Entrez Programming Utilities Help

Last Updated: August 9, 2018
E-utilities Introduction

Please see the Release Notes for details and changes.

The Entrez Programming Utilities (E-utilities) are a set of eight server-side programs that provide a stable interface into the Entrez query and database system at the National Center for Biotechnology Information (NCBI). The E-utilities use a fixed URL syntax that translates a standard set of input parameters into the values necessary for various NCBI software components to search for and retrieve the requested data. The E-utilities are therefore the structured interface to the Entrez system, which currently includes 38 databases covering a variety of biomedical data, including nucleotide and protein sequences, gene records, three-dimensional molecular structures, and the biomedical literature.
# Table of Contents

**E-utilities Quick Start** .................................................................................................................. 1  
  Release Notes .................................................................................................................................. 1  
  Announcement ................................................................................................................................. 1  
  Introduction ...................................................................................................................................... 1  
  Searching a Database ....................................................................................................................... 1  
  Uploading UIDs to Entrez ................................................................................................................ 4  
  Downloading Document Summaries ............................................................................................... 5  
  Downloading Full Records ............................................................................................................. 8  
  Finding Related Data Through Entrez Links .................................................................................. 9  
  Getting Database Statistics and Search Fields ............................................................................... 10  
  Performing a Global Entrez Search ............................................................................................... 12  
  Retrieving Spelling Suggestions .................................................................................................... 13  
  Demonstration Programs ................................................................................................................ 14  
  For More Information .................................................................................................................... 18  

**A General Introduction to the E-utilities** .................................................................................. 19  
  Introduction ...................................................................................................................................... 19  
  Usage Guidelines and Requirements ............................................................................................. 19  
  The Nine E-utilities in Brief ........................................................................................................... 22  
  Understanding the E-utilities Within Entrez ................................................................................ 23  
  Combining E-utility Calls to Create Entrez Applications ............................................................. 27  
  Demonstration Programs ................................................................................................................. 29  
  For More Information ...................................................................................................................... 29  

**Sample Applications of the E-utilities** .................................................................................... 31  
  Introduction ...................................................................................................................................... 31  
  Basic Pipelines ............................................................................................................................... 31  
  ESearch – ESummary/EFetch .......................................................................................................... 31  
  EPost – ESummary/EFetch .............................................................................................................. 32  
  ELink – ESummary/Efetch ............................................................................................................... 33
<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entrez Direct: E-utilities on the UNIX Command Line</td>
<td>71</td>
</tr>
<tr>
<td>Getting Started</td>
<td>71</td>
</tr>
<tr>
<td>Searching and Filtering</td>
<td>75</td>
</tr>
<tr>
<td>Structured Data</td>
<td>79</td>
</tr>
<tr>
<td>Sequence Records</td>
<td>90</td>
</tr>
<tr>
<td>Sequence Coordinates</td>
<td>96</td>
</tr>
<tr>
<td>Complex Objects</td>
<td>97</td>
</tr>
<tr>
<td>Advanced Topics</td>
<td>100</td>
</tr>
<tr>
<td>Automation</td>
<td>105</td>
</tr>
<tr>
<td>Local Data Cache</td>
<td>108</td>
</tr>
<tr>
<td>XML Processing</td>
<td>111</td>
</tr>
<tr>
<td>Examples</td>
<td>114</td>
</tr>
<tr>
<td>Appendices</td>
<td>134</td>
</tr>
<tr>
<td>Release Notes</td>
<td>149</td>
</tr>
<tr>
<td>For More Information</td>
<td>160</td>
</tr>
</tbody>
</table>
E-utilities Quick Start

Eric Sayers, PhD

Created: December 12, 2008; Updated: November 1, 2017.

Release Notes

Please see our Release Notes for details on recent changes and updates.

Announcement

On May 1, 2018, NCBI will begin enforcing the use of new API keys for E-utility calls. Please see Chapter 2 for more details about this important change.

Introduction

This chapter provides a brief overview of basic E-utility functions along with examples of URL calls. Please see Chapter 2 for a general introduction to these utilities and Chapter 4 for a detailed discussion of syntax and parameters.

Examples include live URLs that provide sample outputs.

All E-utility calls share the same base URL:


Searching a Database

Basic Searching

esearch.fcgi?db=<database>&term=<query>

Input: Entrez database (&db); Any Entrez text query (&term)

Output: List of UIDs matching the Entrez query

Example: Get the PubMed IDs (PMIDs) for articles about breast cancer published in Science in 2008

Storing Search Results

esearch.fcgi?db=<database>&term=<query>&usehistory=y

Input: Any Entrez text query (&term); Entrez database (&db); &usehistory=y

Output: Web environment (&WebEnv) and query key (&query_key) parameters
specifying the location on the Entrez history server of the list of UIDs matching the
Entrez query

Example: Get the PubMed IDs (PMIDs) for articles about breast cancer published in Science
in 2008, and store them on the Entrez history server for later use

db=pubmed&term=science[journal]+AND+breast+cancer+AND+2008[pdat]&usehistory=y

Associating Search Results with Existing Search Results

esearch.fcgi?db=<database>&term=<query1>&usehistory=y

# esearch produces WebEnv value ($web1) and QueryKey value ($key1)
esearch.fcgi?db=<database>&term=<query2>&usehistory=y&WebEnv=$web1

# esearch produces WebEnv value ($web2) that contains the results
of both searches ($key1 and $key2)

Input: Any Entrez text query (&term); Entrez database (&db); &usehistory=y; Existing
web environment (&WebEnv) from a prior E-utility call

Output: Web environment (&WebEnv) and query key (&query_key) parameters
specifying the location on the Entrez history server of the list of UIDs matching the
Entrez query

For More Information

Please see ESearch In-Depth for a full description of ESearch.

Sample ESearch Output

<?xml version="1.0" ?>
<!DOCTYPE eSearchResult PUBLIC "-//NLM//DTD eSearchResult, 11 May 2002//EN"
eSearchResult
<Count>255147</Count>  # total number of records matching query
<RetMax>20</RetMax># number of UIDs returned in this XML; default=20
<RetStart>0</RetStart># index of first record returned; default=0
<QueryKey>1</QueryKey># QueryKey, only present if &usehistory=y
<WebEnv>0193yIkBjmM6OUBxuBvPfBIq8-9nIs1dXuMP0hhuMH-8Gjc7F_Dz1XL6z@397033B29A81FB01_0038SID</WebEnv>
# WebEnv; only present if &usehistory=y
<IdList>
   <Id>229486465</Id>    # list of UIDs returned
   <Id>229486321</Id>
   <Id>229485738</Id>
   <Id>229470359</Id>
   <Id>229463047</Id>
   <Id>229463037</Id>
   <Id>229463032</Id>
   <Id>229463019</Id>
   <Id>229463002</Id>
   <Id>229463000</Id>
   <Id>229462974</Id>
   <Id>229462961</Id>
   <Id>229462956</Id>
   <Id>229462921</Id>
   <Id>229462905</Id>
   <Id>229462899</Id>
   <Id>229462873</Id>
   <Id>229462863</Id>
   <Id>229462862</Id>
</IdList>

<TranslationSet>        # details of how Entrez translated the query
   <Translation>
      <From>mouse[orgn]</From>
      <To>"Mus musculus"[Organism]</To>
   </Translation>
</TranslationSet>

<TranslationStack>
   <TermSet>
      <Term>"Mus musculus"[Organism]</Term>
      <Field>Organism</Field>
      <Count>255147</Count>
      <Explode>Y</Explode>
   </TermSet>
   <OP>GROUP</OP>
</TranslationStack>

<QueryTranslation>"Mus musculus"[Organism]</QueryTranslation>
</eSearchResult>

Searching PubMed with Citation Data

citmatch.cgi?db=pubmed&rettype=xml&bdata=<citations>

Input: List of citation strings separated by a carriage return (%0D), where each citation string has the following format:

journal_title|year|volume|first_page|author_name|your_key|

Output: A list of citation strings with the corresponding PubMed ID (PMID) appended.

Example: Search PubMed for the following citations:


db=pubmed&retmode=xml&bdata=proc+natl+acad+sci+u+s+a|1991|88|3248|mann+bj|Art1|%0Dscience|1987|235|182|palmenberg+ac|Art2|

Sample Output (the PMIDs appear in the rightmost field):

proc natl acad sci u s a|1991|88|3248|mann bj|Art1|2014248
science|1987|235|182|palmenberg ac|Art2|3026048

Please see ECitMatch In-Depth for a full description of ECitMatch.

### Uploading UIDs to Entrez

#### Basic Uploading

epost.fcgi?db=<database>&id=<uid_list>

Input: List of UIDs (&id); Entrez database (&db)

Output: Web environment (&WebEnv) and query key (&query_key) parameters specifying the location on the Entrez history server of the list of uploaded UIDs

*Example: Upload five Gene IDs (7173,22018,54314,403521,525013) for later processing.*


#### Associating a Set of UIDs with Previously Posted Sets

epost.fcgi?db=<database1>&id=<uid_list1>

# epost produces WebEnv value ($web1) and QueryKey value ($key1)

epost.fcgi?db=<database2>&id=<uid_list2>&WebEnv=$web1

# epost produces WebEnv value ($web2) that contains the results of both posts ($key1 and $key2)

Input: List of UIDs (&id); Entrez database (&db); Existing web environment (&WebEnv)

Output: Web environment (&WebEnv) and query key (&query_key) parameters specifying the location on the Entrez history server of the list of uploaded UIDs

#### For More Information

Please see EPost In-Depth for a full description of EPost.
Sample EPost Output

```xml
<?xml version="1.0"?>
<ePostResult>
<QueryKey>1</QueryKey>
<WebEnv>NCID_01_268116914_130.14.18.47_9001_1241798628</WebEnv>
</ePostResult>
```

Downloading Document Summaries

Basic Downloading

esummary.fcgi?db=<database>&id=<uid_list>

Input: List of UIDs (&id); Entrez database (&db)

Output: XML DocSums

Example: Download DocSums for these protein GIs:
6678417,9507199,28558982,28558984,28558988,28558990

db=protein&id=6678417,9507199,28558982,28558984,28558988,28558990

Downloading Data From a Previous Search

esearch.fcgi?db=<database>&term=<query>&usehistory=y

# esearch produces WebEnv value ($web1) and QueryKey value ($key1)

esummary.fcgi?db=<database>&query_key=$key1&WebEnv=$web1

Input: Web environment (&WebEnv) and query key (&query_key) representing a set of Entrez UIDs on the Entrez history server

Output: XML DocSums

Sample ESummary Output

The output of ESummary is a series of XML “DocSums” (Document Summaries), the format of which depends on the database. Below is an example DocSum for Entrez Protein.

```xml
<?xml version="1.0"?>
<eSummaryResult>
<DocSum>
<Id>15718680</Id>
```
Sample ESummary version 2.0 Output

Version 2.0 of ESummary is an alternate XML presentation of Entrez DocSums. To retrieve version 2.0 DocSums, the URL should contain the &version parameter with an assigned value of '2.0'. Each Entrez database provides its own unique DTD for version 2.0 DocSums, and a link to the relevant DTD is provided in the header of the version 2.0 XML.

esummary.fcgi?db=<database>&id=<uid_list>&version=2.0

Below is an example version 2.0 DocSum from Entrez Protein (the same record as shown above in the default DocSum XML).

<?xml version="1.0"?>
<!DOCTYPE eSummaryResult PUBLIC "-//NLM//DTD eSummaryResult//EN"
eSummary_protein.dtd">
<eSummaryResult>
   <DocumentSummarySet status="OK">
      <DocumentSummary uid="15718680">
         <Caption>NP_005537</Caption>
         <Title>tyrosine-protein kinase ITK/TSK [Homo sapiens]</Title>
         <Extra>gi|15718680|ref|NP_005537.3|15718680</Extra>
         <Gi>15718680</Gi>
         <CreateDate>1999/06/09</CreateDate>
         <UpdateDate>2011/10/09</UpdateDate>
         <Flags>512</Flags>
         <TaxId>9606</TaxId>
         <Length>620</Length>
         <Status>live</Status>
         <MolType>aa</MolType>
      </DocumentSummary>
   </DocumentSummarySet>
</eSummaryResult>
<Topography linear/>
<SourceDb refseq/>
<SegmentSize 0/>
<ProjectId 0/>
<Genome genomic/>

<SubType chromosome|map/>
<SubName 5|5q31-q32/>
<AssemblyGi 399658/>
<AssemblyAcc D13720.1/>
<Tech/>
<Completeness/>
<GeneticCode 1/>

<Organism Homo sapiens/>

<Statistics>
  <Stat type="all" count="8"/>
  <Stat type="blob_size" count="16154"/>
  <Stat type="cdregion" count="1"/>
  <Stat type="cdregion" subtype="CDS" count="1"/>
  <Stat type="gene" count="1"/>
  <Stat type="org" count="1"/>
  <Stat type="prot" count="1"/>
  <Stat type="prot" subtype="Prot" count="1"/>
  <Stat type="pub" count="14"/>
  <Stat type="pub" subtype="PubMed" count="10"/>
  <Stat type="pub" subtype="PubMed/Gene-ref" count="4"/>
  <Stat type="site" count="1"/>
  <Stat type="site" subtype="Site" count="4"/>
  <Stat type="site" subtype="Site" count="9"/>
  <Stat type="CDD" type="all" count="15"/>
  <Stat type="CDD" type="region" count="6"/>
  <Stat type="CDD" type="region" subtype="Region" count="6"/>
  <Stat type="HPRD" type="all" count="3"/>
  <Stat type="HPRD" type="site" count="3"/>
  <Stat type="HPRD" type="site" subtype="Site" count="3"/>
  <Stat type="SNP" type="all" count="31"/>
  <Stat type="SNP" type="imp" count="31"/>
  <Stat type="SNP" type="imp" subtype="variation" count="31"/>
  <Stat type="all" type="all" count="57"/>
  <Stat type="all" type="blob_size" count="16154"/>
  <Stat type="all" type="cdregion" count="1"/>
  <Stat type="all" type="gene" count="1"/>
  <Stat type="all" type="imp" count="31"/>
  <Stat type="all" type="org" count="1"/>
  <Stat type="all" type="prot" count="1"/>
Downloading Full Records

Basic Downloading

`efetch.fcgi?db=<database>&id=<uid_list>&rettype=<retrieval_type>&retmode=<retrieval_mode>`

Input: List of UIDs (&id); Entrez database (&db); Retrieval type (&rettype); Retrieval mode (&retmode)

Output: Formatted data records as specified

*Example: Download nuccore GIs 34577062 and 24475906 in FASTA format*


Downloading Data From a Previous Search

`esearch.fcgi?db=<database>&term=<query>&usehistory=y`

# esearch produces WebEnv value ($web1) and QueryKey value ($key1)

`efetch.fcgi?db=<database>&query_key=$key1&WebEnv=$web1&rettype=<retrieval_type>&retmode=<retrieval_mode>`

Input: Entrez database (&db); Web environment (&WebEnv) and query key (&query_key) representing a set of Entrez UIDs on the Entrez history server; Retrieval type (&rettype); Retrieval mode (&retmode)

Output: Formatted data records as specified
**Downloading a Large Set of Records**

Please see Application 3 in Chapter 3

Input: Entrez database (&db); Web environment (&WebEnv) and query key (&query_key) representing a set of Entrez UIDs on the Entrez history server; Retrieval start (&retstart), the first record of the set to retrieve; Retrieval maximum (&retmax), maximum number of records to retrieve

Output: Formatted data records as specified

For More Information

Please see EFetch In-Depth for a full description of EFetch.

**Finding Related Data Through Entrez Links**

**Basic Linking**

**Batch mode** – finds only one set of linked UIDs

elink.fcgi?dbfrom=<source_db>&db=<destination_db>&id=<uid_list>

Input: List of UIDs (&id); Source Entrez database (&dbfrom); Destination Entrez database (&db)

Output: XML containing linked UIDs from source and destination databases

*Example: Find one set of Gene IDs linked to nuccore GIs 34577062 and 24475906*


‘By Id’ mode – finds one set of linked UIDs for each input UID

elink.fcgi?dbfrom=<source_db>&db=<destination_db>&id=<uid1>&id=<uid2>&id=<uid3>...

*Example: Find separate sets of Gene IDs linked to nuccore GIs 34577062 and 24475906*


*Note: &db may be a comma-delimited list of databases, so that elink returns multiple sets of linked UIDs in a single call*

**Finding Links to Data from a Previous Search**

esearch.fcgi?db=<source_db>&term=<query>&usehistory=y

# esearch produces WebEnv value ($web1) and QueryKey value ($key1)
elink.fcgi?dbfrom=<source_db>&db=<destination_db>&query_key=$key1&WebEnv=$web1&cmd=neighbor_history

Input: Source Entrez database (&dbfrom); Destination Entrez database (&db); Web environment (&WebEnv) and query key (&query_key) representing the set of source UIDs on the Entrez history server; Command mode (&cmd)

Output: XML containing Web environments and query keys for each set of linked UIDs

Note: To achieve ‘By Id’ mode, one must send each input UID as a separate &id parameter in the URL. Sending a WebEnv/query_key set always produces Batch mode behavior (one set of linked UIDs).

Finding Computational Neighbors Limited by an Entrez Search

elink.fcgi?dbfrom=<source_db>&db=<source_db>&id=<uid_list>&term=<query>&cmd=neighbor_history

Input: Source Entrez database (&dbfrom); Destination Entrez database (&db); List of UIDs (&id); Entrez query (&term); Command mode (&cmd)

Output: XML containing Web environments and query keys for each set of linked UIDs

Example: Find protein UIDs that are rat Reference Sequences and that are sequence similar to GI 15718680


For More Information

Please see ELink In-Depth for a full description of ELink.

Getting Database Statistics and Search Fields

einfo.fcgi?db=<database>

Input: Entrez database (&db)

Output: XML containing database statistics

Note: If no database parameter is supplied, einfo will return a list of all valid Entrez databases.

Example: Find database statistics for Entrez Protein.


For More Information

Please see EInfo In-Depth for a full description of EInfo.
Sample EInfo Output

<?xml version="1.0"?>
<!DOCTYPE eInfoResult PUBLIC "-//NLM//DTD eInfoResult, 11 May 2002//EN" 
<eInfoResult>
<DbInfo>
(DbName)protein/(DbName>
<MenuName>Protein</MenuName>
<Description>Protein sequence record</Description>
<Count>26715092</Count>
<LastUpdate>2009/05/12 04:39</LastUpdate>
<FieldList>
<Field>
<Name>ALL</Name>
<FullName>All Fields</FullName>
<Description>All terms from all searchable fields</Description>
<TermCount>133639432</TermCount>
<IsDate>N</IsDate>
<IsNumerical>N</IsNumerical>
<SingleToken>N</SingleToken>
<Hierarchy>N</Hierarchy>
<IsHidden>N</IsHidden>
</Field>
...
<Field>
<Name>PORG</Name>
<FullName>Primary Organism</FullName>
<Description>Scientific and common names
of primary organism, and all higher levels of taxonomy</Description>
<TermCount>673555</TermCount>
<IsDate>N</IsDate>
<IsNumerical>N</IsNumerical>
<SingleToken>Y</SingleToken>
<Hierarchy>Y</Hierarchy>
<IsHidden>N</IsHidden>
</Field>
</FieldList>
<LinkList>
<Link>
<Name>protein_biosystems</Name>
<Menu>BioSystem Links</Menu>
<Description>BioSystems</Description>
<DbTo>biosystems</DbTo>
</Link>
...
<Link>
<Name>protein_unigene</Name>
<Menu>UniGene Links</Menu>
<Description>Related UniGene records</Description>
<DbTo>unigene</DbTo>
</Link>
</LinkList>
</DbInfo>
</eInfoResult>
Performing a Global Entrez Search

egquery.fcgi?term=<query>

Input: Entrez text query (&term)

Output: XML containing the number of hits in each database.

Example: Determine the number of records for mouse in Entrez.


For More Information

Please see EGQuery In-Depth for a full description of EGQuery.

Sample EGQuery Output

<?xml version="1.0"?>
<!DOCTYPE Result PUBLIC "-//NLM//DTD eSearchResult, January 2004//EN"
<!--
 $Id: egquery_template.xml 106311 2007-06-26 14:46:31Z osipov $
-->
<!-- ================================================================= -->
<Result>
  <Term>mouse[orgn]</Term>
  <eGQueryResult>
    <ResultItem>
      <DbName>pubmed</DbName>
      <MenuName>PubMed</MenuName>
      <Count>0</Count>
      <Status>Term or Database is not found</Status>
    </ResultItem>
    <ResultItem>
      <DbName>pmc</DbName>
      <MenuName>PMC</MenuName>
      <Count>3823</Count>
      <Status>Ok</Status>
    </ResultItem>
    ...
    <ResultItem>
      <DbName>nuccore</DbName>
      <MenuName>Nucleotide</MenuName>
      <Count>1739903</Count>
      <Status>Ok</Status>
    </ResultItem>
    <ResultItem>
      <DbName>nucgss</DbName>
    </ResultItem>
  </eGQueryResult>
</Result>
Retrieving Spelling Suggestions

espell.fcgi?term=\<query\>&db=\<database\>

Input: Entrez text query (&term); Entrez database (&db)

Output: XML containing the original query and spelling suggestions.

Example: Find spelling suggestions for the PubMed Central query ‘fiberblast cell growth’.


For More Information

Please see ESspell In-Depth for a full description of EGQuery.

Sample ESspell Output

<?xml version="1.0"?>
<eSpellResult>
<Database>pmc</Database>
<Query>fiberblast cell growth</Query>
<CorrectedQuery>fibroblast cell growth</CorrectedQuery>
<SpelledQuery>
Demonstration Programs

EBot

EBot is an interactive web tool that first allows users to construct an arbitrary E-utility analysis pipeline and then generates a Perl script to execute the pipeline. The Perl script can be downloaded and executed on any computer with a Perl installation. For more details, see the EBot page linked above.

Sample Perl Scripts

The two sample Perl scripts below demonstrate basic E-utility functions. Both scripts should be copied and saved as plain text files and can be executed on any computer with a Perl installation.

ESearch-EFetch demonstrates basic search and retrieval functions.

```
#!/usr/local/bin/perl -w
#
# =======================================================================
#
#                            PUBLIC DOMAIN NOTICE
#               National Center for Biotechnology Information
#
# This software/database is a "United States Government Work" under the
# terms of the United States Copyright Act. It was written as part of
# the author's official duties as a United States Government employee and
# thus cannot be copyrighted. This software/database is freely available
# to the public for use. The National Library of Medicine and the U.S.
# Government have not placed any restriction on its use or reproduction.
#
# Although all reasonable efforts have been taken to ensure the accuracy
# and reliability of the software and data, the NLM and the U.S.
# Government do not and cannot warrant the performance or results that
# may be obtained by using this software or data. The NLM and the U.S.
# Government disclaim all warranties, express or implied, including
# warranties of performance, merchantability or fitness for any particular
# purpose.
#
# Please cite the author in any work or product based on this material.
#
# =======================================================================
#
# Author:  Oleg Khovayko
#
```

# Subroutine to prompt user for variables in the next section
sub ask_user {
    print "$_[0] [$_[1]]: ";
    my $rc = <>;
    chomp $rc;
    if($rc eq "") { $rc = $_[1]; }
    return $rc;
}

# Define library for the 'get' function used in the next section.
# $utils contains route for the utilities.
# $db, $query, and $report may be supplied by the user when prompted;
# if not answered, default values, will be assigned as shown below.
use LWP::Simple;

my $db = ask_user("Database", "Pubmed");
my $query = ask_user("Query", "zanzibar");
my $report = ask_user("Report", "abstract");

# $esearch contains the PATH & parameters for the ESearch call
# $esearch_result contains the result of the ESearch call
# the results are displayed and parsed into variables
# $Count, $QueryKey, and $WebEnv for later use and then displayed.

my $esearch = "$utils/esearch.fcgi?db=$db&retmax=1&usehistory=y&term=
   "db=$db&retmax=1&usehistory=y&term=";

my $esearch_result = get($esearch . $query);

print "\nESearch RESULT: $esearch_result\n";
$esearch_result =~ /
   m|<Count>(\d+)</Count>.*<QueryKey>(\d+)</QueryKey>.*<WebEnv>(\S+)</WebEnv>|s;

my $Count = $1;
my $QueryKey = $2;
my $WebEnv = $3;

print "Count = $Count; QueryKey = $QueryKey; WebEnv = $WebEnv\n";

# this area defines a loop which will display $retmax citation results from
# Efetch each time the the Enter Key is pressed, after a prompt.
my $retstart;
my $retmax=3;

for($retstart = 0; $retstart < $Count; $retstart += $retmax) {
    my $efetch = "$utils/efetch.fcgi?"
        "rettype=$report&retmode=text&retstart=$retstart&retmax=$retmax&" .
        "db=$db&query_key=$QueryKey&WebEnv=$WebEnv";

    print "\nEF_QUERY=$efetch\n";

    my $efetch_result = get($efetch);

    print "--------\nEFETCH RESULT(".
        ($retstart + 1) . "." . ($retstart + $retmax) . "): ".
        "[$efetch_result]\n"-----PRESS ENTER!!!--------\n";
<>
}

EPost-ESummary demonstrates basic uploading and document summary retrieval.

#!/usr/local/bin/perl -w
# =======================================================================
# #                            PUBLIC DOMAIN NOTICE
#               National Center for Biotechnology Information
# # This software/database is a "United States Government Work" under the
# terms of the United States Copyright Act. It was written as part of
# the author's official duties as a United States Government employee and
# thus cannot be copyrighted. This software/database is freely available
# to the public for use. The National Library of Medicine and the U.S.
# Government have not placed any restriction on its use or reproduction.
# # Although all reasonable efforts have been taken to ensure the accuracy
# and reliability of the software and data, the NLM and the U.S.
# Government do not and cannot warrant the performance or results that
# may be obtained by using this software or data. The NLM and the U.S.
# Government disclaim all warranties, express or implied, including
# warranties of performance, merchantability or fitness for any particular
# purpose.
# # Please cite the author in any work or product based on this material.
# # =======================================================================
# # Author:  Oleg Khovayko
# # File Description: ePost/eSummary calling example
#
# #=====================================================================
my $ePost_url    = "$eutils_root/epost.fcgi";
my $eSummary_url = "$eutils_root/esummary.fcgi";
my $db_name = "PubMed";

# Read input file into variable $file
# File name - first argument $ARGV[0]
undef $/;  # for load whole file
open IF, $ARGV[0] || die "Can't open for read: $!
";
my $file = <IF>;
close IF;
print "Loaded file: [$file]\n";

# Prepare file - substitute all separators to comma
$file =~ s/\s+/,/gs;
print "Prepared file: [$file]\n";

# Create CGI param line
my $form_data = "db=$db_name&id=$file";

# Create HTTP request
my $headers = new HTTP::Headers(
    Accept        => "text/html, text/plain",
    Content_Type    => "application/x-www-form-urlencoded"
);
my $request = new HTTP::Request("POST", $ePost_url, $headers );
$request->content($form_data);

# Create the user agent object
my $ua = new LWP::UserAgent;
$ua->agent("ePost/example");

# send file to ePost by HTTP
my $response = $ua->request($request);

# ---------------------------------------------------------------------
print "Response status message: [" . $response->message . "]\n";
print "Response content: [" . $response->content . "]\n";

# Parse response->content and extract QueryKey & WebEnv
$response->content =~
m|<QueryKey>(\d+)</QueryKey>.*<WebEnv>(\S+)</WebEnv>|s;

my $QueryKey = $1;
my $WebEnv = $2;

print "\nEXTRACTED:\nQueryKey = $QueryKey;\nWebEnv = $WebEnv\n\n";

# Retrieve DocSum from eSummary by simple::get method and print it
#
print "eSummary result: [" .
  get("$eSummary_url?db=$db_name&query_key=$QueryKey&WebEnv=$WebEnv") .
"]\n";

For More Information

Announcement Mailing List

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

Getting Help

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

Suggestions, comments, and questions specifically relating to the EUtility programs may be sent to eutilities@ncbi.nlm.nih.gov.
A General Introduction to the E-utilities

Eric Sayers, PhD

Introduction

The Entrez Programming Utilities (E-utilities) are a set of nine server-side programs that provide a stable interface into the Entrez query and database system at the National Center for Biotechnology Information (NCBI). The E-utilities use a fixed URL syntax that translates a standard set of input parameters into the values necessary for various NCBI software components to search for and retrieve the requested data. The E-utilities are therefore the structured interface to the Entrez system, which currently includes 38 databases covering a variety of biomedical data, including nucleotide and protein sequences, gene records, three-dimensional molecular structures, and the biomedical literature.

To access these data, a piece of software first posts an E-utility URL to NCBI, then retrieves the results of this posting, after which it processes the data as required. The software can thus use any computer language that can send a URL to the E-utilities server and interpret the XML response; examples of such languages are Perl, Python, Java, and C++. Combining E-utilities components to form customized data pipelines within these applications is a powerful approach to data manipulation.

This chapter first describes the general function and use of the eight E-utilities, followed by basic usage guidelines and requirements, and concludes with a discussion of how the E-utilities function within the Entrez system.

Usage Guidelines and Requirements

Use the E-utility URL

All E-utility requests should be made to URLs beginning with the following string:


These URLs direct requests to servers that are used only by the E-utilities and that are optimized to give users the best performance.

1 NCBI; Email: sayers@ncbi.nlm.nih.gov.

* Corresponding author.
Frequency, Timing and Registration of E-utility URL Requests

In order not to overload the E-utility servers, NCBI recommends that users post no more than three URL requests per second and limit large jobs to either weekends or between 9:00 PM and 5:00 AM Eastern time during weekdays. Failure to comply with this policy may result in an IP address being blocked from accessing NCBI. If NCBI blocks an IP address, service will not be restored unless the developers of the software accessing the E-utilities register values of the tool and email parameters with NCBI. The value of tool should be a string with no internal spaces that uniquely identifies the software producing the request. The value of email should be a complete and valid e-mail address of the software developer and not that of a third-party end user. The value of email will be used only to contact developers if NCBI observes requests that violate our policies, and we will attempt such contact prior to blocking access. In addition, developers may request that the value of email be added to the E-utility mailing list that provides announcements of software updates, known bugs and other policy changes affecting the E-utilities. To register tool and email values, simply send an e-mail to eutilities@ncbi.nlm.nih.gov including the desired values along with the name of either a developer or the organization creating the software. Once NCBI establishes communication with a developer, receives values for tool and email and validates the e-mail address in email, the block will be lifted. Once tool and email values are registered, all subsequent E-utility requests from that software package should contain both values. Please be aware that merely providing values for tool and email in requests is not sufficient to comply with this policy; these values must be registered with NCBI. Requests from any IP that lack registered values for tool and email and that violate the above usage policies may be blocked. Software developers may register values of tool and email at any time, and are encouraged to do so.

Coming in May 2018: API Keys

On May 1, 2018, NCBI will begin enforcing the use of API keys that will offer enhanced levels of supported access to the E-utilities. After that date, any site (IP address) posting more than 3 requests per second to the E-utilities without an API key will receive an error message. By including an API key, a site can post up to 10 requests per second by default. Higher rates are available by request (eutilities@ncbi.nlm.nih.gov). Users can obtain an API key now from the Settings page of their NCBI account (to create an account, visit www.ncbi.nlm.nih.gov/account/). After creating the key, users should include it in each E-utility request by assigning it to the new api_key parameter.

Example request including an API key:
esummary.fcgi?db=pubmed&id=123456&api_key=ABCDE12345

Example error message if rates are exceeded:
{"error":"API rate limit exceeded","count":11}\n
Only one API key is allowed per NCBI account; however, a user may request a new key at any time. Such a request will invalidate any existing API key associated with that NCBI account.
We encourage regular E-utility users to obtain an API key as soon as possible and begin the process of incorporating it into code. We also encourage users to monitor their request rates to determine if they will require rates higher than 10 per second. As stated above, we can potentially have higher rates negotiated prior to the beginning of enforcement on May 1, 2018.

**Minimizing the Number of Requests**

If a task requires searching for and/or downloading a large number of records, it is much more efficient to use the Entrez History to upload and/or retrieve these records in batches rather than using separate requests for each record. Please refer to Application 3 in Chapter 3 for an example. Many thousands of IDs can be uploaded using a single EPost request, and several hundred records can be downloaded using one EFetch request.

**Disclaimer and Copyright Issues**

If you use the E-utilities within software, NCBI’s Disclaimer and Copyright notice ([https://www.ncbi.nlm.nih.gov/About/disclaimer.html](https://www.ncbi.nlm.nih.gov/About/disclaimer.html)) must be evident to users of your product. Please note that abstracts in PubMed may incorporate material that may be protected by U.S. and foreign copyright laws. All persons reproducing, redistributing, or making commercial use of this information are expected to adhere to the terms and conditions asserted by the copyright holder. Transmission or reproduction of protected items beyond that allowed by fair use (PDF) as defined in the copyright laws requires the written permission of the copyright owners. NLM provides no legal advice concerning distribution of copyrighted materials. Please consult your legal counsel. If you wish to do a large data mining project on PubMed data, you can enter into a licensing agreement and lease the data for free from NLM. For more information on this please see [http://www.nlm.nih.gov/databases/leased.html](http://www.nlm.nih.gov/databases/leased.html).

**Handling Special Characters Within URLs**

When constructing URLs for the E-utilities, please use lowercase characters for all parameters except &WebEnv. There is no required order for the URL parameters in an E-utility URL, and null values or inappropriate parameters are generally ignored. Avoid placing spaces in the URLs, particularly in queries. If a space is required, use a plus sign (+) instead of a space:

**Incorrect**: &id=352, 25125, 234  
**Correct**:   &id=352,25125,234  

**Incorrect**: &term=biomol.mrna[properties] AND mouse[organism]  
**Correct**:   &term=biomol+mrna[properties]+AND+mouse[organism]  

Other special characters, such as quotation marks (“”) or the # symbol used in referring to a query key on the History server, should be represented by their URL encodings (%22 for “”, %23 for #).
Incorrect: &term=#2+AND+"gene in genomic"[properties]
Correct:   &term=%232+AND+%22gene+in+genomic%22[properties]

The Nine E-utilities in Brief

EInfo (database statistics)
eutils.ncbi.nlm.nih.gov/entrez/eutils/einfo.fcgi
Provides the number of records indexed in each field of a given database, the date of the last update of the database, and the available links from the database to other Entrez databases.

ESearch (text searches)
eutils.ncbi.nlm.nih.gov/entrez/eutils/esearch.fcgi
Responds to a text query with the list of matching UIDs in a given database (for later use in ESummary, EFetch or ELink), along with the term translations of the query.

EPost (UID uploads)
eutils.ncbi.nlm.nih.gov/entrez/eutils/epost.fcgi
Accepts a list of UIDs from a given database, stores the set on the History Server, and responds with a query key and web environment for the uploaded dataset.

ESummary (document summary downloads)
eutils.ncbi.nlm.nih.gov/entrez/eutils/esummary.fcgi
 Responds to a list of UIDs from a given database with the corresponding document summaries.

EFetch (data record downloads)
eutils.ncbi.nlm.nih.gov/entrez/eutils/efetch.fcgi
Responds to a list of UIDs in a given database with the corresponding data records in a specified format.

ELink (Entrez links)
eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi
Responds to a list of UIDs in a given database with either a list of related UIDs (and relevancy scores) in the same database or a list of linked UIDs in another Entrez database; checks for the existence of a specified link from a list of one or more UIDs; creates a hyperlink to the primary LinkOut provider for a specific UID and database, or lists LinkOut URLs and attributes for multiple UIDs.
EGQuery (global query)
eutils.ncbi.nlm.nih.gov/entrez/eutils/egquery.fcgi
Responds to a text query with the number of records matching the query in each Entrez database.

ESpell (spelling suggestions)
eutils.ncbi.nlm.nih.gov/entrez/eutils/espell.fcgi
Retrieves spelling suggestions for a text query in a given database.

ECitMatch (batch citation searching in PubMed)
eutils.ncbi.nlm.nih.gov/entrez/eutils/ecitmatch.cgi
Retrieves PubMed IDs (PMIDs) corresponding to a set of input citation strings.

Understanding the E-utilities Within Entrez

The E-utilities Access Entrez Databases

The E-utilities access the core search and retrieval engine of the Entrez system and, therefore, are only capable of retrieving data that are already in Entrez. Although the majority of data at NCBI are in Entrez, there are several datasets that exist outside of the Entrez system. Before beginning a project with the E-utilities, check that the desired data can be found within an Entrez database.

The Entrez System Identifies Database Records Using UIDs

Each Entrez database refers to the data records within it by an integer ID called a UID (unique identifier). Examples of UIDs are GI numbers for Nucleotide and Protein, PMIDs for PubMed, or MMDB-IDs for Structure. The E-utilities use UIDs for both data input and output, and thus it is often critical, especially for advanced data pipelines, to know how to find the UIDs associated with the desired data before beginning a project with the E-utilities.

See Table 1 for a complete list of UIDs in Entrez.

Table 1 – Entrez Unique Identifiers (UIDs) for selected databases

<table>
<thead>
<tr>
<th>Entrez Database</th>
<th>UID common name</th>
<th>E-utility Database Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>BioProject</td>
<td>BioProject ID</td>
<td>bioproject</td>
</tr>
<tr>
<td>BioSample</td>
<td>BioSample ID</td>
<td>biosample</td>
</tr>
<tr>
<td>Biosystems</td>
<td>BSID</td>
<td>biosystems</td>
</tr>
<tr>
<td>Books</td>
<td>Book ID</td>
<td>books</td>
</tr>
</tbody>
</table>

Table 1 continues on next page...
<table>
<thead>
<tr>
<th>Entrez Database</th>
<th>UID common name</th>
<th>E-utility Database Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conserved Domains</td>
<td>PSSM-ID</td>
<td>cdd</td>
</tr>
<tr>
<td>dbGaP</td>
<td>dbGaP ID</td>
<td>gap</td>
</tr>
<tr>
<td>dbVar</td>
<td>dbVar ID</td>
<td>dbvar</td>
</tr>
<tr>
<td>Epigenomics</td>
<td>Epigenomics ID</td>
<td>epigenomics</td>
</tr>
<tr>
<td>EST</td>
<td>GI number</td>
<td>nucest</td>
</tr>
<tr>
<td>Gene</td>
<td>Gene ID</td>
<td>gene</td>
</tr>
<tr>
<td>Genome</td>
<td>Genome ID</td>
<td>genome</td>
</tr>
<tr>
<td>GEO Datasets</td>
<td>GDS ID</td>
<td>gds</td>
</tr>
<tr>
<td>GEO Profiles</td>
<td>GEO ID</td>
<td>geoprofiles</td>
</tr>
<tr>
<td>GSS</td>
<td>GI number</td>
<td>nucgss</td>
</tr>
<tr>
<td>HomoloGene</td>
<td>HomoloGene ID</td>
<td>homologene</td>
</tr>
<tr>
<td>MeSH</td>
<td>MeSH ID</td>
<td>mesh</td>
</tr>
<tr>
<td>NCBI C++ Toolkit</td>
<td>Toolkit ID</td>
<td>toolkit</td>
</tr>
<tr>
<td>NCBI Web Site</td>
<td>Web Site ID</td>
<td>ncbisearch</td>
</tr>
<tr>
<td>NLM Catalog</td>
<td>NLM Catalog ID</td>
<td>nlmcatalog</td>
</tr>
<tr>
<td>Nucleotide</td>
<td>GI number</td>
<td>nuccore</td>
</tr>
<tr>
<td>OMIA</td>
<td>OMIA ID</td>
<td>omia</td>
</tr>
<tr>
<td>PopSet</td>
<td>PopSet ID</td>
<td>popset</td>
</tr>
<tr>
<td>Probe</td>
<td>Probe ID</td>
<td>probe</td>
</tr>
<tr>
<td>Protein</td>
<td>GI number</td>
<td>protein</td>
</tr>
<tr>
<td>Protein Clusters</td>
<td>Protein Cluster ID</td>
<td>proteinclusters</td>
</tr>
<tr>
<td>PubChem BioAssay</td>
<td>AID</td>
<td>pcassay</td>
</tr>
<tr>
<td>PubChem Compound</td>
<td>CID</td>
<td>pccompound</td>
</tr>
<tr>
<td>PubChem Substance</td>
<td>SID</td>
<td>pcsubstance</td>
</tr>
<tr>
<td>PubMed</td>
<td>PMID</td>
<td>pubmed</td>
</tr>
<tr>
<td>PubMed Central</td>
<td>PMCID</td>
<td>pmc</td>
</tr>
<tr>
<td>SNP</td>
<td>rs number</td>
<td>snp</td>
</tr>
<tr>
<td>SRA</td>
<td>SRA ID</td>
<td>sra</td>
</tr>
<tr>
<td>Structure</td>
<td>MMDB-ID</td>
<td>structure</td>
</tr>
<tr>
<td>Taxonomy</td>
<td>TaxID</td>
<td>taxonomy</td>
</tr>
<tr>
<td>UniGene</td>
<td>UniGene Cluster ID</td>
<td>unigene</td>
</tr>
<tr>
<td>UniSTS</td>
<td>STS ID</td>
<td>unists</td>
</tr>
</tbody>
</table>
The Entrez Core Engine: EGQuery, ESearch, and ESummary

The core of Entrez is an engine that performs two basic tasks for any Entrez database: 1) assemble a list of UIDs that match a text query, and 2) retrieve a brief summary record called a Document Summary (DocSum) for each UID. These two basic tasks of the Entrez engine are performed by ESearch and ESummary. ESearch returns a list of UIDs that match a text query in a given Entrez database, and ESummary returns DocSums that match a list of input UIDs. A text search in web Entrez is equivalent to ESearch-ESummary. EGQuery is a global version of ESearch that searches all Entrez databases simultaneously. Because these three E-utilities perform the two core Entrez functions, they function for all Entrez databases.

equery.fcgi?term=query
esearch.fcgi?db=database&term=query
esummary.fcgi?db=database&id=uid1,uid2,uid3,...

Syntax and Initial Parsing of Entrez Queries

Text search strings entered into the Entrez system are converted into Entrez queries with the following format:

\[ \text{term1}[\text{field1}] \text{ Op term2}[\text{field2}] \text{ Op term3}[\text{field3}] \text{ Op } ... \]

where the terms are search terms, each limited to a particular Entrez field in square brackets, combined using one of three Boolean operators: \(\text{Op} = \text{AND}, \text{ OR}, \text{ or NOT}\). These Boolean operators must be typed in all capital letters.

Example: human[organism] AND topoisomerase[protein name]

Entrez initially splits the query into a series of items that were originally separated by spaces in the query; therefore it is critical that spaces separate each term and Boolean operator. If the query consists only of a list of UID numbers (unique identifiers) or accession numbers, the Entrez system simply returns the corresponding records and no further parsing is performed. If the query contains any Boolean operators (AND, OR, or NOT), the query is split into the terms separated by these operators, and then each term is parsed independently. The results of these searches are then combined according to the Boolean operators.

A full account of how to search Entrez can be found in the Entrez Help Document. Additional information is available from Entrez Help.

Entrez Databases: EInfo, EFetch, and ELink

The NCBI Entrez system currently contains 38 databases. EInfo provides detailed information about each database, including lists of the indexing fields in the database and the available links to other Entrez databases.

einfo.fcgi?db=database
Each Entrez database includes two primary enhancements to the raw data records: 1) software for producing a variety of display formats appropriate to the given database, and 2) links to records in other Entrez databases manifested as lists of associated UIDs. The display format function is performed by EFetch, which generates formatted output for a list of input UIDs. For example, EFetch can produce abstracts from Entrez PubMed or FASTA format from Entrez Protein. EFetch does not yet support all Entrez databases; please see the EFetch documentation for details.

efetch.fcgi?db=database&id=uid1,uid2,uid3&rettype=report_type&retmode=data_mode

The linking function is performed by ELink, which generates a list of UIDs in a specified Entrez database that are linked to a set of input UIDs in either the same or another database. For example, ELink can find Entrez SNP records linked to records in Entrez Nucleotide, or Entrez Domain records linked to records in Entrez Protein.

elink.fcgi?dbfrom=initial_database&db=target_database&id=uid1,uid2,uid3

Using the Entrez History Server

A powerful feature of the Entrez system is that it can store retrieved sets of UIDs temporarily on the servers so that they can be subsequently combined or provided as input for other E-utility calls. The Entrez History server provides this service and is accessed on the Web using either the Preview/Index or History tabs on Entrez search pages. Each of the E-utilities can also use the History server, which assigns each set of UIDs an integer label called a query key (&query_key) and an encoded cookie string called a Web environment (&WebEnv). EPost allows any list of UIDs to be uploaded to the History Server and returns the query key and Web environment. ESearch can also post its output set of UIDs to the History Server, but only if the &usehistory parameter is set to "y". ELink also can post its output to the History server if &cmd is set to "neighbor_history". The resulting query key and Web environment from either EPost or ESearch can then be used in place of a UID list in ESummary, EFetch, and ELink.

In Entrez, a set of UIDs is represented on the History by three parameters:

&db = database; &query_key = query key; &WebEnv = web environment

Upload steps that generate a web environment and query key

esearch.fcgi?db=database&term=query&usehistory=y
epost.fcgi?db=database&id=uid1,uid2,uid3,...
elink.fcgi?dbfrom=source_db&db=destination_db&cmd=neighbor_history&id=uid1,uid2,...

Download steps that use a web environment and query key

esummary.fcgi?db=database&WebEnv=webenv&query_key=key
Generating Multiple Data Sets on the History Server

Each web environment on the History Server can be associated with any number of query keys. This allows different data sets to be combined with the Boolean operators AND, OR, and NOT, or with another Entrez query. It is important to remember that for two data sets (query keys) to be combined, they must be associated with the same web environment. By default, successive E-utility calls produce query keys that are not associated with the same web environment, and so to overcome this, each E-utility call after the initial call must set the &WebEnv parameter to the value of the pre-existing web environment.

Default behavior: These two URLs...

URL 1: epost.fcgi?db=database&id=uid1,uid2,uid3
URL 2: esearch.fcgi?db=database&term=query&usehistory=y

will produce two History sets associated with different web environments:

<table>
<thead>
<tr>
<th>URL</th>
<th>WebEnv</th>
<th>query_key</th>
<th>UIDs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>web1</td>
<td>1</td>
<td>uid1,uid2,uid3</td>
</tr>
<tr>
<td>2</td>
<td>web2</td>
<td>1</td>
<td>uids matching query</td>
</tr>
</tbody>
</table>

Desired behavior: These two URLs...

URL 1: epost.fcgi?db=database&id=uid1,uid2,uid3
(extract web1 from the output of URL 1)
URL 2: esearch.fcgi?db=database&term=query&usehistory=y&WebEnv=web1

will produce two sets associated with the same (new) web environment:

<table>
<thead>
<tr>
<th>URL</th>
<th>WebEnv</th>
<th>query_key</th>
<th>UIDs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>web2</td>
<td>1</td>
<td>uid1,uid2,uid3</td>
</tr>
<tr>
<td>2</td>
<td>web2</td>
<td>2</td>
<td>uids matching query</td>
</tr>
</tbody>
</table>

Combining E-utility Calls to Create Entrez Applications

The E-utilities are useful when used by themselves in single URLs; however, their full potential is realized when successive E-utility URLs are combined to create a data pipeline. When used within such pipelines, the Entrez History server simplifies complex retrieval tasks by allowing easy data transfer between successive E-utility calls. Listed below are several examples of pipelines produced by combining E-utilities, with the
arrows representing the passing of db, WebEnv and query_key values from one E-utility to another. These and related pipelines are discussed in detail in Chapter 3.

Basic Pipelines

Retrieving data records matching an Entrez query
ESearch → ESummary
ESearch → EFetch

Retrieving data records matching a list of UIDs
EPost → ESummary
EPost → EFetch

Finding UIDs linked to a set of records
ESearch → ELink
EPost → ELink

Limiting a set of records with an Entrez query
EPost → ESearch
ELink → ESearch

Advanced Pipelines

Retrieving data records in database B linked to records in database A matching an Entrez query
ESearch → ELink → ESummary
ESearch → ELink → EFetch

Retrieving data records from a subset of an ID list defined by an Entrez query
EPost → ESearch → ESummary
EPost → ESearch → EFetch

Retrieving a set of data records, defined by an Entrez query, in database B from a larger set of records linked to a list of UIDs in database A
EPost → ELink → ESearch → ESummary
EPost → ELink → ESearch → EFetch
Demonstration Programs

Please see Chapter 1 for sample Perl scripts.

For More Information

Please see Chapter 1 for getting additional information about the E-utilities.
Introduction

This chapter presents several examples of how the E-utilities can be used to build useful applications. These examples use Perl to create the E-utility pipelines, and assume that the LWP::Simple module is installed. This module includes the get function that supports HTTP GET requests. One example (Application 4) uses an HTTP POST request, and requires the LWP::UserAgent module. In Perl, scalar variable names are preceded by a "$" symbol, and array names are preceded by a "@". In several instances, results will be stored in such variables for use in subsequent E-utility calls. The code examples here are working programs that can be copied to a text editor and executed directly. Equivalent HTTP requests can be constructed in many modern programming languages; all that is required is the ability to create and post an HTTP request.

Basic Pipelines

All E-utility applications consist of a series of calls that we will refer to as a pipeline. The simplest E-utility pipelines consist of two calls, and any arbitrary pipeline can be assembled from these basic building blocks. Many of these pipelines conclude with either ESummary (to retrieve DocSums) or EFetch (to retrieve full records). The comments indicate those portions of the code that are required for either call.

ESearch – ESummary/EFetch

Input: Entrez text query

ESummary Output: XML Document Summaries

EFetch Output: Formatted data records (e.g. abstracts, FASTA)

use LWP::Simple;

# Download PubMed records that are indexed in MeSH for both asthma and # leukotrienes and were also published in 2009.
$db = 'pubmed';
$query = 'asthma[mesh]+AND+leukotrienes[mesh]+AND+2009[pdat]';
#assemble the esearch URL
$url = $base . "esearch.fcgi?db=$db&term=$query&usehistory=y";

#post the esearch URL
$output = get($url);

#parse WebEnv and QueryKey
$web = $1 if ($output =~ /<WebEnv>(\S+)</WebEnv>/);
$key = $1 if ($output =~ /<QueryKey>(\d+)</QueryKey>/);

### include this code for ESearch-ESummary
#assemble the esummary URL
$url = $base . "esummary.fcgi?db=$db&query_key=$key&WebEnv=$web";

#post the esummary URL
$docsums = get($url);
print "$docsums";

### include this code for ESearch-EFetch
#assemble the efetch URL
$url = $base . "efetch.fcgi?db=$db&query_key=$key&WebEnv=$web";
$url .= '&rettype=abstract&retmode=text';

#post the efetch URL
$data = get($url);
print "$data";

---

EPost – ESummary/EFetch

**Input:** List of Entrez UIDs (integer identifiers, e.g. PMID, GI, Gene ID)

**ESummary Output:** XML Document Summaries

**EFetch Output:** Formatted data records (e.g. abstracts, FASTA)

use LWP::Simple;

# Download protein records corresponding to a list of GI numbers.

$db = 'protein';
$id_list = '194680922,50978626,28558982,9507199,6678417';

#assemble the epost URL
$url = $base . "epost.fcgi?db=$db&id=$id_list";

#post the epost URL
$output = get($url);

#parse WebEnv and QueryKey
$web = $1 if ($output =~ /<WebEnv>(\S+)</WebEnv>/);
$key = $1 if ($output =~ /<QueryKey>(\d+)</QueryKey>/);
### include this code for EPost-ESummary

```php
# assemble the esummary URL
$url = $base . "esummary.fcgi?db=$db&query_key=$key&WebEnv=$web";

# post the esummary URL
$docsums = get($url);
print "$docsums";
```

### include this code for EPost-EFetch

```php
# assemble the efetch URL
$url = $base . "efetch.fcgi?db=$db&query_key=$key&WebEnv=$web";
$url .= "&rettype=fasta&retmode=text";

# post the efetch URL
$data = get($url);
print "$data";
```

**Note:** To post a large number (more than a few hundred) UIDs in a single URL, please use the HTTP POST method for the EPost call (see Application 4).

**ELink – ESummary/Efetch**

**Input:** List of Entrez UIDs in database A (integer identifiers, e.g. PMID, GI, Gene ID)

**ESummary Output:** Linked XML Document Summaries from database B

**EFetch Output:** Formatted data records (e.g. abstracts, FASTA) from database B

use LWP::Simple;

```perl
# Download gene records linked to a set of proteins corresponding to a list of GI numbers.

$db1 = 'protein';  # &dbfrom
$db2 = 'gene';     # &db
$linkname = 'protein_gene'; # desired link &linkname
# input UIDs in $db1 (protein GIs)
$id_list = '194680922,50978626,28558982,9507199,6678417';

# assemble the elink URL
$url = $base . "elink.fcgi?dbfrom=$db1&db=$db2&id=$id_list";
$url .= "&linkname=$linkname&cmd=neighbor_history";

# post the elink URL
$output = get($url);

# parse WebEnv and QueryKey
$web = $1 if ($output =~ /<WebEnv>(\S+)</WebEnv>/);
$key = $1 if ($output =~ /<QueryKey>(\d+)</QueryKey>/);

### include this code for ELink-ESummary
```
#assemble the esummary URL
$url = $base . "esummary.fcgi?db=$db&query_key=$key&WebEnv=$web"

#post the esummary URL
$docsums = get($url);
print "$docsums"

### include this code for ELink-EFetch
#assemble the efetch URL
$url = $base . "efetch.fcgi?db=$db2&query_key=$key&WebEnv=$web"
$url .= "&rettype=xml&retmode=xml"

#post the efetch URL
$data = get($url);
print "$data"

Notes: To submit a large number (more than a few hundred) UIDs to ELink in one URL, please use the HTTP POST method for the Elink call (see Application 4). The &linkname parameter is used to force ELink to return only one set of links (one &query_key) to simplify parsing. If more than one link is desired, the above code must be altered to parse the multiple &query_key values from the ELink XML output. This code uses ELink in "batch" mode, in that only one set of gene IDs is returned and the one-to-one correspondence between protein GIs and gene IDs is lost. To preserve this one-to-one correspondence, please see Application 4 below.

ESearch – ELink – ESummary/EFetch

Input: Entrez text query in database A

ESummary Output: Linked XML Document Summaries from database B

EFetch Output: Formatted data records (e.g. abstracts, FASTA) from database B

use LWP::Simple;
# Download protein FASTA records linked to abstracts published # in 2009 that are indexed in MeSH for both asthma and # leukotrienes.
$db1 = 'pubmed';
$db2 = 'protein';
$linkname = 'pubmed_protein';
$query = 'asthma[mesh]+AND+leukotrienes[mesh]+AND+2009[pdat]';

#assemble the esearch URL
$url = $base . "esearch.fcgi?db=$db1&term=$query&usehistory=y";
#post the esearch URL
$output = get($url);

#parse WebEnv and QueryKey
$web1 = $1 if ($output =~ /<WebEnv>(\S+)</WebEnv>/);
$key1 = $1 if ($output =~ /<QueryKey>(\d+)</QueryKey>/);

#assemble the elink URL
$url = $base . "elink.fcgi?dbfrom=$db1&db=$db2";
$url .= "&query_key=$key1&WebEnv=$web1";
$url .= "&linkname=$linkname&cmd=neighbor_history";
print "$url\n";

#post the elink URL
$output = get($url);
print "$output\n";

#parse WebEnv and QueryKey
$web2 = $1 if ($output =~ /<WebEnv>(\S+)</WebEnv>/);
$key2 = $1 if ($output =~ /<QueryKey>(\d+)</QueryKey>/);

### include this code for ESearch-ELink-ESummary
#assemble the esummary URL
$url = $base . "esummary.fcgi?db=$db2&query_key=$key2&WebEnv=$web2";
#post the esummary URL
$docsums = get($url);
print "$docsums";

### include this code for ESearch-ELink-EFetch
#assemble the efetch URL
$url = $base . "efetch.fcgi?db=$db2&query_key=$key2&WebEnv=$web2";
$url .= "&rettype=fasta&retmode=text";
#post the efetch URL
$data = get($url);
print "$data";

Notes: The &linkname parameter is used to force ELink to return only one set of links (one &query_key) to simplify parsing. If more than one link is desired, the above code must be altered to parse the multiple &query_key values from the ELink XML output. This code uses ELink in "batch" mode, in that only one set of PubMed IDs is returned and the one-to-one correspondence between PubMed IDs and their related PubMed IDs is lost. To preserve this one-to-one correspondence, please see Application 4 below.

EPost – ELink – ESummary/EFetch

Input: List of Entrez UIDs (integer identifiers, e.g. PMID, GI, Gene ID) in database A

ESummary Output: Linked XML Document Summaries from database B

EFetch Output: Formatted data records (e.g. abstracts, FASTA) from database B

use LWP::Simple;

# Downloads gene records linked to a set of proteins corresponding
# to a list of protein GI numbers.
$db1 = 'protein';  # &dbfrom
$db2 = 'gene';     # &db
$linkname = 'protein_gene';
#input UIDs in $db1 (protein GIs)
$id_list = '194680922,50978626,28558982,9507199,6678417';

#assemble the epost URL
$url = $base . "epost.fcgi?db=$db1&id=$id_list";

#post the epost URL
$output = get($url);

#parse WebEnv and QueryKey
$web1 = $1 if ($output =~ /<WebEnv>(\S+)</WebEnv>/);
$key1 = $1 if ($output =~ /<QueryKey>(\d+)</QueryKey>/);

#assemble the elink URL
$url = $base . "elink.fcgi?dbfrom=$db1&db=$db2&query_key=$key1";
$url .= "&WebEnv=$web1&linkname=$linkname&cmd=neighbor_history";

#post the elink URL
$output = get($url);

#parse WebEnv and QueryKey
$web2 = $1 if ($output =~ /<WebEnv>(\S+)</WebEnv>/);
$key2 = $1 if ($output =~ /<QueryKey>(\d+)</QueryKey>/);

### include this code for ESearch-ELink-ESummary
#assemble the esummary URL
$url = $base . "esummary.fcgi?db=$db2&query_key=$key2&WebEnv=$web2";

#post the esummary URL
$docsums = get($url);
print "$docsums";

### include this code for ESearch-ELink-EFetch
#assemble the efetch URL
$url = $base . "efetch.fcgi?db=$db2&query_key=$key2&WebEnv=$web2";
$url .= "&rettype=xml&retmode=xml";

#post the efetch URL
$data = get($url);
print "$data";

Notes: To post a large number (more than a few hundred) UIDs in a single URL, please use the HTTP POST method for the EPost call (see Application 4 below). The &linkname parameter is used to force ELink to return only one set of links (one &query_key) to simplify parsing. If more than one link is desired, the above code must be altered to parse the multiple &query_key values from the ELink XML output. This code uses ELink in "batch" mode, in that only one set of gene IDs is returned and the one-to-one correspondence between protein
**EPost – ESearch**

**Input:** List of Entrez UIDs (integer identifiers, e.g. PMID, GI, Gene ID)

**Output:** History set consisting of the subset of posted UIDs that match an Entrez text query

```perl
use LWP::Simple;

# Given an input set of protein GI numbers, this script creates
# a history set containing the members of the input set that
# correspond to human proteins.
# (Which of these proteins are from human?)

$db = 'protein';
$query = 'human[orgn]';
$id_list = '194680922,50978626,28558982,9507199,6678417';

# assemble the epost URL
$url = $base . "epost.fcgi?db=$db&id=$id_list";

# post the epost URL
$output = get($url);

# parse WebEnv and QueryKey
$web = $1 if ($output =~ /<WebEnv>(\S+)</WebEnv>/);
$key = $1 if ($output =~ /<QueryKey>(\d+)</QueryKey>/);

# assemble the esearch URL
$term = "%23$key+AND+$query";
# %23 places a '#' before the query key
$url = $base . "esearch.fcgi?db=$db&term=$term";
$url .= ";WebEnv=$web&usehistory=y";

# post esearch URL
$limited = get($url);

print "$limited\n";

# Output remains on the history server (&query_key, &WebEnv)
# Use ESummary or EFetch as above to retrieve them

**Note:** To post a large number (more than a few hundred) UIDs in a single URL, please use the HTTP POST method for the EPost call (see Application 4).
**ELink – ESearch**

**Input:** List of Entrez UIDs (integer identifiers, e.g. PMID, GI, Gene ID) in database A

**Output:** History set consisting of the subset of linked UIDs in database B that match an Entrez text query

```perl
use LWP::Simple;

# Given an input set of protein GI numbers, this script creates a
# history set containing the gene IDs linked to members of the input
# set that also are on human chromosome X.
# (Which of the input proteins are encoded by a gene on human
# chromosome X?)

$db1 = 'protein';  # &dbfrom
$db2 = 'gene';     # &db
$linkname = 'protein_gene'; # desired link &linkname
$query = 'human[orgn]+AND+x[chr]';
# Input UIDs in $db1 (protein GIs)
$id_list = '148596974,42544182,187937179,4557377,6678417';

# Assemble the elink URL
$url = $base . 'elink.fcgi?dbfrom=' . $db1 . '&db=' . $db2 . '&id=' . $id_list . '&linkname=' . $linkname . '&cmd=neighbor_history';

# Post the elink URL
$output = get($url);

# Parse WebEnv and QueryKey
$web = $1 if ($output =~ /<WebEnv>(\S+)</WebEnv>/);
$key = $1 if ($output =~ /<QueryKey>(\d+)</QueryKey>/);

# Assemble the esearch URL
$term = '%$key+AND+$query';  # %23 places a '#' before the query key
$url = $base . 'esearch.fcgi?db=' . $db2 . '&term=' . $term . '&WebEnv=' . $web . '&usehistory=y';

# Post esearch URL
$limited = get($url);

print "$limited\n";

# Output remains on the history server (&query_key, &WebEnv)
# Use ESummary or EFetch as in previous examples to retrieve them

**Note:** To submit a large number (more than a few hundred) UIDs to ELink in one URL, please use the HTTP POST method for the ELink call (see Application 4). The &linkname parameter is used to force ELink to return only one set of links (one &query_key) to simplify parsing. If more than one link is desired, the above code must be altered to parse the multiple &query_key values from the ELink XML output. This code uses ELink in "batch" mode, in
that only one set of gene IDs is returned and the one-to-one correspondence between protein GIs and Gene IDs is lost. To preserve this one-to-one correspondence, please see Application 4 below.

**Application 1: Converting GI numbers to accession numbers**

**Goal:** Starting with a list of nucleotide GI numbers, prepare a set of corresponding accession numbers.

**Solution:** Use EFetch with &retttype=acc

**Input:** $gi_list – comma-delimited list of GI numbers

**Output:** List of accession numbers.

```perl
use LWP::Simple;
$gi_list = '24475906,224465210,50978625,9507198';

#assemble the URL
$url = $base . 'efetch.fcgi?db=nucleotide&id=' . $gi_list . '&retttype=acc';

#post the URL
$output = get($url);
print $output;
```

**Notes:** The order of the accessions in the output will be the same order as the GI numbers in $gi_list.

**Application 2: Converting accession numbers to data**

**Goal:** Starting with a list of protein accession numbers, return the sequences in FASTA format.

**Solution:** Create a string consisting of items separated by 'OR', where each item is an accession number followed by '[accn]'.

Example: accn1[accn]+OR+accn2[accn]+OR+accn3[accn]+OR+...

Submit this string as a &term in ESearch, then use EFetch to retrieve the FASTA data.

**Input:** $acc_list – comma-delimited list of accessions

**Output:** FASTA data

```perl
use LWP::Simple;
$acc_list = 'NM_009417,NM_000547,NM_001003009,NM_019353';
@acc_array = split(/,/, $acc_list);

#append [accn] field to each accession
for ($i=0; $i < @acc_array; $i++) {
    $acc_array[$i] .= '[accn];
```
#join the accessions with OR
$query = join('+OR+', @acc_array);

#assemble the esearch URL
$url = $base . 'esearch.fcgi?db=nuccore&term=' . $query . '&usehistory=y';

#post the esearch URL
$output = get($url);

#parse WebEnv and QueryKey
$web = $1 if ($output =~ /<WebEnv>(\S+)</WebEnv>/);
$key = $1 if ($output =~ /<QueryKey>(\d+)</QueryKey>/);

#assemble the efetch URL
$url = $base . 'efetch.fcgi?db=nuccore&query_key=' . $key . '&WebEnv=' . $web . '&rettype=fasta&retmode=text';

#post the efetch URL
$fasta = get($url);
print "$fasta"

Notes: For large numbers of accessions, use HTTP POST to submit the esearch request (see Application 4), and see Application 3 below for downloading the large set in batches.

**Application 3: Retrieving large datasets**

**Goal:** Download all chimpanzee mRNA sequences in FASTA format (>50,000 sequences).

**Solution:** First use ESearch to retrieve the GI numbers for these sequences and post them on the History server, then use multiple EFetch calls to retrieve the data in batches of 500.

**Input:** $query - chimpanzee[orgn]+AND+biomol+mrna[prop]

**Output:** A file named "chimp.fna" containing FASTA data.

```perl
use LWP::Simple;
$search = 'chimpanzee[orgn]+AND+biomol+mrna[prop]';

#assemble the esearch URL
$url = $base . 'esearch.fcgi?db=nucleotide&term=' . $search . '&usehistory=y';

#post the esearch URL
$output = get($url);

#parse WebEnv, QueryKey and Count (# records retrieved)
$web = $1 if ($output =~ /<WebEnv>(\S+)</WebEnv>/);
$key = $1 if ($output =~ /<QueryKey>(\d+)</QueryKey>/);
$count = $1 if ($output =~ /<Count>(\d+)</Count>/);
```
Sample Applications of the E-utilities

#open output file for writing
open(OUT, ">chimp.fna") || die "Can't open file!\n";

#retrieve data in batches of 500
$retmax = 500;
for ($retstart = 0; $retstart < $count; $retstart += $retmax) {
   $efetch_url = $base . "efetch.fcgi?db=nucleotide&WebEnv=$web";
   $efetch_url .= "&query_key=$key&retstart=$retstart";
   $efetch_url .= "&retmax=$retmax&rettype=fasta&retmode=text";
   $efetch_out = get($efetch_url);
   print OUT "$efetch_out";
}
close OUT;

Application 4: Finding unique sets of linked records for each member of a large dataset

Goal: Download separately the SNP rs numbers (identifiers) for each current gene on human chromosome 20.

Solution: First use ESearch to retrieve the Gene IDs for the genes, and then assemble an ELink URL where each Gene ID is submitted as a separate &id parameter.


Output: A file named "snp_table" containing on each line the gene id followed by a colon (":") followed by a comma-delimited list of the linked SNP rs numbers.

use LWP::Simple;
use LWP::UserAgent;
$query = 'human[orgn]+AND+20[chr]+AND+alive[prop]';
$db1 = 'gene';
$db2 = 'snp';
$linkname = 'gene_snp';

#assemble the esearch URL
$url = get($url);

#parse IDs retrieved
while ($output =~ /<Id>(\d+?)</Id>/sg) {
   push(@ids, $1);
}

#assemble the elink URL as an HTTP POST call
$url_params = "dbfrom=$db1&db=$db2&linkname=$linkname";
foreach $id (@ids) {

$url_params .= "&id=$id";
}

#create HTTP user agent
$url = new LWP::UserAgent;
$url->agent("elink/1.0 " . $url->agent);

#create HTTP request object
$req = new HTTP::Request POST => "$url";
$req->content_type('application/x-www-form-urlencoded');
$req->content("$url_params");

#post the HTTP request
$response = $ua->request($req);
$output = $response->content;

open (OUT, ">snp_table") || die "Can't open file!
";
while ($output =~ /<LinkSet>(.*?)</LinkSet>/sg) {

$linkset = $1;
if ($linkset =~ /<IdList>(.*?)</IdList>/sg) {
    $input = $1;
    $input_id = $1 if ($input =~ /<Id>(\d+)</Id>/sg);
}

while ($linkset =~ /<Link>(.*?)</Link>/sg) {
    $link = $1;
    push (@output, $1) if ($link =~ /<Id>(\d+)</Id>/);
}

print OUT "$input_id:" . join(',', @output) . "\n";
}

Notes: This example uses an HTTP POST request for the elink call, as the number of Gene IDs is over 500. The &retmax parameter in the ESearch call is set to 5000, as this is a reasonable limit to the number of IDs to send to ELink in one request (if you send 5000 IDs, you are effectively performing 5000 ELink operations). If you need to link more than 5000 records, add &retstart to the ESearch call and repeat the entire procedure for each batch of 5000 IDs, incrementing &retstart for each batch.

Demonstration Programs
Please see Chapter 1 for sample Perl scripts.

For More Information
Please see Chapter 1 for getting additional information about the E-utilities.
The E-utilities In-Depth: Parameters, Syntax and More

Eric Sayers, PhD

Created: May 29, 2009; Updated: November 1, 2017.

Introduction

This chapter serves as a reference for all supported parameters for the E-utilities, along with accepted values and usage guidelines. This information is provided for each E-utility in sections below, and parameters and/or values specific to particular databases are discussed within each section. Most E-utilities have a set of parameters that are required for any call, in addition to several additional optional parameters that extend the tool’s functionality. These two sets of parameters are discussed separately in each section.

General Usage Guidelines

Please see Chapter 2 for a detailed discussion of E-utility usage policy. The following two parameters should be included in all E-utility requests.

**tool**

Name of application making the E-utility call. Value must be a string with no internal spaces.

**email**

E-mail address of the E-utility user. Value must be a string with no internal spaces, and should be a valid e-mail address.

**api_key – enforced in May 2018**

In May 2018, NCBI will begin enforcing the practice of using an API key for sites that post more than 3 requests per second. Please see Chapter 2 for a full discussion of this new policy.

---

1 NCBI; Email: sayers@ncbi.nlm.nih.gov.

II Corresponding author.
E-utility DTDs

With the exception of EFetch, the E-utilities each generate a single XML output format that conforms to a DTD specific for that utility. Links to these DTDs are provided in the XML headers of the E-utility returns.

ESummary version 2.0 produces unique XML DocSums for each Entrez database, and as such each Entrez database has a unique DTD for version 2.0 DocSums. Links to these DTDs are provided in the version 2.0 XML.

EFetch produces output in a variety of formats, some of which are XML. Most of these XML formats also conform to DTDs or schema specific to the relevant Entrez database. Please follow the appropriate link below for the PubMed DTD:


EInfo

Base URL


Functions

- Provides a list of the names of all valid Entrez databases
- Provides statistics for a single database, including lists of indexing fields and available link names

Required Parameters

None. If no db parameter is provided, einfo will return a list of the names of all valid Entrez databases.

Optional Parameters

db

Target database about which to gather statistics. Value must be a valid Entrez database name.

version

Used to specify version 2.0 EInfo XML. The only supported value is ‘2.0’. When present, EInfo will return XML that includes two new fields: <IsTruncatable> and <IsRangeable>. Fields that are truncatable allow the wildcard character ‘*’ in terms. The wildcard character will expand to match any set of characters up to a limit of 600 unique
expansions. Fields that are rangeable allow the range operator ‘:’ to be placed between a lower and upper limit for the desired range (e.g. 2008:2010[pdat]).

**retmode**

Retrieval type. Determines the format of the returned output. The default value is ‘xml’ for EInfo XML, but ‘json’ is also supported to return output in JSON format.

**Examples**

Return a list of all Entrez database names:


Return version 2.0 statistics for Entrez Protein:


**ESearch**

**Base URL**


**Functions**

- Provides a list of UIDs matching a text query
- Posts the results of a search on the History server
- Downloads all UIDs from a dataset stored on the History server
- Combines or limits UID datasets stored on the History server
- Sorts sets of UIDs

**Required Parameters**

**db**

Database to search. Value must be a valid Entrez database name (default = pubmed).

**term**

Entrez text query. All special characters must be URL encoded. Spaces may be replaced by ‘+’ signs. For very long queries (more than several hundred characters long), consider using an HTTP POST call. See the PubMed or Entrez help for information about search field descriptions and tags. Search fields and tags are database specific.

esearch.fcgi?db=pubmed&term=asthma
Optional Parameters – History Server

**usehistory**

When **usehistory** is set to 'y', ESearch will post the UIDs resulting from the search operation onto the History server so that they can be used directly in a subsequent E-utility call. Also, **usehistory** must be set to 'y' for ESearch to interpret query key values included in **term** or to accept a **WebEnv** as input.

**WebEnv**

Web environment string returned from a previous ESearch, EPost or ELink call. When provided, ESearch will post the results of the search operation to this pre-existing WebEnv, thereby appending the results to the existing environment. In addition, providing **WebEnv** allows query keys to be used in **term** so that previous search sets can be combined or limited. As described above, if **WebEnv** is used, **usehistory** must be set to 'y'.

```
esearch.fcgi?db=pubmed&term=asthma&WebEnv=<webenv string>&usehistory=y
```

**query_key**

Integer query key returned by a previous ESearch, EPost or ELink call. When provided, ESearch will find the intersection of the set specified by **query_key** and the set retrieved by the query in **term** (i.e. joins the two with AND). For **query_key** to function, **WebEnv** must be assigned an existing WebEnv string and **usehistory** must be set to 'y'.

Values for query keys may also be provided in **term** if they are preceded by a '#' (%23 in the URL). While only one **query_key** parameter can be provided to ESearch, any number of query keys can be combined in **term**. Also, if query keys are provided in **term**, they can be combined with OR or NOT in addition to AND.

The following two URLs are functionally equivalent:

```
esearch.fcgi?db=pubmed&term=asthma&query_key=1&WebEnv=<webenv string>&usehistory=y
```

```
esearch.fcgi?db=pubmed&term=%231+AND+asthma&WebEnv=<webenv string>&usehistory=y
```

Optional Parameters – Retrieval

**restart**

Sequential index of the first UID in the retrieved set to be shown in the XML output (default=0, corresponding to the first record of the entire set). This parameter can be used in conjunction with **retmax** to download an arbitrary subset of UIDs retrieved from a search.
**retmax**
Total number of UIDs from the retrieved set to be shown in the XML output (default=20). By default, ESearch only includes the first 20 UIDs retrieved in the XML output. If `usehistory` is set to ‘y’, the remainder of the retrieved set will be stored on the History server; otherwise these UIDs are lost. Increasing `retmax` allows more of the retrieved UIDs to be included in the XML output, up to a maximum of 100,000 records. To retrieve more than 100,000 UIDs, submit multiple esearch requests while incrementing the value of `retstart` (see Application 3).

**rettype**
Retrieval type. There are two allowed values for ESearch: 'uilist' (default), which displays the standard XML output, and 'count', which displays only the <Count> tag.

**retmode**
Retrieval type. Determines the format of the returned output. The default value is ‘xml’ for ESearch XML, but ‘json’ is also supported to return output in JSON format.

**sort**
Specifies the method used to sort UIDs in the ESearch output. The available values vary by database (`db`) and may be found in the Display Settings menu on an Entrez search results page. If `usehistory` is set to ‘y’, the UIDs are loaded onto the History Server in the specified sort order and will be retrieved in that order by ESummary or EFetch. Example values are ‘relevance’ and ‘name’ for Gene and ‘first+author’ and ‘pub+date’ for PubMed. Users should be aware that the default value of `sort` varies from one database to another, and that the default value used by ESearch for a given database may differ from that used on NCBI web search pages.

**field**
Search field. If used, the entire search term will be limited to the specified Entrez field. The following two URLs are equivalent:

```
esearch.fcgi?db=pubmed&term=asthma&field=title
```
```
esearch.fcgi?db=pubmed&term=asthma[title]
```

**Optional Parameters – Dates**

**datetype**
Type of date used to limit a search. The allowed values vary between Entrez databases, but common values are ‘mdat’ (modification date), ‘pdat’ (publication date) and ‘edat’ (Entrez date). Generally an Entrez database will have only two allowed values for `datetype`. 
**reldate**

When `reldate` is set to an integer \( n \), the search returns only those items that have a date specified by `datetype` within the last \( n \) days.

**mindate, maxdate**

Date range used to limit a search result by the date specified by `datetype`. These two parameters (`mindate, maxdate`) must be used together to specify an arbitrary date range. The general date format is YYYY/MM/DD, and these variants are also allowed: YYYY, YYYY/MM.

**Examples**

Search in PubMed with the term *cancer* for abstracts that have an Entrez date within the last 60 days; retrieve the first 100 PMIDs and translations; post the results on the History server and return a WebEnv and query_key:

```plaintext
db=pubmed&term=cancer&reldate=60&datetype=edat&retmax=100&usehistory=y
```

Search in PubMed for the journal PNAS, Volume 97, and retrieve six PMIDs starting with the seventh PMID in the list:

```plaintext
db=pubmed&term=PNAS[ta]+AND+97[vi]&retstart=6&retmax=6&tool=biomed3
```

Search in the NLM Catalog for journals matching the term *obstetrics*:

```plaintext
db=nlmcatalog&term=obstetrics+AND+ncbijournals[filter]
```

Search PubMed Central for free full text articles containing the query *stem cells*:

```plaintext
```

Search in Nucleotide for all tRNAs:

```plaintext
db=nucleotide&term=biomol+trna[prop]
```

Search in Protein for a molecular weight range:

```plaintext
db=protein&term=70000:90000[molecular+weight]
```
EPost

Base URL

Functions
- Uploads a list of UIDs to the Entrez History server
- Appends a list of UIDs to an existing set of UID lists attached to a Web Environment

Required Parameters

db
Database containing the UIDs in the input list. The value must be a valid Entrez database name (default = pubmed).

id
UID list. Either a single UID or a comma-delimited list of UIDs may be provided. All of the UIDs must be from the database specified by db. There is no set maximum for the number of UIDs that can be passed to epost, but if more than about 200 UIDs are to be posted, the request should be made using the HTTP POST method.

epost.fcgi?db=protein&id=15718680,157427902,119703751

Optional Parameter

WebEnv
Web Environment. If provided, this parameter specifies the Web Environment that will receive the UID list sent by post. EPost will create a new query key associated with that Web Environment. Usually this WebEnv value is obtained from the output of a previous ESearch, EPost or ELink call. If no WebEnv parameter is provided, EPost will create a new Web Environment and post the UID list to query_key 1.

epost.fcgi?db=protein&id=15718680,157427902,119703751&WebEnv= <webenv string>

Example
Post records to PubMed:

**ESummary**

**Base URL**


**Functions**

- Returns document summaries (DocSums) for a list of input UIDs
- Returns DocSums for a set of UIDs stored on the Entrez History server

**Required Parameter**

**db**

Database from which to retrieve DocSums. The value must be a valid Entrez database name (default = pubmed).

**Required Parameter – Used only when input is from a UID list**

**id**

UID list. Either a single UID or a comma-delimited list of UIDs may be provided. All of the UIDs must be from the database specified by **db**. There is no set maximum for the number of UIDs that can be passed to ESummary, but if more than about 200 UIDs are to be provided, the request should be made using the HTTP POST method.

esummary.fcgi?db=protein&id=15718680,157427902,119703751

**Required Parameters – Used only when input is from the Entrez History server**

**query_key**

Query key. This integer specifies which of the UID lists attached to the given Web Environment will be used as input to ESummary. Query keys are obtained from the output of previous ESearch, EPost or ELink calls. The **query_key** parameter must be used in conjunction with **WebEnv**.

**WebEnv**

Web Environment. This parameter specifies the Web Environment that contains the UID list to be provided as input to ESummary. Usually this WebEnv value is obtained from the output of a previous ESearch, EPost or ELink call. The **WebEnv** parameter must be used in conjunction with **query_key**.

esummary.fcgi?db=protein&query_key=<key>&WebEnv=<webenv string>
Optional Parameters – Retrieval

**restart**
Sequential index of the first DocSum to be retrieved (default=1, corresponding to the first record of the entire set). This parameter can be used in conjunction with **retmax** to download an arbitrary subset of DocSums from the input set.

**retmax**
Total number of DocSums from the input set to be retrieved, up to a maximum of 10,000. If the total set is larger than this maximum, the value of **restart** can be iterated while holding **retmax** constant, thereby downloading the entire set in batches of size **retmax**.

**retmode**
Retrieval type. Determines the format of the returned output. The default value is ‘xml’ for ESummary XML, but ‘json’ is also supported to return output in JSON format.

**version**
Used to specify version 2.0 ESummary XML. The only supported value is ‘2.0’. When present, ESummary will return version 2.0 DocSum XML that is unique to each Entrez database and that often contains more data than the default DocSum XML.

**Examples**

**PubMed:**


PubMed, version 2.0 XML:


**Protein:**


**Nucleotide:**


**Structure:**

Taxonomy:
db=taxonomy&id=9913,30521

UniSTS:
db=unists&id=254085,254086

**EFetch**

**Base URL**

**Functions**
- Returns formatted data records for a list of input UIDs
- Returns formatted data records for a set of UIDs stored on the Entrez History server

**Required Parameters**

**db**
Database from which to retrieve records. The value must be a valid Entrez database name (default = pubmed). Currently EFetch does not support all Entrez databases. Please see Table 1 in Chapter 2 for a list of available databases.

**Required Parameter – Used only when input is from a UID list**

**id**
UID list. Either a single UID or a comma-delimited list of UIDs may be provided. All of the UIDs must be from the database specified by **db**. There is no set maximum for the number of UIDs that can be passed to EFetch, but if more than about 200 UIDs are to be provided, the request should be made using the HTTP POST method.

efetch.fcgi?db=protein&id=15718680,157427902,119703751

**Required Parameters – Used only when input is from the Entrez History server**

**query_key**
Query key. This integer specifies which of the UID lists attached to the given Web Environment will be used as input to EFetch. Query keys are obtained from the output of
previous ESearch, EPost or ELInk calls. The `query_key` parameter must be used in conjunction with `WebEnv`.

**WebEnv**

Web Environment. This parameter specifies the Web Environment that contains the UID list to be provided as input to EFetch. Usually this WebEnv value is obtained from the output of a previous ESearch, EPost or ELInk call. The `WebEnv` parameter must be used in conjunction with `query_key`.

`efetch.fcgi?db=protein&query_key=<key>&WebEnv=<webenv string>`

**Optional Parameters – Retrieval**

**retmode**

Retrieval mode. This parameter specifies the data format of the records returned, such as plain text, HTML or XML. See Table 1 for a full list of allowed values for each database.

*Table 1 – Valid values of `&retmode` and `&rettype` for EFetch (null = empty string)*

<table>
<thead>
<tr>
<th>Record Type</th>
<th><code>&amp;rettype</code></th>
<th><code>&amp;retmode</code></th>
</tr>
</thead>
<tbody>
<tr>
<td>All Databases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Document summary</td>
<td>docsum</td>
<td>xml, default</td>
</tr>
<tr>
<td>List of UIDs in XML</td>
<td>uilist</td>
<td>xml</td>
</tr>
<tr>
<td>List of UIDs in plain text</td>
<td>uilist</td>
<td>text</td>
</tr>
<tr>
<td>db = bioproject</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full record XML</td>
<td>xml, default</td>
<td>xml, default</td>
</tr>
<tr>
<td>db = biosample</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full record XML</td>
<td>full, default</td>
<td>xml, default</td>
</tr>
<tr>
<td>Full record text</td>
<td>full, default</td>
<td>text</td>
</tr>
<tr>
<td>db = biosystems</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full record XML</td>
<td>xml, default</td>
<td>xml, default</td>
</tr>
<tr>
<td>db = gds</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Summary</td>
<td>summary, default</td>
<td>text, default</td>
</tr>
<tr>
<td>db = gene</td>
<td></td>
<td></td>
</tr>
<tr>
<td>text ASN.1</td>
<td>null</td>
<td>asn.1, default</td>
</tr>
<tr>
<td>XML</td>
<td>null</td>
<td>xml</td>
</tr>
<tr>
<td>Gene table</td>
<td>gene_table</td>
<td>text</td>
</tr>
<tr>
<td>db = homologene</td>
<td></td>
<td></td>
</tr>
<tr>
<td>text ASN.1</td>
<td>null</td>
<td>asn.1, default</td>
</tr>
</tbody>
</table>

*Table 1 continues on next page...*
Table 1 continued from previous page.

<table>
<thead>
<tr>
<th>db</th>
<th>Column 1</th>
<th>Column 2</th>
<th>Column 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>XML</td>
<td>null</td>
<td>xml</td>
<td></td>
</tr>
<tr>
<td>Alignment scores</td>
<td>alignmentscores</td>
<td>text</td>
<td></td>
</tr>
<tr>
<td>FASTA</td>
<td>fasta</td>
<td>text</td>
<td></td>
</tr>
<tr>
<td>HomoloGene</td>
<td>homologene</td>
<td>text</td>
<td></td>
</tr>
<tr>
<td><em>db = mesh</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full record</td>
<td>full, default</td>
<td>text, default</td>
<td></td>
</tr>
<tr>
<td><em>db = nlmcatalog</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full record</td>
<td>null</td>
<td>text, default</td>
<td></td>
</tr>
<tr>
<td>XML</td>
<td>null</td>
<td>xml</td>
<td></td>
</tr>
<tr>
<td><em>db = nuccore, nucest, nucgss, protein or popset</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>text ASN.1</td>
<td>null</td>
<td>text, default</td>
<td></td>
</tr>
<tr>
<td>binary ASN.1</td>
<td>null</td>
<td>text, default</td>
<td></td>
</tr>
<tr>
<td>Full record in XML</td>
<td>native</td>
<td>text, default</td>
<td></td>
</tr>
<tr>
<td>Accession number(s)</td>
<td>acc</td>
<td>text</td>
<td></td>
</tr>
<tr>
<td>FASTA</td>
<td>fasta</td>
<td>text</td>
<td></td>
</tr>
<tr>
<td>TinySeq XML</td>
<td>fasta</td>
<td>xml</td>
<td></td>
</tr>
<tr>
<td>SeqID string</td>
<td>seqid</td>
<td>text</td>
<td></td>
</tr>
<tr>
<td>Additional options for db = nuccore, nucest, nucgss or popset</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GenBank flat file</td>
<td>gb</td>
<td>text</td>
<td></td>
</tr>
<tr>
<td>GBSeq XML</td>
<td>gb</td>
<td>xml</td>
<td></td>
</tr>
<tr>
<td>INSDSeq XML</td>
<td>gbc</td>
<td>xml</td>
<td></td>
</tr>
<tr>
<td>Additional option for db = nuccore and protein</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feature table</td>
<td>ft</td>
<td>text</td>
<td></td>
</tr>
<tr>
<td>Additional option for db = nuccore</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GenBank flat file with full sequence (contigs)</td>
<td>gbwithparts</td>
<td>text</td>
<td></td>
</tr>
<tr>
<td>CDS nucleotide FASTA</td>
<td>fasta_cds_na</td>
<td>text</td>
<td></td>
</tr>
<tr>
<td>CDS protein FASTA</td>
<td>fasta_cds_aa</td>
<td>text</td>
<td></td>
</tr>
<tr>
<td>Additional option for db = nucest</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EST report</td>
<td>est</td>
<td>text</td>
<td></td>
</tr>
<tr>
<td>Additional option for db = nucgss</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GSS report</td>
<td>gss</td>
<td>text</td>
<td></td>
</tr>
<tr>
<td>Additional options for db = protein</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GenPept flat file</td>
<td>gp</td>
<td>text</td>
<td></td>
</tr>
</tbody>
</table>

*Table 1 continues on next page...*
Table 1 continued from previous page.

<table>
<thead>
<tr>
<th>Database</th>
<th>Parameter</th>
<th>Format</th>
</tr>
</thead>
<tbody>
<tr>
<td>GBSeq XML</td>
<td>gp</td>
<td>xml</td>
</tr>
<tr>
<td>INSDDSeq XML</td>
<td>gpc</td>
<td>xml</td>
</tr>
<tr>
<td>Identical Protein XML</td>
<td>ipg</td>
<td>xml</td>
</tr>
<tr>
<td>db = pmc</td>
<td>null</td>
<td>xml, default</td>
</tr>
<tr>
<td>MEDLINE</td>
<td>medline</td>
<td>text</td>
</tr>
<tr>
<td>db = pubmed</td>
<td>null</td>
<td>asn.1, default</td>
</tr>
<tr>
<td>XML</td>
<td>null</td>
<td>xml</td>
</tr>
<tr>
<td>MEDLINE</td>
<td>medline</td>
<td>text</td>
</tr>
<tr>
<td>PMID list</td>
<td>uilist</td>
<td>text</td>
</tr>
<tr>
<td>Abstract</td>
<td>abstract</td>
<td>text</td>
</tr>
<tr>
<td>db = sequences</td>
<td>null</td>
<td>text, default</td>
</tr>
<tr>
<td>text ASN.1</td>
<td>acc</td>
<td>text</td>
</tr>
<tr>
<td>Accession number(s)</td>
<td>acc</td>
<td>text</td>
</tr>
<tr>
<td>FASTA</td>
<td>fasta</td>
<td>text</td>
</tr>
<tr>
<td>SeqID string</td>
<td>seqid</td>
<td>text</td>
</tr>
<tr>
<td>db = sra</td>
<td>null</td>
<td>text, default</td>
</tr>
<tr>
<td>Flat file</td>
<td>flt</td>
<td>text</td>
</tr>
<tr>
<td>FASTA</td>
<td>fasta</td>
<td>text</td>
</tr>
<tr>
<td>RS Cluster report</td>
<td>rsr</td>
<td>text</td>
</tr>
<tr>
<td>SS Exemplar list</td>
<td>sssexemplar</td>
<td>text</td>
</tr>
<tr>
<td>Chromosome report</td>
<td>chr</td>
<td>text</td>
</tr>
<tr>
<td>Summary</td>
<td>docset</td>
<td>text</td>
</tr>
<tr>
<td>UID list</td>
<td>uilist</td>
<td>text or xml</td>
</tr>
<tr>
<td>db = sra</td>
<td>null</td>
<td>xml, default</td>
</tr>
<tr>
<td>XML</td>
<td>full, default</td>
<td>xml, default</td>
</tr>
<tr>
<td>db = taxonomy</td>
<td>null</td>
<td>xml, default</td>
</tr>
<tr>
<td>TaxID list</td>
<td>uilist</td>
<td>text or xml</td>
</tr>
<tr>
<td>db = clinvar</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1 continues on next page...
Table 1 continued from previous page.

| ClinVar Set | clinvarset | xml, default |
| UID list    | uilist     | text or xml  |
| db = gtr    |            |              |

| GTR Test Report | gtracc | xml, default |

**rettype**

Retrieval type. This parameter specifies the record view returned, such as Abstract or MEDLINE from PubMed, or GenPept or FASTA from protein. Please see Table 1 for a full list of allowed values for each database.

**retstart**

Sequential index of the first record to be retrieved (default=0, corresponding to the first record of the entire set). This parameter can be used in conjunction with **retmax** to download an arbitrary subset of records from the input set.

**retmax**

Total number of records from the input set to be retrieved, up to a maximum of 10,000. Optionally, for a large set the value of **retstart** can be iterated while holding **retmax** constant, thereby downloading the entire set in batches of size **retmax**.

**Optional Parameters – Sequence Databases**

**strand**

Strand of DNA to retrieve. Available values are "1" for the plus strand and "2" for the minus strand.

**seq_start**

First sequence base to retrieve. The value should be the integer coordinate of the first desired base, with "1" representing the first base of the sequence.

**seq_stop**

Last sequence base to retrieve. The value should be the integer coordinate of the last desired base, with "1" representing the first base of the sequence.

**complexity**

Data content to return. Many sequence records are part of a larger data structure or "blob", and the **complexity** parameter determines how much of that blob to return. For example, an mRNA may be stored together with its protein product. The available values are as follows:
<table>
<thead>
<tr>
<th>Value of complexity</th>
<th>Data returned for each requested GI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>entire blob</td>
</tr>
<tr>
<td>1</td>
<td>bioseq</td>
</tr>
<tr>
<td>2</td>
<td>minimal bioseq-set</td>
</tr>
<tr>
<td>3</td>
<td>minimal nuc-prot</td>
</tr>
<tr>
<td>4</td>
<td>minimal pub-set</td>
</tr>
</tbody>
</table>

**Examples**

**PubMed**

Fetch PMIDs 17284678 and 9997 as text abstracts:


Fetch PMIDs in XML:


**PubMed Central**

Fetch XML for PubMed Central ID 212403:


**Nucleotide/Nuccore**

Fetch the first 100 bases of the plus strand of GI 21614549 in FASTA format:


Fetch the first 100 bases of the minus strand of GI 21614549 in FASTA format:


Fetch the nuc-prot object for GI 21614549:


Fetch the full ASN.1 record for GI 5:

Fetch FASTA for GI 5:
db=nucleotide&id=5&rettype=fasta

Fetch the GenBank flat file for GI 5:
db=nucleotide&id=5&rettype=gb

Fetch GBSeqXML for GI 5:
db=nucleotide&id=5&rettype=gb&retmode=xml

Fetch TinySeqXML for GI 5:
db=nucleotide&id=5&rettype=fasta&retmode=xml

Popset

Fetch the GenPept flat file for Popset ID 12829836:
db=popset&id=12829836&rettype=gp

Protein

Fetch the GenPept flat file for GI 8:

Fetch GBSeqXML for GI 8:
db=protein&id=8&rettype=gp&retmode=xml

Sequences

Fetch FASTA for a transcript and its protein product (GIs 312836839 and 34577063)
db=sequences&id=312836839,34577063&rettype=fasta&retmode=text

Gene

Fetch full XML record for Gene ID 2:
**ELink**

**Base URL**


**Functions**

- Returns UIDs linked to an input set of UIDs in either the same or a different Entrez database
- Returns UIDs linked to other UIDs in the same Entrez database that match an Entrez query
- Checks for the existence of Entrez links for a set of UIDs within the same database
- Lists the available links for a UID
- Lists LinkOut URLs and attributes for a set of UIDs
- Lists hyperlinks to primary LinkOut providers for a set of UIDs
- Creates hyperlinks to the primary LinkOut provider for a single UID

**Required Parameters**

**db**

Database from which to retrieve UIDs. The value must be a valid Entrez database name (default = pubmed). This is the destination database for the link operation.

**dbfrom**

Database containing the input UIDs. The value must be a valid Entrez database name (default = pubmed). This is the origin database of the link operation. If **db** and **dbfrom** are set to the same database value, then ELink will return computational neighbors within that database. Please see the full list of Entrez links for available computational neighbors. Computational neighbors have linknames that begin with **dbname_dbname** (examples: protein_protein, pcassay_pcassey_activityneighbor).

**cmd**

ELink command mode. The command mode specified which function ELink will perform. Some optional parameters only function for certain values of &cmd (see below).

**cmd=neighbor (default)**

ELink returns a set of UIDs in **db** linked to the input UIDs in **dbfrom**.

*Example: Link from protein to gene*


**cmd=neighbor_score**
Elink returns a set of UIDs within the same database as the input UIDs along with computed similarity scores.

Example: Find related articles to PMID 20210808


**cmd=neighbor_history**

Elink posts the output UIDs to the Entrez History server and returns a **query_key** and **WebEnv** corresponding to the location of the output set.

Example: Link from protein to gene and post the results on the Entrez History


**cmd=acheck**

Elink lists all links available for a set of UIDs.

Example: List all possible links from two protein GIs


Example: List all possible links from two protein GIs to PubMed


**cmd=nccheck**

Elink checks for the existence of links within the same database for a set of UIDs. These links are equivalent to setting **db** and **dbfrom** to the same value.

Example: Check whether two nucore sequences have "related sequences" links.


**cmd=lcheck**

Elink checks for the existence of external links (LinkOuts) for a set of UIDs.

Example: Check whether two protein sequences have any LinkOut providers.


**cmd=llinks**
For each input UID, ELink lists the URLs and attributes for the LinkOut providers that are not libraries.

Example: List the LinkOut URLs for non-library providers for two pubmed abstracts.


For each input UID, ELink lists the URLs and attributes for all LinkOut providers including libraries.

Example: List all LinkOut URLs for two PubMed abstracts.


cmd=prlinks

ELink lists the primary LinkOut provider for each input UID, or links directly to the LinkOut provider's web site for a single UID if retmode is set to ref.

Example: Find links to full text providers for two PubMed abstracts.


Example: Link directly to the full text for a PubMed abstract at the provider's web site.


Required Parameter – Used only when input is from a UID list

id

UID list. Either a single UID or a comma-delimited list of UIDs may be provided. All of the UIDs must be from the database specified by dbfrom. There is no set maximum for the number of UIDs that can be passed to ELink, but if more than about 200 UIDs are to be provided, the request should be made using the HTTP POST method.

Link from protein to gene.


Find related sequences (link from nuccore to nuccore).

If more than one id parameter is provided, ELink will perform a separate link operation for the set of UIDs specified by each id parameter. This effectively accomplishes "one-to-one" links and preserves the connection between the input and output UIDs.

Find one-to-one links from protein to gene.


Required Parameters – Used only when input is from the Entrez History server

query_key
Query key. This integer specifies which of the UID lists attached to the given Web Environment will be used as input to ELink. Query keys are obtained from the output of previous ESearch, EPost or ELink calls. The query_key parameter must be used in conjunction with WebEnv.

WebEnv
Web Environment. This parameter specifies the Web Environment that contains the UID list to be provided as input to ELink. Usually this WebEnv value is obtained from the output of a previous ESearch, EPost or ELink call. The WebEnv parameter must be used in conjunction with query_key.

Link from protein to gene:
elink.fcgi?dbfrom=protein&db=gene&query_key=<key>&WebEnv=<webenv string>

Find related sequences (link from protein to protein):
elink.fcgi?dbfrom=protein&db=protein&query_key=<key>&WebEnv=<webenv string>

Optional Parameter – Retrieval

retmode
Retrieval type. Determines the format of the returned output. The default value is 'xml' for ELink XML, but 'json' is also supported to return output in JSON format.

Optional Parameters – Limiting the Output Set of Links

linkname
Name of the Entrez link to retrieve. Every link in Entrez is given a name of the form dbfrom_db_subset.
The values of subset vary depending on the values of dbfrom and db. Many dbfrom/db combinations have no subset values. See the list of Entrez links for a listing of all available linknames. When linkname is used, only the links with that name will be retrieved.

The linkname parameter only functions when cmd is set to neighbor or neighbor_history.

Find all links from gene to snp.


Find snps with genotype data linked to genes.


term

Entrez query used to limit the output set of linked UIDs. The query in the term parameter will be applied after the link operation, and only those UIDs matching the query will be returned by ELink. The term parameter only functions when db and dbfrom are set to the same database value.

Find all related articles for a PMID.


Find all related review articles published in 2008 for a PMID.

https://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?dbfrom=pubmed&db=pubmed&id=19879512&term=review%5Bfilter%5D+AND+2008%5Bpdat%5Dh

holding

Name of LinkOut provider. Only URLs for the LinkOut provider specified by holding will be returned. The value provided to holding should be the abbreviation of the LinkOut provider’s name found in the <NameAbbr> tag of the ELink XML output when cmd is set to llinks or llinkslib. The holding parameter only functions when cmd is set to llinks or llinkslib.

Find information for all LinkOut providers for a PMID.


Find information from clinicaltrials.gov for a PMID.

Optional Parameters – Dates

These parameters only function when `cmd` is set to `neighbor` or `neighbor_history` and `dbfrom` is `pubmed`.

**datatype**

Type of date used to limit a link operation. The allowed values vary between Entrez databases, but common values are 'mdat' (modification date), 'pdat' (publication date) and 'edat' (Entrez date). Generally an Entrez database will have only two allowed values for `datatype`.

**reldate**

When `reldate` is set to an integer `n`, ELink returns only those items that have a date specified by `datatype` within the last `n` days.

**mindate, maxdate**

Date range used to limit a link operation by the date specified by `datatype`. These two parameters (`mindate, maxdate`) must be used together to specify an arbitrary date range. The general date format is YYYY/MM/DD, and these variants are also allowed: YYYY, YYYY/MM.

EGQuery

Base URL


Function

Provides the number of records retrieved in all Entrez databases by a single text query.

Required Parameter

**term**

Entrez text query. All special characters must be URL encoded. Spaces may be replaced by '+' signs. For very long queries (more than several hundred characters long), consider using an HTTP POST call. See the PubMed or Entrez help for information about search field descriptions and tags. Search fields and tags are database specific.

ESpell

Base URL

Function
Provides spelling suggestions for terms within a single text query in a given database.

Required Parameters

db
Database to search. Value must be a valid Entrez database name (default = pubmed).

term
Entrez text query. All special characters must be URL encoded. Spaces may be replaced by '+' signs. For very long queries (more than several hundred characters long), consider using an HTTP POST call. See the PubMed or Entrez help for information about search field descriptions and tags. Search fields and tags are database specific.


ECitMatch

Base URL

Function
Retrieves PubMed IDs (PMIDs) that correspond to a set of input citation strings.

Required Parameters

db
Database to search. The only supported value is 'pubmed'.

rettype
Retrieval type. The only supported value is 'xml'.

bdata
Citation strings. Each input citation must be represented by a citation string in the following format:
Multiple citation strings may be provided by separating the strings with a carriage return character (%0D). The your_key value is an arbitrary label provided by the user that may serve as a local identifier for the citation, and it will be included in the output. Be aware that all spaces must be replaced by '+' symbols and that citation strings should end with a final vertical bar '|'.


**Release Notes**

**EFetch; ELink JSON output: June 24, 2015**
- EFetch now supports ClinVar and GTR
- ELink now provides output in JSON format

**ESearch &sort; JSON output format: February 14, 2014**
- ESearch now provides a supported sort parameter
- EInfo, ESearch and ESummary now provide output data in JSON format

**ECitMatch, EInfo Version 2.0, EFetch: August 9, 2013**
- ECitMatch is a new E-utility that serves as an API to the PubMed batch citation matcher
- EInfo has an updated XML output that includes two new fields: <IsTruncatable> and <IsRangeable>
- EFetch now supports the BioProject database.

**EFetch Version 2.0. Target release date: February 15, 2012**
- EFetch now supports the following databases: biosample, biosystems and sra
- EFetch now has defined default values for &retmode and &rettype for all supported databases (please see Table 1 for all supported values of these parameters)
- EFetch no longer supports &retmode=html; requests containing &retmode=html will return data using the default &retmode value for the specified database (&db)
- EFetch requests including &rettype=docsum return XML data equivalent to ESummary output

**Release of new Genome database: November 9, 2011**
- Entrez Genome has been completely redesigned, and database records now correspond to a species rather than an individual chromosome sequence. Please see

- Old Genome IDs are no longer valid. A file is available on the NCBI FTP site that maps old Genome IDs to Nucleotide GIs: ftp.ncbi.nih.gov/genomes/old_genomeID2nucGI
- EFetch no longer supports retrievals from Genome (db=genome).
- The ESummary XML for Genome has been recast to reflect the new data model.
- To view the new search fields and links supported for the new Genome database, please see https://eutils.ncbi.nlm.nih.gov/entrez/eutils/einfo.fcgi?db=genome

**ESummary Version 2.0. November 4, 2011**

- ESummary now supports a new, alternative XML presentation for Entrez document summaries (DocSums). The new XML is unique to each Entrez database and generally contains more extensive data about the record than the original DocSum XML.
- There are no plans at present to discontinue the original DocSum XML, so developers can continue to use this presentation, which will remain the default.
- Version 2.0 XML is returned when &version=2.0 is included in the ESummary URL.

**Demonstration Programs**

Please see Chapter 1 for sample Perl scripts.

**For More Information**

Please see Chapter 1 for getting additional information about the E-utilities.
The E-utility Web Service (SOAP)

Eric Sayers, PhD\textsuperscript{1} and Vadim Miller\textsuperscript{2}

Created: January 21, 2010; Updated: January 23, 2015.

Termination Announcement

The SOAP web service for the E-utilities will be **TERMINATED** permanently on July 1, 2015. All requests made to this service after that date will fail.

If you have software that is currently using the E Utility SOAP web service, please plan to transition to using the standard URL interface described in Chapters 1-4 of this book.

Please contact info@ncbi.nlm.nih.gov if you have questions about this change.

For More Information

E-utility DTDs

Please see Chapter 1 for getting additional information about the E-utilities.

\textsuperscript{1} NCBI; Email: sayers@ncbi.nlm.nih.gov. \textsuperscript{2} NCBI; Email: miller@ncbi.nlm.nih.gov.

\textsuperscript{\dagger} Corresponding author.
Entrez Direct: E-utilities on the UNIX Command Line

Jonathan Kans, PhD

Created: April 23, 2013; Updated: August 9, 2018.

Getting Started

Introduction

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

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

Installation

EDirect will run on UNIX and Macintosh computers that have the Perl language installed, and under the Cygwin UNIX-emulation environment on Windows PCs. To install the EDirect software, copy the following commands and paste them into a terminal window:

```bash
cd ~
/bin/bash
perl -MNet::FTP -e \n  '$ftp = new Net::FTP("ftp.ncbi.nlm.nih.gov", Passive => 1);
    $ftp->login; $ftp->binary;
    $ftp->get("/entrez/entrezdirect/edirect.tar.gz");'
gunzip -c edirect.tar.gz | tar xf -
rm edirect.tar.gz
builtin exit
export PATH=$PATH:$HOME/edirect >& /dev/null || setenv PATH "$PATH:$HOME/edirect" ./edirect/setup.sh
```

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

Corresponding author.
This downloads several scripts into an "edirect" folder in the user's home directory. The setup.sh script then downloads any missing Perl modules, and may print an additional command for updating the PATH environment variable in the user's configuration file. Copy that command, if present, and paste it into the terminal window to complete the installation process. The editing instructions will look something like:

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

**Entrez Direct Functions**

Navigation functions support exploration within the Entrez databases:

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

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

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

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

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

Several additional functions are also provided:

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

**Entering Query Commands**

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

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

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

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

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

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

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

Writing Commands on Multiple Lines

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

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

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

Retrieving PubMed Reports

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

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

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

```
... 

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

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

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

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

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

```
...
PMID- 23555569
OWN - NLM
```
Levels of lycopene beta-cyclase 1 modulate carotenoid gene expression and accumulation in Daucus carota.

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]
MDTLLKTPNLDFIPFQHGERLCNPPYPSRVLKVVRKRAIKIVSSVSASALLDLVETKLENLDFA
ELPLYDSKQVVDALAVGGGFPAGLAVAQVSEAGLSIDPSKLIWPNNYGVWDEFEAMLDDLCLDD
TTWSGAVVYVDEVKKDLRSRLPRGRVNRKQLSKMLQKCITNGVQKSKVTVNVHEANSTVVCSDQVKI
QASVVLQATDGSRCLVQDKPYNPYGQVAYGIAEVDGHPDVKMDFMRDKHLDSYPELKERNSKIP
TFLYAMPPFSSNRILIEETSLVARPLRMEDIQRMAARLKHGINKRIEEDERCVIFPPGFLPVLQRRQV
VGIUATGMVHPSTGYMVARTLAAPIVANAIYRGSPSSNLRLGQDQLSAEVWRLWPIEERRQREFFC
FGMDILLLKLLDARTRFFDDLFQHPYWHGFLLSRFFLPLELLVFGLSFLFHASNTSRLEIMTKGTVPLA
KMINNLVQDRD
```

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

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

```
LOCUS AAA81880 501 aa linear PLN ...
DEFINITION lycopene cyclase [Arabidopsis thaliana]..
ACCESSION AAA81880
VERSION AAA81880.1 GI:735882
DBSOURCE locus ATHLYC accession L40176.1
KEYWORDS .
SOURCE Arabidopsis thaliana (thale cress)
ORGANISM Arabidopsis thaliana Eukaryota; Viridiplantae; Streptophyta; Embryophyta;
```
Tracheophyta; Spermatophyta; Magnoliophyta; eudicotyledons; Brassicales; Brassicaceae; Camelineae; Arabidopsis.

REFERENCE 1 (residues 1 to 501)
AUTHORS Scolnik, P.A. and Bartley, G.E.
TITLE Nucleotide sequence of lycopene cyclase (GenBank L40176) from Arabidopsis (PGR95-019)

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 raikivsvv sgsaaldlv
61 petkkenldf elplydtsks qvvdlaivgg gpaglavaqq vseaglsvcs idspklwp
121 nnygvwvdef eamdldcld ttwsgavvyy degvkkdlisr pygrvnrkql ksmlqkcit
181 ngvkfhqskv tnvvhheans tvvcsdgvkl qasvvidatg fsrclvqydk pynpyqvay
241 giiaevdghp fdvdkmvfmd wrdkhldysy elkernskip tflyampfss nriflelets1
301 varpgrpmed igermaarlk hlginvkrie edercvipmg gplpvlpqrv vgiggtagmv
361 hpstgymvar tllaapivan aivrylgspg snsxqgdqsls aevwrdlwpi errrqreffc
421 fmdillkld 1datrrffda ffdlqphywh gflssrlflp ellvglgslf sshasntsrl
481 imtkgtvpla kmnlnlvd dr d

//

Searching and Filtering

Restricting Query Results

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

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

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

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

restrict results to articles published in the previous two months or in the 1990s, respectively.
Qualifying Queries by Indexed Field

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

Commonly-used fields for PubMed queries include:

- [AFFL] Affiliation
- [ALL] All Fields
- [AUTH] Author
- [FAUT] Author - First
- [LAUT] Author - Last
- [PDAT] Date - Publication
- [FILT] Filter
- [JOUR] Journal
- [LANG] Language
- [MAJR] MeSH Major Topic
- [SUBH] MeSH Subheading
- [MESH] MeSH Terms
- [PTYP] Publication Type
- [WORD] Text Word
- [TITL] Title
- [TIAB] Title/Abstract
- [UID] UID

and a qualified query looks like:

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

Filters that limit search results to subsets of PubMed include:

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

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

- [ACCN] Accession
- [ALL] All Fields
- [AUTH] Author
- [GPRJ] BioProject
- [ECNO] EC/RN Number
- [FKEY] Feature key
- [FILT] Filter
- [GENE] Gene Name
and a sample query in the protein database is:

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

Additional examples of subset filters in sequence databases are:

mammalia [ORGN]
mammalia [ORGN:noexp]
cds [FKEY]
lacz [GENE]
beta galactosidase [PROT]
protein snp [FILT]
reviewed [FILT]
biomol genomic [PROP]
dbxref flybase [PROP]
gbd div phg [PROP]
phylogenetic study [PROP]
sequence from mitochondrion [PROP]
src cultivar [PROP]
srcdb refseq validated [PROP]
150:200 [SLEN]
2000:4000 [MLWT]

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

**Examining Intermediate Results**

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

The results of each step in a query can be examined to confirm expected behavior before adding the next step. The Count field in the ENTREZ_DIRECT object contains the number of records returned by the previous step. A good measure of query success is a reasonable (non-zero) count value. For example:
esearch -db protein -query "NP_567004 [ACCN]" |
elink -related |
efilter -query "28000:30000 [MLWT]" |
elink -target structure |
efilter -query "0:2 [RESO]"

produces:

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

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

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

**Combining Independent Queries**

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

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

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

<table>
<thead>
<tr>
<th>Id</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>23962925</td>
<td>Genome analysis reveals insights into physiology and ...</td>
</tr>
<tr>
<td>23959870</td>
<td>Low levels of copper disrupt brain amyloid-β homeostasis ...</td>
</tr>
<tr>
<td>23371554</td>
<td>Genomic diversity and evolution of the head crest in the ...</td>
</tr>
<tr>
<td>23251661</td>
<td>Novel genetic loci identified for the pathophysiology of ...</td>
</tr>
</tbody>
</table>

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

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

will return:

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

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

## Structured Data

### Advantages of XML Format

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

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

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

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

```
```

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

### Conversion of XML Data into Tabular Form

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

will print the number of records in the current query.

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

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

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

**Extraction Arguments**

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

- element Id -first Name Title

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

- pattern DocumentSummary
  - block Author

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

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

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

These commands are issued immediately after an exploration argument.

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

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

and apply to subsequent selection statements.

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

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

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

will generate an XML document summary set:

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

Piping the document summary output to:

```
xtract -outline
```

will give an indented overview of the XML structure hierarchy:

```
DbBuild
DocumentSummary
  Id
  PubDate
  EPubDate
  Source
  Authors
    Author
      Name
      AuthType
      ClusterID
    Author
      Name
      ...
```
The outline view presents a clear, uncluttered picture of the XML hierarchy that is useful in designing the appropriate command for actual data extraction. Copy and paste from the -outline output to xtract arguments can help avoid typographical errors. Thus:

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

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

```
19650888    Cano V        Klebsiella pneumoniae triggers a cytotoxic ...
19262028    Suto J        Metabolic consequence of congenital asplenia ...
19248821    Fukumoto N    Hypoalgesic behaviors of P/Q-type voltage- ...
18822497    Trishin AV    [Protective activity of secreted proteins of ...
18582214    Singh A       Generation and characterization of monoclonal ...
```

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

**Processing Results with UNIX Utilities**

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

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

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

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

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

```
WordAtATime() {
    sed 's/[^a-zA-Z0-9]/ /g; s/^ *//' |
    tr 'A-Z' 'a-z' |
    fmt -w 1
```
Titles can be passed to a pair of these UNIX alias commands:

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

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

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

### Output Format Customization

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

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

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

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

```
2652    OPN1MW    CBD|GCP|GOP|CBBM|COD5|OPN1MW1
5956    OPN1LW    CBP|RCP|ROP|CBBM|COD5
```
The -sep value also applies to unrelated -element items that are grouped with commas. Otherwise the -tab value delineates individual fields.

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

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

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

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

**Pubmed Article XML Records**

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

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

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

```xml
<MedlineCitation>
  <PMID>12345678</PMID>
  <DateCompleted>
    <Year>2000</Year>
    <Month>05</Month>
    <Day>12</Day>
  </DateCompleted>
  <DateRevised>
    <Year>2001</Year>
    <Month>06</Month>
    <Day>15</Day>
  </DateRevised>
  <Article>
    <Journal>
      <ISSN>1234-5678</ISSN>
      <JournalIssue>
        <Volume>56</Volume>
        <Issue>3</Issue>
        <PubDate>
          <Year>2000</Year>
          <Month>05</Month>
          <Day>12</Day>
        </PubDate>
        <Title>Deuteranopia</Title>
        <ISOAbbreviation>Doc</ISOAbbreviation>
      </JournalIssue>
      <Pagination>
        <MedlinePgn>83-84</MedlinePgn>
        <Abstract/>
      </Pagination>
    </Journal>
  </Article>
</MedlineCitation>
```
Using this information to craft a new xtract statement:
```bash
esearch -db pubmed -query "tetrachromacy" |
efetch -format xml |
xtract -pattern PubmedArticle -element MedlineCitation/PMID LastName
```
results in a table of all authors for each record:

<table>
<thead>
<tr>
<th>PMID</th>
<th>Last Name</th>
<th>First Name</th>
<th>Initials</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>23393278</td>
<td>Sabbah</td>
<td>Troje</td>
<td>Gray</td>
<td>Hawryshyn</td>
</tr>
<tr>
<td>20884587</td>
<td>Jordan</td>
<td>Deeb</td>
<td>Bosten</td>
<td>Mollon</td>
</tr>
<tr>
<td>18230593</td>
<td>Koshitaka</td>
<td>Kinoshita</td>
<td>Vorobyev</td>
<td>Arikawa</td>
</tr>
<tr>
<td>17685813</td>
<td>Wachtler</td>
<td>Doi</td>
<td>Lee</td>
<td>Sejnowski</td>
</tr>
</tbody>
</table>

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

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

**Exploration of XML Sets**

Individual PubmedArticle objects can be retrieved directly by efetch:
```bash
efetch -db pubmed -id 20643751 -format xml
```
The resulting XML has authors with separate fields for last name and initials:

```
...<AuthorList>
  <Author>
    <LastName>Inamdar</LastName>
    <ForeName>Arati A</ForeName>
    <Initials>AA</Initials>
  </Author>
  <Author>
    <LastName>Masurekar</LastName>
    <ForeName>Prakash</ForeName>
    <Initials>P</Initials>
  </Author>
...<AuthorList>
```
Without being given any guidance about context, an -element statement with "Initials" and "LastName" arguments:

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

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

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

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

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

which restores the correct association of initials and last name:

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

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

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

results in more desirable formatting of author names:

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

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

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

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

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

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

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

<table>
<thead>
<tr>
<th>PMID</th>
<th>Author(s)</th>
<th>Count</th>
<th>Year, Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>4296474</td>
<td>Friedmann</td>
<td>1</td>
<td>1968 Apr</td>
</tr>
<tr>
<td>4640931</td>
<td>Tager/Steiner</td>
<td>2</td>
<td>1972 Dec</td>
</tr>
<tr>
<td>6092233</td>
<td>Calderon/Contopolou/Mortimer</td>
<td>3</td>
<td>1984 Jul-Aug</td>
</tr>
</tbody>
</table>

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

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

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

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

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

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

will only contribute a single column to the output.)

Nested Exploration of Subsets Within XML Sets

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

```
... 
<MeshHeading>
  <DescriptorName>RNA, Messenger</DescriptorName>
  <QualifierName>genetics</QualifierName>
</MeshHeading>
<MeshHeading>
  <DescriptorName>Transcription, Genetic</DescriptorName>
```
Visiting each MeSH term with a -block statement, and adding a -subset statement within the -block, allows nested exploration of the subheadings for the current MeSH term:

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

and creates a list of MeSH terms with associated subheadings:

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

### Selection of Attributes

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

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

that can be selected as "$\text{DescriptorName@MajorTopicYN}$" or "@$\text{MajorTopicYN}$":

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

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

```
6162838
N|Base Sequence
Y|DNA, Recombinant
```
The results can be processed by the UNIX stream editor "sed":
```
sed -e 's/N\|//g' -e 's/Y\|/*/g'
```
to display an asterisk for major ("starred" MeSH term) concepts:

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

**Recording Values in Variables**

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

```
efetch -db pubmed -id 1413997,6301692,781293 -format xml |
xtract -pattern PubmedArticle -PMID MedlineCitation/PMID |
   -block Author -element "&PMID" |
   -sep " " -tab "\n" -element Initials,LastName
```
produces a list of authors, with the PMID in the first column of each row:

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

**Variable Initialization**

Variables can be initialized with a literal value in parentheses:

```
efetch -db pubmed -id 1413997,6301692,781293 -format xml |
xtract -pattern PubmedArticle -element MedlineCitation/PMID |
   -block Author -sep " " -tab ""
   -element "&COM" Initials,LastName -COM "(, )"
```
This can be used as a placeholder to prevent missing data from shifting columns in a table, or to have additional control over output formatting:
Conditional Processing

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

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

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

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

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

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

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

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

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

Sequence Records

NCBI Data Model for Sequence Records

The NCBI represents sequence records in a data model that is based on the central dogma of molecular biology. Sequences, including genomic DNA, messenger RNAs, and protein products, are "instantiated" with the actual sequence letters, and are assigned identifiers (e.g., accession numbers) for reference. Features carry information about the biology of a given region, with a location that refers to specific intervals on a particular sequence. Some features may also point to the product sequence of a particular transformation.
A gene feature indicates the location of a heritable region of nucleic acid that confers a measurable phenotype. An mRNA feature on genomic DNA represents the exonic and untranslated regions of the message that remain after transcription and splicing. A coding region (CDS) feature has a product reference to the translated protein.

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

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

**Sequence Records in INSDSeq XML**

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

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

returns a set of INSDSeq objects:

```
<INSDSet>
  <INSSeq>
    <INSSeq_locus>AAN78128</INSSeq_locus>
    <INSSeq_length>17</INSSeq_length>
    <INSSeq_moltype>AA</INSSeq_moltype>
    <INSSeq_topology>linear</INSSeq_topology>
    <INSSeq_division>INV</INSSeq_division>
    <INSSeq_update-date>03-JAN-2003</INSSeq_update-date>
    <INSSeq_create-date>10-DEC-2002</INSSeq_create-date>
    <INSSeq_definition>alpha-conotoxin ImI precursor, partial [Conus imperialis]</INSSeq_definition>
    <INSSeq_primary-accession>AAN78128</INSSeq_primary-accession>
    <INSSeq_accession-version>AAN78128.1</INSSeq_accession-version>
    <INSSeq_other-seqids>
      <INSSeqid>gb|AAN78128.1|</INSSeqid>
      <INSSeqid>gi|26418308</INSSeqid>
    </INSSeq_other-seqids>
    <INSSeq_source>Conus imperialis</INSSeq_source>
    <INSSeq_organism>Conus imperialis</INSSeq_organism>
    <INSSeq_taxonomy>Eukaryota; Metazoa; Lophotrochozoa; Mollusca; Gastropoda; Caenogastropoda; Hypsogastropoda; Neogastropoda; Conoidea; Conidae; Conus</INSSeq_taxonomy>
    <INSSeq_references>
      <INSReference>
        ...
      </INSReference>
    </INSSeq_references>
  </INSSeq>
</INSDSet>
```

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

```
<table>
<thead>
<tr>
<th>FEATURES</th>
<th>Location/Qualifiers</th>
</tr>
</thead>
<tbody>
<tr>
<td>source</td>
<td>1..17/organism=&quot;Conus imperialis&quot;/db_xref=&quot;taxon:35631&quot;/country=&quot;Philippines&quot;</td>
</tr>
<tr>
<td>Protein</td>
<td>&lt;1..17/product=&quot;alpha-conotoxin ImI precursor&quot;</td>
</tr>
</tbody>
</table>
| mat_peptide   | 5..16/product="alpha-conotoxin ImI"/note="the C-terminal glycine of the precursor is post translationally removed"
```
in a structured feature table:

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

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

### Generating Qualifier Extraction Commands

Because obtaining specific qualifier values from INSDSeq XML is somewhat more complex than previous cases, the xtract -insd argument can be used to generate extraction instructions.
Running xtract -insd in an isolated command prints a new xtract statement that can then be copied, edited if necessary, and pasted into other queries. Running the -insd command within a multi-step pipe dynamically executes the constructed query.

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

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

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

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

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

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

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

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

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

<table>
<thead>
<tr>
<th>Accession</th>
<th>Length</th>
<th>Product Name</th>
<th>Sequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGO59814.1</td>
<td>32</td>
<td>dell13b conotoxin</td>
<td>DCPTSCPTTCANGWECCCKGYPCVRQHCSGCNH</td>
</tr>
<tr>
<td>AAO33169.1</td>
<td>16</td>
<td>alpha-conotoxin GIC</td>
<td>GCCSHPACAGNNQHIC</td>
</tr>
<tr>
<td>ADB65788.1</td>
<td>20</td>
<td>conotoxin Cal 16</td>
<td>LEMQGCVCNANAKFCCGGEGR</td>
</tr>
<tr>
<td>AAN78128.1</td>
<td>12</td>
<td>alpha-conotoxin ImI</td>
<td>GCCSDPFCAWRCC</td>
</tr>
<tr>
<td>AAF23167.1</td>
<td>31</td>
<td>BeTX toxin</td>
<td>CRAEGTYCENDSQCCLNECCWGGCGHPCRHP</td>
</tr>
<tr>
<td>ADB65789.1</td>
<td>20</td>
<td>conotoxin Cal 16</td>
<td>LEMQGCVCNANAKFCCGGEGR</td>
</tr>
<tr>
<td>AAN78279.1</td>
<td>21</td>
<td>conotoxin Vx-II</td>
<td>WIDPSHYCCCCGGGCTDCCVNC</td>
</tr>
<tr>
<td>ABW16858.1</td>
<td>15</td>
<td>marmophin</td>
<td>DWEYHAHPKPNFSWFT</td>
</tr>
<tr>
<td>...</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Piping the results to a series of UNIX commands:

```
grep -i \"conotoxin\" | 
awk -F \"t\" -v \"OPS=\t\" '{if ( 10 <= $2 && $2 <= 30 ) print}' | 
sort -t \"\t\" -u -k 3,4 | 
sort -t \"\t\" -k 2,2n -k 3,3f | 
cut -f 1,3- | 
column -s \"\t\" -t
```
filters by product name, limits the results to a specified range of peptide lengths, removes redundant accessions, sorts the table by peptide length, deletes the length column, and aligns the columns for cleaner printing:

<table>
<thead>
<tr>
<th>Accession</th>
<th>Name</th>
<th>Peptide Sequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAN78128.1</td>
<td>alpha-conotoxin ImI</td>
<td>GCCSDPRCAWRC</td>
</tr>
<tr>
<td>AAN78127.1</td>
<td>alpha-conotoxin ImII</td>
<td>ACCSDRRCRWRC</td>
</tr>
<tr>
<td>ADB43130.1</td>
<td>conotoxin Cal 1a</td>
<td>KCCKRHHGCHPCGRT</td>
</tr>
<tr>
<td>ADB43131.1</td>
<td>conotoxin Cal 1b</td>
<td>LCCKRHHGCHPCGRT</td>
</tr>
<tr>
<td>AAO33169.1</td>
<td>alpha-conotoxin GIC</td>
<td>GCCSHPACAGNQHIC</td>
</tr>
<tr>
<td>ADB43128.1</td>
<td>conotoxin Cal 5.1</td>
<td>DPAPCCQHPIELCCRR</td>
</tr>
<tr>
<td>AAD31913.1</td>
<td>alpha A conotoxin Tx2</td>
<td>PECCSHPACNDHEPEICR</td>
</tr>
<tr>
<td>ADB43129.1</td>
<td>conotoxin Cal 5.2</td>
<td>MIQRSQCCAVKNCVHV</td>
</tr>
<tr>
<td>ADD97803.1</td>
<td>conotoxin Cal 1.2</td>
<td>AGCCPTIMYKTACRNTNCR</td>
</tr>
<tr>
<td>ADB65789.1</td>
<td>conotoxin Cal 16</td>
<td>LEMQGCVCNANAKFCGCHR</td>
</tr>
<tr>
<td>AAD31912.1</td>
<td>alpha A conotoxin Tx1</td>
<td>PECCSDPRCNSHPELCCGRR</td>
</tr>
<tr>
<td>AAN78279.1</td>
<td>conotoxin Vx-II</td>
<td>WIDPSHYCCGGCGTDCVNC</td>
</tr>
<tr>
<td>ADB43125.1</td>
<td>conotoxin Cal 14.2</td>
<td>GCPADCNTDSNKCSSPGFPG</td>
</tr>
<tr>
<td>ADB97802.1</td>
<td>conotoxin Cal 6.4</td>
<td>GCWCLGPNCACCRSGVCHDCPR</td>
</tr>
<tr>
<td>CAH64846.1</td>
<td>four-loop conotoxin</td>
<td>CRPSGSPCGVTSICGCRCSRGKCT</td>
</tr>
<tr>
<td>AAD31915.1</td>
<td>O-superfamily conotoxin TxO2</td>
<td>CYDGSCTNCGQCSCGWVICFVL</td>
</tr>
<tr>
<td>AAD31916.1</td>
<td>O-superfamily conotoxin TxO3</td>
<td>CYDGGTSCDSGICCSSWGCFVFCL</td>
</tr>
<tr>
<td>AAD31920.1</td>
<td>omega conotoxin SVIA mutant 1</td>
<td>CRPSGSPCGVTSICGCRCSRGKCT</td>
</tr>
<tr>
<td>AAD31921.1</td>
<td>omega conotoxin SVIA mutant 2</td>
<td>CRPSGSPCGVTSICGCRCSRGKCT</td>
</tr>
<tr>
<td>ABE27010.1</td>
<td>conotoxin fe14.1</td>
<td>SPGSTICKMACRTHKYPFCNCR</td>
</tr>
<tr>
<td>ABE27011.1</td>
<td>conotoxin fe14.2</td>
<td>SSGSTVCKMCMRLGHLYFSCGCR</td>
</tr>
<tr>
<td>ABE27007.1</td>
<td>conotoxin pl14.1</td>
<td>GPGSACINMACRGLGQHMYPFCNCR</td>
</tr>
<tr>
<td>ABE27008.1</td>
<td>conotoxin pl14.2</td>
<td>GPGSACINMACRLEHGLYFCHCR</td>
</tr>
<tr>
<td>ABE27009.1</td>
<td>conotoxin pl14.3</td>
<td>GPGSACINMACRLEHGLYFPCNCD</td>
</tr>
</tbody>
</table>

For records where a particular qualifier is missing:

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

a dash is inserted as a placeholder:

<table>
<thead>
<tr>
<th>Accession</th>
<th>Name</th>
<th>Organism</th>
</tr>
</thead>
<tbody>
<tr>
<td>P15919.2</td>
<td></td>
<td>Mus musculus</td>
</tr>
<tr>
<td>AAO61776.1</td>
<td></td>
<td>129/Sv</td>
</tr>
<tr>
<td>NP_033045.2</td>
<td></td>
<td>C57BL/6</td>
</tr>
<tr>
<td>XP_006499075.1</td>
<td></td>
<td>C57BL/6J</td>
</tr>
<tr>
<td>EDL27655.1</td>
<td></td>
<td>mixed</td>
</tr>
<tr>
<td>BAD69530.1</td>
<td></td>
<td>Mus musculus castaneus</td>
</tr>
<tr>
<td>BAD69531.1</td>
<td></td>
<td>Mus musculus domesticus</td>
</tr>
<tr>
<td>BAD69532.1</td>
<td></td>
<td>Mus musculus molossinus</td>
</tr>
</tbody>
</table>

Entrez Direct: E-utilities on the UNIX Command Line
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 catgcattc gttgagttgg aaacaaactt gccggctagc cgcatacccg cggggctgga
61 gaaccggctg tgtgcggcca cagccaccat cctggacaaa cccgaagacg tgagtgaggg
121 tcggcgagaa cttgtgggct agggtcggac ctcccaatga cccgttccca tccccaggga
181 ccccactccc ctggtaacct ctgaccttcc gtgtcctatc ctcccttctt agatcccttc
...```

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

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

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

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

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

Coordinate Conversions

Retrieving the docsum for a particular gene:

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

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

```
...<GenomicInfoType>
  <ChrLoc>13</ChrLoc>
  <ChrAccVer>NC_000013.11</ChrAccVer>
  <ChrStart>32315479</ChrStart>
  <ChrStop>32399671</ChrStop>
  <ExonCount>27</ExonCount>
```
Piping the document summary to an xtract command:

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

obtains the accession and 0-based coordinate values:

```
NC_000013.11 32315479 32399671
```

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

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

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

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

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

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

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

```
NC_000013.11 32315480 32399672
```

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

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

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

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

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

```
NC_000013.11 32315479 32399672
```

**Complex Objects**

**Heterogeneous Data**

XML objects can contain a heterogeneous mix of components. For example:
efetch -db pubmed -id 21433338,17247418 -format xml

returns a mixture of book and journal records:

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

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

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

separately prints the entirety of each XML component:

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

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

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

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

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

Simply exploring with individual arguments:

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

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

```
Coffin   Hughes    Varmus    Fauci    Desrosiers
```

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

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

Retrieving a set of taxonomy records:

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

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

```
<TaxaSet>
  <Taxon>
    <TaxId>9606</TaxId>
    <ScientificName>Homo sapiens</ScientificName>
    ...
    <LineageEx>
      <Taxon>
        <TaxId>131567</TaxId>
        <ScientificName>cellular organisms</ScientificName>
        <Rank>no rank</Rank>
      </Taxon>
      <Taxon>
        <TaxId>2759</TaxId>
        <ScientificName>Eukaryota</ScientificName>
        <Rank>superkingdom</Rank>
      </Taxon>
      ...
    </LineageEx>
  </Taxon>
  ...
  <Taxon>
    <TaxId>7227</TaxId>
    <ScientificName>Drosophila melanogaster</ScientificName>
    ...
  </Taxon>
</TaxaSet>
```

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

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

```
efetch -db taxonomy -id 9606,7227,10090 -format xml |
xtract -pattern Taxon \
  -element TaxId ScientificName GenbankCommonName Division
```
does not examine fields in the internal objects, and returns information only for the main entries:

<table>
<thead>
<tr>
<th>Taxonomy ID</th>
<th>Organism Name</th>
<th>Scientific Name</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>9606</td>
<td>Homo sapiens</td>
<td>human</td>
<td>Primates</td>
</tr>
<tr>
<td>7227</td>
<td>Drosophila melanogaster</td>
<td>fruit fly</td>
<td>Invertebrates</td>
</tr>
<tr>
<td>10090</td>
<td>Mus musculus</td>
<td>house mouse</td>
<td>Rodents</td>
</tr>
</tbody>
</table>

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

```bash
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:

<table>
<thead>
<tr>
<th>Taxonomy ID</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>131567</td>
<td>cellular organisms</td>
</tr>
<tr>
<td>2759</td>
<td>Eukaryota</td>
</tr>
<tr>
<td>33154</td>
<td>Opisthokonta</td>
</tr>
</tbody>
</table>

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

```bash
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:

<table>
<thead>
<tr>
<th>Type</th>
<th>Accession</th>
</tr>
</thead>
<tbody>
<tr>
<td>genomic</td>
<td>NC_000023</td>
</tr>
<tr>
<td>mRNA</td>
<td>XM_006724469</td>
</tr>
<tr>
<td>peptide</td>
<td>XP_006724532</td>
</tr>
<tr>
<td>mRNA</td>
<td>XM_011545467</td>
</tr>
<tr>
<td>peptide</td>
<td>XP_011543769</td>
</tr>
</tbody>
</table>

### Advanced Topics

#### Storing Common Phrases in Alias Files

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

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

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

the esearch line in:

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

will be expanded to:

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

with the query producing:

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

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

`eproxy -alias qAliases`

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

**Additional EDirect Options**

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

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

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

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

produces a ranked list of the ten most cited authors:

```
13    Beadle GW 
8     Ephrussi B 
8     Glass NL 
7     Hawley RS 
7     Mitchell MB 
7     PERKINS DD 
7     Tatum EL 
6     Mitchell HK 
6     YANOFSKY C 
5     Langley CH 
```
Similarly, "-name pubmed_pubmed_refs" returns an article's reference list, again for publications deposited in PMC.

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

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

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

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

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

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

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

**Xtract Special Topics**

Self-closing tags of the standard form:

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

or alternative form:

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

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

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

it can be selected by matching on the specified value:

```
-group Seq-interval_strand \
 -block Seq-interval_strand -if Na-strand@value -equals plus -lbl "+" \
 -block Seq-interval_strand -if Na-strand@value -equals minus -lbl "-"
```
The -pattern, -group, -block, and -subset commands provide a nested hierarchy of loop organizers for exploration of XML objects. Each pattern can contain multiple groups, each group can encompass multiple blocks, and each block can have multiple subsets.

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

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

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

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

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

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

- -pattern
- -division
- -group
- -branch
- -block
- -section
- -subset
- -unit

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

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

```
```

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

```
```

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

```
```

is converted to:

```
```

Multiple values between tags are combined with commas. Thus:

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

is transformed into:

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

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

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

will be sent as:

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

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

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

```
```

so the command:

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

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

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

Entrez Direct Commands Within Scripts

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

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

For example, executing a script file containing:

```bash
#!/bin/bash -norc

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

dbs=`einfo -dbs | sort`
for db in $dbs
do
    eix=`einfo -db $db`
    flds=`parse_fields "$eix"`
    echo "$db"
    echo 
    echo "$flds"
    echo 
    sleep 1
done

will obtain the list of Entrez databases:

annotinfo
assembly
bioproject
...
```
and then return the abbreviations, names, and descriptions of indexed search fields, for each individual database:

```
... mesh

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

The shell script command:

```
sleep 1
```

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

**Xargs/_Sh Loop**

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

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

This produces PubMed article counts for each author:

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

**While Loop**

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

```
cat organisms.txt
```
writes the contents of the file:

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

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

```bash
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:

<table>
<thead>
<tr>
<th>Organism</th>
<th>Family</th>
<th>Division</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arabidopsis thaliana</td>
<td>Brassicaceae</td>
<td>eudicots</td>
</tr>
<tr>
<td>Caenorhabditis elegans</td>
<td>Rhabditidae</td>
<td>nematodes</td>
</tr>
<tr>
<td>Danio rerio</td>
<td>Cyprinidae</td>
<td>bony fishes</td>
</tr>
<tr>
<td>Drosophila melanogaster</td>
<td>Drosophilidae</td>
<td>flies</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>Enterobacteriaceae</td>
<td>enterobacteria</td>
</tr>
<tr>
<td>Homo sapiens</td>
<td>Hominidae</td>
<td>primates</td>
</tr>
<tr>
<td>Mus musculus</td>
<td>Muridae</td>
<td>rodents</td>
</tr>
<tr>
<td>Saccharomyces cerevisiae</td>
<td>Saccharomycetaceae</td>
<td>ascomycetes</td>
</tr>
</tbody>
</table>

(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:

```bash
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:

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

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

**Processing in Groups**

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

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

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

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

**Local Data Cache**

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

**Random Access Archive**

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

Recent advances in computer file system technology now allow all of these published journal article citations to be repackaged as individual files on an inexpensive 500 gigabyte external solid state drive, using a hierarchy of 1 million folders to organize the 28 million PubMed records. This approach uses pairs of digits in the PMID as nodes in the directory structure, providing direct and rapid access to any record. For example, PMID 12345678 would be stored (as a compressed XML file) at /Archive/12/34/56/12345678.xml.gz.

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

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

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

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

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

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

and EDIRECT_PUBMED_MASTER is assumed to be set in subsequent examples.

**Local Query Index**

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

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

For example, the term list that includes "cancer" would be located at /Postings/c/a/n/c/canc.trm. A query on cancer thus only needs to load a very small subset of the total index. This design also supports efficient and unrestricted wildcard truncation (e.g., "therap*"), phrase queries (e.g., "selective serotonin reuptake inhibitor"), and proximity searches (e.g., "tonsillectomy ~ ~ efficacy").
Local Search Commands

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

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

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

translates to:

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

and returns the total counts of the individual words:

    4325      catabolite
    104977    repress*

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

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

For interactive queries, a carefully-crafted wildcard truncation is likely to return more relevant articles than if a rule-based stemming algorithm is used. However, an automated script does not have this luxury, so Porter2 stemming can be selected by appending a dollar sign to the end of a term (e.g., "catabolite repression$". The resulting stem is then used in a truncation search on the term list.

Searching with a phrase:

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

generates a list of PMIDs for records that contain the phrase, and then retrieves the relevant PubmedArticle XML from the local archive.
XML Processing

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

Data Transformation

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

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

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

Sequential Processing

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

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

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

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

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

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

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

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

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

Wrapping Results in XML

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

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

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

```
<Set>
  <Rec>
    <Year>2018</Year>
    <Abst>ammonia</Abst>
    <Abst>plays</Abst>
    <Abst>a</Abst>
    <Abst>key</Abst>
    <Abst>role</Abst>
    <Abst>in</Abst>
    <Abst>the</Abst>
    <Abst>neutralization</Abst>
  </Rec>
</Set>
```
The -wrp argument is a convenience that sets all of the appropriate customization arguments, shown above, given just the XML object names:

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

making it easy to wrap the intermediate values.

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

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

again wrapping the results as structured XML:

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

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

**Selection of XML Subsets**

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

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

```
for yr in {1960..2018}
do
cat countsByYear.xml | 
  xtract -wrp Raw -pattern Pub -select Year -eq "$yr" | 
  xtract -pattern Raw -lblr "$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:
This result can be saved by redirecting to a file, or it can be piped to:

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

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

```
rm countsByYear.xml
```
to remove the intermediate file.

## Examples

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

### Author Frequency

Who are the most prolific authors on rattlesnake phospholipase?

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

This search produces:

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

### Publication Distribution

When were the most papers about Legionnaires disease published?

```
esearch -db pubmed -query "legionnaires disease [TITL]" | efetch -format docsum | xtract -pattern DocumentSummary -element PubDate | 
```

cut -c 1-4 | 
sort-uniq-count-rank

reports the number of selected papers per year:

<table>
<thead>
<tr>
<th>Year</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>1979</td>
<td>173</td>
</tr>
<tr>
<td>1980</td>
<td>102</td>
</tr>
<tr>
<td>1978</td>
<td>96</td>
</tr>
<tr>
<td>1981</td>
<td>92</td>
</tr>
<tr>
<td>1983</td>
<td>66</td>
</tr>
<tr>
<td>...</td>
<td></td>
</tr>
</tbody>
</table>

Treatment Locations

What is the geographic distribution of sepsis treatment studies?

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

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

<table>
<thead>
<tr>
<th>Country</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>567</td>
</tr>
<tr>
<td>Spain</td>
<td>207</td>
</tr>
<tr>
<td>Great Britain</td>
<td>176</td>
</tr>
<tr>
<td>Germany</td>
<td>156</td>
</tr>
<tr>
<td>India</td>
<td>123</td>
</tr>
<tr>
<td>Europe</td>
<td>118</td>
</tr>
<tr>
<td>France</td>
<td>113</td>
</tr>
<tr>
<td>Taiwan</td>
<td>100</td>
</tr>
<tr>
<td>Japan</td>
<td>89</td>
</tr>
<tr>
<td>Thailand</td>
<td>83</td>
</tr>
<tr>
<td>Italy</td>
<td>75</td>
</tr>
<tr>
<td>England</td>
<td>74</td>
</tr>
<tr>
<td>...</td>
<td></td>
</tr>
</tbody>
</table>

Research History

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

```
#!/bin/bash
result=""
for disease in diphtheria pertussis tetanus
do
current=`for (( yr = 2010; yr >= 1900; yr -= 10 ))
do
  esearch -db pubmed -query "disease [TITL] AND $yr:$((yr+9)) [PDAT]" | 
xtract -pattern ENTREZ_DIRECT -lbl "$(yr)s" -element Count
done`
heading=`echo -e "$(disease:0:4)" | tr [a-z] [A-Z]`
```
current=`echo -e "Years\t$heading
-----\t----
$current"`

if [ -n "$result" ]
then
    result=`join -t $'	' <(echo "$result") <(echo "$current")`
else
    result=$current
fi
done
echo "$result"

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

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

**Protein Homolog**

Is there a mammalian equivalent of lycopene cyclase?

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

In the resulting list of GenBank division codes:

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

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

**Longest Sequences**

What are the longest known insulin precursor molecules?
Post-processing excludes the longer "insulin-like receptor" sequences and saves the GenPept results to individual files named by their sequence accessions:

- EFN61235.gpf
- EFN80340.gpf
- EGW08477.gpf
- EKC18433.gpf
- ELK28555.gpf

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

**Archaea Enzyme**

Which archaeabacteria have chloramphenicol acetyltransferase?

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

produces a list of organism names:

- Methanobrevibacter ruminantium
- Methanobrevibacter smithii
- Methanosarcina acetivorans
- ...

**Structural Similarity**

What archaea structures are similar to snake venom phospholipase?

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

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

- Crystal Structure Of Autoprocessed Form Of Tk-Subtilisin
- Crystal Structure Of Ca2 Site Mutant Of Pro-S324a
- Crystal Structure Of Ca3 Site Mutant Of Pro-S324a
- ...
**Taxonomy Search**

Which organisms contain an annotated RefSeq genome MatK gene?

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

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

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

**Chromosome Locations**

Where are mammalian calmodulin genes located?

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

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

<table>
<thead>
<tr>
<th>Id</th>
<th>Name</th>
<th>Location</th>
<th>Species</th>
</tr>
</thead>
<tbody>
<tr>
<td>801</td>
<td>CALM1</td>
<td>14q32.11</td>
<td>Homo sapiens</td>
</tr>
<tr>
<td>808</td>
<td>CALM3</td>
<td>19q13.32</td>
<td>Homo sapiens</td>
</tr>
<tr>
<td>805</td>
<td>CALM2</td>
<td>2p21</td>
<td>Homo sapiens</td>
</tr>
<tr>
<td>24242</td>
<td>Calm1</td>
<td>6q32</td>
<td>Rattus norvegicus</td>
</tr>
<tr>
<td>12313</td>
<td>Calm1</td>
<td>12 E</td>
<td>Mus musculus</td>
</tr>
<tr>
<td>326597</td>
<td>CALM</td>
<td>-</td>
<td>Bos taurus</td>
</tr>
<tr>
<td>50663</td>
<td>Calm2</td>
<td>6q12</td>
<td>Rattus norvegicus</td>
</tr>
<tr>
<td>24244</td>
<td>Calm3</td>
<td>1q21</td>
<td>Rattus norvegicus</td>
</tr>
<tr>
<td>12315</td>
<td>Calm3</td>
<td>7 9.15 cM</td>
<td>Mus musculus</td>
</tr>
<tr>
<td>12314</td>
<td>Calm2</td>
<td>17 E4</td>
<td>Mus musculus</td>
</tr>
<tr>
<td>617095</td>
<td>CALM1</td>
<td>-</td>
<td>Bos taurus</td>
</tr>
<tr>
<td>396838</td>
<td>CALM3</td>
<td>6</td>
<td>Sus scrofa</td>
</tr>
</tbody>
</table>

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

```bash
esearch -db gene -query "calmodulin [PFN] AND mammalia [ORGN]" |
efetch -format docsum |
xtract -pattern DocumentSummary \
```
The `-def` command can achieve the same result for missing elements:

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

### Exon Counts

How many exons are in each dystrophin transcript variant?

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

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

```
NC_000023.11    33339608    31119221
```

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

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

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

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

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

Final processing sorts by number of exons:

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

resulting in a table of exon counts and transcript lengths:

<table>
<thead>
<tr>
<th>Chromosome Accession</th>
<th>Exons</th>
<th>Transcript Accession</th>
<th>Transcript Length</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>NC_000023.11</td>
<td>79</td>
<td>NM_004010.3</td>
<td>14083</td>
<td>Dp427p2</td>
</tr>
<tr>
<td>NC_000023.11</td>
<td>79</td>
<td>NM_000109.3</td>
<td>14069</td>
<td>Dp427c</td>
</tr>
<tr>
<td>NC_000023.11</td>
<td>79</td>
<td>NM_004009.3</td>
<td>14000</td>
<td>Dp427p1</td>
</tr>
<tr>
<td>NC_000023.11</td>
<td>79</td>
<td>NM_004006.2</td>
<td>13993</td>
<td>Dp427m</td>
</tr>
<tr>
<td>NC_000023.11</td>
<td>78</td>
<td>XM_006724468.1</td>
<td>13920</td>
<td>X1</td>
</tr>
<tr>
<td>NC_000023.11</td>
<td>78</td>
<td>XM_006724469.1</td>
<td>13802</td>
<td>X2</td>
</tr>
</tbody>
</table>
Genome Range

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

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

<table>
<thead>
<tr>
<th>Gene Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL3RA</td>
<td>interleukin 3 receptor subunit alpha</td>
</tr>
<tr>
<td>LOC101928032</td>
<td>uncharacterized LOC101928032</td>
</tr>
<tr>
<td>LOC101928055</td>
<td>uncharacterized LOC101928055</td>
</tr>
<tr>
<td>SLC25A6</td>
<td>solute carrier family 25 member 6</td>
</tr>
<tr>
<td>LOC105373102</td>
<td>uncharacterized LOC105373102</td>
</tr>
<tr>
<td>LINC00106</td>
<td>long intergenic non-protein coding RNA 106</td>
</tr>
<tr>
<td>ASMTL-AS1</td>
<td>ASMTL antisense RNA 1</td>
</tr>
<tr>
<td>ASMTL</td>
<td>acetylserotonin O-methyltransferase-like</td>
</tr>
<tr>
<td>P2RY8</td>
<td>purinergic receptor P2Y8</td>
</tr>
<tr>
<td>AKAP17A</td>
<td>A-kinase anchoring protein 17A</td>
</tr>
<tr>
<td>ASMT</td>
<td>acetylserotonin O-methyltransferase</td>
</tr>
</tbody>
</table>

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

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

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

How many genes are on each human chromosome?

```bash
for chr in {1..22} X Y MT
do
  esearch -db gene -query "Homo sapiens [ORGN] AND $chr [CHR]" |
  efilter -query "alive [PROP] AND genotype protein coding [PROP]" |
  efetch -format docsum |
  xtract -pattern DocumentSummary -NAME Name \ 
    -block GenomicInfoType -if ChrLoc -equals "$chr" \ 
    -tab "\n" -element ChrLoc,"&NAME" |
  sort | uniq | cut -f 1 | sort-uniq-count-rank
done
```

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

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

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

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

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

Complete Genomes

What complete genomes are available for Escherichia coli?
This search finds genomic assemblies and sorts the results by sequence length, allowing complete genomes to be easily distinguished from smaller plasmids:

<table>
<thead>
<tr>
<th>Accession</th>
<th>Length</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>NC_002695.1</td>
<td>5498450</td>
<td>Escherichia coli O157:H7 str. Sakai chromosome</td>
</tr>
<tr>
<td>NC_018658.1</td>
<td>5273097</td>
<td>Escherichia coli O104:H4 str. 2011C-3493 ...</td>
</tr>
<tr>
<td>NC_011750.1</td>
<td>5132068</td>
<td>Escherichia coli IAI39 chromosome</td>
</tr>
<tr>
<td>NC_011750.1</td>
<td>5132068</td>
<td>Escherichia coli UMN026 chromosome</td>
</tr>
<tr>
<td>NC_017659.1</td>
<td>147060</td>
<td>Escherichia coli O83:H1 str. NRG 857C plasmid ...</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Accession</th>
<th>Length</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>NC_000001.11</td>
<td>248956422</td>
<td>Homo sapiens chromosome 1</td>
</tr>
<tr>
<td>NC_000002.12</td>
<td>242193529</td>
<td>Homo sapiens chromosome 2</td>
</tr>
<tr>
<td>NC_000003.12</td>
<td>198295559</td>
<td>Homo sapiens chromosome 3</td>
</tr>
<tr>
<td>NC_000004.12</td>
<td>190214555</td>
<td>Homo sapiens chromosome 4</td>
</tr>
<tr>
<td>NC_000005.10</td>
<td>181538259</td>
<td>Homo sapiens chromosome 5</td>
</tr>
<tr>
<td>NC_000006.12</td>
<td>170805979</td>
<td>Homo sapiens chromosome 6</td>
</tr>
<tr>
<td>NC_000007.14</td>
<td>159345973</td>
<td>Homo sapiens chromosome 7</td>
</tr>
<tr>
<td>NC_000008.11</td>
<td>145138636</td>
<td>Homo sapiens chromosome 8</td>
</tr>
<tr>
<td>NC_000009.12</td>
<td>138394717</td>
<td>Homo sapiens chromosome 9</td>
</tr>
<tr>
<td>NC_000010.11</td>
<td>133797422</td>
<td>Homo sapiens chromosome 10</td>
</tr>
<tr>
<td>NC_000011.10</td>
<td>135086622</td>
<td>Homo sapiens chromosome 11</td>
</tr>
<tr>
<td>NC_000012.12</td>
<td>133275309</td>
<td>Homo sapiens chromosome 12</td>
</tr>
<tr>
<td>NC_000013.11</td>
<td>114364328</td>
<td>Homo sapiens chromosome 13</td>
</tr>
<tr>
<td>NC_000014.9</td>
<td>107043718</td>
<td>Homo sapiens chromosome 14</td>
</tr>
<tr>
<td>NC_000015.10</td>
<td>101991189</td>
<td>Homo sapiens chromosome 15</td>
</tr>
<tr>
<td>NC_000016.10</td>
<td>90338345</td>
<td>Homo sapiens chromosome 16</td>
</tr>
<tr>
<td>NC_000017.11</td>
<td>83257441</td>
<td>Homo sapiens chromosome 17</td>
</tr>
<tr>
<td>NC_000018.10</td>
<td>80373285</td>
<td>Homo sapiens chromosome 18</td>
</tr>
<tr>
<td>NC_000019.10</td>
<td>58617616</td>
<td>Homo sapiens chromosome 19</td>
</tr>
<tr>
<td>NC_000020.11</td>
<td>64444167</td>
<td>Homo sapiens chromosome 20</td>
</tr>
<tr>
<td>NC_000021.9</td>
<td>46709983</td>
<td>Homo sapiens chromosome 21</td>
</tr>
</tbody>
</table>
This process can be automated to loop through a list of specified organisms:

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

which generates:

```plaintext
NC_011985.1    4005130    Agrobacterium radiobacter K84 chromosome 1
NC_011983.1    2650913    Agrobacterium radiobacter K84 chromosome 2
NC_005945.1    5228663    Bacillus anthracis str. Sterne chromosome
NC_003997.3    5227293    Bacillus anthracis str. Ames chromosome
NC_002695.1    5498450    Escherichia coli O157:H7 str. Sakai chromosome
NC_018658.1    5273097    Escherichia coli O104:H4 str. 2011C-3493 ...
NC_011751.1    5202090    Escherichia coli UMN026 chromosome
NC_011750.1    5132068    Escherichia coli IAI39 chromosome
NC_017634.1    4747819    Escherichia coli O83:H1 str. NRG 857C chromosome
NC_000913.3    4641652    Escherichia coli str. K-12 substr. MG1655
NC_002946.2    2153922    Neisseria gonorrhoeae FA 1090 chromosome
NC_002516.2    6264404    Pseudomonas aeruginosa PA01 chromosome
NC_004337.2    4607202    Shigella flexneri 2a str. 301 chromosome
NC_003028.3    2160842    Streptococcus pneumoniae TIGR4 chromosome
NC_003098.1    2038615    Streptococcus pneumoniae R6 chromosome
```

**Amino Acid Composition**

What is the amino acid composition of human titin?

```bash
abbrev=( Ala Asx Cys Asp Glu Phe Gly His Ile \ 
       Xle Lys Leu Met Asn Pyl Pro Gln Arg \ 
       Ser Thr Sec Val Trp Xxx Tyr Glx )
efetch -db protein -id "Q8WZ42.4" -format gpc |
xtract -pattern INSDSeq -element INSDSeq_sequence |
tr A-Z a-z |
```
produces a table of residue counts using the three-letter amino acid abbreviations:

<table>
<thead>
<tr>
<th>Amino Acid</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ala</td>
<td>2084</td>
</tr>
<tr>
<td>Arg</td>
<td>1640</td>
</tr>
<tr>
<td>Asn</td>
<td>1111</td>
</tr>
<tr>
<td>Asp</td>
<td>1720</td>
</tr>
<tr>
<td>Cys</td>
<td>513</td>
</tr>
<tr>
<td>Gln</td>
<td>942</td>
</tr>
<tr>
<td>Glu</td>
<td>3193</td>
</tr>
<tr>
<td>Gly</td>
<td>2066</td>
</tr>
<tr>
<td>His</td>
<td>478</td>
</tr>
<tr>
<td>Ile</td>
<td>2062</td>
</tr>
<tr>
<td>Leu</td>
<td>2117</td>
</tr>
<tr>
<td>Lys</td>
<td>2943</td>
</tr>
<tr>
<td>Met</td>
<td>398</td>
</tr>
<tr>
<td>Phe</td>
<td>908</td>
</tr>
<tr>
<td>Pro</td>
<td>2517</td>
</tr>
<tr>
<td>Ser</td>
<td>2463</td>
</tr>
<tr>
<td>Thr</td>
<td>2546</td>
</tr>
<tr>
<td>Trp</td>
<td>466</td>
</tr>
<tr>
<td>Tyr</td>
<td>999</td>
</tr>
<tr>
<td>Val</td>
<td>3184</td>
</tr>
</tbody>
</table>

**Amino Acid Substitutions**

What are the missense products of green-sensitive opsin?

```bash
ApplySNPs() {
    seq=""
    last=""

    while read rsid accn pos res
    do
        if [ "$accn" != "$last" ]
        then
            insd=$(efetch -db protein -id "$accn" -format gbc < /dev/null)
            seq=$(echo $insd | xtract -pattern INSDSeq -element INSDSeq_sequence)
            last=$accn
        fi
        pos=$((pos+1))
        pfx=""
```
sfx=""
echo ">rs$rsid [$acct $res@$pos]"
if [ $pos -gt 1 ]
then
  pfx=$(echo ${seq:0:$pos-1})
fi
if [ $pos -lt ${#seq} ]
then
  sfx=$(echo ${seq:$pos})
fi
echo "$pfx$res$sfx" | fold -w 50
done
}
esearch -db gene -query "CBD [GENE] AND human [ORGN]" |
elink -target snp |
efetch -format xml |
xtract -pattern Rs -RSID Rs@rsId 
 -block FxnSet -if @fxnClass -equals missense 
 -sep "." -element "&RSID" @protAcc,@protVer @aaPosition 
 -tab "\n" -element @residue |
sort -t $'	' -k 2,2 -k 3,3n -k 4,4 | uniq | ApplySNPs

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

104894915    NP_000504.1    93     K
782122931    NP_000504.1    95     V
781899063    NP_000504.1    97     T
781807082    NP_000504.1    102    A
...

The rows are then processed to produce protein sequences with the individual residue substitutions in upper case:

>rs104894915 [NP_000504.1 K@94]
maqqwslqrlagrhpqdsyedstqssiftytnsnstrgpgpnyhiapr
wvyhltsvmifvviasvfntnglvaatmkfkkrlrhplwivlklavaddl
aetviastisvvnqvgygfvlgphmcvegtyvslcgitglwslaiiswe
...

3'UTR Sequences

What are the 3' UTR sequences for lycopene cyclase?

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

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

prints the sequences immediately following the CDS stop codon:

>NM_001328461.1 3'UTR: 1737..1871 lycopene beta cyclase, chloroplastic
gatgaaatatagagttactgtgttgtaagctaatcatcatactgtgcaag
tgcattatcacatttactctcgtcgatgattgatgttcataagattatgagtgt
gccatttatcaaaaaaaaaaaaaaaaaaaaaa

>NM_001316759.1 3'UTR: 1628..1690 lycopene beta cyclase, chloroplastic
atccgagtaatctcgaatct tgtcaattttatatagcctatatta tac

Upstream Sequences

What sequences are upstream of phenylalanine hydroxylase genes?

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

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

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>5053</td>
<td>NC_000012.12</td>
<td>102917603</td>
<td>102838326</td>
</tr>
<tr>
<td>18478</td>
<td>NC_000076.6</td>
<td>87521795</td>
<td>87584137</td>
</tr>
<tr>
<td>38871</td>
<td>NT_037436.4</td>
<td>7760453</td>
<td>7763166</td>
</tr>
<tr>
<td>24616</td>
<td>NC_005106.4</td>
<td>28066639</td>
<td>28129772</td>
</tr>
<tr>
<td>378962</td>
<td>NC_007115.6</td>
<td>17420391</td>
<td>17402704</td>
</tr>
</tbody>
</table>

Given a shell script named "upstream.sh"

#!/bin/bash -norc

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

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

the data lines can be piped through:

    upstream.sh 500

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

Author Combinations

What are the authorship patterns among selected individuals?

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

#!/bin/bash -norc

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

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

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

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

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

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

Running the following command:

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

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

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

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

```
#!/usr/bin/perl

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

my $thisline = "";
my $laststr = "";
my $str = "";
```
my $uid = "";
my $uidlist = "";
my $count = 0;

my $pfx = "";
while ($thisline = <STDIN>) {
    $thisline =~ s///;
    $thisline =~ s/
//;
    if ($thisline =~ /^([^\t\t]+)\t(.+)$/) {
        $uid = $1;
        $str = $2;
        if ( lc ($str) ne lc ($laststr) and $laststr ne "" ) {
            $laststr =~ s/\t/, /g;
            print "<p>(<a href="$base/$db/$uidlist">\$count</a>) - $laststr</p>
";
            $pfx = "";
            $count = 0;
            $uidlist = "";
        }
        $laststr = $str;
        $uidlist .= "$pfx$uid";
        $pfx = ",";
        $count++;
    }
}
if ( $laststr ne "" ) {
    $laststr =~ s/\t/, /g;
    print "<p>(<a href="$base/$db/$uidlist">\$count</a>) - $laststr</p>
";
}

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


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

( 55 ) - Berg CM
( 10 ) - Berg CM, Berg DE
( 1 ) - BERG CM, GARBER ED
( 6 ) - Berg DE, Berg CM
( 39 ) - Casadaban MJ
Clicking on a hyperlinked record count number opens the document summary or individual article page, so the actual publications can be examined.

**Indexed Fields**

What date fields are indexed for PubMed?

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

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

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

**Digital Object Identifiers**

How are digital object identifiers obtained from PubMed articles?

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

extracts the DOIs and constructs the appropriate URL references:

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

These intermediate lines are then piped through:

```bash
xtract -format
```

to produce a minimal HTML document with clickable links:
Phrase Searching

Can phrase searching be simulated in Entrez?

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

For example, running the following command:

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

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

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

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

Gene-Protein Links

What proteins are produced by a given gene?

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

```
esearch -db gene -query "beta galactosidase [PFN]" | 
elink -target protein -name gene_protein_refseq -cmd neighbor | 
xtract -pattern LinkSet -element Id
```
will show the gene ID in the first column and linked RefSeq protein UIDs in subsequent columns.

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

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

while ($line = <STDIN>) {
    chomp ($line);
    @uids = split( /	/, $line);
    $gene = $uids [0];
    $proteins = join (',', @uids [1..$#uids]);
    $symbol = $data = '';

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

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

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

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

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

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

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

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

```bash
grep ".seq.gz" |
grep -e gbmam -e gbpri -e gbrod |
while read file
do
gzcat "$file"
   rm "$file"
done
```

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

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

NCBI-GenBank Flat File Release 206.0

Other Mammalian Sequences (Part 1)

20709 loci, 155323216 bases, from 20709 reported sequences

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

CDS             175..2289
/standard_name="endopeptidase 24.16"
/note="oligopeptidase M :neurolysin :sBAP(soluble angiotensin-binding protein) :MEP(microsomal metalloendopeptidase)"
/codon_start=1
/product="endopeptidase 24.16 type M1"
/protein_id="BAA19060.1"
/db_xref="GI:1783122"
...

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

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

Appendices

Setting Contact Address and Script Name

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

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

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

Command-Line Arguments

Arguments for the EDirect functions are listed below:

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

-\texttt{db} Database name
-\texttt{query} Query string

Document Order

-\texttt{sort} Result presentation order

Date Constraint

-\texttt{days} Number of days in the past
-\texttt{datatype} Date field abbreviation
-\texttt{mindate} Start of date range
-\texttt{maxdate} End of date range

Limit by Field

-\texttt{field} Query words individually in field
-\texttt{pairs} Query overlapping word pairs

Spell Check

-\texttt{spell} Correct misspellings in query

Miscellaneous Arguments

-\texttt{label} Alias for query step

The \texttt{elink} function looks up related articles or associated records:

Destination Database

-\texttt{related} Neighbors in same database
-\texttt{target} Links in different database
-\texttt{name} Link name (e.g., \texttt{pubmed\_protein\_refseq})

Direct Record Selection

-\texttt{db} Database name
-\texttt{id} Unique identifier(s)

Advanced Control

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

Batch Processing

-\texttt{batch} Bypass Entrez history mechanism

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

Query Specification

- **-query** Query string

Document Order

- **-sort** Result presentation order

Date Constraint

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

Limit by Field

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

Spell Check

- **-spell** Correct misspellings in query

Publication Filters

- **-pub** abstract, clinical, english, free, historical, journal, last_week, last_month, last_year, medline, preprint, review, structured

Sequence Filters

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

Gene Filters

- **-status** alive
- **-type** coding, pseudo

Miscellaneous Arguments

- **-label** Alias for query step
The record retrieval function is efetch:

Format Selection

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

Direct Record Selection

- **db** Database name
- **id** Unique identifier or accession number

Sequence Range

- **seq_start** First sequence position to retrieve
- **seq_stop** Last sequence position to retrieve
- **strand** Strand of DNA to retrieve

Gene Range

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

Sequence Flags

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

Miscellaneous

- **raw** Skip database-specific XML modifications

The xtract function is used for processing XML data:

Processing Flags

- **strict** Remove HTML and MathML tags
- **mixed** Allow PubMed mixed content

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

- **stops** Retain stop words in selected phrases

Data Source

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

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

Exploration Constructs

Object DateRevised
Parent/Child Book/AuthorList
Heterogeneous "PubmedArticleSet/**"
Nested "*/Taxon"
Recursive "**/Gene-commentary"

Conditional Execution

-if Element [@attribute] required
-unless Skip if element matches
-and All tests must pass
-or Any passing test suffices
-else Execute if conditional test failed
-position [first|last|outer|inner|all]
-select Select record subset by conditions

String Constraints

-equals String must match exactly
-contains Substring must be present
-starts-with Substring must be at beginning
-ends-with Substring must be at end
-is-not String must not match

Numeric Constraints

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

Format Customization

-ret Override line break between patterns
-tab Replace tab character between fields
-sep Separator between group members
-pfx Prefix to print before group
-sfx Suffix to print after group
-plg Prologue to print once before elements
-elg Epilogue to print once after elements
-rst Reset -sep through -elg
-clr Clear queued tab separator
-pfc Preface combines -clr and -pfx
-wrap Wrap elements in XML object
-def Default placeholder for missing fields
-lbl Insert arbitrary text

Element Selection

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

-element Constructs

<table>
<thead>
<tr>
<th>Tag</th>
<th>Caption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
<td>Initials, LastName</td>
</tr>
<tr>
<td>Parent/Child</td>
<td>MedlineCitation/PMID</td>
</tr>
<tr>
<td>Recursive</td>
<td>&quot;**/Gene-commentary_accession&quot;</td>
</tr>
<tr>
<td>Unrestricted</td>
<td>&quot;PubDate/*&quot;</td>
</tr>
<tr>
<td>Attribute</td>
<td>DescriptorName@MajorTopicYN</td>
</tr>
<tr>
<td>Range</td>
<td>MedlineDate[1:4]</td>
</tr>
<tr>
<td>Substring</td>
<td>&quot;Title[phospholipase</td>
</tr>
<tr>
<td>Object Count</td>
<td>&quot;#Author&quot;</td>
</tr>
<tr>
<td>Item Length</td>
<td>&quot;%Title&quot;</td>
</tr>
<tr>
<td>Element Depth</td>
<td>&quot;^PMID&quot;</td>
</tr>
<tr>
<td>Variable</td>
<td>&quot;&amp;NAME&quot;</td>
</tr>
</tbody>
</table>

Special -element Operations

| Parent Index | "+" |
| XML Subtree | "*" |
| Children | "$" |
| Attributes | "@" |

Numeric Processing

| -num | Count |
| -len | Length |
| -sum | Sum |
| -min | Minimum |
| -max | Maximum |
| -inc | Increment |
| -dec | Decrement |
| -sub | Difference |
| -avg | Average |
| -dev | Deviation |
| -med | Median |
| -bin | Binary |
| -bit | Bit Count |

String Processing

| -encode | URL-encode <, >, &, " and ' characters |
| -upper | Convert text to upper-case |
Text Processing

-terms Partition text at spaces
-words Split at punctuation marks
-pairs Adjacent informative words
-letters Separate individual letters
-clauses Break at phrase separators
-indices Index normalized words

Sequence Processing

-revcomp Reverse-complement nucleotide sequence

Sequence Coordinates

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

Command Generator

-insd Generate INSDSeq extraction commands

-insd Argument Order

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

Miscellaneous

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

Reformatting

-format [copy|compact|flush|indent|expand]

Modification

-filter Object

-validation [retain|remove|encode|decode|shrink|expand|accent]

-contents [content|cdata|comment|object|attributes|container]
-verify Report XML data integrity problems

Summary

-outline Display outline of XML structure
-synopsis Display count of unique XML paths

Documentation

-examples Examples of EDirect and xtract usage

The einfo function returns information on Entrez indexed fields:

Database Selection

-db Database name
-dbs Get all database names

Data Summaries

-fields Print field names
-links Print link names

Several additional functions are provided by EDirect:

epost

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

eproxy

-alias File of aliases
-pipe Read aliases from stdin

econtact

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

nquire

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

In addition, -email and -tool are available in all E-utilities-calling functions to override default values, -http get will force the use of GET instead of POST, -alias will specify a file of shortcut keywords and query strings or URL sections, and -help will print the list of arguments for each function.
For debugging, `-silent` will suppress link failure retry messages, `-verbose` will display the `<ENTREZ_DIRECT>` field values at each step, `-debug` will print the internal URL query and XML results of each step, and `-base` will specify a particular server for quality assurance testing.

**EFetch Formats**

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

<table>
<thead>
<tr>
<th>-db</th>
<th>-format</th>
<th>-mode</th>
<th>Report Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>(all)</td>
<td>docsum</td>
<td>json</td>
<td>DocumentSummarySet XML</td>
</tr>
<tr>
<td></td>
<td>docsum</td>
<td>json</td>
<td>DocumentSummarySet JSON</td>
</tr>
<tr>
<td></td>
<td>full</td>
<td></td>
<td>Same as native except for mesh</td>
</tr>
<tr>
<td></td>
<td>uid</td>
<td></td>
<td>Unique Identifier List</td>
</tr>
<tr>
<td></td>
<td>url</td>
<td></td>
<td>Entrez URL</td>
</tr>
<tr>
<td></td>
<td>xml</td>
<td></td>
<td>Same as <code>-format full</code> <code>-mode xml</code></td>
</tr>
<tr>
<td>bioproject</td>
<td>native</td>
<td>xml</td>
<td>BioProject Report</td>
</tr>
<tr>
<td>biosample</td>
<td>native</td>
<td>xml</td>
<td>BioSample Report</td>
</tr>
<tr>
<td>biosystems</td>
<td>native</td>
<td>xml</td>
<td>BioSampleSet XML</td>
</tr>
<tr>
<td>gds</td>
<td>native</td>
<td>xml</td>
<td>Summary</td>
</tr>
<tr>
<td>gene</td>
<td>gene_table</td>
<td></td>
<td>Gene Table</td>
</tr>
<tr>
<td></td>
<td>native</td>
<td>asn.1</td>
<td>Entrezgene ASN.1</td>
</tr>
<tr>
<td></td>
<td>native</td>
<td>xml</td>
<td>Entrezgene-Set XML</td>
</tr>
<tr>
<td></td>
<td>tabular</td>
<td></td>
<td>Tabular Report</td>
</tr>
<tr>
<td>homologene</td>
<td>alignmentscores</td>
<td></td>
<td>Alignment Scores</td>
</tr>
<tr>
<td></td>
<td>fasta</td>
<td></td>
<td>FASTA</td>
</tr>
<tr>
<td></td>
<td>homologene</td>
<td></td>
<td>Homologene Report</td>
</tr>
<tr>
<td></td>
<td>native</td>
<td></td>
<td>Homologene List</td>
</tr>
<tr>
<td></td>
<td>native</td>
<td>asn.1</td>
<td>HG-Entry ASN.1</td>
</tr>
<tr>
<td></td>
<td>native</td>
<td>xml</td>
<td>Entrez-Homologene-Set XML</td>
</tr>
<tr>
<td>mesh</td>
<td>full</td>
<td></td>
<td>Full Record</td>
</tr>
</tbody>
</table>
native                      MeSH Report
native                     xml       RecordSet XML

nlmcatalog
native                           Full Record
native                     xml       NLMCatalogRecordSet XML

pmc
medline                            MEDLINE
native                     xml       pmc-articleset XML

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

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

snp
chr                             Chromosome Report
docset                          Summary
fasta                           FASTA
flt                             Flat File
native                     asn.1   Rs ASN.1
native                     xml       ExchangeSet XML
rse                          RS Cluster Report
ssexemplar                   SS Exemplar List

sra
native                     xml       EXPERIMENT_PACKAGE_SET XML
runinfo                       xml       SraRunInfo XML
structure

<table>
<thead>
<tr>
<th>mmdb</th>
<th>Ncbi-mime-asn1 strucseq ASN.1</th>
</tr>
</thead>
<tbody>
<tr>
<td>native</td>
<td>MMDB Report</td>
</tr>
<tr>
<td>native</td>
<td>xml</td>
</tr>
<tr>
<td>RecordSet XML</td>
<td></td>
</tr>
</tbody>
</table>

taxonomy

<table>
<thead>
<tr>
<th>native</th>
<th>Taxonomy List</th>
</tr>
</thead>
<tbody>
<tr>
<td>native</td>
<td>xml</td>
</tr>
<tr>
<td>TaxaSet XML</td>
<td></td>
</tr>
</tbody>
</table>

**ESEarch Sort Order**

ESEarch -sort values for several databases are listed below:

<table>
<thead>
<tr>
<th>-db</th>
<th>-sort</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

gene

<table>
<thead>
<tr>
<th>chromosome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gene Weight</td>
</tr>
<tr>
<td>Name</td>
</tr>
<tr>
<td>Relevance</td>
</tr>
</tbody>
</table>

ggeoprofiles

<table>
<thead>
<tr>
<th>Default Order</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deviation</td>
</tr>
<tr>
<td>Mean Value</td>
</tr>
<tr>
<td>Outliers</td>
</tr>
<tr>
<td>Subgroup Effect</td>
</tr>
</tbody>
</table>

pubmed

<table>
<thead>
<tr>
<th>First Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>Journal</td>
</tr>
<tr>
<td>Last Author</td>
</tr>
<tr>
<td>Pub Date</td>
</tr>
<tr>
<td>Recently Added</td>
</tr>
<tr>
<td>Relevance</td>
</tr>
<tr>
<td>Title</td>
</tr>
</tbody>
</table>

(sequences)

<table>
<thead>
<tr>
<th>Accession</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date Modified</td>
</tr>
<tr>
<td>Date Released</td>
</tr>
<tr>
<td>Default Order</td>
</tr>
<tr>
<td>Organism Name</td>
</tr>
<tr>
<td>Taxonomy ID</td>
</tr>
</tbody>
</table>

snp

<table>
<thead>
<tr>
<th>Chromosome Base Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>Default Order</td>
</tr>
<tr>
<td>Heterozygosity</td>
</tr>
<tr>
<td>Organism</td>
</tr>
<tr>
<td>SNP_ID</td>
</tr>
<tr>
<td>Success Rate</td>
</tr>
</tbody>
</table>
**ELink Commands**

ELink -cmd options produce results as LinkSet XML:

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

**EInfo Data**

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

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

**UNIX Utilities**

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

Process by Contents:

```bash
sort     Sorts lines of text
-f       Ignore case
-n       Numeric comparison
```
-r  Reverse result order
-k  Field key (start, stop or first)
-u  Unique lines with identical keys
-b  Ignore leading blanks
-s  Stable sort
-t  Specify field separator

uniq  Removes repeated lines
-c  Count occurrences
-i  Ignore case
-f  Ignore first n fields
-s  Ignore first n characters
-d  Only output repeated lines
-u  Only output non-repeated lines

grep  Matches patterns using regular expressions
-i  Ignore case
-v  Invert search
-w  Search expression as a word
-x  Search expression as whole line
-e  Specify individual pattern
-c  Only count number of matches
-n  Print line numbers

Regular Expressions:

Characters

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

Positions

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

Repeat Matches

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

Modify Contents:

sed Replaces text strings
  -e Specify individual expression
tr Translates characters
  -d Delete character
rev Reverses characters on line

Format Contents:

column Aligns columns by content width
  -s Specify field separator
  -t Create table
expand Aligns columns to specified positions
  -t Tab positions
fold Wraps lines at a specific width
  -w Line width

Filter by Position:

cut Removes parts of lines
  -c Characters to keep
  -f Fields to keep
  -d Specify field separator
  -s Suppress lines with no delimiters
head Prints first lines
  -n Number of lines
tail Prints last lines
  -n Number of lines

Miscellaneous:

wc Counts words, lines, or characters
  -c Characters
  -l Lines
-w   Words

xargs   Constructs arguments
    -n   Number of words per batch

File Compression:

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

gzip   Compress file
    -k   Keep original file
    -9   Best compression

unzip   Decompress .zip archive
    -p   Pipe to stdout

gzcat   Decompress .gz archive and pipe to stdout

Directory and File Navigation:

cd   Changes directory

/   Root
~   Home
.   Current
..  Parent
-   Previous

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

pwd   Prints working directory path

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

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

**Command history:**

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

**Move cursor forward:**

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

**Move cursor backward:**

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

**Delete:**

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

**Autocomplete:**

- `Tab` Completes directory or file names

**Program control:**

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

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

**Release Notes**

**EDirect Version 9.60: August 9, 2018**

- Local archive script removes newlines inside PubMed text fields.
- Efetch adds missing newline at end of PubmedArticleSet XML.
EDirect Version 9.50: July 30, 2018

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

EDirect Version 9.40: July 18, 2018

- Xtract handles misplaced spaces in attributes.
- Xtract -format repairs misplaced spaces in attributes.

EDirect Version 9.30: July 9, 2018

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

EDirect Version 9.20: June 26, 2018

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

EDirect Version 9.10: June 18, 2018

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

EDirect Version 9.00: June 6, 2018

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

EDirect Version 8.90: June 4, 2018

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

EDirect Version 8.80: May 29, 2018

- Efetch removes MathML tags from PubmedArticle XML contents, unless the -raw flag is used.
EDirect Version 8.70: May 14, 2018
- Local phrase indexing now uses positional indices instead of adjacent overlapping word pairs.
- Xtract -select uses conditional expressions to filter records.

EDirect Version 8.60: April 26, 2018
- Efetch -format uid pauses between groups, retries on failure.
- Fetch delay drops from 1/3 to 1/10 second if API key is used.
- Local phrase indexing uses smaller files to avoid memory contention.
- Phrase index removes hyphens from selected prefixes.

EDirect Version 8.50: April 13, 2018
- Efetch markup tag removal modified after change in server.
- Xtract -phrase filter split into -require and -exclude commands.

EDirect Version 8.40: April 9, 2018
- Efetch removes markup tags in all PubMed XML.
- Xtract without -strict prints warnings if markup tags are encountered.
- Xtract proximity search moved from -matches to -phrase.

EDirect Version 8.30: April 4, 2018
- Xtract is now available for ARM processors.

EDirect Version 8.20: March 12, 2018
- Minor changes to local record archiving scripts.

EDirect Version 8.10: March 2, 2018
- Xtract -strict and -mixed support MathML element tags in PubmedArticle XML.

EDirect Version 8.00: February 26, 2018
- Efetch -raw skips database-specific XML modifications.
- Added local-phrase-search script.
- Xtract -strict, -mixed, and -repair flag speed improvements.

EDirect Version 7.90: February 1, 2018
- Minor change to installation commands for tcsh.

EDirect Version 7.80: January 12, 2018
- Updated setup.sh script with additional error checking.
**EDirect Version 7.70: December 27, 2017**
- Added archive-pubmed script to automate local record archiving.

**EDirect Version 7.60: November 15, 2017**
- Epost -id numeric argument bug fixed.
- Xtract conditional tests can now use subrange specifiers.
- Xtract -strict and -mixed use separate -repair flag to normalize Unicode superscripts and subscripts.

**EDirect Version 7.50: October 31, 2017**
- Setup instructions now work with the tcsh shell.
- API key value is taken from the NCBI_API_KEY environment variable.
- Efetchn -format gb supports -style withparts and -style conwithfeat.
- Xtract supports optional element [min:max] substring extraction.
- Xtract -position supports [first|last|outer|inner|all] argument values.
- Added prepare-stash script for local record archive.

**EDirect Version 7.40: September 27, 2017**
- Xtract -hash reports checksums for local record archiving.
- Initial support for API keys.

**EDirect Version 7.30: September 6, 2017**
- Modified stash-pubmed script to work around Cygwin artifact.
- Removed unpack-pubmed script.
- Xtract -archive replaces -stash for local record archiving.
- Xtract -gzip allows compression of archived XML records.

**EDirect Version 7.20: August 28, 2017**
- Added download-pubmed, download-sequence, unpack-pubmed, stash-pubmed, and fetch-pubmed scripts, for experimental local record storage.
- Xtract -flags [strict|mixed] added to support new local storage scripts.
- Removed obsolete, original Perl implementation of xtract.pl.

**EDirect Version 7.10: August 10, 2017**
- Xtract -ascii converts non-ASCII Unicode to hexadecimal numeric character references.
- Setup script recognizes Cygwin running under the MinGW emulator.

**EDirect Version 7.00: July 10, 2017**
- Xtract -mixed and -strict handle multiply-escaped HTML tags.
• Efetch removes normal and escaped HTML tags from PubMed fields.
• Esearch -field processes individual query terms using the designated field, also removing stop words.
• Esearch -pairs splits the query phrase into adjacent overlapping word pairs.

**EDirect Version 6.90: July 5, 2017**
• Xtract -mixed replaces -relaxed, and -accent replaces -plain.
• Efetch uses larger chunks for -format uid, url, and acc.
• Esearch -log shows constructed URL and QueryTranslation result.

**EDirect Version 6.80: June 8, 2017**
• Modified download instructions to use edirect.tar.gz archive.
• The ftp-cp script can now read from stdin without the need for xargs.
• Rerunning ftp-cp or asp-cp only attempts to download missing files.

**EDirect Version 6.70: May 8, 2017**
• Added asp-cp script for faster download of NCBI ftp files using Aspera Connect.
• Xtract -strict and -relaxed handle empty HTML tag variants (e.g., <b/> and <sup/>).

**EDirect Version 6.60: April 25, 2017**
• Xtract -strict replaces -degloss to remove HTML <i>, <b>, <u>, <sup> and <sub> tags from XML contents.
• Xtract -relaxed allows HTML tags in XML contents, to support current PubMed ftp release files.
• Xtract -plain removes Unicode accents.
• The setup.sh script prints an error message if it cannot fetch missing Perl modules.

**EDirect Version 6.50: March 6, 2017**
• Xtract -degloss replaces -html to remove HTML <i>, <b>, <u>, <sup> and <sub> tags.

**EDirect Version 6.40: March 1, 2017**
• Epost detects accession.version input for sequence databases and sets -format acc.
• Xtract -html [remove|encode] converts <i> and <b> tags embedded in XML contents.

**EDirect Version 6.30: February 13, 2017**
• Efetch -format docsum skips GI-less sequences without summaries.
• Xtract local indexing commands moved to -extras documentation.
EDirect Version 6.20: January 30, 2017
- Xtract -limit and -index allow extraction of selected records from XML file.

EDirect Version 6.10: January 19, 2017
- Added run-ncbi-converter script for processing ASN.1 release files.
- Xtract -format flush option added.
- Removed obsolete accession-dot-version conversion code.

EDirect Version 6.00: December 27, 2016
- Efetch -format docsum removes eSummaryResult wrapper.
- Fixed content truncation bug when Xtract encounters very long sequences.

EDirect Version 5.90: December 21, 2016
- Efetch and Elink readied for switch to accession-dot-version sequence identifier.
- Xtract -insd recognizes INSDInterval_iscomp@value and other boolean attributes.
- Xtract adds experimental phrase processing commands for word index preparation.

EDirect Version 5.80: December 12, 2016
- Effilter adds shortcuts for -db gene (e.g., -status alive, -type coding).
- Xtract numeric conditional tests can use an element name for the second argument (e.g., -if ChrStop -lt ChrStart finds minus strand genes).

EDirect Version 5.70: November 30, 2016
- Xtract -format takes an optional [compact|indent|expand] argument. Processing compact XML is about 15% faster than indent form. Using expand places each attribute on a separate line for ease of reading.

EDirect Version 5.60: November 22, 2016
- Fixed bug in -datetype argument for Esearch and Effilter.
- Added optional argument to filter-stop-words script to indicate replacement.

EDirect Version 5.50: November 16, 2016
- Efetch -id allows non-numeric accessions only for sequence databases.
- Xtract element selection no longer considers fields in recursive sub-objects.
- Xtract introduces a double-star "*/Object" construct to flatten recursive child objects for linear exploration.
- Xtract conditional tests ignore empty self-closing tags.
- Xtract -else simplifies insertion of a placeholder to indicate missing data.
EDirect Version 5.40: November 7, 2016

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

EDirect Version 5.30: October 31, 2016

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

EDirect Version 5.20: October 26, 2016

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

EDirect Version 5.10: October 13, 2016

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

EDirect Version 5.00: September 26, 2016

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

EDirect Version 4.90: September 14, 2016

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

EDirect Version 4.80: August 9, 2016
• Xtract -insd controlled vocabularies updated.

EDirect Version 4.70: August 4, 2016
• Einfo -db request can also display -fields and -links data summaries.
• Einfo -dbs prints database names instead of eInfoResult XML.

EDirect Version 4.60: July 18, 2016
• Elink -cmd acheck returns information on all available links for a record.
• Efilter -pub structured limits to articles with structured abstracts.

EDirect Version 4.50: July 1, 2016
• Esearch and Efilter detect and report -query phrase quotation errors.
• Efilter -pub shortcut adds last_week, last_month, and last_year choices.
• Efetch sets -strand 2 for minus strand if -seq_start > -seq_stop or if -chr_start > -chr_stop.

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

EDirect Version 4.30: June 13, 2016
• Efilter -pub preprint limits results to ahead-of-print articles.
• Xtract -pattern Parent/* construct can now process catenated XML files.

EDirect Version 4.20: May 24, 2016
• Xtract command-line argument parsing improvements.
• Nquire -get supersedes -http get.

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

EDirect Version 4.00: April 4, 2016
• Esearch adds -spell to correct known misspellings of biological terms in the query string.
• Efilter adds -spell to correct query misspellings, and -pub, -feature, -location, -molecule, -organism, and -source shortcuts. Run efilter -help to see the choices available for each argument.
EDirect Version 3.90: March 21, 2016
- Code optimizations for increased Xtract speed.

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

EDirect Version 3.70: February 8, 2016
- Xtract performance improvements.

EDirect Version 3.60: January 11, 2016
- The setup.sh configuration script now downloads a precompiled Xtract executable for selected platforms.

EDirect Version 3.50: December 27, 2015
- Xtract reports error for element:value construct outside of -match or -avoid arguments.

EDirect Version 3.40: December 20, 2015
- Xtract -insd supports extraction from multiple features (e.g., CDS,mRNA).

EDirect Version 3.30: December 3, 2015
- Efetch -format docsum can accept a single sequence accession number in the -id argument.

EDirect Version 3.20: November 30, 2015
- Xtract supports -match conditional execution on values recorded in variables.

EDirect Version 3.10: November 18, 2015
- Efetch adds -chr_start and -chr_stop arguments to specify sequence range from 0-based coordinates in gene docsum GenomicInfoType object.

EDirect Version 3.00: October 30, 2015
- Xtract rewritten in the Go programming language for speed. The setup.sh configuration script installs an older Perl version (2.99) if a local Go compiler is unavailable.
- Efetch -format docsum only decodes HTML entity numbers in select situations.
**EDirect Version 2.90: October 15, 2015**
- Xtract warns on use of deprecated arguments -present, -absent, and -trim, in preparation for release of much faster version.

**EDirect Version 2.80: September 9, 2015**
- Xtract uses the "/Child" construct for nested exploration into recursive structures, replacing the -trim argument.

**EDirect Version 2.70: July 14, 2015**
- Added entrez-phrase-search script to query on adjacent word pairs indexed in specific fields.

**EDirect Version 2.60: June 23, 2015**
- Xtract -match and -avoid support "Parent/Child" construct for BLAST XML.

**EDirect Version 2.50: April 9, 2015**
- Xtract capitalized -Pattern handles recursively-defined top-level objects.

**EDirect Version 2.40: March 25, 2015**
- EDirect programs use the http_proxy environment variable to work behind firewalls.

**EDirect Version 2.30: March 11, 2015**
- Cleaned up logic in setup.sh configuration script.
- EPost -format acc works properly on protein accessions.

**EDirect Version 2.20: March 4, 2015**
- Xtract -match and -avoid recognize "@attribute" without element or value.

**EDirect Version 2.10: February 3, 2015**
- Added ftp-ls and ftp-cp scripts for convenient access to the NCBI anonymous ftp server.

**EDirect Version 2.00: August 28, 2014**
- Introduced copy-and-paste installation commands with setup.sh configuration script.

**EDirect Version 1.90: August 8, 2014**
- Xtract -format combines multiple XML results into a single valid object.
• Improved suppression of 0-count failure messages with -silent flag in scripts.

**EDirect Version 1.80: July 15, 2014**
• EPost -format acc accepts accessions in an -id argument on the command line.

**EDirect Version 1.70: April 23, 2014**
• EFetch -format docsum decodes HTML entity numbers embedded in the text.

**EDirect Version 1.60: April 3, 2014**
• Minor enhancements to xtract -insd.

**EDirect Version 1.50: March 29, 2014**
• ESearch -sort specifies the order of results when records are retrieved.
• Xtract exploration arguments (e.g., -block) now work on self-closing tags with data in attributes.

**EDirect Version 1.40: March 17, 2014**
• Xtract -format repairs XML line-wrapping and indentation.
• Implemented -help flag to display the list of command-line arguments for each function.

**EDirect Version 1.30: March 3, 2014**
• Xtract -insd partial logic was corrected to examine both 5' and 3' partial flags, and the location indicator recognizes "+" or "complete" and "-" or "partial".

**EDirect Version 1.20: February 26, 2014**
• Xtract -insd detects if it is part of an EDirect sequence record query, and dynamically executes the extraction request for specific qualifier values. When run in isolation it generates extraction instructions that can be incorporated (with modifications, if necessary) into other queries.

**EDirect Version 1.10: February 10, 2014**
• ESummary was replaced by "efetch -format docsum" to provide a single command for all document retrieval. The esummary command will continue to work for those who prefer it, and to avoid breaking existing scripts.
• Xtract processes each -pattern object immediately upon receipt, eliminating the need for using xargs and sh to split document retrieval into smaller units.

**EDirect Version 1.00: February 6, 2014**
• Initial public release.
For More Information

Announcement Mailing List

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

Getting Help

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

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