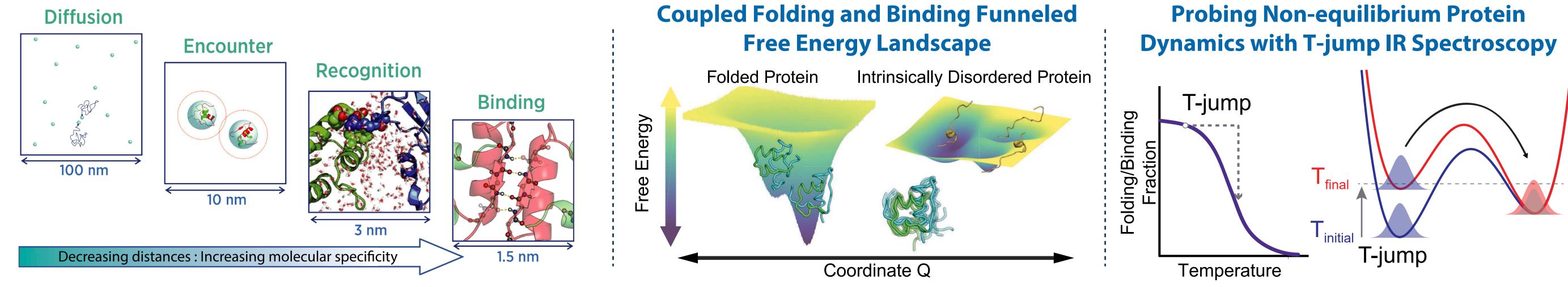


Dynamics of Protein-Protein Interactions

Molecular Dynamics of Protein Association



UL B20B23

Relaxation

A13A16 B24B25

Conformational Disorder in Protein Recognition and Binding

1585 cm⁻¹

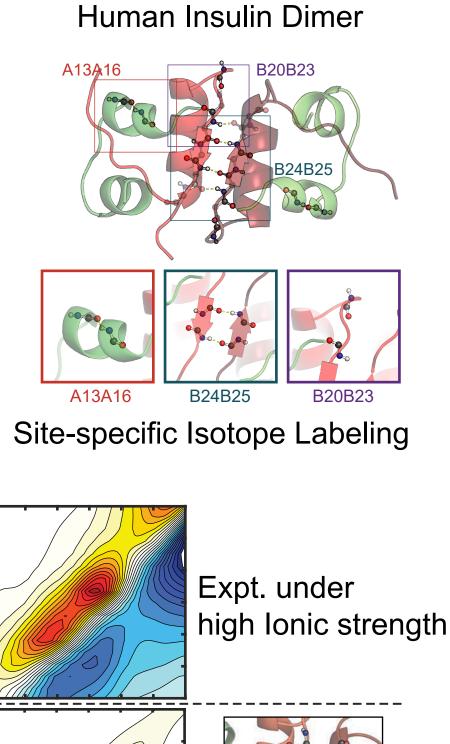
Residue specific T-jump responses

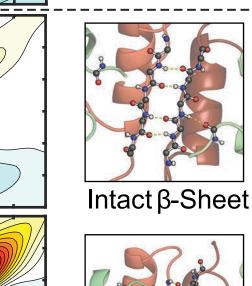
Conformational disorder leads to structural motions that occur over a wide range of timescales and is commonly involved in protein binding and recognition. The course of molecular interactions required for proteins to recognize and bind with specific targets is critical to their cellular functionalities.

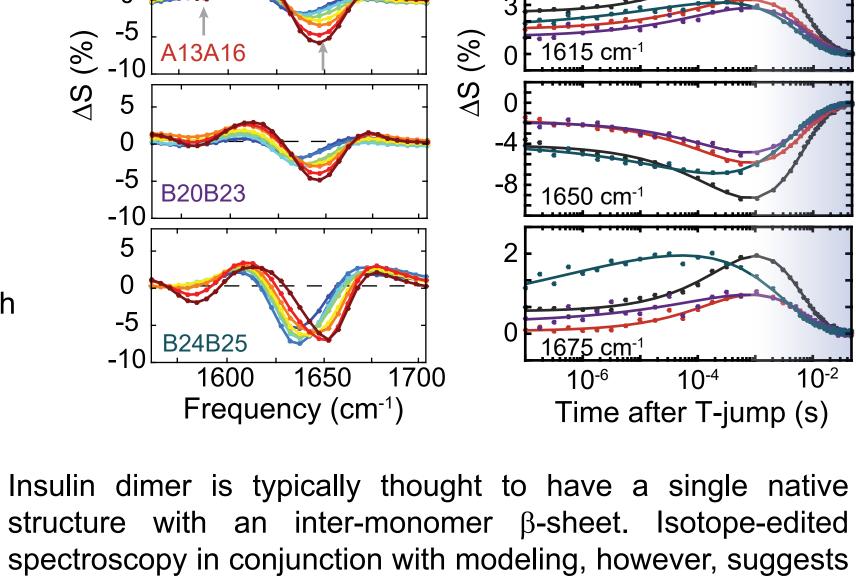
Protein structural transitions often occur in non-equilibrium conditions, through pathways inaccessible at equilibrium. We study coupled folding and binding dynamics using IR spectroscopy, isotope labeling, T-jump spectroscopy, and computational modeling.

Dissociation and Unfolding of Insulin Dimer

 $Time_{T_1}(s)$



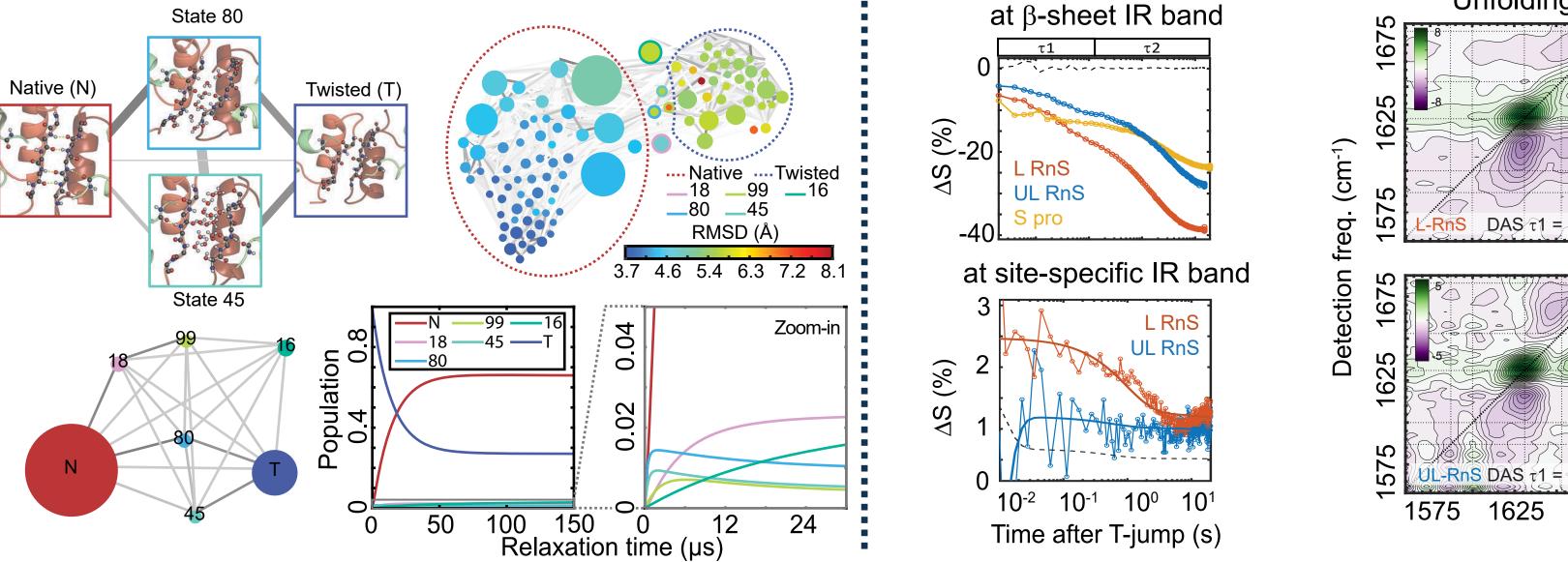




10-3

structure with an inter-monomer β -sheet. Isotope-edited spectroscopy in conjunction with modeling, however, suggests a conformational ensemble containing intact β -sheet and register-shifted strands in the dimer state.

Molecular dynamics simulation of dimer twisting



10-2

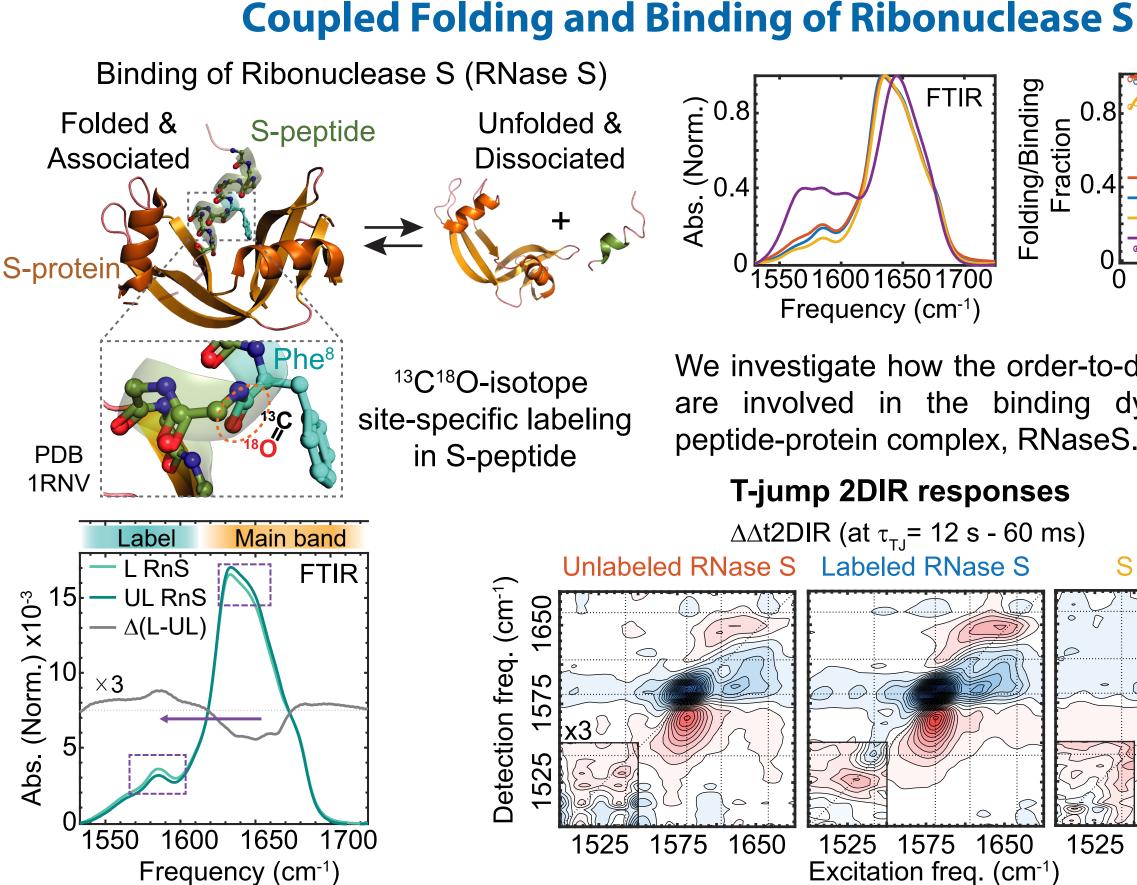
Direct observations from T-jump 2DIR with site-specific isotope-labeled RNase S demonstrate that partial unfolding of the S-protein on ms-timescales destabilizes the hydrophobic binding pocket containing the S peptide, which in turn enables unbinding and unfolding of RNase S on the timescale of seconds.

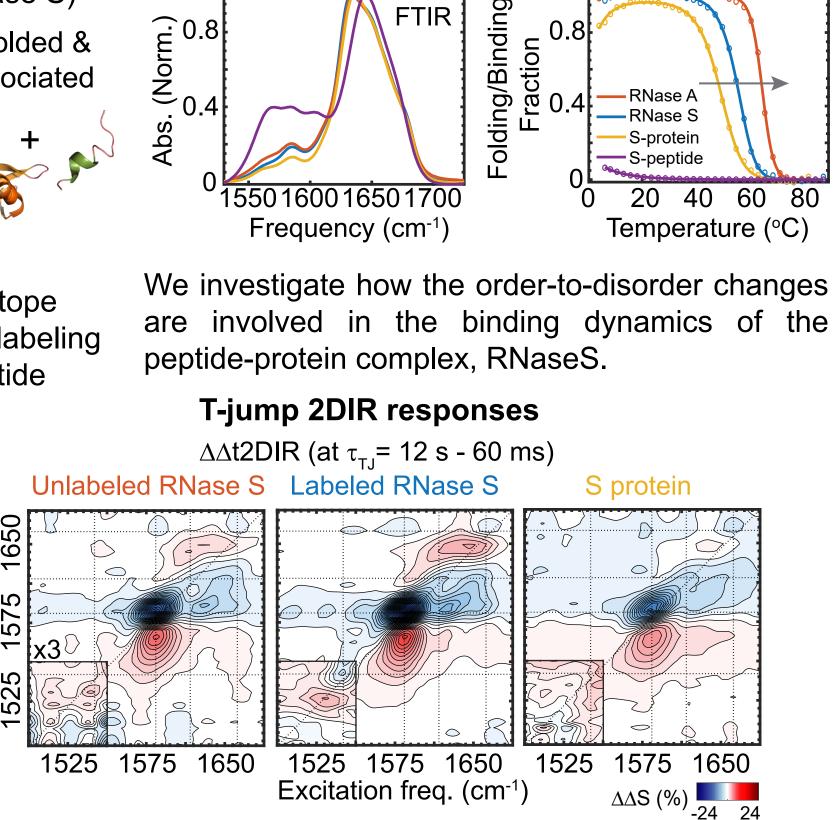
T-jump kinetic traces

Global lifetime analysis

20

Unfolding Unfolding+Unbinding Isotope-labeled region



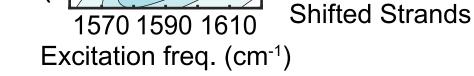


161

590

 (cm^{-1})

Detection freq.



Markov State Models (MSMs) of the dimer reveal a heterogeneous conformational distribution and two dominant conformational states with interconversions occurring on ~20 On-path intermediate μS. structures involve solvation of β -strands, which is also observed in molecular simulations of dimer dissociation.

