

Figure S1. Perl script of the NMODE-monitored energy minimization procedure.

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all.pl

#! /usr/bin/perl

## Perl script of NMODE-monitored energy minimization procedure ##

use Getopt::Long;

$label = 10;
$i = 0;

&GetOptions(
'label|label=s' => \$label,
'i|i=s' => \$i,
);

system ("cp ../para/prm??? .");
system ("rm rms");
system ("rm *.log");
$end = 0;
$num = 0;

system ("min.pl -l $label >> min.log");
system ("rm CHECK");
system ("nmode.pl -l $label -i $i >> nmode.log");

while ($end == 0) {
    if (open (IN, "CHECK") ) {
        system ("cp $label.restrt prmcrd");
        system ("min.pl -l $label >> min.log");
        system ("rm CHECK");
        system ("nmode.pl -l $label -i $i >> nmode.log");
        system ("mv $label.nmode.out $label.$num.nmode.out");
        $num++; print("$num\n");
    }
    else {
        $end = 1;
        print ("The minimization has reached a local minimum!!\n");
    }
}

min.pl

#! /usr/bin/perl

## Perl script for minimization ##

use Getopt::Long;

$label = 10;

&GetOptions(
'label|label=s' => \$label,
);

system ("sed 's/maxcyc =10/maxcyc =$label/g' ../../min.in > tmpmin.in");

$end = 0;
$num = 0;
while ( $end == 0 )
{
    $num++;
    system ("samber5/exe/sander-large -O -i tmpmin.in -o min.out -c prmcrd -p prmtop -r restrt");
    system ("grep ' $label -l $label -i $i >> min.log' min.out | tail -1 > tmp");
    open (IN, "tmp") || die " cannot open tmp, does file tmp exist? Sth wrong with the
minimization.\n";
    while (<IN>)
    {
        $_ = ~/(\s+)(\d+)(\s+)(\S+)(\s+)(\S{1})(\S{6})(\S{1})(\S{2})/ ;
        if ($6 < 6 && $8 eq "-" && $9 > 1) {

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        $end = 1;
    }
    elsif ( $8 eq "-" && $9 > 2) {
        $end = 1;
    }
    else
        {system ("cp restrt prmcrd");}
    }
}
close (IN);

system ("mv restrt $label.restrt");
system ("mv min.out $label.step$num.out");

nmode.pl

#! /usr/bin/perl

## Perl script for normal mode analysis ##

use Getopt::Long;

$label = 10;
$i = 0;

&GetOptions(
'label|label=s' => \$label,
'i|i=s' => $i,
);

system ("$amber8/exe/nmode -O -i ../../nmode$i.in -o $label.nmode.out -c $label.restrt -p
prmtop -r rst");

system ("grep '      1 ' $label.nmode.out > all.check");
system ("grep '      4 ' $label.nmode.out >> all.check");
system ("grep '      5 ' $label.nmode.out >> all.check");
system ("grep '      6 ' $label.nmode.out >> all.check");
system ("grep '      7 ' $label.nmode.out >> all.check");

system ("tail -5 all.check > $label.check");

open (IN, "$label.check") || die " cannot open check, does file exist? Sth wrong with the
minimization.
";
while (<IN>)
{
    if ( $_ =~/(\s+)(\d)(\s+)(\S+)/ ) {
        if ( ($2 == 1 && $4 <= -0.01) || ($2 == 6 && $4 > 10 ) || ($2 == 7 && $4 <= 0 ) ){
            open (OUT, ">>CHECK");
            print OUT ("$label is not a minimum!!\n");
            print ("$label is not a minimum!! The number has been written to file CHECK!!\n");
            close (OUT);
        }
        elsif ($1.$2.$3.$4 eq "      1      0") {
            open (OUT, ">>CHECK");
            print OUT ("$label cannot go through nmode analysis!!\n");
            print ("$label cannot go through nmode analysis!! The number has been written to file
CHECK!!\n");
            close (OUT);
        }
    }
}
}

close (IN);

system ("cp $label.restrt restrt");
system ("$amber8/exe/ptraj prmtop ../../rms.trajin");
system ("echo $label >> rms");
system ("tail -1 rms0.dat >> rms");

system ("$amber8/exe/ptraj prmtop ../../pdb.trajin");
system ("mv restrt.pdb.1 $label.pdb");

```