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| MolTK | |
|  | moltk1 |
|  | User’s Manual |
|  | Release 0.4.0  November 4, 2011 |
|  | Website: moltk.rotatingpenguin.com |

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# Introduction to MolTK

## Overview

### What is MolTK?

There are three faces of MolTK; in order from easiest-to-use to most-powerful:

1. MolTK is a computer application that allows the user to view and align molecular sequences and structures.
2. Moltk is a Python programming language module that allows the user to align and otherwise compute on molecular sequences and structures.
3. Moltk is a C++ API that allow the programmer to compute with molecular sequences and structures with high efficiency.

### Design Goals of MolTK

* Python programming language interactive environment for sequence/structure alignment that is just as easy to use as our (aging) dedicated alignment tool SEQUOIA.
* Flexible architecture that makes it easy to experiment with custom alignment methods and scoring systems.
* Consistent, well documented API for both Python and C++ programmers.
* Units-aware quantity type system. Thus alignment scores are not just numbers, they are information quantities with units of "bits". Atomic coordinates are not just numbers x, y, z, but are vector quantities with units of nanometers. Units-aware quantity types are an important part of scientific computing hygiene:
  + Converting a "quantity" to a raw number requires a "unit" to express the quantity in. This requires the user to pay attention to units at precisely the moment when knowing the unit is most important. The rest of the time is "just works", even if you are wrong about what the current units are!
  + This sort of type safety in scientific computing might help prevent errors such as, say, crashing $100 million orbiters into planets.
  + Type safety: Adding a length to a volume makes no sense, and will result in an error. Dividing a length by a time results in a velocity.
* Next-generation molecular sequence/structure viewer that adheres to our user interface principles.

## Installing MolTK

MolTK download site: <http://code.google.com/p/moltk/downloads/list>

### Installing the MolTK Application

The MolTK application won’t be released until MolTK version 0.7.

### Installing the MolTK Python Module

#### Windows

##### Install 32-bit Python 2.7

http://www.python.org/download/

Python 2.7.2 Windows Installer (current version on November 5, 2011)

##### Put Python on your Path

Start -> Control Panel -> (System and Security) -> System -> Advanced System Settings ->

Environment Variables (in Advanced tab) -> Edit "Path" in System variables ->

Add ";C:\Python27" (without the quotation marks) onto the end of the current text in the

Variable value field -> Click OK

##### Install the MolTK Python module for windows

http://code.google.com/p/moltk/downloads/list

MolTK-0.4.1.win32-py2.7.msi (curren version on November 5, 2011)

#### Macintosh

TODO in MolTK version 0.6

Install Python 2.6

#### Linux

TODO in MolTK version 0.6

### Installing the MolTK C++ SDK

TODO in MolTK version 0.5

### Building MolTK from Source Code

Build from source if you cannot find a binary installer for your system.

#### Additional Prerequisites for Building MolTK from Source

* C++ compiler
  + Windows

Use Visual Studio 9 (2008), if you intend to use the standard python 2.7 install.

http://www.microsoft.com/express/downloads/

* + Mac

Use gcc.

You might need to install XCode developer tools to get gcc.

* + Linux

Use gcc.

* Boost, including iostreams and python libraries
  + Windows

Get it from http://www.boostpro.com/download/ to get prebuilt binary libraries.

Be sure to select the iostream and python libraries, and to select Visual Studio 9. It might take several tries for the install to complete successfully.

* + Mac

I like to build fat binaries supporting both 32-bit and 64-bit architectures. So I build boost like:

./bootstrap.sh --prefix=/usr/local

sudo ./b2 address-model=32\_64 architecture=x86 variant=release link=shared,static install

<or to include PowerPC, which Python still does>

sudo ./b2 address-model=32\_64 architecture=combined variant=release link=shared,static install

* CMake

<http://www.cmake.org>

### Extend MolTK/Regenerate Python Bindings

Only regenerate python bindings if you have changed the moltk API.

#### Additional Prerequisites for Regenerating Python Bindings

* gccxml

(you might need to install cvs first)

cvs -d :pserver:anonymous@www.gccxml.org:/cvsroot/GCC\_XML login

(respond with password gccxml)

cvs -d :pserver:anonymous@www.gccxml.org:/cvsroot/GCC\_XML co gccxml

(install using cmake)

(add location of gccxml.exe to your PATH)

(on windows: run gccxml\_vcconfig.bat from install area)

On Windows, install to a directory without any space characters, i.e. NOT c:/Program Files/whatever

* pygccxml

svn checkout:

https://pygccxml.svn.sourceforge.net/svnroot/pygccxml/pygccxml\_dev pygccxml

cd pygccxml

python setup.py build

python setup.py install

On windows, patch pygccxml/parser/source\_reader.py method

\_\_create\_command\_line to NOT wrap command with double quotes.

* pyplusplus

svn checkout:

https://pygccxml.svn.sourceforge.net/svnroot/pygccxml/pyplusplus\_dev pyplusplus

cd pyplusplus

python setup.py build

python setup.py install

#### Generate API documentation(optional)

* epydoc (for generating python API documentation)

http://sourceforge.net/projects/epydoc/files/epydoc/

* doxygen (C++ API documentation)
* dot (graphs and figures in API documentation)

## Software License

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Commercial users should ask about our dual licensing model.

For questions contact: cmbruns@rotatingpenguin.com

## Resources

Browse the MolTK home page at:

http://rotatingpenguin.com/moltk/

Download MolTK at:

http://code.google.com/p/moltk/downloads/list

Find questions and answers in the moltk-users forum at:

http://groups.google.com/group/moltk-users

Report issues and get the source code at:

http://code.google.com/p/moltk/

Study the MolTK Python API at:

http://www.rotatingpenguin.com/moltk/api\_python/python\_api.html

Study the MolTK C++ API at:

http://www.rotatingpenguin.com/moltk/api\_cxx/cxx\_api.html

# The MolTK Application

# Programming MolTK

## Python

### Tutorial

Download and install MolTK from the MolTK download site:

<http://code.google.com/p/moltk/downloads/list>

In the following examples text following the >>> prompt represents

commands typed by the user. Other lines represent the output of the program.

#### Scenario 1: Aligning 3 Sequences

In this example, the insulin\_shark\_v1.fasta, insulin\_pig\_v1.fasta, and insulin\_human\_v1.fasta are sequences in the FASTA format. Information about the FASTA format can be found at <http://www.ncbi.nlm.nih.gov/BLAST/blastcgihelp.shtml>. A file called test.fasta can be saved with the alignment. The alignment can be also saved as test.pretty which is a nicely formatted but not computer parsable version of the alignment. What follows is an example of performing an alignment of three sequences.

##### Step 1. Download FASTA Test Sequences

Go to download page <http://code.google.com/p/moltk/downloads/list> and download the three FASTA sequences: insulin\_shark\_v1.fasta, insulin\_pig\_v1.fasta, and insulin\_human\_v1.fasta.

##### Step 2. Start an Alignment Session

Open a command prompt window. Navigate to the location of your downloaded FASTA files. In this step “%” represents your command prompt.

% python -i

>>> **import** moltk

##### Step 3. Load test1.fasta Sequence into Seq1

>>> seq1 = moltk.load\_fasta**(**"insulin\_human\_v1.fasta"**)**

##### Step 4. Load test2.fasta Sequence into Seq2

>>> seq2 = moltk.load\_fasta**(**"insulin\_pig\_v1.fasta"**)**

##### Step 5. Align Seq1 and Seq2

>>> align1 = moltk.align**(**seq1, seq2**)**

##### Step 6. Display the Alignment on the Screen

>>> **print** align1

Note: Homo sapiens (human) and Sus scrofa (pig)

##### Step 7. Load test3.fasta Sequence into Seq3

>>> seq3 = moltk.load\_fasta**(**"insulin\_shark\_v1.fasta"**)**

##### Step 8. Align Previous Alignment of test1.fasta and test2.fasta with test3.fasta

>>> align2 = moltk.align**(**align1, seq3**)**

##### Step 9. Save the Alignment to a File

>>> align2.write\_fasta**(**"test.fasta"**)**

You can also save as test.pretty for a nicely formatted but not computer parseable version.

>>> align2.write\_pretty**(**"test.pretty"**)**

##### Step 10. Display a Table of Pairwise Sequence Identities

>>> **print** align2.id\_table**()**

##### Step 11. End Your Alignment Session

>>> quit**()**

#### Scenario 2: Writing a Python Script to Help Automate the Alignment Process

#### Scenario 3: Aligning 2 Sequences and Assessing Significance

#### Scenario 4: Overlaying 2 tertiary structures

### MolTK for SEQUOIA Users

#### % sequoia

MolTK:

% python –i

>>> import moltk

Starts an alignment session

#### SEQUOIA> read SEQ1 test1.fasta

MolTK:

>>> seq1 = moltk.load\_fasta(“test1.fasta”)

Loads a sequence or an alignment into seq1

#### SEQUOIA> read SEQ2 test2.fasta

MolTK:

>>> seq2 = moltk.load\_fasta(“test2.fasta”)

Loads a sequence or an alignment into seq2

#### SEQUOIA> align

MolTK:

>>> align1 = moltk.align(seq1, seq2)

Aligns two sequences/alignments

#### SEQUOIA> print ALIGN

MolTK:

>>> pring align1

Displays the alignment on the screen

#### SEQUOIA> set SEQ1 ALIGN

MolTK:

>>> seq1 = align1

Copies the alignment to seq1

#### SEQUOIA> write ALIGN test.fasta

MolTK:

>>> align1.write\_fasta(“test.fasta”)

Saves the alignment to a file

#### SEQUOIA> print ALIGN test.pretty

MolTK:

>>> align1.write\_pretty(“test.pretty”)

Saves a nicely formatted, but not computer parseable, version of the alignment to a file

#### SEQUOIA> print id ALIGN

MolTK:

>>> print align1.id\_table()

Displays a table of pairwise sequence identities

#### SEQUOIA> quit

MolTK:

>>> quit()

Ends the alignment session

#### SEQUOIA> @test.inp

MolTK:

>>> execfile(“test.py”)

Runs a script file you wrote

#### % sequoia < test.inp

MolTK:

% python test.py

Runs a script file, that you wrote, directly from the command prompt

#### SEQUOIA> COMMENT This is a comment

MolTK:

>>> # This is a comment

Ignores the statement

#### SEQUOIA> help <command>

MolTK:

>>> help(<command>)

Acceses documentation about a command

#### SEQUOIA> system <command>

MolTK:

>>> import os

>>> os.system(“<command>”)

Issues an operating system command

#### SEQUOIA> consensus <sigma>

??? TODO

Creates a consensus sequence with X’s at non-conserved positions

#### SEQUOIA> optimize

??? TODO

Improves an alignment by successively removing and realigning sequences

#### SEQUOIA> print matrix

??? TODO

Displays the current scoring matrix

#### SEQUOIA> read matrix test.mat

??? TODO

Loads a scoring matrix

#### SEQUOIA> random 5

??? TODO

Calculates 5 alignment scores with SEQ2 randomly shuffled

#### SEQUOIA> split 5

??? TODO

Removes sequence 5 from alignment and places it in seq1

#### SEQUOIA> weight

??? TODO

Applies sequence weights to the alignment

#### SEQUOIA> set epen 0.5

MolTK:

>>> moltk.Aligner.shared\_aligner.scorer.default\_gap\_extension\_penalty = 0.5 \* moltk.bit

Sets gap extension penalty

#### SEQUOIA> set gpen 10

MolTK:

>>> moltk.Aligner.shared\_aligner.scorer.default\_gap\_open\_penalty = 10.0 \* moltk.bit

Sets gap opening penalty

#### SEQUOIA> set pretty\_length 50

??? TODO

Sets sequence width of formatted alignments

#### SEQUOIA> set random\_seed 1

??? TODO

Changes seed for RANDOM command

#### SEQUOIA> set suboptimal 0.1

??? TODO

Parameter for allowing suboptimal alignment

#### SEQUOIA> read STRUCT1 test1.pdb

??? TODO in moltk 0.6

Loads a structure into struct1

#### SEQUOIA> salign

??? TODO in moltk 0.6

Creates a structure-based alignment

#### SEQUOIA> overlay

??? TODO in moltk 0.6

Superposes two structures

#### SEQUOIA> equivalence

??? TODO in moltk 0.6

Assigns equivalent residues between two structures

#### SEQUOIA> set acutoff 45

??? TODO in moltk 0.6

Sets max rotation difference, in degrees, for structure alignment

#### SEQUOIA> set dcutoff 4.5

??? TODO in moltk 0.6

Sets max distance difference, in angstroms, for structure alignment

#### SEQUOIA> set runlength 4.5

??? TODO in moltk 0.6

Sets min length required for a run of structurally equivalent residues

#### SEQUOIA> set useangle 0

??? TODO in moltk 0.6

Sets whether to use rotation similarity in structure alignment

#### SEQUOIA> tabulate

There is no tabulate command in MolTK

Populates pairwise residue scores before aligning

Seldom used

#### SEQUOIA> stabulate

There is no stabulate command in MolTK

Populates pairwise residue structure scores before aligning

Seldom used

#### SEQUOIA> set echo 1

Don’t know how to do this in python

Outputs a copy of user’s commands

## C++

### MolTK Coding Style Guidelines

Purpose: To provide a consistent look for both python and C++ MolTK code.

#### Indentation

Use four space characters per indent. No tabs.

#### Class names

Use CapitalizedWords

Use all caps for abbreviations, e.g. PDBStructure.

Class names should be nouns.

#### Macro, enum, and constant names

CAPITALIZED\_WITH\_UNDERSCORES

#### Method and function names

Use lower\_case\_with\_underscores.

Begin method and function names with a verb.

#### Attribute and member names

lower\_case\_with\_underscores

adjective\_noun or noun

b\_variable\_name for boolean values

#### Namespace, package, and module names

lower case, single word, short names

#### Method parameters

lower\_case\_with\_underscores

Remember that method parameter names are more important in python than in C++, because python allows named parameter use. In all C++ header files, every parameter to every exposed method should have an understandable name.

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Needleman, S. & Wunsch, C. D., 1970. A general method applicable to the search for similarities in the amino acid sequence of two proteins. *Journal of Molecular Biology,* Volume 48, pp. 443-453.