Escherichia coli's RfaH studied by all-atom Monte Carlo simulation

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Outline

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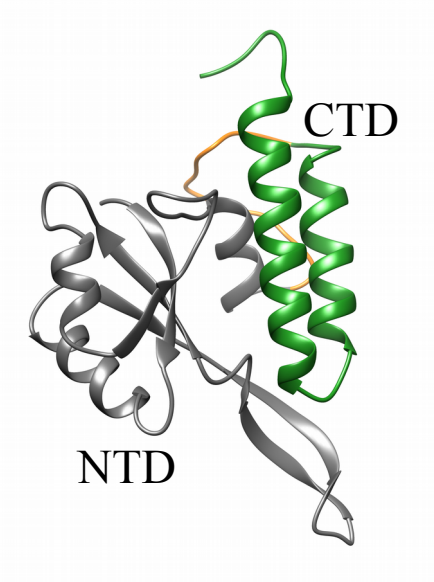
Motivation

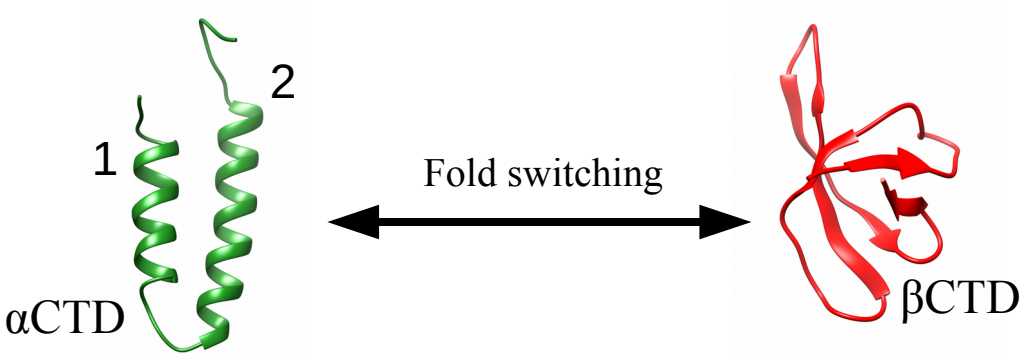
Some proteins can switch fold

RfaH

- Naturally occurring protein in *E. coli*
- 2 interfacing domains (CTD & NTD)
- Dual functional: Regulates transcription and enhances translation
- CTD shown experimentally to be able to switch fold

[Burmann *et al.*, 2012]





Previous computational studies

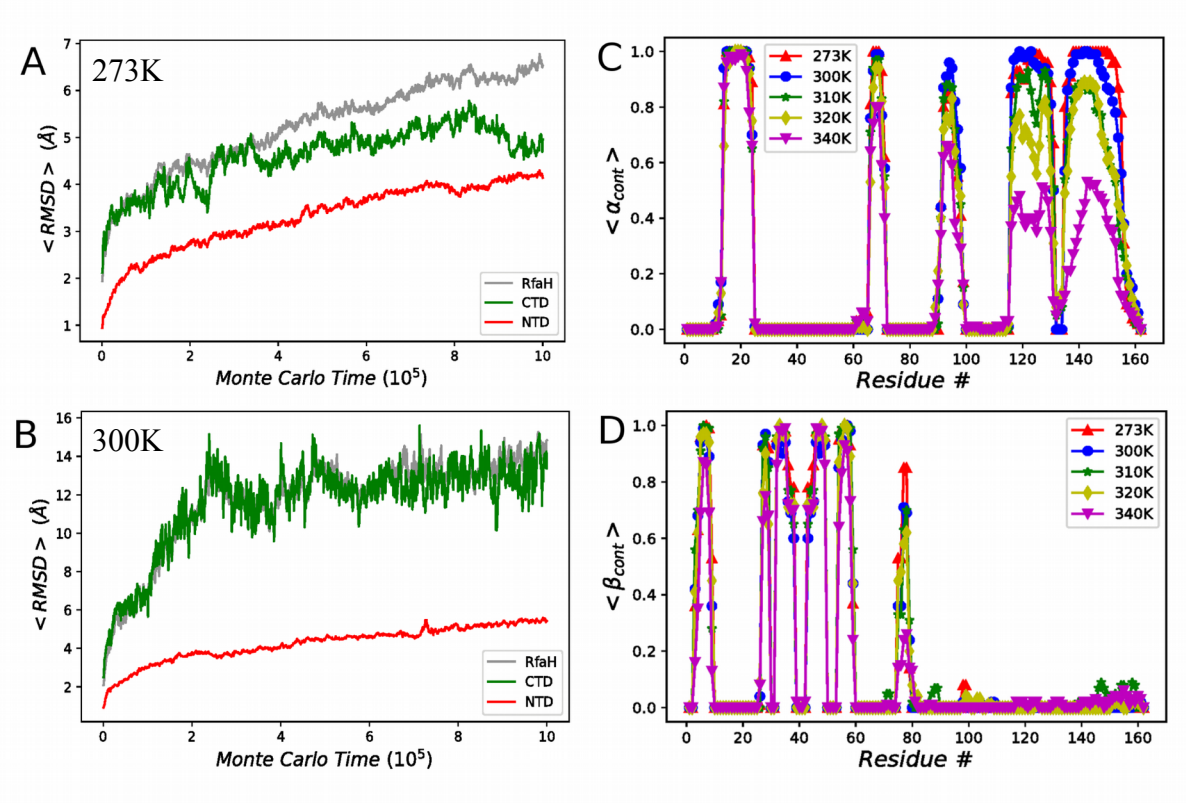
- Some computational studies using molecular dynamics including atomistic and coarse-grained models

- Common observation: NTD is more stable than CTD

Computational study of RfaH

- We employed atomistic Monte Carlo simulations
- Software: PROFASI with a simplified physics-based force field
- Investigated stability properties of full protein, αCTD and βCTD
- Simulations started from experimental structures
- Monitored RMSD and secondary structural content

Results: Full-length RfaH



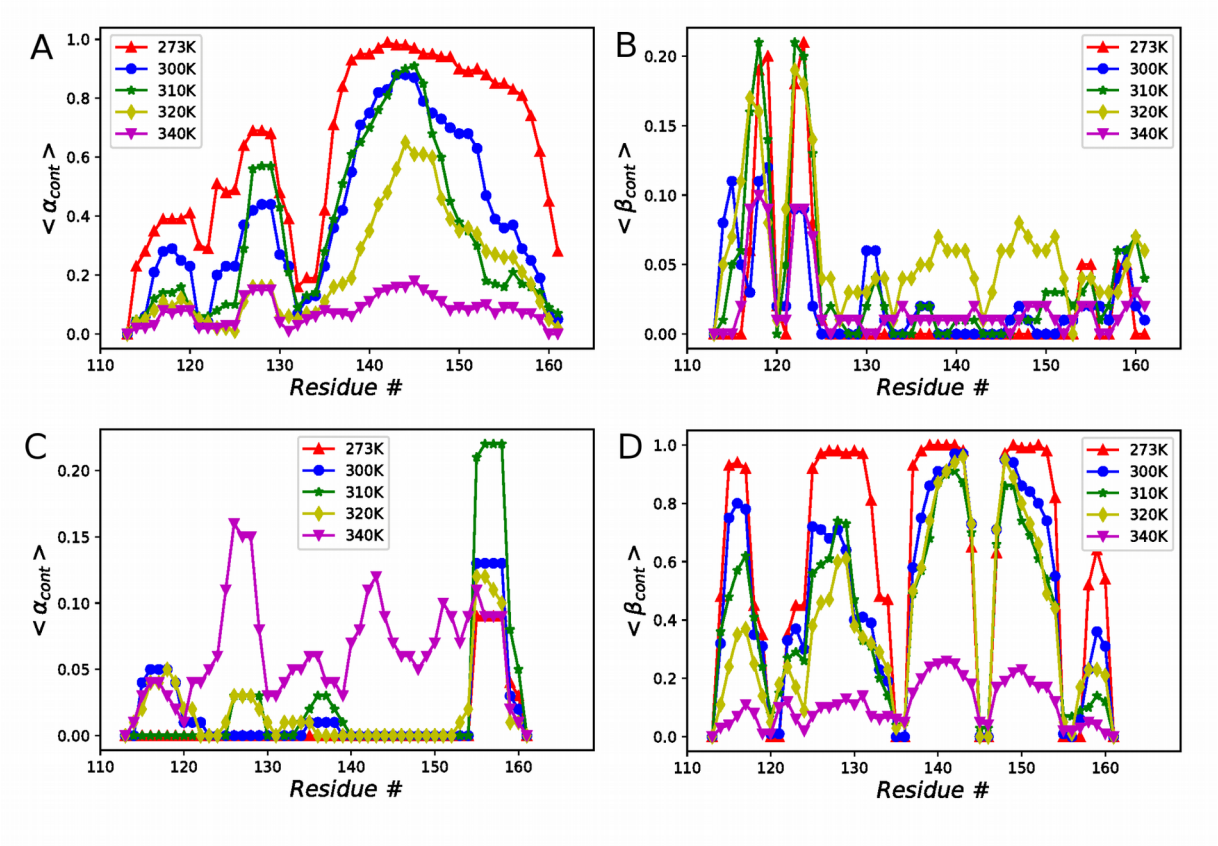
- NTD is highly stable
- CTD is less stable
- Both helices in CTD have similar stability

Results: Isolated CTD

- Helix 2 becomes less stable
- Helix 1 completely losses its helicity
- Inter-domain interactions stabilize CTD

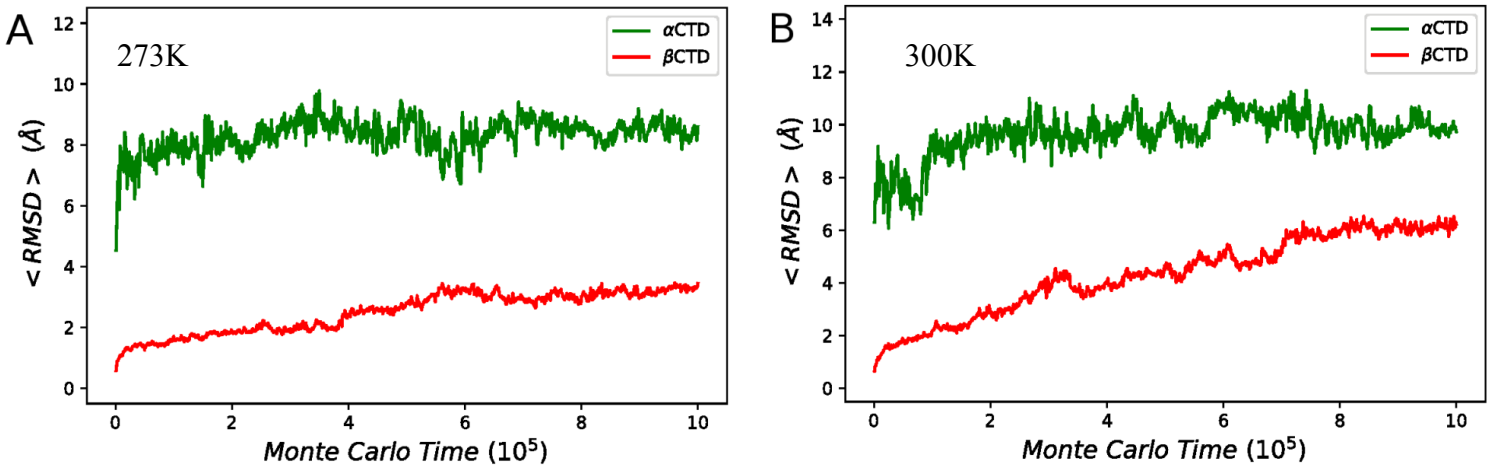
αCTD

βCTD



Results: Isolated CTD

- βCTD is more stable than αCTD
- all-α to all-β fold switch is thermodynamically favored



Conclusion

- Employed all-atom Monte Carlo simulation to investigate both full-length RfaH and isolated CTD
- Simulation able to identify fold switching region in this protein

The relatively low stability of αCTD indicates that it may be primed to switch into the βCTD structural form upon disruption of the stabilizing interface with the NTD.

Future work

PROFASI fails! what next?

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