UNIVERSITY OF GDAŃSK

CHEMIA UG

Using the UNRES server and the standalone UNRES package in SAXS-data-assisted modeling of protein structure

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Outline

- Introduction to UNRES server
- Running a simple job (local energy minimization)
- Unrestricted protein-structure modeling
- Protein structure modeling with SAXS restraints
- Calculations with full UNRES package
- Installing standalone UNRES
- Q&A
- Hands-on part (optional)

UNRES and UNRES server

- Description, download, instructions and more: www.unres.pl

  A. Liwo et al., *J. Molec. Modeling*, 2014, 20

- Server available
  http://unres-server.chem.ug.edu.pl
  (Author: Czarek Czaplewski)

  C. Czaplewski, A. Karczyńska, A.K. Sieradzan, A. Liwo, *Nucleic Acids Research,* 2018, 1, doi: 10.1093/nar/gky328 (web server issue)

UNRES server

UNRES server | Tutorial | Input data | Output files | Changelog | About | Contact

UNRES server: ab initio simulations of protein structure and dynamics by using the coarse-grained UNRES model.

Run a single job without login.

Enter a new job name...

Register/login to run and save multiple jobs (optional).

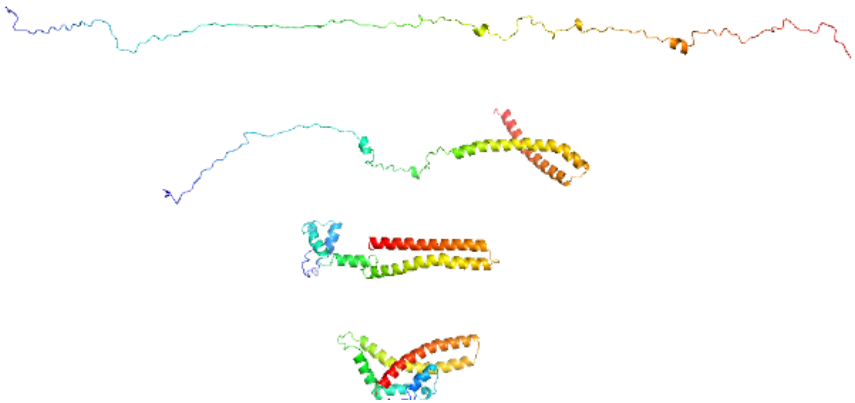
Username:

Password:

Forgot password? Reset it!

Not member? Register!

Log in



Registration

- Registration is optional; jobs can be run in guest mode
- To register
  - Click „Register” on the main server page
  - Type in your login name, password, and email address
  - Check your email and when you receive the activation link, click it

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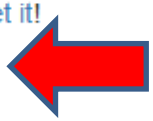


ta Output files Changelog About Contact

Username: johndoe Required. 150 characters or fewer. Letters, digits and @/./+/-/_ only.

Email: john.doe@gmail.com email address

Password: ••••••

- Your password can't be too similar to your other personal information.
- Your password must contain at least 8 characters.
- Your password can't be a commonly used password.
- Your password can't be entirely numeric.

Password confirmation: •••••• Enter the same password as before, for verification.

Submit

Running jobs

- Running jobs in guest mode (no account)
  - one job at a time
  - user data & results kept for 2 weeks
  - access to past jobs possible provided that the web address of the link to a job has been saved
- Running jobs by registered users
  - multiple jobs can be run simultaneously
  - past jobs saved on user's account, easily accessible

Simulation types

- Single energy minimization
- Canonical molecular dynamics
- Simulating conformational ensembles by MREMD
  - Free/secondary-structure restrained simulations
  - SAXS-data assisted simulations

Input data

- Basic and advanced mode enabled
- User-defined input
  - Amino-acid sequence (one-letter code)
  - Type of starting structure (extended or random)
- PDB input
  - Complete information (amino-acid sequence, starting and reference structure) is taken from the PDB structure
- Explicit file name or PDB code (can include chain ID, e.g., G3Q:B) can be supplied to input PDB structure
- Simulation parameters (optional)
- Secondary-structure prediction (PSIPRED format)
- SAXS data

Simulating conformational ensembles by MREMD

Sequence

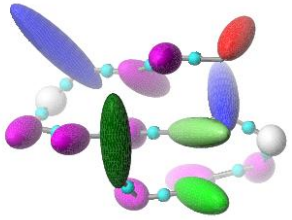
Extra info as restraints

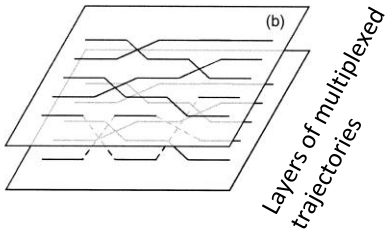
Conformational search with UNRES/MREMD

WHAM: determine the folding temperature.

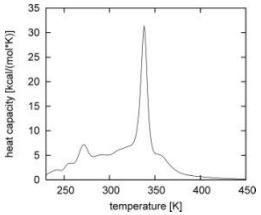
Cluster analysis, cluster ranked by probabilities @T<T_f, NOT energies

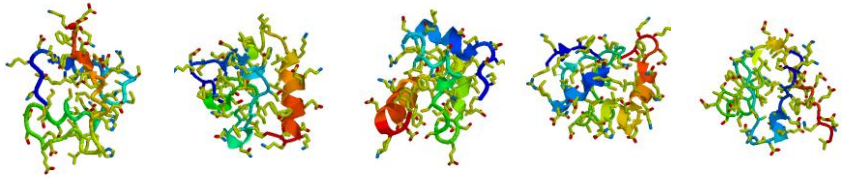
Conversion of CG candidate models to AA models



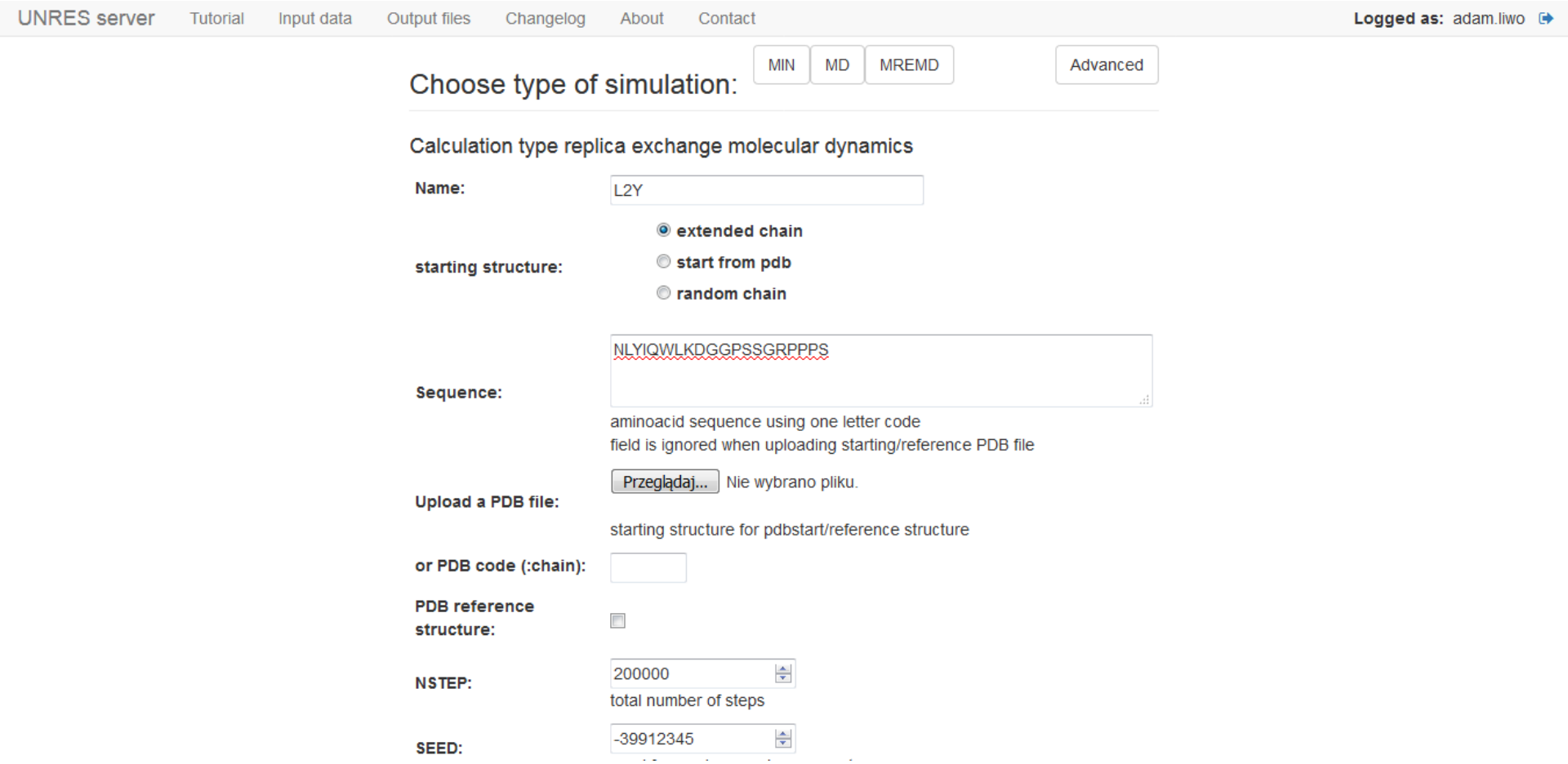


$$P_k(T,\xi) = \exp\left[\omega(\xi) - \frac{U_k}{RT}\right]$$

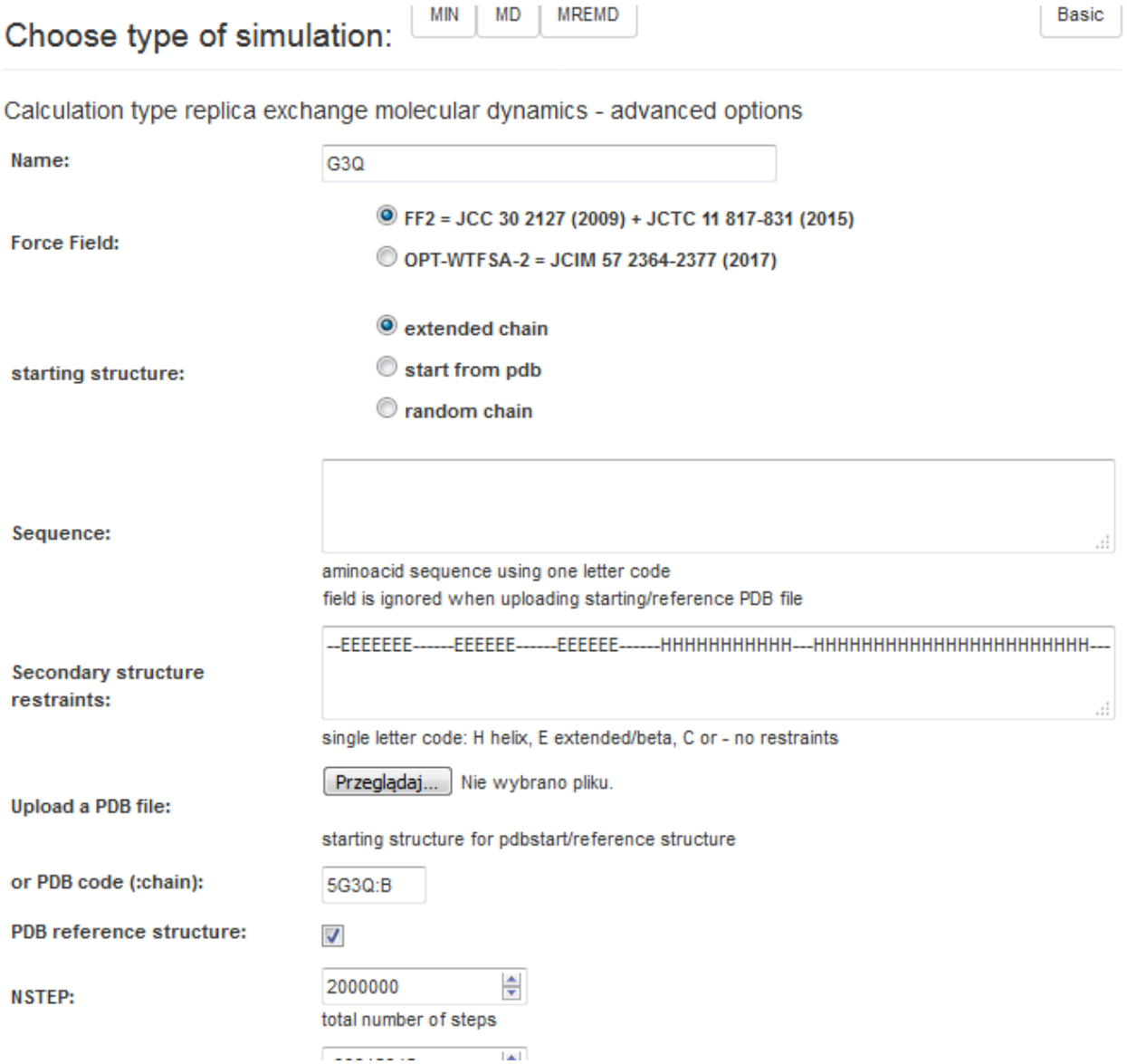




Sample input screen

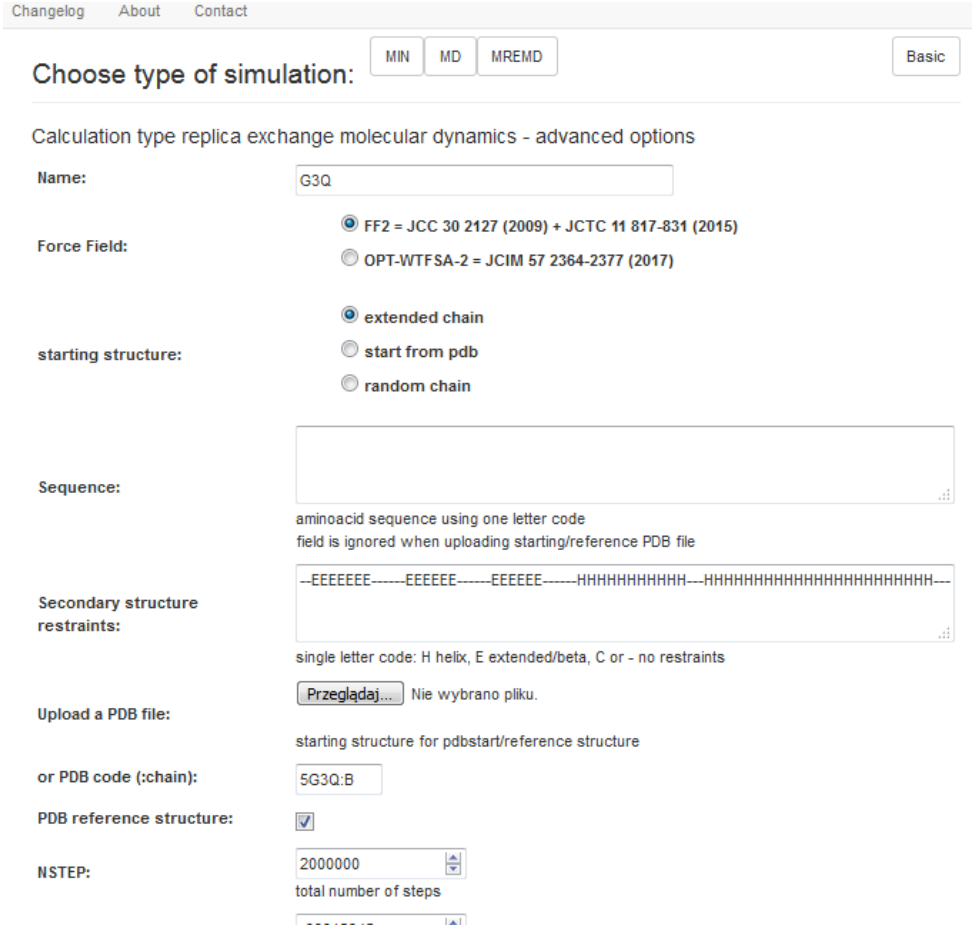


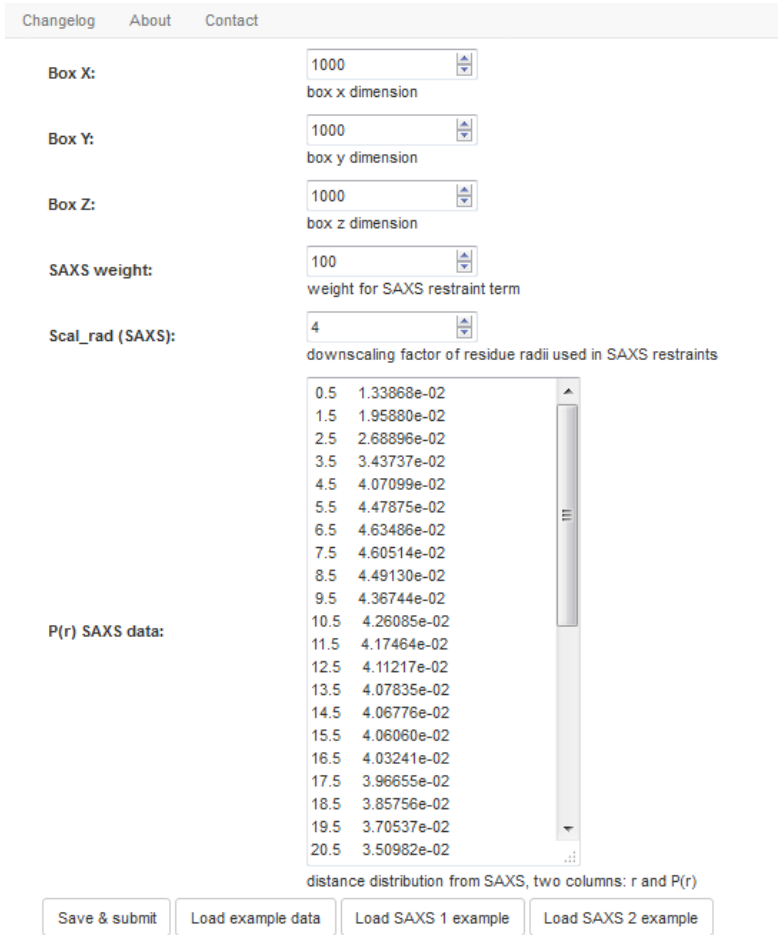
Sample input screen 2



Download by clicking „Load example data” at the bottom of the screen, advanced mode

Sample input screen: SAXS data





Download by clicking „Load SAX1 example” at the bottom of the screen, advanced mode

Tutorial 1: single energy minimization of a PDB structure

- Enter the UNRES server page
- Login to the server (if you have an account)
- Type in the job name and hit „Enter”
- Click on „Load example data” at the bottom of the screen
- Save & submit job
- Wait for the job to finish
- For guest users, the results are displayed immediately, registered users click on the job name to display the results
- Having completed the example try to prepare & run the minimization job on your own (different PDB file/code can be selected)

Tutorial 2: MREMD simulations of tryptophan cage (prediction mode)

- After entering job name click „MREMD”
- Type 1L2Y (the PDB code of tryptophan cage) in the „Upload a PDB file or PDB code” field
- Mark „Reference structure”
- Click „Save & submit job
- Wait for the job to finish and view the results. Notice the 5 clusters of conformations and their populations.
- Another example is available in the advanced mode; click „Load example data” after selecting „Advanced mode”. This example includes secondary-structure-prediction information. It takes long to finish.

Choose type of simulation:

MIN | MD | MREMD

Advanced

Calculation type replica exchange molecular dynamics

Name: L2Y

starting structure:
- (•) **extended chain**
- ( ) **start from pdb**
- ( ) **random chain**

Sequence:

aminoacid sequence using one letter code
field is ignored when uploading starting/reference PDB file

Upload a PDB file: Przeglądaj... Nie wybrano pliku.

starting structure for pdbstart/reference structure

or PDB code (:chain): 1L2Y

PDB reference structure: [x]

NSTEP: 200000

total number of steps

SEED: -10396899

seed for random number generator

Save & submit | Load example data

Tutorial 3: Simulations with simulated SAXS-like restraints on distance distribution

- After setting up the job select „MREMD” „Advanced” and „Load SAXS1 example”. The data are synthetic C$^{\alpha}$-distance distribution from the experimental structure of 5UJQ
- Start the job
- After the job finishes, view the 5 models and the agreement between the calculated and „experimental” distance distribution.
- An example with real data (Schmidt et al.. J. Mol. Biol., 2019, 395, 105-122) can be downloaded by clicking „Load SAXS data 2” however, this calculation takes longer.

Calculations with standalone UNRES

- Calculation types
  - Energy evaluation (single or multiple conformations)
  - Energy minimization
  - Canonical molecular dynamics
  - Replica-exchange molecular dynamics
  - Umbrella-sampling molecular dynamics (canonical and replica-exchange)
  - Global energy minimization by Conformational Space Annealing
  - Energy-map construction
  - Secondary structure, distance (including contact-distance), structure-based, and SAXS restraints in every mode

Calculations with standalone UNRES

- Running calculations in batch mode is strongly recommended
- Text input file must be prepared; however, UNRES server can be used in preparing the input files. Refer to www.unres.pl/docs for the descripton of input files
- Sequence can be input independent of the reference structure (which must have no gaps)
- Postprocessing with WHAM and CLUSTER must be run separately

Installation of standalone UNRES

- Get and unpack the UNRES distribution from www.unres.pl/downloads (select **unres-SAXS.tar.gz**) or from git
- Installation instructions: www.unres.pl/unres-install
- Easy installation can be done using cmake; all components get installed
- Without cmake the user needs to customize the „Makefile”s in each subdirectory and run make separately

Sample installation command flow

```
git clone http://mmka.chem.univ.gda.pl/repo/unres.git
cd unres
git checkout homology
mkdir build
cd build
cmake -DUNRES_MD_FF=E0LL2Y ..
make
make install
```