

# Involvement of Local, Rapid Conformational Dynamics in Binding of Flexible Recognition Motifs

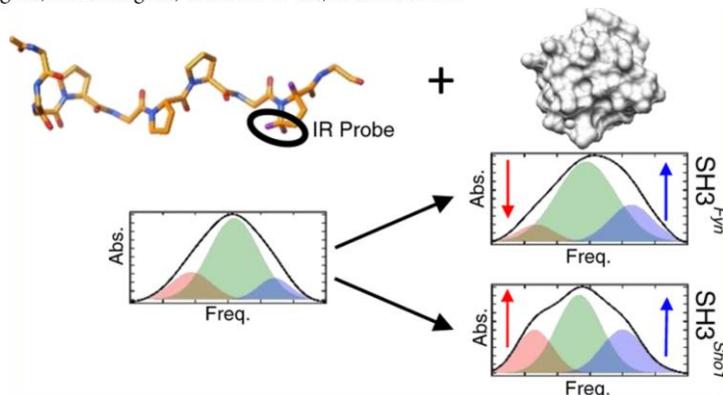
Gregory S. Bukowski, Rachel E. Horness, and Megan C. Thielges\*<sup>✉</sup>

Department of Chemistry, Indiana University, Bloomington, Bloomington, Indiana 47405, United States

 Supporting Information



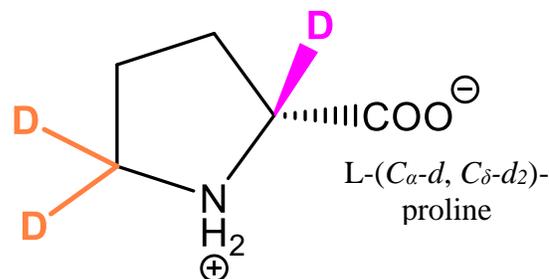
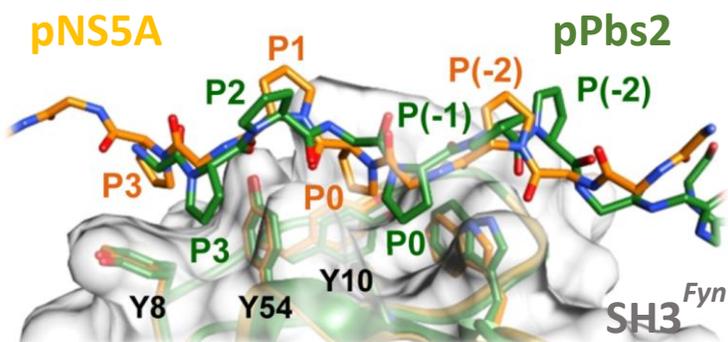
PC:  apis.photography



## Summary

- Changes in conformational heterogeneity (number of states) within and across ligands are SH3 domain and ligand consensus dependent.
- Decreases in conformational heterogeneity upon binding of ligands to SH3s correlates to decreases in binding entropy.
- Ligand flexibility implicated in modulation of conformational heterogeneity, resulting in lower recognition specificity.

PR motif	P x x P						
	P-2	P-1	P0	P1	P2	P3	
<b>pNS5A</b>							
H <sub>2</sub> N-RKRR	P	P	P	I	P	P	A-Ac
<b>pPbs2</b>							
Ac-VNK	P	L	P	P	L	P	VA-NH <sub>2</sub>
<b>pP(-2,1)A)Pbs2</b>							
Ac-VNK	A	L	P	A	L	P	VA-NH <sub>2</sub>



## Techniques Used Throughout Study

- FT IR spectroscopy – observe the individual states/environments of the probe
- Isothermal Titration Calorimetry – measure the thermodynamics of binding
- Molecular Dynamics Simulations – model the SH3:ligand complexes in solution

## Helpful Links

Group Website:

<https://thielges.lab.indiana.edu/>

Publications:

[https://thielges.lab.indiana.edu/Publications/Publications\\_2.html](https://thielges.lab.indiana.edu/Publications/Publications_2.html)

