

# **Drug Delivery Systems examined by NMR**

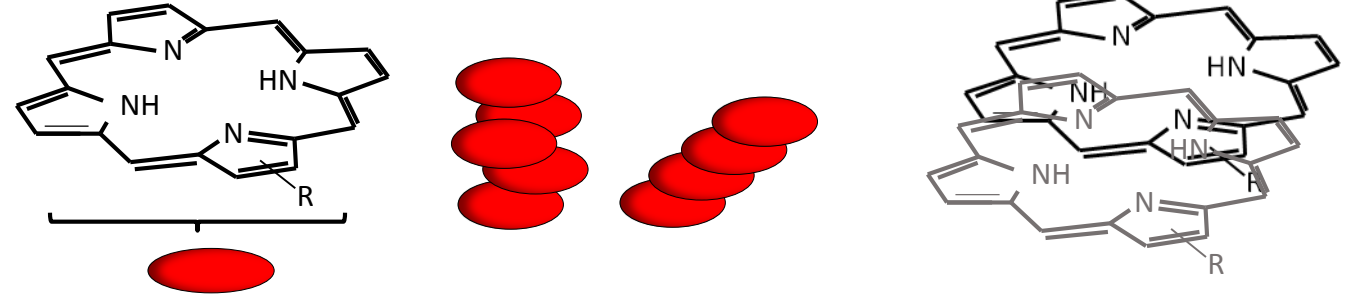
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Luca Sauser, Julien Furrer

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# Drug delivery systems

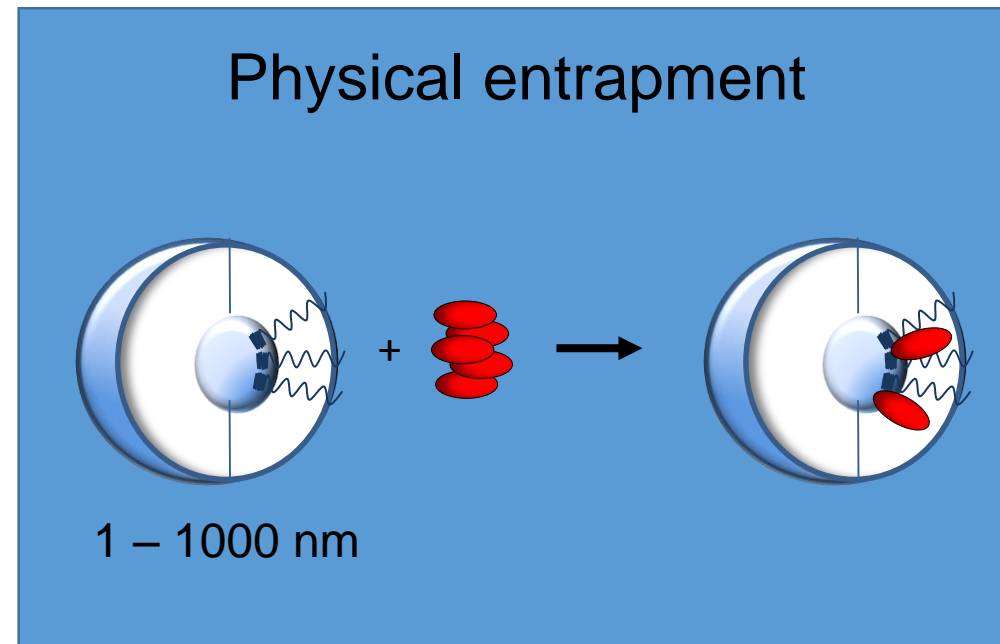
## Porphyritic Photosensitizers

- ❖ Exhibit stacking in water
- ❖ Aggregation reduces PDT efficiency

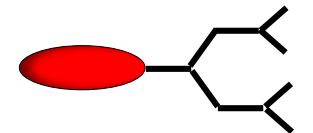


## Polymeric Delivery Systems

- ❖ Monomerize porphyrin aggregates
- ❖ Enhance solubility in water
- ❖ Prolonged stability
- ❖ Nanoparticles  $\Rightarrow$  EPR effect
- ❖ Improved photophysical properties



Chemical bonding

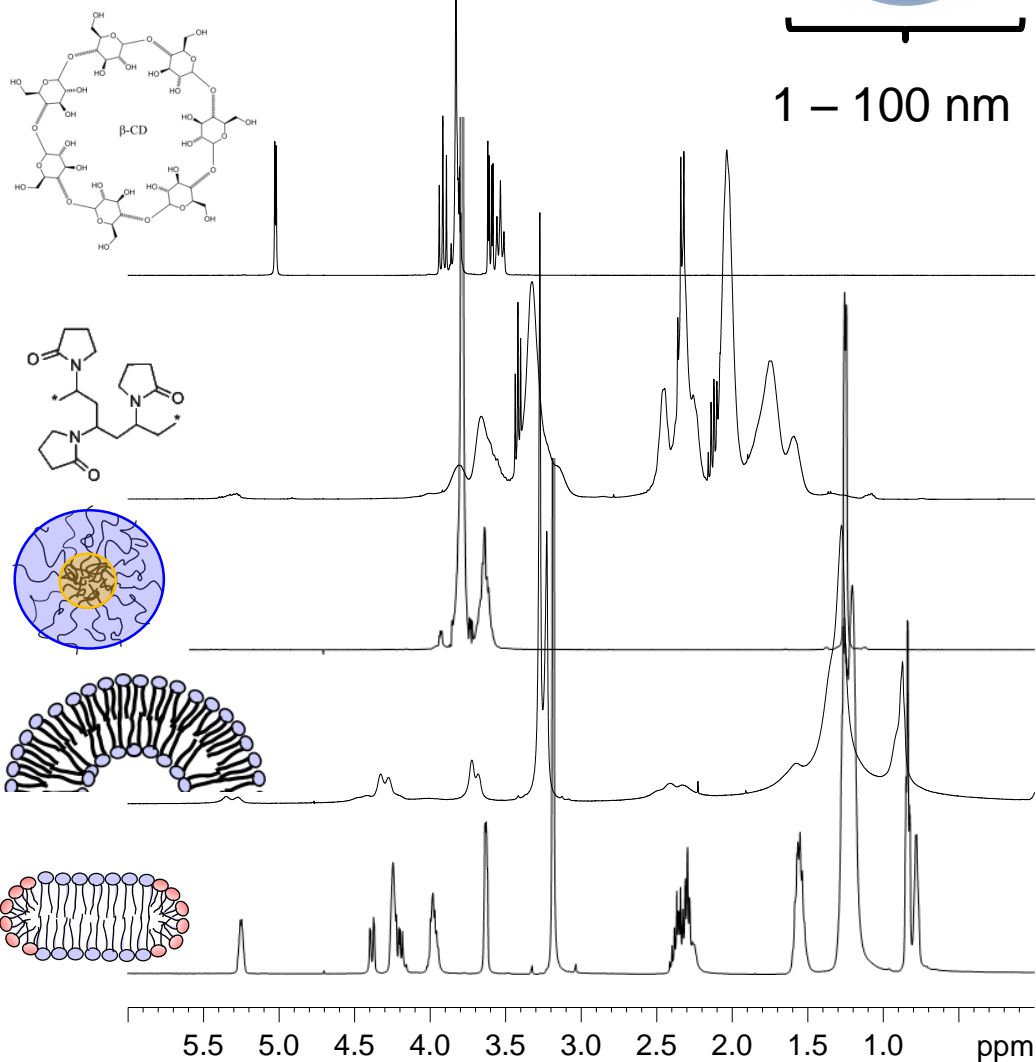




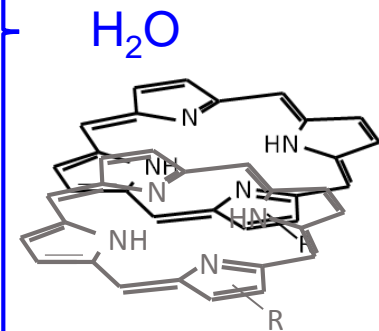
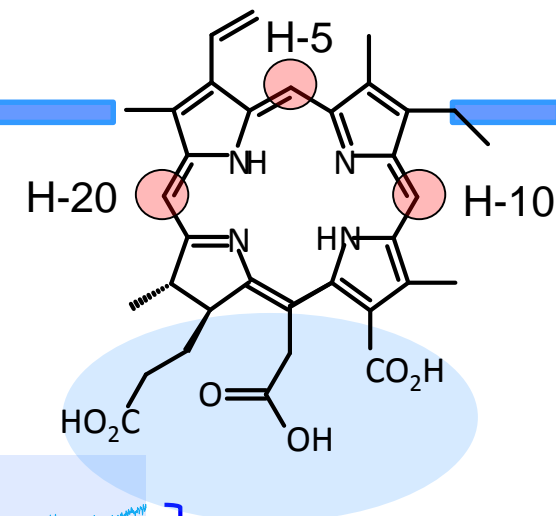
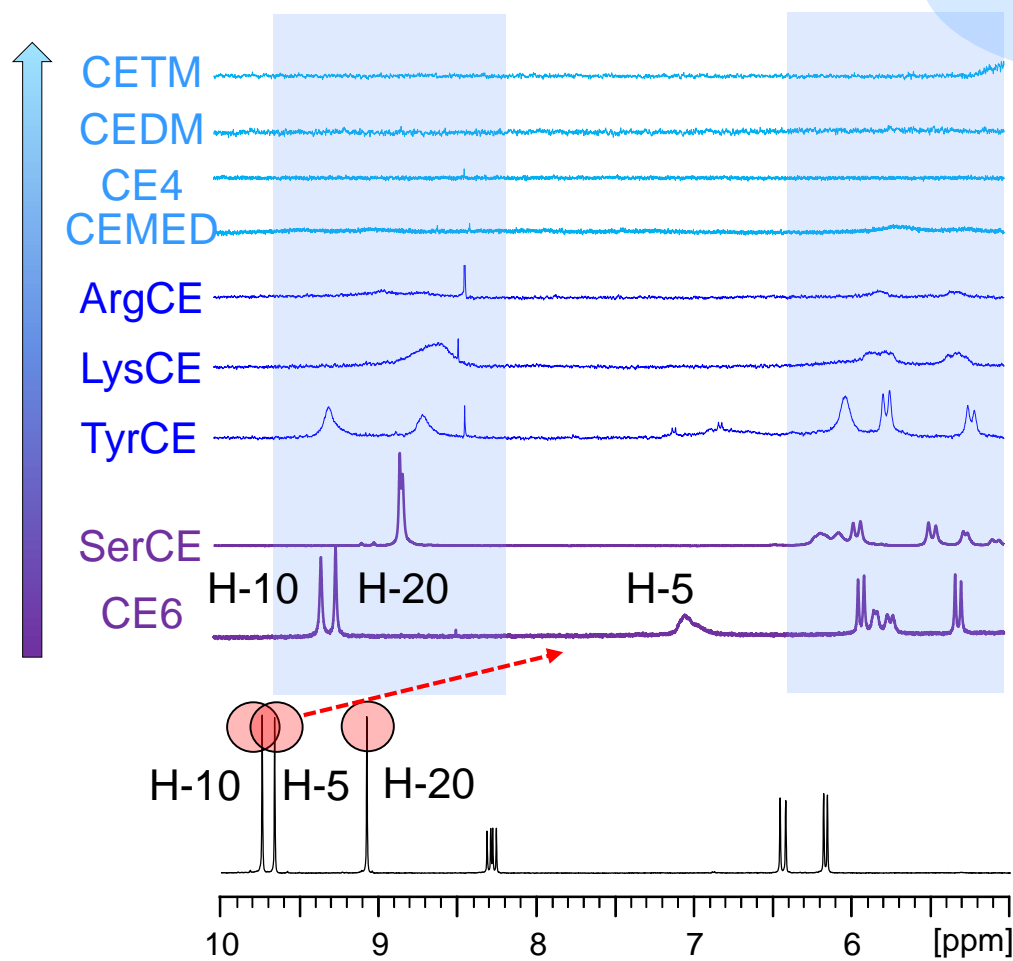
# $^1\text{H}$ NMR spectra

Nanoparticles

Colloidal dispersions



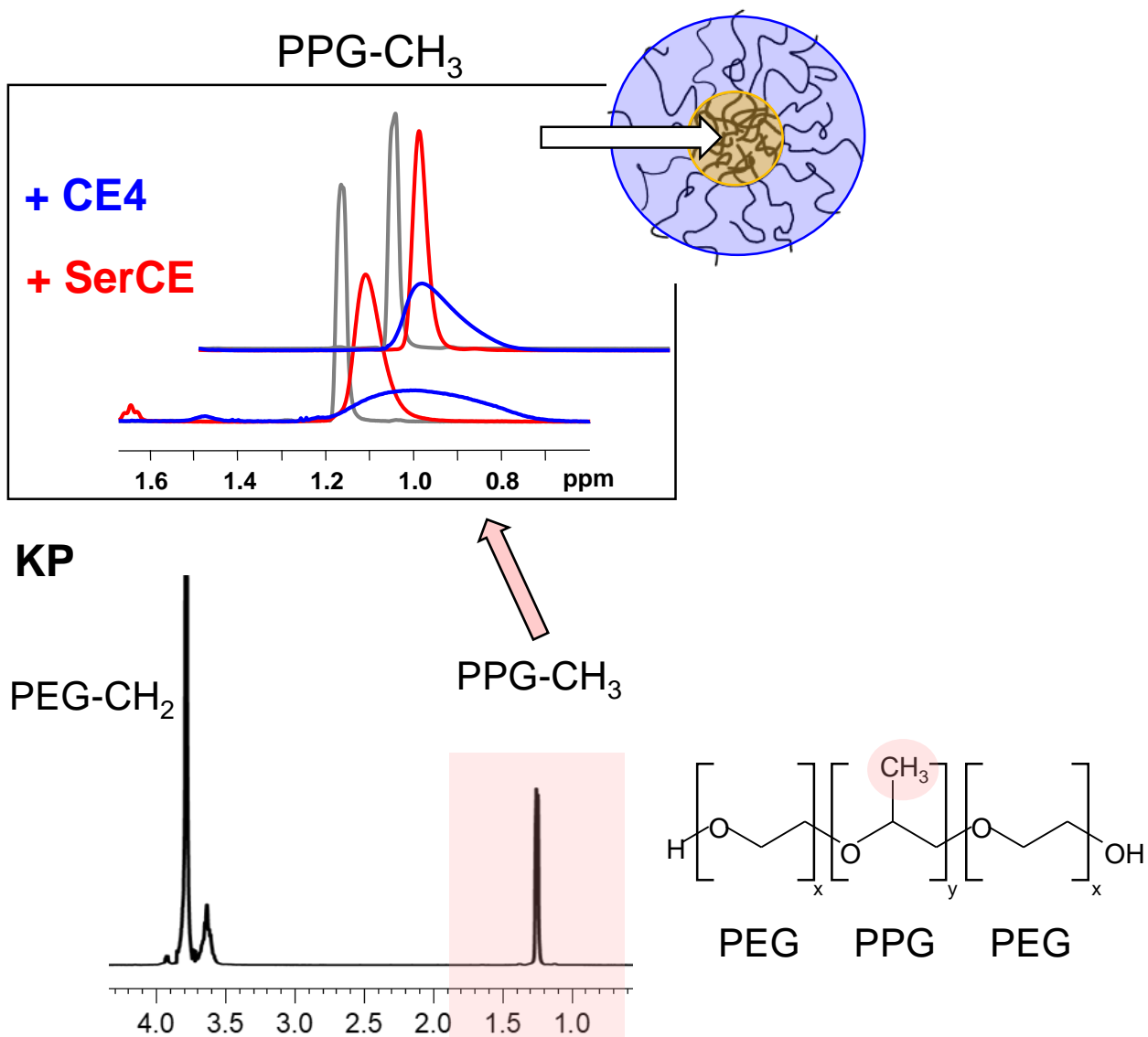
Chlorin e6 derivatives  
Aggregation



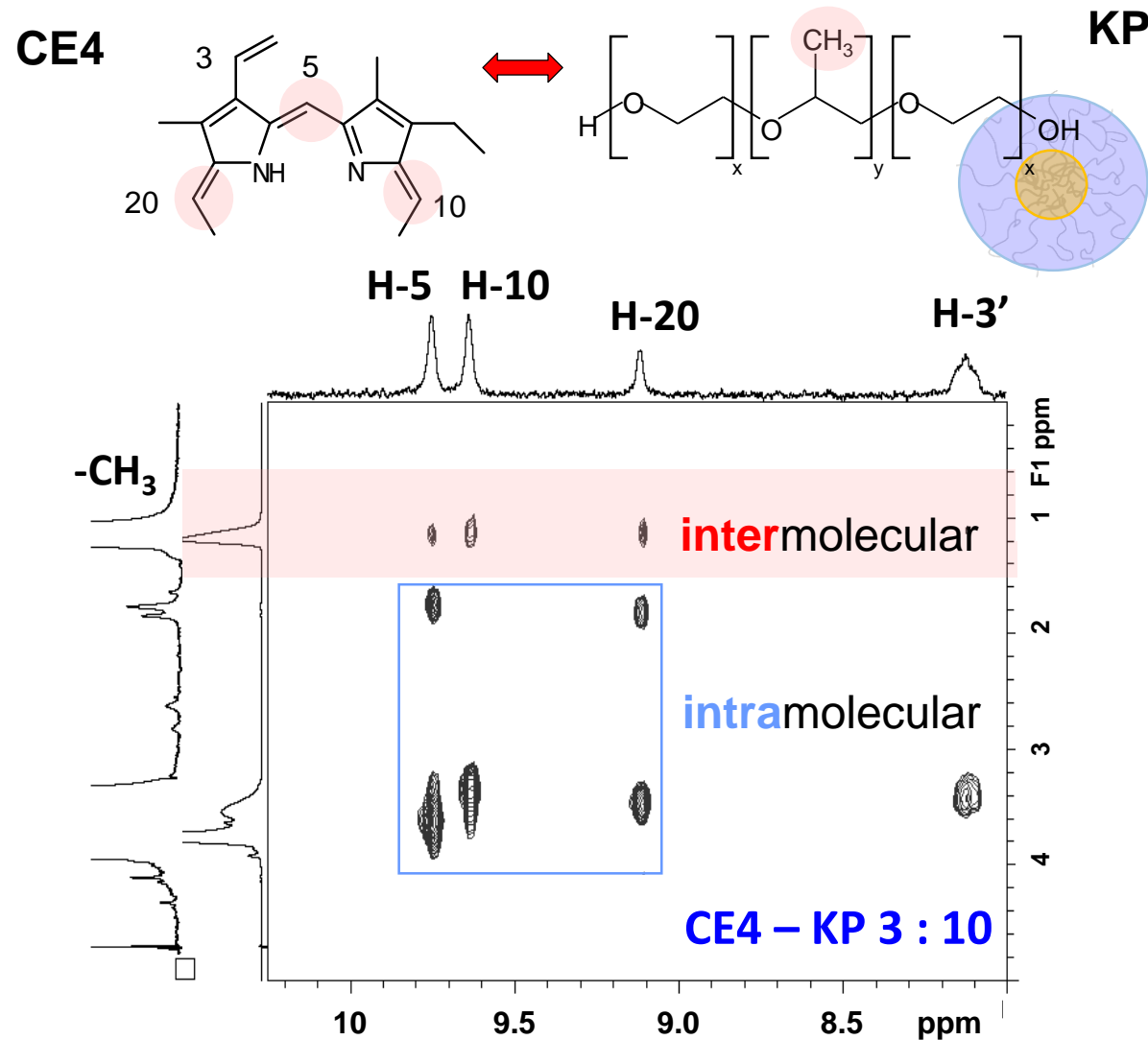
DMSO



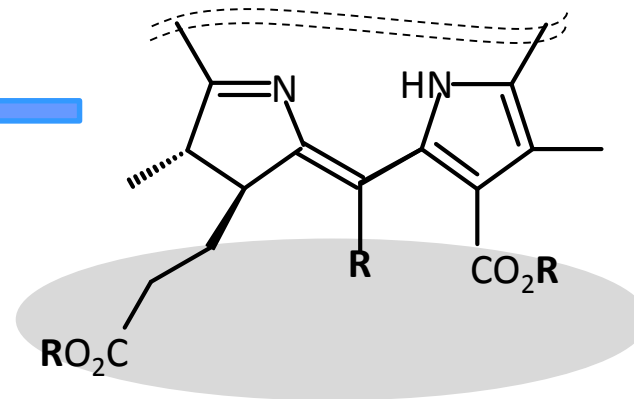
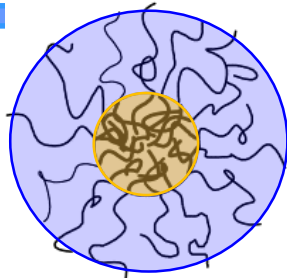
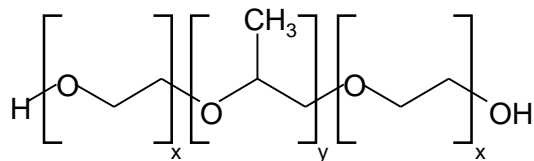
# Monitoring drug encapsulation



## <sup>1</sup>H <sup>1</sup>H NOESY



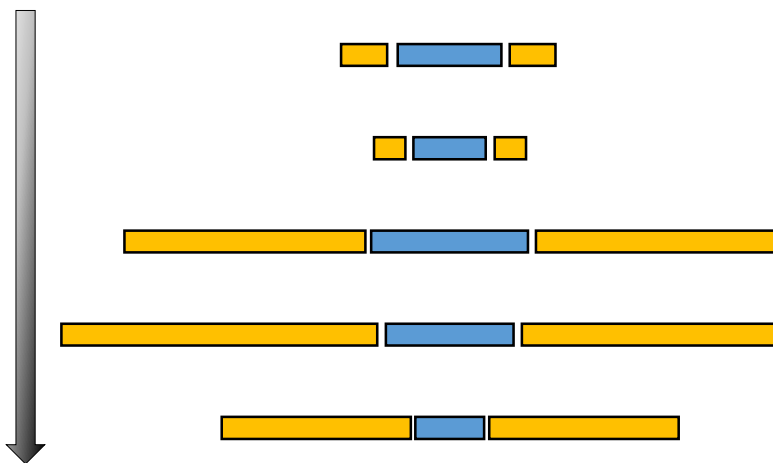
# Monitoring drug encapsulation



## Tuning the micelle properties

HLB

PEG PPG PEG



- HLB
- MW
- PPG units

P84  
L64  
F127  
F108  
KP188  
PBS

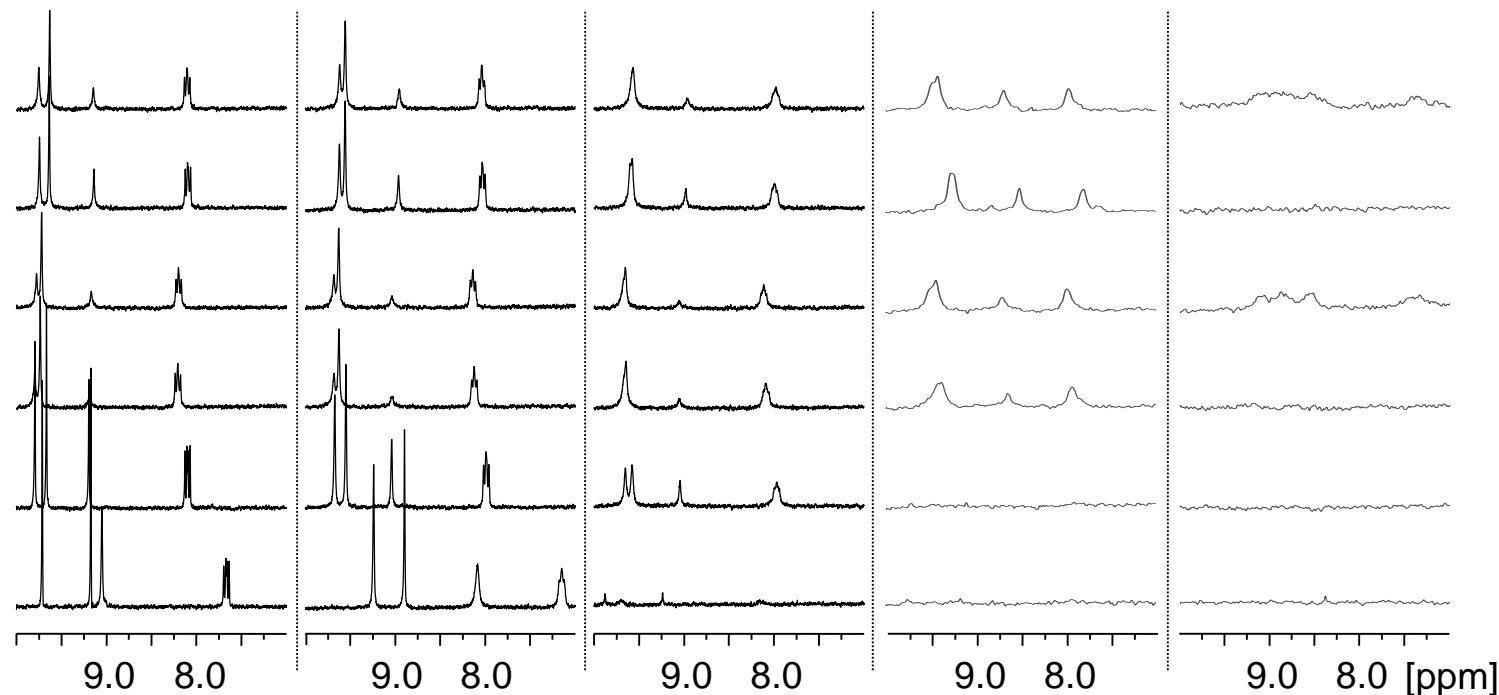
SerCE

CE4

CEMED

CEDM

CETM



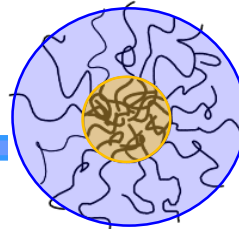
logP

9.0 8.0 [ppm]

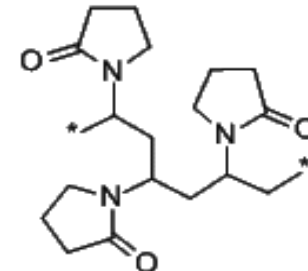




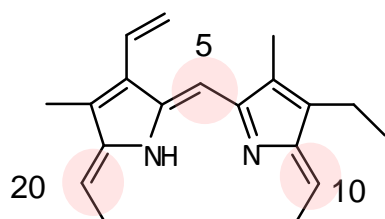
# Comparing micelles and PVP



PVP

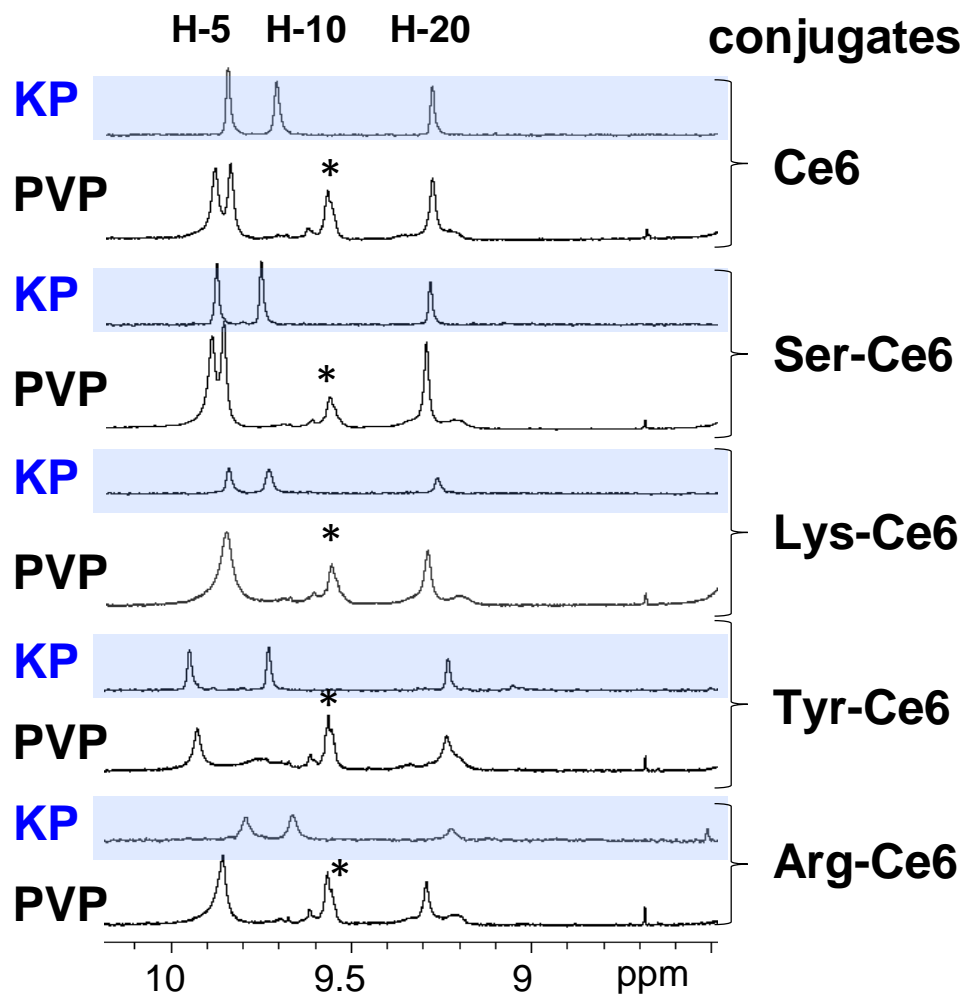


Ce6

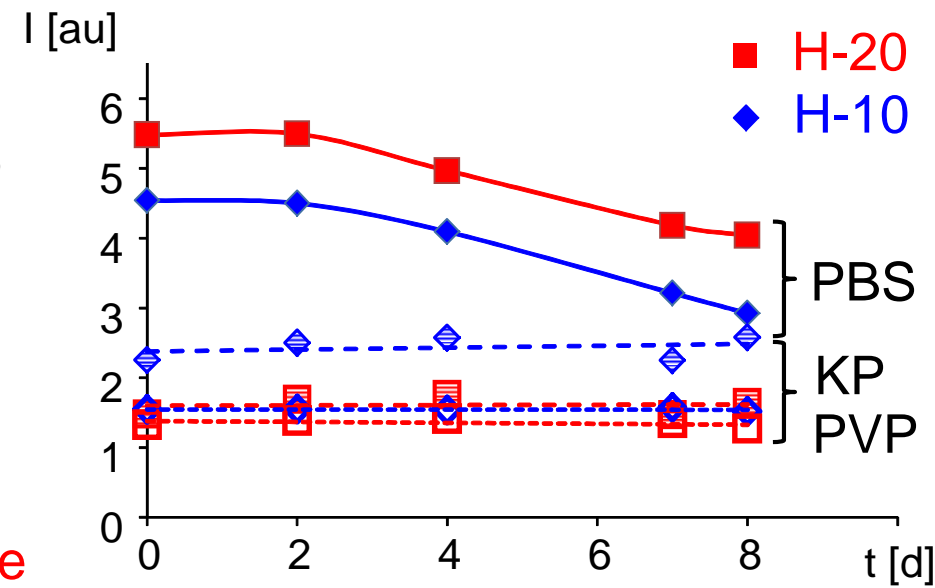
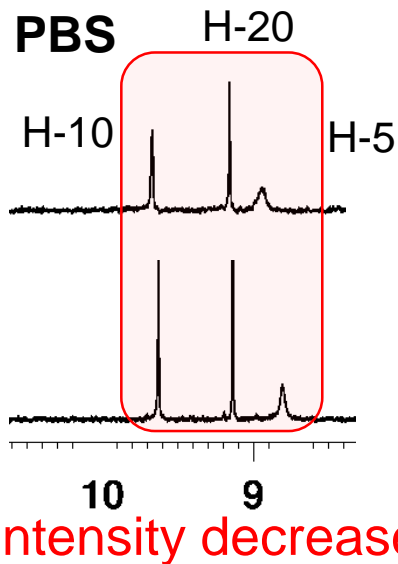


Micelles (KP)

Ce6-Aminoacid  
conjugates



t  
8d  
0d

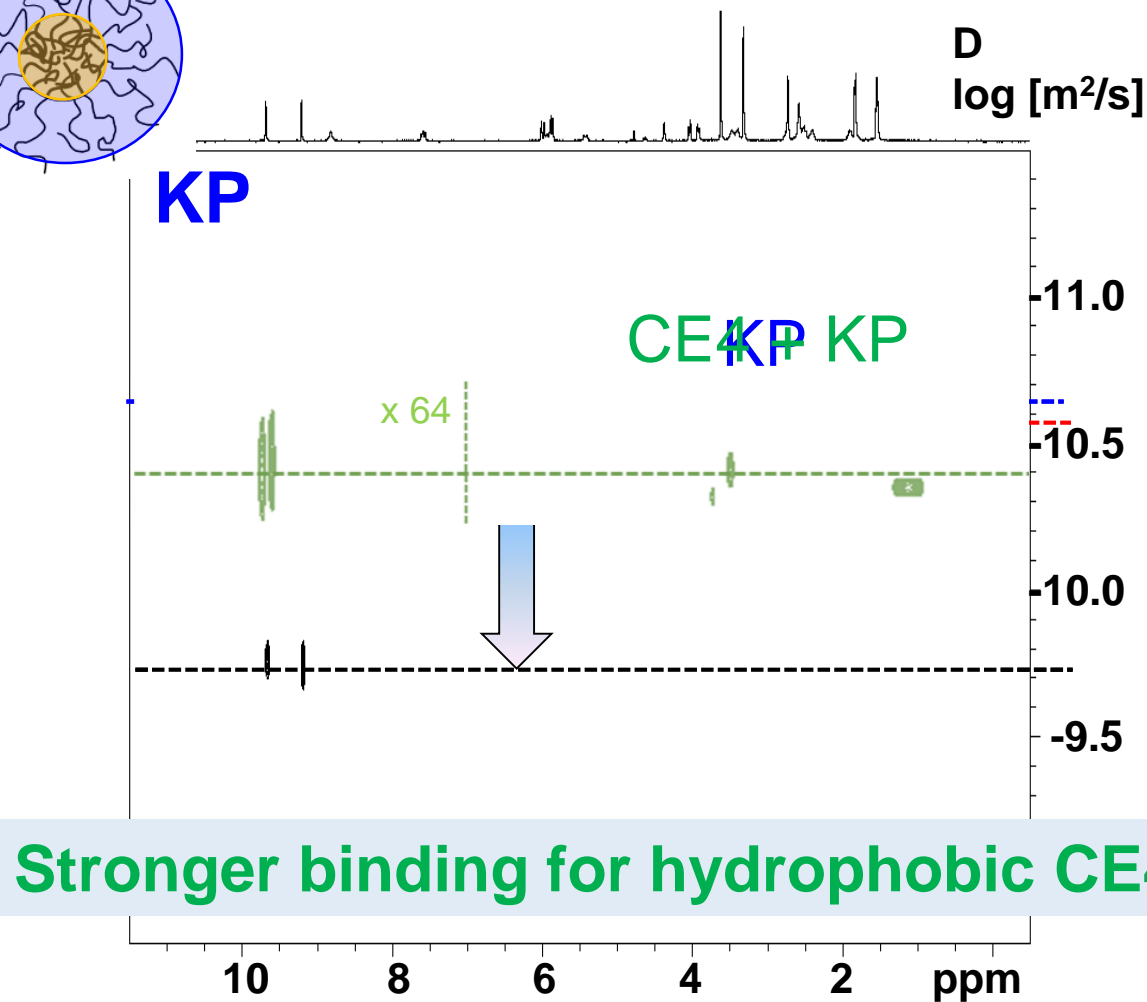
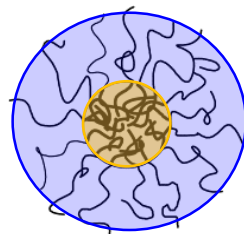
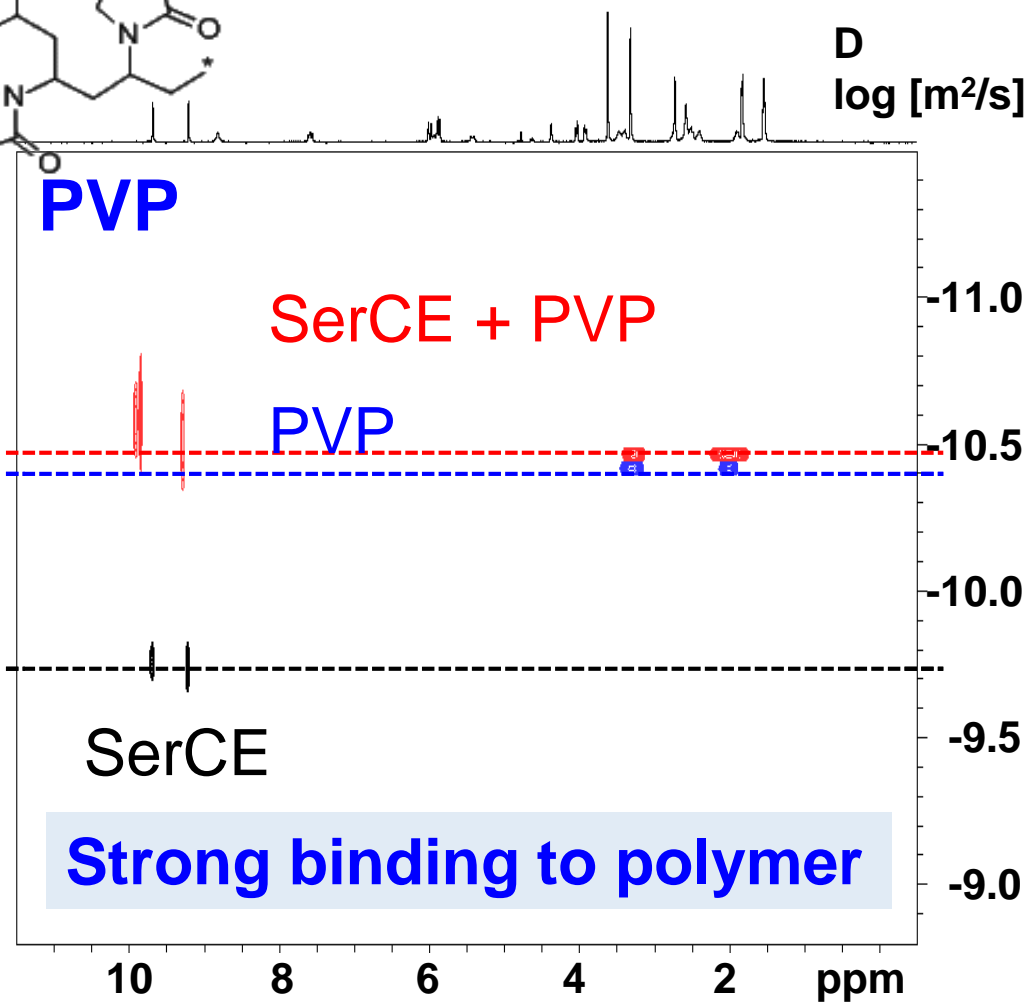
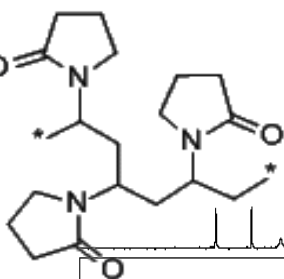


**Micelles and PVP:**

⇒ **Good encapsulation for Ce6-AAs**

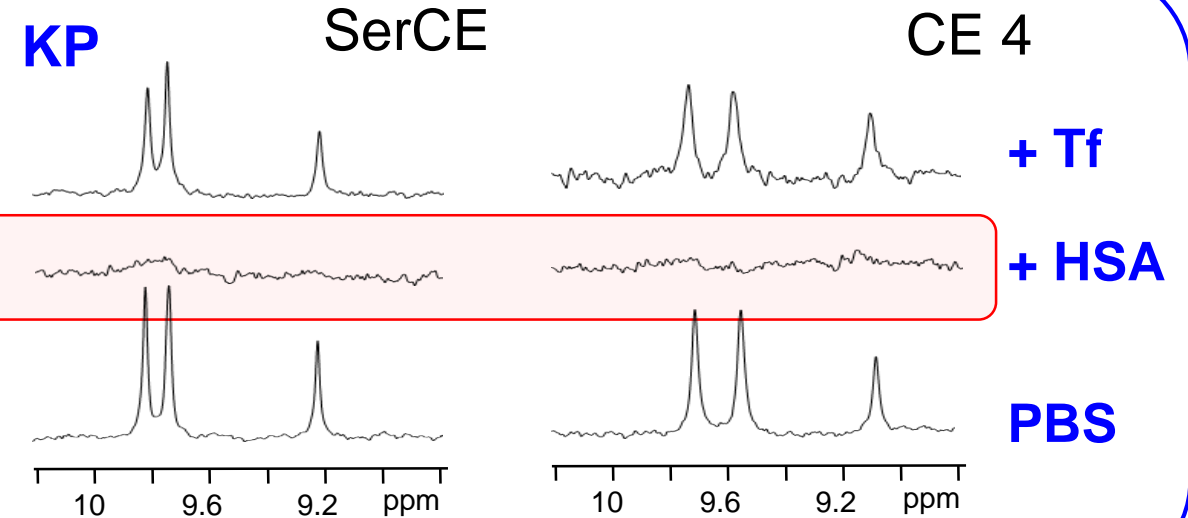
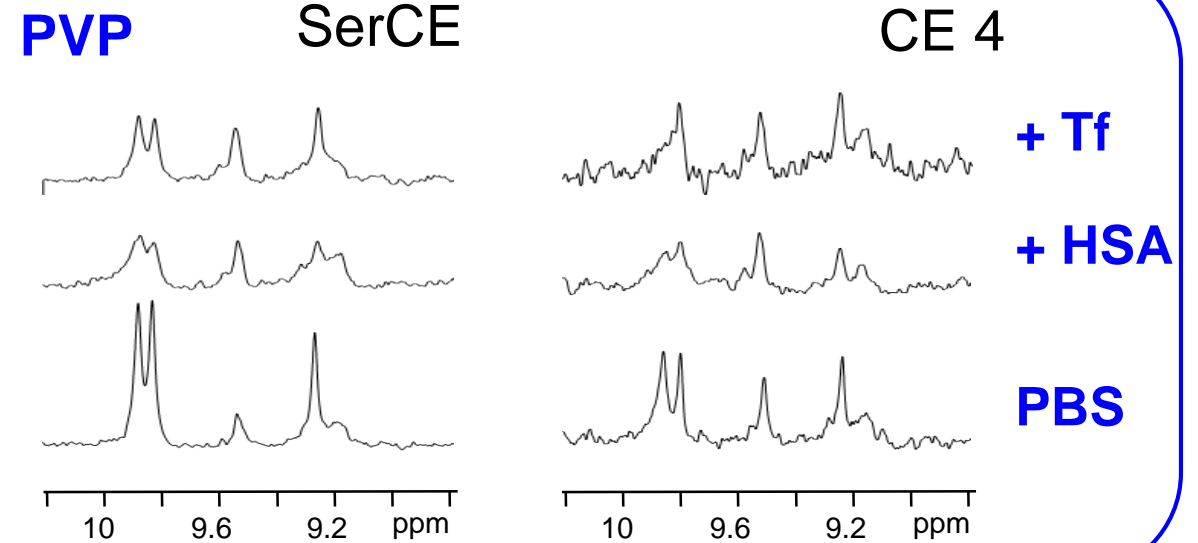
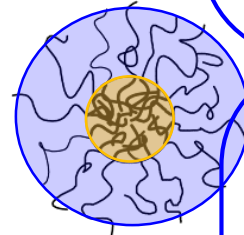
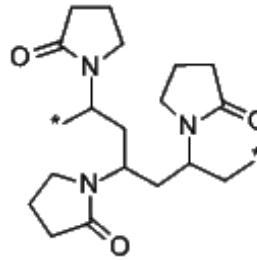
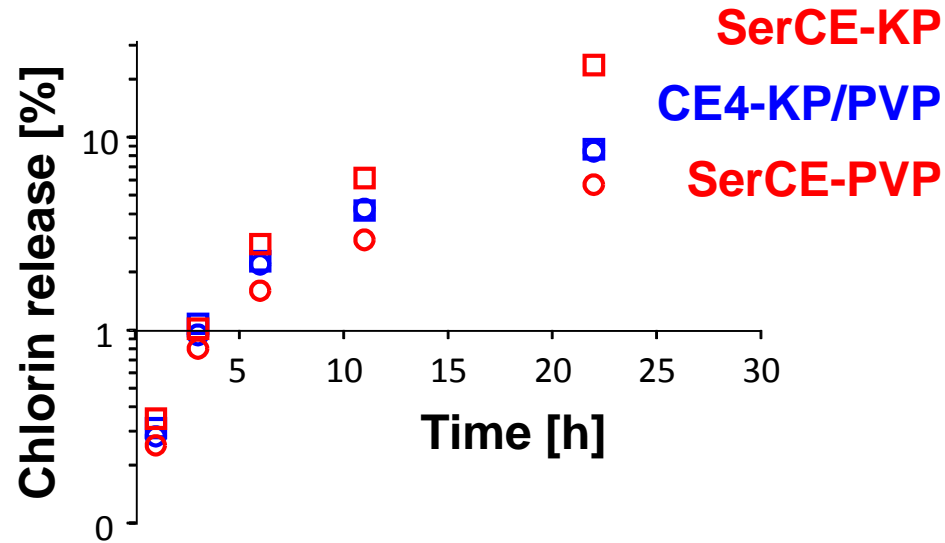
⇒ **Prevention of aggregate growth over time**

# Comparing micelles and PVP: Dynamics



# Comparing micelles and PVP: Release

Release profiles (PBS, 37°C)

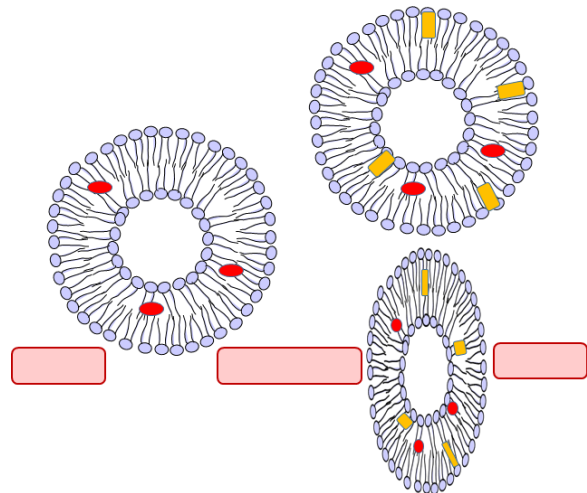
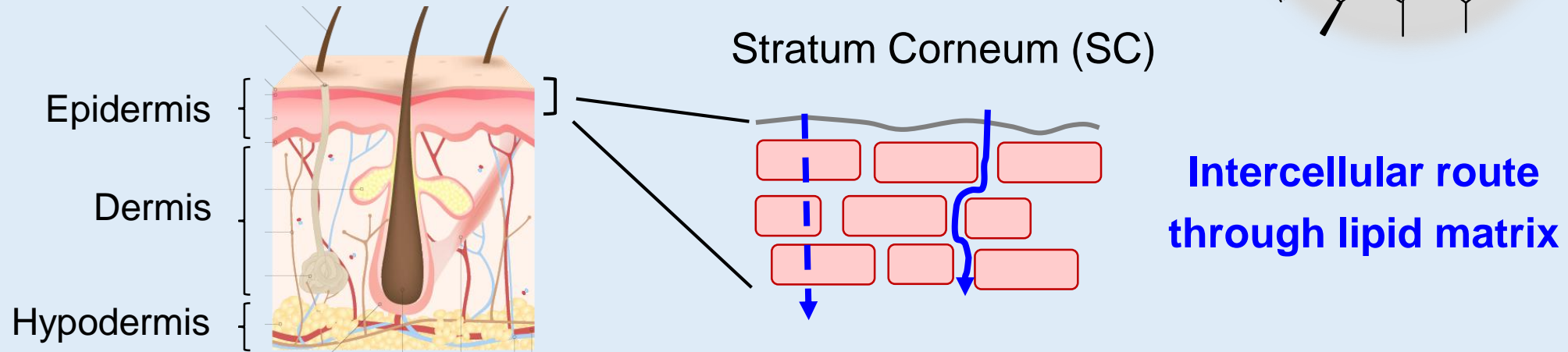
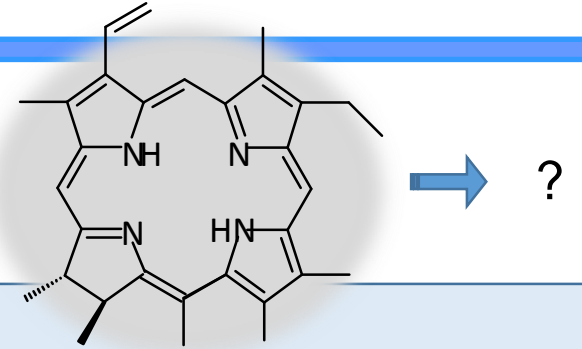
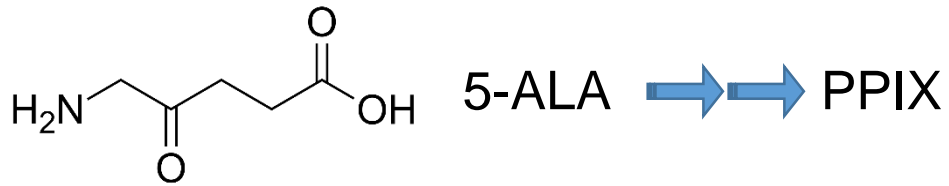


➤ **PVP:**  
Reduced reactivity towards proteins

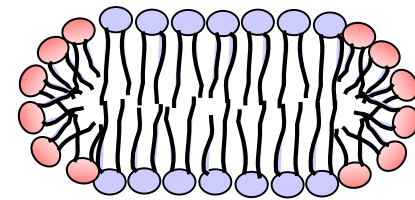
➤ **Micelles (KP):**  
Release in favor of HSA binding

# Bicelles for topical drug delivery

## Topical PDT



Flexible liposomes

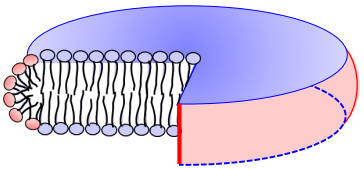


Bicelles

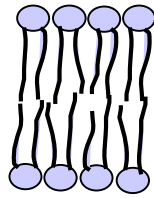
# Bicelles for topical drug delivery

- Small size
- Disc-shaped
- Biocompatible

## Bicelles



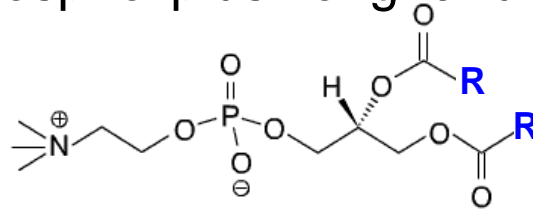
**Bilayer**



**Micelles**

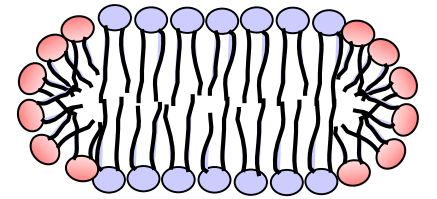


Phospholipids: long- and short-chain



DMPC (C-14) R =  $-(\text{CH}_2)_{12}\text{CH}_3$   
Bilayer-forming

DHPC (C-6) R =  $-(\text{CH}_2)_4\text{CH}_3$   
Edge-forming



DHPC-DMPC  
50 mM, q = 0.5

DHPC

DMPC

5.0

4.5

4.0

3.5

3.0

2.5

2.0

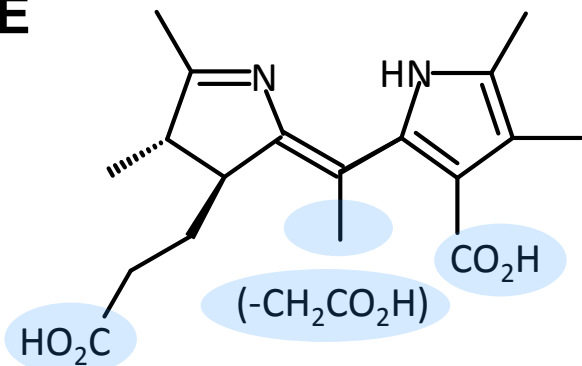
1.5

1.0

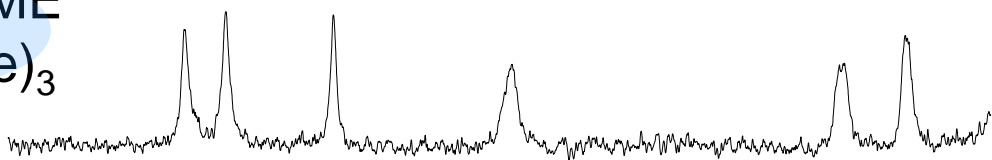
ppm

# Bicelles for topical drug delivery

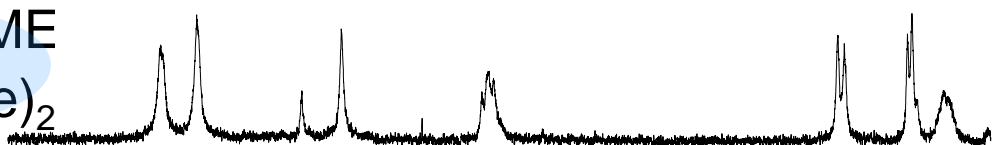
Bicelles 150 mM DHPC/DMPC  $q = 0.5$   
with 5 mM xCE



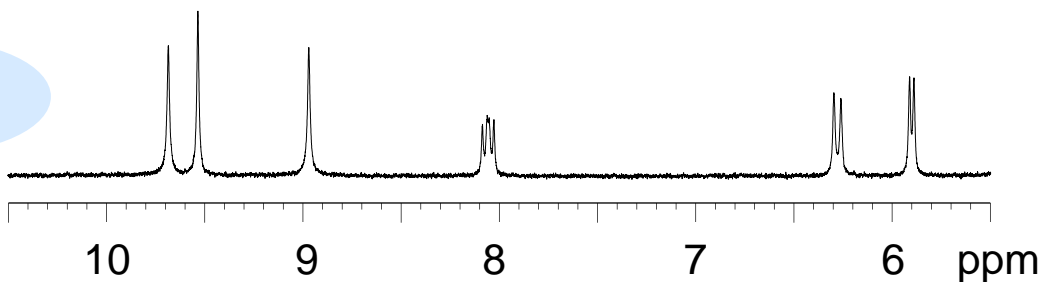
Ce6 TME  
 $-(\text{COMe})_3$



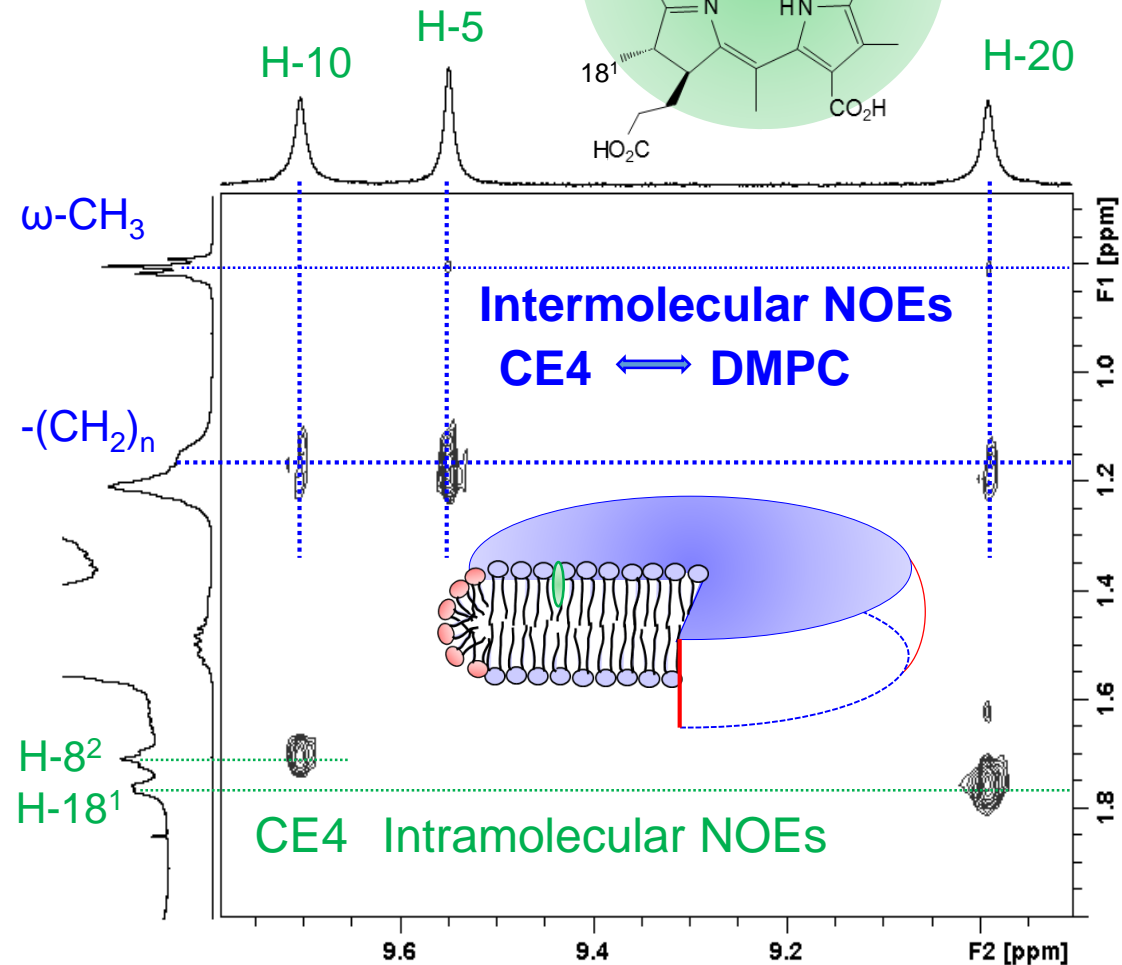
Ce6 DME  
 $-(\text{COMe})_2$



CE4



$^1\text{H}^1\text{H}$  NOESY:  
CE4 – DMPC/DHPC

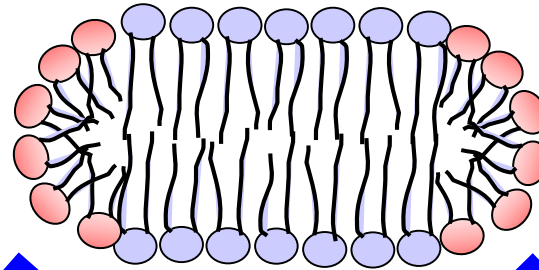


# Bicelles for topical drug delivery: Outlook

## Modifications:

Long chain phospholipids

PEG-ylated PLs  
Charged PLs  
PL- transition temperature  
Additives



Short chain phospholipids

Low water solubility  
Low cmc

q-value

- Prevent fusion
- Keep bicelle morphology
- Enhance stability
- Enhance encapsulation

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Swiss National  
Science Foundation  
SNF



THANK YOU  
FOR  
YOUR ATTENTION

