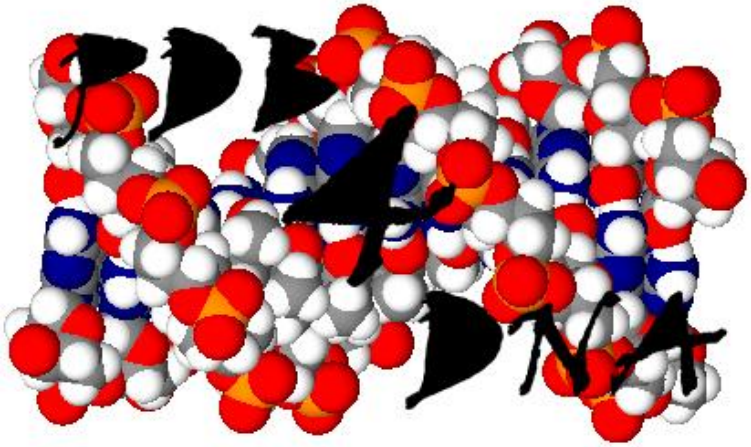

Hands-on pdb4dna

http://pdb4dna.in2p3.fr

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Hands-on **pdb4dna**

1

Scope of the application

- PDB files
- Integration into Geant4
- Algorithm to find the closest atom in DNA
- Strand breaks

2

Application

- Directory content
- Build the example
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- Run in batch mode

3

ROOT analysis

Hands-on **pdb4dna**

1

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ROOT analysis

PDB files - atomistic representation

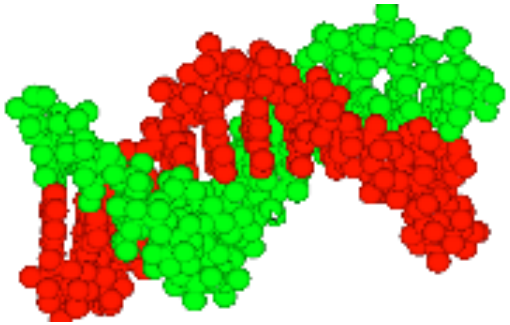
- Protein Data Bank files :
  - A way to **store** and **exchange** polyatomic structures (proteins, **DNA**)
  - File describing the **3D structural information** of molecules
  - A **worlwide free access** to files obtained experimentally by crystallography techniques or computed with geometry optimization codes http://www.rcsb.org/

- File format :
  - ASCII file '.pdb'
  - We mainly extract information from ATOM keyword

```
HEADER                    TRANSFERASE 19-APR-13 4BJP
TITLE   CRYSTAL STRUCTURE OF E. COLI PENICILLIN BINDING PROTEIN 3
...
JRNL    DOI 10.1371/JOURNAL.PONE.0098042
...
REMARK 200 EXPERIMENT TYPE : X-RAY DIFFRACTION
...
ATOM    265  C   ASP  A   149   -38.902  78.078  31.778 C
ATOM    266  O   ASP  A   149   -39.587  78.804  32.500 O
ATOM    267  CB  ASP  A   149   -36.407  78.326  31.747  C
...
TER     3106 ALA A 567
...
END
```

PDB files – DNA example 1/3

- 10 base pairs example – Molecule level



```
HEADER    DNA                          10BP EXAMPLE
...

MODEL     1

ATOM      1  O5'  A   1      9.256  -9.769   4.573  O
ATOM      2  C5'  A   1     10.679  -9.579   4.526  C
...
ATOM     33  OP1  A   2     12.795  -8.381   9.736  O
...
ATOM     65  P    A   3     11.850  -2.418  12.300  P
...
ATOM    445  O5'  A  10      1.100   5.570  32.583  O
TER     445       A  10

ATOM    446  O5'  B  14     -9.356  10.980  33.794  O
...
ATOM    688  C4   B  20      2.805   3.343   8.223  C
TER     688       B  20

ENDMDL
```

This file encodes DNA molecule

Start molecule

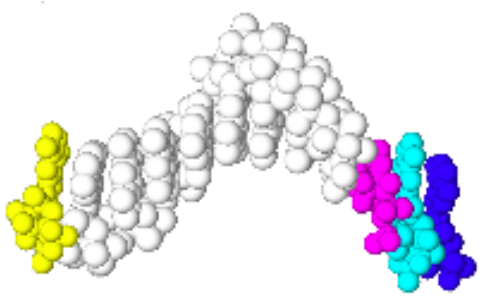
Atom coordinates – first strand (A)

Atom coordinates – second strand (B)

End molecule

PDB files – DNA example 2/3

- 10 base pairs example – nucleotide level

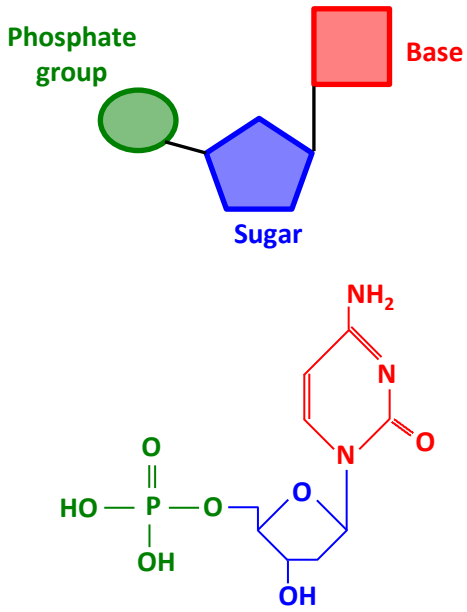


```
HEADER    DNA                          10BP EXAMPLE
…

MODEL    1

ATOM      1  O5‘  A   1     9.256  -9.769   4.573   O
ATOM      2  C5‘  A   1    10.679  -9.579   4.526   C
…
ATOM     33  OP1  A   2    12.795  -8.381   9.736   O
…
ATOM     65  P    A   3    11.850  -2.418  12.300   P
…
ATOM    445  O5‘  A  10     1.100   5.570  32.583   O
TER     445       A  10

ATOM    446  O5‘  B  14    -9.356  10.980  33.794   O
…
ATOM    688  C4   B  20     2.805   3.343   8.223   C
TER     688       B  20

ENDMDL
```

PDB files – DNA example 3/3

- 10 base pairs example – atomic level

Nucleotide structure



Cytosine nucleotide

```
HEADER    DNA                          10BP EXAMPLE
...

ATOM     65  P     DC A   3      11.850  -2.418  12.300      P
ATOM     66  OP1   DC A   3      15.242  -2.080  12.670      O
ATOM     67  OP2   DC A   3      11.107  -3.437  11.073      O
ATOM     68  O5'   DC A   3      12.981  -1.059  12.299      O

ATOM     69  C5'   DC A   3      11.563   0.189  11.896      C
ATOM     70  C4'   DC A   3      12.527   1.314  11.875      C
ATOM     71  O4'   DC A   3      11.455   0.915  11.029      O
ATOM     72  C3'   DC A   3      11.954   1.427  11.278      C
ATOM     73  O3'   DC A   3      12.405   2.645  11.894      O
ATOM     74  C2'   DC A   3      10.453   1.552  11.042      C
ATOM     75  C1'   DC A   3      10.249   1.499  11.527      C

ATOM     76  N1    DC A   3       9.058   0.693  11.174      N
ATOM     77  C2    DC A   3       7.998   1.341  10.557      C
ATOM     78  O2    DC A   3       8.060   2.547  10.316      O
ATOM     79  N3    DC A   3       6.897   0.610  10.230      N
ATOM     80  C4    DC A   3       6.836  -0.699  10.496      C
ATOM     81  N4    DC A   3       5.745  -1.381  10.158      N
ATOM     82  C5    DC A   3       7.924  -1.372  11.112      C
ATOM     83  C6    DC A   3       9.008  -0.643  11.454      C
...
```

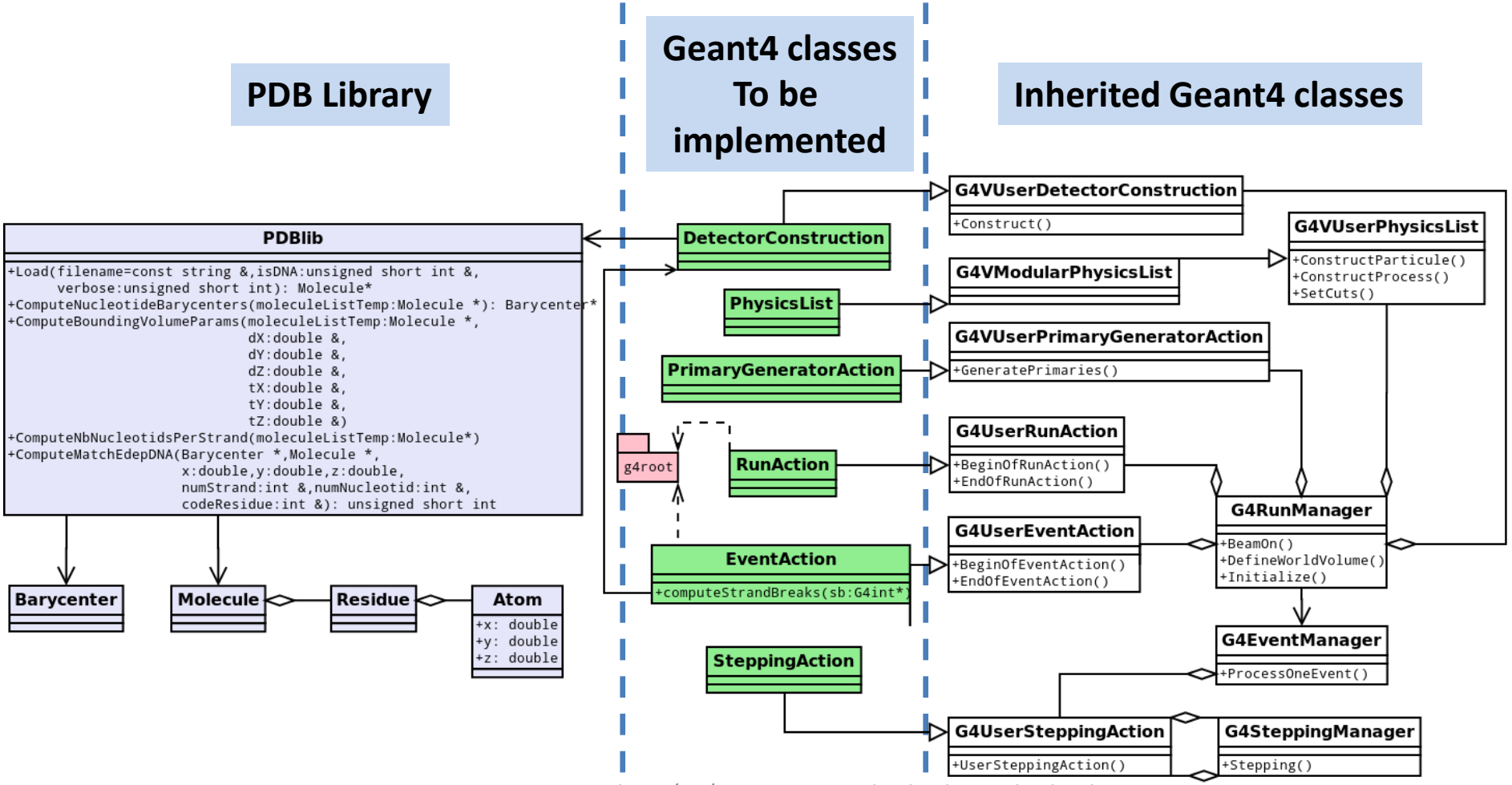
Phosphate group

Sugar

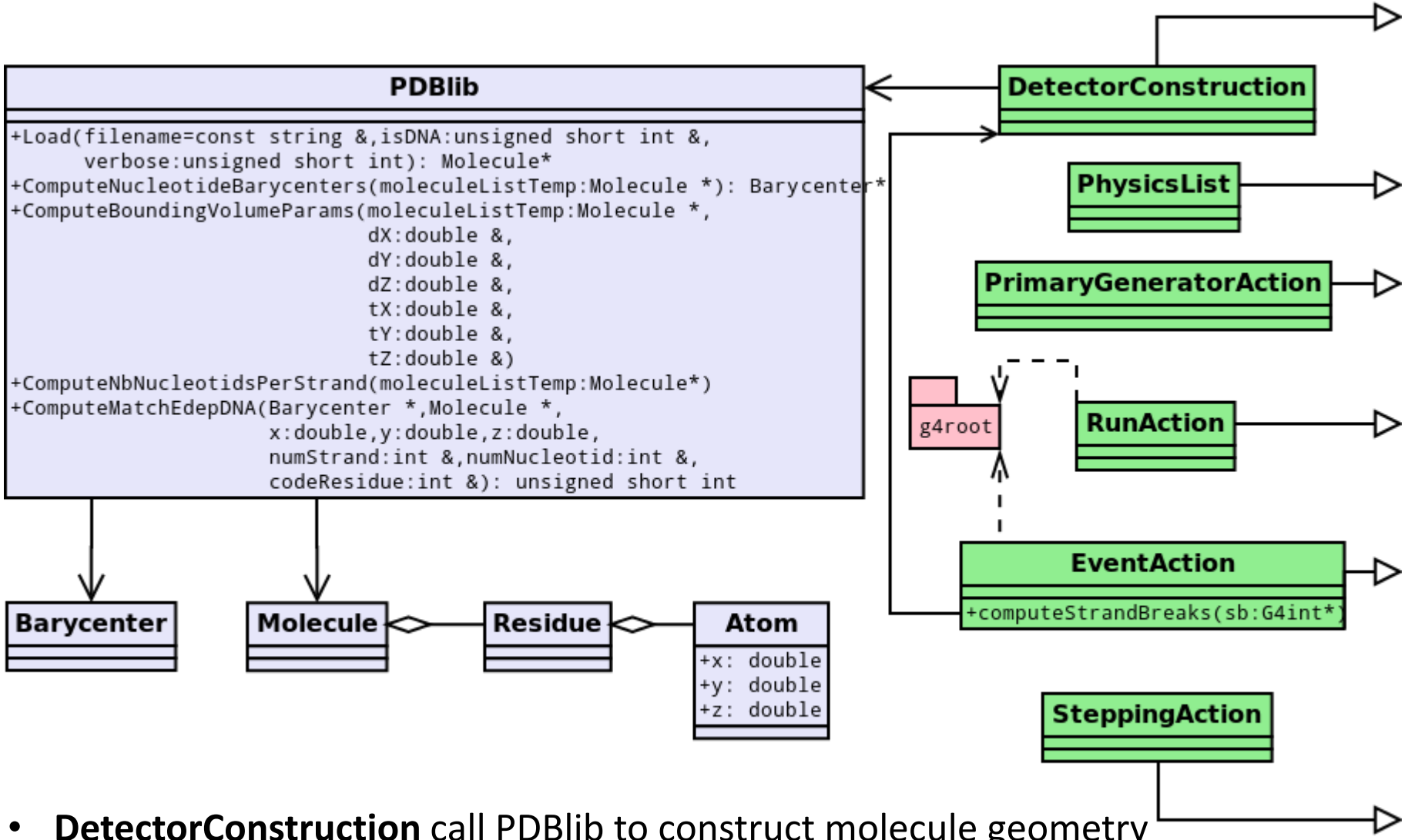
Base

Integration into Geant4 (1/2)

- Pdb4dna example will be provided in the next Geant4 release 10.1



Integration into Geant4 (2/2)

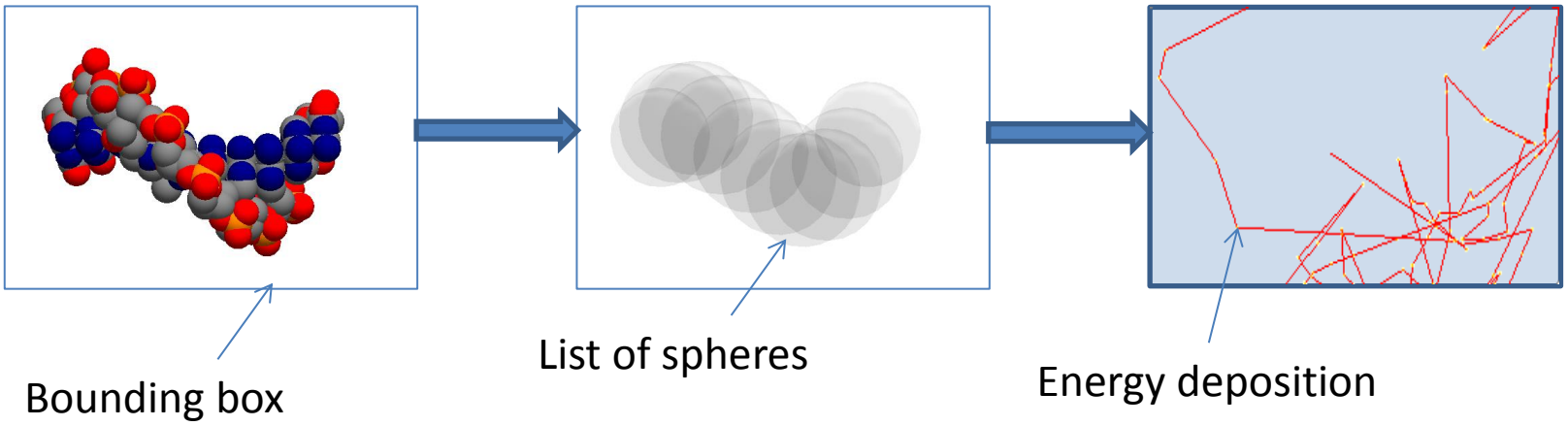


- **DetectorConstruction** call PDBlib to construct molecule geometry
- **EventAction** compute match between Edep and DNA via Detector construction

Algorithm to find the closest atom 1/2

Goal = allocate **energy depositions** to an **element** [sugar, phosphate, base] of nucleotides and then deduce SSB and DSB

- A **bounding box** is calculated with atoms coordinates
- No other Geant4 solid is needed for simulation
- We consider that a sphere is a good approximation to englobe a nucleotide. A **list of spheres** representing nucleotides is calculated
- DNA specific



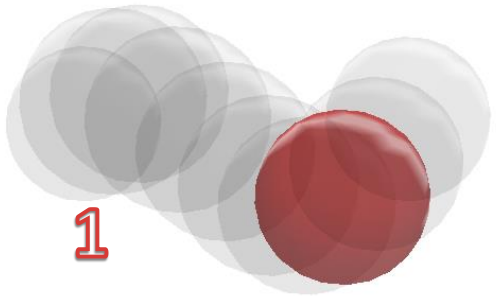
Algorithm to find the closest atom 2/2

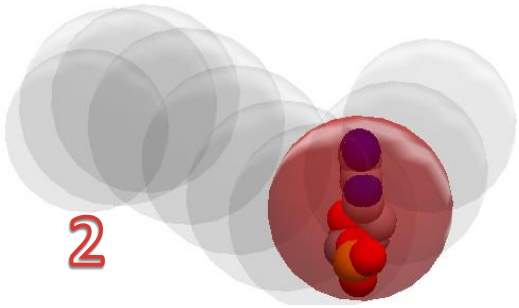
- 1 : Find the closest **nucleotide** from the energy deposition inside the two strands

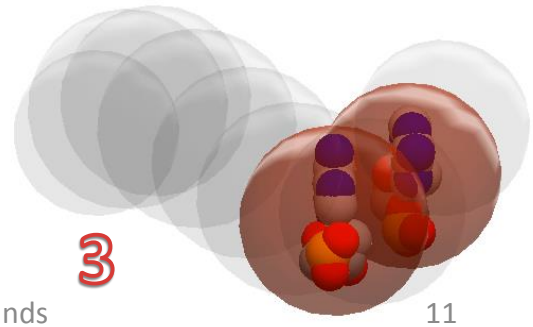
- 2 : Find the closest **atom** from the energy deposition
  - atom by atom inside the selected nucleotide
  - considering Van der Waals radii

- 3 : Due to sphere overlapping, find a better match in the next two nucleotides in the list

- 4 : Return algorithm response:
  - No DNA hit
  - DNA hit, return **nucleotide ID**, **DNA strand**, **group type** (sugar, phosphate or base)



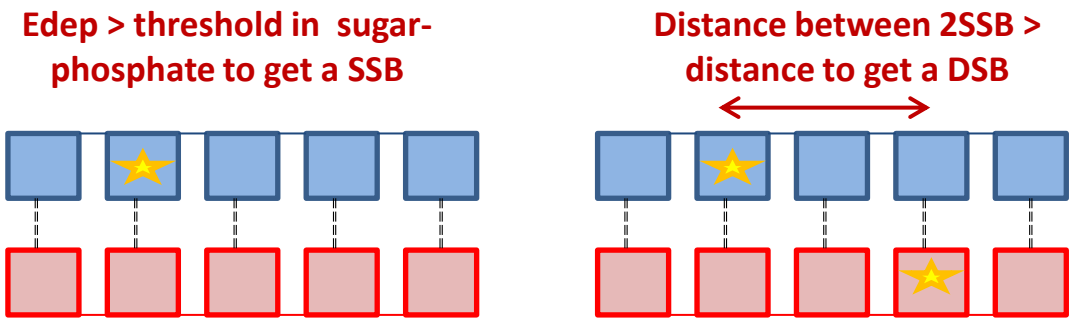




Strand breaks

- Begin of event:
  - A **map** for each strand is created to **store** nucleotide ID and associated energy deposition
- For each step:
  - If the step is in the bounding volume, increment energy deposition per event
  - Ask to PDBlib to **check** the step **position**
    - If the step is in a sugar or a phosphate: get nucleotide ID, strand number, energy deposit, **update** the **map** (ID, Edep+=StepEdep)

- End of event:
  - **Compute** and store **strand breaks**
  - Store energy deposit in the bounding volume



Hands-on **pdb4dna**

1

Scope of the application

- PDB files
- Integration into Geant4
- Algorithm to find the closest atom in DNA
- Strand breaks

2

Application

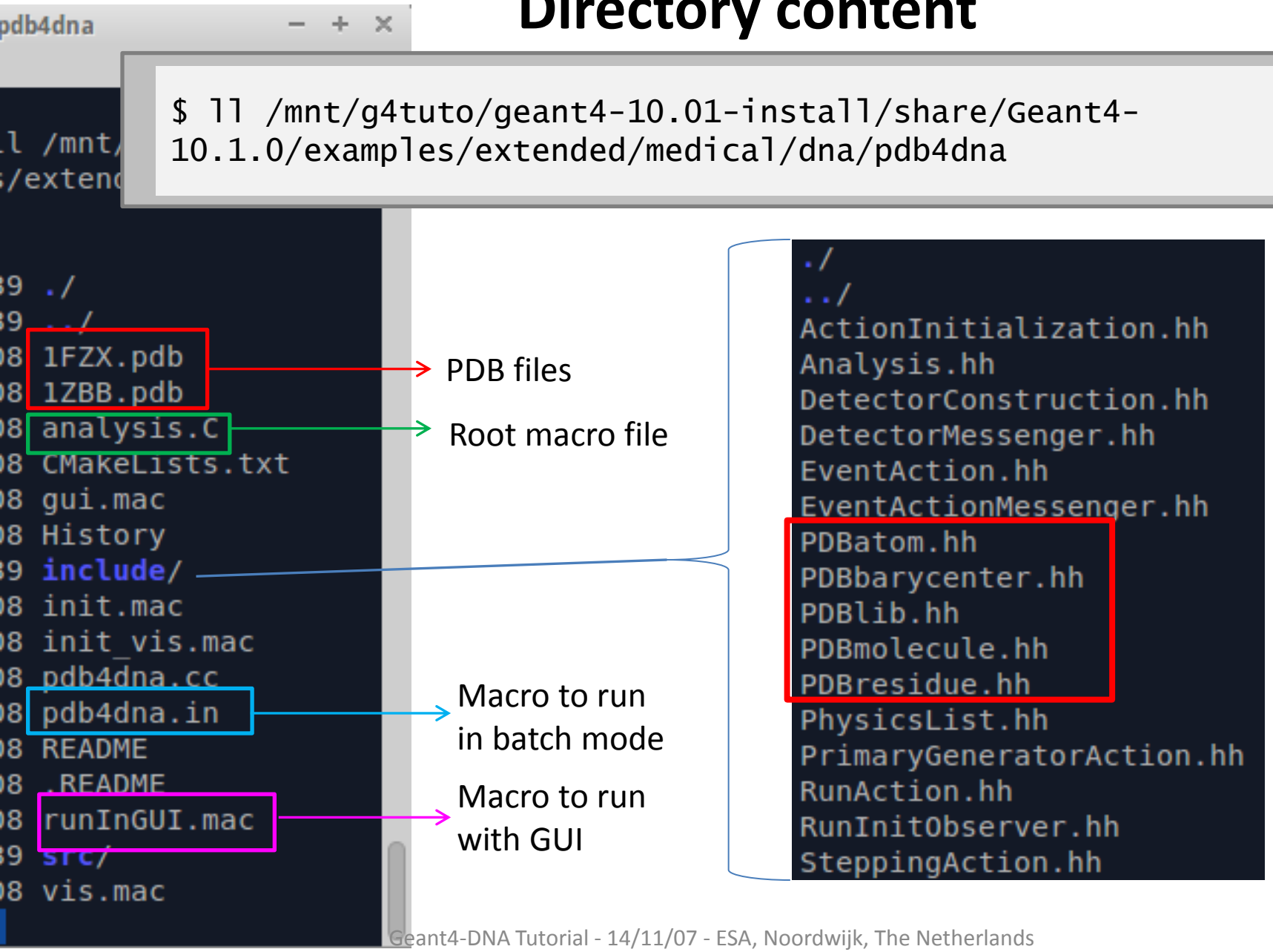
- Directory content
- Build the example
- Preparation before run
- Run with GUI
- Run in batch mode

3

ROOT analysis

Directory content

```
$ ll /mnt/g4tuto/geant4-10.01-install/share/Geant4-10.1.0/examples/extended/medical/dna/pdb4dna
```



Build the example (1/2)

```
$ module load geant4/10.01-mt
$ cd tutorial
$ cp -r /mnt/g4tuto/geant4-10.01-install/share/Geant4-
10.1.0/examples/extended/medical/dna/pdb4dna .
$ mkdir pdb4dna-build
$ cd pdb4dna-build
$ cmake ../pdb4dna
```

```
user@user-VirtualBox:~/tutorial/pdb4dna-build$ cmake ../pdb4dna
-- The C compiler identification is GNU 4.8.2
-- The CXX compiler identification is GNU 4.8.2
-- Check for working C compiler: /usr/bin/cc
-- Check for working C compiler: /usr/bin/cc -- works
-- Detecting C compiler ABI info
-- Detecting C compiler ABI info - done
-- Check for working CXX compiler: /usr/bin/c++
-- Check for working CXX compiler: /usr/bin/c++ -- works
-- Detecting CXX compiler ABI info
-- Detecting CXX compiler ABI info - done
-- Configuring done
-- Generating done
-- Build files have been written to: /home/user/tutorial/pdb4dna-build
user@user-VirtualBox:~/tutorial/pdb4dna-build$
```

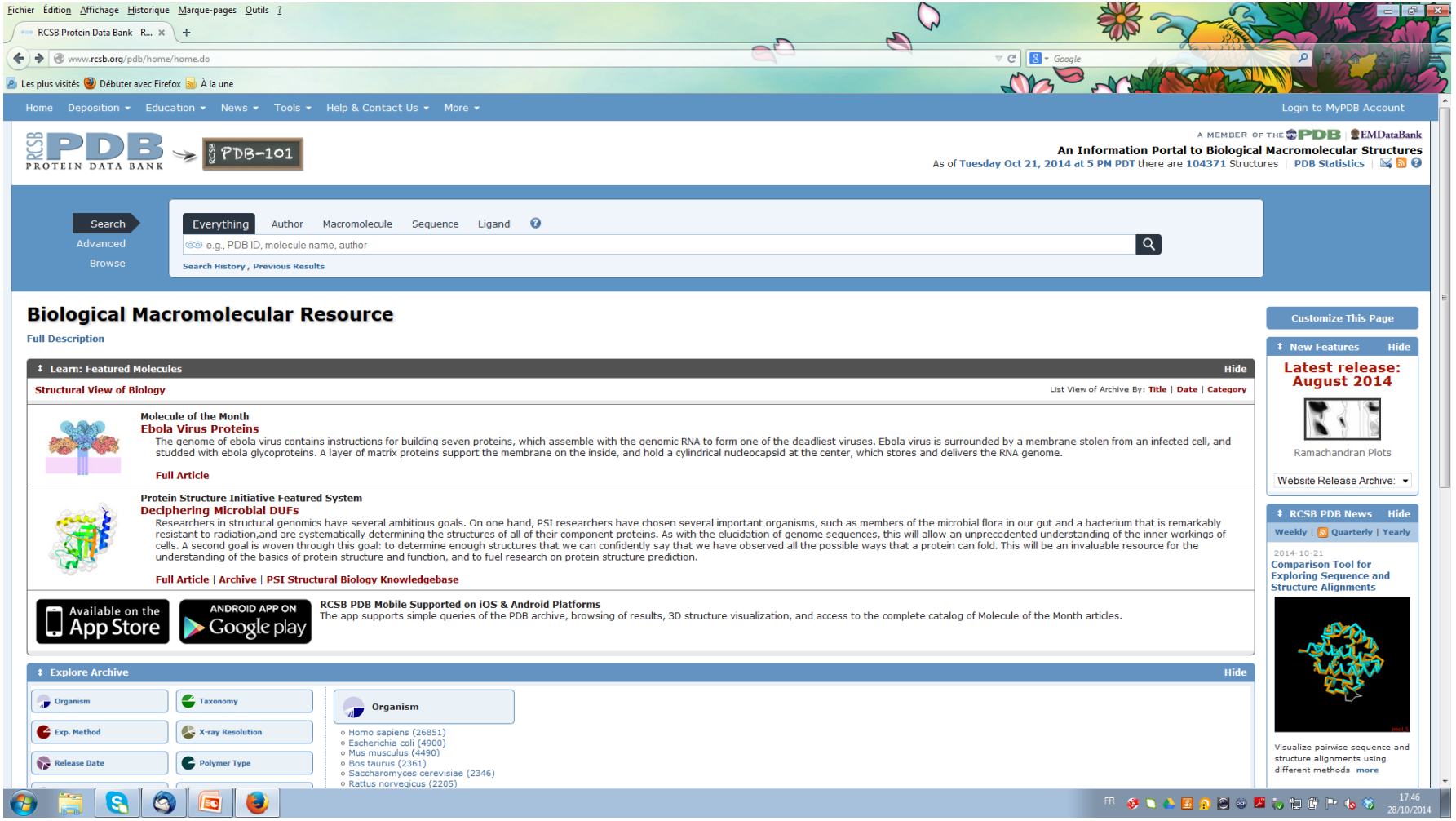
Build the example (1/2)

```
$ make -j2
```

```
user@user-VirtualBox:~/tutorial/pdb4dna-build$ make -j2
Scanning dependencies of target pdb4dna
[  6%] [ 12%] Building CXX object CMakeFiles/pdb4dna.dir/pdb4dna.cc.o
Building CXX object CMakeFiles/pdb4dna.dir/src/PDBlib.cc.o
[ 18%] Building CXX object CMakeFiles/pdb4dna.dir/src/RunAction.cc.o
[ 25%] Building CXX object CMakeFiles/pdb4dna.dir/src/SteppingAction.cc.o
[ 31%] Building CXX object CMakeFiles/pdb4dna.dir/src/PDBresidue.cc.o
[ 37%] Building CXX object CMakeFiles/pdb4dna.dir/src/PDBbarycenter.cc.o
[ 43%] Building CXX object CMakeFiles/pdb4dna.dir/src/DetectorMessenger.cc.o
[ 50%] Building CXX object CMakeFiles/pdb4dna.dir/src/PDBmolecule.cc.o
[ 56%] Building CXX object CMakeFiles/pdb4dna.dir/src/PrimaryGeneratorAction.cc.
o
[ 62%] Building CXX object CMakeFiles/pdb4dna.dir/src/RunInitObserver.cc.o
[ 68%] Building CXX object CMakeFiles/pdb4dna.dir/src/PhysicsList.cc.o
[ 75%] Building CXX object CMakeFiles/pdb4dna.dir/src/DetectorConstruction.cc.o
[ 81%] Building CXX object CMakeFiles/pdb4dna.dir/src/EventActionMessenger.cc.o
[ 87%] Building CXX object CMakeFiles/pdb4dna.dir/src/EventAction.cc.o
[ 93%] Building CXX object CMakeFiles/pdb4dna.dir/src/ActionInitialization.cc.o
[100%] Building CXX object CMakeFiles/pdb4dna.dir/src/PDBatom.cc.o
Linking CXX executable pdb4dna
[100%] Built target pdb4dna
user@user-VirtualBox:~/tutorial/pdb4dna-build$
```

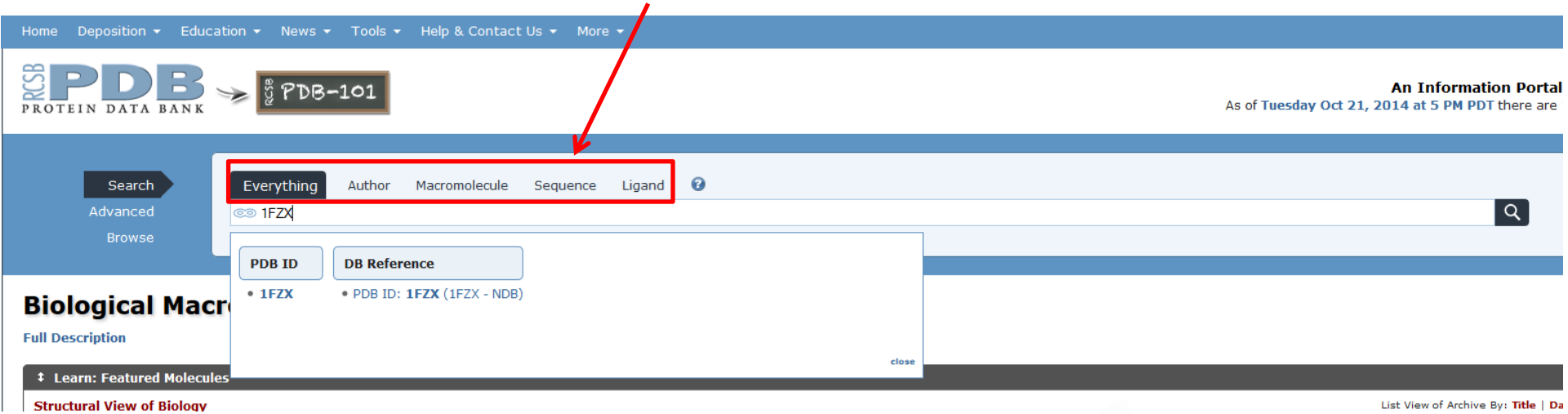
Preparation before run (1/3)

Visit Protein Data Bank website → http://www.rcsb.org/



Preparation before run (2/3)

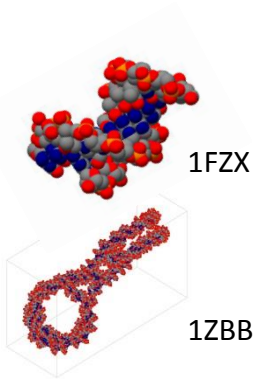
You can find a file by its name, type, sequence, etc…



For the tutorial, we look at:

1FZX file : 12 bp DNA strands (run with GUI)

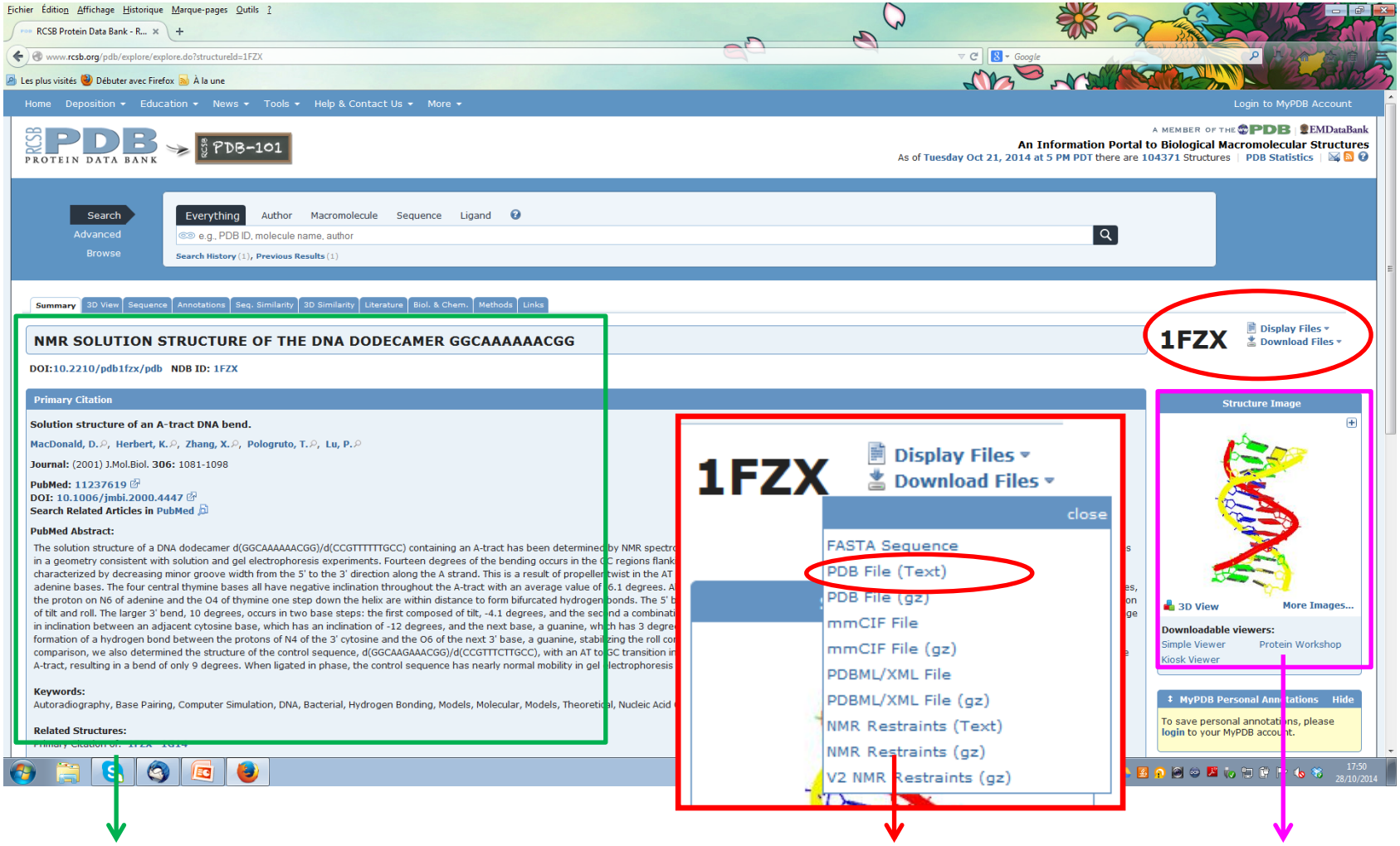
1ZBB file : dinucleosome (run in batch mode)



(Note that for the tutorial, those PDB files are provided in the pdb4dna directory)

« Do you know **1AOI.pdb**? »

Preparation before run (3/3)



Description of the molecule
References

Download the file

Online view
(require Java)

Run in GUI (1/4)

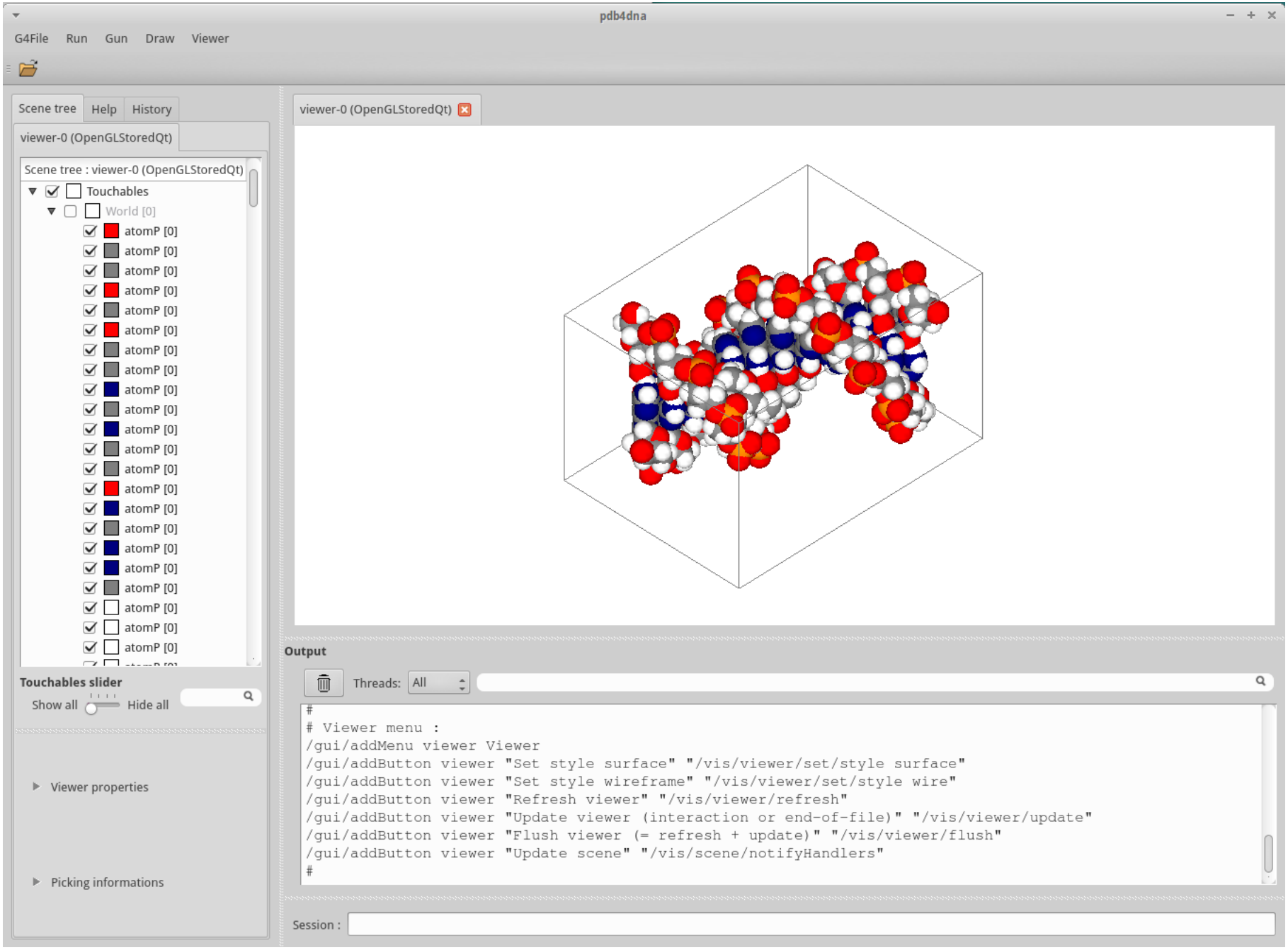
Due to GUI limitation, if you want to select a file into open file dialog you need to rename the extension from pdb to mac.

```
$ cp file.pdb file.mac
```

Run GUI

```
$ ./pdb4dna
```

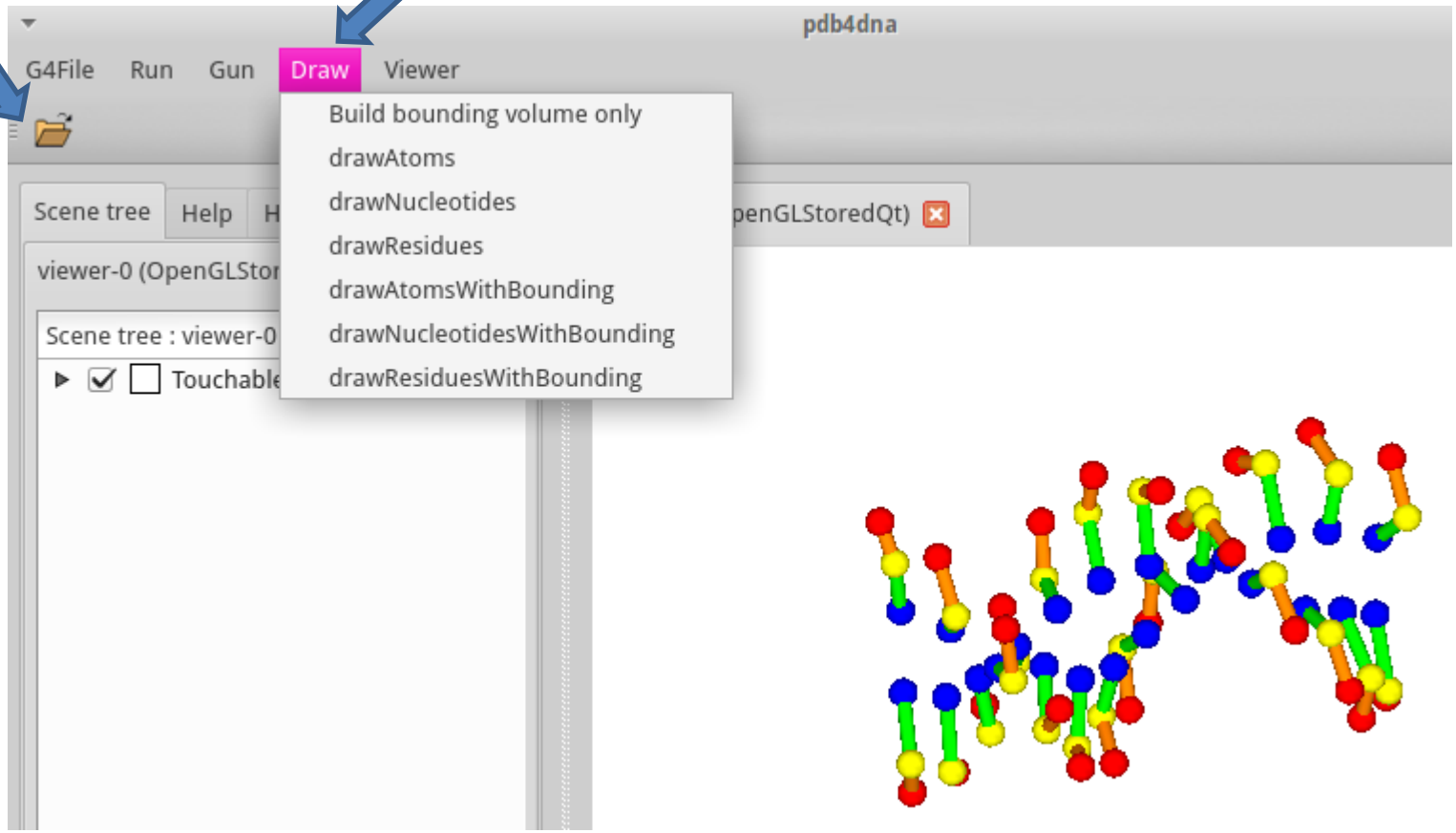
Becarefull, the command will change in the next release to: `./pdb4dna -gui`


pdb4dna
G4File
Run
Gun
Draw
Viewer
Scene tree
Help
History
viewer-0 (OpenGLStoredQt)
Scene tree : viewer-0 (OpenGLStoredQt)
Touchables
World [0]
atomP [0]
Touchables slider
Show all
Hide all
Viewer properties
Picking informations
viewer-0 (OpenGLStoredQt)
Output
Threads:
All
#
Viewer menu :
/gui/addMenu viewer Viewer
/gui/addButton viewer "Set style surface" "/vis/viewer/set/style surface"
/gui/addButton viewer "Set style wireframe" "/vis/viewer/set/style wire"
/gui/addButton viewer "Refresh viewer" "/vis/viewer/refresh"
/gui/addButton viewer "Update viewer (interaction or end-of-file)" "/vis/viewer/update"
/gui/addButton viewer "Flush viewer (= refresh + update)" "/vis/viewer/flush"
/gui/addButton viewer "Update scene" "/vis/scene/notifyHandlers"
#
Session :

Run in GUI (2/4)

Load PDB file (.mac)

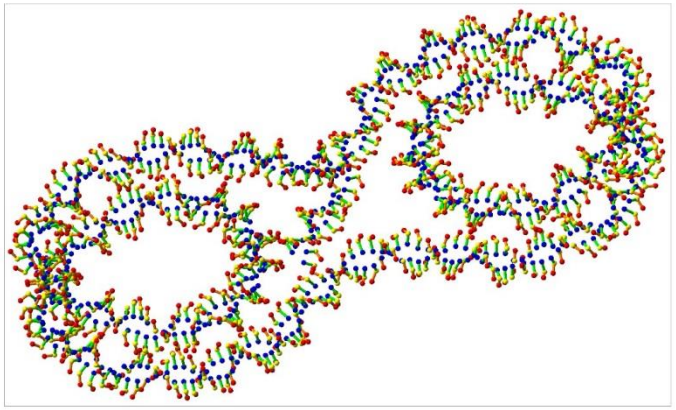
Click on ‘Draw’ menu, and Try different visualisation…



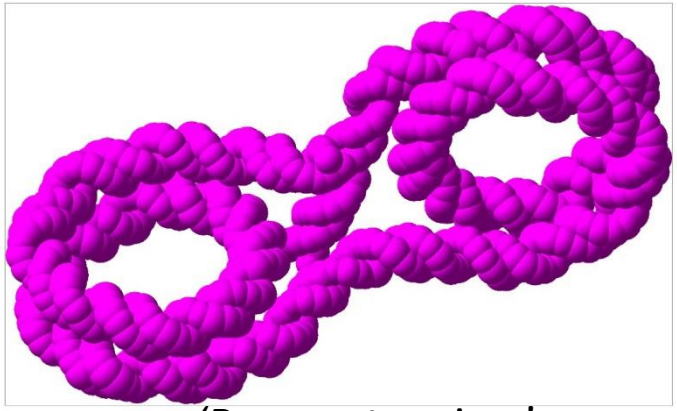
Run in GUI (3/4)

Those screenshots correspond to 1ZBB.pdb (.mac)

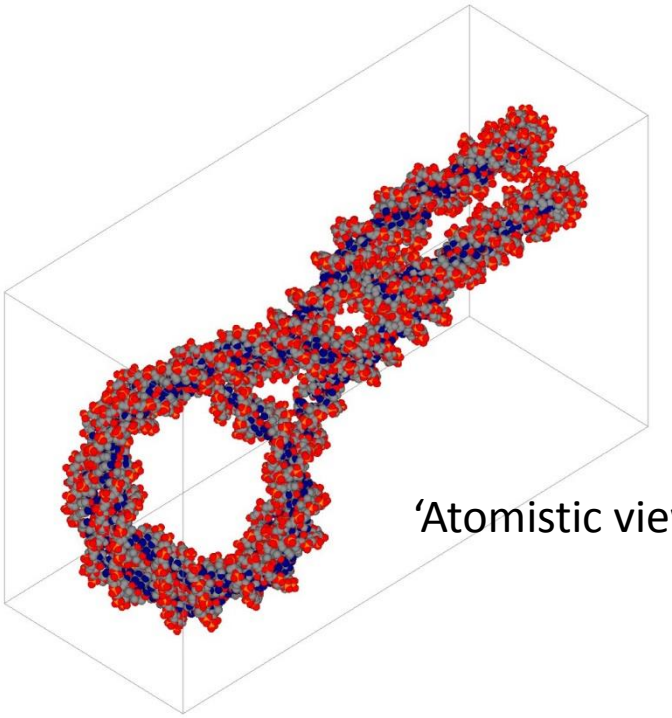
Visualization of a di-nucleosome (Asymmetric Unit of a tetra-nucleosome)



'Residue view'

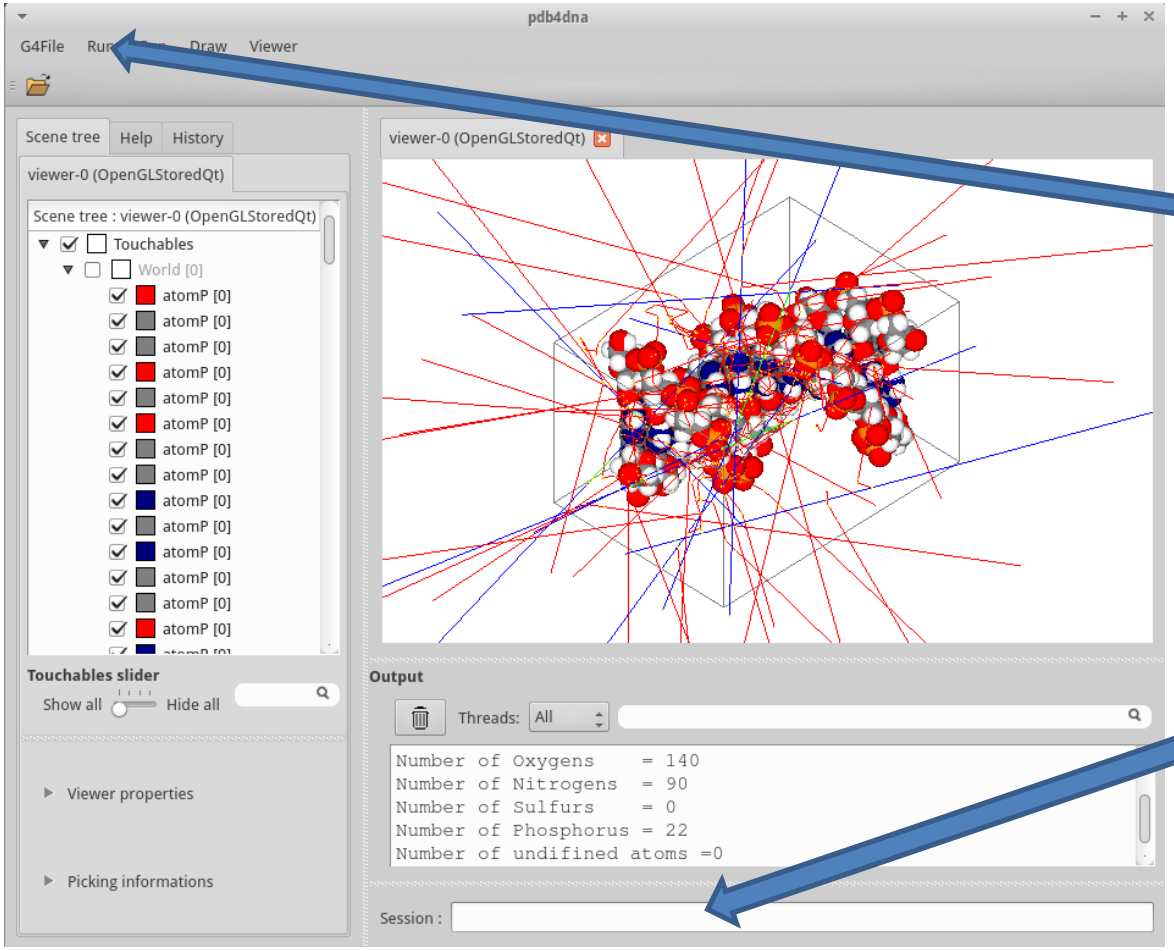


'Barycenter view'



'Atomistic view'

Run in GUI (4/4)



Launch a simulation configured by ‘runInGUI.mac’ in the Run menu

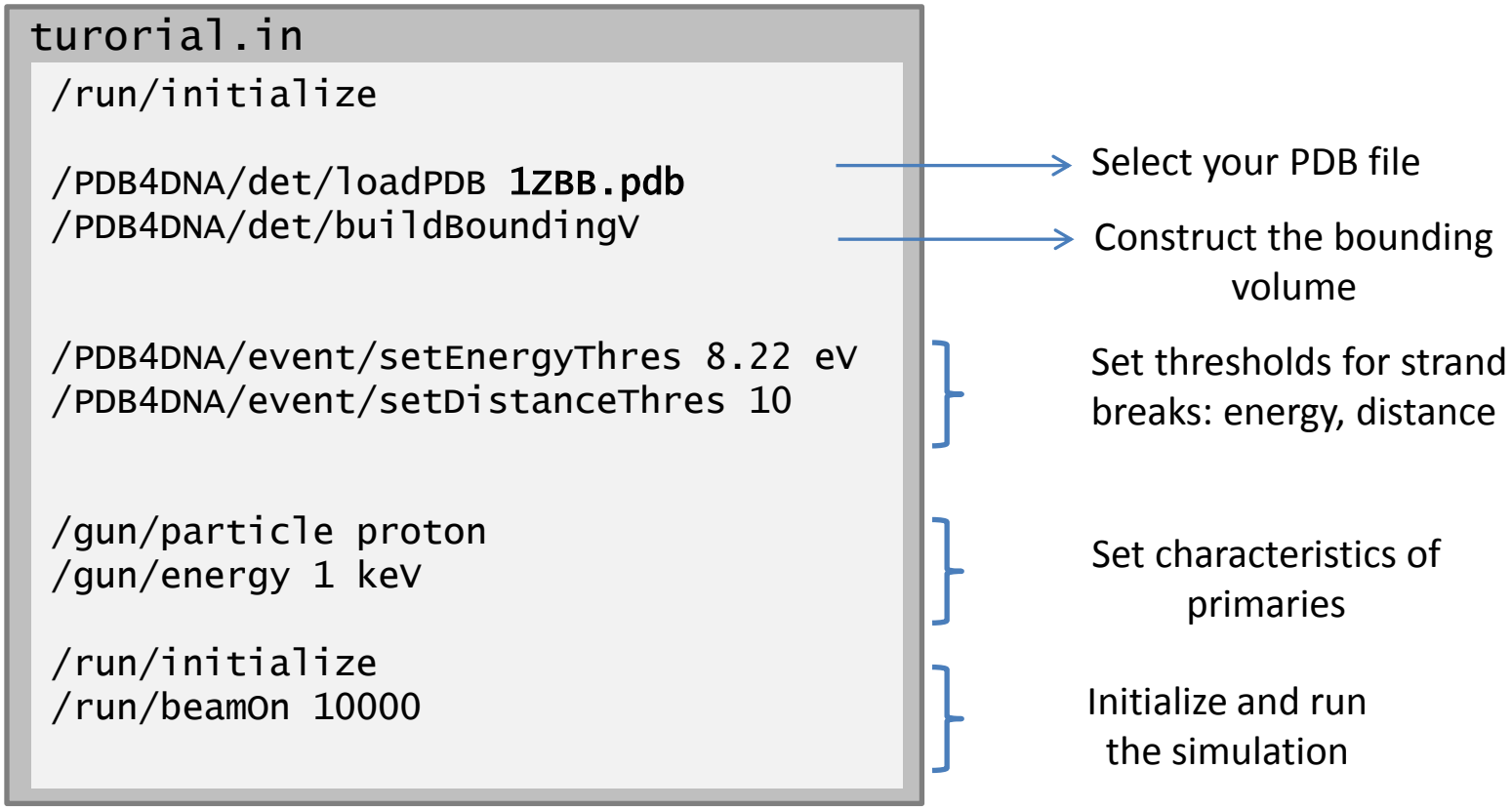
Call run and gun commands in the session text box

/gun/particle e-
/gun/energy 10 keV
/run/beamOn 10
…

Run in batch mode (1/2)

1. Prepare your macro file "`tutorial.in`" using your favorite editor (geany…)

   You can start from the "`pdb4dna.in`" macro file



Run in batch mode (2/2)

2. Run the simulation

```
$ ./pdb4dna -m <your_macro_file> -t <number of threads>
```

Becarefull, the command will change to:
./pdb4dna –mac yourmacrofile –mt numberofthread

```
$ ./pdb4dna -m tutorial.in -t 2
```

```
---> Begin of Event: 9500
G4WT0 >
---> Begin of Event: 9600
G4WT0 >
---> Begin of Event: 9700
G4WT1 >
---> Begin of Event: 9800
G4WT0 >
---> Begin of Event: 9900
Graphics systems deleted.
Visualization Manager deleting...
G4WT1 > Total navigation history collections cleaned: 7
G4WT0 > Total navigation history collections cleaned: 7
Total navigation history collections cleaned: 3
user@user-VirtualBox:~/tutorial/pdb4dna-build$
```

Hands-on **pdb4dna**

1

Scope of the application

- PDB files
- Integration into Geant4
- Algorithm to find the closest atom in DNA
- Strand breaks

2

Application

- Directory content
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ROOT analysis

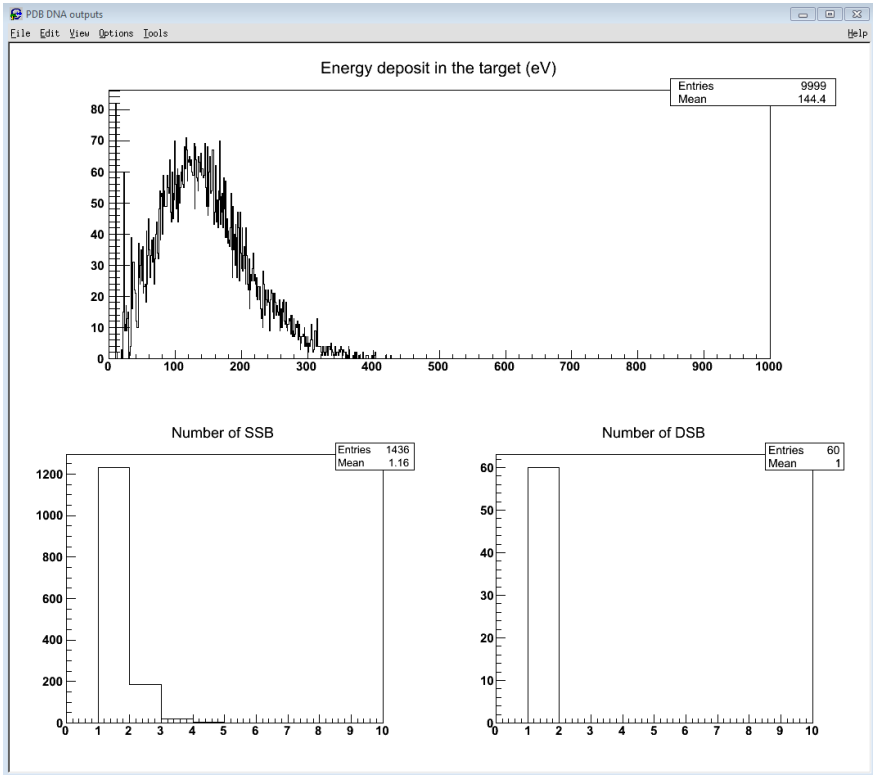
ROOT analysis

- A simulation will produce a root file "**pdb4dna_output.root**"
- 3 histograms: **energy deposits** in the bounding volume per event, **SSB** and **DSB**

```
$ root analysis.C
   ******************************************
   *                                        *
   *        W E L C O M E  to  R O O T      *
   *                                        *
   *   Version   5.32/04      13 July 2012   *
   *                                        *
   *  You are welcome to visit our Web site *
   *          http://root.cern.ch           *
   *                                        *
   ******************************************

ROOT 5.32/04 (tags/v5-32-04@45051, Jul 13 2012,
 15:55:10 on linuxx8664gcc)

CINT/ROOT C/C++ Interpreter version 5.18.00, July 2, 2010
Type ? for help. Commands must be C++ statements.
Enclose multiple statements between { }.
root [0]
Processing analysis.C...
-> Edep in the target : 1.44367 MeV
-> Number of SSB : 1666
-> Number of DSB : 60
root [1]
```



Go further

Now, you have an overview of pdb4dna.

Your feedback is important.

Contact us, we will provide you information concerning technical aspect, implementation, possible improvements…

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Thanks a lot and thanks to the organizers!