

Structural Disorder of IκBα and NF-κB

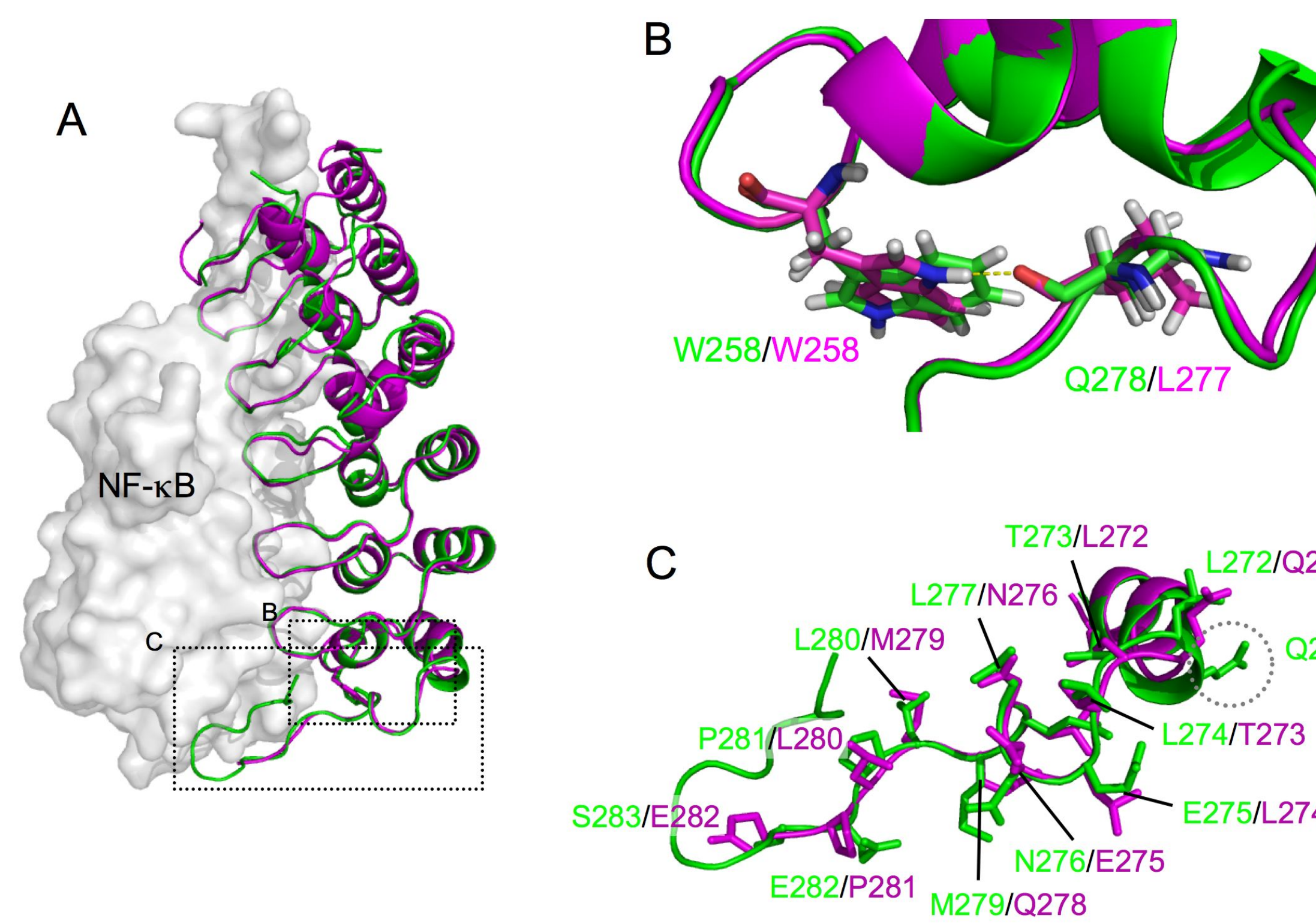
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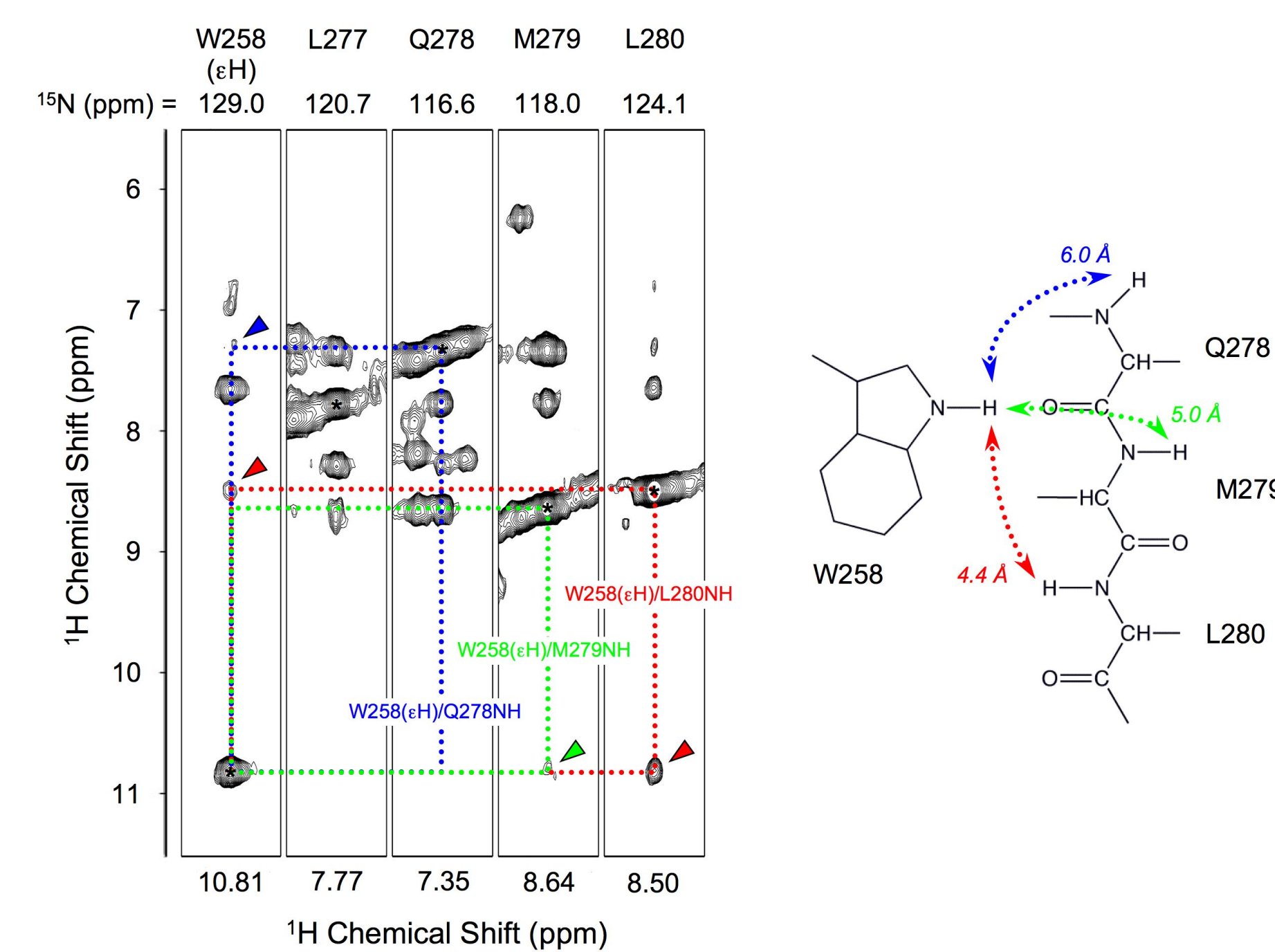
We are studying IκBα and NF-κB in their bound forms. Flexibility is crucial for the function of both proteins. By isotopically labeling only IκBα, we have discovered novel dynamic properties of the ankyrin repeat region of IκBα and determined an interaction site on NF-κB for the flexible PEST sequence of IκBα. Our current goal is to study these complexes by isotopically labeling only certain domains of NF-κB.

PEST Sequence Interaction

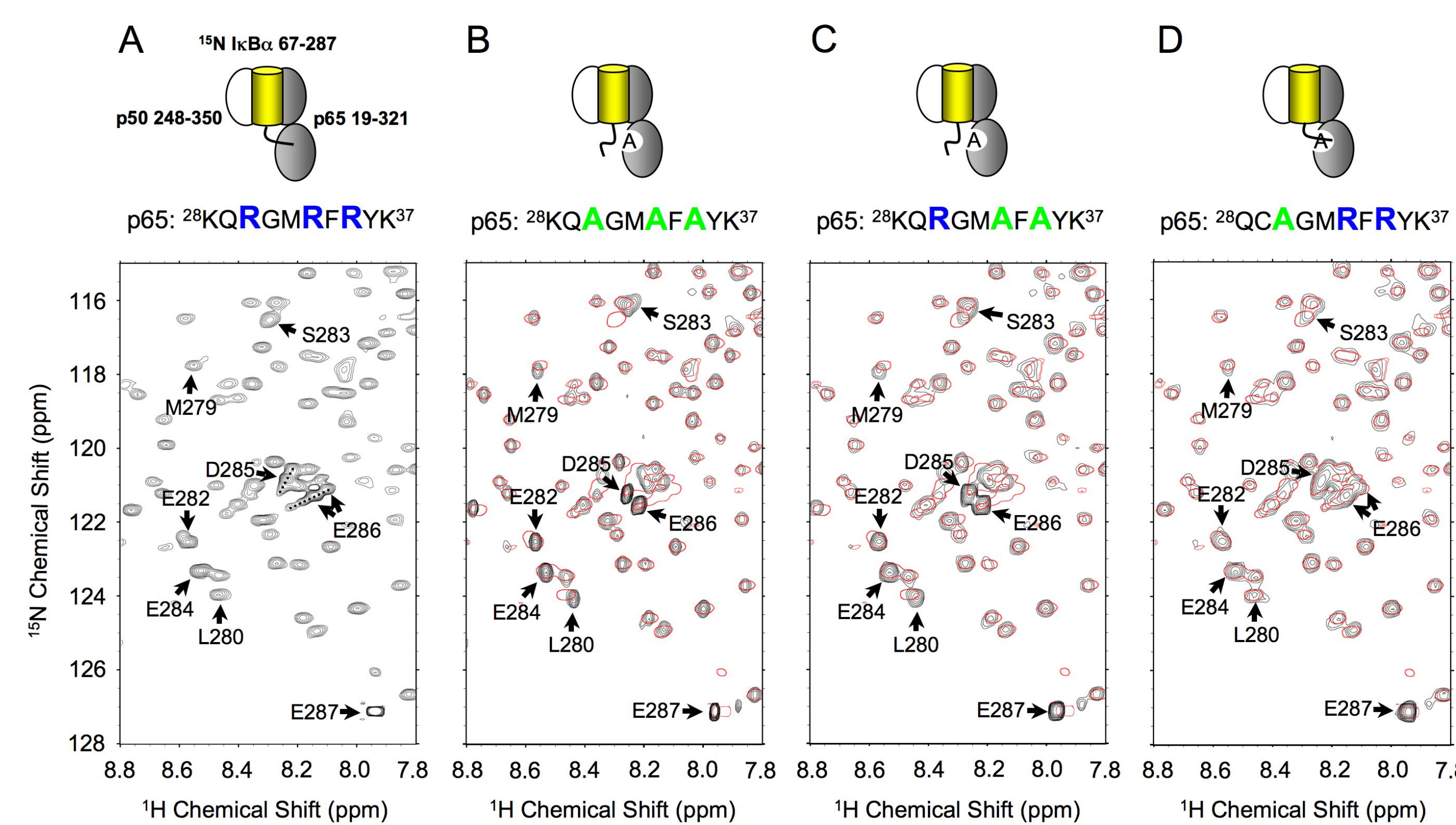
Two published structures show discrepancies in IκBα C-terminus



The C-terminal structure was identified by its NOE pattern

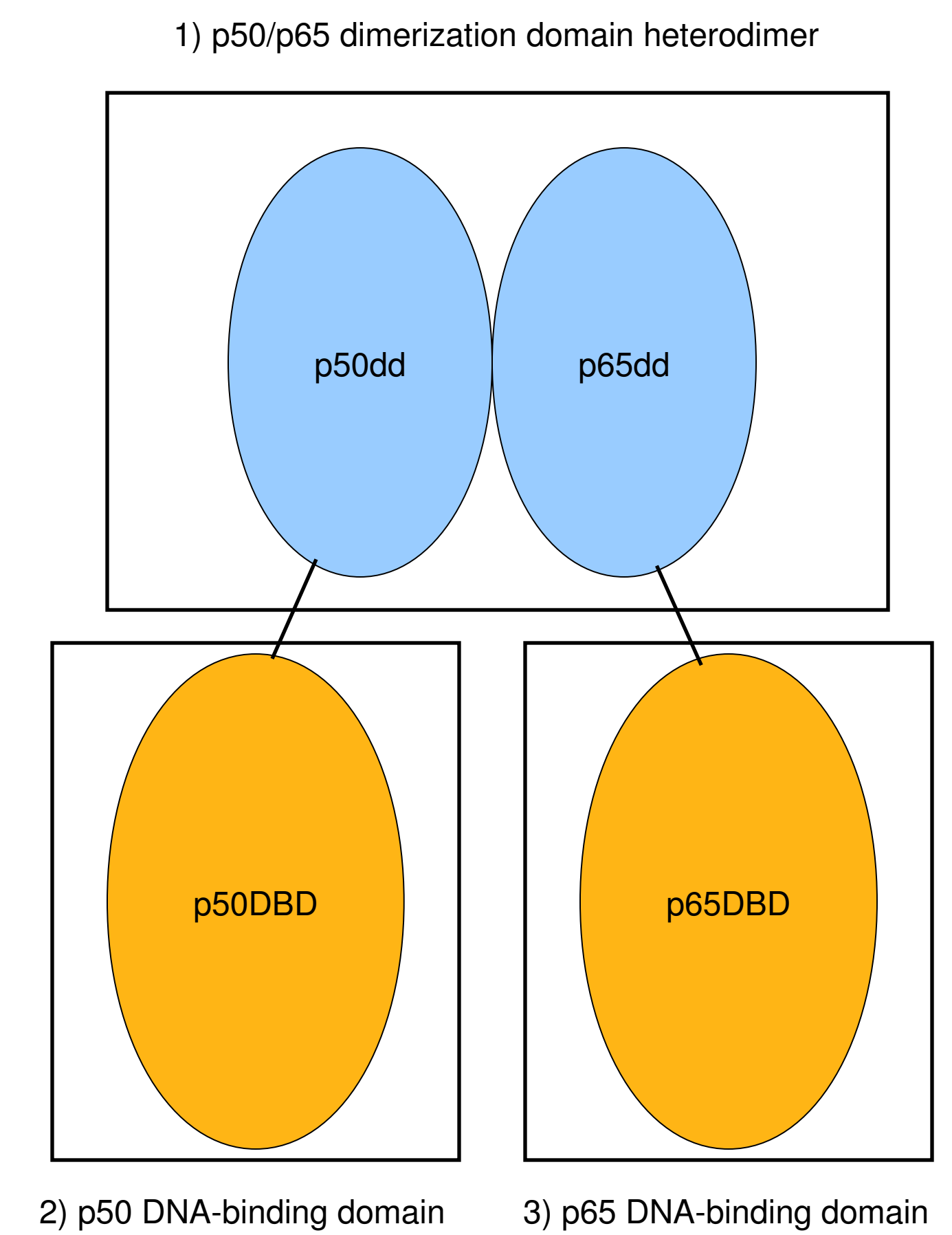


Flexible PEST recognizes the consensus NF-κB Arg-rich sequence



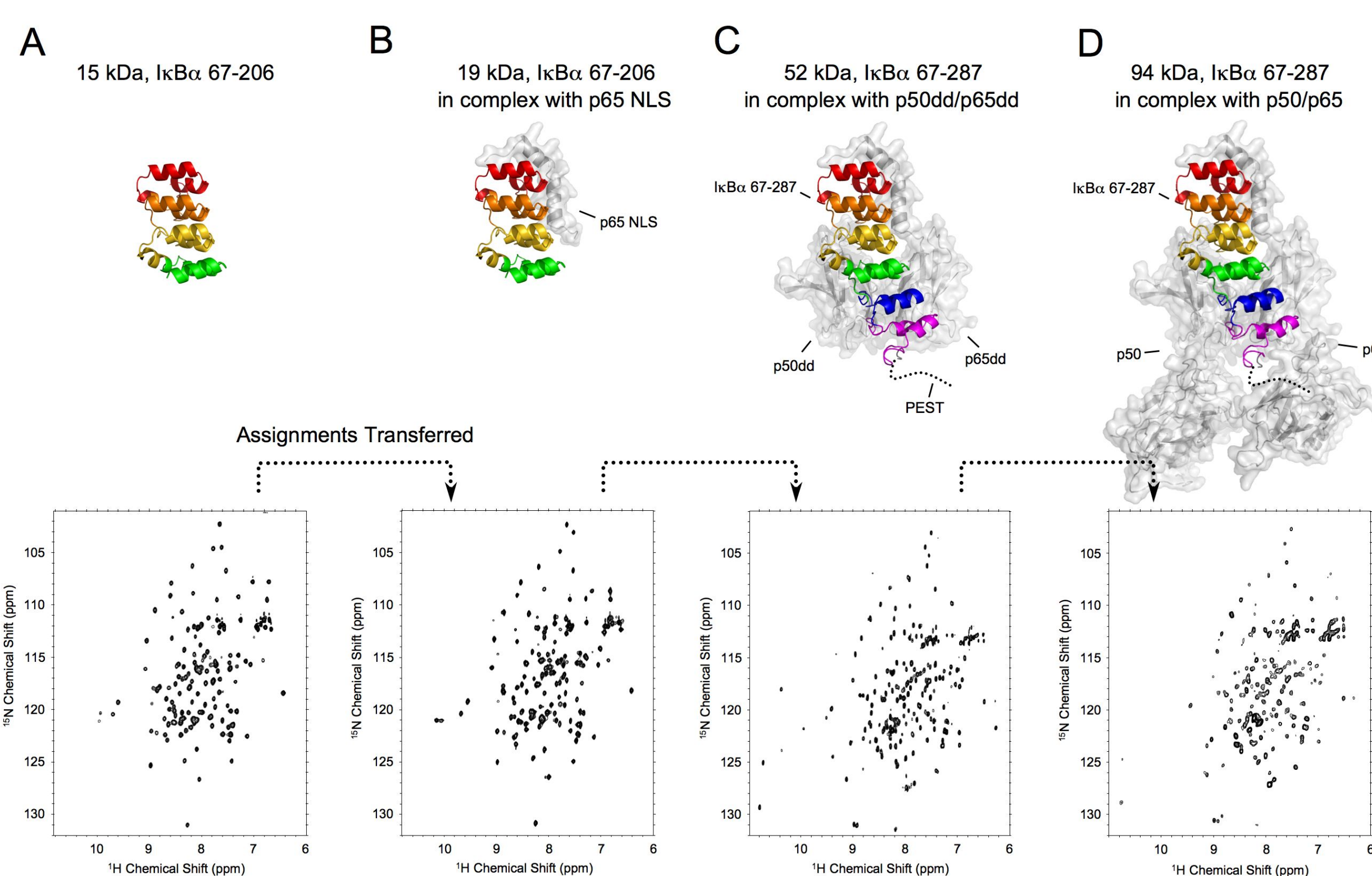
NF-κB Assignments

Because NF-κB is 70 kD, our assignment strategy involves breaking the complex up into three pieces.

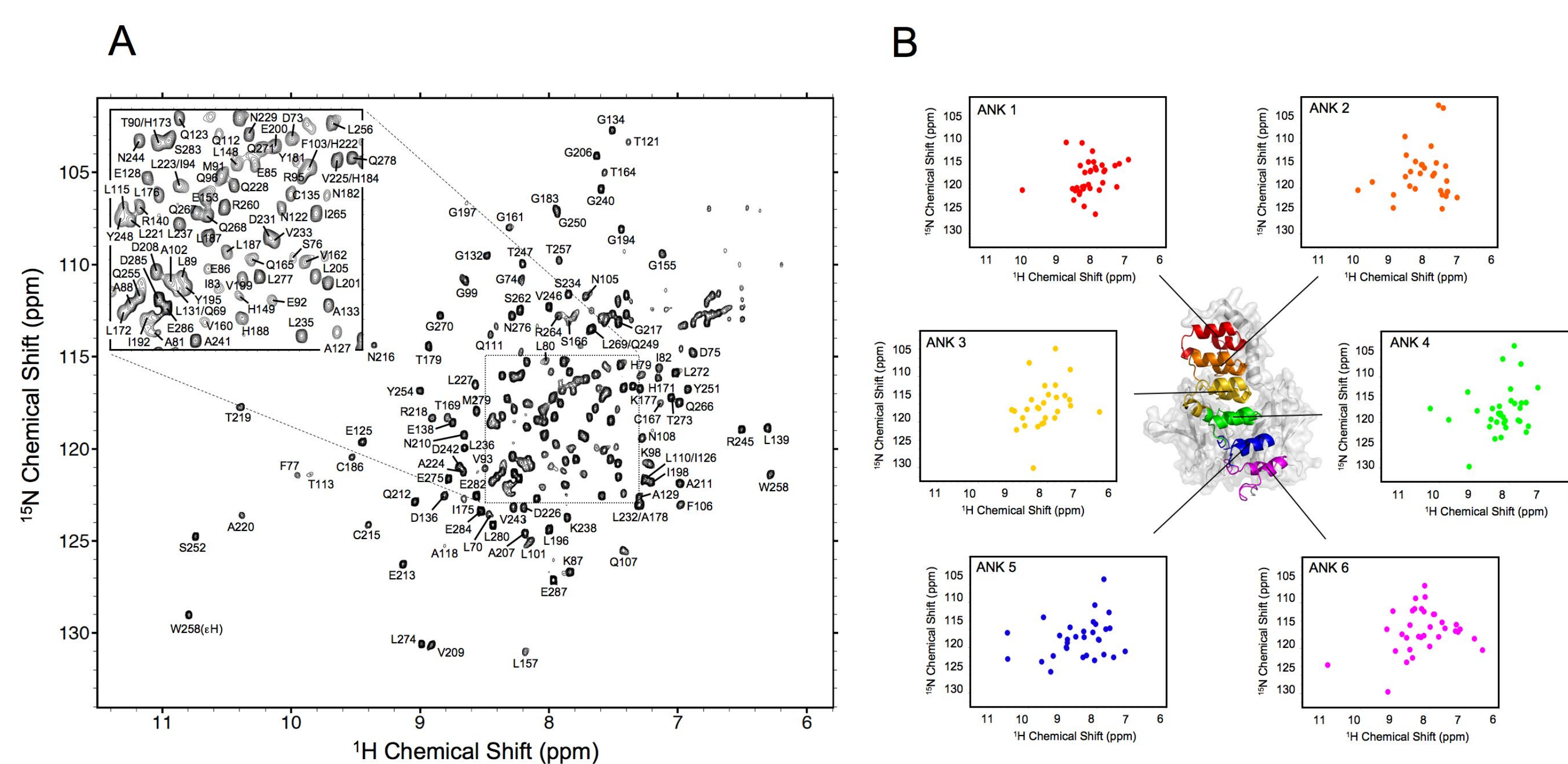


IκBα Assignments

A customized strategy for IκBα backbone assignment

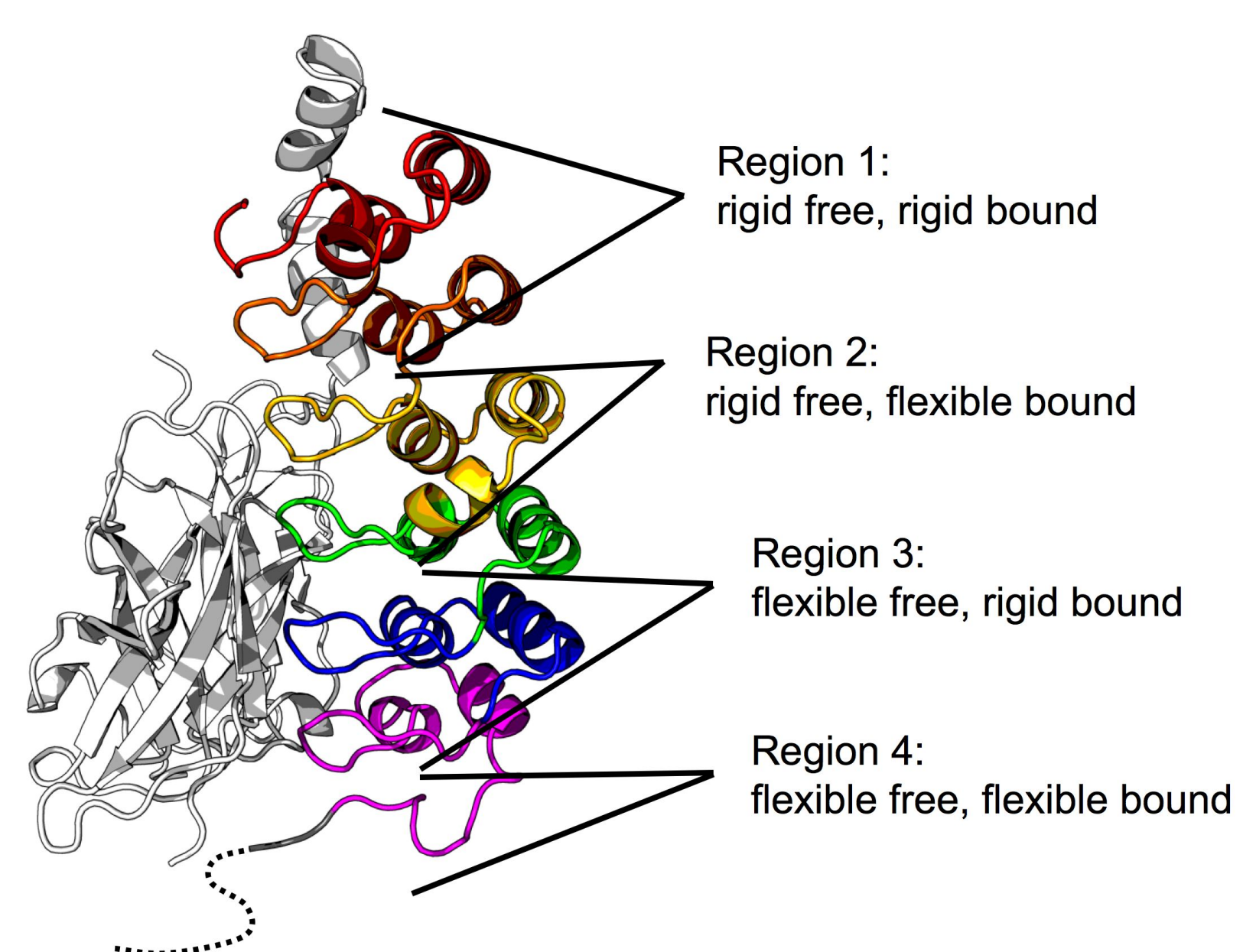


Assignments of the backbone amides and their distributions

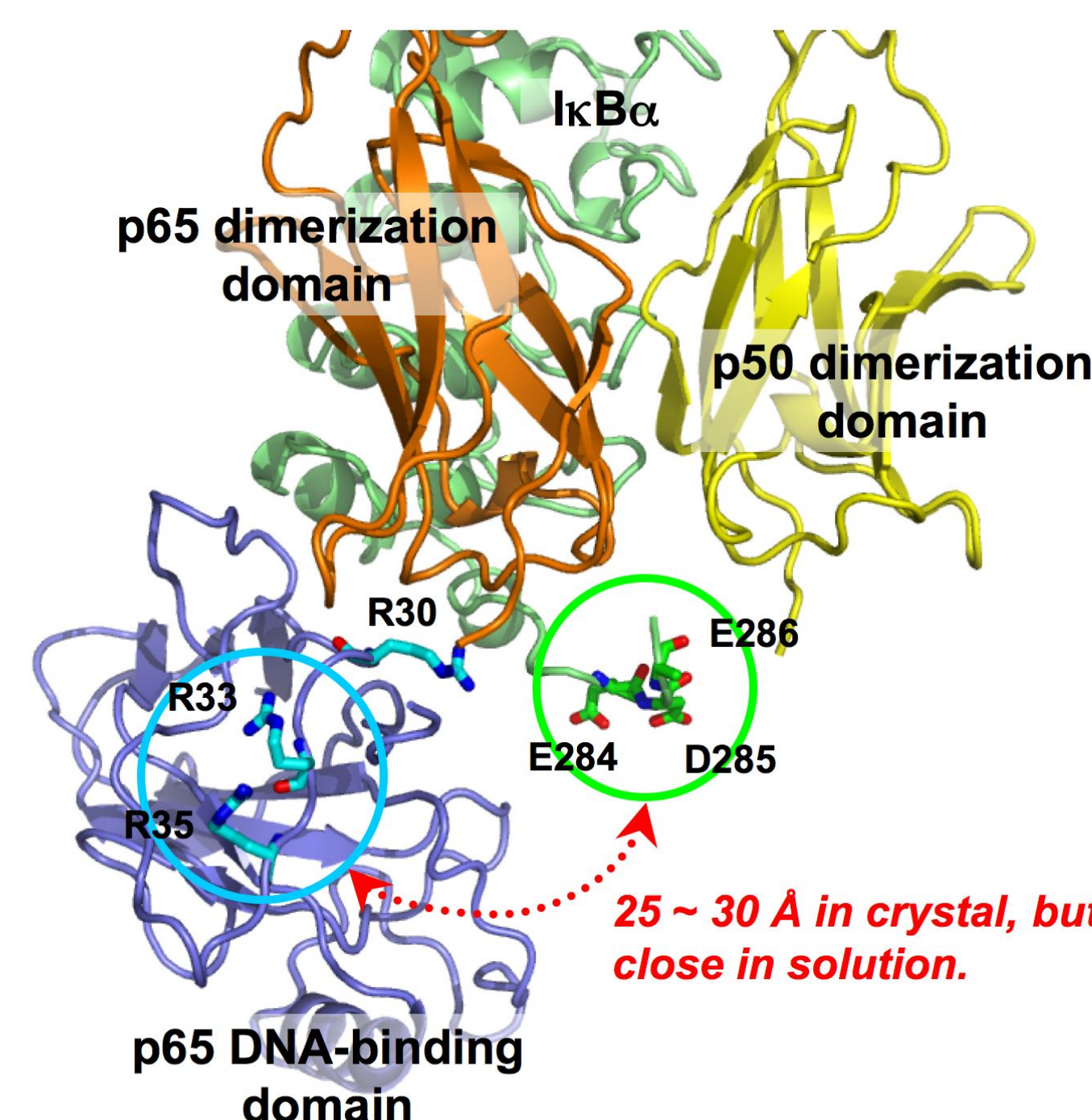


Flexibility of Ankyrin Repeats

Regions of IκBα vary in their dynamic characteristics



For Region 1, average free PF ~ 10⁴ – 10⁵ and average bound PF ~ 10⁴ – 10⁵; for Region 2, average free PF ~ 10⁴ – 10⁵ and average bound PF ~ 10⁴ – 10⁵; for Region 3, average free PF ~ 10⁴ – 10⁵ and average bound PF ~ 10⁴ – 10⁵; for Region 4, average free PF ~ 10⁴ – 10⁵ and average bound PF ~ 10⁴ – 10⁵.



References:

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