BIGNASim: A NoSQL database structure and analysis portal for nucleic acids simulation data

Supplementary Material

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BIGNASim Supplementary Material can be also accessed at
http://mmb.irbbarcelona.org/BIGNASim/SuppMaterial/

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1 Database structure

BIGNaSim is based on the combination of two database engines, Cassandra and MongoDB, and an adapted version of the analysis section of our Nucleic Acids MD portal, NAFlex (1). For trajectory data manipulation, the platform uses MDPlus, an in-house python library that integrates MDAnalysis tools (2) with a developed Cassandra interface.

1.1 Cassandra. The trajectory subsystem.

Cassandra (3) is a distributed and highly scalable key-value database with a strong user community. Cassandra implements a non-centralized architecture, based on peer-to-peer communication, in which all nodes of the cluster are able to receive and serve queries. Data is stored in tables by rows, which are identified by a key chosen by the database user. In each row, users can add different attributes also identified by a chosen name. To each node of the cluster, a token is assigned and become responsible for hosting specific set of rows. The target node for each row is chosen through the partitioner algorithm and the decision is based on the row key and the node token. Cassandra also allows using compound keys and thus, more than one attributes to identify a row. In this case, the users have to specify the partition key (i.e. the attribute that will guide the node assignment) and the clustering keys. When a node receives a query, it finds out which node is responsible for each row involved in the query and partitions, and forwards appropriately the data request. This means that data modelling has a key influence on query performance (4). For this reason, users are encouraged to define their data models considering which queries they are going to perform. Moreover, a common practice is to replicate data in different data models to accommodate different queries. Recently, the authors proposed a mechanism to alleviate users from this requirement (5).

Table S2. Cassandra trajectory database structure.

| Topology table (idSimulation) | Trajectory table (idSimulation) |
|------------------------------|---------------------------------|
| atom_num (Partition Key)     | frame (Partition Key)           |
| atom_name                    | atom_id (Clustering Key)        |
| atom_type                    | x                               |
| chain_code                   | y                               |
| residue_code                 | z                               |
| residue_num                  | (Box size data is included in the same frame as additional pseudo-atoms) |

The Cassandra subsystem (Table S2) was organized in two tables: Topology holds the description of the molecular system using atom number as main indexing key, and storing the atom details, and the usual logical ways of grouping them (residue, chain). The Trajectory table stores the coordinates themselves indexed using frame and atom numbers. Cassandra is a distributed system, and the selection of the partition key has a strong influence on the retrieval efficiency. In our implementation, trajectory data is distributed using frame numbers, improving the retrieval of frame blocks. Indeed, by defining the frame number as Partition Key, we ensure that all the atomic coordinates at a given snapshot are stored contingently in the same node.
Additionally, each frame has atomic identifiers as a second level index, allowing efficient access to any subset of atoms. We have chosen to prioritize frame-based access, after analysing the pattern of access of the MDAnalysis software, used to handle trajectory data. MDAnalysis, constrained by its interface, always access to trajectory a frame at a time. Consequently, with our model the existing algorithms can access to a trajectory in Cassandra seamless, as if it was a common file. At the same time, algorithms that require data of only a subset of atoms may be optimized to take advantage of the second level indexing. To move trajectory data in and out of the Cassandra subsystem, the use of the Python package MDPlus assures a full compatibility with existing molecular dynamics software. Still, when dealing with massive bulk data loading into the database, the overhead introduced by the network communications and the data marshalling between different platforms can be a problem. For that reason, we developed a utility program that takes as input a trajectory file and converts it directly into SSTables, the Cassandra internal data format.

1.2 MongoDB. The analysis and metadata subsystem

The MongoDB database holds simulation metadata and pre-calculated analysis results. MongoDB is a fully flexibly engine and can store heterogeneous collections of documents. The internal structure of each document does not need to be defined beforehand and can match the data structure used in the interacting software, thus simplifying the use of database documents and external analysis software. MongoDB also allows to partition data among different servers (data sharding), using any of the fields as partition key. In our case, the data of the analysis requires both frame-based and atom-based access, hence we have chosen the complete document key as sharding key (See Table S3 below). Although MongoDB is configured with a single entry-point, it processes access queries in parallel among the available nodes, so maximum efficiency is achieved when data is spread evenly among them.

A condition to make the database usable is a very consistent indexing schema, which allows an easy recovery of such documents. Table S3 shows the database collection list together with the primary keys used to store the different objects. Table S4 shows representative data objects as stored in the DB.
Table S3. Structure of main MongoDB collections

| MongoDB collection | Main Index components | Description |
|--------------------|-----------------------|-------------|
| simData            | idSim                 | Simulation metadata, following a specifically defined ontology |
| analDefs           | idSim, idAnal         | Analysis description, one document stored for every analysis result item available. Analysis available could differ from one simulation to another |
| groupDef           | IdSim, (idGroup,nGroup)| Molecular groups (bases, base pairs, base-pair steps, molecular fragments) defined in the simulated system |
| analData           | idSim, (idGroup,nGroup), nFrame (nFrame = 0: Averaged analysis data) (nGroup = 0: All system analysis) | Analysis results. The most appropriate data model for each analysis type is used. |
| analBinFiles       | Id. Above             | Binary files with pre-calculated analysis results (plots, images, etc.) |

1.3 Representation of molecular fragments

MongoDB BIGNASim database has been populated using in-house scripts, and parsing the results obtained from the series of well-known software of analysis implemented in NAFlex (1). Definition of residues and standard groups (nucleotides, base-pair, and base-pair steps) are generated automatically from the simulated sequence and stored in the groupDef collection. Besides of predefined standard groups, the collection can store the definition of any relevant fragment of the simulated molecular system. As a representative example or groupDef structure, Figure S2 shows the complete hierarchy derived from the central tetramer of a Drew-Dickerson dodecamer.

The complete structure of such objects can be found in Table S5. Once the fragments are defined, their id (composed by idSim, idGroup, and nGroup, see Table S3) are used to index analysis results in analData and analBinFiles collections. As shown in Figure S2 above, and Table S5, the collection also holds a hierarchical relationships indicating which are the components of each fragment from the immediate lower level; this allows to navigate from any group down to its composing parts, and to the individual bases (see Use Case 4, for an example of such usage). This would allow linking together analysis corresponding to the related hierarchical levels. At the residue level, the MongoDB analysis subsystem is consistent with data hold in the trajectory subsystem (i.e. idGroup + nGroup corresponds to residue_code + residue_num). As shown in Table S2, results of the analyses are again stored in the three axes space: simulation, the analysed group (split in group id and sequence number for convenience), and frame number. In addition, averages along the trajectory and analysis spanning the whole system can be stored in the same structure. This layout will allow retrieving easily any set of results for any given set of groups and frames and performing the appropriate post-process. Although most data can be retrieved from the BIGNASim portal, more specialized data combination would require specific scripts. See Examples of Use below for sample codes of
such scripts using MongoDB JavaScript. Similar scripts can be prepared using other programming languages (Python, Perl, PHP, or Java). Analyses that may lead to non-numerical results (XY plots, 3D grids, etc.) are also stored under the same coordinate system, although they are kept in a separate collection (analBinFiles) for efficiency reasons. This database layout could be extended to any new type of analysis, without modification, after an appropriate mapping of each individual data item in the group/frame axes. Additionally, the GridFS system provided by MongoDB has been used to handle file based data transfers between application modules, and to hold the temporary user space used for downloading data.

Figure S2. Example of fragment definition on the analysis database. Database entries in groupDef collection derived from the central tetramer of a Drew-Dickerson dodecamer. Primary keys of each data item are indicated. Arrows indicate a container relationship between data objects. Simulation id has been deleted from keys for simplicity.

2 Data Ontology

A strong requirement to organize any field of knowledge is the agreement in the terminology used. This has been a concern in Bioinformatics and has led to the development of a number of ontologies describing several aspects of the discipline (6-9). Here we have developed a partial data ontology to describe Nucleic Acids simulations. Its contents are used to qualify simulations, and power the search facility. Simulation browser tables, and simulation details (Figure S1B) include the set of keywords derived from the ontology. In its present state ontology represents merely a set of normalized terms, but it has been developed in a separate project and will be documented elsewhere. Table S6 show a categorized list of ontology terms.
3 Procedure and instruction to deposit new trajectories in BIGNASim

BIGNASim accepts submissions to incorporate new trajectory data to the repository. Submitted datasets should correspond ideally to finished studies, described by one or more journal publications. Datasets can consist in one or several trajectories. To maintain the consistency of the repository, uploaded trajectories will be limited to 5,000 frames. Authors however, should assure accessibility to the complete trajectories on-demand. Solvent should be removed but ions may remain when its presence is relevant to the study. Authors should assure that the trajectory is of high quality, fulfilling a specific quality checklist (see below), and provide enough metadata to allow to efficiently index the study within the database.

3.1 Submission requirements

The following requirements should be met for a simulated dataset be acceptable in BIGNASim:

1. Dataset should be supported by a scientific publication. Publications in press or submitted could be acceptable, but data will be kept on-hold until the publication is publicly available, and eventually removed if this does not happens after a reasonable time. One or more datasets can be derived from a single publication, but all of them should be referred explicitly in the paper or Supplementary Material. In this sense, BIGNASim could be used as on-line Supp. Material for the publication, provide that enough processing time is allowed.

2. Dataset should correspond to Molecular Dynamics simulation trajectories of nucleic acids (DNA, RNA, PNA), alone or complexed with protein or small ligands.

3. Submitted trajectories should correspond to 5,000 frames, representing the complete simulation time. Solvent should be removed. Ions can be maintained if necessary to the aim of the study. Trajectories should be imaged and individual frames superimposed. Trajectory can be split in multiple files if necessary. Table S7 indicates the available formats.

4. Trajectories should be accompanied by a topology file in the appropriate format that should match the contents of the trajectory files. PDB files are acceptable as topologies. BIGNASim uses MDAnalysis (2) for handling trajectory and topology formats. Refer to MDAnalysis documentation for additional information (Table S7).

5. Submission should include a series of mandatory metadata items (Table S7), but we encourage providing metadata covering the entire ontology (Table S6).

6. Trajectories should fulfil the quality requirements shown in Table S7. Quality will be further checked as part of the analysis step performed in the database.
3.2 Submission procedure

Before starting the submission procedure, authors should prepare the following material:

- One or several trajectory files with a total length of 5000 frames. Chose the frequency of frames to cover the entire simulation. Solvent should be removed, and trajectories properly imaged and superimposed. Acceptable formats appear in Table S7.
- A topology file matching the trajectory file(s). Acceptable formats appear in Table S7
- A quality checklist (Table S7)
- A copy of relevant publications regarding the dataset, unless openly available

1. Register in BIGNASim. Indicate in the registry the intention of deposit new datasets, and follow the instructions.

2. Upload the necessary files (trajectories, and topology) to the workspace. Http upload is provided. For large datasets where transmission could be problematic, other procedures can be arranged.

3. Click on Initiate Deposition to open the Deposit form, and follow the instructions herein. Most Fields are mandatory. Alternatively, a file containing such information can be uploaded to the workspace. A template for this file can be obtained from the web site.

4. The form will allow indicating the uploaded files that correspond to the submission. As a submitted dataset could contain more than one simulation, topology and metadata should be provided for every simulation included. Facilities are provided to allow re-using metadata among trajectories.

5. Click on Complete Submission to start the process. After completing the submission, an accession number will be issued, and a status file will appear in the workspace. Data will be blocked and maintained on-hold until it has been processed. To modify eventually the contents of the submission, contact our team.

6. Trajectories will be checked and the set of BIGNASim analysis will be performed. A detailed log of the analysis performed will be available. The status file will be updated accordingly. In the eventual case that any of the analysis will fail due to issues in the incoming data, authors will be informed and asked to amend the problem. In the absence of errors, the dataset will be incorporated to the database and made public immediately or at the indicated date if any. Note that analysis procedure may take some time.
### Example screenshots of the submission procedure

#### Step 1: File submission

**Dataset** - Group a collection of simulations into a dataset to better search and administrate your data

| Dataset name (*) | Dataset description |
|------------------|---------------------|

**Dataset publication (*)**
- Release once submission is accepted
- Valid dataset until certain date
- The dataset has not a reference publication yet
- Proposed documentation will be uploaded on the following version
- Reference publication is the following

**Files to submit** - Select the files that will compose your submission. Only those files previously uploaded to the workspace can be here selected.

| **Trajectory Files** (*) | **Topology Files** (*) | **Simulation metadata** | **Dataset Documentation** |
|--------------------------|------------------------|--------------------------|----------------------------|
| File Name | File Format | File Name | File Format | File Name | File Format | File Name | File Format |
| Select from uploaded files | * | Select from uploaded files | * | Select from uploaded files | * | Select from uploaded files | * |

(*) Indicates the obligatory fields
4 Software Download

BIGNASim is composed of a rather large and complex set of software units, besides of requiring the installation of two NoSQL database platforms. The installation of local copy of the
server is not generally recommended. However, in cases where data is sensitive, and must be kept private, or for testing purposes an installable reduced version of the software is available. Local stand-alone installations will not be connected with the main BIGNASim database, unless specific agreement in such direction is achieved. Downloadable software will be tuned to avoid the need of an external database system, although they will have the full functionality of the analysis portal. This would obviously limit the amount of data to be handled, but offers a system capable enough to fulfil the needs of a simulations group to a certain extent. Due to the complexity of the software structure, the installable package is being prepared in prepacked Docker images.

4.1 Hardware and software requirements

Local BIGNASim could be installed in any modern Linux system (it has been tested on Ubuntu, and openSuSE). Note that the installation procedure requires reasonable skills in system administration, and root privileges. The downloadable system is designed to run in a single computer or inside a virtual machine.

1. To run BIGNASim Docker images, a Docker server is required. Instructions to install Docker can be found at Docker web site (http://www.docker.com). Note that Docker requires root privileges to be installed. Docker images can be run as part of a virtualized system, refer to Docker instructions to choose the appropriate configuration. Docker should be installed in all nodes performing analysis, but it is not required in database nodes.

3. Download installation package from BIGNASim site. Use the information provided to download Docker images, and perform the basic installation. A series of launching scripts will be created.

4. Install script will ask for data directories for raw trajectory data, and analysis results. These directories should be accessible locally or NFS mounted. Raw trajectory data could be removed after the analysis is performed, but analysis results should be a permanent storage.

5. Follow README files for detailed instructions to install trajectory data.

5 Examples of Use

BIGNASim has been designed in a way that advanced data analysis can be performed straightforwardly, even for types of analysis that were not known at the time of the design. The following cases show some representative examples of the possibilities of data manipulation. Most of the examples can be done within the portal, and are already available as tutorials in BIGNASim web site. The power of the BIGNASim is to store raw data in structures that allow an
easy recovery and combination, either from the analysis or from the trajectory databases. Simple scripts can be used to query the databases and obtain the required analyses. Scripts examples shown here are written in Javascript, the natural language for MongoDB, but most popular scripting languages can be also used. Additional information can be found at BIGNASim Help site.

5.1 Obtaining information about the Drew-Dickerson dodecamer

This use case shows several examples on using the BIGNASim search engine to locate a particular nucleic acid sequence, nucleic acid fragment or base pair step. The search section of the portal is accessed through the main menu:

The search section contains three different possibilities:

- Search by sequence or specific sequence fragments (using regular expressions)
- Search by specific base-pair-steps (with or without flanking regions)
- Search by an extensive nucleic acids ontology (see below)

Examples will show the way of finding three different types of information from the database:

- Information related to the well-known Drew-Dickerson Dodecamer (DDD)
- Information related to the AT Base-Pair Step (central in DDD)
- Information related to a naked duplex B-DNA structure with a particular nucleotidic fragment

5.1.1 Drew Dickerson Dodecamer (DDD)

In this case, the nucleotide sequence of the DDD (CGCGAATTCGCG) can be just searched using the “Search by Sequence” section of the portal:
Javascript code examples

// Finding DDD simulations
SimulationList = db.simData.find({'sequence': 'CGCGAATTCGCG'}).toArray()

// Finding simulations containing DDD sequence using regular expressions
SimulationList = db.simData.find({'sequence': /[CGCGAATTCGCG]/}).toArray()

// Finding simulations containing DDD sequence using possible variations
SimulationList = db.simData.find({'sequence': /^[CGCGA[AC]TTCGCG]/}).toArray()

Due to the importance of DDD in the field, it is specifically included in the Sequence Features section of the nucleic acids ontology, and can be located directly:

Javascript example code

// Finding DDD simulation from ontology search
SimulationList = db.simData.find({'ontology': '10603'}).toArray()

Both access ways open a browse page showing the simulations stored in the database for this particular sequence. In this case, 5 different trajectories are found, the longest one having
10 μs. Each of the simulations can be open individually to look at the MD simulation metadata and trajectory analyses. Combined information from more than one simulation can be obtained, by selecting the desired entries and clicking at **Open analyses for selected simulations**.

5.1.2 AT Base-Pair Step (central in DDD)

The central base-pair step of DDD (CGCGAATTCGCG) can be obtained from the **Search by**

**Javascript equivalent code**

```javascript
// Finding simulations containing AT BpStep with 2 flanking bases
SimulationList = db.simData.find( 
    {'sequence':/..AT../},
    {id:1} 
).toArray();
// Finding simulations containing AT BpStep on any strand
// (not needed for ApT due to symmetry)
SimulationList = db.simData.find(
    {$or:[ {'sequence':/..AT../}, {'rev-sequence':/..AT../} ]},
)
In the selector, the desired base-pair step, in this case AT, must be chosen. There is also the possibility to add a number of required flanking nucleotides, to ensure that information obtained will not be from base-pair steps placed at terminal regions, which can show distorted flexibility parameters. In this example, two flanking nucleotides are forced. The same procedure can be applied for any base-pair step.

The results obtained for the AT base-pair step with the current content of the database are 51 different simulations. Looking at the sequence column, the interesting AT pair, together with the flanking region, can be easily identified thanks to the marking in yellow and orange colours, respectively. The first thing that can be seen in the browse page is that the database contains simulated systems different from DDD containing also the AT base pair. Specifically 46 sequences, some of them having more than one occurrence of it, are recovered. That offers enough information to compare between the flexibility parameters obtained for just the 5 sequences of DDD obtained in the previous section of this example with the remaining sequences having the AT base pair. To exclude DDD simulations from the recovered analyses, selector of records shown should be set to the maximum (100 records): 1) select all

```javascript
[{ _id: 1 }
).toArray();
```
simulations by using the checkbox placed at the left part of the table header, next to the **Id. title**, 2) Filter results using DDD in the Search box, and uncheck all, 3) Remove the DDD filter.

The final step consists on clicking at the **Open Analyses for selected simulations** button at the bottom of the browse page, which will lead to the analysis section of BIGNASim.

In this section, the **AT base-pair step** button will open the available analyses for the AT bp-step. In order to compare the results with the ones corresponding to the **AT base-pairs** from just DDD sequences, the procedure can be repeated for these particular simulations, using an additional browser window.
Continuation Javascript code to retrieve analysis data for ApT steps

```javascript
(idSim = SimulationList[i].idSim;

// retrieve the position of the AT bpSteps (stored as class: 'ATAT')
ATPos = db.groupDef.find(
    {'_id.idSim': idSim, 'class': 'ATAT'},
    {_id: 1}
).toArray()

// obtain available data for a given group
dataCur = db.analData.find(
    {'_id.idSim': idSim, '_id.nGroup': ATPos[i].id.n, '_id.idGroup': ATPos[j].id.idGroup}
);
while (dataCur.hasNext()) {
    printjson(dataCur.next());
}
```

5.1.3 Naked duplex B-DNA structure with a particular nucleotide fragment

The third example shows a more specific search: trajectories having the **DDD** central tetramer (**AATT**), computed on **naked B-DNA duplex** structures, simulated in **equilibrium** conditions, and **electroneutral** charge schema. **AATT** sequence should be included in the **Search by Sequence** section; and then the search refined using the **Search by Ontology**
In the Search by Ontology section, search can be refined using keywords organized in a series of groups. In this case, the keywords chosen should be DNA in Nucleic Acid Type area, Duplex in Structure area, Naked in System Type area, Equilibrium in Trajectory Type, B in Helical Conformation, and, finally, Electroneutral in Simulation Conditions, Ionic Concentration. Every time a search parameter is chosen, the search engine computes the number of results stored for the current selected refinement specification and shows it on-the-fly in the top right part of the Search by Ontology section.
// Finding simulations containing TTAA fragment with 2 flanking bases
// TTAA is palindromic, only one strand need to be considered
// ontology tags: 'DNA' (10101), 'Duplex' (10202),
// 'Naked' (10301), 'B' (10402)
// 'Equilibrium' (20201), 'B', 'Electroneutral' (2010501)
// further check on subclasses has been eliminated for clarity
SimulationList = db.simData.find(
    { 'sequence': /..TTAA../, 'ontology': { $all: ['10101','10202','10301','2010501','20201']} },{_id:1}).toArray();

Again, the results are shown in a browse page. Descriptions show the keywords assigned to each simulation, and confirm that results are indeed duplex naked B-DNA structure simulations, as defined in the search. Still, results obtained contain a sequence different than the DDD having the AATT tetramer: 1rvh (GCAAATTTTGC). For the rest of DDD trajectories, the differences rely on the particular simulation parameters used in the MD, e.g. solvent type, ionic parameters or total length.

From the list of simulations, flexibility analyses can be obtained independently, or combined, clicking at Open Analysis for selected simulations button, or a meta-trajectory with this particular nucleotide fragment can be generated, joining atomic coordinates of the selected set
of simulations. More details on how to build a meta-trajectory with BIGNASim can be found at the section 5.3.

5.2 Visualization of global analysis based in xCGy fragments

The example shows the procedure to extract information from the Global Analyses section of BIGNASim portal. The simple study shown here can be extended to a real use case: the importance of flanking nucleotides in the flexibility of base-pair steps. The effect of the tetranucleotide environment in the sequence-dependent polymorphism of particular base-pair steps has been the target of recent studies. The CG base pair step used for example, shows an interesting bimodal behaviour in one of the six helical base-pair step parameters: Twist (10).

In the study, authors claim that the effect of the flanking bases in the CG base pair step is crucial for the existence of two different conformers: High Twist (HT: ~40°) and Low Twist (LT: ~ 20°). Behaviours for each of the 16 possible tetramers including CG are reported. To illustrate the power of BIGNASim database and its interface, two analyses have been chosen: ACGC showing almost no bimodality, and GCGA showing a clear bimodality. The first step uses the Search section of the portal → Search by sequence (GCGA).

Javascript equivalent code

```javascript
// Direct search of GCGA fragments on both strands
SimulationList = db.simData.find({
   $or: [{'sequence':/GCGA/}, {'rev-sequence': /GCGA/}]
});

// Alternatively search both on only one strand using complementarity
SimulationList = db.simData.find({'sequence':/(GCGA|TCGC)/});
```

In this case, more than 40 simulations containing this particular fragment are available for selection.
Retrieve Analysis for the selected simulations at the bottom of the page, leads to a Global Analyses page, showing the results for the particular GCGA fragment. Since the interest is studying the possible bimodality showed by the CG base pair step in its Twist parameter when it is surrounded by G and A (GCGA), the CG button should be selected:

### Javascript code hint

```javascript
// Available data for all CpG bpstep (in any simulation, and any sequence // position) can be retrieved at using just its idGroup: CGCG
DataforAllCpG = db.analData.find( {'_id.idGroup' : 'CGCG' } );
```

```javascript
// For a simulation SIM and position POS
Datafor1CpG = db.analData.find( {'_id.idSim': SIM, '_id.nGroup': POS, '_id.idGroup': 'CGCG' } );
```

Twist data can be obtained from “Curves → Helical_bpstep”
BIGNASim in its current version contains two kind of analysis for each of the six helical base-pair step parameters: one with the values for every snapshot of all the selected simulations, and one with the time-averaged values for each simulation. To show the bimodality, histogram with all the values for the Twist parameter should be chosen:

In the histogram plot, the average is represented as a vertical blue line, and the experimental value, used as reference, is represented as a vertical red line (see Example of use 5 for a detailed description of the use of experimental data).
Javascript code

// Code to retrieve twist values for a complete trajectory for a given Simulation "SIM",
// and CpG at position "POS"
twistData_c = db.analData.find(
    {'_id.idSim': SIM, '_id.nGroup': POS, '_id.idGroup': 'CGCG'}
).sort('_id.frame':1);
while (twistData_c.hasNext()) {
    Data = twistData_c.next();
    printjson (Data._id.frame + ' ' + Data.CURVES.helical_bpstep.twist);
}

The histogram shows two well defined populations, centred at \(-25^\circ\) and \(-35^\circ\), in good agreement with the previously presented study (10). To analyse the influence of the surrounding bases in the CG base pair step (tetramer influence), the procedure will be repeated seeking for the fragment ACGC. (Search by Sequence → Select All → Open Analysis for the selected simulations).

And CG → Curves → Helical_bpstep Analysis → Twist Analysis.

The new histogram do seems to follow a normal distribution, although a small shoulder to the low twist conformation can still be identified. The clear difference between the two plots show that the GCGA tetramer shows a clear bimodality, whereas the ACGC tetramer is more inclined to be in a High Twist conformation. Additionally, raw histogram data can be downloaded for further analysis.
Complete Javascript code to retrieve twist data from ACGC tetramers

```javascript
SEQ = 'ACGC';
RSEQ = 'GCGT';
/
Search for simulations bearing ACGC
SimulationList = db.simData.find(
    {'$or': [
        {'sequence': {$regex: SEQ}},
        {'rev-sequence': {$regex: RSEQ}},
        {'_id':1}
    ]}
).toArray();
// search for CpG fragments
FragsList = db.groupDef.find(
    {'_id.idSim': {$in: SimulationList}, 'class': 'CGCG'}
).toArray();
// Iterate over fragments
for (i=0; i < FragsList.length; i++) {
    twistData_c = db.analData.find(
        {'_id.idSim': FragsList[i]._id.idSim,
         '_id.nGroup': FragsList[i]._id.n,
         '_id.idGroup': 'CGCG'}
    ).sort('_id.frame':1);
    while (twistData_c.hasNext) {
        Data = twistData_c.next();
        printjson (Data._id.frame + ' ' + Data.CURVES.helical_bpstep.twist);
    }
}
```

5.3 Retrieval, and downloading of xCGy Meta-trajectories

The example show the procedure to build a meta-trajectory containing a particular nucleotide fragment using the BIGNASim portal. Example 3.2 has shown how to extract directly from the database the distribution of a particular helical parameter, recovering the Twist bimodality. However, one can be interested in study different properties, not pre-calculated in BIGNASim database. For that, there is the possibility to generate, download, or send to the NAFlex server a meta-trajectory containing just the nucleotide fragment of interest. It is built joining together the cartesian coordinates from a set of selected simulations stored in our database enclosing the fragment. To illustrate the power of BIGNASim database, the DB is searched for the 16 possible tetramers including CG base-pair, going from 2 (TCGG) to 49 (TCGC) occurrences (see table below), in the present database release.

| Tetramer | #Occurrences | Tetramer | #Occurrences |
|----------|--------------|----------|--------------|
| ACGA     | 5            | ACGG     | 17           |
| CCGA     | 6            | CCGG     | 7            |
| GCCT     | 43           | GCCT     | 15           |
| TCGA     | 9            | TCGG     | 2            |
| ACCT     | 10           | ACCT     | 4            |
| CCCT     | 6            | CCCT     | 11           |
| GCGC     | 19           | GCGT     | 5            |
| TCCT     | 49           | TCCT     | 3            |

As a quick example, we show here the generation of a meta-trajectory of one of the tetramers having less occurrences (ACGT, 4 occurrences). The same procedure could be used to generate meta-trajectories for all of the possible tetranucleotides including CG, thus obtaining
a valuable set of ensembles to analyse and compare. The first step of the procedure consists on accessing the **search section** of the portal from the main menu (see Example 3.1), to locate simulations of normal duplex B-DNA systems containing ACGT.
Results for this specific search are **3 simulations**. The information that will constitute the final meta-trajectory is the combination of all the selected trajectories, **1,290 µs** (500 + 500 + 290 ns). Note that if with the most represented tetramer including **CG** (TCGC) was chosen, the generated meta-trajectory would correspond to up to **39 µs** of simulated time, so this option should be used with care. Meta-trajectory can be obtained from the “Retrieve Meta-trajectory” button, after selecting the appropriate simulations.

The next step for generating the meta-trajectory is to define a desired frame step. In this case, **100 snapshots** as representatives of each trajectory will be extracted (**Frame input section:** **1:5000:50** (for snapshot 1 to snapshot 5000, every 50 snapshots). At this step, trajectory can be downloaded or sent to the **NAFlex** nucleic acid flexibility server.
As the generation of the trajectory is potentially a lengthy process, downloaded trajectories or meta-trajectories, a private user space is created where data is maintained. For registered users, the workspace is permanent, and data can be added in multiple sessions.

5.4 Analysis using fragments hierarchy. Correlation between CpG twist and ζ torsions.

The analysis of nucleic acids flexibility involves a large number of properties, from helical parameters, to hydrogen bonding or stacking energies, dihedral torsions, and distances, among others. Expert users usually combine such analyses in consistent ways, as they are highly correlated, and the combined study gives additional insight in the basis of conformational shifts. This practice requires to combine analyses done at different levels, the base-pair step (two contiguous base pairs), like twist or roll and analysis at the base pair level, like the hydrogen bonding pattern, or backbone torsions of the involved nucleotides. An expert DNA modeller has no problem on doing this manually, but it is a tedious and error-prone activity. BIGNASim includes the hierarchic relationships between sequence fragments (from individual bases to bp-steps), taken automatically (see Figure S1 and Table S5) from the simulation topology, and can be used to perform this kind of analysis in a straightforward way. We present here the necessary pipeline to analyse the correlation between CpG step twist and the ζ torsions of the neighbouring nucleotides. The high twist/low twist conformational change in the d(CpG) base
pair step is one of the most surprising sources of polymorphism in B-DNA. A detailed study of
the phenomena (11) is available. The study relates the twist polymorphism with the BI/BII
transitions related to \( \zeta / \epsilon \) backbone torsions. The key correlation analysis (See Figure 3 on
reference (10)) implies to obtain the Twist helical parameter of the CpG bp-step and the \( \zeta \)
torsion of the two G bases at 3’ of the CpG step. This specific analysis could be done through
the portal, obtaining the twist and \( \zeta \) as described in the previous examples, and downloading the
corresponding raw data. However to illustrate the power of the MongoDB database structure the
following Javascript code shows the pipeline required to obtain such combined set of data from
BIGNASim database.

**Javascript code pipeline to generate a combined analysis of a CpG base pair step Twist and \( \zeta \) torsions of 3’ G nucleotides in the “NAflex_DDD_800ns” simulation.**

```javascript
//Step 1. Locate available CpG bp-steps
// CpG bp-steps are indicated with an idGroup of CGCG.
// CpG is symmetrical, but in other
// cases both strands should be considered.
// The "Class" field combines both possible
// orientations.
var IDSIM = "NAflex_DDD_800ns";
var BPStep = "CGCG";
var BP1 = "CG";
Bpstps = db.groupDef.find({'_id.idSim': IDSIM, 'class': BPStep}).sort({'_id.n': 1}).toArray();

//Alternatively search can be extended to All simulations with CG bpSteps
//Bpstps = db.groupD

var TwCG = [];
var ZetaW = [];
var ZetaC = [];
printjson(Bpstps.length + ' ' + BPStep + ' found')

// Iterate over all CpG steps in the sequence.
for (i = 0; i < Bpstps.length; i++) {
  IDSIM = Bpstps[i]._id.idSim;

  //Step 2. Obtain relevant sequence positions.
  // CGpos: Sequence position (n) of first nucleotide in Watson strand.
  // It is part of the _id fragment key.
  // G1pos: Sequence position of the Watson 3’G: n + 1 nucleotide
  // G2pos: Sequence position of the Crick 3’G. It corresponds to the
  // complementary nucleotide on the first (n) base pair in the CpG step.
  // "comps" field relates CG base pair with its component nucleotides,
  // is this case comps[1] is the G nucleotide.
  CGpos = Bpstps[i]._id.n;
  G1pos = CGpos + 1;
  G2pos = db.groupDef.findOne({
    '_id.n': CGpos,
    '_id.idSim': IDSIM,
    '_id.idGroup': BP1
  }).comps[1].n;

  //Step 3. Collect twist values ordered by frame number.
  TwCG[i] = db.analData.find(
    {'_id.idSim': IDSIM,
     '_id.nGroup': CGpos,
     '_id.idGroup': Bpstps[i]._id.idGroup,
     'CURVES.helical_bpstep.twist': 1}
  ).sort({'_id.frame': 1}).toArray();

  // Step 4. Obtain \( \zeta \) torsions values ordered by frame number
  ZetaW[i] = db.analData.find(
    {'_id.idSim': IDSIM,
     '_id.nGroup': CGpos,
     '_id.idGroup': Bpstps[i]._id.idGroup,
     'CURVES.helical_bpstep.helix': 1}
  ).sort({'_id.frame': 1}).toArray();
```

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5.5 Combining Experimental and MD analysis

The example shows the information integrated in BIGNASim to compare theoretical results obtained with MD simulations with values obtained from experimental structures/trajectories. Comparison with experimental structures in BIGNASim is done at three different levels:

1. Individual helical parameters obtained from the corresponding experimental structure from the PDB
2. Averaged analysis of helical parameters from a complete dataset made from available nucleic acids experimental structures from the PDB
3. Experimental ensembles with PDB structures of equivalent sequences, analysed as pseudotrajectories, superimposed to the appropriate analysis

Individual helical parameters obtained from the corresponding experimental structure from the PDB

In those simulations having a reference PDB structure, the most direct analysis are the comparison between geometrical values extracted from the crystallographic structure and those averaged from the simulation trajectory. From the broad range of possible analyses, the helical parameters, and more specifically, the base-pair step helical parameters are the most used in the last scientific studies (see references section, Ascona B-DNA Consortium articles). In these cases, BIGNASim database store not only the analysis for the simulated trajectory, but also the ones computed on the original PDB structure. Then, just joining both information, a direct comparison can be obtained. The most interesting cases where this comparison can give valuable information are those nucleic acids complexed with protein or ligands. The typical helical conformation of the nucleic acid structure can be distorted due to the influence of the
attached molecule. Studying the time-averaged values for a determined simulated trajectory, with its standard deviation, can give a clue about whether the nucleic acid structure explores the conformation needed to accept the interacting molecule, or it needs a complete change of shape. Additionally, docking regions can be easily identified due to the helical parameters distortions shown (e.g. intercalator ligands). To illustrate the procedure a protein-nucleic acid complex, PDB Code 1hlv, will be chosen. The Quick Search section can be used to select all simulations available related to such PDB entry. Quick search does a global search in any of fields in the database, including ontology terms, or even sequences. It is particularly useful to identify simulations based on experimental structures.

In this case, “1hlv” is found both as PDB reference and in the internal identifier of the simulation. The description column shows the details of the specific simulation, showing that corresponds to “naked” DNA, meaning that the available simulation was done with just the nucleic acid portion of the complex; otherwise, the description would indicate “complex”. This can also be seen in the simulation details, where a straight DNA molecule is depicted.
This will be more evident looking at the helical parameters comparison with the experimental values, which correspond to the complexed conformation.

**Trajectory Analyses → Curves** gives the set of pre-computed helical analyses available

This will open the extended NAFlex interface included in BIGNASim. For a complete description of NAFlex analysis interface and its interactive sequence possibilities, please refer to NAFlex help pages (1). **Average Results** and **Inter-Base Pair Helical Parameters** should be selected.

This will show a set of six different inter-base pair step helical parameters: *Rise, Roll, Shift, Slide, Tilt and Twist*. Each of them have an associated plot with the comparison between the time-averaged theoretical results with the experimental ones. As example, the figure below shows results of the **Twist** parameter along the sequence. Four lines with different colours are shown: NAFlex_1hlv theoretical MD simulation in red, with standard deviation values; average values coming from a set of MD simulations (green) and X-ray structures (blue) (11) and finally the values computed to the corresponding 1hlv PDB experimental structure in violet. One can easily identify the regions of the nucleic acid where the protein is attached, disturbing
the helical conformation. The same analysis can be obtained for the rest of base-pair parameters.

Averaged analysis of helical parameters from a complete dataset made from available nucleic acids experimental structures from the PDB

The second way BIGNASim offers to compare theoretical and experimental values covers a more global vision of nucleic acids flexibility. For that, an averaged analysis of standard fragments (base, base pairs, and base-pairs steps) of a complete dataset made from available nucleic acids experimental structures (taken directly from the PDB), is included in global analyses. See BIGNASim corresponding help section for details of the pipeline to obtain such structures. These averaged values can be used to compare global values extracted from simulations having information from many different simulations on a single base, base pair, and base-pairs step and thus obtain a direct representation of how much our simulations reproduce the experimental observations. To illustrate how this information is added in the BIGNASim interface, the set of global analyses for the CG base-pair step will be used, but any other fragment can be analysed likewise. The procedure required is “Global Analyses → CG → CURVES → Helical_bpstep → Roll”
**BIGNASim** automatically generates a histogram with all the Roll values extracted from the database. Two vertical lines are plotted on the histogram: a blue one, indicating the mean for the represented set of values (MDs) and a red one, which corresponds to the experimental average value obtained from experimental structures.

![Histogram with Roll values](image)

In this case it can be easily seen that the observed values from the simulated systems agree pretty well with the experimental average. The distribution of values follows an almost perfect normal distribution, with the mean value (6.225) distant just 0.5 degrees from the experimental average value (7.35). A second base-pair step parameter, Twist show a different behaviour. It is known from reference (10) that CG-Twist show bimodality with a polymorphism between a high twist (~20°) and a low twist (~40°).
The difference with the previous Roll distribution is clear. In this case, two different distributions can be easily identified, centred at ~25º and ~35º. Interestingly, although the theoretical mean value (33.64) is close to the experimental one (30.66), both averages hide information about the bimodality.

Experimental ensembles with PDB structures of equivalent sequences, analysed as pseudotrajectories, superimposed to the appropriate analysis

The last experimental comparison in BIGNASim is done using analysis taken from experimental ensembles. The procedure to build such ensembles can be found in BIGNASim experimental trajectories help section. Having these experimental ensembles allows to compare theoretical values not just against experimental static information but also the ensemble of conformation found in experimental data. If a particular helical parameter exists in two different conformations (see previous section, CG-Twist example), that information can be obtained from the experimental ensemble and, thus, be compared with the MD simulation values. Unfortunately, due to the scarce number of deposited PDB structures for a determined nucleotide sequence, the number of generated experimental trajectories goes just up to 15 different ensembles (see experimental trajectories table). In this example, a particular structure will be used: a protein-DNA complex with PDB code 2LEF, the structure of a Lymphoid Enhancer-Binding Factor (Lef1 hmg domain, from mouse), complexed with DNA (15bp). As the deposited structure in the PDB was obtained by Nuclear Magnetic Resonance (NMR), it contains 12 different structures, what allows us to construct the experimental ensemble and compute the corresponding helical parameters. The simulation can be easily found from the search section (Search by Ontology → System Type → Complex: Protein-Nuc), and using its nucleotide sequence (CACCCTTGAAGCTC) in the Search by Sequence section, or just browsing the whole database and ordering the results by the id. Once in the simulation page, Trajectory Analyses show a specific section about comparison to experiment when this is available:
The path to obtain the compared analysis is "Average Results → Inter-BasePair Helical parameters"
Please note that direct access to this NAFlex interface for all the sequences having a calculated experimental trajectory is also available in the Experimental Trajectories help section. As this text is intended to be a tutorial, all the previous steps to get to this point are detailed. Two examples will be described: one single parameter (Roll), or two parameters (Roll and Twist).

This is the resulting Roll plot:
The plot shows two lines representing time-averaged values for the Roll parameter: red line corresponds to the MD simulation and green line corresponds to the experimental ensemble. It can be clearly identified a distorted region of the DNA, from the 4th to the 6th base-pair steps of the sequence, probably influenced by the attached protein. The available MD simulation (naked B-DNA) is not exploring these specific Roll values, so the experimental behaviour of the nucleic acid is in this case clearly influenced by the protein.

The Roll and Twist example can be followed in a similar way.

Analyses of helical parameters pairs are done for each of the base-pair steps present in the sequence. In this case, we have 6 different plots, corresponding to (AA/TT), AC, AG, CC/GG, CT, GA, GC and TG).
The following figure shows the base-pair step AA (TT) Twist vs Roll in more detail:

Information shown in these **3D plots** are points corresponding to the correlation between both parameters, where colours represent different population densities, from **higher density in yellow**, to **lower density in blue**. Experimental values are shown as **asterisk symbols in red colour**. As expected from the results found in the previous **Roll** plot, there is a strong deviation in the **Roll** parameter for some of the base-pair steps, placed in a region of the plot almost unexplored by the complete MD simulation. Unsurprisingly, they also have distorted values of the **Twist** parameter.

But comparisons are made also for **backbone torsions, axis base pairs and intra-base pair helical parameters**. As a last example, the following screenshots show a similar example with **Backbone Torsions**:
There are 4 different analyses available: BI/BII population and Puckering percentages, and two angle analysis: $\alpha/\gamma$, $\epsilon/\zeta$. We choose Backbone $\alpha/\gamma$ analysis:

The resulting plot shows the MD (black) vs the experimental (red) values:

No distortion is observed in this case, with the experimental ensemble exploring just a single conformation, whereas the MD simulation is exploring different well-known regions of the conformational space.
## Supplementary Tables

### 6.1 Table S1. Analysis types available in BIGNASim

| Analysis Type                                      | Fragment Scope | Available Data Types                                      | Software                  |
|---------------------------------------------------|----------------|----------------------------------------------------------|---------------------------|
| **Cartesian analysis**                            |                |                                                          |                           |
| • RMSd, RMSf, Radius of Giration, SASA             | Base           | Average values, Plot (Sequence), Plot (Time)             | pTraj (12), Gromacs (13)  |
| **Backbone geometry**                             |                |                                                          |                           |
| • BI/BII population                               | Base           | Average values, Plot (Sequence), Plot (Time)             | Curves+ (14)              |
| • Sugar puckering (N,E,S,W population)            |                |                                                          |                           |
| • Proportion of alpha/gamma torsions              |                |                                                          |                           |
| • Torsions ($\alpha$, $\beta$, $\gamma$, $\epsilon$, $\zeta$, $\chi$, phase) |                |                                                          |                           |
| **Translation Base Pair Axis**                    | Base Pair      | Plot (Sequence), Plot (Time)                             | Curves+ (14)              |
| **Rotational Base Pair Axis**                     | Base Pair      | Plot (Sequence), Plot (Time)                             | Curves+ (14)              |
| **Translation Base Pair Helical parameters**      | Base Pair      | Plot (Sequence), Plot (Time)                             | Curves+ (14)              |
| • Shear, Stretch, Stagger                         |                |                                                          |                           |
| **Rotation Base Pair Helical parameters**         | Base Pair      | Plot (Sequence), Plot (Time)                             | Curves+ (14)              |
| • Buckle, Opening, Propeller                      |                |                                                          |                           |
| **Translation Base Pair Step parameters**         | BP Step        | Plot (Sequence), Plot (Time)                             | Curves+ (14)              |
| • Rise, Slide, Shift                              |                |                                                          |                           |
| **Rotational Base Pair Step parameters**          | BP Step        | Plot (Sequence), Plot (Time)                             | Curves+ (14)              |
| • Roll, Tilt, Twist                               |                |                                                          |                           |
| **Groove dimensions**                             | BP Step        | Plot (Sequence), Plot (Time)                             | Curves+ (14)              |
| • Major and Minor grooves (depth, width)          |                |                                                          |                           |
| **Interactions**                                  |                |                                                          |                           |
| • Base Pair Canonical Hydrogen Bonds (distances)  | Base, BP Step  | Plot (sequence), Plot (Time), Contact Maps               | pTraj (12), in-house       |
| • Hydrogen Bond energies                          |                |                                                          |                           |
| • Stacking Energies                               |                |                                                          |                           |
| **Stiffness analysis**                            | Base Pair Step |                                                          | Curves+ (14)              |
| • Stiffness force constants (Twist, roll, Tilt, Rise, Shift, Slide) | Base, BP Step  | Plot (sequence), Plot (Time), Contact Maps               |                           |
| • Complete stiffness Matrix                       |                |                                                          |                           |
| **NMR Observables**                               |                |                                                          |                           |
| • Vicinal J-Couplings                             | Base           | Values, Plot (Time), 2D NOE Plots                        | in-house                  |
| • Nuclear Overhauser Effect (NOE)                 |                |                                                          |                           |
| **Principal component analysis**                  | Collective     | Values, Animated Traj, 3D view (JsMol) Projections Time Plots | PCASuite (15,16)          |
| • EigenValues & EigenVectors                      |                |                                                          |                           |
| • Collectivity index                              |                |                                                          |                           |
| • EigenVector Stiffness constant                  |                |                                                          |                           |
| • Animated Trajectories                           |                |                                                          |                           |
| • Trajectory projections                          |                |                                                          |                           |
| **Trajectory video**                              | Collective     | Standard video formats, 3D view                          | VMD (17)                  |


6.2 Table S2. Cassandra trajectory database structure.

| Topology table (idSimulation) | Trajectory table (idSimulation) |
|-------------------------------|--------------------------------|
| atom_num (Partition Key)      | frame (Partition Key)          |
| atom_name                     | atom_id (Clustering Key)       |
| atom_type                     | x                              |
| chain_code                    | y                              |
| residue_code                  | z (Box size data is included in the same frame as additional pseudo-atoms) |
| residue_num                   |                                |

6.3 Table S3. Structure of main MongoDB collections

| MongoDB collection | Main Index components | Description |
|--------------------|-----------------------|-------------|
| simData            | idSim                 | Simulation metadata, following a specifically defined ontology |
| analDefs           | idSim, idAnal         | Analysis description, one document stored for every analysis result item available. Analysis available could differ from one simulation to another |
| groupDef           | IdSim, (idGroup,nGroup) | Molecular groups (bases, base pairs, base-pair steps, molecular fragments) defined in the simulated system |
| analData           | idSim, (idGroup,nGroup), nFrame (nFrame = 0: Averaged analysis data) (nGroup = 0: All system analysis) | Analysis results. The most appropriate data model for each analysis type is used. |
| analBinFiles       | Id. Above             | Binary files with pre-calculated analysis results (plots, images, etc.) |
6.4 Table S4. Representative data structures stored in the MongoDB analysis subsystem.

Examples correspond to NAFlex_DDD_bsc1 simulation (Drew Dickerson dodecamer).
Analysis correspond to fragments labelled at position 5.

```json
{
  _id: 'NAFlex_DDD_bsc',
  dataset: 'ParmBSC',
  NucType: 'DNA',
  moleculeType: 'DNA',
  SubType: 'B',
  PDB: '1naj',
  sequence: 'GGCGAATTCGGCG',
  rev_sequence: 'GGCGAATTCGGCG',
  Parts: 'DNA+Iones',
  Chains: 'duplex',
  soluteResidues: 24,
  soluteAtoms: 758,
  soluteCharge: -22,
  CounterIons: 'Na+',
  IonicConcentration: 'Electroneutrality',
  totalIons: 0,
  totalAtoms: 758,
  AdditionalSolvent: 'No',
  solventResidues: 0,
  solventAtoms: 0,
  totalResidues: 24,
  AdditionalMolecules: 'No',
  Ligands: 'No',
  AdditionalIons: 'No',
  IonsParameters: 'Dang',
  ionsModel: '-',
  Water: 'TIP3P',
  Author: 'P.D.',
  Temperature: 298,
  forceField: 'parmbsc0',
  date: '06/23/15',
  saltConcentration: 0,
  totalCharge: -22,
  time: 10000,
  Format: 'netcdf',
  FrameStep: '20ps',
  Frames: 500000,
  Trajectory: 'DDD10micros_nowat.nc',
  Topology: 'DDD10micros_nowat.prmtop',
  RMSd_avg: 1.734,
  RMSd_stddev: 0.368,
  Comments: ',
  ontology: [10101,10402,10202,10301,10603,201010103,2010401,2010501],
  description: 'DNA|B|Duplex|Naked|DDD|ParmBSC1|TIP3P|Electroneutral'
}

// Analyses at base level (5-A)
{
  id: {frame: 0,idSim: 'NAFlex_DDD_bsc1',idGroup: 'A',nGroup: 5},
  CURVES: {
    backbone_torsions: {
      BI_population: [82.26],
      canonical_alpha_gamma: [97.22],
      puckering: [4.34,6.64,88.96,0.06]
    },
    NMR_JC: {
      J1p2p-DNA: [10.011,1.764], J1p2pp-DNA: [5.213,1.430],
      J2p3p-DNA: [6.309,0.999], J2pp3p-DNA: [2.276,1.734],
      J3pp4-DNA: [1.883,1.693]
    },
    NMR_NOE: {
      H1p-H2p: [3.0252,0.0806], H1p-H2pp: [2.3772,0.1157],
    }
  }
}
H2p-H3p: [2.3771, 0.1072], H2p-H4p: [3.7905, 0.0933],
H2pp-H3p: [3.7813, 0.1239], H1p-H4p: [3.5212, 0.6081],
H2p-H8: [3.6553, 0.3865], H2pp-H8: [2.4727, 0.4338],
H3p-H8: [4.6430, 0.4418], H4p-H8: [5.7722, 0.6122],

// Analyses at base pair level (5-AT)
{
  _id: { frame: 0, idSim: 'NAFlex_DDD_bsc1', idGroup: 'AT', nGroup: 5 },
  CURVES: {
    axis_bp: {
      inclin_avg: [3.44, 4.6],
      xdisp_avg: [-0.96, 0.7],
      ydisp_avg: [0.14, 0.5]
    },
    helical_bp: {
      buckle_avg: [5.62, 10.2], opening_avg: [1.87, 5.4],
      propel_avg: [-14.99, 7.7], shear_avg: [0.14, 0.4],
      stagger_avg: [-0.01, 0.4], stretch_avg: [0.03, 0.1]
    }
  }
}

// Analyses at base-pair step level (5-AATT)
{
  _id: { frame: 0, idSim: 'NAFlex_DDD_bsc1', idGroup: 'AATT', nGroup: 5 },
  CURVES: {
    grooves: {
      majd_avg: [5.71, 1.4], majw_avg: [11.93, 1.6],
      mind_avg: [4.95, 0.7], minw_avg: [5.22, 1.4]
    },
    helical_bpstep: {
      rise_avg: [3.37, 0.3], roll_avg: [1.21, 5],
      shift_avg: [-0.27, 0.6], slide_avg: [-0.48, 0.5],
      tilt_avg: [-2.38, 4], twist_avg: [36.35, 4.6]
    }
  },
  STACKING: {
    stW: [-7.1088648, 0.982759350869257],
    stC: [-1.435313399999999, 0.731727353308896],
    HB: [-11.045809, 1.1398008443553]
  },
  STIFFNESS: {
    FORCE_CTES: {
      PRD: [0.01606],
      MAT: [2.31756, 0., 0., 0.00173, 0., 0., 0., 0., 5.57878, 2.97746, 0., -0.01652, -0.20697, 0.2, 2.97747, 11.11783, 0., 0.04616, -0.16052, 0.00173, 0., 0., 0.04624, 0., 0., -0.01652, 0.04616, 0., 0.03597, 0.0064, 0., -0.20696, -0.16051, 0., 0.0064, 0.06717],
      rise_avg: [11.11783], roll_avg: [0.03597],
      shift_avg: [2.31756, 0.04624, 0.57878],
      tilt_avg: [0.04624, 0.06717]
    }
  }
}
Table S5. Complete structure of data objects showing hierarchical relationships derived from the central tetramer of the Drew-Dickerson dodecamer (A₅ATT)

//Fragment definition
// 5-AATT
// TTAA
{ 
  _id: { n: 5, idSim: '0001', idGroup: 'frag1' },
  type: 'fragment',
  fragment_end: 8,
  comps: [
    { n: 5, idSim: '0001', idGroup: 'AATT' },
    { n: 6, idSim: '0001', idGroup: 'ATAT' },
    { n: 7, idSim: '0001', idGroup: 'TTAA' },
  ]
}

//Base pair step definitions
// 5-AA
// TT
{ 
  _id: { n: 5, idSim: '0001', idGroup: 'AATT' },
  class: 'AATT',
  type: 'stepid',
  id: '5-AATT',
  comps: [
    { n: 5, idSim: '0001', idGroup: 'AT' },
    { n: 6, idSim: '0001', idGroup: 'AT' }
  ]
}

// 6-AT
// TA
{ 
  _id: { n: 6, idSim: '0001', idGroup: 'ATAT' },
  class: 'ATAT',
  type: 'stepid',
  id: '6-ATAT',
  comps: [
    { n: 6, idSim: '0001', idGroup: 'AT' },
    { n: 7, idSim: '0001', idGroup: 'TA' }
  ]
}

// 7-TT
// AA
{ 
  _id: { n: 7, idSim: '0001', idGroup: 'TTAA' },
  class: 'AATT',
  type: 'stepid',
  id: '7-TTAA',
  comps: [
    { n: 7, idSim: '0001', idGroup: 'TA' },
    { n: 8, idSim: '0001', idGroup: 'TA' }
  ]
}

//Base pair definitions
// 5-A
// T
{ 
  _id: { n: 5, idSim: '0001', idGroup: 'AT' },
  class: 'AT',
  type: 'bpid',
  id: '5-AT',
  comps: [
    { n: 5, idSim: '0001', idGroup: 'A' },
    { n: 20, idSim: '0001', idGroup: 'T' }
  ]
}

// 6-T
// A
{ 
  _id: { n: 6, idSim: '0001', idGroup: 'AT' },
  class: 'AT',
  type: 'bpid',
  id: '6-AT',
  comps: [
    { n: 6, idSim: '0001', idGroup: 'A' },
    { n: 20, idSim: '0001', idGroup: 'T' }
  ]
}
class: 'AT',
type: 'bpid',
id: '6-AT',
comps: [
  {n: 6, idSim: '0001', idGroup: 'A'},
  {n: 19, idSim: '0001', idGroup: 'T'}
]
// 7-T
// A
{  _id: {n: 7, idSim: '0001', idGroup: 'TA'},
  class: 'AT',
  type: 'bpid',
  id: '7-AT',
  comps: [
    {n: 8, idSim: '0001', idGroup: 'T'},
    {n: 18, idSim: '0001', idGroup: 'A'}
]
// 8-T
// A
{  _id: {n: 8, idSim: '0001', idGroup: 'TA'},
  class: 'AT',
  type: 'bpid',
  id: '8-AT',
  comps: [
    {n: 8, idSim: '0001', idGroup: 'T'},
    {n: 17, idSim: '0001', idGroup: 'A'}
]

//Base definitions
{  _id: {n: 6, idSim: '0001', idGroup: 'A'},
  class: 'A', type: 'bid', id: '6-A'
}
{  _id: {n: 7, idSim: '0001', idGroup: 'A'},
  class: 'A', type: 'bid', id: '7-A'
}
{  _id: {n: 8, idSim: '0001', idGroup: 'T'},
  class: 'T', type: 'bid', id: '8-A'
}
{  _id: {n: 9, idSim: '0001', idGroup: 'T'},
  class: 'A', type: 'bid', id: '6-A'
}
{  _id: {n: 17, idSim: '0001', idGroup: 'A'},
  class: 'A', type: 'bid', id: '17-A'
}
{  _id: {n: 18, idSim: '0001', idGroup: 'A'},
  class: 'A', type: 'bid', id: '18-A'
}
{  _id: {n: 19, idSim: '0001', idGroup: 'T'},
  class: 'T', type: 'bid', id: '19-T'
}
{  _id: {n: 20, idSim: '0001', idGroup: 'T'},
  class: 'T', type: 'bid', id: '20-T'
}
### Table S6. BIGNASim ontology terms

| Hierarchic Id | Label             | Description                          |
|---------------|-------------------|--------------------------------------|
| 1             | System            | Composition of simulated system      |
| 101           | NA_Type           | Type of Nucleic Acid                 |
| 10101         | DNA               | DNA                                  |
| 10102         | RNA               | RNA                                  |
| 1010201       | Viral             | Viral RNA                            |
| 1010202       | Synthetic         | Synthetic RNA                        |
| 1010203       | tRNA              | tRNA                                 |
| 1010204       | Messenger         | Messenger RNA                        |
| 1010205       | Ribosomal         | Ribosomal RNA                        |
| 10103         | DNA-RNA_Hybrid    | DNA-RNA Hybrid                       |
| 10104         | PNA               | PNA                                  |
| 10199         | OtherNA_Type      | Other NA Types                       |
| 102           | Architecture      | Architecture (strand organization)   |
| 10201         | SingleStrand      | Single Strand                        |
| 10202         | Duplex            | Duplex                               |
| 1020201       | Canonical         | Canonical WC pairing                 |
| 102020101     | Linear            | Linear duplex                        |
| 102020102     | Circular          | Circular duplex                      |
| 1020202       | Hogsteen          | Hogsteen pairing                     |
| 10203         | Triplex           | Triplex                              |
| 1020301       | ParallelTrip      | Parallel Triplex                     |
| 1020302       | AntiParallelTrip  | Antiparallel Triplex                 |
| 10204         | Quadruplex        | Quadruplex                           |
| 1020401       | Gloop             | Gloop                                |
| 1020402       | ParallelQuad      | Parallel Quadruplex                  |
| 1020403       | AntiparallelQuad  | Antiparallel Quadruplex              |
| 1020404       | IDNA              | I-DNA                                |
| 1020405       | IRNA              | I-RNA                                |
| 10205         | Holliday.Jnt      | Holliday junction                    |
| 10206         | 3Way.Jnt          | 3-Way junction                       |
| 10207         | RNA PseudoKnot    | RNA PseudoKnot                       |
| 10208         | Ribozymes         | Ribozymes                            |
| 10209         | Large Ribosomal RNA| Large Ribosomal RNA                  |
| 10210         | Riboswitch        | Riboswitch                           |
| 10211         | tRNA              | tRNA fold                            |
| 10212         | G1introns         | G1introns                            |
| 10213         | G2introns         | G2introns                            |
| 10214         | RNA nanostructures| RNA nanostructures                   |
| 10299         | OtherStructureType| Other structure types                |
| 103           | System_Type       | Type of complex involving NA         |
| 10301         | Naked             | Naked, uncomplexed                  |
| 10302         | Complex           | Complexed Nuc. Acid                  |
| 1030201       | Protein-nuc       | Complex Protein Nucl. Acid           |
| 103020101     | Enzymes           | Complexed with Enzyme                |
| 103020102 | Binding | Binding Proteins |
|-----------|---------|------------------|
| 10302010201 | Regulatory | Regulatory Proteins (Trans Factors, etc) |
| 10302010202 | SstrandBind | Single Strand Binders |
| 10302010203 | Nucleosome | Nucleosome proteins |
| 10302010299 | OtherBindProt | Other binding proteins |
| 1030202 | Ligand-nuc | Ligand - Nucleic Acid complexes |
| 103020201 | Intercalator | Intercalator |
| 103020202 | MinGBinder | Minor groove binder |
| 103020203 | MajGBinder | Major groove binder |
| 103020204 | HybridBinder | Hybrid binders |
| 104 | OriginalHelicalConformation | Original helical conformation of the Nucleic Acids |
| 10401 | A | A |
| 10402 | B | B |
| 10403 | Z | Z |
| 10404 | Hogsteen | Hogsteen |
| 10405 | MixedHConf | Mixed conformations |
| 10499 | OtherHConf | Other Conformations |
| 105 | SequenceModifications | Modifications of Nucleic Acids Sequence |
| 10501 | ModifiedNucleotides | Modified Nucleotides |
| 10502 | CrossLinked | CrossLinked |
| 10503 | EpigeneticVariants | Epigenetic Variants |
| 10504 | SequenceMismatches | Sequence Mismatches |
| 10599 | OtherSeqMod | Other modifications |
| 106 | SequenceFeatures | Relevant features related to sequence |
| 10601 | PolyA | Poly A Track |
| 1060101 | BrokenPolyA | Broken Poly A Track |
| 10602 | PolyG | Poly G Track |
| 10603 | DrewDickersonD | Drew Dickerson Dodecamer |
| 10604 | SeqMismatch | Sequence Mismatches |
| 107 | Local structures | Local structure features |
| 10701 | Kink Turn | Kink Turn |
| 10702 | Bulges | Bulges |
| 10703 | Internal loops | Internal loops |
| 10704 | Interacting loops | Interacting loops |
| 1070401 | Kissing loops | Kissing loops |
| 1070402 | Ring RNA | Ring RNA |
| 10705 | Hairpin loops | Hairpin or Stem Loops |
| 1070501 | Triloops | Triloops |
| 1070502 | Tetraloops | Tetraloops |
| 1071503 | Hexaloops | Hexaloops |
| 1071504 | tRNA Fragments | tRNA Fragments |
| 1071505 | Sarcin-Ricin | Sarcin-Ricin |
| 1071506 | TAR RNA | TAR RNA |
| 1071507 | IRES Domains | IRES Domains |
| 2 | Simulation | Simulation Data |
| 201 | SimConditions | Simulation settings |
| 20101 | ForceField | ForceField |
| ID         | Amber   | Cornell ForceField family          |
|------------|---------|------------------------------------|
| 2010101    | Parm99  | Parm99                             |
| 201010102  | ParmBSC0| ParmBSC0                           |
| 201010103  | ParmBSC1| ParmBSC1                           |
| 201010104  | ParmBSC0-OL1| ParmBSC0-OL1                   |
| 201010105  | ParmBSC0-OL4| ParmBSC0-OL4                   |
| 201010106  | ParmBSC0-OL1-OL4| ParmBSC0-OL1-OL4             |
| 201010107  | ParmBSC0-CG| ParmBSC0-Cheng/Garcia           |
| 2010102    | Charmm  | Charmm ForceField family           |
| 201010201  | Charmm36| Charm66                            |
| 2010199    | OtherFF | Other forcefields                  |
| 20102      | Length  | Length of simulations              |
| 2010201    | NanoSecondRange | Between 1 ns and 1 µs |
| 2010202    | MicroSecondRange | Over 1 µs                     |
| 20103      | Temperature | Simulation temperature          |
| 2010301    | Physiological | Physiological (around 298, 300K) |
| 2010302    | NonPhysiological | NonPhysiological             |
| 20104      | Solvent  | Solvent used in the simulation     |
| 2010401    | Water    | Water only                         |
| 2010402    | Mixed    | Mixture water and other solvent    |
| 201040201  | Wat-Ethanol | Water Ethanol mixture           |
| 20105      | Charge   | Charge model                       |
| 2010501    | Electroneutral | Counter ions to compensate NA charge |
| 2010502    | AddedSalt | Added counterions over charge compensation |
| 201050201  | Physiological | Physiological (0.15M)         |
| 201050202  | NonPhysiological | NonPhysiological            |
| 20106      | IonParam | Parameter used for ion description |
| 2010601    | Dang     | Dang                               |
| 2010602    | Cheatham | Cheatham                           |
| 202       | TrajectoryType | Type of trajectory related to conformation changes |
| 20201     | Equilibrium | Equilibrium (thermal fluctuations without major conf. Changes) |
| 20202     | Folding  | Folding or Unfolding              |
| 20203     | Transition | Transition between known conformations |
| 20299     | OtherTrajType | Other type of trajectory |

### Analysis

**Analysis:** any data derived from trajectories (simulated or experimental ensembles)

| ID | Analysis          | Description                                                                 |
|----|-------------------|-----------------------------------------------------------------------------|
| 301 | TimeScope         | Time scope of the analysis                                                  |
| 30101 | Snapshot         | Analysis made on a single snapshot                                          |
| 30102 | TimeAvg          | Time averaged analysis                                                       |
| 302  | FragmentScope     | Fragment scope of the analysis                                               |
| 30201 | SingleBase       | Analysis done on a single residue (base)                                    |
| 30202 | GroupAvg         | Analysis done on a group of residues                                         |
| 3020201 | BP               | Analysis done on a base pair (considering the main NA pairing)              |
| 3020202 | BPStep           | Analysis done on a base pair step (2 consequent base pairs, considering the main pairing) |
| 3020203 | SeqFragment      | Analysis done on other sequence fragments                                   |
| Code  | Type            | Description                                      |
|-------|-----------------|--------------------------------------------------|
| 30203 | FullSystem      | Analysis done on the complete system             |
| 30204 | Metatrajectory  | Analysis done on a group of trajectories         |
| 30205 | ExpStructure    | Analysis done on a experimental structure        |
| 303   | AnalysisType    | Type of analysis                                 |
| 30301 | BackboneTorsions| Backbone Torsions                                |
| 3030101| BI/BIPopulation | Proportion of BI/BII population                  |
| 3030102| SugarPuckering  | Sugar puckering populations (N,E,S,W)            |
| 3030103| AGCanonical     | Proportion of canonical alpha/gamma torsions     |
| 30302 | HelicalParam    | Helical parameters                               |
| 3030201| AxisBP          | Base Pair Axis parameters                        |
| 303020101| Xdisp         | X-Displacement                                   |
| 303020102| Ydisp         | Y-Displacement                                   |
| 3030202 | HelicalBP       | Base Pair Helical parameters                     |
| 303020201| HelicalBPTrans | Translational Base Pair Helical parameters       |
| 30302020101| Shear         | Shear                                            |
| 30302020102| Stretch      | Stretch                                          |
| 30302020103| Stagger      | Stagger                                          |
| 303020202 | HelicalBRRot   | Rotational Base Pair Helical parameters          |
| 30302020201| Buckle        | Buckle                                           |
| 30302020202| Opening       | Opening                                          |
| 30302020203| Propeller    | Propeller                                        |
| 3030203 | HelicalBPStep   | Base Pair Step Helical parameters                |
| 303020301| HelicalBPStepTrans | Translational Base Pair Step Helical parameters |
| 30302030101| Rise          | Rise                                             |
| 30302030102| Slide         | Slide                                            |
| 30302030103| Shift         | Shift                                            |
| 303020302 | HelicalBPStepRot | Rotational Base Pair Step Helical parameters   |
| 30302030201| Roll          | Roll                                             |
| 30302030202| Tilt          | Tilt                                             |
| 30302030203| Twist         | Twist                                            |
| 30303 | GrooveAnalysis  | Groove analysis                                  |
| 3030301| MajorGroove    | Major Groove                                     |
| 303030101| MajGDepth     | Depth of the Major Groove                        |
| 303030102| MinGWidth     | Width of the Major Groove                        |
| 3030302 | MinorGroove    | Minor Groove                                     |
| 303030201| MinGDepth     | Depth of the Minor Groove                        |
| 303030202| MinGWidth     | Width of the Minor Groove                        |
| 30304 | Interactions   | Analysis of interactions                         |
| 3030401| Hbonds        | Hydrogen bonds (distances)                       |
| 303040101| WC            | Watson-Crick Hydrogen Bonds                      |
| 30304199| Other         | Other Hydrogen Bonds                             |
| 3030402 | Stacking      | Stacking interactions                            |
| 30304201| Wstrand       | Stacking on the Watson Strand                   |
| Code    | Term                | Description                                                                 |
|---------|---------------------|-----------------------------------------------------------------------------|
| 303040202 | Cstrand             | Stacking on the Crick Strand                                               |
| 303040203 | Crossed             | Stacking between strands                                                   |
| 30305    | NMR                 | NMR observables                                                             |
| 3030501  | NOE                 | NOE                                                                         |
| 3030502  | JC                  | J-Couplings                                                                 |
| 30306    | Stiffness           | Stiffness analysis                                                          |
| 3030601  | ForceConstant       | Force Constants                                                             |
| 303060101 | Fctwist             | Fctwist                                                                     |
| 303060102 | Fcroll              | Fcroll                                                                      |
| 303060103 | Fctilt              | Fctilt                                                                      |
| 303060104 | Fcrise              | Fcrise                                                                      |
| 303060105 | Fcshift             | Fcshift                                                                     |
| 303060106 | Fcslide             | Fcslide                                                                     |
| 3030602  | ForceMatrix         | Matrix of stiffness constants (twist, roll, tilt, rise, shift, slide)       |
| 3030603  | ForceProduct        | DiagonalProduct                                                             |
| 30307    | TrajectoryVideo     | Video of Trajectory in standard formats                                     |
| 30308    | TrajectoryData      | Trajectory data                                                             |
| 3030801  | PCAZip              | Trajectory in PCZ format                                                    |
| 30309    | Cartesian           | Cartesian analysis                                                          |
| 3030901  | RMSd                | Root Mean Square Deviation (RMSd)                                           |
| 3030902  | RMSf                | Root Mean Square Fluctuation (RMSf)                                         |
| 3030903  | RadGyration         | Radius of Gyration                                                          |
| 3030904  | Bfactor             | B - Factor                                                                  |
| 3030905  | AvgStruct           | Average structure                                                           |
| 30310    | PCAnalysis          | Principal Component analysis                                                |
| 3031001  | EigenValues         | PCA EigenValues                                                             |
| 3031002  | NumberEV            | Number of PCA EigenValues for a given variance                              |
| 3031003  | EigenVal            | Vector of eigenValues                                                       |
| 3031002  | EigenVector         | PCA EigenVectors                                                            |
| 3031003  | TrajectoryProj      | Projections of trajectory                                                   |
| 3031004  | Animated trajectory | Trajectory animated following given eigenvectors                            |
| 3031005  | Entropy             | Entropy prediction                                                          |
| 3031005  | Schlitter           | Entropy prediction using Schlitter protocol                                 |
| 303100502 | Androcioaei        | Entropy prediction using Androcioaei protocol                               |
| 3031006  | Variance            | Variance measured in the trajectory                                         |
| 30311    | ContactMaps         | Contact Maps                                                                |
### 6.7 Table S7. Deposition requirements

| Acceptable topology formats | Preferred: PDB, Amber TOP, Gromacs GRO, ITP, RTP, NAMD PSF http://www.mdanalysis.org/mdanalysis/documentation_pages/topology/init.html |
|-----------------------------|-----------------------------------------------------------------------------------------------------------------------------|
| Acceptable trajectory formats | Preferred: DCD, CRD, XTC, PDB (Models), NetCDF, BINPOS http://www.mdanalysis.org/mdanalysis/documentation_pages/coordinates/init.html |

#### Minimum set of metadata

**Dataset Description**

- Description/aim of the study
- References for supporting publication(s)

**System Description**

- Reference experimental structure (PDB, NDB id)
- Type of Nucleic Acid, Main architecture (S. strand, Duplex, etc.), RNA type
- Composition (Naked NA, Complexes)
- Relevant sequence modifications or features
- Relevant local structures

**Simulation conditions**

- ForceField (type and precise version)
- Simulation length
- Simulation temperature
- Solvent and ions
- Charge settings, added salt
- Type of trajectory (equilibrium, folding/unfolding, transition)
- Number of frames, Time per frame

**Preliminary Analyses**

- RMSd, RMSd/bp, R. Gyration Variation, %Lost WC HBonds, %Lost 3D contacts
- Presence of fraying, Global avg. Roll (degrees), Global avg. Twist (degrees), Groove dimensions (specify measurement method)

**Orientative quality Checklist (applicable to equilibrium trajectories)**

| Simulation length | > 200 ns |
|-------------------|----------|
| RMSd*             | < 5 Å    |
| RMSd/bp*          | < 0.3 Å/bp |
| R. Gyration       | < 0.4 Å/bp |
| Lost H-Bonds SS* | < 20% |
|-----------------|-------|
| Lost 3D contacts* | < 30% |
| Maintenance of global fold | > 90% simulation time |

*RMSd: All-heavy atoms mass weighted. References should be the available experimental structure when available. When not available refer to canonical fiber data. & Applicable to average values in duplex segments
7 Supplementary Figures

7.1 Figure S1. BIGNASim portal screenshot. Expanded view of simulation summary.
A) Simulated system details; B) Simulation details and visualization; C) Access to analysis pages; D) Download trajectories or meta-trajectories
7.2 Figure S2. Example of fragment definition on the analysis database.

Database entries in groupDef collection derived from the central tetramer of a Drew-Dickerson dodecamer. Primary keys of each data item are indicated. Arrows indicate a "container" relationship between data objects. Simulation id has been deleted from keys for simplicity.
8 References

1. Hospital, A., Faustino, I., Collepardo-Guevara, R., Gonzalez, C., Gelpi, J.L. and Orozco, M. (2013) NAFlex: a web server for the study of nucleic acid flexibility. *Nucleic Acids Research*, 41, W47-W55.

2. Michaud-Agrawal, N., Denning, E.J., Woolf, T.B. and Beckstein, O. (2011) Software News and Updates MDAnalysis: A Toolkit for the Analysis of Molecular Dynamics Simulations. *Journal of Computational Chemistry*, 32, 2319-2327.

3. Lakshman, A. and Malik, P. (2010), SIGOPS Oper. Syst. Rev, Vol. 44, pp. 35-40.

4. Hernandez, R., Cugnasco, C., Becerra, Y., Torres, J. and Ayguade, E. (2015), Proceedings of the 23rd Euromicro International Conference on Parallel, Distributed, and Network-Based Processing, pp. 288-295.

5. Hernandez, R., Becerra, Y., Torres, J. and Ayguade, E. (2015), Proceedings of the International Conference on Computational Science, ICCS 2015, pp. 2822-2826.

6. Ison, J., Kalas, M., Jonassen, I., Bolser, D., Uludag, M., McWilliam, H., Malone, J., Lopez, R., Pettifer, S. and Rice, P. (2013) EDAM: an ontology of bioinformatics operations, types of data and identifiers, topics and formats. *Bioinformatics*, 29, 1325-1332.

7. Ashburner, M., Ball, C.A., Blake, J.A., Botstein, D., Butler, H., Cherry, J.M., Davis, A.P., Dolinski, K., Dwight, S.S., Eppig, J.T. *et al.* (2000) Gene Ontology: tool for the unification of biology. *Nature Genetics*, 25, 25-29.

8. Smith, B., Ashburner, M., Rosse, C., Bard, J., Bug, W., Ceusters, W., Goldberg, L.J., Eilbeck, K., Ireland, A., Mungall, C.J. *et al.* (2007) The OBO Foundry: coordinated evolution of ontologies to support biomedical data integration. *Nat Biotechnol*, 25, 1251-1255.

9. Hastings, J., de Matos, P., Dekker, A., Ennis, M., Harsha, B., Kale, N., Muthukrishnan, V., Owen, G., Turner, S., Williams, M. *et al.* (2013) The ChEBI reference database and ontology for biologically relevant chemistry: enhancements for 2013. *Nucleic Acids Research*, 41, D456-D463.

10. Dans, P.D., Faustino, I., Battistini, F., Zakrzewska, K., Lavery, R. and Orozco, M. (2014) Unraveling the sequence-dependent polymorphic behavior of d(CpG) steps in B-DNA. *Nucleic Acids Research*, 42, 11304-11320.

11. Dans, P.D., Perez, A., Faustino, I., Lavery, R. and Orozco, M. (2012) Exploring polymorphisms in B-DNA helical conformations. *Nucleic acids research*, 40, 10668-10678.

12. Roe, D.R. and Cheatham, T.E., III. (2013) PTRAJ and CPPTRAJ: Software for Processing and Analysis of Molecular Dynamics Trajectory Data. *Journal of Chemical Theory and Computation*, 9, 3084-3095.

13. Pronk, S., Pall, S., Schulz, R., Larsson, P., Bjelkmar, P., Apostolov, R., Shirts, M.R., Smith, J.C., Kasson, P.M., van der Spoel, D. *et al.* (2013) GROMACS 4.5: a high-throughput and highly parallel open source molecular simulation toolkit. *Bioinformatics*, 29, 845-854.
14. Blanchet, C., Pasi, M., Zakrzewska, K. and Lavery, R. (2011) CURVES+ web server for analyzing and visualizing the helical, backbone and groove parameters of nucleic acid structures. *Nucleic Acids Res*, 39, W68-73.

15. Meyer, T., Ferrer-Costa, C., Perez, A., Rueda, M., Bidon-Chanal, A., Luque, F.J., Laughton, C.A. and Orozco, M. (2006) Essential dynamics: A tool for efficient trajectory compression and management. *Journal of Chemical Theory and Computation*, 2, 251-258.

16. Camps, J., Carrillo, O., Emperador, A., Orellana, L., Hospital, A., Rueda, M., Cicin-Sain, D., D'Abramo, M., Lluis Gelpi, J. and Orozco, M. (2009) FlexServ: an integrated tool for the analysis of protein flexibility. *Bioinformatics*, 25, 1709-1710.

17. Humphrey, W., Dalke, A. and Schulten, K. (1996) VMD: Visual molecular dynamics. *Journal of Molecular Graphics & Modelling*, 14, 33-38.