Protein Dynamics is Linked to Rigidity

Merging geometrical and topological properties

Geometrical Simulation

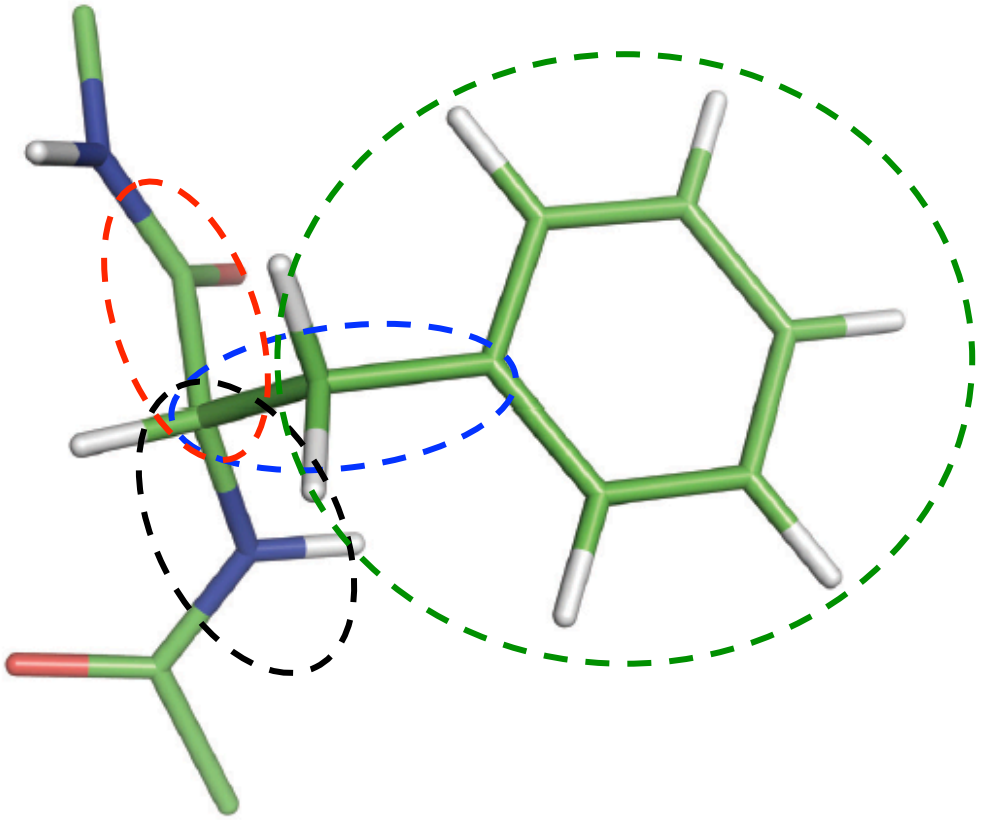
Geometrical Simulation compared to Molecular Dynamics and Elastic Networks:

C. David and D.J. Jacobs, *Characterizing protein motions from structure*, J. Mol. Graph Model, **31**:41-56 (2011)

Geometrical Simulation (GS)

An example of Rigid Cluster Decomposition (RCD)

molecular structure



Identification of rigid clusters using graph rigidity analysis

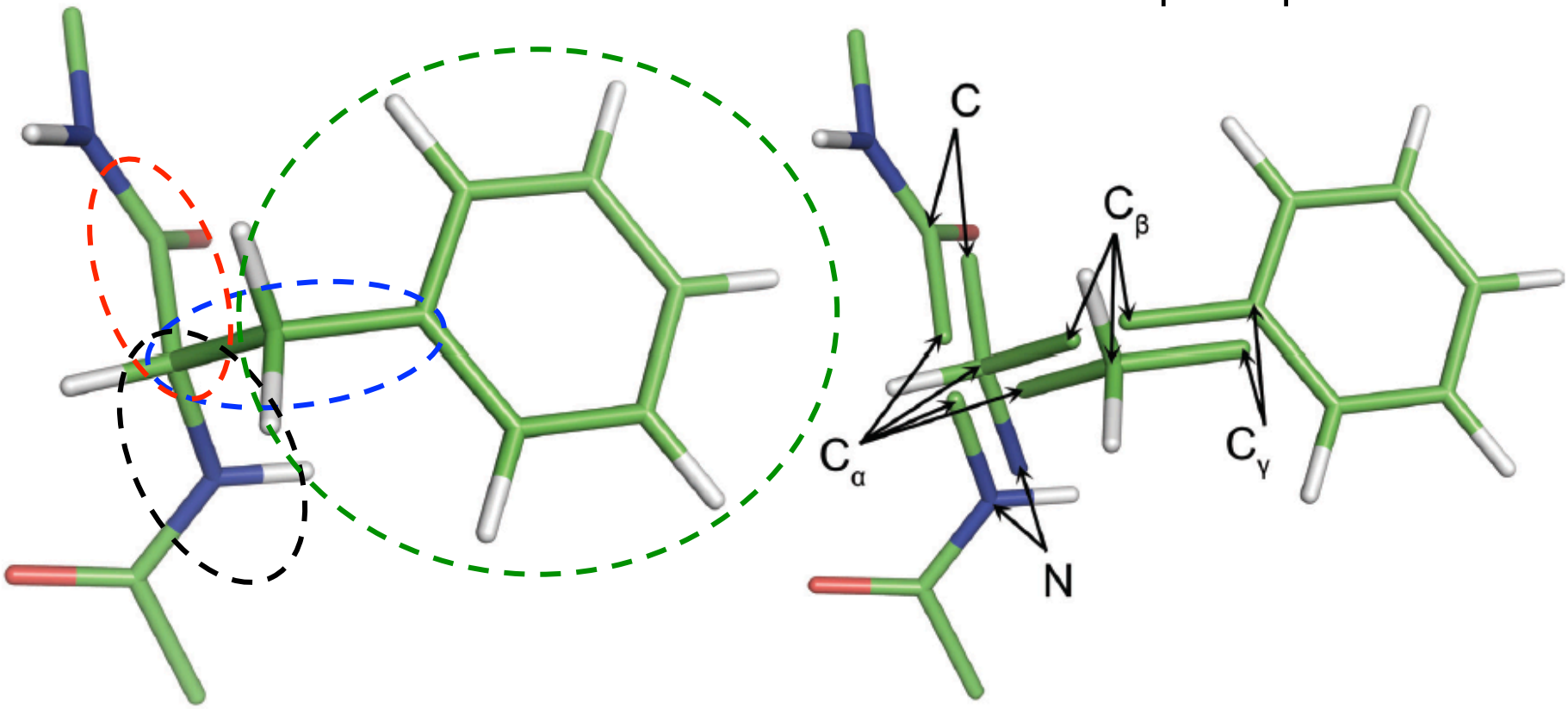
1. D. Farrell, K. Speranskiy and M.F. Thorpe, *Proteins*, **78**:2908–2921 (2010)

2. Daniel W. Farrell, Ph.D. Thesis, *Generating stereochemically acceptable protein pathways*, Arizona State University (2010)

Geometrical Simulation (GS)

An example of Rigid Cluster Decomposition (RCD)

molecular structure → **RCD** creates multiple copies of atoms



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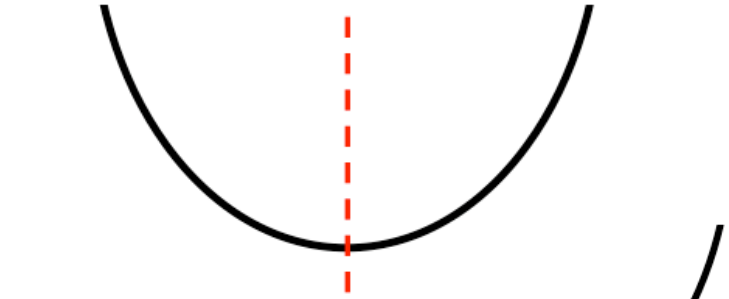
Geometrical Simulation (GS)

Virtual potentials maintain molecular structure

$$V_{POINT} = \tfrac{1}{2} A \sum_{\langle ab \rangle} \left| \vec{r}_a - \vec{r}_b \right|^2$$

Shared atoms merge together



$$V_{MAX} = \tfrac{1}{2} A \sum_{\langle ab \rangle} \begin{cases} \left(\left| \vec{r}_a - \vec{r}_b \right| - d_{ab}^{MAX} \right)^2 & for \ \left| \vec{r}_a - \vec{r}_b \right| \geq d_{ab}^{MAX} \\ 0 & otherwise \end{cases}$$

Prevent atoms from getting too far apart

$$V_{MIN} = \tfrac{1}{2} A \sum_{\langle ab \rangle} \begin{cases} \left(\left| \vec{r}_a - \vec{r}_b \right| - d_{ab}^{MIN} \right)^2 & for \ \left| \vec{r}_a - \vec{r}_b \right| \leq d_{ab}^{MIN} \\ 0 & otherwise \end{cases}$$

Prevent atoms from getting too close

Relaxation Step: Energy minimization method brings constraint network to ZERO energy.

1. D. Farrell, K. Speranskiy and M.F. Thorpe, *Proteins*, **78**:2908–2921 (2010)

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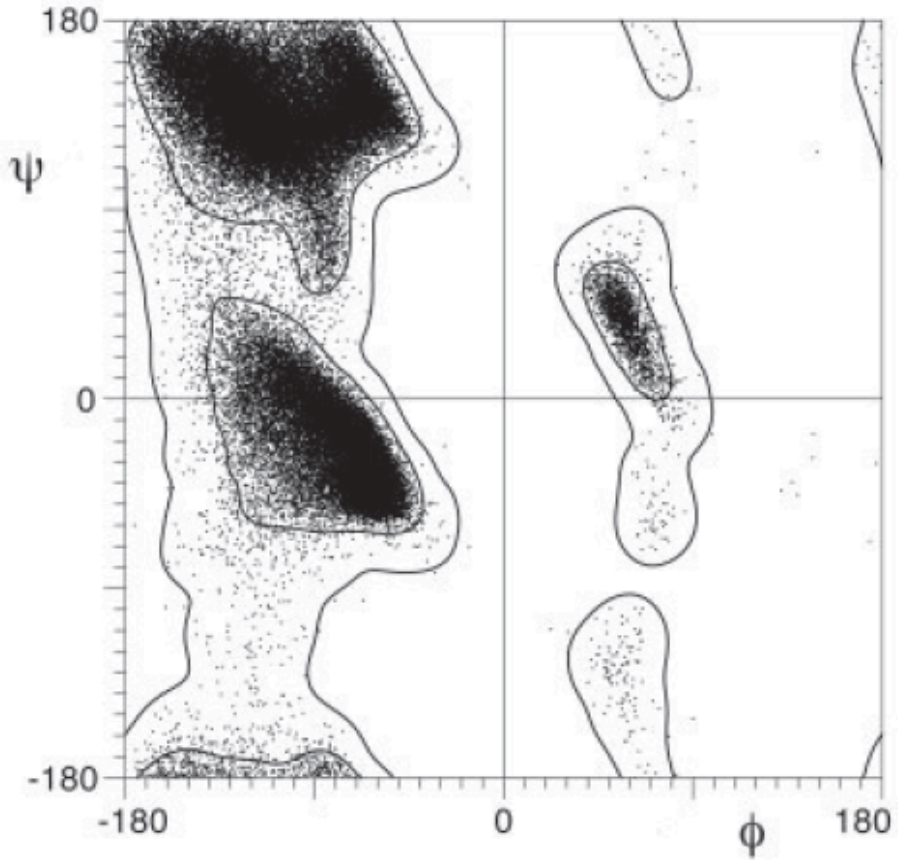
Geometrical Simulation (GS)

Distance inequalities maintain canonical local structural characteristics



Example

Ramachandran plots as well as rotamers are reproduced using distance inequality potentials.

GS parameters were optimized** to keep local geometries that are sampled statistically equivalent to structures from X-ray crystals and that generated by MD simulation.

See: B.K. Ho, A. Thomas and R. Brasseur, Protein Science 12:2508-2522 (2003)

Figure from: S.C. Lovell, J. M. Word, J. S. Richardson and D. C. Richardson. *The penultimate rotamer library*. Proteins 40:389-408 (2000)

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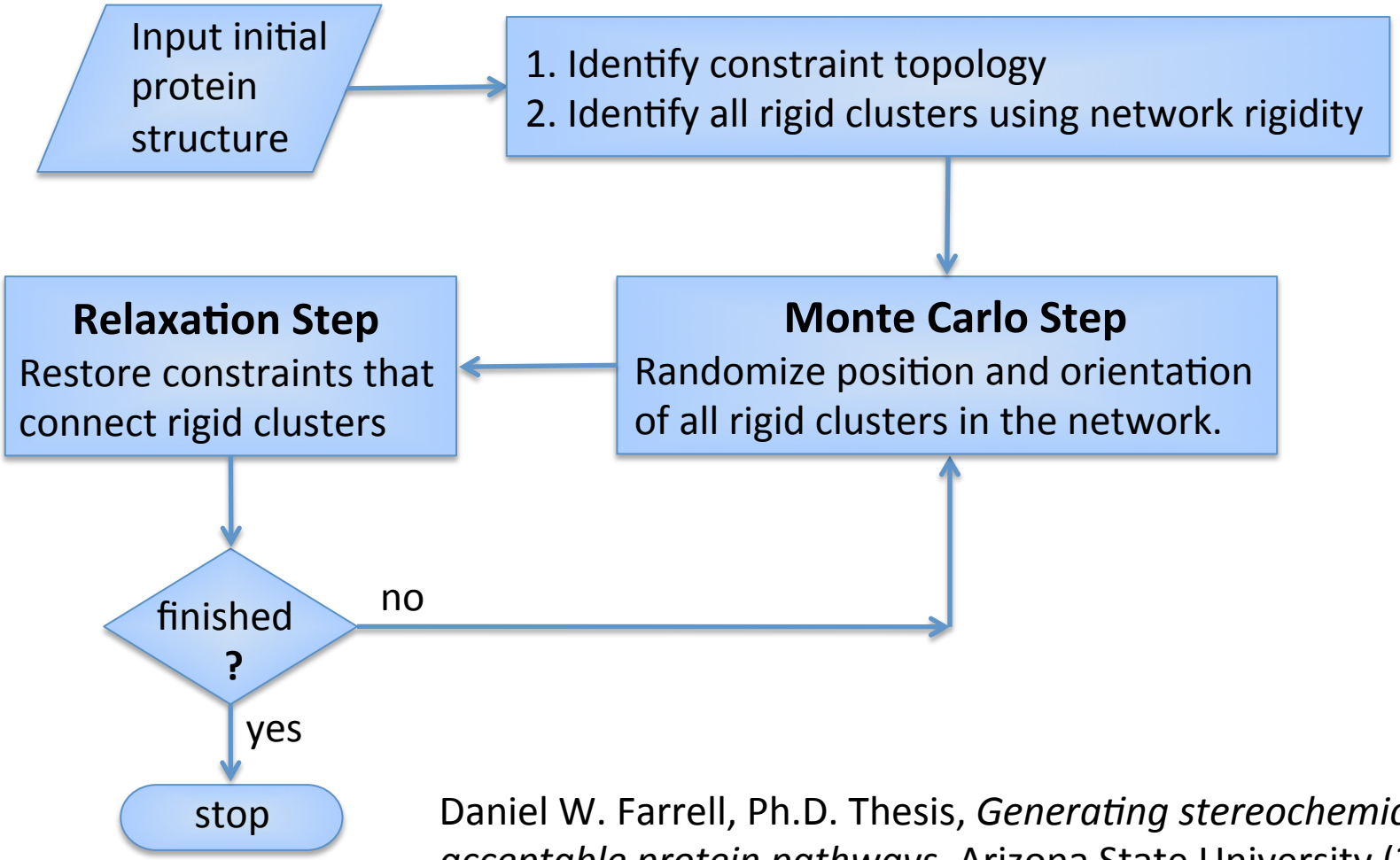
Geometrical Simulation (GS)

Exploration of conformations for fixed constraint topology

High Level Overview



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