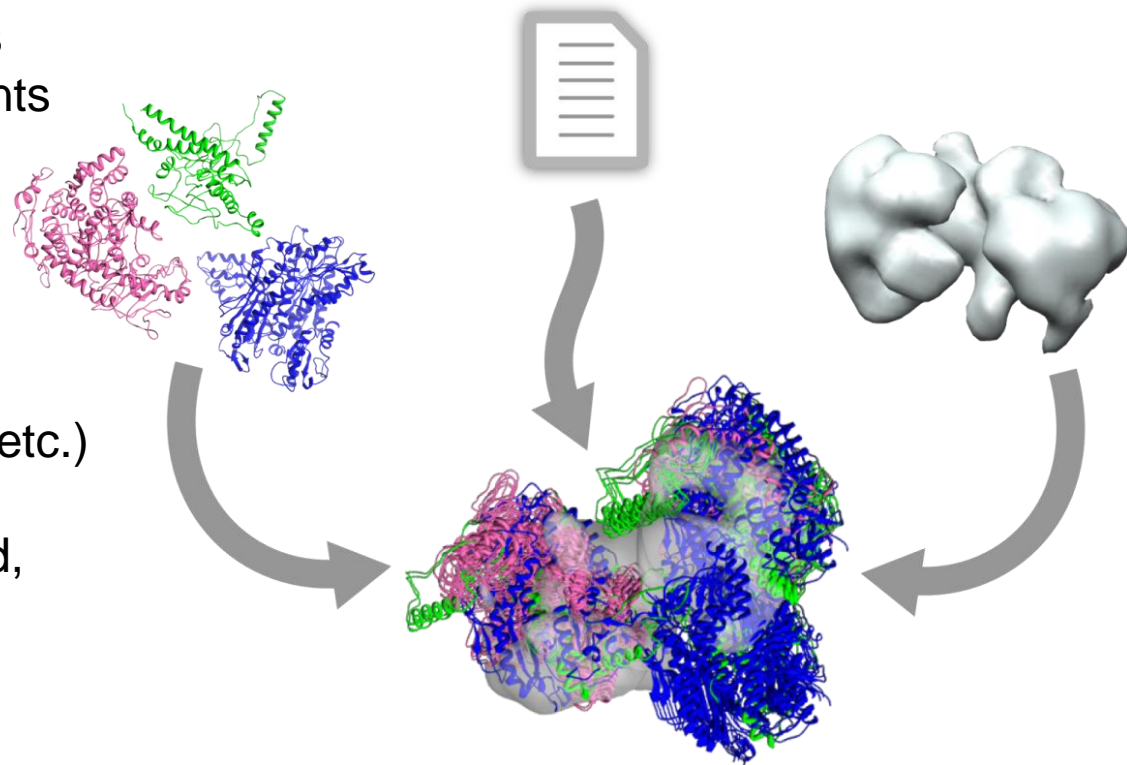


**a software tool for low-resolution modeling
of large macromolecular complexes**

Making sense out of the available data



- sequences of all components
- structures of some components
- models of some components
- disorder / flexibility
- molecule shapes
(**cryoEM, SAXS, SANS**)
- distance restraints
(**FRET, EPR, cross-linking**, etc.)
- accessibility
(enzyme active sites exposed,
footprinting, etc.)

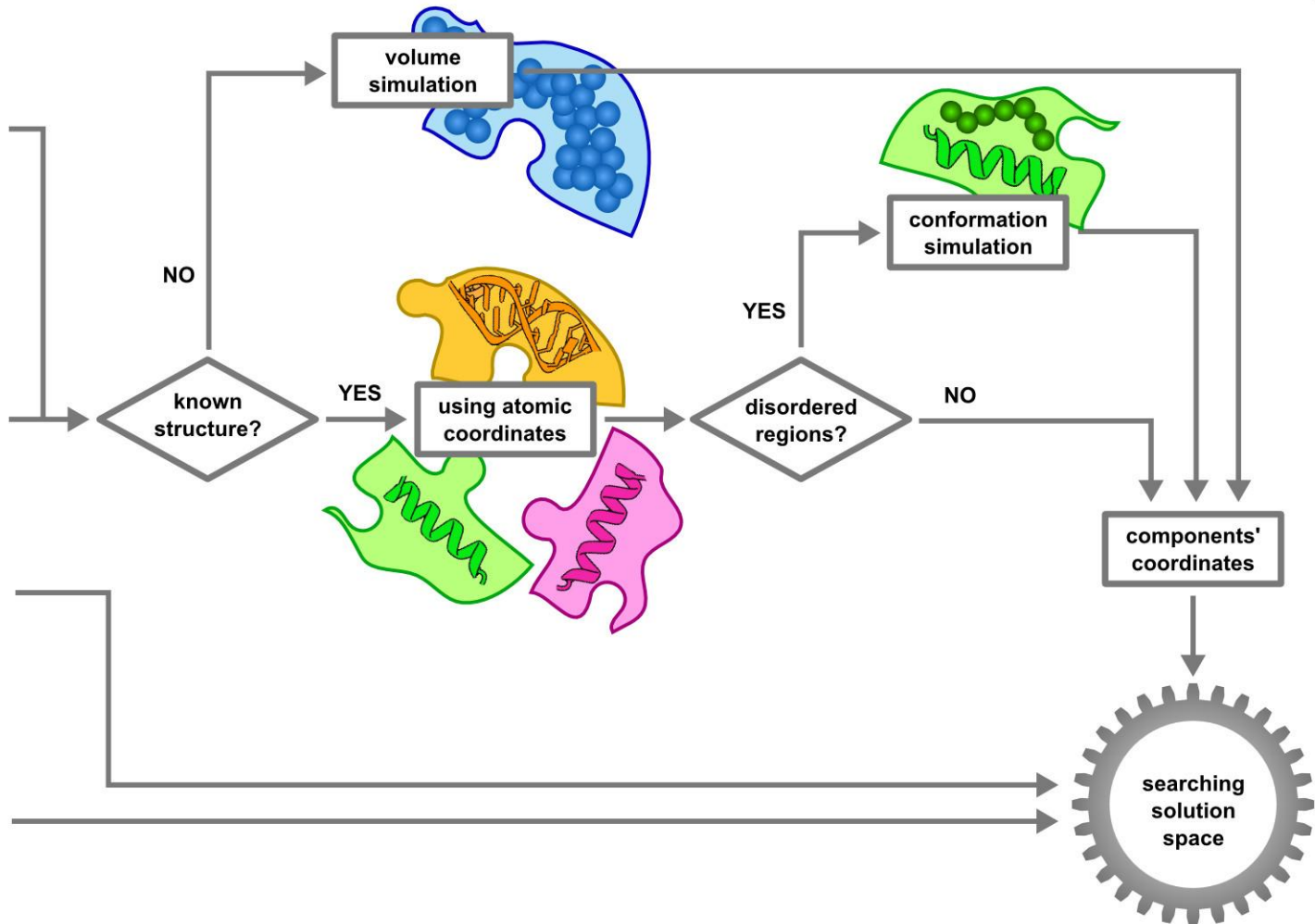
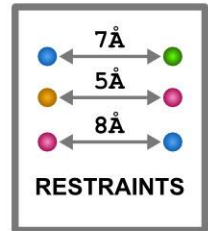
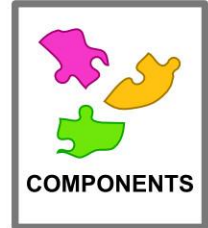


Is it possible to build a 3D model consistent with these data?

Workflow

```
>A  
QVCQGLFNELLENGISV  
>B  
QGKQQLMPQEAAPVPGQ  
>C  
SLEQLYSKYDEMSTIQLM  
>D  
ACUACAGAGGGCAUGGG
```

SEQUENCES



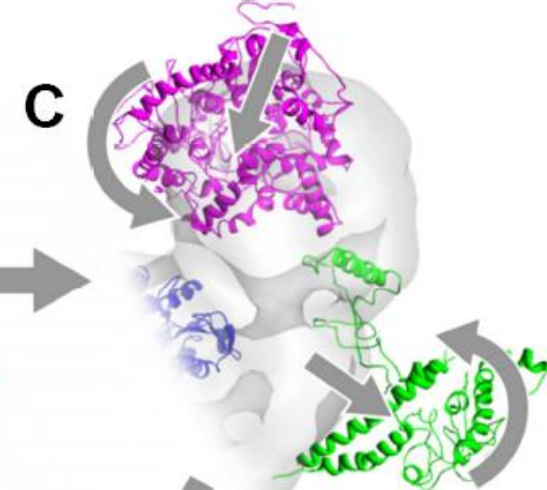
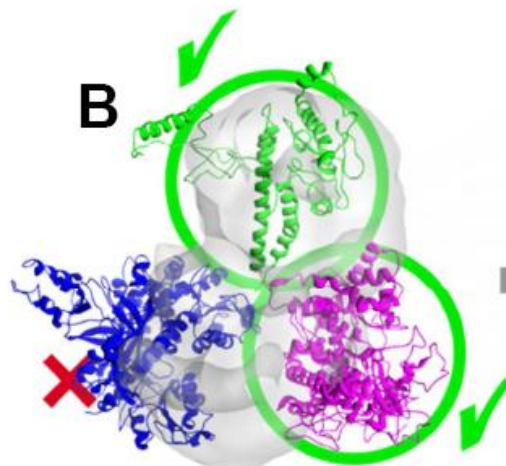
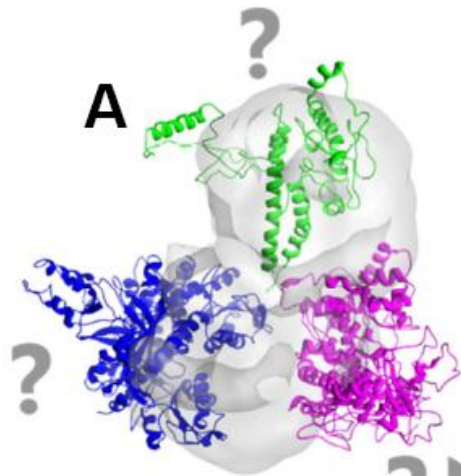
PyRy3D Monte Carlo simulation



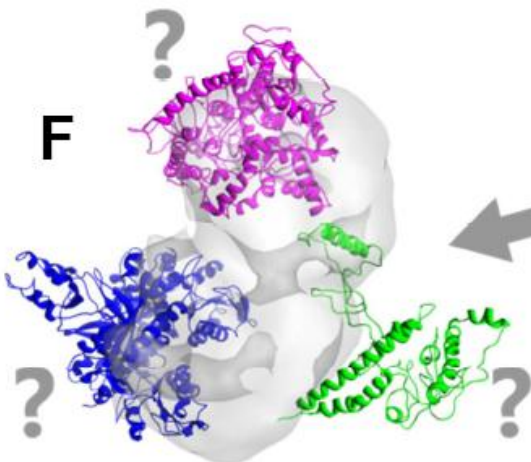
initial conformation

selection of components

random movement

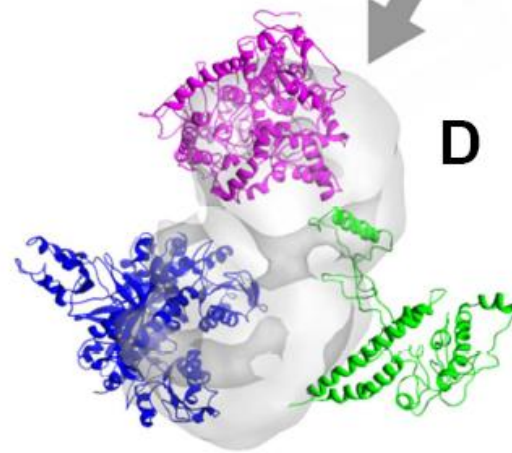


new conformation



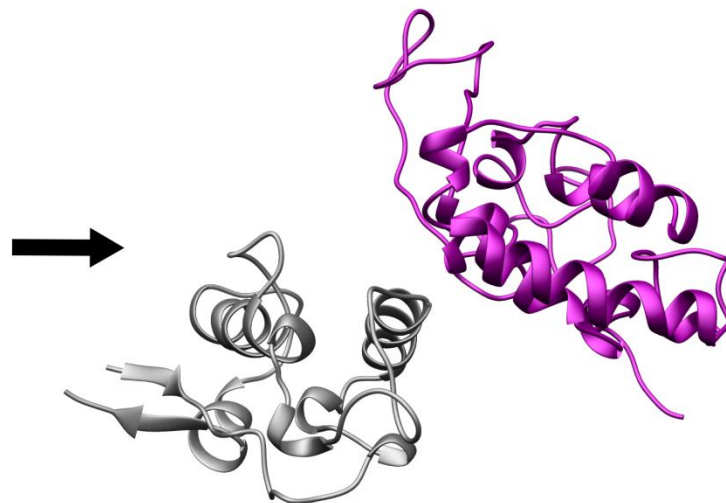
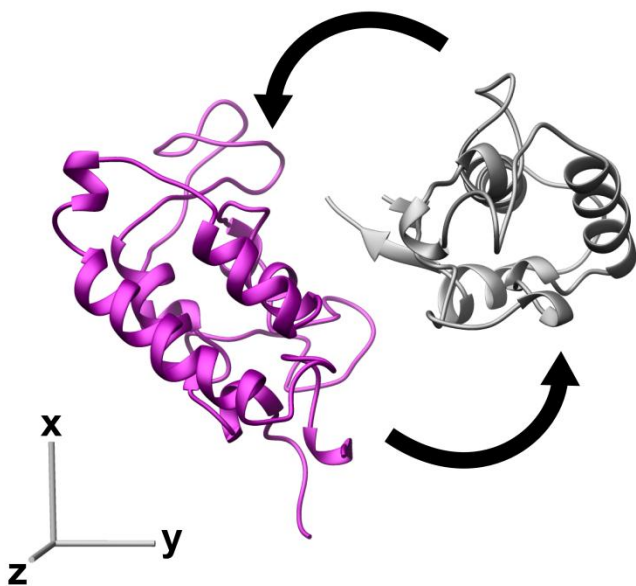
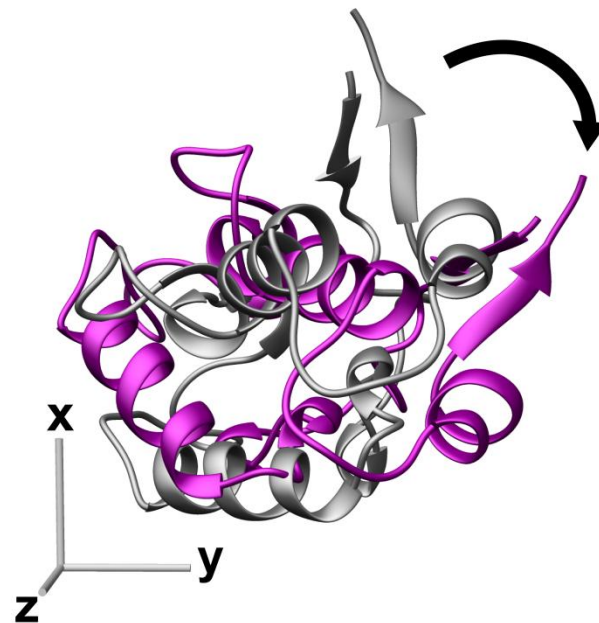
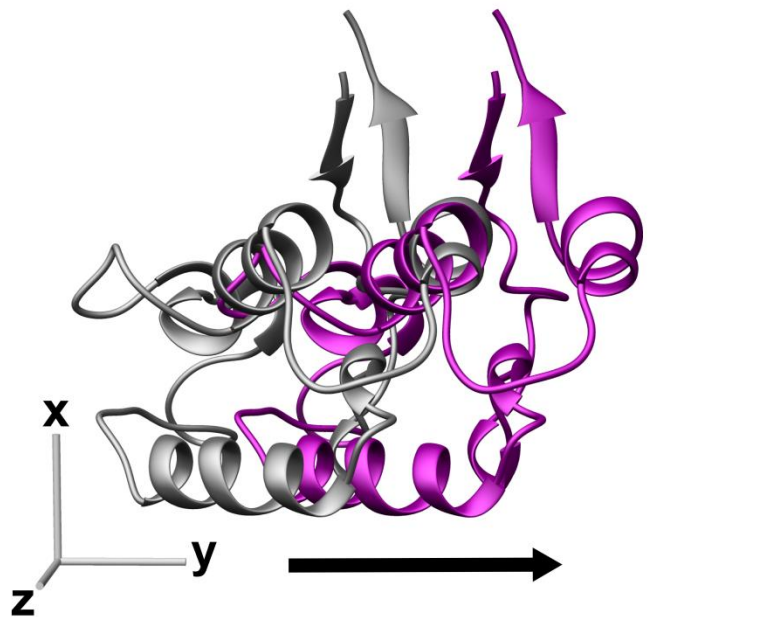
model
scoring

E

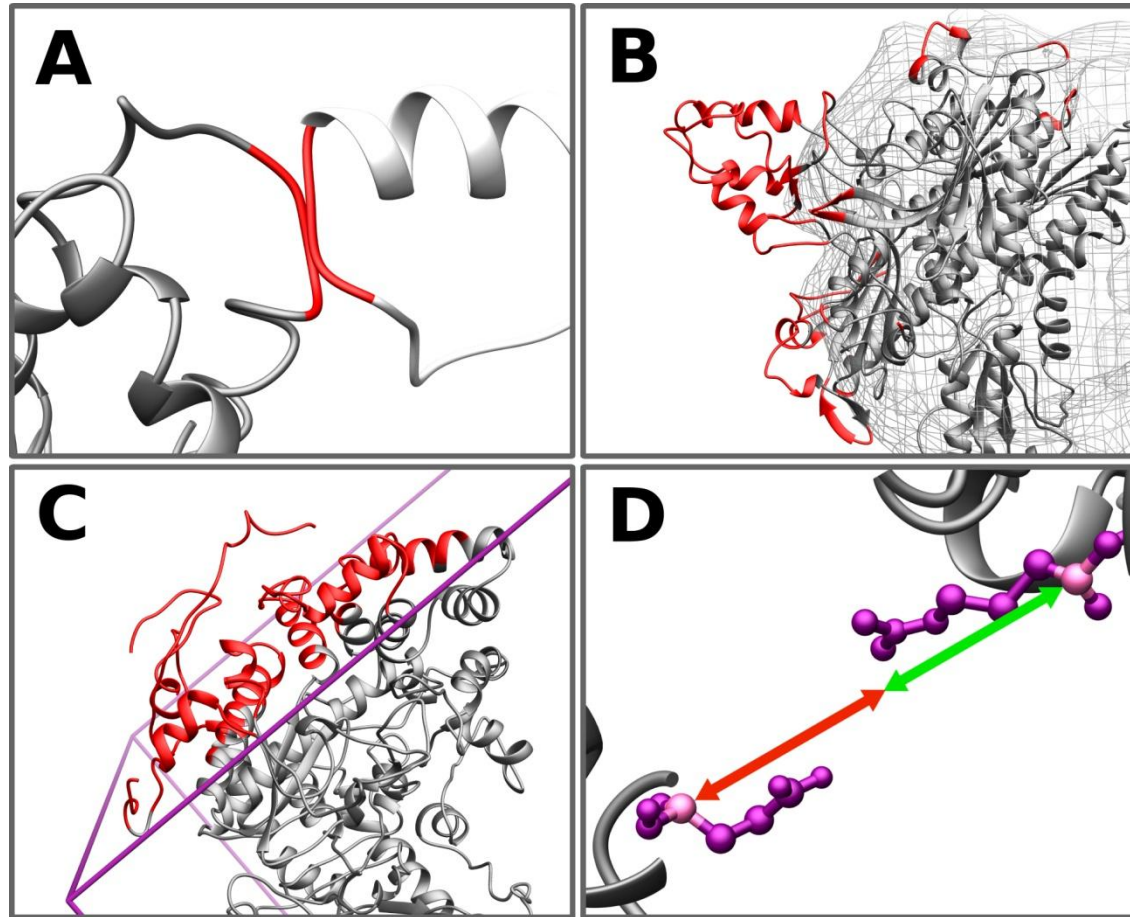


optimization

Set of movements



Scoring function

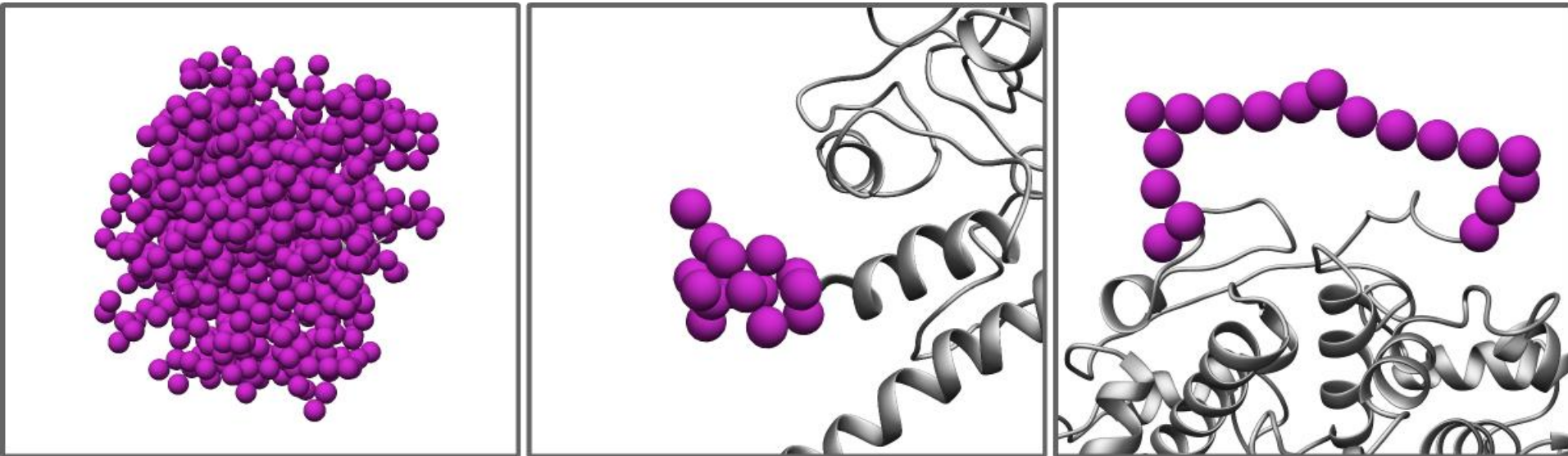


Statistical potentials to evaluate interactions

(to be added soon):

- protein-protein
- protein-RNA/DNA

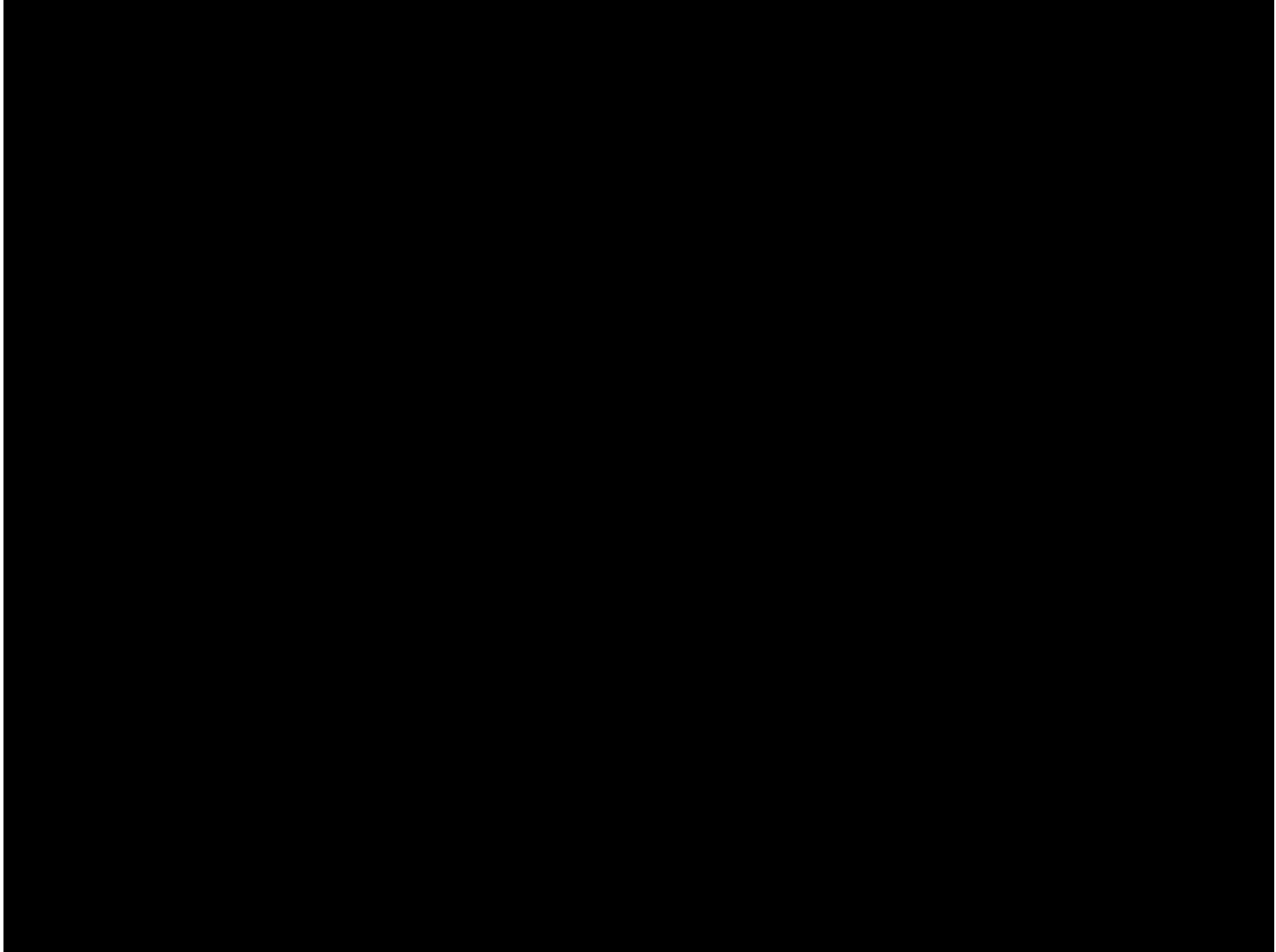
Including information about flexibility



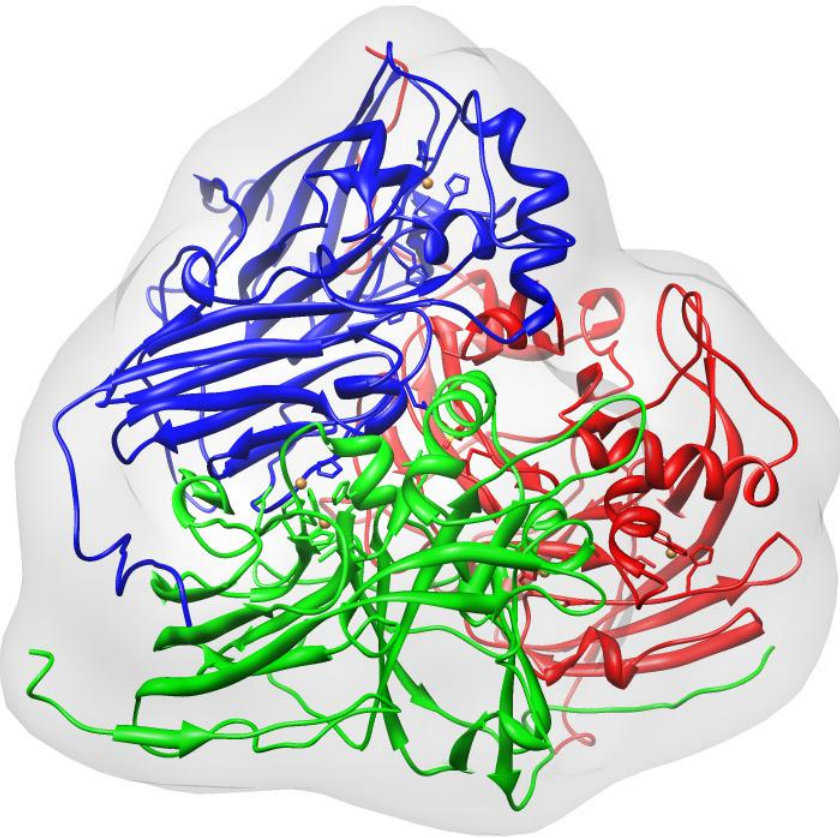
Pseudoatoms are used to build components with:

- no structural data
- missing terminal fragments
- missing internal fragments

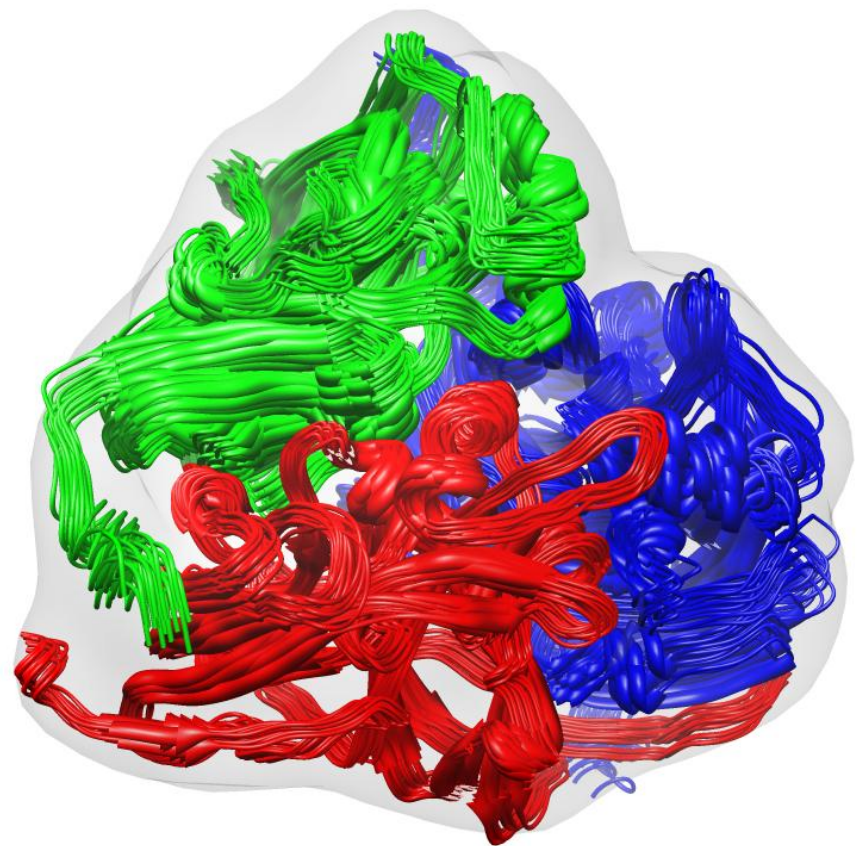
PyRy3D Monte Carlo simulation copper-nitrite reductase (1NIC)



Example results: copper-nitrite reductase (1NIC)



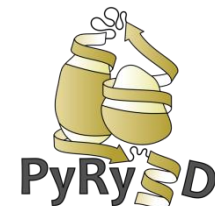
X-ray structure



**models consistent
with cryoEM map**

<http://genesilico.pl/pyry3d/>

PyRy3D usage



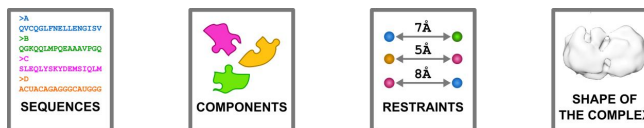
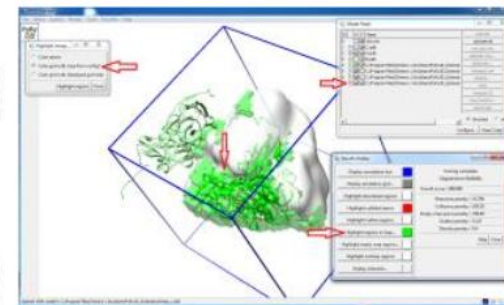
PyRy3D command-line (engine)



```
PyRy3D
program for macromolecular docking into cryoEM maps
(c) 2018 by Joanna M. Kasprzak
usage: python pyry3d.py --help
Usage: pyry3d.py [options]

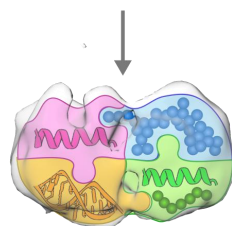
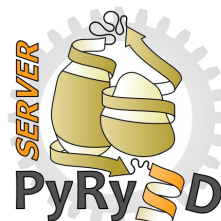
Options:
-h, --help            show this help message and exit
-r FILE, --seq_file=FILE
                    input file with sequences in FASTA format
-d FILE, --dirfile=FILE
                    input file with structure
-r FILE, --restr_file=FILE
                    input file with restraints in Filtrrest3D format
-m FILE, --map_file=FILE
                    input file with complex map
-x FILE, --map_shape=FILE
                    input file with complex map shape
-c CONFIG, --config=CONFIG
                    config file with simulation parameters
-o OUTPUT, --output=OUTPUT
                    write output to file
-t TRAJFILE, --trajfile=TRAJFILE
                    write output to trajectory file
-f FULLATOM, --to_full_atom_model=FULLATOM
                    write best model in fullatom representation
-w MOVIEHISTORY, --save_history_of_moves=MOVIEHISTORY
                    save all moves into a file
-e SCORE_PLOT, --save_plot_with_complex_scores=SCORE_PLOT
                    save plot with complex scores
```

PyRy3D Extension (GUI)



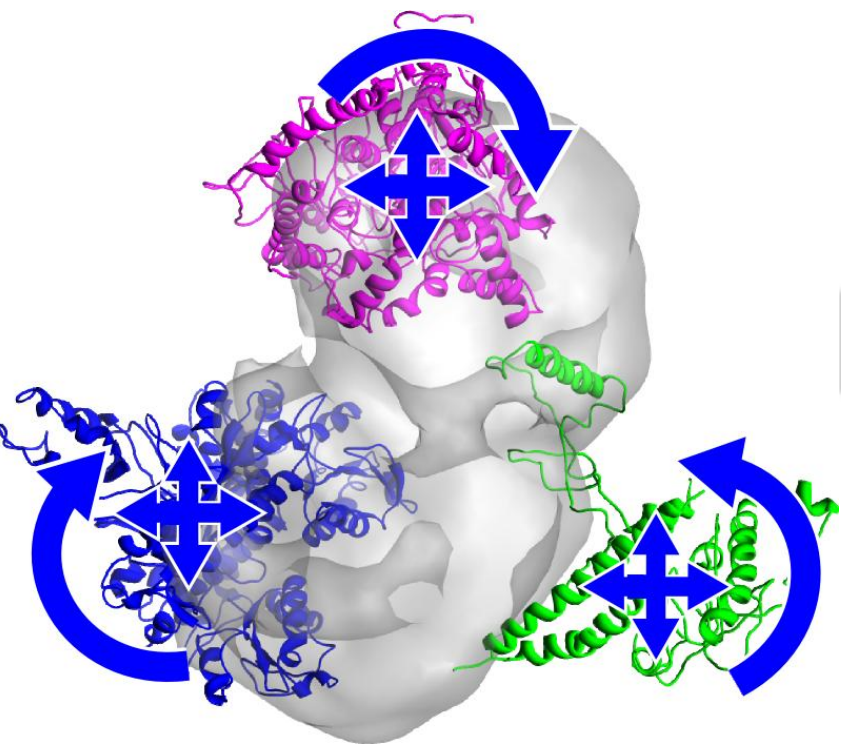
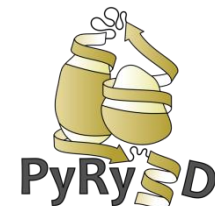
web server

<http://pyry3d.icm.edu.pl>



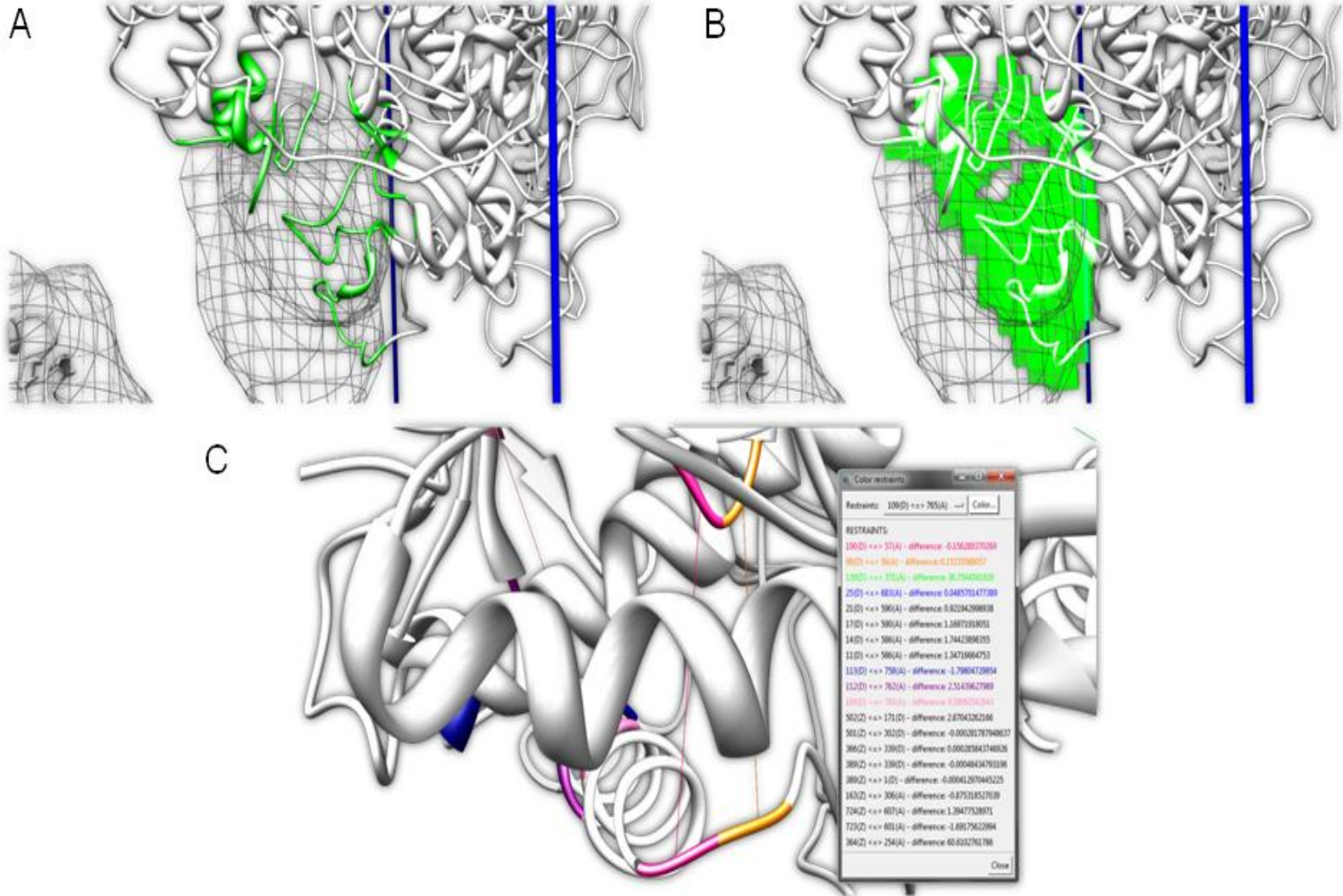
<http://genesilico.pl/pyry3d/>

PyRy3D GUI – UCSF Chimera extension

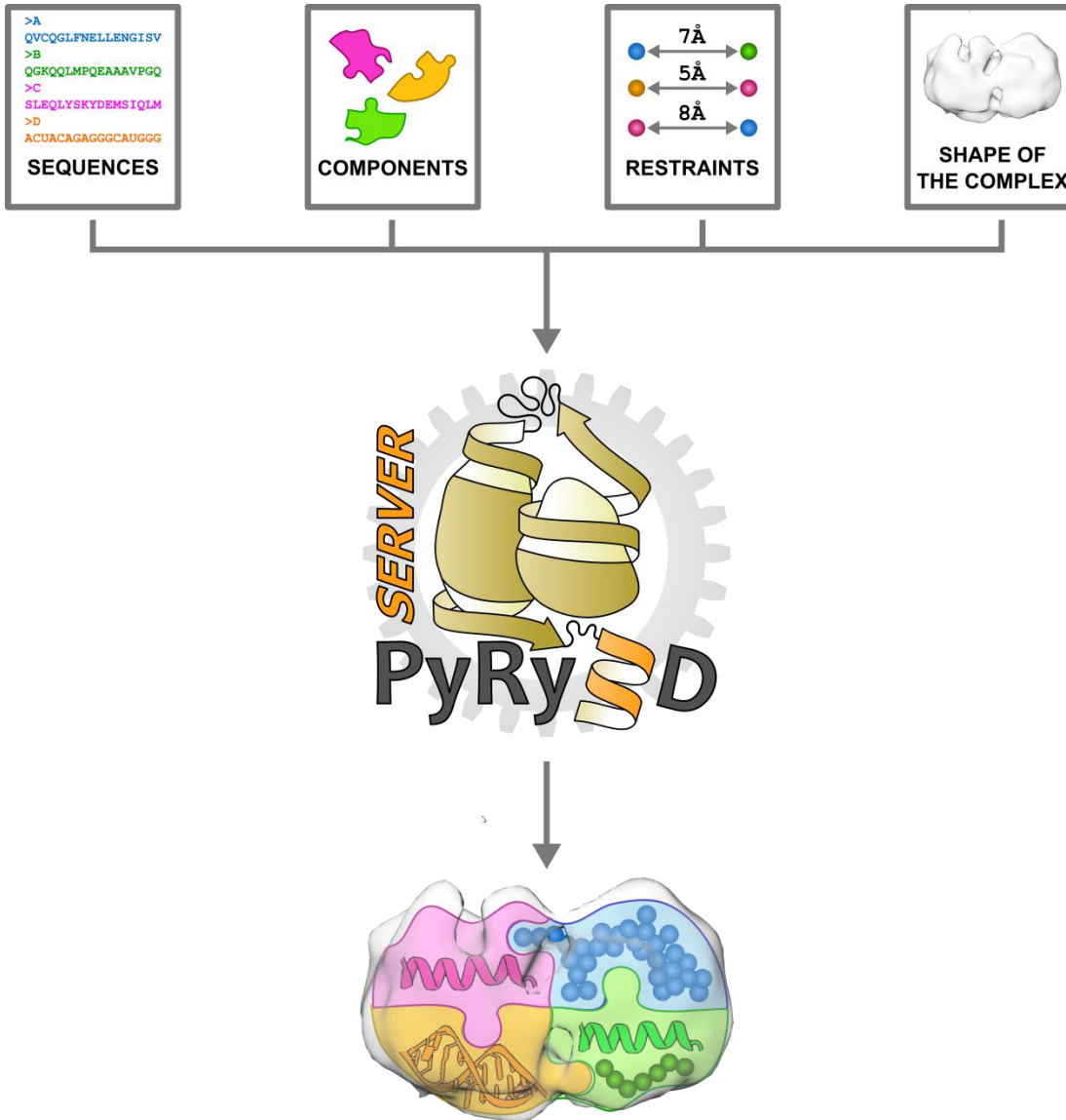


- generate input files for PyRy3D
- run simulations
- rank models
- analyze the scores (e.g. visualize, cluster, rank)
- generate animations
- **and many many more features!!**

PyRy3D GUI – UCSF Chimera extension



PyRy3D server



PyRy3D server



PYRY3D

[Home](#)[Submit](#)[Help](#)[Contact](#)[PyRy3D](#)[Genesisico](#)[Load example](#)

Job title



E-mail



Structures

Upload components' structures

[Przeglądaj...](#)

Nie wybrano pliku.

Sequences

File upload

Upload components' sequences

[Przeglądaj...](#)

Nie wybrano pliku.

Complex shape

density map

Upload complex shape

[Przeglądaj...](#)

Nie wybrano pliku.

Restrains

Upload restrains

[Przeglądaj...](#)

Nie wybrano pliku.

Parameters

File upload

Upload simulation parameters

[Przeglądaj...](#)

Nie wybrano pliku.

[Reset](#)[Submit](#)

Highlights of PyRy3D



Easy to use for non-experts, has a graphical user interface to generate input files, set up simulation parameters, visualize the simulation in real time, change parameters during the simulation etc.

Fully scriptable, expert users can write Python scripts for complicated operations

Enables the use of electron density maps and SAXS/SANS data to describe shapes

Enables the use of many different restraints from experiments and predictions

Can use crystal structures, NMR ensembles, theoretical models, arbitrary shapes

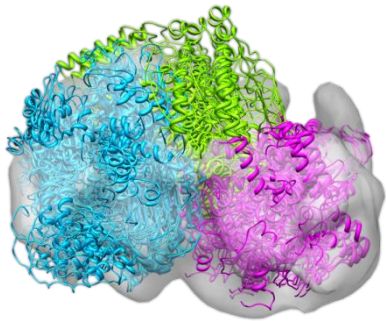
Can model disordered segments and sequences without known structure

<http://genesilico.pl/pyry3d/>

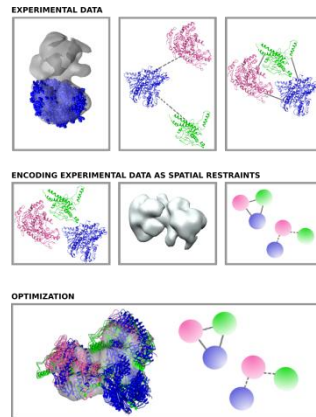
Summary



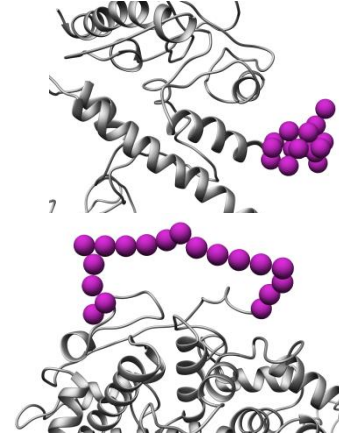
BUILDS LOW-RESOLUTION MODELS



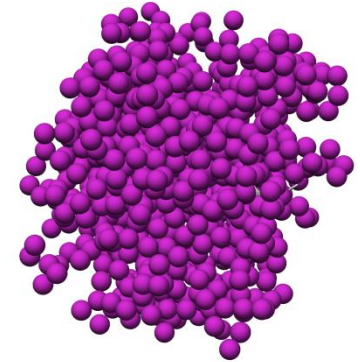
WORKS WITH RESTRAINTS



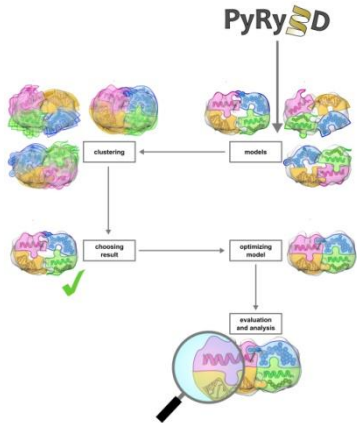
ADDS MISSING FRAGMENTS



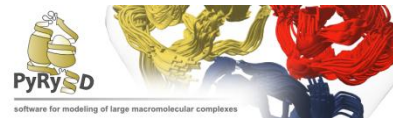
SIMULATES VOLUMES



PROVIDES ENTIRE MODELING PIPELINE



FULLY SCRIPTABLE



software for modeling of large macromolecular complexes

PYRY3D

Modeling of human pentameric gamma complex structure

- This tutorial page can be used to learn how to use PyRy3D commands to build a simple complex model. In particular you will learn how to:
 - Choose input files for analysis
 - Interpretation simulation parameters
 - Analyze results
- [Go to pentameric gamma modeling tutorial]

Modeling of 1982 complex structure using PyRy3D Chimera Extension

- First steps in using PyRy3D/UCSF Chimera Extension
- Molecular complex modeling
- Model analysis
- Choosing PyRy3D Restraints in UCSF Chimera
- Preparing input files for a combined use version of the program
- Monitoring modeling of models
- Decoding a model from simulation

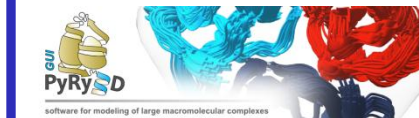
Support from PyRy3D authors

PyRy3D has any comments, recommendations, ideas how to improve the workflow in the software please do not hesitate to contact us

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Marek Szymanski m.szymanski@genetec.pl
Janina Kopycka janina.kopycka@genetec.pl

<http://genesilico.pl/pyry3d>

GRAPHICAL INTERFACE



software for modeling of large macromolecular complexes

GUI PyRy3D

software for modeling of large macromolecular complexes

ONLINE SERVER



software for modeling of large macromolecular complexes

```
graph TD
    SERVER[SERVER PyRy3D] --> SEQUENCES[SEQUENCES]
    SERVER --> COMPONENTS[COMPONENTS]
    SERVER --> RESTRAINTS[RESTRAINTS]
    SERVER --> SHAPE[SHAPE OF THE COMPLEX]
    SEQUENCES --> MODEL[MODEL]
    COMPONENTS --> MODEL
    RESTRAINTS --> MODEL
    SHAPE --> MODEL
```

<http://pyry3d.icm.edu.pl>

3,2,1 START!!!



How to prepare input files?






DATA TYPE	FORMAT	COMMENTS
*STRUCTURES	PDB	<ul style="list-style-type: none">• EACH COMPONENT AS ONE CHAIN;• IF DISORDERED REGIONS OCCUR – NUMBERING OF RESIDUES MATTERS
SEQUENCES	MULTI FASTA	<ul style="list-style-type: none">• REQUIRED ONLY WHEN DISORDERED REGIONS OCCUR
DENSITY MAP AB INITIO MODEL SAXS CURVE	MRC PDB – DAMMIN/IF .DAT	
RESTRAINTS	FILTREST3D	<ul style="list-style-type: none">• POSSIBLE TO ASSIGN WEIGHTS TO RESTRAINTS AND TO COMBINE THEM BY BOOLEAN OPERATORS
CONFIGURATION FILE	TEXT FILE	<ul style="list-style-type: none">• ALL PARAMETERS CAN BE MODIFIED HERE

*** required**

Restraints file – extended Filtrest3D format



```
dist (  
  (G8) "C" - (U9) "D" (<=1.50)  
  (U11) "D" - (C12) "A" (<=1.50)  
  (G59) "A" - (A60) "D" (<=1.50)  
  (C62) "D" - (C63) "B" (<=1.50)  
  (G83) "B" - (U84) "D" (<=1.50)  
  (G88) "D" - (C89) "C" (<=1.50)  
)
```

 residue name and number
 chain ID
 distance in Ångströms

- Boolean operators: AND, OR
- Other types of restraints: PointDistance, SurfaceAccess, Symmetry, Relation

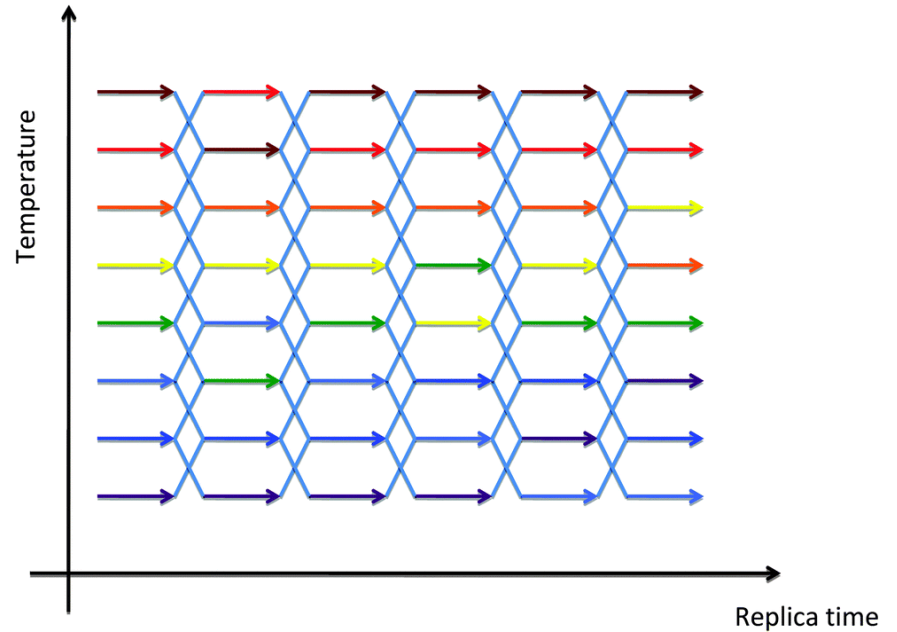
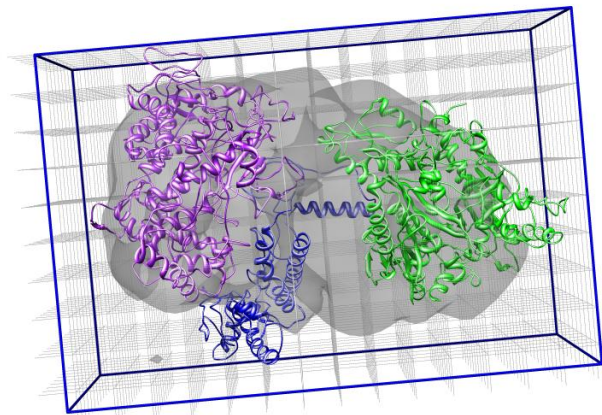
How to set first modeling?



SIMMETHOD SimulatedAnnealing
ANNTEMP 10

STEPS 100
WRITE_N_ITER 10

SIMBOX 1.2
GRIDRADIUS 1.0



How to set scoring function weights

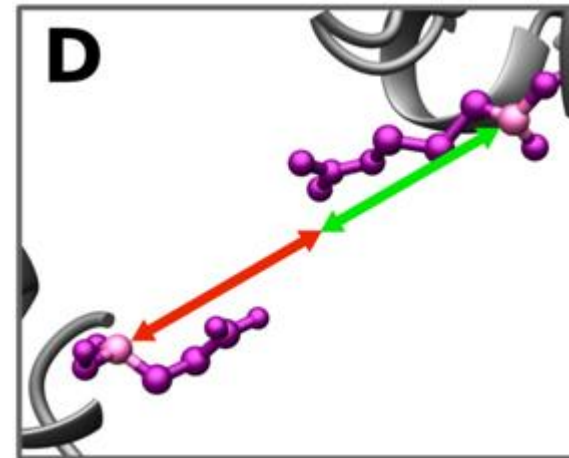
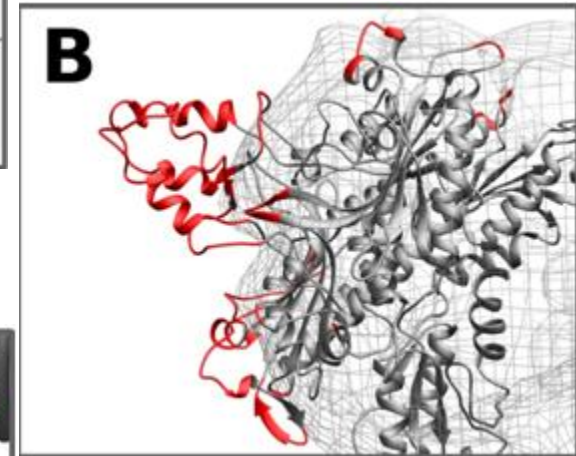
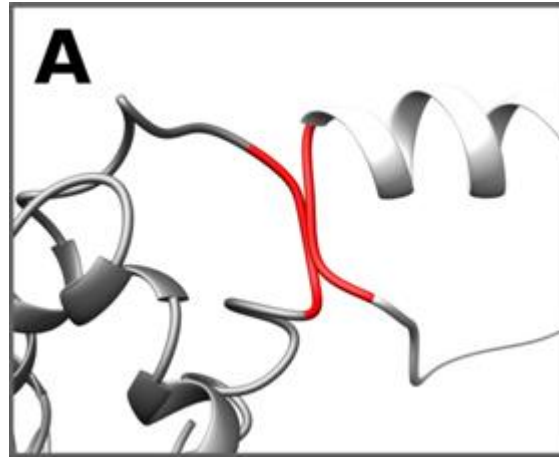


CLASHES 10 10
CLASHES_ALLATOMS 1 1

OUTBOX 10 10
MAP_FREESPACE 5 1
DENSITY 0 3

RESTRAINTS 1 1
SYMMETRY 0 0

CHI2 1 1
RG 1 1

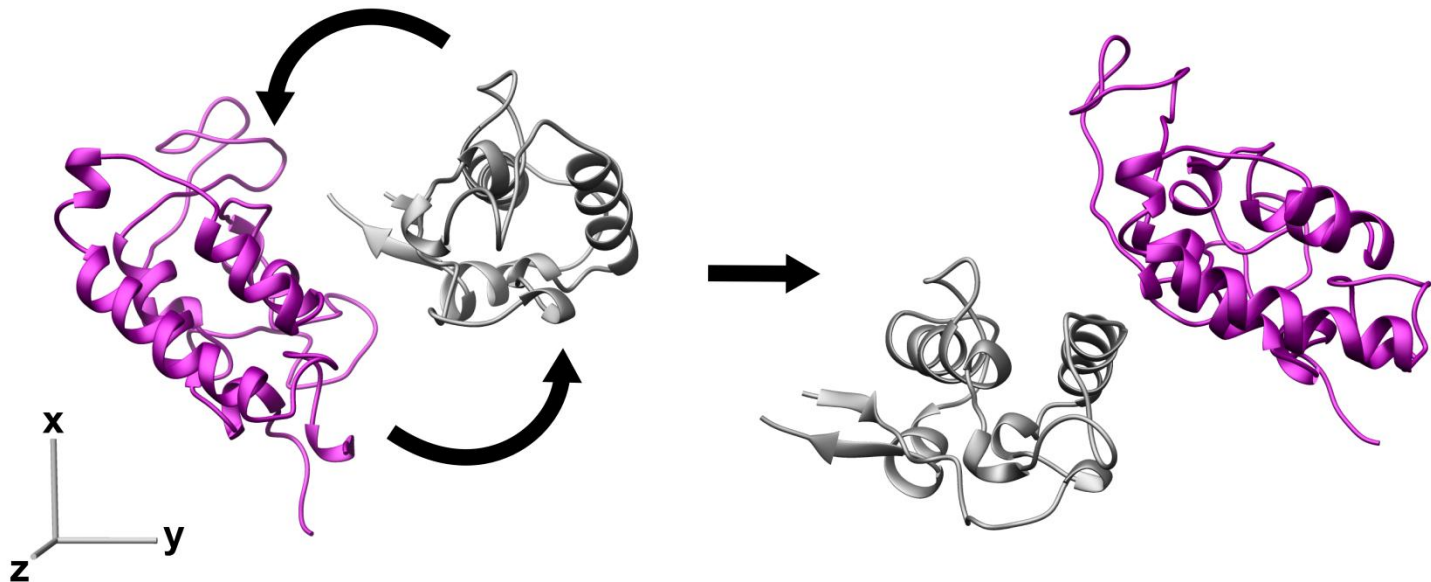
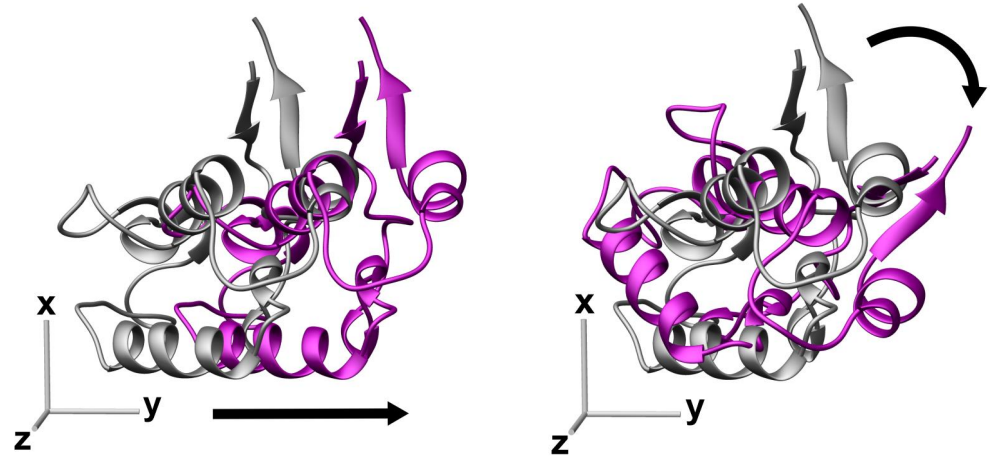


SCALE_PARAMS ON

How to choose allowed moves



ROTATION_FREQ	0.3
ROTATION_COV_FREQ	0.0
TRANSLATION_FREQ	0.3
EXCHANGE_FREQ	0.4
EXCHANGESAMPLE_FREQ	0.0
SIMUL_DD_FREQ	0.0
TRANSLATION_ALL_FREQ	0.0
ROTATION_WHOLE_FREQ	0.0



PyRy3D team



Janusz M. Bujnicki
Joanna Kasprzak
Mateusz Dobrychłop
Wojciech Potrzebowski

Witold Rudnicki
Mateusz Susik
Laura Pogorzelska
Rafał Niemiec





*Bioinformatics
Laboratory*

Thank you for your attention!