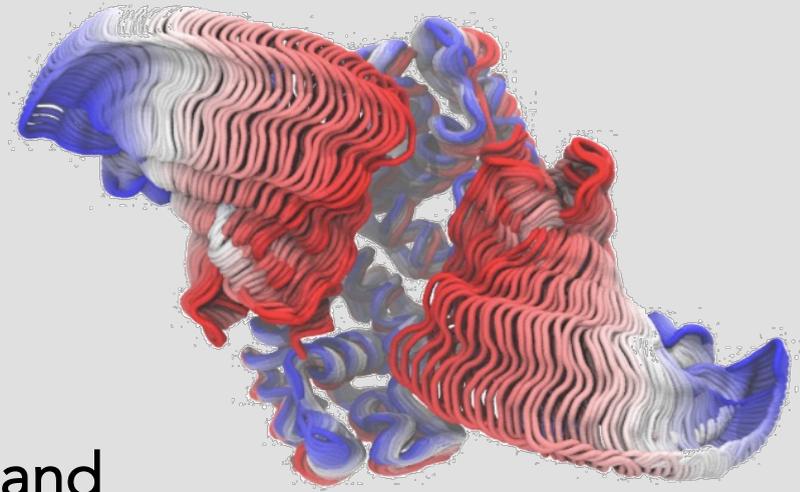


eBDIMS

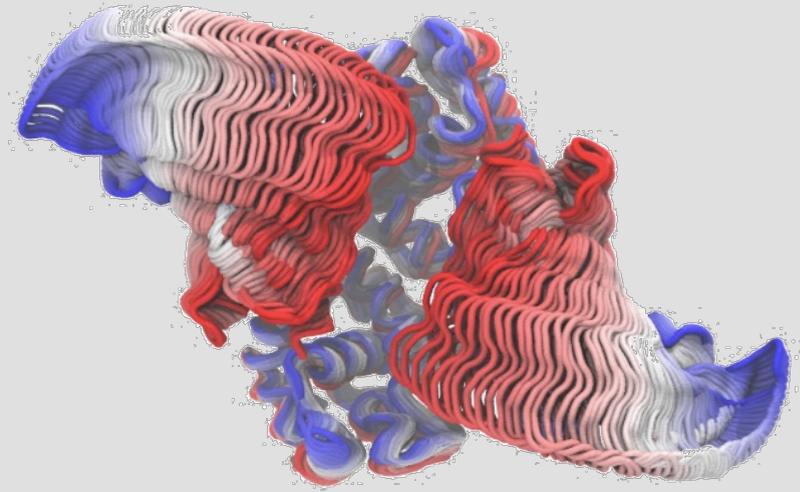
elastic-network driven Brownian Dynamics
Importance Sampling



Step-by-step quick guide and
tutorial

eBDIMS

User Interface



START new eBDIMS simulation

Job description

Job name (required)

project name

Email (optional; to receive job notifications) ?

user@domain.com

Description (optional)

 Download PDB files Upload PDB files

Start PDB structure (required) ?

e.g. 1FA2

Target PDB structure (required)

e.g. 2DRI

SUBMIT JOB

Job name: A job name is specified which allows to monitor job progress on the queue

Description: An optional description of the transition can be added to help the user to identify each job

Email: to receive a direct link to results upon job completion and access other finished jobs

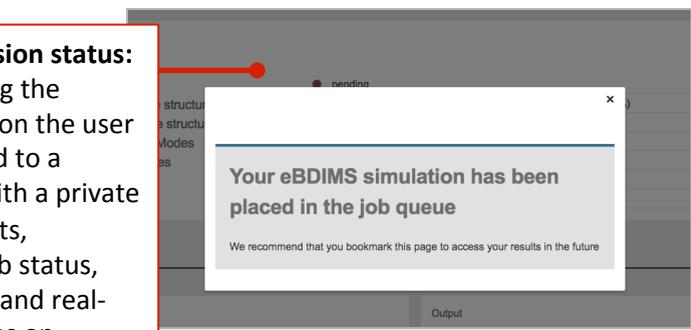
Help icon (?): opens a window explaining how to select chains when downloading from the PDB e.g. [3NJP:B chain B of structure 3NJP](#)

Input files: atomic coordinates can be retrieved from the PDB or be uploaded by the user in strict pdb format

Submission: Upon pressing the submit button the job is placed in the queue

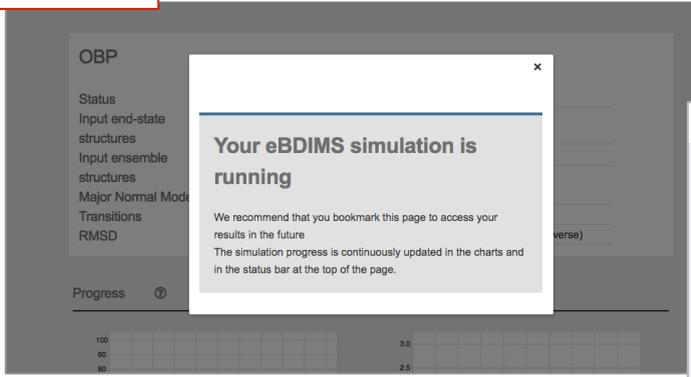
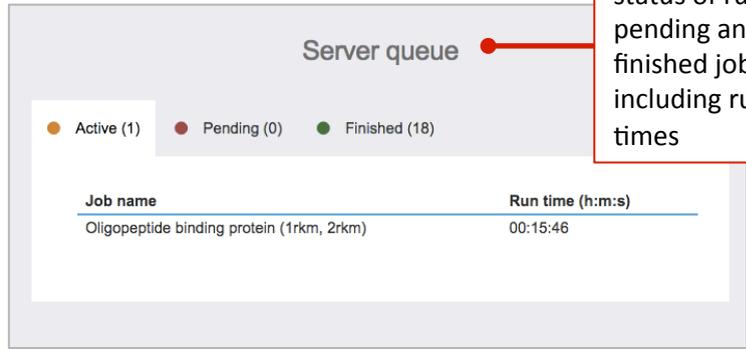
Job submission status:

After clicking the submit button the user is redirected to a webpage with a private link to results, including job status, description and real-time updates on progress



Public queue tab:

status of running, pending and finished jobs including running times



Real-time updates:

as transitions advance, the progress and rMSD are plotted in real-time



Login to access stored results:

If the user has provided an email, he/she will receive a password to log in by clicking on a menu at the upper right corner of the page.

Log in

Email

password

Only for users that provided their email address upon job submission

LOGIN

- Add new job
- Results
- Documentation
- Examples
- Log in

Private user dashboard: upon login, the user can see the status of all his/her jobs (finished/running/queued) and access the results

Dashboard

My jobs

- [sercamd](#)
- [RBP \(1ba2, 2dri\)](#)
- [Maltodextrin binding protein \(1omp, 1anf\)](#)
- [Calmodulin \(1cll, 3ewv\)](#)
- [groelmon2](#)
- [Lactoferrin \(1lfg, 1lfh\)](#)
- [Guanylate kinase \(1ex6, 1ex7\)](#)

General information on the transition:

- initial and final rMSD
- run time, etc

Lactoferrin (1lfg, 1lfh)

Status ● finished ■ Total cpu-time: 00:48:32 (hh:mm:ss)

Input end-state Start PDB code: 1LFG (chains: A)

structures Target PDB code: 1LFH (chains: A)

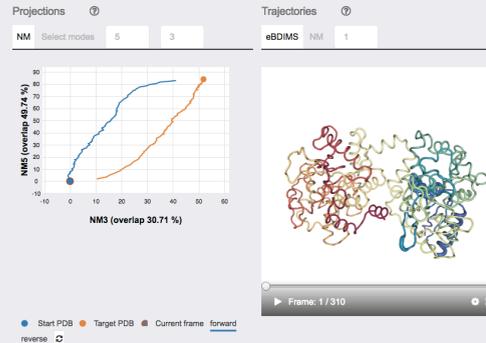
Input ensemble 0 models

Major Normal Modes mode5 (overlap 49.74) mode3 (overlap 30.71)

Transitions Forward: 99.5 % (845.4 s) Reverse: 99.5 % (1030.7 s)

RMSD RMSD initial: 6.429 Å

RMSD final: 0.74 / 0.77 Å (forward/reverse)

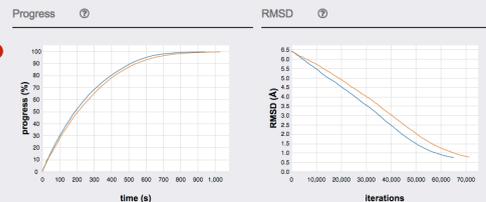


NM/PC 2D-projections linked to 3D-Movies:

- Default modes
- Explore within the 10-subspace

Transition progress and rMSD versus time:

- Convergence
- Final rMSD reached



Files ⓘ

Input

Start structure (1LFG)

Target structure (1LFH)

Input file validation log (.txt file)

Output

Progress log

Analysis

Projections onto NM and PC space (csv)

eBDIMS transitions (pdb files)

Normal modes (pdb files)

Links to download results files:

- Trajectories
- Projections

Commands to run the job in a local machine

Local

eBDIMS transitions can be reproduced on a local machine with the validated input data (i.e. `start.pdb` and `target.pdb`).

Compile the eBDIMS source code and run the executable file from the command line as

```
./eBDIMS_parallel [start.pdb] [target.pdb] [outoff] [mode] [unbiasedSteps]
```

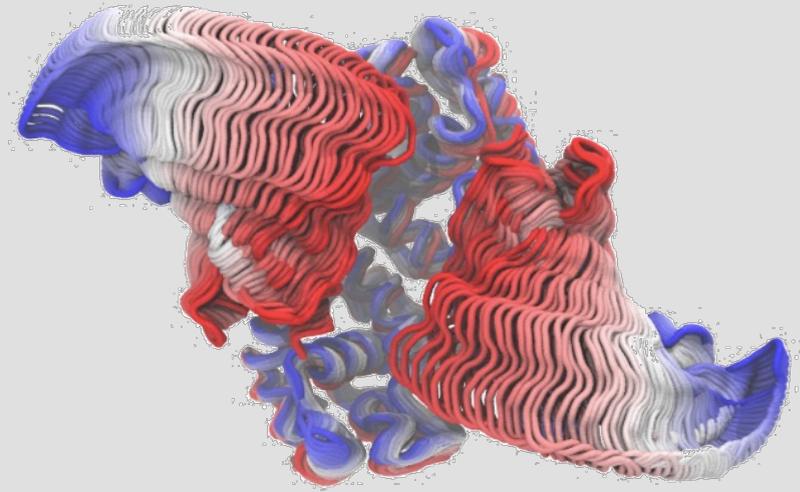
The parameters used were:

- [outoff] = 6
- [mode] = 3
- [unbiasedSteps] = 1

eBDIMS

Example 1: Simple simulation from PDB codes

Example 2: Running eBDIMS uploading files



In this tutorial we will show how to use the eBDIMS server by computing the transition pathways connecting the open (1BA2) and closed (2DRI) conformations of the *E.coli* Ribose Binding Protein (RBP):

START new eBDIMS simulation

Job description

Job name (required) Email (optional; to receive job notifications)

Description (optional)

Download PDB files Upload PDB files

Start PDB structure (required) Target PDB structure (required)

SUBMIT JOB

START new eBDIMS simulation

Job description

Job name (required)

Description (optional)

Start PDB structure Target PDB structure

PDB code examples:

Type or to fetch the entire PDB structure [1NQL](#).

One can specify chains of interest by indicating them immediately after the structure ID (separated by a colon). PDB IDs are case insensitive. Valid chain identifiers are A-Z (i.e. single characters). See examples below:

Example	Interpretation
<input type="text" value="3NJP"/>	All chains of PDB structure 3NJP (i.e. A,B,C,D)
<input type="text" value="3NJP:B"/>	Chain B of PDB structure 3NJP
<input type="text" value="3NJP:A, B, C"/>	Chains A,B,C of PDB structure 3NJP
<input type="text" value="3NJP:A-C"/>	Chains A,B,C of PDB structure 3NJP

PDB codes and chains: since 1BA2 has two chains (A,B) and 2DRI only one (A), by default the server will take chain A which is common to both

Chain selection: For PDBs with the same chains, all are taken unless specified otherwise. Click on the help icon to visualize the syntax for chain selection

RBP codes

Status ● finished ■ Total cpu-time: 00:08:02 (hh:mm:ss)

Input end-state Start PDB code: 1BA2 (chains: A)

structures Target PDB code: ZDRI (chains: A)

Input ensemble 0 models

Project
Major
Trans
RMST

Project
NM

RMS (over the PC space)

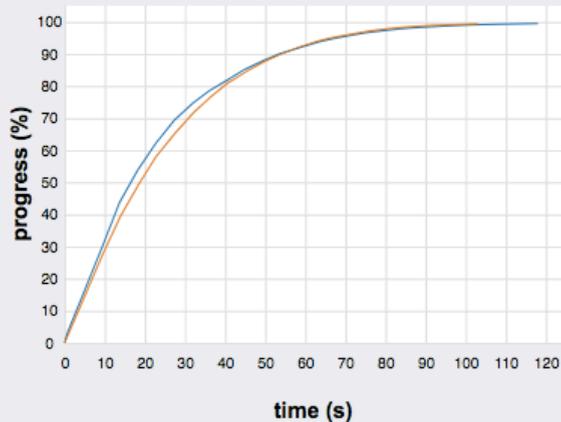
100
90
80
70
60
50
40
30
20
10
0

0 10 20 30 40 50 60 70 80 90 100 110 120

time (s)

progress (%)

Progress



RMSD



Progre



Files

Input

Start structure (1BA2)

Target structure (ZDRI)

Input file validation log (.txt file)

Output

Progress log

Analysis

Projections onto NM and PC space (.csv)

eBDIMS transitions (.pdb files)

Normal modes (.pdb files)

Local

eBDIMS transitions can be reproduced on a local machine with the validated input data (i.e. `start.pdb` and `target.pdb`).

Compile the eBDIMS source code and run the executable file from the command line as

```
./eBDIMS_parallel [start.pdb] [target.pdb] [cutoff] [mode] [unbiasedSteps]
```

The parameters used were:

- `[cutoff]` = 6
- `[mode]` = 3
- `[unbiasedSteps]` = 1

Transition Progress: as the transitions run (first in the forward and then in the reverse direction), the evolution of the rMSD versus their target structure is reported.

Each direction is completed > 95.5% or after 4h.

RBP codes

Status ● finished ■ Total cpu-time: 00:08:02 (hh:mm:ss)

Input end-state structures Start PDB code: 1BA2 (chains: A)
Target PDB code: 2DRI (chains: A)

Input ensemble structures 0 models

Major Normal Modes mode1 (overlap 90.75) mode3 (overlap 20.27)

Transitions Forward: 99.4 % (118.0 s) Reverse: 99.4 % (103.0 s)

RMSD RMSD initial: 6.192 Å
RMSD final: 0.85 / 0.89 Å (forward/reverse)

General information: at the top of the results page, the final rMSD achieved in each direction is reported along with running time

In general transitions proceed until completion (>99%), but in the case of very large proteins or small-scale complex rearrangements they may not be completed in the maximal allowed running time (8h), thus requiring several consecutive runs.

RBP codes

Status

● finished ■ Total cpu-time: 00:08:02 (hh:mm:ss)

Input end-state structures

Start PDB code: 1BA2 (chains: A)

Target PDB code: 2DRI (chains: A)

Input ensemble structures

0 models

Major Normal Modes

mode1 (overlap 90.75) mode3 (overlap 20.27)

Transitions

Forward: 99.4 % (118.0 s) Reverse: 99.4 % (103.0 s)

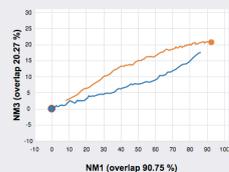
RMSD

RMSD initial: 6.192 Å

RMSD final: 0.85 / 0.89 Å (forward/reverse)

Projections

NM Selected modes 1 3



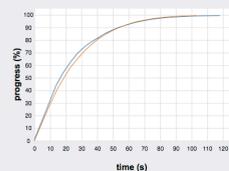
Trajectories

eBDIMS NM 1



Start PDB Target PDB Current frame forward reverse

Progress



RMSD



Files

Input
Start structure (1BA2)
Target structure (2DRI)
Input file validation log (.txt file)

Output
Progress
Analysis
Projections onto NM and PC space (.csv)
eBDIMS transitions (.pdb files)
Normal modes (.pdb files)

Local

eBDIMS transitions can be reproduced on a local machine with the validated input data (i.e. `start.pdb` and `target.pdb`).

Compile the eBDIMS source code and run the executable file from the command line as

```
./eBDIMS_parallel [start.pdb] [target.pdb] [cutoff] [mode] [unbiasedSteps]
```

The parameters used were:

- `[cutoff]` = 6
- `[mode]` = 3
- `[unbiasedSteps]` = 1

RBP codes

Status ● finished ■ Total cpu-time: 00:08:02 (hh:mm:ss)

Input end-state structures ● Start PDB code: 1BA2 (chains: A)

Input ensemble structures ● Target PDB code: 2DRI (chains: A)

Major Normal Modes ● mode1 (overlap 90.75%) ● mode3 (overlap 20.27%)

Transitions ● Forward: 99.4 % (118.0 s) ● Reverse: 99.4 % (103.0 s)

RMSD ● RMSD initial: 6.192 Å ● RMSD final: 0.85 / 0.89 Å (forward/reverse)

Projections



NM-Projections: forward and reverse trajectories are projected by default onto the two better overlapped NMs from the structure defined as “start”, which will appear at (0,0).

Structures with a “open” configuration render NMs with better overlaps with transitions and should be used as reference.

NMs within the 10-lowest frequency modes subspace can be explored.

Significant projections must be:

- Smooth
- Cluster different conformations separately

If projections do not fulfill these conditions, we recommend using the target structure as reference.

Transition 3D-Movies: forward and reverse movie transitions are coupled to the projections onto NMs.

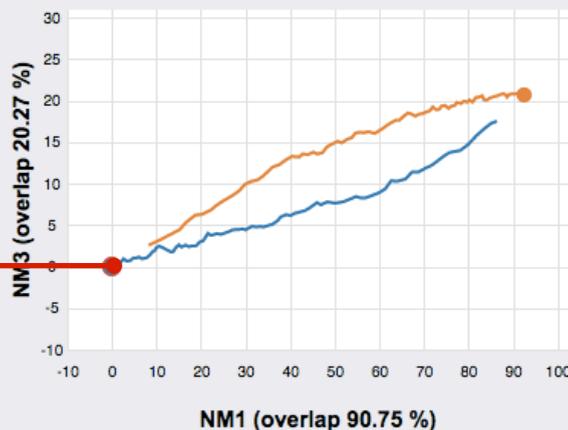
Normal Modes 3D-Movies: All NMs within the first 10-modes subspace can be visualized to better grasp which motions represent the 2D-axes and how they cluster structures

Projections

NM Select modes

1

3



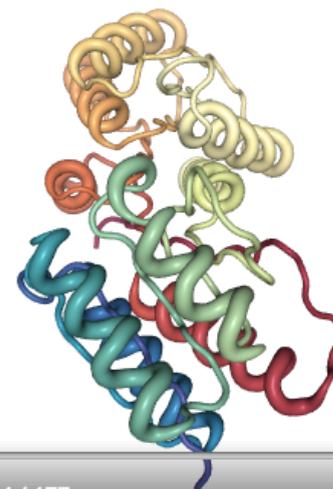
● Start PDB ● Target PDB ● Current frame forward

reverse ↺

Trajectories

eBDIMS

1



▶ Frame: 1 / 177

RBP codes

Status ● finished ■ Total cpu-time: 00:08:02 (hh:mm:ss)

Input end-state structures
Input ensemble structures
Major Normal Modes
Transitions
RMSD

Start PDB code: 1BA2 (chains: A)
Target PDB code: 2DRI (chains: A)
0 models

mode1 (overlap 90.75%) mode3 (overlap 20.27%)
Forward: 99.4 % (118.0 Å) Reverse: 99.4 % (103.0 Å)
RMSD initial: 6.192 Å
RMSD final: 0.85 / 0.89 Å (forward/reverse)

Projections

NM Selected modes: 1, 3

Trajectories

eBDIMS NM 1

Frames: 1 / 177

Legend: Start PDB (blue), Target PDB (orange), Current frame (red), forward (right arrow), reverse (left arrow)

Progress

RMSD

Files

Input

- Start structure (1BA2)
- Target structure (2DRI)
- Input file validation log (.txt file)

Output

- Progress log
- Analysis
- Projections onto NM and PC space (csv)
- eBDIMS transitions (pdb files)
- Normal modes (pdb files)

Local

eBDIMS transitions can be reproduced on a local machine with the validated input data (i.e. [start.pdb](#) and [target.pdb](#)).

Compile the eBDIMS source code and run the executable file from the command line as

```
./eBDIMS_parallel [start.pdb] [target.pdb] [cutoff] [mode] [unbiasedSteps]
```

The parameters used were:

- [cutoff] = 6
- [mode] = 3
- [unbiasedSteps] = 1

Input

- Start structure (1BA2)
- Target structure (2DRI)
- Input file validation log (.txt file)

Output

- Progress log
- Analysis
- Projections onto NM and PC space (csv)
- eBDIMS transitions (pdb files)
- Normal modes (pdb files)

Local

eBDIMS transitions can be reproduced on a local machine with the validated input data (i.e. [start.pdb](#) and [target.pdb](#)).

Compile the eBDIMS source code and run the executable file from the command line as

```
./eBDIMS_parallel [start.pdb] [target.pdb] [cutoff] [mode] [unbiasedSteps]
```

The parameters used were:

- [cutoff] = 6
- [mode] = 3
- [unbiasedSteps] = 1

Links to download results and run locally: at the bottom of the page we can download the forward and reverse trajectories along with the input files, the NM movies in pdb format and the 2D-projections.

We recommend to download the projections and plot them coloring the points versus structure descriptors such as rMSD, key interresidue distances, etc

1. Incomplete/Inconsistent PDBs: PDB files retrieved from the Protein Data Bank can have missing residues, gaps, chimeric constructs, etc:

The screenshot shows the eBDIMS interface with the following elements:

- Buttons: "Download PDB files" (checked) and "Upload PDB files" (unchecked).
- Form fields:
 - "Start PDB structure (required) ?" with input "e.g. 1BA2". Below it, a message says "Missing residues in chain: A".
 - "Target PDB structure (required)" with input "e.g. 2DRI".
- Comparison message: "Start and target have different number of residues (435)" and "Start and target have different number of residues (644)".

2. Fixing and uploading your own PDB files:

- Fixing PDB files for eBDIMS can be as simple as cutting N- or C-terminal residues, or relabeling a broken chain as two separate chains
- Another alternative is to download a special eBDIMS version to run incomplete structures locally (<https://github.com/laura-orellana/eBDIMS>)

You can also use tools as *modeller* to reconstruct full-length structures.

If you want to build an ensemble, you can try our tutorial for ensemble preparation with pdbParser (<https://github.com/ozyo/pdbParser>) or tools such as *Bio3D* or *ProDy*.

Now we imagine our RBP files were “broken” so we took the time to fix them and curate an 11-mer ensemble from the Protein Data Bank. In this case we don’t need to worry about specifying chains since we have prepared our files to be perfectly consistent (otherwise we will get an error message!):

START new eBDIMS simulation

Job description

Job name (required) Email (optional; to receive job notifications) [?](#)

Description (optional)

Download PDB files Upload PDB files

Start PDB structure (required) start.pdb [?](#) Target PDB structure file (required) target.pdb PDB ensemble (optional) ensemble.pdb [?](#)

PDB file format: start, target and all frames in the ensemble need to have the same number of chains and residues.

All chains are processed.

Each coordinate set is delimited as in multipdb files:

```
MODEL
ATOM 1
ATOM 2
.....
ENDMDL
```

Maximal File size should be <15Mb.

RBP (1ba2, 2dri)

Status ● finished ■ Total cpu-time: 00:11:35 (hh:mm:ss)

Input end-state structures Start file: start.pdb (chains: A) Target file: target.pdb (chains: A)

Input ensemble structures 11 models

Major Normal Modes mode1 (overlap 83.19) mode2 (overlap 39.85)

Major PC modes mode1 (variance 97.95%) mode2 (variance 1.47%)

Transitions Forward: 99.5 % (119.9 s) Reverse: 99.4 % (101.1 s)

RMSD RMSD initial: 6.179 Å RMSD final: 0.80 / 0.83 Å (forward/reverse)

Projections

Trajectories

Progress

Files

Local

eBDIMS transitions can be reproduced on a local machine with the validated input data (i.e. start.pdb and target.pdb).
 Compile the eBDIMS source code and run the executable file from the command line as
`./eBDIMS_parallel [start.pdb] [target.pdb] [cutoff] [mode] [unbiasedSteps]`

The parameters used were:

- [cutoff] = 6
- [mode] = 3
- [unbiasedSteps] = 1

General information:

Apart from NMS, information from the two major PCs (capturing the most collective motions of largest variance) is now reported.

The first two PCs typically accumulate > 70-80% of the total ensemble variance.

RBP (1ba2, 2dri)**Status**

● finished ■ Total cpu-time: 00:11:35 (hh:mm:ss)

**Input end-state
structures**

Start file: start.pdb (chains: A)

Target file: target.pdb (chains: A)

**Input ensemble
structures**

11 models

Major Normal Modes

mode1 (overlap 83.19) mode2 (overlap 39.85)

Major PC modes

mode1 (variance 97.95%) mode2 (variance 1.47%)

Transitions

Forward: 99.5 % (119.9 s) Reverse: 99.4 % (101.1 s)

RMSD

RMSD initial: 6.179 Å

RMSD final: 0.80 / 0.83 Å (forward/reverse)

Normal modes (pdb files)

Principal components (pdb files)

RBP (1ba2, 2dri)

Status	finished	Total cpu-time: 00:11:35 (hh:mm:ss)
Input end-state structures	Start file: start.pdb (chains: A)	Target file: target.pdb (chains: A)
Input ensemble structures	11 models	
Major Normal Modes	mode1 (overlap 83.19)	mode2 (overlap 39.86)
Major PC modes	mode1 (variance 97.95%)	mode2 (variance 1.47%)
Transitions	Forward: 99.5 % (119.9 s)	Reverse: 99.4 % (101.1 s)
RMSD	RMSD initial: 6.179 Å	RMSD final: 0.80 / 0.83 Å (forward/reverse)

**Transition 3D-Movies:**

forward and reverse movie transitions are coupled to the projections onto NMs and also PCs.

Principal Components 3D-Movies:

All PCs within the first 10-modes subspace can be visualized to better grasp which motions represent the 2D-axes and how they cluster structures

PC-Projections: apart from projections onto the best NMs from the reference structure, projections onto the two largest-variance PCs of the ensemble are presented.

Intermediates appear as clusters near any of forward/reverse transitions, clearly separated from the end-states.

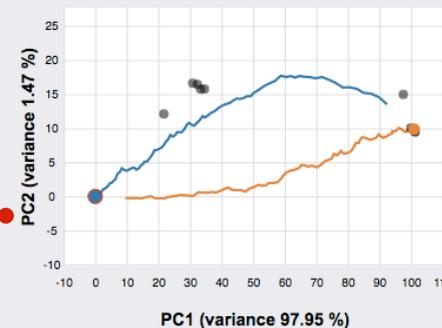
Remember that significant projections must be:

- Smooth
- Cluster different conformations separately

If PC-projections do not fulfill these conditions, we recommend carefully analyzing the ensemble composition and which kind of motions are represented.

Projections

PC NM Select modes 1 2



● Start PDB ● Target PDB ● Ensemble
 ● Current frame forward reverse ↺

Trajectories

eBDIMS PC NM 1



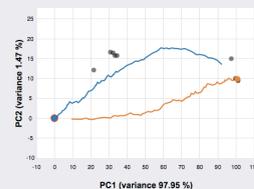
RBP (1ba2, 2dri)

Status
 Input end-state structures
 Input ensemble structures
 Major Normal Modes
 Major PC modes
 Transitions
 RMSD

● finished ■ Total cpu-time: 00:11:35 (hh:mm:ss)
 Start file: start.pdb (chains: A) Target file: target.pdb (chains: A)
 11 modes
 mode1 (overlap 83)
 mode1 (variance 9)
 Forward: 99.5 % (1)
 RMSD initial: 6.179

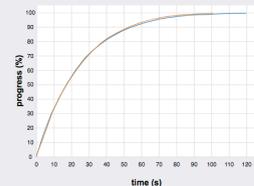
Projections

PC NM Select modes 1 2



● Start PDB ● Target PDB ● Ensemble ● Current frame
 forward reverse ↺

Progress



Files

Input
 Start structure (start.pdb)
 Target structure (target.pdb)
 Ensemble structures (multi pdb file)
 Input file validation log (.txt file)

Local

eBDIMS transitions can be reproduced on a local machine with the validated input data (i.e. start.pdb and target.pdb).
 Compile the eBDIMS source code and run the executable file from the command line as

```
./eBDIMS_parallel [start.pdb] [target.pdb] [cutoff] [mode] [unbiasedSteps]
```


 The parameters used were:

- [cutoff] = 6
- [mode] = 3
- [unbiasedSteps] = 1

Files

Input

Start structure (start.pdb)
 Target structure (target.pdb)
 Ensemble structures (multi pdb file)
 Input file validation log (.txt file)

Output

Progress log
 Analysis
 Projections onto NM and PC space (csv)
 eBDIMS transitions (pdb files)
 Normal modes (pdb files)
 Principal components (pdb files)

Local

eBDIMS transitions can be reproduced on a local machine with the validated input data (i.e. start.pdb and target.pdb).

Compile the eBDIMS source code and run the executable file from the command line as

```
./eBDIMS_parallel [start.pdb] [target.pdb] [cutoff] [mode] [unbiasedSteps]
```

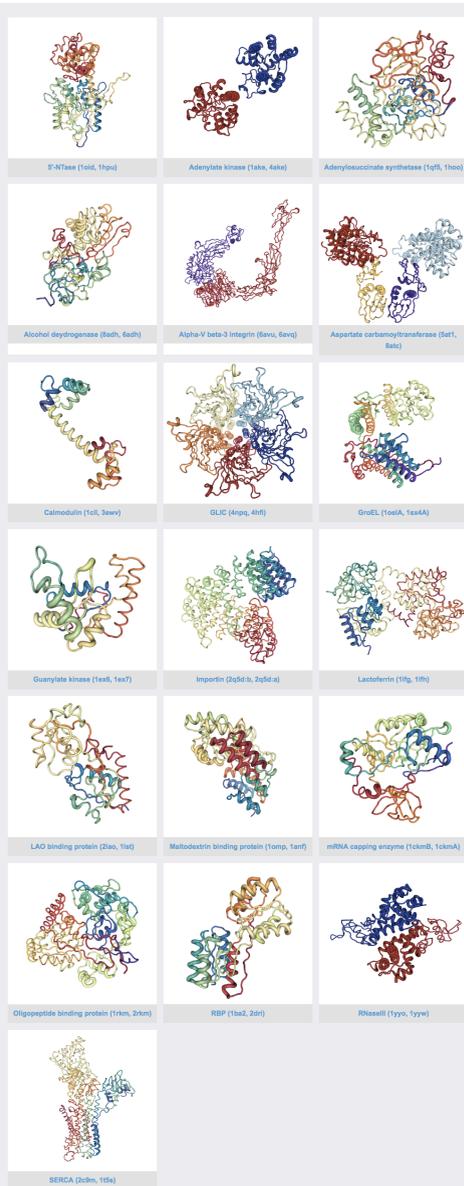
The parameters used were:

- [cutoff] = 6
- [mode] = 3
- [unbiasedSteps] = 1

Links to download results and run locally:

at the bottom of the page we can download the forward and reverse trajectories along with the input files, the NM and PC movies in pdb format and the 2D-projections.

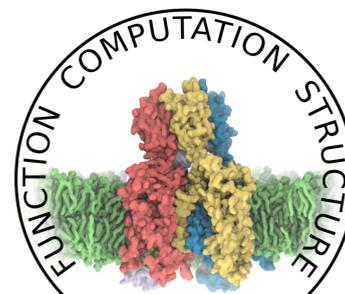
We recommend to download the projections and plot them coloring the points versus structure descriptors such as rMSD, key interresidue distances, etc



- All the examples of the eBDIMS benchmark (with input and output files) are publicly available in the server website, including those discussed in the original publication of the method (Orellana et al, 2016).

- For any questions or comments, contact us at:

ebdimserver@gmail.com



MOLECULAR BIOPHYSICS STOCKHOLM

- To download eBDIMS source codes and related software:

<https://github.com/laura-orellana/eBDIMS>

<https://github.com/cabergh/eBDIMS>

<https://github.com/ozyo/pdbParser>