NIS Colloquia
Turin 28-29 November 2013

Computational NMR spectroscopy applied to bioglasses

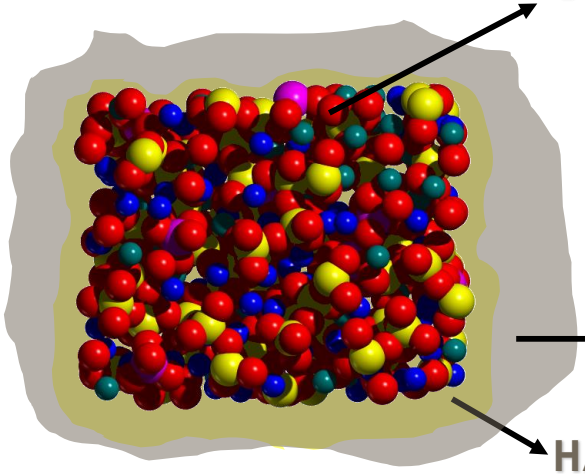
Alfonso Pedone
Department of Chemical and Geological Sciences
University of Modena and Reggio Emilia

Overview of the talk

- **Introduction** (bioglasses & NMR)
- **Methodology**:
  - MD-GIPAW to simulate NMR spectra
- **Application**:
  - 45S5 Bioglass (^{31}**P**, ^{29}**Si**, ^{17}**O**, ^{23}Na)
  - Fluorinated bioglasses (^{19}**F**, ^{29}Si, ^{23}Na)
- Conclusions

Bioglasses

Hench et al *J. Biomed. Mater. Res. Symp*. **1971**, 2, 117



®**Bioglass 45S5** (Hench, 1971)

- SiO_2 45%
- Na_2O 24.5%
- CaO 24.5%
- P_2O_5 6%

SBF [Na^+, K^+, Ca^{2+}, Mg^{2+}, HPO_4^{2-}, HCO_3^-, Cl^- and SO_4^{2-}]

HA [$Ca_{10}(PO_4)_6(OH)_2$]

Prof. Larry Hench

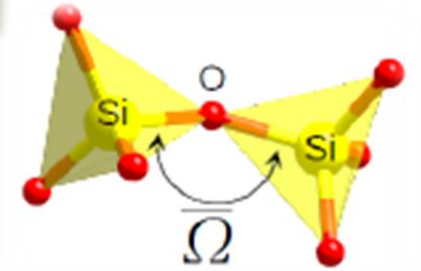
Imperial College London

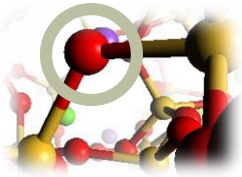
Structure-bioactivity relationships

The crucial issue for the development of bioglasses is an improved understanding of their fundamental structure–bioactivity relationships.

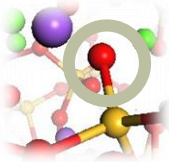
Nuclear Magnetic Resonance spectroscopy is extremely sensitive to chemical environment of active nuclei :

- **Topological disorder** (bond distances and angles, coordination numbers etc..)



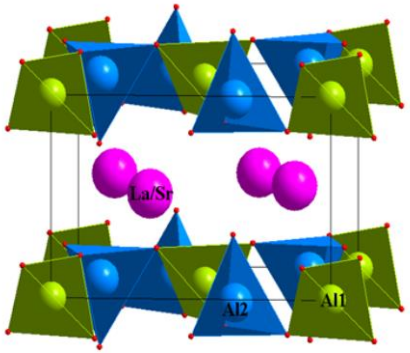


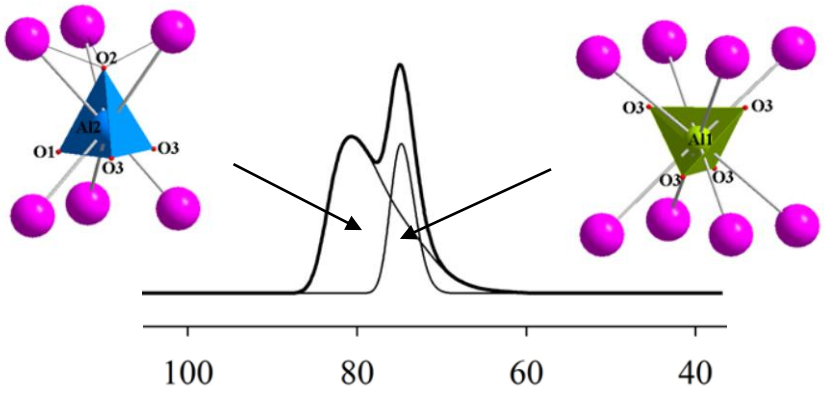
BO



NBO

- the nature of the 2nd coordination sphere (**chemical disorder**)





$$H_{tot} = H_z + H_D + H_Q + H_{CS} + H_{SC} + \dots$$

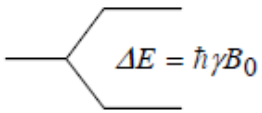
$H_z = \gamma\hbar B_0 I$

$H_D \propto \frac{\gamma_1\gamma_2}{r_{12}^3}\hbar^2$

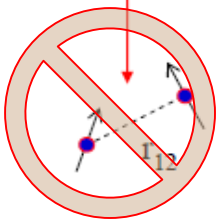
$H_Q \propto \frac{eQ}{2I(2I-1)\hbar}\mathbf{V}$

$H_{CS} = \gamma\hbar \mathbf{I}.\boldsymbol{\sigma}.\mathbf{B}_0$

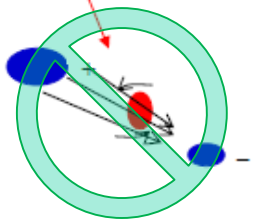
$H_{SC} = \gamma\hbar \mathbf{I}.\mathbf{J}.\mathbf{S}$



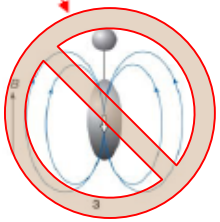
ZEEMAN INT.



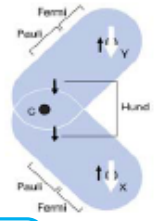
DIPOLAR INT.



QUADRUPOLAR INT. (I>1/2)



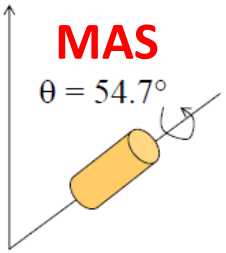
CHEMICAL SHIFT

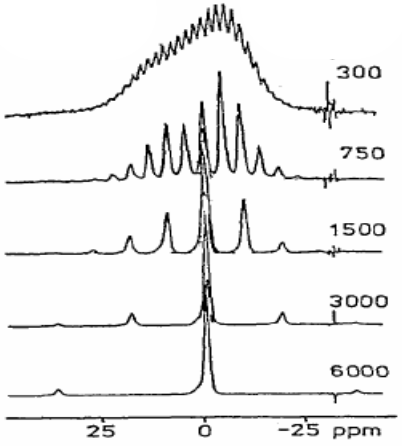


MAS

DAS
DOR
MQMAS

Anisotropic!! → BROAD SOLID STATE SPECTRA



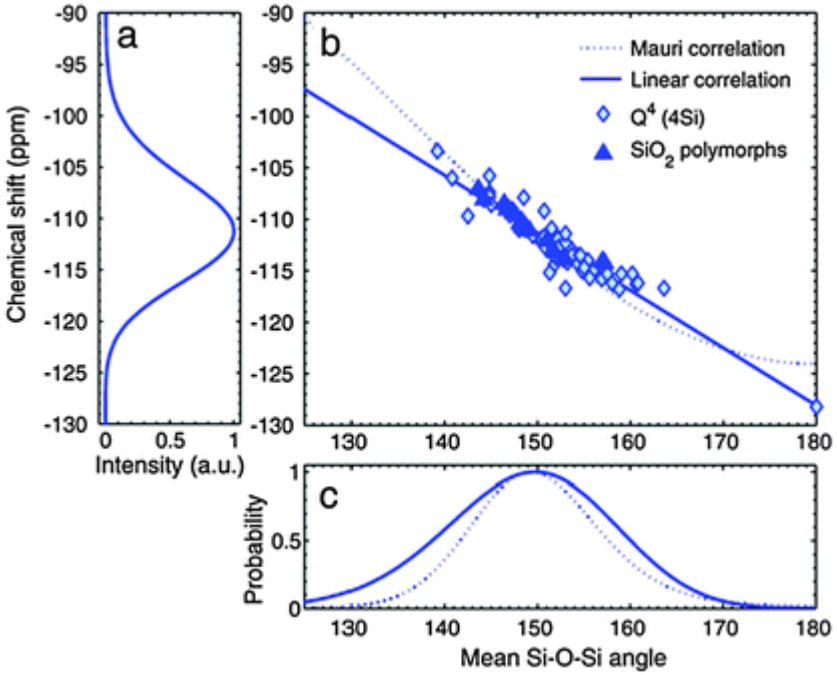


Improved Resolution

Improved Accuracy

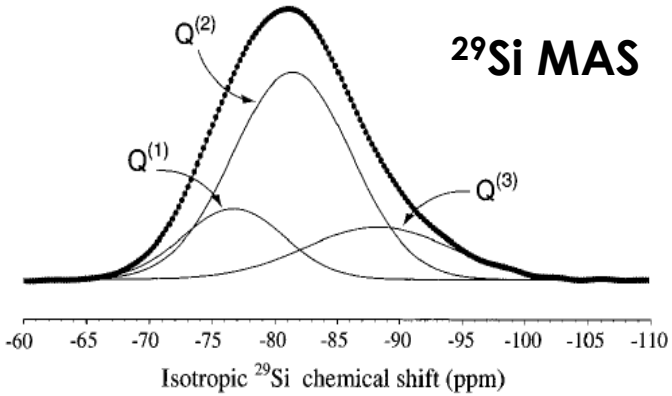
NMR of amorphous systems

Topological disorder

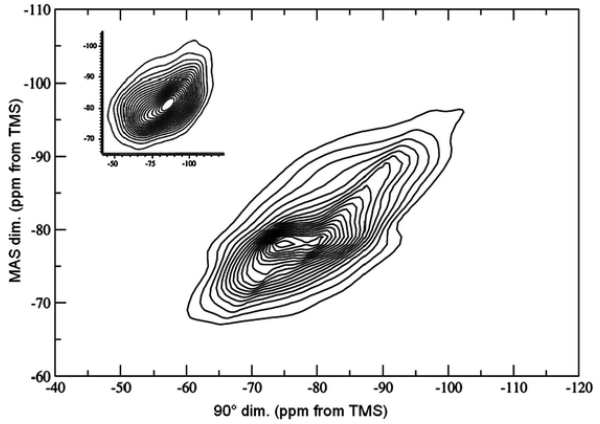


M. Edèn, Annu. Rep. Prog. Chem., Sect. C: Phys. Chem., 2012,108, 177-221

β-$CaSiO_3$ glass



Chemical disorder

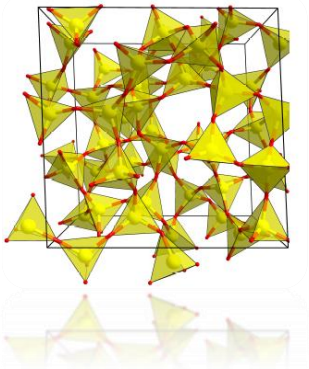


Distribution of structural features → **Distribution of NMR parameters** → **Broad Spectra**

Our Approach

GLASS SAMPLE
3D structure
unknown

GLASS MODEL
3D structure
from MD



Collect NMR spectra & extract NMR parameters

Experiments verify theory

Theory explains experiments

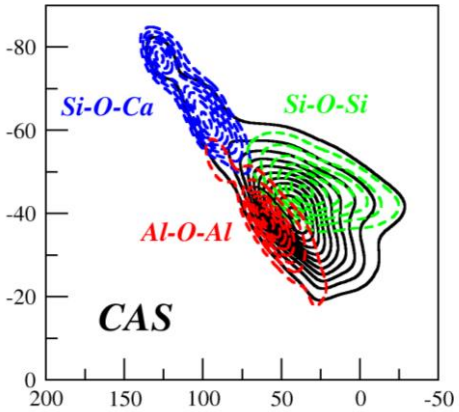
Compute NMR parameters (DFT-GIPAW) & theoretical spectra (fpNMR)

Agreement?

No

Refine the model

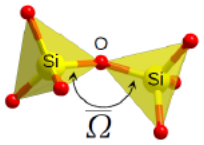
Yes

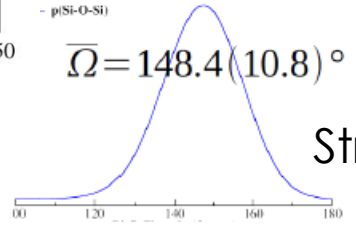


Spectra Interpretation

Peak assignments

NMR - structure relationships

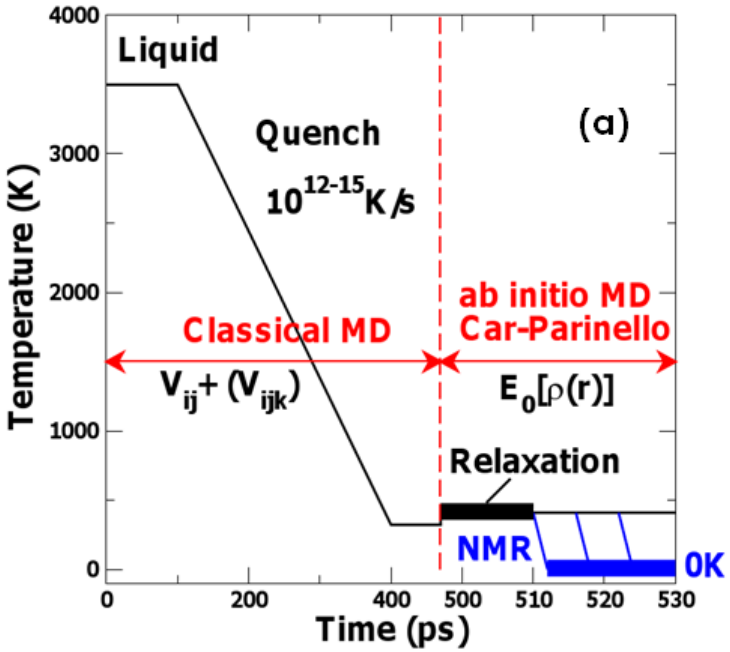


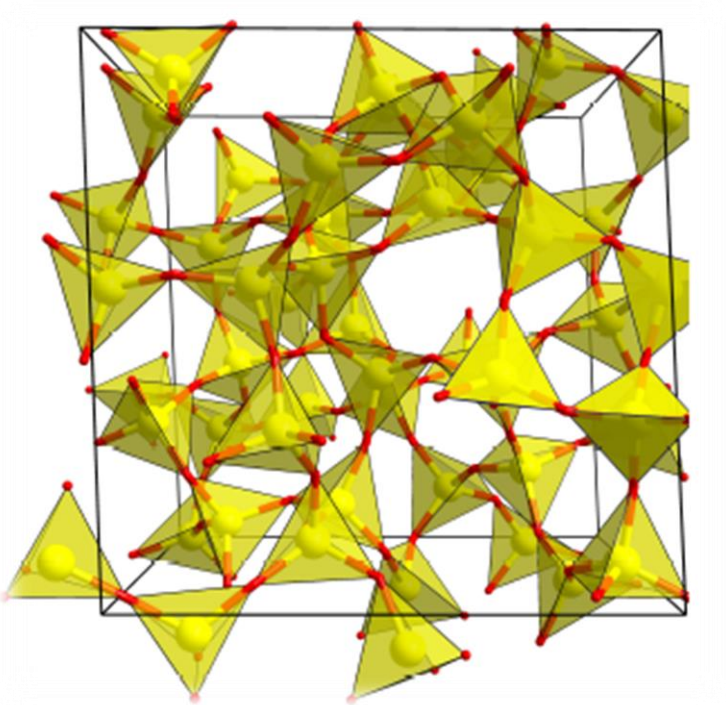


Structural Inversion

Charpentier, T. Menziani, M. C., Pedone A. RSC Advances 2013, 3 (27), 10550 - 10578

Glass Generation: Molecular Dynamics Simulations





• Models of crystalline (or random) systems are melted; the melts are then quenched , freezing the structure into a disordered glassy phase.

Pedone, A. J. Phys. Chem. C 2009, 113, 20773.

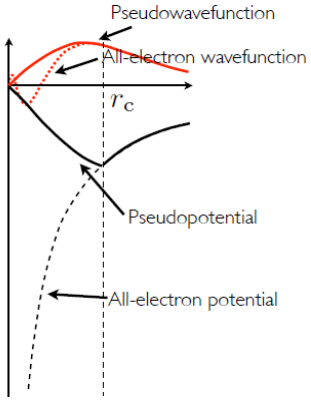
NMR Calculations

DFT-PBE calculations

NMR CASTEP
QUANTUM ESPRESSO

Plane waves Basis set

Pseudo-Potentials



GIPAW: C.J. Pickard, F. Mauri, Physical Review B 63 245101 (2001)

NMR parameters

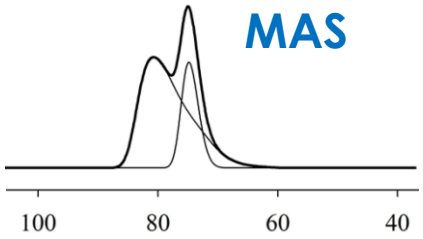
Spin ½ nuclei:
δ_{iso}, Δ_{CSA}, η_{CSA}

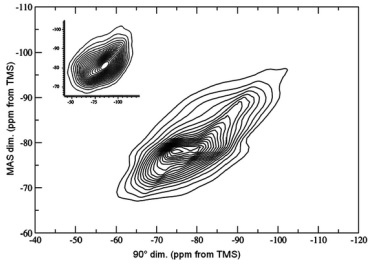
Spin > ½ nuclei:
δ_{iso}, Δ_{CSA}, η_{CSA},
C_Q, η_Q

fpNMR

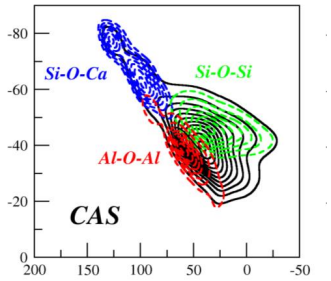
$$\nu_{m,n} = \langle m|\boldsymbol{H}_{tot}|m\rangle - \langle n|\boldsymbol{H}_{tot}|n\rangle$$

Pedone, A.; Charpentier, T.; Menziani, M. C. *Phys. Chem. Chem. Phys.* 2010, *12*, 5064.



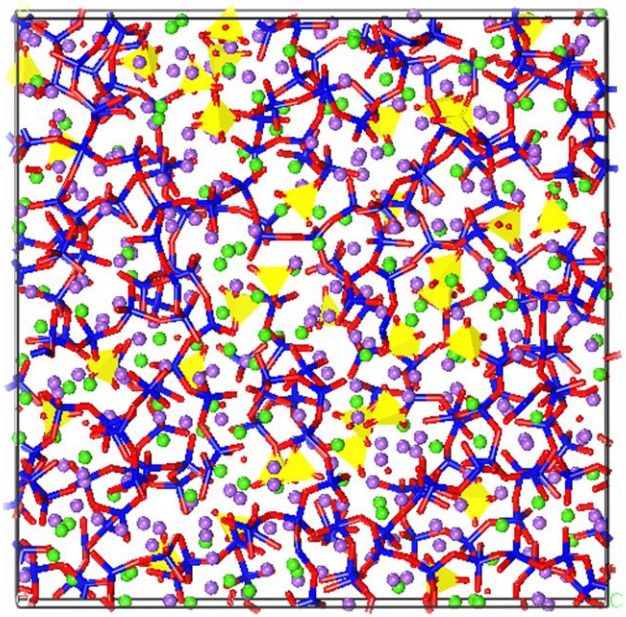


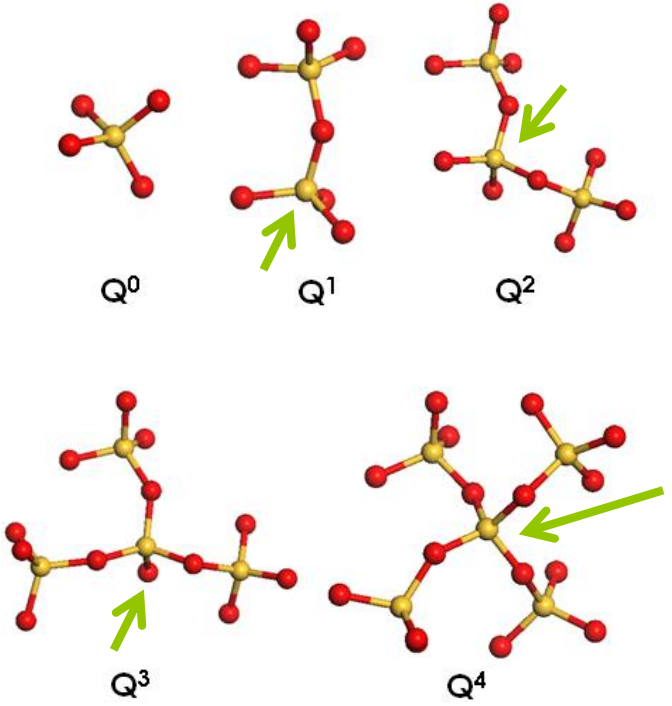
(90°,MAS) 2D NMR



MQMAS

General Microscopic Structure

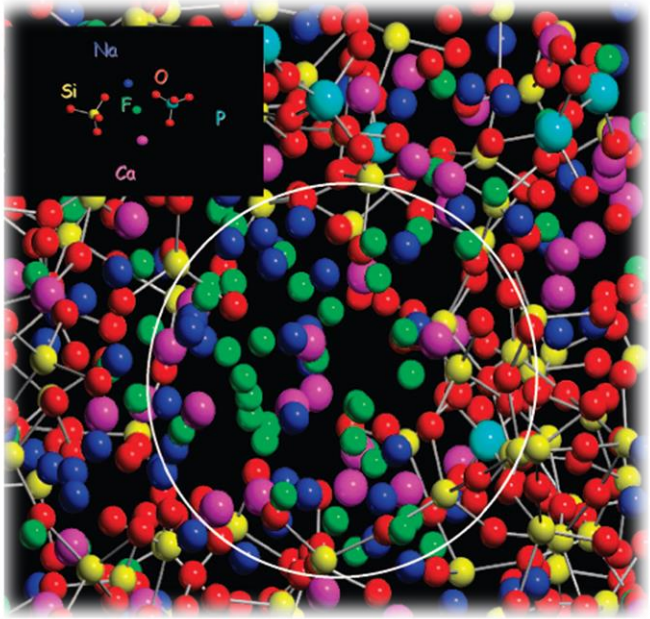




45S5: 46.1% SiO_2, 24.4% Na_2O, 26.9%CaO, 2.6% P_2O_5

- very open silicate network dominated by Q^2 and Q^3 species
- phosphate groups are predominantly isolated Q^0 units associated with modifier cations.
- bioactivity appears for glasses with network connectivity (NC) < 3

General Microscopic Structure



CaF_2

↓

CaO

Network connectivity increases

45S5F: 46.1% SiO_2, 24.4% Na_2O, 16.9%CaO, 10CaF_2 2.6% P_2O_5

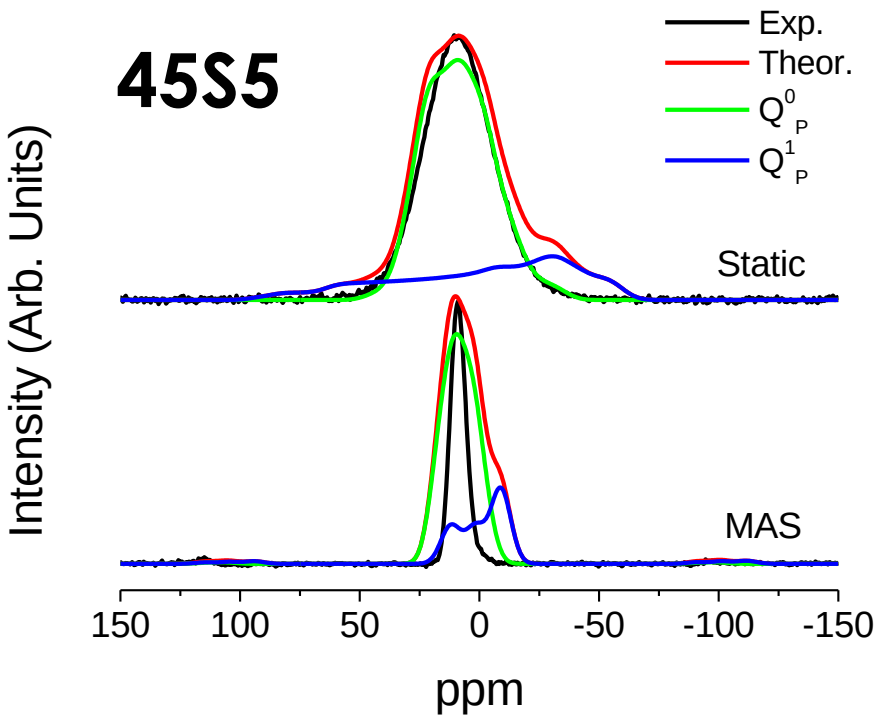
- Fluoride prefers to form FM_n moieties (M=Na/Ca)
- The high affinity of F for Na and Ca modifier cations determines the separation of a highly polymerized phosphosilicate matrix from an ionic phase rich in Na, Ca and F.

Lusvardi et al. J. Phys. Chem. B 2008, 112, 12730. Christie et al. J. Phys. Chem. B 2011, 115, 2038-2045.

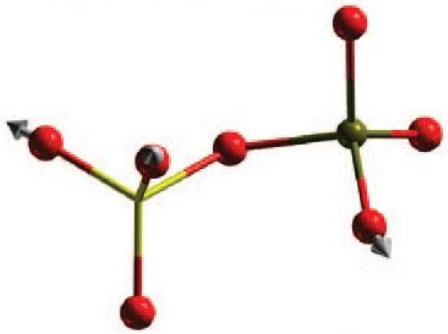
Open Questions on the structure

- Bi- or Trinomial Q^n(Si) distributions?
- Are P-O-Si bonds present in the glass?
- Nature of Cation Mixing around NBOs. Random or Non-Random distributions?
- Fluorine environment? Are Si-F bonds present in the glass?
- Does Fluorine prefer to bond with Na or Ca?

PHOSPHOROUS ENVIRONMENT



δ_{iso} = 8.7 ppm, CSA=-11.2 ppm

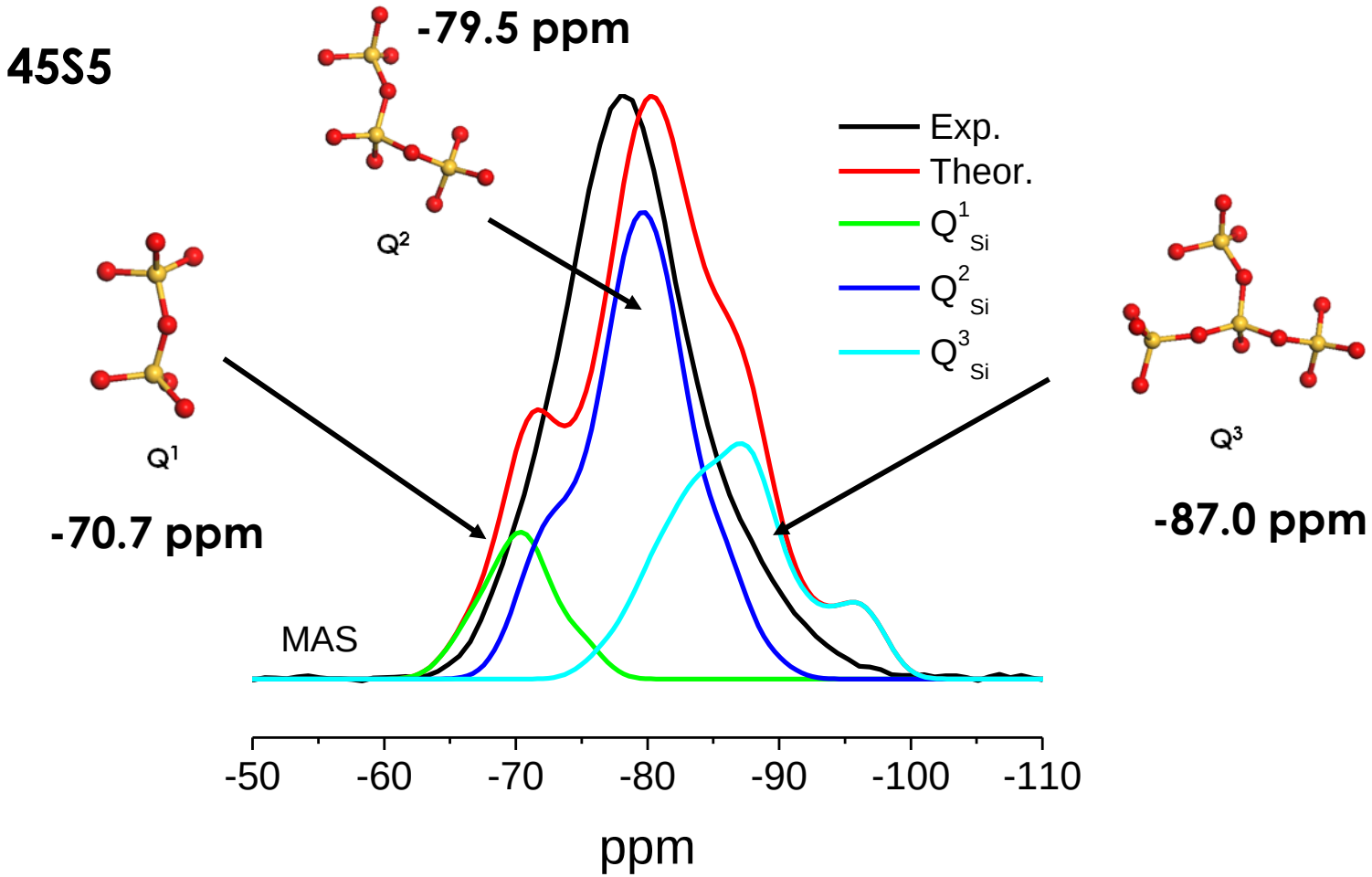


δ_{iso} = -0.7 ppm, CSA=-70.2 ppm

➢**No Si-O-P bonds are present in the real structure**

Pedone, A.; Charpentier, T.; Malavasi, G.; Menziani, M. C. *Chem. Mater.* 2010, 22, 5644.

SILICON ENVIRONMENT



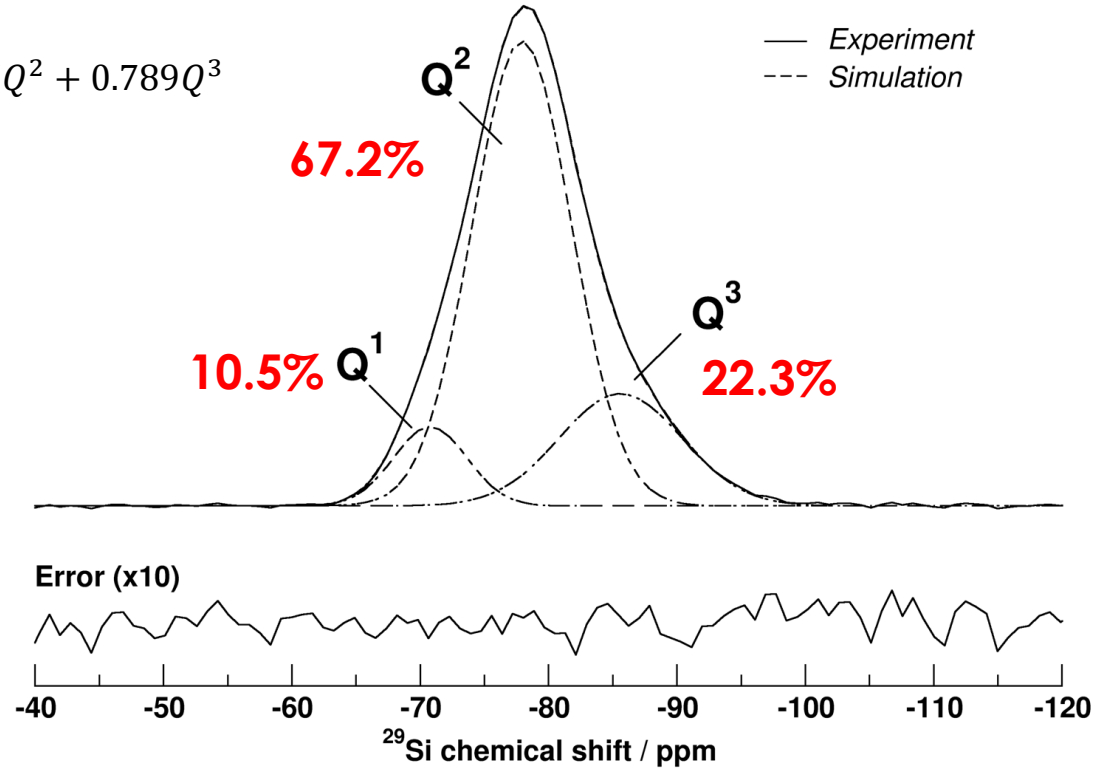
Pedone, A. et al. *Chem. Mater.* 2010, *22*, 5644.

Direct fitting of the ^{29}Si MAS spectrum

Compositional constraints:

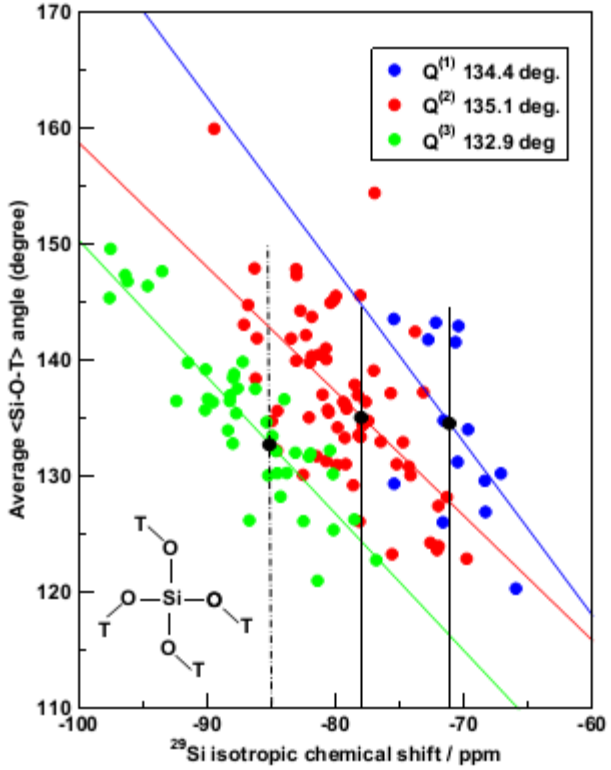
$$\frac{Si - NBO}{Si - BO - Si} = \frac{(3Q^1 + 2Q^2 + Q^3)}{(0.5Q^1 + Q^2 + 1.5Q^3)}$$

$$Q^1 = -0.1087Q^2 + 0.789Q^3$$



Pedone, A. et al. *Chem. Mater.* 2010, *22*, 5644.

^{29}Si δ_{iso} is a good probe of the Bond Angle Distribution (BAD).



$Q^{(n)}$ Analysis

	$\#Ca^{(a)}$	$\#Na^{(a)}$	$Q^{(n)}$-O-Si
$Q^{(3)}$	1.6 (1.1)	4.4 (1.6)	135.1 (11.5)
$Q^{(2)}$	2.7 (1.0)	4.6 (1.3)	136.4 (10.4)
$Q^{(1)}$	4.1 (0.7)	4.9 (1.0)	134.1 (7.26)

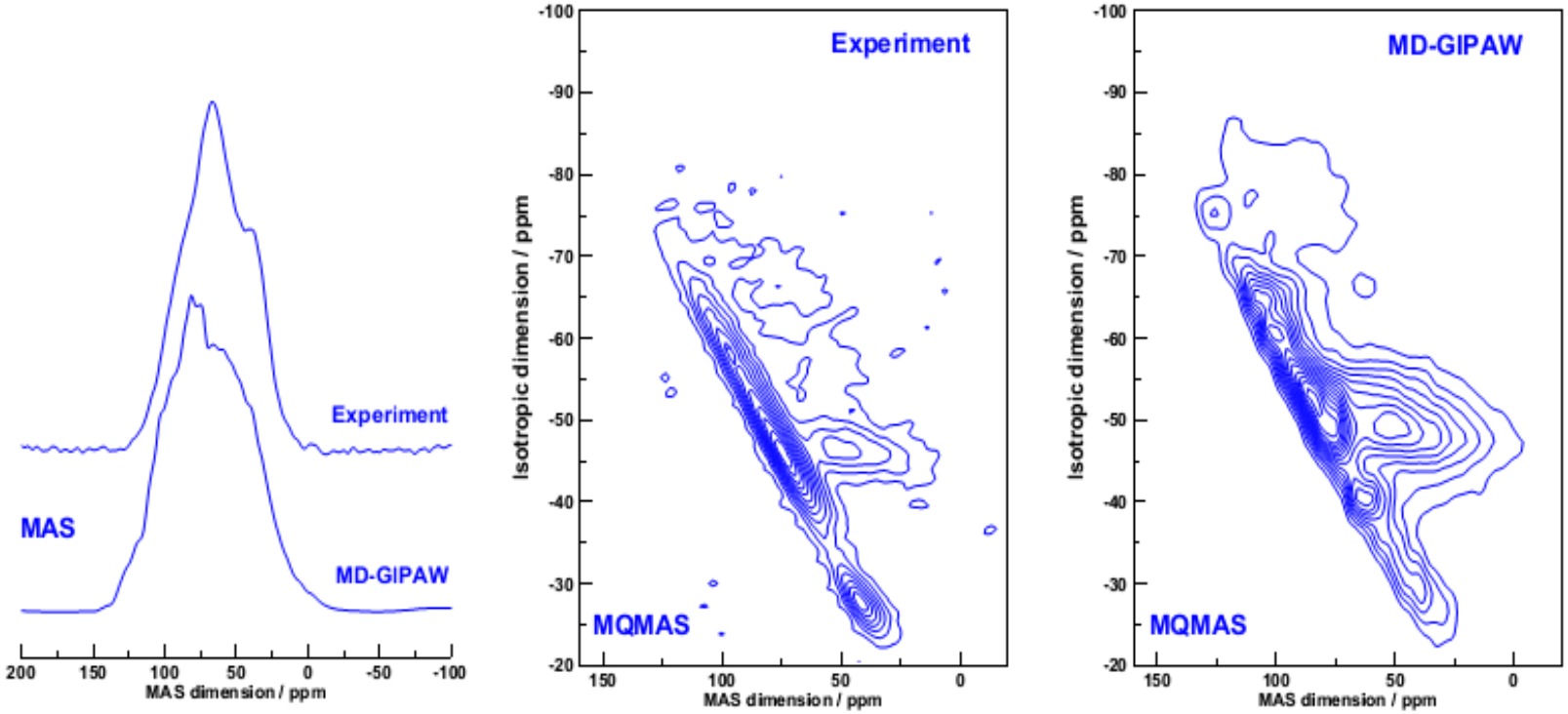
$^{(a)}$ Number of neighbours within r_c=4 Å.

- #Na $\approx$ constant
- #Ca decreases with n

$\Rightarrow$ Influence of the (Na,Ca) cation ordering around Si atoms

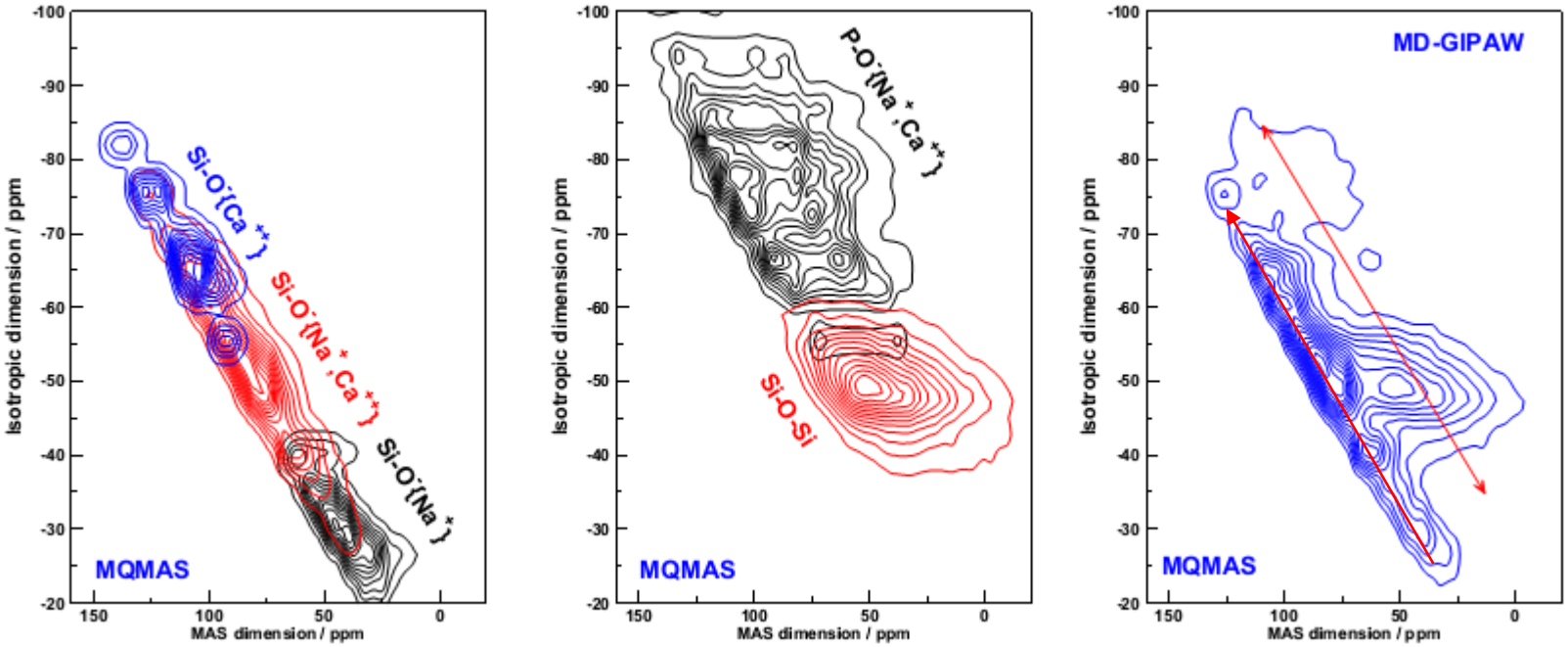
^{17}O NMR

Good agreement between the experimental and theoretical ^{17}O NMR spectra



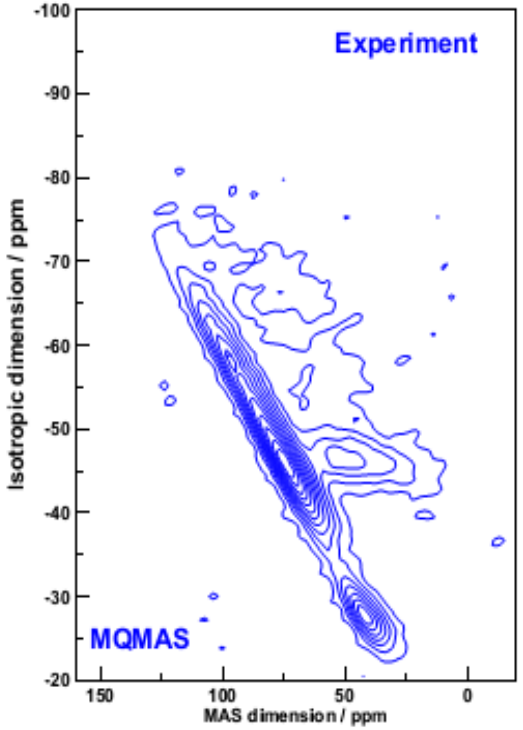
Analysis of the ^{17}O NMR parameters for each oxygen species

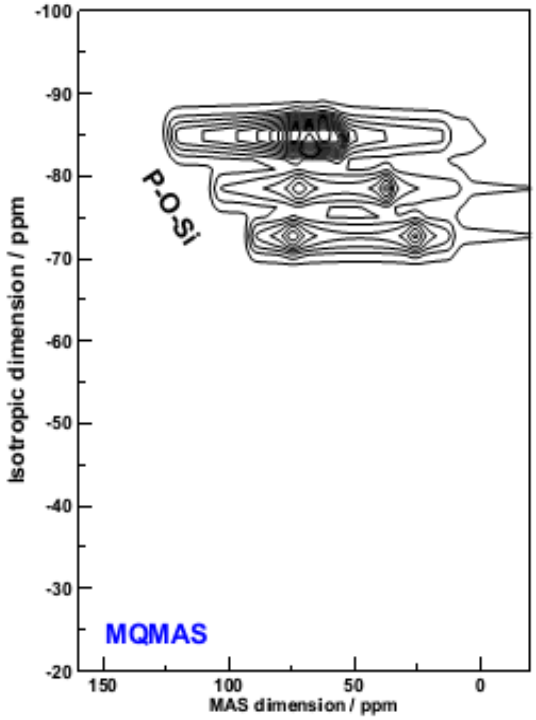
Oxygen sites



MD-GIPAW assisted the deconvolution of ^{17}O NMR

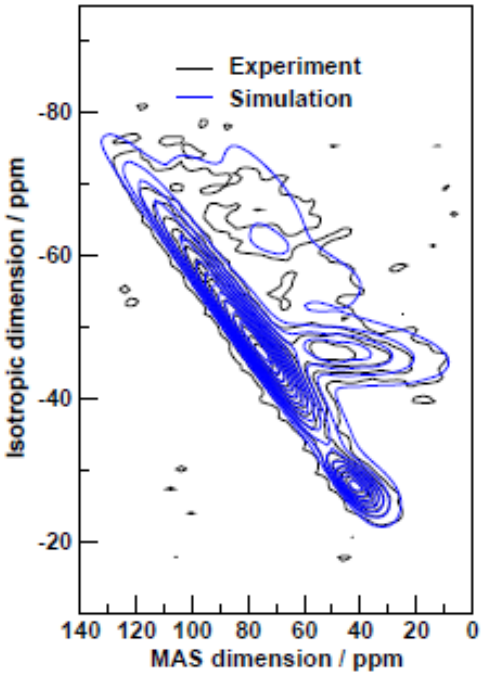
Si-O-P sites

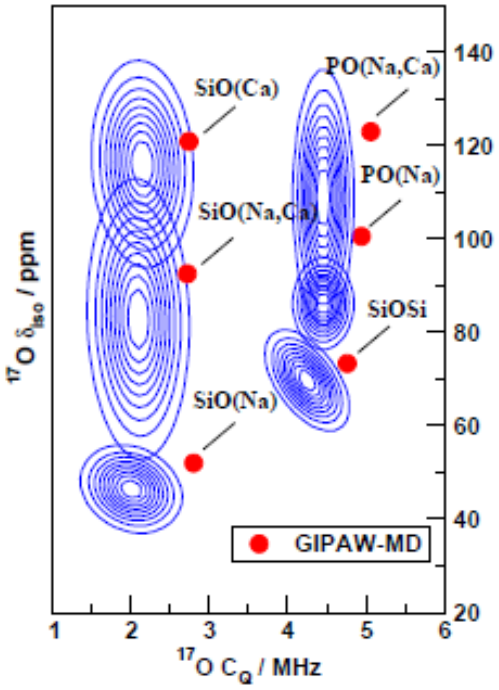

Experiment
MQMAS
Isotropic dimension / ppm
MAS dimension / ppm
-100
-90
-80
-70
-60
-50
-40
-30
-20
150
100
50
0


P-O-Si
MQMAS
Isotropic dimension / ppm
MAS dimension / ppm
-100
-90
-80
-70
-60
-50
-40
-30
-20
150
100
50
0

OXYGEN ENVIRONMENT

The theoretical calculations have been used to guide the fitting of the experimental **^{17}O 3QMAS** spectra



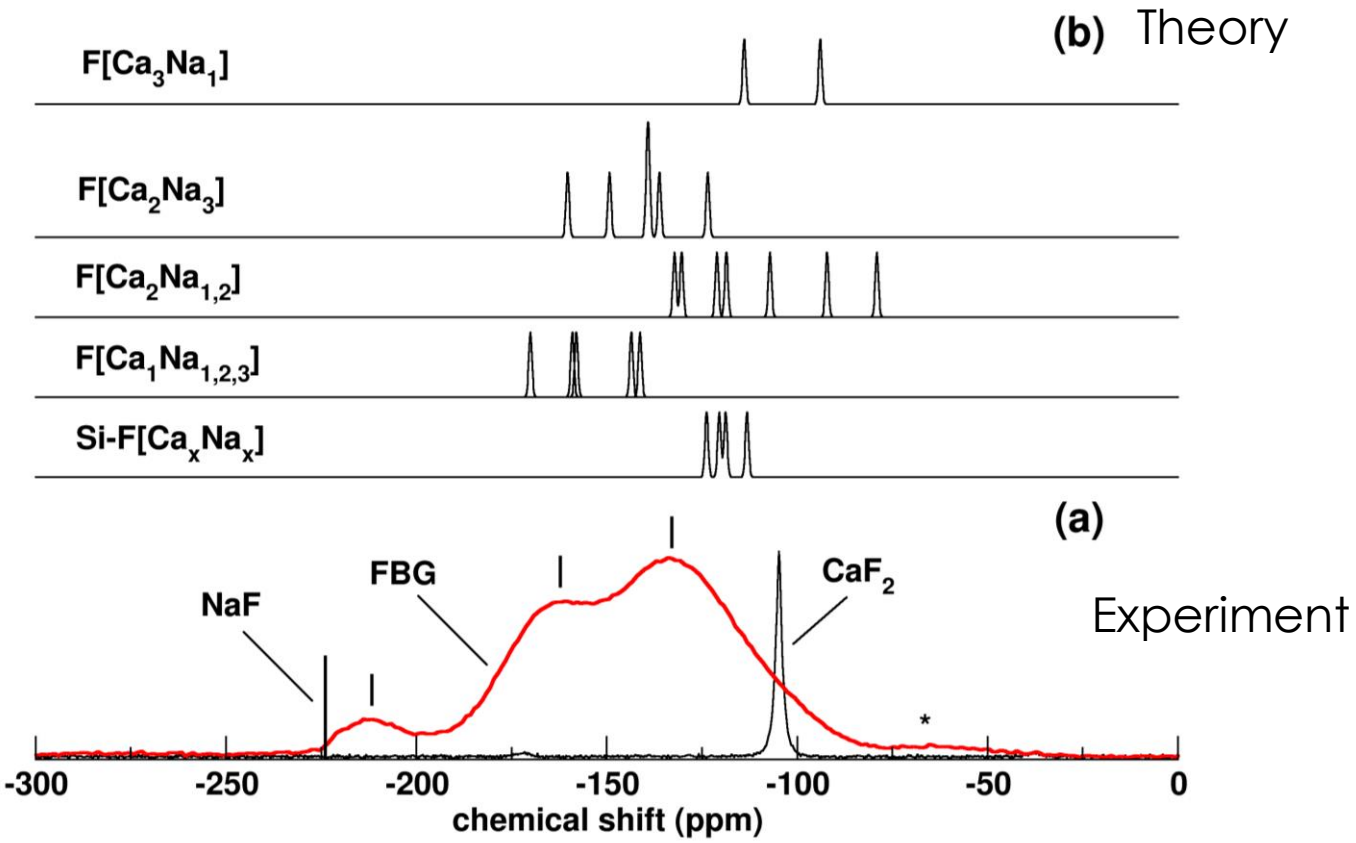


Site Populations

Site	MQMAS
P-O(Ca,Na)	14.7%
P-O(Na)	5.9%
P-O(Ca)	-
Si-O(Ca,Na)	37.3%
Si-O(Na)	6.5%
Si-O(Ca)	7.1%
Si-O-Si	28.1%

NON RANDOM DISTRIBUTION OF Na & Ca AROUND OXYGEN

45S5F Bioglass



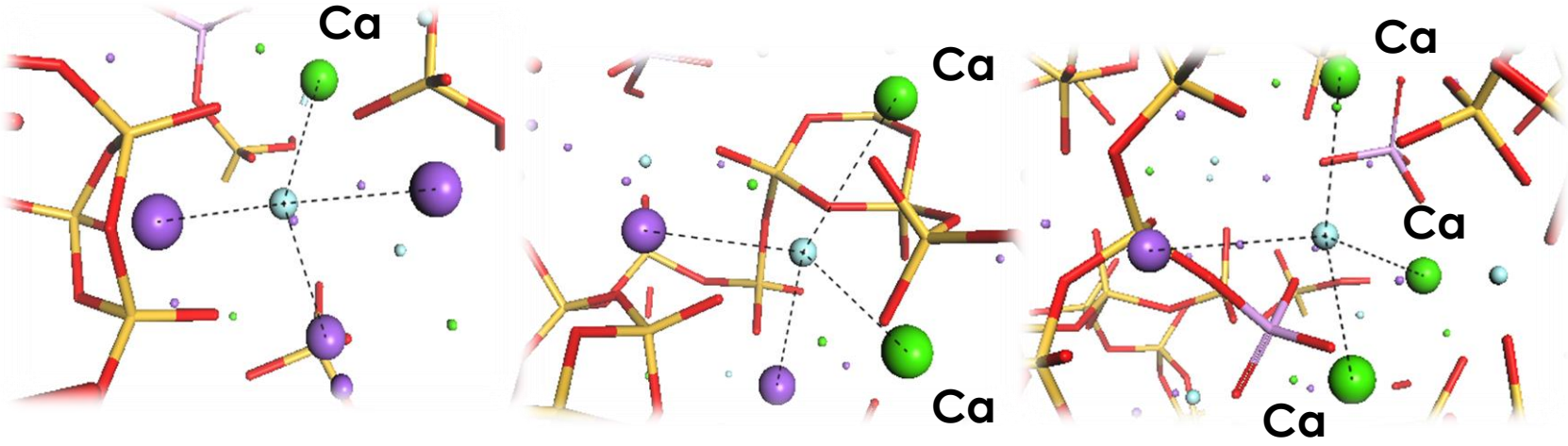
The calculated spectra of the various F sites fall within the experimental isotropic chemical shift ranges denoting a satisfactory agreement.

Pedone et al. J. Mater. Chem. 2012 22 12599

F[$CaNa_3$] 12%

F[Ca_2Na_2] 24%

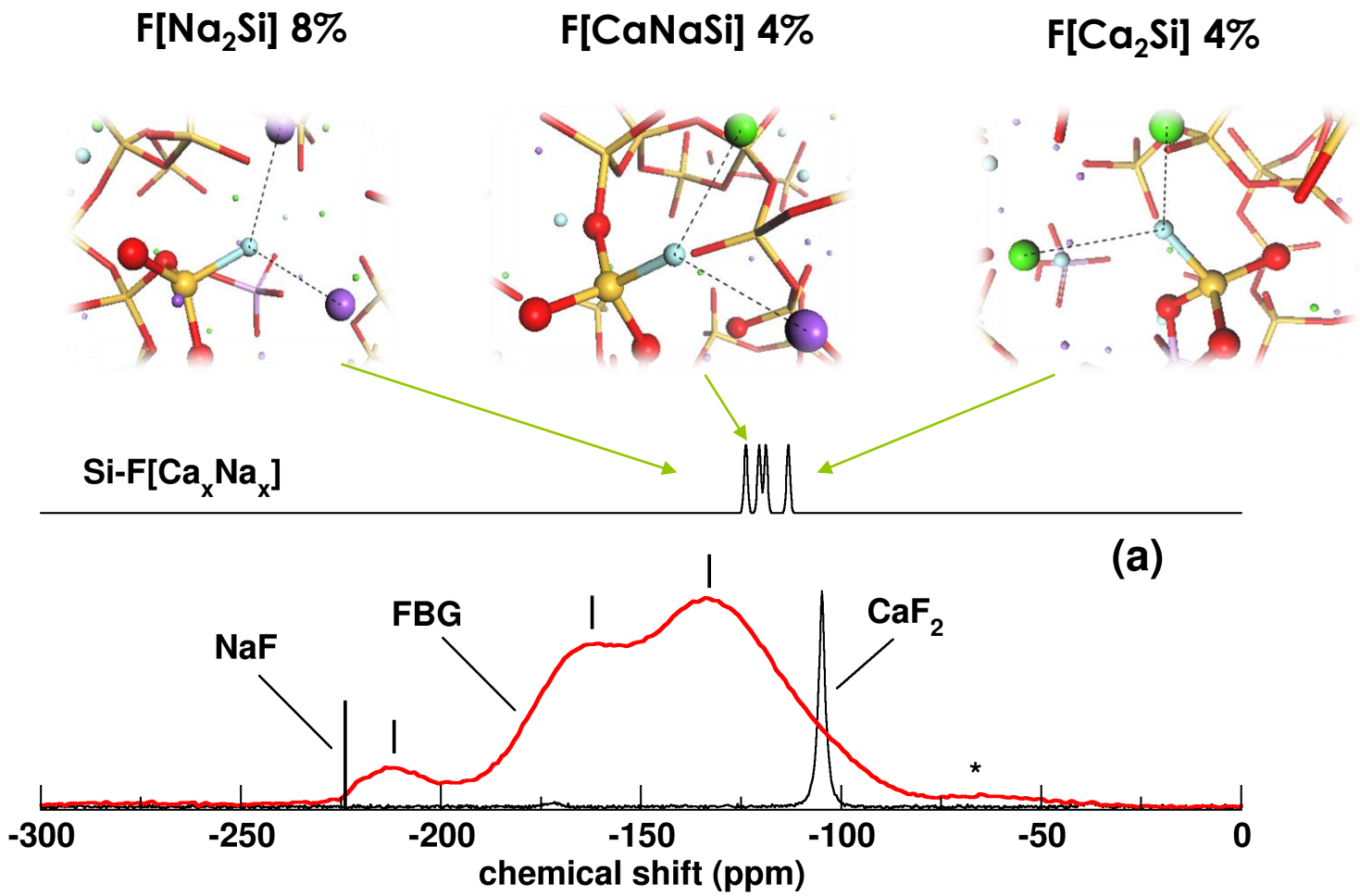
F[Ca_3Na] 8%



High δiso → **low δiso**

- ✓ de-shielding due to the partial covalence of the Ca-F bonds.

Contribution of Si-F bonds to ^{19}F MAS spectra…



- ✓ it is difficult to assess the presence of Si–F bonds by means of the MAS NMR spectra only.

Conclusions

- **NMR spectroscopy + MD-GIPAW is a powerfull tool to improve amorphous system structural characterization**

- P is present as orthophosphate units (No Si-O-P bonds in the compositions studied)
- Trinomial distribution of Q^n(Si) species
- Non-random distribution of Na/Ca around NBO
- Si-F bonds are not detectable by means of ^{29}Si MAS NMR but REDOR experiments must be used
- F atoms are coordinated to the modifiers in a mixed state

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