rotag: generating rotamer libraries for protein side-chains

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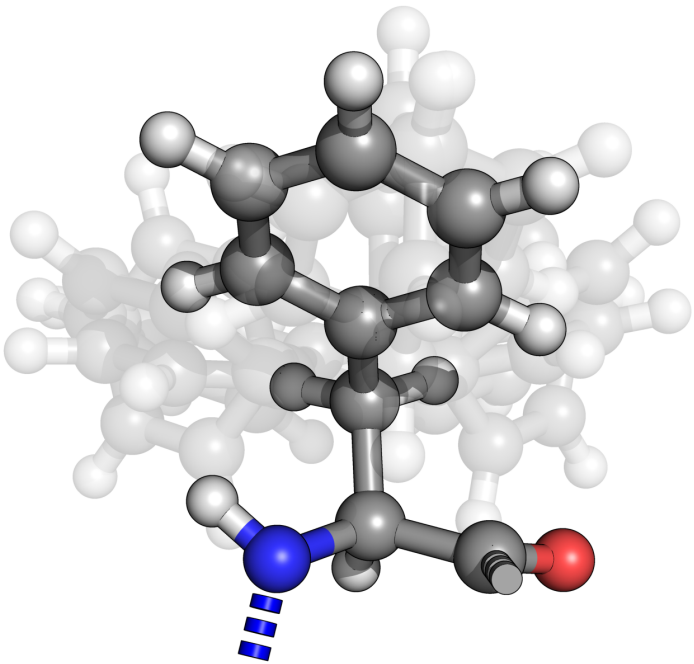
Side-chain rotamer libraries



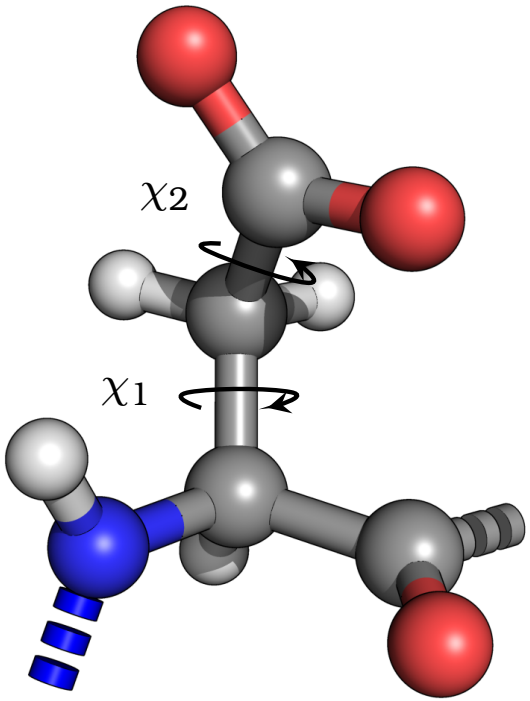
Rotamer – a conformational isomer whose structure is determined only by rotation around the bond or bonds.

Rotamer library – a collection of rotamers most commonly found in crystal structures.

Usage of rotamer libraries:

- studies of how mutations affect side-chain atom interactions with ligands;
- protein structure prediction and refinement.

Method utilising physics-based constraints (1)

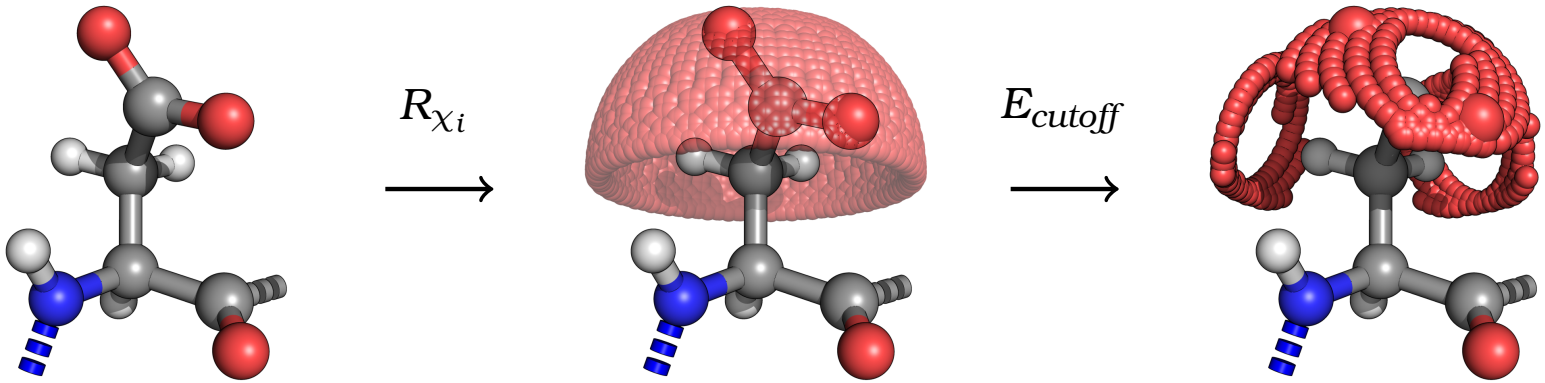


Rotational model

$$\boldsymbol{p}^{0\prime} = \boldsymbol{T}_n^0 \cdot (\prod_{i=1}^{n} \boldsymbol{R}_{\chi i} \cdot \boldsymbol{T}_{i-1}^i) \cdot \boldsymbol{p}^0$$

$\boldsymbol{p}^{0\prime}$	- transformed atom coordinates;
$\boldsymbol{T}$	- reference frame changing operator;
i	- reference frame;
$\boldsymbol{R}$	- dihedral angle changing operator;
χ	- dihedral angle;
$\boldsymbol{p}^0$	- atom coordinates of the observed atom;

Method utilising physics-based constraints (2)



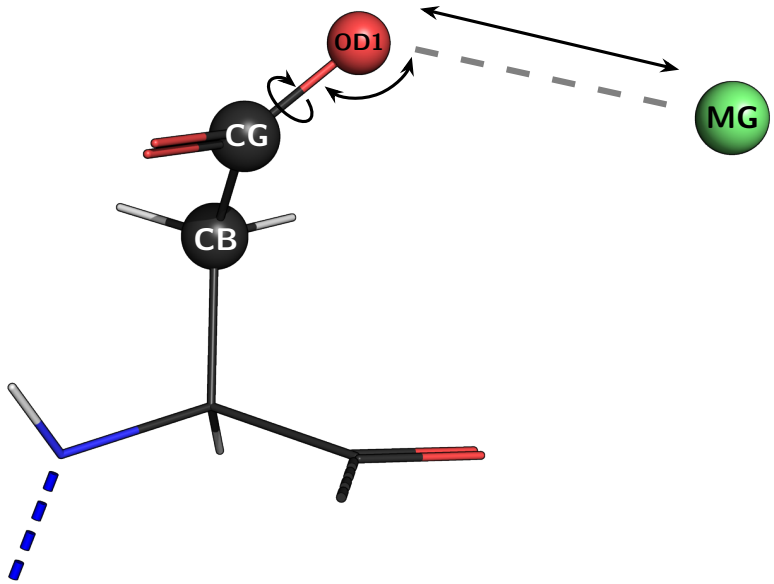
Energy calculation

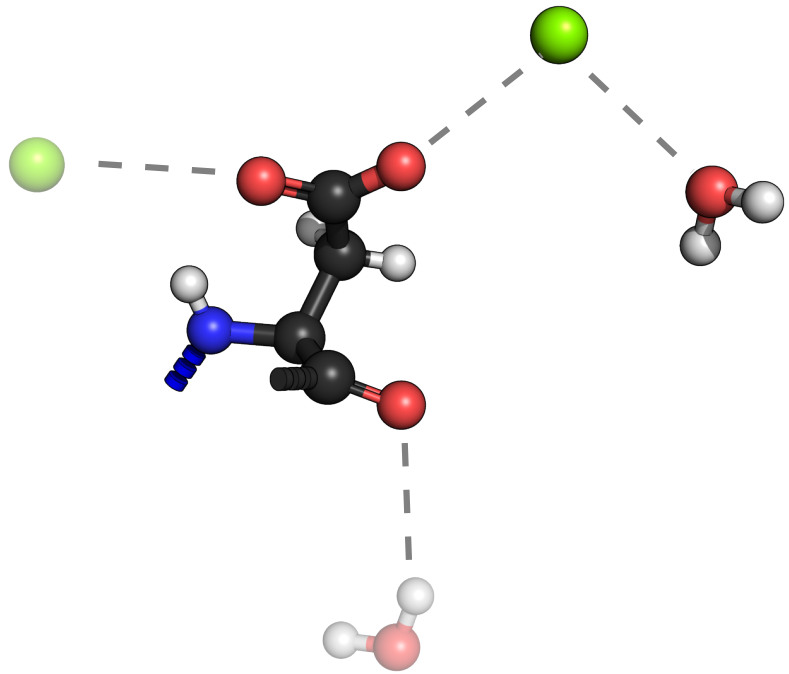
$$E_{\text{Total}} = \sum_{i} \sum_{j \neq i} Q_{ij} (w_1 E_{ij}^{LJ} + w_2 E_{ij}^{C} + w_3 E_{ij}^{H}) + \sum_{\text{d}} w_4 E_d^T \tag{2}$$

where:

E	–	energy value;	LJ	–	Lennard-Jones;
w	–	weight;	C	–	Coulomb;
i,j	–	atom indexes;	H	–	hydrogen bond;
d	–	dihedral angle index;	T	–	torsional.
Q	–	distance cutoff function;			

Extending rotamer libraries including ions and ligands





Method's advantages and disadvantages

Advantages:

- single protein structure is needed to produce possible rotamers for each protein residue;
- non-canonical amino acids could be also analysed;
- rotamer scanning resolution can be chosen based on computational resources.

Disadvantages:

- current implementation of the method in Perl programming language is slow.

References:

- Algirdas Grybauskas, Saulius Gražulis, Building protein structure-specific rotamer libraries, Bioinformatics, Volume 39, Issue 7, July 2023, btad429. https://doi.org/10.1093/bioinformatics/btad429