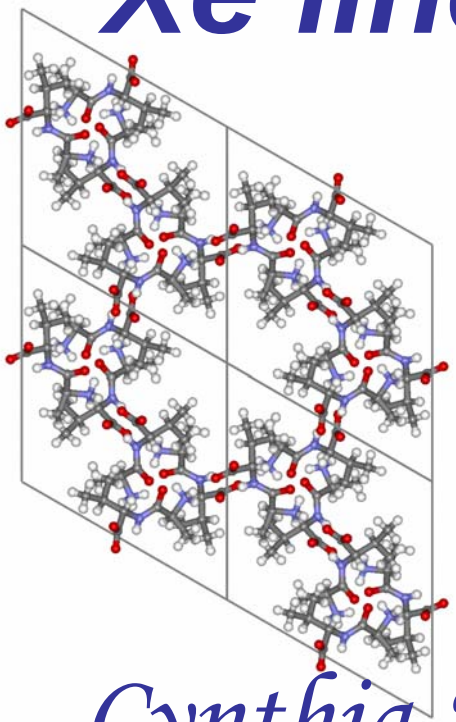
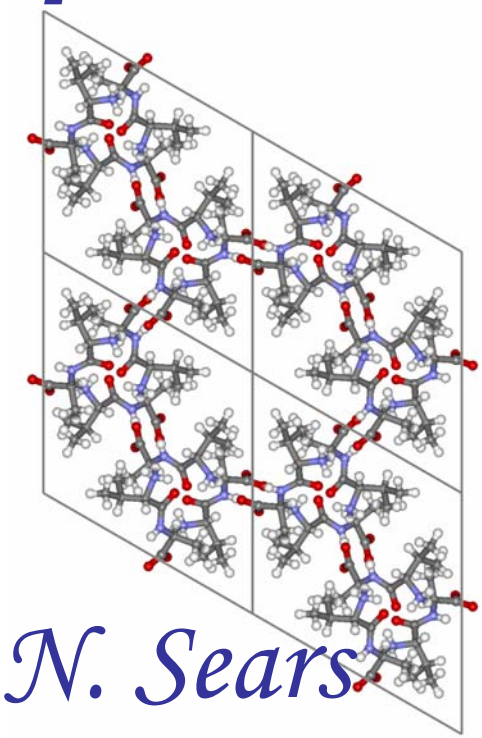
Xe line shapes in dipeptide channels: AV and VA





Cynthia J. Jameson and Devin N. Sears

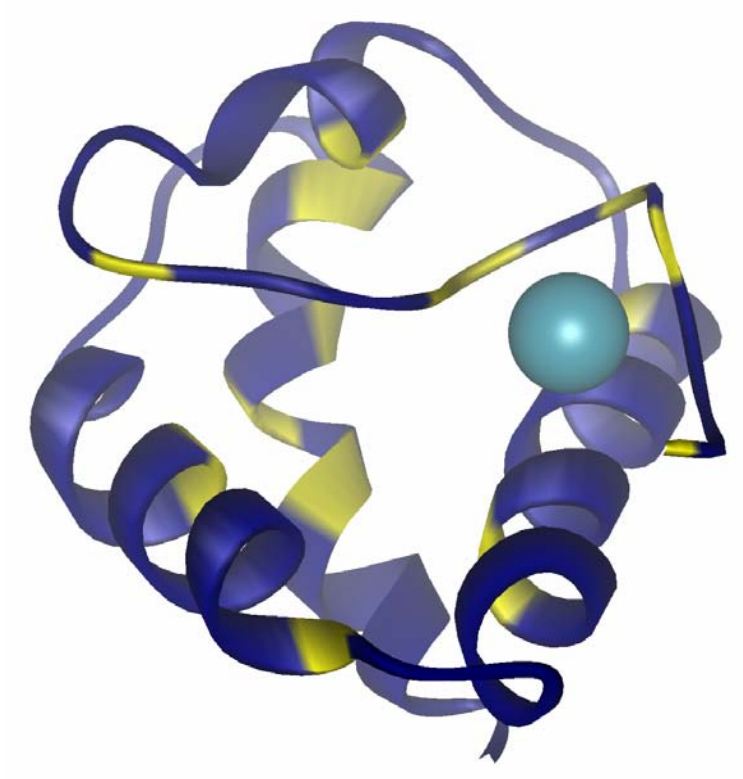
University of Illinois at Chicago

with *Ripmeester et al.*

Motivation:

- Xenon has an affinity for hydrophobic cavities and pockets in proteins

- NMR demonstrates Xe binding in protein pockets in solution



Wheat nonspecific lipid transfer protein
Yellow residues indicate amino acids which have SPINOE enhanced ^{1}H NMR signals indicating close proximity to a hyperpolarized ^{129}Xe atom

Xe in pockets

C. Landon,
P. Berthault,
F. Vovelle,
and H. Desvaux

Simulations constrained by SPINOE data provide Xe positions in wheat nonspecific lipid transfer protein.

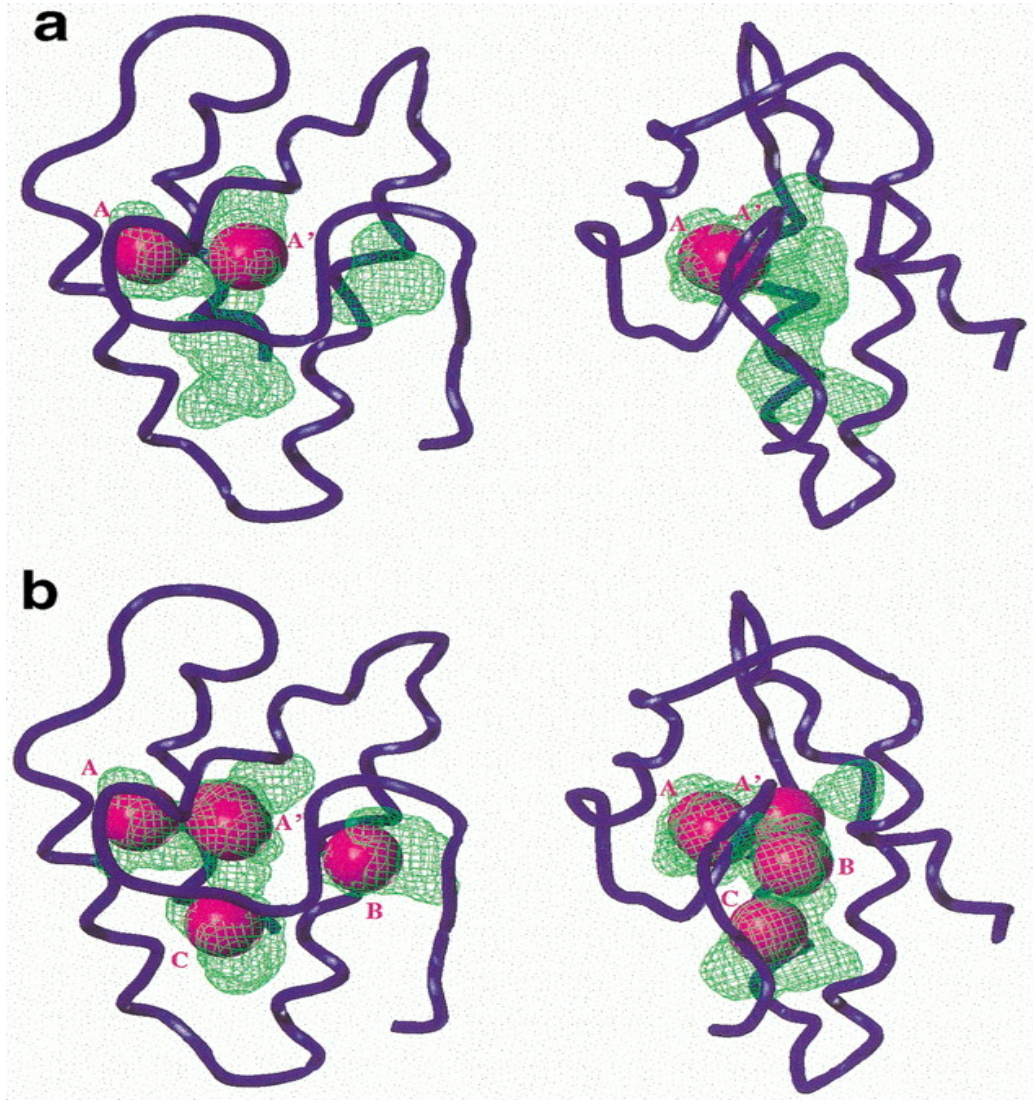
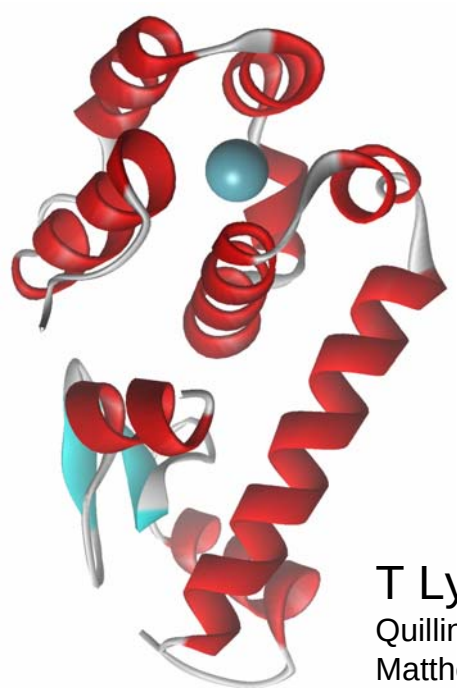


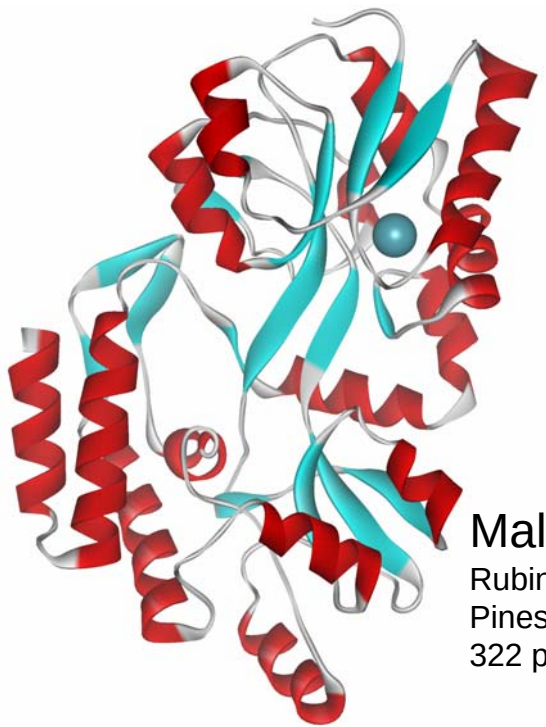
Figure taken from
Protein Science (2001), 10:762-770.

Xenon sequestered in protein cavities and pockets observed by x-ray crystallography



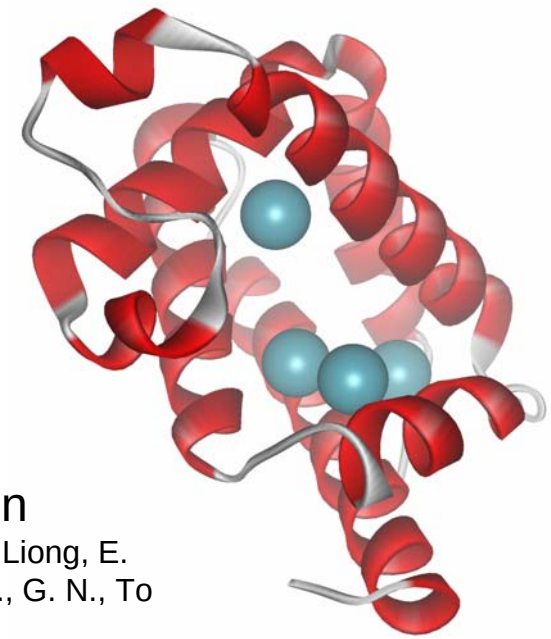
T Lysozyme

Quillin, M. L., Breyer, W. A., Griswold, I. J., Matthews, B. W. J.Mol.Biol. 302 pp. 955 (2000)



Maltose binding protein

Rubin, S. M., Lee, S.-Y., Ruiz, E. J., Pines, A., Wemmer, D. E., J.Mol.Biol. 322 pp. 425 (2002)



Myoglobin

Radding, W., Liong, E. C., Phillips Jr., G. N., To be published

Chemical shifts of Xe in protein pockets requires an understanding of the nature of Xe-protein interactions

Our approach:

Start with molecular crystalline systems of known structure

Dipeptide molecular crystals form 1-D channels ideal for understanding Xe-protein interaction

L-Val-L-Ala

VA

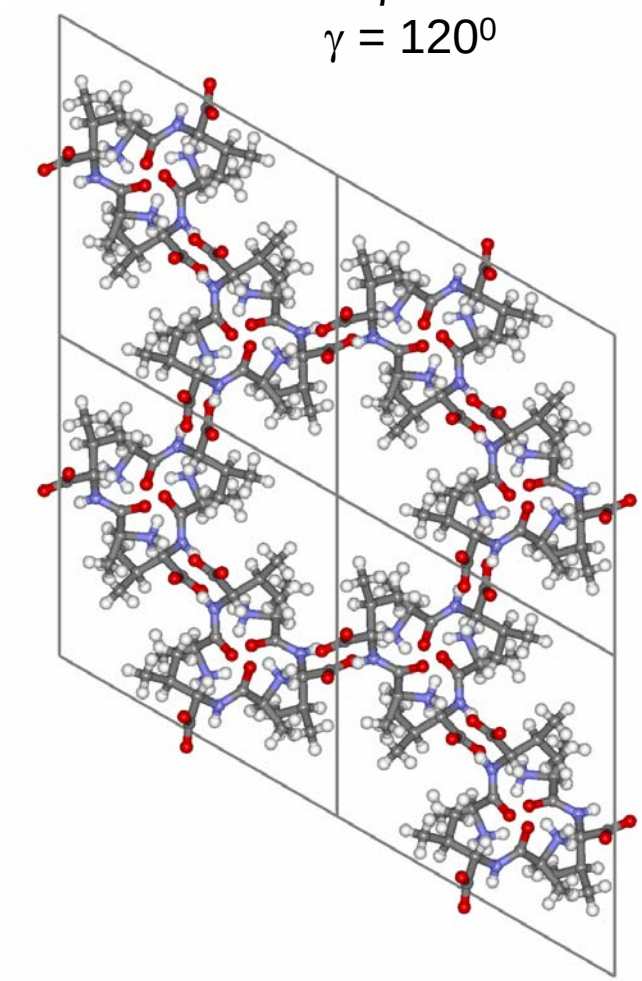
P61

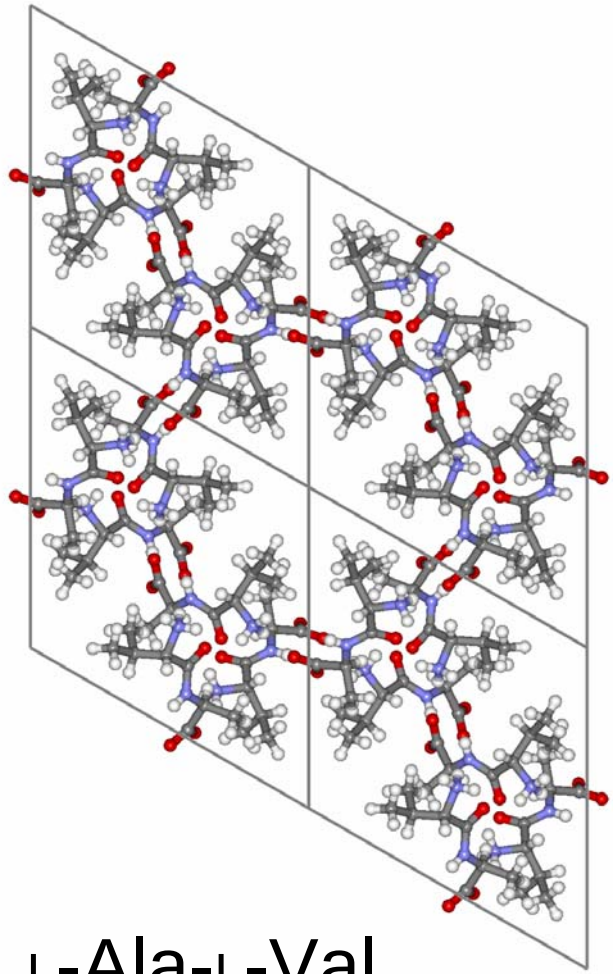
a = b= 14.461 Å

c = 10.083 Å

$\alpha = \beta = 90^0$

$\gamma = 120^0$





L-Ala-L-Val

AV

P61

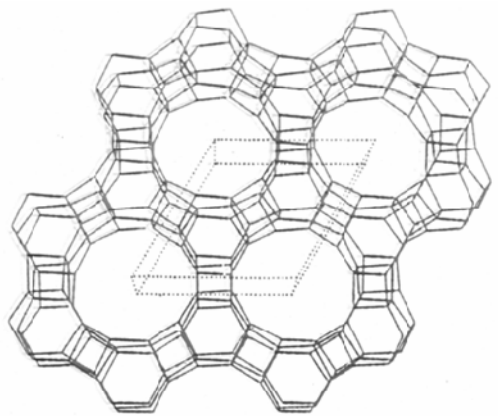
a = b= 14.462 Å

c = 10.027 Å

$\alpha = \beta = 90^0$

$\gamma = 120^0$

Xe in nanochannels



QUESTION:
Is information about
the architecture and
constitution of the nanochannel
encoded into the Xe NMR lineshape in
polycrystalline samples?

- nature of geometric confinement, i. e., size and shape of the nanochannel or cavity
- electronic structure of the channel atoms

How is information encoded into the average Xe chemical shift?

The Xe chemical shift encodes any structural or dynamic information that depends on:

- **Electronic structure of the neighbors of the Xe atom**
- **Configurations of neighbor atoms, how many, at what distances**
- **The relative probabilities of the various configurations**

Information that is encoded in observed Xe spectra:

known from Xe in zeolitic channels

- **structural as well as dynamic information**
- **the diameter of the channel**
- **the aspect ratio of the cross section of the channel**
- **the architecture of the channel**
- **average number of Xe atoms per unit cell**
- **electronic structure of atoms constituting the cavity walls**

Grand Canonical Monte Carlo Simulations

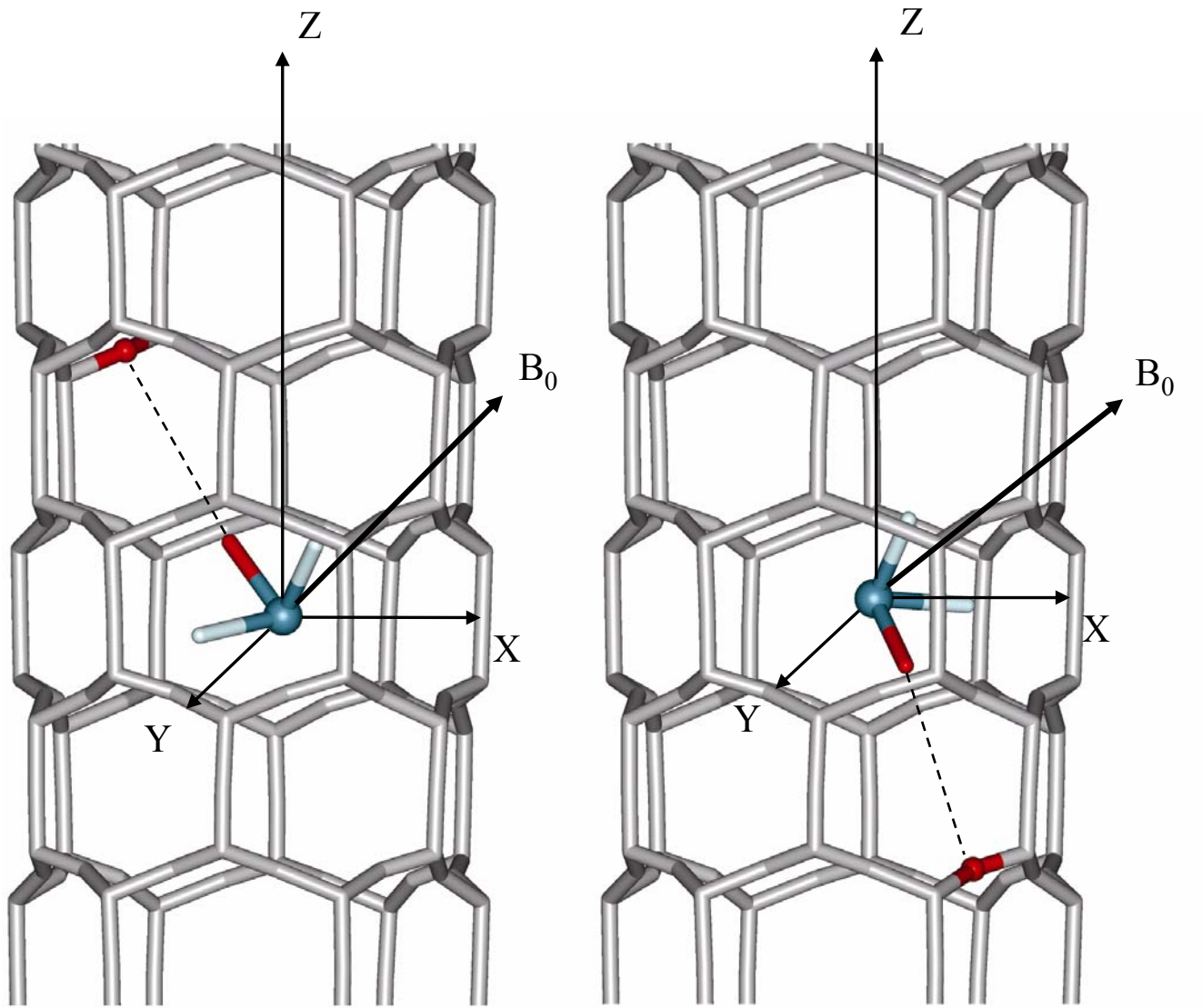
- Impose the condition that the chemical potential of Xe in the overhead bulk gas is the same as the chemical potential of Xe in the adsorbed phase (decide to create, destroy, displace Xe atoms, accordingly)
- Choose a B_0 direction, taking steps of equal probability in $\zeta\phi$ space
- Sum the tensor components along the B_0 direction from each Xe-O (or other channel atom), from each Xe-Xe

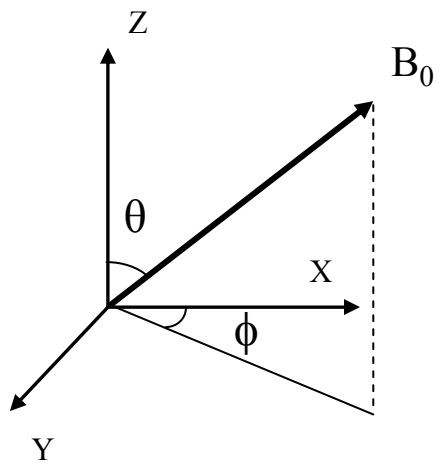
Xe shielding tensor in a channel in an external magnetic field (B_0) along direction (θ,ϕ):

$$\sigma_{B0}(\theta, \phi) = \sigma_{xx} \sin^2\theta\cos^2\phi + \sigma_{yy} \sin^2\theta\sin^2\phi + \sigma_{zz} \cos^2\theta + \tfrac{1}{2}(\sigma_{xy}+\sigma_{yx})\sin^2\theta\sin2\phi + \tfrac{1}{2}(\sigma_{xz}+\sigma_{zx})\sin2\theta\cos\phi + \tfrac{1}{2}(\sigma_{yz}+\sigma_{zy})\sin2\theta\sin\phi$$

one Xe tensor from interaction with ALL channel atoms

Lineshapes by grand canonical Monte Carlo





Random orientation of crystallites:
Probability that B_0 lies in any infinitesimal solid angle is
$d\zeta\, d\phi / 4\pi$, where
$\zeta = (-\cos\theta)$
Equal areas in $\zeta\phi$ plane correspond to equal probabilities

Consider one Xe-O at a time
(and one Xe-Xe at a time)

How do we model the structure?

First we obtain from the literature or from a crystallographic data base the positions of the atoms in the crystal. Then we make up several unit cells in our computer so as to visualize what atoms the Xe actually will interact with in the channel.

These are valyl-alanine and alanyl-valine. They are called retro-analogs.

L-Val-L-Ala

VA

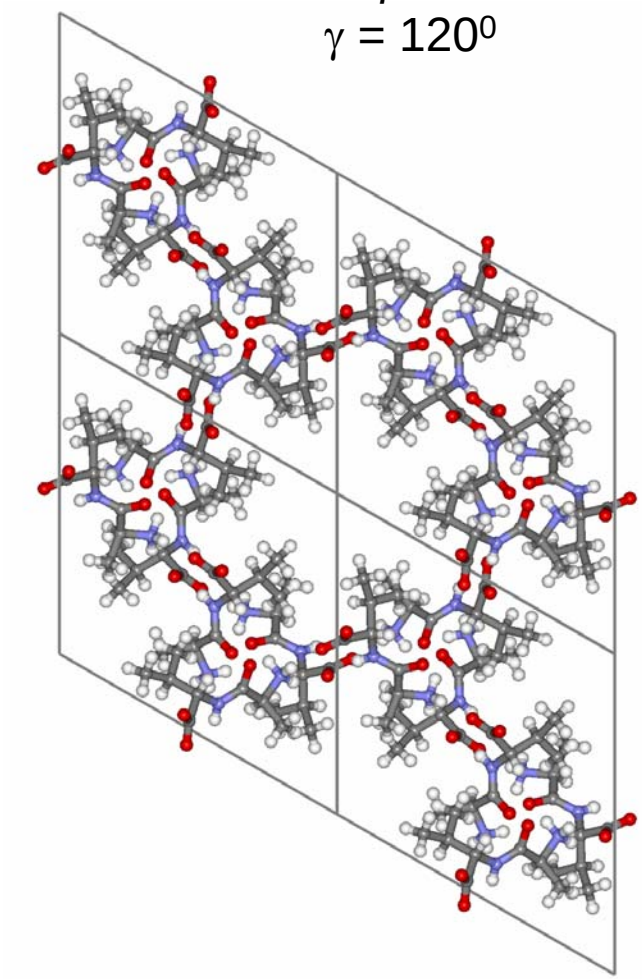
P61

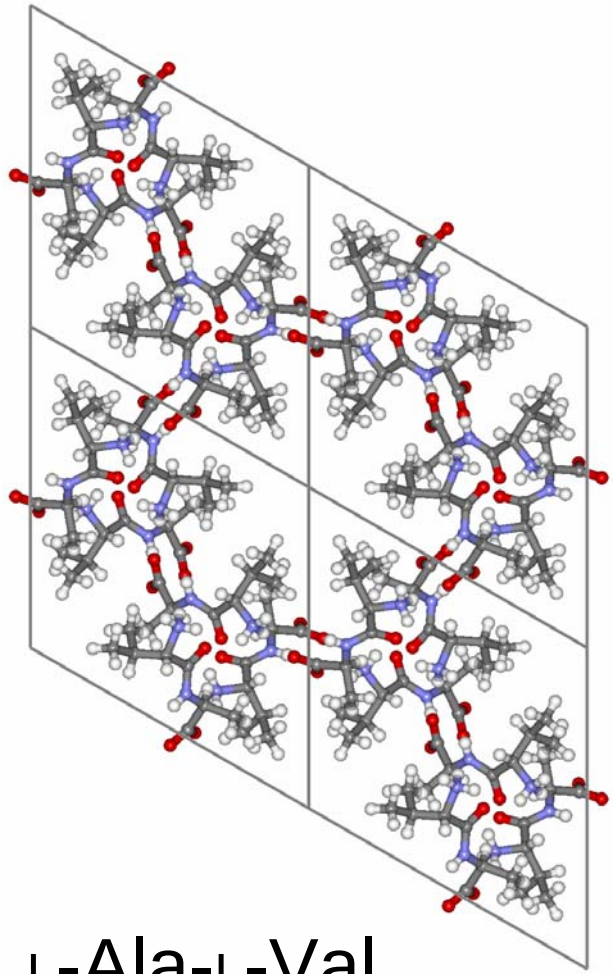
a = b= 14.461 Å

c = 10.083 Å

$\alpha = \beta = 90^0$

$\gamma = 120^0$





L-Ala-L-Val

AV

P61

a = b= 14.462 Å

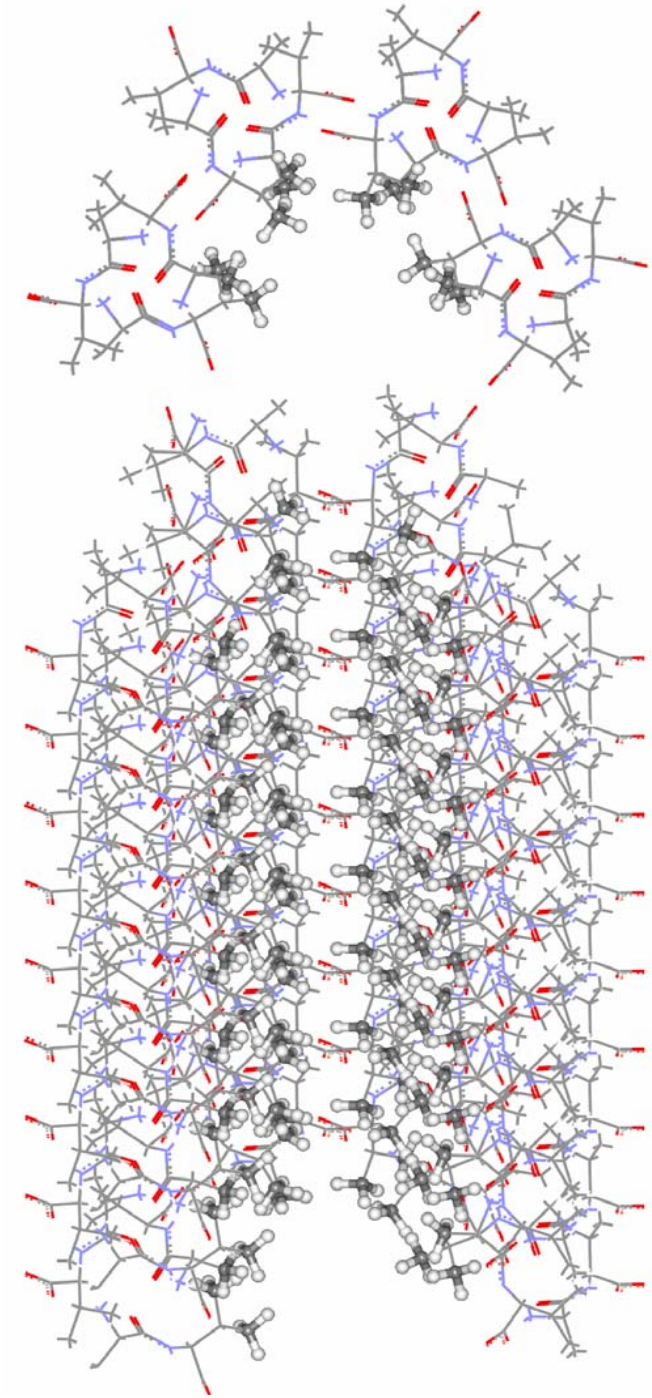
c = 10.027 Å

$\alpha = \beta = 90^0$

$\gamma = 120^0$

•From the perspective of the Xe only the side chain methyl groups are accessible

•Can we use the **Xe- CH_4** shielding response surface and potential energy surface for our simulations?



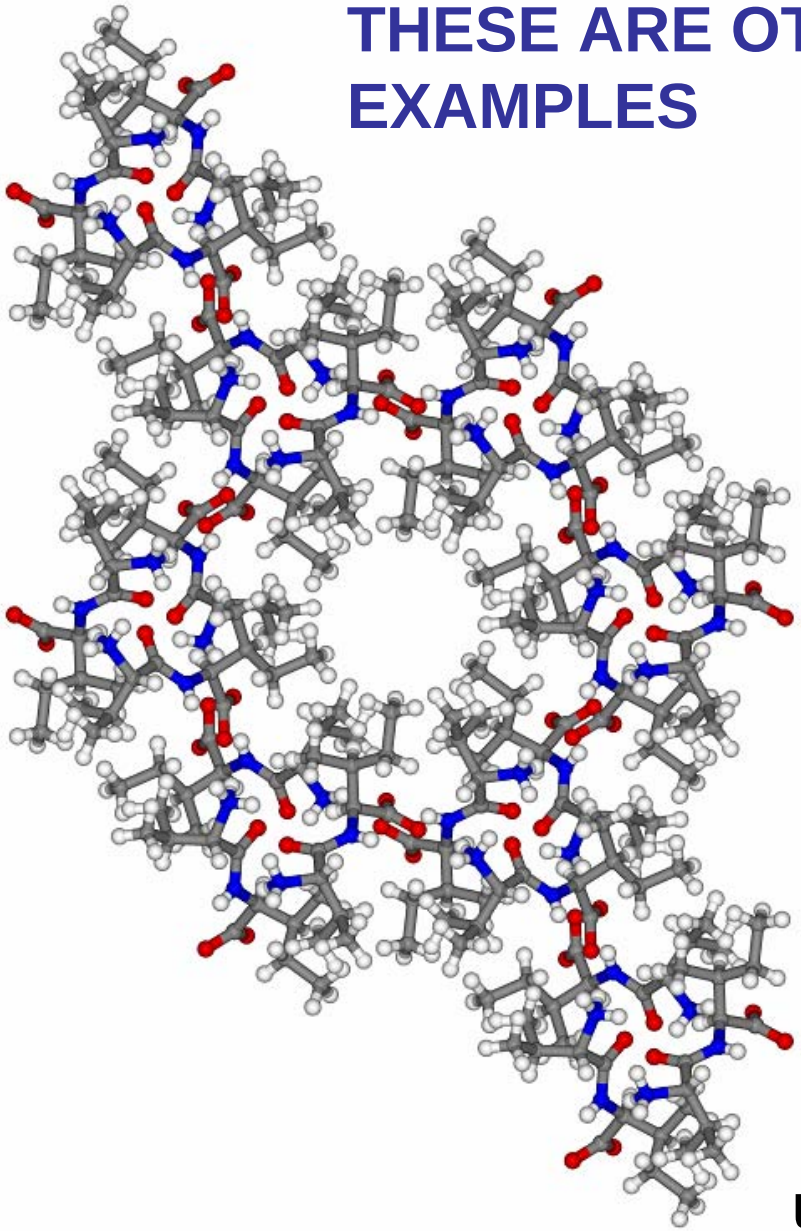
Top view

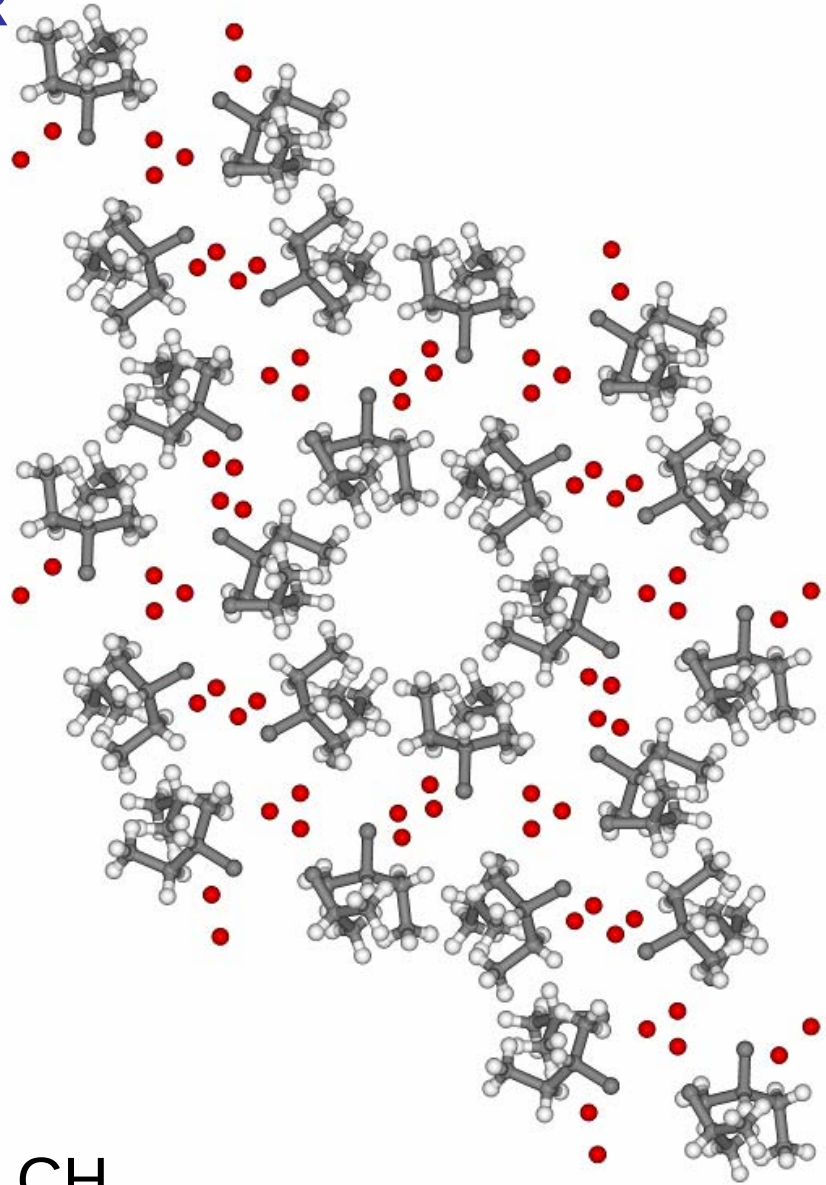
Tilted view

Modeling

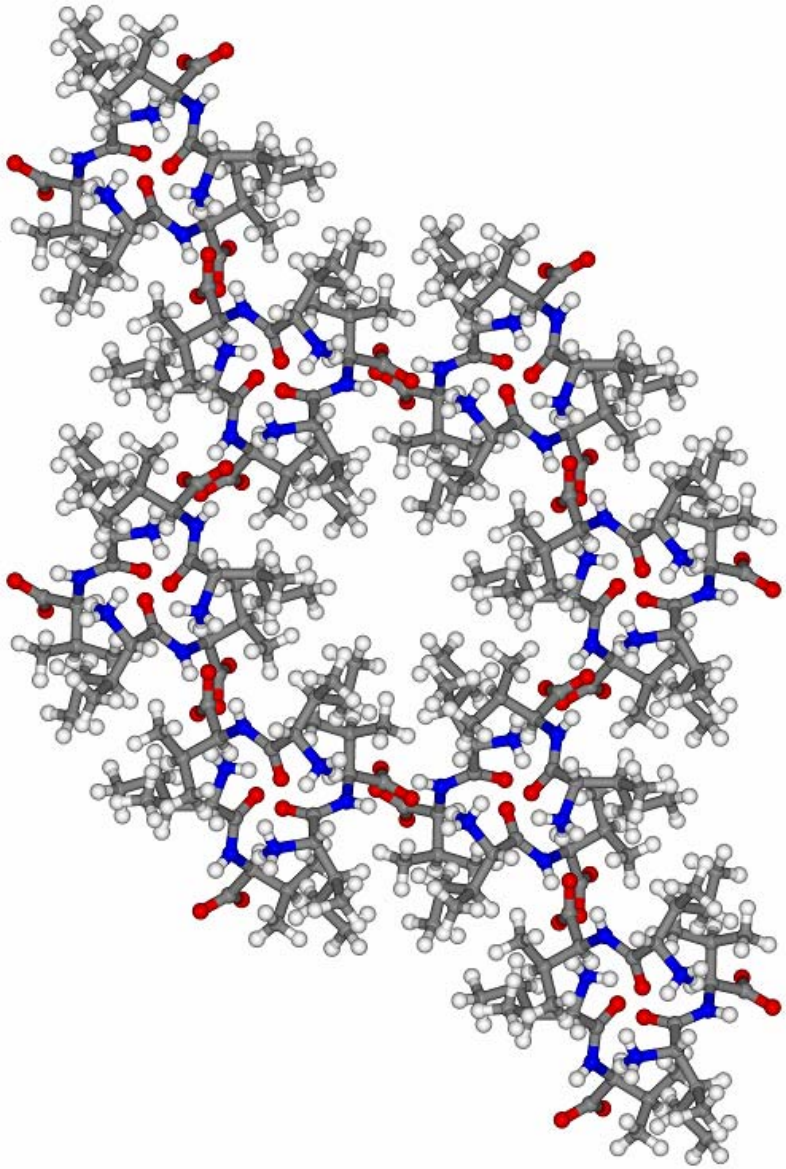
- C and H atom positions in the channel wall retain the electronic structure of C and H atoms in CH_4 molecule with respect to potential energy of interactions and intermolecular shielding contributions to Xe
- replace O and N atoms and all other C atoms by dummy atoms which have no contributions to the Xe chemical shift but which have repulsive interaction potentials with Xe in the Monte Carlo simulations

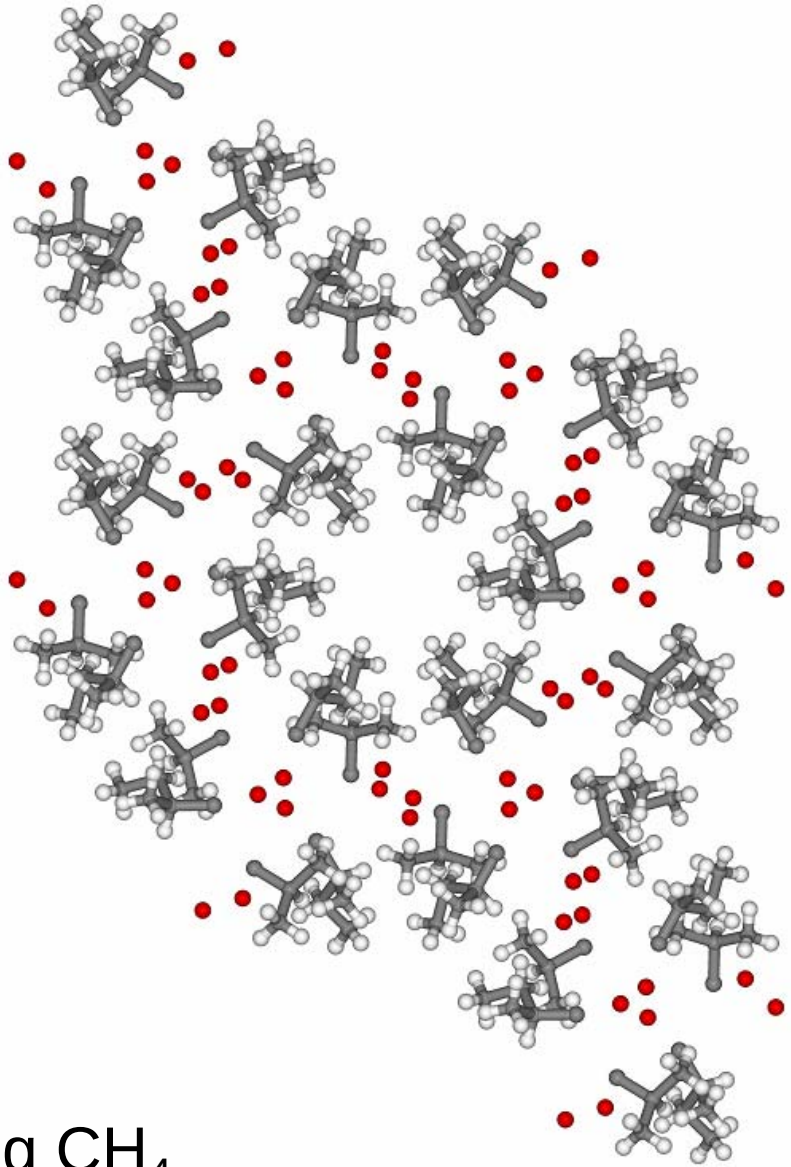
THESE ARE OTHER EXAMPLES





VI X-Ray Structure —using CH_4→ GCMC Structure





using CH_4

IV X-Ray Structure → GCMC Structure

The **dimer tensor model** for Xe shielding tensor in a channel

The contribution to the shielding of Xe at point J due to i_{th} C atom located at (x_i, y_i, z_i) is given by the ab initio tensor components for the XeC dimer, the functions $\sigma_{\perp}(r_{XeC})$, $\sigma_{||}(r_{XeC})$.

Likewise, we use the functions $\sigma_{\perp}(r_{XeH})$, $\sigma_{||}(r_{XeH})$ in:

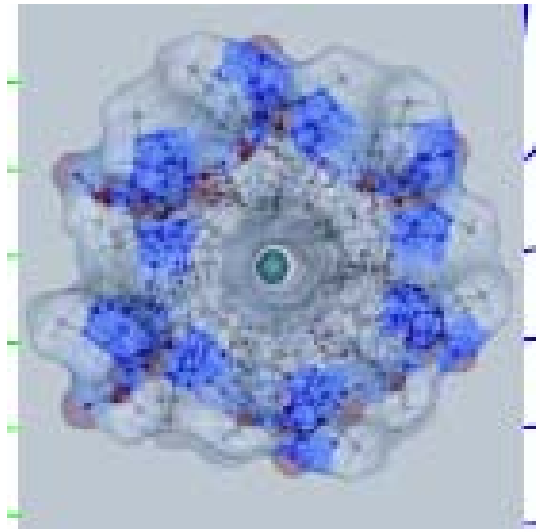
$$\sigma_{XX} = [(x_i - x_J)/r_{iJ}]^2\sigma_{||} + \{[(y_i - y_J)/r_{iJ}]^2 + [(z_i - z_J)/r_{iJ}]^2\}\,\sigma_{\perp}$$

$$\tfrac{1}{2}(\sigma_{XY}+\sigma_{YX}) = [(x_i - x_J)/r_{iJ}]\bullet[(y_i - y_J)/r_{iJ}](\sigma_{||} - \sigma_{\perp})$$

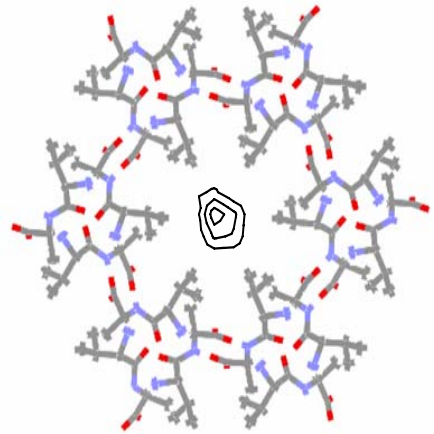
The contribution to the shielding of Xe at point J due to the K_{th} Xe atom located at (x_K, y_K, z_K) is given by the ab initio tensor components for the XeXe dimer, the functions $\sigma_{\perp}(r_{XeXe})$, $\sigma_{||}(r_{XeXe})$.

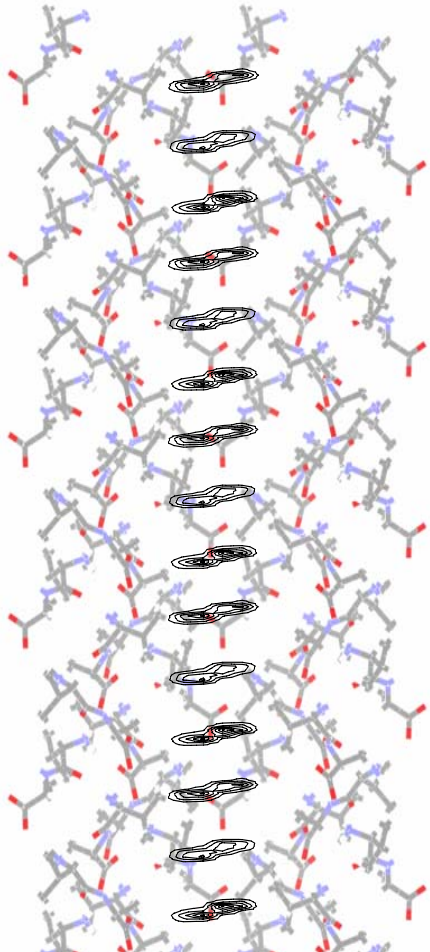
From GCMC simulations the **one-body distribution function** shows the probability of finding a Xe atom as a function of position within the channel

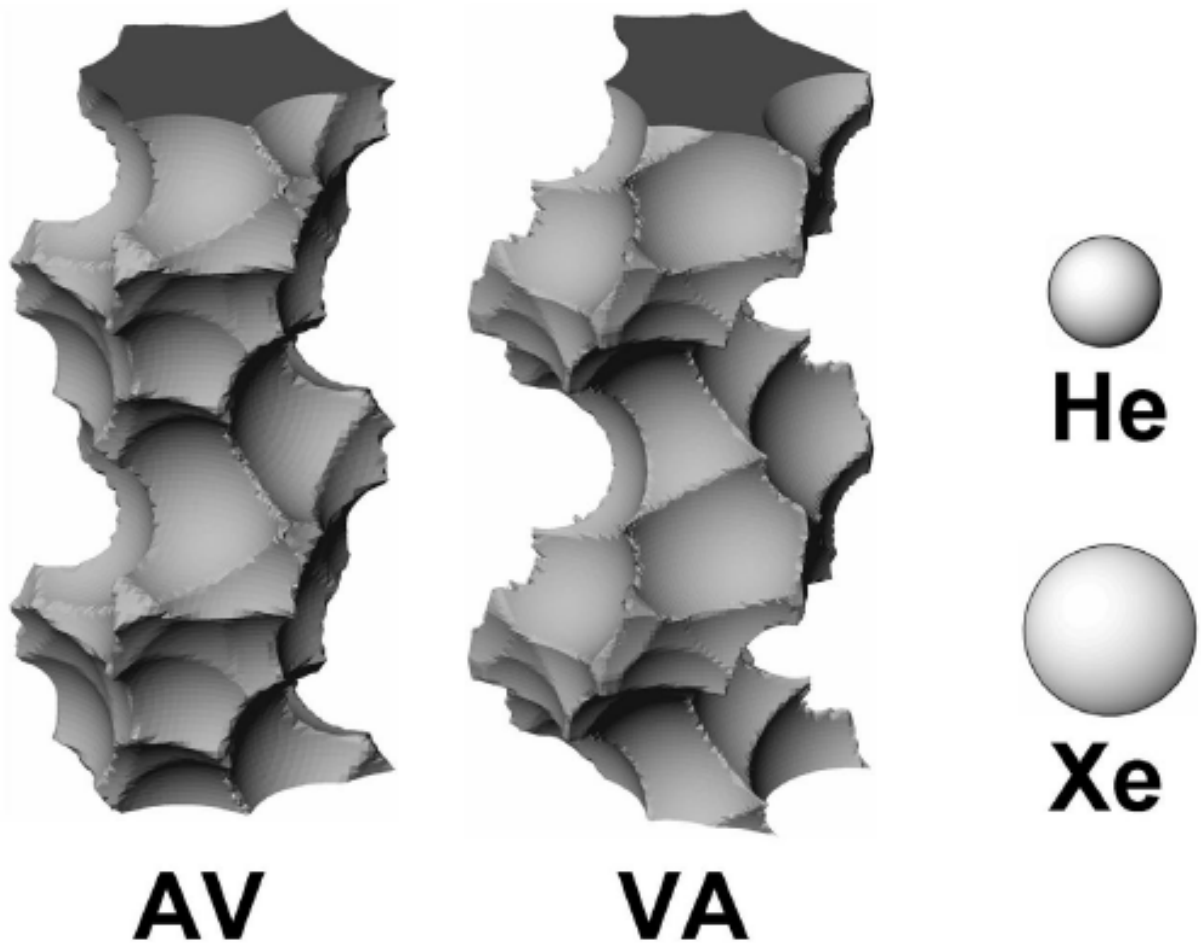
Xe in VA



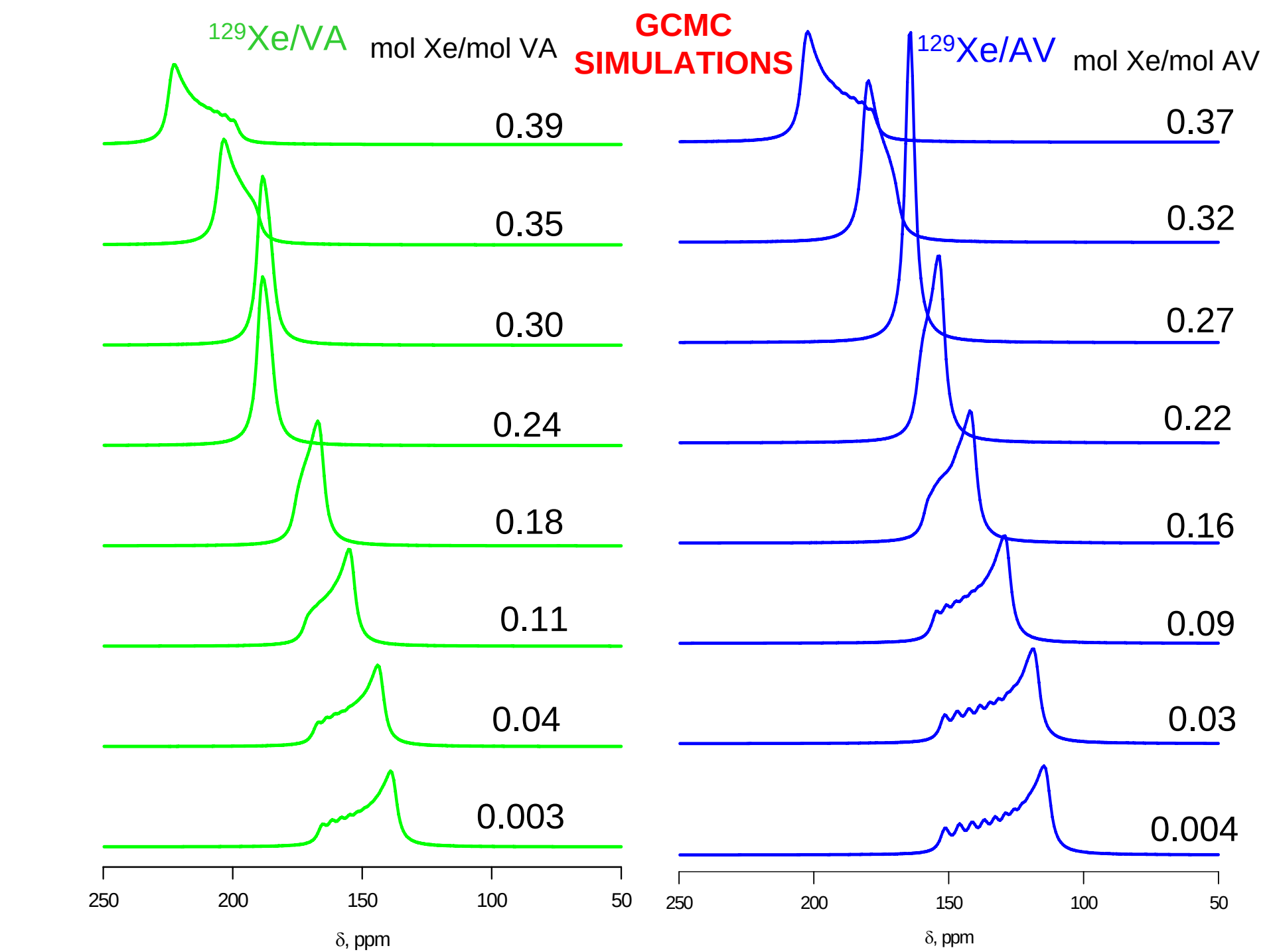
a helical channel!



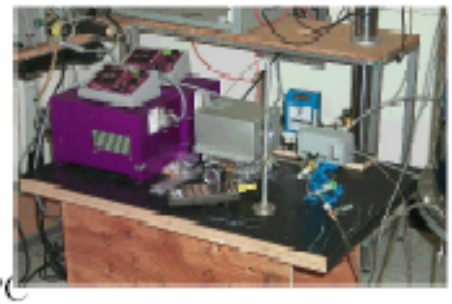




Figures from Soldatov et al. J. Am. Chem. Soc. 128, 6737-44 (2006)


^{129}Xe/VA
mol Xe/mol VA
GCMC
SIMULATIONS
^{129}Xe/AV
mol Xe/mol AV
0.39
0.35
0.30
0.24
0.18
0.11
0.04
0.003
0.37
0.32
0.27
0.22
0.16
0.09
0.03
0.004
250
200
150
100
50
δ, ppm
250
200
150
100
50
δ, ppm

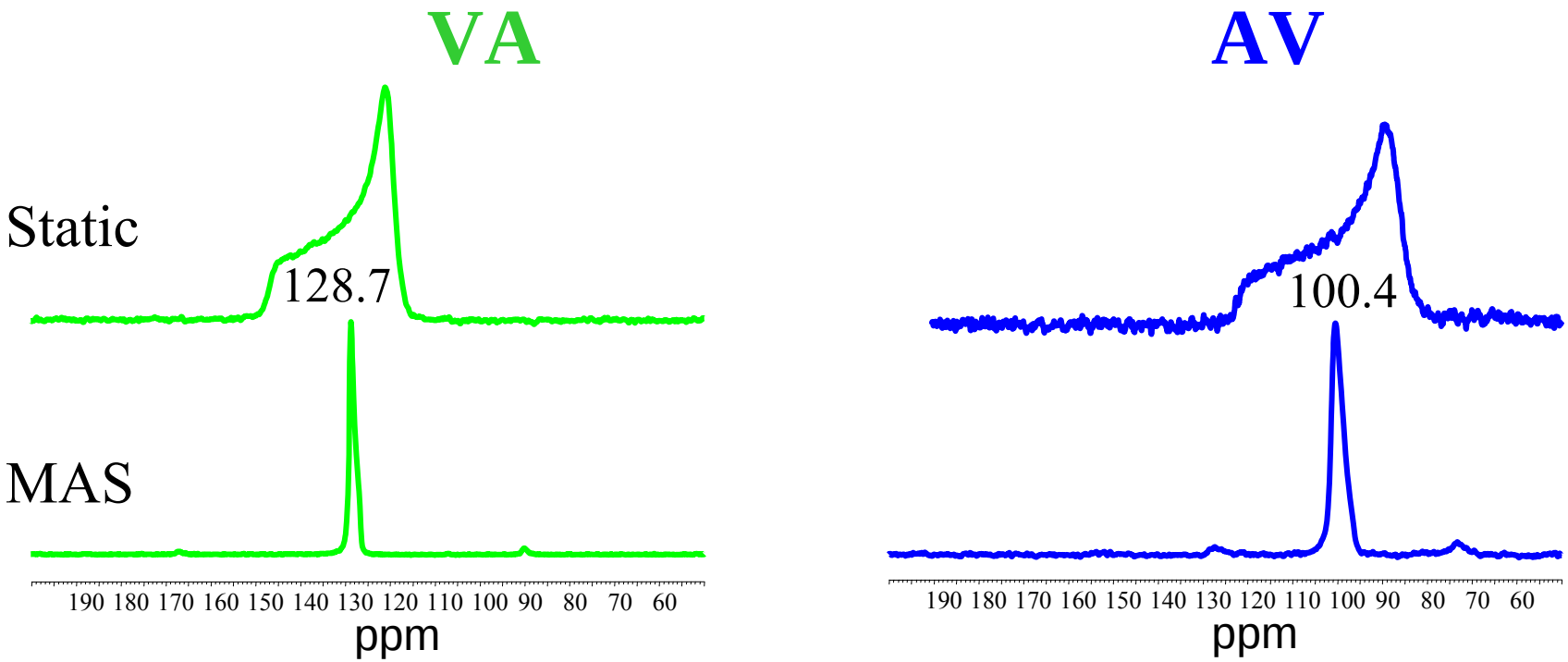
Experimental setup



Open circuit:

- Constant composition of the gas phase
- Concentration on the surface changed by T

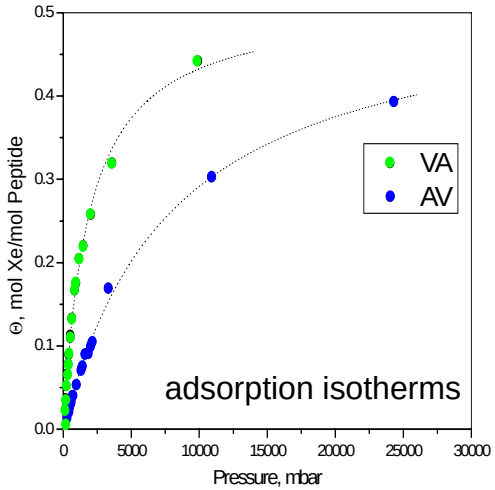
Continuous flow hyperpolarized ^{129}Xe NMR

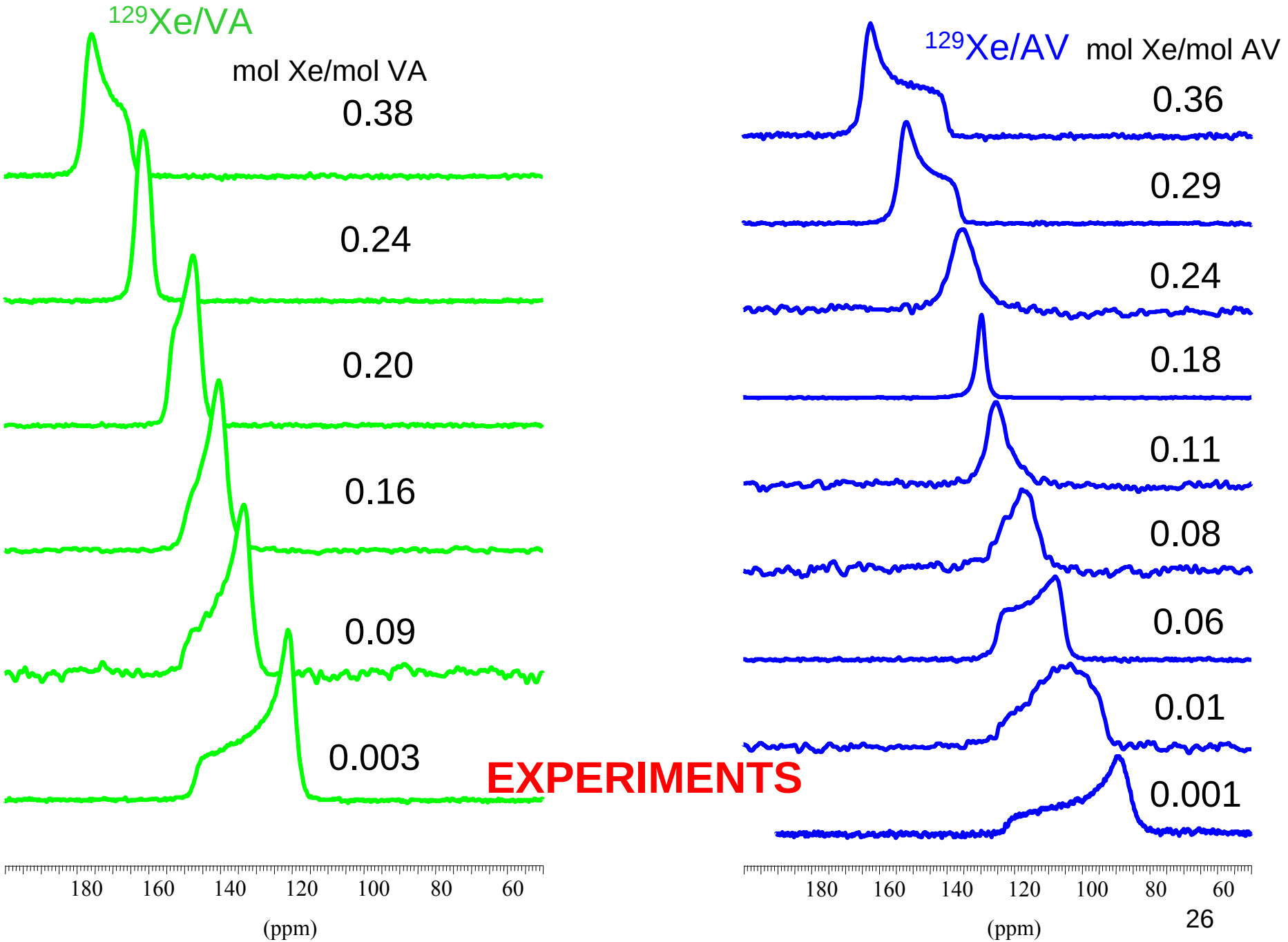


CSA fits of the static spectra

δ_i	128.9 ppm	δ_i	98.7 ppm
Δ	18.0 ppm	Δ	23.0 ppm
η	0.15	η	0.2

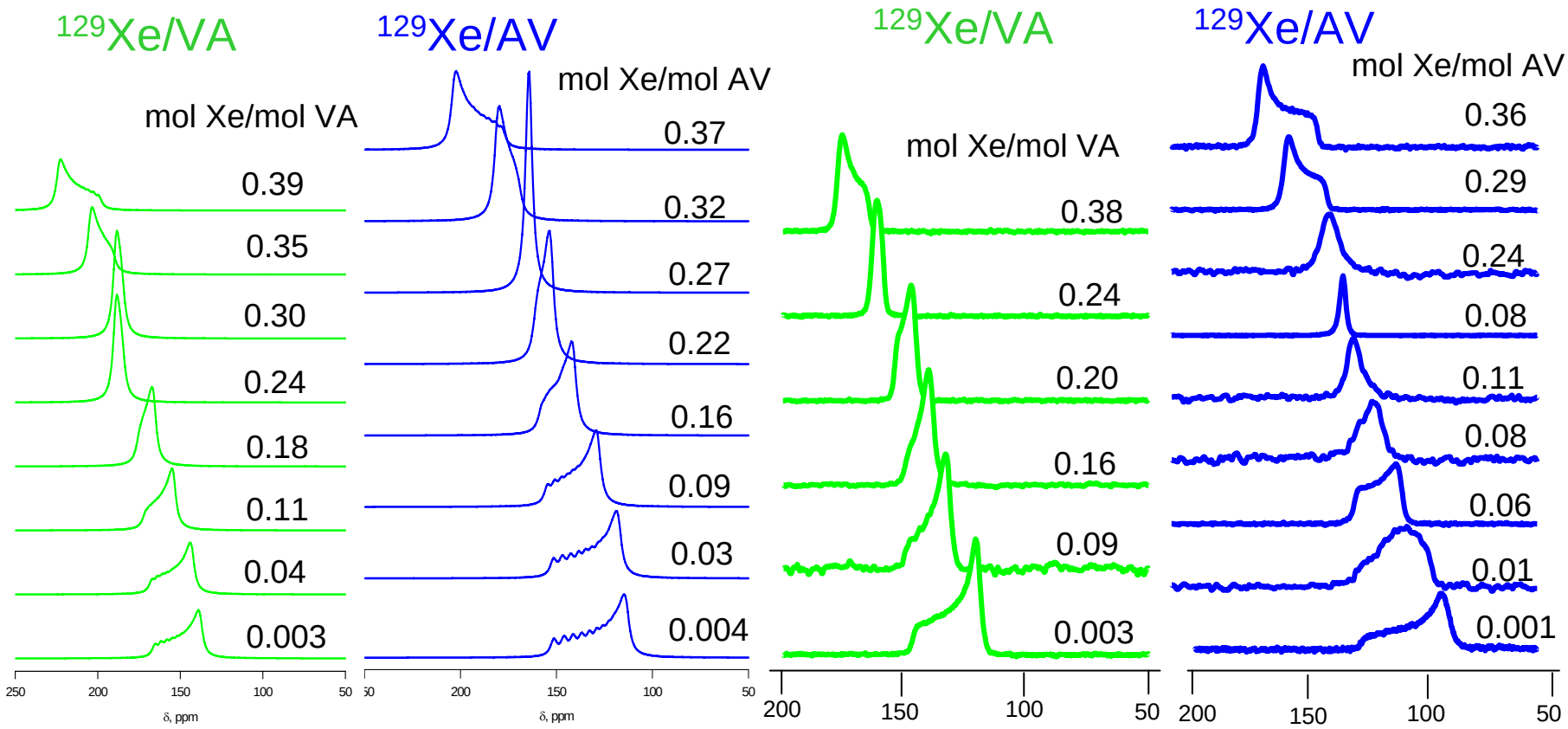
Adsorption isotherms of Xe in VA and AV




129Xe/VA
mol Xe/mol VA
0.38
0.24
0.20
0.16
0.09
0.003
180 160 140 120 100 80 60
(ppm)
129Xe/AV
mol Xe/mol AV
0.36
0.29
0.24
0.18
0.11
0.08
0.06
0.01
0.001
180 160 140 120 100 80 60
(ppm)
EXPERIMENTS

GCMC SIMULATIONS

EXPERIMENTS



Jameson and Sears

Ripmeester et al.

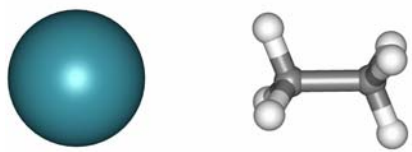
COMPARISON OF PREDICTIONS AND EXPERIMENTS

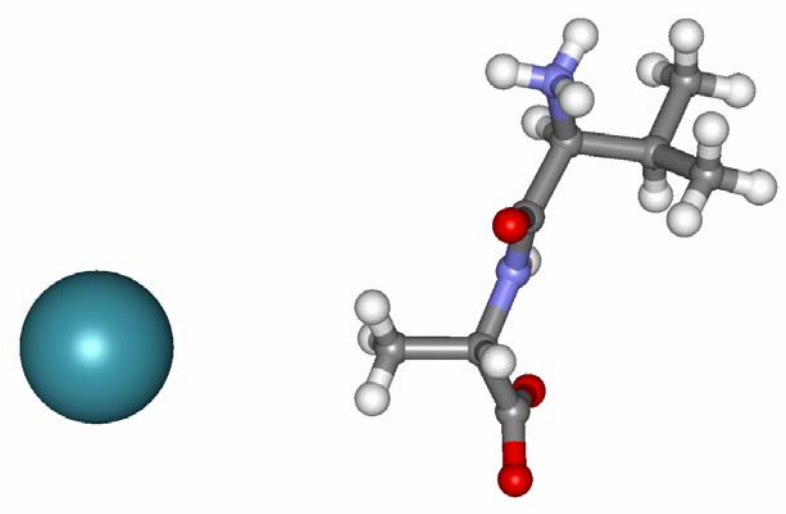
Xe NMR Spectra

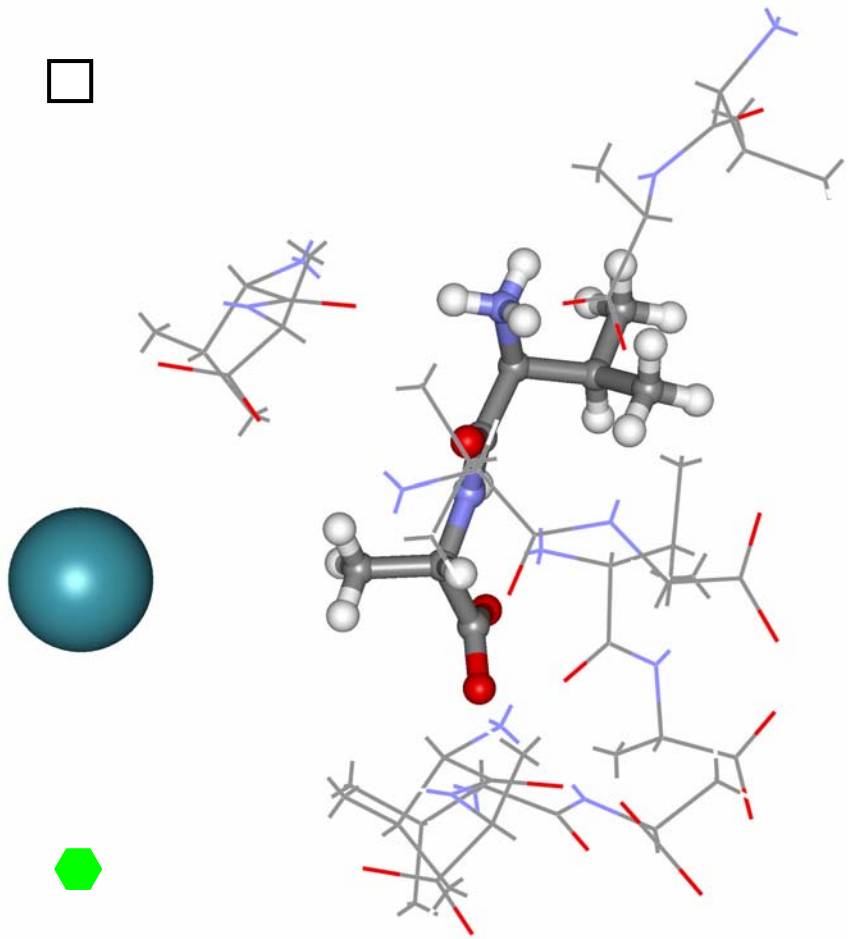
What is wrong with using Xe-C and Xe-H shielding tensors from the Xe-CH_4 shielding response in the dipeptide channel? How may we improve the model?

Models for shielding response calculation:

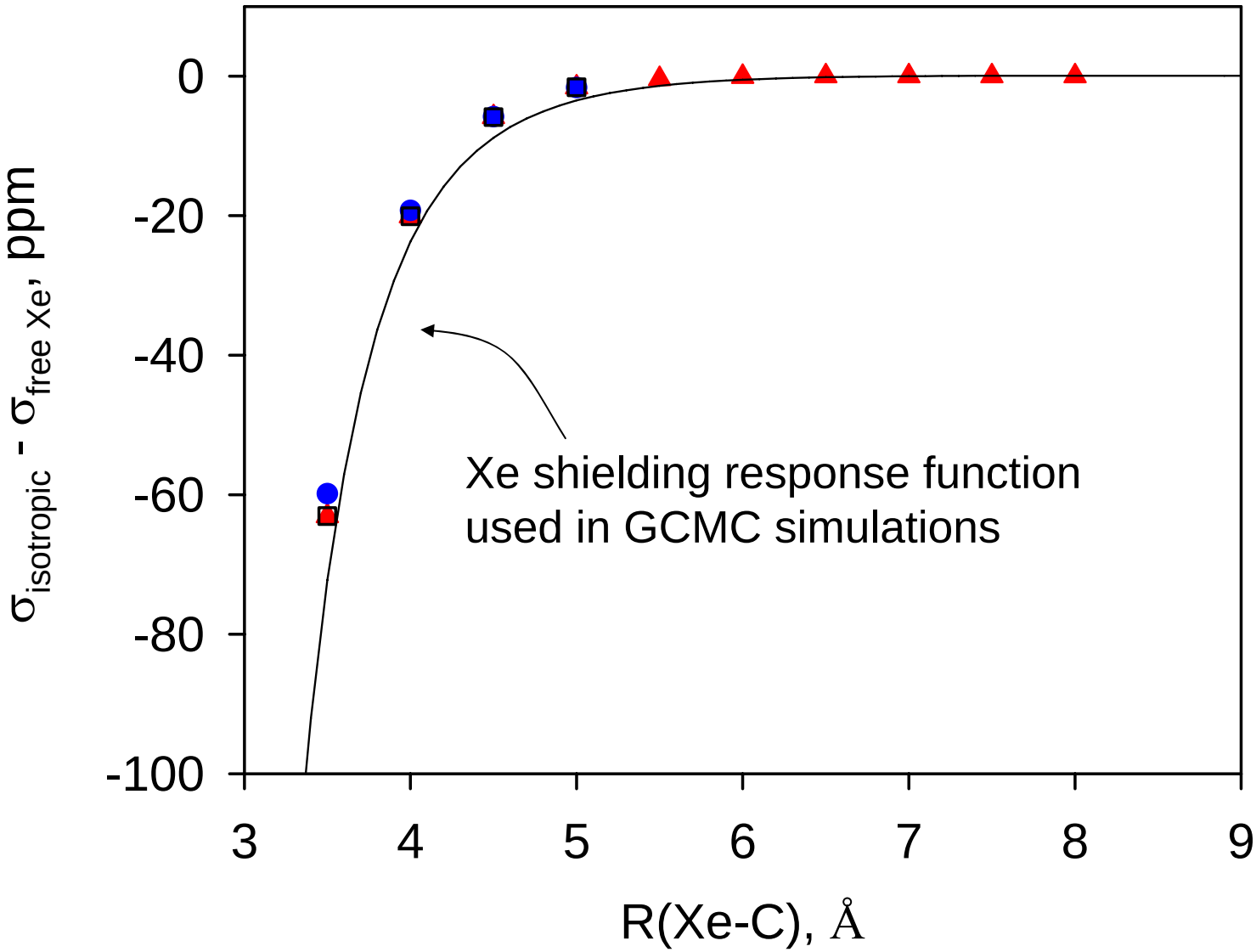
CH_4







DFT calculations suggest a smaller Xe shielding response for Xe-C and Xe-H for the Xe@dipeptide compared to Xe@CH_4



Xe approach normal to the plane of the three H atoms in H_3C

r(Xe-C), Å	First Model Xe@H_3CH	Xe@ H_3CCH_3	Model A Xe@VA
3.5	-66.5963	-63.0607	-53.4822
4.0	-21.3146	-20.0875	-17.3036
4.5	-6.2307	-5.8652	-5.2406
5.0	-1.6730	-1.5802	-1.4988

we used

smaller response

CONCLUSIONS

- Hyperpolarized ^{129}Xe experiments have been carried out as a function of Xe occupancy in two dipeptide molecular crystal nanochannels

- GCMC simulations compare favorably with experiment indicating that use of only Xe-C and Xe-H shielding response functions is sufficient to describe the Xe response to this hydrophobic environment

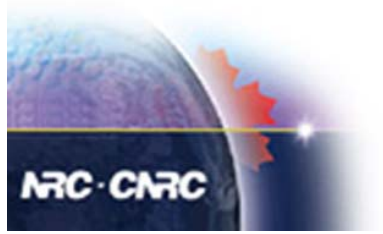
- Peptide sidechains provide the major contributions to the observed Xe chemical shift in these types of systems

Acknowledgments

Funding for CJJ's lab

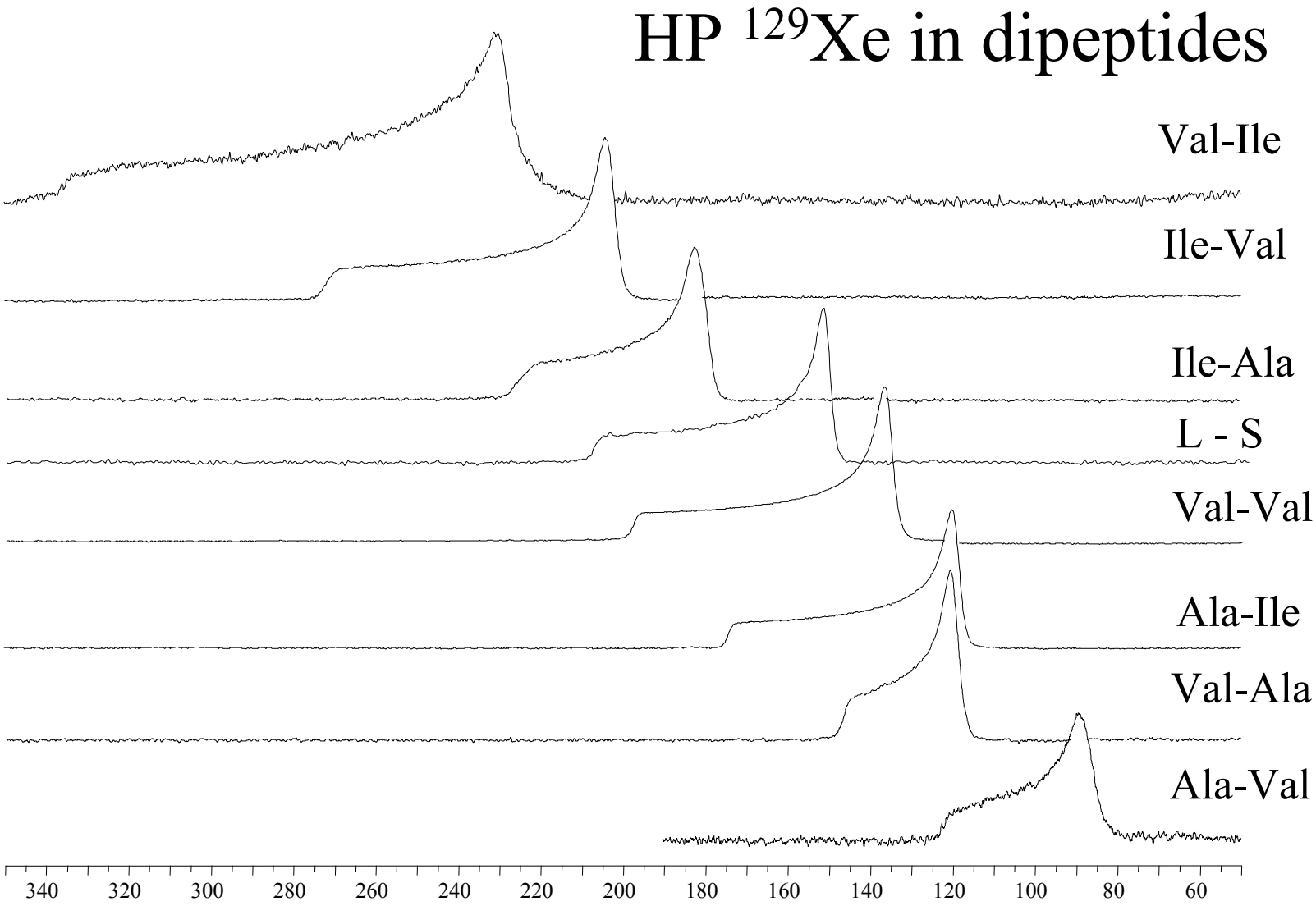
Collaborators

Igor Moudrakovski
Dmitriy V. Soldatov
John A. Ripmeester
Chris Ratcliffe



Devin N. Sears

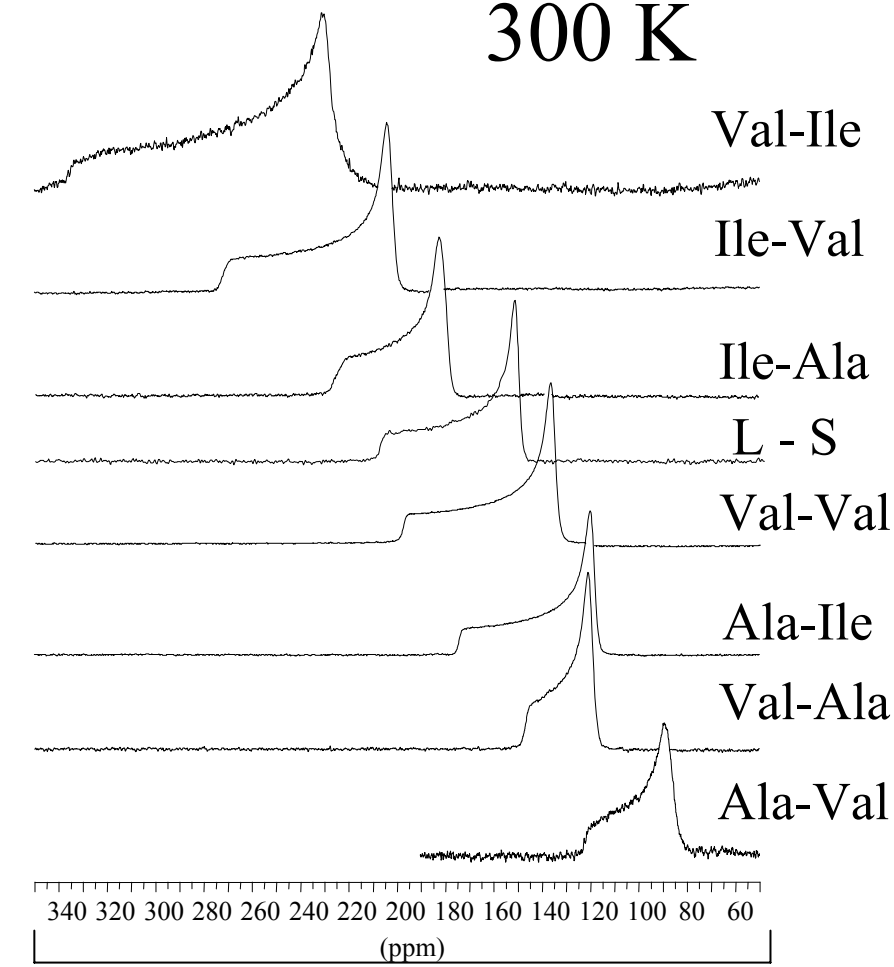
EPILOGUE



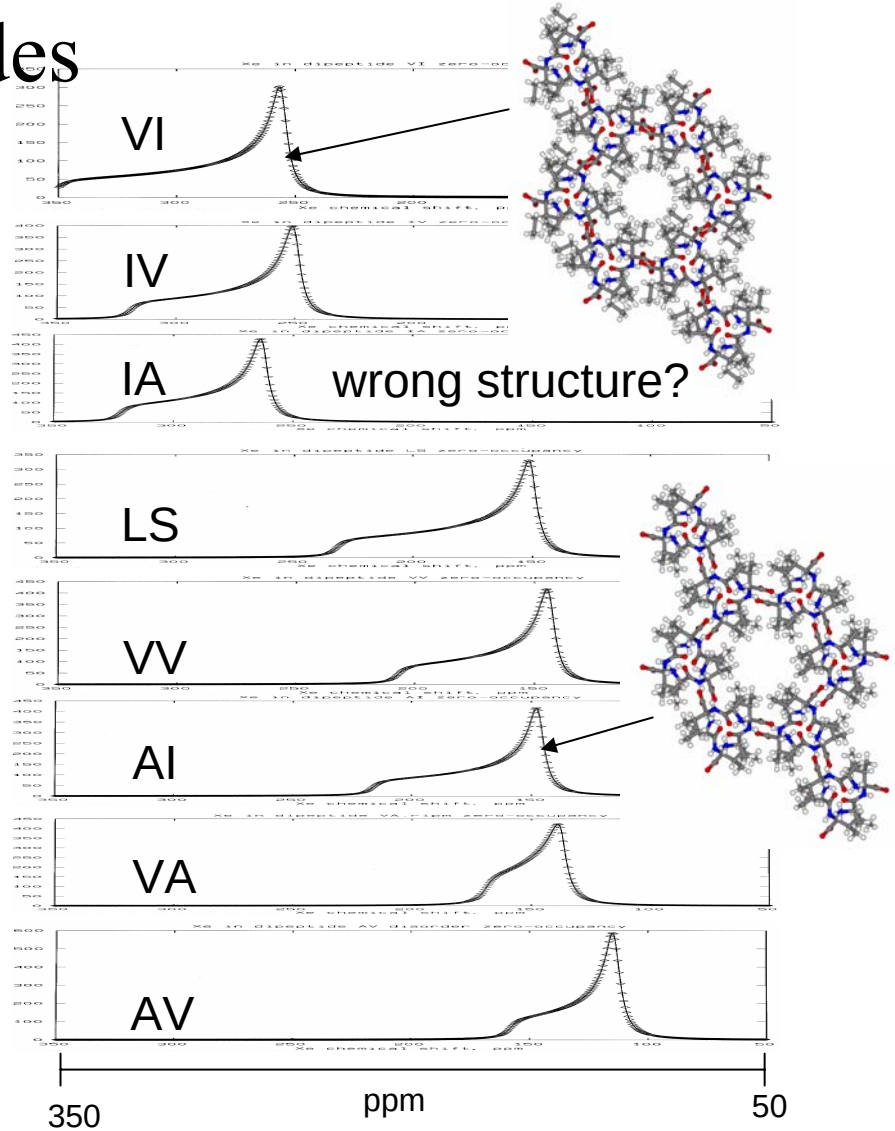
D.V. Soldatov, I.L. Moudrakovski, J.A. Ripmeester 300 K

^{129}Xe NMR in dipeptides

300 K



350 50



EXPERIMENTS

SIMULATIONS

EPILOGUE

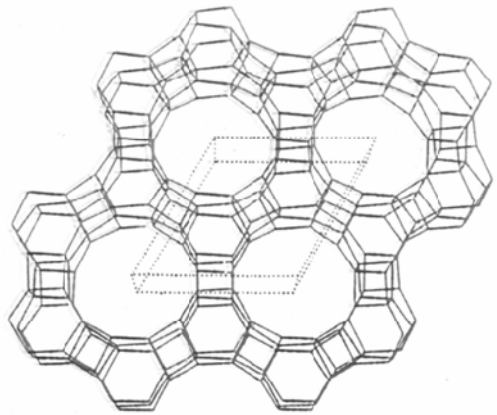
HP Xe in other dipeptides experiments

- Micropores in crystalline dipeptides as seen from the crystal structure, He pycnometry, and ^{129}Xe NMR spectroscopy, D.V. Soldatov, I.L. Moudrakovski, E.V. Grachev, J.A. Ripmeester, J. Am. Chem. Soc. 128, 6737-44 (2006).
- A New Approach to Characterizing Sorption in Materials with Flexible Micropores, R. Anedda, D.V. Soldatov, I.L. Moudrakovski, M. Casu, J. A. Ripmeester, Chem. Mat. 20, 2908-2920 (2008)

EPILOGUE

Xe in nanochannels

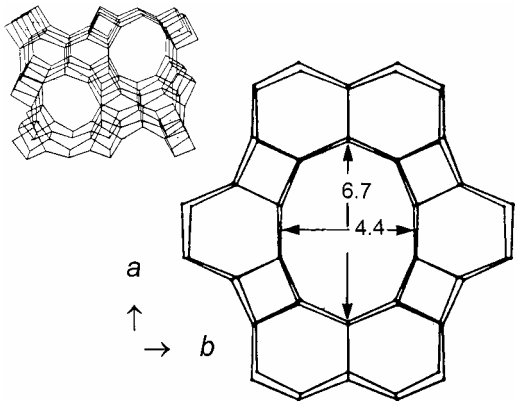
MORE GENERAL QUESTION:



Is information about the architecture and constitution of the nanochannel encoded into the Xe NMR lineshape in polycrystalline samples?

- nature of geometric confinement, i. e., size and shape of the nanochannel or cavity
- electronic structure of the channel atoms

Architecture of the channel determines the lineshape

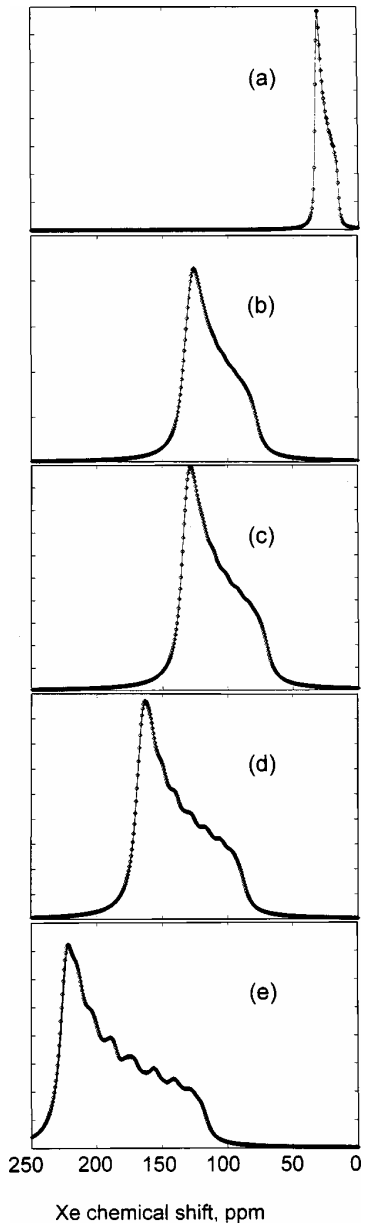


$ALPO_4$-11 architecture

One Xe atom
in a neon channel

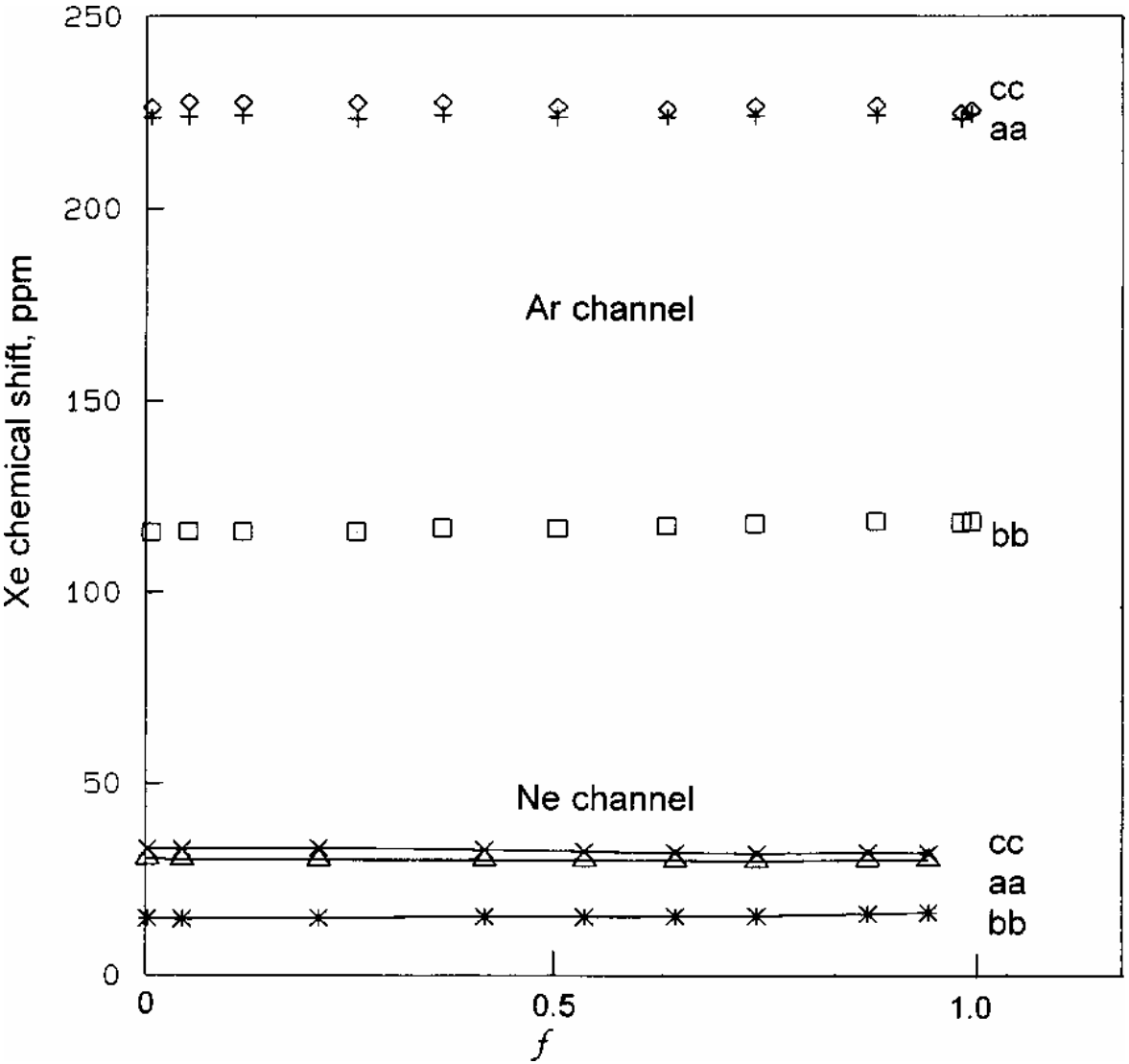
Electronic structure of the channel atoms determines the isotropic chemical shift and width at zero-loading

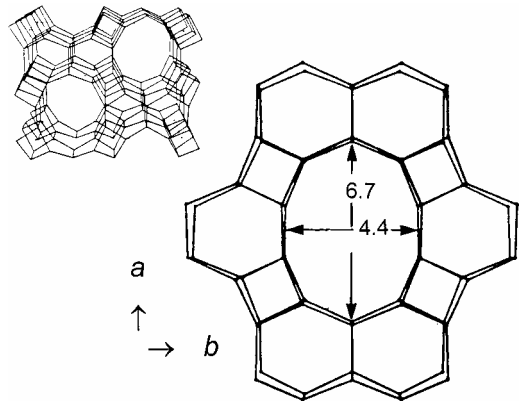
One Xe atom
in an argon channel



Jameson, JCP 116, 8912 (2002)

signature of the channel architecture: Xe-channel contributions



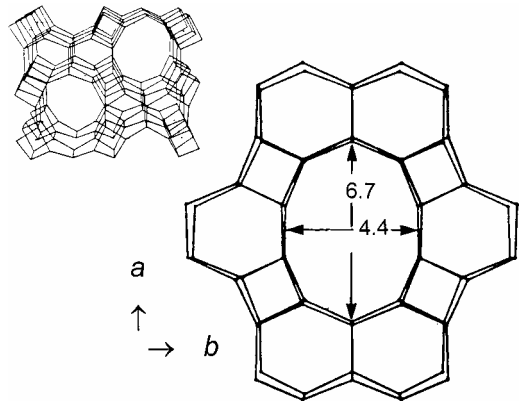


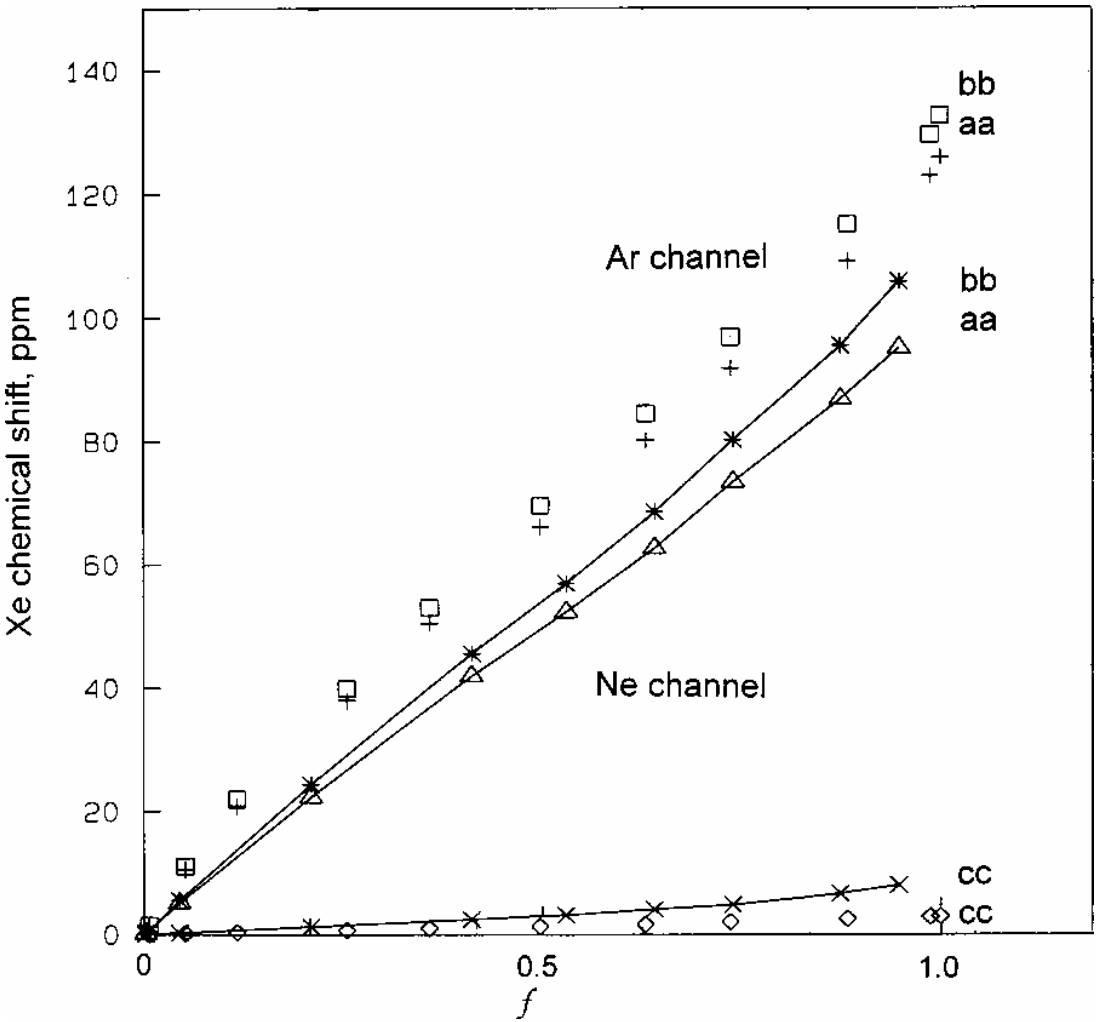
larger component is δ_{aa}

smaller is δ_{bb}, clearly not circular cross section

larger response from Ar than Ne

signature of the channel architecture: Xe-Xe contributions





almost no δ_{cc} component, not enough space for two Xe atoms to overlap densities in one cross-sectional plane

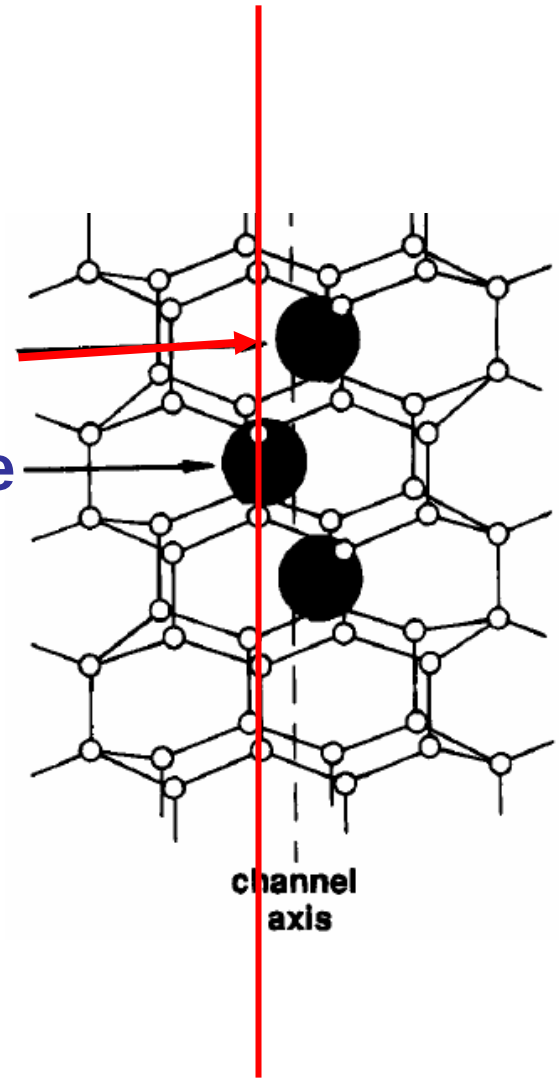
larger contribution to δ_{bb}

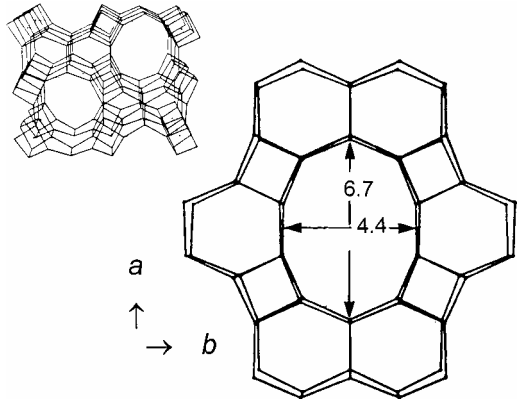
smaller to δ_{aa}

WHY?

look on the plane shown in red for electron densities which can contribute to δ_{aa}

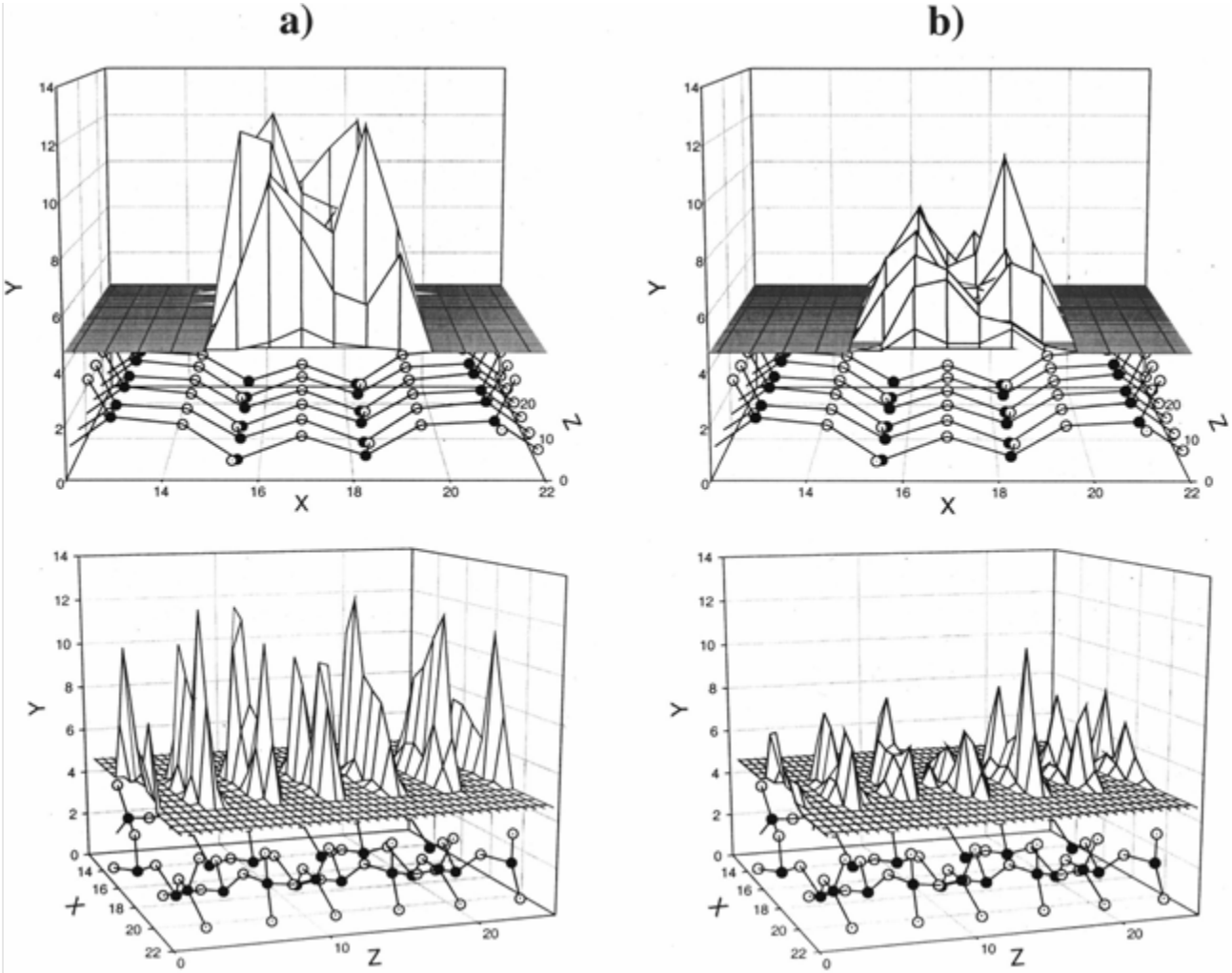
consider the shielding of this Xe





look on the plane of the screen for electron densities which can contribute to δ_{bb}

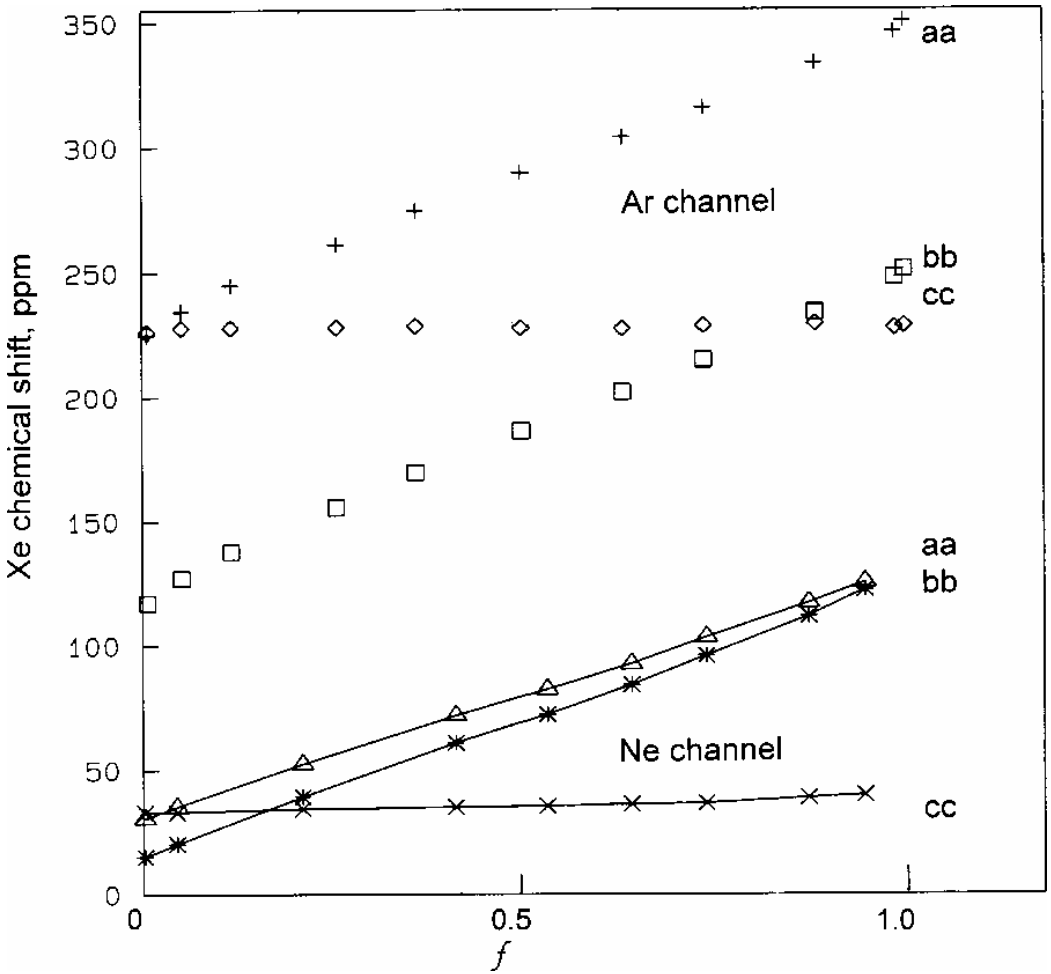
One-body distribution functions of Xe in ALPO4-11

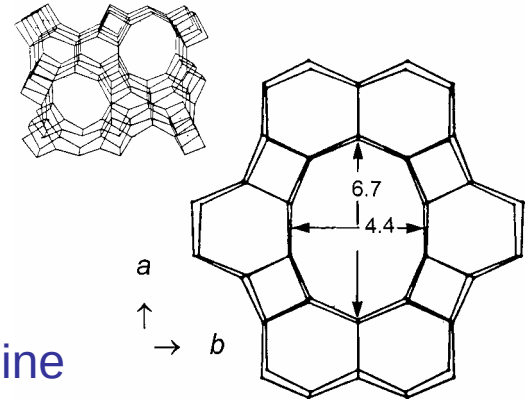


at full loading

0.26% occupancy

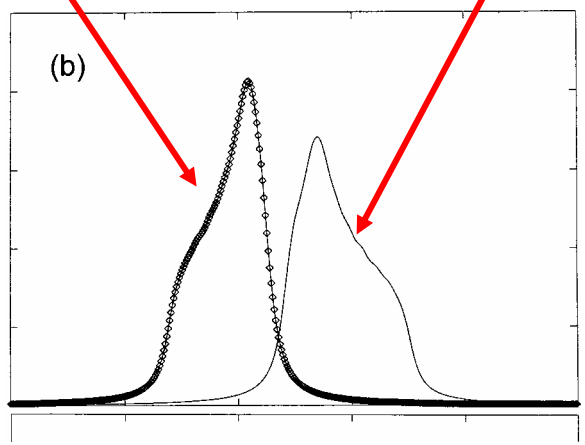
average tensor components





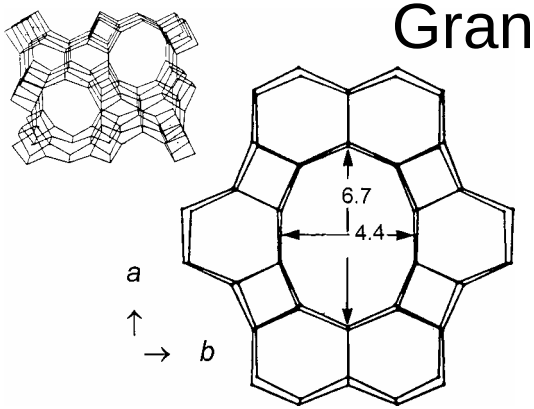
total line shape

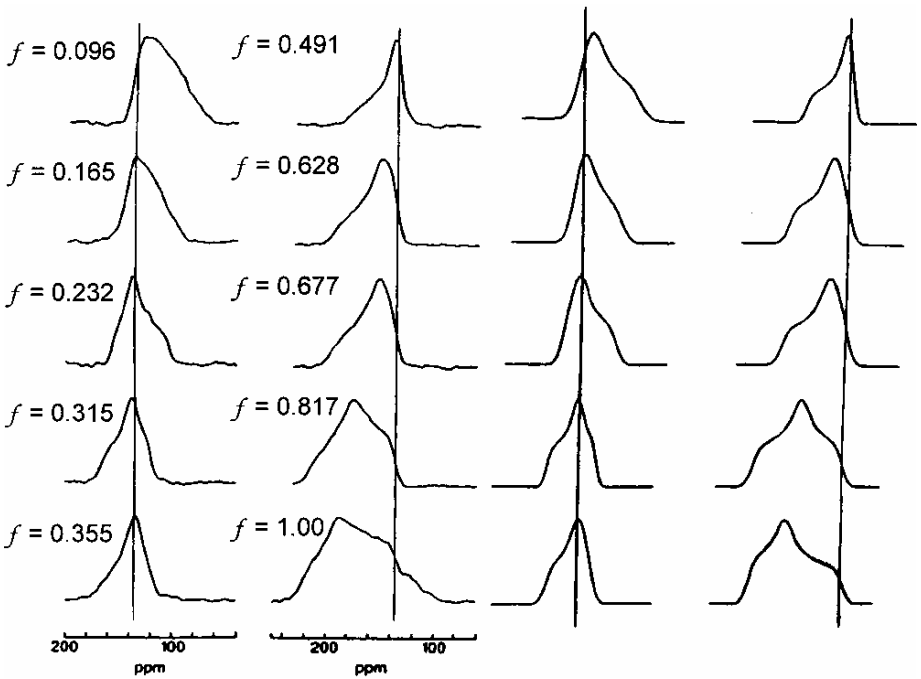
Xe-channel contrib

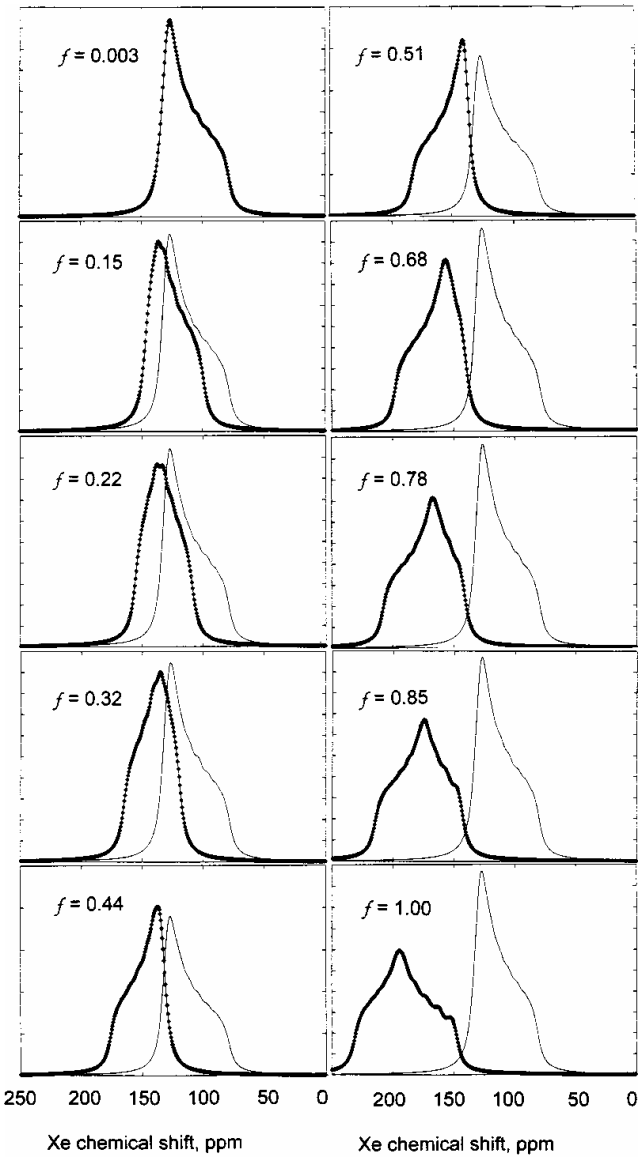


Xe in the channels of $ALPO_4$-11

Grand Canonical Monte Carlo **SIMULATIONS**







Jameson J Chem Phys 116, 8912 (2002)

EXPERIMENTS J.A. Ripmeester and C.I. Ratcliffe, J. Phys. Chem. 99, 619 (1995)

NMR lineshapes in nanochannels and nanocavities can provide the average Xe shielding tensor in confined geometries.

- Simulations demonstrate separately which part of the observed NMR lineshape characteristics provides the **signature of the channel architecture**, and which part provides information on the **electronic structure of the atoms constituting the channel**.
- The variation in lineshape as a function of loading in real systems can be reproduced.
- The additive dimer tensor model can work well in channels and cavities of arbitrary size and shape.