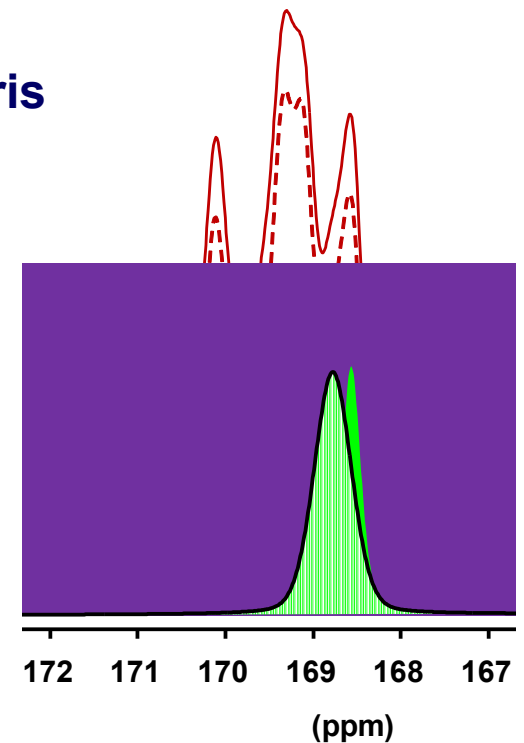
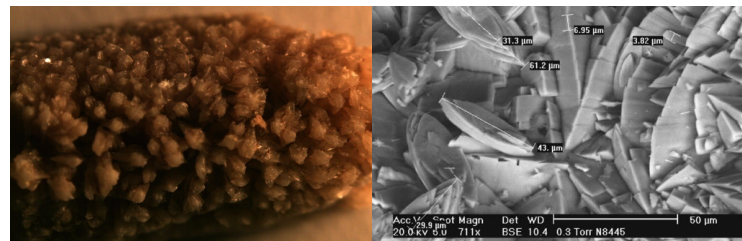


New Potentialities of NMR and DNP for the Study of Biomaterials: Experiments and Theory

C. Bonhomme*, W. Teh, C. Leroy, A. Rankin

Laboratoire de Chimie de la Matière Condensée de Paris

Sorbonne Université, Paris, France



Pathological calcifications (kidney stones, KS)

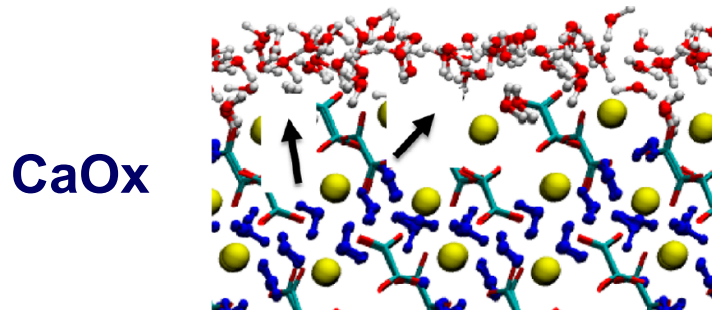
a major societal/health problem worldwide
(in France, related costs *per year* > 800 millions €)

an intrinsic structural/chemical complexity

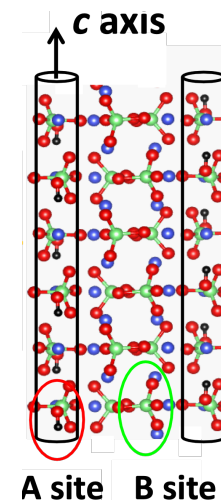
- minerals
- fatty acids, triglycerides, proteins
- ... ↔ Hybrid organic/inorganic materials

Ca Oxalates (Mono-, Di-, Tri-hydrate, CaOx)

Ca Phosphates (hydroxyapatite, HAp)



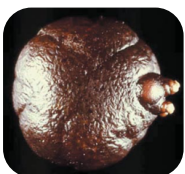
HAp



Pathological calcifications (kidney stones, KS)



Tenon hospital, Paris



a major societal/health problem worldwide
(in France, related costs per year > 800 millions €)

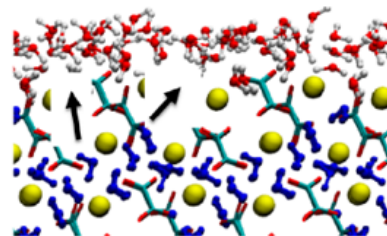
an intrinsic structural/chemical complexity

- minerals
- fatty acids, triglycerides, proteins
- ... ↔ Hybrid organic/inorganic materials

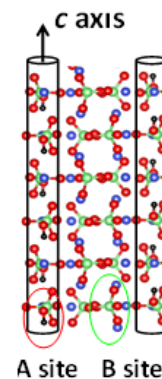
Ca Oxalates (mono-, di-, tri-hydrate)

Ca Phosphates (hydroxyapatite, HAp)

CaOx



HAp



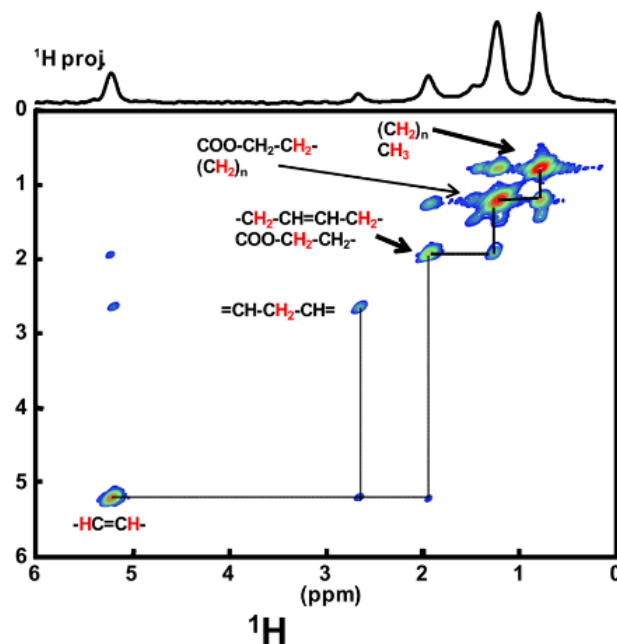
→ diagnosis

→ prevention



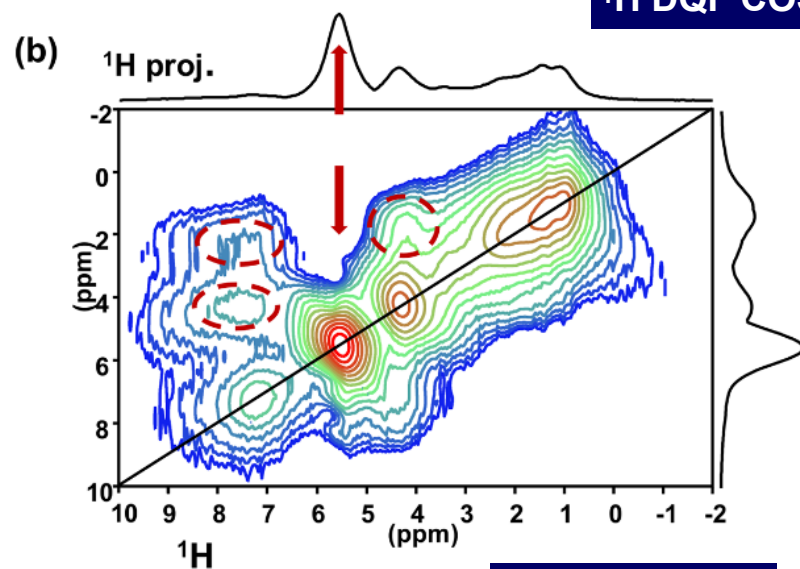
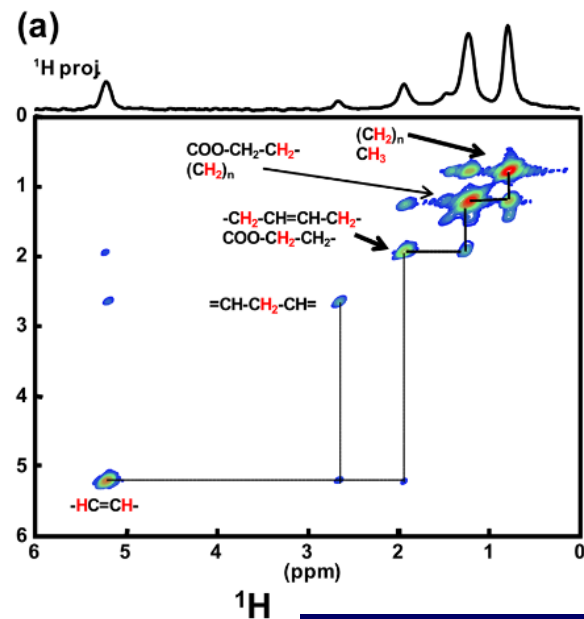
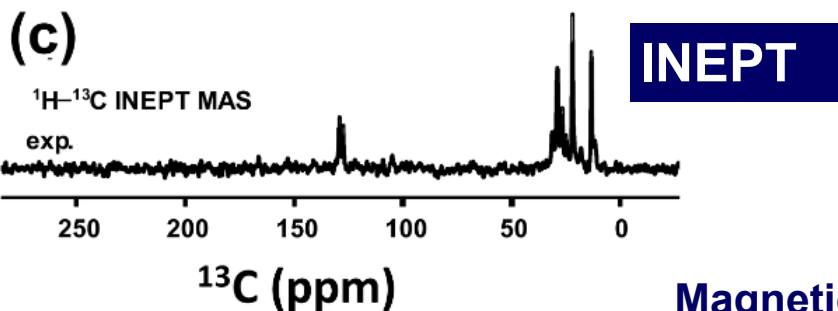
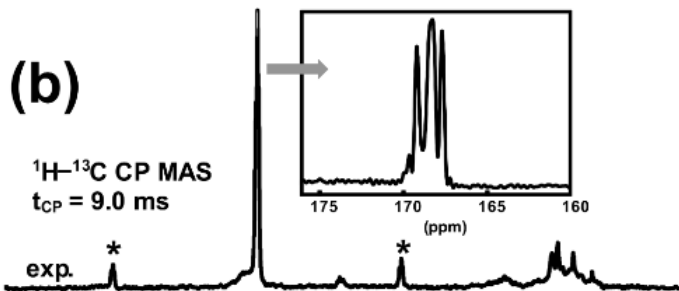
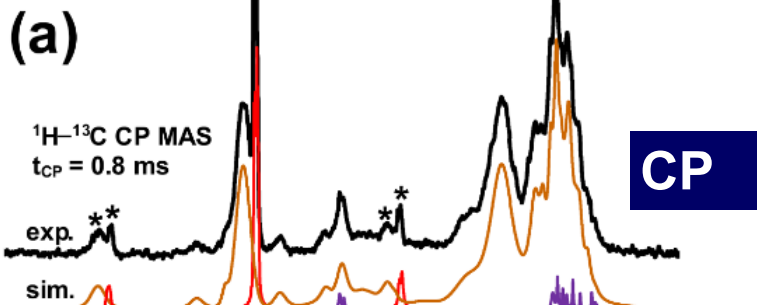
NMR / DNP ?

- NMR as a unique platform of characterization
- *in situ* transformations, *artificial* kidney stones
- Sensitivity enhancement
- DNP crystallography



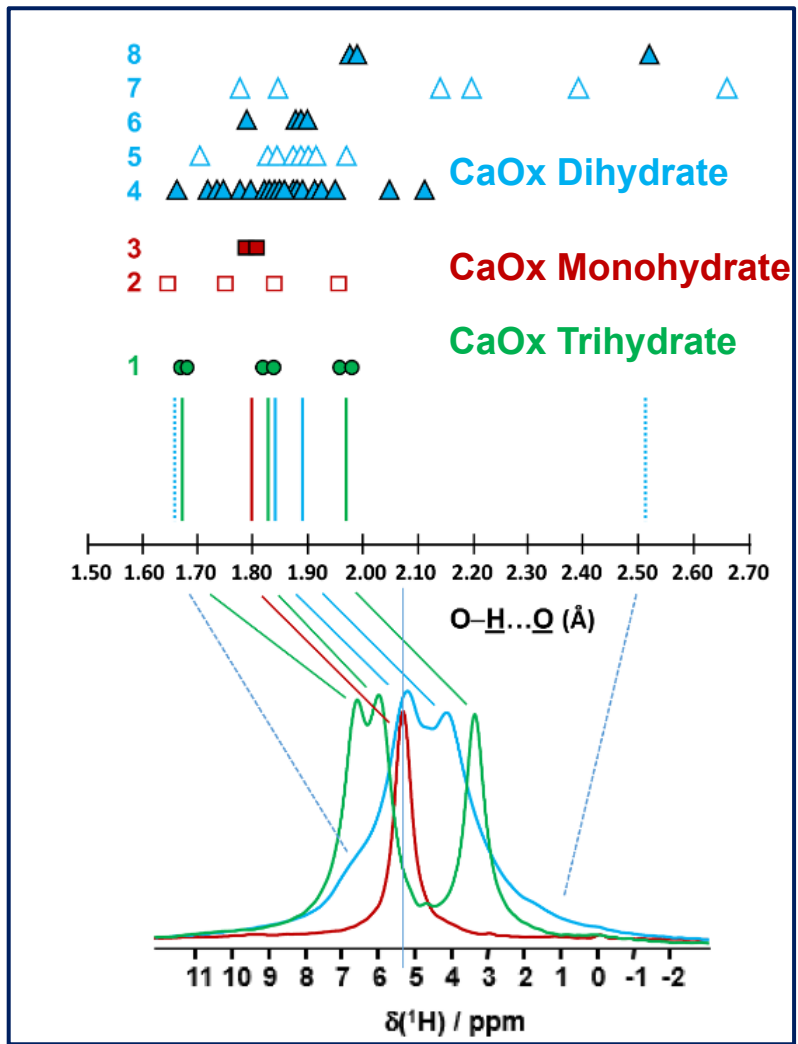
Structure, dynamics and interfaces in KS

^{13}C CP MAS, ^1H DQ MAS NMR, dynamics, interfaces

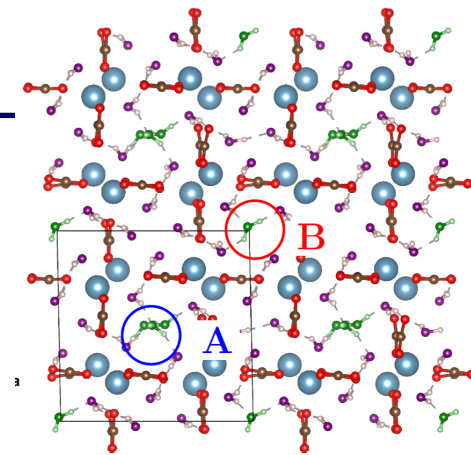


Fast characterization of KS by ^1H solid state NMR

^1H DUMBO MAS NMR & local dynamics

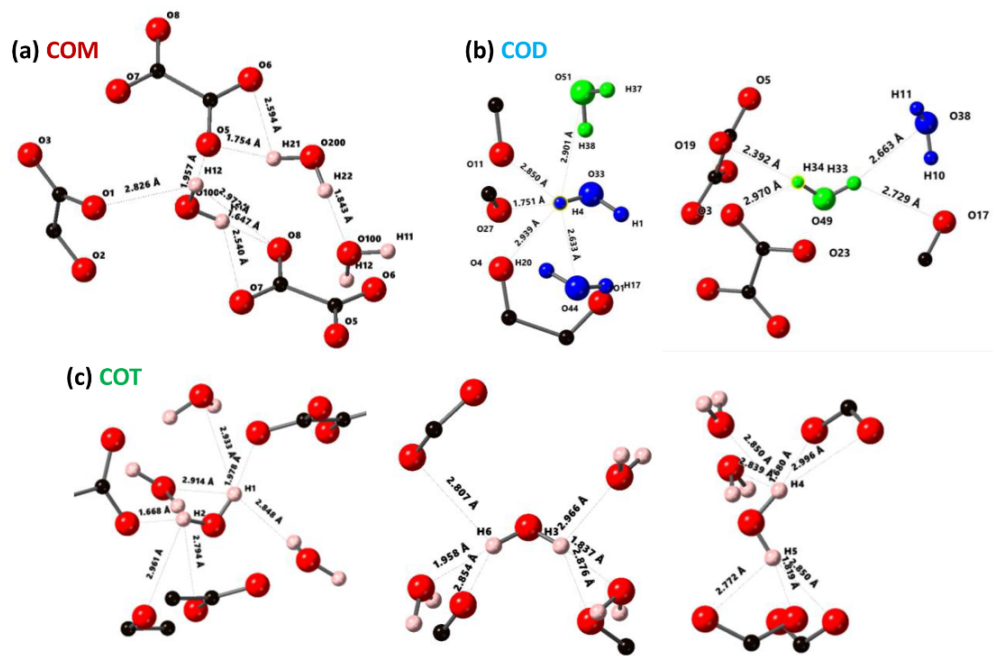


Sakellariou,
Emsley *et al.*...



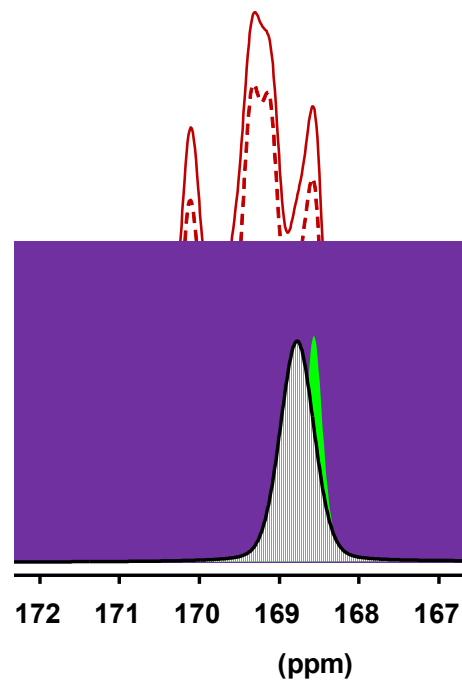
CaOx Dihydrate: a zeolite (natural MOF)

DFT optimized



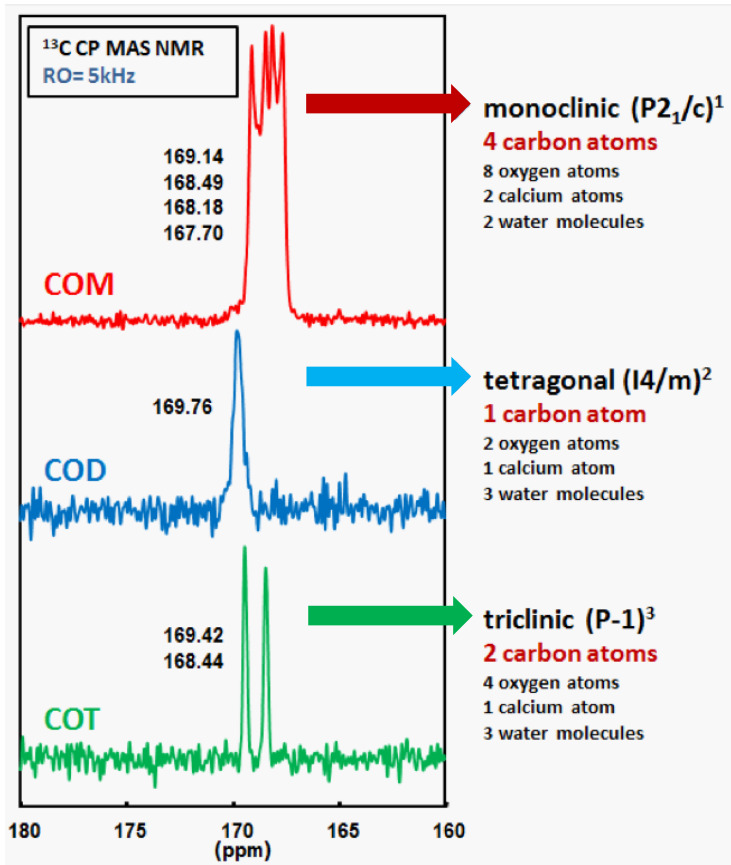
H-bonds networks

- NMR as a unique platform of characterization
- ***in situ* transformations, *artificial* kidney stones**
- Sensitivity enhancement
- DNP crystallography



In situ transformations (700 MHz, Φ 2.5 mm)

^{13}C CP MAS @ 5 kHz

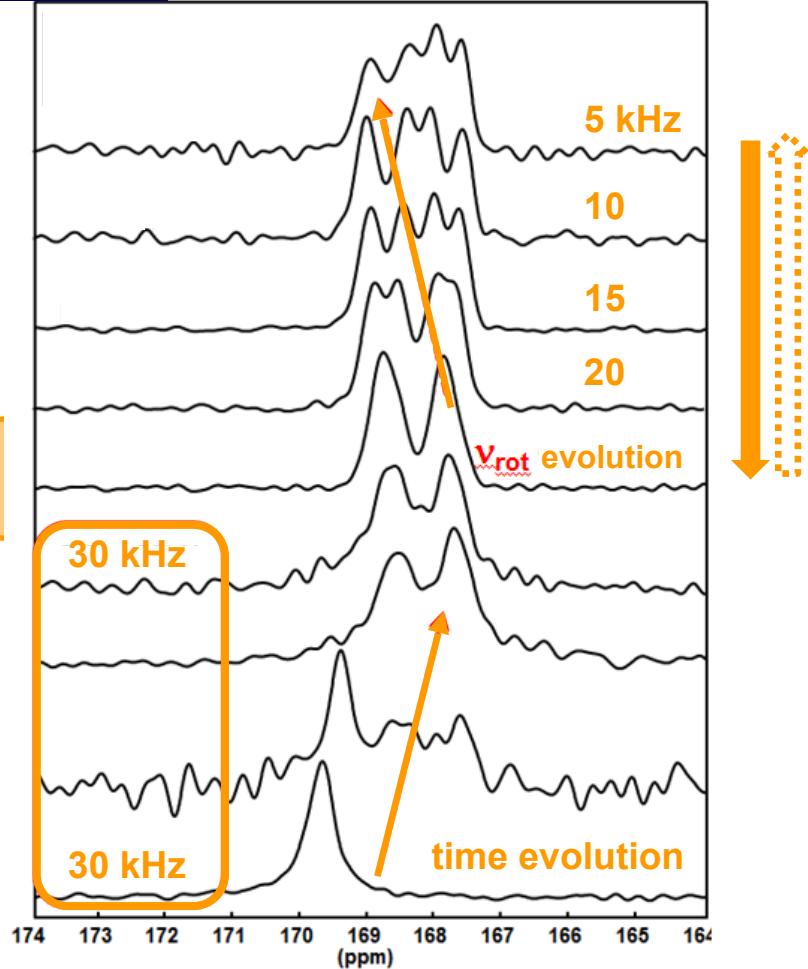
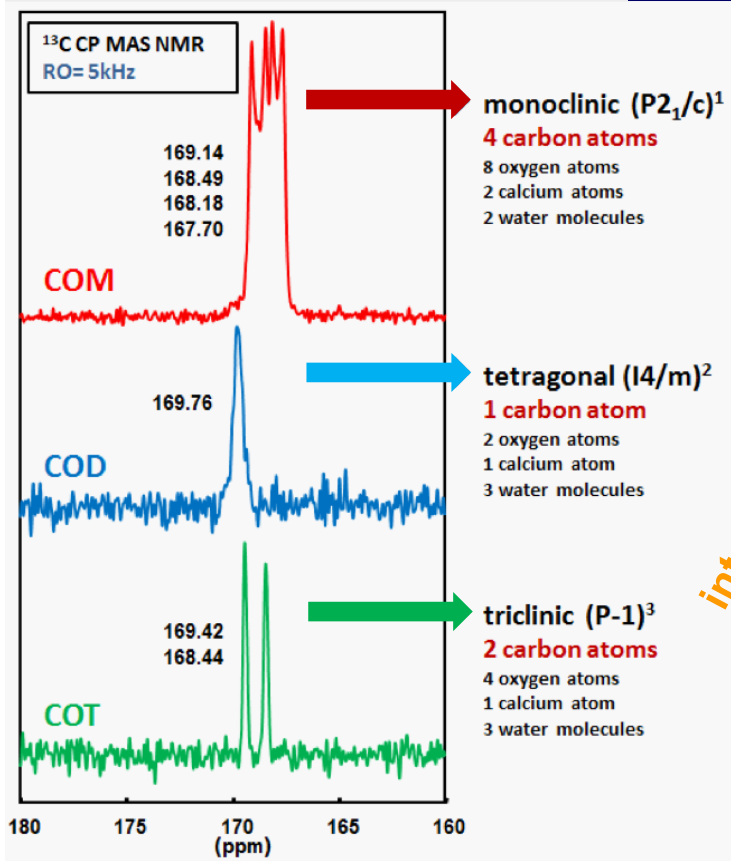


In situ transformations (700 MHz, Φ 2.5 mm)

^{13}C CP MAS @ 5 kHz

^{13}C CP MAS @ 30 kHz

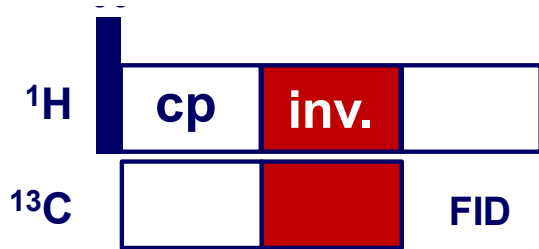
...to : CaOx Monohydrate



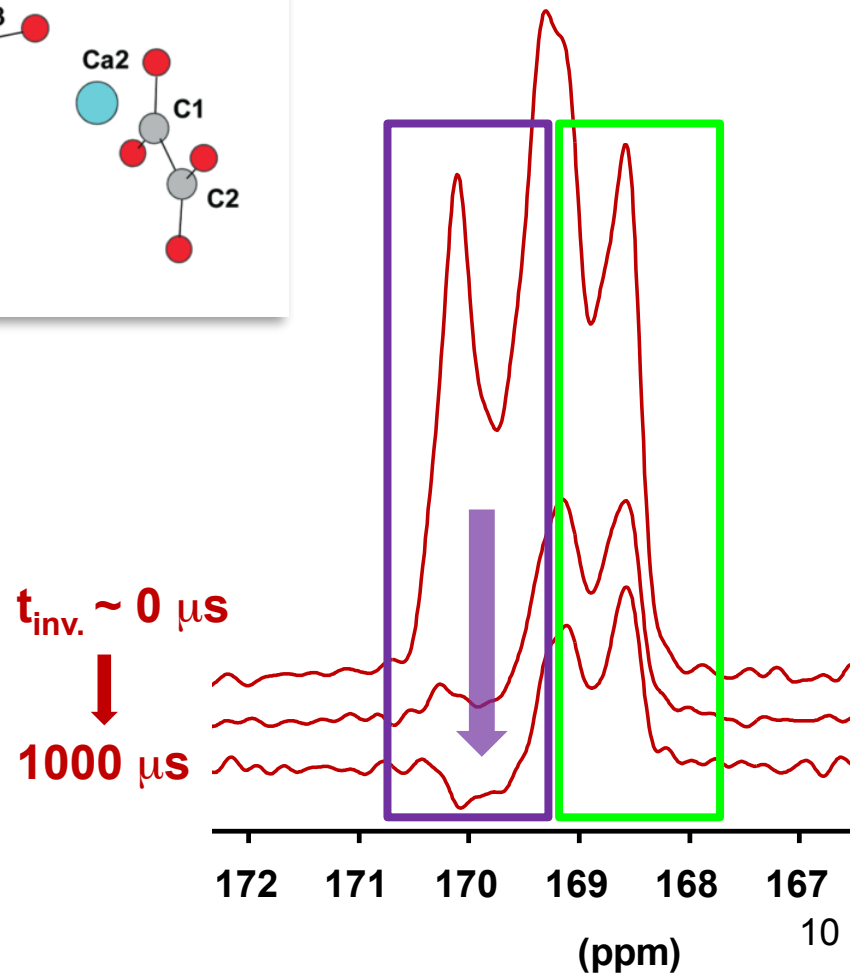
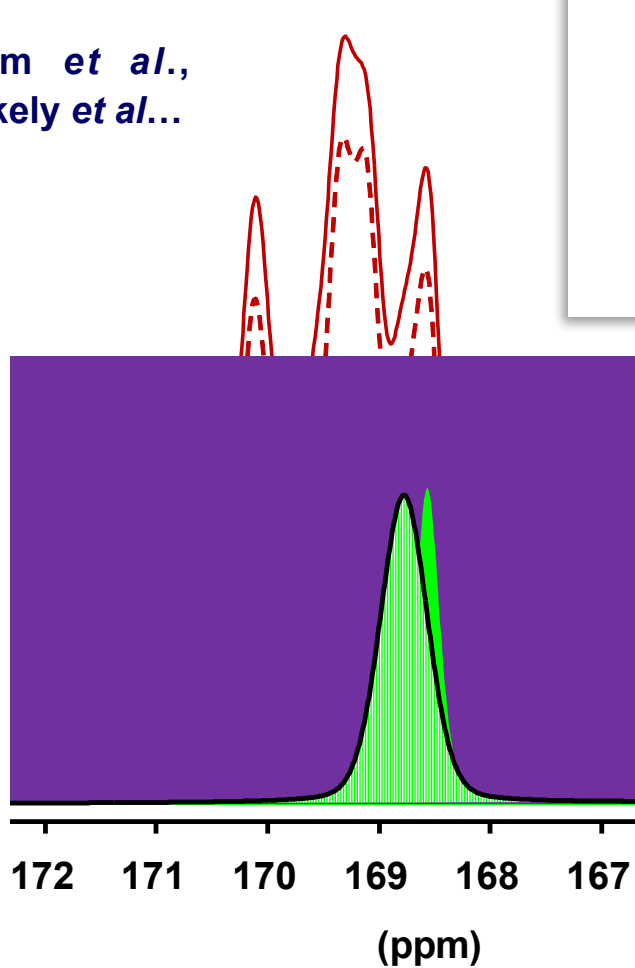
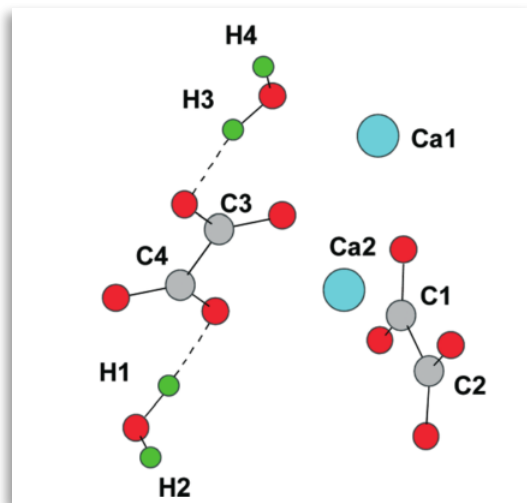
from: CaOx Dihydrate

^1H - ^{13}C spectral editing by inversion of polarization

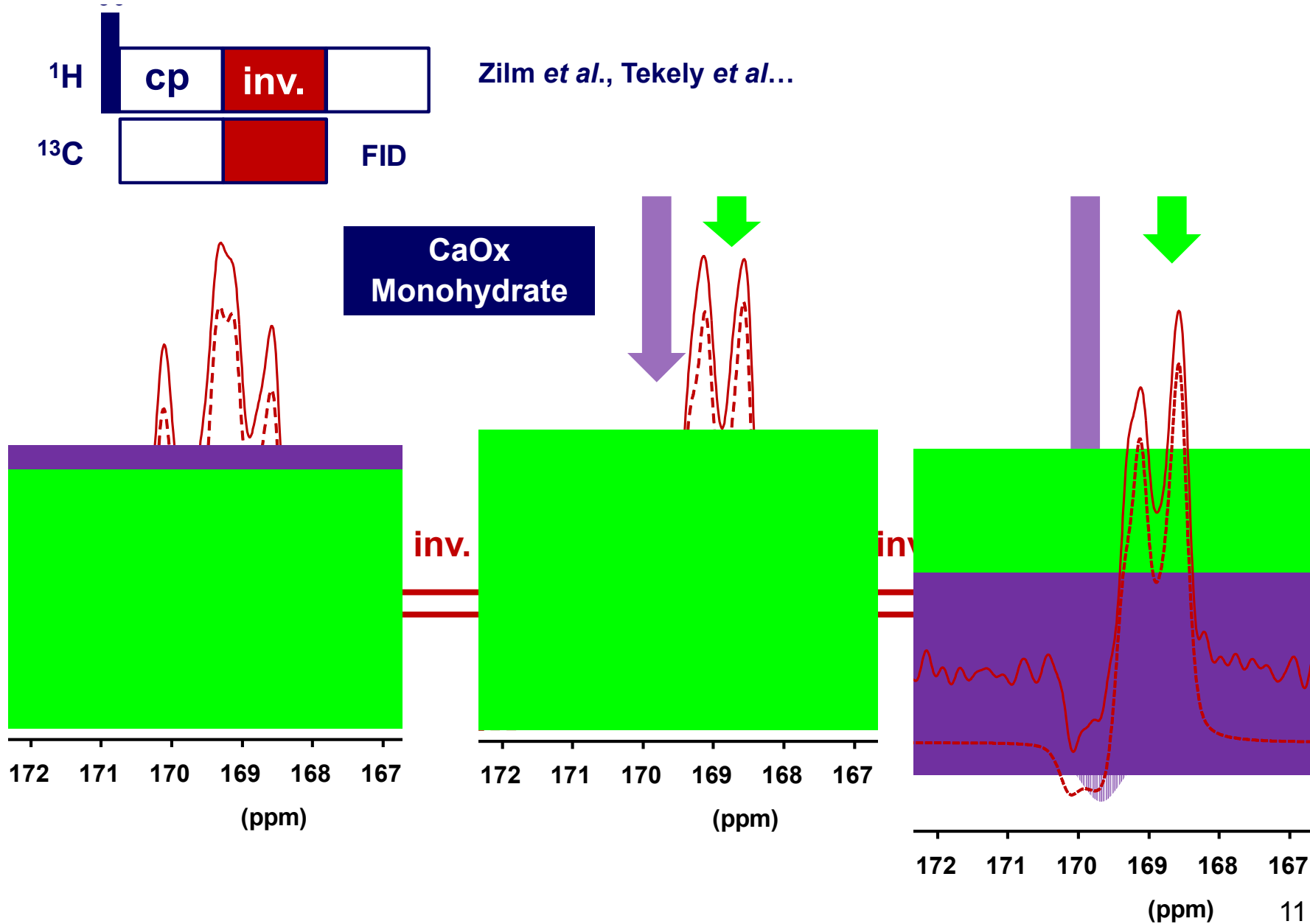
CaOx
Monohydrate



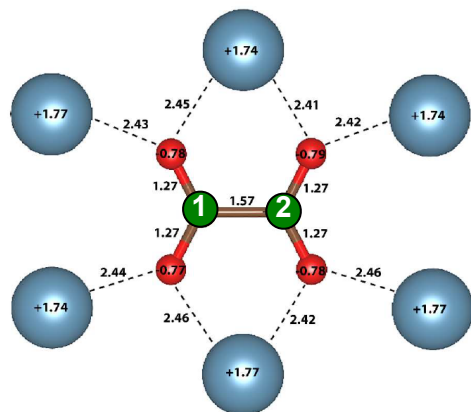
Zilm *et al.*,
Tekely *et al.*...



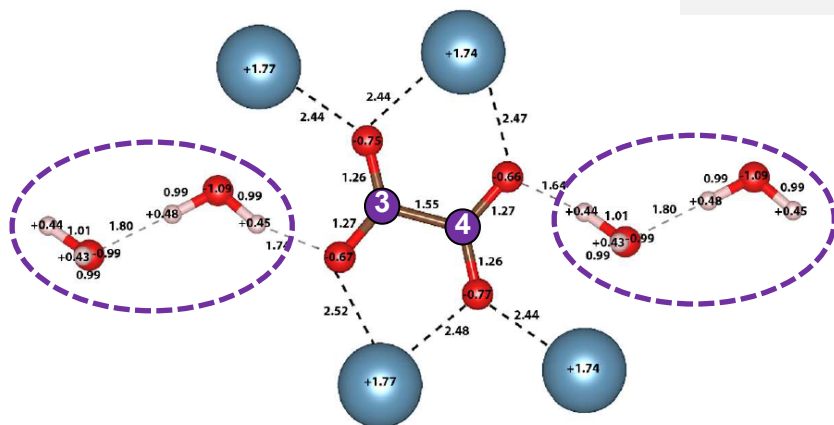
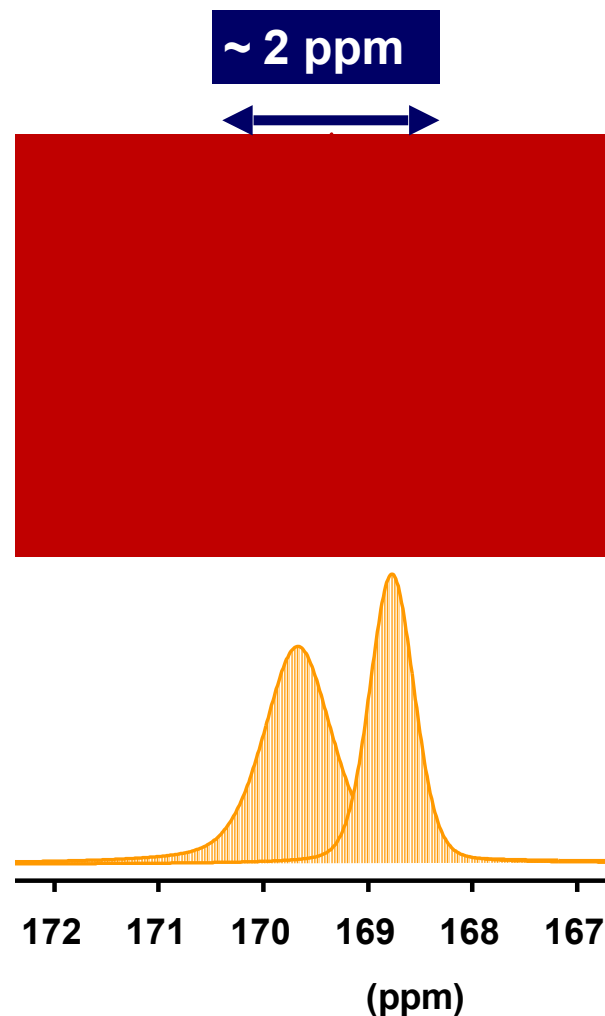
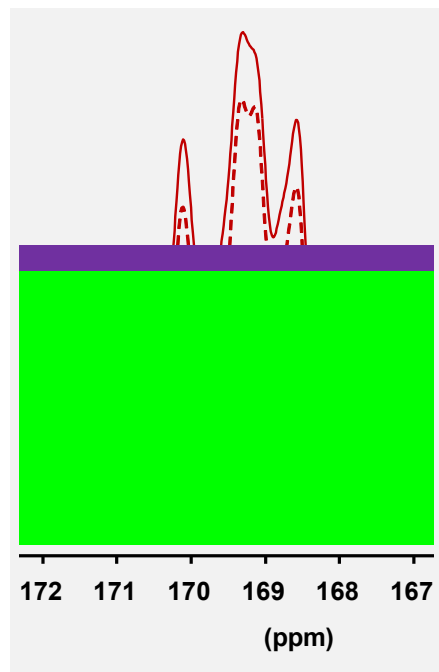
^1H - ^{13}C spectral editing by inversion of polarization



Full interpretation of the ^{13}C CP MAS NMR spectra



$P2_1/c$: C_1, C_2, C_3, C_4

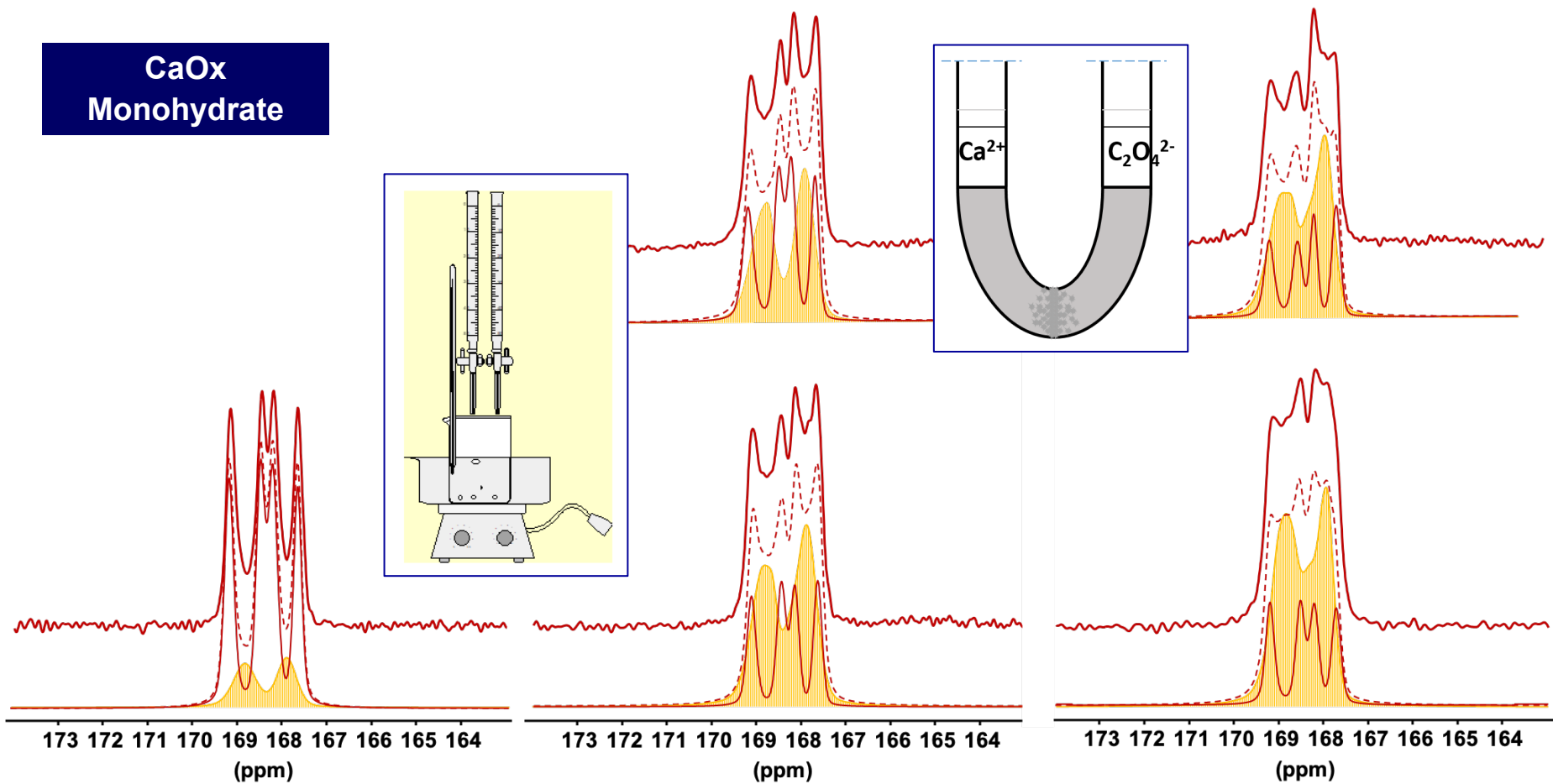


✓ COM phase: $P2_1/c$ space group

✓ disordered COM phase: statistical $I2/m$ space group (Shepelenko *et al.*, 2020)

The new phase is ubiquitous in COM syntheses

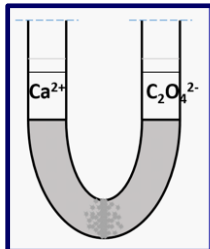
CaOx
Monohydrate



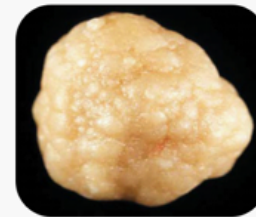
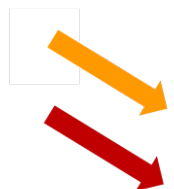
✓ COM phase: $P2_1/c$ space group

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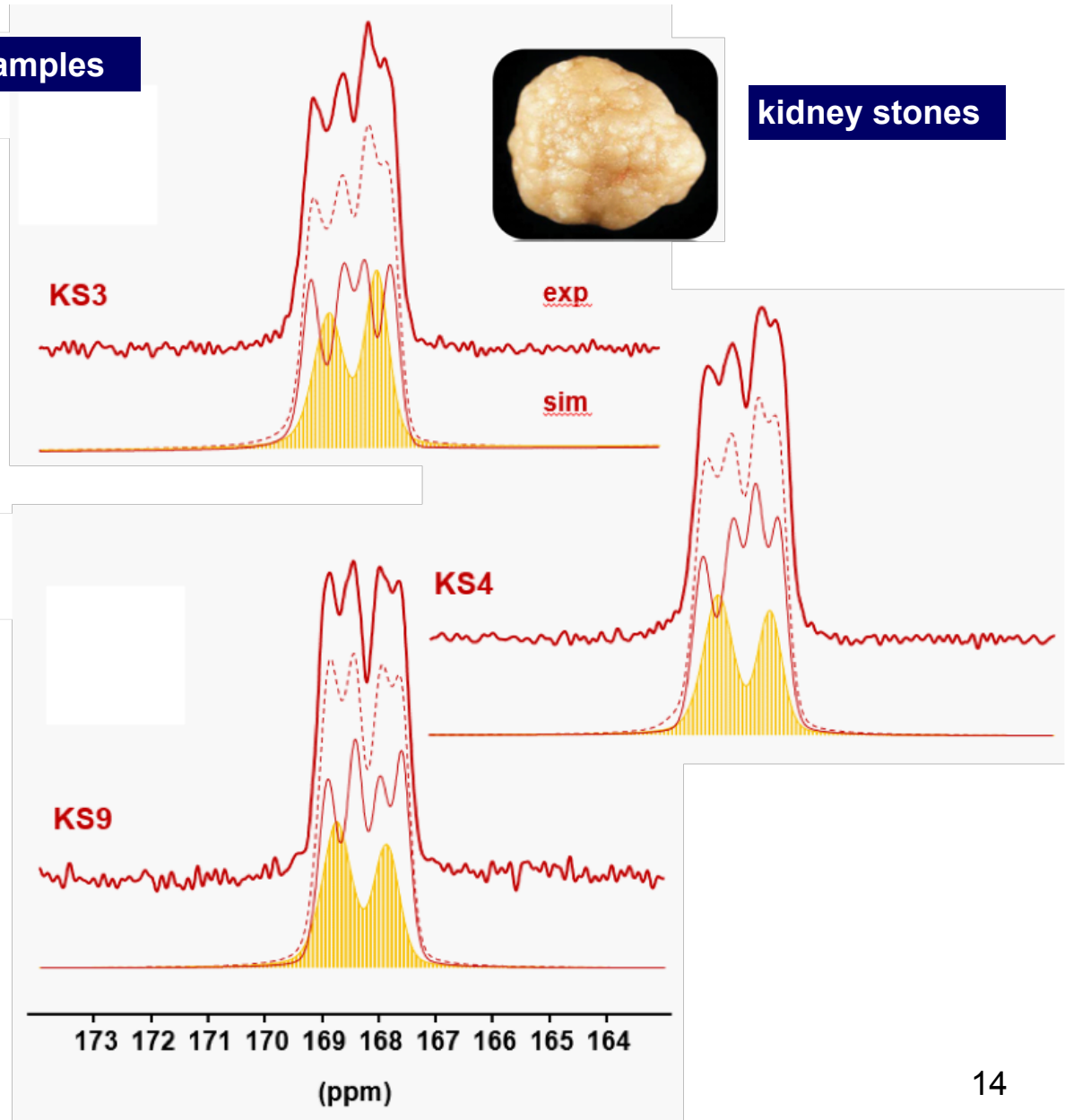
Towards *artificial* kidney stones



synthetic samples

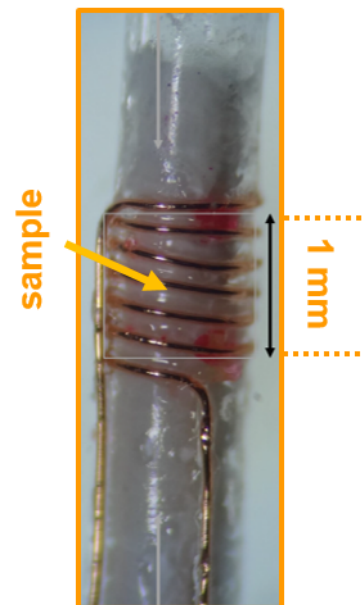


kidney stones



→ diagnosis

- NMR as a unique platform of characterization
- *in situ* transformations, *artificial* kidney stones
- **Sensitivity enhancement**
- DNP crystallography

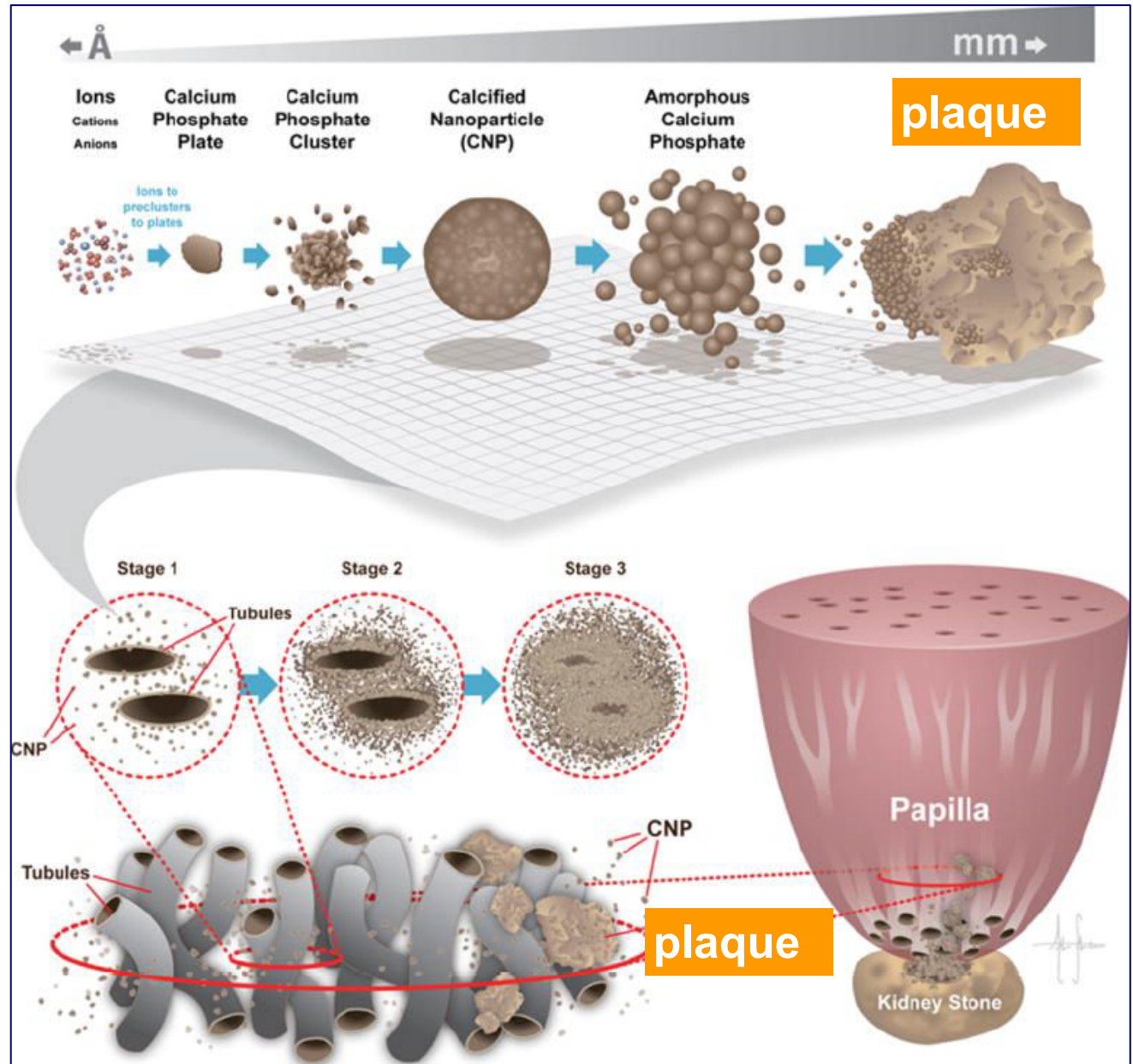


The Randall's plaque



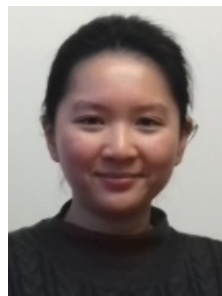
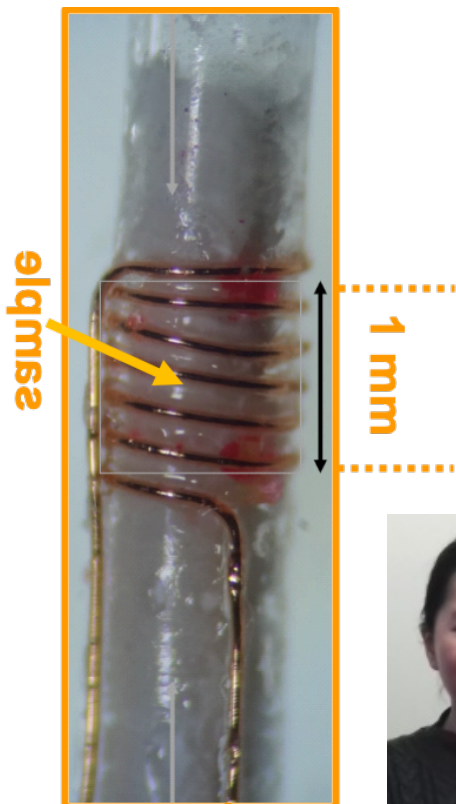
$d < 1 \text{ mm}$

Sherer *et al.*,
Acta Biomater.,
2018



Magic Angle Coil Spinning (MACS)

Sakellariou *et al.*, 2007

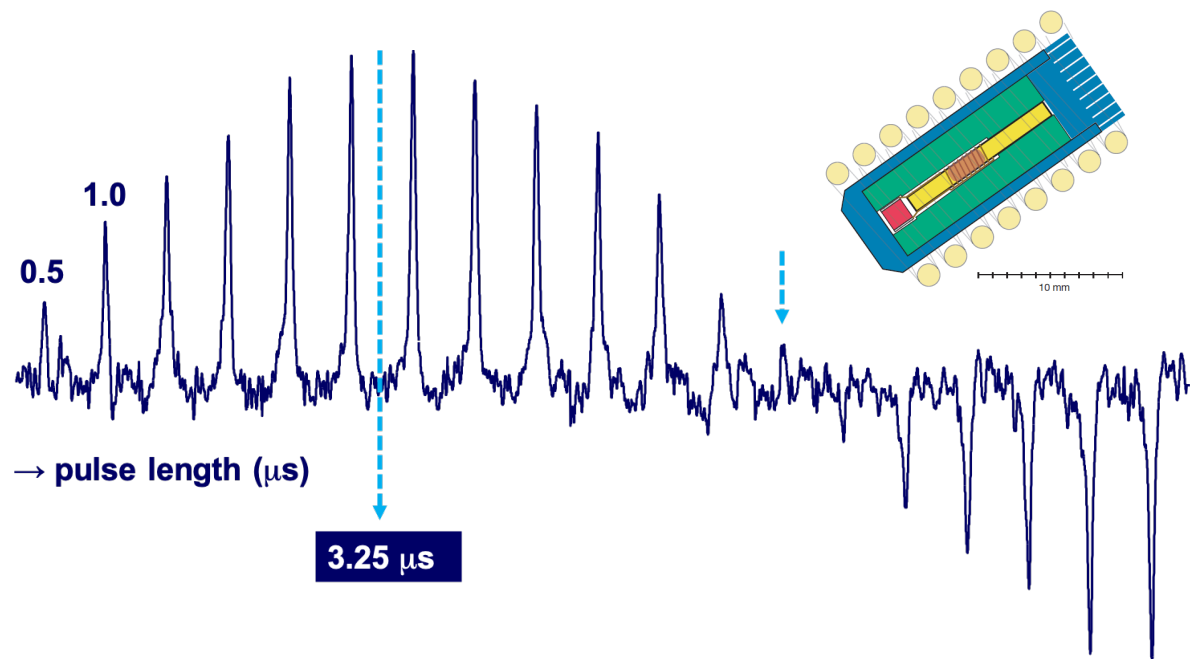


W. Teh

chip

~ few €

^{31}P nutation (micro-coil @ 50W)



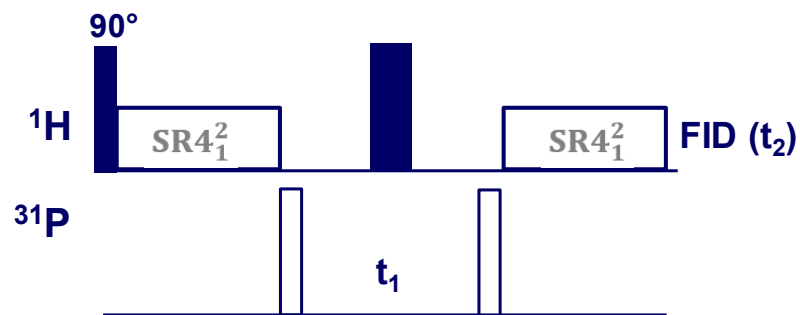
gain in time

~ 10

^1H , ^{31}P ...

m ~ 100 μg

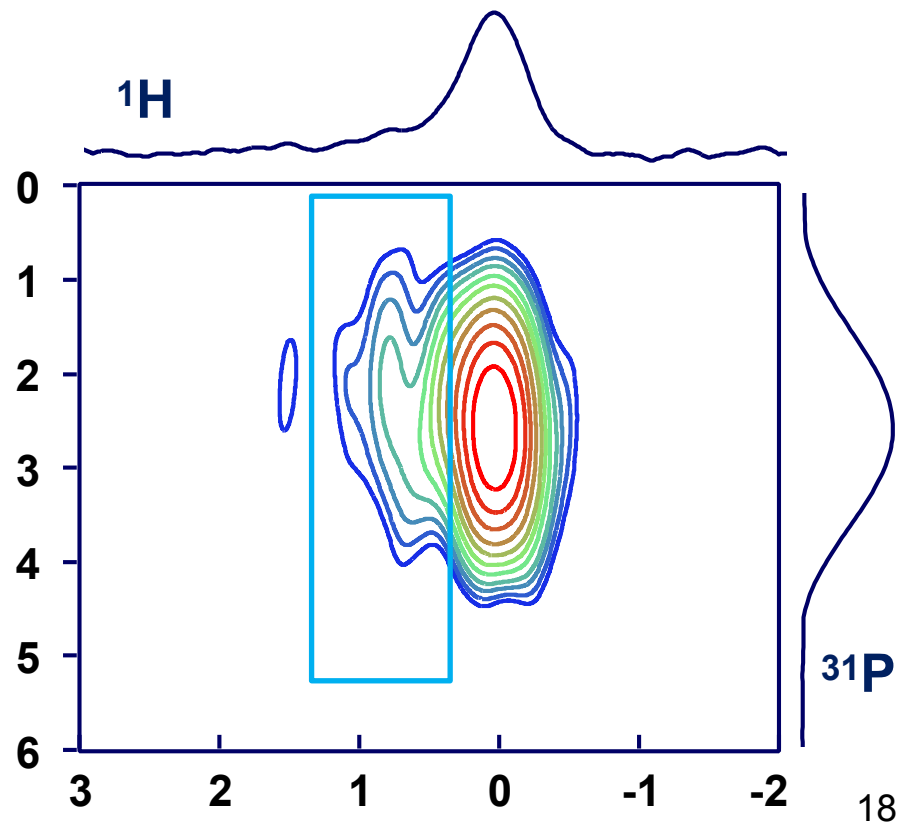
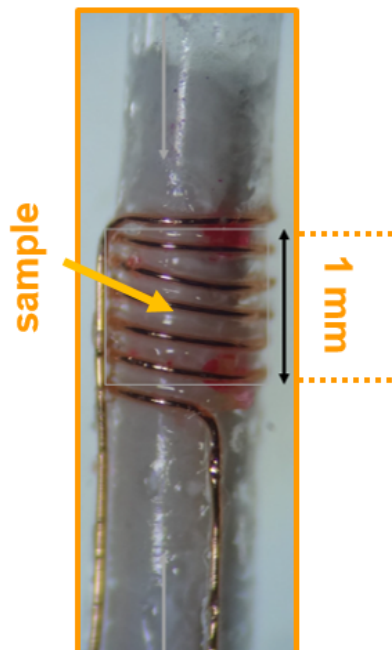
2D experiments on small mass samples



Amoureux *et al.*, Kentgens *et al.*

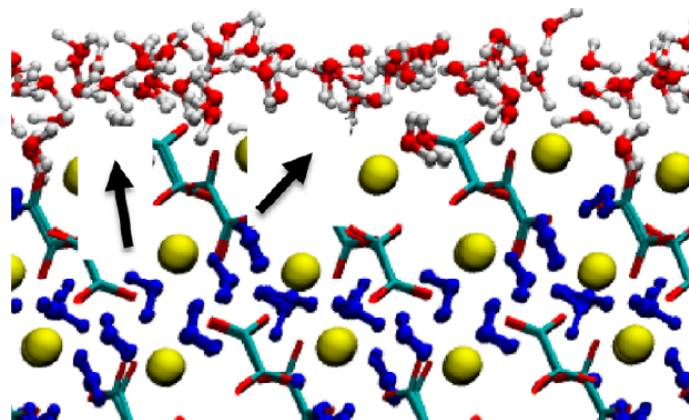
^1H - ^{31}P D-HMQC MAS
synthetic HAp ~ 100 μg

~ 4 hours



Outline

- NMR as a unique platform of characterization
- *in situ* transformations, *artificial* kidney stones
- Sensitivity enhancement
- **DNP crystallography**



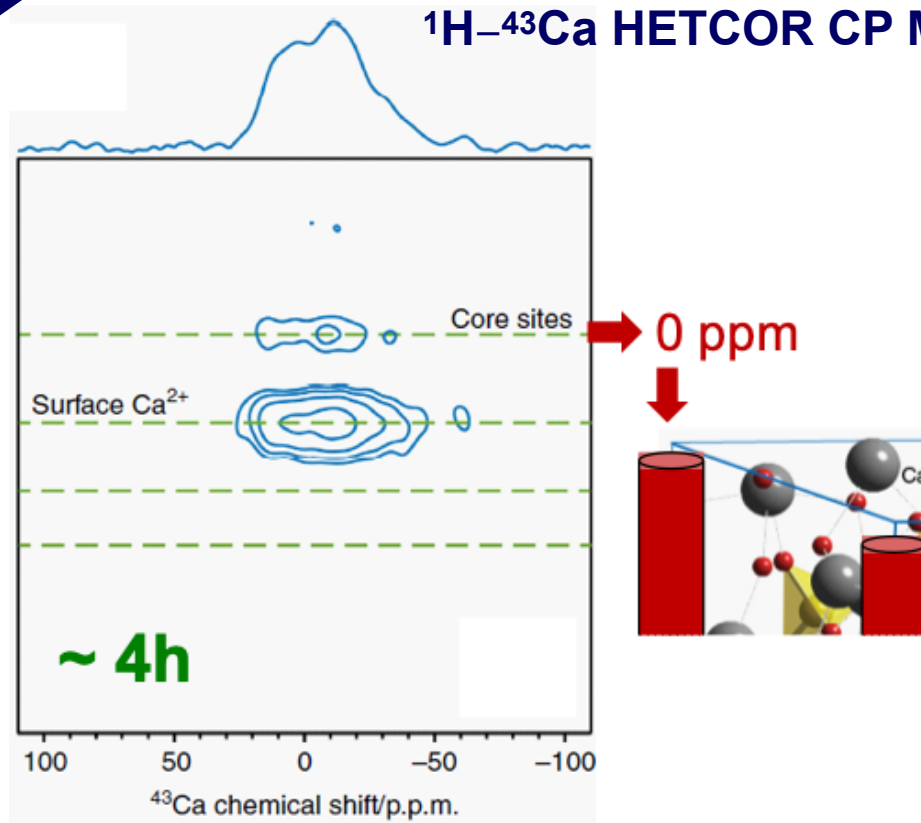
Dynamic Nuclear Polarization for biomaterials

100 K, DNP juice: glycerol- d_8 /D₂O/H₂O (60/30/10; v/v/v) + AMUPol,

sample: ~ 20 mg

low NA, low γ nuclei

0.14% nat. abundance
 ^1H - ^{43}Ca HETCOR CP MAS



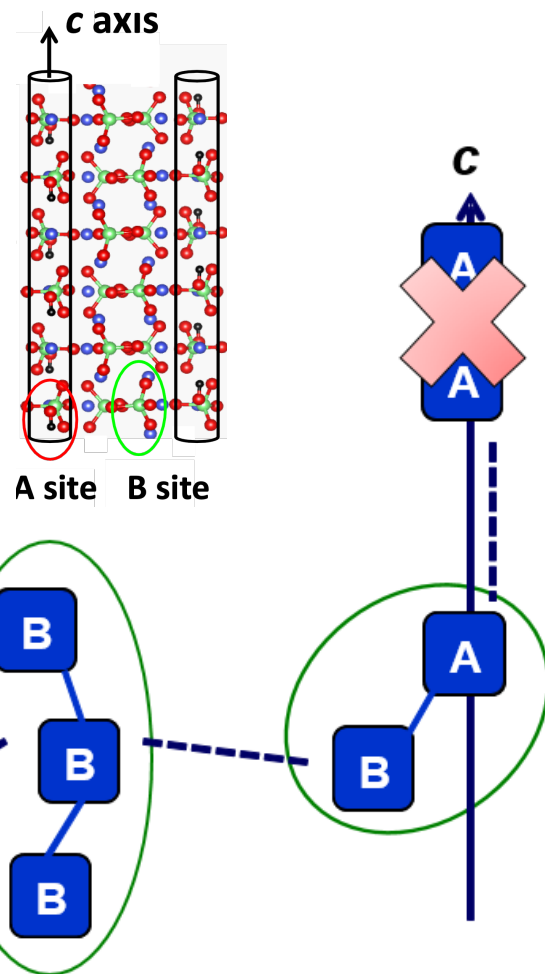
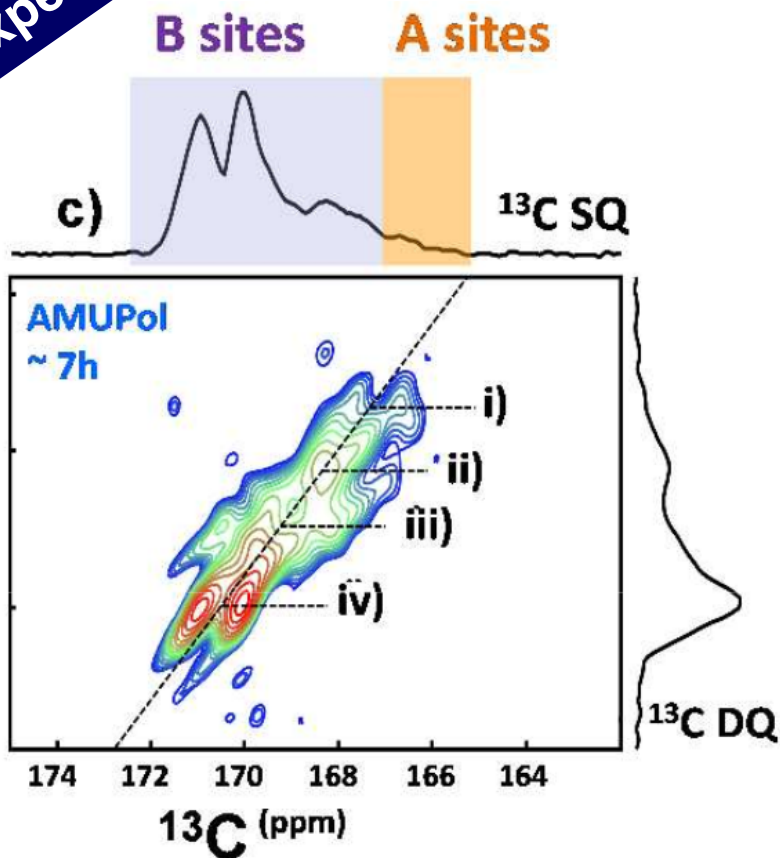
Nature Commun., 2017 (with D. Lee, G. de Paëpe, D. Laurencin)

Dynamic Nuclear Polarization for biomaterials

100 K, DNP juice: D₂O/H₂O (60/30/10; v/v/v) + AMUPol,

sample: ~ 20 mg

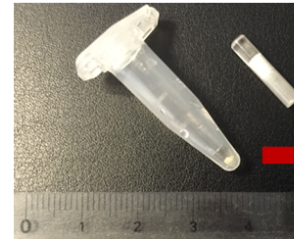
DQ-SQ experiments



Dynamic Nuclear Polarization for biomaterials

100 K, DNP juice: D₂O/H₂O (60/30/10; v/v/v) + AMUPol,

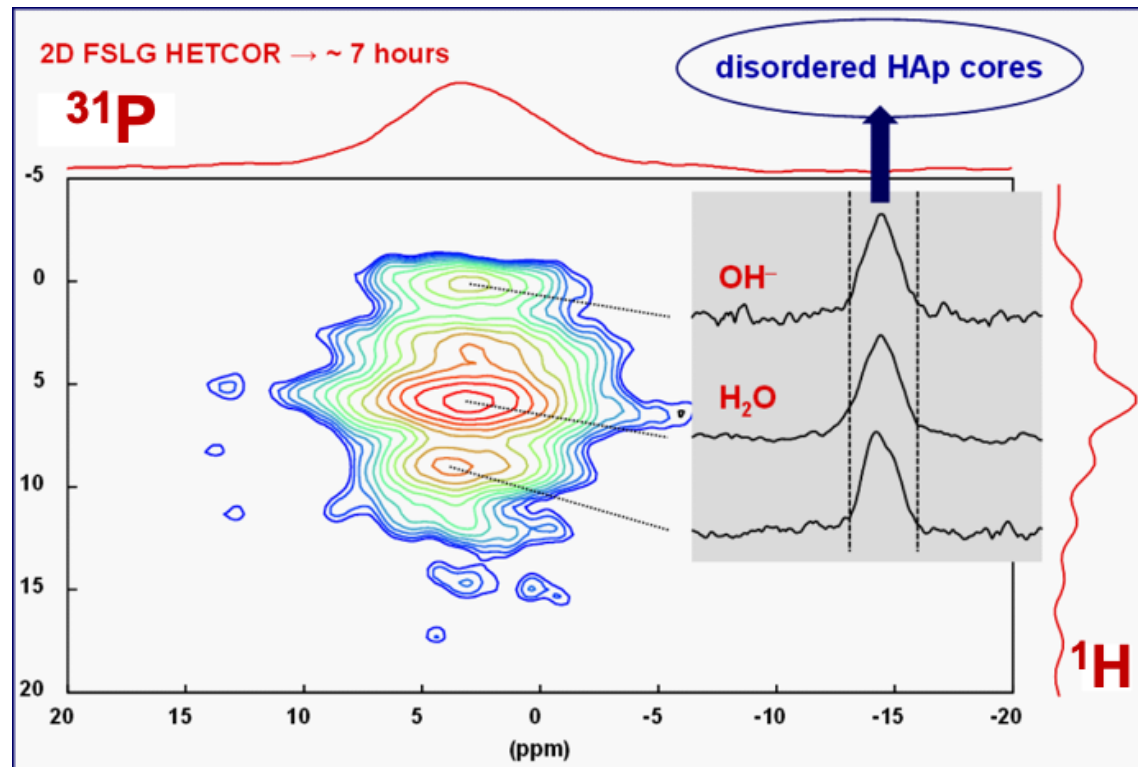
low mass samples



sapphire rotor

unique R plaque

+ {AMUpol in D₂O/H₂O (9:1)}

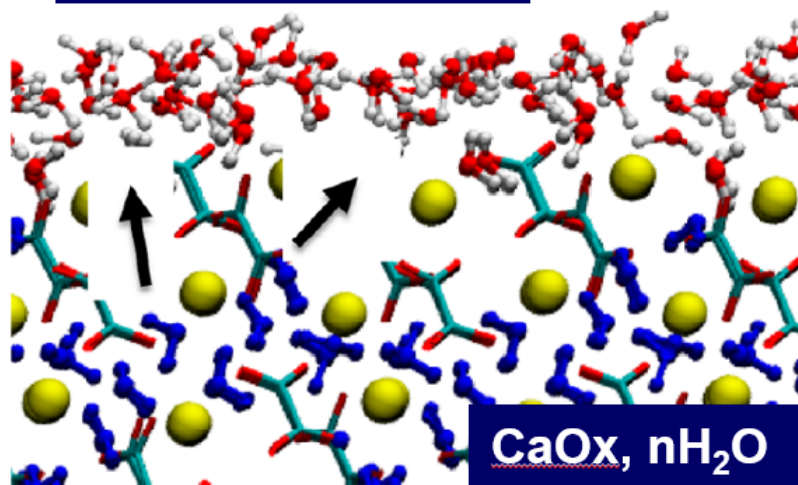


unpublished results

First principles calculations of realistic CaOx structures

bulk (water, organics...)

surface / interface



CP2K/quickstep DFT

Gaussian plane wave hybrids

PBE / D3 Grimme / OptPBE-vdW

BO-MD

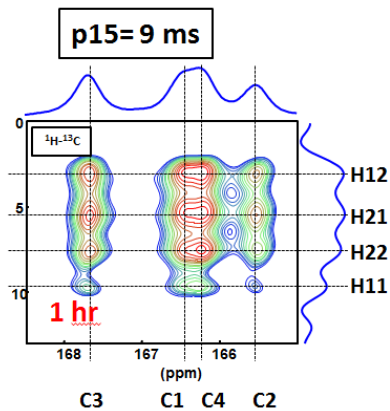
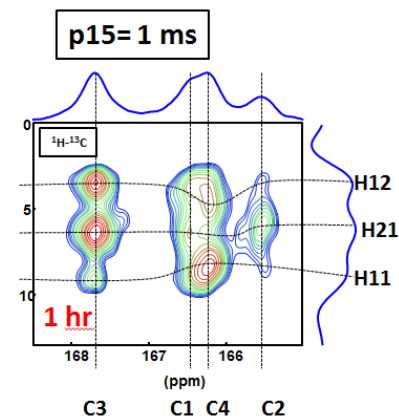
GROMACS, Gromos force field 54a7



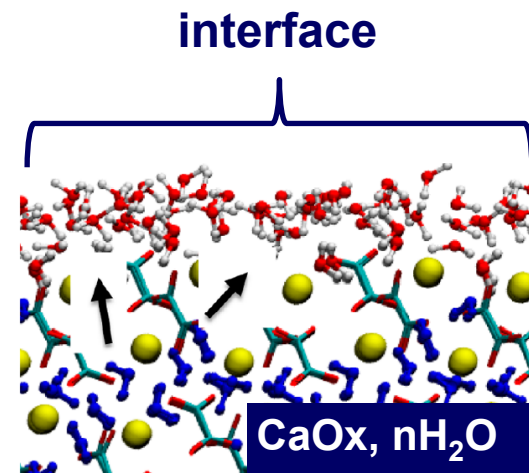
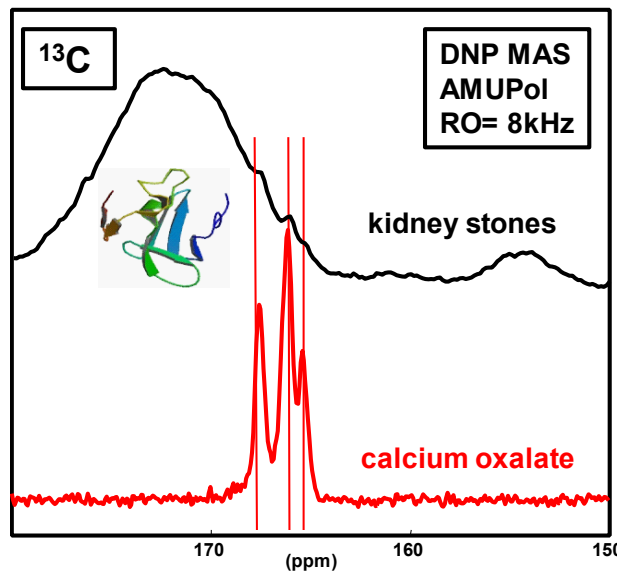
role of water, layers of solvation at
DFT level...

TEKpol in d-TCE/TCE (9:1)

^1H - ^{13}C FSLG HETCOR



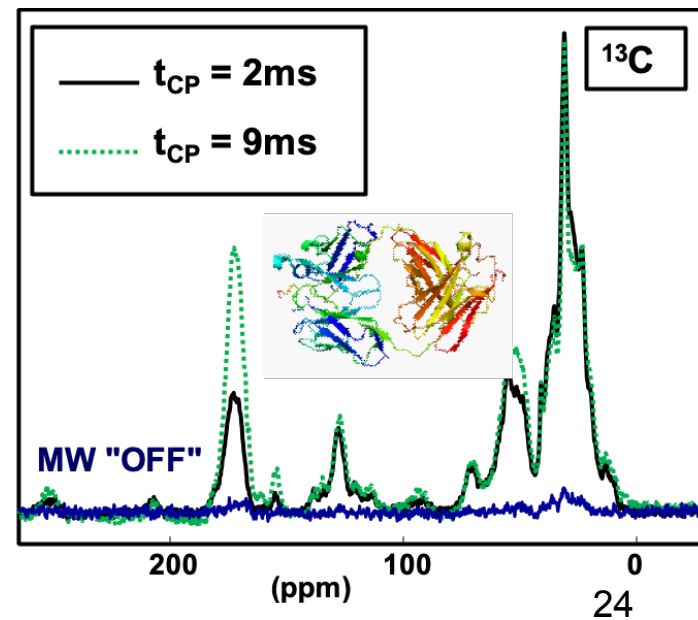
→ assignments



- heterogeneity
- choice of the solvent / radical

→ towards interfaces
→ GIPAW (slabs...)

(with C. Gervais)



Conclusions and acknowledgments

- ^1H and ^{13}C nuclei as pertinent targets for diagnosis at hospitals
- *in situ* monitored phase transformations, a new polymorph of CaOx
- More sensitivity offered by MACS and DNP (+ crystallography)

W. Teh, C. Leroy, A. Rankin, T. Debroise, Y. Petit

D. Laurencin, C. Gervais, F. Tielens

G. De Paëpe, D. Lee, F. Aussenac

D. Sakellariou

U. Scheler

M. Daudon, E. Letavernier, D. Bazin (Tenon Hospital)

