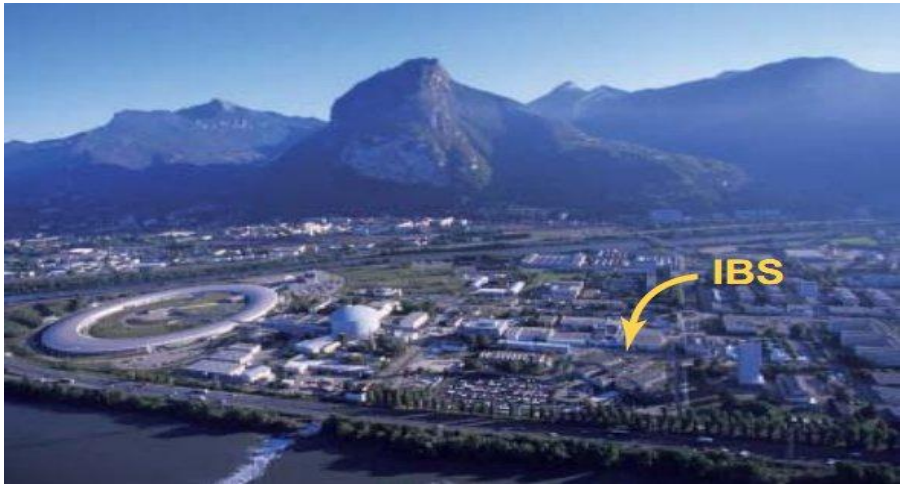
Institute of Structural Biology J-P. Ebel (IBS) – CNRS, Grenoble



Zsófia Sólyom

ESR

Annual Intensive Training Course – Budapest, Hungary

Outline

- Academic record
- Master thesis
- Results from the internship in Grenoble and subject of PhD

2006–2009 Budapest University of Technology and Economics, Chemical engineering

- Bachelor thesis: Stabilization of phosphinidenes by complexation
- Internship: Hoffmann la Roche Ltd.-Molecular Biology Laboratories, Basel

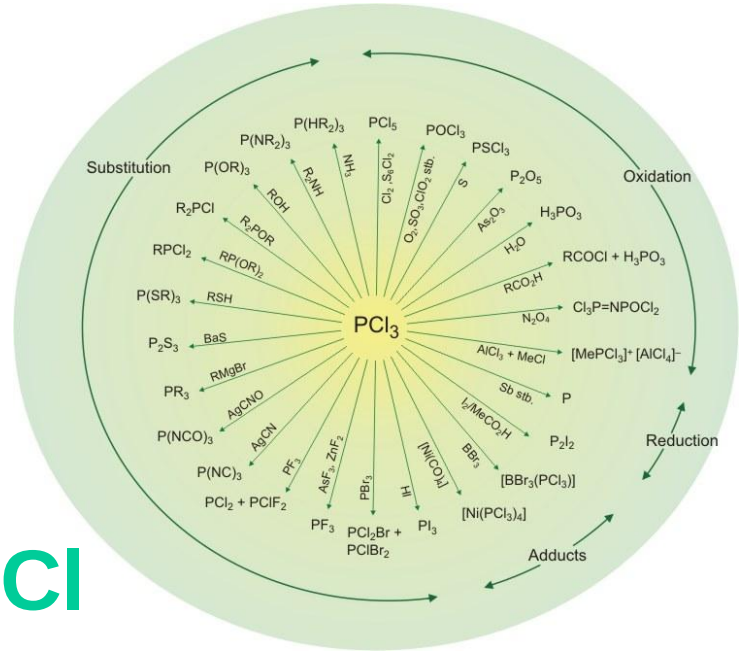
2009–2011 Chemical engineering MSc – analytical chemistry and structure research

2009–2010 academic year in Joseph Fourier University, Chemistry and Life Sciences

- Internship: Institute of Structural Biology, NMR laboratory
- Master thesis: A theoretical study on the hydrolysis of phosphorus trichloride

1 September 2011– PhD studies in University of Grenoble

Hydrolysis of phosphorus trichloride



- PCl_3 is important raw material of organophosphorus industry
- Highly moisture sensitive, rapid hydrolysis

$$PCl_3 + 3\,H_2O \longrightarrow H_3PO_3 + 3\,HCl$$

- **PCl_3 is stable <u>stirred on air</u> for up to a week in certain ionic liquids (ILs)**

Amigues, E.; Hardacre, C.; Keane, G.; Migaud, M.; O'Neill, M.; *Chem. Commun.* **2005**, *1*, 72.

- <u>Understanding the phenomenon</u>:
  - the structure of water in ILs ⟶ literature

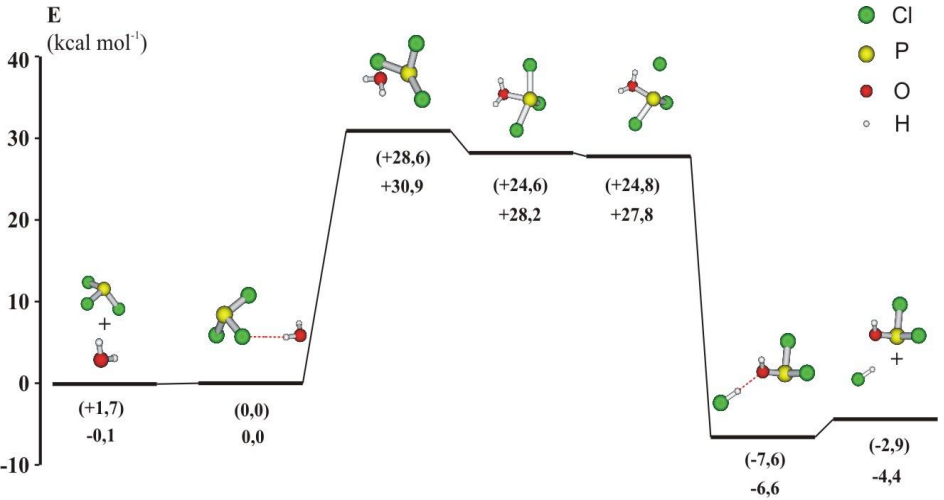
    <u>Isolated</u> water molecules, no clusters
  - the mechanism of hydrolysis ⟶ master thesis

Transition states and activation energies

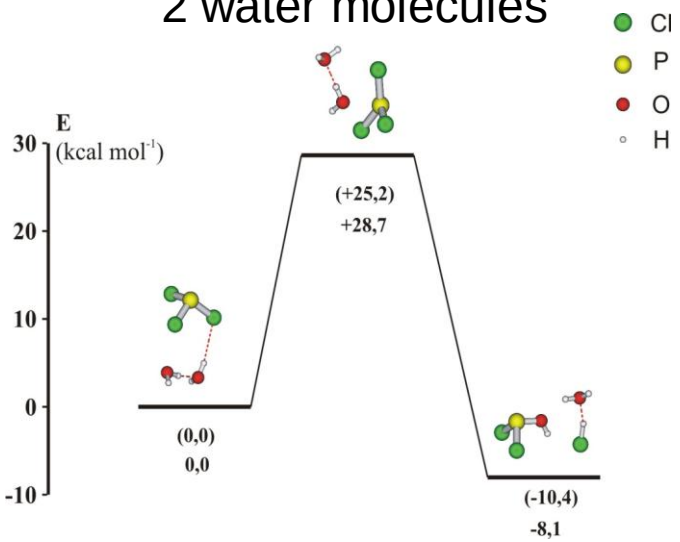
E_a = ?

$$PCl_3 + \mathbf{n}\ H_2O \longrightarrow PCl_2OH + HCl + n\text{-}1\ H_2O$$

1 water molecule

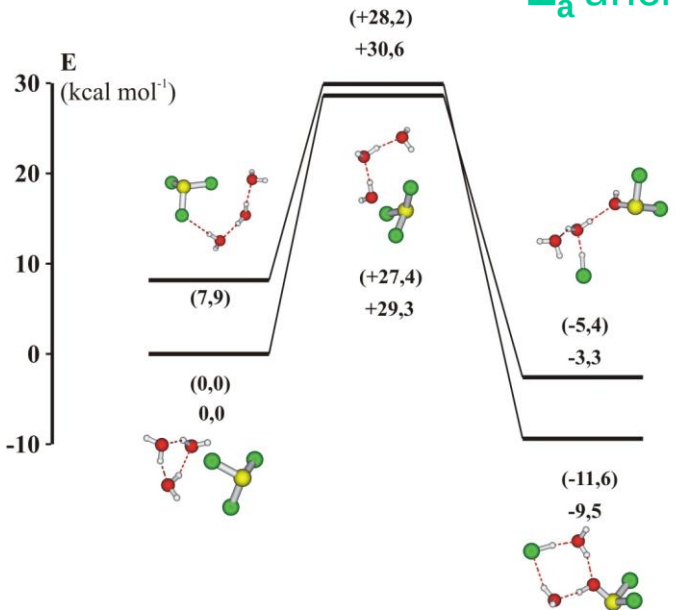


2 water molecules



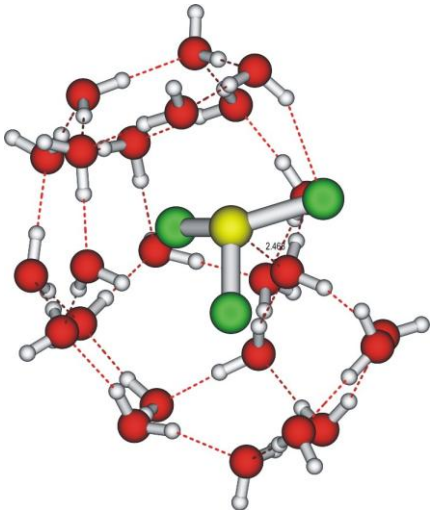
3 water molecules

E_a unchanged

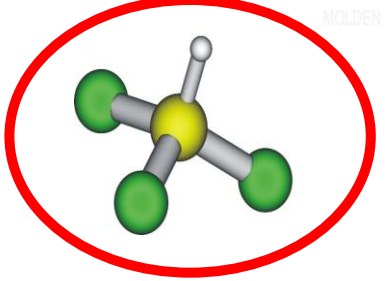


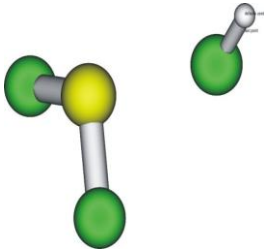
4,5,6,…30 water molecules

E_a increases



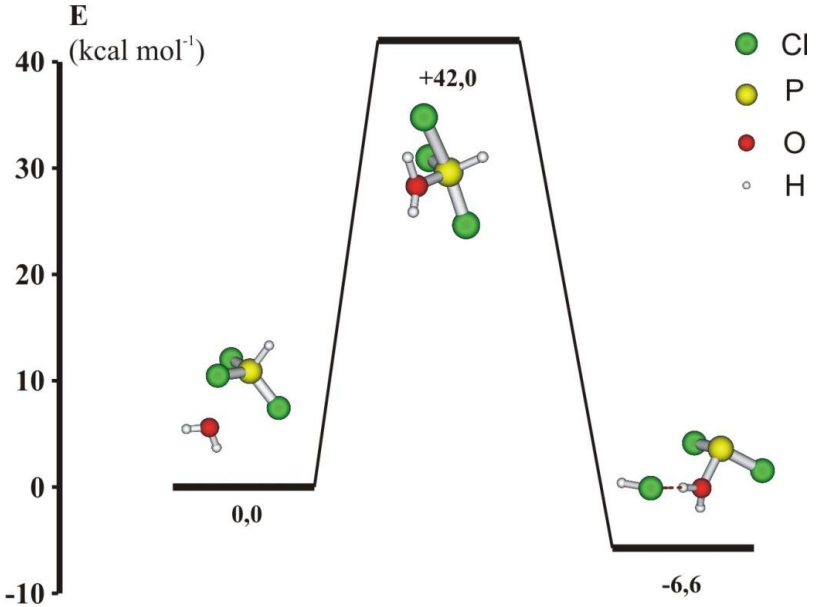
Role of acid catalysis



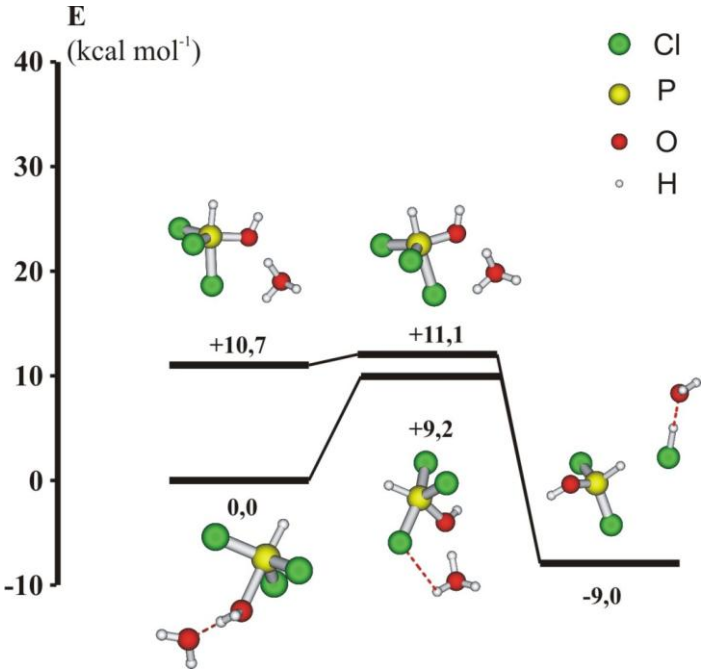


ΔE_{rel} **0,0 kcal/mol** **+15,8 kcal/mol**

1 water molecule + acid



2 water molecules + acid



Autocatalytic reaction

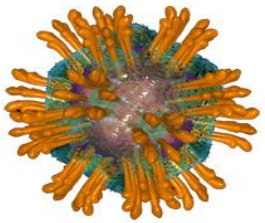
In ionic liquids the water molecules are isolated → hydrolysis is hampered

PhD project

Investigating structure and dynamics in intrinsically disordered proteins by multidimensional NMR spectroscopy

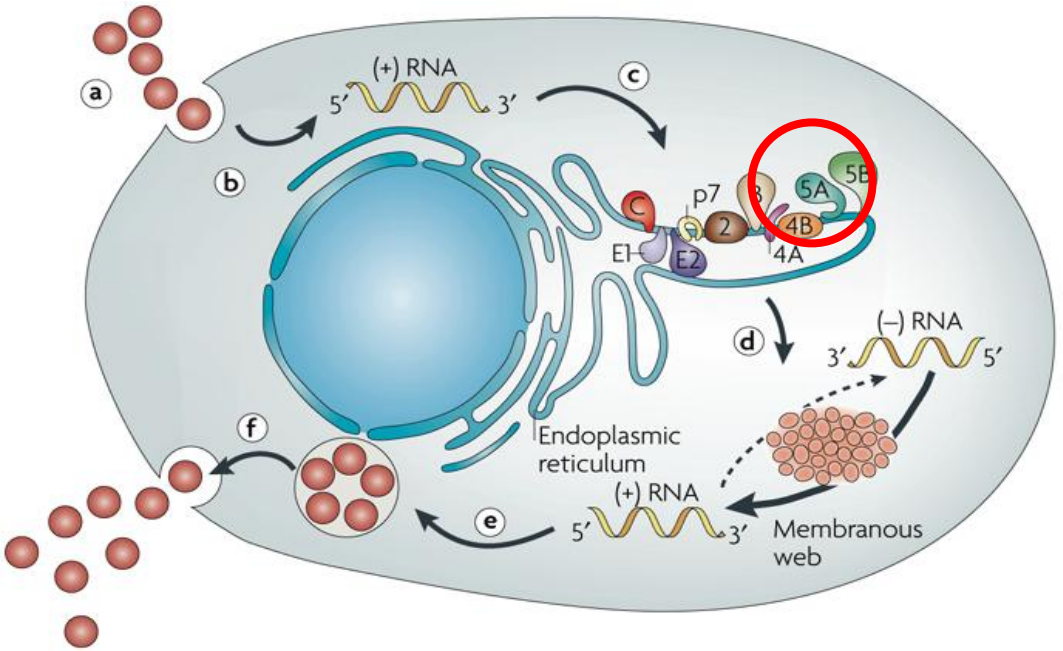
IDPs studied:

- NS5A protein of Hepatitis C virus
- a disordered RNA chaperone protein

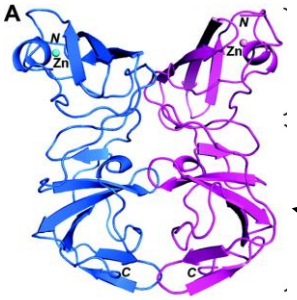


HCV NS5A protein

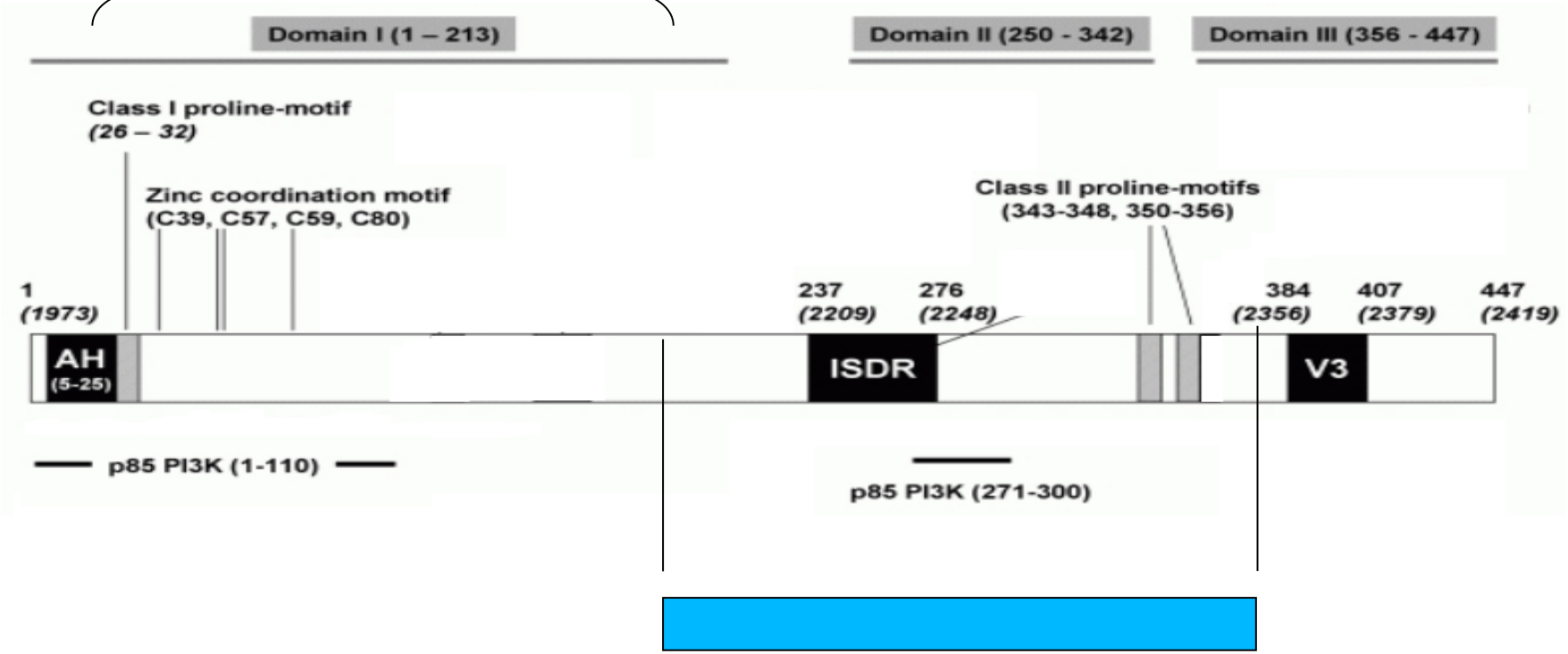
- Importance in the life cycle of the Hepatitis C virus, binding to many partners, cellular and viral proteins
- NS5A is highly disordered



Nature Reviews | Microbiology



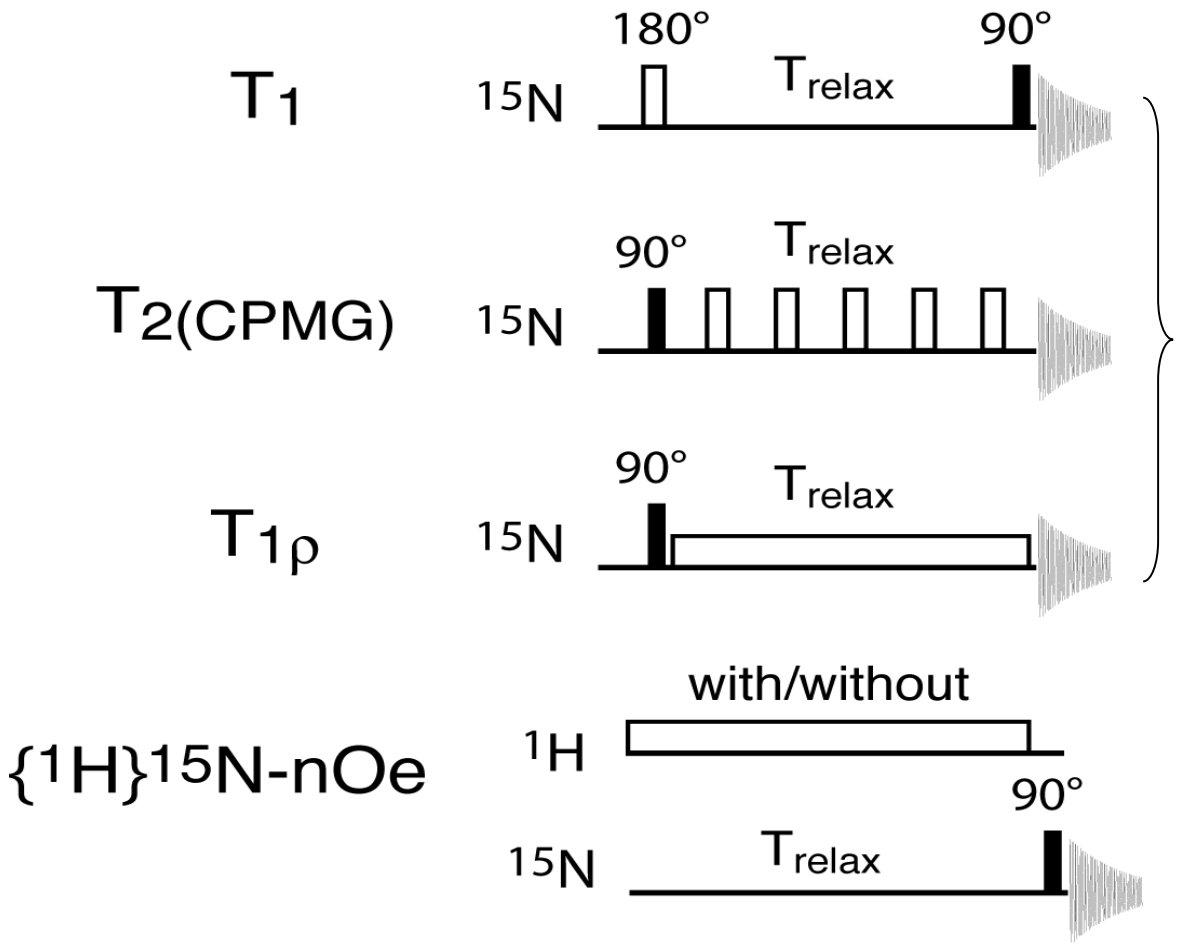
The NS5A protein fragment

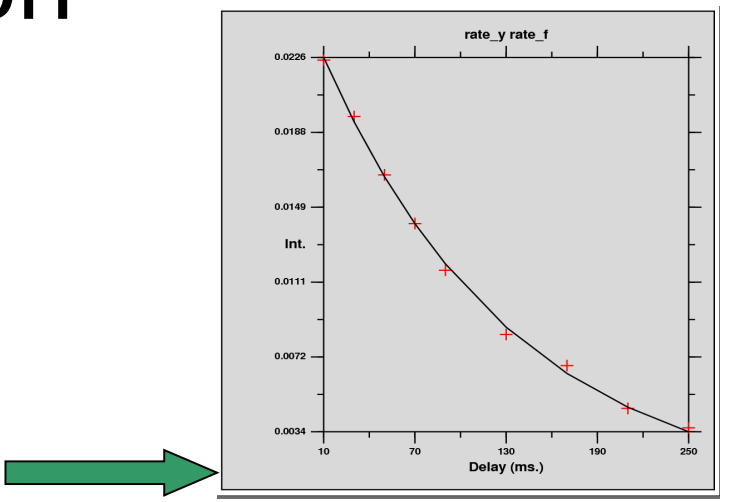


My internship project: study of the temperature dependence of the conformational backbone dynamics of NS5A fragment (2010)

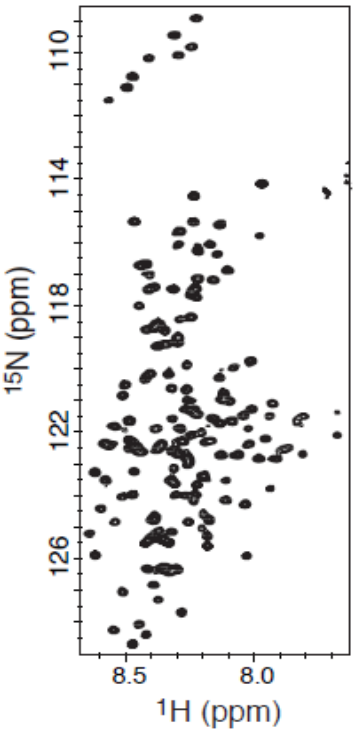
^{15}N Relaxation

The principle of the relaxation experiments





Isat/I



On assigned peaks

Results

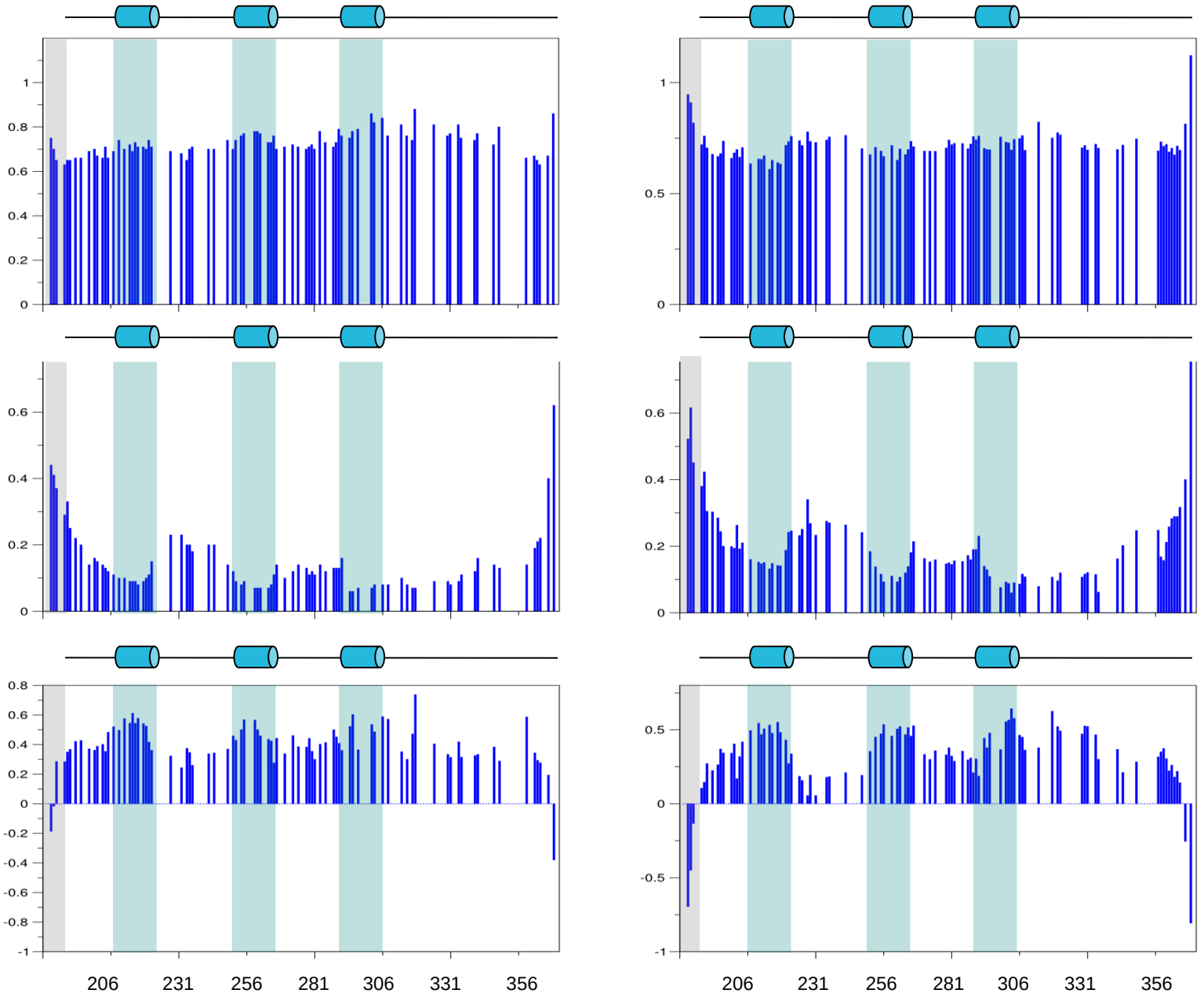
5 ˚C

20 ˚C

T1

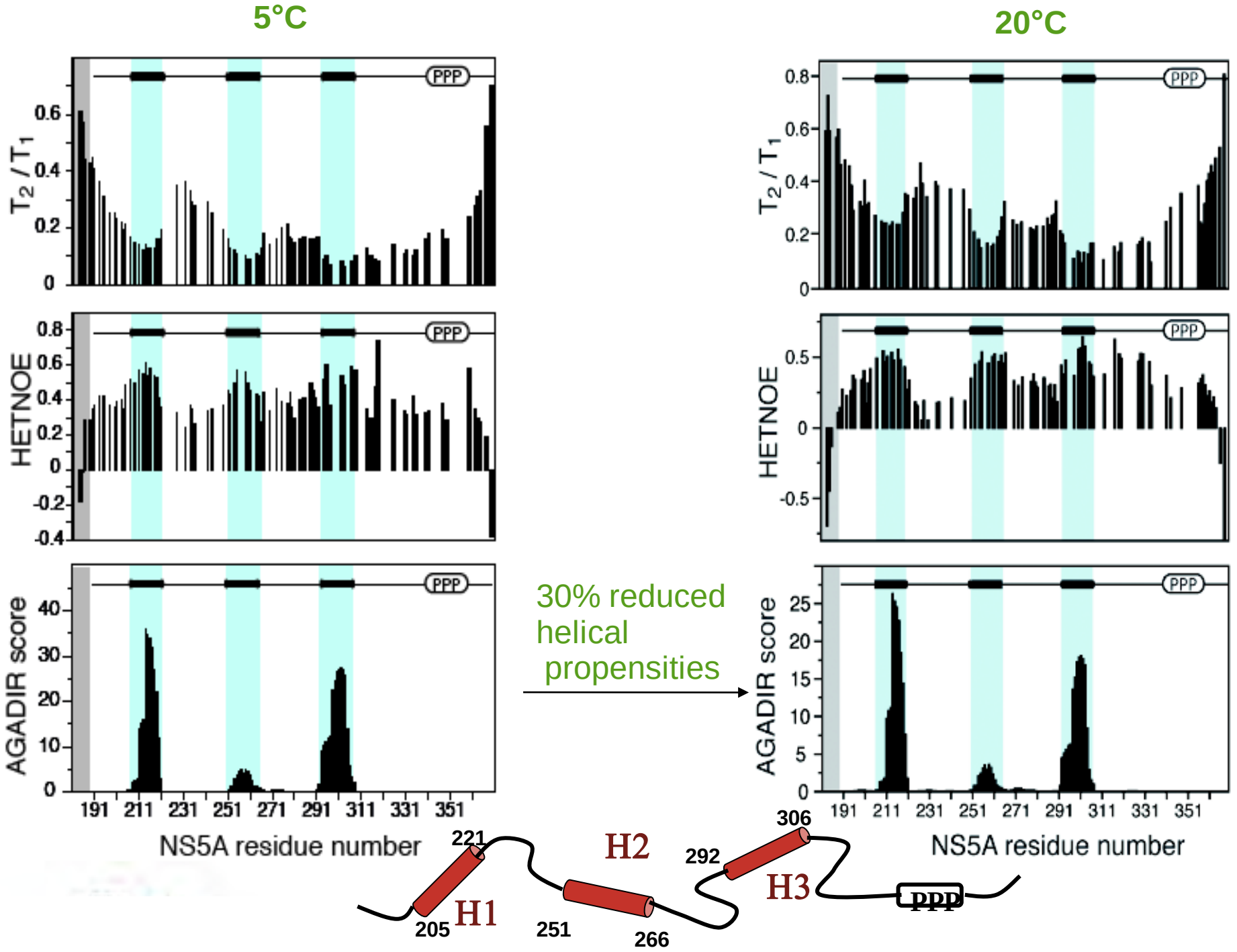
T1ρ

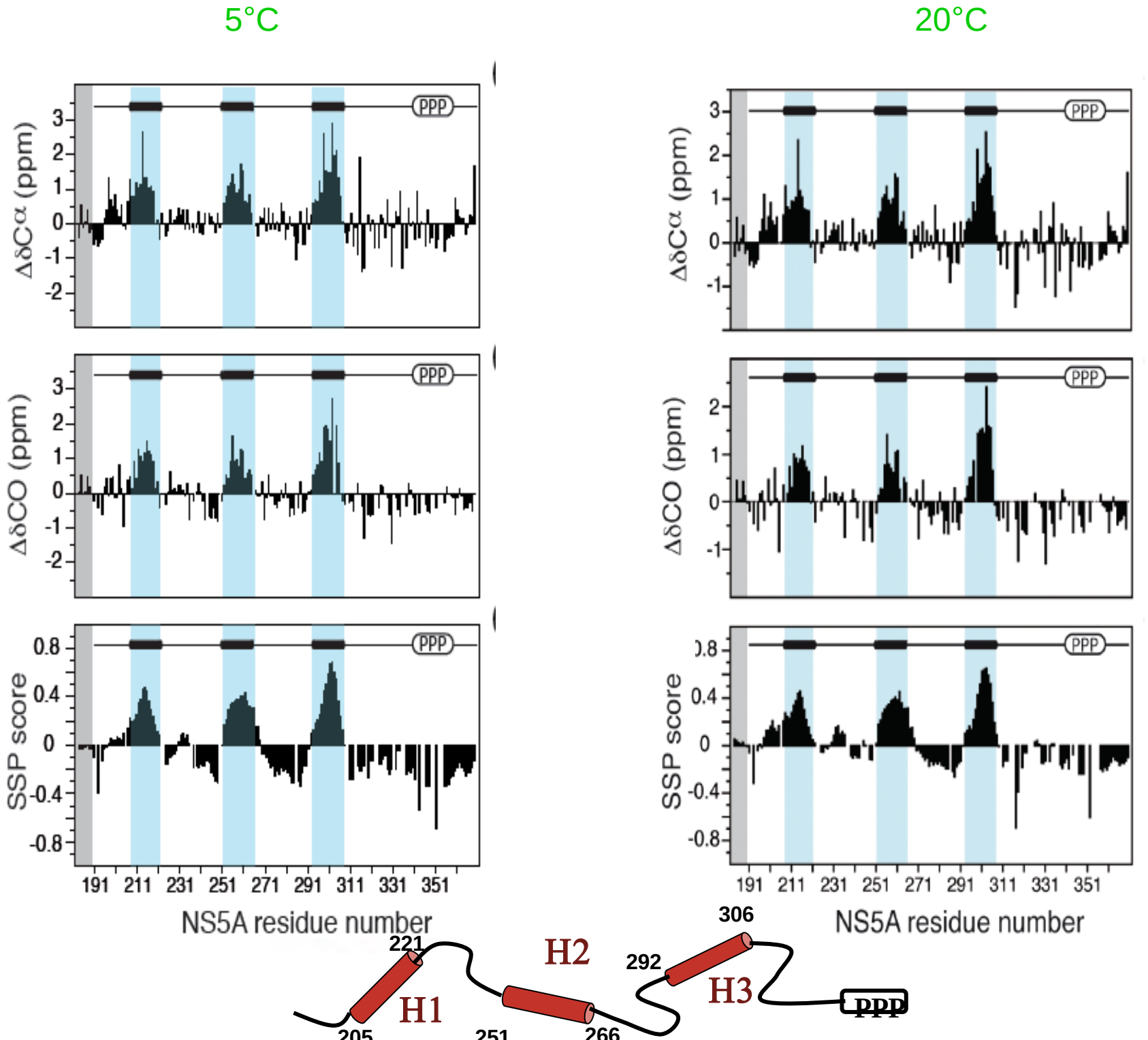
HETNOE



No significant changes

NMR Results vs Agadir predictions

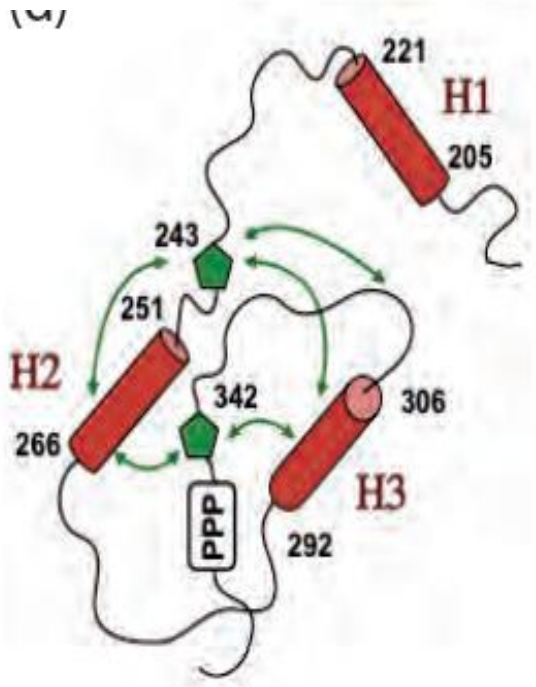



5°C
20°C
ΔδCα (ppm)
ΔδCO (ppm)
SSP score
PPP
191 211 231 251 271 291 311 331 351
NS5A residue number
221
205
H1
H2
251
266
292
306
H3
PPP

Conclusions

The temperature change (5°C→20°C) has only a slight influence on the dynamics, tumbling changes

AGADIR results, chemical shift deviations and relaxation results: tertiary interactions stabilize the helices



Objectives

Development of fast multidimensional NMR methods to study IDPs

Apply those methods to biologically interesting systems

NS5A:

- production of protein for interaction studies with SH3 domains
- RDC measurements


Thank you for your attention!