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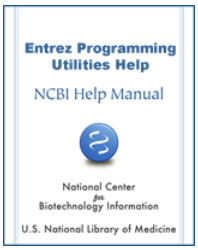

Entrez Direct: E-utilities on the Unix Command Line

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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. Search terms are entered as command-line arguments. Individual operations are connected with Unix pipes to construct multi-step queries. Selected records can then be retrieved in a variety of formats.

Installation

EDirect will run on Unix and Macintosh computers, and under the Cygwin Unix-emulation environment on Windows PCs. To install the EDirect software, open a terminal window and execute one of the following two commands:

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

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

This will download a number of scripts and several precompiled programs into an "edirect" folder in the user's home directory. It may then 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=\$HOME/edirect:\$PATH" >> $HOME/.bash_profile
```

As a convenience, the installation process 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.

Once installation is complete, run:

```
export PATH=${HOME}/edirect:${PATH}
```

to set the PATH for the current terminal session.

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Quick Start

The **readme.pdf** file included in the edirect folder contains a highly-abridged version of this document. It is intended to convey the most important points in the least amount of time for the new user, while still presenting the minimal essential details. It also covers subtle issues in several Entrez biological databases, demonstrates integration of data from external sources, and has a brief introduction to scripting and programming.

The full documentation gives a much more in-depth exploration of the underlying topics, especially in the Complex Objects section, and in the Additional Examples web page, which is organized by Entrez database. This document also introduces other worthy topics, such as identifier lookup and sequence coordinate conversions, and has a more thorough treatment of automation.

Programmatic Access

EDirect connects to Entrez through the Entrez Programming Utilities interface. It supports searching by indexed terms, looking up precomputed neighbors or links, filtering results by date or category, and downloading record summaries or reports.

Navigation programs (**esearch**, **elink**, **efilter**, and **efetch**) communicate by means of a small structured message, which can be passed invisibly between operations with a Unix pipe. The message includes the current database, so it does not need to be given as an argument after the first step.

Accessory programs (**nquire**, **transmute**, and **xtract**) can help eliminate the need for writing custom software to answer ad hoc questions. Queries can move seamlessly between EDirect programs and Unix utilities or scripts to perform actions that cannot be accomplished entirely within Entrez.

All EDirect programs are designed to work on large sets of data. They handle many technical details behind the scenes (avoiding the learning curve normally required for E-utilities programming). Intermediate results are either saved on the Entrez history server or instantiated in the hidden message. For best performance, obtain an API Key from NCBI, and place the following line in your .bash_profile and .zshrc configuration files:

```
export NCBI_API_KEY=unique_api_key
```

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.

Each program has a **–help** command that prints detailed information about available arguments.

Navigation Functions

Esearch performs a new Entrez search using terms in indexed fields. It requires a **–db** argument for the database name and uses **–query** for the search terms. For PubMed, without field qualifiers, the server uses automatic term mapping to compose a search strategy by translating the supplied query:

```
esearch -db pubmed -query "selective serotonin reuptake inhibitor"
```

Search terms can also be qualified with a bracketed field name to match within the specified index:

```
esearch -db nuccore -query "insulin [PROT] AND rodents [ORGN]"
```

Elink looks up precomputed neighbors within a database, or finds associated records in other databases:

```
elink -related
```

```
elink -target gene
```

Elink also connects to the NIH Open Citation Collection dataset to find publications that cite the selected PubMed articles, or to follow the reference lists of PubMed records:

```
elink -cited
```

```
elink -cites
```

Efilter limits the results of a previous query, with shortcuts that can also be used in esearch:

```
efilter -molecule genomic -location chloroplast -country sweden -mindate 1985
```

Efetch downloads selected records or reports in a style designated by **–format**:

```
efetch -format abstract
```

There is no need to use a script to loop over records in small groups, or write code to retry after a transient network or server failure, or add a time delay between requests. All of those features are already built into the EDirect commands.

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:

```
esearch -db pubmed -query "tn3 transposition immunity" | efetch -format medline
```

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.

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

Continuing the query looks up precomputed neighbors of the original papers, next links to all protein sequences published in the related articles, then limits those to the rodent division of GenBank, and finally retrieves the records in FASTA format:

```
elink -related | \
elink -target protein | \
efilter -division rod | \
efetch -format fasta
```

In most modern versions of Unix the vertical bar pipe symbol also allows the query to continue on the next line, without the need for an additional backslash.

Accessory Programs

Nquire retrieves data from remote servers with URLs constructed from command line arguments:

```
nquire -get https://icite.od.nih.gov api/pubs -pmids 2539356 |
```

Transmute converts a concatenated stream of JSON objects or other structured formats into XML:

```
transmute -j2x |
```

Xtract can use waypoints to navigate a complex XML hierarchy and obtain data values by field name:

```
xtract -pattern data -element cited_by |
```

The resulting output can be post-processed by Unix utilities or scripts:

```
fmt -w 1 | sort -V | uniq
```

Discovery by Navigation

PubMed related articles are calculated by a statistical text retrieval algorithm using the title, abstract, and medical subject headings (MeSH terms). The connections between papers can be used for making discoveries. An example of this is finding the last enzymatic step in the vitamin A biosynthetic pathway.

Lycopene cyclase in plants converts lycopene into β-carotene, the immediate biochemical precursor of vitamin A. An initial search on the enzyme finds 303 articles. Looking up precomputed neighbors returns 18,943 papers, some of which might be expected to discuss other enzymes in the pathway:

```
esearch -db pubmed -query "lycopene cyclase" | elink -related |
```

β-carotene is known to be an essential nutrient, required in the diet of herbivores. This indicates that lycopene cyclase is not present in animals (with a few exceptions caused by horizontal gene transfer), and that the enzyme responsible for converting β-carotene into vitamin A is not present in plants.

Applying this knowledge, by linking the publication neighbors to their associated protein records and then filtering those candidates using the NCBI taxonomy, can help locate the desired enzyme.

Linking from pubmed to the protein database finds 520,222 protein sequences:

```
elink -target protein |
```

Limiting to mice excludes plants, fungi, and bacteria, which eliminates the earlier enzymes:

```
efilter -organism mouse -source refseq |
```

This matches only 26 sequences, which is small enough to examine by retrieving the individual records:

```
efetch -format fasta
```

As anticipated, the results include the enzyme that splits β-carotene into two molecules of retinal:

```
...
>NP_067461.2 beta,beta-carotene 15,15'-dioxygenase isoform 1 [Mus musculus]
MEIIFGQNKKEQLEPVQAKVTGSIPAWLQGTLLRNGPGMHTVGESKYNHWFDGLALLHSFSIRDGEVFYR
SKYLQSDTYIANIEANRIVVSEFGTMAYPDPCKNIFSKAFSYLSHTIPDFTDNCLINIMKCGEDFYATTE
TNYIRKIDPQTLETLEKVDYRKYVAVNLATSHPHYDEAGNVLNMGTSVVDKGRTKYVIFKIPATVPDSKK
...
```

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:

```
...
85. 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
  ...
```

If "medline" format is used instead:

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

the output 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
...
```

Sequence records can also be obtained as GenBank or GenPept flatfiles:

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

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 errqreffc
      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"
```

Limiting by Date

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

```
efilter -days 60 -datetype PDAT

efilter -mindate 2000

efilter -maxdate 1985

efilter -mindate 1990 -maxdate 1999
```

restrict results to articles published in the previous two months, since the beginning of 2000, through the end of 1985, or in the 1990s, respectively. YYYY/MM and YYYY/MM/DD date formats are also accepted.

Fetch by Identifier

Efetch and elink can take a list of numeric identifiers or accessions in an **−id** argument:

```
efetch -db pubmed -id 7252148,1937004 -format xml

efetch -db nuccore -id 1121073309 -format acc

efetch -db protein -id 3OQZ_a -format fasta

efetch -db bioproject -id PRJNA257197 -format docsum

efetch -db pmc -id PMC209839 -format medline

elink -db pubmed -id 2539356 -cites
```

without the need for a preceding esearch command.

Non-integer accessions will be looked up with an internal search, using the appropriate field for the database:

```
esearch -db bioproject -query "PRJNA257197 [PRJA]" |
efetch -format uid | ...
```

Most databases use the [ACCN] field for identifier lookup, but there are a few exceptions:

```
annotinfo      [ASAC]
assembly       [ASAC]
bioproject     [PRJA]
books          [AID]
clinvar        [VACC]
gds            [ALL]
genome         [PRJA]
geoprofiles    [NAME]
gtr            [GTRACC]
mesh           [MHUI]
nuccore        [ACCN] or [PACC]
pcsubstance    [SRID]
snp            [RS] or [SS]
```

(For −db pmc it merely removes any "PMC" prefix from the integer identifier.)

For backward compatibility, **esummary** is a shortcut for esearch −format docsum:

```
esummary -db bioproject -id PRJNA257197

esummary -db sra -id SRR5437876
```

Reading Large Lists of Identifiers

Efetch and elink can also read a large list of identifiers or accessions piped in through stdin:

```
cat "file_of_identifiers.txt" |
efetch -db pubmed -format docsum
```

or from a file indicated by an **–input** argument:

```
efetch -input "file_of_identifiers.txt" -db pubmed -format docsum
```

As mentioned above, there is no need to use a script to split the identifiers into smaller groups or add a time delay between individual requests, since that functionality is already built into EDirect.

Indexed Fields

The **einfo** command can report the fields and links that are indexed for each database:

```
einfo -db protein -fields
```

This will return a table of field abbreviations and names indexed for proteins:

```
ACCN    Accession
ALL     All Fields
ASSM    Assembly
AUTH    Author
BRD     Breed
CULT    Cultivar
DIV     Division
ECNO    EC/RN Number
FILT    Filter
FKEY    Feature key
...
```

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           [LANG]    Language
[ALL]     All Fields            [MAJR]    MeSH Major Topic
[AUTH]    Author                [SUBH]    MeSH Subheading
[FAUT]    Author - First        [MESH]    MeSH Terms
[LAUT]    Author - Last         [PTYP]    Publication Type
[CRDT]    Date - Create         [WORD]    Text Word
[PDAT]    Date - Publication    [TITL]    Title
[FILT]    Filter                [TIAB]    Title/Abstract
[JOUR]    Journal               [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       [MLWT]    Molecular Weight
[ALL]     All Fields      [ORGN]    Organism
[AUTH]    Author          [PACC]    Primary Accession
[GPRJ]    BioProject      [PROP]    Properties
[BIOS]    BioSample       [PROT]    Protein Name
[ECNO]    EC/RN Number    [SQID]    SeqID String
[FKEY]    Feature key     [SLEN]    Sequence Length
[FILT]    Filter          [SUBS]    Substance Name
[GENE]    Gene Name       [WORD]    Text Word
[JOUR]    Journal         [TITL]    Title
[KYWD]    Keyword         [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]
txid40674 [ORGN]
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.)

See **efilter –help** for a list of filter shortcuts available for several Entrez databases.

Examining Intermediate Results

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

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 "tryptophan synthase alpha chain [PROT]" |
efilter -query "28000:30000 [MLWT]" |
elink -target structure |
efilter -query "0:2 [RESO]"
```

produces:

```
<ENTREZ_DIRECT>
  <Db>structure</Db>
  <WebEnv> MCID_5fac27e119f45d4eca20b0e6</WebEnv>
  <QueryKey>32</QueryKey>
  <Count>58</Count>
  <Step>4</Step>
</ENTREZ_DIRECT>
```

with 58 protein structures being within the specified molecular weight range and having the desired (X-ray crystallographic) atomic position resolution.

(The QueryKey value differs from Step because the elink command splits its query into smaller chunks to avoid server truncation limits and timeout errors.)

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.)

Because elink splits a large query into multiple smaller link requests, the new QueryKey value cannot be predicted in advance. The −label argument is used to get around this artifact. The label value is prefixed by a "#" symbol and placed in parentheses in the final search. For example, the query:

```
esearch -db protein -query "amyloid* [PROT]" |
elink -target pubmed -label prot_cit |
esearch -db gene -query "apo* [GENE]" |
elink -target pubmed -label gene_cit |
esearch -query "(#prot_cit) AND (#gene_cit)" |
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 ...
...
```

Structured Data

Advantages of XML Format

The ability to obtain Entrez records in structured eXtensible Markup Language (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 information is 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 into Tables

The xtract program uses command-line arguments to direct the selective conversion of data in XML format. It allows record detection, path exploration, element selection, conditional processing, and report formatting to be controlled independently.

The **–pattern** command partitions an XML stream by object name into individual records that are processed separately. Within each record, the **–element** command does an exhaustive, depth-first search to find data content by field name. Explicit paths to objects are not needed.

By default, the –pattern argument divides the results into rows, while placement of data into columns is controlled by –element, to create a tab-delimited table.

Format Customization

Formatting commands allow extensive customization of the output. The line break between –pattern rows is changed with **–ret**, while the tab character between –element columns is modified by **–tab**. Multiple instances of the same element are distinguished using **–sep**, which controls their separation independently of the –tab command. The following query:

```
efetch -db pubmed -id 6271474,6092233,16589597 -format docsum |
xtract -pattern DocumentSummary -sep "|" -element Id PubDate Name
```

returns a tab-delimited table with individual author names separated by vertical bars:

```
6271474     1981            Casadaban MJ|Chou J|Lemaux P|Tu CP|Cohen SN
6092233     1984 Jul-Aug    Calderon IL|Contopoulou CR|Mortimer RK
16589597    1954 Dec        Garber ED
```

The –sep value also applies to distinct –element arguments that are grouped with **commas**. This can be used to keep data from multiple related fields in the same column:

```
-sep " " -element Initials,LastName
```

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

The **−def** command sets a default placeholder to be printed when none of the comma-separated fields in an −element clause are present:

```
-def "-" -sep " " -element Year,Month,MedlineDate
```

Repackaging commands (**−wrp**, **−enc**, and **−pkg**) wrap extracted data values with bracketed XML tags given only the object name. For example, "−wrp Word" issues the following formatting instructions:

```
-pfx "<Word>" -sep "</Word><Word>" -sfx "</Word>"
```

and also ensures that data values containing encoded angle brackets, ampersands, quotation marks, or apostrophes remain properly encoded inside the new XML.

Additional commands (**−tag**, **−att**, **−atr**, **−cls**, **−slf**, and **−end**) allow generation of XML tags with attributes. Running:

```
-tag Item -att type journal -cls -element Source -end Item \
-deq "\n" -tag Item -att type journal -atr name Source -slf
```

will produce regular and self-closing XML objects, respectively:

```
<Item type="journal">J Bacteriol</Item>
<Item type="journal" name="J Bacteriol" />
```

Element Variants

Derivatives of −element were created to eliminate the inconvenience of having to write post-processing scripts to perform otherwise trivial modifications or analyses on extracted data. They are subdivided into several categories. Substitute for −element as needed. A representative selection is shown below:

```
Positional:       -first, -last, -even, -odd, -backward

Numeric:          -num, -len, -inc, -dec, -bin, -hex, -bit

Statistics:       -sum, -acc, -min, -max, -dev, -med

Averages:         -avg, -geo, -hrm, -rms

Logarithms:       -lge, -lg2, -log

Character:        -encode, -upper, -title, -mirror, -alnum

String:           -basic, -plain, -simple, -author, -journal, -prose

Text:             -words, -pairs, -letters, -order, -reverse

Citation:         -year, -month, -date, -page, -auth

Sequence:         -revcomp, -fasta, -ncbi2na, -molwt, -pentamers

Translation:      -cds2prot, -gcode, -frame

Coordinate:       -0-based, -1-based, -ucsc-based

Variation:        -hgvs
```

```
Frequency:        -histogram

Expression:       -reg, -exp, -replace

Substitution:     -transform, -translate

Indexing:         -aliases, -classify

Miscellaneous:    -doi, -wct, -trim, -pad, -accession, -numeric
```

The original −element prefix shortcuts, "#" and "%", are redirected to **−num** and **−len**, respectively.

See xtract **−help** for a brief description of each command.

Exploration Control

Exploration commands provide fine control over the order in which XML record contents are examined, by separately presenting each instance of the chosen subregion. This limits what subsequent commands "see" at any one time, and allows related fields in an object to be kept together.

In contrast to the simpler DocumentSummary format, records retrieved as PubmedArticle XML:

```
efetch -db pubmed -id 1413997 -format xml |
```

have authors with separate fields for last name and initials:

```
<Author>
  <LastName>Mortimer</LastName>
  <Initials>RK</Initials>
</Author>
```

Without being given any guidance about context, an −element command on initials and last names:

```
efetch -db pubmed -id 1413997 -format xml |
xtract -pattern PubmedArticle -element Initials LastName
```

will explore the current record for each argument in turn, printing all initials followed by all last names:

```
RK    CR    JS    Mortimer    Contopoulou    King
```

Inserting a **−block** command adds another exploration layer between −pattern and −element , and redirects data exploration to present the authors one at a time:

```
efetch -db pubmed -id 1413997 -format xml |
xtract -pattern PubmedArticle -block Author -element Initials LastName
```

Each time through the loop, the −element command only sees the current author's values. This restores the correct association of initials and last names in the output:

```
RK    Mortimer    CR    Contopoulou    JS    King
```

Grouping the two author subfields with a comma, and adjusting the −sep and −tab values:

```
efetch -db pubmed -id 1413997 -format xml |
xtract -pattern PubmedArticle -block Author \
  -sep " " -tab ", " -element Initials,LastName
```

produces a more traditional formatting of author names:

```
RK Mortimer, CR Contopoulou, JS King
```

Sequential Exploration

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. For example:

```
efetch -db pubmed -id 6092233,4640931,4296474 -format xml |
xtract -pattern PubmedArticle -element MedlineCitation/PMID \
  -block PubDate -sep " " -element Year,Month,MedlineDate \
  -block AuthorList -num Author -sep "/" -element LastName |
sort-table -k 3,3n -k 4,4f
```

generates a table that allows easy parsing of author last names, and sorts the results by author count:

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

Like −element arguments, the individual −block statements are executed sequentially, in order of appearance.

Note that "−element MedlineCitation/PMID" uses the **parent / child** construct to prevent the display of additional PMID items that might be present later in CommentsCorrections objects.

Note also 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

Exploration command names (**−group**, **−block**, and **−subset**) are assigned to a precedence hierarchy:

```
-pattern > -group > -block > -subset > -element
```

and are combined in ranked order to control object iteration at progressively deeper levels in the XML data structure. Each command argument acts as a "nested for-loop" control variable, retaining information about the context, or state of exploration, at its level.

(Hypothetical) census data would need several nested loops to visit each unique address in context:

```
-pattern State -group City -block Street -subset Number -element Resident
```

A nucleotide or protein sequence record can have multiple features. Each feature can have multiple qualifiers. And every qualifier has separate name and value nodes. Exploring this natural data hierarchy, with **−pattern** for the sequence, **−group** for the feature, and **−block** for the qualifier:

```
efetch -db nuccore -id NG_008030.1 -format gbc |
xtract -pattern INSDSeq -element INSDSeq_accession-version \
  -group INSDFeature -deq "\n\t" -element INSDFeature_key \
    -block INSDQualifier -deq "\n\t\t" \
      -element INSDQualifier_name INSDQualifier_value
```

keeps qualifiers, such as gene and product, associated with their parent features, and keeps qualifier names and values together on the same line:

```
NG_008030.1
    source
              organism         Homo sapiens
              mol_type         genomic DNA
              db_xref          taxon:9606
    gene
              gene             COL5A1
    mRNA
              gene             COL5A1
              product          collagen type V alpha 1 chain, transcript variant 1
              transcript_id    NM_000093.4
    CDS
              gene             COL5A1
              product          collagen alpha-1(V) chain isoform 1 preproprotein
              protein_id       NP_000084.3
              translation      MDVHTRWKARSALRPGAPLLPPLLLLLLWAPPPSRAAQP...
              ...
```

Saving Data in Variables

A value can be recorded in a variable and used wherever needed. Variables are created by a hyphen followed by a name consisting of a string of capital letters or digits (e.g., **−KEY**). Variable values are retrieved by placing an ampersand before the variable name (e.g., "**&KEY**") in an −element statement:

```
efetch -db nuccore -id NG_008030.1 -format gbc |
xtract -pattern INSDSeq -element INSDSeq_accession-version \
  -group INSDFeature -KEY INSDFeature_key \
    -block INSDQualifier -deq "\n\t" \
      -element "&KEY" INSDQualifier_name INSDQualifier_value
```

This version prints the feature key on each line before the qualifier name and value, even though the feature key is now outside of the visibility scope (which is the current qualifier):

```
NG_008030.1
    source    organism         Homo sapiens
    source    mol_type         genomic DNA
    source    db_xref          taxon:9606
    gene      gene             COL5A1
    mRNA      gene             COL5A1
    mRNA      product          collagen type V alpha 1 chain, transcript variant 1
    mRNA      transcript_id    NM_000093.4
    CDS       gene             COL5A1
    CDS       product          collagen alpha-1(V) chain isoform 1 preproprotein
    CDS       protein_id       NP_000084.3
    CDS       translation      MDVHTRWKARSALRPGAPLLPPLLLLLLWAPPPSRAAQP...
    ...
```

Variables can be (re)initialized with an explicit literal value inside parentheses:

```
-block Author -sep " " -tab "" -element "&COM" Initials,LastName -COM "(, )"
```

They can also be used as the first argument in a conditional statement:

```
-CHR Chromosome -block GenomicInfoType -if "&CHR" -differs-from ChrLoc
```

Using a double-hyphen (e.g., **−−STATS**) appends a value to the variable.

In addition, a variable can also save the the modified data resulting from an **−**element variant operation. This allows multiple sequential transitions within a single xtract command:

```
-END -sum "Start,Length" -MID -avg "Start,&END"
```

All variables are reset when the next record is processed.

Conditional Execution

Conditional processing commands (**−if**, **−unless**, **−and**, **−or**, and **−else**) restrict object exploration by data content. They check to see if the named field is within the scope, and may be used in conjunction with string, numeric, or object constraints to require an additional match by value. For example:

```
esearch -db pubmed -query "Havran W [AUTH]" |
efetch -format xml |
xtract -pattern PubmedArticle -if "#Author" -lt 14 \
  -block Author -if LastName -is-not Havran \
    -sep ", " -tab "\n" -element LastName,Initials[1:1] |
sort-uniq-count-rank
```

selects papers with fewer than 14 authors and prints a table of the most frequent collaborators, using a range to keep only the first initial so that variants like "Berg, CM" and "Berg, C" are combined:

```
34    Witherden, D
15    Boismenu, R
12    Jameson, J
10    Allison, J
10    Fitch, F
...
```

Numeric constraints can also compare the integer values of two fields. This can be used to find genes that are encoded on the minus strand of a nucleotide sequence:

```
-if ChrStart -gt ChrStop
```

Object constraints will compare the string values of two named fields, and can look for internal inconsistencies between fields whose contents should (in most cases) be identical:

```
-if Chromosome -differs-from ChrLoc
```

The **−position** command restricts presentation of objects by relative location or index number:

```
-block Author -position last -sep ", " -element LastName,Initials
```

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 "\-"
```

but setting a default value with −def may be more convenient in simple cases.

Parallel −if and −unless statements can be used to provide a more complex response to alternative conditions that include nested explorations.

Post-processing Functions

Elink **−cited** can perform a reverse citation lookup, thanks to a data service provided by the NIH Open Citation Collection. The extracted author names can be processed by piping to a chain of Unix utilities:

```
esearch -db pubmed -query "Beadle GW [AUTH]" |
elink -cited |
efetch -format docsum |
xtract -pattern Author -element Name |
sort -f | uniq -i -c
```

which produces an alphabetized count of authors who cited the original papers:

```
1 Abellan-Schneyder I
1 Abramowitz M
1 ABREU LA
1 ABREU RR
1 Abril JF
1 Abächerli E
1 Achetib N
1 Adams CM
2 ADELBERG EA
1 Adrian AB
...
```

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. For example:

```
SortUniqCountRank() {
  grep '.' |
  sort -f |
  uniq -i -c |
  awk '{ n=$1; sub(/[ \t]*[0-9]+[ \t]/, ""); print n "\t" $0 }' |
  sort -t "$(printf '\t')" -k 1,1nr -k 2f
}
alias sort-uniq-count-rank='SortUniqCountRank'
```

(An enhanced version of **sort-uniq-count-rank** that accepts customization arguments is now included with EDirect as a stand-alone script.)

The raw author names can be passed directly to the sort-uniq-count-rank script:

```
esearch -db pubmed -query "Beadle GW [AUTH]" |
elink -cited |
efetch -format docsum |
xtract -pattern Author -element Name |
sort-uniq-count-rank
```

to produce a tab-delimited ranked list of authors who most often cited the original papers:

```
17    Hawley RS
13    Beadle GW
13    PERKINS DD
11    Glass NL
11    Vécsei L
10    Toldi J
```

```
9     TATUM EL
8     Ephrussi B
8     LEDERBERG J
...
```

Similarly, elink **–cites** uses NIH OCC data to return an article's reference list.

Other scripts for tab-delimited files include **sort-table**, **reorder-columns**, and **align-columns**. Unix parameter expansion requires **filter-columns** and **print-columns** arguments to be in single quotes.

Note that EDirect commands can also be used inside Unix functions or scripts.

Viewing an XML Hierarchy

Piping a PubmedArticle XML object to xtract **–outline** will give an indented overview of the XML hierarchy:

```
PubmedArticle
  MedlineCitation
    PMID
    DateCompleted
      Year
      Month
      Day
    ...
    Article
      Journal
        ...
        Title
        ISOAbbreviation
      ArticleTitle
      ...
      Abstract
        AbstractText
      AuthorList
        Author
          LastName
          ForeName
          Initials
          AffiliationInfo
            Affiliation
        Author
          ...
```

Using xtract **–synopsis** or **–contour** will show the full paths to all nodes or just the terminal (leaf) nodes, respectively. Piping those results to "sort-uniq-count" will produce a table of unique paths.

Code Nesting Comparison

Sketching with indented 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
```

where the rank of the argument name controls the nesting depth, could be represented as a computer program in pseudo code by:

```
for pat = each PubmedArticle {
  for blk = each pat.Author {
    print blk.Initials blk.LastName
  }
  for blk = each pat.MeSHTerm {
    if blk.Qual is present {
      print blk.MeshName
      for sbs = each blk.Qual {
        print sbs.QualName
      }
    }
  }
}
```

where the brace indentation count controls the nesting depth.

Extra arguments 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 exploration commands below −pattern, in order of rank, are:

```
-path
  -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.

Complex Objects

Author Exploration

What's in a name? That which we call an author by any other name may be a consortium, investigator, or editor:

```
<PubmedArticle>
  <MedlineCitation>
    <PMID>99999999</PMID>
    <Article>
      <AuthorList>
        <Author>
          <LastName>Tinker</LastName>
        </Author>
        <Author>
          <LastName>Evers</LastName>
        </Author>
        <Author>
          <LastName>Chance</LastName>
        </Author>
        <Author>
          <CollectiveName>FlyBase Consortium</CollectiveName>
        </Author>
      </AuthorList>
    </Article>
    <InvestigatorList>
```

```
        <Investigator>
          <LastName>Alpher</LastName>
        </Investigator>
        <Investigator>
          <LastName>Bethe</LastName>
        </Investigator>
        <Investigator>
          <LastName>Gamow</LastName>
        </Investigator>
      </InvestigatorList>
    </MedlineCitation>
  </PubmedArticle>
```

Within the record, −element exploration on last name:

```
xtract -pattern PubmedArticle -element LastName
```

prints each last name, but does not match the consortium:

```
Tinker    Evers    Chance    Alpher    Bethe    Gamow
```

Limiting to the author list:

```
xtract -pattern PubmedArticle -block AuthorList -element LastName
```

excludes the investigators:

```
Tinker    Evers    Chance
```

Using −num on each type of object:

```
xtract -pattern PubmedArticle -num Author Investigator LastName CollectiveName
```

displays the various object counts:

```
4    3    6    1
```

Date Selection

Dates come in all shapes and sizes:

```
<PubmedArticle>
  <MedlineCitation>
    <PMID>99999999</PMID>
    <DateCompleted>
      <Year>2011</Year>
    </DateCompleted>
    <DateRevised>
      <Year>2012</Year>
    </DateRevised>
    <Article>
      <Journal>
        <JournalIssue>
          <PubDate>
            <Year>2013</Year>
          </PubDate>
        </JournalIssue>
      </Journal>
      <ArticleDate>
        <Year>2014</Year>
      </ArticleDate>
    </Article>
```

```
    </MedlineCitation>
    <PubmedData>
      <History>
        <PubMedPubDate PubStatus="received">
          <Year>2015</Year>
        </PubMedPubDate>
        <PubMedPubDate PubStatus="accepted">
          <Year>2016</Year>
        </PubMedPubDate>
        <PubMedPubDate PubStatus="entrez">
          <Year>2017</Year>
        </PubMedPubDate>
        <PubMedPubDate PubStatus="pubmed">
          <Year>2018</Year>
        </PubMedPubDate>
        <PubMedPubDate PubStatus="medline">
          <Year>2019</Year>
        </PubMedPubDate>
      </History>
    </PubmedData>
  </PubmedArticle>
```

Within the record, −element exploration on the year:

```
xtract -pattern PubmedArticle -element Year
```

finds and prints all nine instances:

```
2011    2012    2013    2014    2015    2016    2017    2018    2019
```

Using −block to limit the scope:

```
xtract -pattern PubmedArticle -block History -element Year
```

prints only the five years within the History object:

```
2015    2016    2017    2018    2019
```

Inserting a conditional statement to limit element selection to a date with a specific attribute:

```
xtract -pattern PubmedArticle -block History \
  -if @PubStatus -equals "pubmed" -element Year
```

surprisingly still prints all five years within History:

```
2015    2016    2017    2018    2019
```

This is because the −if command uses the same exploration logic as −element, but is designed to declare success if it finds a match anywhere within the current scope. There is indeed a "pubmed" attribute within History, in one of the five PubMedPubDate child objects, so the test succeeds. Thus, −element is given free rein to do its own exploration in History, and prints all five years.

The solution is to explore the individual PubMedPubDate objects:

```
xtract -pattern PubmedArticle -block PubMedPubDate \
  -if @PubStatus -equals "pubmed" -element Year
```

This visits each PubMedPubDate separately, with the −if test matching only the indicated date type, thus returning only the desired year:

```
2018
```

PMID Extraction

Because of the presence of a CommentsCorrections object:

```
<PubmedArticle>
  <MedlineCitation>
    <PMID>99999999</PMID>
    <CommentsCorrectionsList>
      <CommentsCorrections RefType="ErratumFor">
        <PMID>88888888</PMID>
      </CommentsCorrections>
    </CommentsCorrectionsList>
  </MedlineCitation>
</PubmedArticle>
```

attempting to print the record's PubMed Identifier:

```
xtract -pattern PubmedArticle -element PMID
```

also returns the PMID of the comment:

```
99999999    88888888
```

Using an exploration command cannot exclude the second instance, because it would need a parent node unique to the first element, and the chain of parents to the first PMID:

```
PubmedArticle/MedlineCitation
```

is a subset of the chain of parents to the second PMID:

```
PubmedArticle/MedlineCitation/CommentsCorrectionList/CommentsCorrections
```

Although **–first** PMID will work in this particular case, the more general solution is to limit by subpath with the parent / child construct:

```
xtract -pattern PubmedArticle -element MedlineCitation/PMID
```

That would work even if the order of objects were reversed.

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 / star** construct is used to visit the individual components, even though they may have different names. Piping the 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 −db taxonomy and Gene-commentary in −db gene. Thus, they can contain 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 closed by the </Taxon> stop tag on line 6, and not by the first </Taxon> encountered on line 3.

When a recursive object (e.g., Taxon) is given to an exploration command:

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

subsequent −element commands are blocked from descending into the internal objects, and return information only for the main entries:

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

The **star / 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 / child** construct:

```
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
...
```

Additional Elink Options

Elink has several additional modes that 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, the "neighbor" command:

```
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     ...
...
```

The "acheck" command returns all available link names for each record:

```
esearch -db pubmed -query "Federhen S [AUTH]" |
elink -cmd acheck |
xtract -pattern LinkSet -tab "\n" -element IdLinkSet/Id \
  -block LinkInfo -tab "\n" -element LinkName
```

printing each on its own line:

```
25510495
pubmed_images
pubmed_pmc
pubmed_pmc_local
pubmed_pmc_refs
pubmed_pubmed
pubmed_pubmed_citedin
...
```

The "prlinks" command can obtain the URL reference to the publisher web page for an article. The Unix "xargs" command calls elink separately for each identifier:

```
epost -db pubmed -id 22966225,19880848 |
efetch -format uid |
xargs -n 1 elink -db pubmed -cmd prlinks -id |
xtract -pattern LinkSet -first Id -element ObjUrl/Url
```

Repackaging XML Results

Splitting abstract paragraphs into individual words, while using XML reformatting commands:

```
efetch -db pubmed -id 2539356 -format xml |
xtract -stops -rec Rec -pattern PubmedArticle \
  -enc Paragraph -wrp Word -words AbstractText
```

generates:

```
...
<Paragraph>
  <Word>the</Word>
  <Word>tn3</Word>
  <Word>transposon</Word>
  <Word>inserts</Word>
  ...
```

```
    <Word>was</Word>
    <Word>necessary</Word>
    <Word>for</Word>
    <Word>immunity</Word>
  </Paragraph>
  ...
```

with the words from each abstract instance encased in a separate parent object. Word counts for each paragraph could then be calculated by piping to:

```
xtract -pattern Rec -block Paragraph -num Word
```

Multi-Step Transformations

Although xtract provides −element variants to do simple data manipulation, more complex tasks are sometimes best handled by being broken up into a series of simpler transformations. These are also known as structured data "processing chains".

Document summaries for two bacterial chromosomes:

```
efetch -db nuccore -id U00096,CP002956 -format docsum |
```

contain several individual fields and a complex series of self-closing Stat objects:

```
<DocumentSummary>
  <Id>545778205</Id>
  <Caption>U00096</Caption>
  <Title>Escherichia coli str. K-12 substr. MG1655, complete genome</Title>
  <CreateDate>1998/10/13</CreateDate>
  <UpdateDate>2020/09/23</UpdateDate>
  <TaxId>511145</TaxId>
  <Slen>4641652</Slen>
  <Biomol>genomic</Biomol>
  <MolType>dna</MolType>
  <Topology>circular</Topology>
  <Genome>chromosome</Genome>
  <Completeness>complete</Completeness>
  <GeneticCode>11</GeneticCode>
  <Organism>Escherichia coli str. K-12 substr. MG1655</Organism>
  <Strain>K-12</Strain>
  <BioSample>SAMN02604091</BioSample>
  <Statistics>
    <Stat type="Length" count="4641652"/>
    <Stat type="all" count="9198"/>
    <Stat type="cdregion" count="4302"/>
    <Stat type="cdregion" subtype="CDS" count="4285"/>
    <Stat type="cdregion" subtype="CDS/pseudo" count="17"/>
    <Stat type="gene" count="4609"/>
    <Stat type="gene" subtype="Gene" count="4464"/>
    <Stat type="gene" subtype="Gene/pseudo" count="145"/>
    <Stat type="rna" count="187"/>
    <Stat type="rna" subtype="ncRNA" count="79"/>
    <Stat type="rna" subtype="rRNA" count="22"/>
    <Stat type="rna" subtype="tRNA" count="86"/>
    <Stat source="all" type="Length" count="4641652"/>
    <Stat source="all" type="all" count="13500"/>
    <Stat source="all" type="cdregion" count="4302"/>
    <Stat source="all" type="gene" count="4609"/>
    <Stat source="all" type="prot" count="4302"/>
```

```
      <Stat source="all" type="rna" count="187"/>
    </Statistics>
    <AccessionVersion>U00096.3</AccessionVersion>
  </DocumentSummary>
  <DocumentSummary>
    <Id>342852136</Id>
    <Caption>CP002956</Caption>
    <Title>Yersinia pestis A1122, complete genome</Title>
    ...
```

which make extracting the single "best" value for gene count a non-trivial exercise.

In addition to repackaging commands that surround extracted values with XML tags, the −element "*" construct prints the entirety of the current scope, including its XML wrapper. Piping the document summaries to:

```
xtract -set Set -rec Rec -pattern DocumentSummary \
  -block DocumentSummary -pkg Common \
    -wrp Accession -element AccessionVersion \
    -wrp Organism -element Organism \
    -wrp Length -element Slen \
    -wrp Title -element Title \
    -wrp Date -element CreateDate \
    -wrp Biomol -element Biomol \
    -wrp MolType -element MolType \
  -block Stat -if @type -equals gene -pkg Gene -element "*" \
  -block Stat -if @type -equals rna -pkg RNA -element "*" \
  -block Stat -if @type -equals cdregion -pkg CDS -element "*" |
```

encloses several fields in a Common block, and packages statistics on gene, RNA, and coding region features into separate sections of a new XML object:

```
...
<Rec>
  <Common>
    <Accession>U00096.3</Accession>
    <Organism>Escherichia coli str. K-12 substr. MG1655</Organism>
    <Length>4641652</Length>
    <Title>Escherichia coli str. K-12 substr. MG1655, complete genome</Title>
    <Date>1998/10/13</Date>
    <Biomol>genomic</Biomol>
    <MolType>dna</MolType>
  </Common>
  <Gene>
    <Stat type="gene" count="4609"/>
    <Stat type="gene" subtype="Gene" count="4464"/>
    <Stat type="gene" subtype="Gene/pseudo" count="145"/>
    <Stat source="all" type="gene" count="4609"/>
  </Gene>
  <RNA>
    <Stat type="rna" count="187"/>
    <Stat type="rna" subtype="ncRNA" count="79"/>
    <Stat type="rna" subtype="rRNA" count="22"/>
    <Stat type="rna" subtype="tRNA" count="86"/>
    <Stat source="all" type="rna" count="187"/>
  </RNA>
  <CDS>
    <Stat type="cdregion" count="4302"/>
    <Stat type="cdregion" subtype="CDS" count="4285"/>
    <Stat type="cdregion" subtype="CDS/pseudo" count="17"/>
```

```
      <Stat source="all" type="cdregion" count="4302"/>
    </CDS>
  </Rec>
  ...
```

With statistics from different types of feature now segregated in their own substructures, total counts for each can be extracted with the −first command:

```
xtract -set Set -rec Rec -pattern Rec \
  -block Common -element "*" \
  -block Gene -wrp GeneCount -first Stat@count \
  -block RNA -wrp RnaCount -first Stat@count \
  -block CDS -wrp CDSCount -first Stat@count |
```

This rewraps the data into a third XML form containing specific feature counts:

```
...
<Rec>
  <Common>
    <Accession>U00096.3</Accession>
    <Organism>Escherichia coli str. K-12 substr. MG1655</Organism>
    <Length>4641652</Length>
    <Title>Escherichia coli str. K-12 substr. MG1655, complete genome</Title>
    <Date>1998/10/13</Date>
    <Biomol>genomic</Biomol>
    <MolType>dna</MolType>
  </Common>
  <GeneCount>4609</GeneCount>
  <RnaCount>187</RnaCount>
  <CDSCount>4302</CDSCount>
</Rec>
...
```

without requiring extraction commands for the individual elements in the Common block to be repeated at each step.

Assuming the contents are satisfactory, passing the last structured form to:

```
xtract \
  -head accession organism length gene_count rna_count \
  -pattern Rec -def "-" \
    -element Accession Organism Length GeneCount RnaCount
```

produces a tab-delimited table with the desired values:

```
accession     organism                 length     gene_count    rna_count
U00096.3      Escherichia coli ...     4641652    4609          187
CP002956.1    Yersinia pestis A1122    4553770    4217          86
```

If a different order of fields is desired after the final xtract has been run, piping to:

```
reorder-columns 1 3 5 4
```

will rearrange the output, including the column headings:

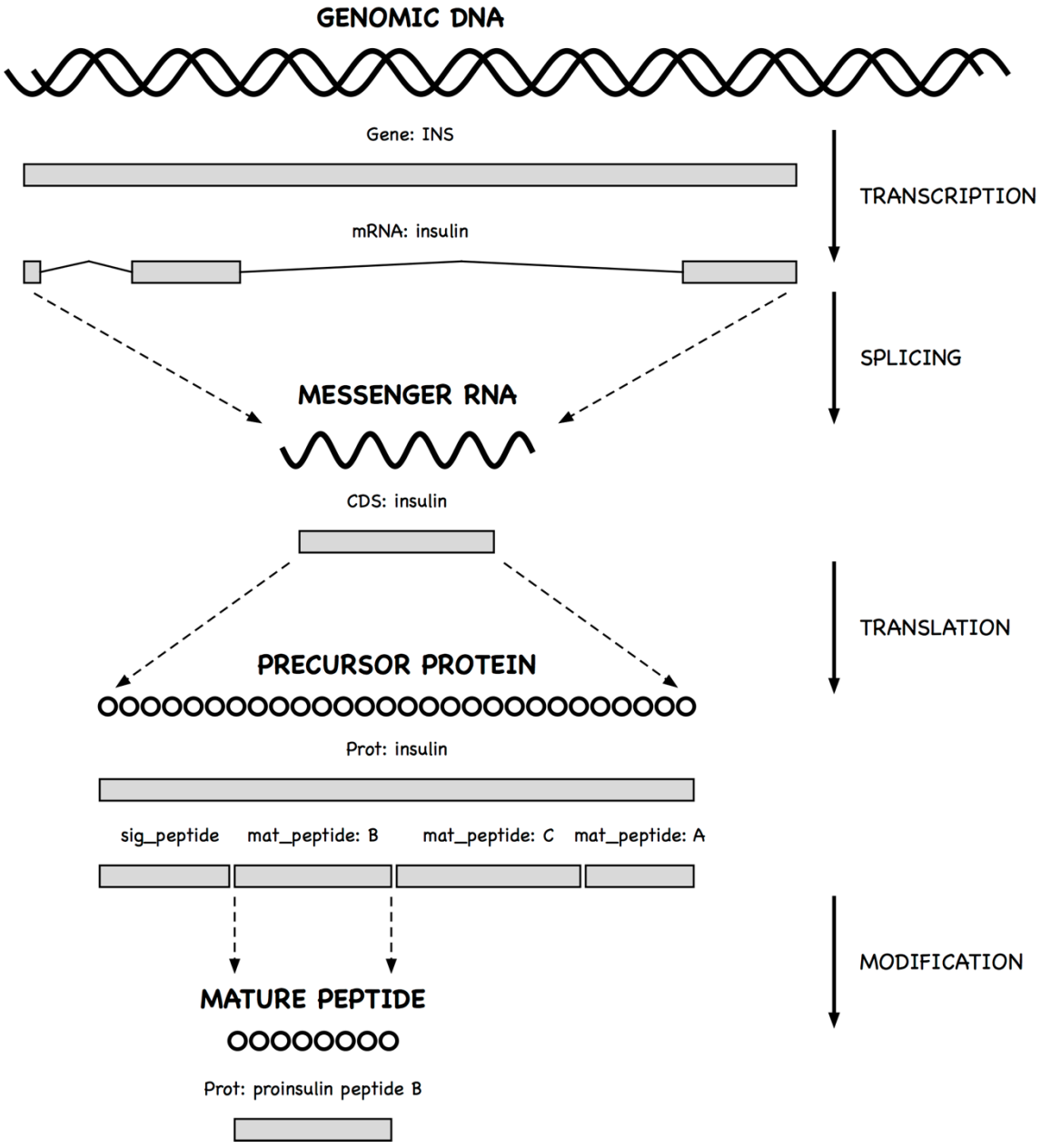
```
accession     length     rna_count    gene_count
U00096.3      4641652    187          4609
CP002956.1    4553770    86           4217
```

Sequence Records

NCBI Data Model for Sequence Records

The NCBI data model for sequence records 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.

Each sequence can have multiple features, which contain information about the biology of a given region, including the transformations involved in gene expression. Each feature can have multiple qualifiers, which store specific details about that feature (e.g., name of the gene, genetic code used for protein translation, accession of the product sequence, cross-references to external databases).



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.

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>
      ...
```

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"
```

are presented in INSDSeq XML as structured objects:

```
...
<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>
...
```

The data hierarchy is easily explored using a **–pattern** {sequence} **–group** {feature} **–block** {qualifier} construct. However, 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.

Generating Qualifier Extraction Commands

As a convenience for exploring sequence records, the xtract **–insd** helper function generates the appropriate nested extraction commands from feature and qualifier names on the command line. (Two computed qualifiers, **sub_sequence** and **feat_location**, are also supported.)

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 automatically-constructed query.

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

```
xtract -insd complete mat_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 -SEQ INSDSeq_sequence \
  -group INSDFeature -if INSDFeature_key -equals mat_peptide \
    -branch INSDFeature -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 product \
    -element INSDQualifier_value
```

Snail Venom Peptide Sequences

Incorporating the xtract −insd command in a search on cone snail venom:

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

prints the accession number, mature peptide length, product name, calculated molecular weight, and amino acid sequence for a sample of neurotoxic peptides:

```
AAN78128.1    12    alpha-conotoxin ImI    1357    GCCSDPRCAWRC
ADB65789.1    20    conotoxin Cal 16       2134    LEMQGCVCNANAKFCCGEGR
ADB65788.1    20    conotoxin Cal 16       2134    LEMQGCVCNANAKFCCGEGR
AGO59814.1    32    del13b conotoxin       3462    DCPTSCPTTCANGWECCKGYPCVRQHCSGCNH
AAO33169.1    16    alpha-conotoxin GIC    1615    GCCSHPACAGNNQHIC
AAN78279.1    21    conotoxin Vx-II        2252    WIDPSHYCCCGGGCTDDCVNC
AAF23167.1    31    BeTX toxin             3433    CRAEGTYCENDSQCCLNECCWGGCGHPCRHP
ABW16858.1    15    marmophin              1915    DWEYHAHPKPNSFWT
...
```

Piping the results to a series of Unix commands and EDirect scripts:

```
grep -i conotoxin |
filter-columns '10 <= $2 && $2 <= 30' |
sort-table -u -k 5 |
sort-table -k 2,2n |
align-columns -
```

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

```
AAN78127.1    12    alpha-conotoxin ImII           1515    ACCSDRRCRWRC
AAN78128.1    12    alpha-conotoxin ImI            1357    GCCSDPRCAWRC
ADB43130.1    15    conotoxin Cal 1a               1750    KCCKRHHGCHPCGRK
ADB43131.1    15    conotoxin Cal 1b               1708    LCCKRHHGCHPCGRT
AAO33169.1    16    alpha-conotoxin GIC            1615    GCCSHPACAGNNQHIC
ADB43128.1    16    conotoxin Cal 5.1              1829    DPAPCCQHPIETCCRR
AAD31913.1    18    alpha A conotoxin Tx2          2010    PECCSHPACNVDHPEICR
ADB43129.1    18    conotoxin Cal 5.2              2008    MIQRSQCCAVKKNCCHVG
ADB65789.1    20    conotoxin Cal 16               2134    LEMQGCVCNANAKFCCGEGR
ADD97803.1    20    conotoxin Cal 1.2              2206    AGCCPTIMYKTGACRTNRCR
AAD31912.1    21    alpha A conotoxin Tx1          2304    PECCSDPRCNSSHPELCGGRR
```

```
AAN78279.1    21    conotoxin Vx-II                 2252    WIDPSHYCCCGGGCTDDCVNC
ADB43125.1    22    conotoxin Cal 14.2              2157    GCPADCPNTCDSSNKCSPGFPG
ADD97802.1    23    conotoxin Cal 6.4               2514    GCWLCLGPNACCRGSVCHDYCPR
AAD31915.1    24    O-superfamily conotoxin TxO2    2565    CYDSGTSCNTGNQCCSGWCIFVCL
AAD31916.1    24    O-superfamily conotoxin TxO3    2555    CYDGGTSCDSGIQCCSGWCIFVCF
AAD31920.1    24    omega conotoxin SVIA mutant 1   2495    CRPSGSPCGVTSICCGRCYRGKCT
AAD31921.1    24    omega conotoxin SVIA mutant 2   2419    CRPSGSPCGVTSICCGRCSRGKCT
ABE27006.1    25    conotoxin p114a                 2917    FPRPRICNLACRAGIGHKYPFCHCR
ABE27007.1    25    conotoxin p114.1                2645    GPGSAICNMACRLGQGHMYPFCNCN
...
```

The xtract **–insdx** variant:

```
esearch -db protein -query "conotoxin" |
efilter -query "mat_peptide [FKEY]" |
efetch -format gpc |
xtract -insdx complete mat_peptide "%peptide" product mol_wt peptide |
xtract -pattern Rec -select product -contains conotoxin |
xtract -pattern Rec -sort mol_wt
```

saves the output table directly as XML, with the XML tag names taken from the original qualifier names:

```
...
  <Rec>
  <accession>AAO33169.1</accession>
  <feature_key>mat_peptide</feature_key>
  <peptide_Len>16</peptide_Len>
  <product>alpha-conotoxin GIC</product>
  <mol_wt>1615</mol_wt>
  <peptide>GCCSHPACAGNNQHIC</peptide>
</Rec>
<Rec>
  <accession>AIC77099.1</accession>
  <feature_key>mat_peptide</feature_key>
  <peptide_Len>16</peptide_Len>
  <product>conotoxin Im1.2</product>
  <mol_wt>1669</mol_wt>
  <peptide>GCCSHPACNVNNPHIC</peptide>
</Rec>
...
```

Qualifier names with prefix shortcuts "**#**" and "**%**" are modified to use "_Num" and "_Len" suffixes, respectively.

Missing Qualifiers

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-table -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
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 "zero-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 using −element:

```
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**, were created to allow direct use of the 0-based coordinates:

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

Xtract now 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 docsum ChrStart and ChrStop fields are 0-based, sees that the desired output is 1-based, and translates the command to convert coordinates internally using the −inc logic. 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
```

Gene Records

Genes in a Region

To list all genes between two markers flanking the human X chromosome centromere, first retrieve the protein-coding gene records on that chromosome:

```
esearch -db gene -query "Homo sapiens [ORGN] AND X [CHR]" |
efilter -status alive -type coding | efetch -format docsum |
```

Gene names and chromosomal positions are extracted by piping the records to:

```
xtract -pattern DocumentSummary -NAME Name -DESC Description \
  -block GenomicInfoType -if ChrLoc -equals X \
    -min ChrStart,ChrStop -element "&NAME" "&DESC" |
```

Exploring each GenomicInfoType is needed because of pseudoautosomal regions at the ends of the X and Y chromosomes:

```
...
<GenomicInfo>
  <GenomicInfoType>
    <ChrLoc>X</ChrLoc>
    <ChrAccVer>NC_000023.11</ChrAccVer>
```

```
      <ChrStart>155997630</ChrStart>
      <ChrStop>156013016</ChrStop>
      <ExonCount>14</ExonCount>
    </GenomicInfoType>
    <GenomicInfoType>
      <ChrLoc>Y</ChrLoc>
      <ChrAccVer>NC_000024.10</ChrAccVer>
      <ChrStart>57184150</ChrStart>
      <ChrStop>57199536</ChrStop>
      <ExonCount>14</ExonCount>
    </GenomicInfoType>
  </GenomicInfo>
  ...
```

Without limiting to chromosome X, the copy of IL9R near the "q" telomere of chromosome Y would be erroneously placed with genes that are near the X chromosome centromere, shown here in between SPIN2A and ZXDB:

```
...
57121860    FAAH2     fatty acid amide hydrolase 2
57133042    SPIN2A    spindlin family member 2A
57184150    IL9R      interleukin 9 receptor
57592010    ZXDB      zinc finger X-linked duplicated B
...
```

With genes restricted to the X chromosome, results can be sorted by position, and then filtered and partitioned:

```
sort-table -k 1,1n | cut -f 2- |
grep -v pseudogene | grep -v uncharacterized | grep -v hypothetical |
between-two-genes AMER1 FAAH2
```

to produce an ordered table of known genes located between the two markers:

```
FAAH2      fatty acid amide hydrolase 2
SPIN2A     spindlin family member 2A
ZXDB       zinc finger X-linked duplicated B
NLRP2B     NLR family pyrin domain containing 2B
ZXDA       zinc finger X-linked duplicated A
SPIN4      spindlin family member 4
ARHGEF9    Cdc42 guanine nucleotide exchange factor 9
AMER1      APC membrane recruitment protein 1
```

Gene Sequence

Genes encoded on the minus strand of a sequence:

```
esearch -db gene -query "DDT [GENE] AND mouse [ORGN]" |
efetch -format docsum |
xtract -pattern GenomicInfoType -element ChrAccVer ChrStart ChrStop |
```

have coordinates ("zero-based" in docsums) where the start position is greater than the stop:

```
NC_000076.6    75773373    75771232
```

These values can be read into Unix variables by a "while" loop:

```
while IFS=$'\t' read acn str stp
do
  efetch -db nuccore -format gb \
    -id "$acn" -chr_start "$str" -chr_stop "$stp"
done
```

The variables can then be used to obtain the reverse-complemented subregion in GenBank format:

```
LOCUS       NC_000076               2142 bp    DNA     linear   CON 08-AUG-2019
DEFINITION  Mus musculus strain C57BL/6J chromosome 10, GRCm38.p6 C57BL/6J.
ACCESSION   NC_000076 REGION: complement(75771233..75773374)
...
     gene            1..2142
                     /gene="Ddt"
     mRNA            join(1..159,462..637,1869..2142)
                     /gene="Ddt"
                     /product="D-dopachrome tautomerase"
                     /transcript_id="NM_010027.1"
     CDS             join(52..159,462..637,1869..1941)
                     /gene="Ddt"
                     /codon_start=1
                     /product="D-dopachrome decarboxylase"
                     /protein_id="NP_034157.1"
                     /translation="MPFVELETNLPASRIPAGLENRLCAATATILDKPEDRVSVTIRP
                     GMTLLMNKSTEPCAHLLVSSIGVVGTAEQNRTHSASFFKFLTEELSLDQDRIVIRFFP
                     ...
```

The reverse complement of a plus-strand sequence range can be selected with efetch −revcomp

External Data

Querying External Services

The nquire program uses command-line arguments to obtain data from RESTful, CGI, or FTP servers. Queries are built up from command-line arguments. Paths can be separated into components, which are combined with slashes. Remaining arguments (starting with a dash) are tag/value pairs, with multiple values between tags combined with commas.

For example, a POST request:

```
nquire -url http://w1.weather.gov/xml/current_obs/KSFO.xml |
xtract -pattern current_observation -tab "\n" \
  -element weather temp_f wind_dir wind_mph
```

returns the current weather report at the San Francisco airport:

```
A Few Clouds
54.0
Southeast
5.8
```

and a GET query:

```
nquire -get http://collections.mnh.si.edu/services/resolver/resolver.php \
  -voucher "Birds:321082" |
xtract -pattern Result -tab "\n" -element ScientificName StateProvince Country
```

returns information on a ruby-throated hummingbird specimen:

```
Archilochus colubris
Maryland
United States
```

while an FTP request:

```
nquire -ftp ftp.ncbi.nlm.nih.gov pub/gdp ideogram_9606_GCF_000001305.14_850_V1 |
grep acen | cut -f 1,2,6,7 | awk '/^X\t/'
```

returns data with the (estimated) sequence coordinates of the human X chromosome centromere (here showing where the p and q arms meet):

```
X    p    58100001    61000000
X    q    61000001    63800000
```

Nquire can also produce a list of files in an FTP server directory:

```
nquire -lst ftp://nlmpubs.nlm.nih.gov online/mesh/MESH_FILES/xmlmesh
```

or a list of FTP file names preceded by a column with the file sizes:

```
nquire -dir ftp.ncbi.nlm.nih.gov gene/DATA
```

Finally, nquire can download FTP files to the local disk:

```
nquire -dwn ftp.nlm.nih.gov online/mesh/MESH_FILES/xmlmesh desc2021.zip
```

If Aspera Connect is installed, the nquire −asp command will provide faster retrieval from NCBI servers:

```
nquire -asp ftp.ncbi.nlm.nih.gov pubmed baseline pubmed22n0001.xml.gz
```

Without Aspera Connect, nquire −asp defaults to using the −dwn logic.

XML Namespaces

Namespace prefixes are followed by a colon, while a leading colon matches any prefix:

```
nquire -url http://webservice.wikipathways.org getPathway -pwId WP455 |
xtract -pattern "ns1:getPathwayResponse" -decode ":gpml" |
```

The embedded Graphical Pathway Markup Language object can then be processed:

```
xtract -pattern Pathway -block Xref \
  -if @Database -equals "Entrez Gene" \
    -tab "\n" -element @ID
```

Automatic Xtract Format Conversion

Xtract can now detect and convert input data in JSON, text ASN.1, and GenBank/GenPept flatfile formats. The transmute commands or shortcut scripts, described below, are only needed if you want to inspect the intermediate XML, or to override default conversion settings.

JSON Arrays

Consolidated gene information for human β-globin retrieved from a curated biological database service developed at the Scripps Research Institute:

```
nquire -get http://mygene.info/v3 gene 3043 |
```

contains a multi-dimensional array of exon coordinates in JavaScript Object Notation (JSON) format:

```
"position": [
  [
    5225463,
    5225726
  ],
  [
```

```
      5226576,
      5226799
    ],
    [
      5226929,
      5227071
    ]
  ],
  "strand": -1,
```

This can be converted to XML with transmute **–j2x** (or the **json2xml** shortcut script):

```
transmute -j2x |
```

with the default"**–nest** element" argument assigning distinct tag names to each level:

```
<position>
  <position_E>5225463</position_E>
  <position_E>5225726</position_E>
</position>
...
```

JSON Mixtures

A query for the human green-sensitive opsin gene:

```
nquire -get http://mygene.info/v3/gene/2652 |
transmute -j2x |
```

returns data containing a heterogeneous mixture of objects in the pathway section:

```
<pathway>
  <reactome>
    <id>R-HSA-162582</id>
    <name>Signal Transduction</name>
  </reactome>
  ...
  <wikipathways>
    <id>WP455</id>
    <name>GPCRs, Class A Rhodopsin-like</name>
  </wikipathways>
</pathway>
```

The parent / star construct is used to visit the individual components of a parent object without needing to explicitly specify their names. For printing, the name of a child object is indicated by a question mark:

```
xtract -pattern opt -group "pathway/*" \
  -pfc "\n" -element "?,name,id"
```

This displays a table of pathway database references:

```
reactome        Signal Transduction               R-HSA-162582
reactome        Disease                           R-HSA-1643685
...
reactome        Diseases of the neuronal system   R-HSA-9675143
wikipathways    GPCRs, Class A Rhodopsin-like     WP455
```

Xtract **–path** can explore using multi-level object addresses, delimited by periods or slashes:

```
xtract -pattern opt -path pathway.wikipathways.id -tab "\n" -element id
```

Conversion of ASN.1

Similarly to −j2x, transmute **−a2x** (or **asn2xml**) will convert Abstract Syntax Notation 1 (ASN.1) text files to XML.

Tables to XML

Tab-delimited files are easily converted to XML with transmute **−t2x** (or **tbl2xml**):

```
nquire -ftp ftp.ncbi.nlm.nih.gov gene/DATA gene_info.gz |
gunzip -c | grep -v NEWENTRY | cut -f 2,3 |
transmute -t2x -set Set -rec Rec -skip 1 Code Name
```

This takes a series of command-line arguments with tag names for wrapping the individual columns, and skips the first line of input, which contains header information, to generate a new XML file:

```
...
<Rec>
  <Code>1246500</Code>
  <Name>repA1</Name>
</Rec>
<Rec>
  <Code>1246501</Code>
  <Name>repA2</Name>
</Rec>
...
```

The transmute −t2x **−header** argument will obtain tag names from the first line of the file:

```
nquire -ftp ftp.ncbi.nlm.nih.gov gene/DATA gene_info.gz |
gunzip -c | grep -v NEWENTRY | cut -f 2,3 |
transmute -t2x -set Set -rec Rec -header
```

CSV to XML

Similarly to −t2x, transmute **−c2x** (or **csv2xml**) will convert comma-separated values (CSV) files to XML.

GenBank Download

The entire set of GenBank format release files be downloaded with:

```
fls=$( nquire -lst ftp.ncbi.nlm.nih.gov genbank )
for div in \
  bct con env est gss htc htg inv mam pat \
  phg pln pri rod sts syn tsa una vrl vrt
do
  echo "$fls" |
  grep ".seq.gz" | grep "gb${div}" |
  sort -V | skip-if-file-exists |
  nquire -asp ftp.ncbi.nlm.nih.gov genbank
done
```

Unwanted divisions can be removed from the "for" loop to limit retrieval to specific sequencing classes or taxonomic regions.

GenBank to XML

The most recent GenBank virus release file can also be downloaded from NCBI servers:

```
nquire -lst ftp.ncbi.nlm.nih.gov genbank |
grep "^gbvrl" | grep ".seq.gz" | sort -V |
tail -n 1 | skip-if-file-exists |
nquire -asp ftp.ncbi.nlm.nih.gov genbank
```

GenBank flatfile records can be selected by organism name or taxon identifier, or by presence or absence of an arbitrary text string, with transmute **–gbf** (or **filter-genbank**):

```
gunzip -c *.seq.gz | filter-genbank -taxid 11292 |
```

Since xtract can now read JSON, ASN.1, and GenBank formats, the filtered flatfiles can be piped to xtract to obtain feature location intervals and underlying sequences of individual coding regions:

```
xtract -insd CDS gene product feat_location sub_sequence
```

without the need for an explicit transmute **–g2x** (or **gbf2xml**) step.

GenPept to XML

The latest GenPept daily incremental update file can be downloaded:

```
nquire -ftp ftp.ncbi.nlm.nih.gov genbank daily-nc Last.File |
sed "s/flat/gnp/g" |
nquire -ftp ftp.ncbi.nlm.nih.gov genbank daily-nc |
gunzip -c | transmute -g2x |
```

and the extracted INSDSeq XML can be processed in a similar manner:

```
xtract -pattern INSDSeq -select INSDQualifier_value -equals "taxon:2697049" |
xtract -insd mat_peptide product sub_sequence
```

Local PubMed Cache

Fetching data from Entrez 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.

Recent advances in technology provide an affordable and practical alternative. High-performance NVMe solid-state drives (which eliminate rotational delays for file access and bookkeeping operations) are readily available for purchase. Modern high-capacity file systems, such as APFS (which uses 64-bit inodes) or Ext4 (which can be configured for 100 million inodes), are now ubiquitous on contemporary computers. A judicious arrangement of multi-level nested directories (each containing no more than 100 subfolders or record files) ensures maximally-efficient use of these enhanced capabilities.

This combination of features allows local record storage (populated in advance from the PubMed FTP release files) to be an effective replacement for on-demand network retrieval, while avoiding the need to install and support a legacy database product on your computer.

Random Access Archive

EDirect can now preload over 35 million live PubMed records onto an inexpensive external 500 GB (gigabyte) solid-state drive as individual files for rapid retrieval. For example, PMID 2539356 would be stored at:

```
/pubmed/Archive/02/53/93/2539356.xml.gz
```

using a hierarchy of folders to organize the data for random access to any record.

The local archive is a completely self-contained turnkey system, with no need for the user to download, configure, and maintain complicated third-party database software.

Set an environment variable in your configuration file(s) to reference a section of your external drive:

```
export EDIRECT_LOCAL_ARCHIVE=/Volumes/external_drive_name/
```

or set separate environment variables to keep the intermediate steps on the external SSD but leave the resulting archive in a designated area of the computer's internal storage:

```
export EDIRECT_LOCAL_ARCHIVE=$HOME/internal_directory_name/
export EDIRECT_LOCAL_WORKING=/Volumes/external_drive_name/
```

In the latter case it will store around 180 GB on the internal drive for the local archive, or up to 250 GB if the local search index (see below) is also built.

Then run **archive-pubmed** to download the PubMed release files and distribute each record on the drive. This process will take several hours to complete, but subsequent updates are incremental, and should finish in minutes.

Retrieving over 125,000 compressed PubMed records from the local archive:

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

takes about 20 seconds. Retrieving those records from NCBI's network service, with efetch −format xml, would take around 40 minutes.

Even modest sets of PubMed query results can benefit from using the local cache. A reverse citation lookup on 191 papers:

```
esearch -db pubmed -query "Cozzarelli NR [AUTH]" | elink -cited |
```

requires 13 seconds to match 9620 subsequent articles. Retrieving them from the local archive:

```
efetch -format uid | fetch-pubmed |
```

takes less than one second. Printing the names of all authors in those records:

```
xtract -pattern PubmedArticle -block Author \
  -sep " " -tab "\n" -element LastName,Initials |
```

allows creation of a frequency table:

```
sort-uniq-count-rank
```

that lists the authors who most often cited the original papers:

```
145    Cozzarelli NR
108    Maxwell A
86     Wang JC
81     Osheroff N
...
```

Fetching from the network service would extend the 14 second running time to over 2 minutes.

Local Search Index

A similar divide-and-conquer strategy is used to create a local information retrieval system suitable for large data mining queries. Run **archive-pubmed −index** to populate retrieval index files from records stored in the local archive. The initial indexing will also take a few hours. Since PubMed updates are released once per day, it may be convenient to schedule reindexing to start in the late evening and run during the night.

For PubMed titles and primary abstracts, 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" in the title or abstract would be located at:

```
/pubmed/Postings/TIAB/c/a/n/c/canc.TIAB.trm
```

A query on cancer thus only needs to load a very small subset of the total index. The software supports expression evaluation, wildcard truncation, phrase queries, and proximity searches.

The **phrase-search** script (with an implied **–db pubmed**) provides access to the local search system.

Names of indexed fields, all terms for a given field, and terms plus record counts, are shown by:

```
phrase-search -fields

phrase-search -terms TITL

phrase-search -totals PROP
```

Terms are truncated with trailing asterisks, and can be expanded to show individual postings counts:

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

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

Query evaluation includes Boolean operations and parenthetical expressions:

```
phrase-search -query "(literacy AND numeracy) NOT (adolescent OR child)"
```

Adjacent words in the query are treated as a contiguous phrase:

```
phrase-search -query "selective serotonin reuptake inhibitor"
```

Each plus sign will replace a single word inside a phrase, and runs of tildes indicate the maximum distance between sequential phrases:

```
phrase-search -query "vitamin c + + common cold"

phrase-search -query "vitamin c ~ ~ common cold"
```

An exact substring match, without special processing of Boolean operators or indexed field names, can be obtained with -title (on the article title) or -exact (on the title or abstract), while ranked partial term matching in any field is available with -match:

```
phrase-search -title "Genetic Control of Biochemical Reactions in Neurospora."

phrase-search -match "tn3 transposition immunity [PAIR]" | just-top-hits 1
```

MeSH identifier code, MeSH hierarchy key, and year of publication are also indexed, and MESH field queries are supported by internally mapping to the appropriate CODE or TREE entries:

```
phrase-search -query "C14.907.617.812* [TREE] AND 2015:2019 [YEAR]"

phrase-search -query "Raynaud Disease [MESH]"
```

The phrase-search **–filter** command allows PMIDs to be generated by an EDirect search and then incorporated as a component in a local query:

Data Analysis and Visualization

All query commands return a list of PMIDs, which can be piped directly to **fetch-pubmed** to retrieve the uncompressed records. For example:

```
phrase-search -query "selective serotonin ~ ~ ~ reuptake inhibit*" |
fetch-pubmed |
xtract -pattern PubmedArticle -num AuthorList/Author |
sort-uniq-count -n |
reorder-columns 2 1 |
head -n 25 |
align-columns -g 4 -a lr
```

performs a proximity search with dynamic wildcard expansion (matching phrases like "selective serotonin and norepinephrine reuptake inhibitors") and fetches 12,966 PubMed records from the local archive. It then counts the number of authors for each paper (a consortium is treated as a single author), printing a frequency table of the number of papers per number of authors:

```
0      51
1    1382
2    1897
3    1906
...
```

The phrase-search and fetch-pubmed scripts are front-ends to the **rchive** program, which is used to build and search the inverted retrieval system. Rchive is multi-threaded for speed, retrieving records from the local archive in parallel, and fetching the positional indices for all terms in parallel before evaluating the title words as a contiguous phrase.

The cumulative size of PubMed can be calculated with a running sum of the annual record counts. Exponential growth over time will appear as a roughly linear curve on a semi-logarithmic graph:

```
phrase-search -totals YEAR |
print-columns '$2, $1, total += $1' |
print-columns '$1, log($2)/log(10), log($3)/log(10)' |
ilter-columns '$1 >= 1800 && $1 < YR' |
xy-plot annual-and-cumulative.png
```

Natural Language Processing

NCBI's Biomedical Text Mining Group performs computational analysis to extract chemical, disease, and gene references from article contents. NLM indexing of PubMed records assigns Gene Reference into Function (GeneRIF) mappings.

Running **archive-ncbinlp −index** periodically (monthly) will automatically refresh any out-of-date support files and then index the connections in CHEM, DISZ, GENE, and several gene subfields (GRIF, GSYN, and PREF):

```
phrase-search -terms DISZ | grep -i Raynaud

phrase-search -counts "Raynaud* [DISZ]"

phrase-search -query "Raynaud Disease [DISZ]"
```

Following Citation Links

Running **archive-nihocc −index** will download the latest NIH Open Citation Collection monthly release and build CITED and CITES indices, the local equivalent of elink −cited and −cites commands.

Citation links are retrieved by piping one or more PMIDs to phrase-search **–link**:

```
phrase-search -db pubmed -query "Havran W* [AUTH]" |
phrase-search -link CITED |
```

This returns PMIDs for 6504 articles that cite the original 96 papers. The records are then fetched and analyzed:

```
fetch-pubmed |
xtract -pattern PubmedArticle -histogram Journal/ISOAbbreviation |
sort-table -nr | head -n 10
```

to display the most popular journals in which the subsequent articles were published:

```
921    J Immunol
293    Eur J Immunol
248    J Exp Med
168    Front Immunol
149    Proc Natl Acad Sci U S A
139    Cell Immunol
121    Int Immunol
106    J Invest Dermatol
105    Immunol Rev
99     Immunity
```

Rapidly Scanning PubMed

If the **expand-current** script is run, an ad hoc scan can be performed on the nonredundant set of live PubMed records:

```
cat $EDIRECT_LOCAL_WORKING/pubmed/Scratch/Current/*.xml |
xtract -timer -turbo -pattern PubmedArticle -PMID MedlineCitation/PMID \
  -group AuthorList -if "#LastName" -eq 7 -element "&PMID" LastName
```

finding 1,700,652 articles with seven authors. (This query excludes consortia and additional named investigators. Author count is now indexed in the ANUM field.)

Xtract uses the Boyer-Moore-Horspool algorithm to partition an XML stream into individual records, distributing them among multiple instances of the data exploration and extraction function for concurrent execution. A multi-core computer with a solid-state drive can process all of PubMed in under 4 minutes.

The expand-current script now calls xtract -index to place an XML size object immediately before each PubMed record:

```
...
</PubmedArticle>
<NEXT_RECORD_SIZE>6374</NEXT_RECORD_SIZE>
<PubmedArticle>
...
```

The xtract **–turbo** flag reads this precomputed information to approximately double the speed of record partitioning, which is the rate-limiting step when many CPU cores are available. With proper cooling, it should allow up to a dozen cores to contribute to batch data extraction throughput.

User-Specified Term Index

Running **custom-index** with a PubMed indexer script and the names of the fields it populates:

```
custom-index $( which idx-grant ) GRNT
```

integrates user-specified indices into the local search system. The **idx-grant** script:

```
xtract -set IdxDocumentSet -rec IdxDocument -pattern PubmedArticle \
  -wrp IdxUid -element MedlineCitation/PMID -clr -rst -tab "" \
  -group PubmedArticle -pkg IdxSearchFields \
    -block PubmedArticle -wrp GRNT -element Grant/GrantID
```

has reusable boilerplate in its first three lines, and indexes PubMed records by Grant Identifier:

```
...
<IdxDocument>
  <IdxUid>2539356</IdxUid>
  <IdxSearchFields>
    <GRNT>AI 00468</GRNT>
    <GRNT>GM 07197</GRNT>
    <GRNT>GM 29067</GRNT>
  </IdxSearchFields>
</IdxDocument>
...
```

Once the final inversion:

```
...
<InvDocument>
  <InvKey>ai 00468</InvKey>
  <InvIDs>
    <GRNT>2539356</GRNT>
  </InvIDs>
</InvDocument>
<InvDocument>
  <InvKey>gm 07197</InvKey>
  <InvIDs>
    <GRNT>2539356</GRNT>
  </InvIDs>
</InvDocument>
<InvDocument>
  <InvKey>gm 29067</InvKey>
  <InvIDs>
    <GRNT>2539356</GRNT>
  </InvIDs>
</InvDocument>
..
```

and posting steps are completed, the new fields are ready to be searched.

Processing by XML Subset

A query on articles with abstracts published in a chosen journal, retrieved from the local cache, and followed by a multi-step transformation:

```
esearch -db pubmed -query "PNAS [JOUR]" -pub abstract |
efetch -format uid | fetch-pubmed |
xtract -stops -rec Rec -pattern PubmedArticle \
  -wrp Year -year "PubDate/*" -wrp Abst -words Abstract/AbstractText |
xtract -rec Pub -pattern Rec \
  -wrp Year -element Year -wrp Num -num Abst > countsByYear.xml
```

returns structured data with the year of publication and number of words in the abstract for each record:

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

(The ">" redirect saves the results to a file.)

The following "for" loop limits the processed query results to one year at a time with xtract −select, passing the relevant subset to a second xtract command:

```
for yr in {1960..2021}
do
  cat countsByYear.xml |
  xtract -set 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    122
1970    120
1971    127
...
2018    207
2019    207
2020    208
```

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.

Identifier Conversion

The archive-pubmed script also downloads MeSH descriptor information from the NLM FTP server and generates a conversion file:

```
...
<Rec>
  <Code>D064007</Code>
  <Name>Ataxia Telangiectasia Mutated Proteins</Name>
  ...
  <Tree>D12.776.157.687.125</Tree>
  <Tree>D12.776.660.720.125</Tree>
</Rec>
...
```

that can be used for mapping MeSH codes to and from chemical or disease names. For example:

```
cat $EDIRECT_LOCAL_ARCHIVE/pubmed/Data/meshconv.xml |
xtract -pattern Rec \
  -if Name -starts-with "ataxia telangiectasia" \
    -element Code
```

will return:

```
C565779
C576887
```

```
D001260
D064007
```

More information on a MeSH term could be obtained by running:

```
efetch -db mesh -id D064007 -format docsum
```

Integration with Entrez

Use phrase-search -filter to combine the UID results of a search (here followed by a link step) with a local query:

```
phrase-search -query "Berg CM [AUTH]" |
phrase-search -link CITED |
phrase-search -filter "Transposases [MESH]"
```

Intermediate lists of PMIDs can be saved to a file and piped (with "cat") into a subsequent phrase-search −filter query. They can also be uploaded to the Entrez history server by piping to **epost**:

```
epost -db pubmed
```

or piped directly to **efetch**.

Solid-State Drive Preparation

To initialize a solid-state drive for hosting the local archive on a Mac, log into an admin account, run Disk Utility, choose View -> Show All Devices, select the top-level external drive, and press the Erase icon. Set the Scheme popup to GUID Partition Map, and APFS will appear as a format choice. Set the Format popup to APFS, enter the desired name for the volume, and click the Erase button.

To finish the drive configuration, disable Spotlight indexing on the drive with:

```
sudo mdutil -i off "${EDIRECT_LOCAL_ARCHIVE}"
sudo mdutil -E "${EDIRECT_LOCAL_ARCHIVE}"
```

and disable FSEvents logging with:

```
sudo touch "${EDIRECT_LOCAL_ARCHIVE}/.fseventsd/no_log"
```

Also exclude the disk from being backed up by Time Machine or scanned by a virus checker.

Automation

Unix Shell Scripting

A shell script can be used to repeat the same sequence of operations on a number of input values. The Unix shell is a command interpreter that supports user-defined variables, conditional statements, and repetitive execution loops. Scripts are usually saved in a file, and referenced by file name.

Comments start with a pound sign ("#") and are ignored. Quotation marks within quoted strings are entered by "escaping" with a backslash ("\"). Subroutines (functions) can be used to collect common code or simplify the organization of the script.

Combining Data from Adjacent Lines

Given a tab-delimited file of feature keys and values, where each gene is followed by its coding regions:

```
gene    matK
CDS     maturase K
gene    ATP2B1
```

```
CDS     ATPase 1 isoform 2
CDS     ATPase 1 isoform 7
gene    ps2
CDS     peptide synthetase
```

the **cat** command can pipe the file contents to a shell script that reads the data one line at a time:

```
#!/bin/bash

gene=""
while IFS=$'\t' read feature product
do
  if [ "$feature" = "gene" ]
  then
    gene="$product"
  else
    echo "$gene\t$product"
  fi
done
```

The resulting output lines, printed by the **echo** command, have the gene name and subsequent CDS product names in separate columns on individual rows:

```
matK      maturase K
ATP2B1    ATPase 1 isoform 2
ATP2B1    ATPase 1 isoform 7
ps2       peptide synthetase
```

Dissecting the script, the first line selects the Bash shell on the user's machine:

```
#!/bin/bash
```

The latest gene name is stored in the "gene" variable, which is first initialized to an empty string:

```
gene=""
```

The **while** command sequentially reads each line of the input file, **IFS** indicates tab-delimited fields, and **read** saves the first field in the "feature" variable and the remaining text in the "product" variable:

```
while IFS=$'\t' read feature product
```

The statements between the **do** and **done** commands are executed once for each input line. The **if** statement retrieves the current value stored in the feature variable (indicated by placing a dollar sign (**$**) in front of the variable name) and compares it to the word "gene":

```
if [ "$feature" = "gene" ]
```

If the feature key was "gene", it runs the **then** section, which copies the contents of the current line's "product" value into the persistent "gene" variable:

```
then
  gene="$product"
```

Otherwise the **else** section prints the saved gene name and the current coding region product name:

```
else
  echo "$gene\t$product"
```

separated by a tab character. The conditional block is terminated with a **fi** instruction ("if" in reverse):

```
fi
```

In addition to else, the **elif** command can allow a series of mutually-exclusive conditional tests:

```
if [ "$feature" = "gene" ]
then
  ...
elif [ "$feature" = "mRNA" ]
then
  ...
elif [ "$feature" = "CDS" ]
then
  ...
else
  ...
fi
```

A variable can be set to the result of commands that are enclosed between "**$(**" and "**)**" symbols:

```
mrna=$( echo "$product" | grep 'transcript variant' |
        sed 's/^.*transcript \(variant .*\).*$/\1/' )
```

Entrez Direct Commands Within Scripts

EDirect commands can also be run inside scripts. Saving the following text:

```
#!/bin/bash

printf "Years"
for disease in "$@"
do
  frst=$( echo -e "${disease:0:1}" | tr [a-z] [A-Z] )
  printf "\t${frst}${disease:1:3}"
done
printf "\n"

for (( yr = 2020; yr >= 1900; yr -= 10 ))
do
  printf "${yr}s"
  for disease in "$@"
  do
    val=$(
      esearch -db pubmed -query "$disease [TITL]" |
      efilter -mindate "${yr}" -maxdate "$((yr+9))" |
      xtract -pattern ENTREZ_DIRECT -element Count
    )
    printf "\t${val}"
  done
  printf "\n"
done
```

to a file named "scan_for_diseases.sh" and executing:

```
chmod +x scan_for_diseases.sh
```

allows the script to be called by name. Passing several disease names in command-line arguments:

```
scan_for_diseases.sh diphtheria pertussis tetanus |
```

returns the counts of papers on each disease, by decade, for over a century:

```
Years    Diph    Pert    Teta
2020s    104     281     154
```

```
2010s    860     2558    1296
2000s    892     1968    1345
1990s    1150    2662    1617
1980s    780     1747    1488
...
```

A graph of papers per decade for each disease is generated by piping the table to:

```
xy-plot diseases.png
```

Passing the data instead to:

```
align-columns -h 2 -g 4 -a ln
```

right-justifies numeric data columns for easier reading or for publication:

```
Years    Diph    Pert    Teta
2020s     104     281     154
2010s     860    2558    1296
2000s     892    1968    1345
1990s    1150    2662    1617
1980s     780    1747    1488
...
```

while piping to:

```
transmute -t2x -set Set -rec Rec -header
```

produces a custom XML structure for further comparative analysis by xtract.

Time Delay

The shell script command:

```
sleep 1
```

adds a one second delay between steps, and can be used to help prevent overuse of 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

EDirect supplies a **join-into-groups-of** script that combines lines of unique identifiers or sequence accession numbers into comma-separated groups:

```
#!/bin/sh
xargs -n "$@" echo |
sed 's/ /,/g
```

The following example demonstrates processing 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'
```

Programming in Go

A program written in a compiled language is translated into a computer's native machine instruction code, and will run much faster than an interpreted script, at the cost of added complexity during development.

Google's Go language (also known as "golang") is "an open source programming language that makes it easy to build simple, reliable, and efficient software". Go eliminates the need for maintaining complicated "make" files. The build system assumes full responsibility for downloading external library packages. Automated dependency management tracks module release numbers to prevent version skew.

As of 2020, the Go development process has been streamlined to the point that it is now easier to use than some popular scripting languages.

To build Go programs, the latest Go compiler must be installed on your computer. A link to the installation URL is in the Documentation section at the end of this web page.

basecount.go Program

Piping FASTA data to the basecount binary executable (compiled from the basecount.go source code file shown below):

```
efetch -db nuccore -id J01749,U54469 -format fasta | basecount
```

will return rows containing an accession number followed by counts for each base:

```
J01749.1    A 983    C 1210    G 1134    T 1034
U54469.1    A 849    C 699     G 585     T 748
```

The full (uncommented) source code for basecount.go is shown here, and is discussed below:

```
package main

import (
    "eutils"
    "fmt"
    "os"
    "sort"
)

func main() {

    fsta := eutils.FASTAConverter(os.Stdin, false)

    countLetters := func(id, seq string) {

        counts := make(map[rune]int)
        for _, base := range seq {
            counts[base]++
        }

        var keys []rune
        for ky := range counts {
            keys = append(keys, ky)
        }
        sort.Slice(keys, func(i, j int) bool { return keys[i] < keys[j] })

        fmt.Fprintf(os.Stdout, "%s", id)
        for _, base := range keys {
            num := counts[base]
            fmt.Fprintf(os.Stdout, "\t%c %d", base, num)
        }
        fmt.Fprintf(os.Stdout, "\n")
    }

    for fsa := range fsta {
        countLetters(fsa.SeqID, fsa.Sequence)
    }
}
```

Performance can be measured with the Unix "time" command:

```
time basecount < NC_000014.fsa
```

The program reads and counts the 107,043,718 bases of human chromosome 14, from an existing FASTA file, in under 2.5 seconds:

```
NC_000014.9    A 26673415    C 18423758    G 18559033    N 16475569    T 26911943
2.287
```

basecount.go Code Review

Go programs start with **package main** and then **import** additional software libraries (many included with Go, others residing in commercial repositories like github.com):

```
package main

import (
    "eutils"
    "fmt"
```

```
    "os"
    "sort"
)
```

Each compiled Go binary has a single **main** function, which is where program execution begins:

```
func main() {
```

The fsta **variable** is assigned to a data **channel** that streams individual FASTA records one at a time:

```
    fsta := eutils.FASTAConverter(os.Stdin, false)
```

The countLetters **subroutine** will be called with the identifier and sequence of each FASTA record:

```
    countLetters := func(id, seq string) {
```

An empty counts **map** is created for each sequence, and its memory is freed when the subroutine exits:

```
        counts := make(map[rune]int)
```

A **for** loop on the **range** of the sequence string visits each sequence letter. The map keeps a running count for each base or residue, with "++" incrementing the current value of the letter's map entry:

```
        for _, base := range seq {
           counts[base]++
        }
```

(String iteration by range returns position and letter pairs. Since the code does not use the position, its value is absorbed by an underscore ("_") character.)

Maps are not returned in a defined order, so map keys are loaded to a keys **array**, which is then sorted:

```
        var keys []rune
        for ky := range counts {
            keys = append(keys, ky)
        }
        sort.Slice(keys, func(i, j int) bool { return keys[i] < keys[j] })
```

(The second argument passed to sort.Slice is an **anonymous** function literal used to control the sort order. It is also a **closure**, implicitly inheriting the keys array from the enclosing function.)

The sequence identifier is printed in the first column:

```
       fmt.Fprintf(os.Stdout, "%s", id)
```

Iterating over the array prints letters and base counts in alphabetical order, with tabs between columns:

```
        for _, base := range keys {
            num := counts[base]
            fmt.Fprintf(os.Stdout, "\t%c %d", base, num)
        }
```

A newline is printed at the end of the row, and then the subroutine exits, clearing the map and array:

```
        fmt.Fprintf(os.Stdout, "\n")
    }
```

The remainder of the main function uses a loop to **drain** the fsta channel, passing the identifier and sequence string of each successive FASTA record to the countLetters function. The main function then ends with a final closing brace:

```
    for fsa := range fsta {
        countLetters(fsa.SeqID, fsa.Sequence)
    }
}
```

Note that the sequence of human chromosome 14, processed above, is stored in its entirety as a single contiguous Go string. No special coding considerations are needed for input, access, or memory management, even though it is over 107 million characters long.

Go Dependency Management

EDirect includes source code for the **eutils** helper library, which consolidates common functions used by xtract, transmute, and rchive, including the FASTA parser/streamer used by the basecount program shown above.

In addition to around two dozen eutils "*.go" files, the distribution contains "go.mod" and "go.sum" module files for the eutils package. They were created by running "./build.sh" in the eutils directory prior to release on the FTP site.

Modules provide a mechanism for automatically managing external dependencies. They record version numbers and checksums for the packages imported by eutils source files during development. Go will then retrieve the same versions of those packages, along with all of their internal support packages, if the eutils library is later incorporated into other software development projects.

Use of modules allows external Go packages to evolve independently, publishing newer versions with incompatible function argument signatures on their own schedules, while ensuring that this natural software development cycle does not break a working library or application build at some inopportune time in the future.

Compiling a Go Project

Each project typically resides in its own directory. The source code can be split into multiple files, and the build process will normally compile all of the "*.go" files together.

Create a new directory named "basecount" with:

```
cd ~
mkdir basecount
```

and copy the **basecount.go** source code file into that directory.

The program can then be compiled by running:

```
cd basecount
go mod init basecount
echo "replace eutils => $HOME/edirect/eutils" >> go.mod
go get eutils
go mod tidy
go build
```

but for convenience these commands are usually incorporated into a build script. To do this, save the following script to a file named **build.sh** in the same directory:

```
#!/bin/bash

if [ ! -f "go.mod" ]
then
  go mod init "$( basename $PWD )"
  echo "replace eutils => $HOME/edirect/eutils" >> go.mod
  go get eutils
```

```
fi

if [ ! -f "go.sum" ]
then
  go mod tidy
fi

go build
```

To compile the executable, enter the basecount directory, set the Unix execution permission bit, and run the build script:

```
cd basecount
chmod +x build.sh
./build.sh
```

The build script runs "**go mod init**" to generate "go.mod", and "**go mod tidy**" to generate " go.sum", if either module file is not already present.

(The "$(basename $PWD)" construct sets the executable's default name to match the parent directory, without needing to manually customize the "go mod init" line for each project.)

(The "replace eutils => $HOME/edirect/eutils" construct computes the path for finding the local eutils source code directory in the standard EDirect installation location.)

The "**go build**" instruction compiles the source file(s) for the application and all dependent libraries (caching the compiled object files for faster use later). It will then link these into a binary executable file that can run on the development machine.

You can select specific input files, change the executable program's name, and cross-compile for a different platform, with additional arguments to "go build":

```
env GOOS=darwin GOARCH=arm64 go build -o basecount.Silicon basecount.go
```

Separate projects in a single directory could be built by changing the "go build" line to:

```
for fl in *.go
do
  go build -o "${fl%.go}" "$fl"
done
```

Python Integration

Controlling EDirect from Python scripts is easily done with assistance from the **edirect.py** library file, which is included in the EDirect archive:

```
import subprocess
import shlex

def execute(cmmd, data=""):
    if isinstance(cmmd, str):
        cmmd = shlex.split(cmmd)
    res = subprocess.run(cmmd, input=data,
                         capture_output=True,
                         encoding='UTF-8')
    return res.stdout.strip()

def pipeline(cmmds, data=""):
    def flatten(cmmd):
```

```
        if isinstance(cmmd, str):
            return cmmd
        else:
            return shlex.join(cmmd)
    if not isinstance(cmmds, str):
        cmmds = ' | '.join(map(flatten, cmmds))
    res = subprocess.run(cmmds, input=data, shell=True,
                         capture_output=True,
                         encoding='UTF-8')
    return res.stdout.strip()

def efetch(*, db, id, format, mode=""):
    cmmd = ('efetch', '-db', db, '-id', str(id), '-format', format)
    if mode:
        cmmd = cmmd + ('-mode', mode)
    return execute(cmmd))
```

At the beginning of your program, import the edirect module with the following commands:

```
#!/usr/bin/env python3

import sys
import os
import shutil

sys.path.insert(1, os.path.dirname(shutil.which('xtract')))
import edirect
```

(Note that the import command uses "edirect", without the ".py" extension.)

The first argument to **edirect.execute** is the Unix command you wish to run. It can be provided either as a string:

```
edirect.execute("efetch -db nuccore -id NM_000518.5 -format fasta")
```

or as a sequence of strings, which allows a variable's value to be substituted for a specific parameter:

```
accession = "NM_000518.5"
edirect.execute(('efetch', '-db', 'nuccore', '-id', accession, '-format', 'fasta'))
```

An optional second argument accepts data to be passed to the Unix command through stdin. Multiple steps are chained together by using the result of the previous command as the data argument in the next command:

```
seq = edirect.execute("efetch -db nuccore -id NM_000518.5 -format fasta")
sub = edirect.execute("transmute -extract -1-based -loc 51..494", seq)
prt = edirect.execute(('transmute', '-cds2prot', '-every', '-trim'), sub)
```

Data piped to the script itself is relayed by using "**sys.stdin.read()**" as the second argument.

Alternatively, the **edirect.pipeline** function can accept a sequence of individual command strings to be piped together for execution:

```
edirect.pipeline(('efetch -db protein -id NP_000509.1 -format gp',
                  'xtract -insd Protein mol_wt sub_sequence'))
```

or execute a string containing several piped commands:

```
edirect.pipeline('''efetch -db nuccore -id J01749 -format fasta |
  transmute -replace -offset 1907 -delete GG -insert TC |
  transmute -search -circular GGATCC:BamHI GAATTC:EcoRI CTGCAG:PstI |
  align-columns -g 4 -a rl''')
```

Hiding details (e.g., isinstance, shlex.join, shlex.split, and subprocess.run) inside a common module means that biologists who are new to coding could control an entire analysis pipeline from their first Python program.

An **edirect.efetch** shortcut that uses named arguments is also available:

```
edirect.efetch(db="nuccore", id="NM_000518.5", format="fasta")
```

To run a custom shell script, make sure the execute permission bit is set, supply the full execution path, and follow it with any command-line arguments:

```
db = "pubmed"
res = edirect.execute(("./datefields.sh", db), "")
```

NCBI C++ Toolkit Access

EDirect scripts can be called from the NCBI C++ toolkit using the **ncbi::edirect::Execute** function:

```
#include <misc/eutils_client/eutils_client.hpp>
```

The function signature has separate parameters for the script name and its command-line arguments, followed by an optional string to be passed via stdin:

```
string Execute (
  const string& cmmd,
  const vector<string>& args,
  const string& data = kEmptyStr
);
```

Multiple steps are chained together by using the previous result as the data argument in the next command:

```
string seq = ncbi::edirect::Execute
  ( "efetch", { "-db", "nuccore", "-id", "NM_000518.5", "-format", "fasta" } );
string sub = ncbi::edirect::Execute
  ( "transmute", { "-extract", "-1-based", "-loc", "51..494" }, seq );
string prt = ncbi::edirect::Execute
  ( "transmute", { "-cds2prot", "-every", "-trim" }, sub );
```

The argument vector can also be generated dynamically, under program control:

```
vector<string> args;

args.push_back("-db");
args.push_back("pubmed");
args.push_back("-format");
args.push_back("abstract");
args.push_back("-id");
args.push_back(uid);
```

Citation matching can be performed on a CPub object reference with the -asn argument:

```
string uid = ncbi::edirect::Execute
  ( "cit2pmid", { "-asn", FORMAT(MSerial_FlatAsnText << pub) } );
```

or you can use -title, -author, -journal, -volume, -issue, -pages, and -year arguments.

If a matching PMID is found, it can be retrieved as PubmedArticle XML and transformed into Pubmed-entry ASN.1:

```
string xml = ncbi::edirect::Execute
  ( "efetch", { "-db", "pubmed", "-format", "xml" }, uid );
```

```
string asn = ncbi::edirect::Execute
  ( "pma2pme", { "-std" }, xml );
```

The ASN.1 string can then be read into memory with an object loader for further processing:

```
#include <objects/pubmed/Pubmed_entry.hpp>

unique_ptr<CObjectIStream> stm;
stm.reset ( CObjectIStream::CreateFromBuffer
  ( eSerial_AsnText, asn.data(), asn.length() ) );

CRef<CPubmed_entry> pme ( new CPubmed_entry );
stm->Read ( ObjectInfo ( *pme ) );
```

Additional Examples

EDirect examples demonstrate how to answer ad hoc questions in several Entrez databases. The detailed examples have been moved to a separate document, which can be viewed by clicking on the ADDITIONAL EXAMPLES link.

Appendices

Command-Line Arguments

Each EDirect program has a **–help** command that prints detailed information about available arguments. These include –**sort** values for esearch, **–format** and **–mode** choices for efetch, and **–cmd** options for elink.

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>280005319</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
  -A    Number of lines after match
  -B    Number of lines before match
```

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

Escape Sequences

  \n    Line break
  \t    Tab character
```

Modify Contents:

```
  sed         Replaces text strings

    -e        Specify individual expression
    s///      Substitute
        /g    Global
        /I    Case-insensitive
        /p    Print

  tr          Translates characters

    -d        Delete character
    -s        Squeeze runs of characters

  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

  mktemp    Make temporary file

  join      Join columns in files by common field

  paste     Merge columns in files by line number
```

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
    .*    Current and parent directory

  pwd     Prints working directory path
```

File Redirection:

```
  <         Read stdin from file
  >         Redirect stdout to file
  >>        Append to file
  2>        Redirect stderr
  2>&1      Merge stderr into stdout
  |         Pipe between programs
  <(cmd)    Execute command, read results as file
```

Shell Script Variables:

```
$0      Name of script
$n      Nth argument
$#      Number of arguments
"$*"    Argument list as one argument
"$@"    Argument list as separate arguments
$?      Exit status of previous command
```

Shell Script Tests:

```
-d      Directory exists
-f      File exists
-s      File is not empty
-n      Length of string is non-zero
-x      File is executable
-z      Variable is empty or not set
```

Shell Script Options:

```
set        Set optional behaviors

  -e       Exit immediately upon error
  -u       Treat unset variables as error
  -x       Trace commands and argument
```

File and Directory Extraction:

```
         BAS=$(printf pubmed%03d $n)
         DIR=$(dirname "$0")
         FIL=$(basename "$0")
```

Remove Prefix:

```
         FILE="example.tar.gz"
#        ${FILE#.*}  -> tar.gz
##       ${FILE##.*} -> gz
```

Remove Suffix:

```
         FILE="example.tar.gz"
         TYPE="http://identifiers.org/uniprot_enzymes/"
%        ${FILE%.*}  -> example.tar
         ${TYPE%/}   -> http://identifiers.org/uniprot_enzymes
%%       ${FILE%%.*} -> example
```

Loop Constructs:

```
         while IFS=$'\t' read ...
         for sym in HBB BRCA2 CFTR RAG1
         for col in "$@"
         for yr in {1960..2020}
         for i in $(seq $first $incr $last)
         for fl in *.xml.gz
```

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

Release Notes

EDirect release notes describe the history of incremental development and refactoring, from the original implementation in Perl to the redesign in Go and shell script. The detailed notes have been moved to a separate document, which can be viewed by clicking on the RELEASE NOTES link.

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.

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Documentation

EDirect navigation functions call the URL-based Entrez Programming Utilities:

```
https://www.ncbi.nlm.nih.gov/books/NBK25501
```

NCBI database resources are described by:

https://www.ncbi.nlm.nih.gov/pubmed/37994677

Information on how to obtain an API Key is described in this NCBI blogpost:

https://ncbiinsights.ncbi.nlm.nih.gov/2017/11/02/new-api-keys-for-the-e-utilities

An introduction to shell scripting for non-programmers is at:

https://missing.csail.mit.edu/2020/shell-tools/

An article on the Go programming language, written by its creators, is at:

https://cacm.acm.org/research/the-go-programming-language-and-environment/

and transcripts of talks on design philosophy and retrospective experience of Go are at:

https://commandcenter.blogspot.com/2012/06/less-is-exponentially-more.html

https://commandcenter.blogspot.com/2024/01/what-we-got-right-what-we-got-wrong.html

Instructions for downloading and installing the Go compiler are at:

https://golang.org/doc/install#download

Additional NCBI website and data usage policy and disclaimer information is located at:

https://www.ncbi.nlm.nih.gov/home/about/policies/

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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.