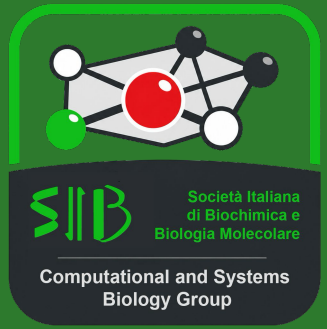
S3 · 15:00–15:15

Towards RING 5.0: An Updated Tool for the Analysis of Protein Structures Through Residue Interaction Networks



Sol Clara Begué

University of Padua

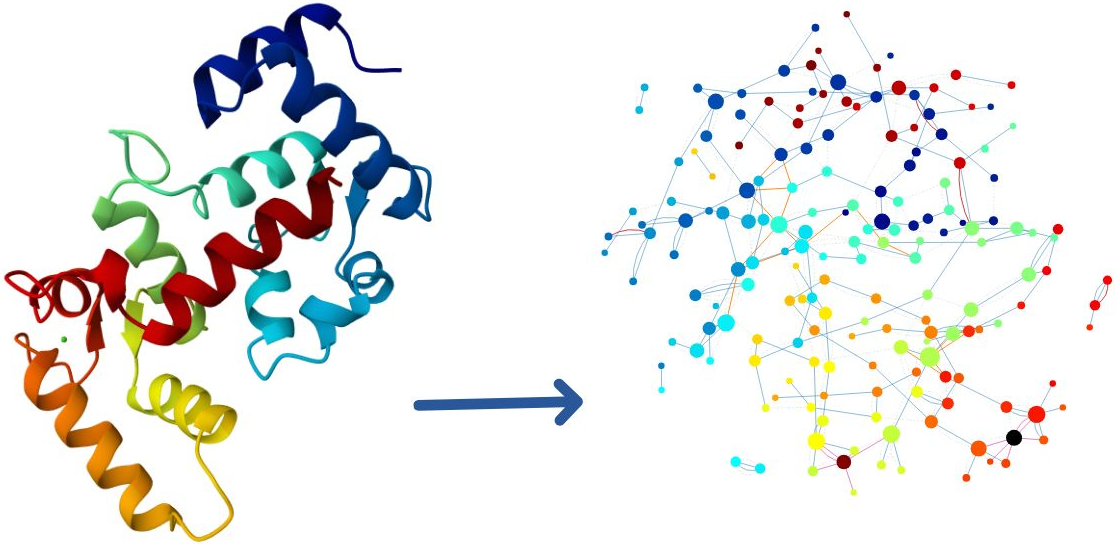
RING **generates RINs** from protein structures using **geometric paremeters**

Current version: RING 4.0

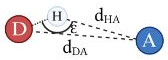
What is a RIN?

A **graph representation** of a protein structure, where:

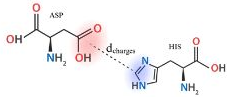
- Residues ⟶ **Nodes**
- Noncovalent Interactions ⟶ **Edges**



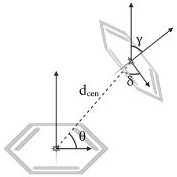
Interactions supported and their geometries



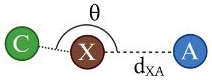
H-bond



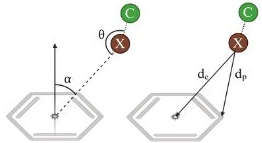
Ionic Bond



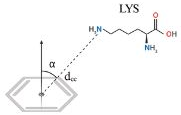
π-π stacking



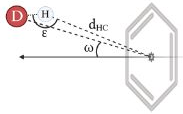
Halogen-acceptor bond



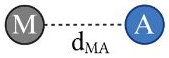
Halogen-π bond



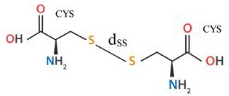
π-cation bond



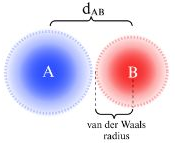
π-H bond



Metal-ion coordination



Disulphide bond



VdW forces

Allowed components

Single chain proteins

Multimers

Ligands

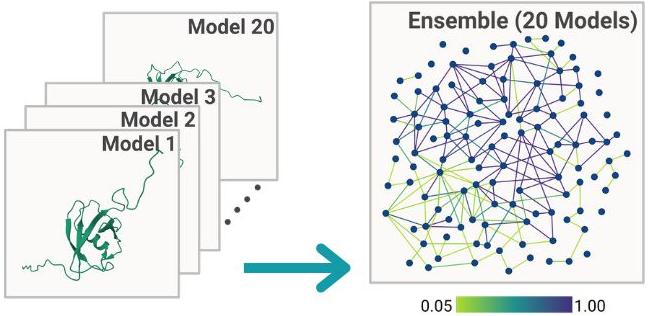
RNA

DNA

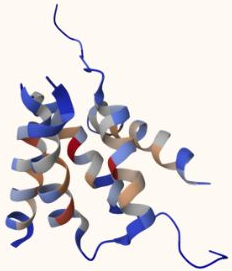
Cofactors

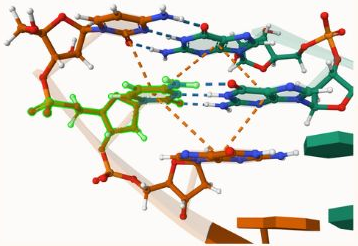
Mixed complexes

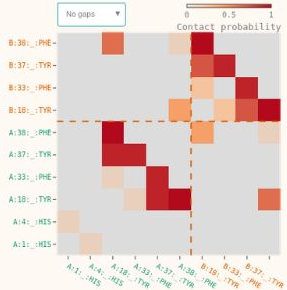
Protein ensembles



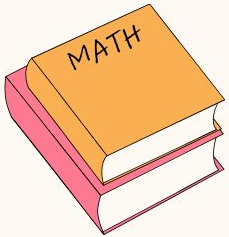
Qualitative

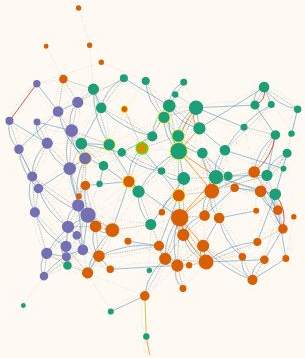






Quantitative





$$C_C(v) = \frac{1}{\sum_{u \neq v} d(v,u)}$$

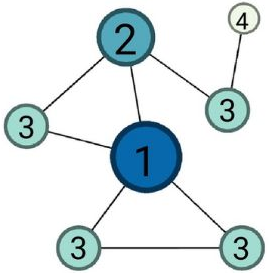
$$x_i = \frac{1}{\lambda} \sum_{j=1}^{n} A_{ij} x_j$$

$$C_B(v) = \sum_{\substack{s \neq v \neq t \\ s \neq t}} \frac{\sigma_{st}(v)}{\sigma_{st}}$$

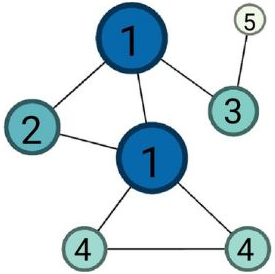
RING

JSON

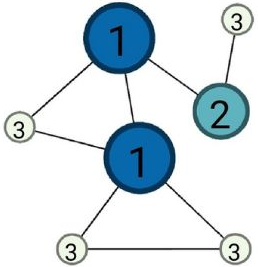
Cytoscape



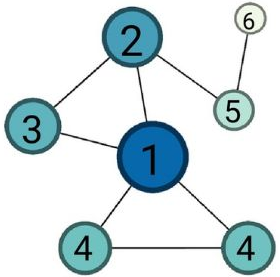
Degree Centrality



Closeness Centrality



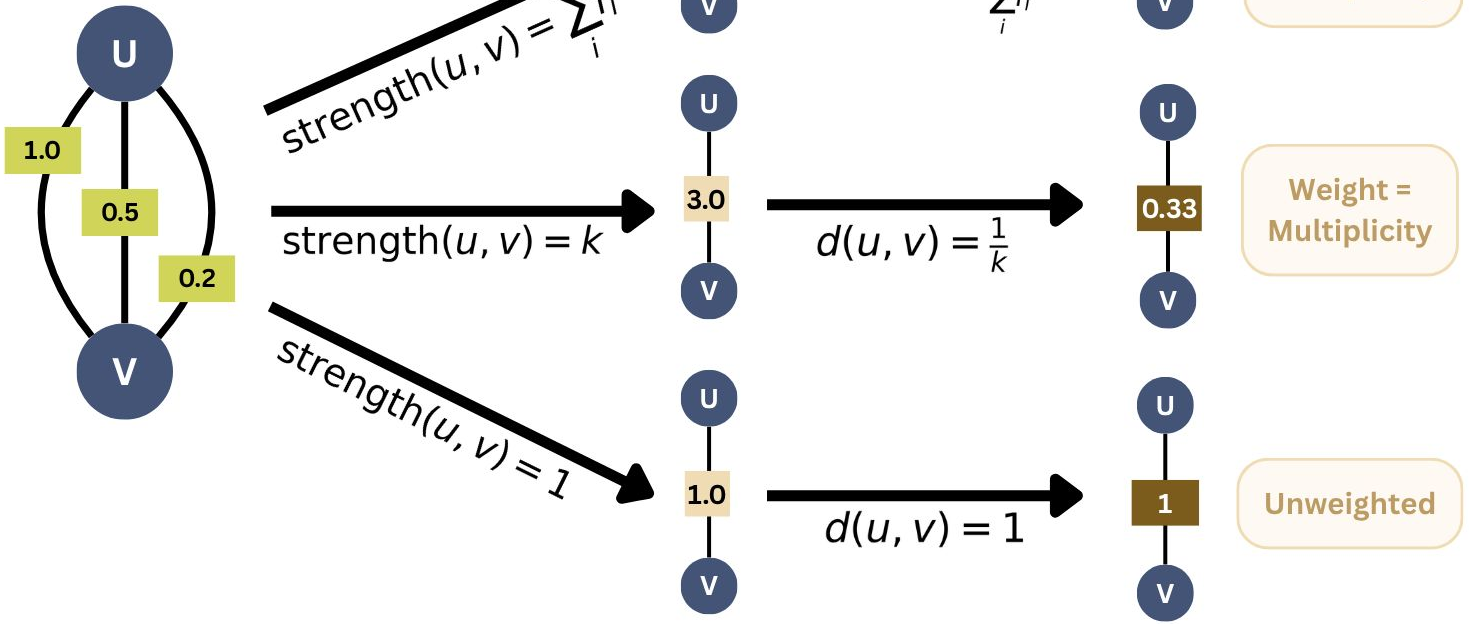
Betweenness Centrality



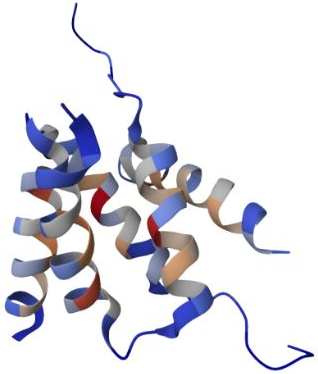
Eigenvector Centrality

RINs have some peculiarities

- Each edge has a frequency associated
- Multiple edges can connect the same nodes
- Strength? Distance?



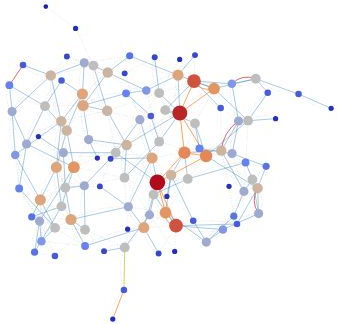
Centralities

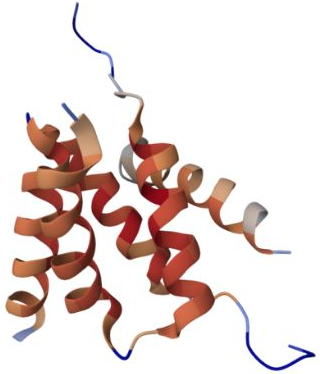


Color scheme

Degree centrality

0 18

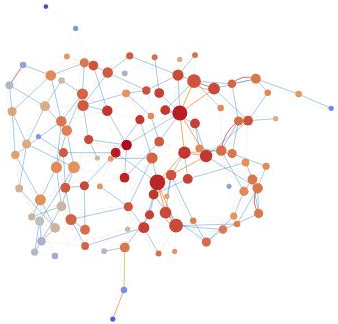


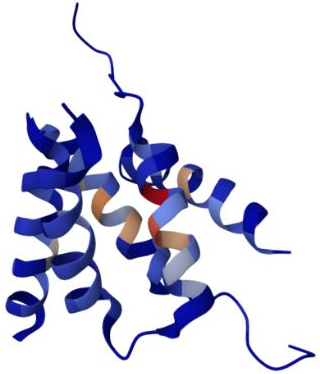


Color scheme

Closeness centrality

0 0.26305

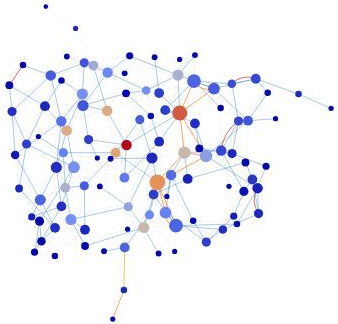


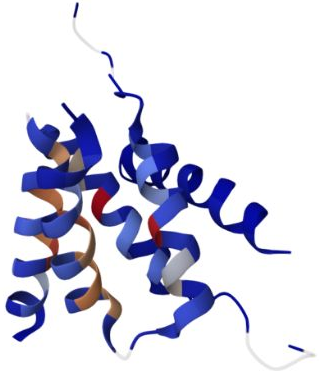


Color scheme

Betweenness centrality

0 0.20512

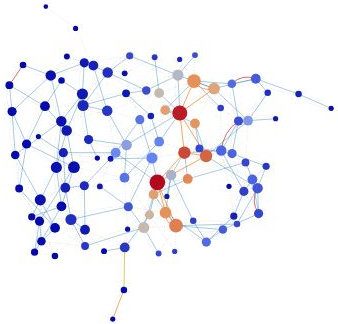




Color scheme

Eigenvector centrality

0.000022 1



Right hydrogens

Right atom charges

Right hydrogen bond donor/acceptor behaviour

More biologically accurate results

...

LYR

LYS

LYT

...

LYS

- **Prot. State 1** → 0 ≤ pH ≤ 3.5
- **Prot. State 2** → 3.5 < pH ≤ 8.0
- **Prot. State 3** → 8.0 < pH ≤ 10.5
- **Prot. State 4** → 10.5 < pH ≤ 14

- **Prot. State 2**

H Geometries

- H1: at ang1 at1 ang2 at2
- H2: at ang1 at1 ang2 at2
- H3: at ang1 at1 ang2 at2
- ...

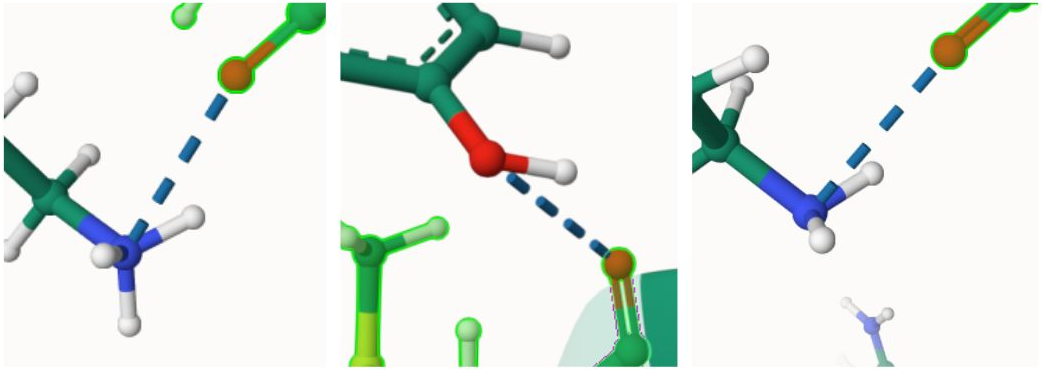
Atom labels

- HBOND donors: At1, At2
- HBOND acceptors: At3, At4
- Cationic atoms: At5
- Anionic atoms: At6, At7

One big problem:

HBONDs and **PIHBONDs** depend on the position of the H atoms (orientation and distance requirements).

Can we always tell which is the best H placement?



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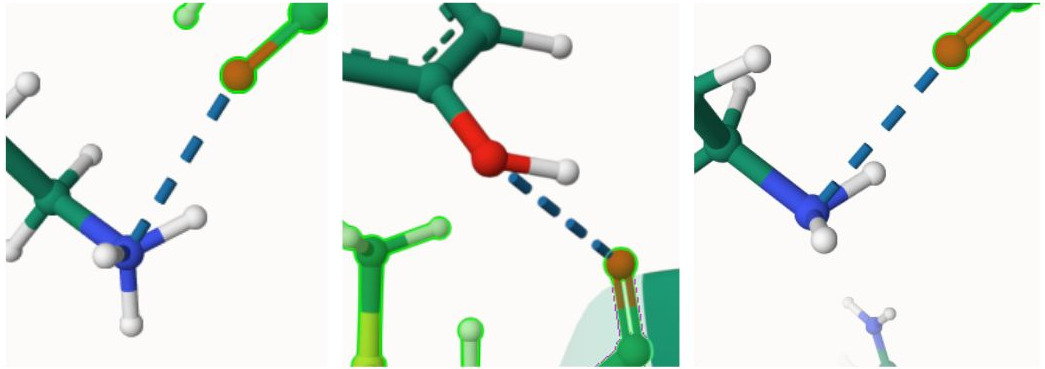
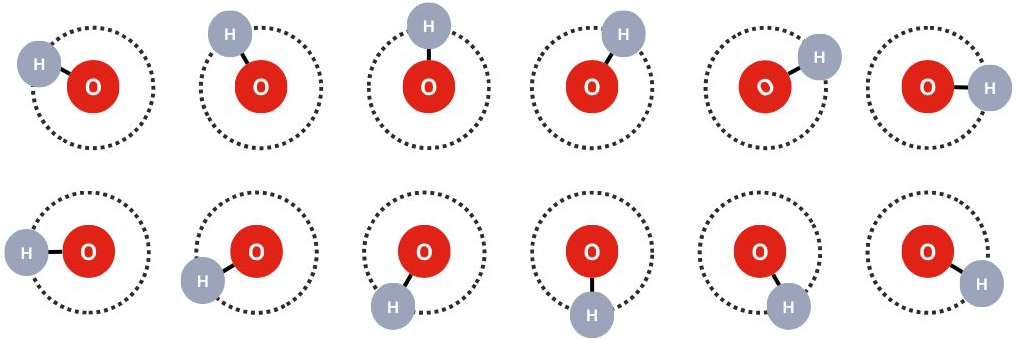




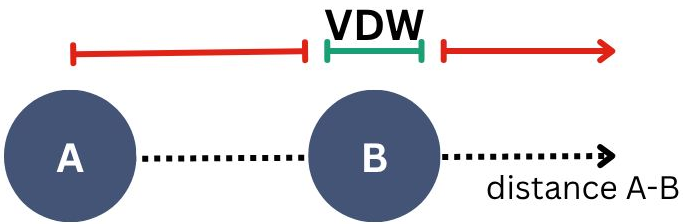
Proposed solution:

For HBOND candidates, we can actually **sample different H rotations** and test for the best one

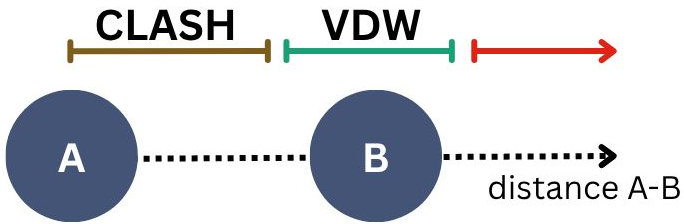
We choose the "rotamer" with most HBONDs

VDW forces update

RING 4.0



RING 5.0

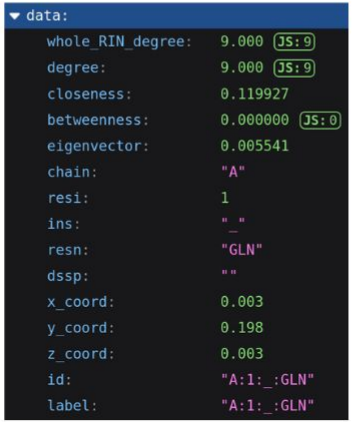


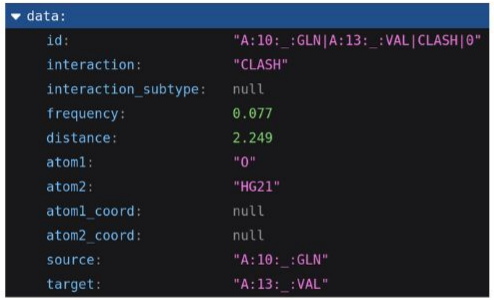
... + refinements in most interactions

Other new developments…

New exporters

- JSON file now available for CLI users.
- New graphML network file.





New non-std amino acids and nucleotides handling

- No more LIG treatment.
- Residuea like HYP are now recognized as amino acids.
- Makes RING better at handling PTMs (phosphorylation, acetylation, hydroxylation, etc).

Web Server updates

- Easier analysis + more flexibility
- New filters
- New visualization options

New interaction coming soon…

Thank you for the attention!

You can find RING on:
https://ring.biocomputingup.it/

Acknowledgements:

Sol C. Begue has been co-funded by the European Union under the MSCA-COFUND-DP ArchiFun GA n. 101126656