# Point de vue sur les propriétés locales de phases moléculaires piégées

Ronan Lefort

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**Université de Rennes 1**

**Université Européenne de Bretagne**

# Point of view on trapped molecular phases

## Synthesis document

defended on february $6^{th}$ 2009

in order to obtain the

### National Recognition for Research Supervision (Habilitation à diriger des recherches)

**in Physics**

by

Ronan Lefort

**Composition of the jury**

| | | |
|---|---|---|
| *President :* | **Marc Descamps** | Univ. Lille |
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**Institut de Physique de Rennes — UMR 6251**

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## Dynamics of Confined Complex Fluids

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# 1

# Curriculum Vitae

## Titles

**1998 :** PhD in Physics, Université de Rennes 1, Mention **Très Honorable avec Félicitations du Jury**

**1995 :** Master degree in physics, sp. Materials Science Université de Rennes 1, **Top of the year**

**1995 :** Ingeneer degree **INSA Rennes**, sp. **Génie Physique**

## Professional experience

### *2005 - today :*

- **Assistant professor, Université de Rennes 1, UFR SPM**
  - 16h/y - Master course in Nanoscience, ”Thermodynamics in confinement, Inverse systems”
  - 90h/y - 3rd year in materials science (vibrations, waves)
  - 48h/y - L1/L2 (waves and particles, point mechanics, oscillators)
  - Practical courses in physics (3rd year in electronics)
  - 40h - Practical courses, Master of physics
- **Researche at the Institut de Physique de Rennes, UMR 6251**
  - Nanoconfinement of complex fluids
  - Large scale facilities, Solid State NMR

### *1999-2005 :*

- **Assistant professor, Department of Chemistry, l'IUT ”A”, Université de Lille 1.**
  - General physics (Electricity, Geometrical optics), Practical courses
  - Coordinator of pedagogic projects for training sandwich courses

**• Researcher at the Laboratoire de Dynamique et Structure des Matériaux Moléculaires, LDSMM, UMR 8024**

Université de Lille 1

- Analysis by $^{13}C$, $^{1}H$ and $^{2}H$ NMR of dynamic and structural properties of out of equilibrium molecular materials. Polymorphism and polyamorphism in "forced" pharmaceutical materials (thermal and non thermal routes of amorphization).
- Development of analysis methods by coupling NMR and ab initio or molecular mechanics calculations.

***1998 - 1999 :***

Military service as Scientist, military schools of Saint-Cyr Coëtquidan (56) (physics teacher)

***1995 - 1999 :***

Assistant teacher in physics at the université de Rennes I

## Research supervising

- **PhD director** of Gilbert Chahine, Remarkable properties and ultra-slow dynamics of nanoconfined liquid crystals (2007 - 2010)
- Member of the PhD jury of Vincent Caron (defended on december 12th 2006, Université de Lille 1)
- Rémi Busselez, PhD in physics, Dynamics of bioprotecting fluids confined in porous silicon, Rennes (2005 - 2008)
- Régis Guégan, PhD in physics, Structure of liquid crystals confined in porous silicon, Rennes (2005 - 2006)
- Vincent Caron, PhD in physics, Stable and metastable phases of lactose under mechanical forcing, Lille (2003 - 2005)
- Armelle De Gusseme, PhD in physics, Solid state phase transformations of pharmaceutical materials : fananserin and trehalose, Lille (2003 - 2004)
- Vincent Caron, Master of physics, Solid state NMR of lactose, Lille (2003)
- Alain Bailly, PhD in physics, Local structural analysis by solid state NMR of quadrupolar nuclei : MQ-REDOR methods, Lille (1999-2000)

## Collective functions

- Coordinator of the interregion Master of physics "Nanoscience, Nanomaterials and Nanotechnologies" for the Université de Rennes 1
- Contact for the IPR for the CPER project "Solid state NMR".

- Member of the ”commission de spécialistes” (recruitment commitee), CNU 28, Université de Rennes 1 (2006-2008)
- Member of the pedagogic commitee for sandwich courses by training, IUT ”A” of Lille (2002-2005)

## Actions of animation, communication and popularization of research

- Co-organizer of the workshop ”Réseau RMN Grand Bassin Parisien”, *Rennes*, june 12th 2008
- Leader of the CNRS project *Passion-Recherche* ”Cinéma - Sciences” (2008 - 2009), (elementary school)
- Leader of conferences cycle, preparatory classes, lycée Châteaubriand, Rennes
- Leader of the action ”Cherche - Musique”, **Nuit des Chercheurs**, *Rennes*, september 26th 2008

# 2

# Publications

## Journals with referring commitee

1. Q. JI, R. LEFORT, R. BUSSELEZ, and D. MORINEAU, "Phase transition and dynamics of a gay-berne liquid crystal confined in cylindrical nanopores", *Journal of Chemical Physics*, **Soumis**, (2008).

2. R. BUSSELEZ, R. LEFORT, M. GUENDOUZ, B. FRICK, O. MERDRIGNAC-CONANEC, and D. MORINEAU, "Molecular dynamics of glycerol and glycerol-trehalose bioprotectant solutions nanoconfined in porous silicon", *Journal of Chemical Physics*, **Soulmis**, (2008).

3. A. V. KITYK, M. WOLFF, K. KNORR, D. MORINEAU, R. LEFORT, and P. HUBER, "Continuous Paranematic-to-Nematic Ordering Transitions of Liquid Crystals in Tubular Silica Nanochannels", *Physical Review Letters*, **101**, 187801(2008).

4. R. LEFORT, D. MORINEAU, R. GUEGAN, M. GUENDOUZ, J.-M. ZANOTTI AND B. FRICK, "Relation between static short-range order and dynamic heterogeneities in a nanoconfined liquid crystal", *Physical Review E*, **78**, 040701(R)(2008).

5. R. BUSSELEZ, C. ECOLIVET, R. GUEGAN, R. LEFORT, D. MORINEAU, B. TOUDIC, M. GUENDOUZ AND F. AFFOUARD, "Sliding and translational diffusion of molecular phases confined into nanotubes", *Int. J. Nanotechnology*, **5**, 867(2008).

6. R. LEFORT, D. MORINEAU, R. GUEGAN, C. ECOLIVET, M. GUENDOUZ, J.-M. ZANOTTI and B. FRICK, "Incoherent quasielastic neutron scattering study of molecular dynamics of 4-n-octyl-4'-cyanobiphenyl", *Physical Chemistry Chemical Physics*, **10**, 2993 - 2999 (2008).

7. R. GUEGAN, D. MORINEAU, R. LEFORT, W. BEZIEL, M. GUENDOUZ, L. NOIREZ, A. HENSCHEL and P. HUBER, "Rich polymorphism of a rod-like liquid crystal (8CB) confined in two types of unidirectional nanopores", *Eur. Phys. Journal E*, **26**, 261 - 273(2008).

8. R. GUEGAN, R. LEFORT, D. MORINEAU, A. MOREAC, M. GUENDOUZ, W. BEZIEL, J. M. ZANOTTI, AND B. FRICK, "Molecular dynamics of a short range ordered smectic phase nanoconfined in porous silicon.", *Journal of Chemical Physics*, **126(6)**, 064902, (2007)

9. R. LEFORT, P. BORDAT, A. CESARO AND M. DESCAMPS, "Exploring conformational energy landscape of glassy disaccharides by CPMAS 13C NMR and DFT / GIAO simulations. I. Methologdical aspects.", *Journal of Chemical Physics*, **126(2)**, 014510 (2007)
10. R. LEFORT, P. BORDAT, A. CESARO AND M. DESCAMPS, "Exploring conformational energy landscape of glassy disaccharides by CPMAS 13C NMR and DFT / GIAO simulations. II. Enhanced molecular flexibility in amorphous trehalose.", *Journal of Chemical Physics*, **126(2)**, 014511 (2007)
11. R. LEFORT, V. CARON, J.-F. WILLART AND M. DESCAMPS, "Mutarotational Kinetics and Glass Transition of Lactose ", *Solid State Com.*, **140**, 329-334, (2006)
12. R. LEFORT, D. MORINEAU, R. GUEGAN, A. MOREAC, C. ECOLIVET AND M. GUENDOUZ, "Structure and relaxation processes of an anisotropic molecular fluid confined into 1D nanochannels", *Philosophical Magazine*, **87**, 469 (2007)
13. R. GUEGAN, R. LEFORT, W. BEZIEL, D. MORINEAU, M. GUENDOUZ AND B. FRICK, "Dynamics of 8CB confined into porous silicon probed by incoherent neutron backscattering experiments.", *European Physical Journal S.T.*, **141**, 29-34 (2007)
14. J. LEFEBVRE, J.-F. WILLART, V. CARON, R. LEFORT, F. AFFOUARD AND F. DANÈDE, "Structure determination of the 1/1 $\alpha/\beta$ mixed lactose by X-ray powder diffraction", *Acta Crystallographica Section B*, **61(4)**, (2005), 455-463
15. R. LEFORT, A. de GUSSEMME, J.-F. WILLART, F. DANEDE, M. DESCAMPS, "Solid State NMR and DSC methods for quantifying the amorphous content in solid dosage forms : an application to ball-milling of trehalose", *International Journal of Pharmaceutics*, **280**, (2004), 209-219
16. J.-F. WILLART, V. CARON, R. LEFORT, F. DANEDE, D. PREVOST, M. DESCAMPS, "Athermal character of the solid state amorphization of lactose induced by ball-milling", *Solid State Communications*, **132**, (2004) 693-696
17. R. LEFORT, A.HEDOUX, Y.GUINET, E.COCHIN, M.DESCAMPS, "Fast intramolecular dynamics of triphenyl phosphite investigated by 2H NMR", *European Physical Journal*, **B30**, (2002) 519-525
18. A.HEDOUX, Y.GUINET, P. DEROLLEZ, O. HERNANDEZ, R. LEFORT, M. DESCAMPS, "A contribution to the understanding of the polyamorphism situation in Triphenyl Phosphite", *Physical Chemistry Chemical Physics*, **6**, (2004), 3192-3199
19. R. LEFORT, J.W. WIENCH, M. PRUSKI, J.-P. AMOUREUX, "A Carr-Purcell-Meiboom-Gill Approach to Multidimensional Solid-State NMR of Quadrupolar Nuclei", *Journal of Chemical Physics*, **116(6)**, 2493 (2002)
20. R. LEFORT, J. ETRILLARD, B. TOUDIC, F. GUILLAUME, P. BOURGES, R. CURRAT, T. BRECZEWSKI, "Dynamical Molecular Disorder and Diffuse Scattering in an Alkane/Urea Incommensurate Inclusion Compound", *European Physical Journal*, **B24** , (2001) 51-57
21. P.R. BODART, J.-P. AMOUREUX, Y. DUMAZY, R. LEFORT, "Theoretical and Experimental Study of Quadrupolar Echoes for Half-Integer Spins in Static Solid-State NMR", *Molecular Physics*, **98(19)**, 1545-1551, (2000)

22. H. LE LANN, B. TOUDIC, R. LEFORT, J. ETRILLARD, F. GUILLAUME, B. RUFFLE, J. OLLIVIER, R.E. LECHNER, T. BRECZEWSKI, ”Coherent Neutron Analysis of Diffuse Scattering in an Alkane-Urea Composite”, *Physica B*, **276-278**, 298-299 (2000)

23. R. LEFORT, J. ETRILLARD, B. TOUDIC, F. GUILLAUME, T. BRECZEWSKI, P. BOURGES, ”Incommensurate Intermodulation of an Organic Intergrowth Compound Observed by Neutron Scattering”, *Physical Review Letters*, **77(19)**, 4027-4030, (1996)

## Other publications

1. HIGHLIGHTS, Institut Laüe-Langevin, *Annual Reports*, 2006

2. HIGHLIGHTS, Laboratoire Léon Brillouin, 2006

3. *Virtual Journal of Nanoscale Science & Technology*, http://www.vjnano.org, 26 février 2007

4. *Virtual Journal of Biological Physics Research*, http://www.vjbio.org, 15 février 2007

5. HÉDOUX A., GUINET Y., DEROLLEZ P., HERNANDEZ O., LEFORT R., DESCAMPS M., ”Description and origin of the polyamorphism situation in triphenyl phosphite”, Dans ”Recent Research Developments in Physics”, *Transworld Research Network (Ed.)* (2004) 887 - http://hal.archives-ouvertes.fr/hal-00090325/fr/

6. H. LE LANN, B. TOUDIC, J. OLLIVIER, B. RUFFLE, R. E. LECHNER, F. GUILLAUME, R. LEFORT, ”Coherent versus incoherent neutron scattering study of dynamical disorder in intergrowth crystals”, Proceedings of the VIIIth Polish-French seminar ”Dynamics and transformations of the molecular materials”, *Biuletyn Instytutu Chemii Fizycznej I Teoretycznej Politechniki Wroclawskiej*,**11**, 183-186 (2001)

7. R. LEFORT, J. ETRILLARD, B. TOUDIC, F. GUILLAUME, T. BRECZEWSKI, ”Aperiodic Features of Urea/Alkane Intergrowth Organic Compounds”, *Proceedings of the International Conference on Aperiodic Crystals ”Aperiodic 97”*, World Scientific, 679-683 (1998)

## Oral communications

1. R. BUSSELEZ, R. LEFORT, Q. JI, R. GUEGAN, G. CHAHINE, M. GUENDOUZ, J.-M. ZANOTTI, B. FRICK and D. MORINEAU, ”Bioprotectant glassforming solutions confined in porous silicon nanocapillaries”, 2008 MRS Fall Meeting, Symposium TT, december 2008, Boston (invited conference)

2. D. MORINEAU, R. GUEGAN, R. LEFORT, M. GUENDOUZ, ”Dynamics of nanoconfined liquid crystals”, *3rd International Workshop on Dynamics in Confinement*, ILL, Grenoble, 23-26 mars 2006 (invited conference)

3. D. MORINEAU, R. GUEGAN, R. LEFORT, R. BUSSELEZ, M. GUENDOUZ, ”General aspects of the nanoconfinement of molecular phases”, *France-Japan Symposium on Molecular Materials*, Université de Rennes 1, 16-19 mars 2006 (invited conference)

4. R. BUSSELEZ, D. MORINEAU, F. AFFOUARD, R. LEFORT, M. GUENDOUZ, "Nanoconfinement et hétérogénéités dynamiques de mélanges bioprotecteurs vitrifiables.", *XIèmes Jounrées de la Matière Condensée*, 25-29 août 2008, Strasbourg
5. R. LEFORT, D. MORINEAU, R. GUEGAN, M. GUENDOUZ, J.-M. ZANOTTI and B. FRICK, "Effets de désordre gelé et de basse dimensionalité sur la dynamique moléculaire de fluides anisotropes confinés.", *XIèmes Jounrées de la Matière Condensée*, 25-29 août 2008, Strasbourg
6. R. BUSSELEZ, D. MORINEAU, F. AFFOUARD, R. LEFORT, M. GUENDOUZ, "Etude de solutions bioprotectrices Glycérol/Tréhalose confinées dans des nanocanaux de silicium poreux", *IIèmes Journées Nanosciences de Bretagne*, 5-6 juin 2008, Nantes
7. R. LEFORT, R. GUEGAN, D. MORINEAU, M. GUENDOUZ, J.-M. ZANOTTI, B. FRICK, "Quenched disorder and low dimensional nanoconfinement effects on the structure and molecular dynamics of an anisotropic fluid", *IVth European Conference on Neutron Scattering*, 25-29 juin 2007
8. D. MORINEAU, R. GUEGAN, R. LEFORT, A. MOREAC, M. GUENDOUZ, "Structure and relaxation processes of an anisotropic molecular fluid confined into 1D nanochannels", *Xth International Workshop on Disordered Systems*, 18-21 mars 2006, Molveno, Italie
9. R. GUEGAN, D. MORINEAU, W. BEZIEL, R. LEFORT, M. GUENDOUZ, "Structure et dynamique individuelle d'un cristal liquide (8CB) confiné dans des nanopores unidirectionnels de silicium poreux», *14èmes Journées de la diffusion neutronique*, 13-19 mai 2006, Clermont-Ferrand, France
10. R. GUEGAN, W. BEZIEL, A. MOREAC, R. LEFORT, M. GUENDOUZ, D. MORINEAU, "An anisotropic molecular fluid confined into 1D nanochannels : low dimensionality and surface disorder effects", *Vth International Discussion Meeting on Relaxations in Complex Systems*, 7-13 juillet 2005, Lille, France
11. R. GUÉGAN, D. MORINEAU, W. BÉZIEL, R. LEFORT, C. LOVERDO, A. MORÉAC, M. GUENDOUZ and M. STCHAKOVSKY, "Transition smectique du 8CB confiné dans des nanocanaux 1D orientés présentant un fort désordre de surface. », *Colloque Francophone sur les Cristaux Liquides*, 13-16 septembre 2005, Montpellier, France
12. R. LEFORT, P. BODART, J.-P. AMOUREUX, J.W. WIENCH, M. PRUSKI, F. TAULELLE, "Improving Signal-to-Noise Ratio of Solid-State NMR experiments : Combination of Acquisition Schemes and Data Processing", *19e reunion de travail en RMN du solide*, 16-18 octobre 2000, Eveux, France
13. L. MONTAGNE, V. KOSTOJ, G. PALAVIT, G. MAIRESSE, R. LEFORT, J.-P. AMOUREUX, C. JÄGER, M. ZEIER, " 17O NMR of phosphate glasses and BIMEVOX compounds", *19e reunion de travail en RMN du solide*, 16-18 octobre 2000, Eveux, France
14. R. LEFORT, "Spectroscopie RMN", 48e journées de l'Union des Physiciens, 28-31 octobre 2000, Lille, France
15. H. LE LANN, R. LEFORT, B. TOUDIC, J. ETRILLARD, F. GUILLAUME, P. BOURGES, R. CURRAT, T. BRECZEWSKI, "Phase Transition and Molecular Disorder in Urea/Alkane Incommensurate Composites", *VIIIe séminaire Franco-Polonais*, 13-17 septembre 2000, Zamek Czocha, Pologne

16. R. LEFORT, P. BODART, J.-P. AMOUREUX, J.W. WIENCH, M. PRUSKI, F. TAULELLE, ”New methods for increasing sensitivity in solid-state NMR of quadrupolar nuclei : CPMG-MQMAS and specialized processing”, *Franco-Italian Conference on Magnetic Resonance*, GERM, 02-05 mai 2000, La Londe Les Maures (83), France
17. P. RABILLER, L. TOUPET, R. LEFORT, J. ETRILLARD, B. TOUDIC, F. GUILLAUME, T. BRECZEWSKI, P. BOURGES, R. CURRAT, ”Analyse par diffraction X et cohérente de neutrons d'un composite moléculaire incommensurable : aspects statiques et dynamiques du désordre”, *AFC 98, colloque de l'association française de cristallographie*, 1998, Orléans, France
18. J. ETRILLARD, R. LEFORT, B. TOUDIC, P. RABILLER, L. TOUPET, F. GUILLAUME, T. BRECZEWSKI, P. BOURGES, R. CURRAT, ”Analyse structurale et dynamique de cristaux composites organiques”, *7émes journées de la diffusion neutronique*, 1998, Albé, France
19. P. RABILLER, R. LEFORT, J. ETRILLARD, L. TOUPET, B. TOUDIC, F. GUILLAUME, ”X ray and neutron scattering analysis of short range order in composite incommensurate crystals”, *VII Polish-French seminar on dynamics transformations of molecular materials*, 14-18 septembre 1998, Stella-Plage, France
20. R. LEFORT, B. TOUDIC, J. ETRILLARD, P. RABILLER, L. TOUPET, ”Caractérisation par Cristallographie de Superespace de l'Intermodulation de Systèmes Quasipériodiques Composites”, *Séminaires de l'Ecole Doctorale de Physique*, 1998, Rennes, France
21. R. LEFORT, J. ETRILLARD, B. TOUDIC, F. GUILLAUME, T. BRECZEWSKI, ”Aperiodic Features of Urea/Alkane Intergrowth Organic Compounds”, International Conference on Aperiodic Crystals ”Aperiodic 97”, 27-31 août 1997, Alpe d'Huez, France
22. R. LEFORT, B. TOUDIC, J. ETRILLARD, P. RABILLER, L. TOUPET, ”Intermodulation de Systèmes Composites Quasipériodiques”, *Physique en Herbe*, 30 juin - 04 juillet 1997, Caen, France
23. B. TOUDIC, J. ETRILLARD, R. LEFORT, J. OLLIVIER, ”From modulated to composite incommensurate crystals”, *VI Polish-French seminar on dynamics transformations of molecular materials*, 12-14 septembre 1996, Rydzyna, Pologne

## Poster communications

1. R. BUSSELEZ, D. MORINEAU, F. AFFOUARD, R. LEFORT, M. GUENDOUZ, ”Nanoconfinement et hétérogénéités dynamiques de mélanges bioprotecteurs vitrifiables.”, *XIèmes Jounrées de la Matière Condensée*, 25-29 août 2008, Strasbourg
2. G. CHAHINE, R. LEFORT, J.-M. ZANOTTI, D. MORINEAU, ”Propriétés structurales remarquables de cristaux-liquides nanoconfinés”, *IIèmes Journées Nanosciences de Bretagne*, 5-6 juin 2008, Nantes, *Prix du meilleur poster*
3. R. GUÉGAN, D. MORINEAU, R. LEFORT, A. MORÉAC, M. GUENDOUZ, J.-M. ZANOTTI AND B. FRICK, ”Unidirectional quenched disorder effects on the structure and molecular dynamics of a nanoconfined liquid crystal”, *International Soft Matter Conference 2007*, 1 - 4 Octobre 2007, Eurogress, Aachen, Allemagne

4. R. BUSSELEZ, R. LEFORT, D. MORINEAU, F. AFFOUARD AND M. GUENDOUZ, "Glycerol/trehalose bioprotectant solutions confined in nanoporous silicon", *International Soft Matter Conference 2007*, 1 - 4 Octobre 2007, Eurogress, Aachen, Allemagne
5. R. LEFORT, R. GUÉGAN, D. MORINEAU, A. MORÉAC, W. BÉZIEL, M. GUENDOUZ, J.-M. ZANOTTI, B. FRICK, "Mise en ordre smectique et dynamique relaxationnelle d'un cristal-liquide sous contrainte de désordre aléatoire gelé en confinement nanométrique unidimensionnel », *Congrès général de la SFP*, 29 août 2005, Lille, France
6. R. LEFORT, P. BORDAT, A. CESARO, M. DESCAMPS, "Exploring conformational energy landscape of glassy dissacharides by CPMAS 13C NMR and DFT/GIAO simulations"", *Vth IDMRCS*, 7-13 juillet 2005, Lille, France
7. R. LEFORT, J.-P. AMOUREUX, P. BODART, M. PRUSKI, "Optimized CPMG-MQMAS methods with ANAFOR treatment", 42nd ENC, 11-16 mars 2001, Orlando, Florida, USA
8. H. LE LANN, B. TOUDIC, R. LEFORT, J. OLLIVIER, B. RUFFLE , R. LECHNER, F. GUILLAUME, P. BOURGES, R. CURRAT ET T. BRECZEWSKI, "Coherent versus Incoherent Neutron Scattering Study of Dynamical Disorder in an Incommensurate Inclusion Compound", *VIIIe séminaire Franco-Polonais*, 13-17 septembre 2000, Zamek Czocha, Pologne
9. R. LEFORT, P. BODART, J.-P. AMOUREUX, J. W. WIENCH, M. PRUSKI, F. TAULELLE, "Sensitivity enhancement of Solis-State NMR experiments : Application of CPMG to MQ-MAS and New Data Processing", *15e European Experimental NMR Conference (EENC)*, 12-17 juin 2000, Leipzig, Allemagne
10. M. PRUSKI, J. W. WIENCH, J.-P. AMOUREUX, P. BODART, R. LEFORT, F. TAULELLE, "CPMG-MQMAS in Solid-State NMR of Quadrupolar Nuclei", *41st ENC*, 9-14 avril 2000, Pacific Grove, California, USA
11. H. LE LANN, J. GALLIER, J.C. AMELINE, J. ETRILLARD, R. LEFORT, C. ODIN, P. RABILLER B. TOUDIC, F. GUILLAUME ET T. BRECZEWSKI, "Pretransitional and ordering processes around structural phase transition in an incommensurate inclusion compound", *DIPROSO XXVII*, 13-16 sept 1999, Tours, France and VIIIe séminaire Franco-Polonais, 13-17 septembre 2000, Zamek Czocha, Pologne
12. H. LE LANN, J. ETRILLARD, R. LEFORT, J. GALLIER, B. TOUDIC, J. OLLIVIER, B. RUFFLE , R. LECHNER, F. GUILLAUME, P. BOURGES, R. CURRAT ET T. BRECZEWSKI, "Coherent neutron analysis of diffuse scattering in urea-alkane incommensurate composite", *European Conference on Neutron Scattering*, 1-4 sept 1999, Budapest, Hongrie
13. H. LE LANN, R. LEFORT, J. GALLIER, B. TOUDIC, J.C. AMELINE, A. GIRARD, Y. MARQUETON , C. ECOLIVET, F. GUILLAUME, M. COUZI, "Static and dynamic features of the incommensuratly modulated organic crystal of urea-alkane", VIIth French-Polish *Seminar on dynamics and transformations of molecular materials*, 14-18 sept 1998, Stella-plage, France
14. R. LEFORT, J. ETRILLARD, B. TOUDIC, F. GUILLAUME, T. BRECZEWSKI, P. BOURGES "A Coherent Neutron Scattering Study of Urea/Alkane Composite Systems",

*VIth polish-french meeting on dynamics and transformations of molecular materials*, 12-14 Septembre 1996, Rydzyna, Pologne

## Recent seminars

1. R. LEFORT, "Forcing Molecular Materials", *Institut für FestkörperPhysik, Darmstadt*, sept. 2008
2. R. LEFORT, D. MORINEAU, R. GUEGAN, "Structure et dynamique de phases mésogènes sous nanoconfinement de basse dimensionalité", *CRMD, Orléans*, 19 avril 2007
3. R. LEFORT, "Bioprotection par les sucres : le cas du trehalose vu par RMN", *Journée du réseau RMN Grand bassin Parisien*, Lille, 05 février 2007

## Recent collaborations

- S. MAGAZU, Université de Messine, Italie
- P. HUBER, Universität des Saarlandes, Saarbrücken, Allemagne
- F. AFFOUARD, Laboratoire de Dynamique et Structure des Matériaux Moléculaires, Lille
- J.-M. ZANOTTI, Laboratoire Léon Brillouin, CEA-Saclay
- B. FRICK, Institut Laue-Langevin, Grenoble
- M. GUENDOUZ, Laboratoire d'Optronique, Lannion
- A. CESARO, Université de Trieste, Italie

# Part II

# Synthesis Document

The two first chapters of this synthesis document provide a summary of my main research activities. Of course, my two consecutive research positions in the *Laboratoire de Dynamique et Structure des Matériaux Moléculaires* of Lille, then at the *Institut de Physique* of Rennes have been the occasion of various scientific and personal exchanges within different environments, and sometimes of new thematic choices and changes. For these reasons, I have been careful to emphasize the coherence and progression of my works, rather than simply follow their chronology.

Two particular key points are underlined : first, the subjects I developed about transformations of molecular materials, often out of equilibrium, when they are submitted to external forcing. Secondly, I have recurrently promoted the choice of a local approach of these problems (structural and dynamic effects at the molecular scale or in its immediate neighbourhood). The importance of this local point of view has always been a major scientific motivation, that I have always put forward, especially in the supervising of PhD works. This has led to the development of incoherent neutron scattering or solid state NMR methods [125, 135], and also to original approaches of more general problems, related to polymorphic, polyamorphic or glassy transformations of molecular fluids or solids.

The last chapter of the present document details the research projects I wish to develop at the Institut de Physique of Rennes, in the frame of the theme "Nanoconfinement of complex fluids".

# 1

# General Context

It is well known since a long time that many molecular materials possess an exceptional richness of equilibrium phases. This *polymorphism* is a sign of a very complex energy landscape, and can be seen as the result of a contrast between strong intramolecular bonds and weak intermolecular cohesion, characteristic of these materials. This contrast is often associated to an important number of conformational degrees of freedom, and can result in a subtle balance between enthalpic and entropic effects, which equilibrium appears very sensitive to temperature and pressure conditions, as well as to the kinetics of external actions [27, 53].

For the same reasons, a molecular compound can often possess a large number of metastable or out of equilibrium states, that are rather easy to reach (and maintain) in standard thermodynamic conditions. Such states take on a considerable importance in some domains of pharmaceutics or food industry, where they have a decisive influence on solubility or bioavailability of drugs [44, 184], or on the texture and stability of food [175, 176].

As an example, the glass transition properties of sugars and of their aqueous solutions have often been evoked as determining their bioprotective skills [46, 84]. Beyond thermal treatments close to equilibrium, other actions allow to easily trap such states, and are often encountered in industrial processes (metallurgy, galenic design, lyophilization, nanofiltration...). Among them can be found mechanical forcing [76], irradiation [150], or topological confinement at very small scales[1] [99, 186, 190, 209]. Whereas these trapping mechanisms begin to be well known in case of the glass transition, those implied in non thermal transformations far from equilibrium are still today a matter of open fundamental questions.

The following sections detail the most important aspects of the state of the art in these domains, at the moment where my own research activities have begun.

## 1.1 The glass transition

### 1.1.1 Phenomenology

One of the most famous out of equilibrium transformations consists in quenching a liquid fast enough (if possible) to avoid its crystallization (figure 1.1, left). This results in maintaining the liquid in a supercooled metastable state, going along on cooling with a tremendous increase of the viscosity (figure 1.1, right). This leads below a temperature $T_g$ to a vitreous out of equilibrium solid state characterized by a complete freezing of the molecular relaxations on the time scale of the experiment. The phenomenology associated to this *glass transition* of the liquid is now well

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[1] this point is illustrated in section 3.2.2

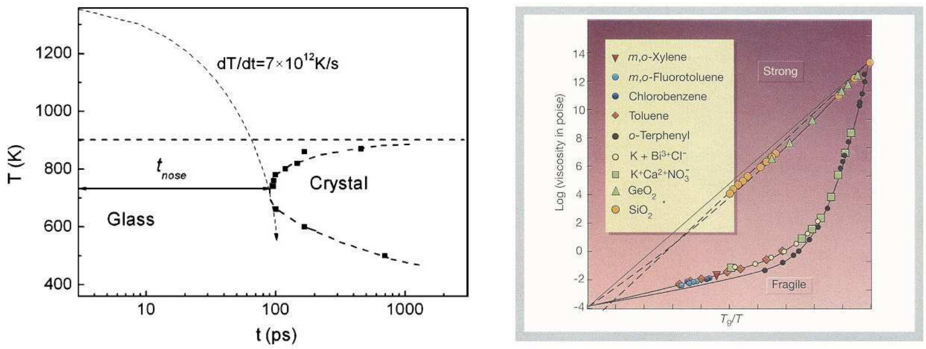


Figure 1.1: **left :** Diagram *Temperature - Time - Crystallization fraction* ("TTT") of a pure compound. **right :** Angell "strong - fragile" diagram of some glass former compounds [51].

established, and its universal character is supported by a large number of experimental data on various systems [51].

Two essential characters of this transformation are systematically observed. One is the non Arrhenian temperature dependence of the viscosity, and therefore of the average structural relaxation time of the liquid. On these grounds, molecular materials are remarkable, as this effect is very pronounced for many of them, which are classified within "fragile" liquids (figure 1.1, right). The second signature is the non exponential shape of the average impulsional response of the supercooled liquid.

Although these observations attest the intrinsic kinetic nature of the glass transition, the global understanding of the associated effects within a unified theoretical frame remains today one of the major problems of condensed matter physics. However, some theoretical approaches have emerged since the founding works of Kauzmann [110]. Some of them try to relate the slowing down of the molecular dynamics with the thermodynamical variables qualifying the liquid state. Adam and Gibbs [3] propose that it is exponentially related to the decrease of the configurational entropy of the liquid, the number of accessible states being reduced by a more pronounced cooperativity inside zones (CRR) which size increases when temperature is lowered. More recent works (Kivelson [114, 115]) relate the non Arrhenian dynamics to the topological frustration that can be induced by a preferential local order of the liquid, incompatible with long range order (crystalline order).

A second point of view relies on a microscopic description of the dynamics, and provides particularly efficient descriptions of the properties of the supercooled liquid at relatively high temperatures, when the cooperative effects essentially concern the first coordination shell of the molecule ("cage effect"). On this basis, the mode coupling theory (MCT) introduced by Götze [83] predicts a break of ergodicity at a critical temperature $T_c$, whereas so-called "energy landscape" approaches introduced by Stillinger [177, 51] predict a decoupling of local (energy well bottom) and strongly correlated (inter wells) dynamics below a temperature $T_a$.

The universal non exponentiality of the relaxation functions of glass forming liquids have led the scientific community to progressively adopt the idea of an intrinsic heterogeneity of the dynamics of these systems, scaling on a typical correlation length $\xi_{dyn}$ increasing when approaching the glass transition temperature $T_g$. An evidence of such dynamic heterogeneities has been provided experimentally, in particular by local techniques like nuclear magnetic resonance (c.f. figure 1.2 [185, 199]).

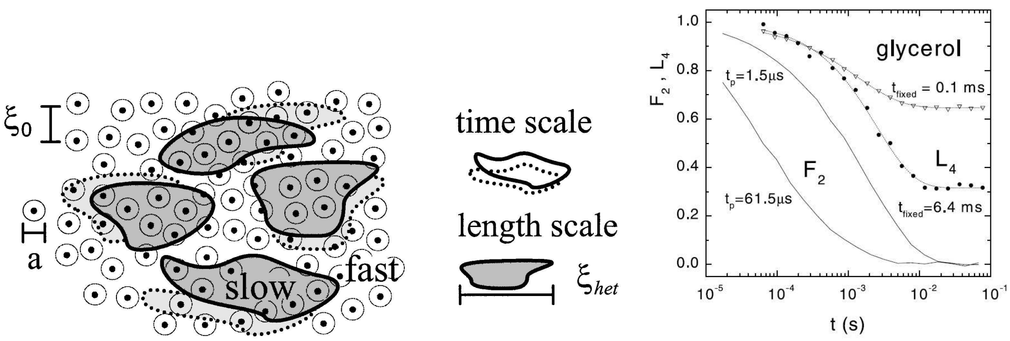


Figure 1.2: (a) Space and time scales of the dynamic heterogeneities of a glass forming liquid [199] (b) Average orientational correlation functions of dynamical sub ensembles measured on glycerol by NMR [185].

### 1.1.2 Bioprotectant solutions

These observations go largely beyond the frame of inorganic or molecular liquids. An intense activity of research is still going on, which underlines the universality of behaviours associated with glass transitions in liquids, *jamming* transitions in granular and colloidal media [20, 37, 43], or dynamic transitions of biological macromolecules [111, 206, 218, 85]. As an example, a growing number of studies have focused on this last point since the last ten years, at the frontiers of physics, chemistry and biology, aiming to understand the mechanisms preventing biological cellular matter from denaturation under chemical or physical stress (temperature, osmotic pressure...) [9, 22, 34, 62, 216]. Binary solutions implying disacharides (trehalose, sucrose) or polyalcohols (glycerol) belong to categories of solvents able to prevent at best thermal denaturations of proteins as well as intracellular water crystallization. Among the invoked mechanisms, the highly associated nature of these solutions, and also their glassy dynamics appear to be recognized as key elements determining their bioprotective skills [10, 22, 46, 57, 147, 46]. Within this frame, part of my works concentrated on the particular local structure of the trehalose glass (section 2.1), and on the nanometric confinement effects on the dynamics of trehalose/glycerol solutions in their supercooled state, around their $T_g$ (section 3.2.1).

## 1.2 Nanoconfined molecular phases

### 1.2.1 Confinement and glass transition

The nature of the dynamic heterogeneity of supercooled liquids still focus today a considerable effort of theoretical and experimental research, as well as its potential relation with local order [47, 21, 19, 60]. These concepts have opened new routes of investigation of finite size effect when approaching the glass transition, in particular by using nanoporous materials as confinement matrices for liquids [72, 99, 179, 166, 219, 105]. New opportunities have been allowed by new materials with controlled nanoporosities (c.f. figure 1.3) for studying the properties of confined simple or glass forming liquids [12, 143, 221, 15].

The structure of a confined system is heterogeneous, mainly due to the solid interface of large specific area introduced by the porous medium. This interface prints its topology, characteristic sizes and possible disorder on the confined phase, and also often modifies significantly surface tension. On the fundamental point of view, the structure factor $S(\mathbf{q})$ of a confined phase displays static correlations of topological order, even before ant molecular contribution, and this print can have dynamical consequences [116]. On the experimental point of view, these effects have revealed important in case of some liquids, as they impose to take into account *excluded volume* terms [157]. Confinement effects on the structure can be for instance observed on density, which tends to decrease with the size of the pore size [158, 4]. For the moment, only numerical simulations can provide a spatially resolved picture of static correlations in confined fluids. In an invariable way, such simulations predict a layering structure of the liquid near the solid interface [200, 90]. Most striking and almost universal results also concern the decrease of the melting temperature of the confined phases [72]. This decrease, more pronounced in smaller pores, is in agreement with the *Gibbs-Thompson* representation for pores larger than 10 nm. Most of the widely used porosimetry methods are based on this representation, such as NMR cryoporosimetry [204], or adsorption isotherms [79, 93]. For smaller pores, the effect is often dramatically more pronounced, and the transition can even disappear. The confinement effect appears in that case as a trapping of the system in metastable states [4].

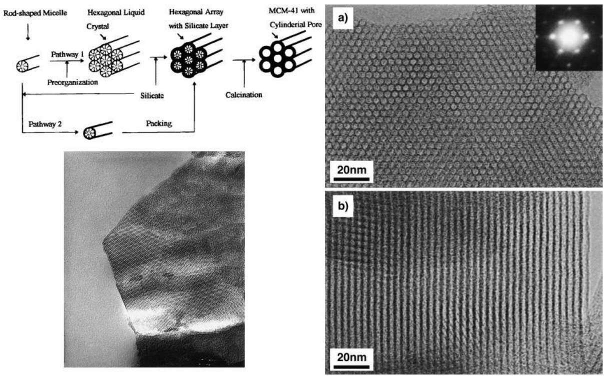


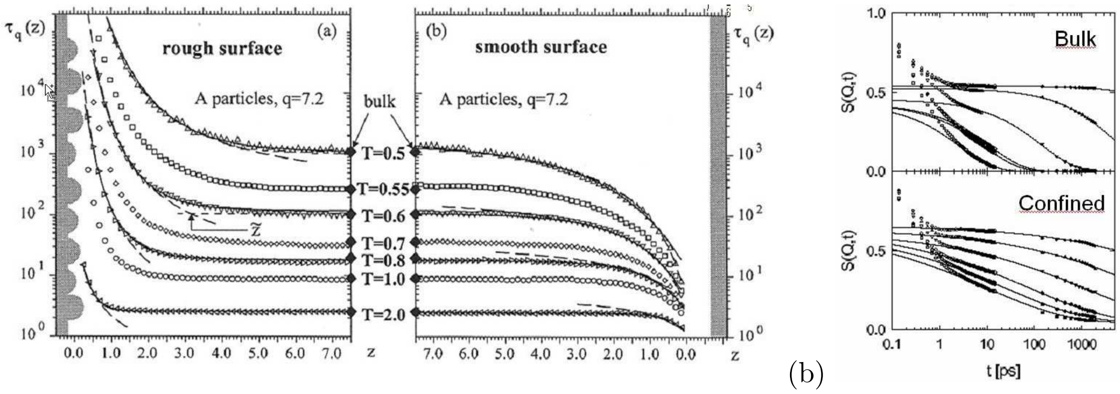
Figure 1.3: Synthesis and TEM images of nanoporous silica MCM41-x (taken from [12, 143]).

Beyond these topological aspects and their possible dynamical consequences, it has been shown that the supplementary heterogeneity introduced by the solid/liquid interface could sometimes play a decisive role on molecular dynamics, such as interfacial slowing-down (c.f. figure 1.4).

For most simple liquids, no clear structural (static) signature of these heterogeneities does exist. In the aim to contribute to a better understanding of the relation between dynamic and structural spatial scales, some of my most recent research works have focused on more complex fluids, like liquid crystals. Indeed, such systems share many dynamic features in common with glass forming liquids [28, 29], while they display orientational and translational order parameters easily accessible to the experiment 3.2.3.

### 1.2.2 Confinement and quenched disorder

The fundamental interest of confined liquids is not restricted to questions related to the glass transition. Another problem which remains today one of the most difficult challenges of statistical physics concerns the influence of disorder on phase transitions. Since the pioneering argument of Imry and Ma, predicting the instability of systems with order parameters of continuous symmetry with respect to any arbitrary weak *quenched disorder* [103], numerous fluids confined in solid porous matrices have been studied as possible experimental realizations of the Random



(a) (b)

Figure 1.4: (a) Average correlation time of the molecular dynamics of a Leenard-Jones system confined in a slit pore [179]. (b) Response functions of confined salol (neutron scattering), compared to a heterogeneous model [223]

Field Ising Model (RFIM). Binary solutions with gap of miscibility have very early been recognized by de Gennes as archetype examples of such systems [49]. More recently, Radziovsky and Toner have addressed a considerable theoretical breakthrough, by giving a detailed description of the $nematic(N) \rightarrow smectic(Sm_A)$ transition of liquid crystals confined in aerogels [17].

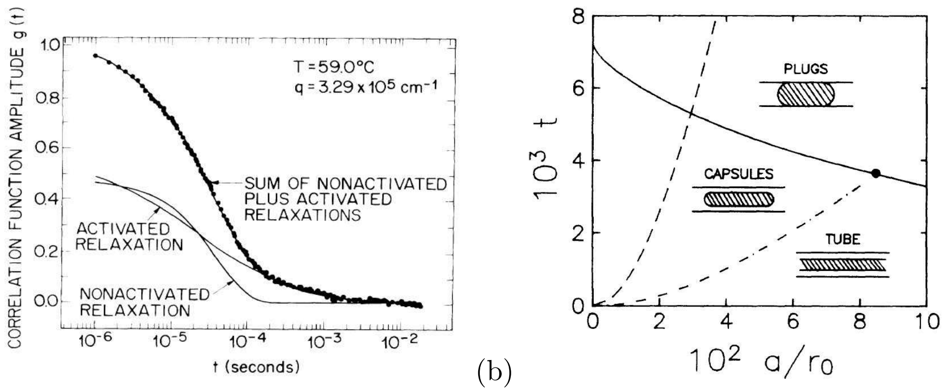
These works establish that the presence of quenched disorder (even weak) makes the ordinary order phase systematically unstable with respect to only short range correlated structures (SRO). Two universal features of this SRO are established. The first one is a direct signature of the disorder on the structure factor of the confined phase, which adds to the usual thermal contribution (eqn. 1.1) [49, 17].

$$S(q) = \left(\frac{\sigma_1}{1+q^2\xi^2}\right)_{thermal} + \left(\frac{a_2\xi^3}{[1+q^2\xi^2]^2}\right)_{disorder} \tag{1.1}$$

Moreover, an extreme slowing down of the transformation kinetics, associated to non exponential response functions reminiscent of glassy dynamics are observed (fig. 1.5a) [56].

Still today, the behaviour of such transitions submitted to anisotropic quenched disorder raises numerous questions. I chose to address this particular point in an important part of my most recent works, focusing on the $N \rightarrow Sm_A$ transition of mesogenic compounds confined in porous silicon, which topology is essentially one-dimensional. At low temperature, this system provides a striking illustration of the trapping of metastable states trapped by nanoconfinement 3.2.2.

Studies led on a growing variety of systems have demonstrated that quenched disorder effects only dominate when the topology of the porous medium allows the correlation length of the fluid's order parameter to grow larger than the one characterizing the disorder [79]. Opposite cases are encountered for instance in low porosity media (Vycor, alumina membranes...), where interfacial wetting forces seem to prevail and favour a nanostructured demixion of the binary system, in agreement with "single pore" models (c.f. figure 1.5b) [69, 141, 142, 156].



(a) (b)

Figure 1.5: (a) Logarithmic scaling of the dynamic light scattering response function on a 2,6-lutidine/water solution confined in Vycor [56]. (b) Theoretical diagram of wetting nanostructures expected under confinement [142].

## 1.3 Molecular phases trapped by mechanical forcing

As described in the previous sections, situations where a liquid is confined or thermally quenched is a way to trap it in a metastable state. Other routes can be used to obtain amorphous, inhomogeneous or far from equilibrium phases. These routes are often encountered in some processes of metallurgic, pharmaceutical or food industries. In the last two cases, an efficient control of the amorphous fraction in products is a major problem, as it impacts several physical properties such as texture, solubility or bioavailability [184, 94].

Among these processes, mechanical milling has been one of the most studied and rationalized, due to its importance in mecanosynthesis [18] and activation of metallic alloys [76, 169, 38]. Usually employed in order to reduce the particle size, ball milling implies other structural transformations, which can lead to amorphous alloys [97] and repel solubility limits [182], induce *order→disorder* [13] or polymorphic [100] phase transitions. The first systematic studies on molecular compounds are more recent and report similar observations [101, 108, 202, 68]. It is obvious that such final states are far from thermodynamic equilibrium. Before controlling their stability degree, it is necessary to reach a deep understanding of the kinetic phenomena that take place during the first stages of their formation. In particular, self-diffusion of defects, together with molecular relaxation and associated ageing processes are expected to play a central role in the competition between amorphization and recrystallization during ball milling. Molecular materials offer particularly interesting opportunities to analyze these mechanisms, as their glass transition and melting temperatures can be close to ambient milling conditions.

Several formal approaches have been proposed, aiming to predict the nature of the states of matter obtained versus different milling conditions. The first ones are based on thermodynamic quasi-equilibrium arguments, and address specifically the amorphization transition. An idea widely discussed in the literature supposes that amorphization results from a local raise of the temperature induced by friction, higher that the melting temperature, and immediately followed by a quench to room temperature [210]. Okamoto has proposed that the energy accumulated during the milling process is partially converted into a vibrational contribution, large enough to destabilize the crystal (generalized Lindemann criterion [159]). The Fecht model is more complete [65, 66], and takes into account the contribution of mechanically induced defects in the free energy of the crystal, and predicts a lowering of the melting temperature, that can become lower than the glass temperature of the liquid (c.f. figure 1.6).

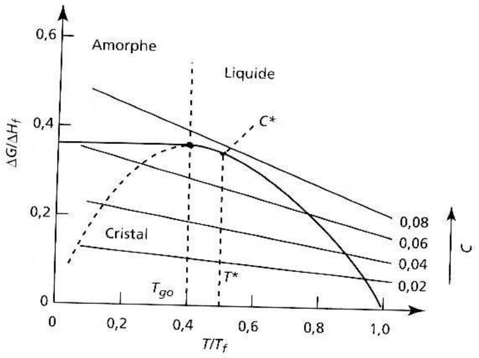


Figure 1.6: Fecht model of amorphization by ballistic defects [65].

Although the latter description explicitly takes into account microscopic effects of ball milling amorphization, its remains unable to predict other polymorphic out of equilibrium transitions, or transformations of the glass itself [38]. A more detailed approach has been proposed by Martin and Bellon, who recognize the ballistic nature of the action of milling in their *theory of driven materials*, as it is the case for irradiation [150, 151]. Final states are not simply metastable, but are the consequence of the steady-state equilibrating the rate $\Gamma_{bal}$ of ballistic defects and the rate $\Gamma_{th}$ of thermal reconfiguration (thermally activated relaxation towards equilibrium). A phase characterized by an order parameter $\eta$ evolves dynamically under ball milling, and it is not possible any more to describe it by a thermodynamic state function like the free energy $G$. However, a general picture can be drawn introducing a Lyapunov functional $L$ obeying equation 1.2.

$$\frac{d\eta}{dt} = -\Gamma_{th}\frac{\partial G}{\partial \eta} + \Gamma_{bal} = -\frac{dL}{d\eta} \tag{1.2}$$

This equation predicts steady states ($\frac{d\eta}{dt} = 0$) associated to minima of $L$. These minima can correspond to values of the order parameter $\eta$ shifted from the stable equilibrium or metastable states of the system (extension of solubility, alloys unreachable by thermal routes, a.s.o.). In the case where the ballistic contributions are dominant, these steady states can correspond to phases of the unmilled compound, but of higher free energy: the concept of *effective temperature* then allows to rationalize these observations (c.f. equation 1.3) [150].

$$T_{eff} = T\left(1 + \frac{\Gamma_{bal}}{\Gamma_{th}}\right) \tag{1.3}$$

At low temperature, thermally activated relaxations are not efficient, and $\Gamma_{th} << \Gamma_{bal}$. The steady-state reached by ball milling is therefore the one that would be obtained by heating the unmilled compound at a temperature $T_{eff} >> T$. If $T_{eff} > T_m$, the compound is made amorphous. On the other hand, at high temperature, the effective temperature remains close to the real one, and the ball milling can have only a weak effect (metallic compounds), or trap the system in a polymorphic state (molecular compounds).

In that frame, I could address two questions related to transformations of molecular materials submitted to ball milling. The first one deals with the evaluation of ballistic effects playing a role during the first stages of ball milling amorphization of sugars (section 2.2). The second one is related to the putative polyamorphism of the sugar glasses obtained by ball milling, which could be addressed by analyzing their local order by solid state nuclear magnetic resonance 2.1.

# 2

# Mechanical Milling of Sugars

## Contents

One of the major piece of my research activities has stood during several years at the interface between the problems of ball milling of molecular materials and bioprotection by sugars. In the frame of the *technologic research team* ”Therapeutic forced materials” (university of Lille), I’ve been interested in the evolution of the local structure of disaccharides under the action of mechanical milling. On this subject, magnetic resonance techniques have revealed very powerful, and could contribute to a better understanding of the amorphization mechanisms of molecular compounds through non thermal routes. In parallel, I could address in detail the conformational degrees of freedom of amorphous phases of sugars, and underline the impact they might have on their bioprotective skills.

The main results of these structural studies are summarized in the following sections.

## 2.1 Local order of sugar glasses

Alike, and even more than other molecular compounds, sugars reveal an impressive polymorphism. In addition to a large number of stable or metastable crystalline phases of pure compounds, their strong affinity with water, together with their local functional properties (reducing or not, asymmetric carbons) result in chemical dgrees of freedom responsible for mono or polyhydrated structures, or in anomeric defined compounds [123, 33]. This crystalline richness is complemented by an equivalent panel of amorphous phases, that can be obtained by multiple ways (quench of the liquid, ball milling, sray-drying, dehydration... see figure 2.2)

A major question, which is still matter of debate, concerns the potential universality of the structural and dynamic properties of these amorphous states. Whereas indirect observations (revealing different propensities for recrystallization) are in favor of a real *polyamorphism*

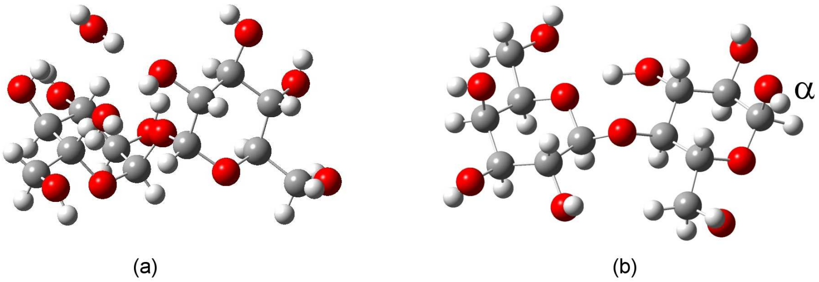


Figure 2.1: Molecular structures in crystalline forms of disaccharides (a) trehalose dihydrate (b) lactose $\alpha$ (the anomer $\alpha$ is defined by the conformation of the asymmetric carbon $C_1'$ of the glucose cycle)

of trehalose [192], no direct observation of any liquid-liquid transition nor different relaxation properties have been reported so far on amorphous forms prepared through different routes.

Solid state NMR, especially on carbon, is a unique tool for investigating local structure of sugars. Indeed, every change in the geometry of covalent bonds in the vicinity of a carbon nucleus can perturb the electronic density enough so that it can be detected through the chemical shift. $^{13}C$ NMR therefore provides an ”ID card” of molecular conformations, in the form of thin lines if these conformations are in small numbers (or unique in a crystal), or in the form of broad lines for disordered phases in which molecular geometries are distributed (c.f. figure 2.2).

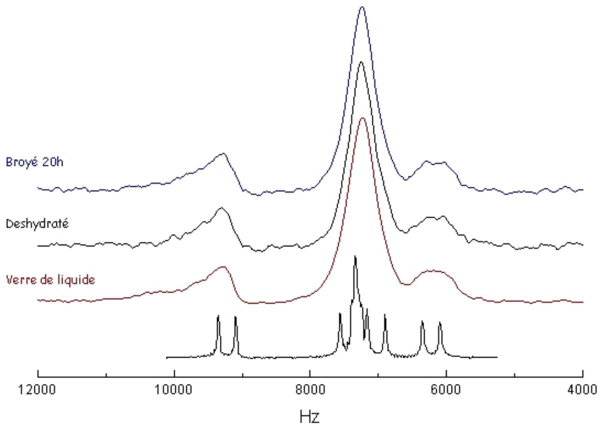


Figure 2.2: $^{13}C$ CPMAS spectra of crystalline anhydrous trehalose and of amorphous trehalose obtained by different routes

In case of trehalose, these conformational distributions appear identical for all studied amorphous compounds, whatever their preparation method can be. This reveals no structural polyamorphism (figure 2.2).

### 2.1.1 Methodological aspects

Although the NMR spectra of amorphous trehalose only displays three broad lines including unresolved contributions of different carbons of the molecule, it keeps a well identified structure. This is in contrast with X ray or neutron diffractograms, which usually show a structure factor

$S(\mathbf{q})$ essentially made of one principal peak in addition to a small intramolecular contribution. Conversely, the $^{13}C$ CPMAS lines can be only moderately broadened, and can display easily recognizable shape elements. This is remarkable on the spectra of amorphous trehalose in the region between 9 and 10 kHz, where stands the line attributed to the carbons $C_1$ and $C_1^{'}$ involved in the glycosidic bond. This broadening is due to the heterogeneous addition of all contributions of the distributed molecular conformations. In the present case, it is particularly asymmetric, and shows a marked discontinuity close to $\nu_{NMR}$=9 kHz.

These remarkable features are susceptible to provide precise information on the underlying conformational distribution. Hence, the local structure of the glass can be probed, even if intermolecular correlations cannot be addressed directly. On this basis, I have been interested in applying this approach to amorphous states obtained by mechanical milling. In a first stage, I found necessary to evaluate the exact amount of information that can be extracted from such an experiment.

In the case of disaccharides, the broadening of the line attributed to the $C_x$ carbons of the glycosidic bond is mainly due to a distribution of torsion angles around this bond [193, 220]. A purely intramolecular model can therefore be proposed.

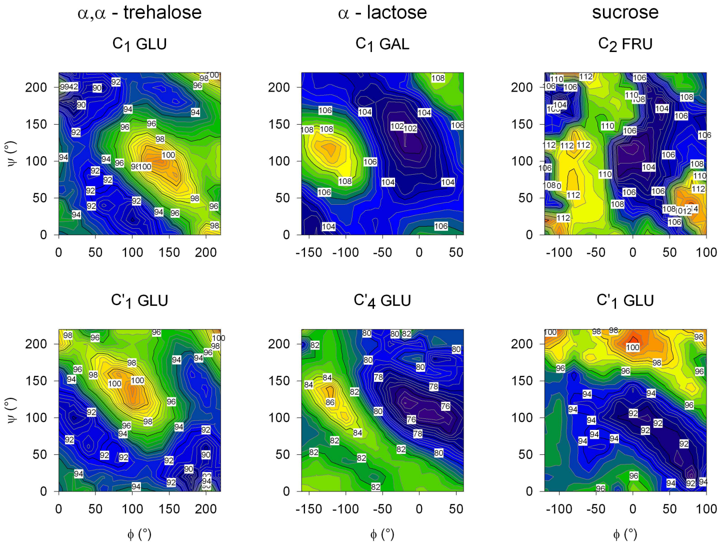


Figure 2.3: Isotropic chemical shift $\sigma(C_x, \phi, \psi)$ of the $C_x$ carbons implied in the glycosidic bond of trehalose, lactose and sucrose. The maps are calculated by DFT methods (B3PW91/3-21+G**), keeping the torsion angles $\phi$ and $\psi$ constant, and relaxing the other degrees of freedom by molecular mechanics simulations (empirical potentials).

The figure 2.3 shows the chemical shift maps calculated for trehalose, lactose and sucrose. They give its variations versus the molecular conformation, as defined by two torsion angles $(\phi, \psi)$ around the glycosidic bond. The other degrees of freedom are relaxed for each couple of values $(\phi, \psi)$ in order to obtain energetically realistic conformations. The NMR spectrum can then be calculated by mapping the contours at constant chemical shift, weighted by an occupation factor $\chi(\phi, \psi)$ (equation 2.1). This occupation probability carries thoroughly the structural information contained in the NMR line shape. This function must be chosen in the frame of a structural model, which parameters can be refined by fitting equation 2.1 to the experimental spectrum.

$$S(\nu) = \oint_{\sigma(\phi,\psi)=\nu} \frac{\chi(\phi,\psi)}{\left|\vec{\nabla}\,\sigma(\phi,\psi)\right|_{\sigma=\nu}} d\phi d\psi \tag{2.1}$$

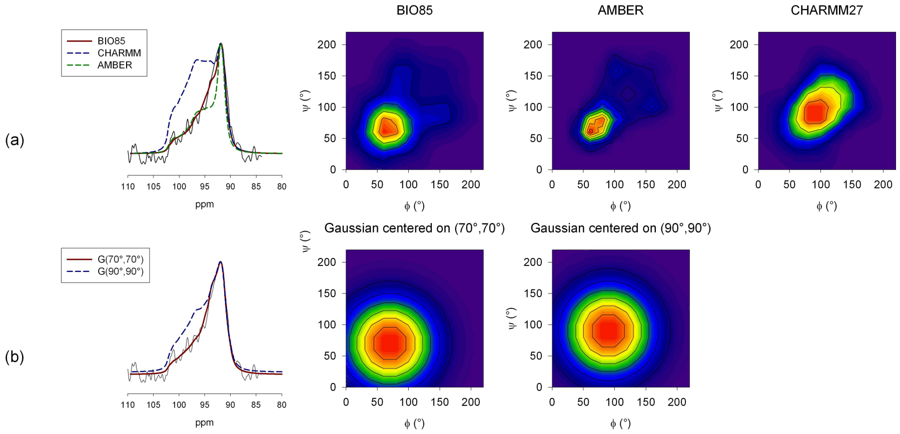


Figure 2.4: Best fits of the glycosidic part of the $^{13}C$ NMR spectrum of amorphous trehalose obtained by ball milling. Different conformational occupation factors are compared: (a) $\chi(\phi,\psi) \propto exp(-\frac{E(\phi,\psi)}{RT})$ with $E(\phi,\psi)$ calculated by molecular mechanics simulations using different empirical force fields, and (b) $\chi(\phi,\psi)$ of gaussian form with standard deviation $\Delta$

Application to the particular case of trehalose is extremely illustrative of the exact amount of information that can be extracted from the NMR spectrum [125]. The figure 2.4 shows that either a Boltzmann or a gaussian choice for the function $\chi(\phi,\psi)$ can equally lead to satisfactory agreement with the experiment. In both cases, a first significant parameter can be deduced: the maximum of the function $\chi(\phi,\psi)$, which corresponds to the most probable molecular conformation populated in the glass (around $(70°, 70°)$ for trehalose). The figure 2.4b indicates how the method is sensitive to this parameter: a simple shift of a few degrees in the model of its position leads to unacceptable results. The second parameter that can be extracted is the standard deviation of the distribution. In the case of figure 2.4a, the function $\chi(\phi,\psi)$ is supposed to be strongly correlated to the conformational energy $E(\phi,\psi)$, the most likely position corresponding naturally to the conformation of the lowest energy. Assuming that it only depends on intramolecular contributions, the function $E(\phi,\psi)$ can be estimated by simulation methods using classic molecular mechanics. However, it appears that the global accuracy of the method is not sufficient to describe in a more detailed way than a standard deviation the actual shape of the distribution of conformations in amorphous trehalose.

### 2.1.2 Application to different sugar glasses

We applied this method to other disaccharides (c.f. figure 2.5), in order to compare the local structures of their amorphous forms obtained by mechanical grinding [126]. In agreement with the previous discussion, the main parameters which can be extracted from the model of the CPMAS spectra are the most probable molecular conformation and the standard deviation of the conformational distribution. For the three studied disaccharides, the most probable conformations are found in agreement with the minima of energy calculated on crystal structures by classic molecular dynamics [126]. On the other hand, the shapes of the distributions $\chi(\phi,\psi)$ based on these force fields are not consistent with the experimental data, contrary to gaussian

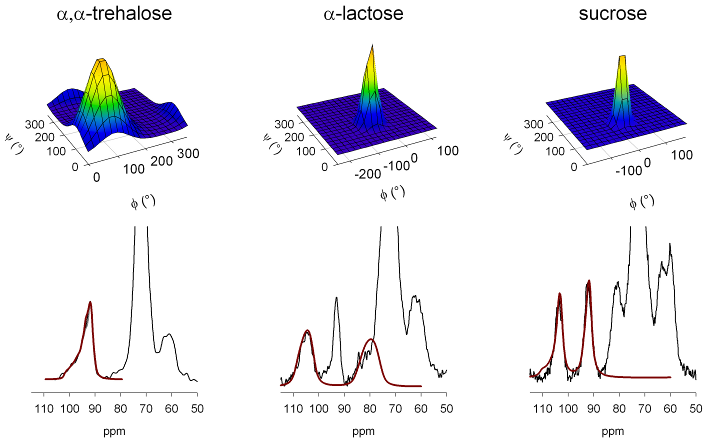


Figure 2.5: En bas : Meilleurs fits (ligne noire continue) des distributions expérimentales (ligne pointillée) de déplacement chimique du $^{13}C$ des carbones glycosidiques du trehalose, lactose et sucrose amorphes obtenus par broyage. En haut : distributions conformationnelles gaussiennes $\chi(\phi, \psi)$ correspondantes.

shapes. This simple fact suggests that the local structure of the disaccharide glasses cannot be completely described on the basis of purely intramolecular energy considerations.

The main result lies in the extent of the conformational distributions measured in the three sugar glasses. While the gaussian standard deviations found for the lactose and the sucrose are close to $\Delta \approx 15\,^{\circ}$, that of the trehalose reaches $\Delta \approx 50\,^{\circ}$, which represents an extremely large apparent flexibility. A coarse interpretation of these differences can be made by examining the crystalline structures of the three sugars, which reveal for lactose and sucrose the presence of intramolecular hydrogen bonds stabilizing a particular conformation of the glycosidic bond, while for trehalose, this intramolecular bond is absent. These results suggest that this situation might persist in the amorphous forms obtained by grinding. However, it is also possible in the case of trehalose that conformations of relatively high energy could be stabilized by intermolecular correlations, unobservable by a purely local technique like NMR [164, 165].

Although this apparent flexibility anomaly of glassy trehalose tends to contradict some *ab initio* calculations on isolated molecules (calculations however not directly confronted with the experiment) [70, 71], it is strongly supported by recent molecular dynamics simulations of aqueous solutions [137, 138]. Such an agreement would be expected if the structural properties of the glass were essentially of intramolecular origin. All these results suggest that conformational flexibility could be an essential ingredient participating in the microscopic mechanisms responsible for high bioprotective qualities of the dissacharide.

## 2.2 Amorphization by ball milling

An relatively large number of systematic works on the mechanisms of milling have been carried out on inorganic compounds, within the framework of metallurgical applications. More recently, the influence of the temperature of grinding (with respect to $T_g$) on the nature of the final state could be be clarified on molecular compounds [32, 52, 54, 184], as well as the transformations observed at the early stages of milling [214, 128].

### 2.2.1 Early stages of the amorphization by ball milling

The $^{13}C$ CPMAS NMR spectra presented figure 2.6a illustrate the amorphization of pure anhydrous trehalose by mechanical milling [128]. They reveal an increasing quantity of amorphous trehalose that appears during the mechanical action. The sample is made totally amorphous after a period that depends on the grinding power and on the mass of powder.

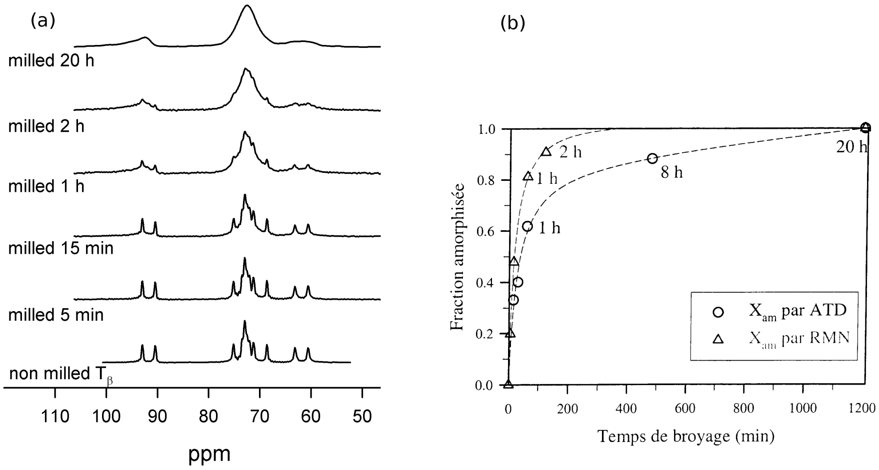


Figure 2.6: (a) $^{13}C$ CPMAS spectra of trehalose $T_\beta$ measured after different milling times. (b) Fraction of amorphous trehalose versus milling time, as determined by NMR (trinagles) or DSC (circles) [50].

Trehalose having a temperature of high glassy transition ($T_g \approx 373$ K), the grinding is made in a much lower (ambient) temperature. The notion of *effective temperature* proposed by Martin and Bellon [150, 151] allows to report qualitatively the behavior of the sugar (equation 1.3). Hence, the steady state stabilized by milling is the amorphous phase.

An more detailed analysis of the NMR spectra presented in figure 2.6a reveals some information on the mechanisms of amorphzation, in the first stages of the transformation. Until very long times (and thus high amorphous contents), the characteristic lines of the trehalose $T_\beta$ are clearly visible, and present no broadening. They add to a second contribution with on the contrary very broad lines, typical of fully amorphous trehalose. This second broad contribution is already present from the very first times of grinding.

This consitution of the CPMAS NMR spectrum in two independent components allows a very simple deconvolution by an elementary linear refinement. This supplies a robust method for evaluating the amorphous content of trehalose. More direct than alternative methods like scanning calorimetry (DSC), its local character makes it also less sensitive to the quality of lots. Therefore, it provides a simple answer to one of the major problems encountered in phamaceutical industry [128].

One essential point is the significant difference of the amorphous contents measured by NMR and by DSC *at short milling times* (c.f. figure 2.6b), whereas they perfectly agree for artificial mixtures of totally crystalline and totally amorphous volumes [128]. The DSC measures this content by identifying the jump of specific heat at the $T_g$ of the glassy part. The NMR measures it by identifying the fraction of molecules presenting important conformational distortions. The fact that the amorphous content measured by NMR at short milling times is much more important than that measured by DSC indicates the appearance of an important number of conformational defects, which distribution is the same as in the amorphous trehalose, but do not have a glassy character (do not contribute to the $C_p$ jump). It is noteworthy that the NMR linewidth associated to this apparently amorphous part is consistent with rather high energy defects (c.f. section 2.1). This is in agreement with the ballistic picture of ball milling. On the other hand, the non vitreous character of at least part of these defects leads to wonder about their actual static correlations at short milling times. They do not seem extended enough to confer to the disordered molecular set significant collective properties before longer milling times.

These observations are to move closer to structural analyses led by X-ray diffraction on various molecular compounds [31, 214]. They show that the short milling times first of all result in a reduction of the size of crystallites, accompanied by important deformations. It is thus reasonable to think that these structural modifications generate an accumulation of the conformational defects located on topological defects (dislocations, grain boundaries...). The reduction of the size of crystallites affects rapidly and significantly the surface/volume ratio. The surface contribution to the amorphous content as measured by NMR can become important. Surface can also be the privileged location for the appearance of the effectively glassy trehalose detectable by thermal analysis.

### 2.2.2 Athermal character of ball milling

As illustrated in the previous section, the mechanism of amorphization is similar to an actual rapid and inhomogeneous fusion under $T_g$, rather than a progressive and homogeneous disruptance of the crystalline network. At a given milling power, the grinding time seems to be the only parameter supplying the energy necessary for the complete conversion of the whole sample volume. This observation raises the question of the mechanisms of milling at the first stages of the amorphization, at the microscopic scale (c.f. section 1.3).

I could address this point by analyzing the properties of another disaccharide, *lactose*. It has the peculiarity to possess two molecular anomeric forms $\alpha$ and $\beta$. They only differ by the equatorial or planar position the hydroxyl function carried by the carbon $C_1'$ of the glucose cycle (figure 2.1). The conversion between the $\alpha$ and $\beta$ forms depends on a chemical balance. The kinetics of this reaction (called *mutarotation*) is very fast in aqueous solution [31]. This peculiarity is also at the origin of a particular crystalline polymorphism, as shown in figure 2.7.

Discriminating both anomers is particularly easy with NMR. Either observing the proton in aqueous solution or $^{13}C$ in solid phase. The integration of the corresponding peaks area (c.f. figure 2.7 (left *a*) allows to quantify the relative fraction of both anomers in the solid phase. The number of "chemical" polymorphs $\alpha : \beta \;/\; x : (1-x)$ reported in the literature is important. Therefore, this simple quantitative information is an essential prerequisite for the determination of the number of molecules by unit cell during the crystalline structure refinement by powder X-ray diffraction. Hence, the structure of the defined compound $\alpha : \beta/50 : 50$ obtained by heating of the amorphous milled lactose could be be determined (c.f. figure 2.7 (right) [123]).

Mutarotation is a highly thermally activated reaction. The coexistence of both anomers in aqueous solution is therefore unavoidable, as well as the appearance of the $\beta$ form by heating over the melting point of the crystalline forms of $\alpha$L [31]. As a consequence, it provides a direct and simple way to probe the thermal hypothesis for the amorphization by ball milling: if its mechanism is related to a local raise of temperature, the amorphization of pure $\alpha$L must go along with an important isomerization.

Figure 2.8a shows the NMR response measured of the amorphous lactose obatined by ball milling ($>$ 20h) pure crystalline $\alpha$L. Just after milling, and before any other thermal treatment,

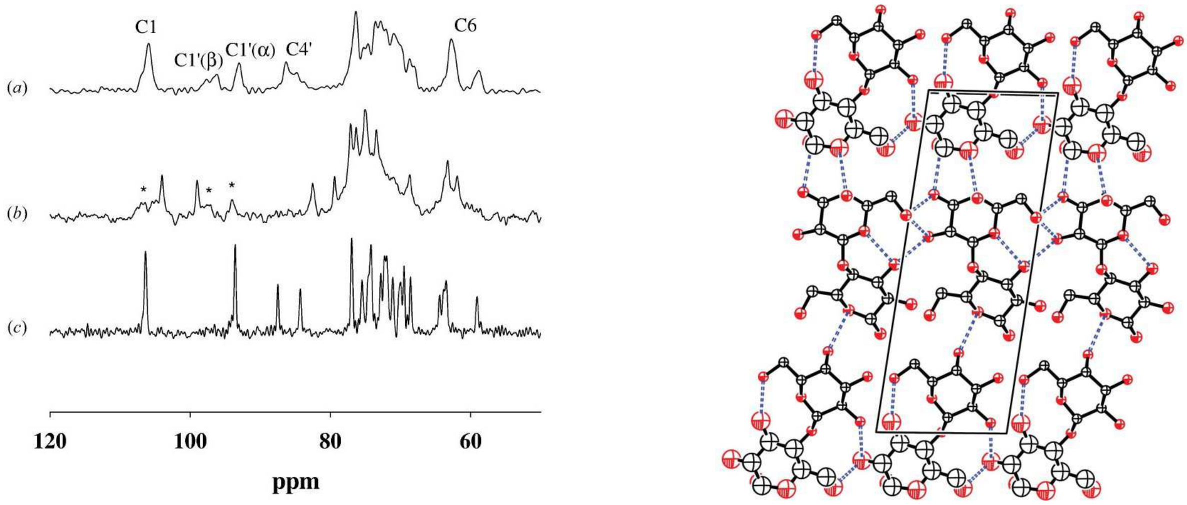


Figure 2.7: Gauche : Spectres CPMAS $^{13}C$ des polymorphes cristallins du lactose : (a) composé défini $\alpha : \beta$ 50 : 50, (b) $\beta$L commercial et (c) $\alpha$L commercial ; Droite : Représentation de la maille cristalline du polymorphe $\alpha : \beta$ 50 : 50 du lactose

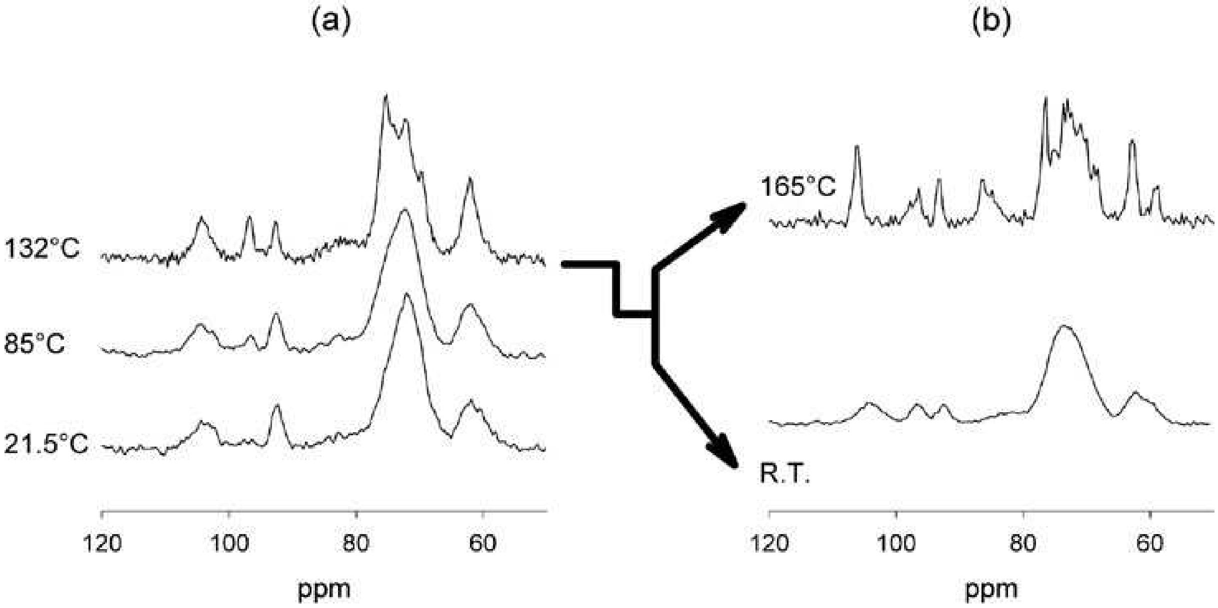


Figure 2.8: $^{13}C$ CPMAS spectra during thermal treatment of amorphous lactose obtained by ball milling of crystalline $\alpha$L.

there is no NMR line characteristic of the $\beta$ anomer (at most <4 %). Ball milling under dry atmosphere appears to our knowledge as the only preparation method of amorphous lactose leading to a sgnificant anomeric purity. Heating this pure amorphous $\alpha$L form from room temperature to a temperature slightly higher than $T_g$ ($\approx$110 °C) reveals the progressive appearance of the anomer $\beta$ (figure 2.8a). From this point, further heating above 160 °C induces recystallization into the defined compound $\alpha : \beta/50 : 50$, whereas going back to room temperature is reminiscent of a thermal quench, and leads to a $\alpha : \beta/50 : 50$ glass of lactose (figure 2.8b). Alike its crystalline polymorphism, lactose also displays an anomeric *polyamorphism*.

These simple observations are signture of the strong thermal activation of the mutarotation reaction in the solid state. They prove unambiguously that the actual temperature never exceeds, even locally, the melting temperature during the milling process. This allows to exclude the *melt - quench* mechanism hypothesis. More generally, this reveals the athermal character of the amorphization by mechanical routes [213].

## 2.3 Mutarotation of lactose and glass transition

A very simple reaction pathway is inspired from that proposed long ago for glucose [144, 217, 78], and accounts for the essential characteristics of mutarotation of lactose. It assumes a passage from one anomer to the other through an intermediate opened-cycle aldehyde form, separated by energy barriers (transition states, c.f. figure 2.9b). These barriers result in thermal activation, and determine the kinetic constants of the reaction.

The figure 2.8 discussed in the previous section shows an increase of $\beta$ lactose content when temperature approaches $T_g$. Above $T_g$, the two anomers appear in equal quantities. This proportion seems thereafter to remain irreversibly independent on temperature (see figure 2.9a).

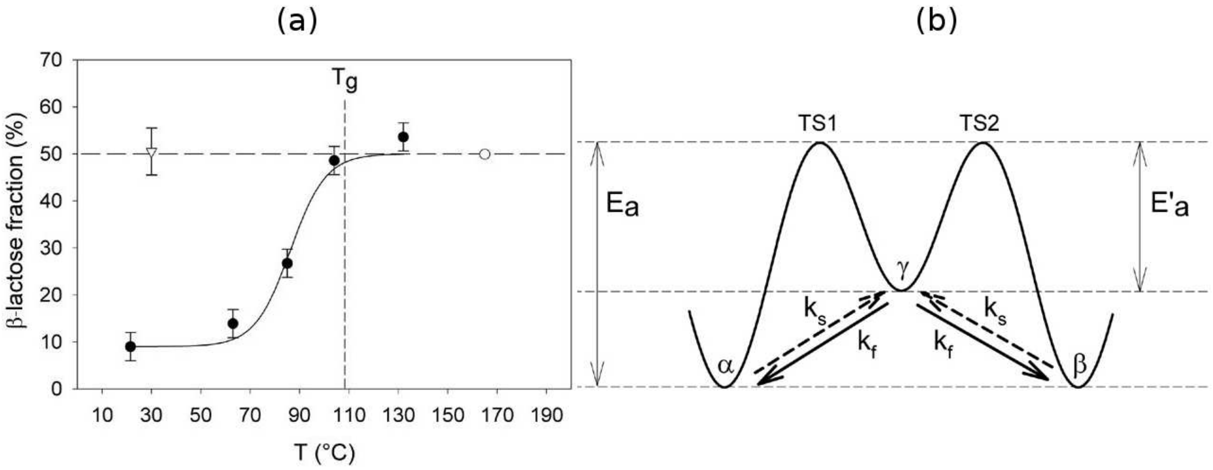


Figure 2.9: (a) : Evolution of the $\beta$ anomer content measured by solid state NMR versus temperature (solid circles). After reaching 132 °C, the amorphous $\alpha : \beta/50 : 50$ sample is either quenched to room temperature (triangle), either heated until recrystallization (open circles). (b) Energetic pathway for solid state mutarotation.

The $\alpha : \beta$=50 : 50 content appears therfore as the equilibrium value of the reaction. It suggests that the energy difference between the two anomers is almost zero in the solid state. This underlines the fundamental difference between the isolated molecule in solution, for which the coupling with the solvent determines the favored conformation, and the same molecule in a solid phase, for which this conformational part becomes very small compared to intermolecular contributions (hydrogen bond network).

The fact that this content of 50% is not reached below $T_g$ reveals the collective kinetic properties of amorphous lactose obtained by ball milling. Indeed, for $T > T_g$ the reaction reaches instaneously equilibrium, whereas for $T < T_g$ it is observed out-of-equilibrium: the reaction time exceeds that of the NMR experiment ($\approx$ 1 hour). The glass transition temperature therefore signals a cross-over between two reactional kinetic regimes. Mutarotation cannot proceed without water unless local structures and intermolecular favorable conditions appear. These conditions occur at a frequency driven by the structural $\alpha$ relaxation of the amorphous lactose. Mutarotation is an example of reaction with "dispersive" kinetics below $T_g$ [168], alike some curing reactions [117, 171], of photoisomerizations of proteins [91], which kinetic constants couple to the viscosity of the environment and therefore display all charateristic features of glassy dynamics (non arrhenian slowing-down, distribution of kinetic constants).

This illustrates how a purely local phenomenon like mutarotation can reveal as an interesting tool for studying more into the detail phenomena associated to the relaxational dynamics of an amorphous compound prepared by ball milling, such as heterogeneous dynamics, or ageing effects below $T_g$ [127].

# 3

# Dynamics of Confined Complex Fluids

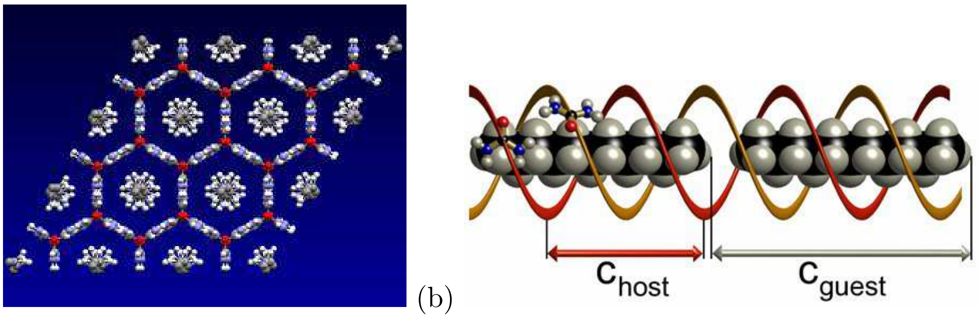
## Contents

In this second chapter, I will develop another aspect of my work, which concerns the dynamic properties of confined condensed molecular phases. An important point common to all these studies is the choice of highly anisotropic (quasi 1D) systems [25]. It is readily expected that a low dimensional topology should strongly impact the structure of the confined phases. A purely one dimensional character is for instance not compatible with a long range crystalline order, and implies finite size effects that can influence the nature of phase transitions or electronic properties of the system [63, 162]. Generally, a molecular phase will show a shifted thermodynamic equilibrium when it is confined in an anisotropic environment. This shift can range from a simple perturbation (if the interaction with the host matrix is weak) to the stabilization of out of equilibrium states, observable or not in the bulk phase [5].

## 3.1 Preamble: local dynamics and collective properties

A system can be ”ultra confined” if the characteristic radius $R$ of the confining matrix reaches molecular sizes. The contribution of the *guest-host* interaction to the free energy of the system there becomes of the same order of the *guest-guest* interactions, which cannot determine alone the nature of the order in the confined phase any more. Such a phase cannot be separated from its host, and forms with it a crystalline or quasicrystalline network. Only topological arguments, or the asymmetry of the local interactions (ionic/metallic, hydrogen bond network/van de Waals...) allow to formally distinguish the host from the ultra confined guest sublattice. Hence, the whole system possesses common vibrational collective dynamics. In some cases, the two interacting sublattices show a long range aperiodic order[2]. This particular structure displays additional degrees of freedom that induce specific phonon bands [11, 23]. The analysis of this collective dynamics in intergrowth compounds of alkanes in urea has been a major part of my PhD thesis [124]. In the present document, these works can be revisited, in order to underline how collective and individual effects in these systems can be intimately interrelated, and how the hierarchy of long and short range orders and of static or dynamic disorders can be revealed both by collective or local probes.

Figure 3.1 shows schematically the structure of the supramolecular urea/alkane aperiodic self-assembly [198]. In these compounds, the alkanes prevent the urea network from remaining in their pure quadratic form. Instead, urea molecules adopt a double helix configuration, building one dimensional channels arranging in a honeycomb way (average space group $P6_122$ at high temperature). The hydrogen bond stabilization of this host network generates cell parameters that are essentially independent of the length of the guest alkane chains [124].



(a) (b)

Figure 3.1: Schematic structure of the $C_nH_{2n+2}urea$ compounds, in view (a) parallel or (b) perpendicular to the $c$ crystallographic axis [197, 198]).

Alkanes stack in the free volume as a single file with average periodicity $c_{guest}$. The ratio $c_{host}/c_{guest}$ is most often irrational: the self-assembly is aperiodic. This relative independence of both sublattices reveals the asymmetry of interactions *host-host* and *guest-guest*. This asymmetry results at least partially in a one dimensional organization of the alkane chains, as it is revealed by diffuse scattering planes in the diffraction pattern of the crystal [124]. However, the interaction between the two sublattices is strong, and results in an incommensurate intermodulation (c.f. figure 3.2a).

This intermodulation generates important and complex collective phenomena in these compounds, some of which have been recently reported: analyticity breaking and phase transition mechanism in a crystallographic superspace, selective compressibility [198]. Another feature of these supramolecular materials is the disorder revealed by diffraction: beyond the Bragg peaks that demonstrate crystalline order, and the type "s" diffuse scattering associated to the 1D ordering of the alkane chains, another type of diffuse scattering (type "d") is observed. It forms broad stripes in reciprocal space, as an evidence of much shorter correlation lengths (order <1D) (figure 3.2b).

We have investigated the nature of this disorder by coherent neutron scattering. The stripes associated to the type "d" diffuse scattering are separated along the $c^*$ axis by a reciprocal period corresponding to that of the $-(CH_2)-$ groups of an alkane molecule. The conditions of extinction along this axis is also in agreement with the pseudo $2_1$ symmetry axis of the molecule.

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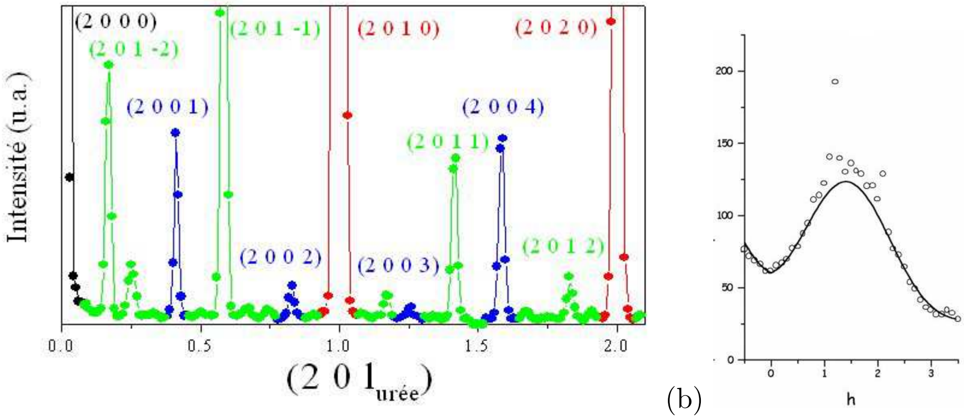
[2] if $a$ and $b$ represent the periodicities of the host and guest sublattices when their interaction vanishes, then an aperiodic order is obtained if the ratio $\frac{a}{b}$ is irrational



(a) (b)

Figure 3.2: (a) (2 0 $l$) neutron diffraction line measured on a single crystal of $C_{19}D_{40}/urea$ at T = 250 K. Different Bragg peaks are attributed to the urea (red) or alkane (blue) sublattices, and satellite peaks (green) are the sign of an incommensurate intermodulation [129]. (b) Diffuse scattering of type "d", measured by neutron diffraction on a single crystal of $C_{19}D_{40}/urea$ and compared to the molecular form factor of the alkane [134].

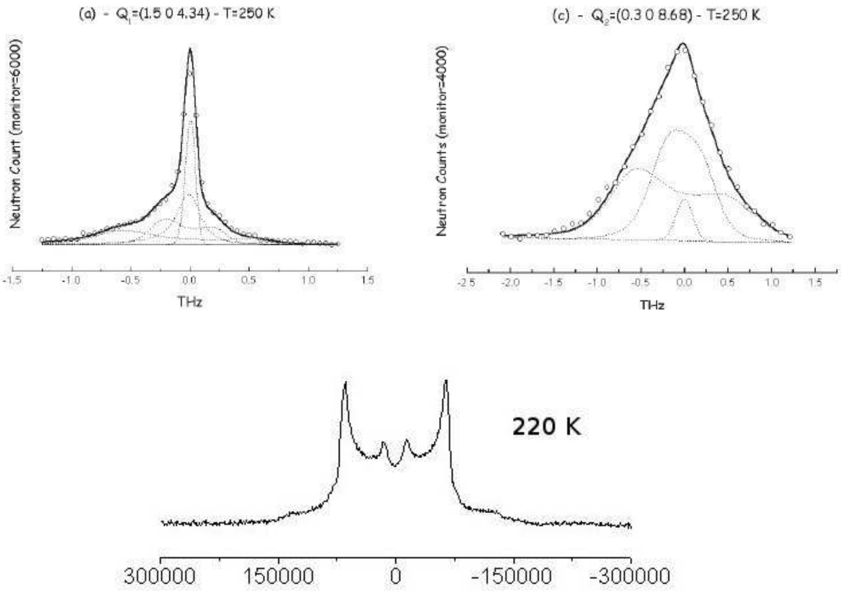
The "d" diffuse scattering is therefore reminiscent of the intensity that would be scattered by a single alkane molecule, which can be easily calculated within a given model of molecular geometry: $I(\vec{Q}) = \left\langle F_m(\vec{Q})F_m(\vec{Q})^* \right\rangle$, with $F_m(\vec{Q}) = \sum_{i\in molécule} b_i exp(\vec{Q}\ .\ \vec{r_i})$.

Coherent neutron elastic scans across the "d" diffuse scattering [134] have confirmed that its intensity is indeed well described by the form factor of a single alkane molecule in its *all-trans* conformation, and averages over all possible orientations of the molecule plane around its long axis (aligned with the urea channel, c.f. figure 3.2b). The agreement is all the more satisfactory as there is no other adjustable parameters than experimental normalizations. Therefore, this suggests that the translational and rotational fluctuations responsible for the diffuse scattering are very weakly correlated. The energy analysis of these diffuse stripes is reported in figure 3.3a. The scattering appears completely inelastic, the coherent elastic intensity is thoroughly rejected into the diffraction pattern (Bragg of type "s" diffuse scattering) [134].

This analysis illustrates how a purely local property can be blatantly revealed while using a coherent probe. This situation is reminiscent of that encountered when studying glass forming liquids or polymers, for which the coherent and incoherent inelastic structure factors are intimately related [80, 224]. It is however opposite to the situation discussed in section 2, where information on the extent of collective effects could be extracted out of purely local dynamic observables. As illustrated in figure 3.3b, very broad distributions of self-correlation times associated to intramolecular rapid motions can be evidenced by $^2H$ NMR in molecular amorphous states [130]. Hence, these distributions reveal indirectly pronounced heterogeneities related to dynamic cooperative phenomena.

## 3.2 Nanoconfinement of complex fluids

This last section summarizes my most recent research works, in the frame of the theme "Nanoconfinement of complex fluids" at the Institut de physique of Rennes. Beyond solid state physics, I am developing within this theme an activity opened to new problems raised by the radically



(a)

(b)

Figure 3.3: (a) Q constant scans on a single crystal of $C_{19}D_{40}/urea - d_4$, across the two first diffuse scattering stripes of type "d". (b) $^2H$ NMR spectra of perdeuterated triphenyl phosphite (TPP-$d_{15}$) in its supercooled liquid phase at 220 K.

new behaviour of glass forming or more generally soft matter that is observed when it is trapped by nanometric confinement.

Starting from the relatively completed knowledge on simple confined liquids (see introduction 1.2.1), our approach aims to enlarge experimental studies to nanoconfinement of more complex systems. Beyond the stinking interest they presently focus in the application domains of the nano and biotechnologies (nanofluidics, lab-on-chip...) [30, 81, 104, 121], these systems are more and more encountered as intermediates for the synthesis of new objects (magnetic nanowires, conducting polymer nanotubes ... [58, 139, 187]) and raise important new fundamental questions. Ranging from biologic mixtures to thermo or lyotropic mesogens, these complex fluids generally display very rich bulk phase and states diagrams. Under confinement, the order parameters that drive transitions between those states can strongly couple to the topology or to the details of the interface imposed by the confining medium, and therefore show a totally new behaviour.

Within this general frame, we chose to open our activity to the analysis of anisotropic properties of confined phases, and were in consequence particularly interested in the use of the columnar form of porous silicon (PSi) as a model confining matrix. PSi is obtained by an electrochemical etching of a crystalline Si wafer in an aqueous solution of HF and ethanol [77]. The obtained layer displays a non-interconnected pores topology, macroscopically oriented perpendicularly to the wafer surface. The average pore diameter is about 8 nm [26], the length of which can reach several hundreds of microns (fig. 3.4).

This specific anisotropy allows to carry out experiments with a precise knowledge of the orientation of the wafer (then the pore axis) within a laboratory frame (incident beam, magnetic field...), and therefore avoid the need of powder averaging which is necessary when using other types of anisotropic porous materials like MCM or SBA.

I will first present confinement effects observed on several original dynamic properties ob-

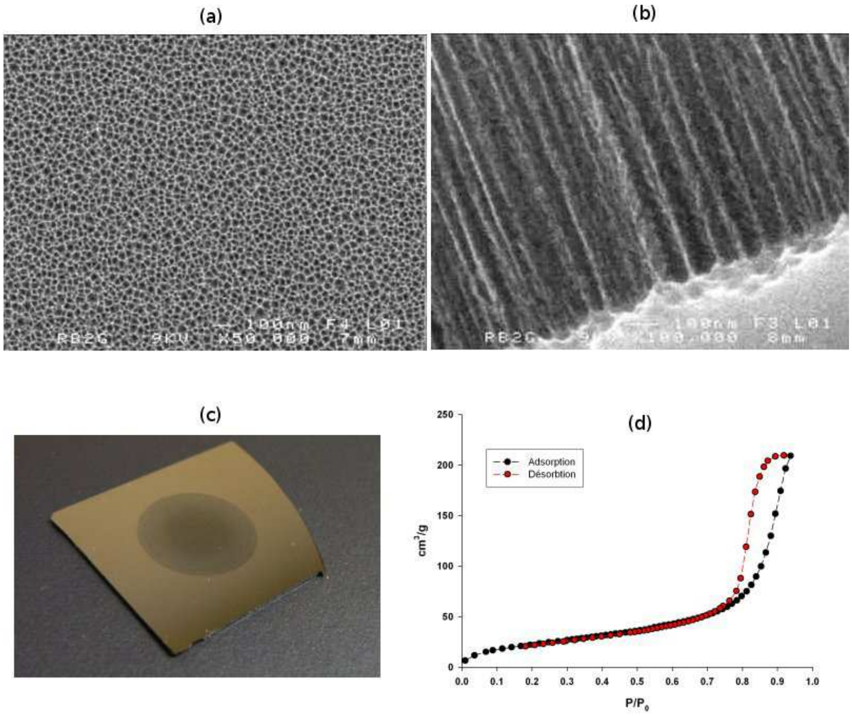


Figure 3.4: SEM images: (a) top view and (b) side view of a porous silicon layer. (c) Photograph of a wafer with its porous layer (black disk). (d) $N_2$ adsorption and desorption isotherms measured on porous silicon [26].

served on glass forming binary mixtures (section 3.2.1). Then (section 3.2.2), I will discuss some results that illustrate structural effects in a confined smectic phase submitted to *anisotropic* quenched disorder. Finally, the main elements of the molecular heterogeneous dynamic properties associated to this smectic ordering under confinement will be summarized (section 3.2.3).

### 3.2.1 Confined biopretectant binary systems

One of the striking results obtained on simple confined liquids is the tendency of average properties like density or dynamic properties like diffusivity to become highly heterogeneous in nanometric pores (c.f. figure 1.4). These observations are supported by number of *all-atoms* molecular dynamics simulations, and make questionable the validity of *continuous media* approaches [109, 73]. Confined fluids of biotechnological interest are often mixtures, and this adds a new very important complexity. For homogeneous bulk mixtures, concentration can be submitted to local fluctuations, in the same way as the density in simple liquids (c.f. figure 3.5). Some binary systems can also display a gap of miscibility, and then become under confinement very sensitive to the topology of the porous medium, that can be responsible for quenched disorder effects, or nanostructured demixions (see introduction 1.1.2, and outlooks 4.1.2).

Within bioprotectant systems, the fundamental properties of bulk disaccharides solutions have been studied in detail [9, 10, 22, 34, 46, 57, 62, 147, 216]. The hydrogen bonded nature of these solutions, together with the glassy character of their dynamics have been put forward as key parameters driving the bioprotection mechanisms. Within the most studied sugars, trehalose shows exceptional bioprotective skills. In section 2.1, we showed that the local structure of

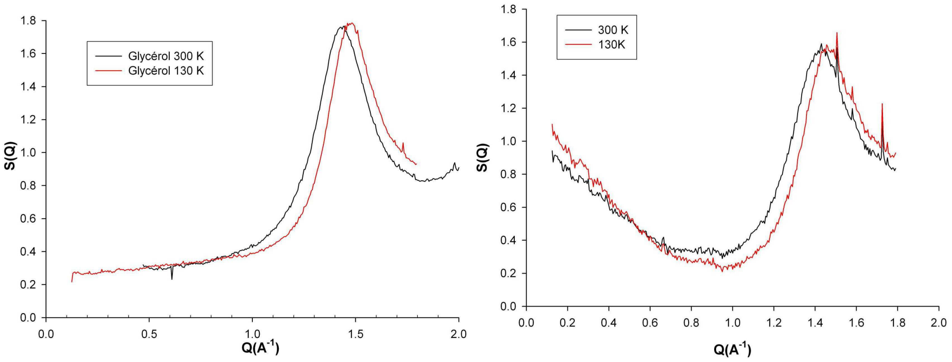


Figure 3.5: Neutron diffraction pattern of bulk bioprotectant solutions [24]. **left:** Structure factor of pure glycerol. **right:** Structure factor of a 30%w trehalose in glycerol solution. The increase of the signal at low angles is due to concentration inhomogeneities in the solution.

the pure trehalose glass displays very particular features, related to a broad distribution of molecular conformations. Moreover, the *in vivo* mechanisms of bioprotection occur in crowded cellular environments [195], within often interfacial solutions [163] for which spatial confinement at the nanometer scale become a relevant parameter. The detailed study of confinement effects (in PSi) on trehalose/glycerol solutions have been undertaken in our team during the PhD work of Rémi Busselez [24].

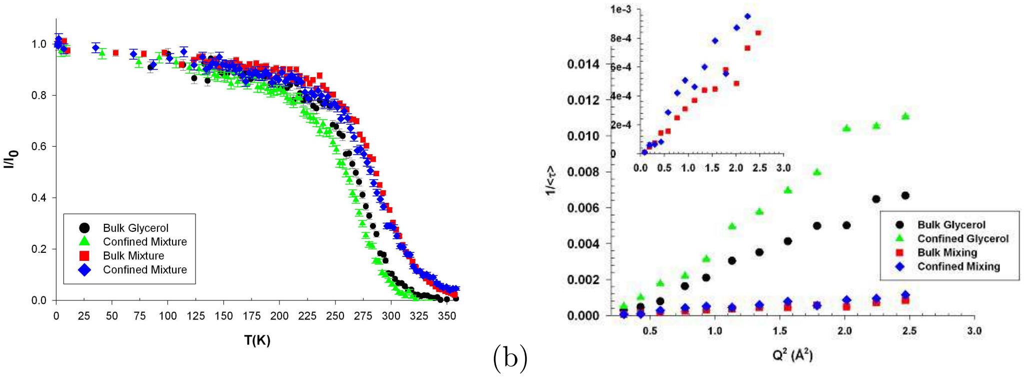

(a)
(b)

Figure 3.6: Quasielastic neutron scattering (backscattering) on on bioprotectant solutions. (a) Elastic scans. (b) Average self-correlation time as extracted from quasielastic spectra at 310 K.

The incoherent neutron scattering analysis (in the nanosecond time window) allows to separate clearly the antagonist effects of sugar addition (marked slowing down) from confinement (acceleration) on the average parameters qualifying the dynamics of these solutions (figure 3.6, tableau 3.1).

As usual on glass forming systems, the intermediate scattering functions of the solutions can be refined by stretched exponential functions ($exp[-(DQ^2t)^\beta]$), which parameters are listed in table 3.1. Both the introduction of sugar and the confinement tend to lower the stretching exponent $\beta$, and these effects are additive. This lowering can be interpreted as an increase of the heterogeneity of the molecular dynamics. Conversely, the fundamental reason why the confinement leads in this case to an average acceleration remains to clarify, as no sharp tendency can

| | Glycerol | Confined glycerol | Solution | Confined solution |
|---|---|---|---|---|
| $\beta$ | 0.6 | 0.5 | 0.5 | 0.4 |
| $< D >$ $(10^{-8} cm^2.s^{-1})$ | 5.0 | 7.6 | 0.52 | 0.77 |

Table 3.1: Average self-diffusion coefficient and Kohlraush stretching exponent extracted from the refinement of the quasielastic neutron scattering data at T = 310 K on glycerol and a 20w% trehalose/glycerol solution.

still be synthesized today that could help rationalizing the observations reported on numerous systems [6]. Hence, it appears all the more necessary to combine a sufficient number of techniques with complementary time windows (magnetic resonance, dielectric relaxation, molecular dynamics simulation), in order to precisely qualify the relations between confinement, glassy dynamics, and possibly out-of-equilibrium trapping of such mixtures.

### 3.2.2 Structure of nanoconfined liquid crystals

Since the pioneering works on smectic liquid crystals confined to the nanometer scale in isotropic materials such as aerogels or aerosils [17, 136], a growing interest has been focused on the use of random anisotropic materials [140, 75]. Such new geometries are indeed susceptible to allow decoupling the quenched disorder effects on the nematic and smectic order parameters [170]. The solution proposed by Leheny and co-workers was to strain aerosil suspensions under static shear. The resulting random disorder was in that case anisotropic, but not systematically quenched [140]. Our contribution has been to propose an experimental realization of anisotropic quenched disorder by taking advantage both on the quasi unidimensional topology and of the pronounced corrugation of the internal surface of porous silicon, randomly coupling to the anchoring field of the confined liquid crystal [89].

The figure 3.7 shows the evolution of the Bragg peaks of a confined model liquid crystal (4-octyl-4'-n-cyanobiphenyl, 8CB) , observed by small angle neutron diffraction. A diffuse peak appears below 300 K, and reveals the growth of smectic correlations. This peak is not a full ring as in the bulk, but its intensity concentrates for scattering wave vectors aligned with the silicon pores axis. Such an observation demonstrates the strong coupling between the anisotropy of the confined phase and the one dimensional topology of the porous medium. A precise analysis of the shape of the Bragg peak was carried out on a two axis neutron diffractometer. It reveals that the smectic correlations remain short ranged in their whole temperature domain of existence, and that their structure factor can be modelled by the sum of two terms (eqn. 1.1): one of thermal origin (same shape as a bulk smectic peak), and a second with characteristic shape attributed to quenched disorder effects [17, 172]. In case of PSi, the amplitude of the *anisotropic quenched disorder* appears large [89], and one can expect specific effects that are at present not taken into account within the available theoretical frames [173].

At lower temperatures, the smectic peak disappears when crystallization occurs. This crystallization takes place during several steps towards phases ($K'$, $K'_s$) distinct from the stable phase ($K$) of bulk 8CB (c.f. fig 3.7). These new phases also display preferential orientations with respect to the pores axis [87]. The anisotropic confinement therefore promotes at low temperature the stabilization of new phases or phases that are metastable for the bulk fluid. It also cancels the *nematic→smectic* transition, and replaces it by a short range smectic order which temperature domain is significantly extended (crystallization temperatures are lowered by c.a. 50 K), and which correlation lengths always remain finite [87, 89].

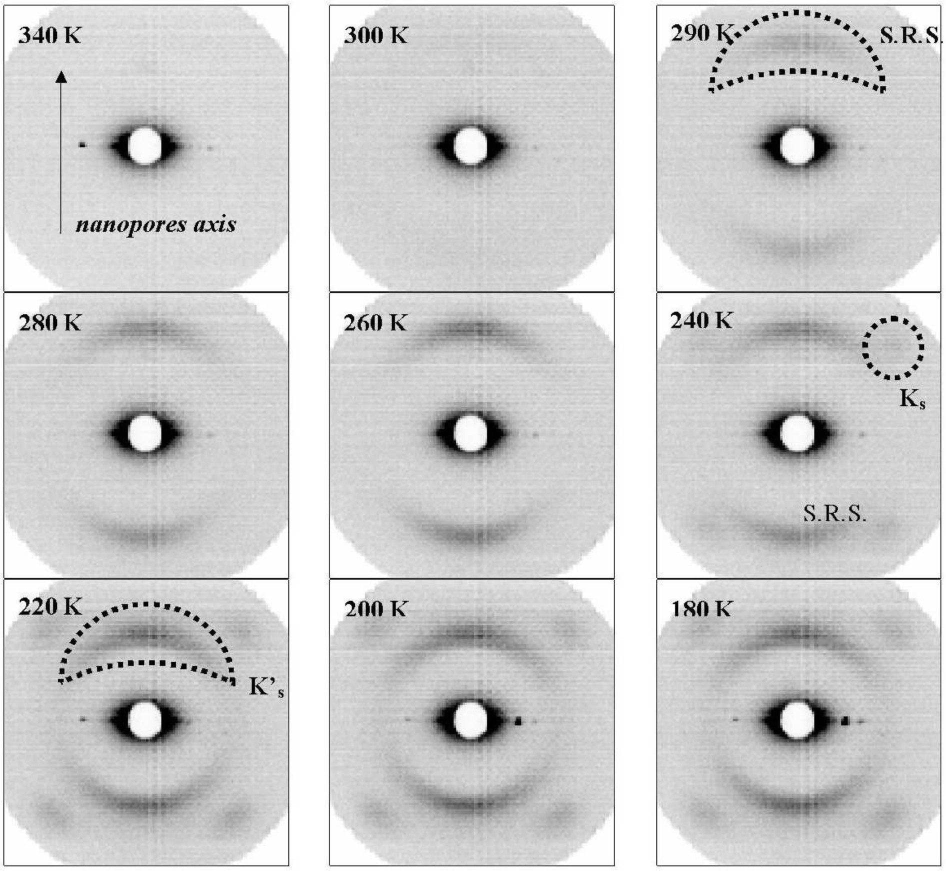


Figure 3.7: Small angle diffraction patterns of 8CB confined in porous silicon, at different temperatures.

### 3.2.3 Dynamic heterogeneities and local order

These quenched disorder effects on the smectic ordering result in a static order of very short range ($\xi_{stat}$<12 nm in case of 8CB in PSi). However, the nature of this order and the extent of its correlation remain clearly identified and measurable. This situation contrasts with the case of more simple or glass forming liquids, for which such a local order is neither of translational nature nor of sufficient extent for a non ambiguous signature in a diffraction experiment. The nanoconfinement of liquid crystals provides therefore a unique opportunity to analyze the molecular dynamics of a system for which short range static correlations grow continuously when temperature is lowered. Whereas the evidence of such a relation is still a matter of debate in supercooled liquids, the study of liquid crystals is susceptible to enlight some aspects of the problem. Indeed, surprising analogies have recently been reported between the molecular dynamics of mesogens at the approach of their *isotropic→nematic* transition (fluctuations of the orientational order parameter) and supercooled liquids at the approach of the glass transition (structural relaxation $\alpha$) [29]. Such an evidence suggests a possible unified description of the heterogeneity of molecular dynamics (of characteristic length $\xi_{dyn}$) when it is driven by a coupling with local order (of characteristic size $\xi_{stat}$). Such a unified point of view has been proposed in the frame of mode coupling theory [28].

In case of 8CB confined in PSi, the molecular dynamics seems to follow the same continuous

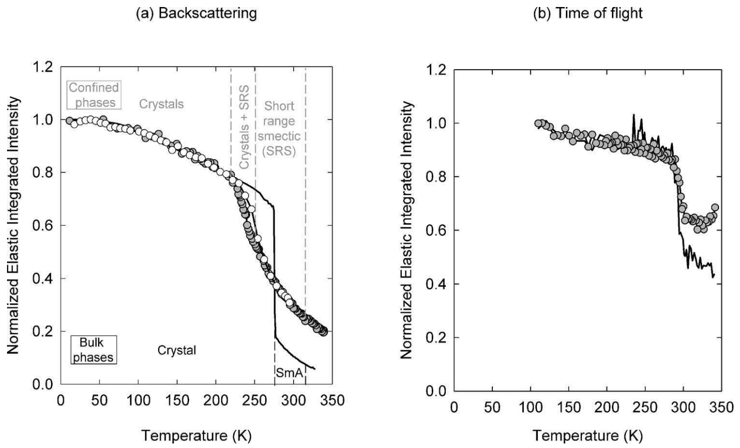


Figure 3.8: Elastic scans measured by quasielastic neutron (a) backscattering or (b) time of flight.

behaviour as the static correlation length (figure 3.8), suggesting a possible generalization of this point of view in the case of a short range smectic phase [88].

### Molecular dynamics of bulk 8CB

Another major advantage of liquid crystals compared to supercooled liquids allows to greatly simplify the analysis of their molecular dynamics. In case of glass formers, the frequency overlap of diffusional and reorientational processes, together with their intrinsic heterogeneity results in dynamic response functions of complex shape, that are usually described by semi-empiric laws such as the Kohlraush decay ($f(t) \propto exp[-(\frac{t}{\tau})^{\beta}]$). Conversely, these processes are often decoupled for liquid crystals, which allows a description in terms of relaxation modes (translational self diffusion, molecular rotations or librations...). Consequently, it has been possible for many liquid crystals to provide a clear image of their molecular dynamics, especially by quasielastic neutron scattering [55, 98, 122, 153]. Finally, this decomposition into simple modes in the direct space also provides realistic analytical laws [207, 133], and opens the way to study the molecular dynamics of liquid crystals in more complex environments.

Despite abundant literature, the individual dynamics of cyanobiphenyls has been poorly studied [122]. In order to better understand the dynamic behaviour of 8CB confined in PSi, the knowledge of its bulk dynamic properties is mandatory. We therefore carried out quasielastic neutron scattering experiments on a large scale of relaxation times (> 3 decades), by combining data recorded on time of flight and backscattering spectrometers (fig. 3.9) [133].

In the considered time window, two modes essentially dominate the dynamics of the liquid crystal, from the isotropic phase down to crystallization: a rapid uniaxial rotational diffusion (≈ 10 ps) and slow translational self-diffusion (≈ a few ns). Corresponding characteristic times for these two processes as measured by neutron scattering are in very good agreement with those measured by other techniques like light scattering [131] or pulsed field gradient NMR [59]. The complete set of intermediate functions can therefore be in a first approximation by a very simple *analytical* model [133]:

$$f_{bulk}\left(Q,t\right) = exp\left(-Q^2\left\langle u_{vib}^2\right\rangle\right) f_{rot}\left(Q,\tau_c,t\right) exp\left(-DQ^2t\right) \tag{3.1}$$

A simple Debye-Waller factor (effective mean square displacement $\left\langle u_{vib}^2\right\rangle$) takes into account

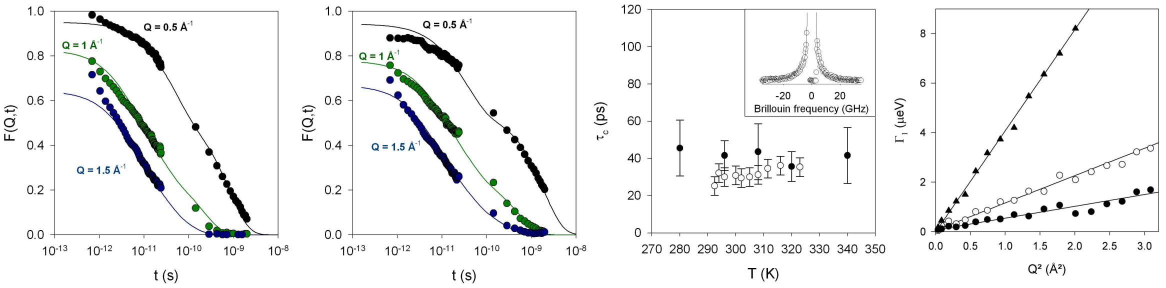


Figure 3.9: (a) and (b): Intermediate incoherent neutron scattering functions measured at 320 K and 296 K on bulk 8CB. (c) Rotational correlation time measured by Brillouin and neutron scattering. (d) Spatial dependence of the quasielastic linewidth (backscattering) associated to the diffusional mode [133].

both rapid vibrations and also part of the librations and rotations of the aliphatic chain ends of 8CB. The complete knowledge of this analytic form, together with the values of diffusion coefficients for the bulk provides a solid basis for studying the dynamics in confinement [133].

### Characteristic length of dynamic heterogeneities

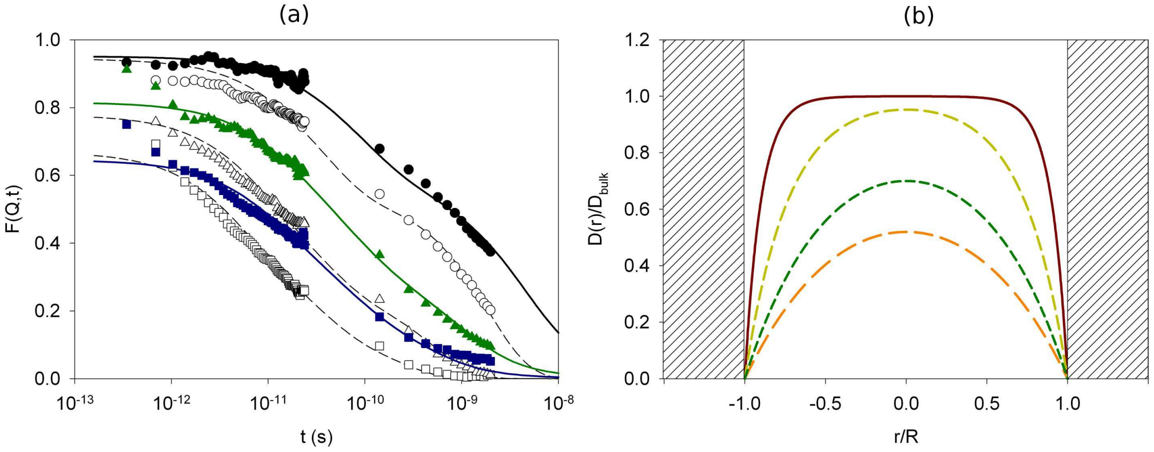


Figure 3.10: (a) Intermediate incoherent neutron scattering functions of 8CB confined in PSi at 296 K for different Q moduli. The response of bulk 8CB is recalled in light gray. (b) Model of the spatial heterogeneity of the dynamic parameters (rotational and translational diffusion coefficients) of 8CB confined in PSi [132].

When 8CB is confined in PSi, the molecular dynamics is globally strongly slowed down with respect to the bulk phase at the same temperature, even in the isotropic and nematic phases (figure 3.8). Moreover, its intermediate scattering function displays a very pronounced stretching towards longer times (figure 3.10a). On the time scale of the experiment, the molecular dynamics is no longer fully relaxed, which indicates an important slowing down of translational diffusion modes. This is also noticeable at shorter times, corresponding to more localized modes. This situation is strongly reminiscent of the confinement induced stretching already observed on molecular glass forming liquids [223]. This suggests an heterogeneous origin mediated by the surface of the pores, driving a slowing down of the interfacial molecules (anchoring). A simple model taking this heterogeneity into account is depicted in figure 3.10b, and based on three hypothesis: *i)* the surface dynamics is much slower than the experimental resolution ($D(R) \to 0$), *ii)* far from the surface, the dynamics tends to that of the bulk, following a simple exponential law $D(r) \propto exp(-\frac{r-R}{\xi_{wall}})$, and *iii)* the relaxation modes remain the same as in the bulk. This approach provides a definition of a *dynamical correlation length* $\xi_{wall}$ that can be evaluated from the experiment, after averaging over the sample volume (eqn 3.2).

$$f_{conf}\left(Q,t\right)=\frac{1}{V}\int_{V}f_{bulk}\left(r,Q,t\right)dV \tag{3.2}$$

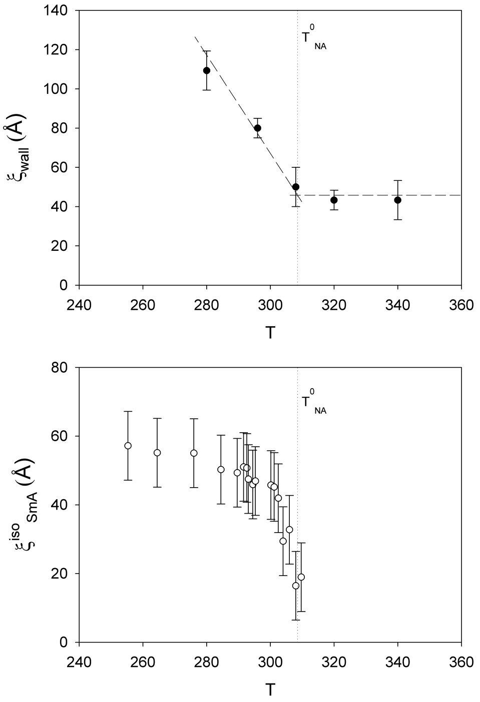


Figure 3.11: Comparison of the (a) dynamic $\xi_{wall}$ and (b) static $\xi^{iso}_{SmA}$ correlation lengths of 8CB confined in PSi

The figure 3.11 reveals that this dynamic correlation length $\xi_{wall}$ is constant and relatively weak at high temperature (bimodal distribution of dynamical populations), and grows significantly (continuous distribution of the dynamic parameters in the pore) in the temperature domain where the short range smectic correlations tend to appear. This analysis therefore constitutes the first direct observation of the growth of dynamic heterogeneities driven by a local static order of growing size $\xi^{iso}_{SmA}$ [132]. This coupling between dynamic and static lengths measuring the memory of interfacial effects in the confined phase is supported by recent molecular dynamics simulations carried out in our team on a mesogenic model (Gay Berne system) in the frame of a CNRS postdoctoral position (Qing Ji [106]).

# 4

# Outlooks

## Contents

My research projects are naturally planned within the theme ”Nanoconfinement of complex fluids” at the Institut de Physique of Rennes. They rely on the axes that I have developed in the previous chapters, both thematically (complex molecular phases, nanoconfinement) and methodologically (importance of the local approach). Some of them represent short or medium term outlooks, in the direct continuity of the most recent works, and will be particularly carried out in the frame of PhD supervising (Gilbert Chahine). Some other works are longer term outlooks, and constitute a widening to new problems raised by complex binary or ternary confined systems. The complete set of these scientific projects will be in strong connection with the other parts of the team's activity. In particular, the investment on large scale facilities will be continued (co-worker: Denis Morineau), and new tools of molecular dynamics simulation will be explored (co-worker: Aziz Ghoufi). These outlooks also strongly rely on the new possibilities provided by new equipments, which installation in the laboratory is supported by our team (dielectric spectroscopy, solid state 600 MHz NMR, pulsed field gradient NMR).

## 4.1 Short term outlooks

### 4.1.1 Confinement of liquid crystals

The following projects have been initiated in the frame of the PhD work of Gilbert Chahine, started in 2008 under my supervision.

Up to now, quenched disorder effects on smectic phases have most of the time been studied on model mesogens, on the *nematic* → *smectic* phase transition which essentially second order character is well established in the bulk. Other liquid crystals display however different phase diagrams, as illustrated in case of the cyanobiphenyls (nCB) family (figure 4.1).

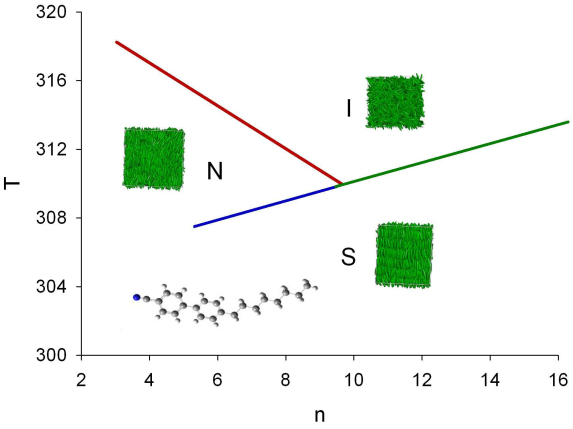


Figure 4.1: Phase diagram of the cyanobiphenyls family.

In this very case, increasing the length of the aliphatic chain leads to an increase of the coupling between nematic and smectic order parameters, inducing a more and more pronounced first order character of the transition [48]. Above 10 carbons, the domain of existence of the nematic phase vanishes, and the smectic order establishes directly from the isotropic liquid through a discontinuous transition. Although the low temperature phase remains unstable versus quenched disorder, the mechanism leading to this order is in that case very different, at least for the bulk phase: the transition is no longer driven by the order parameter fluctuations, but rather by a nucleation and growth process. An fundamental change in the the relative importance of thermal and disorder terms in the structure factor can therefore be anticipated. Also, one can wonder whether the universality of the scaling laws observed on $N \rightarrow Sm_A$ transitions still holds. The nature of the interaction with the inner surface can also express in an original way in confined systems, for which ladder-type anchoring transitions have been evidenced [102]. A metastability domain associated to hysteresis phenomena with temperature can also be expected, although it has never been observed up to now on confined liquid crystals (while they dominate other first order transitions like capillary condensation). The importance of kinetic effects able for instance to lead to a coexistence of phases remains a matter of debate [16, 174].

Another essential aspect concerns the nature of the *nematic* order, which is no longer a prerequisite for the translational ordering. Up to now, numerous studies have focused on compounds displaying a nematic phase [41, 113, 45]. In case of $I \rightarrow Sm_A$ transitions, the topology, the nature of the interfacial interaction or the dimensionality of the confinement can gain importance with respect to the coupling between orientational and translational order parameters that drives the bulk phase behaviour. In the continuity of the optical birefringence measurements that we have reported on 7CB and 8CB in collaboration with A. Kityk and P. Huber at the university of Saarbrücken [113], the precise analysis of the nematic and paranematic orders of 10CB and 12CB will be carried out at the Intitut de physique, using $^2H$ magnetic resonance on selectively deuterated samples confined in PSi. Here again, the macroscopic orientation of the porous matrix provides a particularly favourable opportunity to discriminate the interfacial contribution to the nematic order parameter [41].

Finally, there is still no description of the molecular dynamics of confined liquid crystals accepted by a large scientific community. In the bulk, striking analogies between reorientational relaxations in thermoplastic mesogens and in glass formers have been recently evidenced on systems with a $I \rightarrow N$ transition. These observations raise today a considerable attention, because they open the way to a better understanding of collective dynamic phenomena in complex liquids [28, 29, 35, 36]. They also provide a new point of view on the often reported glassy character of the molecular relaxations in confined fluids [7, 74], that in particular associated to the collective fluctuations in presence of quenched disorder [17]. We have shown that these concepts of heterogeneous dynamics, usually invoked for glass formers, appear equally relevant for describing the stretched response of confined smectics (c.f. sections 3.2.3) [132].

However, these questions remain open for liquid crystals without nematic stable phase, and for which an essential arrhenian behaviour of the relaxation modes seems to be recovered [74]. As a first step, a systematic study of the molecular dynamics of 10CB and 12CB will be undertaken, taking advantage of the new equipment of broad band dielectric spectroscopy installed in the laboratory, especially for discriminating interfacial modes [74]. In parallel, some aspects of the collective dynamics on the same systems (this time perdeuterated) will be analyzed by coherent neutron scattering by *spin-echo* spectroscopy, in the frame of the PhD work of Gilbert Chahine, in collaboration with the CEA in Saclay.

### 4.1.2 Bioprotectant binary mixtures

Beyond the PhD works of Rémi Busselez (c.f. section 3.2.1), a detailed understanding of the influence of confinement of the glassy dynamics of binary bioprotectants requires a complete analysis of the response at long time scales, accessible to calorimetry or magnetic resonance techniques.

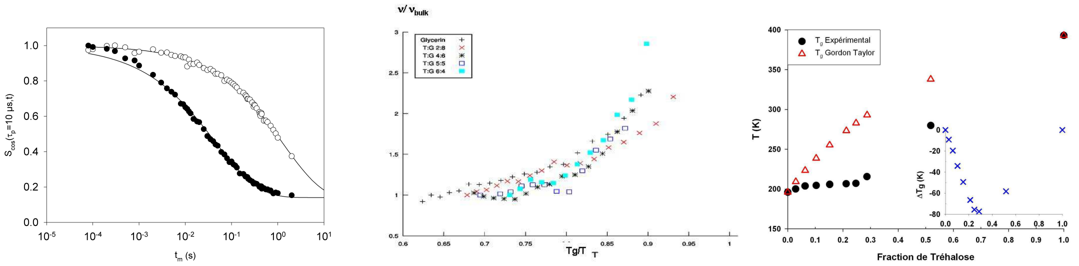


Figure 4.2: (a) Reorientational correlation functions of bulk (open circles) or confined (solid circles) glycerol, as measured by $^2H$ NMR (stimulated echoes) at 210 K. (b) Ratio of the average frequencies associated to the structural relaxation of bulk and confined glycerol (coll. R. Pelster, Saarbrücken). (c) Glass transition temperature of trehalose/glycerol mixtures versus their sugar concentration [82, 24].

$^2H$ NMR stimulated echo methods will be developed in Rennes [67], in order to characterize the slow (around ms) rotational dynamics of the confined solutions. Preliminary results at $T_g$+20 K (c.f. figure 4.2a) show that the confinement induces an average acceleration. It is much more pronounced than the one observed at higher temperature with neutron scattering. This magnifying of confinement effects at the approach of the glass transition is in agreement with observations by dielectric spectroscopy, made in collaboration with Rolf Pelster from the university of Saarbrücken (c.f. figure 4.2b).

There is still important work to do to understand in detail the reasons of this marked effect on the dynamics of the binary solutions near $T_g$. A key parameter seems to be the asymmetry of the solvent-solvent and solute-solvent interactions, which go along with a strong non ideal character of the solution. This is indirectly revealed by the departure of the $T_g$ from the Gordon-Taylor law (figure 4.2c) [82, 24]. A systematic analysis of a broad range of concentrations shall be undertaken, in order to unravel this point. The study of the solutions highly concentrated with sugar will be made through a collaboration with the group of S. Magazù (Milano). Moreover, the consequences of confinement on the density of the mixture, together with the role of the interface on the homogeneity of structural and dynamic properties will be probed by modulating the nature of the interfacial interaction, by chemical of functional treatment of the surface (hydrophilic/phobic, grafting of functions with preferential affinity with one of the components). Finally, pulsed field gradient NMR techniques will allow to extend the range of wave vectors on which the dynamics will be probed [67, 215].

## 4.2 Nanoconfined complex mixtures

A new tendency is emerging today, aiming to reduce the size of devices for detection or manipulation of complex fluids, in the domains of imaging [152], pharmaceutical prospective [42] or even medicine [208]. For the design of such components, the potentiality of hybrid porous-organic nanostructures (fig. 4.3) retain considerable attention in a growing number of applications from electronics [39, 1], optics [225, 212], or nanofluidics [61, 2]. In most cases, the fluids implied in the realization of use of these systems are complex mixtures, which must be driven in restricted environments.

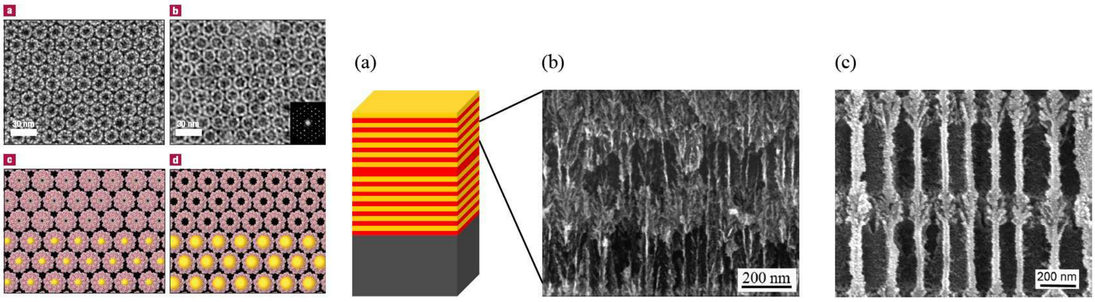


Figure 4.3: (a) Ordered network of chaperonin complexes and modelling of their coupling with gold quantum dots [152]. (b) Optical microcavities based on a micro and mesoporous silicon heterostructure functionalized with liquid crystals [212].

One research axis I wish to promote is to study the effects of confinement on binary and ternary model systems, which properties are representative of the fundamental problems raised by some of these applications. In a first time, this project will focus on the behaviour of mixtures possessing a gap of miscibility, by opposition to the bioprotectant solutions studied so far, which are miscible in all proportions. In a second time, the novel questions raised by the addition of a third component will be addressed. For instance, the mechanisms of the bioprotectant function will be studied in the presence of biological macromolecules. In that case, the coupling between the multiscale character of these solutions with the topology of the porous medium shall be investigated. Also the effects of confinement on the coupling between the solvent dynamics and the properties of the folding-denaturation transition of simple proteins will be addressed. In parallel, the fundamental question of the behaviour under confinement of such class of entropy driven transitions shall be analyzed on model ternary systems.

### 4.2.1 Binary systems with gap of miscibility

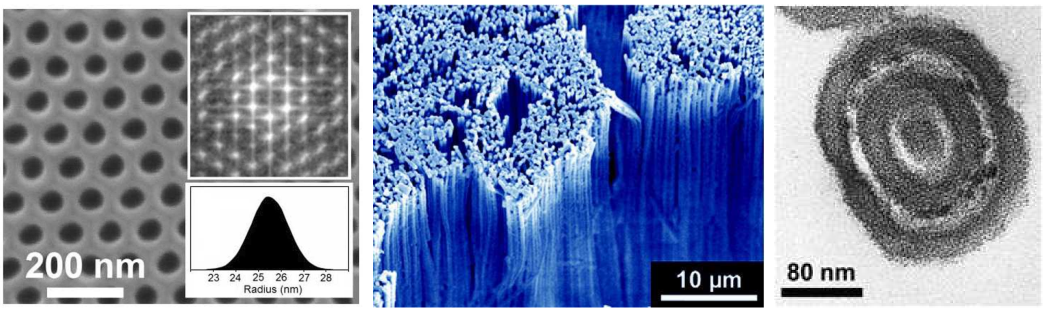


Figure 4.4: (a) SEM image of the surface of a porous alumina membrane [41]. (b) Liquid crystal nanotubes [188] and (c) nanostripes of PS-$\beta$-PMMA demixed in an epoxy resin [191]. Both (b) and (c) are obtained through *template* methods.

During the past few years, the development of *template* methods has allowed to master the synthesis of a growing variety of organic functional nanotubes, from polymer [58, 187] to liquid crystalline systems (figure 4.4) [188]. Very recently, the use of binary mixtures could lead to new composite nanoobjects [178]. From the fundamental point of view, the key element making the design of these nanoobjects possible stands in the ability to initiate phase separation of the confined binary in the template, in order to obtain a controlled nanostructure.

This mechanism entirely relies on the demixion of a mixture under confinement. Hence, it can be greatly influenced by the nature of the interfacial interaction, or the porous topology. In contrary to interconnected and isotropic porous media, where quenched disorder effects can dominate the dynamic properties of the solutions enough to prevent demixion (c.f. section 1.2.2), templates with highly anisotropic topology (such as Anopore$^{(R)}$ membranes) seem to favour sharp interfaces between the separated phases, leading to ”plug”, nanotube or ”capsule” structures (c.f. figure 4.5).

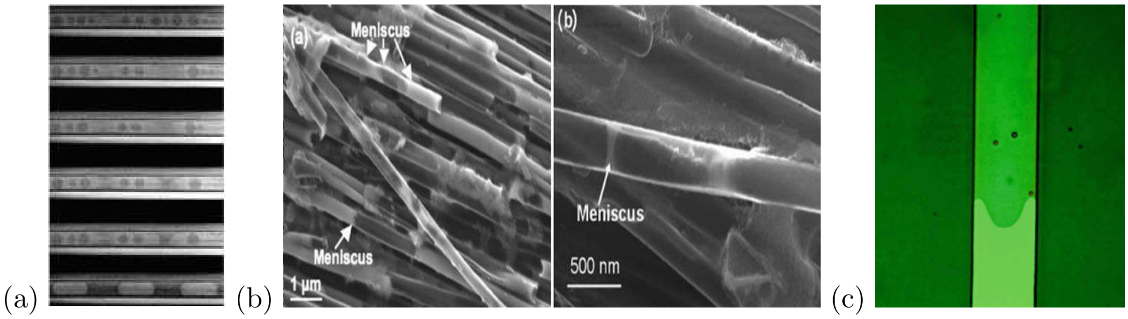


Figure 4.5: Formation steps of ”plug” type morphologies in (a) aqueous solutions confined in capillaries of 250 $\mu$m [201], or (b) in nematic liquid crystals confined in carbon nanopipes ($\phi \approx$ 200 nm) [183]. (c) Front meniscus of a water ”plug” in a nanochannel of height 100 nm [61].

Until now, the ultimate size reached for these wetting synthesized structures is around 20 nm, whereas emphasized effects are expected for smaller diameters [58]. Going beyond requires a better understanding of the mechanisms of the demixion transition under confinement in pores of very small size. Formally, columnar matrices of alumina or porous silicon can be particularly representative realizations of the demixion model in a single pore (c.f. section 1.2.2 and references [69, 141, 142, 156]). They provide good opportunities to analyze the nanostructures obtained and their growth kinetics.

In the frame of a project in collaboration with the *Institut des Matériaux* in Nantes (J.-L. Duvail), supported by the competence center *C'Nano Nord-Ouest*, we propose to carry out such study in model binary solutions (water/triethylamine, water/isobutyric acid). The nature of the potential nanostructures obtained after demixion in porous alumina membranes shall be investigated by small angle neutron scattering [180], and some dynamic aspects such molecular self diffusion approaching the transition will also be scrutinized by pulsed field gradient NMR [204]. In a second part of this project, the objective will be to evaluate the possibility to synthesize nanoobjects out of the obtained nanostructures. In this purpose, one of the first direction we will explore will consist in including a functional monomer with a high affinity with one of the constituents of the mixture, and which polymerization can be induced after demixion in the template.

### 4.2.2 Ternary systems

The project detailed in the previous section illustrates the interest in prorogating our research by the investigation of confined ternary systems. Another example in the continuity of our works on bioprotectant binary solutions (section 3.2.1) is the *folding-denaturation* transition of proteins in solution and in restricted environment. Understanding the mechanisms of this transition *in-vivo* is a very difficult task, as a whole hierarchy of dynamic processes is involved. Most of them are heterogeneous (glassy dynamics), dissipative, sometimes out of equilibrium and irreversible, and strongly coupled to the thermodynamic state and molecular dynamics of the solvent [196, 92, 91]. The study of such physical processes driving the protein denaturation in bulk solutions stimulates a growing number of experimental studies [218, 148, 96]. The role of the solvent, and in particular that of hydration layers of the macromolecule in aqueous solutions focuses a particular interest: the influence of a putative strong-fragile transition in this layer is a matter of recent controversy [85, 149, 161, 206].

Since the discovery of an intracellular mechanism of folding assisted by macromolecular complexes (chaperonins) [95], spatial confinement has appeared as an essential parameter promoting stabilization of native conformations of proteins (figure 4.6).

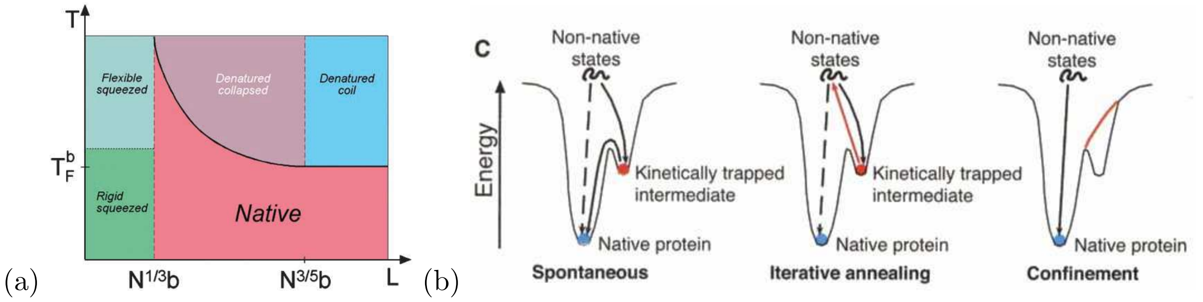


Figure 4.6: (a) Confinement stabilization of the native conformation of a protein [195]. (b) Folding mechanism assisted by confinement in a molecular chaperonin [95].

Recent thermodynamic models [222] or simulations [145, 194] have aimed to discriminate the respective roles of *cellular crowding* and *molecular confinement* within the mechanisms allowing in the same time to accelerate folding and to avoid aggregation. Clearly, finite size effects, together with coupling to the solvent allow a sufficient modulation of the energetic landscape of the protein so that activation barriers between intermediate states (figure 4.6). Although the number of experimental studies that could support such scenario remain today relatively scarce [64], there is no doubt that it is of general interest, for it minimizes the importance of dissipative or out of equilibrium aspects (as mediated through ATP hydrolysis for instance), while it presents the *folding-denaturation* transition as essentially driven by *entropic* effects [203, 194].

The latter remark suggests the relevance of a "pedestrian" approach of such problems in biological ternary mixtures, by focusing on model systems and studying the generic effects of nanometric confinement on a phase transition driven by entropy. Within this general frame, I propose two main axes of research. The first (exploratory) one will aim to analyze structural and transport equilibrium properties in simple confined solutions (water/sugar/protein or glycerol/sugar/protein). The choice of the system will be guided by its simplicity, the proper knowledge of its bulk properties in the literature, as well as its size adequation with the porous medium (lysozyme, cytochrome C...). These data are essential for a better understanding of the respective roles of the solvent and interfacial effects on the protein dynamics. The second axis is more fundamental, and will focus on the investigation of confinement effects on model entropy driven transitions, such as *inverse melting* in simple molecular ternary mixtures.

### Multiscale systems

In the first axis, I will as a first step try to discriminate the structural and dynamic properties which are driven either by the macromolecule-solvent coupling of by the coupling with the topology of the pore. This approach requires a global account of the multiscale nature of the system, which involves different characteristic lengths ranging from a few nanometers (solvent heterogeneities, interfacial layers) to several microns according to the geometry of the confining matrix (clustering, pore topology).

From the structural point of view, it will be essential to determine the importance of macromolecular aggregation, as an ultimate expression of concentration heterogeneities in systems with large size distributions [189]. This study shall be carried out for instance by small angle neutron scattering, on samples which porous geometry will be controlled (track-etched or alumina membranes), as well as the nature of the interfacial interaction (hydrophilic/phobic or covalent grafting).

From a dynamic point of view, the multiscale nature of the system will also require a global experimental approach. At first, dielectric spectroscopies will be allied to quasielastic neutron scattering in order to better understand the influence of the macromolecule on the solvent dynamics in restricted environment. Modulating isotopic contrast, or using complementary probes like NMR can prove to be decisive, allowing to reduce the complexity of the system by selecting partial observables. Secondly, I propose to analyse more deeply the influence of the porous topology on the transport properties of the confined macromolecules. Dynamics will be probed, that spread over times several orders of magnitude longer than that of the solvent, and that can strongly couple to the low dimensionality of the confining matrix. For example, generic processes of *single-file diffusion* can be expected to take place, as it is the case in numerous micro to macroscopic systems (figure 4.7a and b) [120, 211]. Comparative studies in controlled cylindrical pores (track-etched, alumina) or with diameters voluntary modulated at different length scales (figures 4.3b and 4.7c) will help disentangling the influence of the confinement topology on such transport processes.

A *coarse-grain* approach of the macromolecular dynamics can be employed, by selectively measuring the self-diffusion properties by pulsed field gradient NMR, over mean square dis-

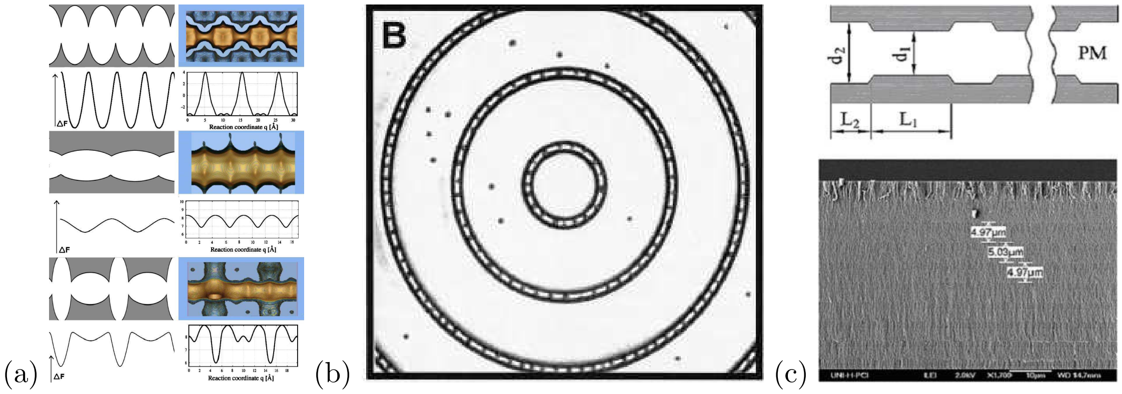


Figure 4.7: (a) Modelling structure/mobility coupling in zeolites [14]. (b) Single-file diffusion of confined colloids [211]. (c) Porous silicon structure with nanometric modulated diameter [112].

placements of the order of microns. This technique has long revealed as a particularly successful tool for studying the relation between structure and mobility in restricted environment [119], on scales ranging from a few molecular diameters in zeolites [118], a few tens of nanometers in mesoporous materials [205, 146] up to microns in colloidal systems [160].

### Entropic drive under confinement

The second axis I propose to develop is more fundamental. Its goal is to better understand the generic effects of confinement on entropy driven transitions, of which the protein folding-denaturation seems to be representative [96, 149, 194, 218]. The study of the latter is still hindered by the need to take into account a large number of secondary parameters in the analysis of experimental data (chemical and conformational details of the macromolecule, coupled time and space scales...). Moreover, this transition is not a genuine phase transition: it is a dynamic transition for which collective effects are restricted to the protein size and its immediate surrounding, making the system more sensitive to local heterogeneities and easy to trap in out of equilibrium states.

For these reasons, the studies we should undertake will concentrate on simpler model systems, featuring only reversible transitions between homogeneous states, stable or metastable. As an example, aqueous solutions of *methyl cellulose* can mimic in an interesting way the transition between native and aggregated states of biological materials. Such solutions display at low temperature a fluid phase that transforms reversibly on heating into a gel phase [181]. This transformation can be considered as an inverse glass transition, for which the low temperature phase is a solution of folded polymers energetically favoured, while at high temperature, it is formed of open conformations in hydrophobic interaction (entropically favoured, c.f. figure 4.8c).

More generally, the whole set of *inverse transitions* constitute representative models of transitions driven by entropic effects, that can be strongly affected by confinement. *Inverse melting* has been predicted as soon as 1903 by Tammann for pure compounds, and described as singularities at high pressure (reminiscent of the water density anomaly at the ice→liquid transition) accounted in the frame of the Clapeyron equation [107, 86]. Only recently, experimental evidence of such transitions have been reported, first at high pressure in quantum fluids or simple liquid crystals (figure 4.8a) [107, 181].

Rapidly, it has appeared that pressure is not the only thermodynamical parameter leading

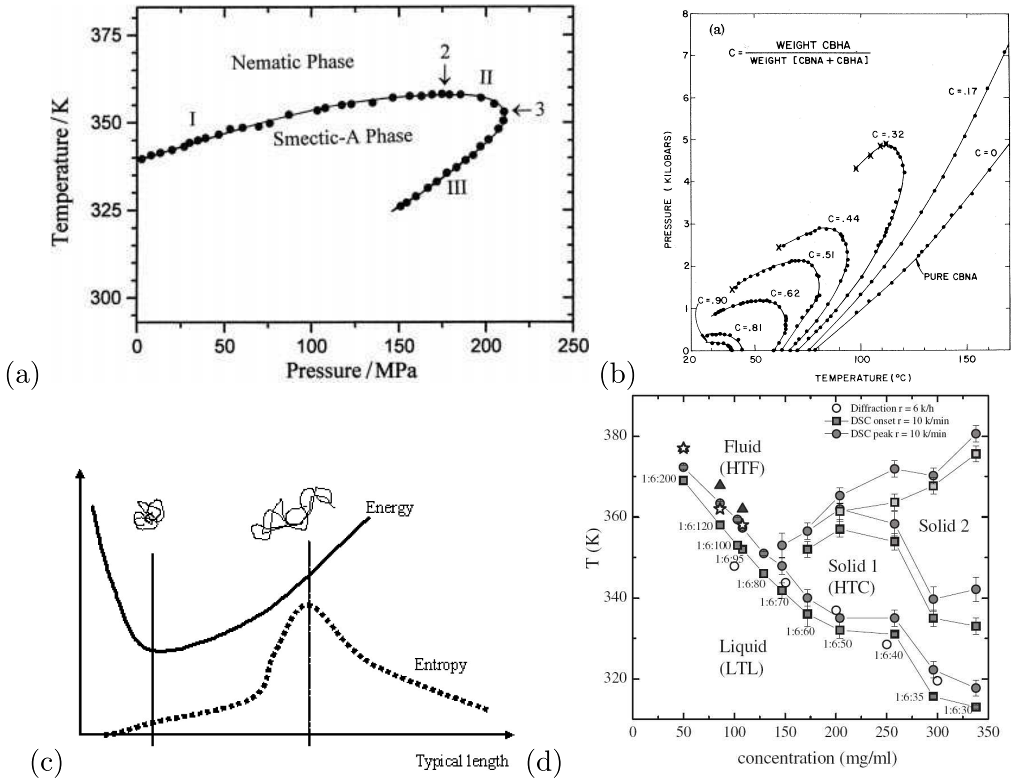


Figure 4.8: (a) and (b) Reentrant smectic phase of pure 8OCB [107] and of 8OCB/6OCB binaries [40]. (c) Entropic mechanisms of an inverse glass transition [181]. (d) Phase diagram of the ternary molecular system water/$\alpha$-cyclodextrin/4MP [8].

to this type of inverse transition. The introduction of binary liquid crystal mixtures allowed to considerably reduce the pressure range where a reentrant smectic phase appears (figure 4.8b). Very recently, inverse melting could be observed at atmospheric pressure in a ternary aqueous solution between a low temperature fluid phase and a high temperature crystal phase (figure 4.8d) [8]. Although the microscopic mechanisms leading to this inverse melting in such simple molecular systems are far from being completely understood, the formal analogy with folding-aggregation transitions in biological solutions has been underlined [167]. In both cases, the high entropy state (stabilized at high T) paradoxally corresponds to a long range order [181]. In the continuity to our present works and short term outlooks, the study of such model systems under confinement provides new opportunities to better understand the effects of entropic drive in restricted environment, which recent theoretical works attempt to embed within a very general framework [154, 155].

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# Résumé

Il est très facile de ”piéger” des phases moléculaires complexes dans des états métastables ou hors-équilibre, en usant d’actions complexes (voies athermiques), d’environnements complexes (topologie), ou en manipulant la complexité intrinsèque du système (réseaux d’interactions). Des procédés industriels les plus courants aux nanotechnologies les plus poussées, on rencontre des phases moléculaires piégées par des processus de forçage (trempe thermique, irradiation, broyage mécanique...) ou de confinement nanométrique (basse dimensionalité, hétérogénéité, champs aléatoires, phases interfaciales...). Ce document de synthèse met en avant les problématiques physiques communes à ces situations, au travers d’études expérimentales de systèmes modèles. Des matériaux forcés à intérêt pharmaceutique aux fluides complexes nanoconfinés, la puissance des approches complémentaires par des techniques locales (résonance magnétique du solide) ou collectives (diffusion de neutrons) est soulignée.

**Mots-clés:** Nanoconfinement, fluides complexes, broyage mécanique, matériaux moléculaires, résonance magnétique du solide, diffusion de neutrons

# Abstract

It apprears quite easy to ”trap” complex molecular phases in metastable or out-of-equililbrium states, by using complex actions (athermal routes), complex environments (topology) or by manipulating the intrinsic complexity of the system (interactions network). From usual industrial processes to most recent nanotechnologies, trapped molecular phases are encountered in forcing procedures (thermal quench, irradiation, ball milling...) or nanoscale confinement (low dimensionality, heterogeneity, random fields, interfacial phases...). This synthesis document enlights the physical promlems common to these situations, through experimental studies of model systems. From forced molecular materials of pharmaceutical interest to nanoconfined complex fluids, the power of complemetary approaches using local (NMR) or collective (neutron scattering) techniques is underlined.

**Keywords:** nanoconfinement, complex fluids, ball milling, molecular materials, solid state magnetic resonance, neutron scattering