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Trieste

# *UV RESONANCE RAMAN SCATTERING AT ELETTRA: PRINCIPLE AND APPLICATIONS*

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***Elettra - Sincrotrone Trieste – Italy***

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# I. Principles:

I. Inelastic light scattering experiment

II. Raman effect

III. Resonance Raman scattering

IV. UV RR setup at IUVS@Elettra

# II. Examples of applications

- Dynamical properties of aqueous solutions and complex molecular systems
- Structural characterization of biological systems, i.e. peptides and DNA
- Molecular structure and dynamics in hydrogel phases

# Inelastic scattering experiments

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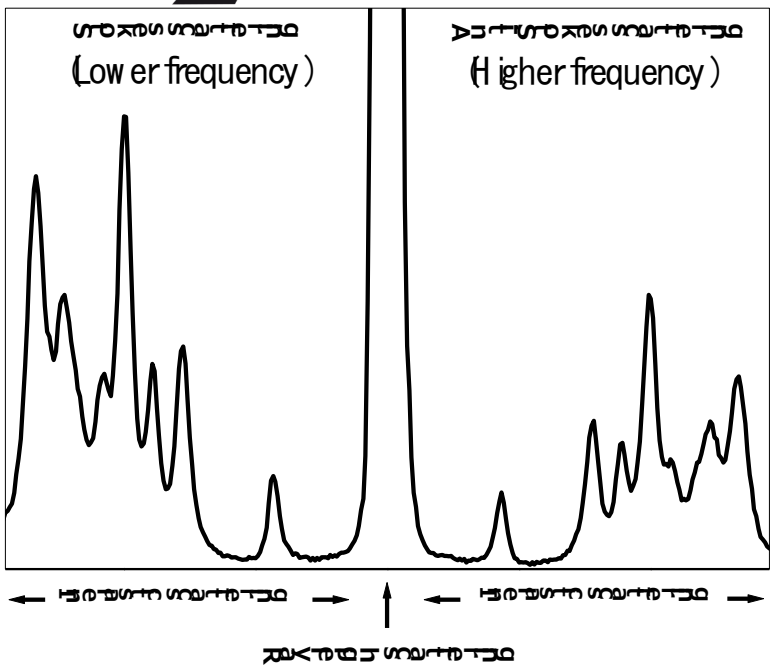
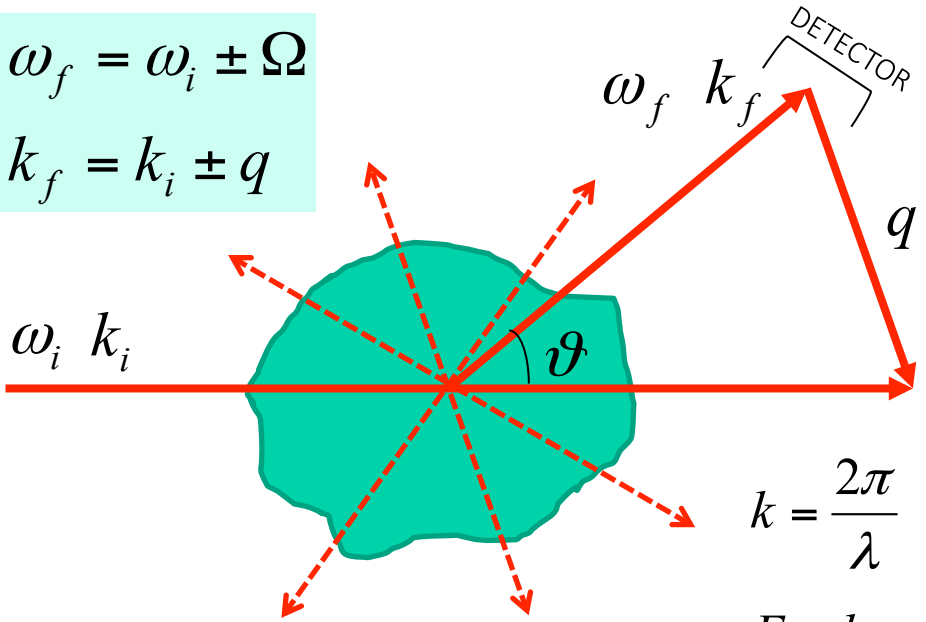



$$\omega_f = \omega_i \pm \Omega$$

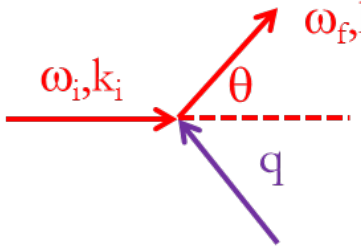
$$k_f = k_i \pm q$$




$$k = \frac{2\pi}{\lambda} \qquad q \cong 2k\,sen\frac{\vartheta}{2}$$

$$E = h\nu = \qquad \omega = hc/\lambda$$

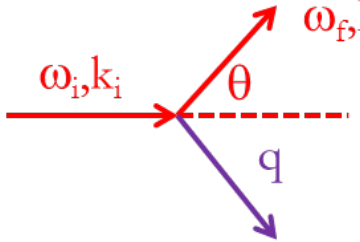
*ANTI-STOCKES PROCESS* — *absorption of phonon* $\Omega, q$




$$\omega_f = \omega_i + \Omega$$

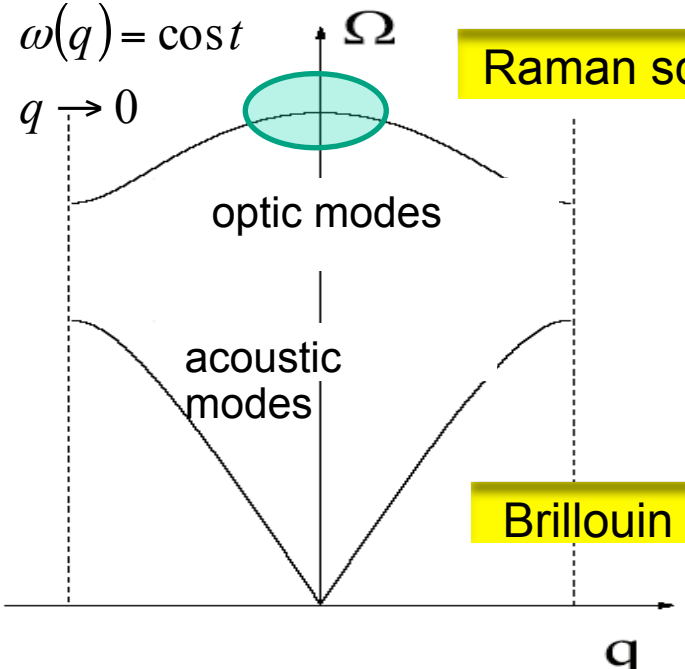
$$k_f = k_i + q$$

*STOCKES PROCESS* — *emission of phonon* $\Omega, q$




$$\omega_f = \omega_i - \Omega$$

$$k_f = k_i - q$$




Raman scattering

Brillouin scattering

# Raman effect

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*Raman bands arise from changes in the molecular polarizability during the vibrations*

$$P(t) = \alpha_0 E_0 \cos\omega_0 t + \frac{1}{2}\delta\alpha_k Q_k^0 E_0 \left[\cos(\omega_0 - \omega_k)t - \phi_k + \cos(\omega_0 + \omega_k)t + \phi_k\right]$$

$$= P(\omega_0) + P(\omega_0 - \omega_k) + P(\omega_0 + \omega_k)$$

$P(\omega_0) \propto \cos\omega_0 t$

Rayleight or elastic scattering

$P(\omega_0 - \omega_k) \propto \cos(\omega_0 - \omega_k)t - \phi_k$

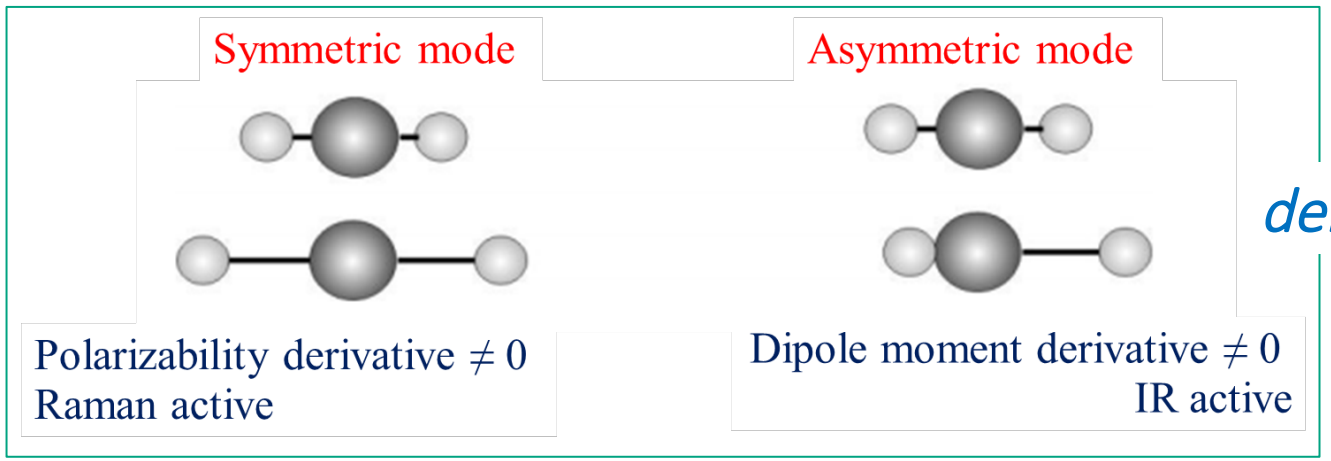
Stockes Raman scattering

$P(\omega_0 + \omega_k) \propto \cos(\omega_0 + \omega_k)t + \phi_k$

Anti-Stockes Raman scattering

*Raman scattering total intensity:* $I(\theta)_{av} = B(\nu_0 \pm \nu)^4 I_0 \left(\frac{\partial \alpha_{xx}}{\partial Q_1}\right)_0^2 \sin^2\theta$

*derived polarizability tensor*



# Resonance Raman scattering

*Raman scattering intensities of totally symmetric vibrations of the molecular moiety involved in the electronic transition are enhanced by a factor of $10^2$ to $10^6$*

$\pi$-$\pi^*$ electronic transition at 197 nm

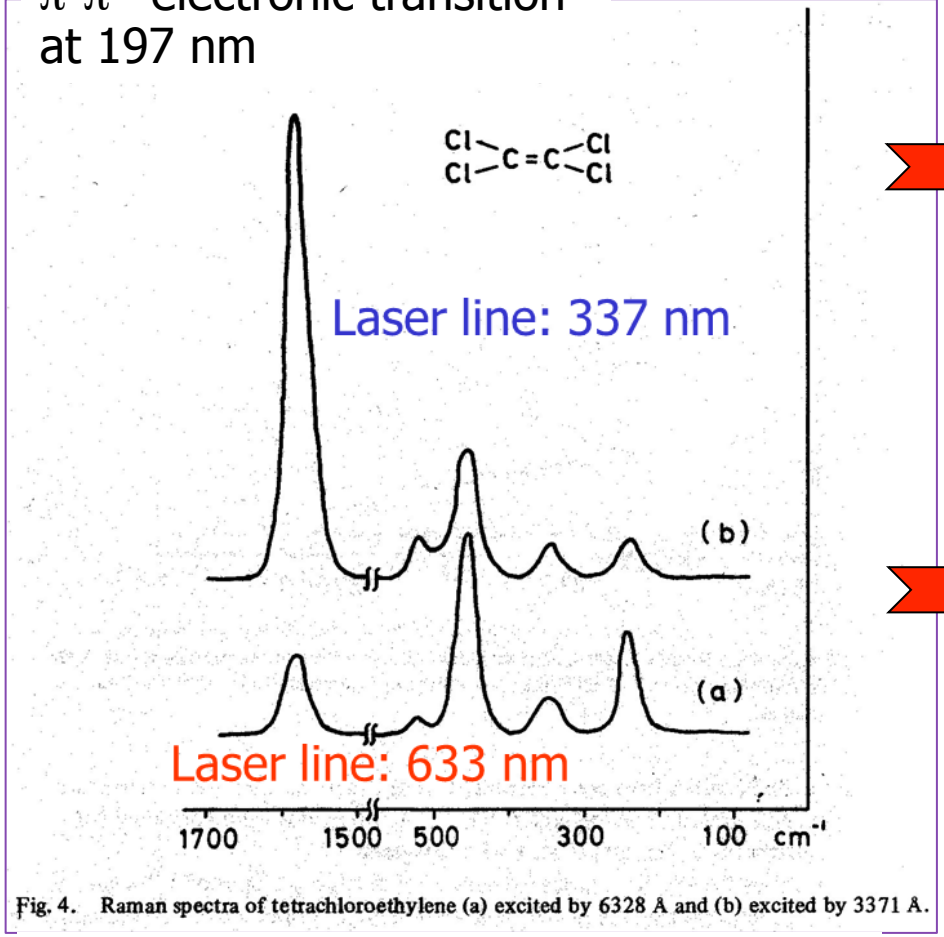



Fig. 4. Raman spectra of tetrachloroethylene (a) excited by 6328 Å and (b) excited by 3371 Å.

Ref:"Advances in Raman spectroscopy-Vol. 1", edited by J. P. Mathieu

***High sensitivity:*** components at low concentrations can now be detected and analyzed

***Specificity:*** The Raman modes associated to specific parts of the molecule is selectively enhanced in the spectra

# Resonance Raman scattering

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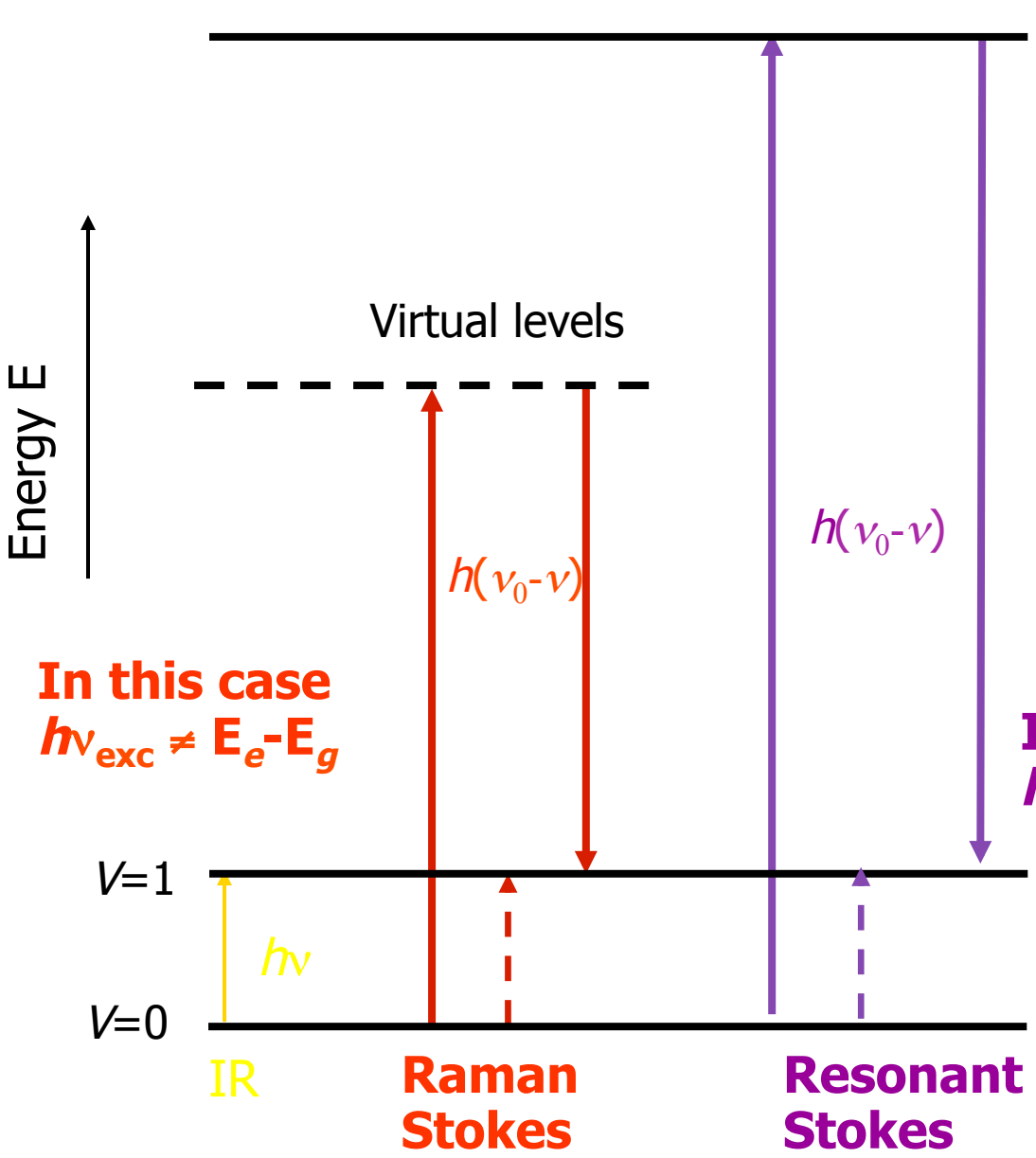
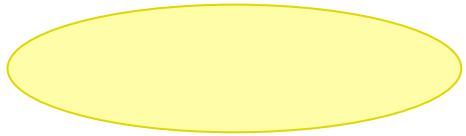



Raman scattering tensor:



In RR conditions:

# *Resonance Raman scattering in the UV range (below 400 nm)*

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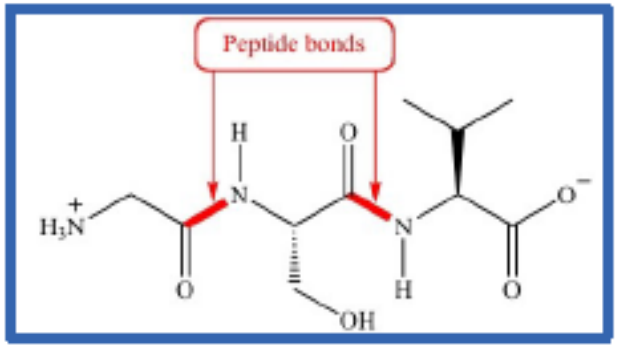
## < 250 nm

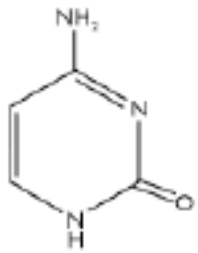
**amide π-π* transition**



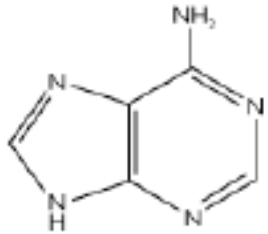

## 250-300 nm

**Chromophore transition**

**nucleotides**



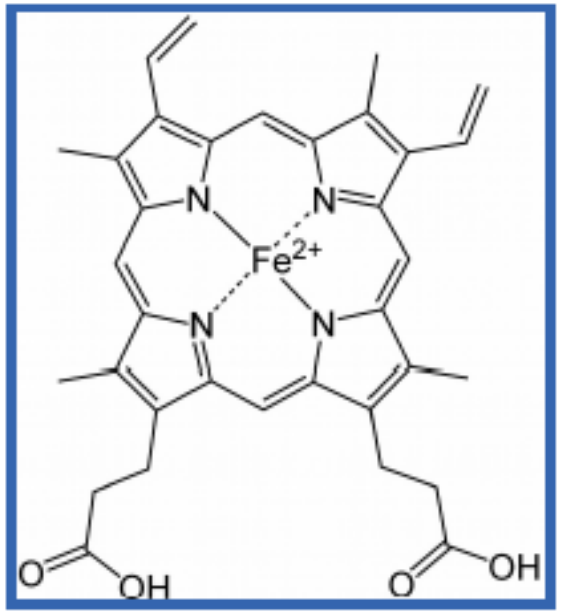

cytosine




adenine

## 400 nm

**HEME in-plane ring vibrations**



# *Sensitive and selective spectral probing of specific molecular moieties in complex systems*

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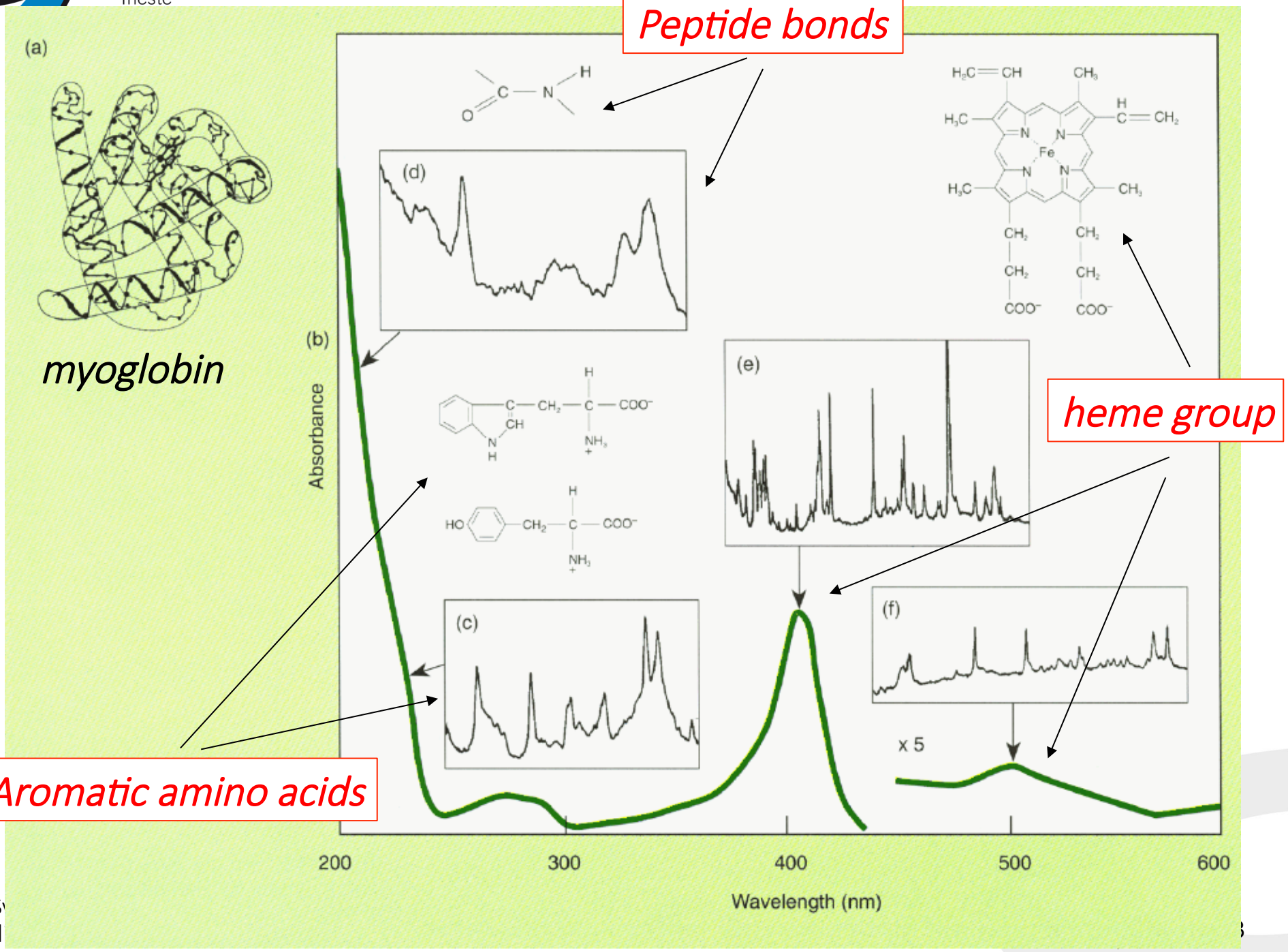

# Strong reduction of the interfering fluorescence background in Raman spectra

*Pre-resonance conditions can be obtained by selectively changing the exciting radiation wavelength*

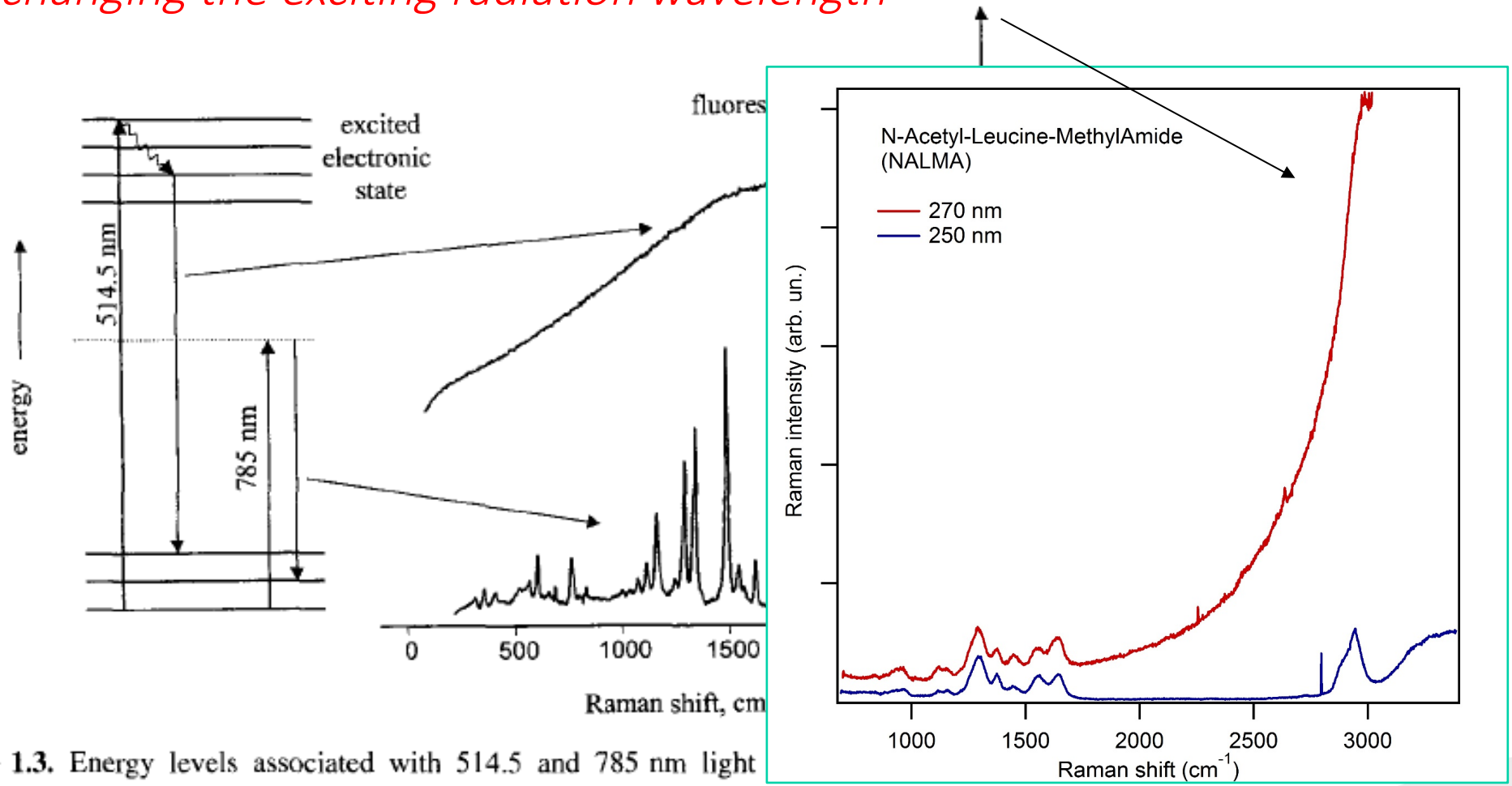


**Figure 1.3.** Energy levels associated with 514.5 and 785 nm light sample. Energy and intensity scales are not to scale, and fluorescence intensity is several orders of magnitude greater than Raman scattering. Raman shift axis is relative to the incident laser frequency.

# UV Raman set-up at IUVS@Elettra

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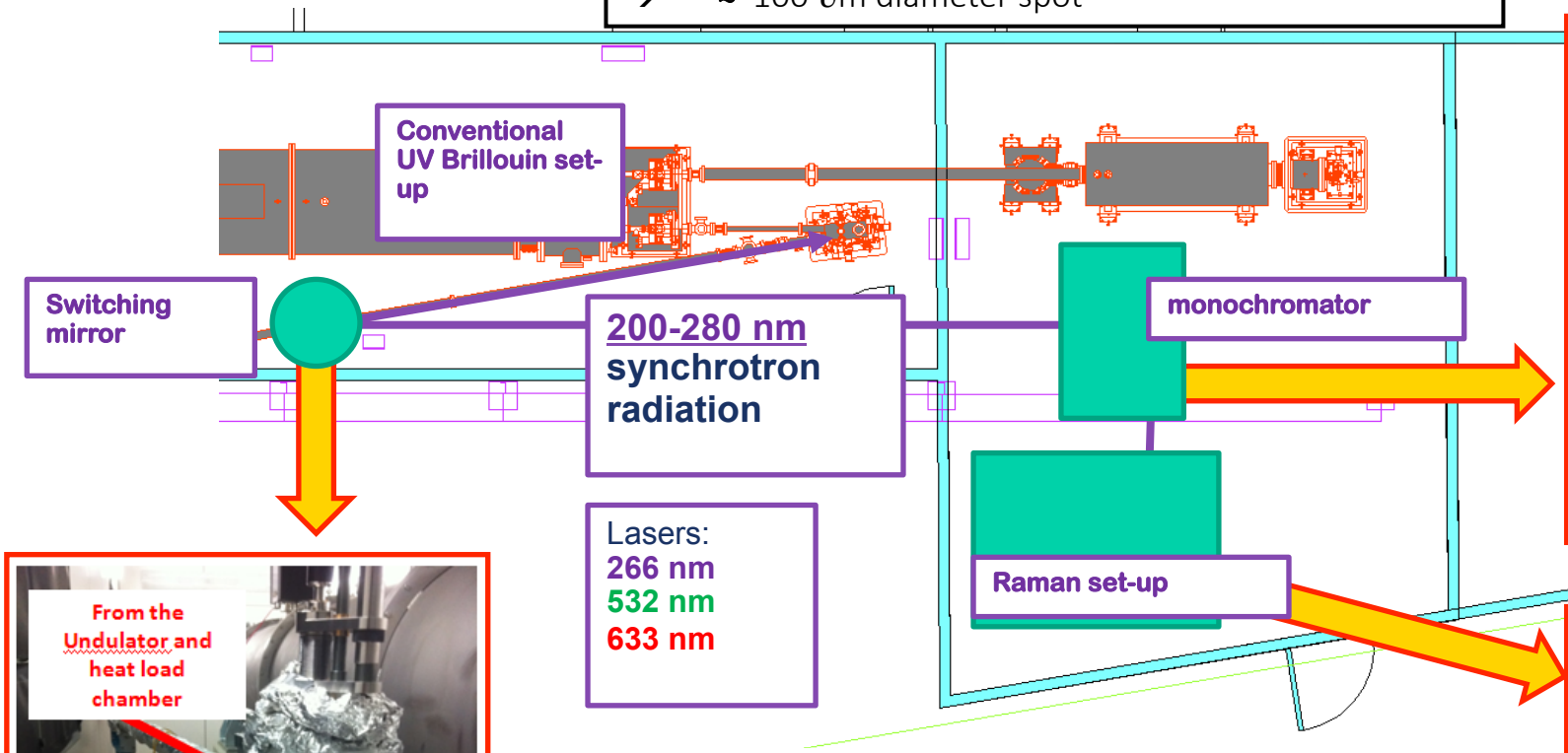
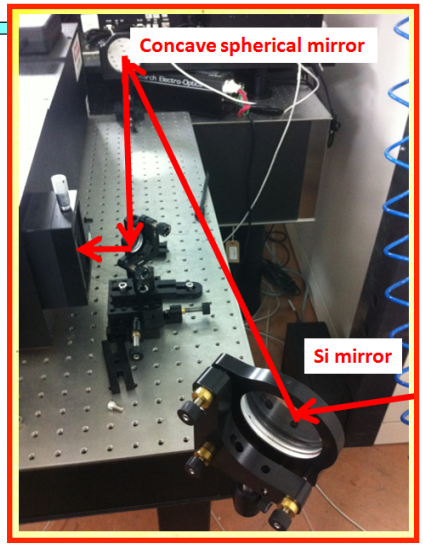
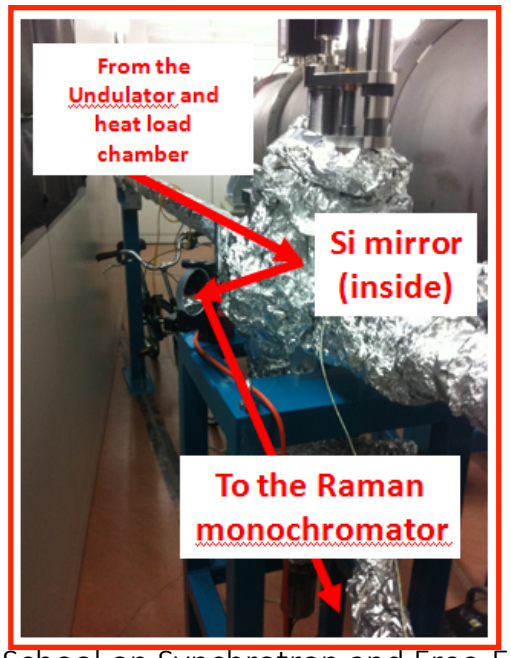
**Main features of the Raman set-up**

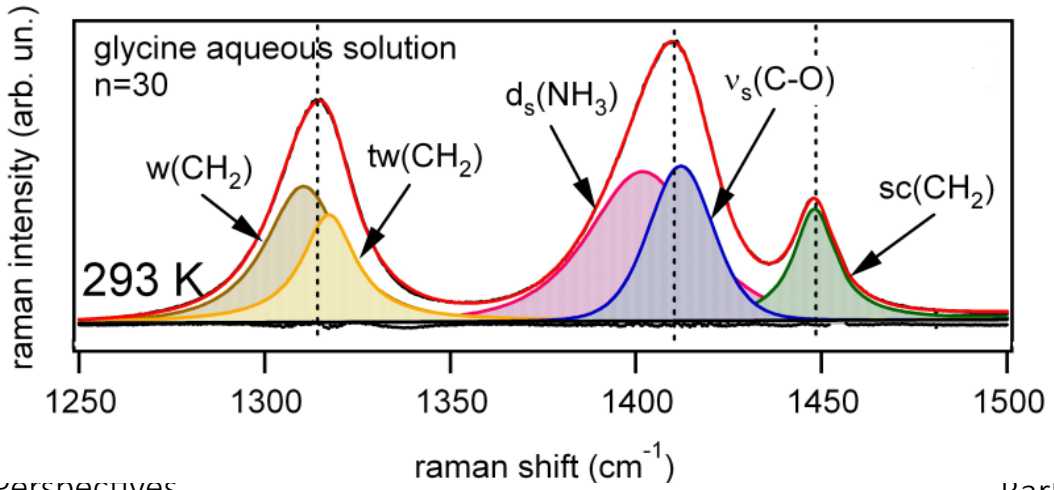
Beam @ sample:
- → $E_i$ = 4.6 ÷ 6.2 eV (200 - 270 nm)
- → ≈ 10 uW (@ 270 nm)
- → ≈ 100 υm diameter spot

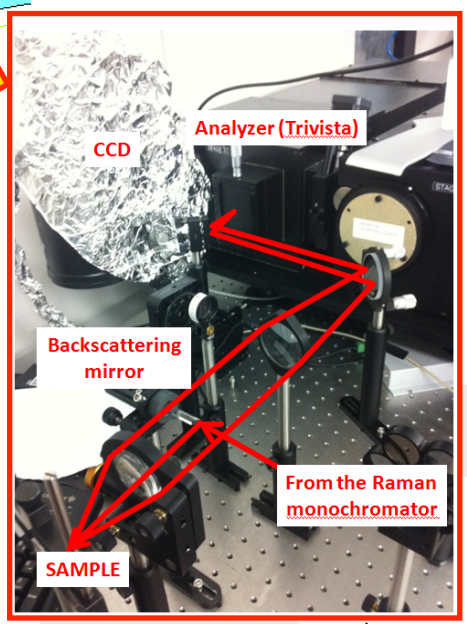
Experimental Resolution
≈ 1 $cm^{-1}$ @ 270 nm
≈ 0.3 $cm^{-1}$ @ 633 nm



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# *Examples of applications of UV Raman scattering technique:*

- Dynamical properties of aqueous solutions and complex molecular systems

Saito M, Bull. Chem. Soc. Jpn., Vol. 88 - 4, pp. 591-596 (2015)
D'Amico F, Phys. Chem. Chem. Phys., Vol. 17 - 16, pp. 10987-10992 (2015)
D'Amico F, J. Chem. Phys. 139 - 1, pp. 015101-5 (2013)
D'Amico F, J. Phys. Chem. B, Vol. 116 - 44, pp. 13219-13227 (2012)

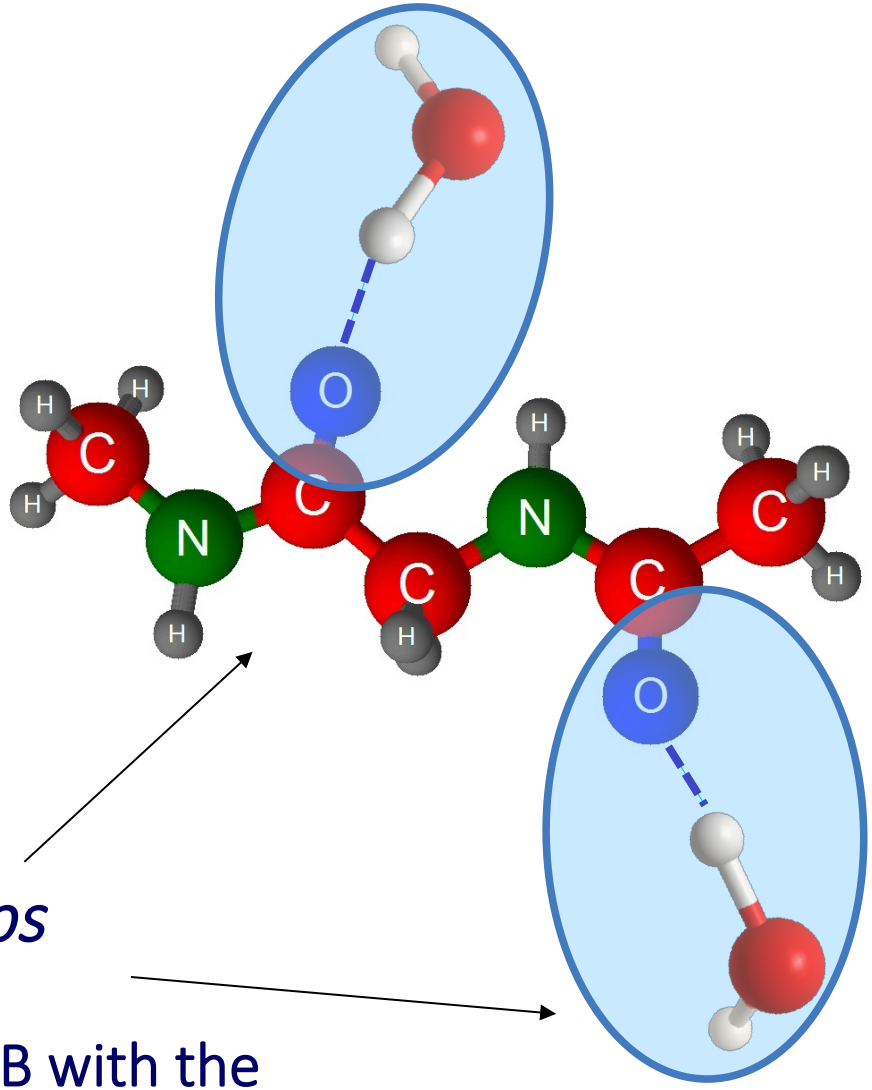
- Structural characterization of biological systems, i.e. peptides and DNA

D'Amico F, Analyst, Vol. 140 - 5, pp. 1477-1485 (2015)

- Molecular structure and dynamics in hydrogel phases

Rossi B. et al., Soft Matter (2015) 11, 2183
Rossi B, et al. Phys. Chem. Chem. Phys., Vol. 17 - 2, pp. 963-971 (2015)
Rossi B, et al. J. Chem. Phys. Vol. 142, pp. 014901 (2015)
Venuti V, Phys. Chem. Chem. Phys., Vol. 17 - 15, pp. 10274-10282 (2015)

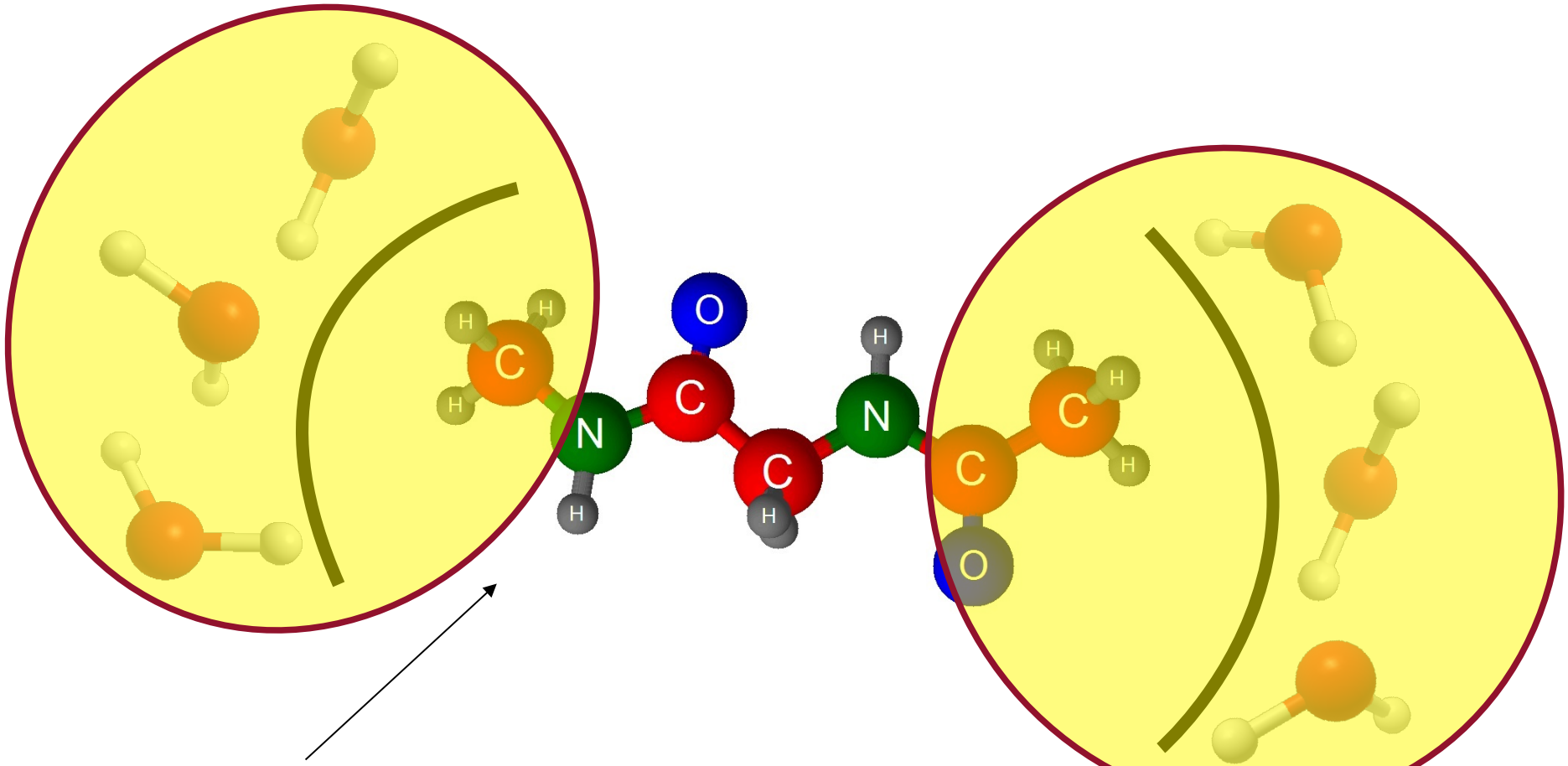
# *Hydrophobic/hydrophilic effects*




*Hydrophilic groups*

C=O groups forms HB with the surrounding water molecules

# *Hydrophobic/hydrophilic effects*




*Hydrophobic groups*

CH3 groups repels the surrounding water molecules

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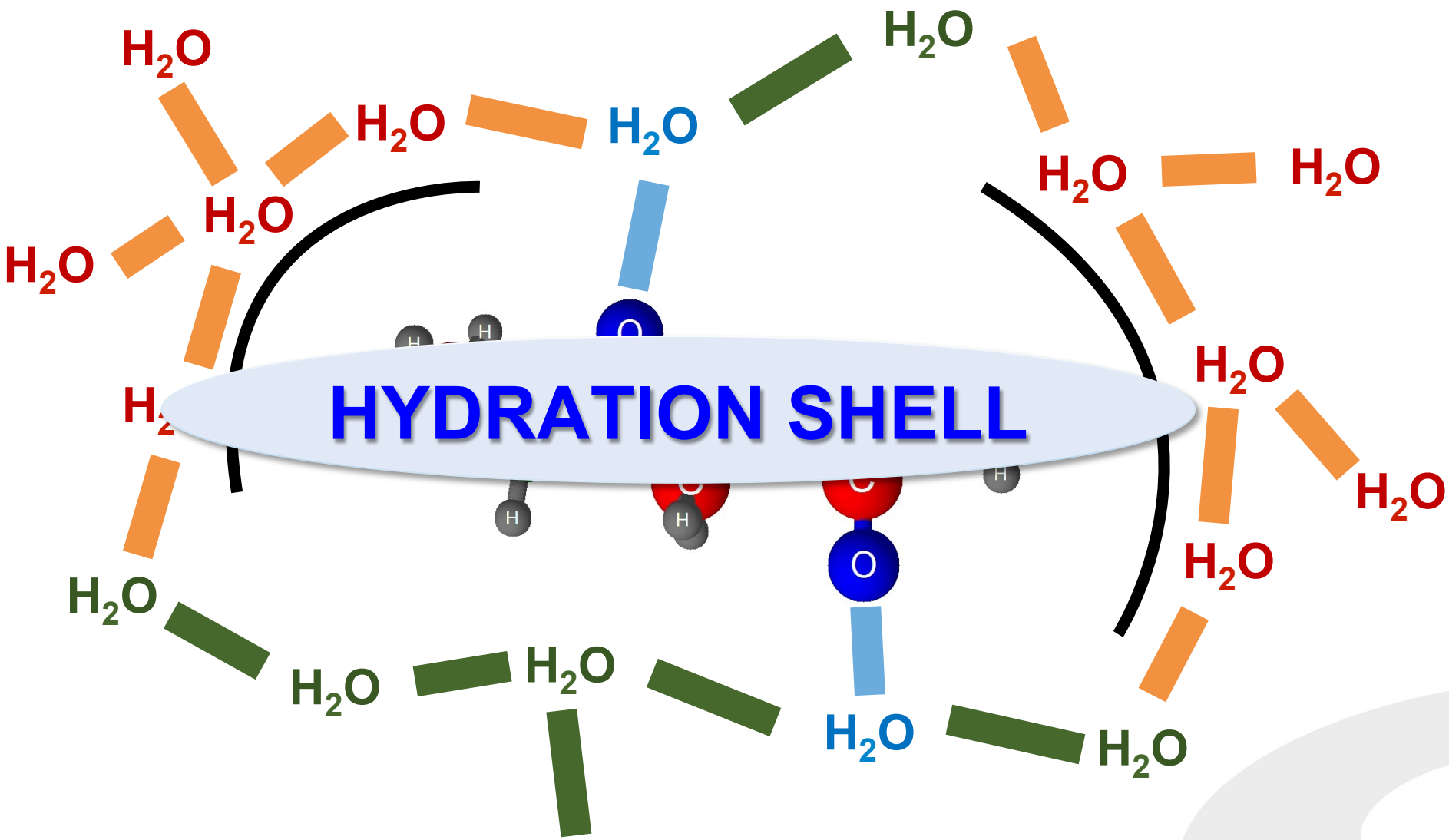
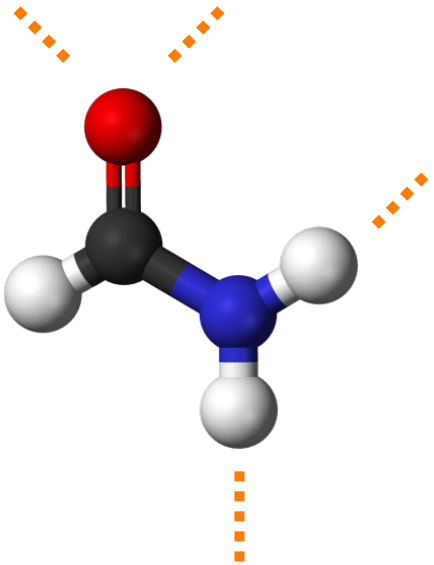
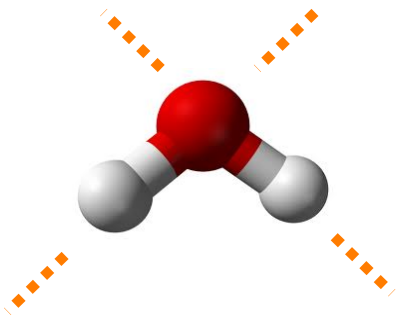
*How water behaves around the hydrophilic/hydrophobic groups?*



# *Formamide aqueous solutions: molecular dynamics on hydrogen bonding systems*

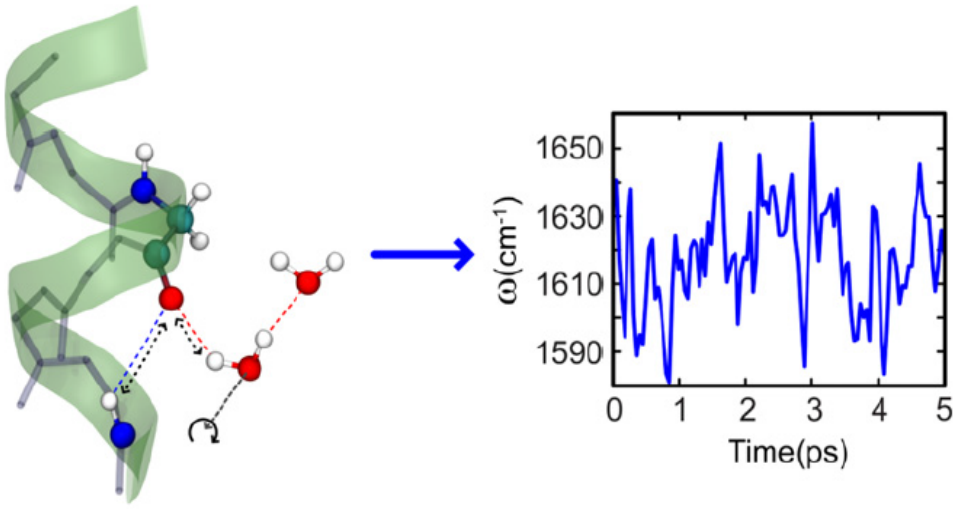


*FA – MW45*



*W – MW18*

- It is a small ***hydrogen bonding*** molecule
- It forms an ***extended network*** in the liquid phase
- It's to some extent ***similar*** to water (intermolecular structure, dynamics and spectral properties)
- It's fully miscible with water
- It contains a peptide bond: ***model for protein-water interactions*** C=O···H-N C=O···H-O N-H···O-H




**A. Ghosh, R. M. Hochstrasser CP 390, 1 (2011)**

# Neat FA and FA-water mixtures

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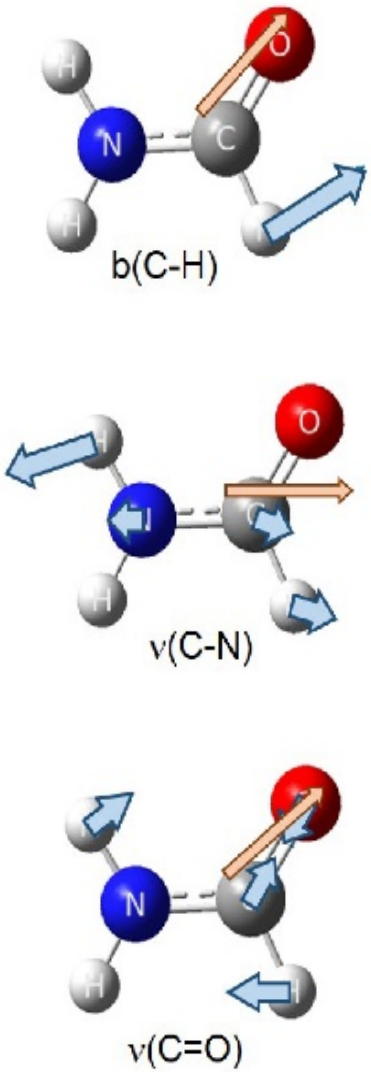
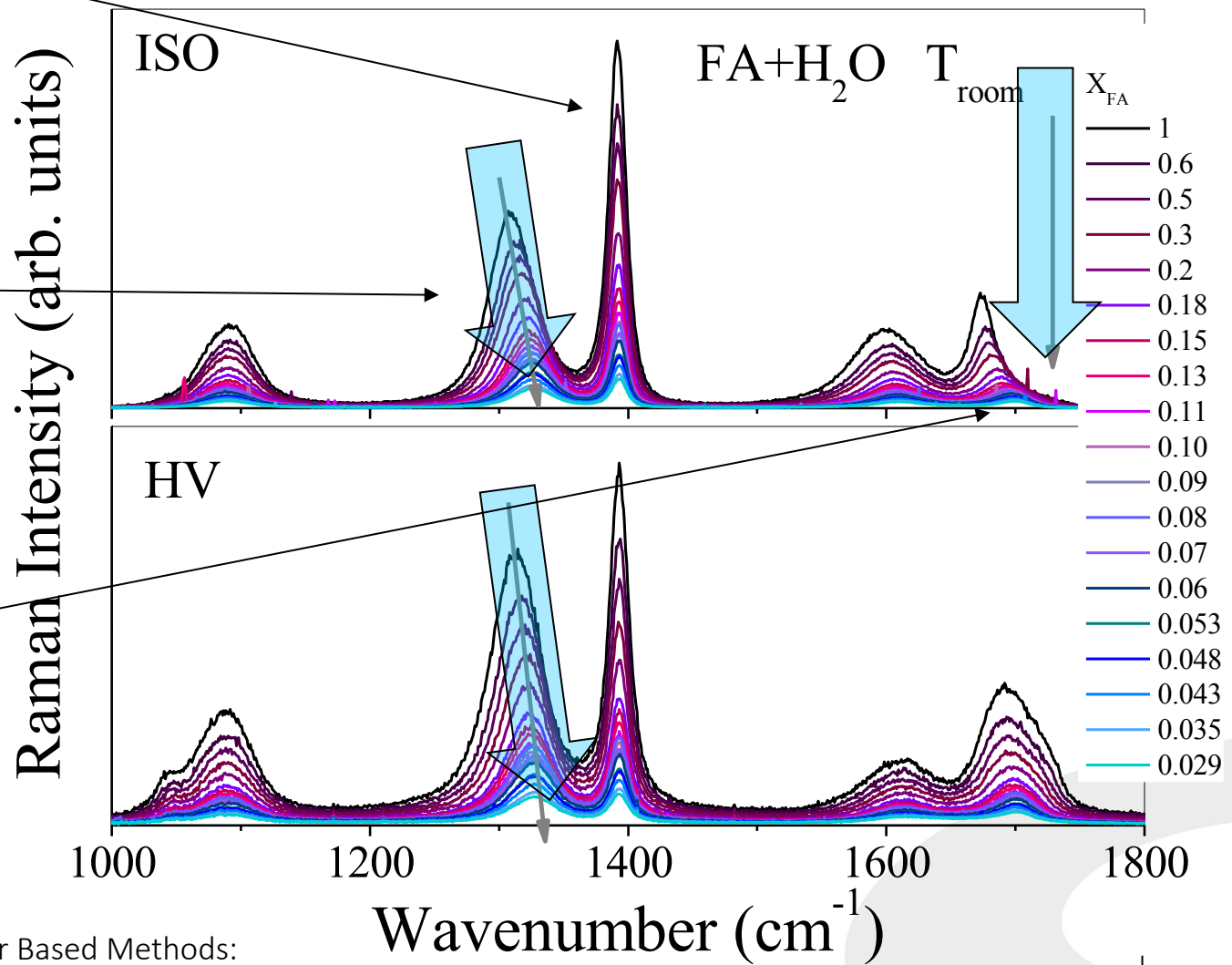
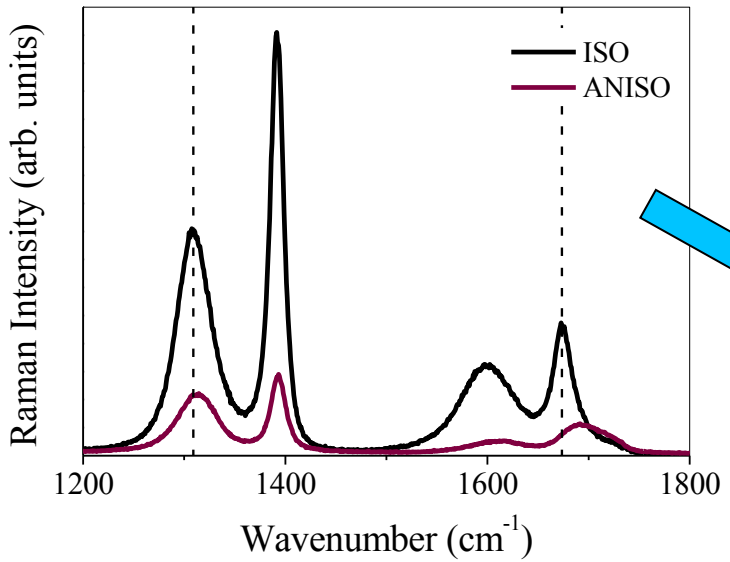
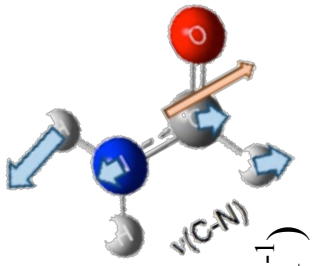
*Isotropic and anisotropic Raman spectra are probes of molecular interactions*

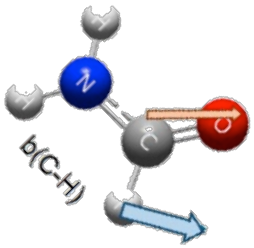


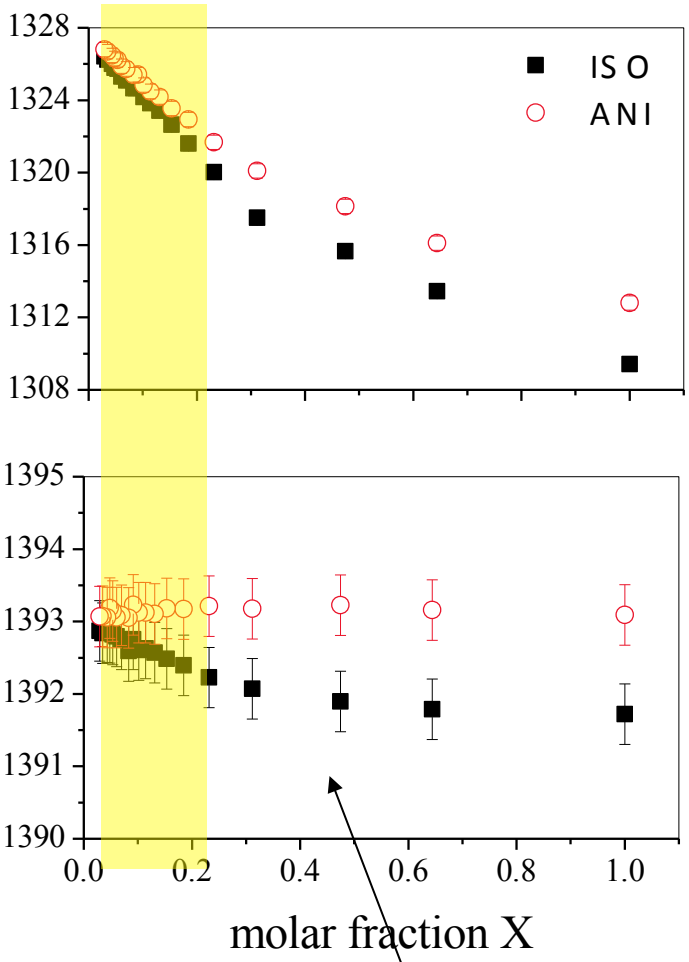



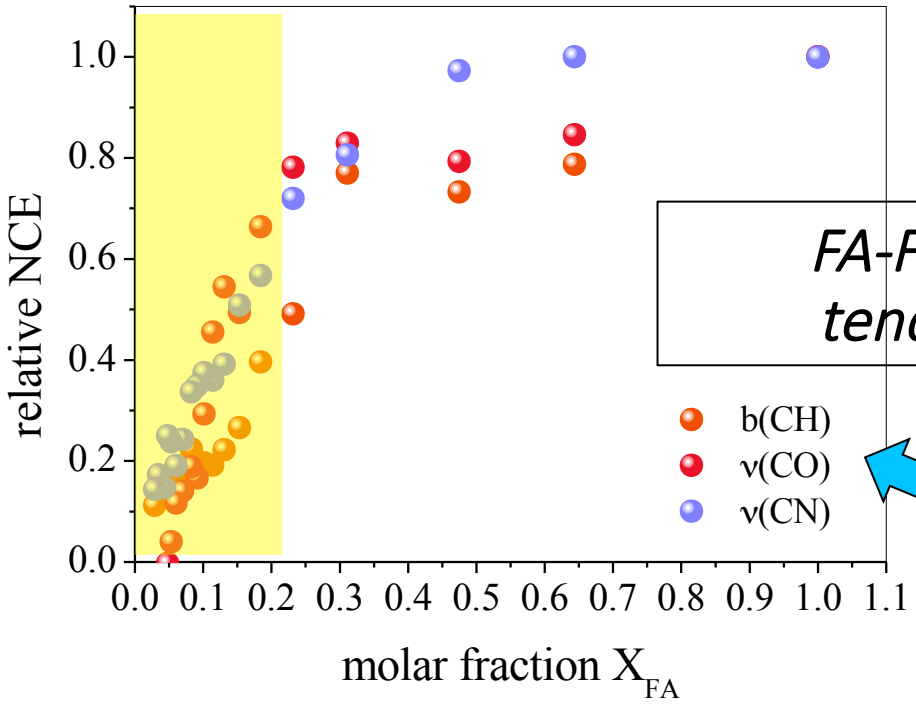
# *Raman non-coincidence effect*




*FA-FA interactions tend to vanish for* $X_{FA}<0.2$

NCE is sensitive to the ***local liquid structure***

(translational and orientational order)

# Rotational dynamics of FA in diluted regime

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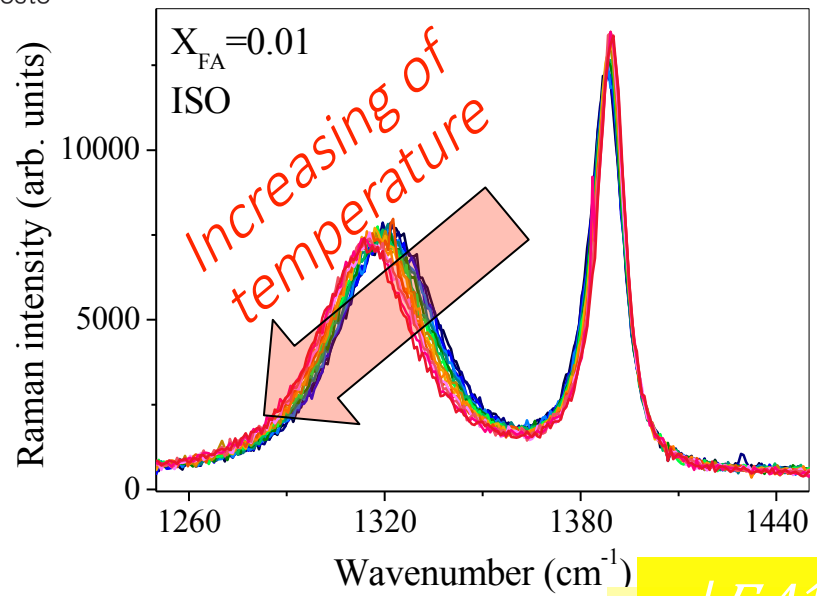
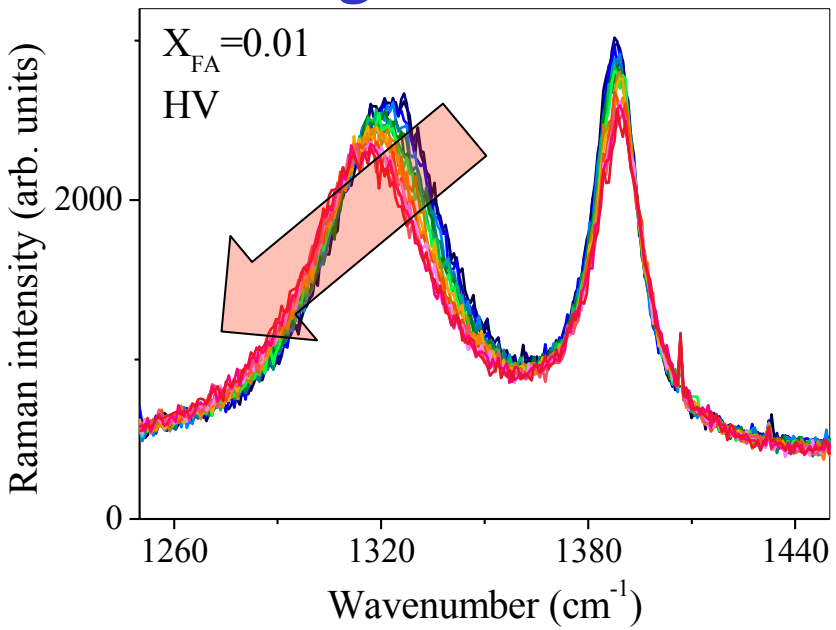
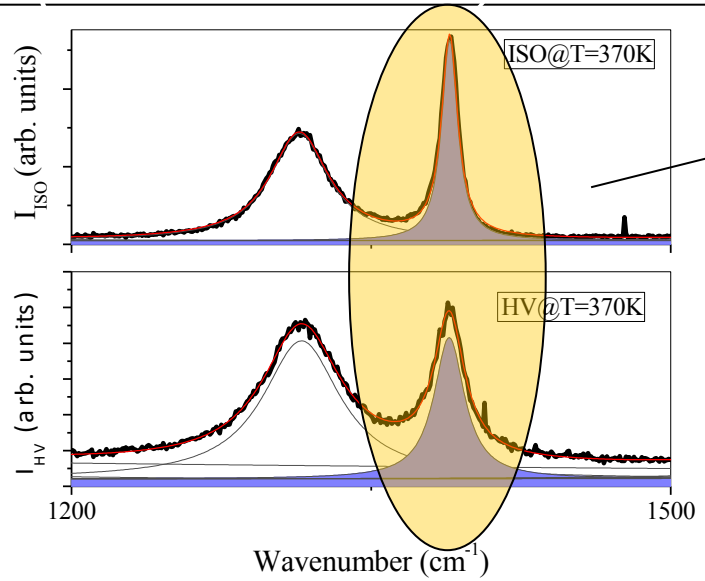
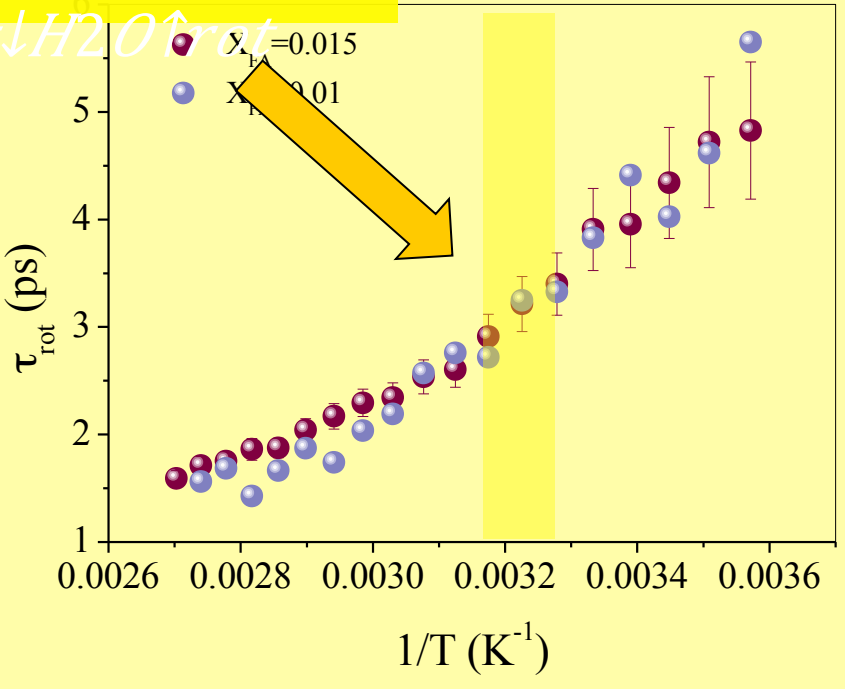



$\tau_{FA}^{rot} \approx \tau_{H2O}^{rot}$




Sch ethods:

# *Restructuring of water in the Hydration Shell of Salty Solutions probed by Resonant Raman Spectrum of Water*

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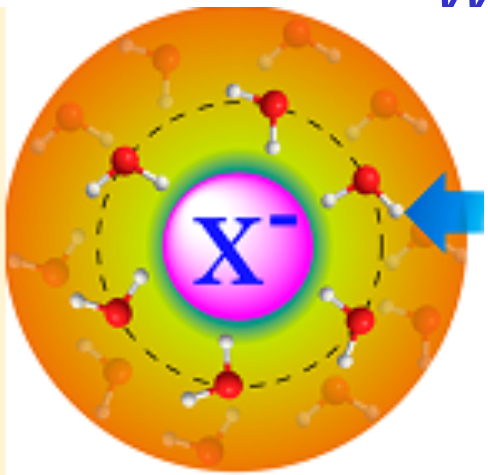
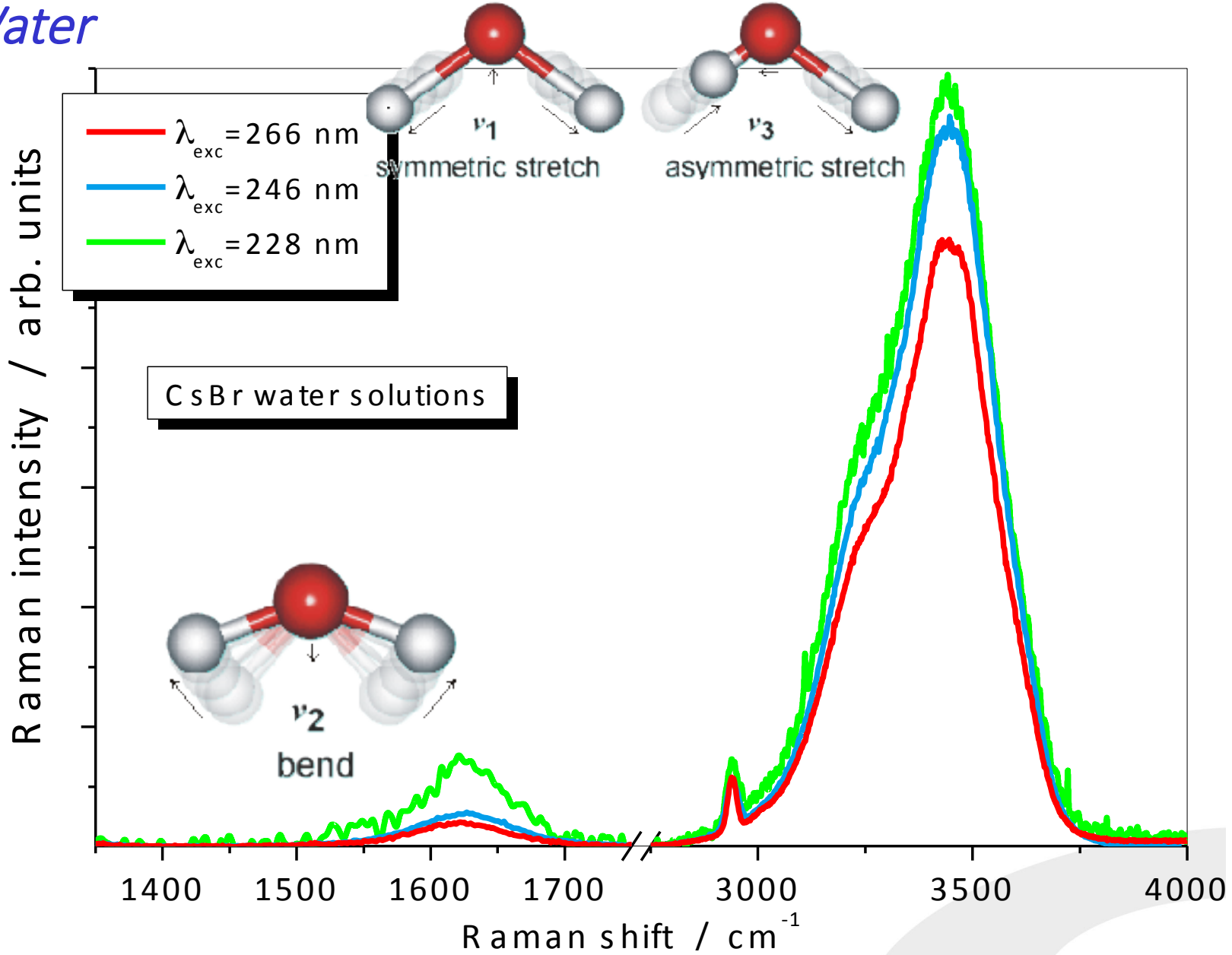
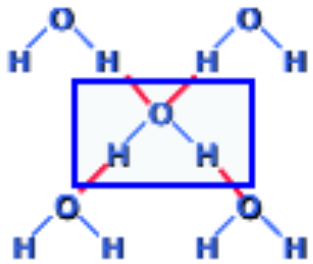



$X^- = Br$

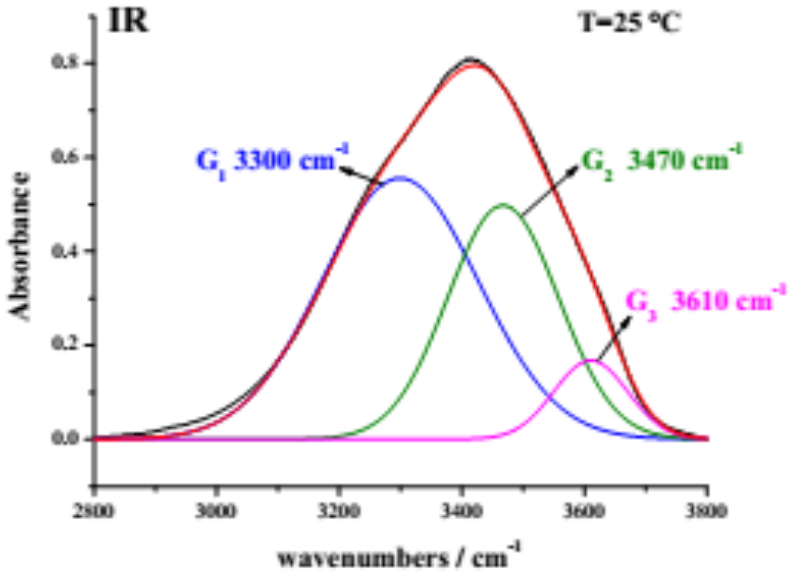
$C^- = Li$
$K$
$Cs$

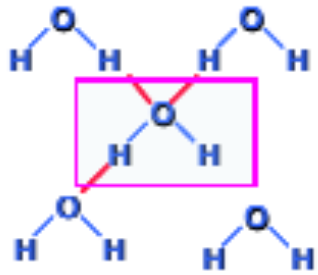


# OH stretching mode: probe of HB organization of water

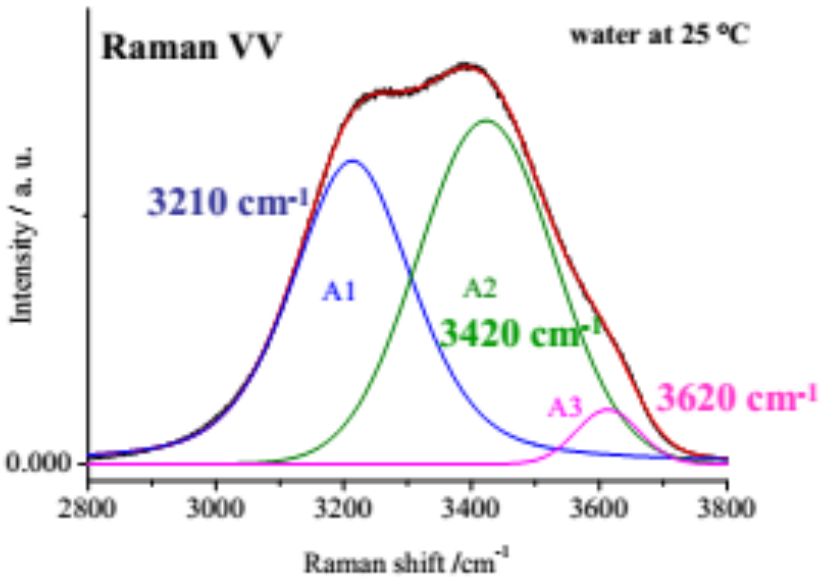


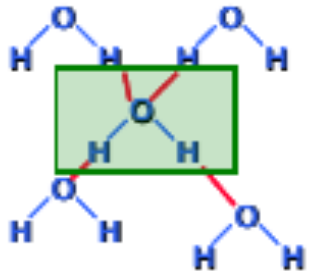
ordered H-bonded $H_2O$



free OH



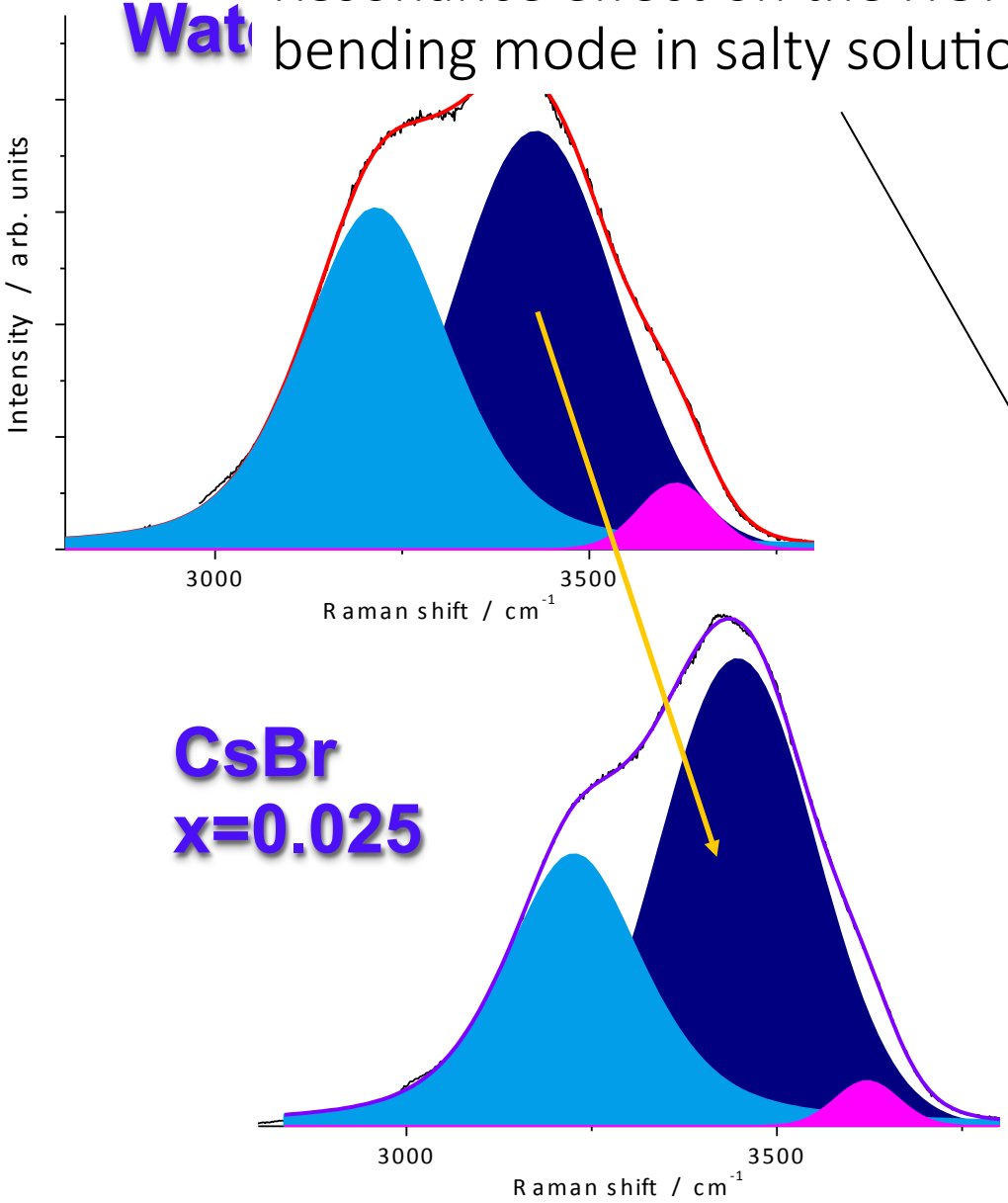



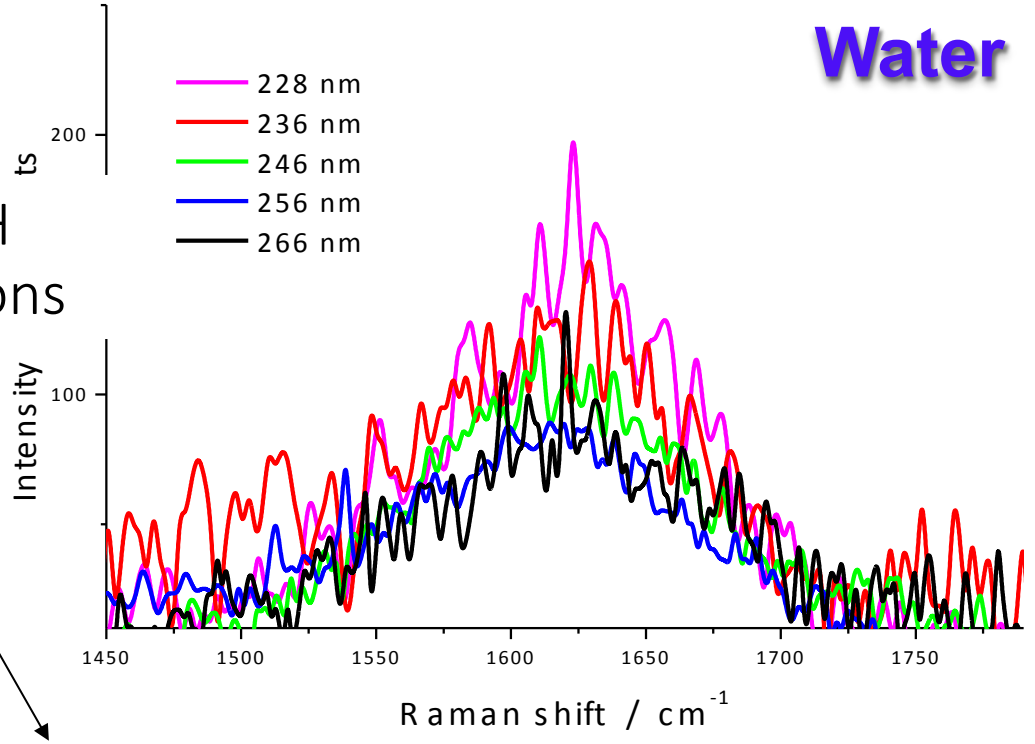
disordered H-bonded $H_2O$

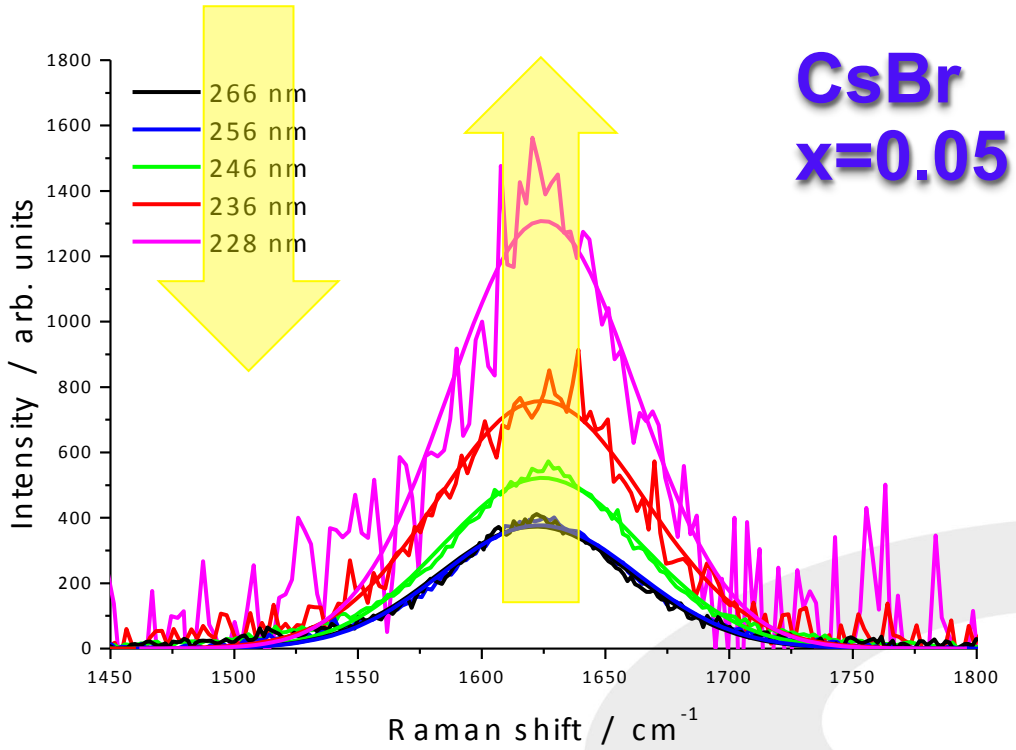
# Resonance effect on the HOH bending mode in salty solutions

λ=266 nm

Water



# HYDRATION SHELL DYNAMICS IN CYCLODEXTRIN AQUEOUS SOLUTIONS

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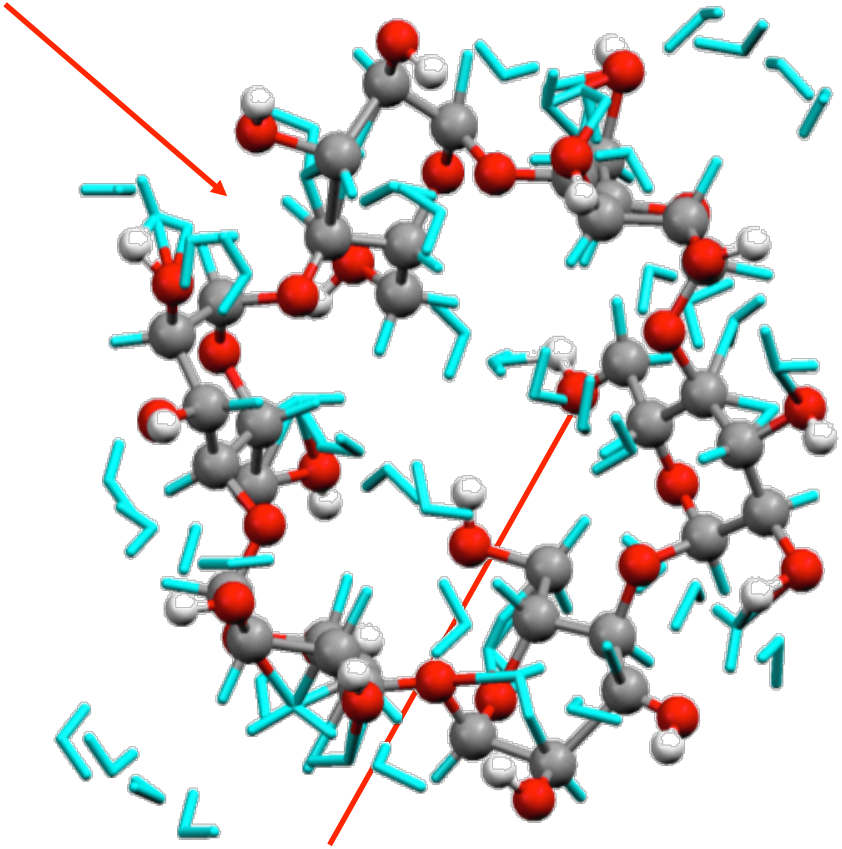
- ✓ *natural and biodegradable compounds*
- ✓ *relatively low costs of production for industrial uses (5 Euro/Kg)*
- ✓ *low toxicity*
- ✓ *hight versatility*

**Water-soluble surface**



**Hydrophobic central cavity**

# HOW WATER REARRANGES AROUND CD?

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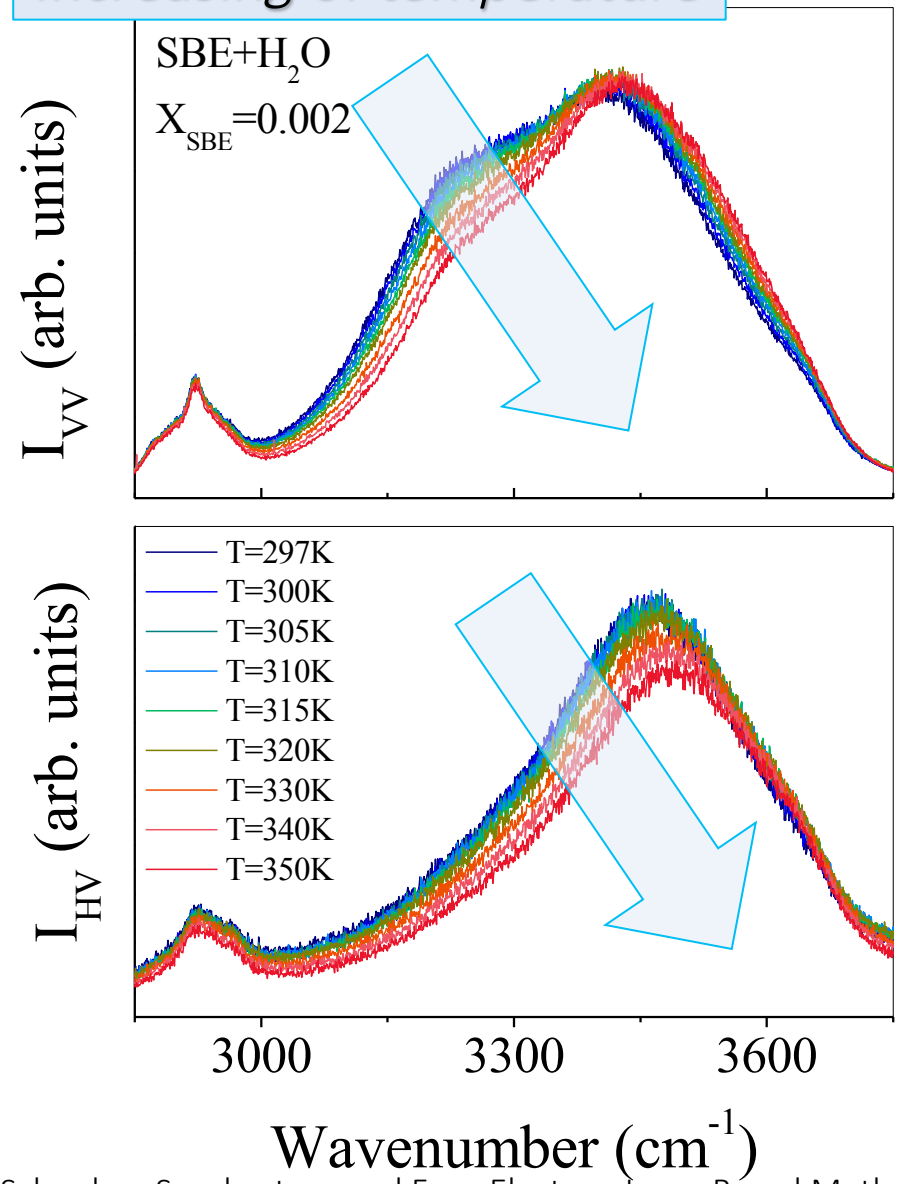
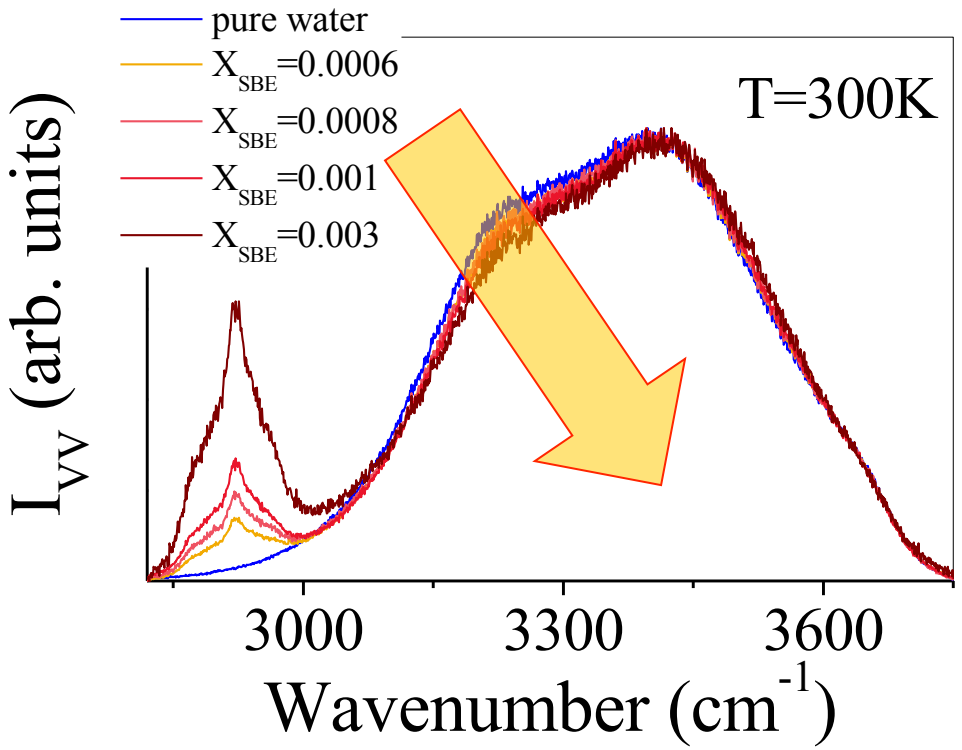
*Increasing of temperature*




*Increasing of concentration*




*Decrement in intensity of the low-wavenumber side of the O-H stretching profile*

*destructuring effect on the tetrahedral HB structures of water molecules*

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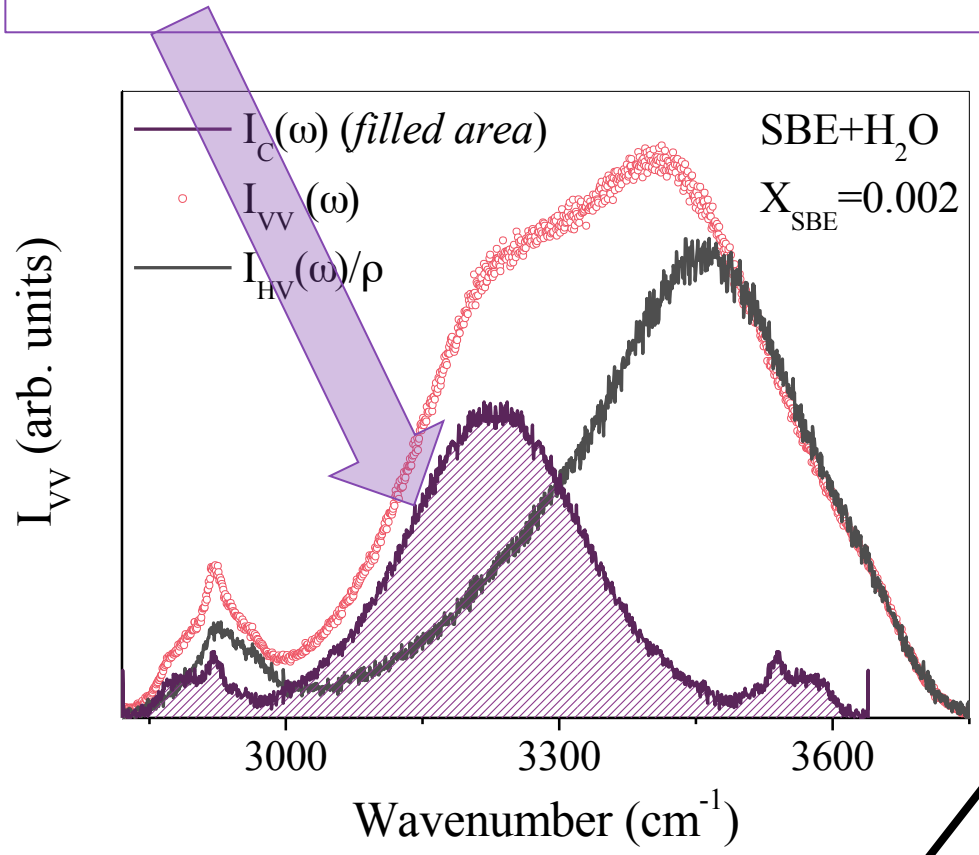
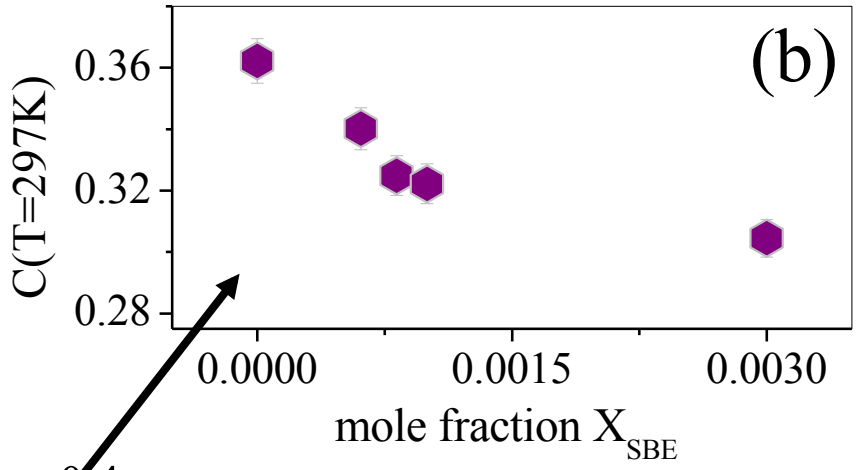
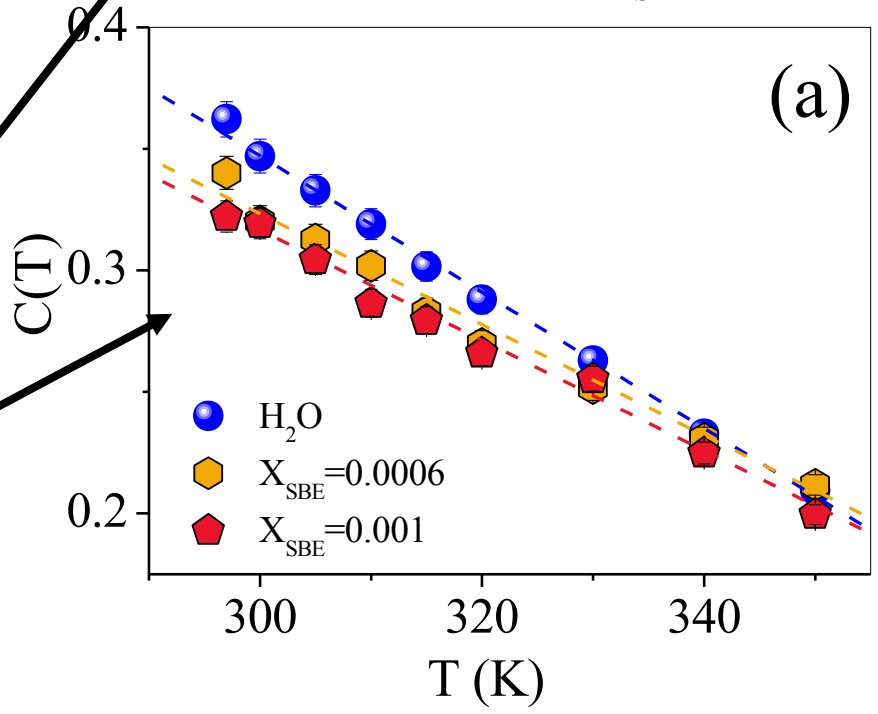
Sincrotrone
Trieste

*fraction of ordered HB water species present in solution*




***Lessening of ordered HB assemblies of water as a function of T and $X_{SBE}$***

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# *Examples of applications of UV Raman scattering technique:*

- Dynamical properties of aqueous solutions and complex molecular systems

Saito M, Bull. Chem. Soc. Jpn., Vol. 88 - 4, pp. 591-596 (2015)
D'Amico F, Phys. Chem. Chem. Phys., Vol. 17 - 16, pp. 10987-10992 (2015)
D'Amico F, J. Chem. Phys. 139 - 1, pp. 015101-5 (2013)
D'Amico F, J. Phys. Chem. B, Vol. 116 - 44, pp. 13219-13227 (2012)

- Structural characterization of biological systems, i.e. peptides and DNA

D'Amico F, Analyst, Vol. 140 - 5, pp. 1477-1485 (2015)

- Molecular structure and dynamics in hydrogel phases

Rossi B. et al., Soft Matter (2015) 11, 2183
Rossi B, et al. Phys. Chem. Chem. Phys., Vol. 17 - 2, pp. 963-971 (2015)
Rossi B, et al. J. Chem. Phys. Vol. 142, pp. 014901 (2015)
Venuti V, Phys. Chem. Chem. Phys., Vol. 17 - 15, pp. 10274-10282 (2015)

# Resonance raman spectra of Nucleobases

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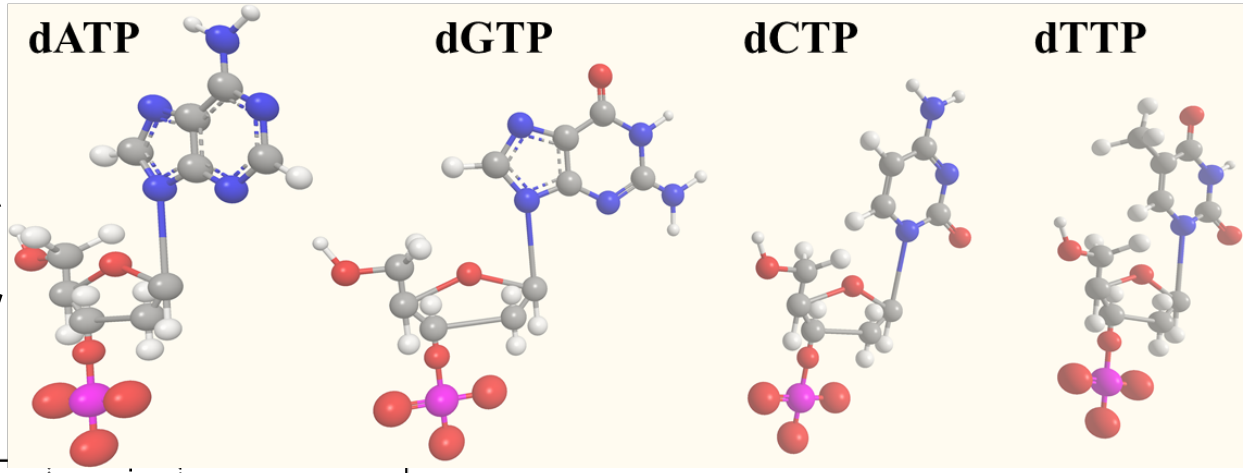
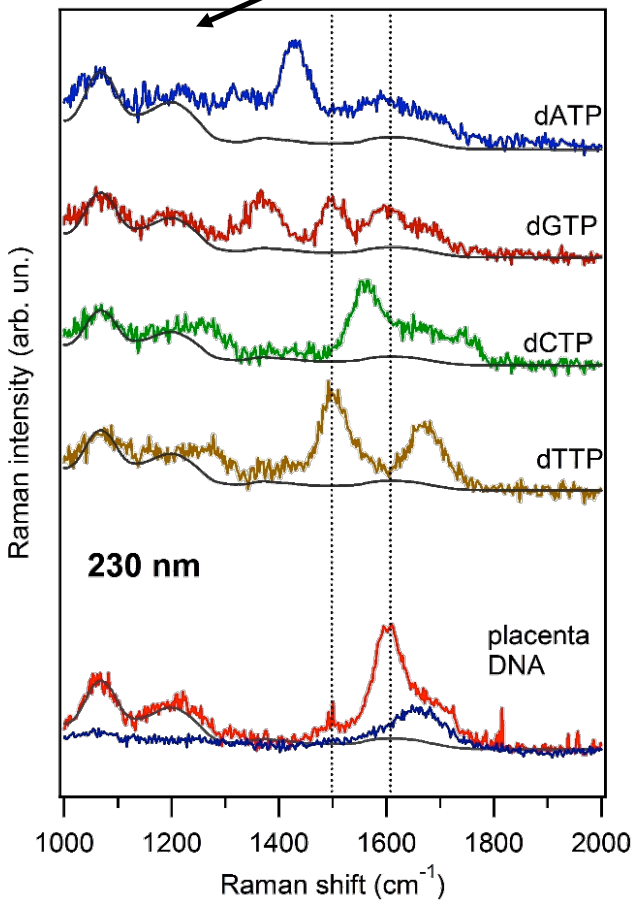
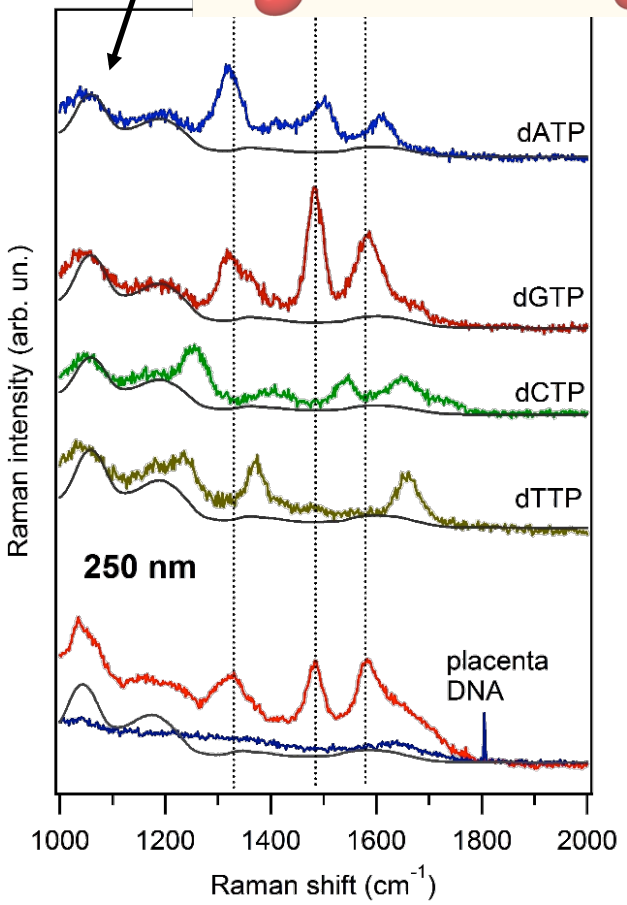
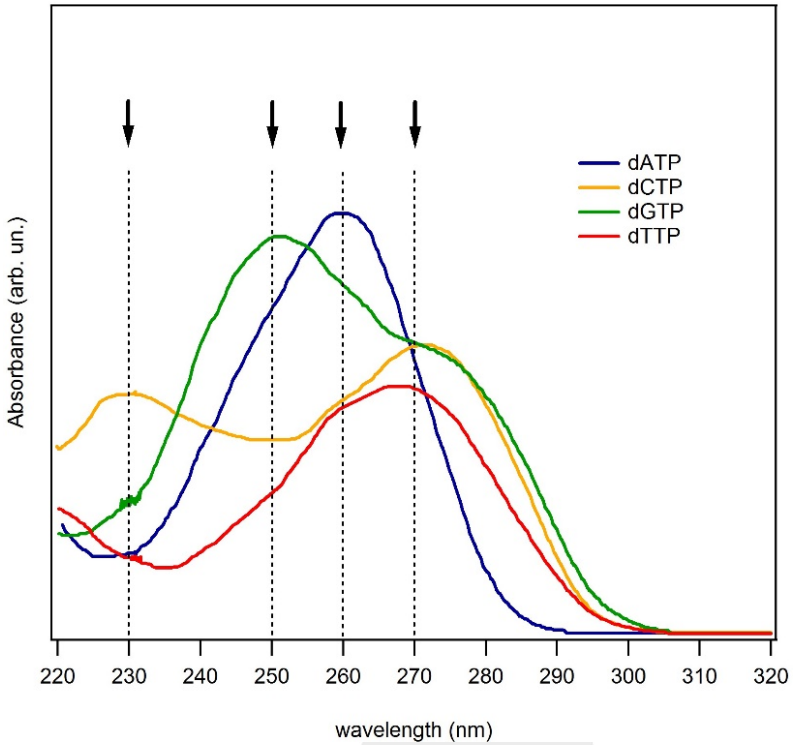



$E_{exc}$=230nm

$E_{exc}$=250nm

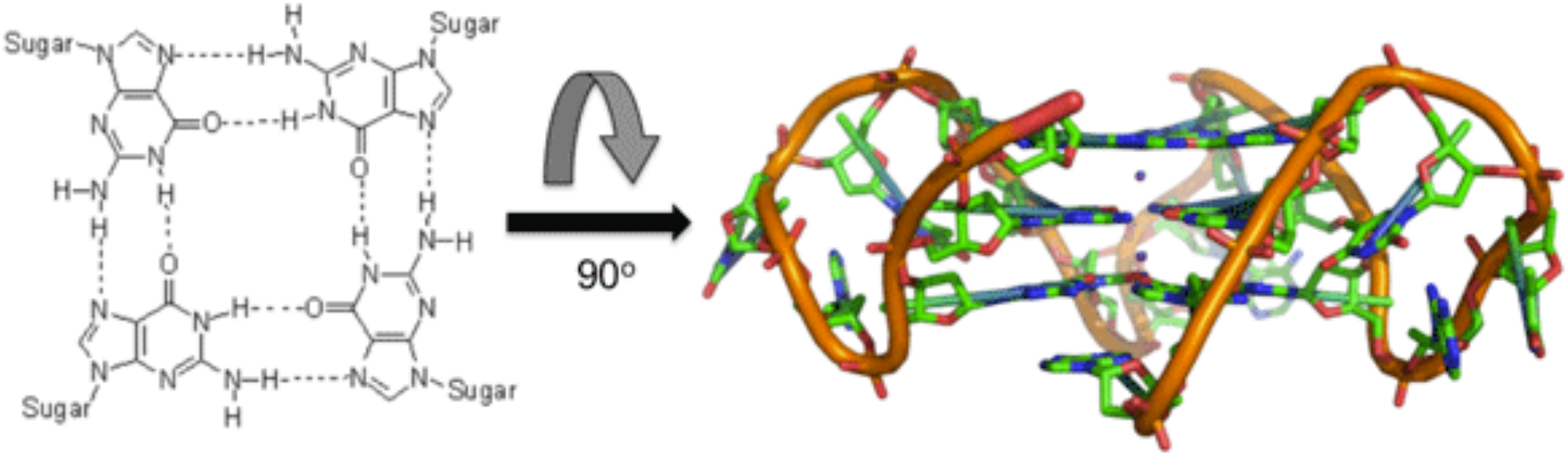


# Stabilitation of G-quadruplex structures of DNA

Elettra Sincrotrone Trieste

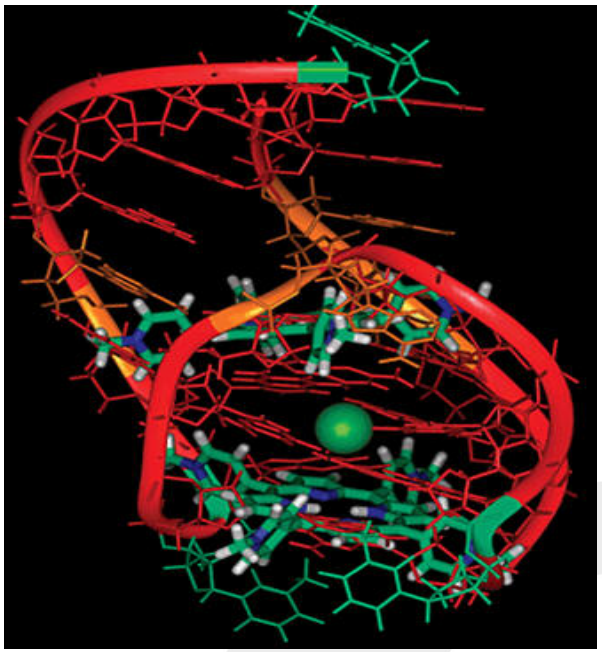



The formation of G-quadruplex structures in telomeres has been shown to decrease the activity of the enzyme telomerase, which is responsible for mantaining the length of telomeres and is involved in around 85% of all cancers

→ Active target of drug discovery

Human telomeric quadruplex (22mer):

$AG_3 (T_2AG_3)_3$



MW ~ 7000 Da

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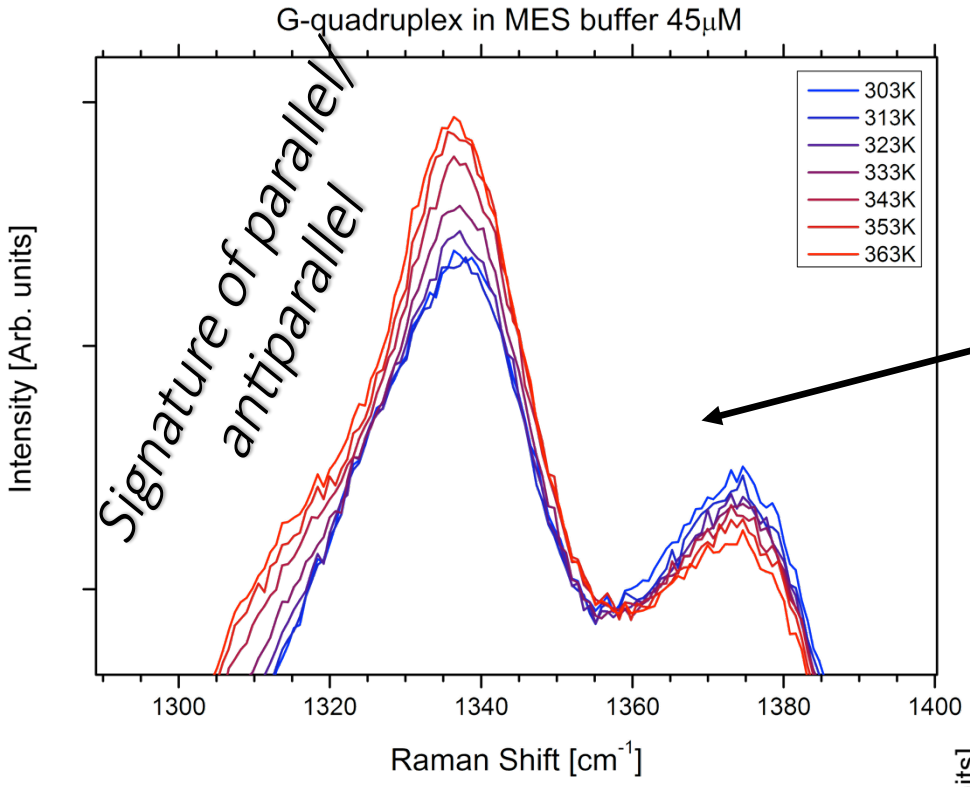


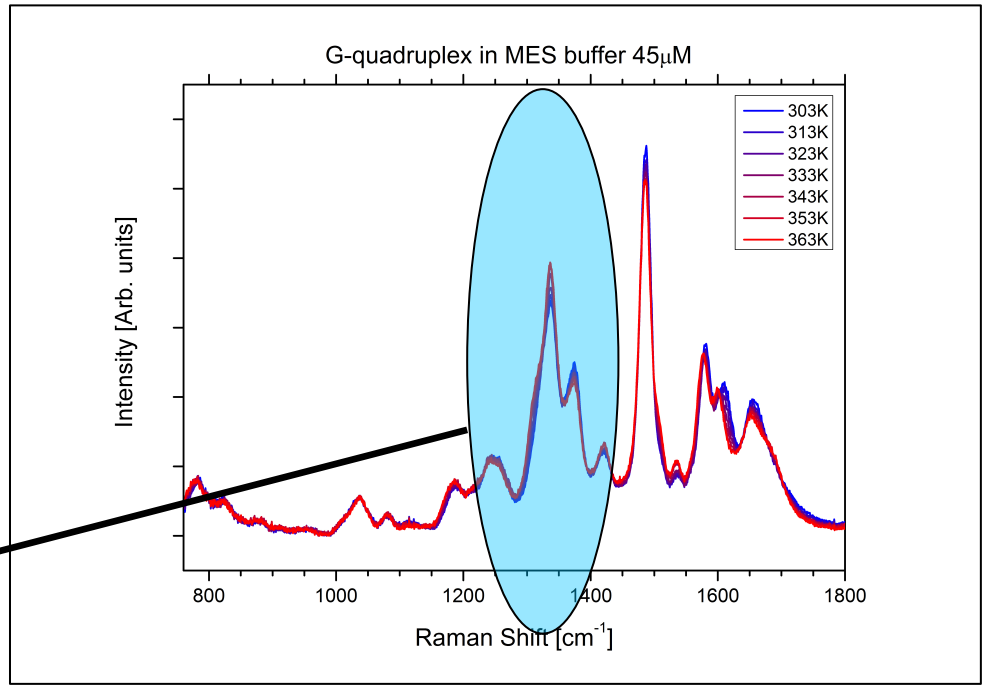


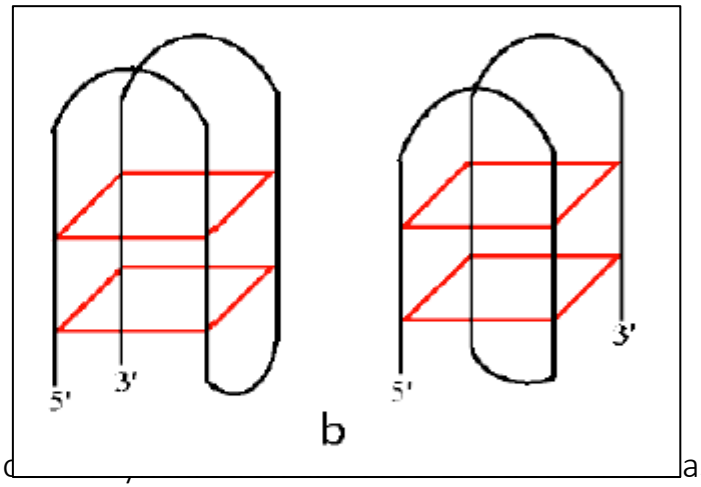


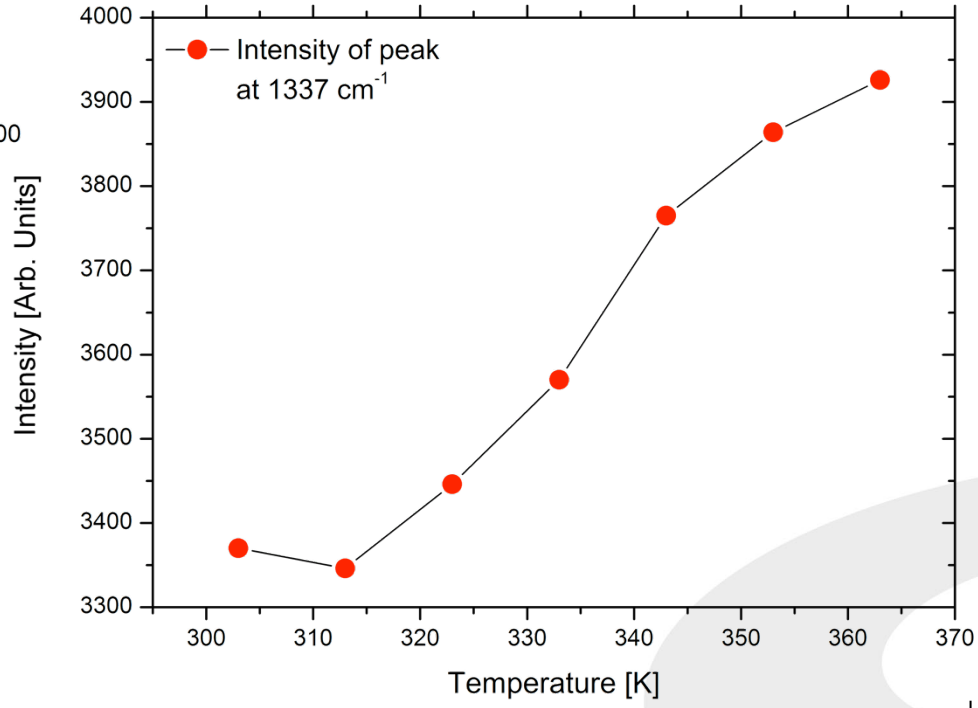


Sch ased Methods:
Multidisciplinary Applications and Perspectives

# *RESONANCE RAMAN SPECTRA OF PEPTIDES*

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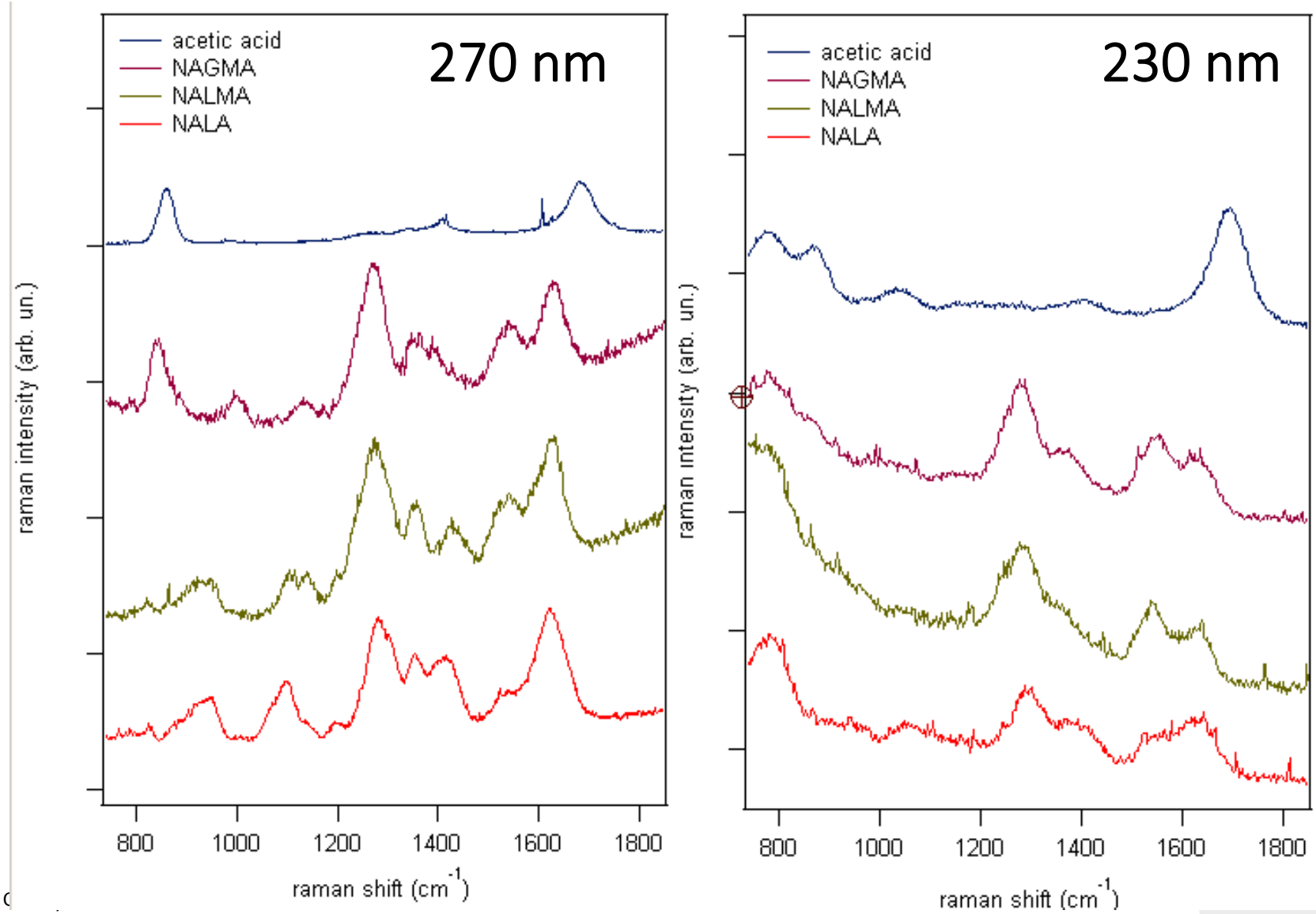
N-acetyl-leucinemethylamide (NALMA)
N-acetyl-leucineamide (NALA)
N-acetyl glycine methyl amide (NAGMA)



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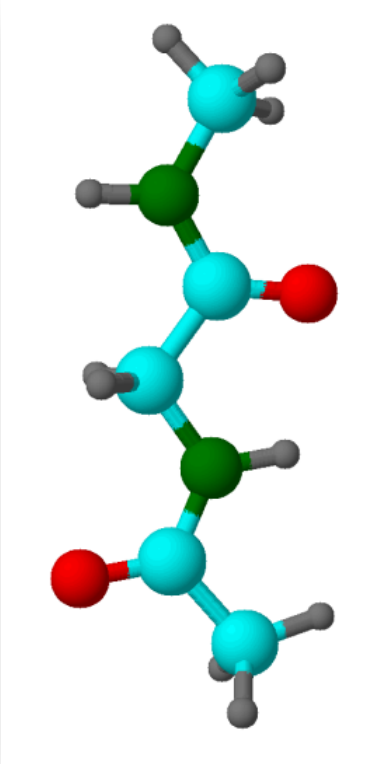
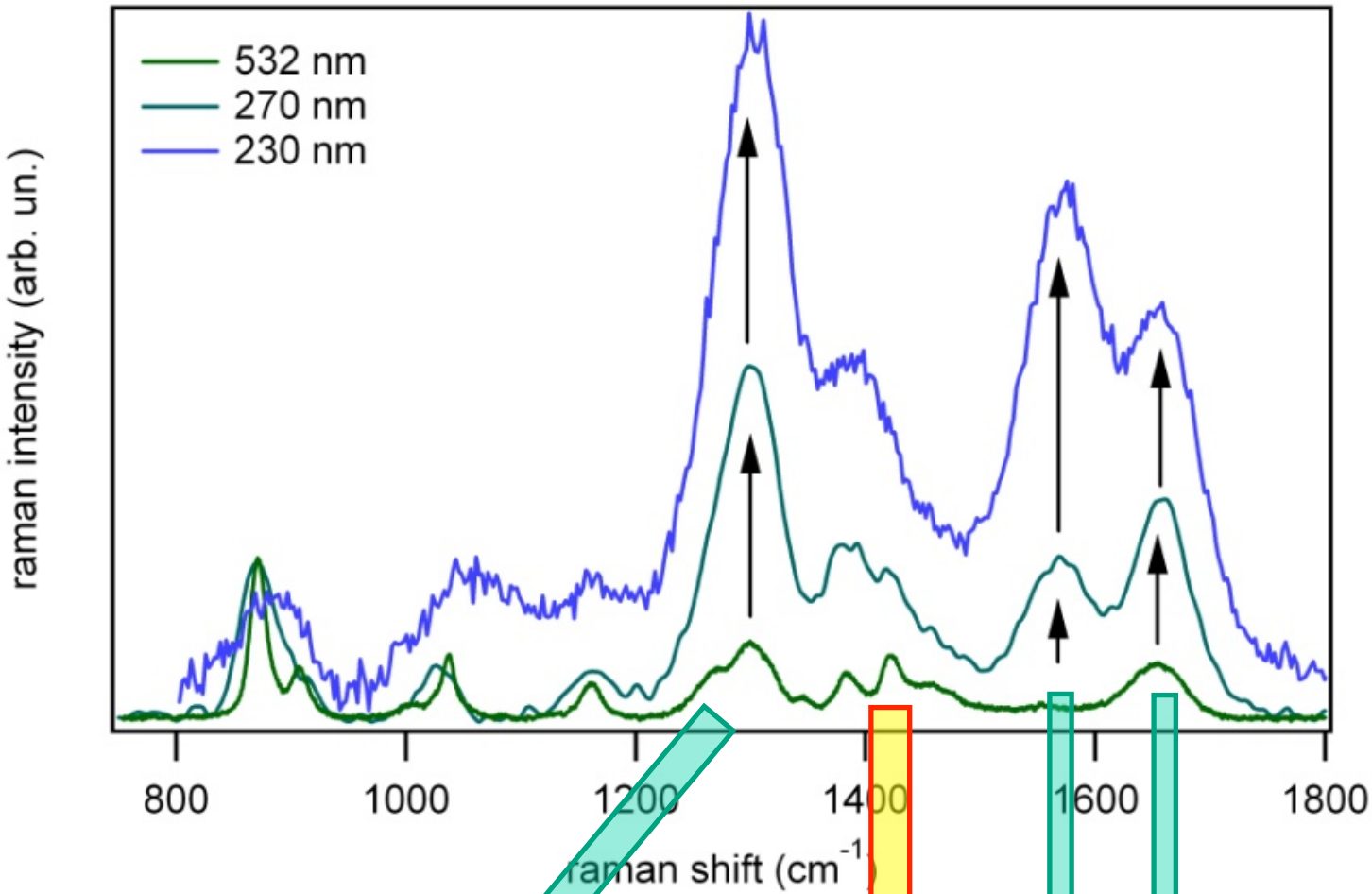
# NAGMA






$CH_2$ $CH_3$ bending+
C-C, C=O wagging
Resonant
(involving the whole molecules)

$CH_2$ $CH_3$ rocking
Not resonant

C=O stretching
Resonant

# *Resonance effect on oligopeptides: Amide II band*

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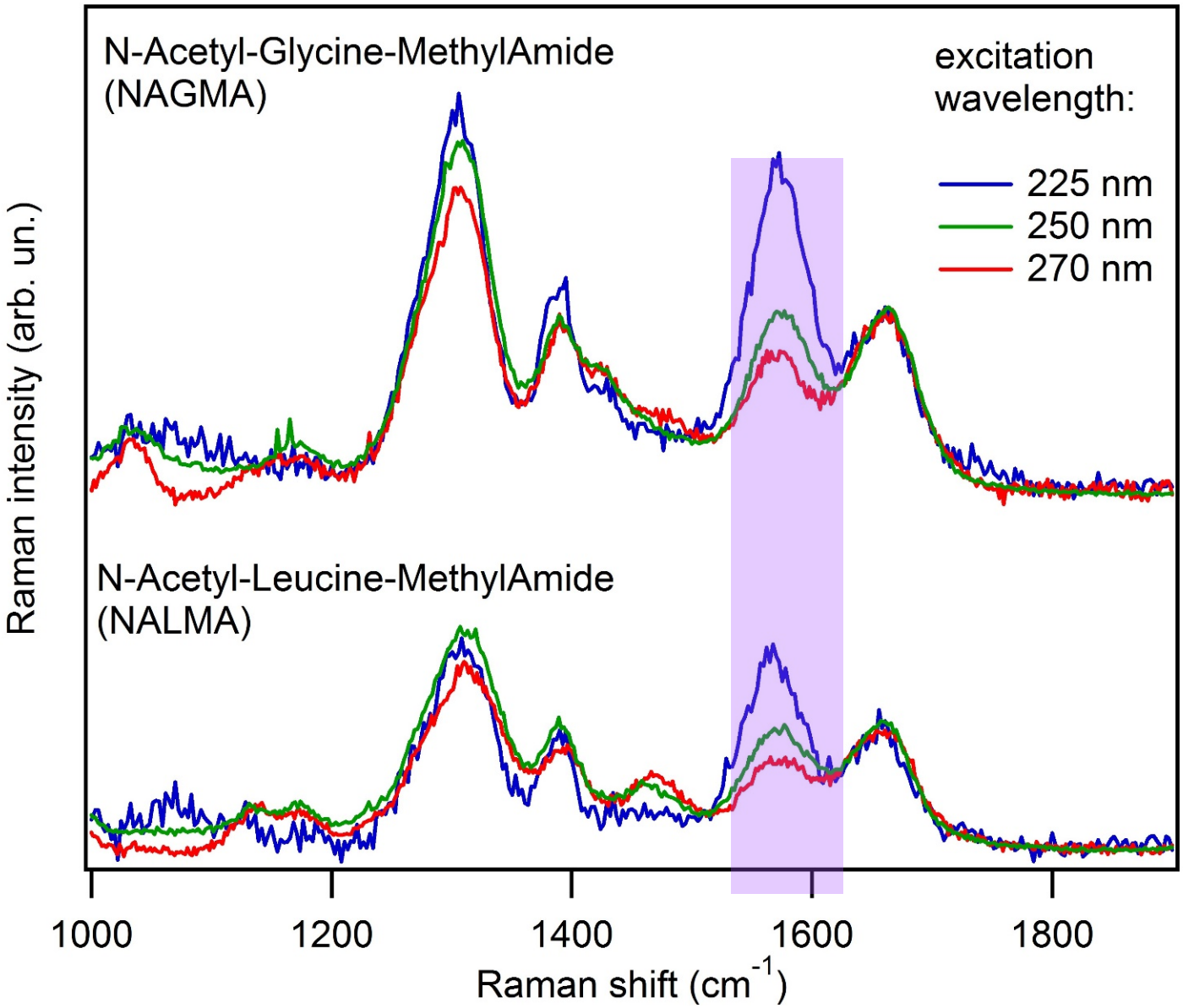


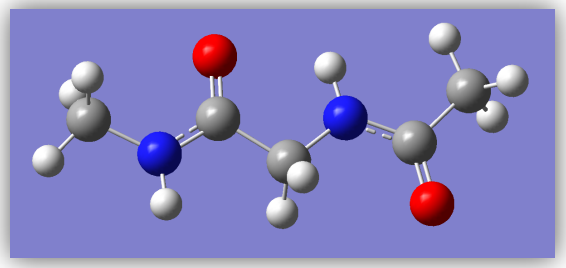

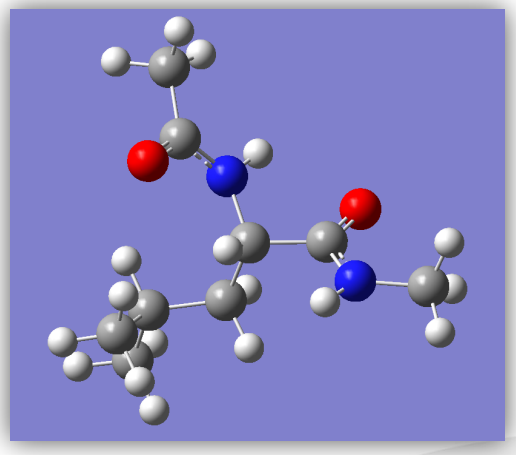

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D'Amico F, J. Chem. Phys. 139 - 1, pp. 015101-5 (2013)
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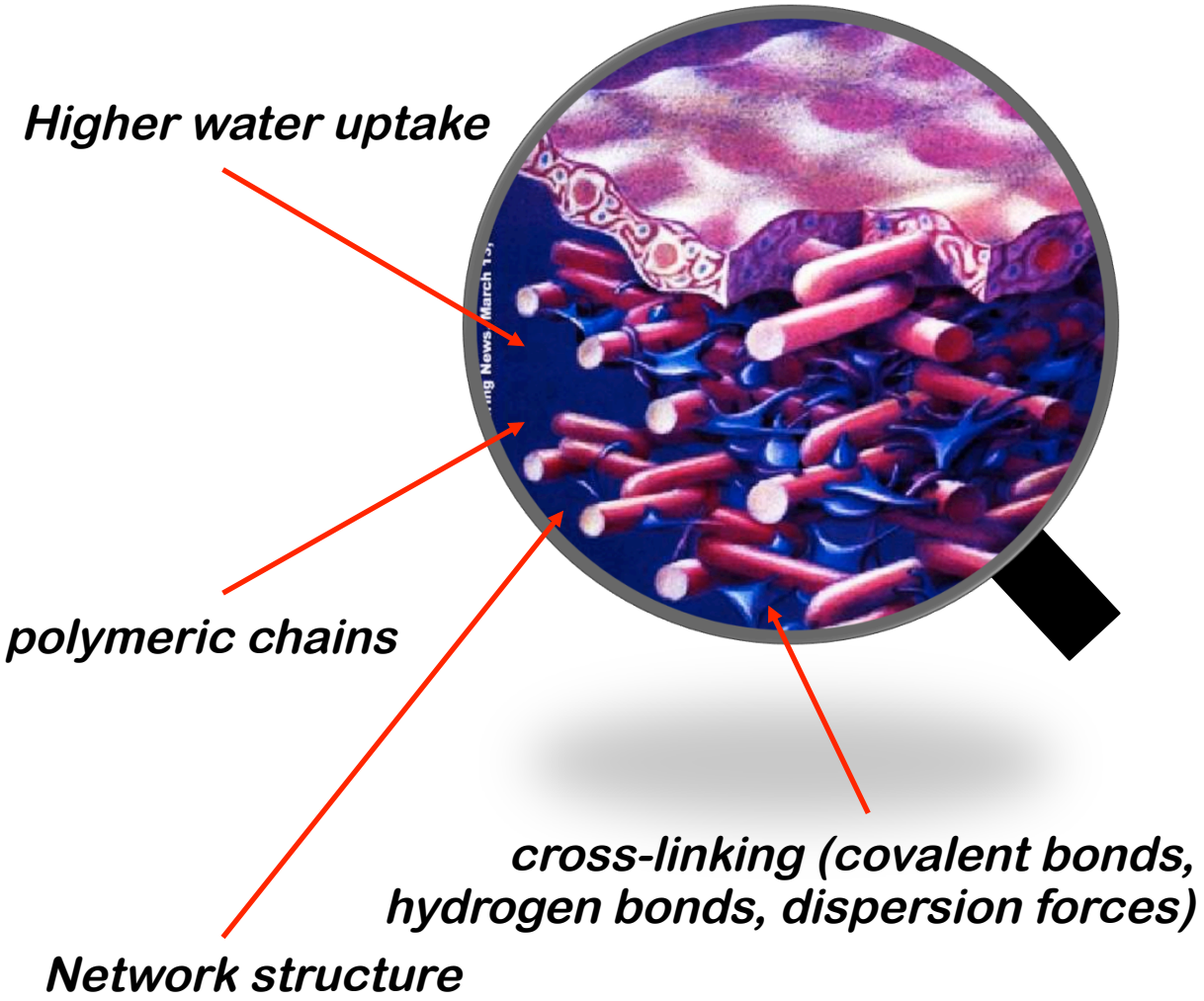
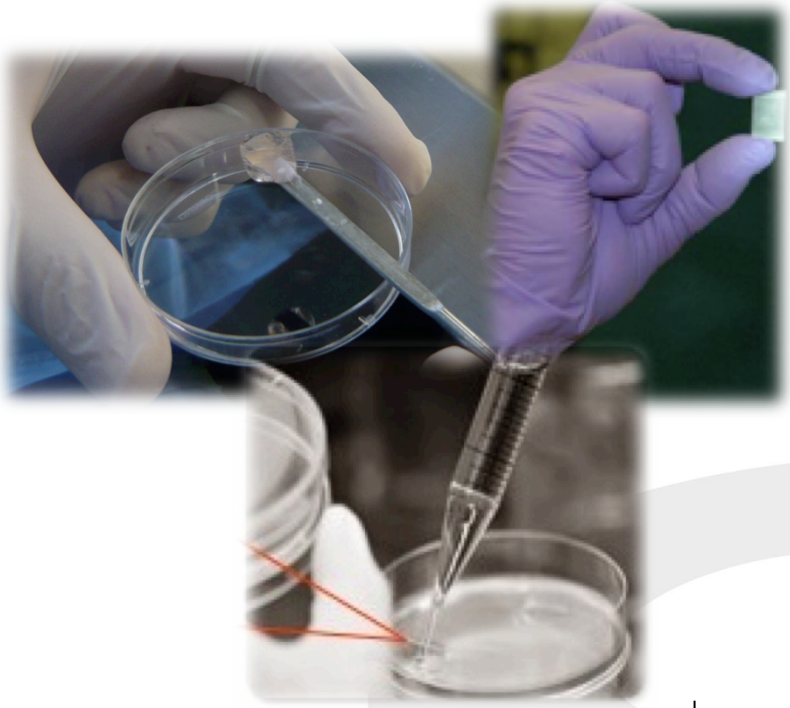
Rossi B, et al. J. Chem. Phys. Vol. 142, pp. 014901 (2015)
Venuti V, Phys. Chem. Chem. Phys., Vol. 17 - 15, pp. 10274-10282 (2015)

# Hydrogels as biomaterials

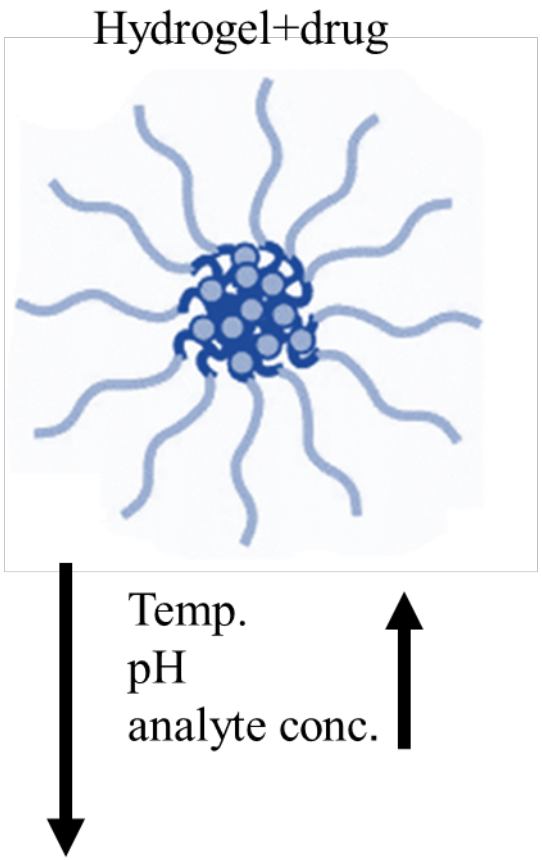
***The high water content (up to 99%) and the biocompatibility of hydrogels makes them resembling to natural soft tissue more than any other type of biomaterials***




- *scaffolding matrices for 3D culturing cells*
- *Drug-delivery*
- *Controlled release systems*



# *Environmentally sensitive hydrogels*



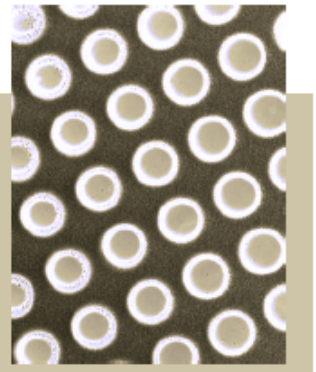

ADVANCED MATERIALS

REVIEW

DOI: 10.1002/adma.200501612

## Hydrogels in Biology and Medicine: From Molecular Principles to Bionanotechnology**

By *Nicholas A. Peppas*, J. Zach Hilt, Ali Khademhosseini*, and *Robert Langer**



*Hydrophilic polymers are the center of research emphasis in nanotechnology because of their perceived "intelligence". They can be used as thin films, scaffolds, or nanoparticles in a wide range of biomedical and biological applications. Here we highlight recent developments in engineering uncrosslinked and crosslinked hydrophilic polymers for these applications. Natural, biohybrid, and synthetic hydrophilic polymers and hydrogels are analyzed and their thermodynamic responses are discussed. In addition, examples of the use of hydrogels for various therapeutic applications are given. We show how such systems' intelligent behavior can be used in sensors, microarrays, and imaging. Finally, we outline challenges for the future in integrating hydrogels into biomedical applications.*

*polymer networks that are capable of **sensing** and **responding** to external stimuli, by varying their structure and chemical-physical properties*

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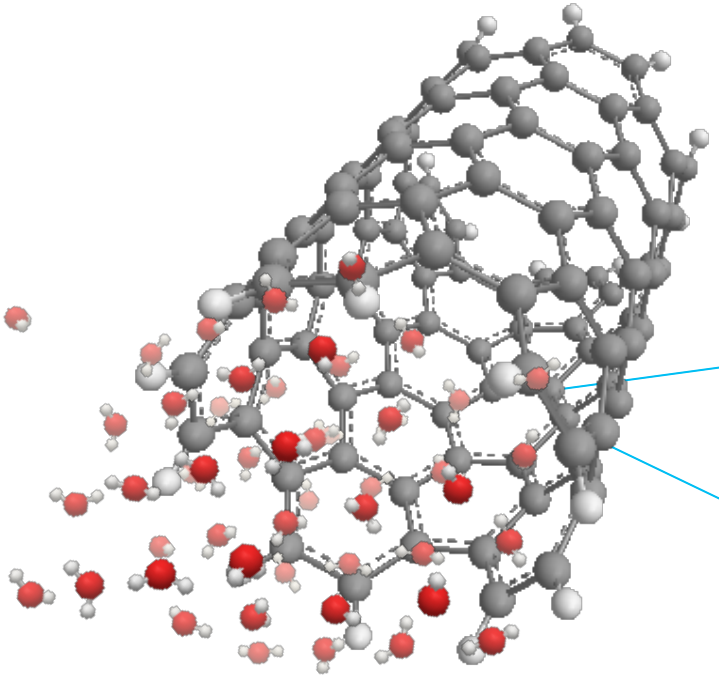
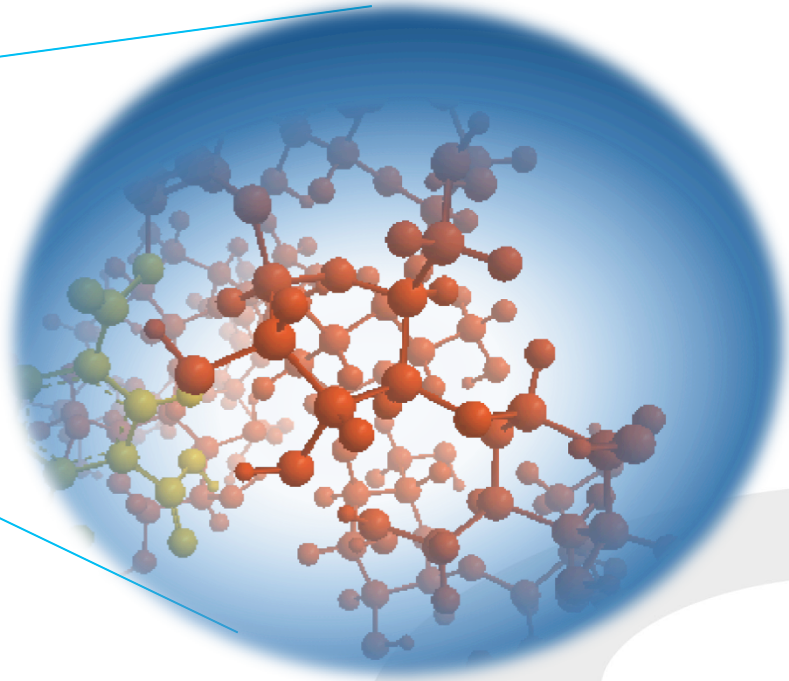
# *Hydrogels as model systems*

*Hydrogels as well-controlled* ***soft confining medium*** *for investigating the HB dynamics of water*

*What is the effect on the nano-scale confinement of water?*



*How water behaves around the hydrophilic/hydrophobic groups?*



# Hydrogels: the open issues

*The need of precise control of mechanical and physico-chemical properties of hydrogels starting from their molecular architecture*

1 *to monitor the **polymer response to external stimuli** (hydration level, T, pH)*

2 *to spot on the state of **water** in the hydrogels*

3 *to study the molecular state and transport properties of the **entrapped guest (as in drug-loaded hydrogels)***

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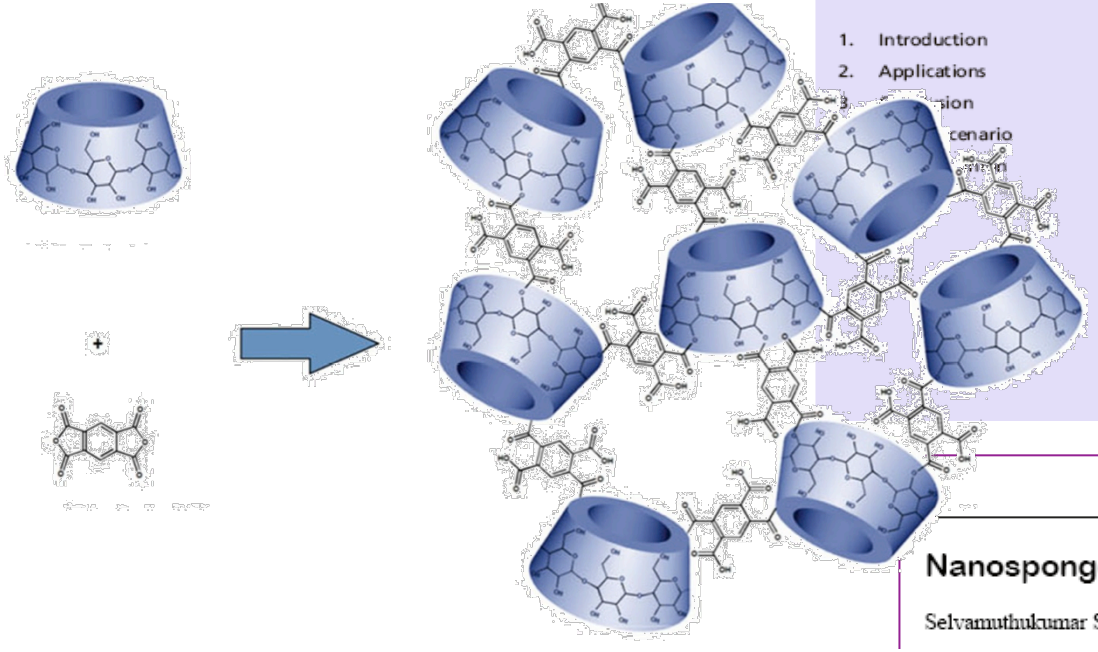


EXPERT OPINION

1. Introduction
2. Applications
3. ion
4. cenario

Review

# Cyclodextrin-based nanosponges: a propitious platform for enhancing drug delivery

Sai V Chilajwar†, Priti P Pednekar, Kisan R Jadhav, Gajendra JC Gupta & Vilasrao J Kadam
*University of Mumbai, Bharati Vidyapeeth's College of Pharmacy, Department of Pharmaceutics, Navi-Mumbai, India*

***Introduction:*** Recently, Nanotechnology is receiving considerable acknowledgment due to its potential to combine features that are difficult to achieve by making use of a drug alone. Cyclodextrin-based nanosponges are yet another contemporary approach for highlighting the advancements which could be brought about in a drug delivery system. Statistical analyses have shown that around 40% of currently marketed drugs and about 90% of drugs in their developmental phase encounter solubility-related problems. Cyclodextrin-based nanosponges have the capacity to emerge as a productive approach over conventional cyclodextrins by overcoming the disadvantages associated with the latter.

J Pharm Pharmaceut Sci (www.cspsCanada.org) 15(1) 103 - 111, 2012

## Nanosponges: A Novel Class of Drug Delivery System - Review

Selvamuthukumar Subramanian, Anandam Singireddy, Kannan Krishnamoorthy and Manavalan Rajappan

culty of Engineering and Technology, Annamalai University, Annamalai Nagar, Tamil

ised, January 9, 2012; Accepted, January 11, 2012; Published, January 12, 2012.

targeted drug delivery systems have been a dream for a long time, but it has been complex chemistry that is involved in the development of new systems. The has become a significant step toward overcoming these problems. Nanosponges ze of about a virus, which can be filled with a wide variety of drugs. These tiny und the body until they encounter the specific target site and stick on the surface ug in a controlled and predictable manner. Because the drug can be released at the of circulating throughout the body it will be more effective for a particular given t character of these sponges is their aqueous solubility; this allows the use of these igs with poor solubility.

Advanced Review

## Cyclodextrin-based nanosponges: a versatile platform for cancer nanotherapeutics development

Shankar Swaminathan[1], Roberta Cavalli[2] and Francesco Trotta[3,*]

Article first published online: 22 JAN 2016
DOI: 10.1002/wnan.1384

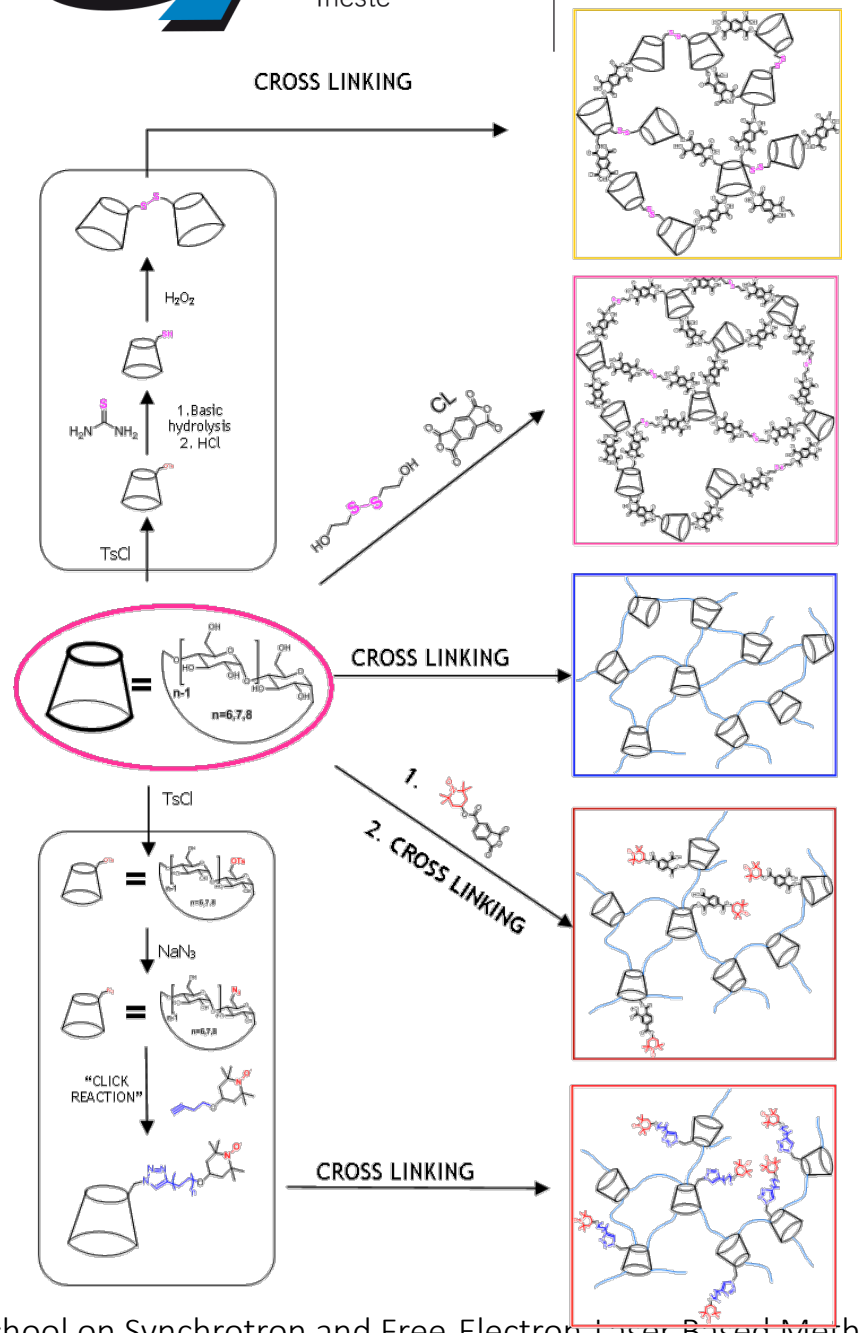


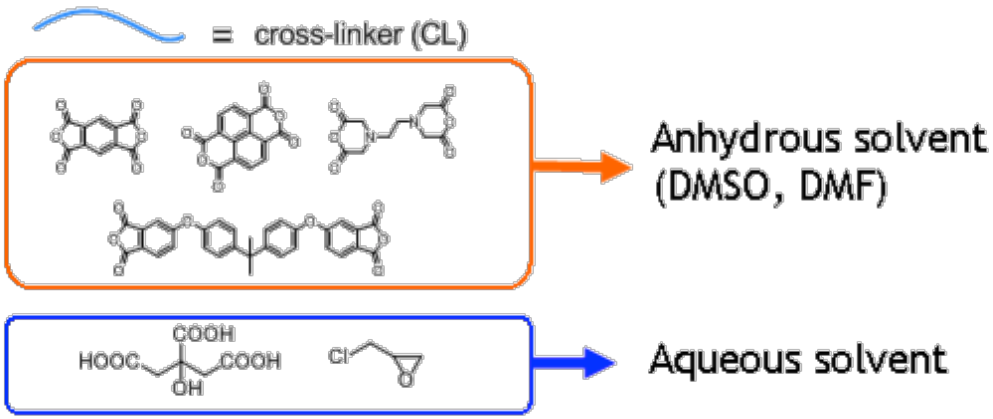
Issue


Wiley Interdisci
Reviews: Nanor
Nanobiotechnol

Early View (Onli
Record publishe
inclusion in an is

# *High versatility, simple synthetic routes*



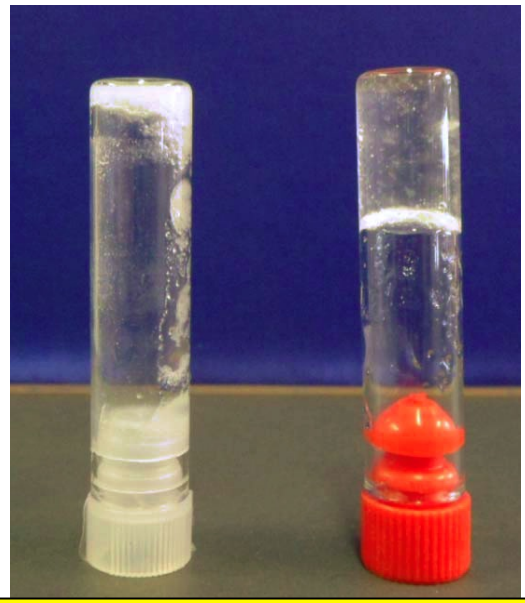




- *Hydrophobic/hydrophilic balance*
- *Grade of entanglement*
- *Swelling equilibrium*
- *Water-retaining ability*
- *pH- and temperature stimuli response*

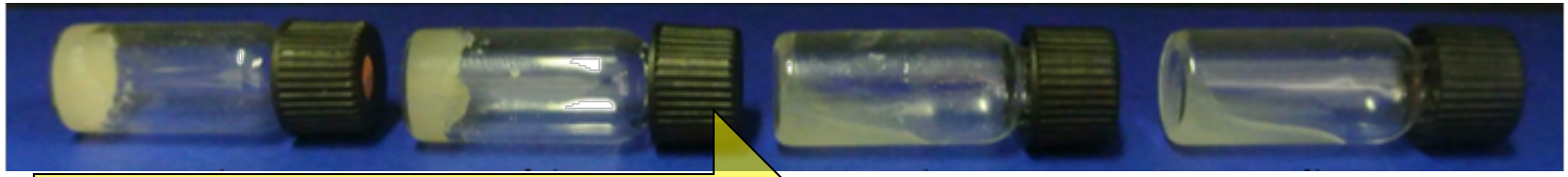
# NS hydrogels: a complex behaviour

Elettra Sincrotrone Trieste

Soft Matter 9 (2013) 6457
Soft Matter 10 (2014) , 2320
J. Incl. Phenom. Macrocycl. Chem, (2014) 80, 69
J. Incl. Phenom. Macrocycl. Chem, (2014) 80, 77
B. Rossi et al. Soft Matter (2015)



**pH sensitive**



*Temperature*
*Hydration h=mg water/mg NS*

**gel-sol phase transition**

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# NS hydrogels as molecular carriers

## Sponge-like structure with high performances of molecular encapsulation

BEILSTEIN JOURNAL OF ORGANIC CHEMISTRY

### Anomalous diffusion of Ibuprofen in cyclodextrin nanosponge hydrogels: an HRMAS NMR study

Monica Ferro[1], Franca Castiglione[*1], Carlo Punta[1], Lucio Melone[1], Walter Panzeri[2], Barbara Rossi[3], Francesco Trotta[4] and Andrea Mele[*1,2]

Full Research Paper

Open Access

Address:
[1]Department of Chemistry, Materials and Chemical Engineering "G. Natta", Politecnico di Milano, Piazza L. da Vinci 32 – 20133 Milano Italy, [2]CNR-ICRM, Via L. Mancinelli, 7 20131 Milano, Italy, [3]Elettra - Sincrotrone Trieste, Strada Statale 14 km 163.5, Area Science Park, 34149 Trieste, Italy and Department of Physics, University of Trento, via Sommarive 14, 38123 Povo, Trento, Italy and [4]Department of Chemistry, University of Torino, Via Pietro Giuria 7, 10125 Torino, Italy

Email:
Franca Castiglione* - franca.castiglione@polimi.it; Andrea Mele* - andrea.mele@polimi.it

* Corresponding author

Keywords:
cross-linked polymers; cyclodextrin nanosponges; diffusion; HRMAS NMR spectroscopy; TEM

*Beilstein J. Org. Chem.* **2014**, *10*, 2715–2723.
doi:10.3762/bjoc.10.286

Received: 28 July 2014
Accepted: 06 November 2014
Published: 19 November 2014

This article is part of the Thematic Series "Superstructures with cyclodextrins: Chemistry and applications II".

Guest Editor: G. Wenz



## ...towards environmentally sensitive hydrogels

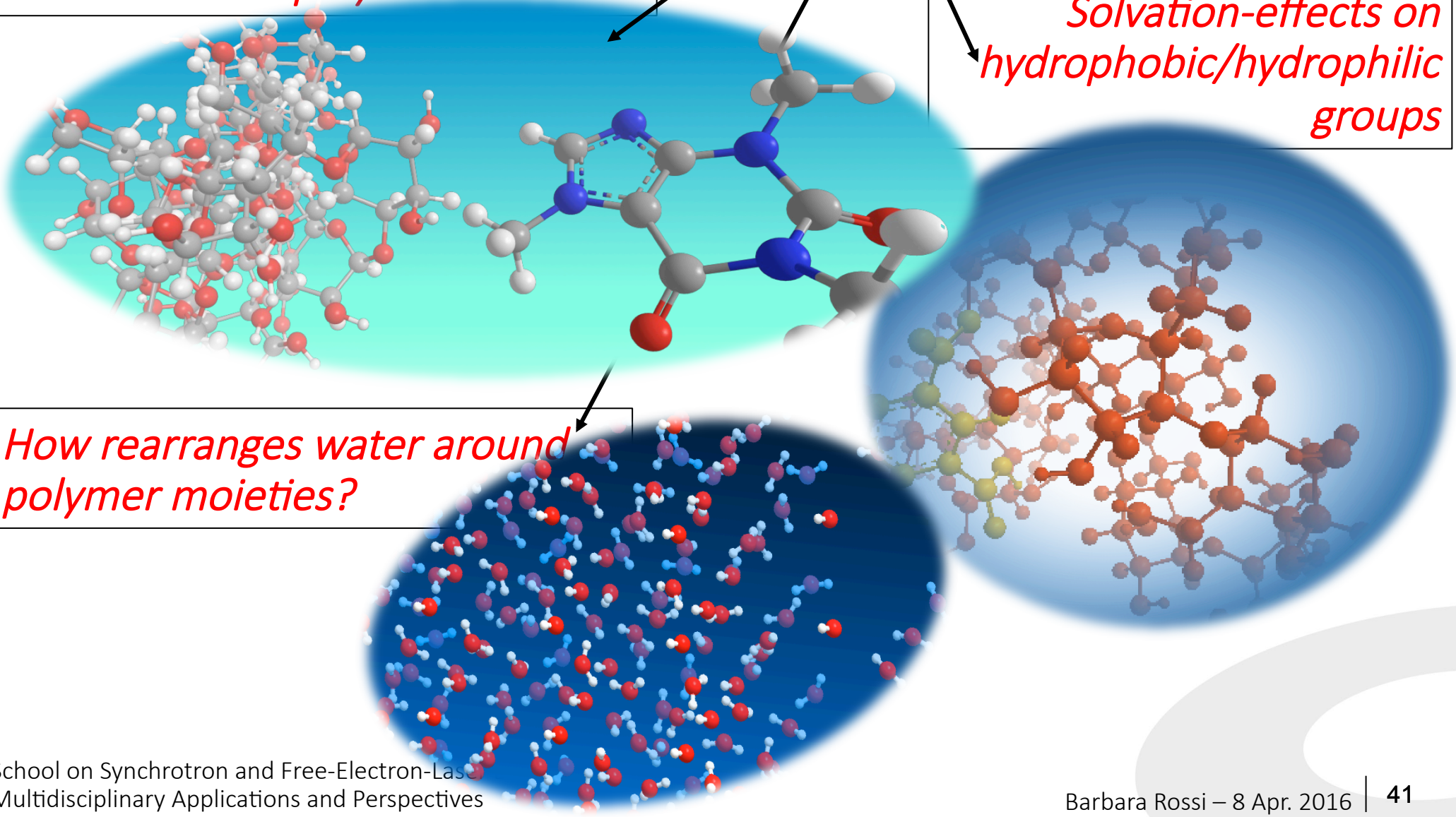
Elettra Sincrotrone Trieste

# ...how is changed the polymer dynamics?

*Interactions between guest molecules and polymer skeleton*

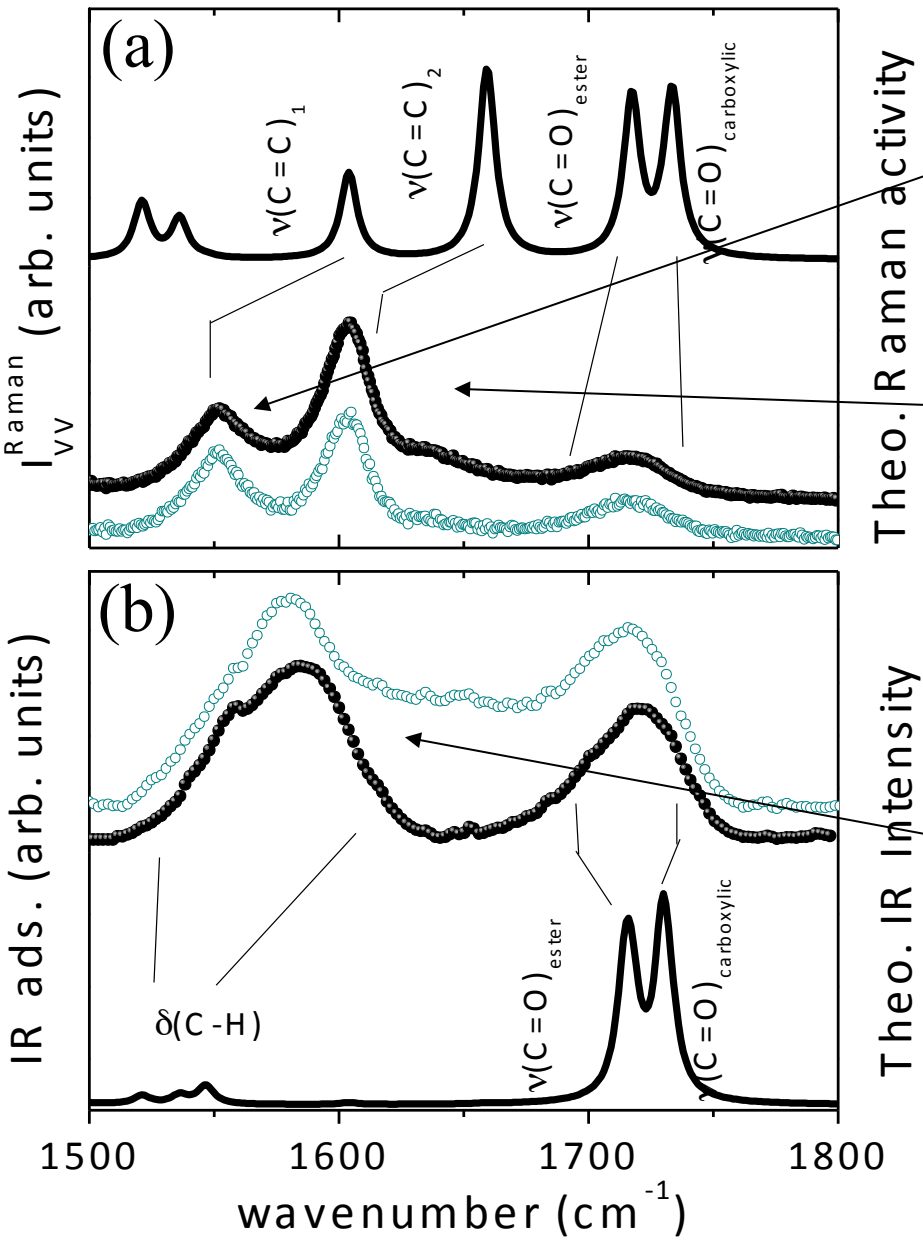
*Solvation-effects on hydrophobic/hydrophilic groups*

*How rearranges water around polymer moieties?*



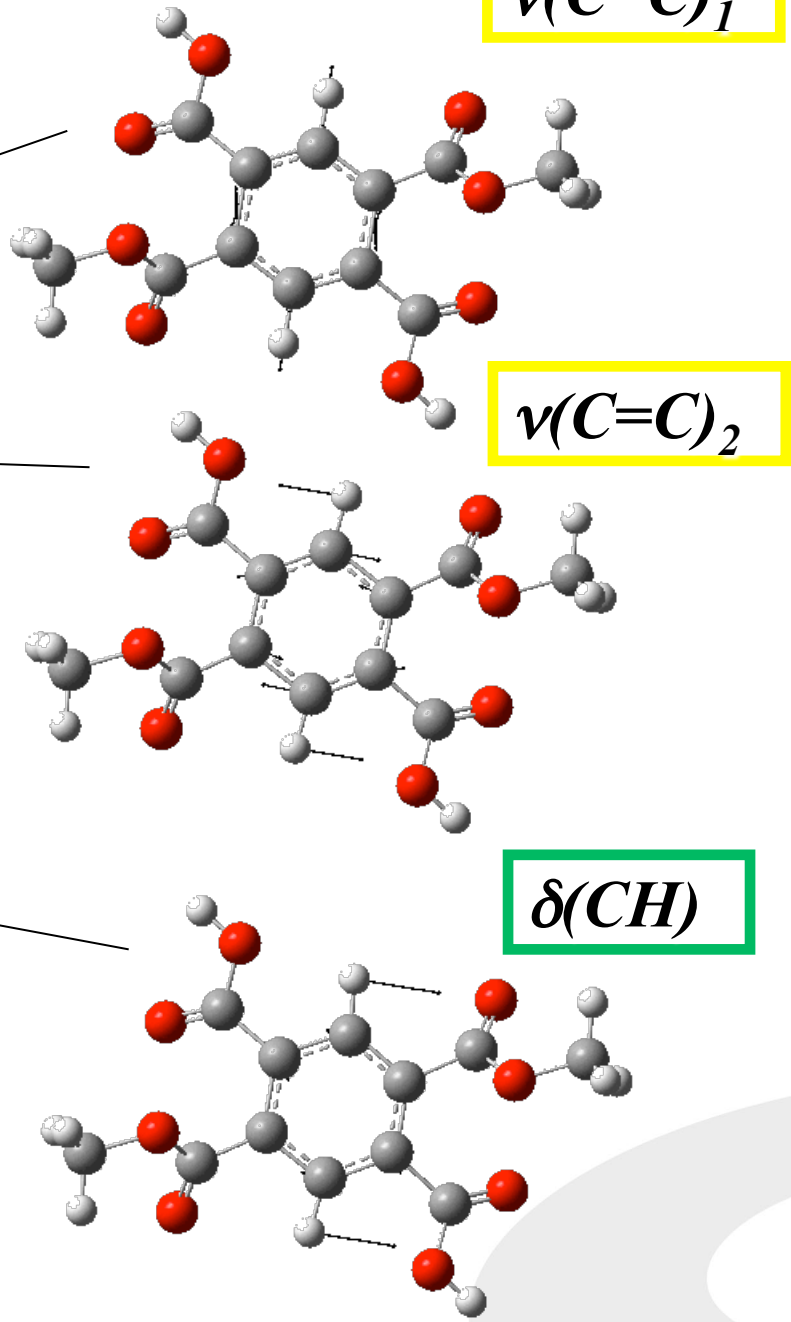
Elettra Sincrotrone Trieste

F. Castiglione et al. JPCB 2012, **116**, 7952
B. Rossi, et al. *PCCP* 2015, **17**, 963
V. Venuti et al. PCCP 2015, *17,* 10274

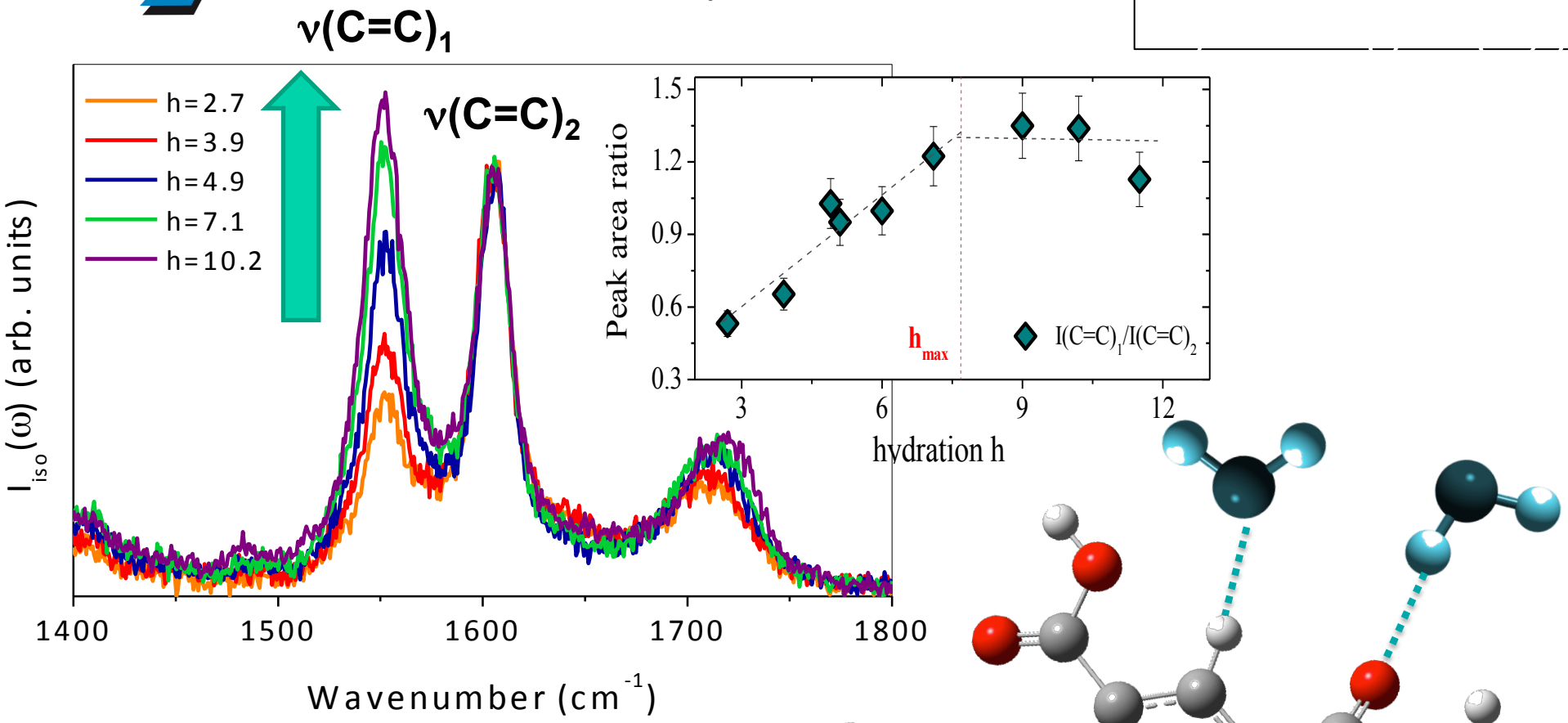


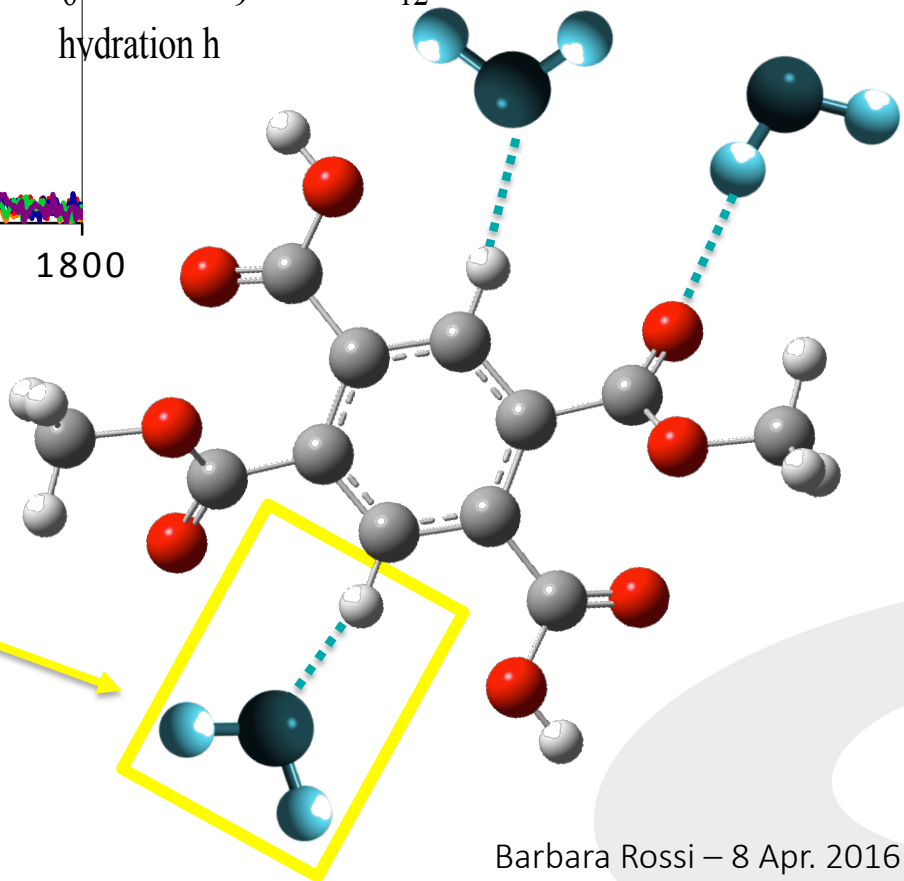

Theo. Raman activity

Theo. IR Intensity



# Hydration-dependence of Raman spectra

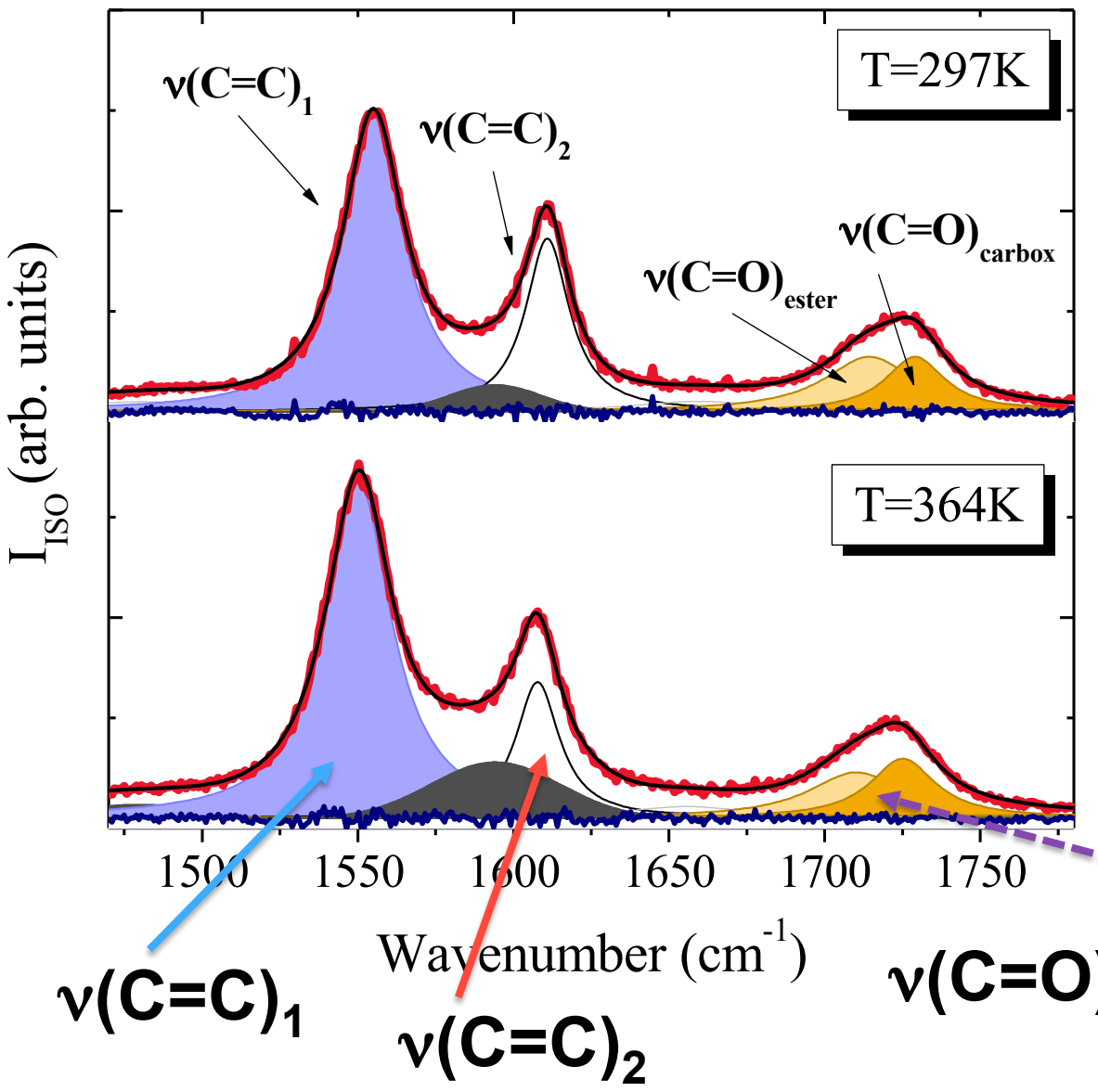


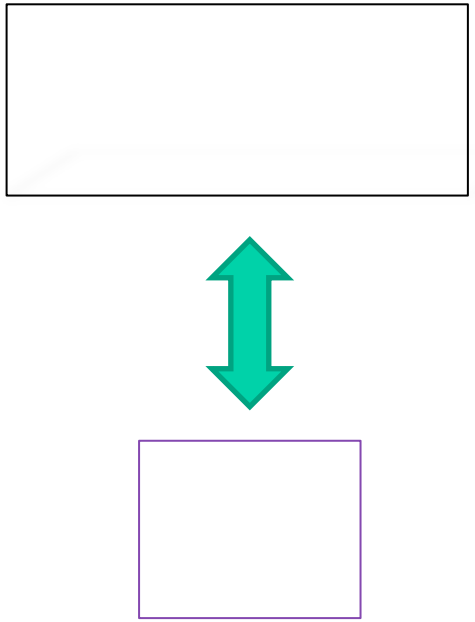



*C–H…O–H non-conventional hydrogen bond with $H_2O$*

D'Amico et al., JPCB 2012, 116, 1321
B. Rossi, et al. *PCCP* 2015, **17**, 963

# Kubo-Anderson line shape analysis



*collision rate of the molecules in the liquid phase on the vibrating groups*

**ν(C=C)$_1$**

**ν(C=C)$_2$**

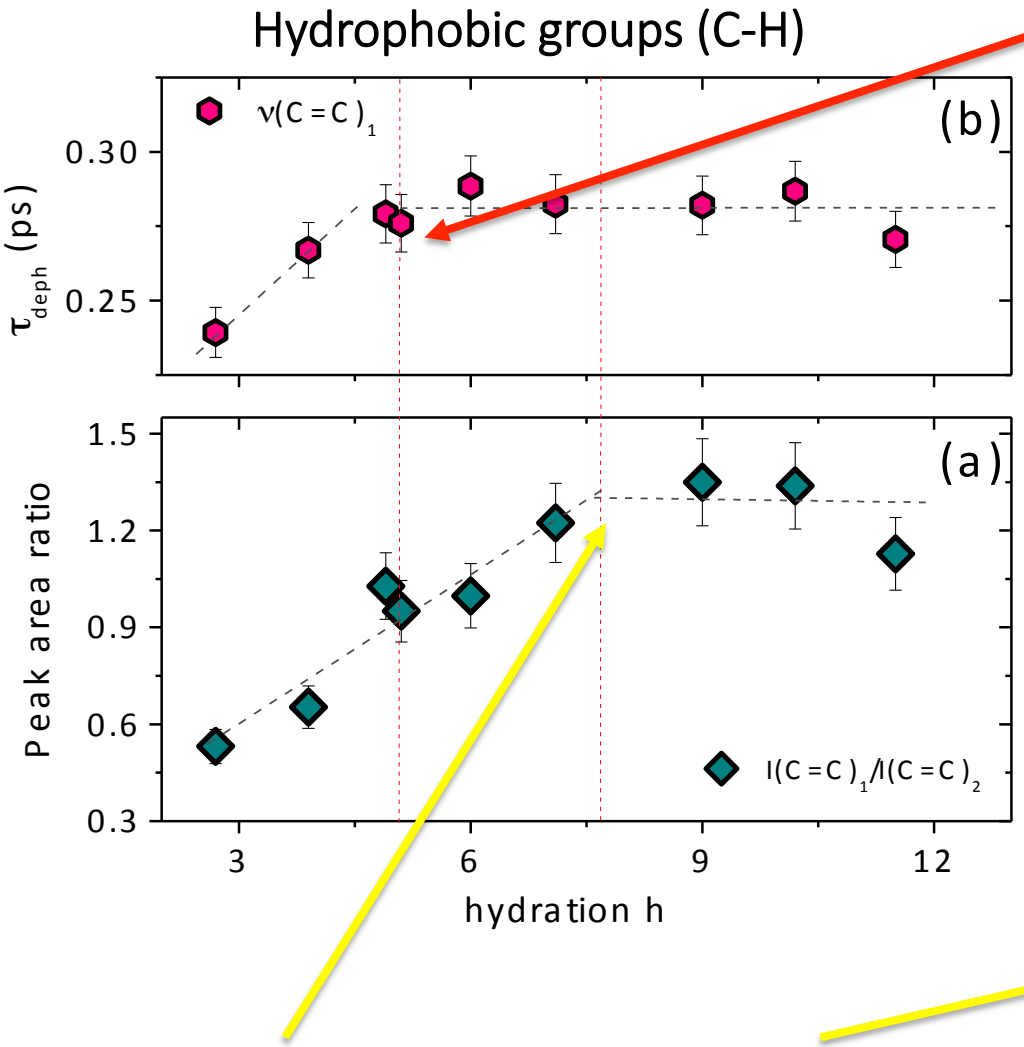
**ν(C=O)+HOH bend. $H_2O$**

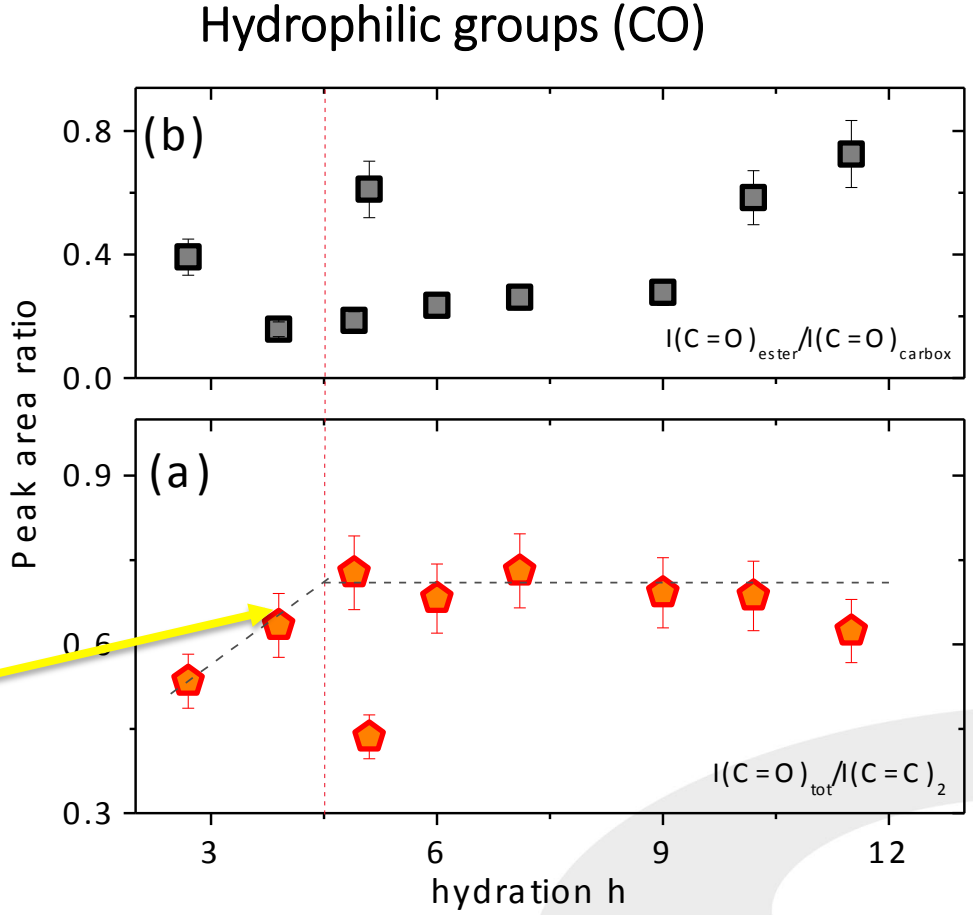
B. Rossi, et al. *PCCP* 2015, **17**, 963
F. D'Amico et al., JPCB 2012, 116, 1321
F. D'Amico, B. Rossi et al. PCCP 2015, **17**, 10987

# *Dynamic perturbation of $H_2O$ on polymer groups*

B. Rossi, et al. *PCCP* 2015, **17**, 963

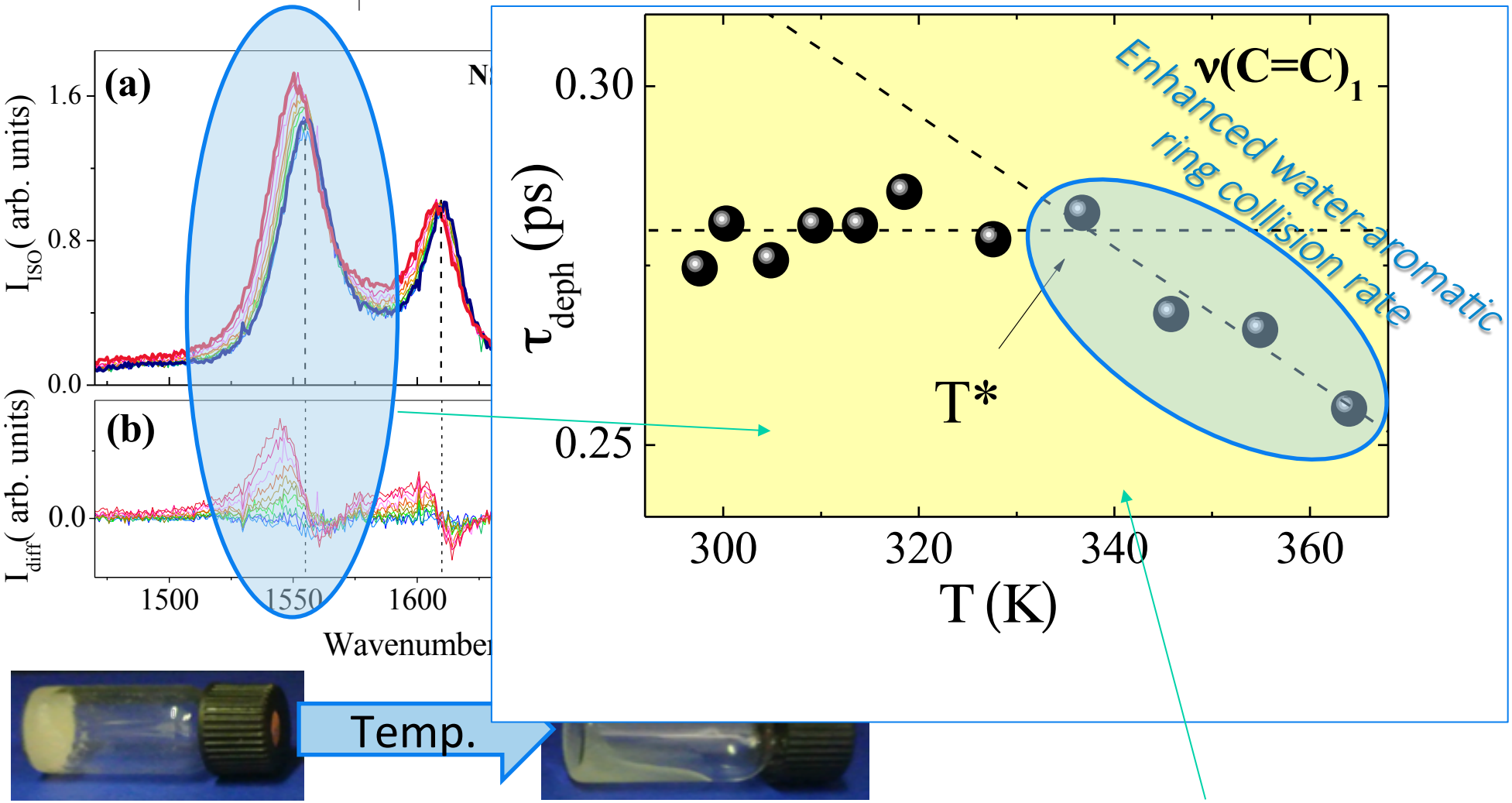
*becomes maximum at h corresponding to cross-over hydration level*




*Extension of $H_2O$ perturbation on polymer groups*

# Thermo-activation of NS hydrogel




*Increased dynamic perturbation of water around the hydrophobic groups, i.e. increased solvation of the system*

# *pH- dependence*

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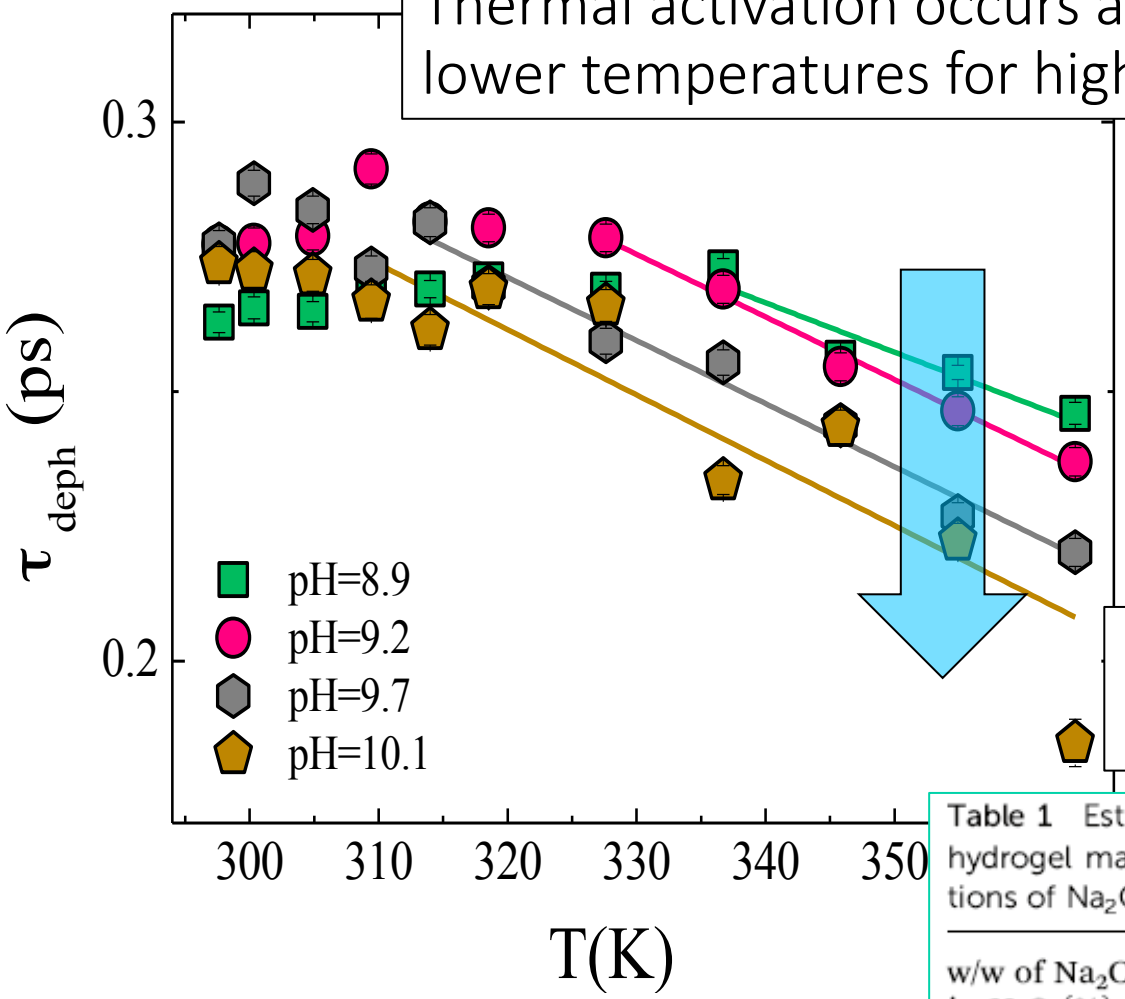
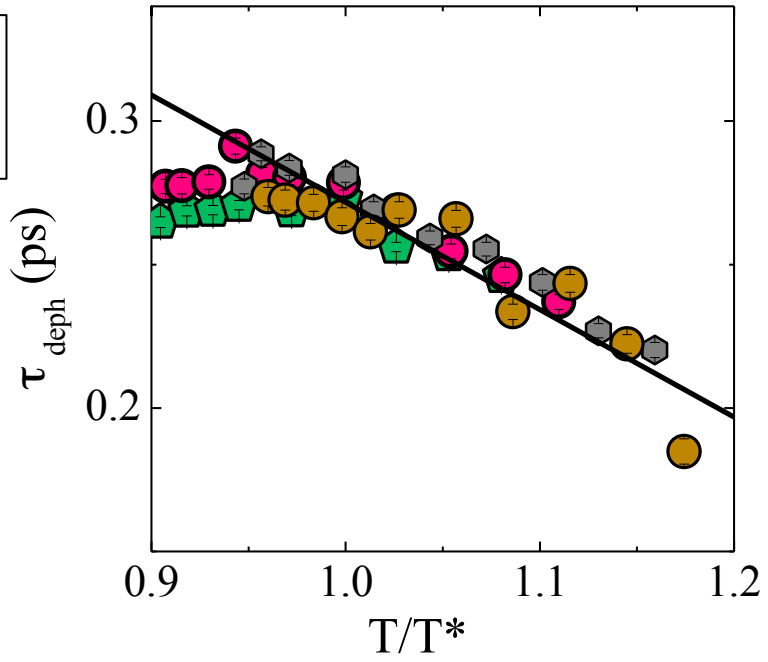
Thermal activation occurs at lower temperatures for high pH



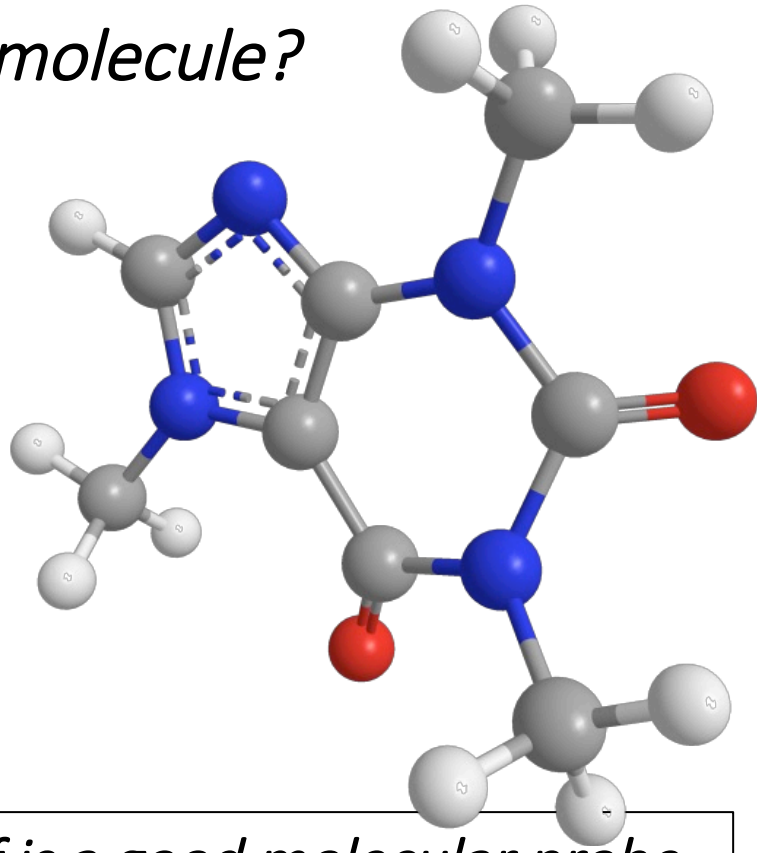

*increased accessibility of water molecules to the hydrophobic sites*

Table 1 Estimated values of $T^*$ as a function of pH measured in the NS hydrogel matrix, obtained by hydrating β-CDPMA14 with aqueous solutions of $Na_2CO_3$ at different concentrations

| w/w of $Na_2CO_3$ in $H_2O$ (%) | Measured pH of gel | Estimated $T^*$ (K) |
|---|---|---|
| 10 | 8.9 | 337 |
| 15 | 9.2 | 328 |
| 20 | 9.7 | 314 |
| 25 | 10.1 | 310 |

B. Rossi, et al. *Soft Matter* 2015, **11**, 5862

# Why caffeine as guest molecule?



Elettra Sincrotrone Trieste

CHEMISTRY OF MATERIALS

Article

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## Rationale of Drug Encapsulation and Release from Biocompatible Porous Metal–Organic Frameworks

Denise Cunha,[†] Mouna Ben Yahia,[†,‡] Shaun Hall,[‡] Stuart R. Miller,[†] Hubert Chevreau,[†] Erik Elkaïm,[§] Guillaume Maurin,[‡] Patricia Horcajada,*[,†] and Christian Serre*[,†]

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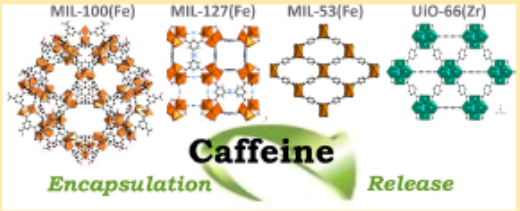
Supporting Information

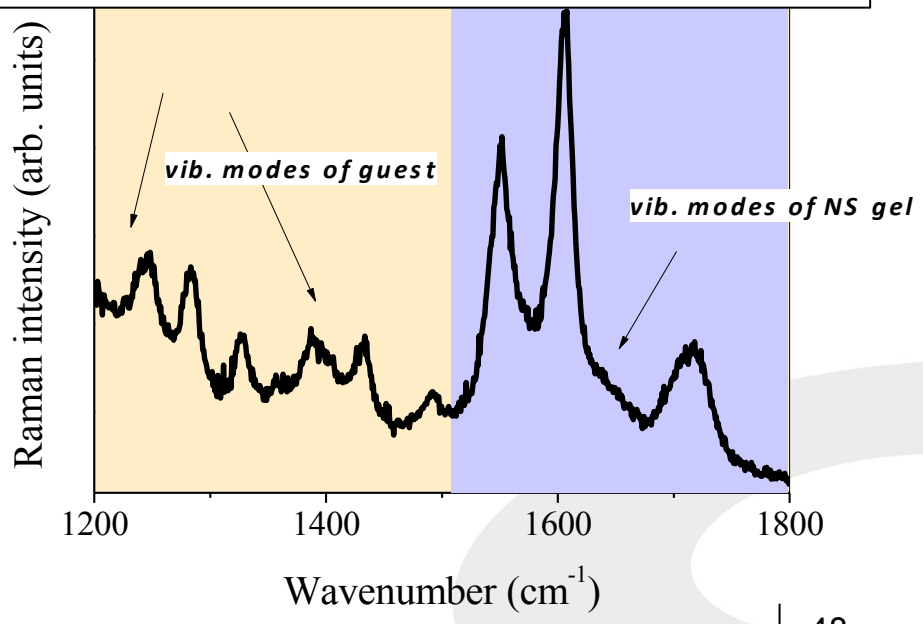
**ABSTRACT:** A joint experimental and computational systematic exploration of the driving forces that govern (i) encapsulation of active ingredients (solvent, starting material dehydration, drug/material ratio, immersion time, and several consecutive impregnations) and (i) its kinetics of delivery (structure, polarity, ...) was performed using a series of porous biocompatible metal–organic frameworks (MOFs) that bear different topologies, connectivities, and chemical compositions. The liporeductor cosmetic caffeine was selected as the active molecule. Its encapsulation is a challenge for the cosmetic industry due to its high tendency to crystallize leading to poor loadings (<5 wt %) and uncontrolled releases with a subsequent low efficiency. It was evidenced that caffeine entrapping reaches exceptional payloads up to 50 wt %, while progressive release of this cosmetic agent upon immersion in the simulated physiological media (phosphate buffer solution pH = 7.4 or distilled water pH = 6.3, 37 °C) occurred mainly depending on the degree of MOF stability, caffeine mobility, and MOF–caffeine interactions. Thus, MIL-100 and UiO-66 appear as very promising carriers for topical administration of caffeine with both spectacular cosmetic payloads and progressive releases within 24 h.




**KEYWORDS:** *MOFs, encapsulation, release, cosmetic, caffeine*

*Large interest in realizing new promising carriers for controlled topical administration of caffeine in cosmetic formulations*

*Caf is a good molecular probe*



# Thermo-activation of NS hydrogel loaded with Caf

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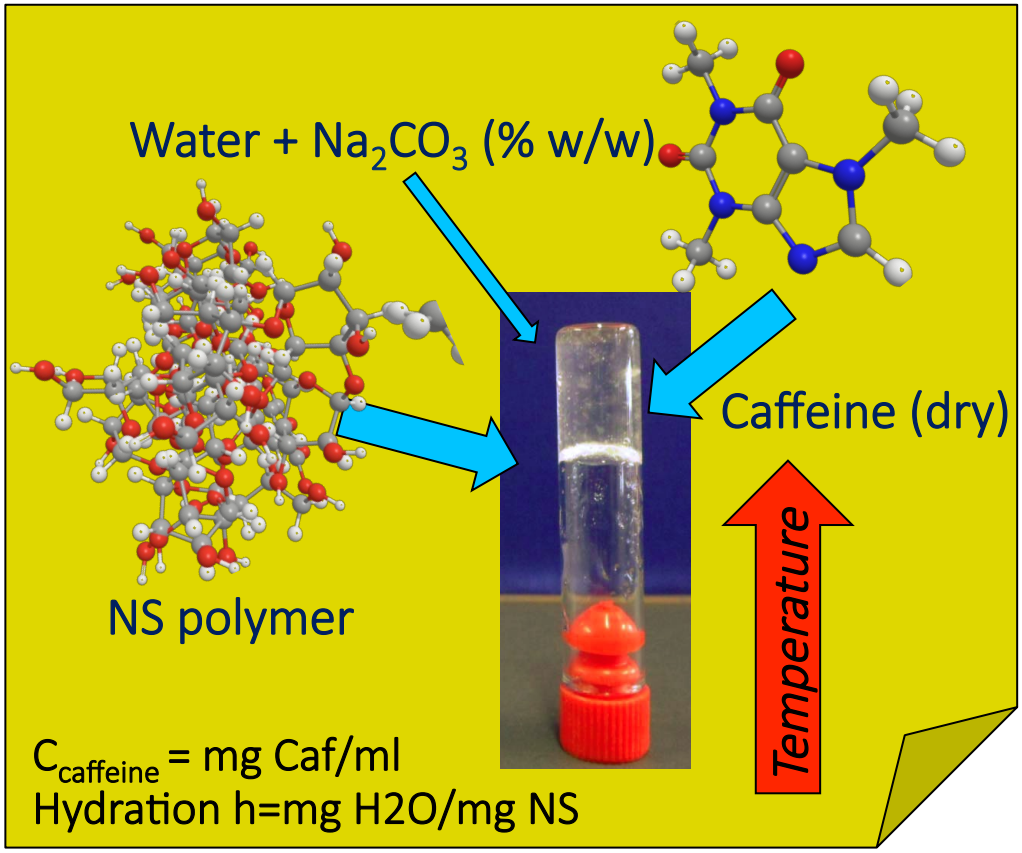


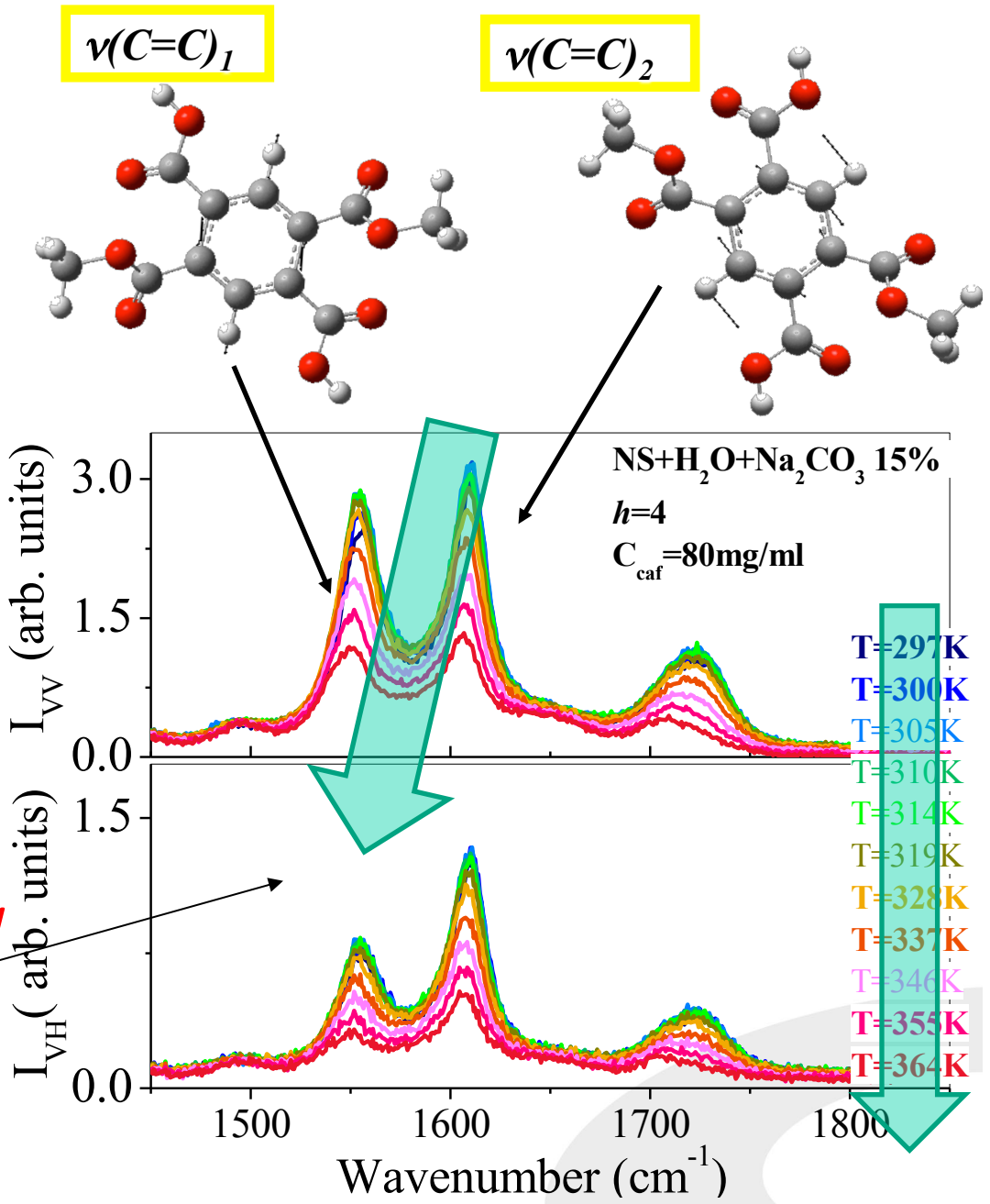


## Temperature-dependence of vibrational modes of NS polymer matrix

F. Castiglione et al. JPCB 2012, **116**, 7952
B. Rossi, et al. *PCCP* 2015, **17**, 963

# Analysis of drug-free spectra

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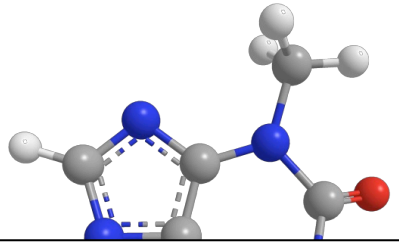

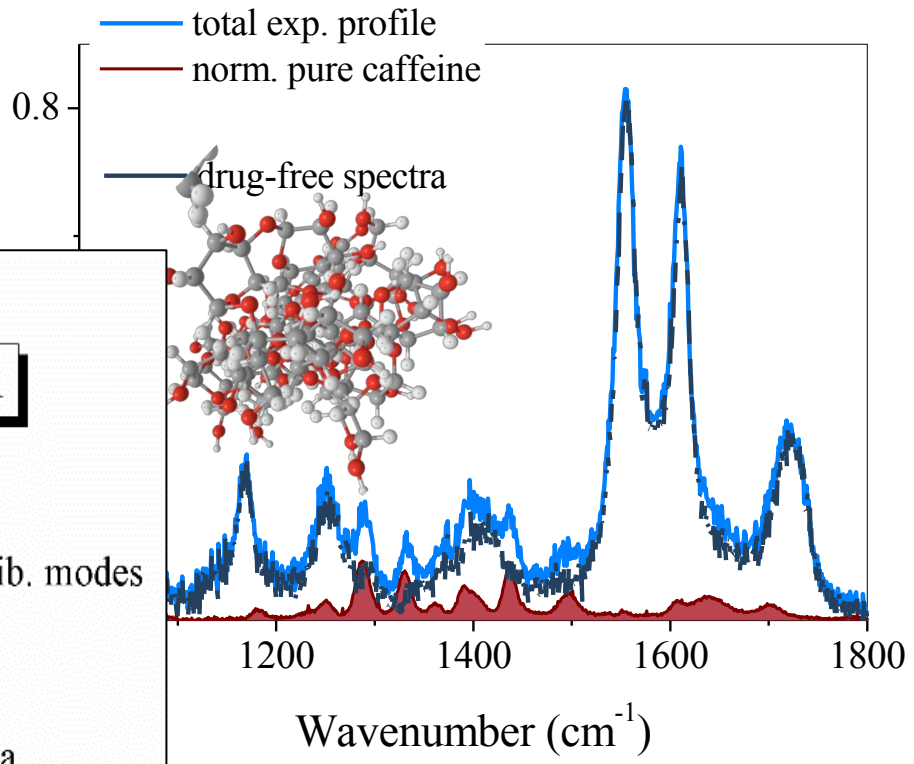


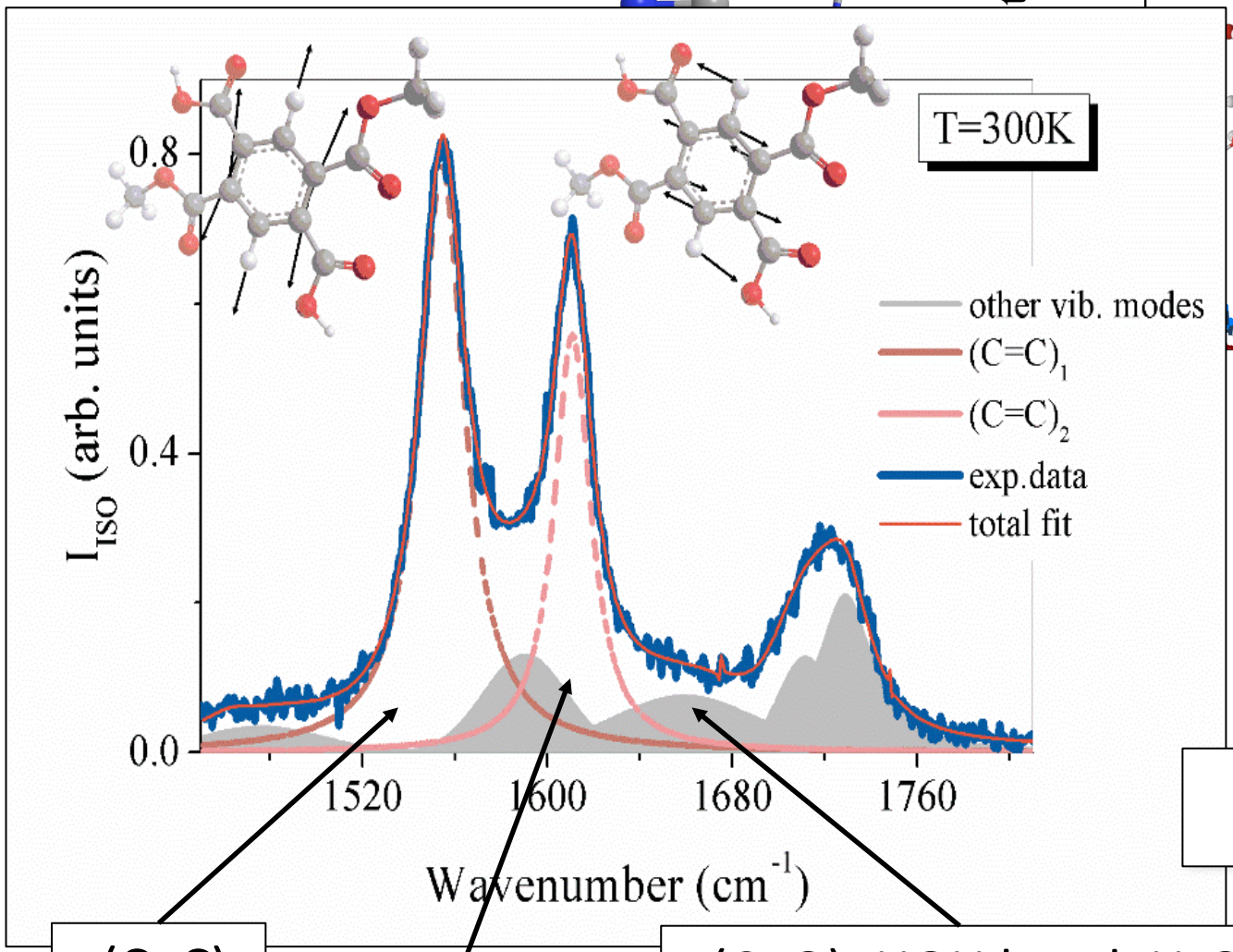


inverse of collision rate of the liquid molecules on the vibrating groups

$\nu(C=C)_1$

$\nu(C=C)_2$

$\nu(C=O)$+HOH bend. $H_2O$

B. Rossi, et al. *PCCP* 2015, **17**, 963
F. D'Amico et al., JPCB 2012, 116, 1321
F. D'Amico, B. Rossi et al. PCCP 2015, **17**, 10987

# *Temperature-dependence of dephasing time*

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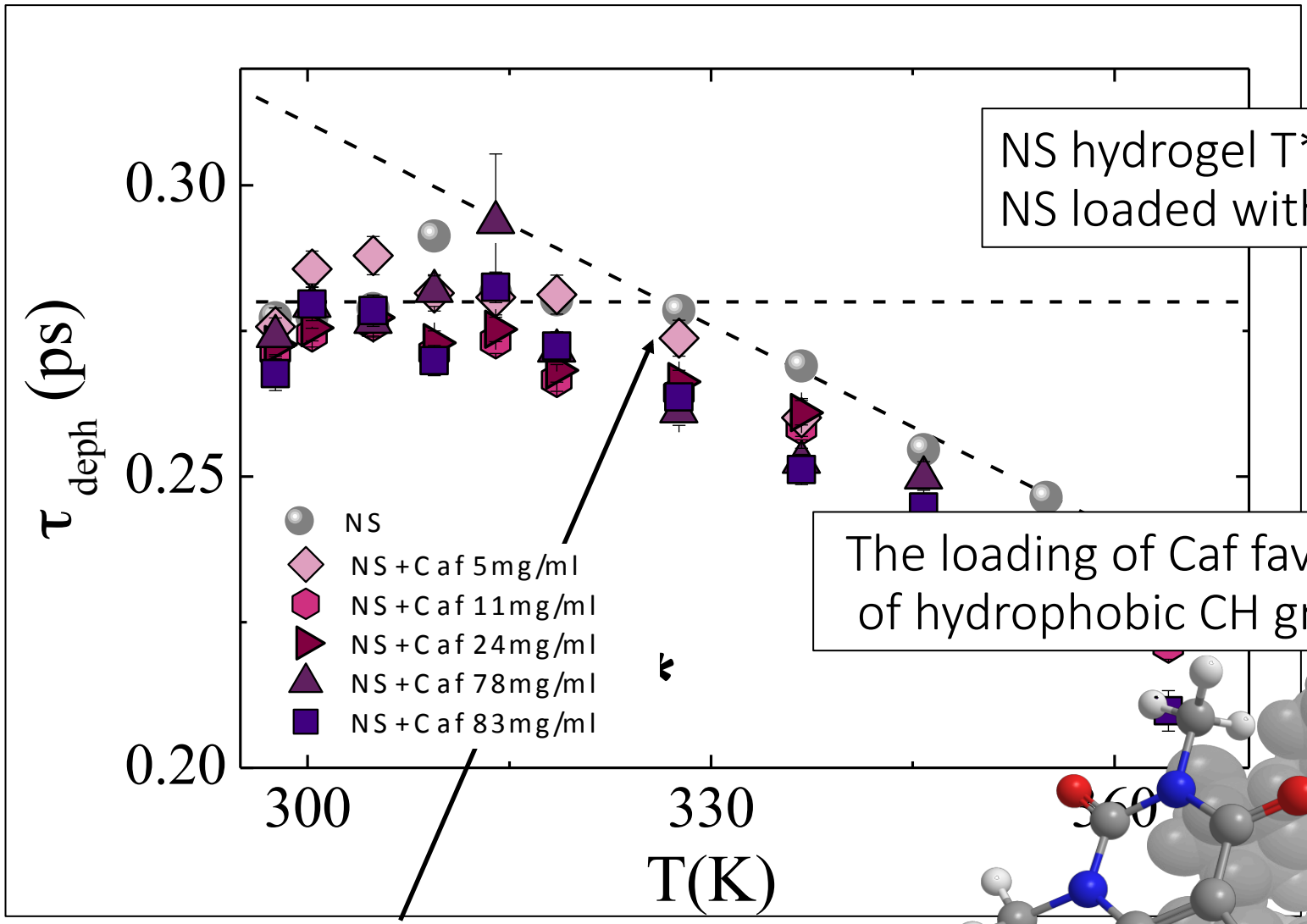
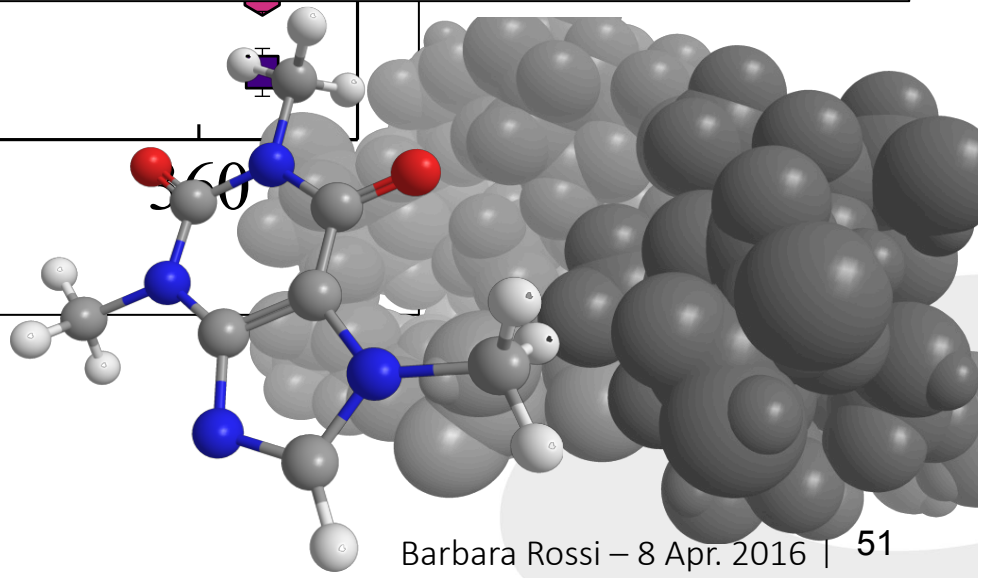



NS hydrogel T*=328K
NS loaded with Caf T*≈315K

The loading of Caf favours the ***solvation*** of hydrophobic CH groups of NS matrix



*Activation temperature T* describes hydrophobic/hydrophilic behaviour of CH groups*

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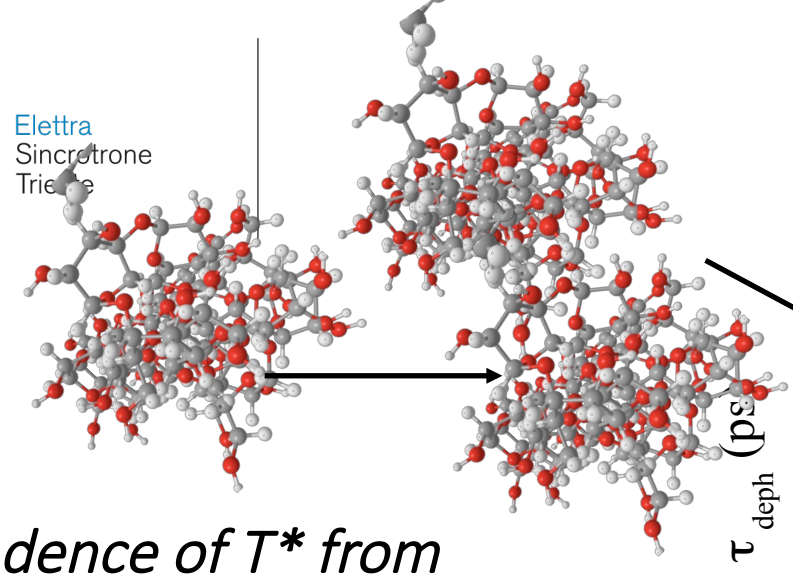
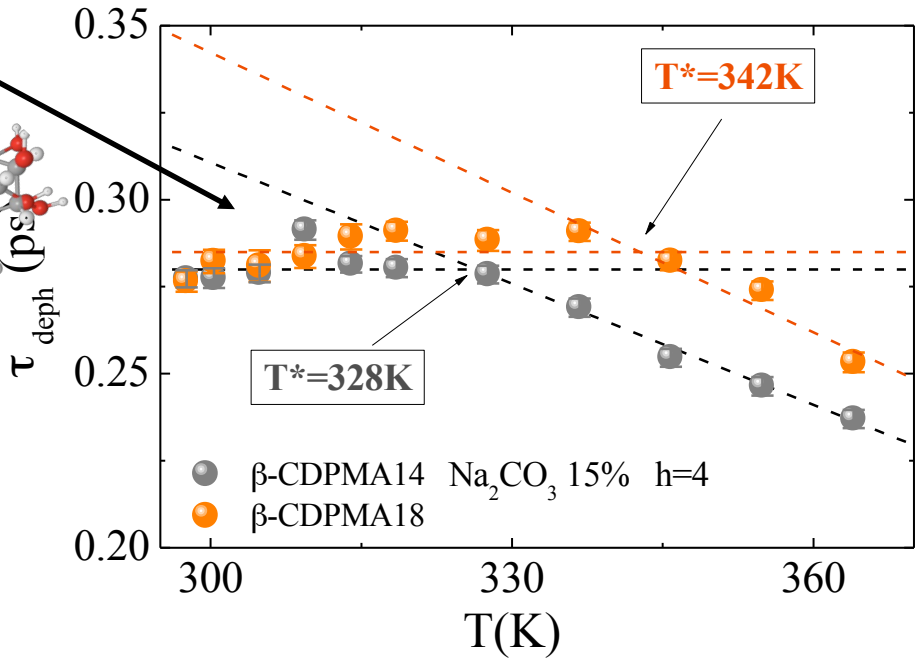
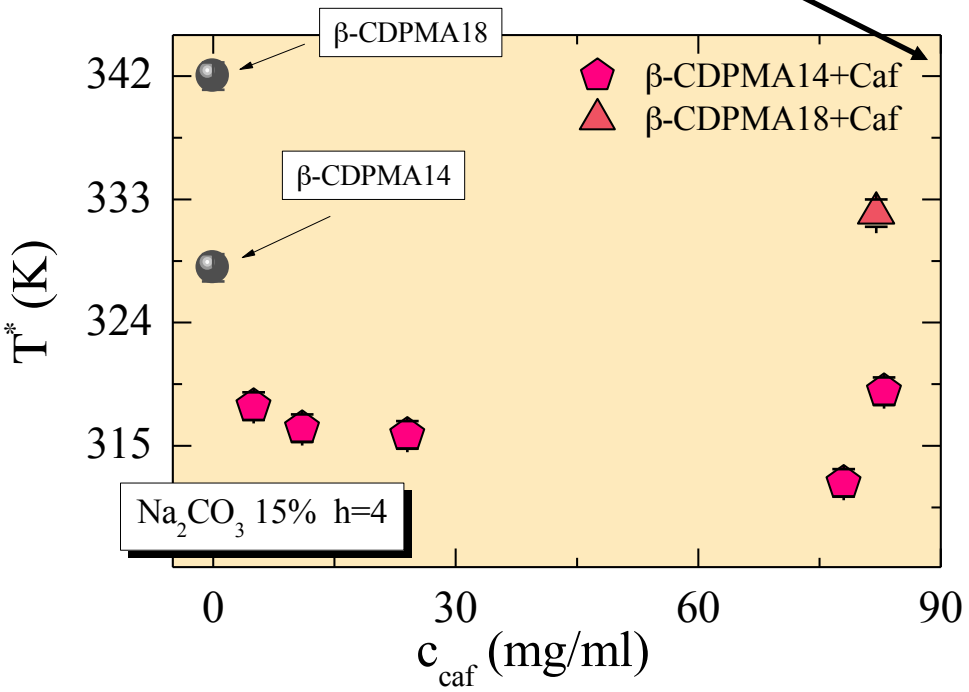
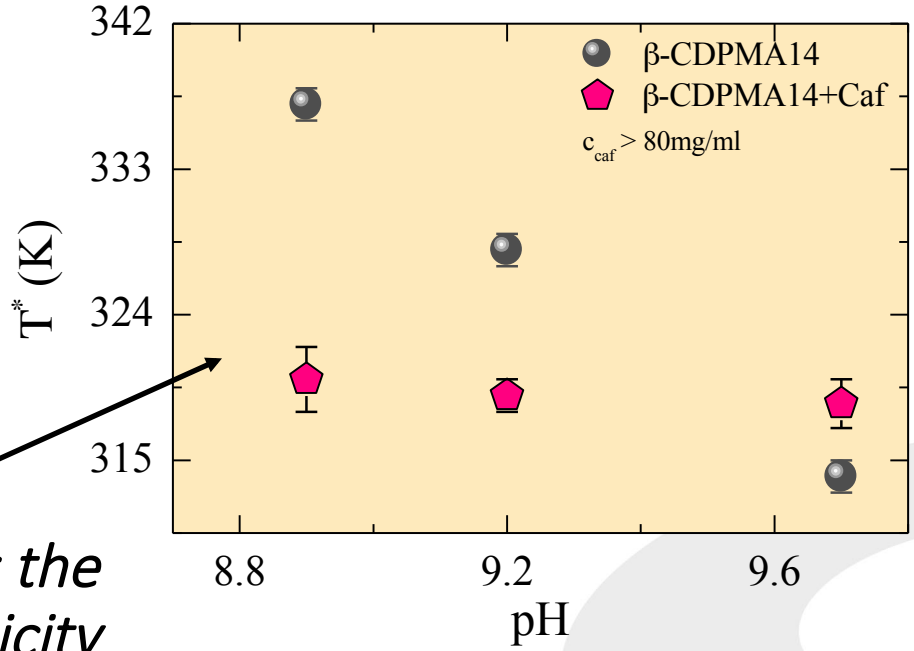


## *Reticulation increases the hydrophobicity of NS polymer*

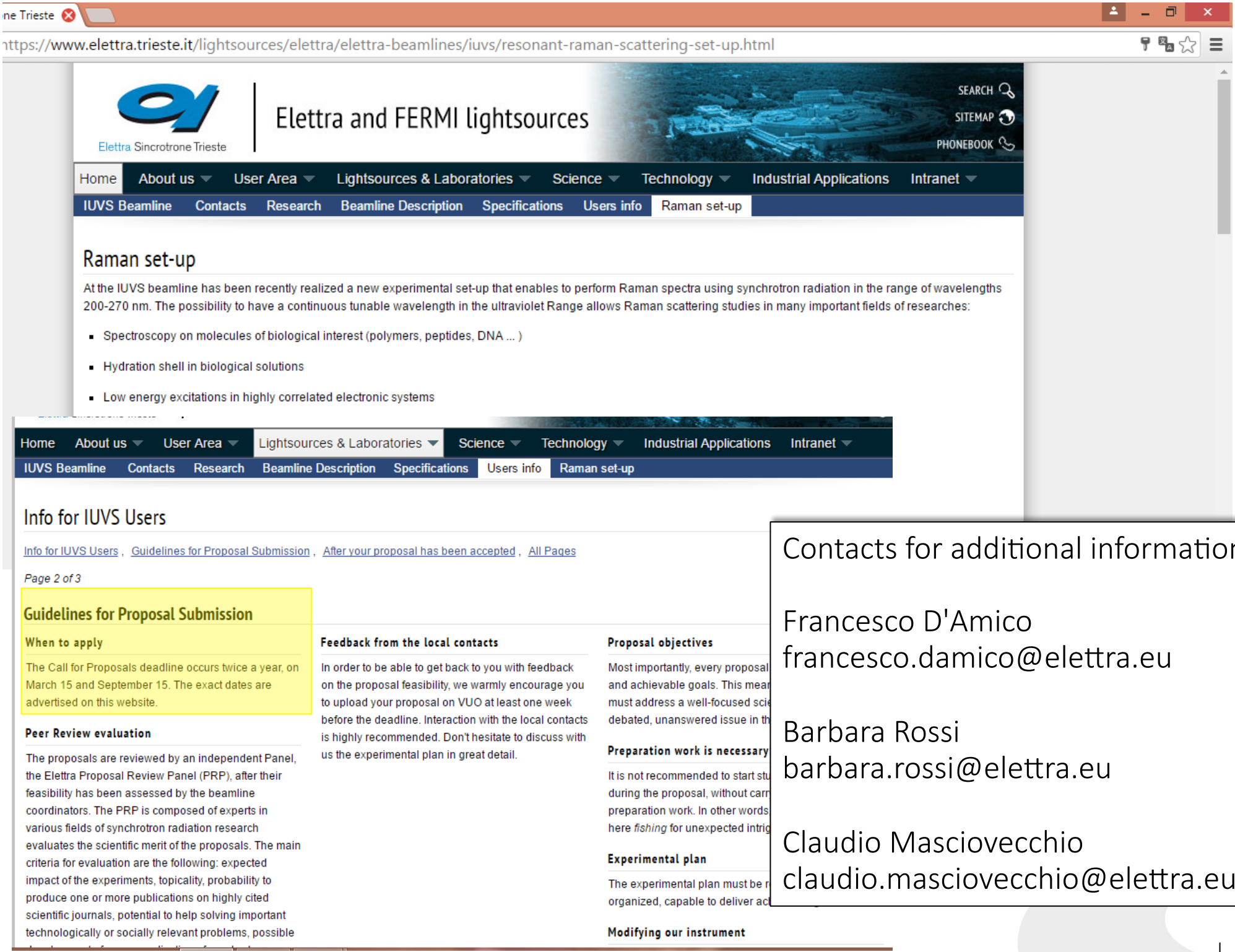



## *Slight dependence of T* from concentration of caffeine*




## *The addition of Caf balances the pH-effects on hydrophobicity*

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# Thank you for your attention

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