
```

Titles can be passed to a pair of these UNIX alias commands:

```
esearch -db pubmed -query "Casadaban transposition immunity" |
elink -related |
efetch -format docsum |
xtract -pattern DocumentSummary -element Title |
word-at-a-time |
sort-uniq-count-rank
```

to generate a table of word occurrence counts, sorted by frequency:

```
296    of
175    the
114    transposition
102    and
94     in
93     mu
83     a
61     dna
61     tn3
55     transposon
...
```

Output Format Customization

The line break between -pattern objects can be overridden with -ret, and the tab character between fields can be replaced by -tab.

The -sep argument is used to distinguish multiple elements of the same type and control their separation independently of the -tab argument. For example:

```
esearch -db gene -query "deuteranopia" |
efetch -format xml |
xtract -pattern Entrezgene \
  -element Gene-track_geneid Gene-ref_locus \
  -sep "|" -element Gene-ref_syn_E
```

combines all synonyms for a gene into a single column, separated by vertical bars:

```
2652    OPN1MW    CBD|GCP|GOP|CBBM|COD5|OPN1MW1
5956    OPN1LW    CBP|RCP|ROP|CBBM|COD5
```

The -sep value also applies to unrelated -element items that are grouped with commas. Otherwise the -tab value delineates individual fields.

Groups or fields are preceded by the -pfx value and followed by the -sfx value, both of which are initially empty.

Missing data values can be marked by the -def argument. For example:

```
esearch -db pubmed -query "deuteranopia" |
efetch -format xml |
xtract -pattern PubmedArticle -def "-" \
  -first MedlineCitation/PMID Author/LastName Keyword
```

inserts a dash in a column where the specified element is missing.

Pubmed Article XML Records

The PubmedArticle object (for -db pubmed) has a more detailed structure than the DocumentSummary:

```
esearch -db pubmed -query "tetrachromacy" |
efetch -format xml |
xtract -outline
```

More information is fielded, including author names, dates, and the abstract:

```
PubmedArticle
  MedlineCitation
    PMID
```

```
      DateCompleted
        Year
        Month
        Day
      DateRevised
        Year
        Month
        Day
      Article
        Journal
          ISSN
          JournalIssue
            Volume
            Issue
            PubDate
              Year
              Month
              Day
          Title
          ISOAbbreviation
        ArticleTitle
        Pagination
          MedlinePgn
        Abstract
          AbstractText
          CopyrightInformation
        AuthorList
          Author
            LastName
            ForeName
            Initials
            AffiliationInfo
              Affiliation
          Author
            LastName
            ...
```

Using this information to craft a new xtract statement:

```
esearch -db pubmed -query "tetrachromacy" |
efetch -format xml |
xtract -pattern PubmedArticle -element MedlineCitation/PMID LastName
```

results in a table of all authors for each record:

```
23393278    Sabbah       Troje        Gray        Hawryshyn
20884587    Jordan       Deeb         Bosten      Mollon
18230593    Koshitaka    Kinoshita    Vorobyev    Arikawa
17685813    Wachtler     Doi          Lee         Sejnowski
...
```

(Note that "-element MedlineCitation/PMID" uses the "Parent/Child" construct to prevent the display of additional PMID items that may occur later in CommentsCorrections objects.)

The -first or -last arguments can be used instead of -element, if appropriate.

Exploration of XML Sets

Individual PubmedArticle objects can be retrieved directly by efetch:

```
efetch -db pubmed -id 20643751 -format xml
```

The resulting XML has authors with separate fields for last name and initials:

```
...
<AuthorList>
  <Author>
    <LastName>Inamdar</LastName>
    <ForeName>Arati A</ForeName>
    <Initials>AA</Initials>
  </Author>
  <Author>
    <LastName>Masurekar</LastName>
    <ForeName>Prakash</ForeName>
    <Initials>P</Initials>
  </Author>
  <Author>
    <LastName>Bennett</LastName>
    <ForeName>Joan Wennstrom</ForeName>
    <Initials>JW</Initials>
  </Author>
</AuthorList>
...
```

Without being given any guidance about context, an -element statement with "Initials" and "LastName" arguments:

```
efetch -db pubmed -id 1413997,6301692,781293 -format xml |
xtract -pattern PubmedArticle -element MedlineCitation/PMID \
  -element Initials LastName
```

will explore the current record for each argument separately, and thus print all author initials followed by all author last names:

```
1413997    RK    CR           JS         Mortimer      Contopoulou    King
6301692    MA    NR           Krasnow    Cozzarelli
781293     MJ    Casadaban
```

Inserting a -block statement redirects data exploration to consider each author one at a time. Subsequent -element statements only see the current author's values:

```
efetch -db pubmed -id 1413997,6301692,781293 -format xml |
xtract -pattern PubmedArticle -element MedlineCitation/PMID \
  -block Author -element Initials LastName
```

which restores the correct association of initials and last name:

```
1413997    RK    Mortimer     CR    Contopoulou    JS    King
6301692    MA    Krasnow      NR    Cozzarelli
781293     MJ    Casadaban
```

Adding a -sep statement to replace the normal tab between group members, and using a comma to combine the two arguments ("Initials,LastName") into a group:

```
efetch -db pubmed -id 1413997,6301692,781293 -format xml |
xtract -pattern PubmedArticle -element MedlineCitation/PMID \
  -block Author -sep " " -element Initials,LastName
```

results in more desirable formatting of author names:

```
1413997    RK Mortimer     CR Contopoulou    JS King
6301692    MA Krasnow      NR Cozzarelli
781293     MJ Casadaban
```

The first or last structured object can be selected by the -position statement:

```
efetch -db pubmed -id 1413997,6301692,781293 -format xml |
xtract -pattern PubmedArticle -element MedlineCitation/PMID \
  -block Author -position first -sep " " -element Initials,LastName
```

Exploring Separate XML Regions

Multiple -block statements can be used in a single xtract to explore different areas of the XML. This limits element extraction to the desired subregions, and allows disambiguation of fields with identical names.

Combining independent fields with commas allows them to be treated as sets. The tab that normally separates these can be replaced with a -sep argument:

```
efetch -db pubmed -id 6092233,4640931,4296474 -format xml |
xtract -pattern PubmedArticle -element MedlineCitation/PMID \
  -block AuthorList -sep "/" -element LastName "#Author" \
  -block PubDate -sep " " -element Year,Month MedlineDate |
sort -t $'\t' -k 3,3n -k 2,2f
```

This generates a table that allows easy parsing of author last names, counts the number of authors present, and prints the date each record was published, sorting the results by author count:

```
4296474    Friedmann                         1    1968 Apr
4640931    Tager/Steiner                     2    1972 Dec
6092233    Calderon/Contopoulou/Mortimer     3    1984 Jul-Aug
```

(Note that the PubDate object can exist either in a structured form:

```
<PubDate>
  <Year>1968</Year>
  <Month>Apr</Month>
  <Day>25</Day>
</PubDate>
```

(with the Day field frequently absent), or in a string form:

```
<PubDate>
  <MedlineDate>1984 Jul-Aug</MedlineDate>
</PubDate>
```

but would not contain a mixture of both types, so the directive:

```
-element Year,Month MedlineDate
```

will only contribute a single column to the output.)

Nested Exploration of Subsets Within XML Sets

Medical Subject Headings (MeSH terms) in a record may be assigned subheadings:

```
  ...
  <MeshHeading>
    <DescriptorName>RNA, Messenger</DescriptorName>
    <QualifierName>genetics</QualifierName>
  </MeshHeading>
  <MeshHeading>
```

```
      <DescriptorName>Transcription, Genetic</DescriptorName>
    </MeshHeading>
    <MeshHeading>
      <DescriptorName>beta-Galactosidase</DescriptorName>
      <QualifierName>genetics</QualifierName>
      <QualifierName>metabolism</QualifierName>
    </MeshHeading>
  </MeshHeadingList>
  ...
```

Visiting each MeSH term with a -block statement, and adding a -subset statement within the -block, allows nested exploration of the subheadings for the current MeSH term:

```
  efetch -db pubmed -id 6162838 -format xml |
  xtract -pattern PubmedArticle -tab "" -element MedlineCitation/PMID \
    -block MeshHeading -pfx "\n" -tab "" -element DescriptorName \
      -subset QualifierName -pfx " / " -tab "" -element QualifierName
```

and creates a list of MeSH terms with associated subheadings:

```
  6162838
  Base Sequence
  DNA, Recombinant
  Escherichia coli / genetics
  ...
  RNA, Messenger / genetics
  Transcription, Genetic
  beta-Galactosidase / genetics / metabolism
```

Selection of Attributes

The MeSH term and subheading fields actually have major topic attributes:

```
  ...
  <MeshHeading>
    <DescriptorName MajorTopicYN="N">beta-Galactosidase</DescriptorName>
    <QualifierName MajorTopicYN="Y">genetics</QualifierName>
    <QualifierName MajorTopicYN="N">metabolism</QualifierName>
  </MeshHeading>
  ...
```

that can be selected as "DescriptorName@MajorTopicYN" or "@MajorTopicYN":

```
  efetch -db pubmed -id 6162838 -format xml |
  xtract -pattern PubmedArticle -tab "" -element MedlineCitation/PMID \
    -block MeshHeading -pfx "\n" -sep "|" -tab "" \
      -element DescriptorName@MajorTopicYN,DescriptorName \
      -subset QualifierName -pfx " / " -sep "|" -tab "" \
        -element "@MajorTopicYN,QualifierName"
```

The major topic value is placed before each MeSH term or subheading:

```
  6162838
  N|Base Sequence
  Y|DNA, Recombinant
  N|Escherichia coli / N|genetics
  ...
  N|RNA, Messenger / Y|genetics
  N|Transcription, Genetic
  N|beta-Galactosidase / Y|genetics / N|metabolism
```

The results can be processed by the UNIX stream editor "sed":

```
sed -e 's/N|//g' -e 's/Y|/*/g'
```

to display an asterisk for major ("starred" MeSH term) concepts:

```
6162838
Base Sequence
*DNA, Recombinant
Escherichia coli / genetics
...
RNA, Messenger / *genetics
Transcription, Genetic
beta-Galactosidase / *genetics / metabolism
```

Recording Values in Variables

A value can be recorded in a variable and then displayed multiple times as needed. Variables are indicated by a hyphen followed by a string of capital letters or digits. The variable "-PMID" is referred to as "&PMID" in an -element argument. For example:

```
efetch -db pubmed -id 1413997,6301692,781293 -format xml |
xtract -pattern PubmedArticle -PMID MedlineCitation/PMID \
  -block Author -element "&PMID" \
    -sep " " -tab "\n" -element Initials,LastName
```

produces a list of authors, with the PMID in the first column of each row:

```
1413997    RK Mortimer
1413997    CR Contopoulou
1413997    JS King
6301692    MA Krasnow
6301692    NR Cozzarelli
781293     MJ Casadaban
```

Variable Initialization

Variables can be initialized with a literal value in parentheses:

```
efetch -db pubmed -id 1413997,6301692,781293 -format xml |
xtract -pattern PubmedArticle -element MedlineCitation/PMID \
  -block Author -sep " " -tab "" \
    -element "&COM" Initials,LastName -COM "(, )"
```

This can be used as a placeholder to prevent missing data from shifting columns in a table, or to have additional control over output formatting:

```
1413997    RK Mortimer, CR Contopoulou, JS King
6301692    MA Krasnow, NR Cozzarelli
781293     MJ Casadaban
```

All variables are reset when the next record is processed.

Conditional Processing

Xtract provides -if and -unless arguments that filter by element name or name plus data value. For example:

```
esearch -db pubmed -query "Cozzarelli NR [AUTH]" |
efetch -format xml |
xtract -pattern PubmedArticle -if "#Author" -eq 3 \
  -block Author -if LastName -is-not Cozzarelli \
    -sep ", " -tab "\n" -element LastName,Initials |
sort | uniq
```

will select papers with exactly 3 authors and print the coauthor names:

```
  Ackerman, RS
  Adams, DE
  Alexandrov, AI
  Arimondo, PB
  Bauer, WR
  ...
```

Multiple conditions are specified with -and and -or commands:

```
  -if @score -equals 1 -or @score -starts-with 0.9
```

The -else command can supply alternative -element or -lbl instructions to be run if the condition is not satisfied:

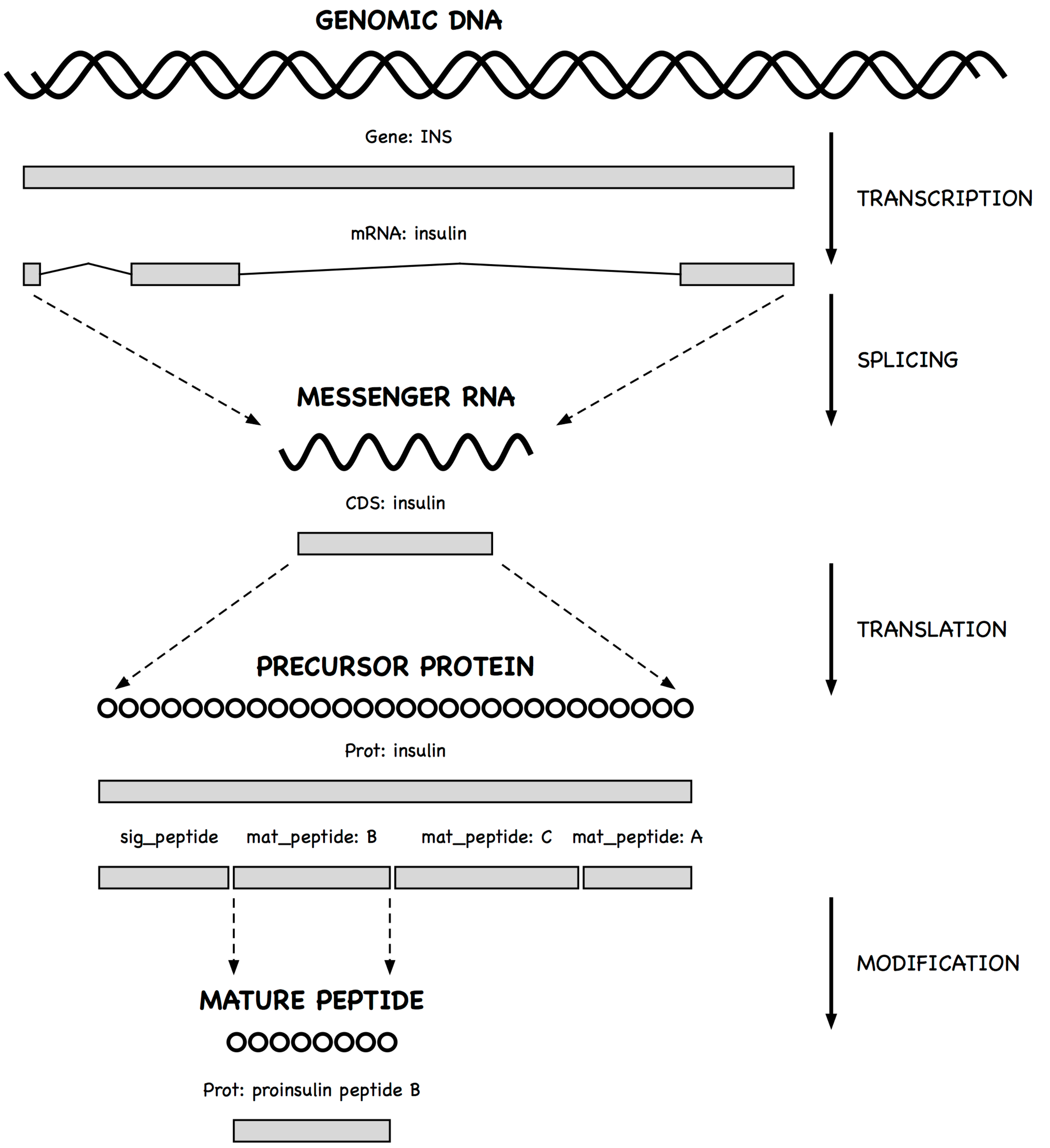
```
  -if MapLocation -element MapLocation -else -lbl "\-"
```

Parallel -if and -unless statements can be used to provide a more complex response to alternative conditions that includes nested exploration.

Sequence Records

NCBI Data Model for Sequence Records

The NCBI represents sequence records in a data model that is based on the central dogma of molecular biology. Sequences, including genomic DNA, messenger RNAs, and protein products, are "instantiated" with the actual sequence letters, and are assigned identifiers (e.g., accession numbers) for reference. Features carry information about the biology of a given region, with a location that refers to specific intervals on a particular sequence. Some features may also point to the product sequence of a particular transformation.



A gene feature indicates the location of a heritable region of nucleic acid that confers a measurable phenotype. An mRNA feature on genomic DNA represents the exonic and untranslated regions of the message that remain after transcription and splicing. A coding region (CDS) feature has a product reference to the translated protein.

Since messenger RNA sequences are not always submitted with a genomic region, CDS features (which model the travel of ribosomes on transcript molecules) are traditionally annotated on the genomic sequence, with locations that encode the exonic intervals.

Features display specific biological annotation in qualifiers. For example, the name of a gene is shown in the / gene qualifier. A qualifier can be dynamically generated from underlying data for the convenience of the user. Thus, the sequence of a mature peptide may be extracted from the mat_peptide feature's location on the precursor protein and displayed in a /peptide qualifier, even if a mature peptide is not instantiated.

Sequence Records in INSDSeq XML

Sequence records can be retrieved in an XML version of the GenBank or GenPept flatfile. The query:

```
efetch -db protein -id 26418308,26418074 -format gpc
```

returns a set of INSDSeq objects:

```
<INSDSet>
  <INSDSeq>
    <INSDSeq_locus>AAN78128</INSDSeq_locus>
    <INSDSeq_length>17</INSDSeq_length>
    <INSDSeq_moltype>AA</INSDSeq_moltype>
    <INSDSeq_topology>linear</INSDSeq_topology>
    <INSDSeq_division>INV</INSDSeq_division>
    <INSDSeq_update-date>03-JAN-2003</INSDSeq_update-date>
    <INSDSeq_create-date>10-DEC-2002</INSDSeq_create-date>
    <INSDSeq_definition>alpha-conotoxin ImI precursor, partial [Conus
       imperialis]</INSDSeq_definition>
    <INSDSeq_primary-accession>AAN78128</INSDSeq_primary-accession>
    <INSDSeq_accession-version>AAN78128.1</INSDSeq_accession-version>
    <INSDSeq_other-seqids>
      <INSDSeqid>gb|AAN78128.1|</INSDSeqid>
      <INSDSeqid>gi|26418308</INSDSeqid>
    </INSDSeq_other-seqids>
    <INSDSeq_source>Conus imperialis</INSDSeq_source>
    <INSDSeq_organism>Conus imperialis</INSDSeq_organism>
    <INSDSeq_taxonomy>Eukaryota; Metazoa; Lophotrochozoa; Mollusca;
       Gastropoda; Caenogastropoda; Hypsogastropoda; Neogastropoda;
       Conoidea; Conidae; Conus</INSDSeq_taxonomy>
    <INSDSeq_references>
      <INSDReference>
      ...
```

INSDSeq XML presents biological features and qualifiers (shown here in GenPept format):

```
FEATURES             Location/Qualifiers
     source          1..17
                     /organism="Conus imperialis"
                     /db_xref="taxon:35631"
                     /country="Philippines"
     Protein         <1..17
                     /product="alpha-conotoxin ImI precursor"
     mat_peptide     5..16
                     /product="alpha-conotoxin ImI"
                     /note="the C-terminal glycine of the precursor is post
                     translationally removed"
                     /calculated_mol_wt=1357
                     /peptide="GCCSDPRCAWRC"
     CDS             1..17
                     /coded_by="AY159318.1:<1..54"
                     /note="nAChR antagonist"
```

in a structured feature table:

```
...
<INSDFeature>
  <INSDFeature_key>mat_peptide</INSDFeature_key>
  <INSDFeature_location>5..16</INSDFeature_location>
  <INSDFeature_intervals>
    <INSDInterval>
      <INSDInterval_from>5</INSDInterval_from>
      <INSDInterval_to>16</INSDInterval_to>
      <INSDInterval_accession>AAN78128.1</INSDInterval_accession>
    </INSDInterval>
  </INSDFeature_intervals>
  <INSDFeature_quals>
    <INSDQualifier>
      <INSDQualifier_name>product</INSDQualifier_name>
      <INSDQualifier_value>alpha-conotoxin ImI</INSDQualifier_value>
    </INSDQualifier>
    <INSDQualifier>
      <INSDQualifier_name>note</INSDQualifier_name>
      <INSDQualifier_value>the C-terminal glycine of the precursor is
         post translationally removed</INSDQualifier_value>
    </INSDQualifier>
    <INSDQualifier>
      <INSDQualifier_name>calculated_mol_wt</INSDQualifier_name>
      <INSDQualifier_value>1357</INSDQualifier_value>
    </INSDQualifier>
    <INSDQualifier>
      <INSDQualifier_name>peptide</INSDQualifier_name>
      <INSDQualifier_value>GCCSDPRCAWRC</INSDQualifier_value>
    </INSDQualifier>
  </INSDFeature_quals>
</INSDFeature>
...
```

Feature and qualifier names are indicated in data values, not XML element tags, and require -if and -equals to select the desired object and content. The xtract -insd argument simplifies this process, as shown below.

Generating Qualifier Extraction Commands

Because obtaining specific qualifier values from INSDSeq XML is somewhat more complex than previous cases, the xtract -insd argument can be used to generate extraction instructions.

Running xtract -insd in an isolated command prints a new xtract statement that can then be copied, edited if necessary, and pasted into other queries. Running the -insd command within a multi-step pipe dynamically executes the constructed query.

Providing an optional (complete/partial) location indication, a feature key, and then one or more qualifier names:

```
xtract -insd complete mat_peptide "%peptide" product peptide
```

creates a new xtract statement that will produce a table of qualifier values from mature peptide features with complete locations. The statement starts with instructions to record the accession and find features of the indicated type:

```
xtract -pattern INSDSeq -ACCN INSDSeq_accession-version \
  -group INSDFeature -if INSDFeature_key -equals mat_peptide \
    -unless INSDFeature_partial5 -or INSDFeature_partial3 \
      -clr -pfx "\n" -element "&ACCN"
```

Each qualifier then generates custom extraction code that is appended to the growing query. For example:

```
-block INSDQualifier \
  -if INSDQualifier_name -equals peptide \
    -element INSDQualifier_value
```

Incorporating the xtract -insd command in a query for marine snail venom peptides:

```
esearch -db pubmed -query "conotoxin" |
elink -target protein |
efilter -query "mat_peptide [FKEY]" |
efetch -format gpc |
xtract -insd complete mat_peptide "%peptide" product peptide
```

produces a table with columns for accession number, calculated peptide length, product name, and peptide sequence:

```
AGO59814.1    32    del13b conotoxin       DCPTSCPTTCANGWECCKGYPCVRQHCSGCNH
AAO33169.1    16    alpha-conotoxin GIC    GCCSHPACAGNNQHIC
ADB65788.1    20    conotoxin Cal 16       LEMQGCVCNANAKFCCGEGR
AAN78128.1    12    alpha-conotoxin ImI    GCCSDPRCAWRC
AAF23167.1    31    BeTX toxin             CRAEGTYCENDSQCCLNECCWGGCGHPCRHP
ADB65789.1    20    conotoxin Cal 16       LEMQGCVCNANAKFCCGEGR
AAN78279.1    21    conotoxin Vx-II        WIDPSHYCCCGGGCTDDCVNC
ABW16858.1    15    marmophin              DWEYHAHPKPNSFWT
...
```

Piping the results to a series of UNIX commands:

```
grep -i conotoxin |
awk -F '\t' -v 'OFS=\t' '{if ( 10 <= $2 && $2 <= 30 ) print}' |
sort -t $'\t' -u -k 3,4 |
sort -t $'\t' -k 2,2n -k 3,3f |
cut -f 1,3- |
column -s $'\t' -t
```

filters by product name, limits the results to a specified range of peptide lengths, removes redundant accessions, sorts the table by peptide length, deletes the length column, and aligns the columns for cleaner printing:

```
AAN78128.1  alpha-conotoxin ImI            GCCSDPRCAWRC
AAN78127.1  alpha-conotoxin ImII           ACCSDRRCRWRC
ADB43130.1  conotoxin Cal 1a               KCCKRHHGCHPCGRK
ADB43131.1  conotoxin Cal 1b               LCCKRHHGCHPCGRT
AAO33169.1  alpha-conotoxin GIC            GCCSHPACAGNNQHIC
ADB43128.1  conotoxin Cal 5.1              DPAPCCQHPIETCCRR
AAD31913.1  alpha A conotoxin Tx2          PECCSHPACNVDHPEICR
ADB43129.1  conotoxin Cal 5.2              MIQRSQCCAVKKNCCHVG
ADD97803.1  conotoxin Cal 1.2              AGCCPTIMYKTGACRTNRCR
ADB65789.1  conotoxin Cal 16               LEMQGCVCNANAKFCCGEGR
AAD31912.1  alpha A conotoxin Tx1          PECCSDPRCNSSHPELCGGRR
AAN78279.1  conotoxin Vx-II                WIDPSHYCCCGGGCTDDCVNC
ADB43125.1  conotoxin Cal 14.2             GCPADCPNTCDSSNKCSPGFPG
ADD97802.1  conotoxin Cal 6.4              GCWLCLGPNACCRGSVCHDYCPR
CAH64846.1  four-loop conotoxin            CRPSGSPCGVTSICCGRCSRGKCT
AAD31915.1  O-superfamily conotoxin TxO2   CYDSGTSCNTGNQCCSGWCIFVCL
AAD31916.1  O-superfamily conotoxin TxO3   CYDGGTSCDSGIQCCSGWCIFVCF
AAD31920.1  omega conotoxin SVIA mutant 1  CRPSGSPCGVTSICCGRCYRGKCT
AAD31921.1  omega conotoxin SVIA mutant 2  CRPSGSPCGVTSICCGRCSRGKCT
ABE27010.1  conotoxin fe14.1               SPGSTICKMACRTGNGHKYPFCNCR
ABE27011.1  conotoxin fe14.2               SSGSTVCKMMCRLGYGHLYPSCGCR
```

```
  ABE27007.1  conotoxin p114.1               GPGSAICNMACRLGQGHMYPFCNCN
  ABE27008.1  conotoxin p114.2               GPGSAICNMACRLEHGHLYPFCHCR
  ABE27009.1  conotoxin p114.3               GPGSAICNMACRLEHGHLYPFCNCD
  ...
```

For records where a particular qualifier is missing:

```
  esearch -db protein -query "RAG1 [GENE] AND Mus musculus [ORGN]" |
  efetch -format gpc |
  xtract -insd source organism strain |
  sort -t $'\t' -u -k 2,3
```

a dash is inserted as a placeholder:

```
  P15919.2          Mus musculus                -
  AAO61776.1        Mus musculus                129/Sv
  NP_033045.2       Mus musculus                C57BL/6
  XP_006499075.1    Mus musculus                C57BL/6J
  EDL27655.1        Mus musculus                mixed
  BAD69530.1        Mus musculus castaneus      -
  BAD69531.1        Mus musculus domesticus     BALB/c
  BAD69532.1        Mus musculus molossinus     MOA
```

Sequence Coordinates

Gene Positions

An understanding of sequence coordinate conventions is necessary in order to use gene positions to retrieve the corresponding chromosome subregion with efetch or with the UCSC browser.

Sequence records displayed in GenBank or GenPept formats use a "one-based" coordinate system, with sequence position numbers starting at "1":

```
      1 catgccattc gttgagttgg aaacaaactt gccggctagc cgcatacccg cggggctgga
     61 gaaccggctg tgtgcggcca cagccaccat cctggacaaa cccgaagacg tgagtgaggg
    121 tcggcgagaa cttgtgggct agggtcggac ctcccaatga cccgttccca tccccaggga
    181 ccccactccc ctggtaacct ctgaccttcc gtgtcctatc ctcccttcct agatcccttc
    ...
```

Under this convention, positions refer to the sequence letters themselves:

```
  C   A   T   G   C   C   A   T   T   C
  1   2   3   4   5   6   7   8   9  10
```

and the position of the last base or residue is equal to the length of the sequence. The ATG initiation codon above is at positions 2 through 4, inclusive.

For computer programs, however, using "zero-based" coordinates can simplify the arithmetic used for calculations on sequence positions. The ATG codon in the 0-based representation is at positions 1 through 3. (The UCSC browser uses a hybrid, half-open representation, where the start position is 0-based and the stop position is 1-based.)

Software at NCBI will typically convert positions to 0-based coordinates upon input, perform whatever calculations are desired, and then convert the results to a 1-based representation for display. These transformations are done by simply subtracting 1 from the 1-based value or adding 1 to the 0-based value.

Coordinate Conversions

Retrieving the docsum for a particular gene:

```
esearch -db gene -query "BRCA2 [GENE] AND human [ORGN]" |
efetch -format docsum
```

returns the chromosomal position of that gene in 0-based coordinates:

```
...
<GenomicInfoType>
  <ChrLoc>13</ChrLoc>
  <ChrAccVer>NC_000013.11</ChrAccVer>
  <ChrStart>32315479</ChrStart>
  <ChrStop>32399671</ChrStop>
  <ExonCount>27</ExonCount>
</GenomicInfoType>
...
```

Piping the document summary to an xtract command:

```
xtract -pattern GenomicInfoType -element ChrAccVer ChrStart ChrStop
```

obtains the accession and 0-based coordinate values:

```
NC_000013.11    32315479    32399671
```

EFetch has -seq_start and -seq_stop arguments to retrieve a gene segment, but these expect the sequence subrange to be in 1-based coordinates.

To address this problem, two additional efetch arguments, -chr_start and -chr_stop, allow direct use of the 0-based coordinates:

```
efetch -db nuccore -format gb -id NC_000013.11 \
  -chr_start 32315479 -chr_stop 32399671
```

and eliminate the need for writing a UNIX shell command to increment the two values.

Xtract has numeric extraction commands to assist with coordinate conversion. Selecting fields with an -inc argument:

```
xtract -pattern GenomicInfoType -element ChrAccVer -inc ChrStart ChrStop
```

obtains the accession and 0-based coordinates, then increments the positions to produce 1-based values:

```
NC_000013.11    32315480    32399672
```

EDirect knows the policies for sequence positions in all relevant Entrez databases (e.g., gene, snp, dbvar), and provides additional shortcuts for converting these to other conventions. For example:

```
xtract -pattern GenomicInfoType -element ChrAccVer -1-based ChrStart ChrStop
```

understands that gene ChrStart and ChrStop fields are 0-based, sees that the desired output is 1-based, and translates the command to convert coordinates using the -inc argument. Similarly:

```
-element ChrAccVer -ucsc-based ChrStart ChrStop
```

leaves the 0-based start value unchanged but increments the original stop value to produce the half-open form that can be passed to the UCSC browser:

```
NC_000013.11    32315479    32399672
```

Complex Objects

Heterogeneous Data

XML objects can contain a heterogeneous mix of components. For example:

```
efetch -db pubmed -id 21433338,17247418 -format xml
```

returns a mixture of book and journal records:

```
<PubmedArticleSet>
  <PubmedBookArticle>
    <BookDocument>
    ...
    </PubmedBookData>
  </PubmedBookArticle>
  <PubmedArticle>
    <MedlineCitation>
    ...
    </PubmedData>
  </PubmedArticle>
</PubmedArticleSet>
```

The "Parent/*" construct is used to visit the individual components, even though they may have different names. Piping the XML output to:

```
xtract -pattern "PubmedArticleSet/*" -element "*"
```

separately prints the entirety of each XML component:

```
<PubmedBookArticle><BookDocument> ... </PubmedBookData></PubmedBookArticle>
<PubmedArticle><MedlineCitation> ... </PubmedData></PubmedArticle>
```

Use of the "Parent/Child" construct can isolate objects of the same name that differ by their location in the XML hierarchy. For example:

```
efetch -db pubmed -id 21433338,17247418 -format xml |
xtract -pattern "PubmedArticleSet/*" \
  -group "BookDocument/AuthorList" -tab "\n" -element LastName \
  -group "Book/AuthorList" -tab "\n" -element LastName \
  -group "Article/AuthorList" -tab "\n" -element LastName
```

writes separate lines for book/chapter authors, book editors, and article authors:

```
Fauci        Desrosiers
Coffin       Hughes        Varmus
Lederberg    Cavalli       Lederberg
```

Simply exploring with individual arguments:

```
-group BookDocument -block AuthorList -element LastName
```

would visit the editors (at BookDocument/Book/AuthorList) as well as the authors (at BookDocument/AuthorList), and print names in order of appearance in the XML:

```
Coffin    Hughes    Varmus    Fauci    Desrosiers
```

(In this particular example the book author lists could be distinguished by using -if "@Type" -equals authors or -if "@Type" -equals editors, but exploring by "Parent/Child" is a general position-based approach.)

Recursive Definitions

Certain XML objects returned by efetch are recursively defined, including Taxon in TaxaSet (-db taxonomy) and Gene-commentary in Entrezgene (-db gene). Thus, they can have nested objects with the same XML tag.

Retrieving a set of taxonomy records:

```
  efetch -db taxonomy -id 9606,7227 -format xml
```

produces XML with nested Taxon objects (marked below with line references) for each rank in the taxonomic lineage:

```
    <TaxaSet>
1     <Taxon>
        <TaxId>9606</TaxId>
        <ScientificName>Homo sapiens</ScientificName>
        ...
        <LineageEx>
2         <Taxon>
            <TaxId>131567</TaxId>
            <ScientificName>cellular organisms</ScientificName>
            <Rank>no rank</Rank>
3         </Taxon>
4         <Taxon>
            <TaxId>2759</TaxId>
            <ScientificName>Eukaryota</ScientificName>
            <Rank>superkingdom</Rank>
5         </Taxon>
          ...
        </LineageEx>
        ...
6     </Taxon>
7     <Taxon>
        <TaxId>7227</TaxId>
        <ScientificName>Drosophila melanogaster</ScientificName>
        ...
8     </Taxon>
    </TaxaSet>
```

Xtract tracks XML object nesting to determine that the <Taxon> start tag on line 1 is actually closed by the </Taxon> stop tag on line 6, and not by the first </Taxon> encountered on line 3.

When a recursive object is given to an exploration command, selection of data using the -element command:

```
  efetch -db taxonomy -id 9606,7227,10090 -format xml |
  xtract -pattern Taxon \
    -element TaxId ScientificName GenbankCommonName Division
```

does not examine fields in the internal objects, and returns information only for the main entries:

```
  9606     Homo sapiens               human          Primates
  7227     Drosophila melanogaster    fruit fly      Invertebrates
  10090    Mus musculus               house mouse    Rodents
```

The "*/Child" construct will skip past the outer start tag:

```
  efetch -db taxonomy -id 9606,7227,10090 -format xml |
  xtract -pattern Taxon -block "*/Taxon" \
    -tab "\n" -element TaxId,ScientificName
```

to visit the next level of nested objects individually:

```
131567    cellular organisms
2759      Eukaryota
33154     Opisthokonta
...
```

Recursive objects can be fully explored with a double-star-slash prefix:

```
esearch -db gene -query "DMD [GENE] AND human [ORGN]" |
efetch -format xml |
xtract -pattern Entrezgene -block "**/Gene-commentary" \
  -tab "\n" -element Gene-commentary_type@value,Gene-commentary_accession
```

which visits every child object regardless of nesting depth:

```
genomic    NC_000023
mRNA       XM_006724469
peptide    XP_006724532
mRNA       XM_011545467
peptide    XP_011543769
...
```

Advanced Topics

Storing Common Phrases in Alias Files

Long or complicated search phrases can be saved in a file to avoid having to retype (or copy and paste) the full text for each query. Each line of the file has a shortcut keyword, a tab character, and the expanded search term. Shortcuts are referenced by placing them in parentheses after prefixing with a pound ("#") sign.

For example, given a file named "q_aliases" containing:

```
jour_filt    [MULT] AND ncbijournals [FILT]
trans_imm    (transposition OR target) immunity
```

the esearch line in:

```
esearch -alias q_aliases -db nlmcatalog -query "Science (#jour_filt)" |
efetch -format docsum |
xtract -pattern DocumentSummary -element ISOAbbreviation \
  -subset ISSNInfo -sep "|" -element issn,issntype
```

will be expanded to:

```
esearch -db nlmcatalog -query "Science [MULT] AND ncbijournals [FILT]"
```

with the query producing:

```
J. Zhejiang Univ. Sci.    1009-3095|Print    1009-3095|Linking
Science (80- )            0193-4511|Print    0193-4511|Linking
Science                   0036-8075|Print    1095-9203|Electronic    ...
```

An alias file can also be read in a separate instruction at the beginning of a pipeline or script:

```
eproxy -alias q_aliases
```

For maximum flexibility, separate eproxy commands can be piped together to load multiple shortcut files, as long as the shortcut strings are all unique.

Additional EDirect Options

ESearch and EFilter can be given a -sort argument to specify the order of results when the records are retrieved:

```
esearch -db pubmed -query "opsin gene conversion" -sort "last author" |
efetch -format docsum |
xtract -pattern DocumentSummary -element Id LastAuthor PubDate Title
```

ELink can return links to the citation list using "-name pubmed_pubmed_citedin", but only for publications with full text deposited in PubMed Central (PMC). For example, the query:

```
esearch -db pubmed -query "Beadle GW [AUTH]" |
elink -related -name pubmed_pubmed_citedin |
efetch -format docsum |
xtract -pattern Author -element Name |
sort-uniq-count-rank |
head -n 10
```

produces a ranked list of the ten most cited authors:

```
13    Beadle GW
8     Ephrussi B
8     Glass NL
7     Hawley RS
7     Mitchell MB
7     PERKINS DD
7     Tatum EL
6     Mitchell HK
6     YANOFSKY C
5     Langley CH
```

Similarly, "-name pubmed_pubmed_refs" returns an article's reference list, again for publications deposited in PMC.

ELink has several command modes, and these can be specified with the -cmd argument. When not using the default "neighbor_history" command, elink will return an eLinkResult XML object, with the links for each UID presented in separate blocks. For example:

```
esearch -db pubmed -query "Hoffmann PC [AUTH] AND dopamine [MAJR]" |
elink -related -cmd neighbor |
xtract -pattern LinkSetDb -element Id
```

will show the original PMID in the first column and related article PMIDs in subsequent columns:

```
1504781    11754494    3815119    1684029    14614914    12128255    ...
1684029    3815119     1504781    8097798    17161385    14755628    ...
2572612    2903614     6152036    2905789    9483560     1352865     ...
...
```

When the elink command "prlinks" is used with "ref" mode, it can obtain HTML containing or referencing full text articles directly from the publishers. The UNIX "xargs" command calls elink separately for each identifier:

```
epost -db pubmed -id 22966225,19880848 |
efilter -query "freetext [FILT]" |
efetch -format uid |
xargs -n 1 elink -db pubmed -cmd prlinks -mode ref -http get -id
```

The elink -batch flag will bypass the Entrez history mechanism for large queries.

Xtract Special Topics

Self-closing tags of the standard form:

```
<Na-strand/>
```

or alternative form:

```
<Na-strand></Na-strand>
```

have no text content and thus cannot be selected with an -element command. If the tag contains an attribute:

```
<Seq-interval_strand>
  <Na-strand value="plus"/>
</Seq-interval_strand>
```

it can be selected by matching on the specified value:

```
-group Seq-interval_strand \
  -block Seq-interval_strand -if Na-strand@value -equals plus -lbl "+" \
  -block Seq-interval_strand -if Na-strand@value -equals minus -lbl "-"
```

The -pattern, -group, -block, and -subset commands provide a nested hierarchy of loop organizers for exploration of XML objects. Each pattern can contain multiple groups, each group can encompass multiple blocks, and each block can have multiple subsets.

Use of different argument names allows a linear representation of loop nesting, and provides sufficient flexibility to identify and extract arbitrary data from XML records in Entrez.

Sketching in pseudo code can clarify relative nesting levels. The extraction command:

```
xtract -pattern PubmedArticle \
  -block Author -element Initials,LastName \
  -block MeshHeading \
    -if QualifierName \
      -element DescriptorName \
      -subset QualifierName -element QualifierName
```

could be represented as a computer program in pseudo code by:

```
for each Pubmed record {
  for each Author {
    print Initials LastName
  }
  for each MeSH term {
    if Subheadings are present {
      print Term Name
      for each Subheading {
        print Subheading Name
      }
    }
  }
}
```

Extra arguments (-division, -branch, -section, and -unit) are held in reserve to provide additional levels of organization, should the need arise in the future for processing complex, deeply-nested XML data. The full set of commands, in order of rank, are:

```
-pattern
-division
```

```
-group
-branch
-block
-section
-subset
-unit
```

Starting xtract exploration with -block, and expanding with -group and -subset, leaves additional level names that can be used wherever needed without having to redesign the entire command.

Querying External Web Services

The EDirect nquire function can be used to obtain data from an arbitrary URL. Queries are built up from command-line arguments. For example:

```
nquire -url "https://eutils.ncbi.nlm.nih.gov/entrez/eutils/esearch.fcgi" \
  -db pubmed -term insulin
```

reads the URL and then tag/value pairs to generate an E-utilities query:

```
https://eutils. ... .gov/entrez/eutils/esearch.fcgi?db=pubmed&term=insulin
```

Paths can be separated into components, which are combined with slashes, so:

```
-url https://eutils.ncbi.nlm.nih.gov entrez/eutils efetch.fcgi
```

is converted to:

```
https://eutils.ncbi.nlm.nih.gov/entrez/eutils/efetch.fcgi
```

Multiple values between tags are combined with commas. Thus:

```
-db nuccore -id U54469 V00328 -rettype fasta
```

is transformed into:

```
db=nuccore&id=U54469,V00328&rettype=fasta
```

A value that starts with a hyphen (or minus sign) can be distinguished from a tag by prefixing it with a backslash, so:

```
nquire -url http://api.geonames.org/countryCode -lat 41.796 -lng "\-87.577"
```

will be sent as:

```
http://api.geonames.org/countryCode?lat=41.796&lng=-87.577
```

and will return "US" for coordinates within Chicago, which has a negative (western hemisphere) longitude value.

The -alias argument can read a file of shortcut keywords and URL aliases. The following aliases are always available:

```
ncbi_url      https://www.ncbi.nlm.nih.gov
eutils_url    https://eutils.ncbi.nlm.nih.gov/entrez/eutils
```

so the command:

```
nquire -url "(#eutils_url)" esearch.fcgi \
  -db gds -term "GSE22309 [ACCN] AND gse [ETYP]" -retmax 200
```

will run an ESearch query and return an eSearchResult XML object.

Raw XML with inconsistent line-wrapping and indentation can be reformatted for easier visual inspection of the data structure and content by piping it through:

```
xtract -format
```

Automation

Entrez Direct Commands Within Scripts

Taking an adventurous plunge into the world of programming, a shell script can be written when each output line of one step needs to be processed independently, instead of output being piped in its entirety to the next command. (The simplest shell script is merely a copy of a set of commands that are typed into the terminal for execution.)

In scripts, variables can be set to the results of a command by enclosing the statements in backtick ("`") characters. The variable name is prefixed by a dollar sign ("$") to use its value as an argument in another command. Comments start with a pound sign ("#") and are ignored. Quotation marks within quoted strings are entered by "escaping" with a backslash ("\"). Subroutines can be used to collect common code or simplify the organization of the script.

For example, executing a script file containing:

```
#!/bin/bash -norc

parse_fields() {
  echo "$1" |
  xtract -pattern Field \
    -pfx "[" -sfx "]" -element Name \
    -pfx "" -sfx "" -element FullName Description |
  sort -t $'\t' -k 2,2f | column -s $'\t' -t
}

dbs=`einfo -dbs | sort`

for db in $dbs
do
  eix=`einfo -db $db`
  flds=`parse_fields "$eix"`

  echo "$db"
  echo ""
  echo "$flds"
  echo ""

  sleep 1
done
```

will obtain the list of Entrez databases:

```
annotinfo
assembly
bioproject
...
```

and then return the abbreviations, names, and descriptions of indexed search fields, for each individual database:

```
...
mesh
```

```
  [ALL]   All Fields          All terms from all searchable fields
  [FILT]  Filter              Limits the records
  [MESH]  MeSH Terms          MeSH Terms
  [MHUI]  MeSH Unique ID      NLM MeSH Browser Unique ID
  [MULT]  Multi               Multi
  [PREV]  Previous Indexing   Previous Indexing
  [TYPE]  Record Type         Record type
  [REG]   Registry Number     Registry Number
  [NOTE]  Scope Note          Scope Note
  [ALSO]  See Also            See Also
  [SUBS]  Substance Name      Substance Name
  [WORD]  Text Word           Free text
  [TN]    Tree Number         Tree Number
  [UID]   UID                 Unique number assigned to publication
  ...
```

The shell script command:

```
  sleep 1
```

adds a one second delay between steps in a loop, and can be used to help prevent overuse of the Entrez servers by advanced scripts.

Xargs/Sh Loop

Writing a script to loop through data can sometimes be avoided by creative use of the UNIX xargs and sh commands. Within the "sh -c" command string, the last name and initials arguments (passed in pairs by "xargs -n 2") are substituted at the "$0" and "$1" variables. All of the commands in the sh string are run separately on each name:

```
  echo "Garber ED Casadaban MJ Mortimer RK" |
  xargs -n 2 sh -c 'esearch -db pubmed -query "$0 $1 [AUTH]" |
  xtract -pattern ENTREZ_DIRECT -lbl "$1 $0" -element Count'
```

This produces PubMed article counts for each author:

```
  ED Garber      35
  MJ Casadaban   46
  RK Mortimer    85
```

While Loop

A "while" loop can also be used to independently process lines of data. Given a file "organisms.txt" containing genus-species names, the UNIX "cat" command:

```
  cat organisms.txt
```

writes the contents of the file:

```
  Arabidopsis thaliana
  Caenorhabditis elegans
  Danio rerio
  Drosophila melanogaster
  Escherichia coli
  Homo sapiens
  Mus musculus
  Saccharomyces cerevisiae
```

This can be piped to a loop that reads one line at a time:

```
  while read org
  do
    esearch -db taxonomy -query "$org [LNGE] AND family [RANK]" < /dev/null |
    efetch -format docsum |
    xtract -pattern DocumentSummary -lbl "$org" \
      -element ScientificName Division
  done
```

looking up the taxonomic family name and BLAST division for each organism:

```
  Arabidopsis thaliana        Brassicaceae          eudicots
  Caenorhabditis elegans      Rhabditidae           nematodes
  Danio rerio                 Cyprinidae            bony fishes
  Drosophila melanogaster     Drosophilidae         flies
  Escherichia coli            Enterobacteriaceae    enterobacteria
  Homo sapiens                Hominidae             primates
  Mus musculus                Muridae               rodents
  Saccharomyces cerevisiae    Saccharomycetaceae    ascomycetes
```

(The "< /dev/null" input redirection construct prevents esearch from "draining" the remaining lines from stdin.)

For Loop

The same results can be obtained with organism names embedded in a "for" loop:

```
  for org in \
    "Arabidopsis thaliana" \
    "Caenorhabditis elegans" \
    "Danio rerio" \
    "Drosophila melanogaster" \
    "Escherichia coli" \
    "Homo sapiens" \
    "Mus musculus" \
    "Saccharomyces cerevisiae"
  do
    esearch -db taxonomy -query "$org [LNGE] AND family [RANK]" |
    efetch -format docsum |
    xtract -pattern DocumentSummary -lbl "$org" \
      -element ScientificName Division
  done
```

File Exploration

A for loop can also be used to explore the computer's file system:

```
  for i in *
  do
    if [ -f "$i" ]
    then
      echo $(basename "$i")
    fi
  done
```

visiting each file within the current directory. The asterisk ("*") character indicates all files, and can be replaced by any pattern (e.g., "*.txt") to limit the file search. The if statement "-f" operator can be changed to "-d" to find directories instead of files, and "-s" selects files with size greater than zero.

Processing in Groups

Because of technical limits in the Entrez link server, it may be necessary to perform an elink operation on a large set of records by using a function that splits unique identifiers or sequence accession numbers into smaller groups:

```
JoinIntoGroupsOf() {
  xargs -n "$@" echo |
  sed 's/ /,/g'
}
alias join-into-group-of='JoinIntoGroupsOf'
```

The following example will process sequence records in groups of 200 accessions at a time:

```
...
efetch -format acc |
join-into-groups-of 200 |
xargs -n 1 sh -c 'epost -db nuccore -format acc -id "$0" |
elink -target pubmed |
efetch -format abstract'
```

Local Data Cache

Entrez Direct users normally obtain selected data records with efetch, which makes calls to the efetch.fcgi network server. This solution works well when a few thousand records are needed, but it does not scale for much larger sets of data, where the time it takes to download becomes a limiting factor.

Random Access Archive

As an alternative, the entire set of PubMed records can be obtained by file transfer protocol, and can be kept current by retrieving daily update files. The release files can be decompressed and piped through xtract for bulk analysis, but they do not provide random access to individual records.

Recent advances in computer file system technology now allow all of these published journal article citations to be repackaged as individual files on an inexpensive 500 gigabyte external solid state drive, using a hierarchy of folders to organize the 28 million PubMed records. This approach uses pairs of digits in the PMID as nodes in the directory structure, providing direct and rapid access to any record. For example, PMID 12345678 would be stored (as a compressed XML file) at /Archive/12/34/56/12345678.xml.gz.

EDirect now includes an archive-pubmed script to fully automate the download, update, extraction, and storage process. The path to the dedicated solid state drive is passed to the script on the command-line:

```
archive-pubmed -path /Volumes/alexandria
```

It can be rerun on a daily or weekly basis to keep the archive up to date. Once the archive is populated, PMIDs can be piped to the fetch-pubmed script in order to retrieve PubmedArticle XML records from the local data cache. fetch-pubmed requires the path to the Archive subdirectory in order to find the data. For example:

```
esearch -db pubmed -query "cancer AND regulation" |
efetch -format uid |
fetch-pubmed -path /Volumes/alexandria/Archive
```

The -path argument is not needed by either script if an environment variable is set up in the user's .bash_profile configuration file:

```
export EDIRECT_PUBMED_MASTER=/Volumes/alexandria
```

and EDIRECT_PUBMED_MASTER is assumed to be set in subsequent examples.

Local Query Index

A similar divide-and-conquer strategy can be used to create a local information retrieval index suitable for large data mining queries. A second new script, index-pubmed, automates this activity. (It is a superset of archive-pubmed, and can also be run at regular intervals.)

For selected PubMed text fields (the title and primary abstract), the indexing process deletes hyphens after specific prefixes, removes accents and diacritical marks, splits words at punctuation characters, corrects encoding artifacts, and spells out Greek letters for easier searching on scientific terms. It then prepares inverted indices with term positions, and uses them to build distributed term lists and postings files.

For example, the term list that includes "cancer" would be located at /Postings/NORM/c/a/n/c/canc.trm. A query on cancer thus only needs to load a very small subset of the total index.

This design supports efficient Boolean expression evaluation (e.g., "(literacy AND numeracy) NOT (adolescent OR child)"), unrestricted wildcard truncation (e.g., "therap*"), phrase queries (e.g., "selective serotonin reuptake inhibitor"), and proximity searches (e.g., "vitamin c ~ ~ common cold").

Local Search Commands

The phrase-search script controls access to the local indices. The actual underlying work is done by the rchive program. Term counts are returned by -count (combining wildcard expansions into a single number) or by -counts (which expands wildcards and displays the individual terms and counts). Using -query returns the PMIDs that match the search expression.

For example, examining the term list with a truncated phrase:

```
phrase-search -count "catabolite repress*"
```

translates to:

```
rchive -path /Volumes/alexandria/Postings -count "catabolite repress*"
```

and returns the total counts of the individual words:

```
4325      catabolite
104977    repress*
```

Using -counts instead of -count returns the expanded terms and the individual postings counts:

```
4325     catabolite
12002    repress
1        repressa
5        repressable
1        repressae
1        repressant
2        repressants
1        repressc
1        represse
26322    repressed
1        repressedm
...
```

Searching with a phrase:

```
phrase-search -query "selective serotonin reuptake inhibitor*" |
fetch-pubmed
```

generates a list of PMIDs for records that contain the phrase, and then retrieves the relevant PubmedArticle XML from the local archive. Appending the query with [STEM] evaluates the same expression using words that have been processed through the Porter2 stemming algorithm.

XML Processing

In addition to -first and -last commands, xtract has other -element variants that return transformed versions of the selected data values. It also has methods that make it easy to wrap extracted values in XML tags for further processing by xtract.

Data Transformation

Numeric evaluation commands work on a set of data with the same tag names. For example, -num will count the number of named objects (with the -element "#Author" shortcut translated to -num Author). Integer values in XML objects can be added with -sum, and their arithmetic mean can be calculated with -avg. The number of characters in selected contents is returned by -len (with -element "%Title" implemented as -len Title).

Text and string commands work on individual string values. Sentences are split at punctuation marks with -words, or converted to upper case with -upper. The -year command returns the first four-digit token encountered in the data, so it works correctly with an integer Year or the semi-structured MedlineDate string. Applying -year to "PubDate/*" will examine the values of all internal objects, regardless of tag name, and is a general solution for obtaining the PubMed publication year.

The full set of -element variants can be seen by running xtract -help.

Sequential Processing

Data analysis frequently involves several sequential steps of text or numeric processing. Examining the growth of PubMed abstracts over time, for example, requires isolating individual words per abstract, counting the words per article, filtering the results by year, and then computing the average word count per year. The individual operations are all supported by xtract functions, so wrapping intermediate values in XML can eliminate the need for a separate script to perform the calculations.

Running an esearch query on articles published in a chosen journal, limiting the results to articles with abstracts, obtaining the individual PMIDs, and fetching the records from the local data cache:

```
esearch -db pubmed -query "PNAS [JOUR]" -pub abstract |
efetch -format uid |
fetch-pubmed
```

returns an XML PubmedArticleSet containing just over 115,000 PubmedArticle records. The next step will be to extract the year of publication and the individual words from the article's abstract. The desired fields in the original XML are:

```
...
<PubDate>
  <Year>2018</Year>
  ...
</PubDate>
...
<Abstract>
  <AbstractText>Ammonia plays a key role in the ....</AbstractText>
</Abstract>
...
```

Piping the PubmedArticleSet to an initial version of the extraction commands:

```
xtract -stops -pattern PubmedArticle \
  -year "PubDate/*" \
  -pfc "\n" -sep "\n" -words Abstract/AbstractText
```

prints the year and each individual abstract word on a separate line:

```
2018
ammonia
plays
a
key
role
in
the
neutralization
of
atmospheric
acids
...
```

Wrapping Results in XML

Customization arguments make it possible to wrap intermediate values (e.g., individual words per abstract, and word counts per article) back into XML form, so they can be sent to another xtract command for the next processing step. Piping the PubmedArticleSet to:

```
xtract -stops -head "<Set>" -tail "</Set>" -hd "<Rec>" -tl "</Rec>" \
  -pattern PubmedArticle \
  -pfx "<Year>" -sfx "</Year>" -year "PubDate/*" \
  -pfx "<Abst>" -sfx "</Abst>" -sep "</Abst><Abst>" \
  -words Abstract/AbstractText
```

allows extracted values to be written as structured XML fragments (shown reformatted for easier reading):

```
<Set>
  <Rec>
    <Year>2018</Year>
    <Abst>ammonia</Abst>
    <Abst>plays</Abst>
    <Abst>a</Abst>
    <Abst>key</Abst>
    <Abst>role</Abst>
    <Abst>in</Abst>
    <Abst>the</Abst>
    <Abst>neutralization</Abst>
    <Abst>of</Abst>
    <Abst>atmospheric</Abst>
    <Abst>acids</Abst>
    ...
```

The -wrp argument is a convenience that sets all of the appropriate customization arguments, shown above, given just the XML object names:

```
xtract -stops -wrp Set,Rec -pattern PubmedArticle \
  -wrp "Year" -year "PubDate/*" \
  -wrp "Abst" -words Abstract/AbstractText
```

making it easy to wrap the intermediate values.

The results are then piped to the next step, which uses -num to count the number of words that were in the abstract of each article:

```
xtract -wrp Set,Pub -pattern Rec \
  -wrp "Year" -element Year \
  -wrp "Num" -num Abst
```

again wrapping the results as structured XML:

```
<Set>
  <Pub><Year>2018</Year><Num>198</Num></Pub>
  <Pub><Year>2018</Year><Num>167</Num></Pub>
  <Pub><Year>2018</Year><Num>242</Num></Pub>
  ...
```

Redirecting the output with "> countsByYear.xml" saves the results in a file, to be used for all subsequent processing.

Selection of XML Subsets

The xtract -select argument allows record subsetting by data value, such as the year of publication. It acts as an "-if" statement, and is followed by conditionals, but with no -element, since its purpose is to pass along the entirety of all records that satisfy the condition.

This can be more convenient, and is significantly faster, than running a separate esearch query for each year, and it can look at data elements that are not indexed by Entrez. It is used in the loop below to limit the processed query results to one year at a time, passing the relevant subset to a second xtract command:

```
for yr in {1960..2018}
do
  cat countsByYear.xml |
  xtract -wrp Raw -pattern Pub -select Year -eq "$yr" |
  xtract -pattern Raw -lbl "$yr" -avg Num
done
```

that applies -avg to the word counts in order to compute the average number of abstract words per article for the current year:

```
1969    121
1970    119
1971    126
...
2016    207
2017    206
2018    205
```

This result can be saved by redirecting to a file, or it can be piped to:

```
tee /dev/tty |
xy-plot pnas.png
```

to print the data to the terminal and then display the results in graphical format. The last step should be:

```
rm countsByYear.xml
```

to remove the intermediate file.

Examples

Additional examples of using EDirect to answer ad hoc questions are shown in this section.

Author Frequency

Who are the most prolific authors on rattlesnake phospholipase?

```
esearch -db pubmed -query \
  "crotalid venoms [MAJR] AND phospholipase [TIAB]" |
efetch -format xml |
xtract -pattern PubmedArticle \
  -block Author -sep " " -tab "\n" -element LastName,Initials  |
sort-uniq-count-rank
```

This search produces:

```
74    Lomonte B
73    Gutiérrez JM
49    Soares AM
48    Marangoni S
43    Giglio JR
39    Bon C
...
```

Publication Distribution

When were the most papers about Legionnaires disease published?

```
esearch -db pubmed -query "legionnaires disease [TITL]" |
efetch -format docsum |
xtract -pattern DocumentSummary -element PubDate |
cut -c 1-4 |
sort-uniq-count-rank
```

reports the number of selected papers per year:

```
173    1979
102    1980
96     1978
92     1981
66     1983
...
```

Treatment Locations

What is the geographic distribution of sepsis treatment studies?

```
esearch -db pubmed -query \
  "sepsis/therapy [MESH] AND geographic locations [MESH]" |
efetch -format xml |
xtract -pattern PubmedArticle \
  -block MeshHeading -if DescriptorName@Type -equals Geographic \
    -tab "\n" -element DescriptorName |
sort-uniq-count-rank
```

returns the number of articles ranked by country (or region) of study:

```
567    United States
207    Spain
```

```
176     Great Britain
156     Germany
123     India
118     Europe
113     France
100     Taiwan
89      Japan
83      Thailand
75      Italy
74      England
...
```

Research History

What is the historic pattern of publication on diphtheria, pertussis, and tetanus?

```
#!/bin/bash
result=""
for disease in diphtheria pertussis tetanus
do
  current=`for (( yr = 2010; yr >= 1900; yr -= 10 ))
    do
      esearch -db pubmed -query "$disease [TITL] AND $yr:$((yr+9)) [PDAT]" |
      xtract -pattern ENTREZ_DIRECT -lbl "${yr}s" -element Count
    done`
  heading=`echo -e "${disease:0:4}" | tr [a-z] [A-Z]`
  current=`echo -e "Years\t$heading\n-----\t----\n$current"`
  if [ -n "$result" ]
  then
    result=`join -t $'\t' <(echo "$result") <(echo "$current")`
  else
    result=$current
  fi
done
echo "$result"
```

gives per-decade counts of relevant papers for each disease:

```
Years    DIPH    PERT    TETA
-----    ----    ----    ----
2010s    577     1708    914
2000s    892     1966    1344
1990s    1150    2661    1615
1980s    780     1746    1485
1970s    749     698     1524
1960s    1152    635     2086
1950s    1226    491     1540
1940s    452     173     239
1930s    157     26      46
1920s    128     5       21
1910s    83      7       41
1900s    93      3       28
```

Protein Homolog

Is there a mammalian equivalent of lycopene cyclase?

```
esearch -db protein -query \
  "lycopene beta cyclase [PROT] AND tomato [ORGN]" |
elink -related |
efetch -format gpc |
xtract -pattern INSDSeq -element INSDSeq_division |
sort-uniq-count-rank
```

In the resulting list of GenBank division codes:

```
  905    BCT
  856    ENV
  609    PLN
  197    CON
  127    PAT
  2      SYN
```

there are no similar sequences (protein neighbors) in the HUM, PRI, ROD, MAM, VRT, or INV divisions, so lycopene cyclase is not present in animals.

Longest Sequences

What are the longest known insulin precursor molecules?

```
  esearch -db protein -query "insulin [PROT]" |
  efetch -format docsum |
  xtract -pattern DocumentSummary -element Caption Slen Title |
  grep -v receptor | sort -k 2,2nr | head -n 5 | cut -f 1 |
  xargs -n 1 sh -c 'efetch -db protein -id "$0" -format gp > "$0".gpf'
```

Post-processing excludes the longer "insulin-like receptor" sequences and saves the GenPept results to individual files named by their sequence accessions:

```
  EFN61235.gpf
  EFN80340.gpf
  EGW08477.gpf
  EKC18433.gpf
  ELK28555.gpf
```

using the right angle bracket (">") UNIX output redirection character.

Archaea Enzyme

Which archaebacteria have chloramphenicol acetyltransferase?

```
  esearch -db protein -query \
    "chloramphenicol acetyltransferase [PROT] AND archaea [ORGN]" |
  efetch -format gpc |
  xtract -pattern INSDSeq -element INSDSeq_organism INSDSeq_definition |
  grep -i chloramphenicol | cut -f 1 | sort -f | uniq
```

produces a list of organism names:

```
  Methanobrevibacter ruminantium
  Methanobrevibacter smithii
  Methanosarcina acetivorans
  ...
```

Structural Similarity

What archaea structures are similar to snake venom phospholipase?

```
esearch -db structure -query "crotalus [ORGN] AND phospholipase A2" |
elink -related |
efilter -query "archaea [ORGN]" |
efetch -format docsum |
xtract -pattern DocumentSummary \
  -if PdbClass -equals Hydrolase \
    -element PdbDescr |
sort -f | uniq -i
```

This query uses geometric comparison (structure neighboring) to find proteins that are too divergent to be detected by sequence similarity with a BLAST search:

```
Crystal Structure Of Autoprocessed Form Of Tk-Subtilisin
Crystal Structure Of Ca2 Site Mutant Of Pro-S324a
Crystal Structure Of Ca3 Site Mutant Of Pro-S324a
...
```

Taxonomy Search

Which organisms contain an annotated RefSeq genome MatK gene?

```
esearch -db nuccore -query "MatK [GENE] AND NC_0:NC_999999999 [PACC]" |
efetch -format docsum |
xtract -pattern DocumentSummary -element TaxId |
sort -n | uniq |
epost -db taxonomy |
efetch -format docsum |
xtract -pattern DocumentSummary -element ScientificName |
sort
```

The first query obtains taxonomy UIDs from nucleotide document summaries and uploads them for separate retrieval from the taxonomy database:

```
Acidosasa purpurea
Acorus americanus
...
Zingiber spectabile
Zygnema circumcarinatum
```

Chromosome Locations

Where are mammalian calmodulin genes located?

```
esearch -db gene -query "calmodulin [PFN] AND mammalia [ORGN]" |
efetch -format docsum |
xtract -pattern DocumentSummary -MAP "(-)" -MAP MapLocation \
  -element Id Name "&MAP" ScientificName
```

The MAP variable is initialized with a literal dash to prevent missing data from shifting columns in the table:

```
801       CALM1    14q32.11     Homo sapiens
808       CALM3    19q13.32     Homo sapiens
805       CALM2    2p21         Homo sapiens
24242     Calm1    6q32         Rattus norvegicus
12313     Calm1    12 E         Mus musculus
326597    CALM     -            Bos taurus
50663     Calm2    6q12         Rattus norvegicus
24244     Calm3    1q21         Rattus norvegicus
12315     Calm3    7 9.15 cM    Mus musculus
12314     Calm2    17 E4        Mus musculus
```

```
  617095    CALM1    -            Bos taurus
  396838    CALM3    6            Sus scrofa
  ...
```

The -else command can also be used to insert placeholders for missing data:

```
  esearch -db gene -query "calmodulin [PFN] AND mammalia [ORGN]" |
  efetch -format docsum |
  xtract -pattern DocumentSummary \
    -if MapLocation -element Id Name MapLocation ScientificName \
      -else -element Id Name -lbl "\-" -element ScientificName
```

The -def command can achieve the same result for missing elements:

```
  esearch -db gene -query "calmodulin [PFN] AND mammalia [ORGN]" |
  efetch -format docsum |
  xtract -pattern DocumentSummary \
    -def "-" -element Id Name MapLocation ScientificName
```

Exon Counts

How many exons are in each dystrophin transcript variant?

```
  esearch -db gene -query "DMD [GENE] AND human [ORGN]" |
  efetch -format docsum |
  xtract -pattern DocumentSummary \
    -block GenomicInfoType -tab "\n" -element ChrAccVer,ChrStart,ChrStop |
```

This search returns the chromosome accession and the (0-based) gene start and stop positions:

```
  NC_000023.11    33339608    31119221
```

These are then passed to efetch in (0-based) -chr_start and -chr_stop arguments:

```
  xargs -n 3 sh -c 'efetch -db nuccore -format gbc \
    -id "$0" -chr_start "$1" -chr_stop "$2"' |
```

which converts them to (1-based) -seq_start and -seq_stop arguments and retrieves an INSDSeq XML subset record for the indicated region. That contains a number of alternatively-spliced dystrophin mRNA and CDS features.

Data extraction computes the number of intervals for each mRNA location (corresponding to individual exons or UTRs), and obtains the transcript sequence accession, transcript length, and product name from qualifiers:

```
  xtract -insd complete mRNA "#INSDInterval" \
    transcript_id "%transcription" product |
```

Final processing sorts by number of exons:

```
  grep -i dystrophin |
  sed 's/dystrophin, transcript variant //g' |
  sort -k 2,2nr -k 4,4nr
```

resulting in a table of exon counts and transcript lengths:

```
  NC_000023.11    79    NM_004010.3       14083    Dp427p2
  NC_000023.11    79    NM_000109.3       14069    Dp427c
  NC_000023.11    79    NM_004009.3       14000    Dp427p1
  NC_000023.11    79    NM_004006.2       13993    Dp427m
  NC_000023.11    78    XM_006724468.1    13920    X1
  NC_000023.11    78    XM_006724469.1    13802    X2
  NC_000023.11    77    XM_006724470.1    13881    X3
  ...
```

Genome Range

What genes are in a given range on the human Y chromosome?

```
  esearch -db gene -query "Homo sapiens [ORGN] AND Y [CHR]" |
  efilter -status alive | efetch -format docsum |
  xtract -pattern DocumentSummary -NAME Name -DESC Description \
    -block GenomicInfoType -if ChrLoc -equals Y \
      -min ChrStart,ChrStop -element "&NAME" "&DESC" |
  sort -k 1,1n | cut -f 2- |
  between-two-genes ASMT IL3RA
```

This query returns a table of gene names and descriptions, for the human "Y" chromosome, in the region between the ASMT and IL3RA genes:

```
  IL3RA           interleukin 3 receptor subunit alpha
  LOC101928032    uncharacterized LOC101928032
  LOC101928055    uncharacterized LOC101928055
  SLC25A6         solute carrier family 25 member 6
  LOC105373102    uncharacterized LOC105373102
  LINC00106       long intergenic non-protein coding RNA 106
  ASMTL-AS1       ASMTL antisense RNA 1
  ASMTL           acetylserotonin O-methyltransferase-like
  P2RY8           purinergic receptor P2Y8
  AKAP17A         A-kinase anchoring protein 17A
  ASMT            acetylserotonin O-methyltransferase
```

(The "-if ChrLoc -equals Y" test is necessary because certain genes (e.g., IL9R) are present in the pseudoautosomal regions common to both X and Y chromosomes:

```
  ...
  <GenomicInfo>
    <GenomicInfoType>
      <ChrLoc>Y</ChrLoc>
      <ChrAccVer>NC_000024.10</ChrAccVer>
      <ChrStart>57184100</ChrStart>
      <ChrStop>57197336</ChrStop>
      <ExonCount>10</ExonCount>
    </GenomicInfoType>
    <GenomicInfoType>
      <ChrLoc>X</ChrLoc>
      <ChrAccVer>NC_000023.11</ChrAccVer>
      <ChrStart>155997580</ChrStart>
      <ChrStop>156010816</ChrStop>
      <ExonCount>10</ExonCount>
    </GenomicInfoType>
  </GenomicInfo>
  ...
```

with each gene copy annotated in its own GenomicInfoType block.)

Gene Counts

How many genes are on each human chromosome?

```
  for chr in {1..22} X Y MT
  do
```

```
    esearch -db gene -query "Homo sapiens [ORGN] AND $chr [CHR]" |
    efilter -query "alive [PROP] AND genetype protein coding [PROP]" |
    efetch -format docsum |
    xtract -pattern DocumentSummary -NAME Name \
      -block GenomicInfoType -if ChrLoc -equals "$chr" \
        -tab "\n" -element ChrLoc,"&NAME" |
    sort | uniq | cut -f 1 | sort-uniq-count-rank
  done
```

returns a count of unique protein-coding genes per chromosome:

```
2067    1
1268    2
1071    3
755     4
873     5
1034    6
935     7
690     8
801     9
739     10
1288    11
1027    12
335     13
607     14
608     15
862     16
1181    17
277     18
1402    19
545     20
248     21
445     22
844     X
71      Y
13      MT
```

The range construct cannot be used for Roman numerals, so the equivalent query on Saccharomyces cerevisiae would need to explicitly list all chromosomes:

```
for chr in I II III IV V VI VII VIII IX X XI XII XIII XIV XV XVI MT
```

Plastid genes can be selected with "source plastid [PROP]".

Complete Genomes

What complete genomes are available for Escherichia coli?

```
esearch -db assembly -query \
  "Escherichia coli [ORGN] AND representative [PROP]" |
elink -target nuccore -name assembly_nuccore_refseq |
efetch -format docsum |
xtract -pattern DocumentSummary -element AccessionVersion Slen Title |
sed 's/,.*//' |
sort -t $'\t' -k 2,2nr
```

This search finds genomic assemblies and sorts the results by sequence length, allowing complete genomes to be easily distinguished from smaller plasmids:

```
NC_002695.1    5498450    Escherichia coli O157:H7 str. Sakai chromosome
NC_018658.1    5273097    Escherichia coli O104:H4 str. 2011C-3493 ...
NC_011751.1    5202090    Escherichia coli UMN026 chromosome
NC_011750.1    5132068    Escherichia coli IAI39 chromosome
NC_017634.1    4747819    Escherichia coli O83:H1 str. NRG 857C chromosome
NC_000913.3    4641652    Escherichia coli str. K-12 substr. MG1655
NC_017659.1    147060     Escherichia coli O83:H1 str. NRG 857C plasmid ...
...
```

The sed command removes extraneous text in the title (e.g., complete genome, complete sequence, primary assembly) after a comma.

A similar query for humans, additionally filtering out scaffolds, contigs, and plasmids:

```
esearch -db assembly -query "Homo sapiens [ORGN] AND representative [PROP]" |
elink -target nuccore -name assembly_nuccore_refseq |
efetch -format docsum |
xtract -pattern DocumentSummary -element AccessionVersion Slen Title |
sed 's/,.*//' | grep -v scaffold | grep -v contig | grep -v plasmid | sort
```

returns the assembled chromosome and mitochondrial sequence records:

```
NC_000001.11    248956422    Homo sapiens chromosome 1
NC_000002.12    242193529    Homo sapiens chromosome 2
NC_000003.12    198295559    Homo sapiens chromosome 3
NC_000004.12    190214555    Homo sapiens chromosome 4
NC_000005.10    181538259    Homo sapiens chromosome 5
NC_000006.12    170805979    Homo sapiens chromosome 6
NC_000007.14    159345973    Homo sapiens chromosome 7
NC_000008.11    145138636    Homo sapiens chromosome 8
NC_000009.12    138394717    Homo sapiens chromosome 9
NC_000010.11    133797422    Homo sapiens chromosome 10
NC_000011.10    135086622    Homo sapiens chromosome 11
NC_000012.12    133275309    Homo sapiens chromosome 12
NC_000013.11    114364328    Homo sapiens chromosome 13
NC_000014.9     107043718    Homo sapiens chromosome 14
NC_000015.10    101991189    Homo sapiens chromosome 15
NC_000016.10    90338345     Homo sapiens chromosome 16
NC_000017.11    83257441     Homo sapiens chromosome 17
NC_000018.10    80373285     Homo sapiens chromosome 18
NC_000019.10    58617616     Homo sapiens chromosome 19
NC_000020.11    64444167     Homo sapiens chromosome 20
NC_000021.9     46709983     Homo sapiens chromosome 21
NC_000022.11    50818468     Homo sapiens chromosome 22
NC_000023.11    156040895    Homo sapiens chromosome X
NC_000024.10    57227415     Homo sapiens chromosome Y
NC_012920.1     16569        Homo sapiens mitochondrion
```

This process can be automated to loop through a list of specified organisms:

```
for org in \
  "Agrobacterium tumefaciens" \
  "Bacillus anthracis" \
  "Escherichia coli" \
  "Neisseria gonorrhoeae" \
  "Pseudomonas aeruginosa" \
  "Shigella flexneri" \
  "Streptococcus pneumoniae"
do
  esearch -db assembly -query "$org [ORGN]" |
  efilter -query "representative [PROP]" |
  elink -target nuccore -name assembly_nuccore_refseq |
  efetch -format docsum |
  xtract -pattern DocumentSummary -element AccessionVersion Slen Title |
  sed 's/,.*//' |
  grep -v -i -e scaffold -e contig -e plasmid -e sequence -e patch |
  sort -t $'\t' -k 2,2nr
done
```

which generates:

```
  NC_011985.1    4005130    Agrobacterium radiobacter K84 chromosome 1
  NC_011983.1    2650913    Agrobacterium radiobacter K84 chromosome 2
  NC_005945.1    5228663    Bacillus anthracis str. Sterne chromosome
  NC_003997.3    5227293    Bacillus anthracis str. Ames chromosome
  NC_002695.1    5498450    Escherichia coli O157:H7 str. Sakai chromosome
  NC_018658.1    5273097    Escherichia coli O104:H4 str. 2011C-3493 ...
  NC_011751.1    5202090    Escherichia coli UMN026 chromosome
  NC_011750.1    5132068    Escherichia coli IAI39 chromosome
  NC_017634.1    4747819    Escherichia coli O83:H1 str. NRG 857C chromosome
  NC_000913.3    4641652    Escherichia coli str. K-12 substr. MG1655
  NC_002946.2    2153922    Neisseria gonorrhoeae FA 1090 chromosome
  NC_002516.2    6264404    Pseudomonas aeruginosa PAO1 chromosome
  NC_004337.2    4607202    Shigella flexneri 2a str. 301 chromosome
  NC_003028.3    2160842    Streptococcus pneumoniae TIGR4 chromosome
  NC_003098.1    2038615    Streptococcus pneumoniae R6 chromosome
```

Genes in Pathways

What genes are in the phenylketonuria pathway?

```
  esearch -db gene -query "PAH [GENE]" -organism human |
  elink -target biosystems |
  efilter -pathway wikipathways |
  elink -target gene |
  efetch -format docsum |
  xtract -pattern DocumentSummary -element Name Description |
  grep -v pseudogene | grep -v uncharacterized |
  sort -f
```

returns the entire set of genes in the selected biosystems:

```
  AANAT      aralkylamine N-acetyltransferase
  ACADM      acyl-CoA dehydrogenase medium chain
  ACHE       acetylcholinesterase (Cartwright blood group)
  ADCYAP1    adenylate cyclase activating polypeptide 1
  ...
```

Amino Acid Composition

What is the amino acid composition of human titin?

```
  abbrev=( Ala Asx Cys Asp Glu Phe Gly His Ile \
           Xle Lys Leu Met Asn Pyl Pro Gln Arg \
           Ser Thr Sec Val Trp Xxx Tyr Glx )
  efetch -db protein -id "Q8WZ42.4" -format gpc |
  xtract -pattern INSDSeq -element INSDSeq_sequence |
  tr A-Z a-z |
  sed 's/[^a-z]//g' |
  fold -w 1 |
  sort-uniq-count |
  while read num lttr
  do
    idx=$(printf %i "'$lttr'")
    ofs=$((idx-97))
    echo -e "${abbrev[$ofs]}\t$num"
  done |
  sort
```

produces a table of residue counts using the three-letter amino acid abbreviations:

```
  Ala    2084
  Arg    1640
  Asn    1111
  Asp    1720
  Cys    513
  Gln    942
  Glu    3193
  Gly    2066
  His    478
  Ile    2062
  Leu    2117
  Lys    2943
  Met    398
  Phe    908
  Pro    2517
  Ser    2463
  Thr    2546
  Trp    466
  Tyr    999
  Val    3184
```

Amino Acid Substitutions

What are the missense products of green-sensitive opsin?

```
  esearch -db gene -query "OPN1MW [GENE] AND human [ORGN]" |
  elink -target snp | efetch -format json |
  xtract -j2x -set - -rec RS |
  xtract -pattern RS -pfx "rs" -RSID RS/refsnp_id \
    -group protein -if name -contains missense \
      -block variant -element "&RSID" seq_id \
        inserted_sequence -tab "\n" -inc position |
  sort -t $'\t' -k 2,2 -k 4,4n -k 3,3f -k 1.3n | uniq
```

The query returns an intermediate table of non-synonymous amino acid substitutions (with 0-based location coordinates) derived from single nucleotide polymorphisms:

```
  rs1238141906    NP_000504.1    K    41
  rs1189783086    NP_000504.1    L    43
  rs1284438666    NP_000504.1    I    64
  rs1223726997    NP_000504.1    T    65
  ...
```

The rows are then processed in a while loop:

```
  while read rsid accn res pos
  do
    if [ "$accn" != "$last" ]
    then
```

```
      seq=$(efetch -db protein -id "$accn" -format gpc < /dev/null |
            xtract -pattern INSDSeq -element INSDSeq_sequence)
      last=$accn
    fi
    echo ">$rsid [$accn $res@$pos]"
    echo "${seq:0:$pos-1}$res${seq:$pos}" | fold -w 50
  done
```

to produce protein sequences with the individual residue substitutions in upper case:

```
  >rs1238141906 [NP_000504.1 K@41]
  maqqwslqrlagrhpqdsyedstqssiftytnsnstrgpfKgpnyhiapr
  wvyhltsvwmifvviasvftnglvlaatmkfkklrhplnwilvnlavadl
  aetviastisvvnqvygyfvlghpmcvlegytvslcgitglwslaiiswe
  ...
```

3'UTR Sequences

What are the 3' UTR sequences for lycopene cyclase?

```
  ThreePrimeUTRs() {
    xtract -pattern INSDSeq -ACC INSDSeq_accession-version -SEQ INSDSeq_sequence \
      -group INSDFeature -if INSDFeature_key -equals CDS -PRD "(-)" \
        -block INSDQualifier -if INSDQualifier_name \
          -equals product -PRD INSDQualifier_value \
        -block INSDFeature -pfc "\n" -element "&ACC" -rst \
          -last INSDInterval_to -element "&SEQ" "&PRD" |
    while read acc pos seq prd
    do
      if [ $pos -lt ${#seq} ]
      then
        echo -e ">$acc 3'UTR: $((pos+1))..${#seq} $prd"
        echo "${seq:$pos}" | fold -w 50
      elif [ $pos -ge ${#seq} ]
      then
        echo -e ">$acc NO 3'UTR"
      fi
    done
  }

  esearch -db nuccore -query "5.5.1.19 [ECNO]" |
  efilter -molecule mrna -source refseq |
  efetch -format gbc | ThreePrimeUTRs
```

prints the sequences immediately following the CDS stop codon:

```
  >NM_001328461.1 3'UTR: 1737..1871 lycopene beta cyclase, chloroplastic
  gatgaatatagagttactgtgttgtaagctaatcatcatactgatgcaag
  tgcattatcacatttacttctgctgatgattgttcataagattatgagtt
  agccatttatcaaaaaaaaaaaaaaaaaaaaaaaaa
  >NM_001316759.1 3'UTR: 1628..1690 lycopene beta cyclase, chloroplastic
  atccgagtaattcggaatcttgtccaattttatatagcctatattaatac
  ...
```

Upstream Sequences

What sequences are upstream of phenylalanine hydroxylase genes?

```
  esearch -db nuccore -query "U49897 [ACCN]" |
  elink -target gene |
  elink -target homologene |
  elink -target gene |
  efetch -format docsum |
  xtract -pattern DocumentSummary -if GenomicInfoType -element Id \
    -block GenomicInfoType -element ChrAccVer ChrStart ChrStop |
  awk -F '\t' -v 'OFS=\t' '{print $1, $2, $3+1, $4+1}'
```

obtains a series of homologous genes, converting the gene coordinates to 1-based positions suitable for retrieving sequence regions:

```
5053      NC_000012.12    102917603    102838326
18478     NC_000076.6     87521795     87584137
38871     NT_037436.4     7760453      7763166
24616     NC_005106.4     28066639     28129772
378962    NC_007115.6     17420391     17402704
...
```

Given a shell script named "upstream.sh":

```
#!/bin/bash -norc

bases=1500
if [ -n "$1" ]
then
  bases=$1
fi

while read id accn start stop
do
  if [[ $start -eq 0 || $stop -eq 0 || $start -eq $stop ]]
  then
    echo "Skipping $id due to ambiguous coordinates"
    continue
  fi
  if [ $start -gt $stop ]
  then
    stop=$(( start + bases ))
    start=$(( start + 1 ))
    strand=2
  else
    stop=$(( start - 1 ))
    start=$(( start - bases ))
    strand=1
  fi
  rslt=`efetch -db nuccore -id $accn -format fasta \
        -seq_start $start -seq_stop $stop -strand $strand < /dev/null`
  echo "$rslt"
done
```

the data lines can be piped through:

```
upstream.sh 500
```

to extract and print the 500 nucleotides immediately upstream of each gene. (Without the argument it will default to 1500 nucleotides.)

Author Combinations

What are the authorship patterns among selected individuals?

The "coauthors.sh" script takes author name arguments to construct a custom data extraction command for analyzing research collaboration patterns:

```
#!/bin/bash -norc

if [ "$#" -lt 2 ]
then
  echo "Must supply at least two author names"
  exit 1
fi

query="xtract -pattern PubmedArticle -element MedlineCitation/PMID"

# append a -block statement for each author argument
for auth in "$@"
do
  query=`echo "$query -block Author -if LastName -equals \"$auth\"" \
              "-sep \" \" -element LastName,Initials"`
done

query=`echo "$query | sort -t \$'\\t' -k 2f -k 1,1n"`

if [ -t 0 ]
then
  # stand-alone command, print constructed query for later use
  echo "$query"
else
  # dynamically execute query on XML data piped to script
  res=`eval "$query"`
  echo "$res"
fi
```

If XML publication data are piped to the script, it will read the data and immediately execute the generated xtract query. Otherwise, if called as a stand-alone command, it will print the custom query instructions for later use.

Running the following command:

```
esearch -db pubmed -query "Casadaban MJ [AUTH] OR Berg CM [AUTH]" |
efetch -format xml |
./coauthors.sh Casadaban Groisman Berg Garber |
./extract-fuse.pl pubmed > author_patterns.htm
```

first produces an internal result table of PMIDs grouped by author combination:

```
...
7635839    Casadaban MJ
9634770    Casadaban MJ
1827084    Casadaban MJ    Groisman EA
2954879    Casadaban MJ    Groisman EA
3020001    Casadaban MJ    Groisman EA
3525518    Casadaban MJ    Groisman EA
3542967    Casadaban MJ    Groisman EA
6324195    Casadaban MJ    Groisman EA
3301525    Casadaban MJ    Groisman EA    Berg CM
```

The sorted lines are then piped to the "extract-fuse.pl" script:

```
#!/usr/bin/perl
```

```
my $max = scalar @ARGV;
if ( $max < 1 ) {
  die "Need argument for database\n";
}
my $db = $ARGV[0];

my $thisline = "";
my $laststr = "";
my $str = "";
my $uid = "";
my $uidlist = "";
my $count = 0;
my $base = "https://www.ncbi.nlm.nih.gov";

my $pfx = "";
while ($thisline = <STDIN>) {
  $thisline =~ s/\r//;
  $thisline =~ s/\n//;

  if ($thisline =~ /^([^\t]+)\t(.+)$/) {
    $uid = $1;
    $str = $2;

    if ( lc ($str) ne lc ($laststr) and $laststr ne "" ) {
      $laststr =~ s/\t/, /g;
      print "<p>(<a href=\"$base/$db/$uidlist\">";
      print " $count </a>) - $laststr</p>\n";
      $pfx = "";
      $count = 0;
      $uidlist = "";
    }
    $laststr = $str;

    $uidlist .= "$pfx$uid";
    $pfx = ",";
    $count++;
  }
}

if ( $laststr ne "" ) {
  $laststr =~ s/\t/, /g;
  print "<p>(<a href=\"$base/$db/$uidlist\">";
  print " $count </a>) - $laststr</p>\n";
}
```

which combines them into PubMed query URLs, one for each author pattern:

```
https://www.ncbi.nlm.nih.gov/pubmed/1827084,2954879,3020001,...
```

Those are then wrapped, along with a record count, in the appropriate HTML tags for web display. If the resulting file is opened with a browser, it presents an argument-order-dependent view of author collaboration:

```
( 55 ) - Berg CM

( 10 ) - Berg CM, Berg DE

( 1 ) - BERG CM, GARBER ED

( 6 ) - Berg DE, Berg CM
( 39 ) - Casadaban MJ

( 6 ) - Casadaban MJ, Groisman EA

( 1 ) - Casadaban MJ, Groisman EA, Berg CM
```

Clicking on a hyperlinked record count number opens the document summary or individual article page, so the actual publications can be examined.

Indexed Fields

What date fields are indexed for PubMed?

```
einfo -db pubmed |
xtract -pattern Field \
  -if IsDate -equals Y -and IsHidden -equals N \
    -pfx "[" -sfx "]" -element Name \
    -pfx "" -sfx "" -element FullName |
sort -k 2f | expand
```

This produces a list of field abbreviations and names filtered by index type:

```
[CDAT]  Date - Completion
[CRDT]  Date - Create
[EDAT]  Date - Entrez
[MHDA]  Date - MeSH
[MDAT]  Date - Modification
[PDAT]  Date - Publication
```

Digital Object Identifiers

How are digital object identifiers obtained from PubMed articles?

```
esearch -db pubmed -query "Rowley JD [AUTH]" |
efetch -format xml |
xtract -head '<html><body>' -tail '</body></html>' \
  -pattern PubmedArticle -PMID MedlineCitation/PMID \
  -block ArticleId -if @IdType -equals doi \
  -tab '\n' -pfx '<p><a href="http://dx.doi.org/' \
  -sep '">' -sfx '</a></p>' -encode ArticleId,"&PMID"
```

extracts the DOIs and constructs the appropriate URL references:

```
<html><body>
<p><a href="http://dx.doi.org/10.1038/leu.2013.340">24496283</a></p>
<p><a href="http://dx.doi.org/10.1073/pnas.1310656110">23818607</a></p>
<p><a href="http://dx.doi.org/10.1126/science.1241318">23788787</a></p>
...
```

These intermediate lines are then piped through:

```
xtract -format
```

to produce a minimal HTML document with clickable links:

```
<?xml version="1.0"?>
<!DOCTYPE html>
<html>
  <body>
    <p>
```

```
        <a href="http://dx.doi.org/10.1038/leu.2013.340">24496283</a>
      </p>
      <p>
        <a href="http://dx.doi.org/10.1073/pnas.1310656110">23818607</a>
      </p>
      ...
    </body>
  </html>
```

Phrase Searching

Can phrase searching be simulated in Entrez?

The "entrez-phrase-search" script included with EDirect takes advantage of the fact that some short phrases are indexed in certain Entrez fields. Given an input phrase, the script generates overlapping pairs of adjacent words, separately queries on each pair to determine which are present in the pubmed title or abstract index, and keeps those that appear in at least 10 articles. Independent phrases are separated by a plus ("+") sign.

For example, running the following command:

```
  entrez-phrase-search -db pubmed -field WORD \
    selective serotonin reuptake inhibitor + monoamine oxidase inhibitor
```

will generate word pairs from each phrase and run a query on each pair. The individual term counts are:

```
  11343    selective serotonin
  11892    serotonin reuptake
   6714    reuptake inhibitor
  21722    monoamine oxidase
   3680    oxidase inhibitor
```

The combined query will return a search result with 36 articles, and these can then be retrieved by piping to efetch. The script in its current form will not match phrases with plurals (e.g., serotonin reuptake inhibitors) or hyphens (e.g., monoamine-oxidase inhibitor).

Gene-Protein Links

What proteins are produced by a given gene?

Given a query in the gene database, the following commands:

```
  esearch -db gene -query "beta galactosidase [PFN]" |
  elink -target protein -name gene_protein_refseq -cmd neighbor |
  xtract -pattern LinkSet -element Id
```

will show the gene ID in the first column and linked RefSeq protein UIDs in subsequent columns.

Piping the results to a Perl script named "gene-protein-links.pl" will read the identifiers and run separate efetch queries on the gene and protein databases:

```
  #!/usr/bin/perl

  while ($line = <STDIN>) {

    chomp ($line);
    @uids = split( /\t/, $line);
    $gene = $uids [0];
    $proteins = join (',', @uids [1..$#uids]);
    $symbol = $data = '';

    $cmd = "efetch -format docsum -db gene -id $gene | ";
    $cmd .= "xtract -pattern DocumentSummary -element Name CommonName";
    open (CMD, "$cmd|");
    while (<CMD>) {
      $symbol .= $_;
    }
    close CMD;

    if ($proteins ne "") {
      $cmd = "efetch -format docsum -db protein -id $proteins | ";
      $cmd .= "xtract -pattern DocumentSummary -element Caption Slen Title";
      open (CMD, "$cmd|");
      while (<CMD>) {
        $data .= $_;
      }
      close CMD;
    }

    print "$symbol$data\n";
  }
```

printing the gene symbol and organism common name, followed by the protein accessions, lengths, and titles:

```
  GLB1            human
  NP_001129074    546    beta-galactosidase isoform c preproprotein ...
  NP_001073279    647    beta-galactosidase isoform b [Homo sapiens]
  NP_000395       677    beta-galactosidase isoform a preproprotein ...

  Glb1            house mouse
  NP_033882       647    beta-galactosidase preproprotein [Mus musculus]

  Glb1            Norway rat
  NP_001101662    647    beta-galactosidase precursor [Rattus norvegicus]
  ...
```

Bulk Downloads

How can the entire set of GenBank records for mammals be obtained?

```
  ftp-ls ftp.ncbi.nlm.nih.gov genbank |
  grep ".seq.gz" |
  grep -e gbmam -e gbpri -e gbrod |
  while read file
  do
    ftp-cp ftp.ncbi.nlm.nih.gov genbank "$file"
    gzcat "$file"
    rm "$file"
  done
```

will use the ftp-ls and ftp-cp scripts (included with the EDirect software) to retrieve and print GenBank flatfiles for human, primate, rodent, and other mammals:

```
  GBMAM1.SEQ          Genetic Sequence Data Bank
                          February 15 2015

                  NCBI-GenBank Flat File Release 206.0
```

```
                Other Mammalian Sequences (Part 1)

     20709 loci,   155323216 bases, from    20709 reported sequences


LOCUS       AB000170                2732 bp    mRNA    linear   MAM ...
DEFINITION  Sus scrofa mRNA for endopeptidase 24.16, complete cds.
ACCESSION   AB000170
VERSION     AB000170.1  GI:1783121
KEYWORDS    endopeptidase 24.16 type M3; endopeptidase 24.16 type M1.
SOURCE      Sus scrofa (pig)
  ORGANISM  Sus scrofa
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata;
            Euteleostomi; Mammalia; Eutheria; Laurasiatheria;
            Cetartiodactyla; Suina; Suidae; Sus.
REFERENCE   1
  AUTHORS   Kato,A., Sugiura,N., Saruta,Y., Hosoiri,T., Yasue,H. and
            Hirose,S.
  TITLE     Targeting of endopeptidase 24.16 to different subcellular
            compartments by alternative promoter usage
  JOURNAL   J. Biol. Chem. 272 (24), 15313-15322 (1997)
   PUBMED   9182559
REFERENCE   2  (bases 1 to 2732)
  AUTHORS   Hirose,S.
  TITLE     Direct Submission
  JOURNAL   Submitted (27-DEC-1996) Shigehisa Hirose, Tokyo Institute of
            Technology, Department of Biological Sciences; 4259
            Nagatsuta-cho, Midori-ku, Yokohama, Kanagawa 226-8501, Japan
FEATURES             Location/Qualifiers
     source          1..2732
                     /organism="Sus scrofa"
                     /mol_type="mRNA"
                     /db_xref="taxon:9823"
                     /tissue_type="Liver"
                     /dev_stage="Adult"
                     /note="porcine"
     mRNA            1..2732
                     /note="corresponding to exon1,5-16 of this gene;
                     endopeptidase 24.16 type 1"
     CDS             175..2289
                     /standard_name="endopeptidase 24.16"
                     /note="oligopeptidase M :neurolysin :sBAP(soluble
                     angiotensin-binding protein) :MEP(microsomal
                     metalloendopeptidase)"
                     /codon_start=1
                     /product="endopeptidase 24.16 type M1"
                     /protein_id="BAA19060.1"
                     /db_xref="GI:1783122"
                     ...
```

For systems with Aspera Connect installed, the asp-ls and asp-cp scripts can be used for faster retrieval:

```
asp-ls genbank |
grep ".seq.gz" |
grep -e gbmam -e gbpri -e gbrod |
while read file
do
  asp-cp genbank "$file"
  gzcat "$file"
```

```
    rm "$file"
  done
```

Appendices

Setting Contact Address and Script Name

EDirect automatically obtains the user's e-mail address from the system, to have someone to notify in case a runaway script causes problems with an Entrez server, but if another contact address is desired (e.g., that of a system administrator or software developer) it can be explicitly set at the beginning of a pipeline or script:

```
  econtact -email author_email_address -tool name_of_script
```

That way the NCBI has information on who to contact if an infinite loop in a script accidentally abuses NCBI resources. (For convenience, the preferred e-mail address and software tool name can also be set in all E-utilities-calling operations.)

Command-Line Arguments

Arguments for the EDirect functions are listed below:

Use esearch to start a new Entrez search on indexed terms:

```
  Query Specification

    -db          Database name
    -query       Query string

  Document Order

    -sort        Result presentation order

  Date Constraint

    -days        Number of days in the past
    -datetype    Date field abbreviation
    -mindate     Start of date range
    -maxdate     End of date range

  Limit by Field

    -field       Query words individually in field
    -pairs       Query overlapping word pairs

  Spell Check

    -spell       Correct misspellings in query

  Miscellaneous Arguments

    -label       Alias for query step
```

The elink function looks up related articles or associated records:

```
  Destination Database

    -related    Neighbors in same database
    -target     Links in different database
    -name       Link name (e.g., pubmed_protein_refseq)

  Direct Record Selection

    -db         Database name
    -id         Unique identifier(s)

  Advanced Control

    -cmd        Command type (returns eLinkResult XML)
    -mode       "ref" uses LinkOut provider's web site
    -holding    Name of LinkOut provider

  PubMed Citation Lookup

    -cited      References to this paper
    -cites      Publication reference list

  Batch Processing

    -batch      Bypass Entrez history mechanism

  Miscellaneous Arguments

    -label      Alias for query step
```

Use efilter to restrict search or link results by indexed terms:

```
  Query Specification

    -query       Query string

  Document Order

    -sort        Result presentation order

  Date Constraint

    -days        Number of days in the past
    -datetype    Date field abbreviation
    -mindate     Start of date range
    -maxdate     End of date range

  Limit by Field

    -field       Query words individually in field
    -pairs       Query overlapping word pairs

  Spell Check

    -spell       Correct misspellings in query

  Publication Filters

    -pub         abstract, clinical, english, free, historical,
                 journal, medline, preprint, published, review,
                 structured
    -journal     pnas, "j bacteriol", ...
    -released    last_week, last_month, last_year, prev_years
  Sequence Filters

    -country     usa:minnesota, united_kingdom, "pacific ocean", ...
    -feature     gene, mrna, cds, mat_peptide, ...
    -location    mitochondrion, chloroplast, plasmid, plastid
    -molecule    genomic, mrna, trna, rrna, ncrna
    -organism    animals, archaea, bacteria, eukaryotes, fungi,
                 human, insects, mammals, plants, prokaryotes,
                 protists, rodents, viruses
    -source      genbank, insd, pdb, pir, refseq, swissprot, tpa

  Gene Filters
    -status      alive
    -type        coding, pseudo

  SNP Filters

    -class       acceptor, donor, frameshift, indel, intron,
                 missense, nonsense, synonymous

  Biosystems Filters

    -kind        pathway
    -pathway     reactome, wikipathways

  Miscellaneous Arguments

    -label       Alias for query step
```

The record retrieval function is efetch:

```
  Format Selection

    -format        Format of record or report
    -mode          text, xml, asn.1, json
    -style         withparts, conwithfeat

  Direct Record Selection

    -db            Database name
    -id            Unique identifier or accession number

  Sequence Range

    -seq_start     First sequence position to retrieve
    -seq_stop      Last sequence position to retrieve
    -strand        1 = forward DNA strand, 2 = reverse complement
    -revcomp       Shortcut for strand 2

  Gene Range

    -chr_start     Sequence range from 0-based coordinates
    -chr_stop        in gene docsum GenomicInfoType object

  Sequence Flags

    -complexity    0 = default, 1 = bioseq, 3 = nuc-prot set
    -extend        Extend sequence retrieval in both directions
    -extrafeat     Bit flag specifying extra features

  Subset Retrieval

    -start         First record to fetch
    -stop          Last record to fetch

  Miscellaneous

    -raw           Skip database-specific XML modifications
    -json          Convert adjusted XML output to JSON
```

The xtract function is used for processing XML data:

```
  Processing Flags

    -strict          Remove HTML and MathML tags
    -mixed           Allow mixed content XML

    -accent          Excise Unicode accents and diacritical marks
    -ascii           Unicode to numeric HTML character entities
    -compress        Compress runs of spaces

    -stops           Retain stop words in selected phrases

  Data Source

    -input           Read XML from file instead of stdin
    -transform       File of substitutions for -translate

  Exploration Argument Hierarchy

    -pattern         Name of record within set
    -group             Use of different argument
    -block               names allows command-line
    -subset                control of nested looping

  Path Navigation

    -path            Explore by list of adjacent object names

  Exploration Constructs

    Object           DateRevised
    Parent/Child     Book/AuthorList
    Path             MedlineCitation/Article/Journal/JournalIssue/PubDate
    Heterogeneous    "PubmedArticleSet/*"
    Exhaustive       "History/**"
    Nested           "*/Taxon"
    Recursive        "**/Gene-commentary"

  Conditional Execution

    -if              Element [@attribute] required
    -unless          Skip if element matches
    -and             All tests must pass
    -or              Any passing test suffices
    -else            Execute if conditional test failed
    -position        [first|last|outer|inner|even|odd|all]
```

```
String Constraints

  -equals          String must match exactly
  -contains        Substring must be present
  -is-within       String must be present
  -starts-with     Substring must be at beginning
  -ends-with       Substring must be at end
  -is-not          String must not match
  -is-before       First string < second string
  -is-after        First string > second string
  -matches         Matches without commas or semicolons
  -resembles       Requires all words, but in any order

Object Constraints

  -is-equal-to     Object values must match
  -differs-from    Object values must differ

Numeric Constraints

  -gt              Greater than
  -ge              Greater than or equal to
  -lt              Less than
  -le              Less than or equal to
  -eq              Equal to
  -ne              Not equal to

Format Customization

  -ret             Override line break between patterns
  -tab             Replace tab character between fields
  -sep             Separator between group members
  -pfx             Prefix to print before group
  -sfx             Suffix to print after group
  -rst             Reset -sep through -elg
  -clr             Clear queued tab separator
  -pfc             Preface combines -clr and -pfx
  -deq             Delete and replace queued tab separator
  -def             Default placeholder for missing fields
  -lbl             Insert arbitrary text

XML Generation

  -wrp             Wrap elements in XML object
  -plg             Prologue to print before elements
  -elg             Epilogue to print after elements
  -fwd             Foreword to print before set
  -awd             Afterword to print after set

Element Selection

  -element         Print all items that match tag name
  -first           Only print value of first item
  -last            Only print value of last item
  -NAME            Record value in named variable

-element Constructs
```

```
  Tag               Caption
  Group             Initials,LastName
  Parent/Child      MedlineCitation/PMID
  Recursive         "**/Gene-commentary_accession"
  Unrestricted      "PubDate/*"
  Attribute         DescriptorName@MajorTopicYN
  Range             MedlineDate[1:4]
  Substring         "Title[phospholipase | rattlesnake]"
  Object Count      "#Author"
  Item Length       "%Title"
  Element Depth     "^PMID"
  Variable          "&NAME"

Special -element Operations

  Parent Index      "+"
  Object Name       "?"
  XML Subtree       "*"
  Children          "$"
  Attributes        "@"

Numeric Processing

  -num              Count
  -len              Length
  -sum              Sum
  -min              Minimum
  -max              Maximum
  -inc              Increment
  -dec              Decrement
  -sub              Difference
  -avg              Average
  -dev              Deviation
  -med              Median
  -mul              Product
  -div              Quotient
  -mod              Remainder
  -bin              Binary
  -bit              Bit Count

String Processing

  -encode           URL-encode <, >, &, ", and ' characters
  -plain            Remove embedded mixed-content markup tags
  -upper            Convert text to upper-case
  -lower            Convert text to lower-case
  -chain            Change_spaces_to_underscores
  -title            Capitalize initial letters of words
  -order            Rearrange words in sorted order
  -year             Extract first 4-digit year from string
  -translate        Substitute values with -transform table

Text Processing

  -terms            Partition text at spaces
  -words            Split at punctuation marks
  -pairs            Adjacent informative words
  -reverse          Reverse words in string
  -letters          Separate individual letters
```

```
    -clauses          Break at phrase separators

  Sequence Processing

    -revcomp          Reverse-complement nucleotide sequence
    -nucleic          Subrange determines forward or revcomp
    -molwt            Calculate molecular weight of peptide

  Sequence Coordinates

    -0-based          Zero-Based
    -1-based          One-Based
    -ucsc-based       Half-Open

  Command Generator

    -insd             Generate INSDSeq extraction commands

  -insd Argument Order

    Descriptors       INSDSeq_sequence INSDSeq_definition INSDSeq_division
    Flags             [complete|partial]
    Feature(s)        CDS,mRNA
    Qualifiers        INSDFeature_key "#INSDInterval" gene product sub_sequence

  Frequency Table

    -histogram        Collects data for sort-uniq-count on entire set of records

  Entrez Indexing

    -e2index          Create Entrez index XML
    -indices          Index normalized words

  Miscellaneous

    -head             Print before everything else
    -tail             Print after everything else
    -hd               Print before each record
    -tl               Print after each record

  Reformatting

    -format           [copy|compact|flush|indent|expand]
                        [-unicode fuse|space|period|brackets|markdown|slash|tag]
                        [-script brackets|markdown]
                        [-mathml terse]

  Modification

    -filter           Object
                        [retain|remove|encode|decode|shrink|expand|accent]
                          [content|cdata|comment|object|attributes|container]

  Validation

    -verify           Report XML data integrity problems

  Summary
```

```
    -outline         Display outline of XML structure
    -synopsis        Display individual XML paths
    -contour         Display XML paths to leaf nodes
                       [delimiter]

  Record Selection

    -select          Select record subset by conditions
    -retaining       File of identifiers to use for selection
    -excluding       Exclude records listed in identifier file
    -appending       Identifier-tab-metadata must be in record order

  Data Conversion

    -j2x             Convert JSON stream to XML suitable for -path navigation
                       [-set setWrapper]
                       [-rec recordWrapper]
                       [-nest flat|recurse|plural|depth]

    -t2x             Convert tab-delimited table to XML
                       [-set setWrapper]
                       [-rec recordWrapper]
                       [-skip linesToSkip]
                       [-lower | -upper]
                       [-indent | -flush]
                       XML object names per column

  Documentation

    -examples        Examples of EDirect and xtract usage
```

The einfo function returns information on Entrez indexed fields:

```
  Database Selection

    -db        Database name
    -dbs       Get all database names

  Data Summaries

    -fields    Print field names
    -links     Print link names
```

Several additional functions are provided by EDirect:

```
  epost

    -db        Database name
    -id        Unique identifier(s) or accession number(s)
    -format    uid or acc
    -input     Read from file instead of stdin
    -label     Alias for query step

  eproxy

    -alias     File of aliases
    -pipe      Read aliases from stdin
```

```
econtact

  -email     Contact person's address
  -tool      Name of script or program

nquire

  -get       Uses HTTP GET instead of POST
  -url       Base URL for external search
```

In addition, -email and -tool are available in all E-utilities-calling functions to override default values, -http get will force the use of GET instead of POST, -alias will specify a file of shortcut keywords and query strings or URL sections, and -help will print the list of arguments for each function.

For debugging, -silent will suppress link failure retry messages, -verbose will display the <ENTREZ_DIRECT> field values at each step, -debug will print the internal URL query and XML results of each step, and -base will specify a particular server for quality assurance testing.

EFetch Formats

EFetch -format and -mode values for each database are shown below:

-db	-format	-mode	Report Type
(all)			
	docsum		DocumentSummarySet XML
	docsum	json	DocumentSummarySet JSON
	full		Same as native except for mesh
	uid		Unique Identifier List
	url		Entrez URL
	xml		Same as -format full -mode xml
bioproject			
	native		BioProject Report
	native	xml	RecordSet XML
biosample			
	native		BioSample Report
	native	xml	BioSampleSet XML
biosystems			
	native	xml	Sys-set XML
clinvar			
	variation		Older Format
	variationid		Transition Format
	vcv		VCV Report
	clinvarset		RCV Report
gds			
	native	xml	RecordSet XML
	summary		Summary
gene			
	full_report		Detailed Report
	gene_table		Gene Table
	native		Gene Report

```
               native              asn.1    Entrezgene ASN.1
               native              xml      Entrezgene-Set XML
               tabular                      Tabular Report

homologene
               alignmentscores              Alignment Scores
               fasta                        FASTA
               homologene                   Homologene Report
               native                       Homologene List
               native              asn.1    HG-Entry ASN.1
               native              xml      Entrez-Homologene-Set XML

mesh
               full                         Full Record
               native                       MeSH Report
               native              xml      RecordSet XML

nlmcatalog
               native                       Full Record
               native              xml      NLMCatalogRecordSet XML

pmc
               bioc                         PubTator Central BioC XML
               medline                      MEDLINE
               native              xml      pmc-articleset XML

pubmed
               abstract                     Abstract
               bioc                         PubTator Central BioC XML
               medline                      MEDLINE
               native              asn.1    Pubmed-entry ASN.1
               native              xml      PubmedArticleSet XML

(sequences)
               acc                          Accession Number
               est                          EST Report
               fasta                        FASTA
               fasta               xml      TinySeq XML
               fasta_cds_aa                 FASTA of CDS Products
               fasta_cds_na                 FASTA of Coding Regions
               ft                           Feature Table
               gb                           GenBank Flatfile
               gb                  xml      GBSet XML
               gbc                 xml      INSDSet XML
               gene_fasta                   FASTA of Gene
               gp                           GenPept Flatfile
               gp                  xml      GBSet XML
               gpc                 xml      INSDSet XML
               gss                          GSS Report
               ipg                          Identical Protein Report
               ipg                 xml      IPGReportSet XML
               native              text     Seq-entry ASN.1
               native              xml      Bioseq-set XML
               seqid                        Seq-id ASN.1

snp
               json                         Reference SNP Report

sra
```

```
               native            xml      EXPERIMENT_PACKAGE_SET XML
               runinfo           xml      SraRunInfo XML

  structure
               mmdb                       Ncbi-mime-asn1 strucseq ASN.1
               native                     MMDB Report
               native            xml      RecordSet XML

  taxonomy
               native                     Taxonomy List
               native            xml      TaxaSet XML
```

ESearch Sort Order

ESearch -sort values for several databases are listed below:

```
  -db          -sort
  ___          _____

  gene
               Chromosome
               Gene Weight
               Name
               Relevance

  geoprofiles
               Default Order
               Deviation
               Mean Value
               Outliers
               Subgroup Effect

  pubmed
               First Author
               Journal
               Last Author
               Pub Date
               Recently Added
               Relevance
               Title

  (sequences)
               Accession
               Date Modified
               Date Released
               Default Order
               Organism Name
               Taxonomy ID

  snp
               Chromosome Base Position
               Default Order
               Heterozygosity
               Organism
               SNP_ID
               Success Rate
```

ELink Commands

ELink -cmd options produce results as LinkSet XML:

-cmd	Result
neighbor	Neighbors or links
neighbor_score	Neighbors with computed similarity scores
acheck	All links available
ncheck	Existence of neighbors
lcheck	Existence of external links (LinkOuts)
llinks	Non-library LinkOut providers
llinkslib	All LinkOut providers
prlinks	Primary LinkOut provider, or URL for single UID with -mode ref

EInfo Data

EInfo field data contains status flags for several term list index properties:

```
<Field>
  <Name>ALL</Name>
  <FullName>All Fields</FullName>
  <Description>All terms from all searchable fields</Description>
  <TermCount>138982028</TermCount>
  <IsDate>N</IsDate>
  <IsNumerical>N</IsNumerical>
  <SingleToken>N</SingleToken>
  <Hierarchy>N</Hierarchy>
  <IsHidden>N</IsHidden>
  <IsTruncatable>Y</IsTruncatable>
  <IsRangable>N</IsRangable>
</Field>
```

UNIX Utilities

Several useful classes of UNIX text processing filters, with selected arguments, are presented below:

Process by Contents:

```
sort    Sorts lines of text

  -f    Ignore case
  -n    Numeric comparison
  -r    Reverse result order

  -k    Field key (start,stop or first)
  -u    Unique lines with identical keys

  -b    Ignore leading blanks
  -s    Stable sort
```

```
    -t    Specify field separator

  uniq    Removes repeated lines

    -c    Count occurrences
    -i    Ignore case

    -f    Ignore first n fields
    -s    Ignore first n characters

    -d    Only output repeated lines
    -u    Only output non-repeated lines

  grep    Matches patterns using regular expressions

    -i    Ignore case
    -v    Invert search
    -w    Search expression as a word
    -x    Search expression as whole line

    -e    Specify individual pattern

    -c    Only count number of matches
    -n    Print line numbers
```

Regular Expressions:

```
  Characters

    .     Any single character (except newline)
    \w    Alphabetic [A-Za-z], numeric [0-9], or underscore (_)
    \s    Whitespace (space or tab)
    \     Escapes special characters
    []    Matches any enclosed characters

  Positions

    ^     Beginning of line
    $     End of line
    \b    Word boundary

  Repeat Matches

    ?     0 or 1
    *     0 or more
    +     1 or more
    {n}   Exactly n
```

Modify Contents:

```
  sed     Replaces text strings

    -e    Specify individual expression

  tr      Translates characters

    -d    Delete character

  rev     Reverses characters on line
```

Format Contents:

```
  column  Aligns columns by content width

    -s    Specify field separator
    -t    Create table

  expand  Aligns columns to specified positions

    -t    Tab positions

  fold    Wraps lines at a specific width

    -w    Line width
    -s    Fold at spaces
```

Filter by Position:

```
  cut     Removes parts of lines

    -c    Characters to keep
    -f    Fields to keep
    -d    Specify field separator

    -s    Suppress lines with no delimiters

  head    Prints first lines

    -n    Number of lines

  tail    Prints last lines

    -n    Number of lines
```

Miscellaneous:

```
  wc      Counts words, lines, or characters

    -c    Characters
    -l    Lines
    -w    Words

  xargs   Constructs arguments

    -n    Number of words per batch
```

File Compression:

```
  tar     Archive files

    -c    Create archive
    -f    Name of output file
    -z    Compress archive with gzip

  gzip    Compress file

    -k    Keep original file
    -9    Best compression

  unzip   Decompress .zip archive
```

```
    -p    Pipe to stdout

  gzcat   Decompress .gz archive and pipe to stdout
```

Directory and File Navigation:

```
  cd      Changes directory

    /     Root
    ~     Home
    .     Current
    ..    Parent
    -     Previous

  ls      Lists file names

    -1    One entry per line
    -a    Show files beginning with dot (.)
    -l    List in long format
    -R    Recursively explore subdirectories
    -S    Sort files by size
    -t    Sort by most recently modified

  pwd     Prints working directory path
```

Additional documentation with detailed explanations and examples can be obtained by typing "man" followed by a command name.

Terminal Keyboard Shortcuts

Control and escape sequences can be used within a terminal session to navigate through the command history and to move the cursor for editing the command currently being entered:

Command history:

```
  Ctrl-n     Next command
  Ctrl-p     Previous command
```

Move cursor forward:

```
  Ctrl-e     To end of line
  Ctrl-f     By one character
  Esc-f      By one argument
```

Move cursor backward:

```
  Ctrl-a     To beginning of line
  Ctrl-b     By one character
  Esc-b      By one argument
```

Delete:

```
  Del        Previous character
  Ctrl-d     Next character
  Ctrl-k     To end of line
  Ctrl-u     Entire line
  Ctrl-w     Previous word
  Esc-Del    Previous argument
  Esc-d      Next argument
```

Autocomplete:

```
  Tab       Completes directory or file names
```

Program control:

```
  Ctrl-c    Quit running program
  ^x^y      Run last command replacing x with y
```

(Note that Control sequences are typed by holding down Control, hitting the other key, and releasing Control, while Escape sequences are typed by hitting Escape and then hitting the other key.)

Release Notes

EDirect Version 13.6: April 17, 2020

- Efilter -db snp -class shortcuts mappings updated to reflect changes to FXN index.
- Xtract adds -matches and -resembles string conditional tests, -order string processing command.
- Minor change to term granularity for MeSH [TREE] index creation.

EDirect Version 13.5: February 21, 2020

- Xtract -select -streaming uses case-insensitive test, concurrent processing.
- Minor change to term granularity for reenabled [CODE] index creation.

EDirect Version 13.4: February 4, 2020

- Local [CONV] term list indexes GNBR theme plus relationship plus identifier pair.
- Theme indexing splits genes at semicolons, adds M prefix to OMIM, H to ChEBI identifiers.
- Run "source theme-aliases" to load commands for navigating theme identifier connections.

EDirect Version 13.3: January 28, 2020

- Index-extras downloads newest version of Global Network of Biomedical Relationships theme data.
- Xtract -contour replaces -synopsis -leaf variant.

EDirect Version 13.2: January 7, 2020

- Expand-current can be run after archive-pubmed as well as index-pubmed.

EDirect Version 13.1: December 30, 2019

- Local index only builds TREE fields for A, C, D, E, F, G, and Z categories.
- Stop word list now includes "studies" and "study" in addition to "studied".
- Xtract -select driver file command names changed to -retaining, -excluding, and -appending.
- New efetch -format types documented for -db clinvar.
- Updated MeSH tree category descriptions in phrase-search -help.

EDirect Version 13.0: December 16, 2019

- Xtract -histogram collects data for sort-uniq-count on entire set of records.
- Xtract -wrp with empty string or dash resets -sep, -pfx, -sfx, -plg, and -elg customization values.
- Xtract -fwd and -awd print once before and once after a set of object instances.
- Xtract -t2x uses asterisk before column name to indicate XML contents, will not escape angle brackets in string.

EDirect Version 12.9: December 9, 2019

- Xtract -plain, an -element variant that removes embedded mixed-content markup, now also converts Unicode subscripts/superscripts, cleans bad spaces.
- Xtract -select -in changed to -select -using.
- Xtract -select -adding matches by identifier and appends XML metadata.
- Xtract -select -merging requires original records and identifier-metadata file to be in same order.
- Moved xtract -examples text to separate hlp-xtract.txt file.
- Efetch -format asn maps to -format asn.1.
- Disabled building of [CODE] field in local index.
- Minor changes to term granularity for faster local index creation.
- Index-pubmed takes optional [-collect | -index | -invert | -merge | -promote] argument to resume processing in an intermediate step.

EDirect Version 12.8: December 3, 2019

- Xtract -molwt sequence processing command added.
- Xtract -len triggers -def instead of returning 0 for missing object.
- Xtract -pairs does not drop the first component of hyphenated terms (e.g., site-specific).
- Xtract -synopsis with optional -leaf argument only reports content nodes.
- Adjusted test-eutils -esummary dbvar test.
- Local archive asks user to check TRIM status on slow update.
- Local archive checks that volume is actually a solid-state drive.

EDirect Version 12.7: November 21, 2019

- Local archive detects slow performance, reminds user about antivirus scanning and content indexing.
- Local archive warns if Mac file system is not APFS, prints instructions on how to reformat drive.
- Xtract -examples adds namespace prefix and Base64 decoding example.
- Efetch -db nucleotide/nuccore -style withparts/conwithfeat processes -id accession list one record at a time.

EDirect Version 12.6: November 15, 2019

- Added support for automatic fallback to IPv4.
- Xtract -insd adds mol_wt as a synonym for calculated_mol_wt.
- Changed granularity of local index for [YEAR] field.
- If archiving is slow, ask user to ensure that antivirus scanning and content indexing are disabled.

EDirect Version 12.5: November 6, 2019

- Efetch -start and -stop subset retrieval arguments are now documented.
- Efetch -format docsum rescues uid attribute if no existing <Id> tag, now using case-sensitive test to prevent <id> from blocking.
- Added efetch -revcomp flag, sets -strand 2.
- Einfo sorts -fields and -links results by tag name.
- Fixed stdin-vs-argument bug in ftp-cp introduced when moving code into edirect.pl for Anaconda issue.
- Local search system [THME] field also indexes disambiguated themes - Jc (chemical-disease) and Jg (gene-disease) - under original code J (role in disease pathogenesis).

EDirect Version 12.4: October 28, 2019

- Expanded README file to cover more advanced features of potential interest to codeathon participants.
- Elink -released also accepts four-digit year.
- Local search system builds separate [CODE] and [TREE] indices for MeSH code and hierarchy values.

EDirect Version 12.3: October 23, 2019

- Added single-line copy-and-execute commands, in curl and wget flavors, as convenient options for EDirect installation.
- Elink -db pubmed supports -cited and -cites to follow reference connections from the NIH Open Citation Collection dataset.
- Added missing retry code to esearch and esummary.
- Xtract -t2x converts tab-delimited table to XML.
- Xtract -sort rearranges records by designated identifier.
- Xtract -split breaks up a large XML stream into multiple files.
- Xtract -chain changes_spaces_to_underscores.
- Efetch -db gtr -format docsum -mode json downloads in smaller groups to avoid timeouts.
- Nquire -get does not need -url command if followed immediately by URL argument.
- Consolidated code for perl-based commands (e.g., nquire, transmute) into master edirect.pl script.
- Wrappers to all perl-based commands now handle conflict with Anaconda installation.
- Moved external resource indexing code from xtract to rchive.
- Added phrase-search -filter command to pipe efetch -format uid results into local query.
- Download-ncbi-data script updated to use desc2020.xml and supp2020.xml for mesh lookup table.
- Experimental index-extras script loads natural language processing results into local retrieval system.
- Experimental fetch-extras scripts retrieves indexed NLP fields per PMID saved in local archive.

EDirect Version 12.2: September 27, 2019

- Added install-edirect.sh script, with download link in web documentation, for easier installation.
- Updated setup.sh script to ask permission to edit the PATH setting in the user's .bash_profile file.
- Xtract -is-before and -is-after tests compare order of strings.
- Xtract -mul, -div, and -mod numeric processing commands added.

EDirect Version 12.1: August 29, 2019

- Local query index now creates field-specific subdirectories immediately below Postings folder.
- Term position index files, needed for phrase and proximity searching in [NORM] and [STEM] fields, not made for [CODE] and [YEAR].
- Phrase-search -terms [field] prints complete term list for given field.
- Rchive -help gives example of how to sequentially ascend the MeSH [CODE] hierarchy index.
- Added expand-current script, to be run after index-pubmed, to prepare for fast scanning of all PubMed records.
- Added -repeat option to test-eutils monitoring script.

EDirect Version 12.0: August 14, 2019

- Efetch adds -format bioc for -db pubmed and -db pmc, retrieving annotated records from PubTator Central.
- Added download-ncbi-data script to consolidate and replace special-case scripts.

EDirect Version 11.9: August 5, 2019

- Updated test-eutils driver files due to retirement of unigene.
- Test-eutils progress line prints a period for success, x for failure.
- Test-eutils -timer prints response times in milliseconds for each query.
- Added exclude-uid-lists script.
- Added download-pmc-bioc script.
- Nquire supports -bioc-pubmed and -bioc-pmc shortcuts.
- Fetch-pubmed -fresh generates uncompressed PubMed files from local archive for fast data extraction.
- Index-pubmed retains compressed PubMed intermediate files for batch scanning.
- Xtract supports -select parent/element@attribute^version -in file_of_identifiers.

EDirect Version 11.8: July 23, 2019

- Xtract -j2x converts newline to space, compresses runs of spaces.
- Xtract -j2x supports JSON null tags.

EDirect Version 11.7: July 3, 2019

- Efetch -format docsum -mode json reads 500 records at a time, in conformance with the server limit.
- Fetch-pubmed -all sequentially streams all live records from the local cache.
- Xtract -plain removes embedded mixed-content markup tags.
- Added download-pmc-oa to fetch the open-access subset of PubMed Central.

EDirect Version 11.6: June 11, 2019

- Xtract -path implementation was simplified.
- Einfo -db all returns a combined eInfoResult XML, containing field and link names, and record and term counts, for all Entrez databases in one operation.

EDirect Version 11.5: June 7, 2019

- Xtract -is-equal-to and -differs-from conditional arguments compare values in two named elements.

EDirect Version 11.4: May 23, 2019

- Efetch -db snp -format json reads 10 records at a time for the initial server deployment.
- Updated SNP examples to use efetch -format json and xtract -j2x.
- Added Genes in Pathways example.
- Added xml2tbl script.

EDirect Version 11.3: May 3, 2019

- Xtract -j2x converts JSON stream to XML suitable for -path navigation.
- Xtract -format -self retains self-closing tabs with no attributes.
- Esample replaces xtract -samples.

EDirect Version 11.2: April 15, 2019

- Efetch -db snp only supports -format docsum and -format json.
- Efilter -db biosystems has -kind and -pathway shortcuts.

EDirect Version 11.1: April 3, 2019

- Xtract optimizes performance for 6 CPUs with hyperthreading.

EDirect Version 11.0: March 11, 2019

- Xtract -path generates exploration commands from dotted object path.
- Xtract -format -separate retains internal </parent><parent>.

EDirect Version 10.9: February 1, 2019

- Xtract -insd supports a sub_sequence qualifier that uses -nucleic and produces upper-case sequence.
- Xtract now has an -is-within string conditional test.

EDirect Version 10.8: January 20, 2019

- EDIRECT_DO_AUTO_ABBREV environment variable restores relaxed matching of command-line arguments.
- Efilter shortcut -journal added for -db pubmed.
- Efilter -pub last_* shortcuts moved to -released.
- Efilter -pub and -feature can take comma-separate list of choices.
- Transmute -docsum command added.
- Transmute -decode and -encode commands renamed to -unescape and -escape.
- Transmute -decode64 and -encode64 commands added.

EDirect Version 10.7: January 14, 2019

- Xtract -nucleic uses bracketed range direction to determine whether to reverse complement the sequence.

EDirect Version 10.6: December 13, 2018

- Local archive script creates command for saving data path in configuration file.
- Xtract -reverse returns -words output in reverse order.
- Efilter shortcut added for -db snp (e.g., -class missense).
- Efetch -format gbc (INSDSeq XML) supports -style withparts and -style conwithfeat.

EDirect Version 10.5: December 4, 2018

- EDirect commands and pipelines support faster access with API keys.
- Xtract attributes can be delimited by quotation marks or apostrophes.
- Transmute -encode and -decode commands added.
- Simplified processing of local inverted index intermediate files.

EDirect Version 10.4: November 13, 2018

- Rchive local indexing code refactored for faster performance.
- Xtract -deq deletes and replaces queued tab separator after the fact.
- Efilter -organism queries in [ORGN] field if argument is not in shortcut list.

EDirect Version 10.3: November 1, 2018

- Rchive -invert, -merge, -promote, and -query steps make better use of multiple processor cores.
- New phrase-search script replaces local-phrase-search.

EDirect Version 10.2: October 15, 2018

- Transmute -x2j joins -j2x to simplify the use of JSON-based services.
- Efetch -json converts adjusted XML output to JSON as a convenience.
- Xtract tag alphabet expanded to accommodate converted JSON data.
- Nquire -ftp takes server, directory, and filename arguments, sends data to stdout.

EDirect Version 10.1: October 9, 2018

- Xtract -mixed improves support for mixed-content XML.

EDirect Version 10.0: September 27, 2018

- Efilter can search for sequence records by sample collection location (e.g., -country "canada new brunswick").
- Xtract parsing code was refactored in preparation for improvements in handling mixed-content XML data.
- Added transmute script for format conversions (e.g., -j2x for JSON to XML).

EDirect Version 9.90: September 17, 2018

- Normalized archive path for low-value PMIDs in preparation for incremental indexing.

EDirect Version 9.80: September 4, 2018

- Xtract XML block reader can run on separate thread for improved performance on computers with surplus processor cores.
- Fixed bug in string cleanup when text starts with a non-ASCII Unicode character.
- Efetch regular expression pattern for detecting mixed-content tags was adjusted.

EDirect Version 9.70: August 22, 2018

- Local archive builds parallel stemmed and non-stemmed indices of terms in the title and abstract.
- Rchive and local-phrase-search use -query for evaluation of non-stemmed terms, -search for evaluation using the stemmed index.

EDirect Version 9.60: August 9, 2018

- Local archive script removes newlines inside PubMed text fields.
- Efetch adds missing newline at end of PubmedArticleSet XML.

EDirect Version 9.50: July 30, 2018

- Local indexing scripts adjusted to accommodate projected range of PMID values.
- Fixed inconsistency in positional indexing of terms with embedded non-alphanumeric characters.
- EDIRECT_PUBMED_WORKING environment variable keeps local archive intermediate files on a separate volume.
- Rchive and local-phrase-search use -exact to round-trip ArticleTitle contents without interpretation as a query formula.

EDirect Version 9.40: July 18, 2018

- Xtract handles misplaced spaces in attributes.

- Xtract -format repairs misplaced spaces in attributes.

EDirect Version 9.30: July 9, 2018

- Local data indexing retains intermediate products, allows rapid streaming of non-redundant current records.
- Index preparation removes apostrophe in trailing 's possessives.
- Wildcard minimum varies with prefix-driven posting character depth.

EDirect Version 9.20: June 26, 2018

- Portability and efficiency improvements to local data cache scripts.
- Xtract handles misplaced spaces in self-closing tags.

EDirect Version 9.10: June 18, 2018

- Added Parent/* element exploration construct to xtract.
- Xtract -year reliably obtains the year from "PubDate/*".

EDirect Version 9.00: June 6, 2018

- Fetch-pubmed -path supplies missing Archive directory if root path is given.
- Efetch cleanup of MathML markup properly handles parentheses.

EDirect Version 8.90: June 4, 2018

- Xtract -transform and -translate allow data value substitution.
- Xtract -wrp simplifies wrapping of extracted values in XML tags.

EDirect Version 8.80: May 29, 2018

- Efetch removes MathML tags from PubmedArticle XML contents, unless the -raw flag is used.

EDirect Version 8.70: May 14, 2018

- Local phrase indexing now uses positional indices instead of adjacent overlapping word pairs.
- Xtract -select uses conditional expressions to filter records.

EDirect Version 8.60: April 26, 2018

- Efetch -format uid pauses between groups, retries on failure.
- Fetch delay drops from 1/3 to 1/10 second if API key is used.
- Local phrase indexing uses smaller files to avoid memory contention.
- Phrase index removes hyphens from selected prefixes.

EDirect Version 8.50: April 13, 2018

- Efetch markup tag removal modified after change in server.
- Xtract -phrase filter split into -require and -exclude commands.

EDirect Version 8.40: April 9, 2018

- Efetch removes markup tags in all PubMed XML.
- Xtract without -strict prints warnings if markup tags are encountered.
- Xtract proximity search moved from -matches to -phrase.

EDirect Version 8.30: April 4, 2018

- Xtract is now available for ARM processors.

EDirect Version 8.20: March 12, 2018

- Minor changes to local record archiving scripts.

EDirect Version 8.10: March 2, 2018

- Xtract -strict and -mixed support MathML element tags in PubmedArticle XML.

EDirect Version 8.00: February 26, 2018

- Efetch -raw skips database-specific XML modifications.
- Added local-phrase-search script.
- Xtract -strict, -mixed, and -repair flag speed improvements.

EDirect Version 7.90: February 1, 2018

- Minor change to installation commands for tcsh.

EDirect Version 7.80: January 12, 2018

- Updated setup.sh script with additional error checking.

EDirect Version 7.70: December 27, 2017

- Added archive-pubmed script to automate local record archiving.

EDirect Version 7.60: November 15, 2017

- Epost -id numeric argument bug fixed.
- Xtract conditional tests can now use subrange specifiers.
- Xtract -strict and -mixed use separate -repair flag to normalize Unicode superscripts and subscripts.

EDirect Version 7.50: October 31, 2017

- Setup instructions now work with the tcsh shell.
- API key value is taken from the NCBI_API_KEY environment variable.
- Efetch -format gb supports -style withparts and -style conwithfeat.
- Xtract supports optional element [min:max] substring extraction.
- Xtract -position supports [first|last|outer|inner|all] argument values.
- Added prepare-stash script for local record archive.

EDirect Version 7.40: September 27, 2017

- Xtract -hash reports checksums for local record archiving.
- Initial support for API keys.

EDirect Version 7.30: September 6, 2017

- Modified stash-pubmed script to work around Cygwin artifact.
- Removed unpack-pubmed script.
- Xtract -archive replaces -stash for local record archiving.

- Xtract -gzip allows compression of archived XML records.

EDirect Version 7.20: August 28, 2017

- Added download-pubmed, download-sequence, unpack-pubmed, stash-pubmed, and fetch-pubmed scripts, for experimental local record storage.
- Xtract -flags [strict|mixed] added to support new local storage scripts.
- Removed obsolete, original Perl implementation of xtract.pl.

EDirect Version 7.10: August 10, 2017

- Xtract -ascii converts non-ASCII Unicode to hexadecimal numeric character references.
- Setup script recognizes Cygwin running under the MinGW emulator.

EDirect Version 7.00: July 10, 2017

- Xtract -mixed and -strict handle multiply-escaped HTML tags.
- Efetch removes normal and escaped HTML tags from PubMed fields.
- Esearch -field processes individual query terms using the designated field, also removing stop words.
- Esearch -pairs splits the query phrase into adjacent overlapping word pairs.

EDirect Version 6.90: July 5, 2017

- Xtract -mixed replaces -relaxed, and -accent replaces -plain.
- Efetch uses larger chunks for -format uid, url, and acc.
- Esearch -log shows constructed URL and QueryTranslation result.

EDirect Version 6.80: June 8, 2017

- Modified download instructions to use edirect.tar.gz archive.
- The ftp-cp script can now read from stdin without the need for xargs.
- Rerunning ftp-cp or asp-cp only attempts to download missing files.

EDirect Version 6.70: May 8, 2017

- Added asp-cp script for faster download of NCBI ftp files using Aspera Connect.
- Xtract -strict and -relaxed handle empty HTML tag variants (e.g., <b/> and <sup/>).

EDirect Version 6.60: April 25, 2017

- Xtract -strict replaces -degloss to remove HTML <i>, <b>, <u>, <sup> and <sub> tags from XML contents.
- Xtract -relaxed allows HTML tags in XML contents, to support current PubMed ftp release files.
- Xtract -plain removes Unicode accents.
- The setup.sh script prints an error message if it cannot fetch missing Perl modules.

EDirect Version 6.50: March 6, 2017

- Xtract -degloss replaces -html to remove HTML <i>, <b>, <u>, <sup> and <sub> tags.

EDirect Version 6.40: March 1, 2017

- Epost detects accession.version input for sequence databases and sets -format acc.
- Xtract -html [remove|encode] converts <i> and <b> tags embedded in XML contents.

EDirect Version 6.30: February 13, 2017

- Efetch -format docsum skips GI-less sequences without summaries.
- Xtract local indexing commands moved to -extras documentation.

EDirect Version 6.20: January 30, 2017

- Xtract -limit and -index allow extraction of selected records from XML file.

EDirect Version 6.10: January 19, 2017

- Added run-ncbi-converter script for processing ASN.1 release files.
- Xtract -format flush option added.
- Removed obsolete accession-dot-version conversion code.

EDirect Version 6.00: December 27, 2016

- Efetch -format docsum removes eSummaryResult wrapper.
- Fixed content truncation bug when Xtract encounters very long sequences.

EDirect Version 5.90: December 21, 2016

- Efetch and Elink readied for switch to accession-dot-version sequence identifier.
- Xtract -insd recognizes INSDInterval_iscomp@value and other boolean attributes.
- Xtract adds experimental phrase processing commands for word index preparation.

EDirect Version 5.80: December 12, 2016

- Efilter adds shortcuts for -db gene (e.g., -status alive, -type coding).
- Xtract numeric conditional tests can use an element name for the second argument (e.g., -if ChrStop -lt ChrStart finds minus strand genes).

EDirect Version 5.70: November 30, 2016

- Xtract -format takes an optional [compact|indent|expand] argument. Processing compact XML is about 15% faster than indent form. Using expand places each attribute on a separate line for ease of reading.

EDirect Version 5.60: November 22, 2016

- Fixed bug in -datetype argument for Esearch and Efilter.
- Added optional argument to filter-stop-words script to indicate replacement.

EDirect Version 5.50: November 16, 2016

- Efetch -id allows non-numeric accessions only for sequence databases.
- Xtract element selection no longer considers fields in recursive sub-objects.
- Xtract introduces a double-star "**/Object" construct to flatten recursive child objects for linear exploration.
- Xtract conditional tests ignore empty self-closing tags.
- Xtract -else simplifies insertion of a placeholder to indicate missing data.

EDirect Version 5.40: November 7, 2016

- Added filter-stop-words and xy-plot scripts.

EDirect Version 5.30: October 31, 2016

- Added support for ecitmatch utility.
- Added amino-acid-composition and between-two-genes scripts.
- The sort-uniq-count and sort-uniq-count-rank scripts take an optional argument (e.g., -n for numeric comparisons, -r to reverse order).

EDirect Version 5.20: October 26, 2016

- Setup script no longer modifies the user's configuration file to update the PATH variable. Instead, it now prints customized instructions for the user to execute. The user may choose to run these commands, but is free to edit the .bash_profile file manually.
- Xtract deprecates -match and -avoid functions and the Element:Value conditional shortcut.
- Xtract -if and -unless commands use compound statements for conditional execution (e.g., -if Element -equals Value).
- Colon now separates namespace prefix from element name in xtract arguments (e.g., -block jats:abstract). Colon at start of element name matches any namespace prefix.
- Xtract -insd uses a dash as placeholder for missing field. Experimental -insdx command is deprecated.
- Precompiled versions of xtract are now provided for Darwin, Linux, and CYGWIN_NT platforms. The appropriate executable is downloaded by the setup script.

EDirect Version 5.10: October 13, 2016

- Xtract adds -0-based, -1-based, and -ucsc numeric extraction/conversion commands for sequence positions from several Entrez databases.

EDirect Version 5.00: September 26, 2016

- Efetch -format fasta removes blank lines between records.
- Xtract -insdx uses a dash to indicate a missing field.
- Xtract -insd no longer has blank lines between records.
- Xtract -input allows reading XML data from a file.

EDirect Version 4.90: September 14, 2016

- Epost -input allows reading from an input file instead of using data piped through stdin.
- Efilter now supports the -sort argument.
- Xtract -filter can recover information in XML comments and CDATA blocks.

EDirect Version 4.80: August 9, 2016

- Xtract -insd controlled vocabularies updated.

EDirect Version 4.70: August 4, 2016

- Einfo -db request can also display -fields and -links data summaries.
- Einfo -dbs prints database names instead of eInfoResult XML.

EDirect Version 4.60: July 18, 2016

- Elink -cmd acheck returns information on all available links for a record.
- Efilter -pub structured limits to articles with structured abstracts.

EDirect Version 4.50: July 1, 2016

- Esearch and Efilter detect and report -query phrase quotation errors.
- Efilter -pub shortcut adds last_week, last_month, and last_year choices.
- Efetch sets -strand 2 for minus strand if -seq_start > -seq_stop or if -chr_start > -chr_stop.

EDirect Version 4.40: June 21, 2016

- Transitioning to use of https for access to NCBI services.
- Epost -db assembly -format acc uses [ASAC] field instead of [ACCN].

EDirect Version 4.30: June 13, 2016

- Efilter -pub preprint limits results to ahead-of-print articles.
- Xtract -pattern Parent/* construct can now process catenated XML files.

EDirect Version 4.20: May 24, 2016

- Xtract command-line argument parsing improvements.
- Nquire -get supersedes -http get.

EDirect Version 4.10: May 3, 2016

- Xtract -format removes multi-line XML comments and CDATA blocks.

EDirect Version 4.00: April 4, 2016

- Esearch adds -spell to correct known misspellings of biological terms in the query string.
- Efilter adds -spell to correct query misspellings, and -pub, -feature, -location, -molecule, -organism, and -source shortcuts. Run efilter -help to see the choices available for each argument.

EDirect Version 3.90: March 21, 2016

- Code optimizations for increased Xtract speed.

EDirect Version 3.80: February 29, 2016

- Xtract can distribute its work among available processor cores for additional speed.

EDirect Version 3.70: February 8, 2016

- Xtract performance improvements.

EDirect Version 3.60: January 11, 2016

- The setup.sh configuration script now downloads a precompiled Xtract executable for selected platforms.

EDirect Version 3.50: December 27, 2015

- Xtract reports error for element:value construct outside of -match or -avoid arguments.

EDirect Version 3.40: December 20, 2015

- Xtract -insd supports extraction from multiple features (e.g., CDS,mRNA).

EDirect Version 3.30: December 3, 2015

- Efetch -format docsum can accept a single sequence accession number in the -id argument.

EDirect Version 3.20: November 30, 2015

- Xtract supports -match conditional execution on values recorded in variables.

EDirect Version 3.10: November 18, 2015

- Efetch adds -chr_start and -chr_stop arguments to specify sequence range from 0-based coordinates in gene docsum GenomicInfoType object.

EDirect Version 3.00: October 30, 2015

- Xtract rewritten in the Go programming language for speed. The setup.sh configuration script installs an older Perl version (2.99) if a local Go compiler is unavailable.
- Efetch -format docsum only decodes HTML entity numbers in select situations.

EDirect Version 2.90: October 15, 2015

- Xtract warns on use of deprecated arguments -present, -absent, and -trim, in preparation for release of much faster version.

EDirect Version 2.80: September 9, 2015

- Xtract uses the "*/Child" construct for nested exploration into recursive structures, replacing the -trim argument.

EDirect Version 2.70: July 14, 2015

- Added entrez-phrase-search script to query on adjacent word pairs indexed in specific fields.

EDirect Version 2.60: June 23, 2015

- Xtract -match and -avoid support "Parent/Child" construct for BLAST XML.

EDirect Version 2.50: April 9, 2015

- Xtract capitalized -Pattern handles recursively-defined top-level objects.

EDirect Version 2.40: March 25, 2015

- EDirect programs use the http_proxy environment variable to work behind firewalls.

EDirect Version 2.30: March 11, 2015

- Cleaned up logic in setup.sh configuration script.
- EPost -format acc works properly on protein accessions.

EDirect Version 2.20: March 4, 2015

- Xtract -match and -avoid recognize "@attribute" without element or value.

EDirect Version 2.10: February 3, 2015

- Added ftp-ls and ftp-cp scripts for convenient access to the NCBI anonymous ftp server.

EDirect Version 2.00: August 28, 2014

- Introduced copy-and-paste installation commands with setup.sh configuration script.

EDirect Version 1.90: August 8, 2014

- Xtract -format combines multiple XML results into a single valid object.
- Improved suppression of 0-count failure messages with -silent flag in scripts.

EDirect Version 1.80: July 15, 2014

- EPost -format acc accepts accessions in an -id argument on the command line.

EDirect Version 1.70: April 23, 2014

- EFetch -format docsum decodes HTML entity numbers embedded in the text.

EDirect Version 1.60: April 3, 2014

- Minor enhancements to xtract -insd.

EDirect Version 1.50: March 29, 2014

- Esearch -sort specifies the order of results when records are retrieved.
- Xtract exploration arguments (e.g., -block) now work on self-closing tags with data in attributes.

EDirect Version 1.40: March 17, 2014

- Xtract -format repairs XML line-wrapping and indentation.
- Implemented -help flag to display the list of command-line arguments for each function.

EDirect Version 1.30: March 3, 2014

- Xtract -insd partial logic was corrected to examine both 5' and 3' partial flags, and the location indicator recognizes "+" or "complete" and "-" or "partial".

EDirect Version 1.20: February 26, 2014

- Xtract -insd detects if it is part of an EDirect sequence record query, and dynamically executes the extraction request for specific qualifier values. When run in isolation it generates extraction instructions that can be incorporated (with modifications, if necessary) into other queries.

EDirect Version 1.10: February 10, 2014

- ESummary was replaced by "efetch -format docsum" to provide a single command for all document retrieval. The esummary command will continue to work for those who prefer it, and to avoid breaking existing scripts.
- Xtract processes each -pattern object immediately upon receipt, eliminating the need for using xargs and sh to split document retrieval into smaller units.

EDirect Version 1.00: February 6, 2014

- Initial public release.

For More Information

Announcement Mailing List

NCBI posts general announcements regarding the E-utilities to the utilities-announce announcement mailing list. This mailing list is an announcement list only; individual subscribers may **not** send mail to the list. Also, the list of subscribers is private and is not shared or used in any other way except for providing announcements to list members. The list receives about one posting per month. Please subscribe at the above link.

Getting Help

Please refer to the PubMed and Entrez help documents for more information about search queries, database indexing, field limitations and database content.

Suggestions, comments, and questions specifically relating to the EUtility programs may be sent to eutilities@ncbi.nlm.nih.gov.