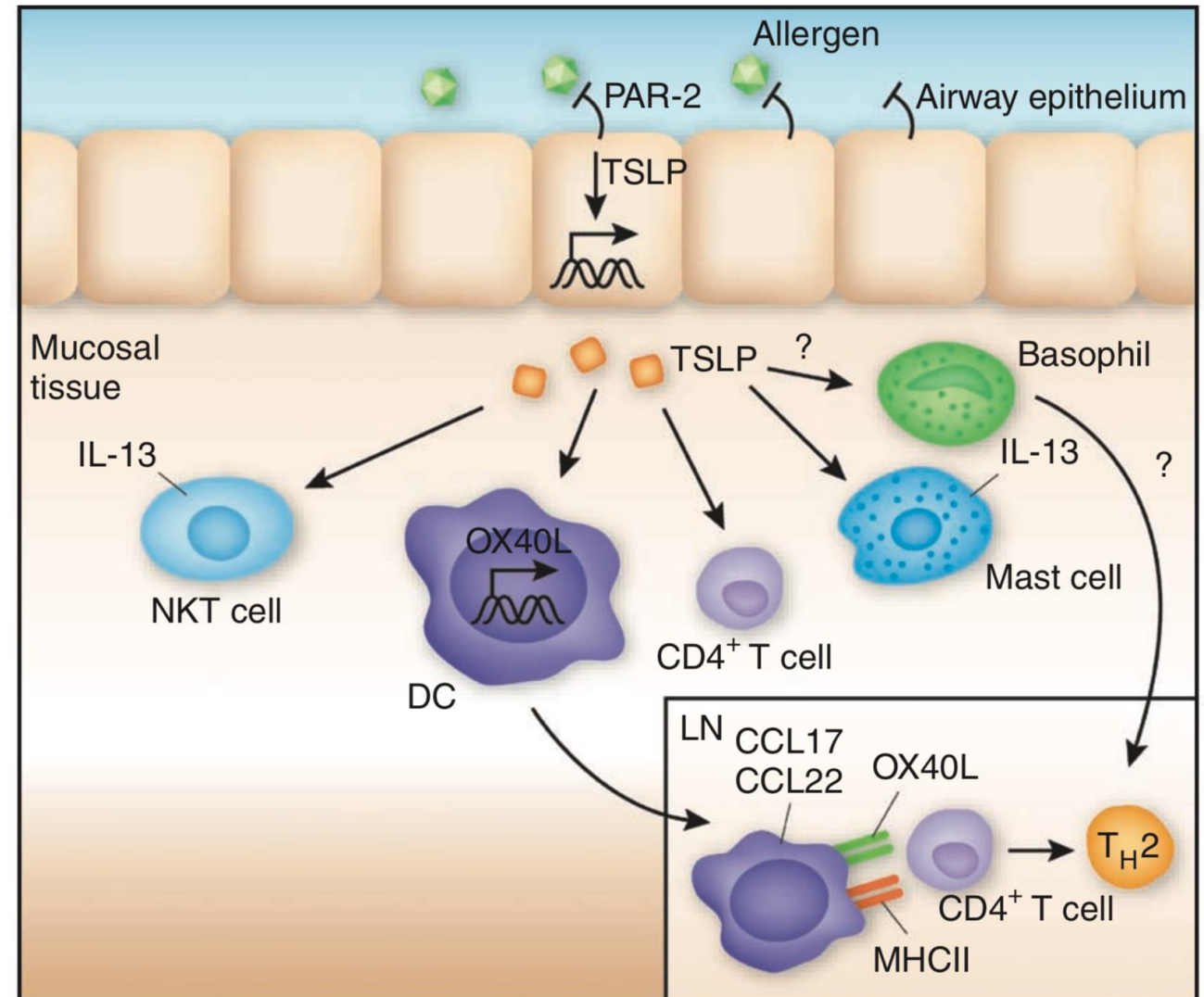


TSLP

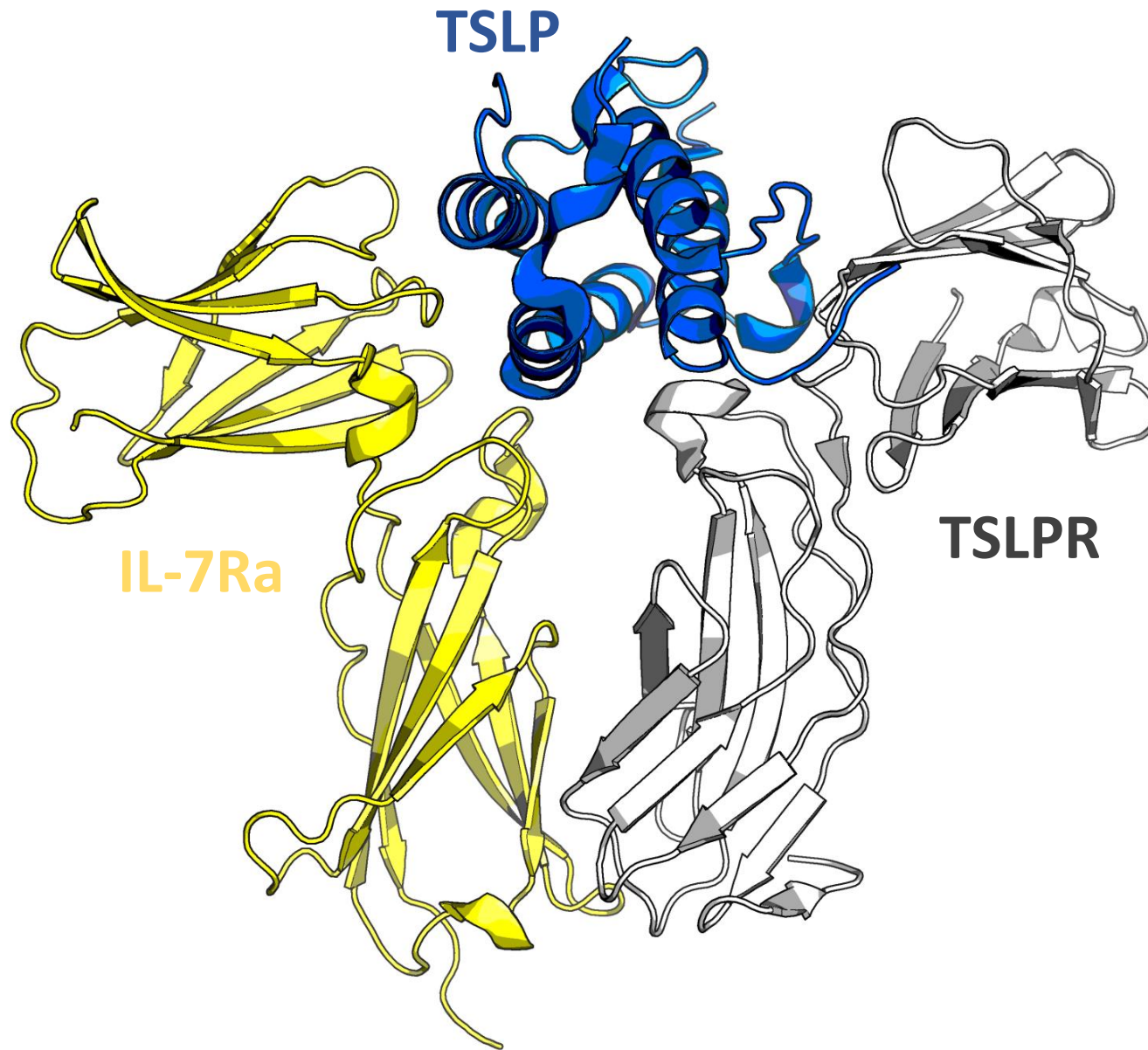
A molecular modelling study

What is TSLP?

- Cytokine
- Pro-inflammatory
- Master switch for asthma, allergic rhinitis and eczema



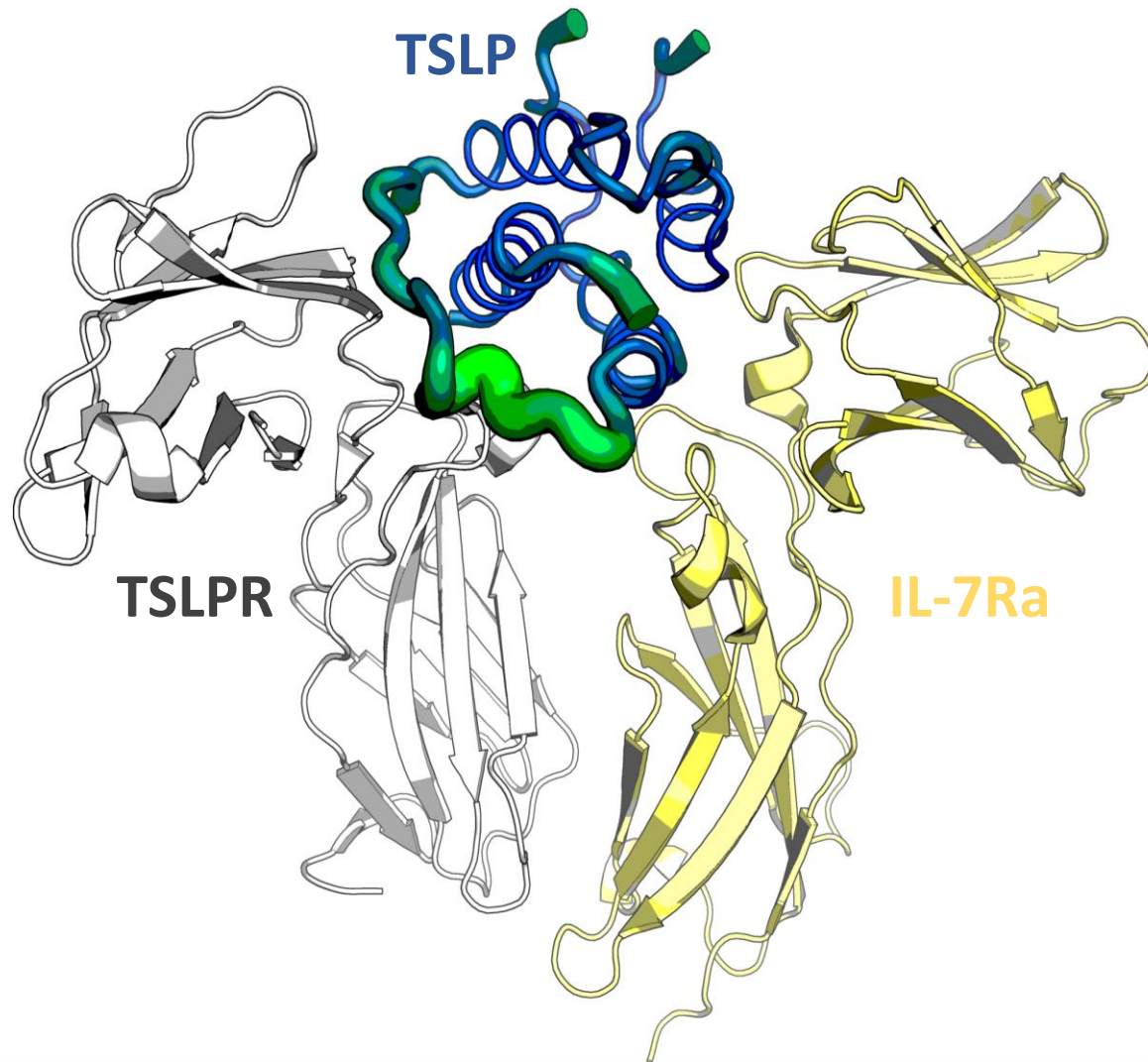
TSLP:TSLPR:IL-7Ra complex



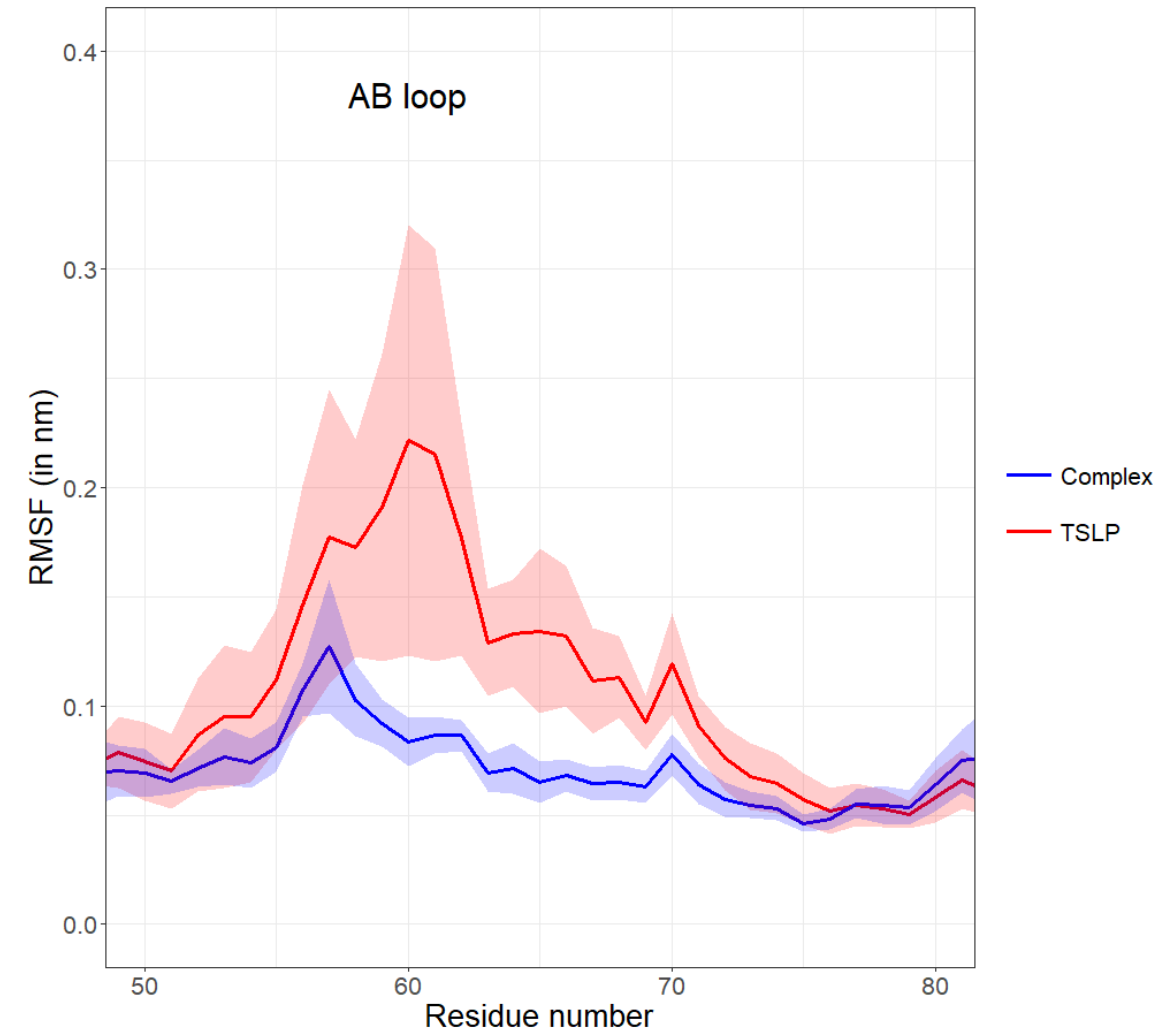
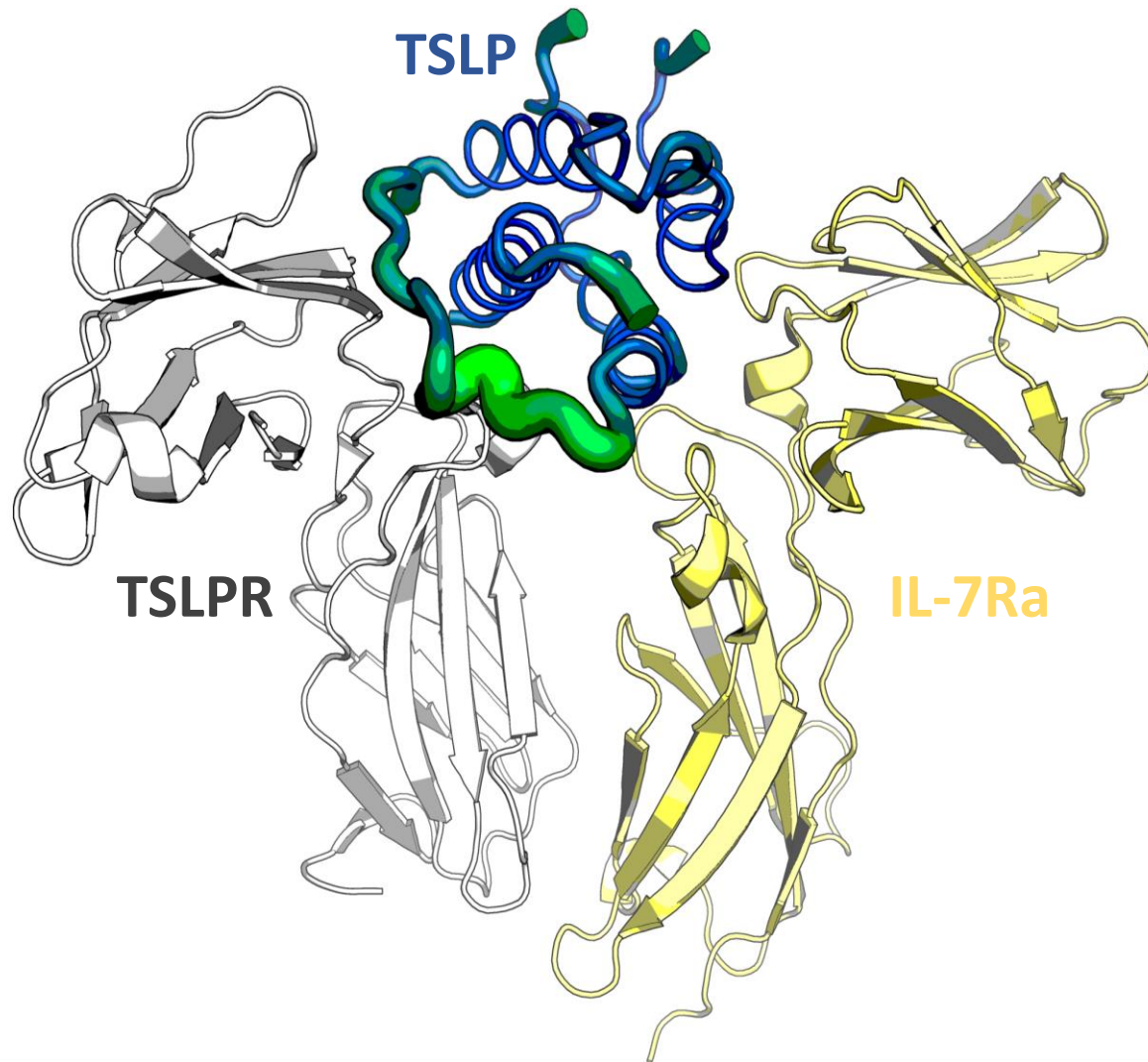
Molecular dynamics simulations

- Make molecules move (in a physics-consistent way)
- Answer biological questions

Priming of TSLP by TSLPR

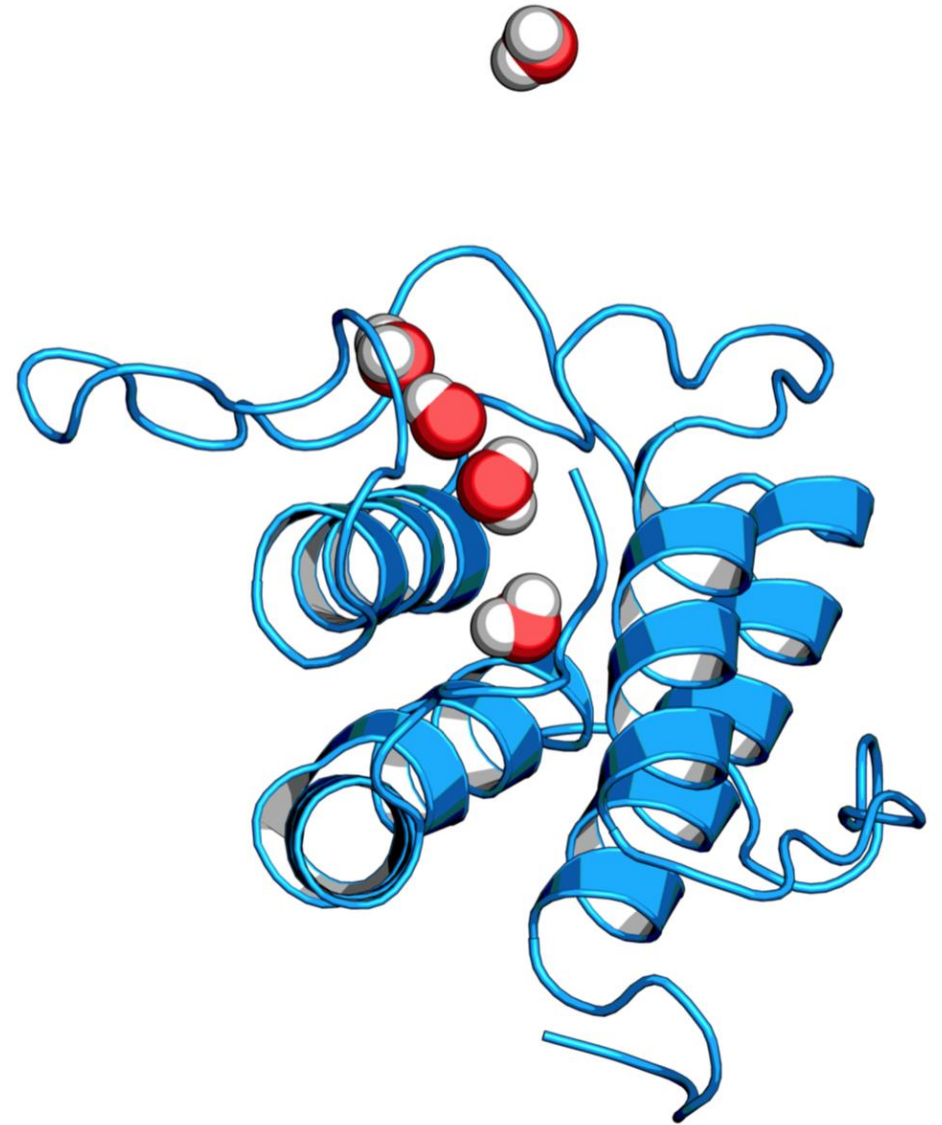


Priming of TSLP by TSLPR



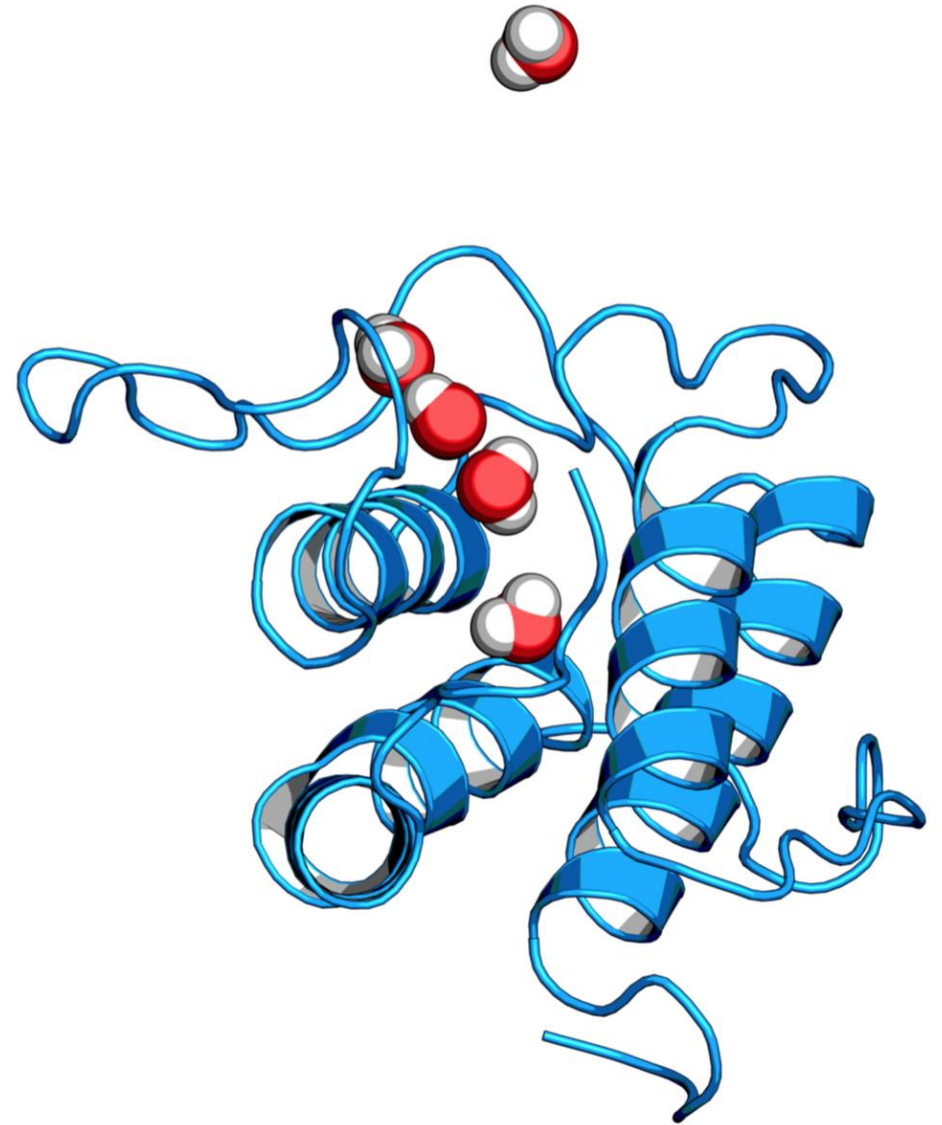
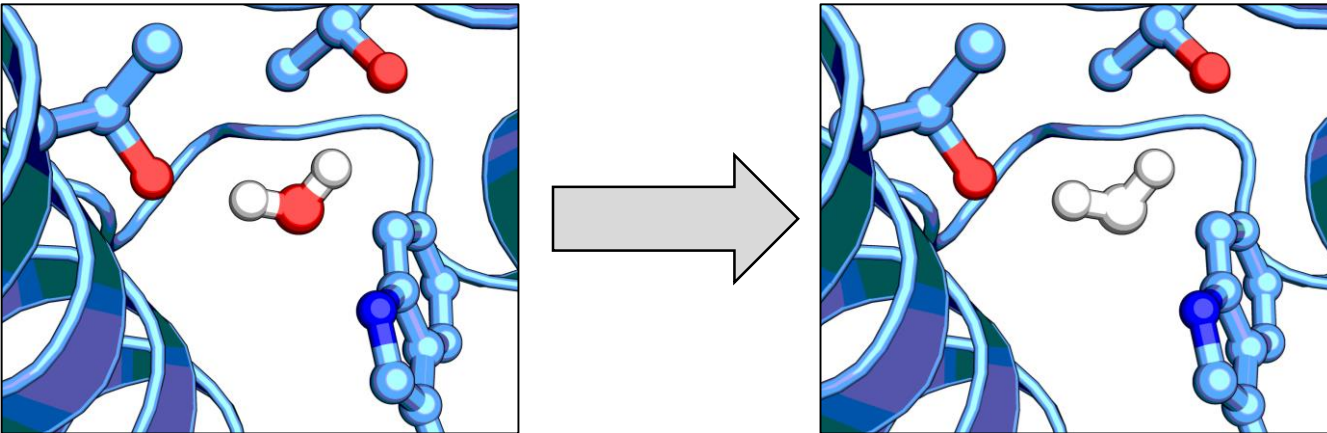
Central water molecule

- Unique in the cytokine world
- TSLP can get new water molecule from bulk solvent when it is removed

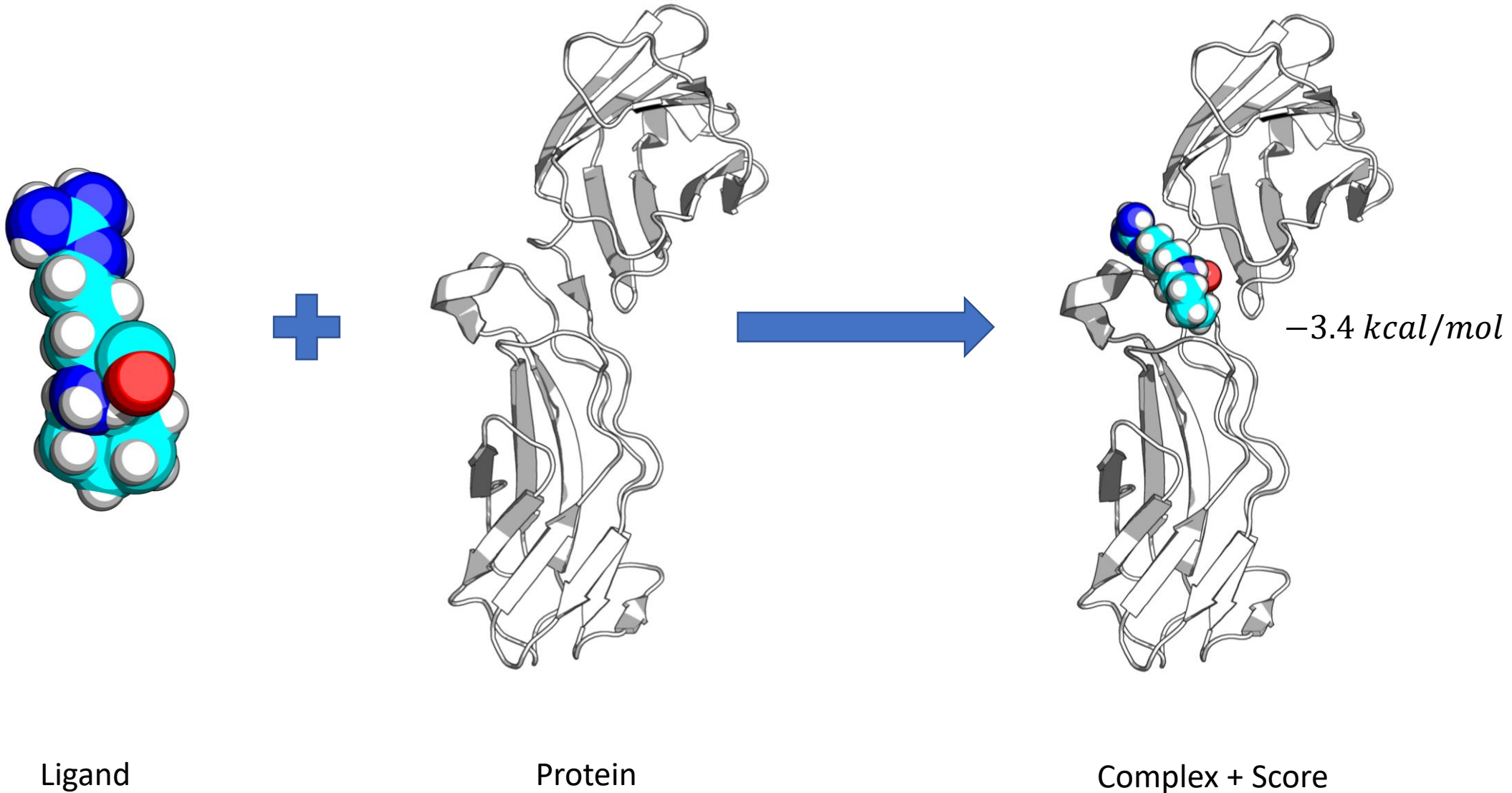


Central water molecule

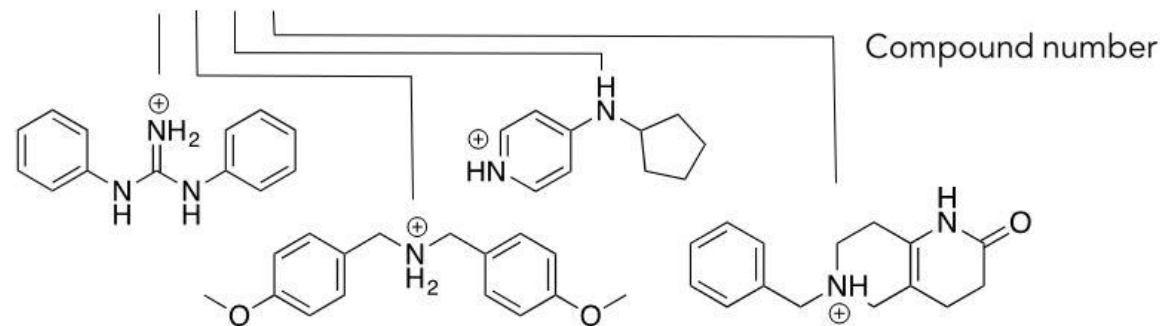
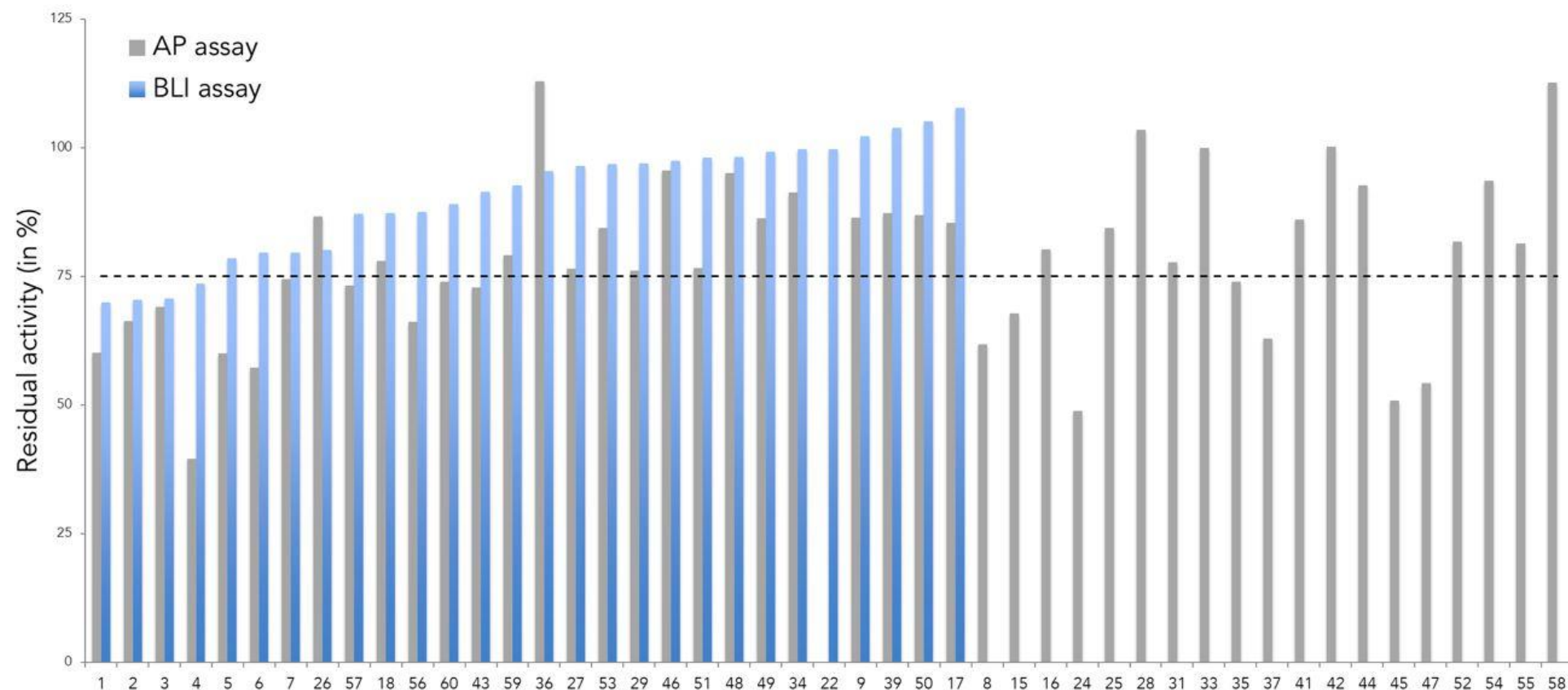
- Unique in the cytokine world
- TSLP can get new water molecule from bulk solvent when it is removed
- Calculate energy by transforming into a 'ghost' molecule: $-3.6 \text{ kcal.mol}^{-1}$



Inhibitor development: molecular docking

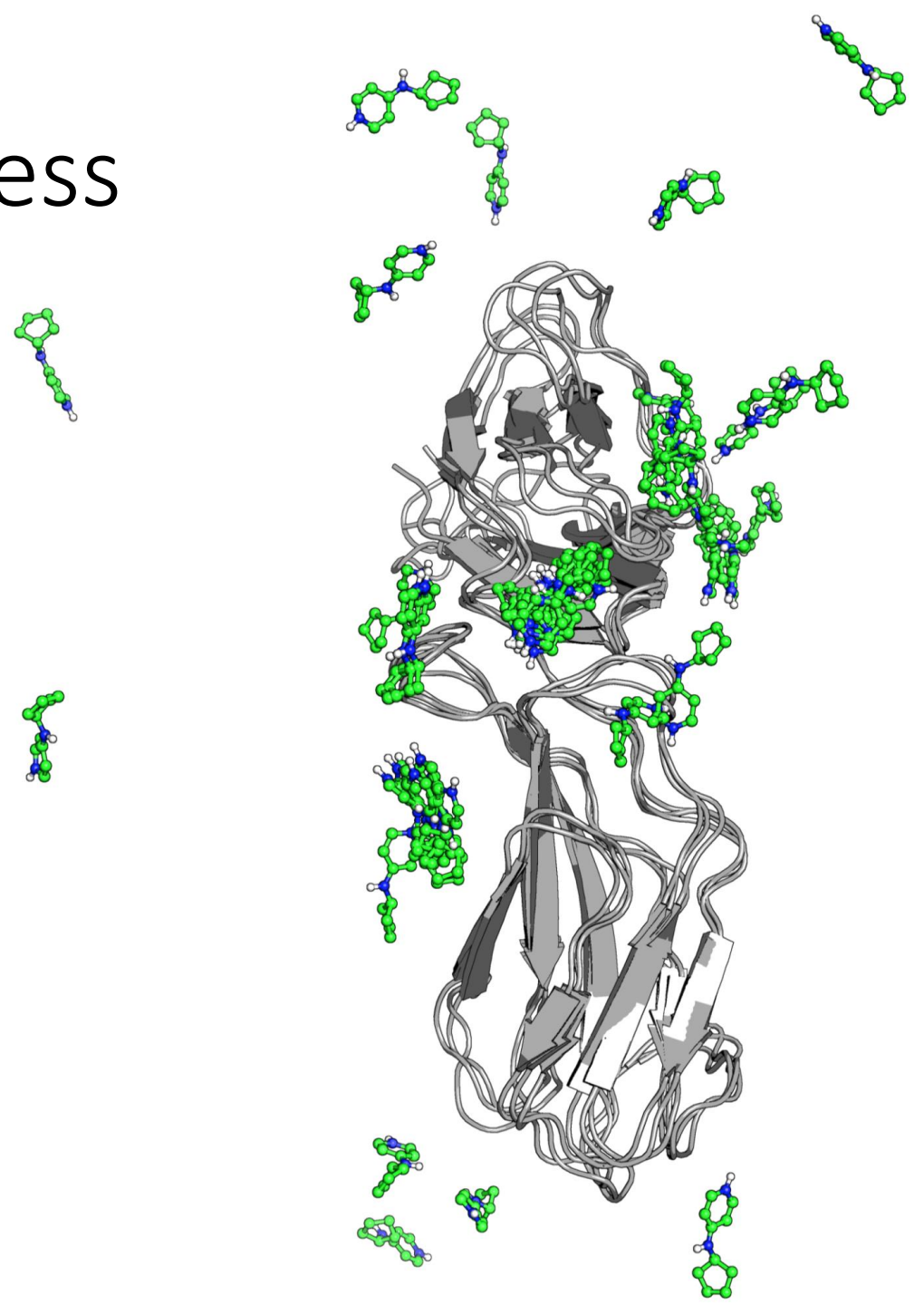


In vitro testing

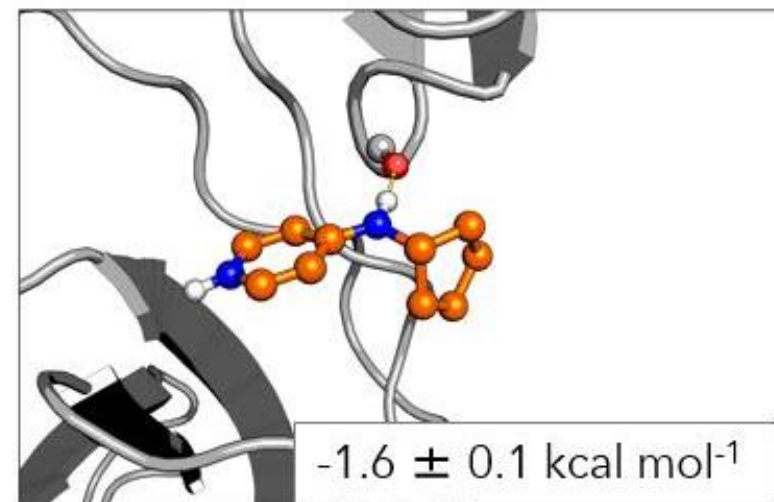
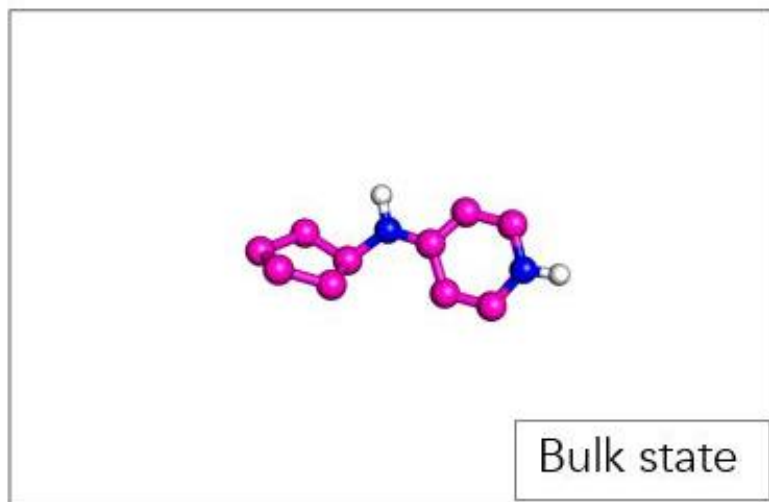
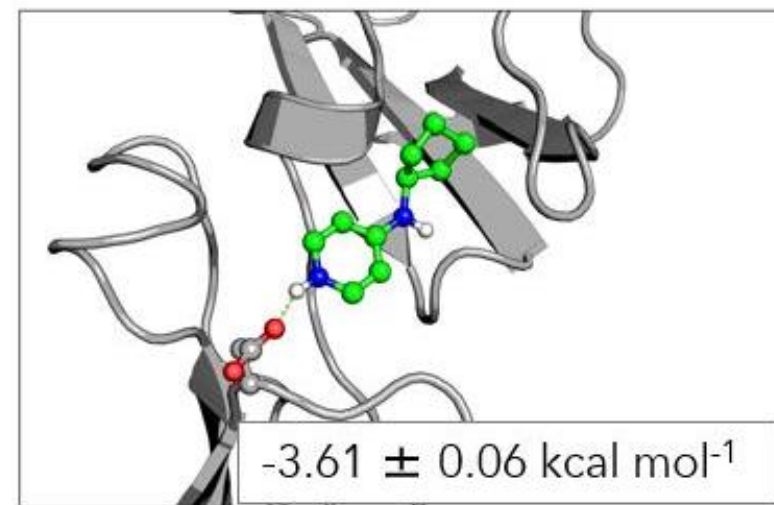
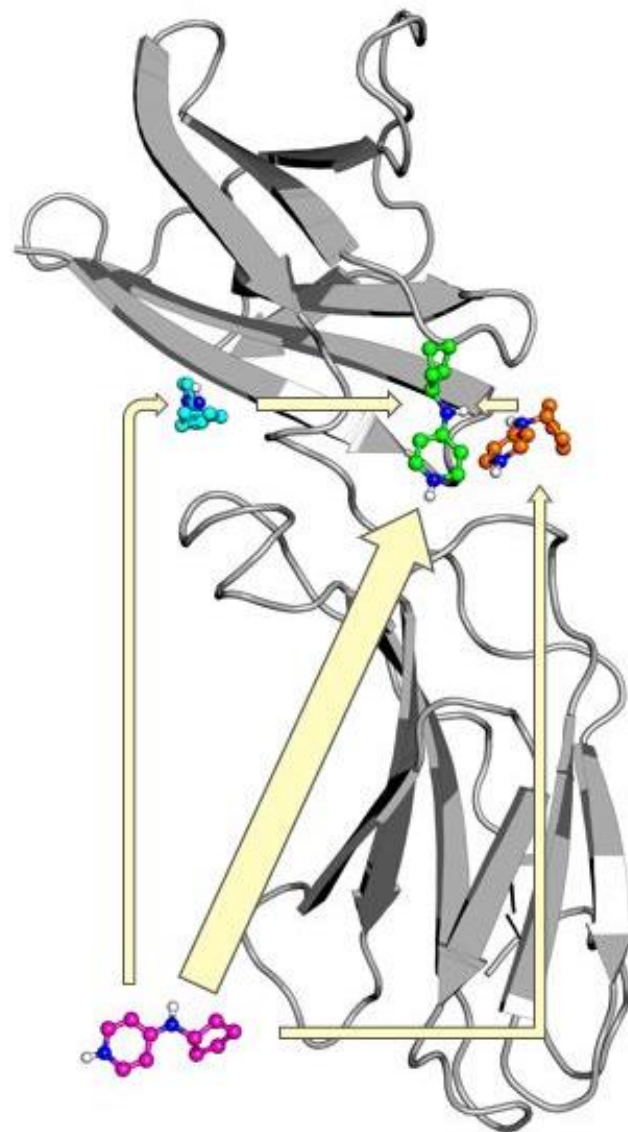
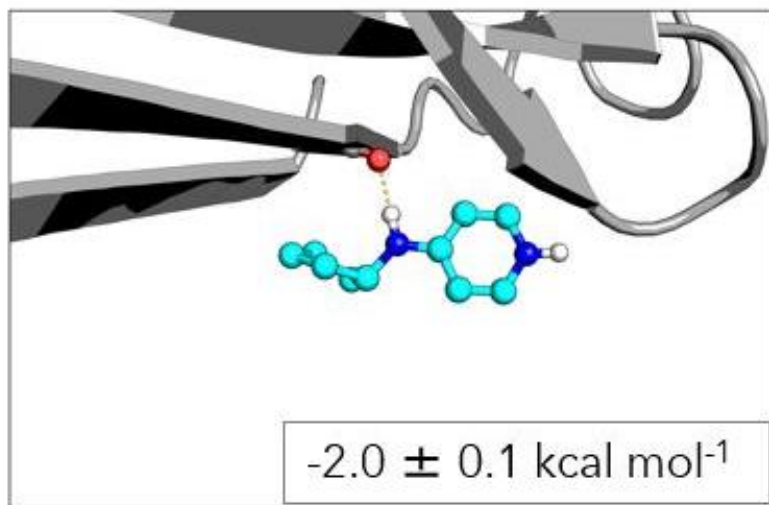


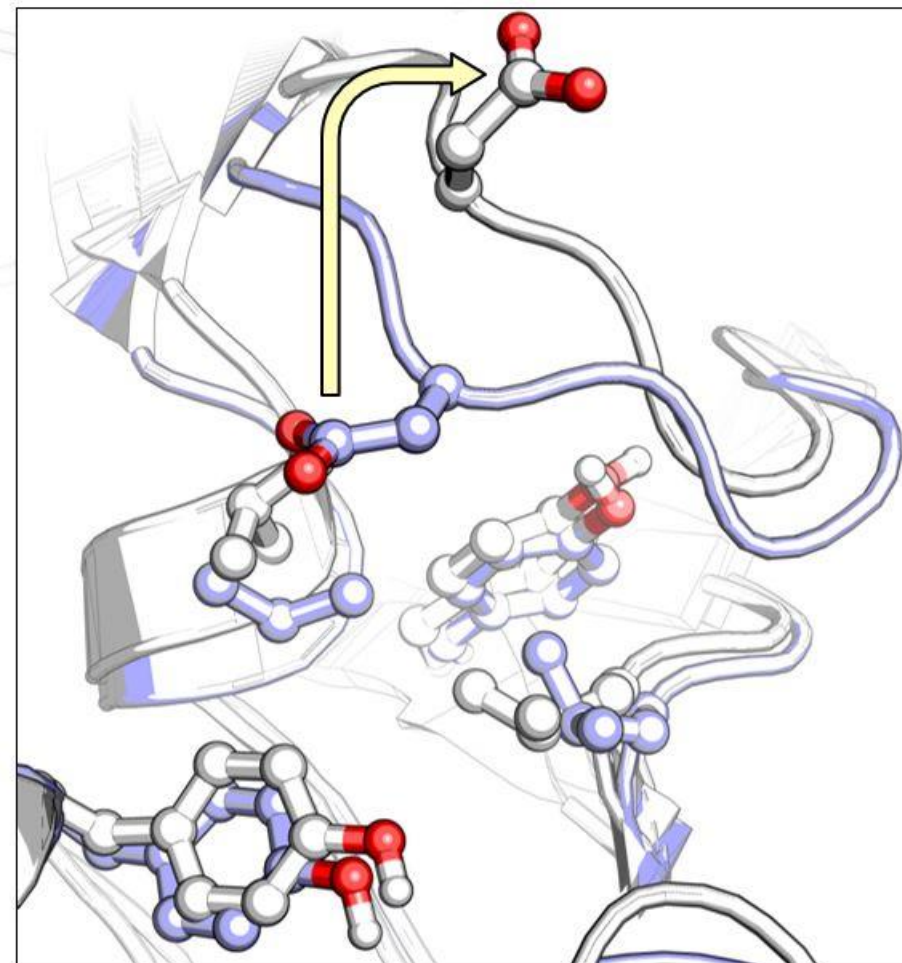
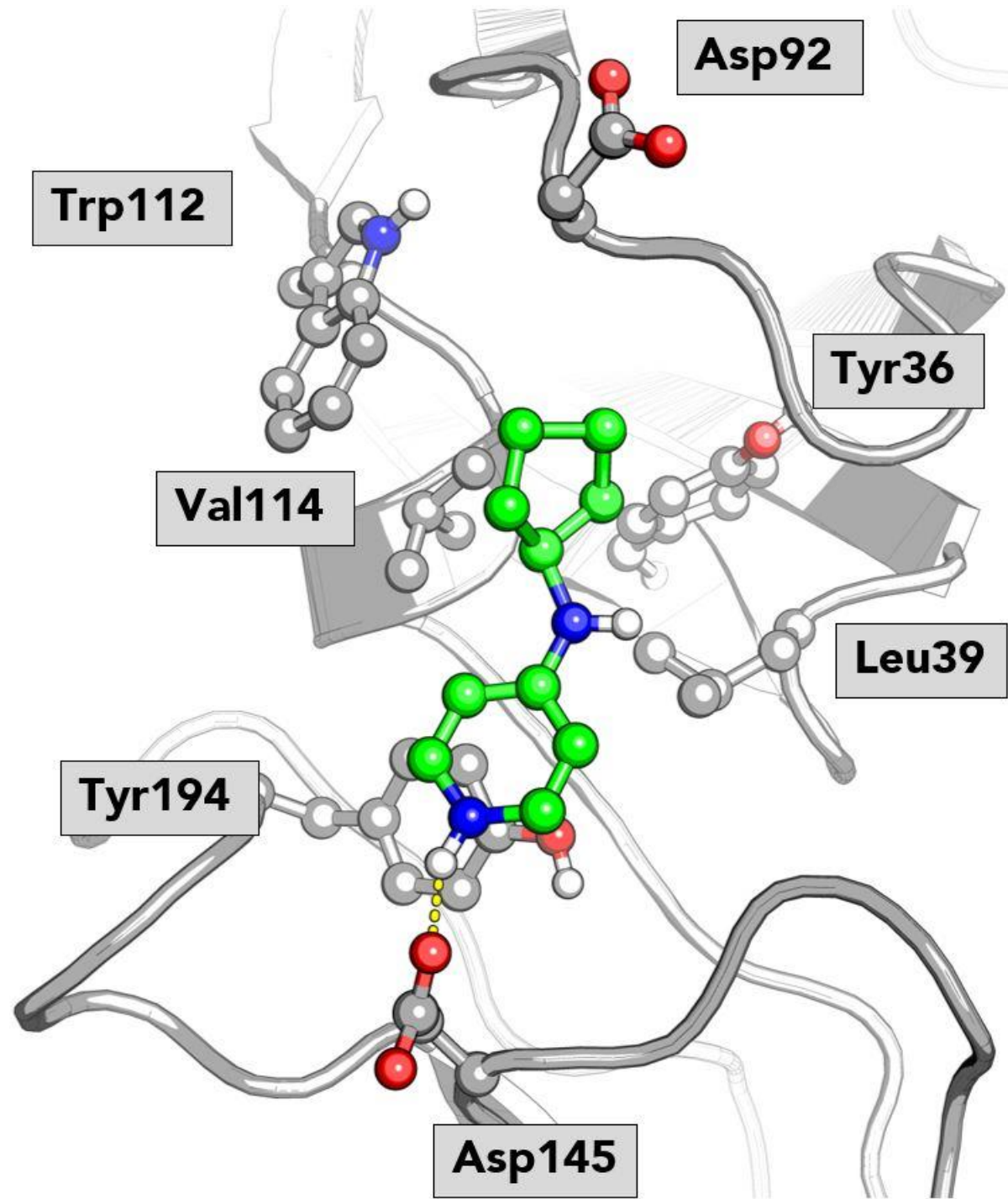
Simulating the binding process

- Put ligand and protein into a box
- Run 150 medium-length simulations



Markov Model





Thank you!

