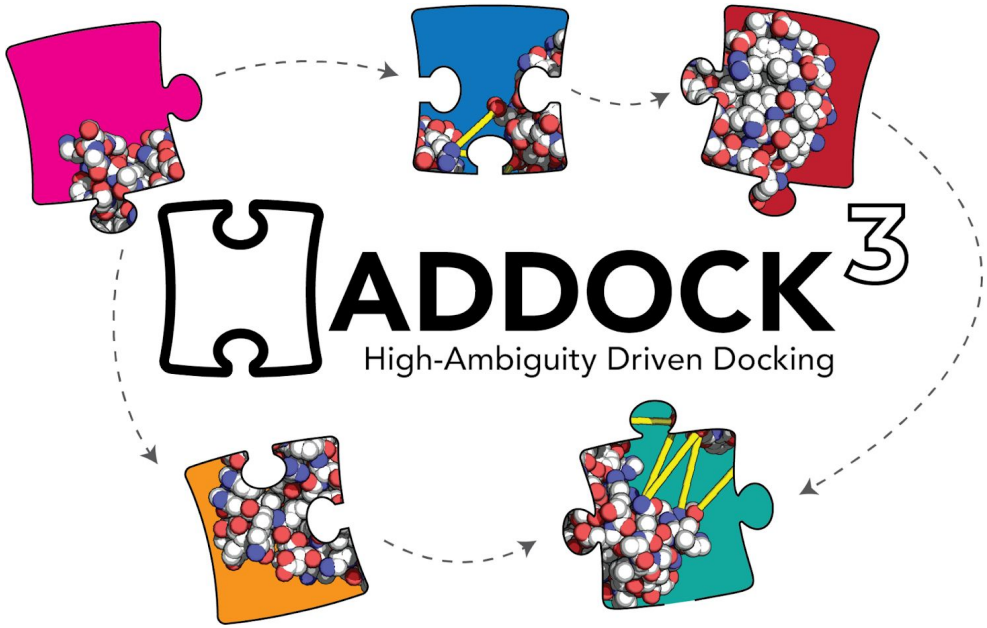
Introducing HADDOCK3, Enabling modular integrative modelling pipelines



speaker

João MC Teixeira

@joaomcteixeira

www.bonvinlab.org

Utrecht University

bioexcel

Thanks to the whole HADDOCK team (past and present)

Thanks to you

HADDOCK v2

> 28,900 registered users
> 430,000 jobs since 2010
> 1,500 local installations
> 130 countries

Alexandre Bonvin
Full Professor

Marco Giulini
Postdoctoral Researcher

João Teixeira
Postdoctoral Researcher

Rodrigo Vargas Honorato
Postdoctoral Researcher

Siri van Keulen
Postdoctoral Researcher

Charlotte van Noort
Ph.D Candidate

René Monté
IT support

Ivar de Leeuw
M.Sc Student

Jesús Lopez Rivera
M.Sc Student

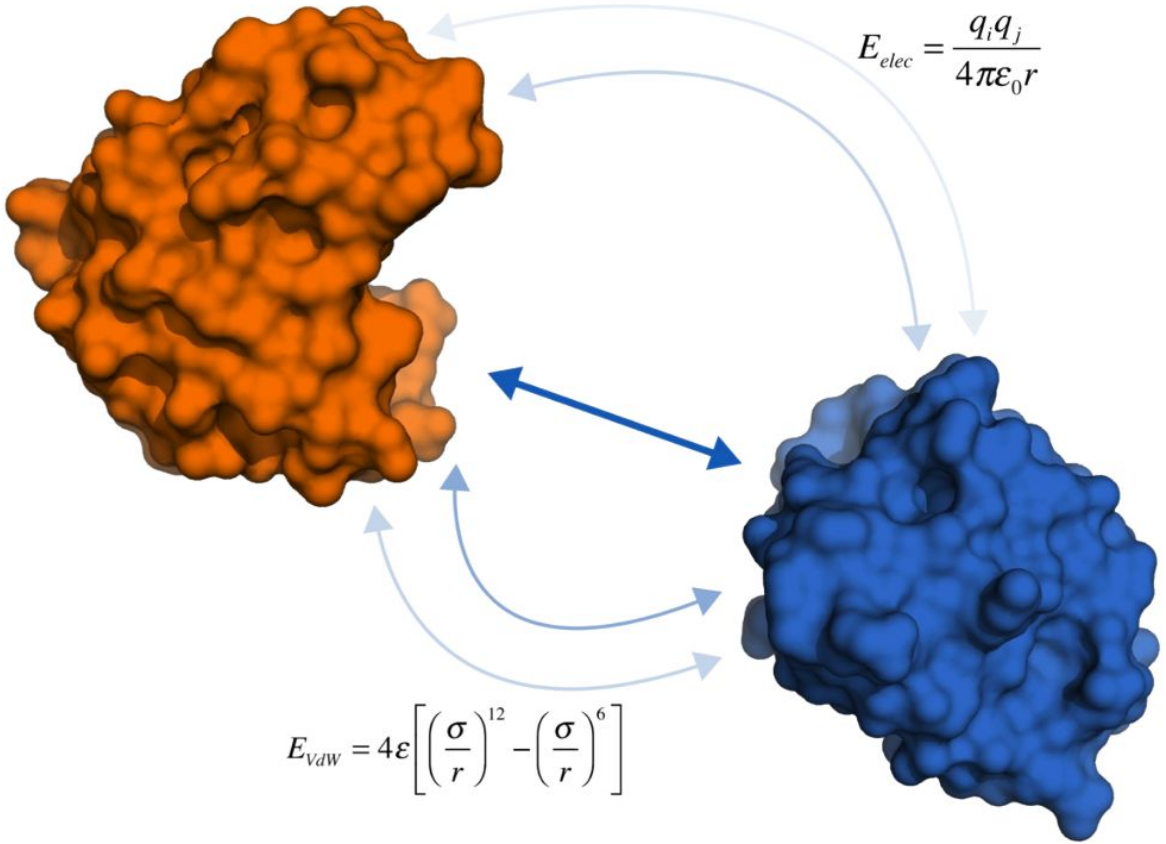
Douwe chulte
M.Sc Student

Rafaella Buzatu
M.Sc Student

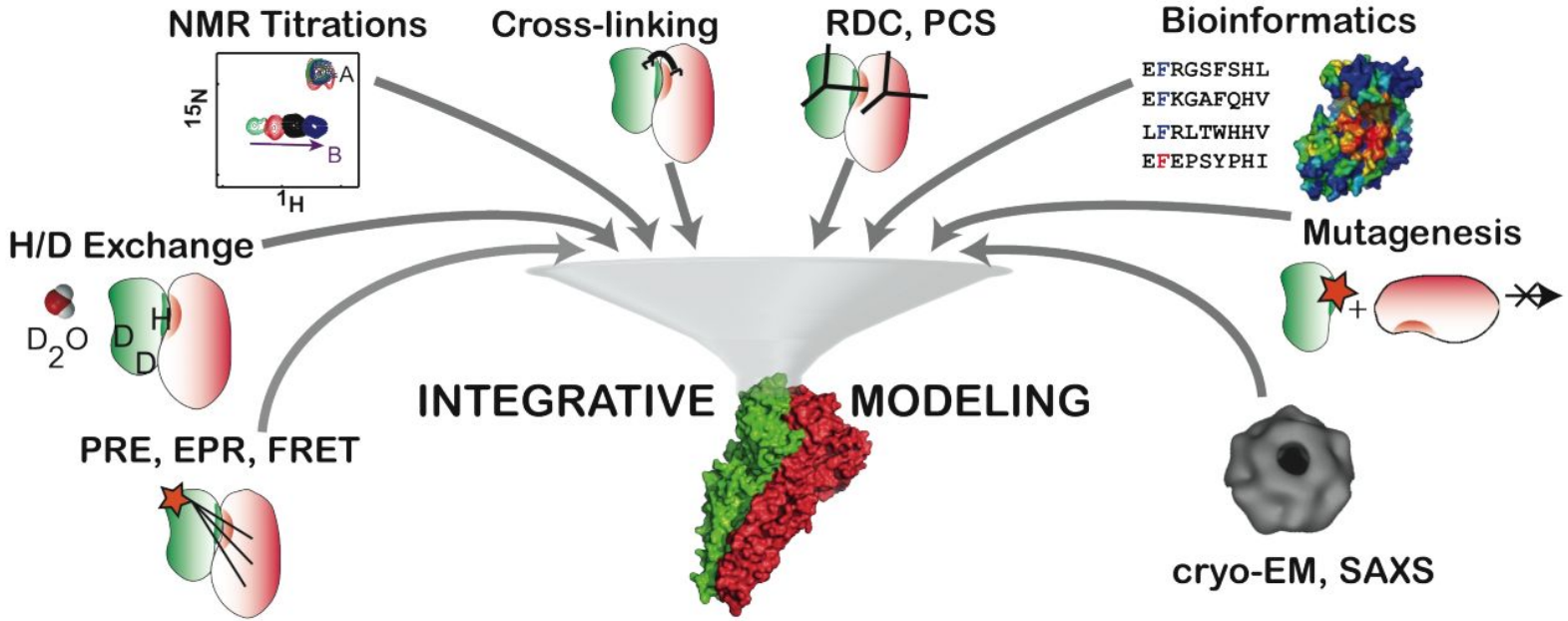
Aldo van den Nieuwendijk
M.Sc Student

www.bonvinlab.org

Overview of HADDOCK v2



Overview of HADDOCK v2



HADDOCK v2 additional resources

Our group's webpage:

https://www.bonvinlab.org/software/#haddock

Integrative modelling of biomolecular complexes with HADDOCK:

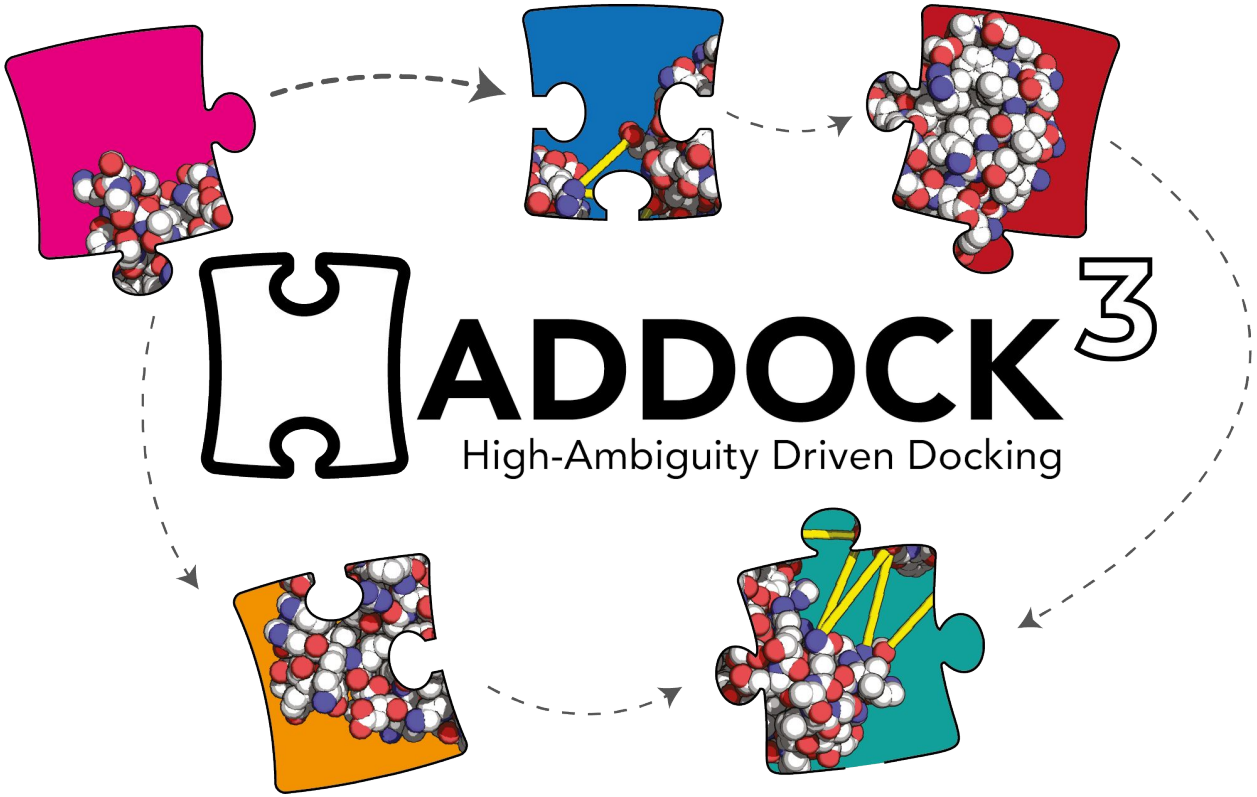
https://youtu.be/kxEidXfUUB4?t=360

The HADDOCK 2.4 server - new features and a guided demo:

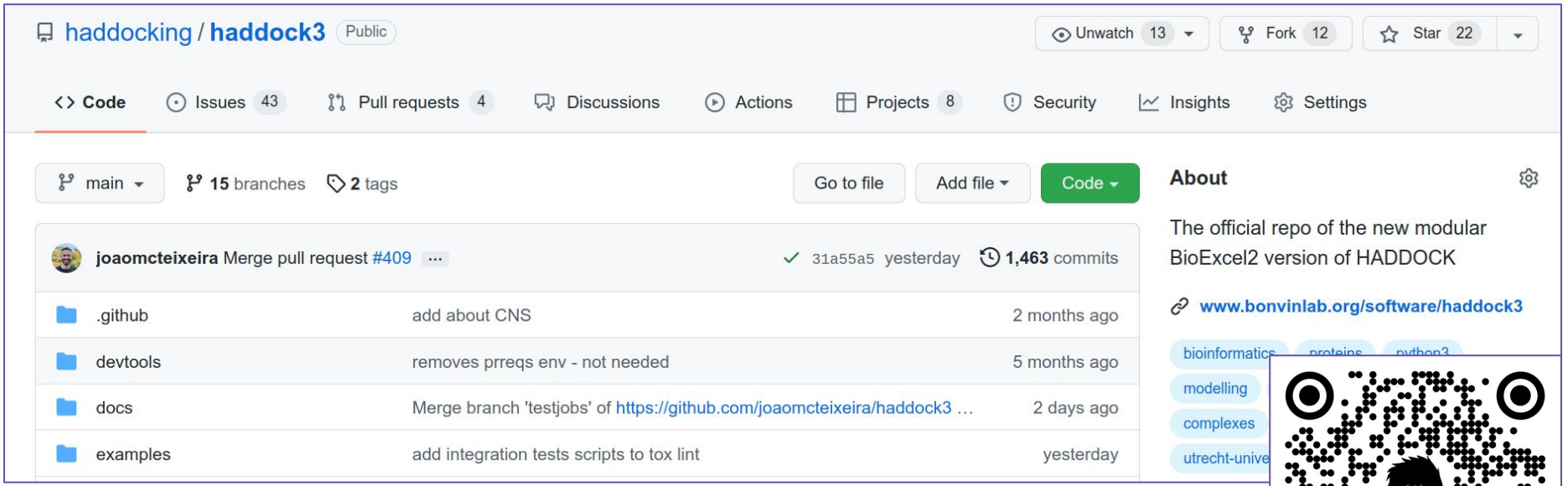
https://youtu.be/9dWdaJ5jBqo

@BioExcelCoE

Introducing HADDOCK v3



HADDOCK3's open-source repository



https://github.com/haddocking/haddock3

A modular workflow as the main feature

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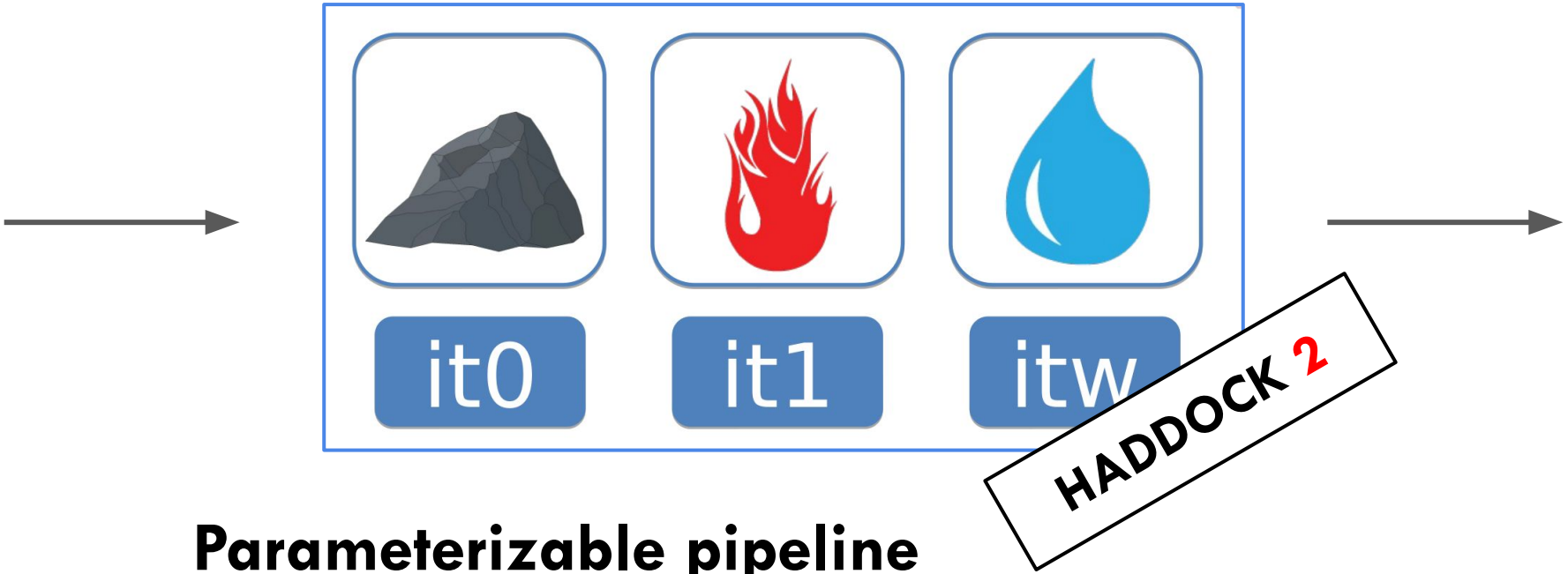
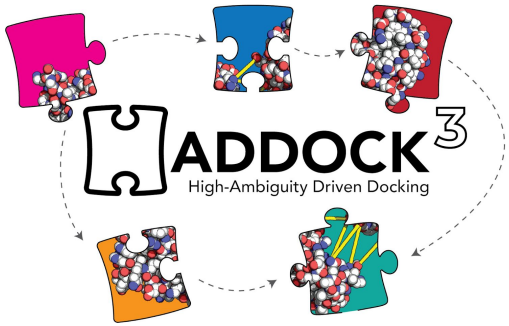
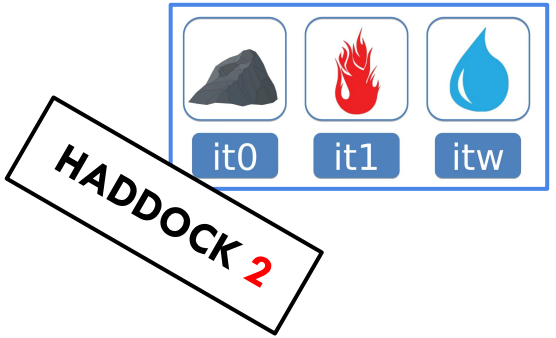


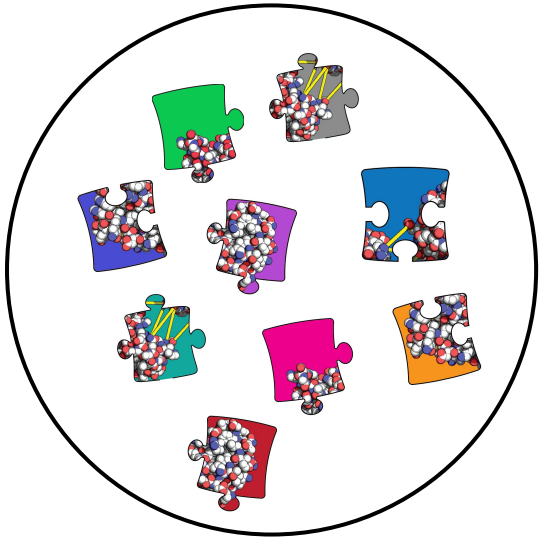
Parameterizable pipeline

A modular workflow as the main feature

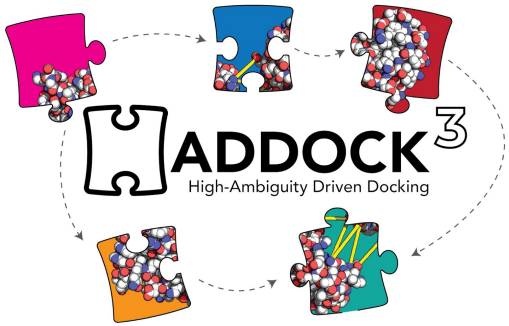




Catalogue of independent **modules**



Combining the different pieces



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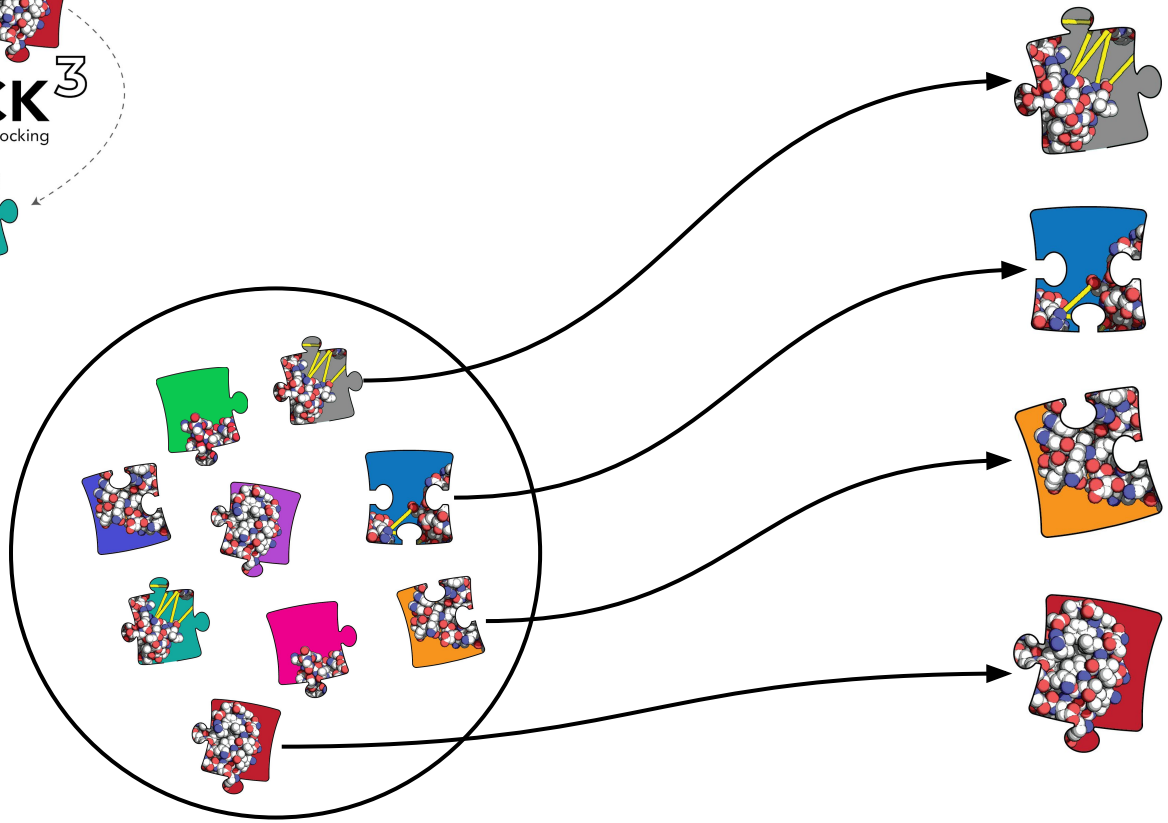

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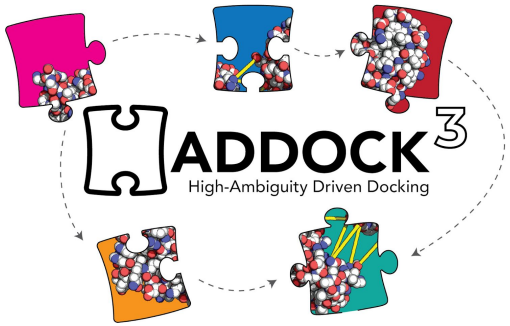

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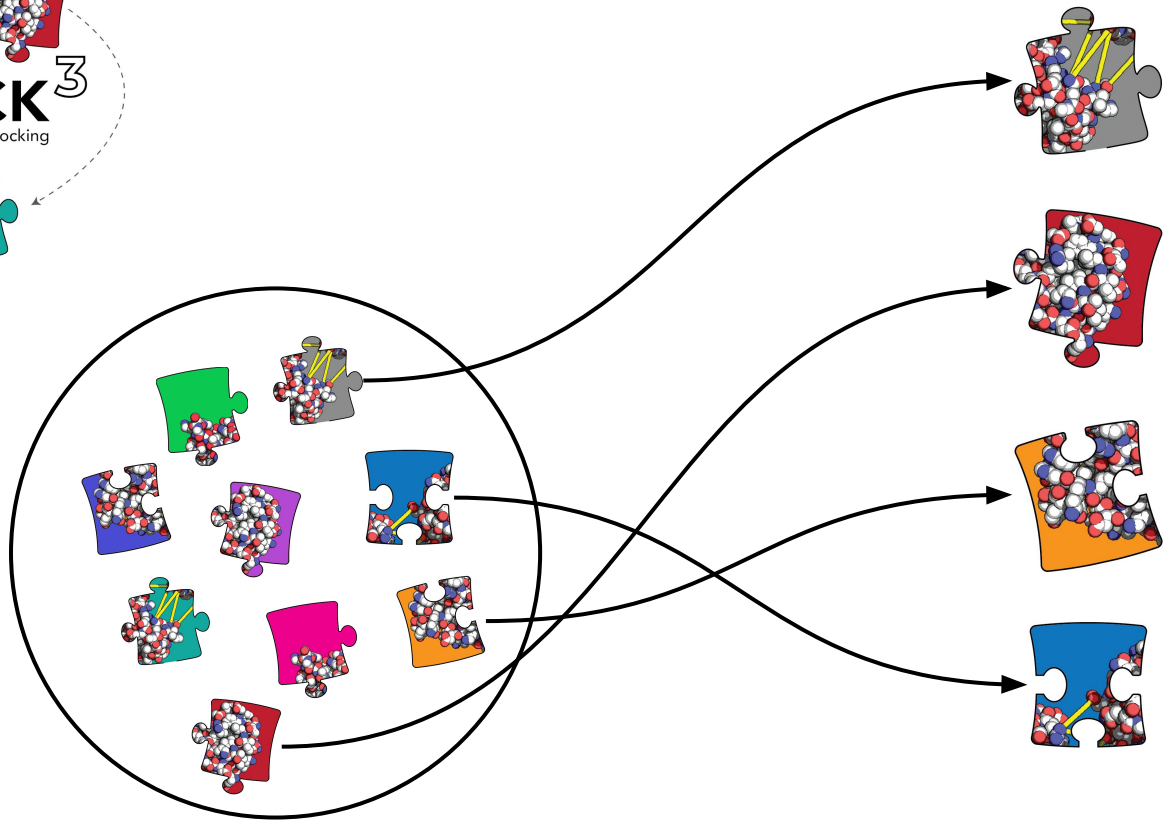

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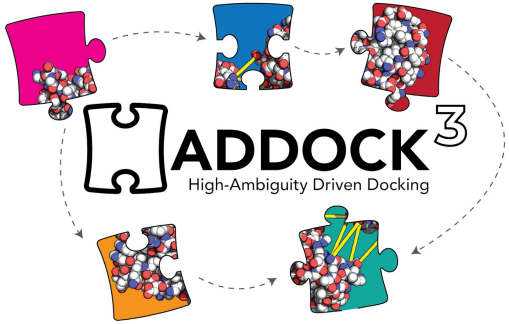

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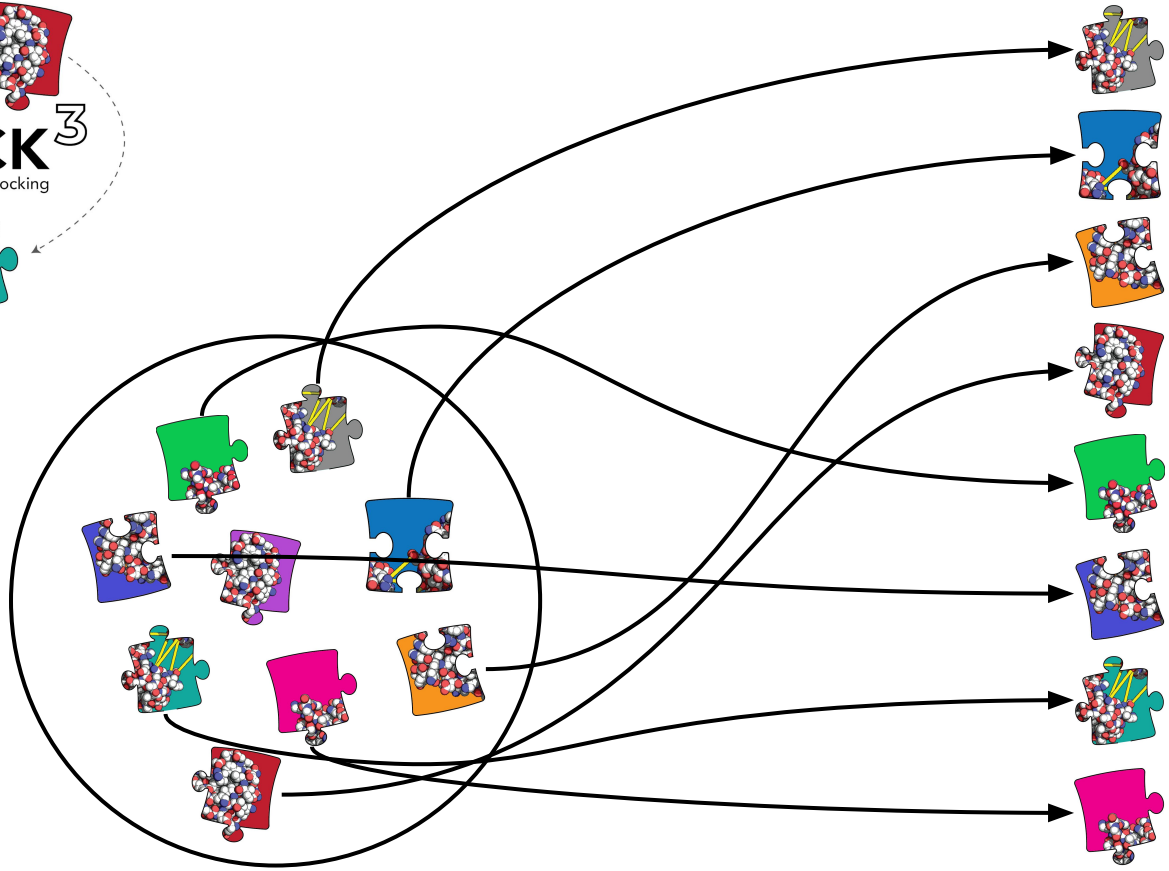

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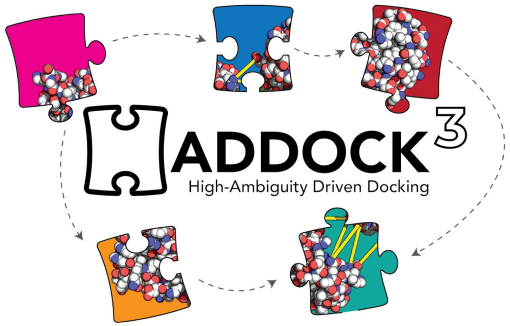

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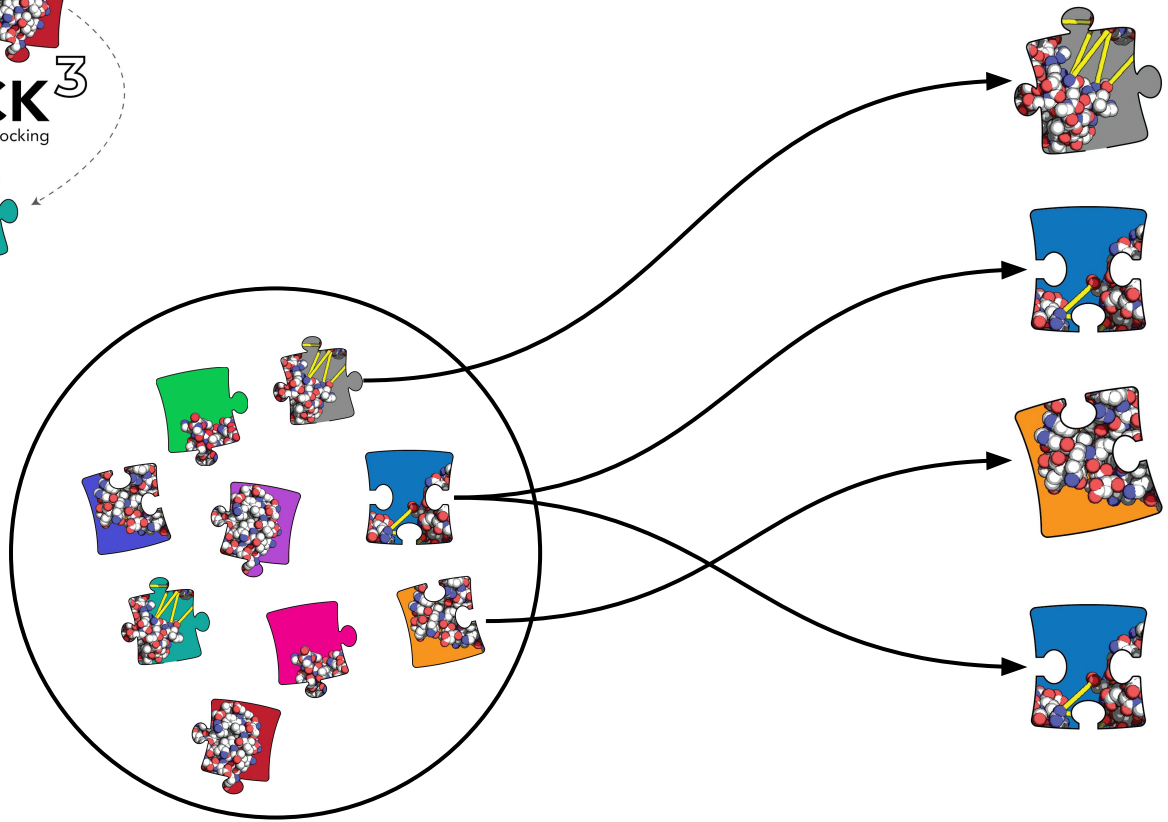

Implemented modules

topology

All-atom topology

sampling

Rigid Body

lightdock

gdock

refinement

Semi-Flexible ref.

Energy minimization

Short MD w/ explicit water

analysis

CAPRI eval

RMSD matrix

Clust by FCC

Clust by RMSD

Select top model

Select top cluster

scoring

All-atom scoring

All-atom scoring w/ $MD_{exp.\ water}$

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How to run

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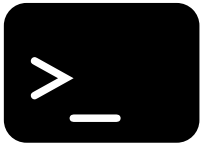

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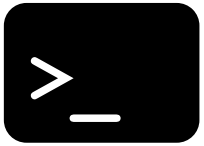
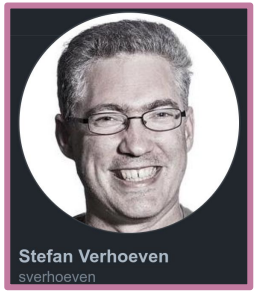
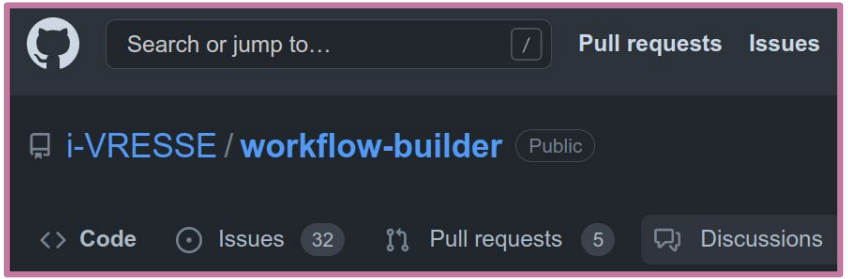


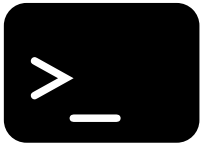
netherlands eScience center



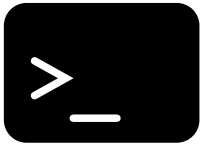


https://github.com/i-VRESSE/workflow-builder

How to run



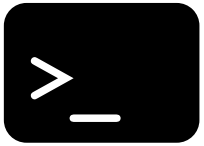
How to run



```
$ haddock3 my-file.cfg
```

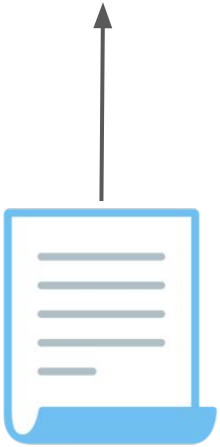
Config file

How to run



results folder

```
$ haddock3 my-file.cfg
```



Config file

Configuration file

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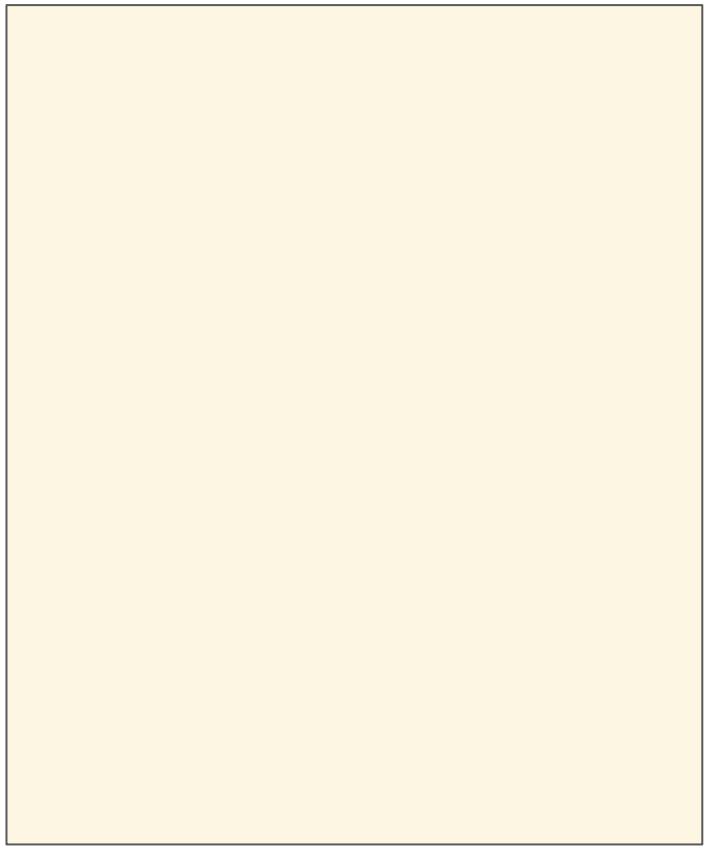

Configuration file

```
run_dir = "run1-test"
molecules =  [
    "data/mol1.pdb",
    "data/mol2.pdb"
    ]
```

Mandatory parameters

Configuration file

```
run_dir = "run1-test"
molecules =  [
    "data/mol1.pdb",
    "data/mol2.pdb"
    ]

ncores = 40
```

Mandatory parameters

Optional parameters

Configuration file

```
run_dir = "run1-test"
molecules =  [
    "data/mol1.pdb",
    "data/mol2.pdb"
    ]

ncores = 40

[topoaa]
autohis = false
[topoaa.mol1]
nhisd = 0
nhise = 1
hise_1 = 75
```

Mandatory parameters

Optional parameters

Step #1

(topoaa module)

Configuration file

```
run_dir = "run1-test"
molecules =  [
    "data/mol1.pdb",
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    ]

ncores = 40

[topoaa]
autohis = false
[topoaa.mol1]
nhisd = 0
nhise = 1
hise_1 = 75


[rigidbody]
tolerance = 20
ambig_fname = "data/mol1-mol2_air.tbl"
sampling = 20
```

Mandatory parameters

Optional parameters

Step #1

(topoaa module)

Step #2

(rigidbody module)

Configuration file

```
run_dir = "run1-test"
molecules =  [
    "data/mol1.pdb",
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ncores = 40

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[rigidbody]
tolerance = 20
ambig_fname = "data/mol1-mol2_air.tbl"
sampling = 20

[caprieval]
reference_fname = "data/complex.pdb
```

Mandatory parameters

Optional parameters

Step #1

(topoaa module)

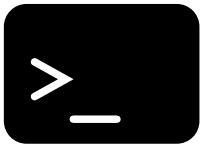
Step #2

(rigidbody module)

Step #3

(caprieval module)

How to run



results folder

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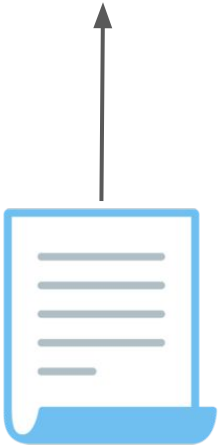
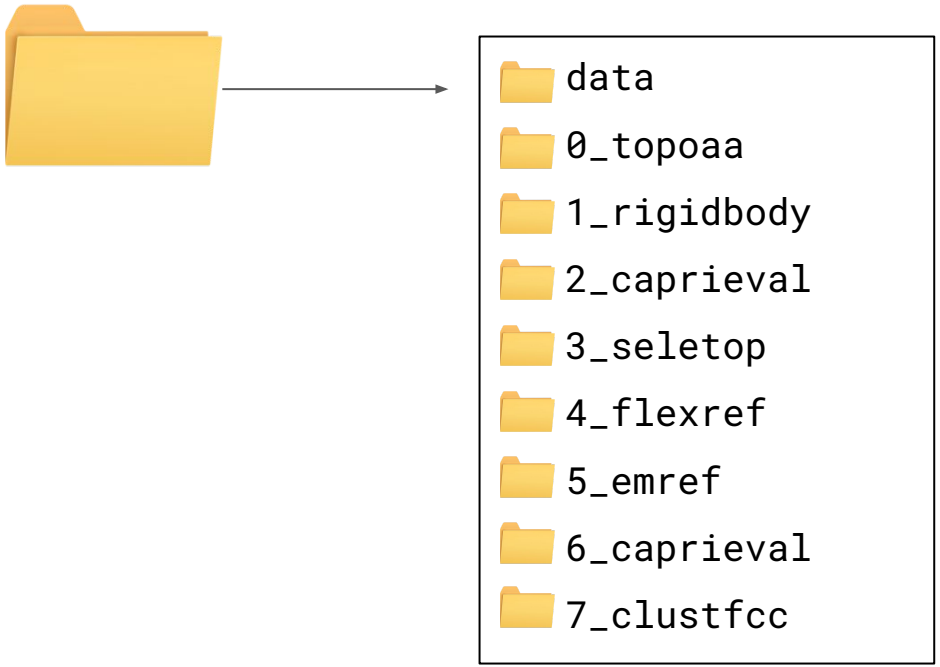


Config file

The results folder

The results folder



The results folder

- data
- 0_topoaa
- 1_rigidbody
- 2_caprieval
- 3_seletop
- 4_flexref
- 5_emref
- 6_caprieval
- 7_clustfcc

```
run_dir = "run1-test"
molecules =  [
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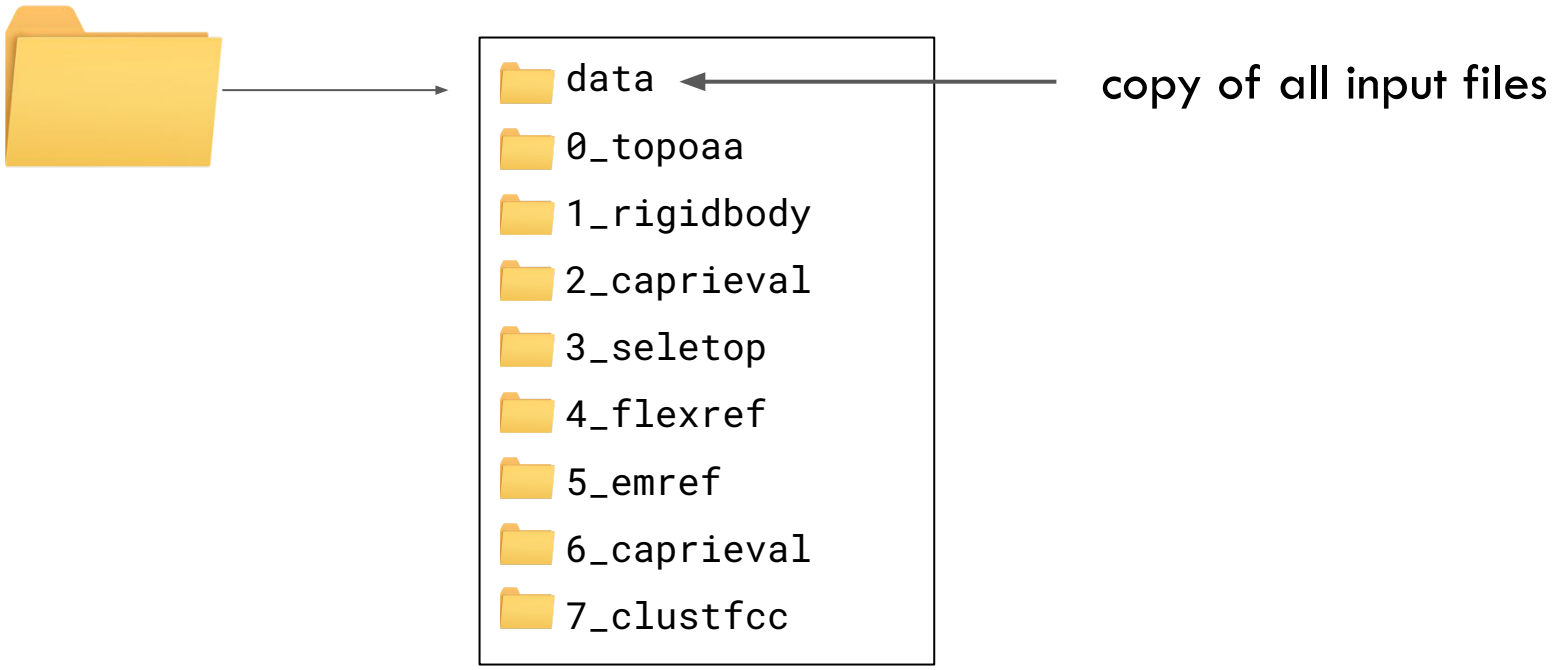
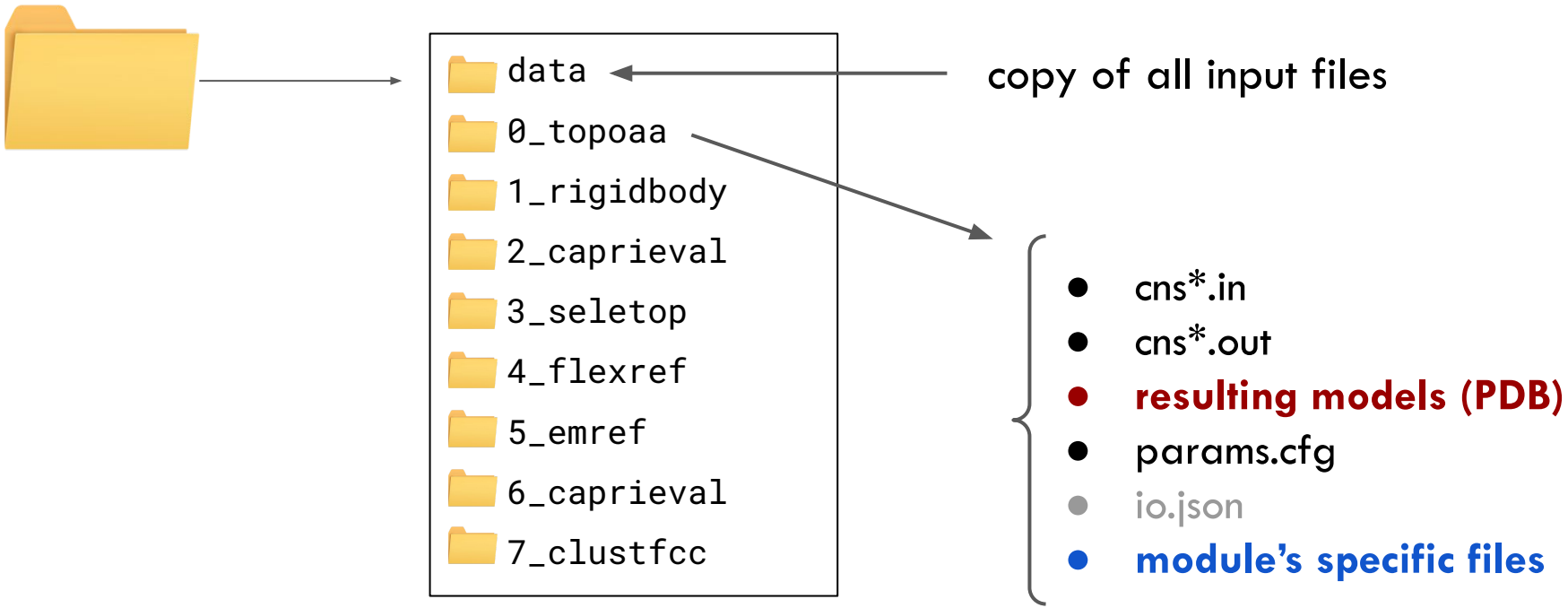
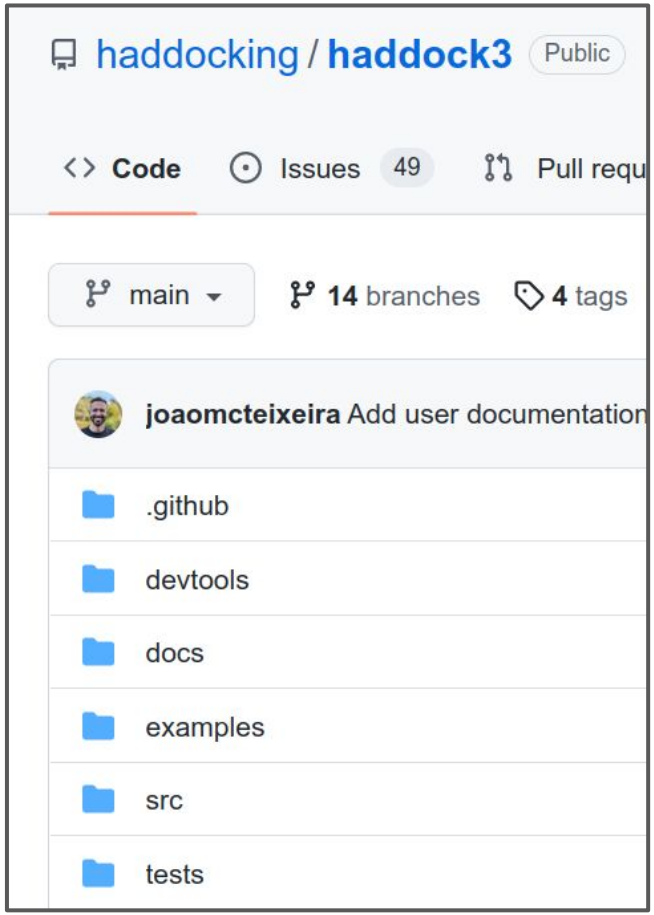


The results folder



Examples

Examples



GitHub

Examples

haddocking / haddock3 Public

Code Issues 49 Pull requ

main 14 branches 4 tags

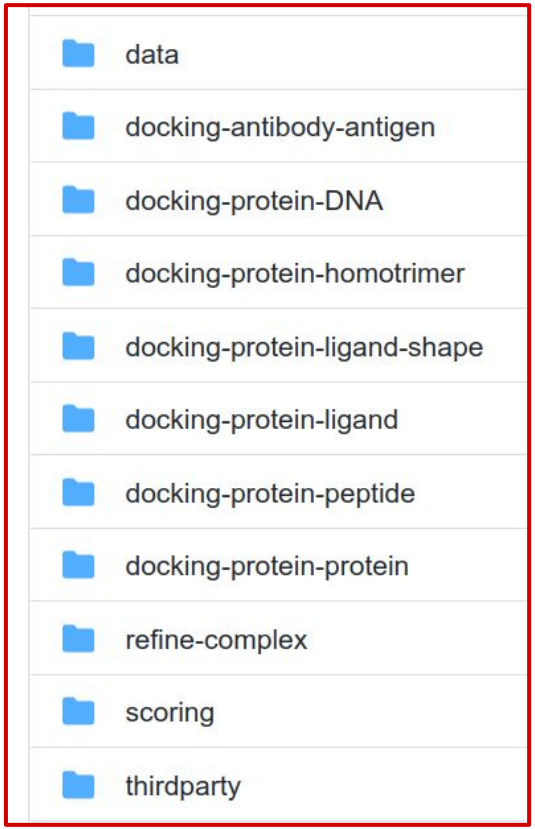
joaomcteixeira Add user documentation

- .github
- devtools
- docs
- examples
- src
- tests

- data
- docking-antibody-antigen
- docking-protein-DNA
- docking-protein-homotrimer
- docking-protein-ligand-shape
- docking-protein-ligand
- docking-protein-peptide
- docking-protein-protein
- refine-complex
- scoring
- thirdparty

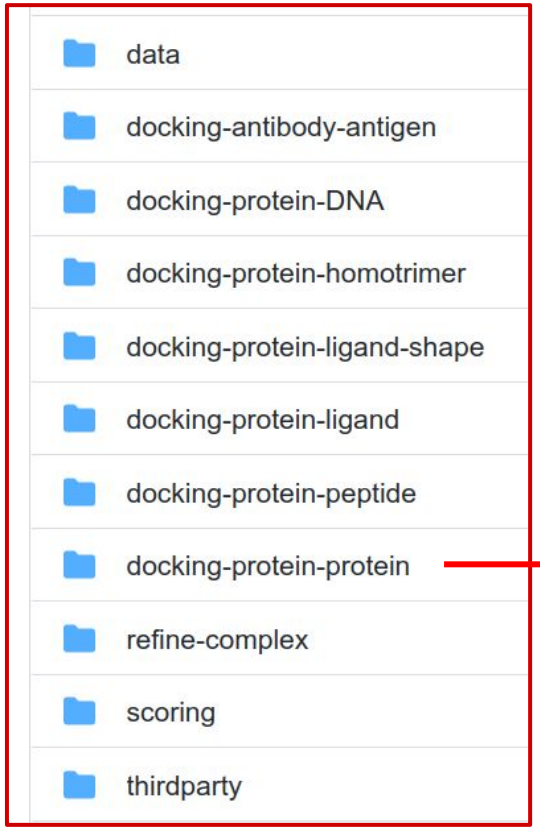
GitHub

Examples

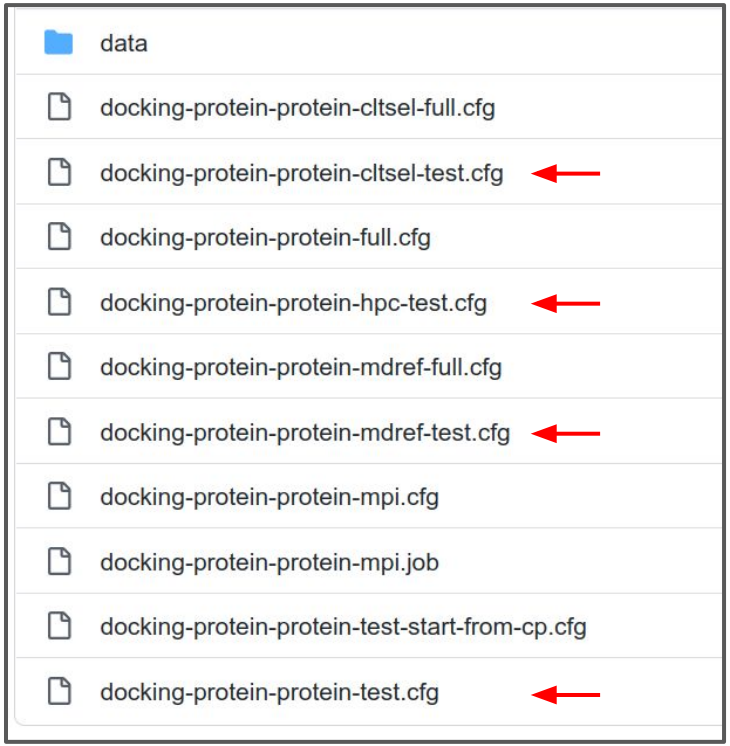


GitHub

Examples



haddock3 / examples / **docking-protein-protein** /



GitHub

Running an example

haddock3 / examples / docking-protein-protein /

```
$ haddock3 docking-protein-protein-test.cfg
```

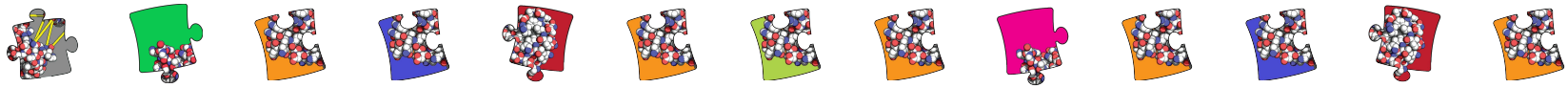
Config file

HADDOCK 3 modularity - Antibody-antigen docking

examples/docking-antibody-antigen/

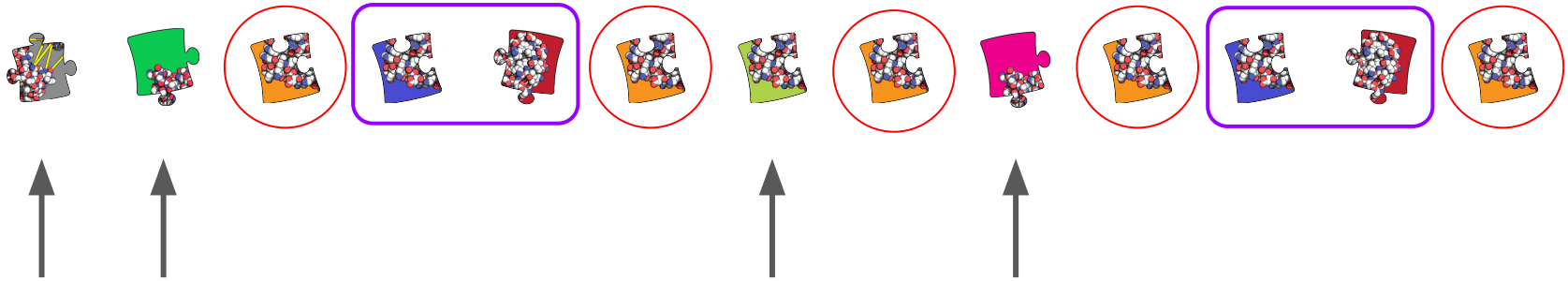
1. docking-antibody-antigen-CDR-accessible-clt-test.cfg
2. docking-antibody-antigen-CDR-accessible-test.cfg
3. docking-antibody-antigen-ranairCDR-clt-test.cfg
4. docking-antibody-antigen-ranairCDR-test.cfg

HADDOCK 3 modularity - Antibody-antigen docking

1. 

HADDOCK 3 modularity - Antibody-antigen docking

1.

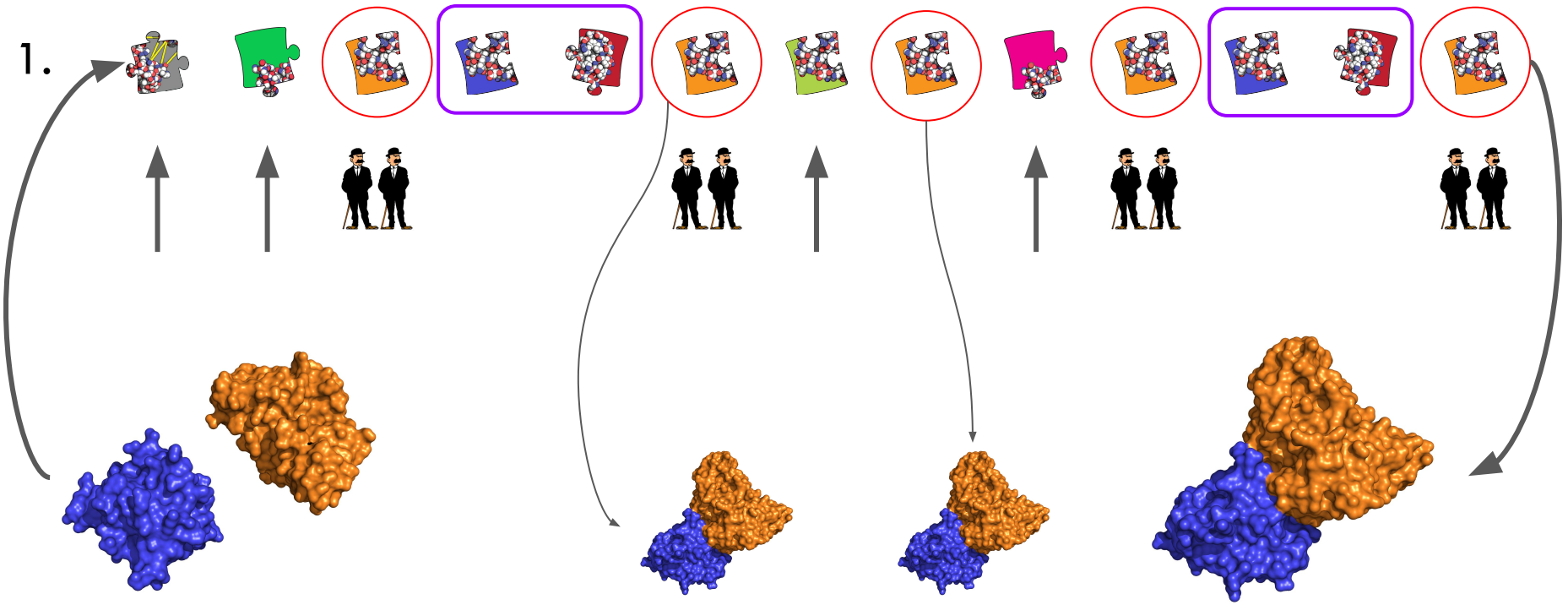


simulation

analysis

cluster and selection

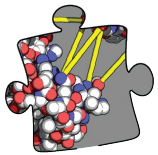
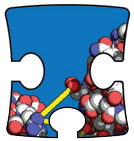
HADDOCK 3 modularity - Antibody-antigen docking



HADDOCK 3 modularity - Antibody-antigen docking

HADDOCK 3 modularity - Use it for scoring

haddock3 / examples / **scoring** /

1.   → PDB files
Scoring tables

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topology

All-atom topology

sampling

Rigid Body

lightdock

gdock

refinement

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Energy minimization

Short MD w/ explicit water

analysis

CAPRI eval

RMSD matrix

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Clust by RMSD

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Select top cluster

scoring

All-atom scoring

All-atom scoring w/ MD$_{\text{exp. water}}$

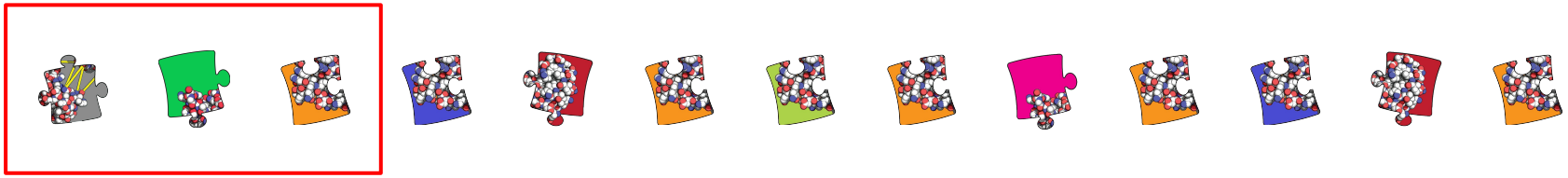
Navigating the results folder

Navigating the results folder

Navigating the results folder

1. docking-antibody-antigen-CDR-accessible-clt-test.cfg

Navigating the results folder



1. All-atom topology
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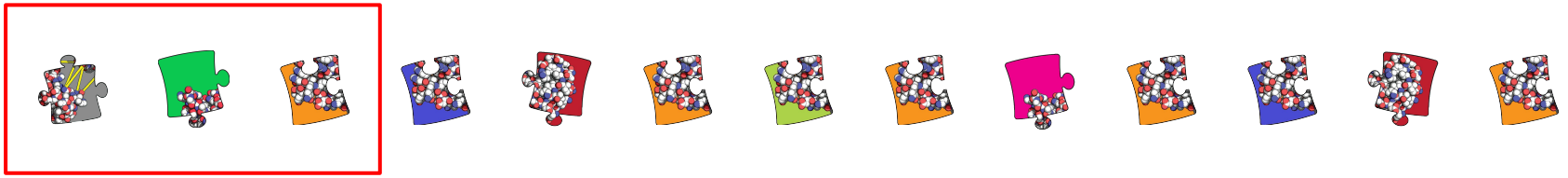

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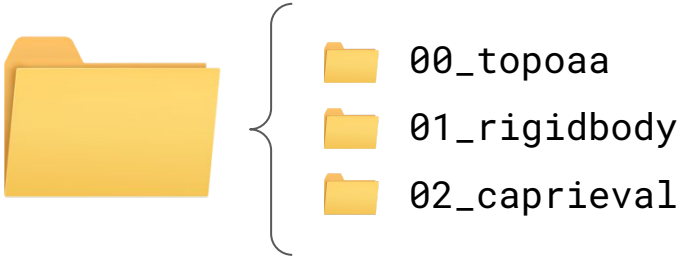

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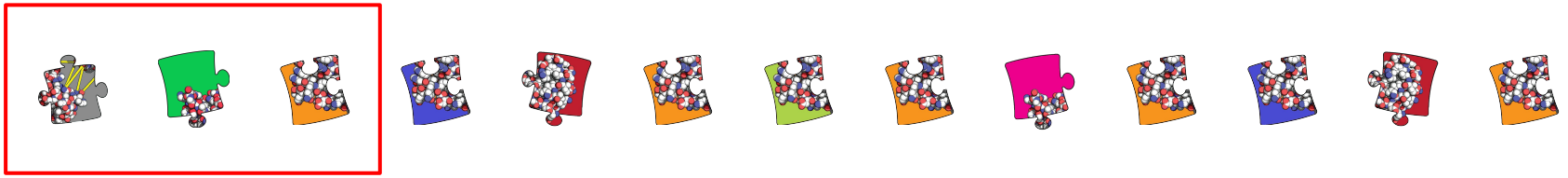

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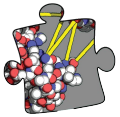

```
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├── 4G6K_fv.inp
├── 4G6K_fv.out
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```

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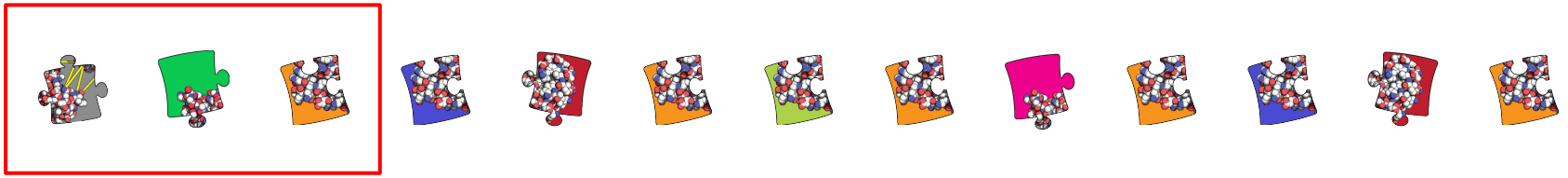

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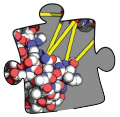

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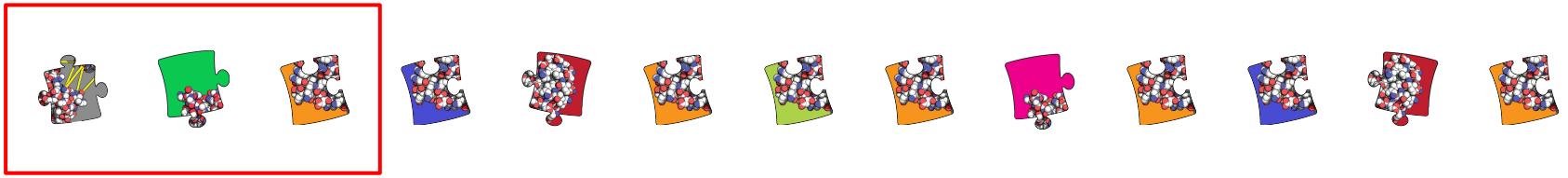

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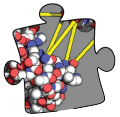

- 00_topoaa ←
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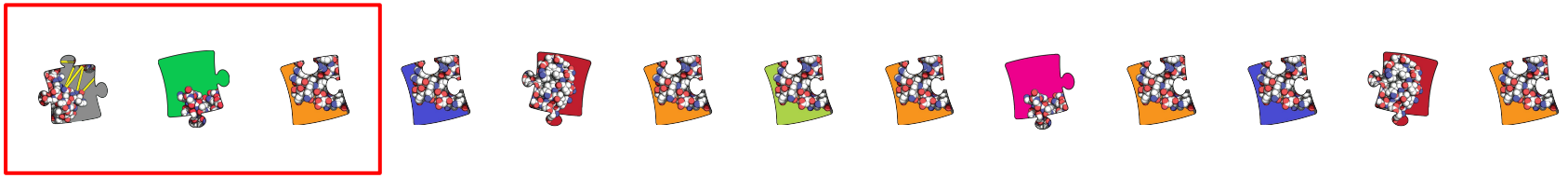

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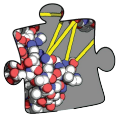

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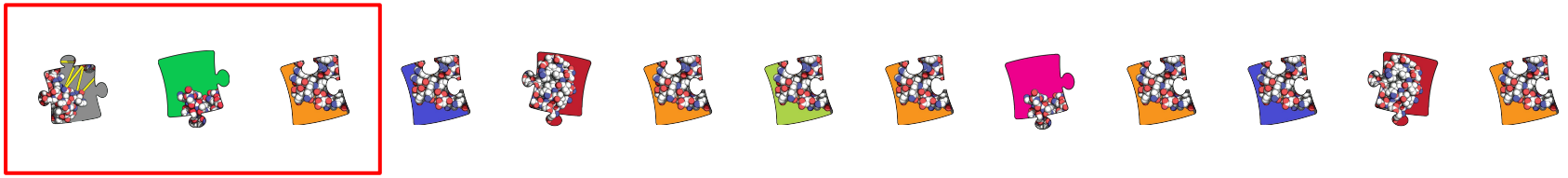

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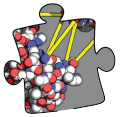

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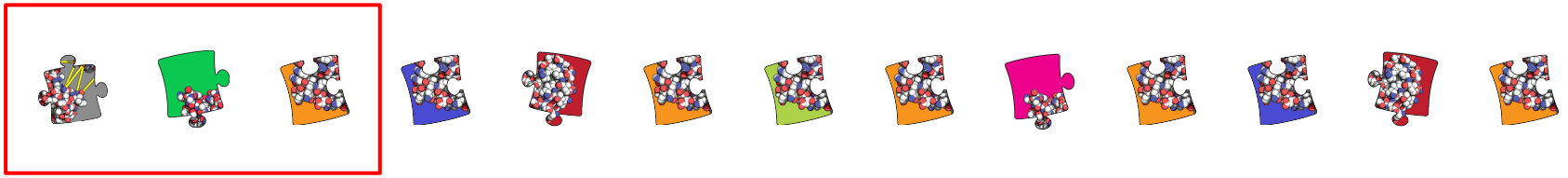

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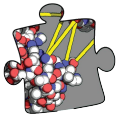

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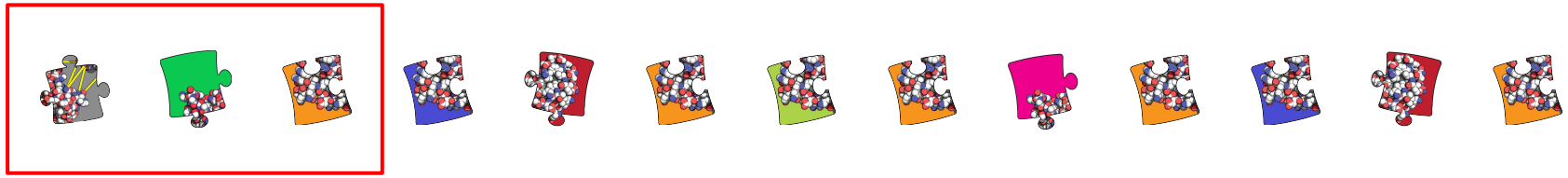

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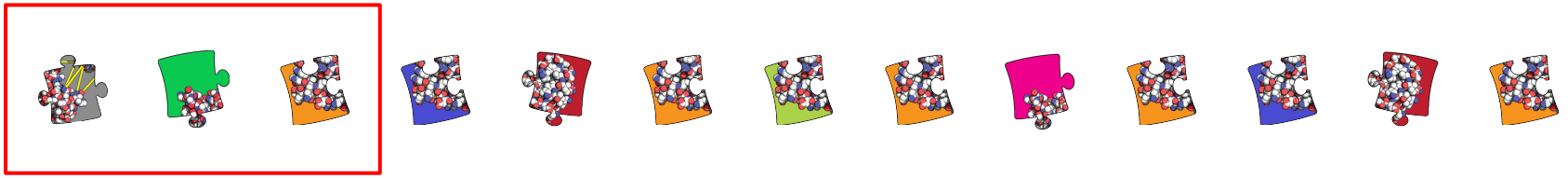

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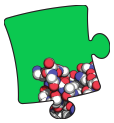

```
.
├── io.json
├── params.cfg
├── rigidbody_10.inp
├── rigidbody_10.out
├── rigidbody_10.pdb
└── rigidbody_10.seed
```

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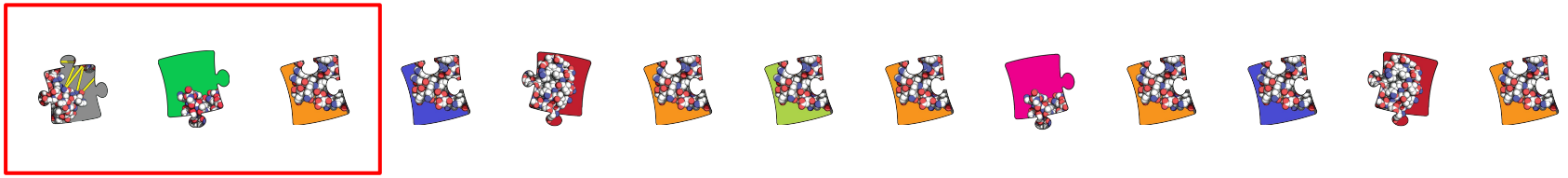

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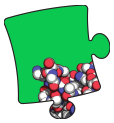

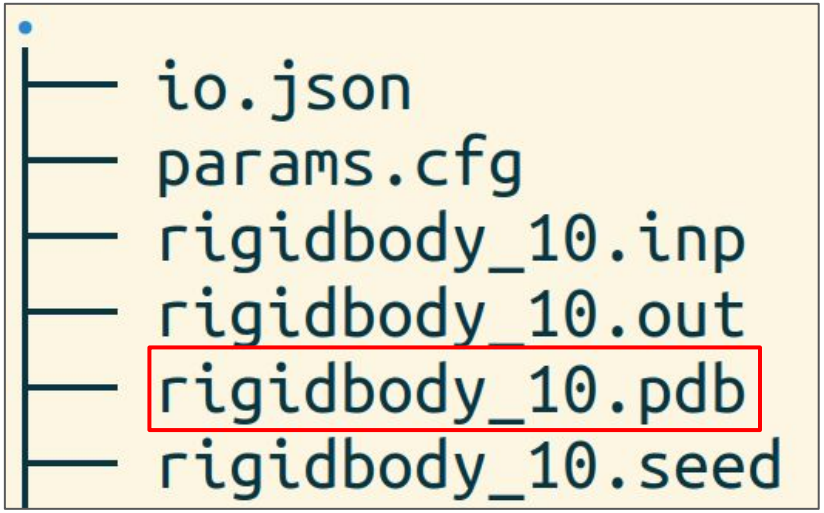

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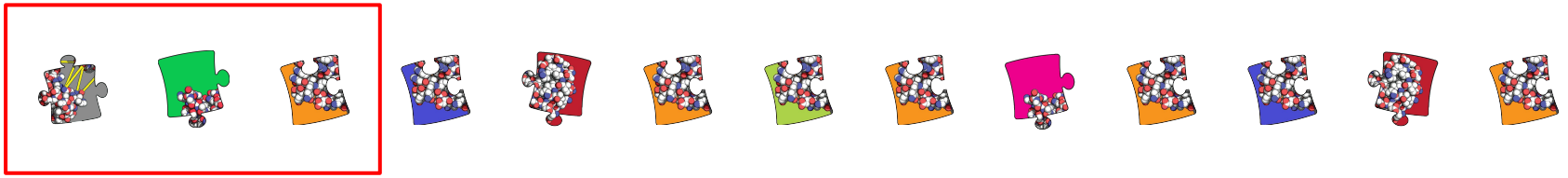

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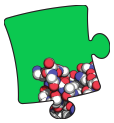

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io.json
params.cfg
rigidbody_10.inp
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rigidbody_10.seed
```

```
sampling = 20
```

rigidbody_1.* (...) _20.*

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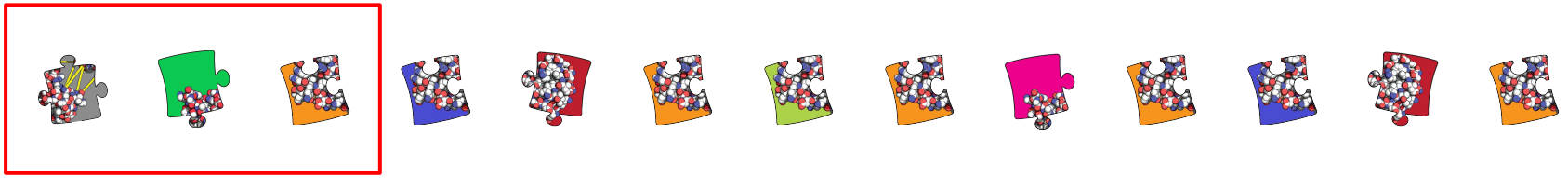

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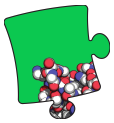

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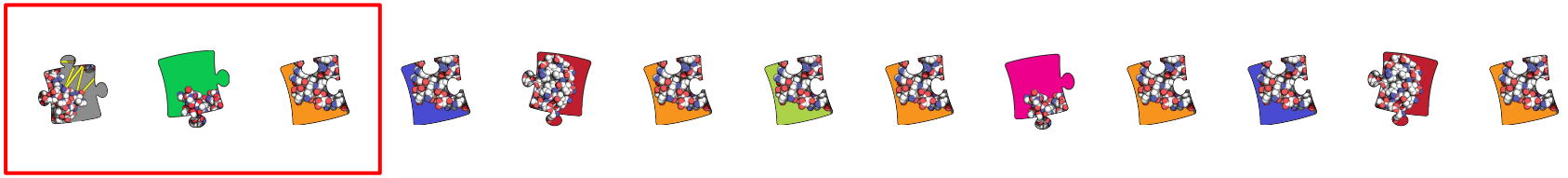

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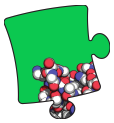

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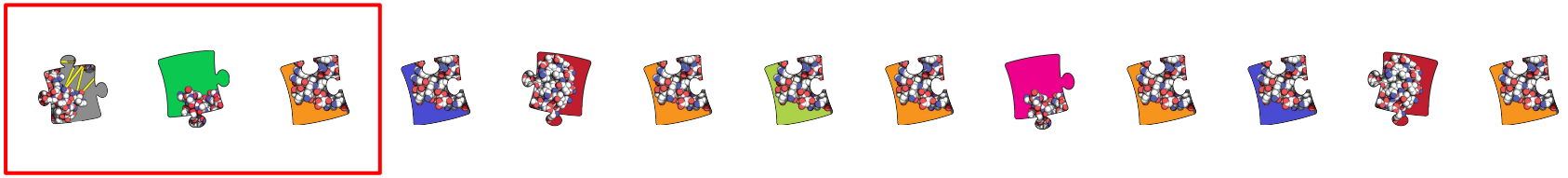

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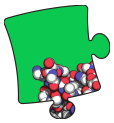

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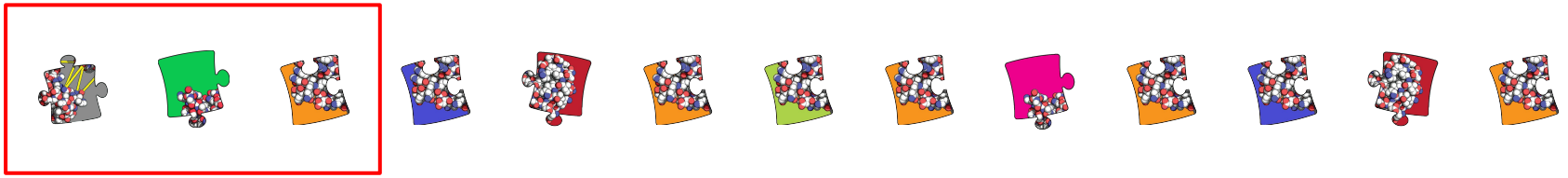

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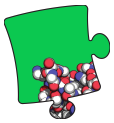

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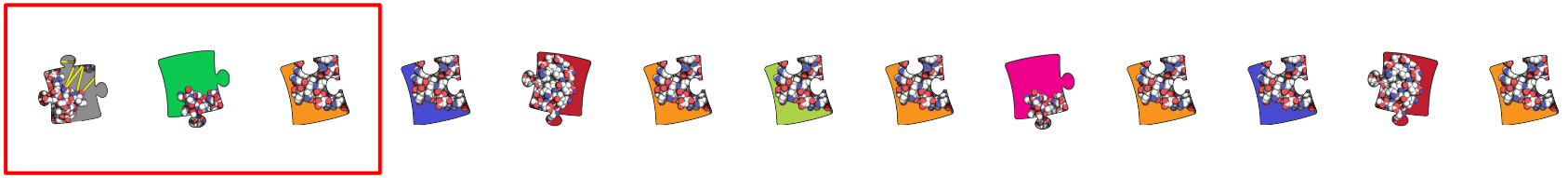

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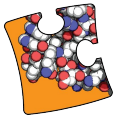

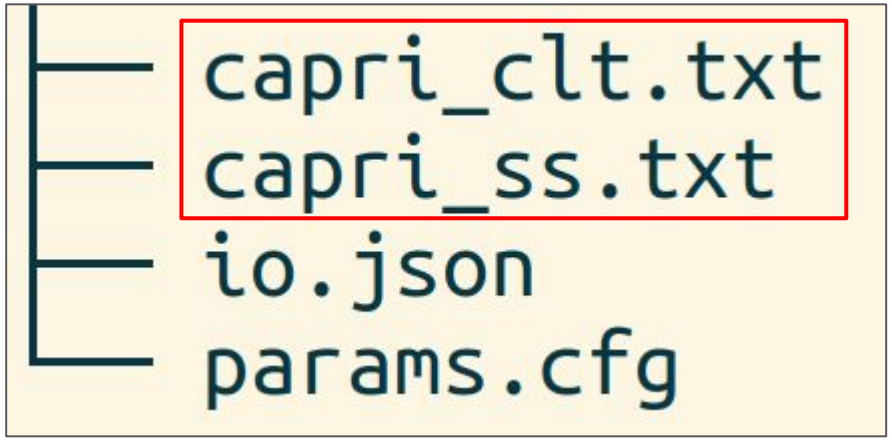

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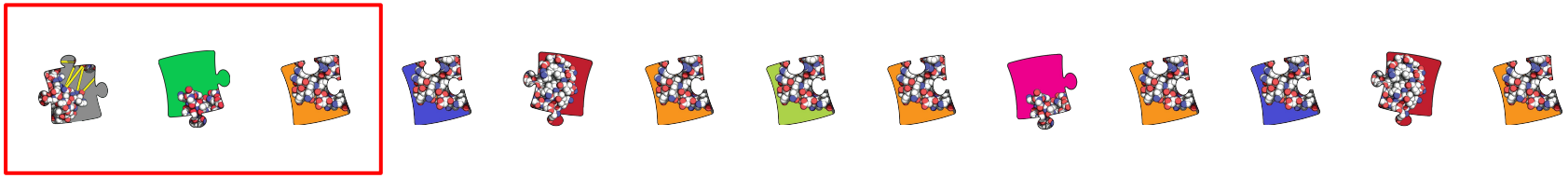
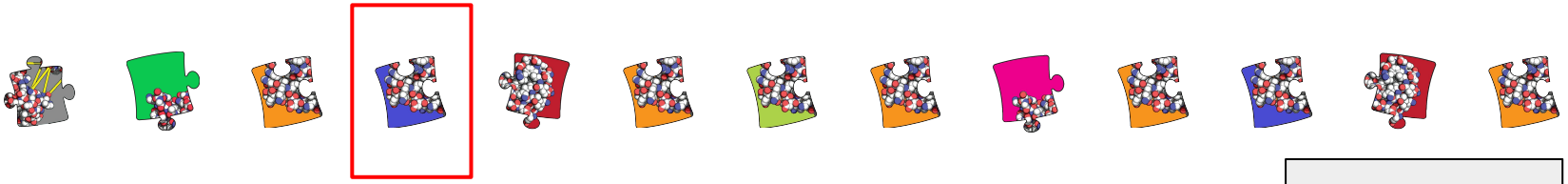


capri_ss.txt

```
· cat capri_ss.txt
```

model	md5	caprieval_rank	score	irmsd	fnat	lrmsd	ilrmsd	dockq	cluster-id	cluster-ranking	model-cluster-ranking
../01_rigidbody/rigidbody_10.pdb	-	1	-7.255	16.081	0.000	23.850	23.454	nan	-	-	-
../01_rigidbody/rigidbody_2.pdb	-	2	-2.476	11.816	0.069	19.209	15.440	0.083	-	-	-
../01_rigidbody/rigidbody_18.pdb	-	3	-0.654	8.562	0.034	14.570	12.225	0.106	-	-	-
../01_rigidbody/rigidbody_6.pdb	-	4	0.915	13.201	0.017	20.638	18.004	0.058	-	-	-
../01_rigidbody/rigidbody_9.pdb	-	5	1.231	13.682	0.000	21.034	19.911	nan	-	-	-
../01_rigidbody/rigidbody_14.pdb	-	6	1.466	9.977	0.000	15.779	13.939	nan	-	-	-
../01_rigidbody/rigidbody_4.pdb	-	7	3.026	15.357	0.000	22.964	22.286	nan	-	-	-
../01_rigidbody/rigidbody_12.pdb	-	8	3.342	12.260	0.000	20.027	20.263	nan	-	-	-
../01_rigidbody/rigidbody_17.pdb	-	9	4.378	13.175	0.017	20.598	17.960	0.059	-	-	-
../01_rigidbody/rigidbody_5.pdb	-	10	4.592	16.149	0.000	24.648	23.385	nan	-	-	-
../01_rigidbody/rigidbody_13.pdb	-	11	5.574	13.770	0.000	19.958	18.354	nan	-	-	-
../01_rigidbody/rigidbody_11.pdb	-	12	5.964	10.180	0.000	15.936	14.417	nan	-	-	-
../01_rigidbody/rigidbody_3.pdb	-	13	6.279	16.125	0.000	23.742	23.226	nan	-	-	-
../01_rigidbody/rigidbody_15.pdb	-	14	7.290	11.221	0.000	17.690	14.717	nan	-	-	-
../01_rigidbody/rigidbody_19.pdb	-	15	8.055	10.801	0.017	17.974	15.462	0.073	-	-	-
../01_rigidbody/rigidbody_16.pdb	-	16	8.962	13.857	0.017	20.803	20.439	0.057	-	-	-
../01_rigidbody/rigidbody_20.pdb	-	17	13.244	12.724	0.017	20.616	16.883	0.059	-	-	-
../01_rigidbody/rigidbody_8.pdb	-	18	13.432	9.740	0.000	14.530	12.858	nan	-	-	-
../01_rigidbody/rigidbody_1.pdb	-	19	16.938	16.797	0.000	24.808	24.279	nan	-	-	-
../01_rigidbody/rigidbody_7.pdb	-	20	17.373	8.544	0.052	14.686	12.397	0.111	-	-	-

Navigating the results folder

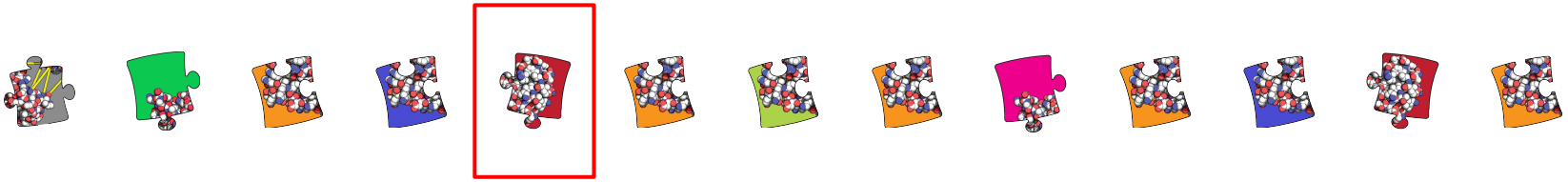


4. Cluster FCC

clustfcc.txt

```
Total # of clusters: 5

-----------------------------------------------
Cluster 1 (#3, n=2, top2_avg_score = -0.49 +-6.77)

clt_rank        model_name      score
1       rigidbody_10.pdb        -7.26
2       rigidbody_3.pdb 6.28    *

-----------------------------------------------
Cluster 2 (#5, n=2, top2_avg_score = 2.65 +-1.73)

clt_rank        model_name      score
1       rigidbody_6.pdb 0.91
2       rigidbody_17.pdb        4.38    *
```

Navigating the results folder

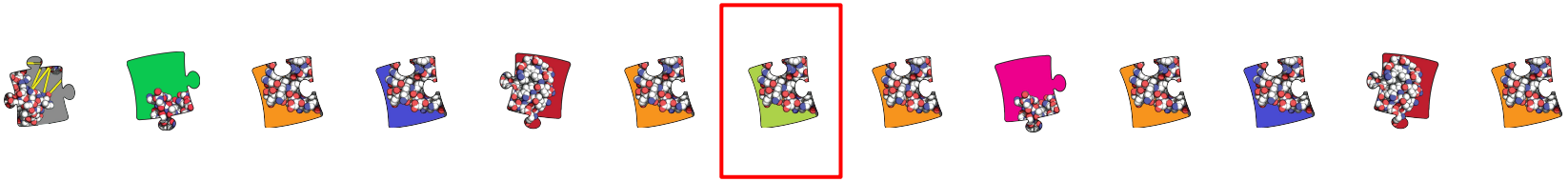


5. Select top clusters

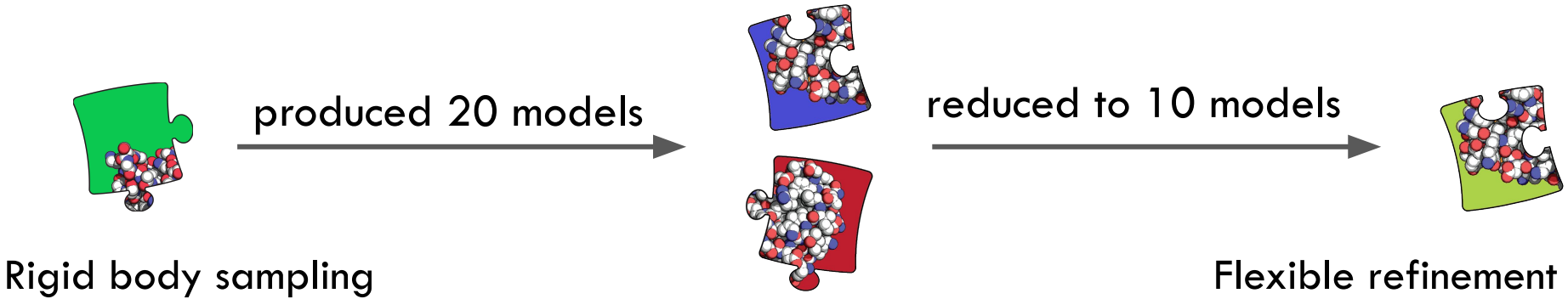
seletopclusts.txt

```
· cat seletopclusts.txt
                rel_path                        cluster_name
../01_rigidbody/rigidbody_10.pdb  cluster_1_model_1.pdb
../01_rigidbody/rigidbody_3.pdb   cluster_1_model_2.pdb
../01_rigidbody/rigidbody_6.pdb   cluster_2_model_1.pdb
../01_rigidbody/rigidbody_17.pdb  cluster_2_model_2.pdb
../01_rigidbody/rigidbody_14.pdb  cluster_3_model_1.pdb
../01_rigidbody/rigidbody_11.pdb  cluster_3_model_2.pdb
../01_rigidbody/rigidbody_2.pdb   cluster_4_model_1.pdb
../01_rigidbody/rigidbody_20.pdb  cluster_4_model_2.pdb
../01_rigidbody/rigidbody_18.pdb  cluster_5_model_1.pdb
../01_rigidbody/rigidbody_7.pdb   cluster_5_model_2.pdb
```

Navigating the results folder



7. Flexible refinement



Advanced features

Continuing and extending runs

Continuing and extending runs

Config file

```
$ haddock3 my-file.cfg
```

```
0_topoaa
1_rigidbody
2_caprieval
3_seletop
4_flexref
5_emref
6_caprieval
7_clustfcc
```

Something went wrong,
or you don't like these modules' results...

Continuing and extending runs

Config file

```
$ haddock3 my-config.cfg --restart 4
```

```
0_topoaa
1_rigidbody
2_caprieval
3_seletop
4_flexref
5_emref
6_caprieval
7_clustfcc
```

Reruns from 4 onward

Continuing and extending runs

```
$ haddock3 edited-params.cfg --restart 4
```

Config file

Edited parameters

```
0_topoaa
1_rigidbody
2_caprieval
3_seletop
4_flexref
5_emref
6_caprieval
7_clustfcc
```

Reruns from 4 onward

Additional command-line clients

```
$ haddock3 -h
```

```
$ haddock3-cfg -h
```

```
$ haddock3-pp -h
```

```
$ haddock3-bm -h
```

```
$ haddock3-dmn -h
```

How to start testing/using it

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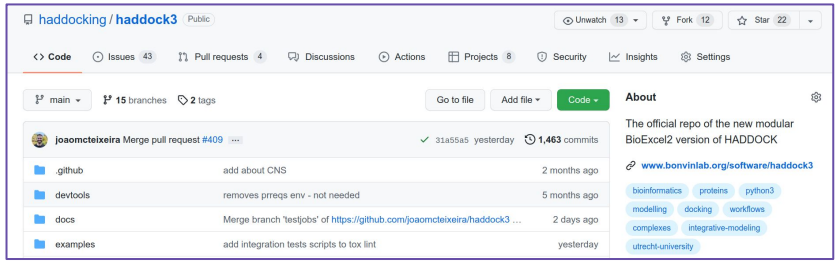
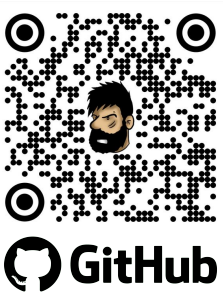
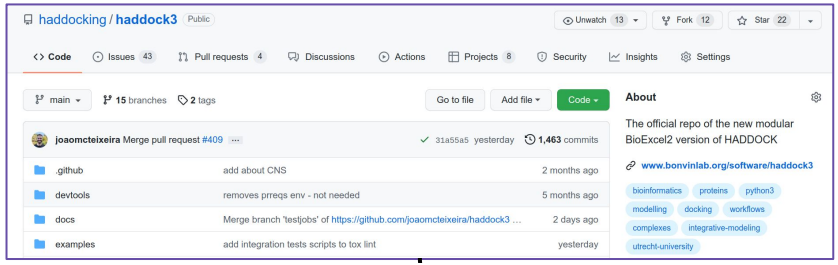


https://github.com/haddocking/haddock3

How to start testing/using it





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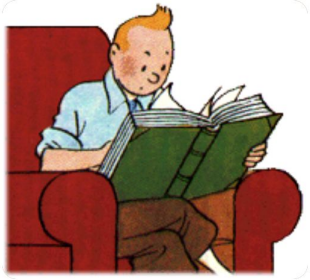


Installation

Open a `terminal` window and navigate to the folder where you want to install HADDOCK3; for example: `software`. The current installation instructions are local and will affect only your user.

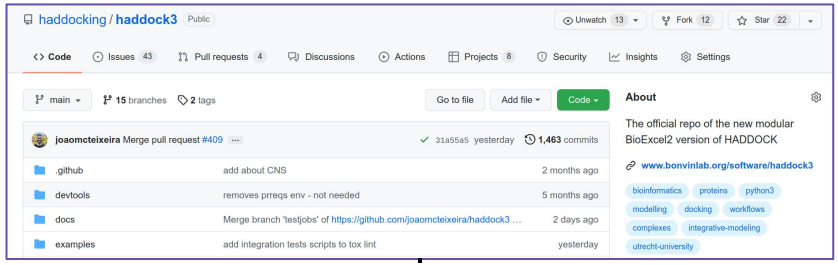
1 Clone this repository:

Mind the `--recursive` flag when cloning!

```
git clone --recursive https://github.com/haddocking/haddock3.git
cd haddock3
cd src/fcc/src
chmod u+x Makefile
make
cd -
```

By the end of the above commands, you should be back to the `haddock3` main folder.

How to start testing/using it



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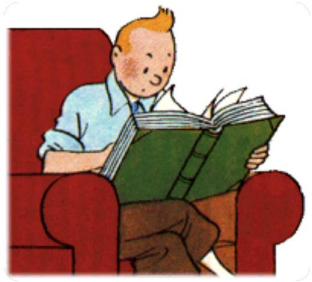

Ask for CNS

A.M.J.J.Bonvin@uu.nl

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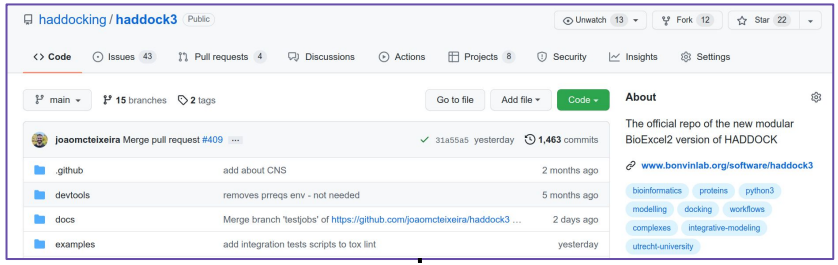
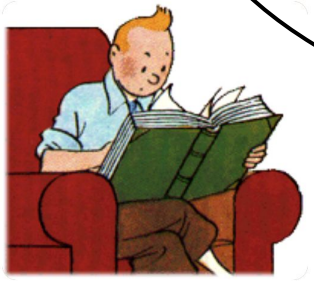


https://github.com/haddocking/haddock3



Ask for CNS

A.M.J.J.Bonvin@uu.nl

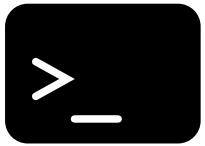
2. Documentation

HADDOCK3-beta documentation is not yet hosted online. You need to generate it locally. First, install HADDOCK3 and activate the `haddock3` python environment as explained in the installation instructions. Then, in your terminal window, run:

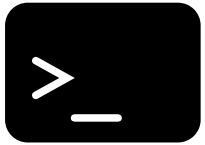
```
tox -e docs
```

Ignore any warning messages. After, use your favorite browser to open the file `haddock3-docs/index.html`. This will open a local webpage with the complete HADDOCK3 documentation. Navigate around, enjoy, and contribute.

How to start testing/using it



How to start testing/using it



```
$ haddock3 -h
```

HADDOCK3 as a Python library

```python
from haddock.clis.cli import main

main("path/to/my/file.cfg")
```

```python
from haddock.modules.sampling.rigidbody import HaddockModule

rigidbody = HaddockModule(...)
print(rigidbody.params)  # default parameters
rigidbody.updateparameters(sampling=10000)
rigidbody.run()
```

Contribute

Contributing to HADDOCK3

Welcome, we made many efforts to facilitate your contribution to this fantastic project. There

- you can improve tutorials and/or documentation
- improve the code itself (maybe you even found some bug 🐛?)
- improve error messages so they become clearer
- add a new simulation module altogether
- write more unittests (we dare you to do that 🤦)

Before attempting any development, please install HADDOCK3 following the instructions in the INSTALL file. Afterwards, follow the instructions in this file.

haddock3
3.0.0

Search docs

Installation
Installing third-party packages
Usage
Examples
Tutorials
Command-line interfaces
Modules
Testing
Contributing to HADDOCK3
Citing
Library Reference

» Welcome to HADDOCK3 Documentation!

Welcome to HADDOCK3 Documentation!

You can read now through the **contents** bellow.

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- Installation
- Installing third-party packages
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Future developments

1. pre-processing and cleaning of input PDBs *(almost implemented PR#144)*
2. Porting experimental restraints support from Haddock2 to Haddock3
3. Workflow branching and merge
4. Continue developing documentation and tutorials

Where to find us

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@amjjbonvin

João MC Teixeira

@joaomcteixeira

Thanks to the whole HADDOCK team (past and present)

Thanks to you

HADDOCK v2

> 28,900 registered users
> 430,000 jobs since 2010
> 1,500 local installations
> 130 countries

Alexandre Bonvin
Full Professor

Marco Giulini
Postdoctoral Researcher

João Teixeira
Postdoctoral Researcher

Rodrigo Vargas Honorato
Postdoctoral Researcher

Siri van Keulen
Postdoctoral Researcher

Charlotte van Noort
Ph.D Candidate

René Monté
IT support

Ivar de Leeuw
M.Sc Student

Jesús Lopez Rivera
M.Sc Student

Douwe chulte
M.Sc Student

Rafaella Buzatu
M.Sc Student

Aldo van den Nieuwendijk
M.Sc Student

www.bonvinlab.org