Supplementary Method 1: Software installation (*ShapeMapper*)

This guide assumes the user is familiar with basic Unix/Linux commands to change directories, extract archived files, move files, display and edit text files, and run executables. These steps only need to be performed once. Example data for the 16S rRNA and TPP riboswitch is available at the Sequence Read Archive SRP052065 (sequencing files).

1. Obtain the latest version of *ShapeMapper* from www.chem.unc.edu/rna/software.html
2. Extract *ShapeMapper* files to any directory.
3. Add this *ShapeMapper* directory location to the system PATH (see Supporting Protocol 2).
4. Build the C and C++ *ShapeMapper* modules.
    a. Browse to the *ShapeMapper* directory from a command line terminal.
    b. Execute the command "*make*".
5. Ensure the files ShapeMapper.py and pvclient.py are executable with your user permissions. If not, add executable permissions with the "*chmod*" command.
6. Verify or install all non-optional third-party programs (see Table 1).
7. Ensure the *bowtie2* executables *bowtie2-build* and *bowtie2* are present in the system PATH.
8. If modeling structures, install RNAstructure, add to the system PATH, and add the RNAstructure/data_tables folder to the system DATAPATH (see Supporting Protocol 2)
9. If rendering secondary structures and running python 2.6, install the python module "httplib2".
10. If rendering secondary structures, ensure an internet connection is active to query the Pseudoviewer web service.

***ShapeMapper* dependencies**

Dependencies	**Optional**
Unix-based operating system such as Linux	no
Unix utility "*make*" (needed for building pipeline modules)	no
Unix utility "*gcc*" (needed for compiling one pipeline module)	no
Unix utility "*g++*" (needed for compiling two pipeline modules)	no
Python 2.7	no
Python module matplotlib (tested with version 1.3.1)	no
Bowtie2	no
Python module httplib2 (only needed for secondary structure rendering)	yes
RNAstructure (only needed for structure modeling)	yes

Supplementary Method 2: Software installation (*SuperFold*)

This guide assumes the user is familiar with basic Unix/Linux commands to change directories, extract archived files, move files, display and edit text files, and run executables. These steps only need to be performed once.

1. Use a package manager, such as apt-get on Debian, Ubuntu, or Linux or MacPorts on OSX, to install Numpy and Matplotlib. Using apt-get:

   ```
   $ sudo apt-get install python-matplotlib
   ```

2. To install RNAstructure, download the compiled version of the text interfaces for your system from the Mathews lab web site (http://rna.urmc.rochester.edu/RNAstructureDownload.html). Unzip the tarball and move it to the home directory:

   ```
   $ tar –xzvf RNAstructureTextInterfaces*.tgz
   $ mv RNAstructure ~/
   ```

3. Add the RNAstructure programs and data tables to the PATH:

   ```
   $ export DATAPATH=$HOME/RNAstructure/data_tables
   $ export PATH=$HOME/RNAstructure/exe:$PATH
   ```

4. To install *SuperFold*, Obtain the latest version of ShapeMapper from www.chem.unc.edu/rna/software.html, move it to your home directory, and add it to the PATH:

   ```
   $ tar –xzvf SuperFold.tgz
   $ mv SuperFold ~/
   $ export PATH=$HOME/SuperFold:$PATH
   ```

5. **Example data.** SHAPE-MaP data for the *E. coli* 16S rRNA are included in the *SuperFold* tarball. Copy the .map file to a working directory "my_superfold_analysis"

   ```
   $ cd
   $ mkdir my_superfold_analysis
   $ cp ~/SuperFold/16SrRNA.map my_superfold_analysis/
   $ cd my_superfold_analysis
   ```

***SuperFold* dependencies**

Dependency	**Optional**
Unix-based operating system such as Linux	no
Python 2.6 or 2.7	no
Python module matplotlib (tested with version 1.3.1)	no
Python module Numpy (tested with 1.4)	no
RNAstructure	no
Python module httplib2 (only needed for secondary structure rendering)	yes