

Structural Determinants of Protein Evolution : buriedness vs. flexibility vs. design

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Presented at

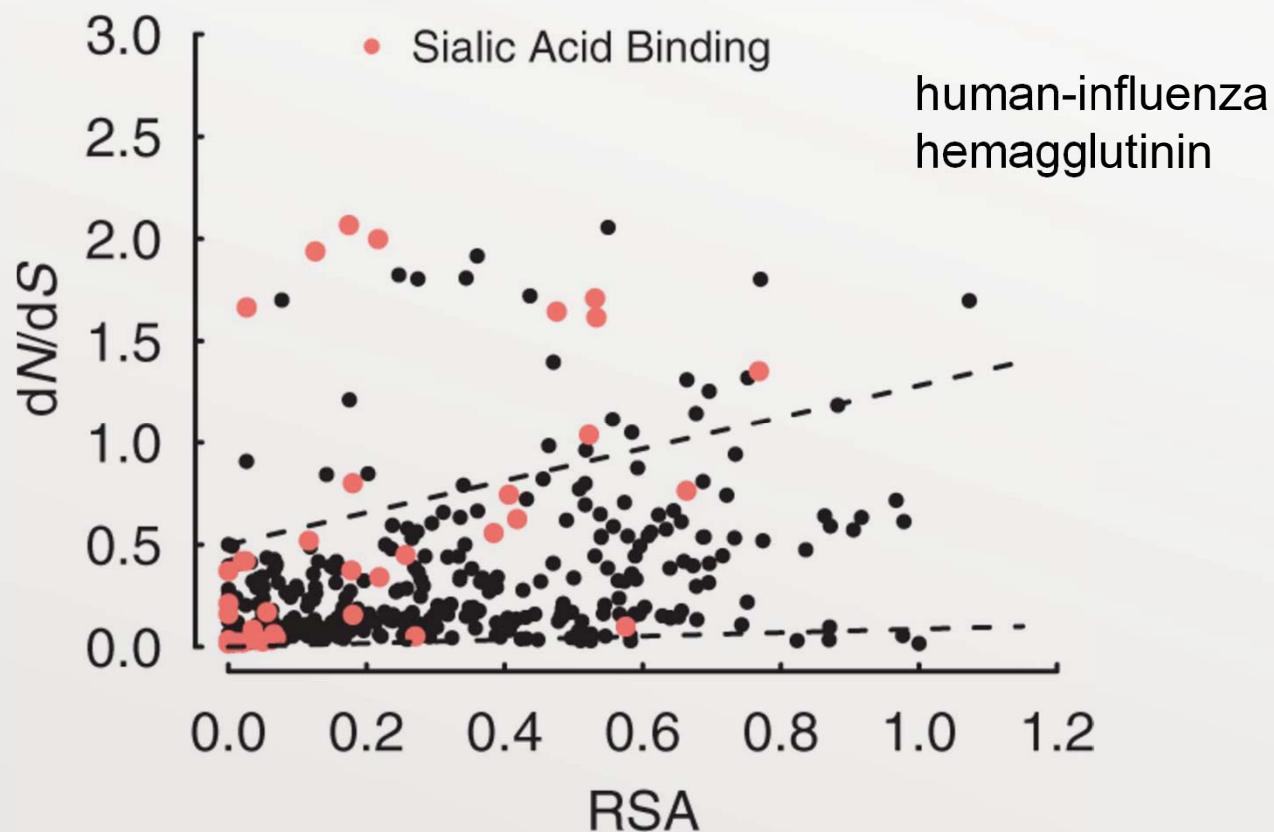
SMBE Annual Meeting, June 10 2014
Puerto Rico, USA

Why are some sites in viral proteins more variable than others?

Influenza virus hemagglutinin

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... GTIKSWDESYIELKVEVP ...  
... GTIKSWDESYTELKVDVP ...  
... GTIKSWDENYTELKVDVP ...  
... GTIKSWDENYAELKVDVP ...  
... GTIKSWDESYTELKVEVP ...  
... GTIKSWDESYTELKVDVP ...  
... GTIKSWDESYTELKVDVP ...
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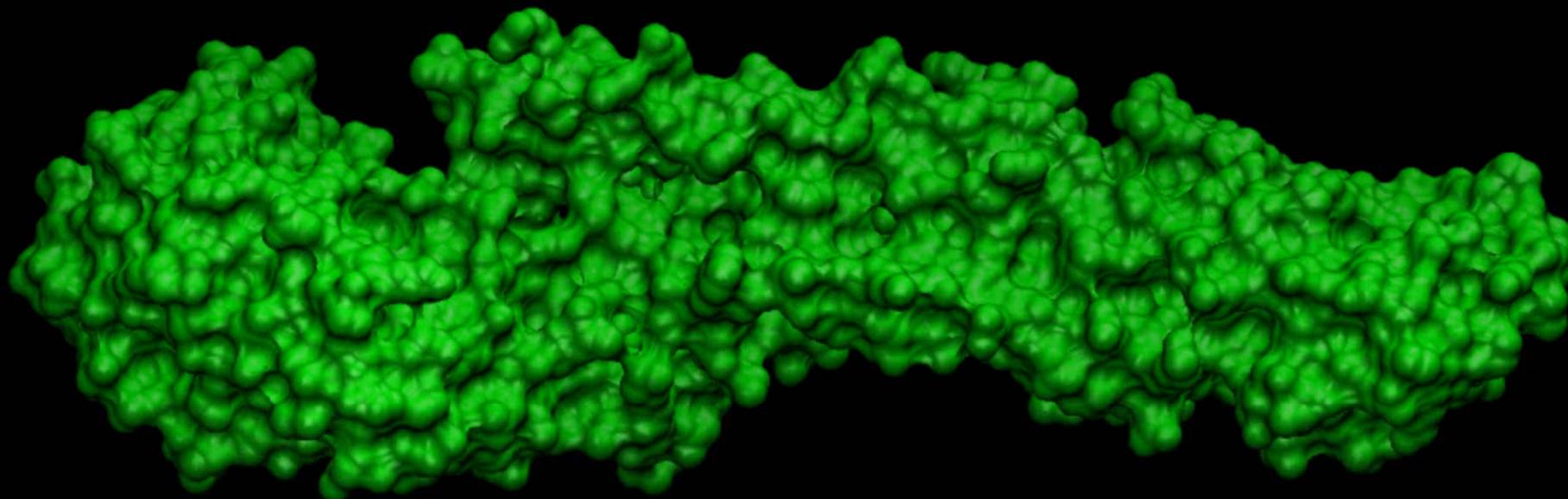
Buried residues (sites) evolve more slowly than exposed residues



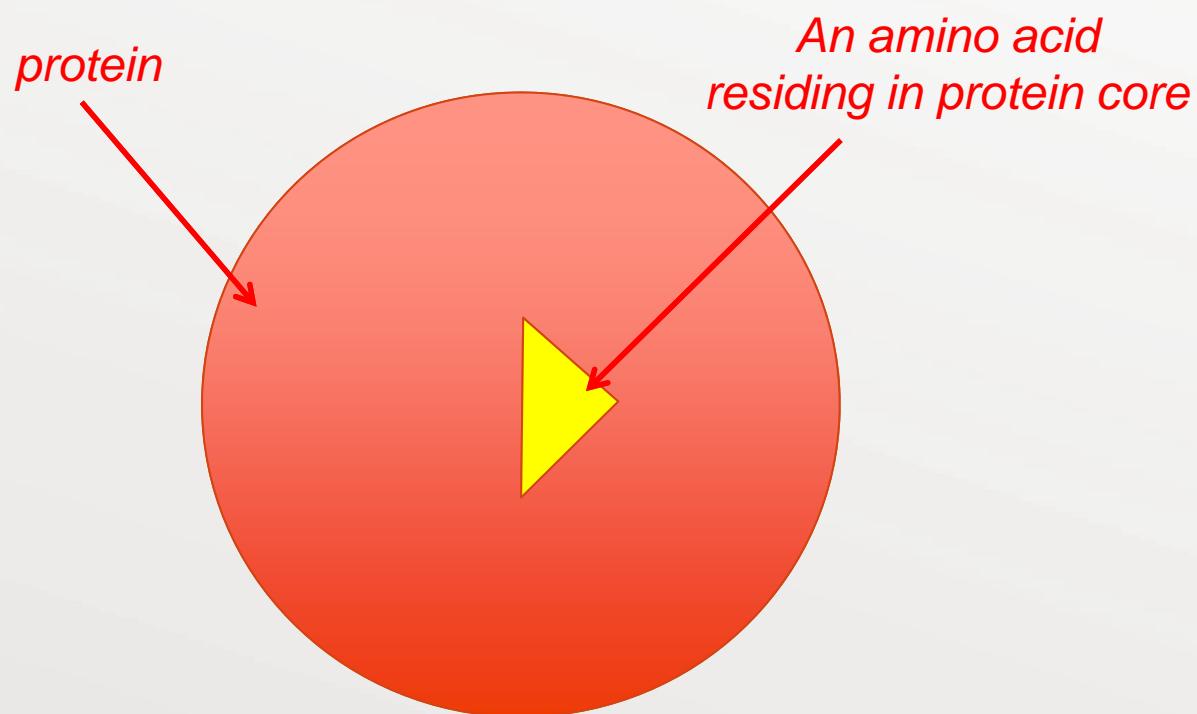
Meyer & Wilke, 2013, MBE, **30**, 36-44

Amino acid sites in the core of proteins have lower solvent accessible surface area

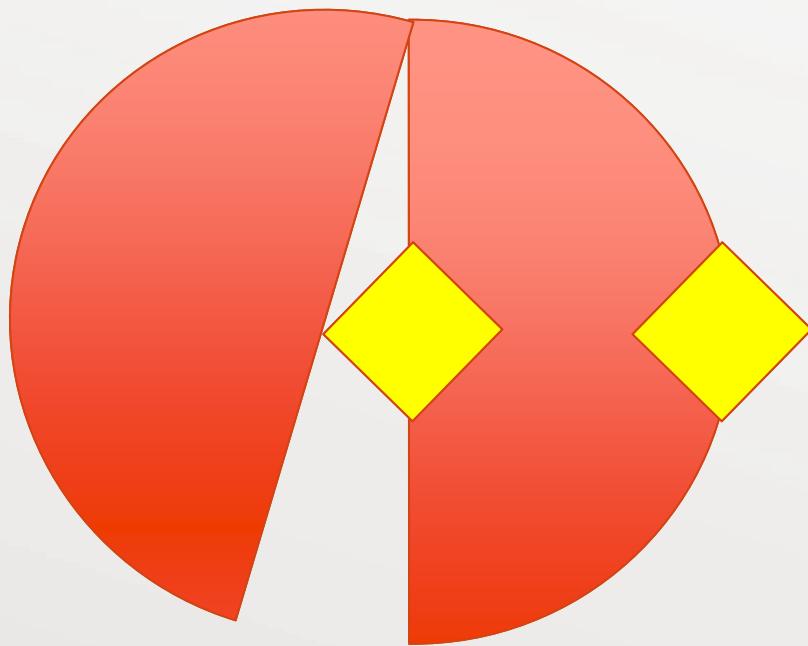
Influenza virus hemagglutinin



Amino acid substitutions in the core are disruptive

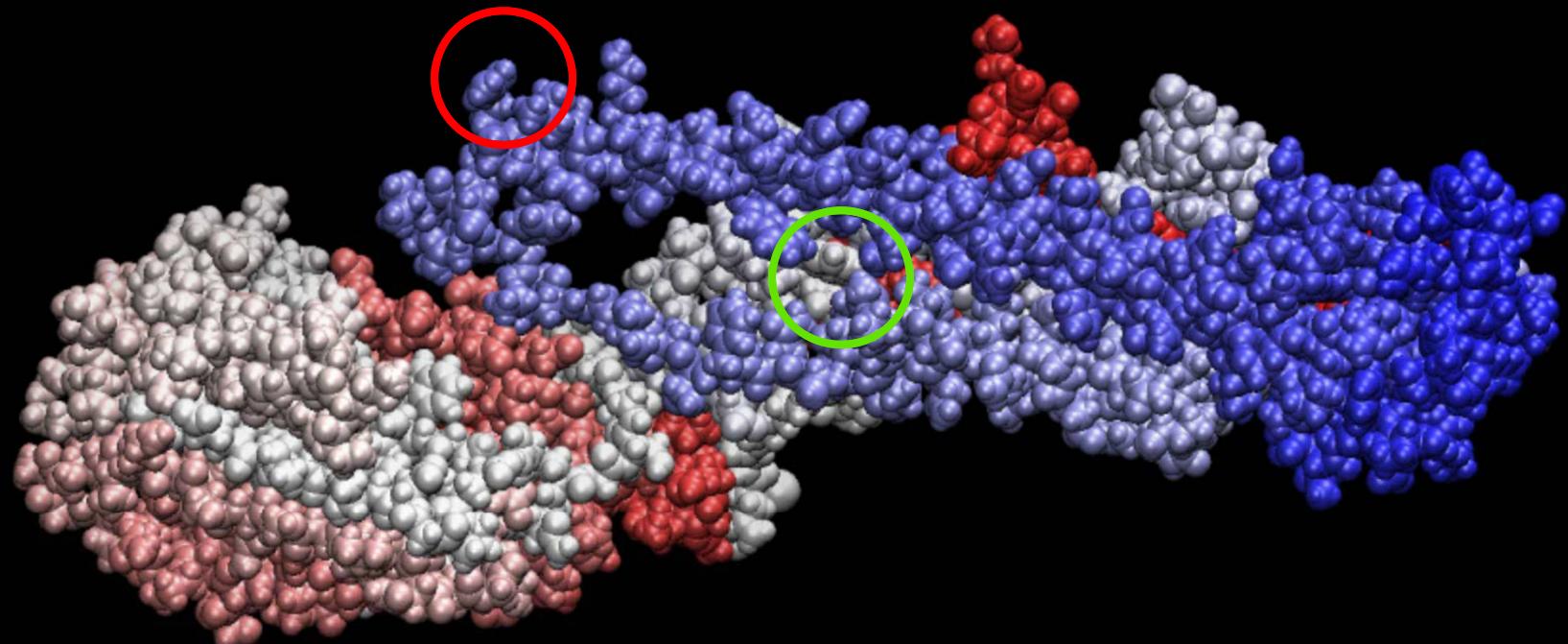


Amino acid substitutions in the core are disruptive

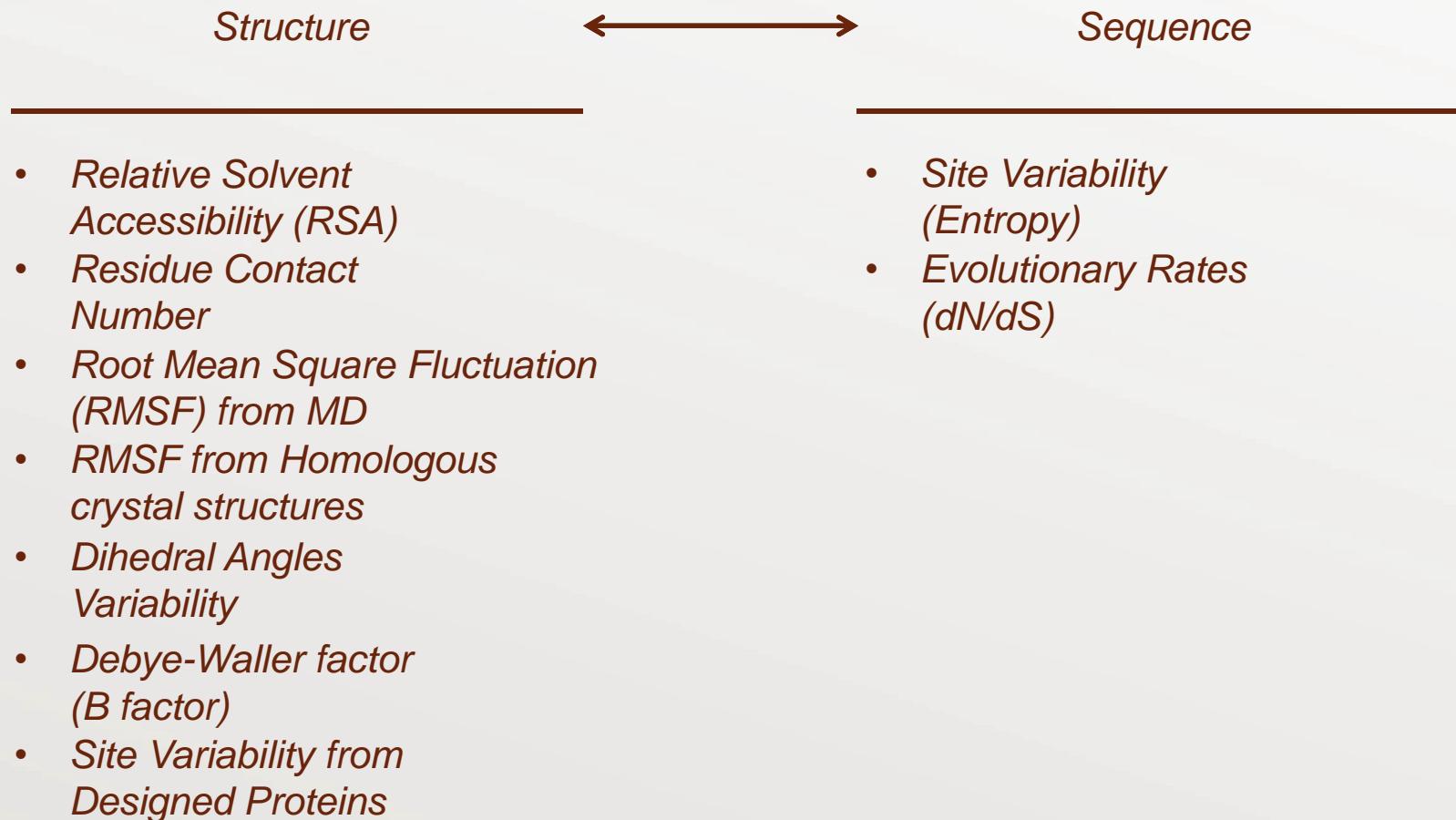


Proteins are dynamic 3D entities

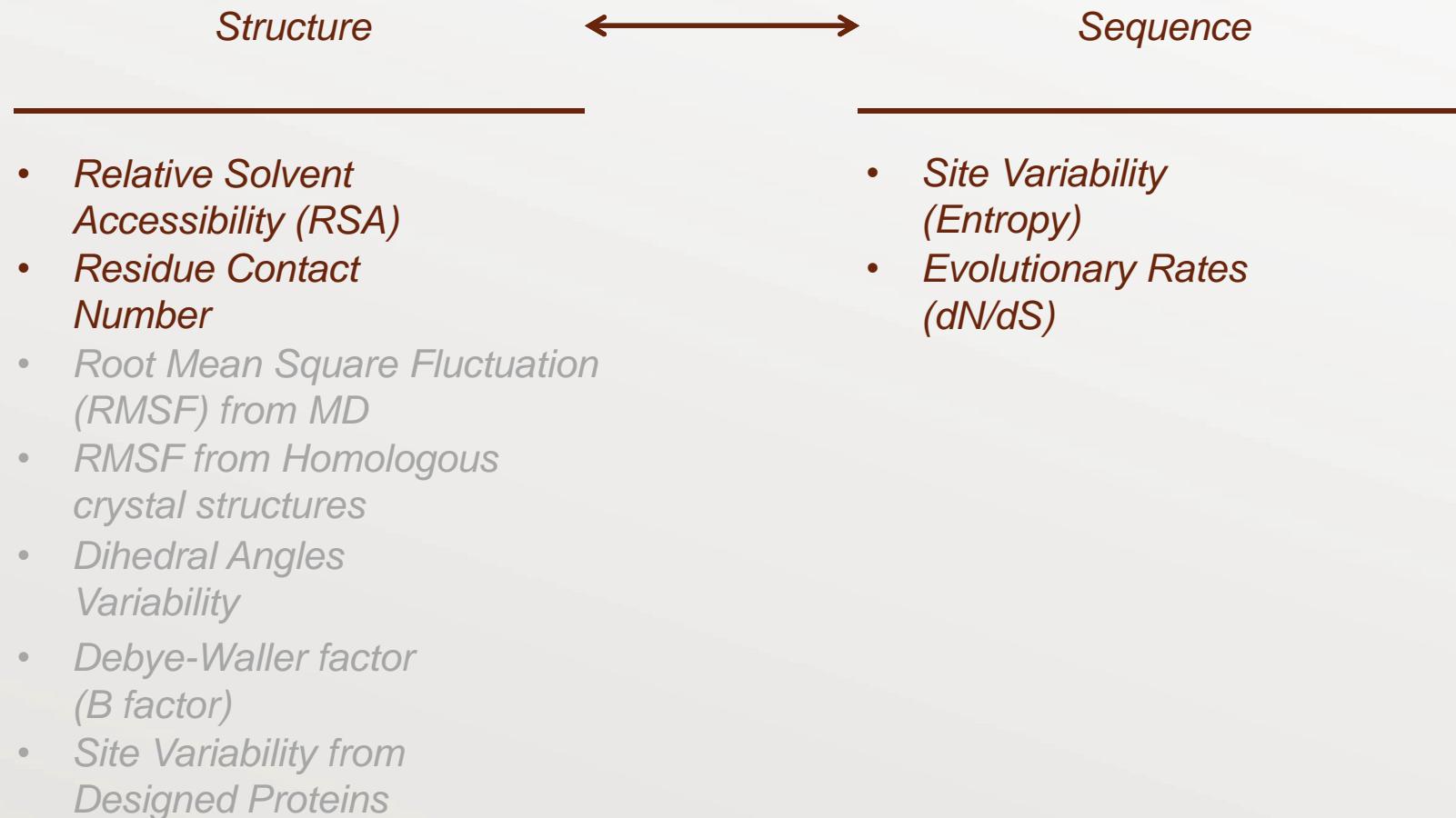
Influenza virus hemagglutinin



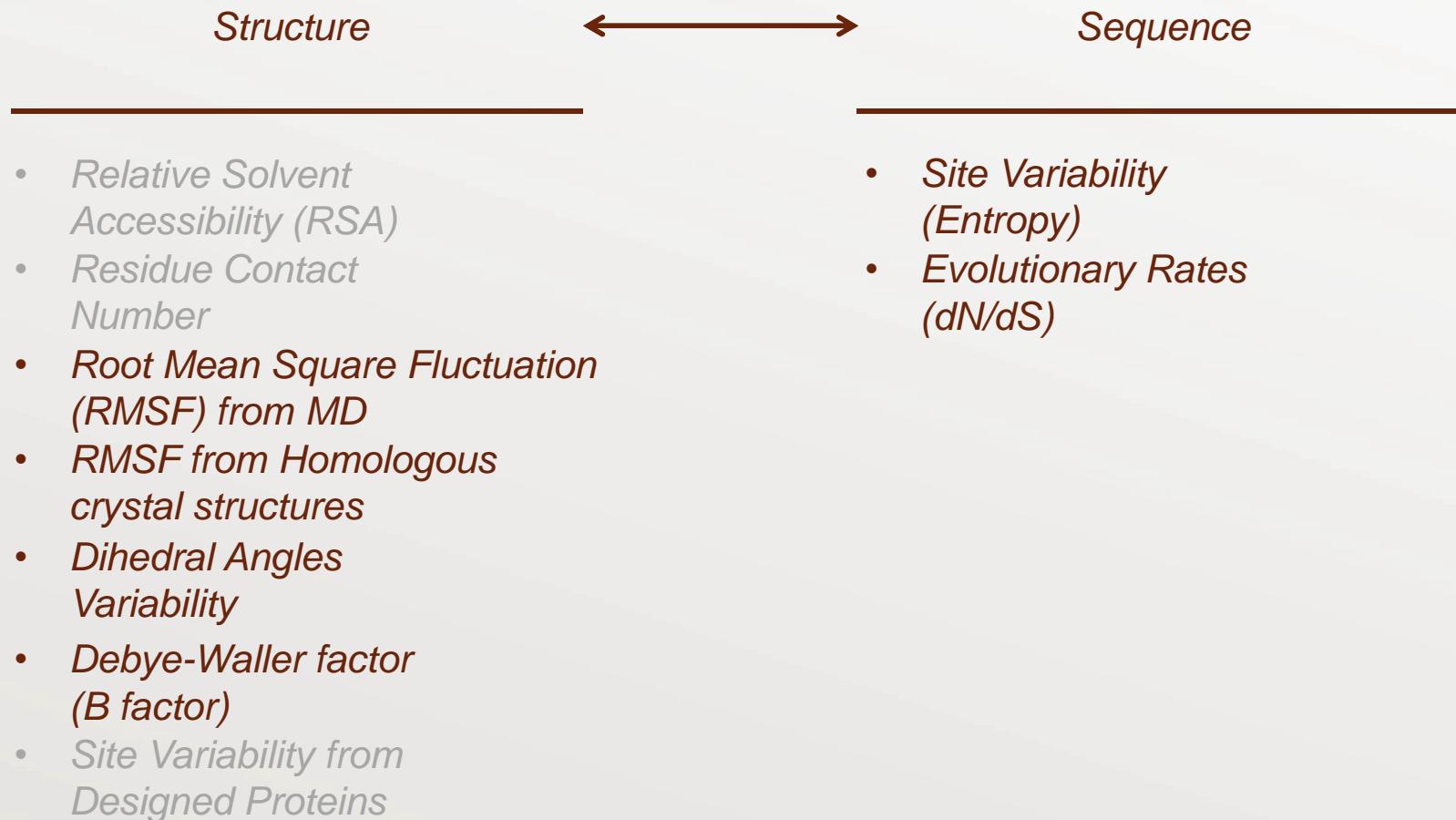
Does structural variation have any prediction power for the sequence evolution of the protein?



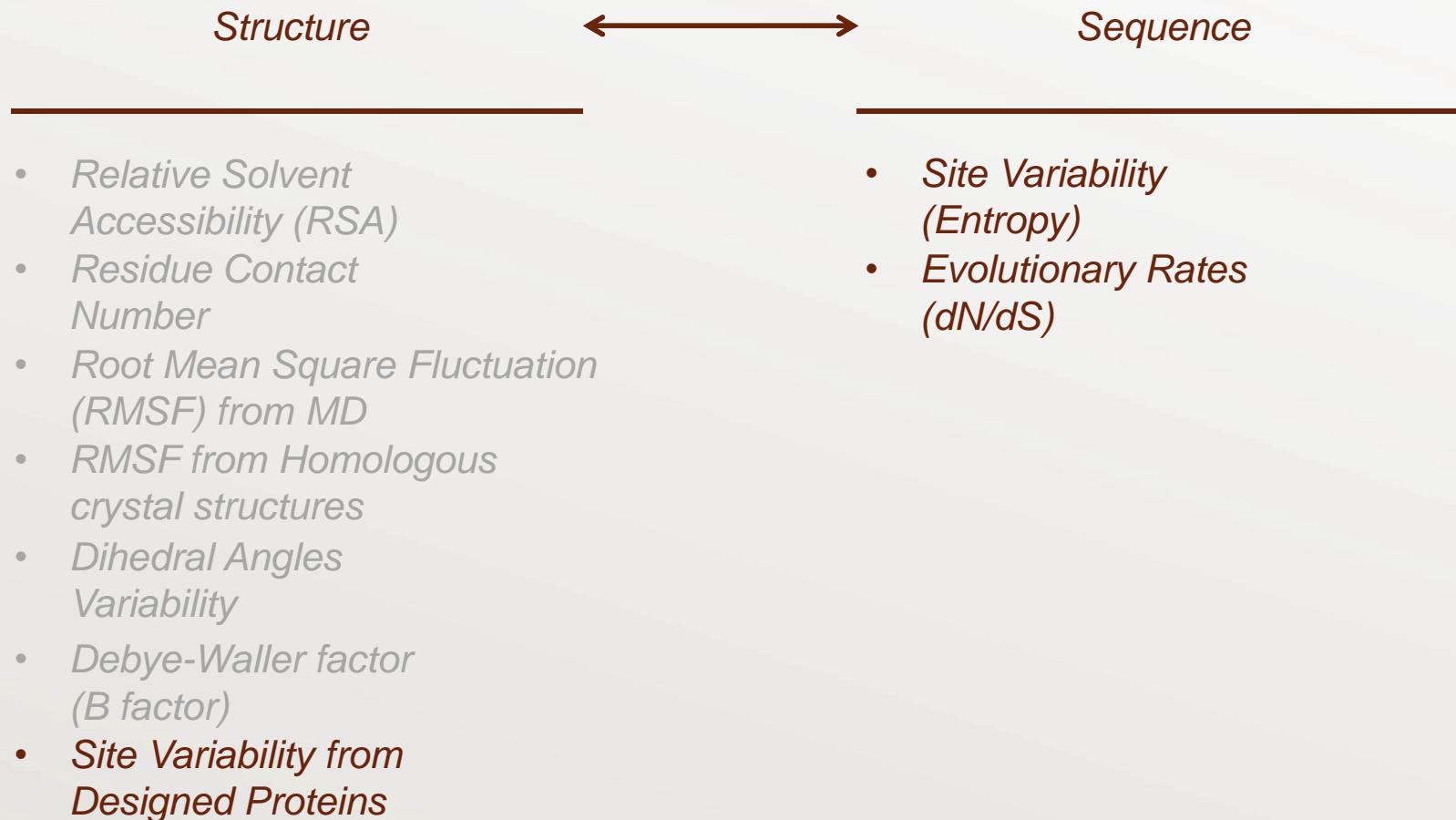
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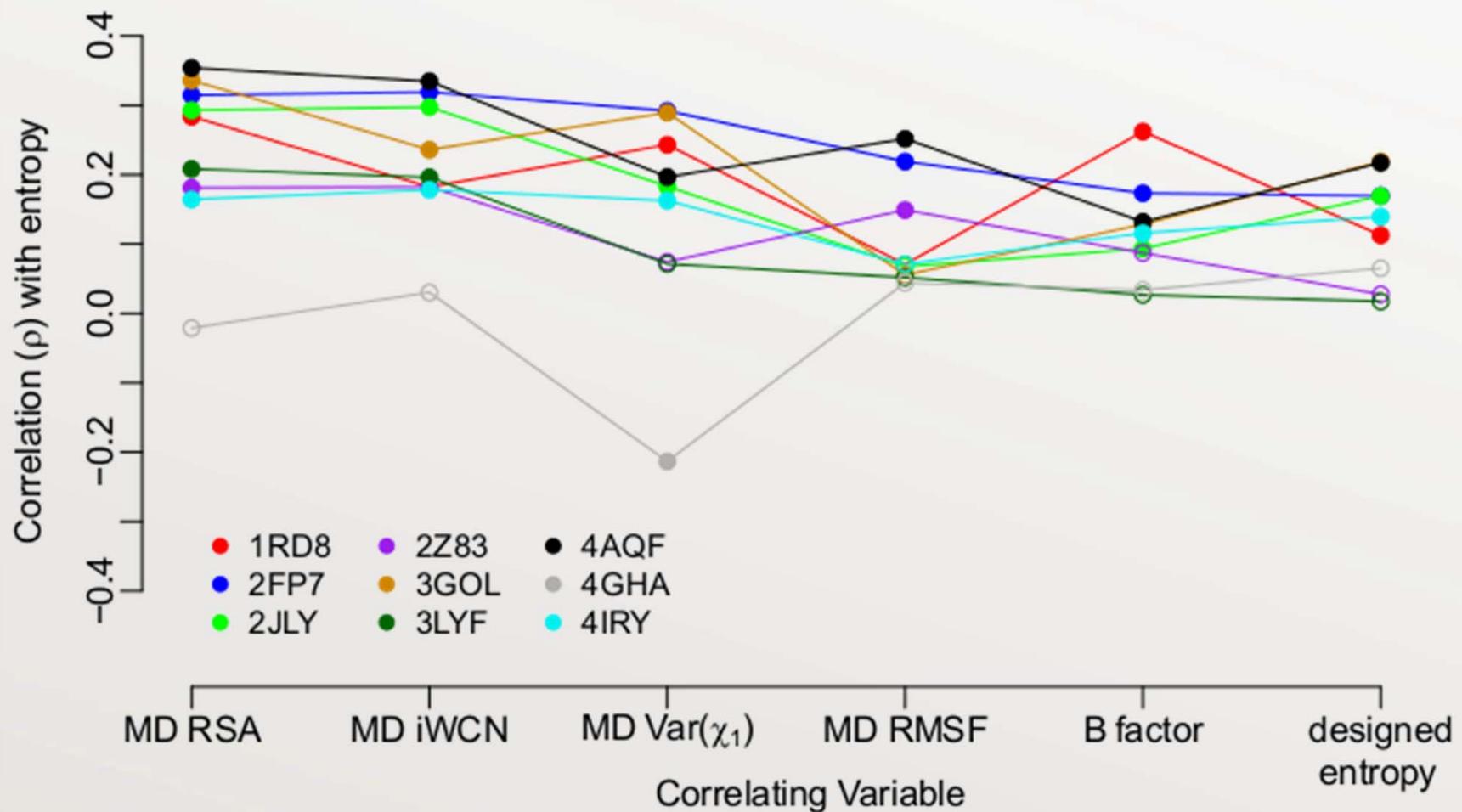
Does structural variation have any prediction power for the sequence evolution of the protein?



9 viral proteins were analyzed

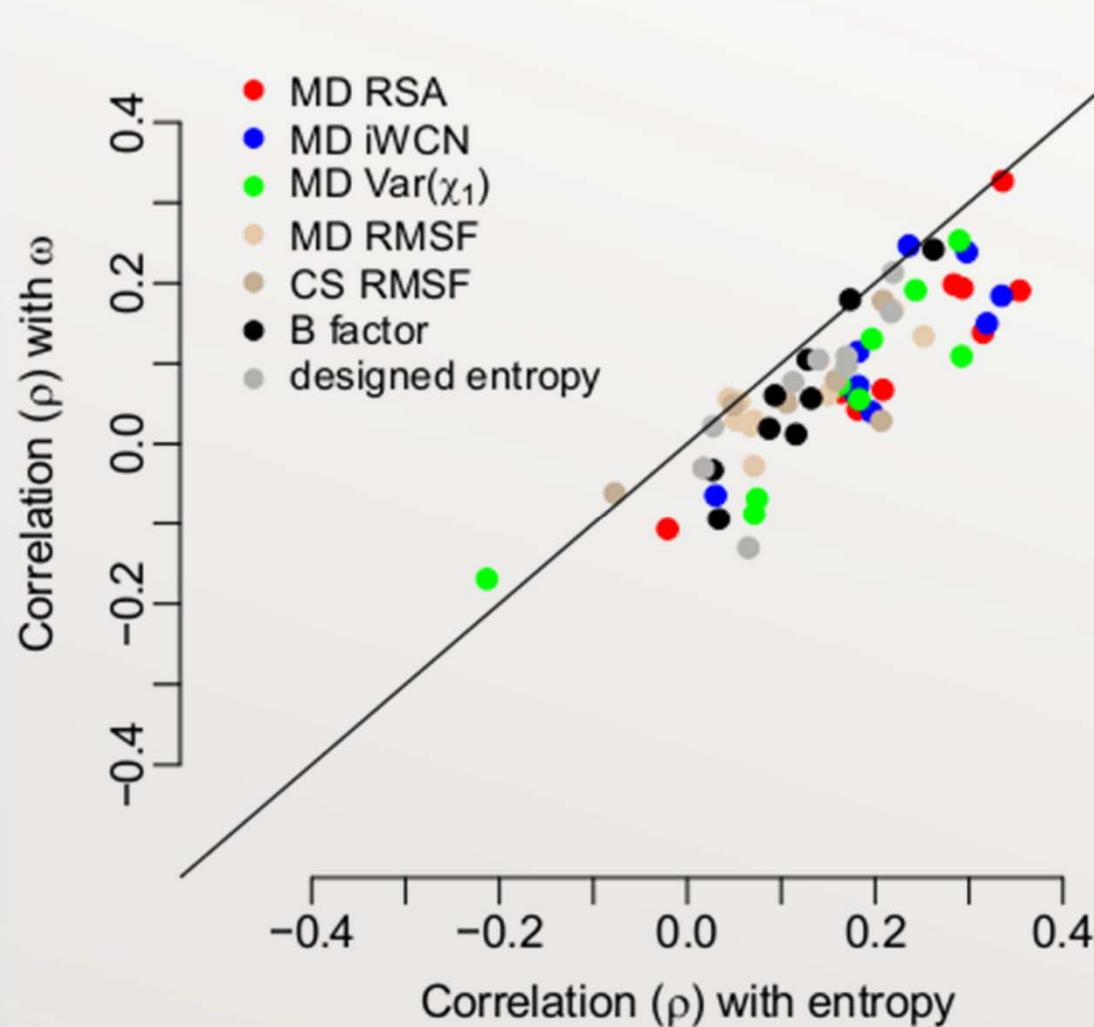
- Crimean-Congo Hemorrhagic Fever Virus Nucleocapsid
- Dengue Protease – Helicase
- West Nile Protease
- Influenza Nucleoprotein
- Marburg Virus RNA Binding Domain
- Hepatitis C Protease
- Japanese Encephalitis Helicase/Nucleoside
- Hemagglutinin Precursor
- Rift Valley Fever Virus Nucleoprotein

Buriedness measures outperform flexibility measures

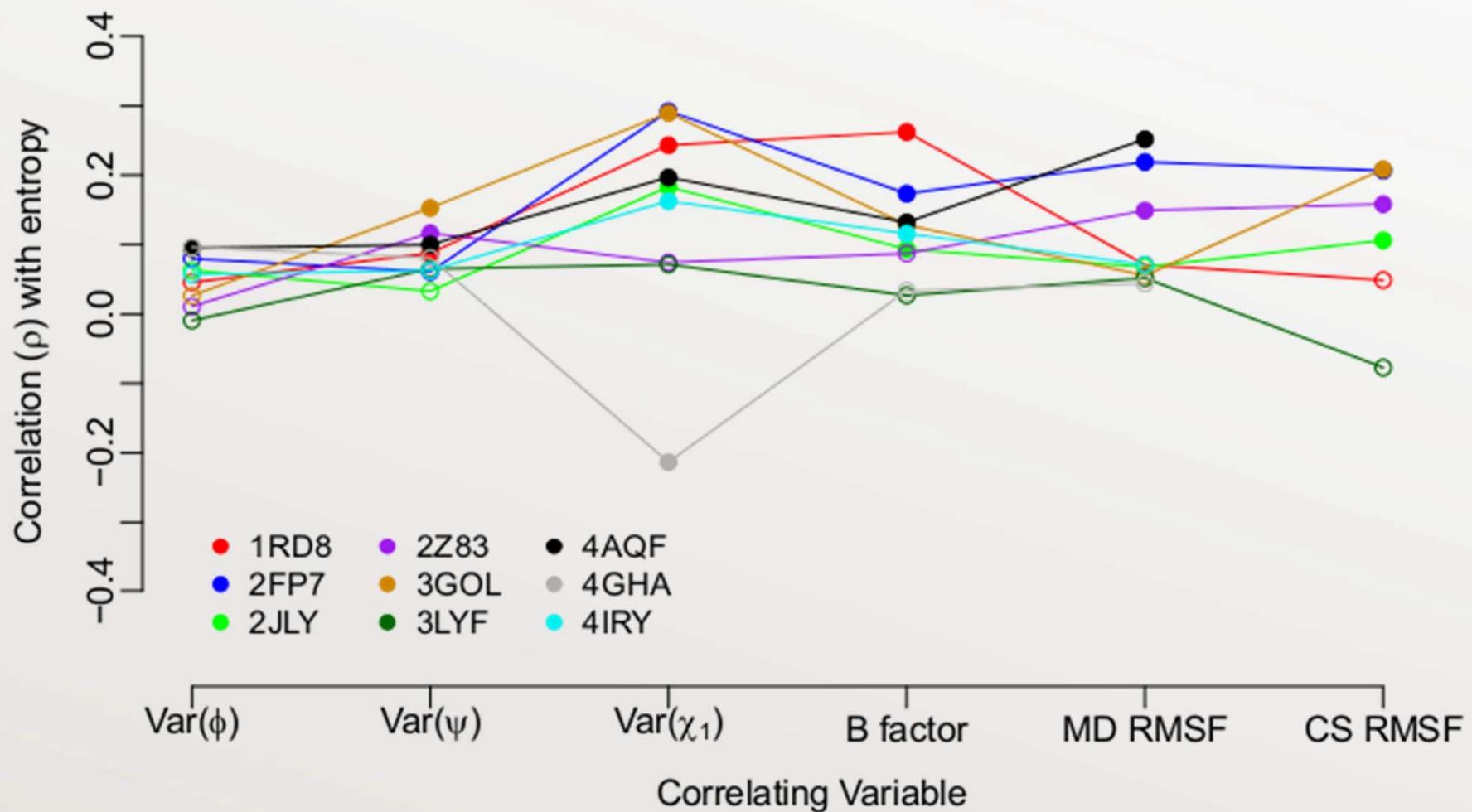


Sequence Entropy vs. Evolutionary Rates

Which one is a better measure of sequence variability?



Flexibility measures: Not strong indicators of sequence variability



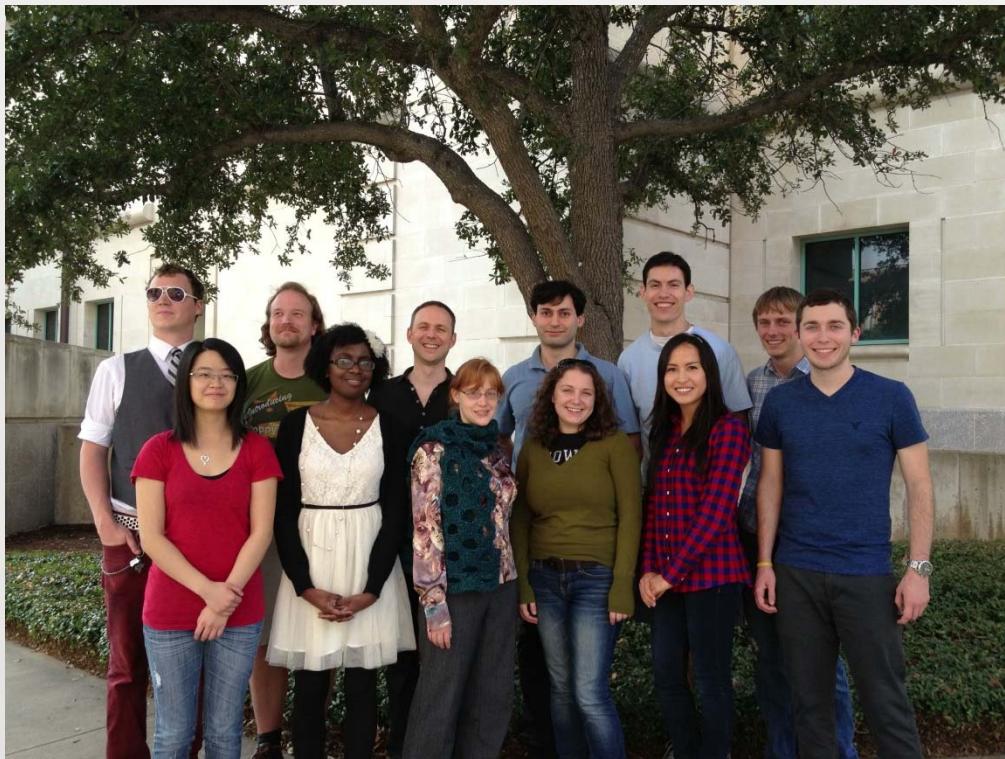
Summary

- Structural Measures of site flexibility correlate positively, but weakly in general, with sequence variability measures ($\rho \sim 0.1 - 0.3$) .
- Relative Solvent Accessibility and Contact Number are moderately good indicators of the site variability in viral proteins ($\rho \sim 0.2 - 0.4$) .
- Huang et al., 2014, BMC Evol. Bio., **14**, 78 “ A mechanistic stress model of protein evolution accounts for site-specific evolutionary rates and their relationship with packing density and flexibility ”
- Shahmoradi et al. 2014, **arXiv:1404.7511**, “ Predicting evolutionary site variability from structure in viral proteins: buriedness, flexibility, and design ”
- Dariya Sydkova, **Poster U-2280**, “ Structural Variation and Site Variability in Viral Proteins ”

Acknowledgments



Claus Wilke (PI)



Wilke Lab members

Daria Sydkova

Eleisha Jackson

Stephanie Spielman

Austin Meyer

Art Covert

Dakota DerryBerry

Viswanadham Sridhara

References

1. Predicting evolutionary site variability from structure in viral proteins: buriedness, packing, flexibility, and design, Shahmoradi, Amir and Sydykova, Dariya K and Spielman, Stephanie J and Jackson, Eleisha L and Dawson, Eric T and Meyer, Austin G and Wilke, Claus O, *Journal of Molecular Evolution (JME)* 79, 3-4, 130–142, 2014.
2. Intermediate divergence levels maximize the strength of structure--sequence correlations in enzymes and viral proteins, Jackson, Eleisha L and Shahmoradi, Amir and Spielman, Stephanie J and Jack, Benjamin R and Wilke, Claus O, *Protein Science*, 25, 7, 1341-1353, 2016.
3. Dissecting the roles of local packing density and longer-range effects in protein sequence evolution, Shahmoradi, Amir and Wilke, Claus O, *Proteins: Structure, Function, and Bioinformatics*, 84, 6, 841-854, 2016.

References

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@article{shahmoradi2014predicting,  
  title={Predicting evolutionary site variability from structure in viral proteins:  
buriedness, packing, flexibility, and design},  
  author={Shahmoradi, Amir and Sydykova, Dariya K and Spielman, Stephanie J  
and Jackson, Eleisha L and Dawson, Eric T and Meyer, Austin G and Wilke, Claus  
O},  
  journal={Journal of molecular evolution},  
  volume={79},  
  number={3-4},  
  pages={130--142},  
  year={2014},  
  publisher={Springer US}  
}
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@article{jackson2016intermediate,  
  title={Intermediate divergence levels maximize the strength of structure--  
sequence correlations in enzymes and viral proteins},  
  author={Jackson, Eleisha L and Shahmoradi, Amir and Spielman, Stephanie J  
and Jack, Benjamin R and Wilke, Claus O},  
  journal={Protein Science},  
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}
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