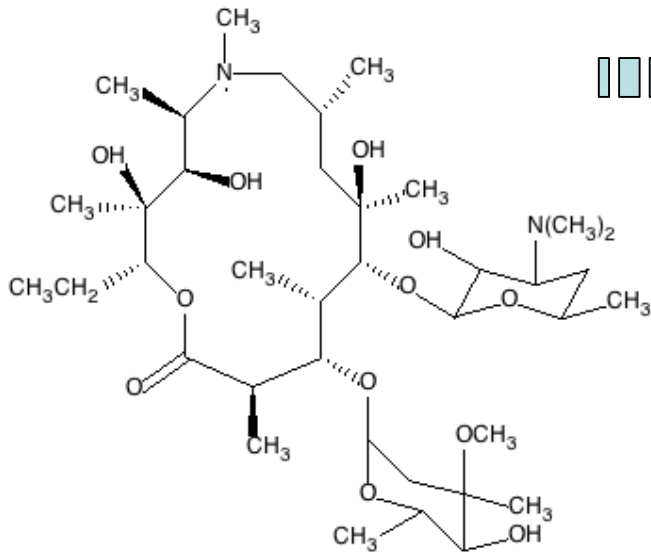


Interaction of the macrolide antibiotic azithromycin, with model of membranes



Inhibits endocytosis in
macrophages

- I. AFM on bilayers
- II. Experiments with GUV
- III. Langmuir on monolayers
- IV. Experiments on MLVs

Collaboration :

M.-P. Mingeot-Leclercq (UCL)

A. Schanck (UCL)

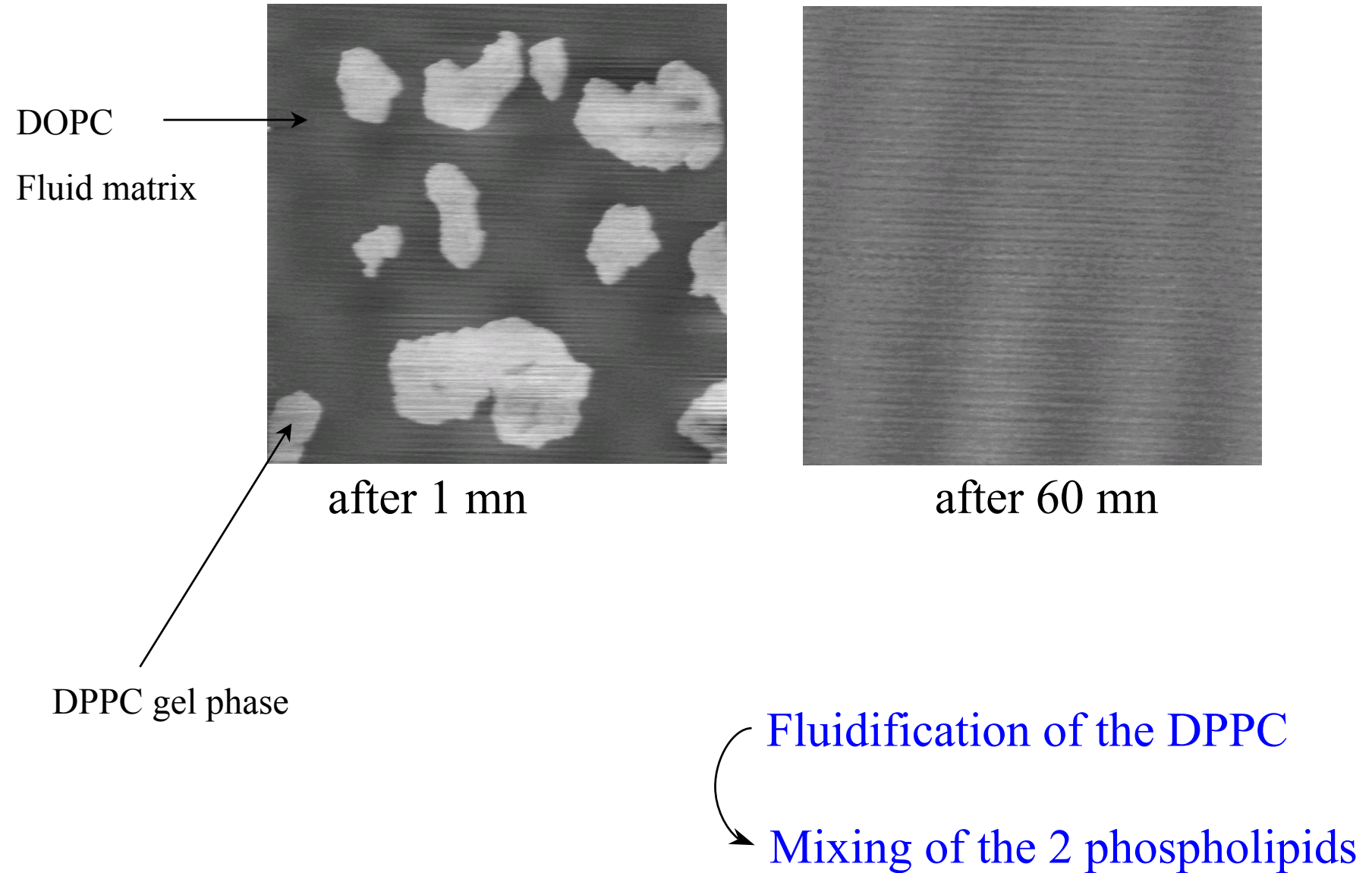
S. Ronkart (FSAGx)

A. Berquand (UCL)

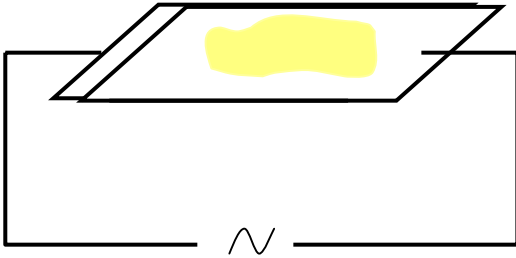
Nathalie FA

*Cellular and Molecular Pharmacology Lab.,
UCL 73.70 av E.Mounier 73, B-1200 Bruxelles (Belgique)*

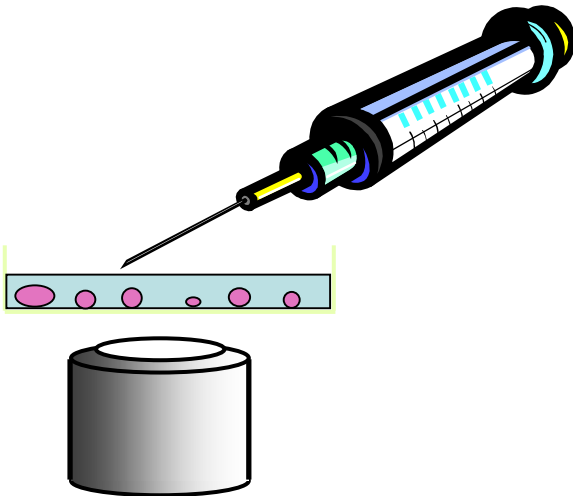
I AFM experiments on DOPC:DPPC 1:1 bilayers



II Experiences with DOPC GUV



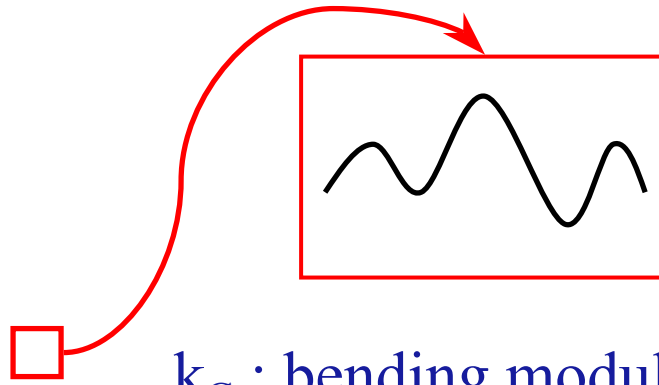
- lipidic film hydrated under an electric field
- GUV : diameter 10--> 80 microns
- unilamellar



- experiences at **high concentration in azithro.** :
(lipid/azi \approx 5/1)
-> High deformations or destruction
of the GUV
- experiences at **low concentration in azithro.** :
(lipid/azi $>$ 50/1)

At low concentration in azithromycin (DOPC:azi = 50:1) ...

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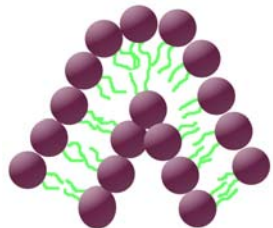


k_C : bending modulus ($k_B T$)

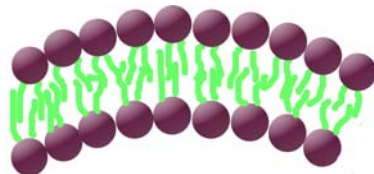
= energy necessary to bend the membrane

-> depends on the chemical nature of the bilayer

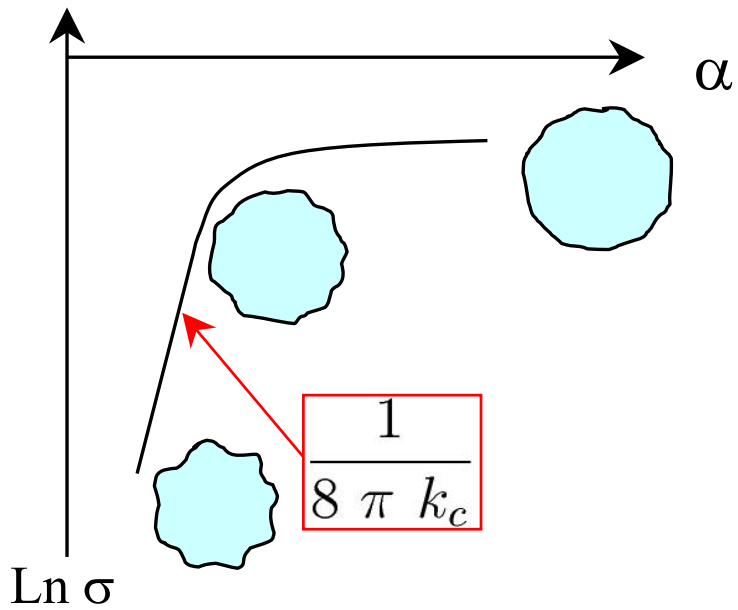
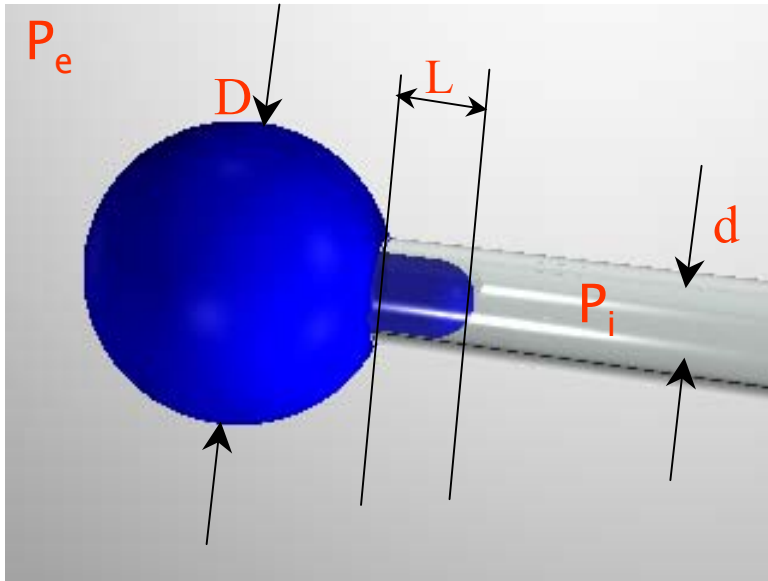
DLPC (C12:0)
 $k_C = 7 k_B T$

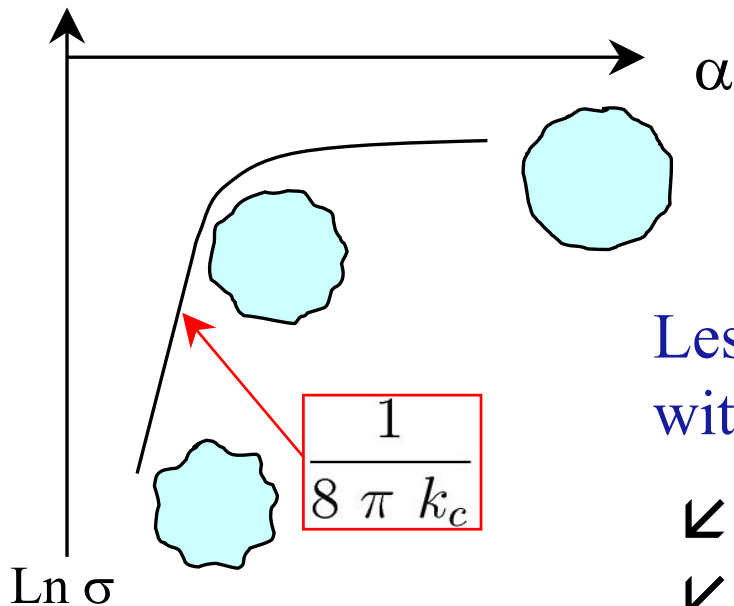
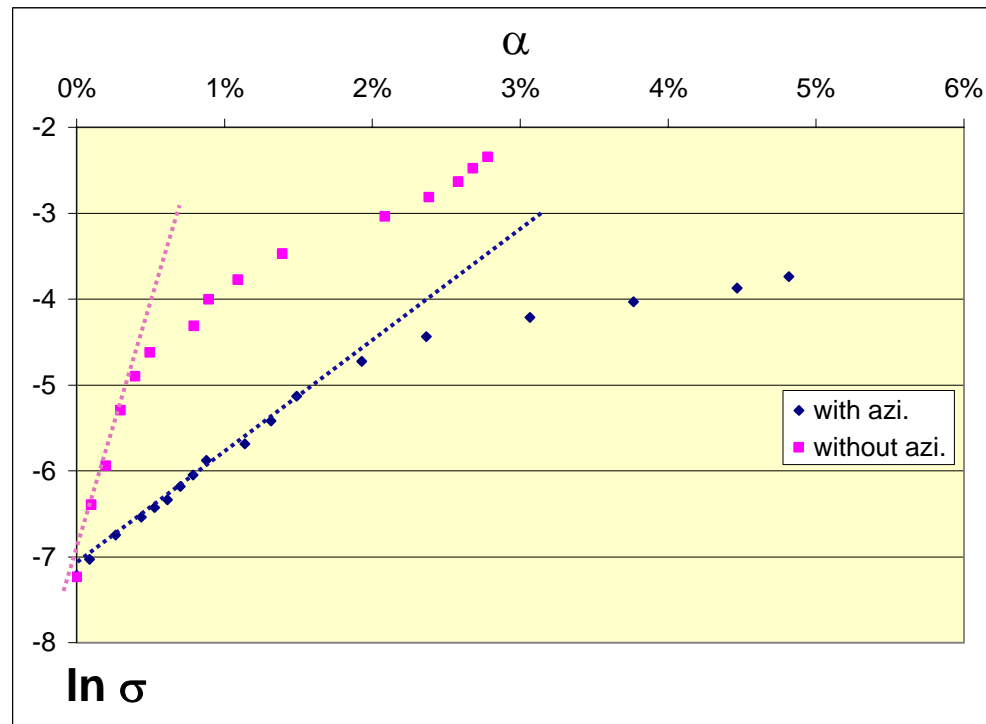
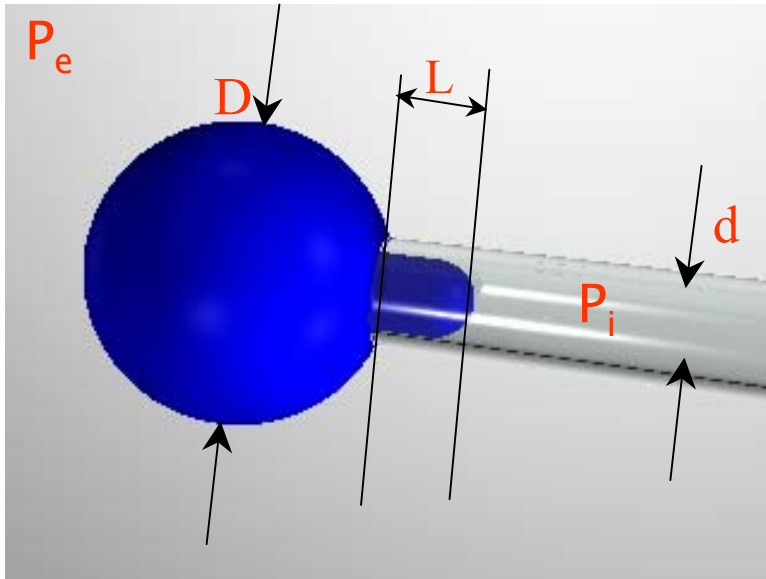


DOPC (C16:1)
 $k_C = 22 k_B T$



Measurement of the k_C by aspiration of the GUV in a micropipet





with azithromycin :
 $k_C = 9,6 \pm 1,5 \text{ kBT}$

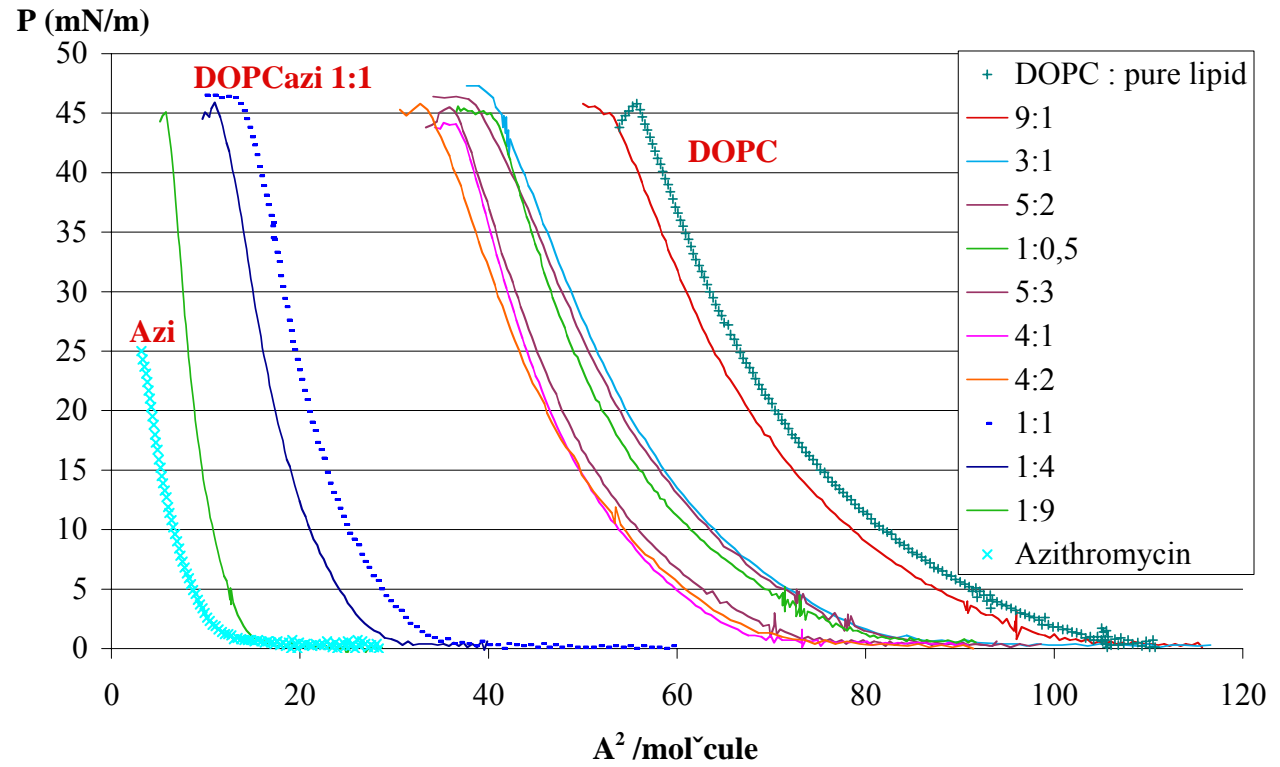
without azithromycin :
 $k_C = 22 \pm 2 \text{ k}_B\text{T}$

Less energy necessary to bend a membrane with azithromycin

- ↙ Insertion of azithromycin in the bilayer
- ↙ Higher fluidity of the lipids

III Langmuir isotherms on monolayers

DOPC + azithromycin

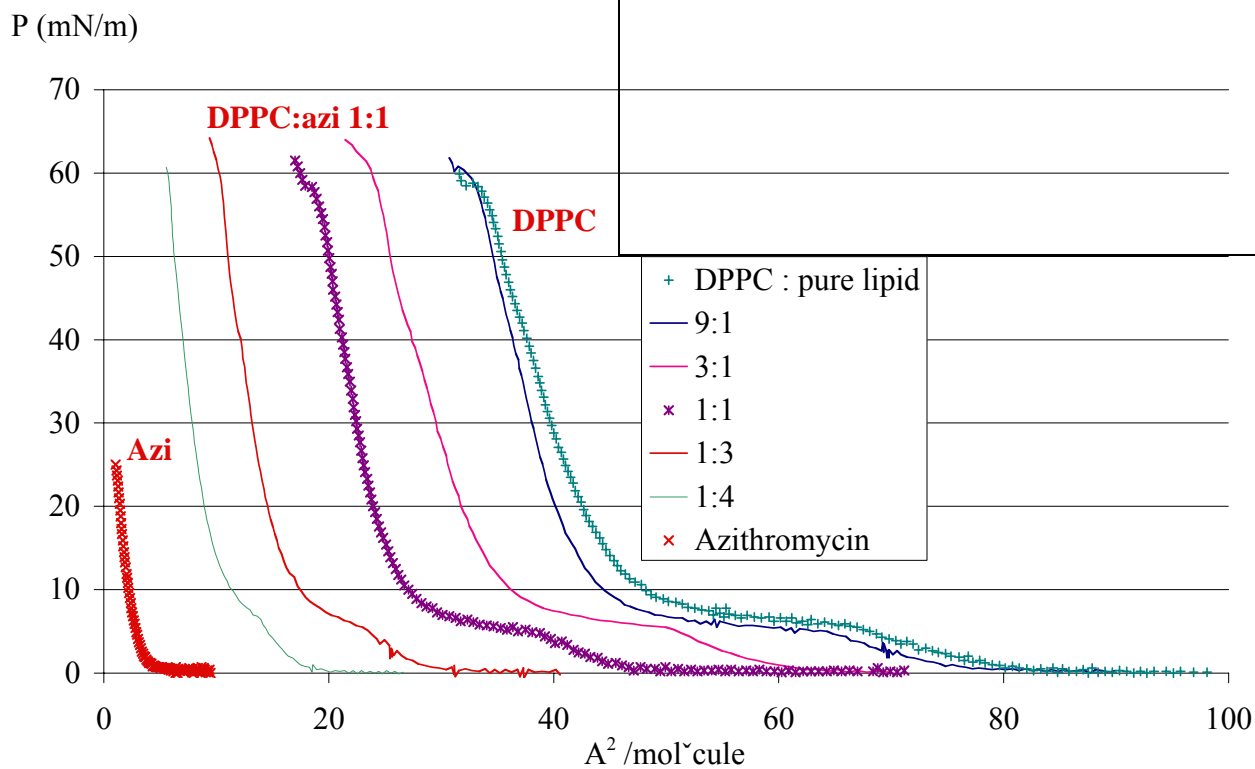


Ideal mixing of DOPC
and azithromycin

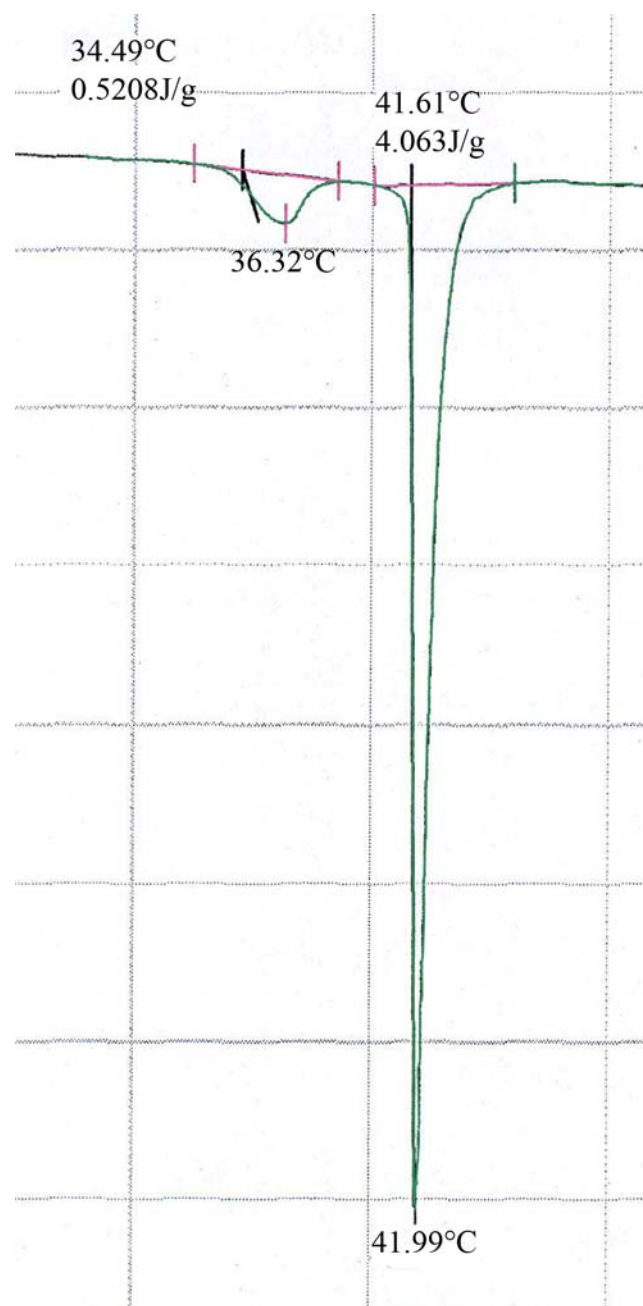
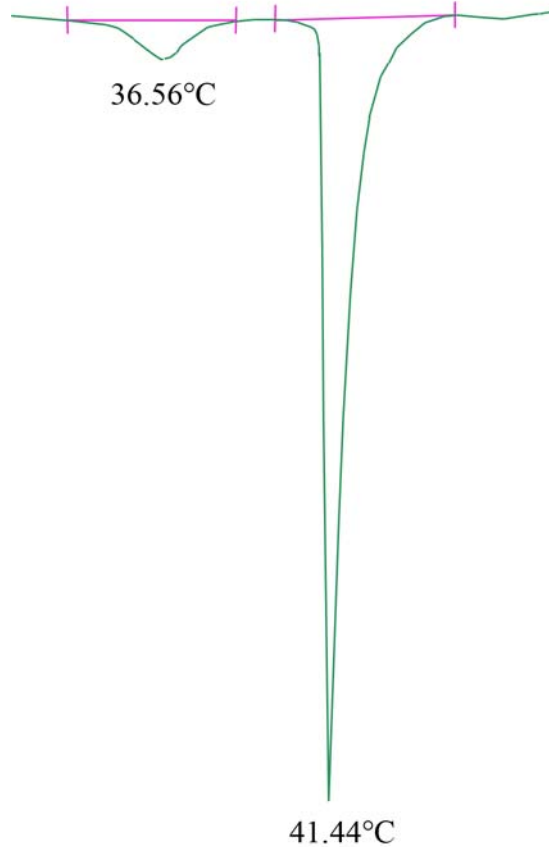
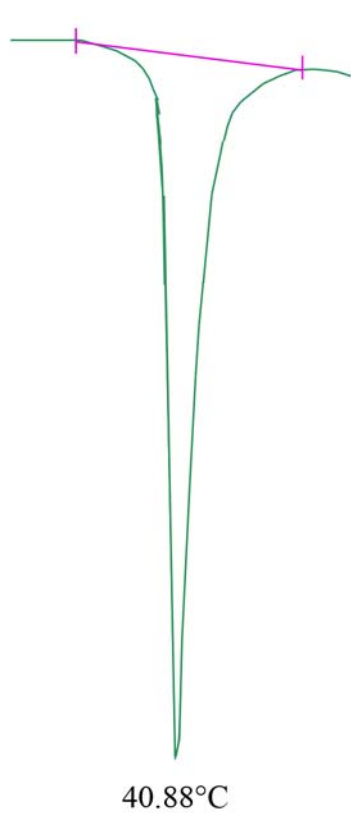
III Langmuir isotherms on monolayers

DPPC + azithromycin

Ideal mixing of DPPC and azithromycin



IV Experiments on MLV : DSC



DPPC:azi = 6:1

DPPC:azi = 26:1

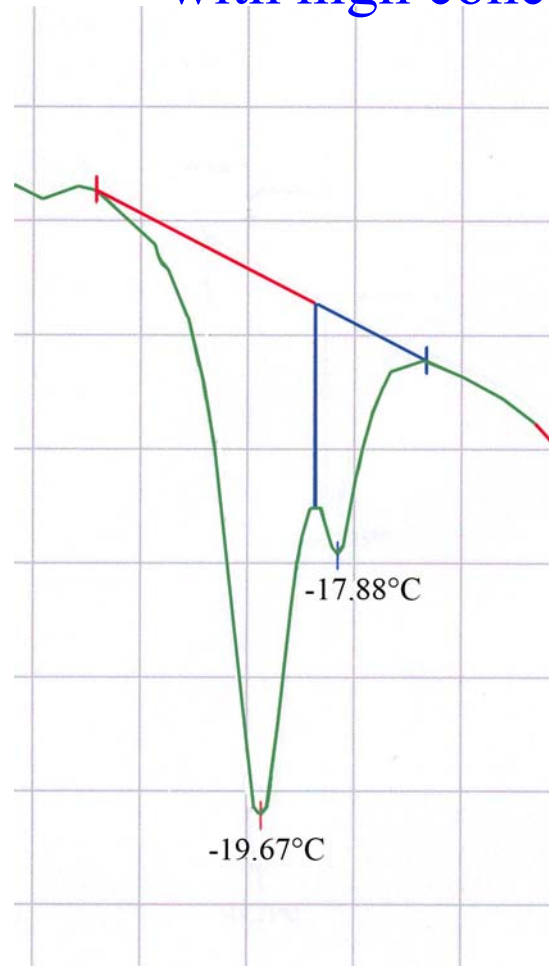
DPPC

pretransition of DPPC disappears
with high concentration of azi.

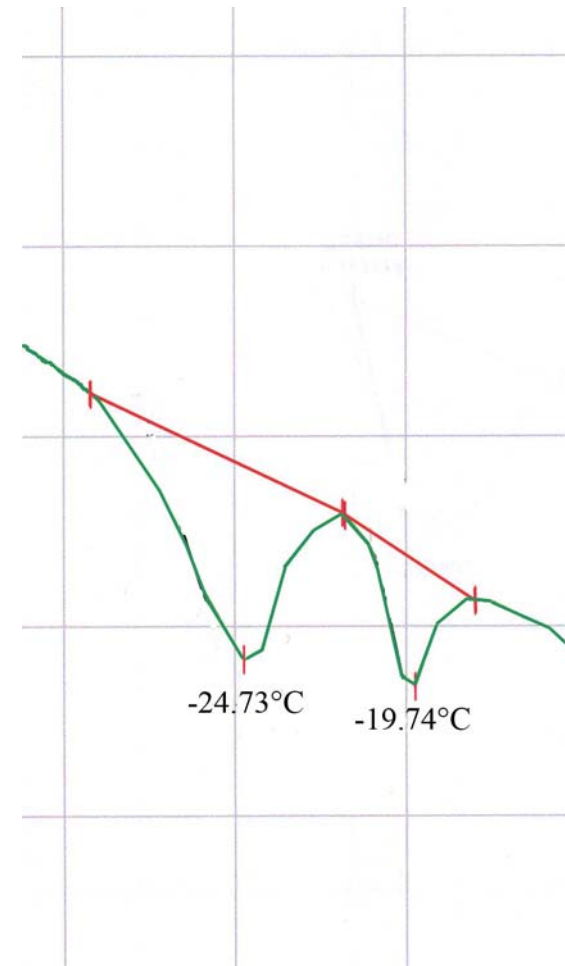
A pretransition of DOPC appears with high concentration of azi.



DOPC:azi = 63:1

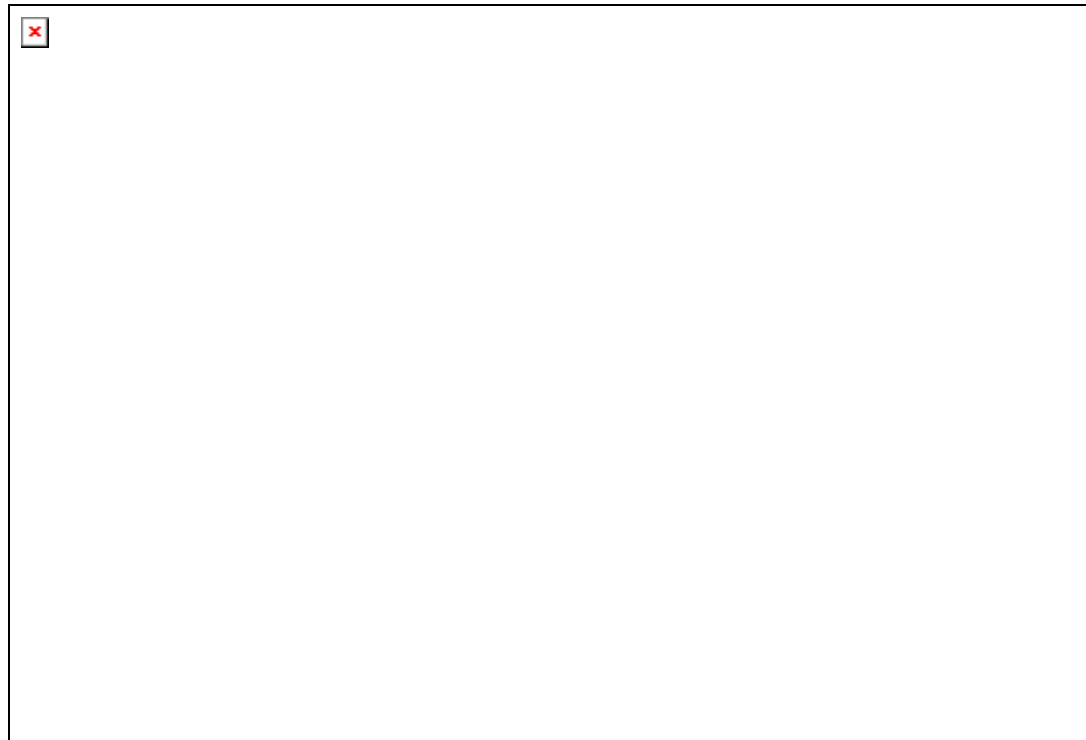
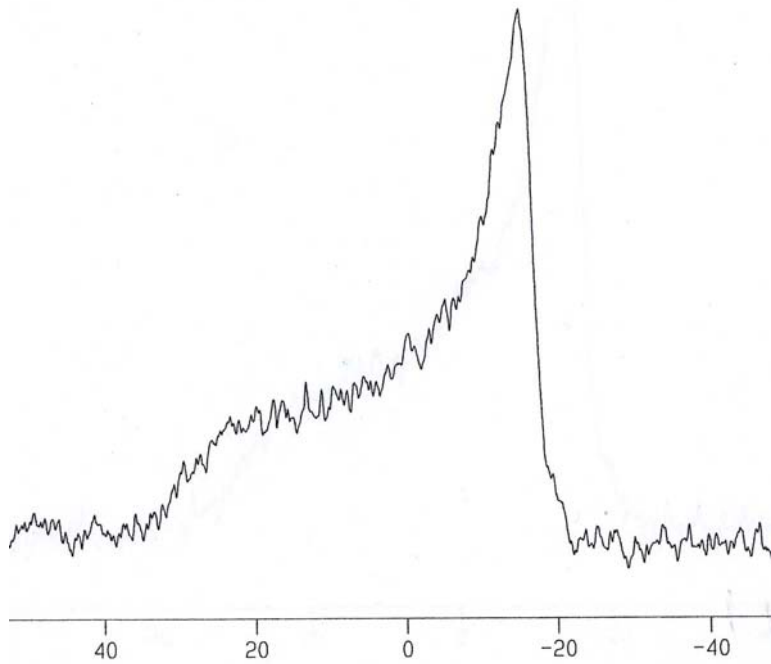


DOPC:azi = 16:1



DOPC:azi = 2:1

IV Experiments on MLV : ^{31}P NMR



Conclusions

- easy insertion of azithromycin in DOPC bilayer :
modification of the bending modulus
- ideal mixing of azithromycin with DOPC and DPPC monolayers
- disappearance of the pretransition of DPPC AND
diminution of the transition temperature
- increase of the fluidity of DOPC and DPPC

Thanks to...

M.-P. Mingeot-Leclercq (UCL)

A. Schanck (UCL)

S. Ronkart (FSAGx)

A. Berquand (UCL)

Carlos Marques, André Schroder (LDFC, Strasbourg, France)