Nano-assemblies on materials :

Mechanically responding functionalized polyelectrolyte multilayer films

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Technologies pour la santé Inserm

Biomaterials & Polyelectrolyte multilayers

One of the main objective :

Modify biomaterial surfaces to provide them

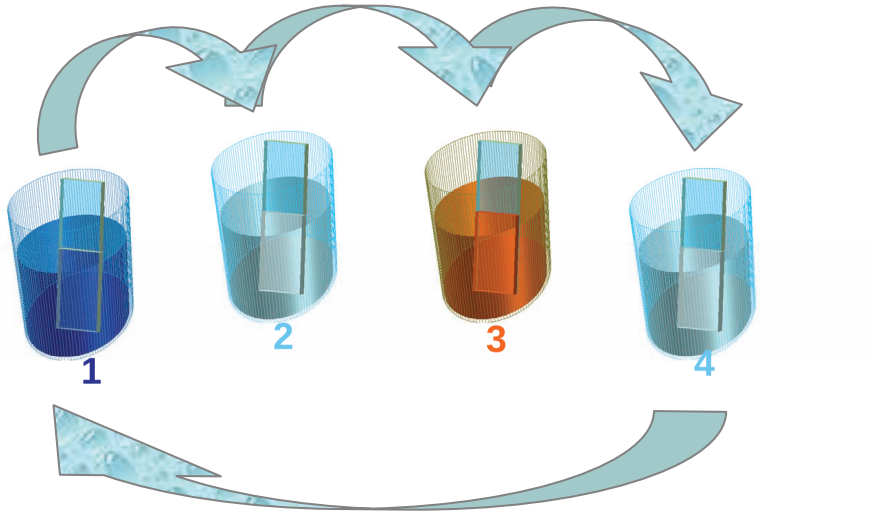
- Biomimetic properties
- Multifunctional properties
- Sequential release of drugs
- Cover all materials

+ *Simple method*

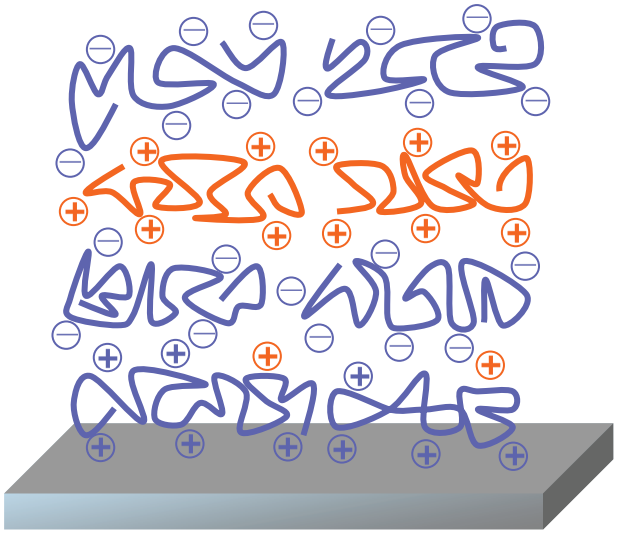
+ *Structures well defined*

Approach = ***polyelectrolyte multilayer film coatings***
Layer-by-Layer method (LbL)

Polyelectrolyte multilayer films as nanoassemblies



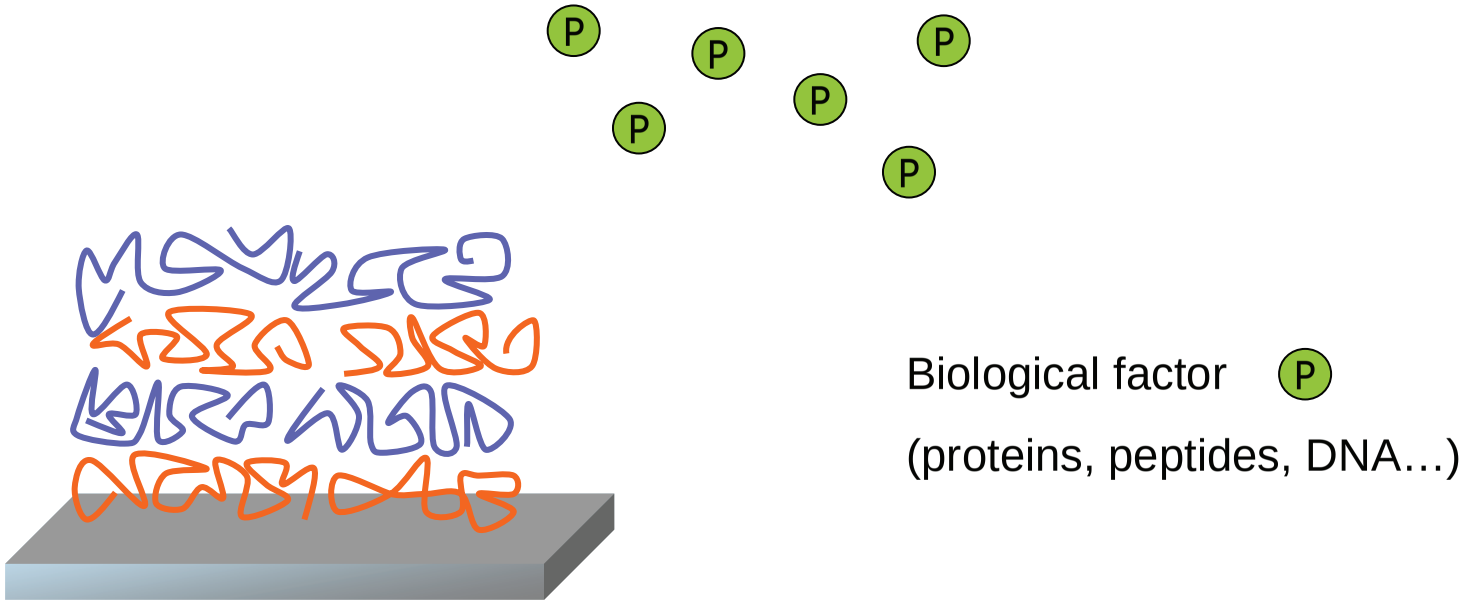
1. Polycation solution
2. Buffer
3. Polyanion solution
4. Buffer



Decher, *Science* 277:1232-1237 (1997)

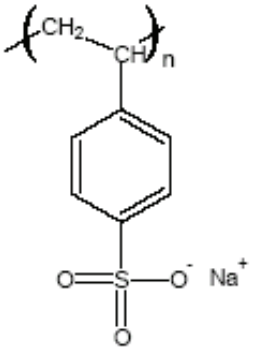
Biological interest

- Films made of biopolymers : polysaccharides, polypeptides
- Confer a biological activity by embedding biological factors

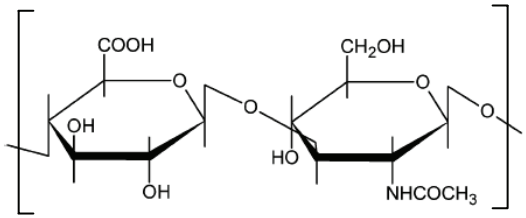


Build up of the Polyelectrolyte multilayers

Polyanions

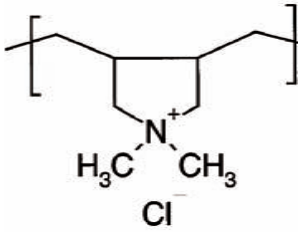


Poly(styrene sulfonate)
PSS

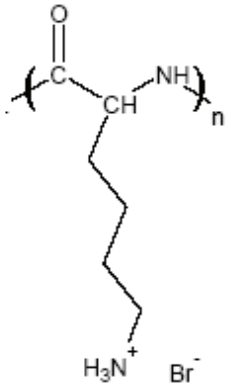


Hyaluronic acid
HA

Polycations

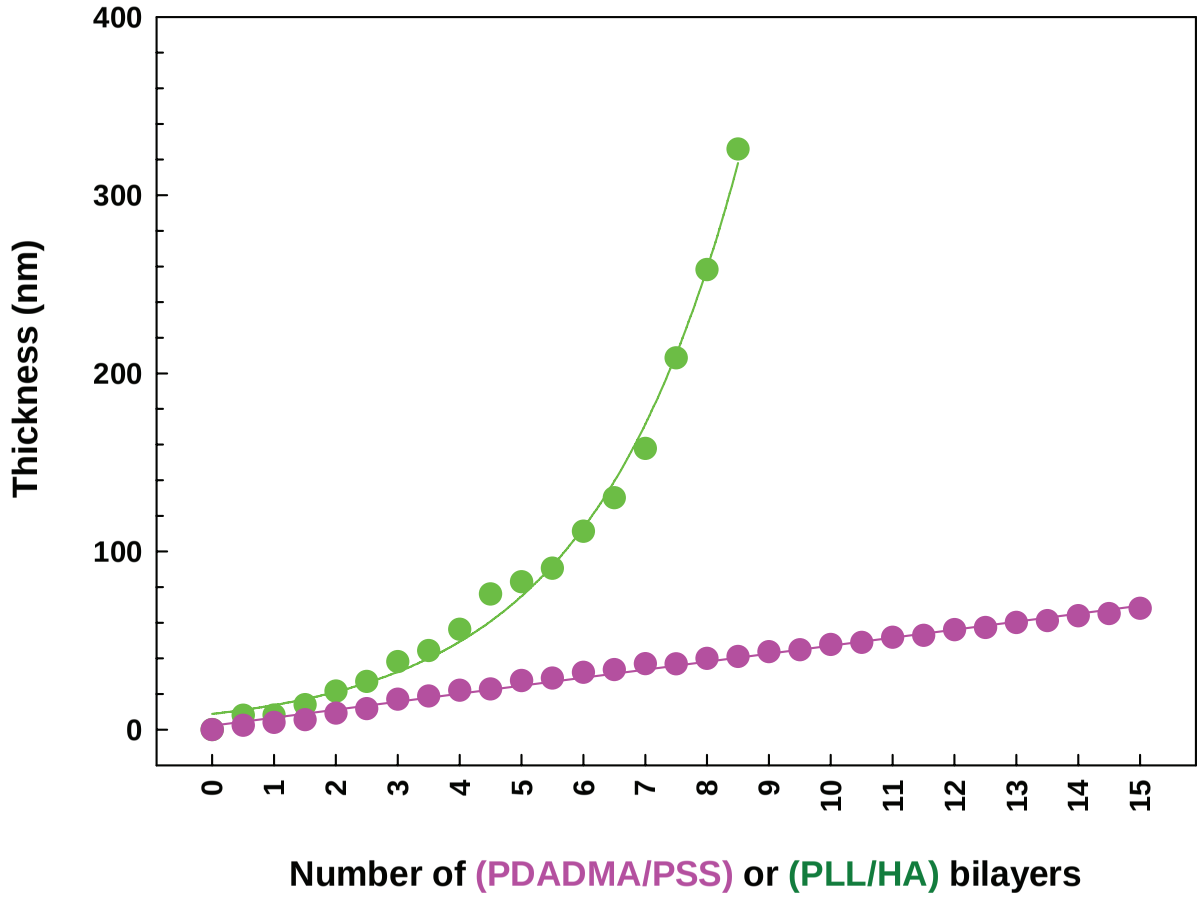


Poly(diallyl-dimethyl-ammonium chloride)
PDADMA



Poly-L-Lysine
PLL

*Build up of the Polyelectrolyte multilayers : **QCM** (Quartz Crystal Microbalance)*

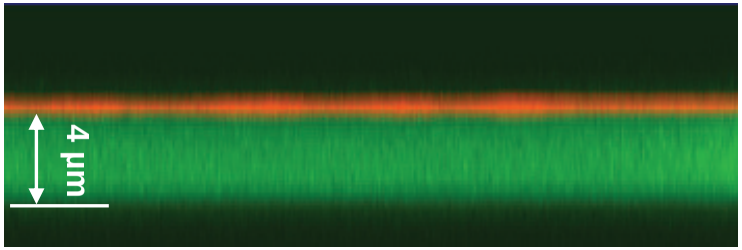


Linear growth regime** **vs** **Exponential growth regime

***Macromolecules* 2002**; 35: 4458

***Macromolecules* 2004**; 37: 1159

Growth Mechanism for (PLL/HA) films : confocal microscopy



Film section

(PLL / HA)$_{19}$ / PLL$_{20}$

with PLL$_{19}^{FITC}$ and HA$_{19}^{TR}$

Diffusion of PLL chains through the film section

***Proc. Natl. Acad. Sci. USA* 2002**; 99:12531

***Langmuir* 2001**; 17:7414

PDADMA / PSS vs PLL / HA films

(PDADMA/PSS)

- ***Linear growth***
- ***Thin***
- ***No diffusion through film section***
- ***Dense***

(PLL/HA)

- ***Exponential growth***
- ***Thick***
- ***Diffusion of PLL through film section***
- ***Hydrated***

Multilayer Films with compartments / barriers

BARRIERS

- films with **no diffusion** of polymers, peptides, proteins… through the film section

= *films with linear growth regime like* (PAH/PSS) or (PDADMA/PSS) films

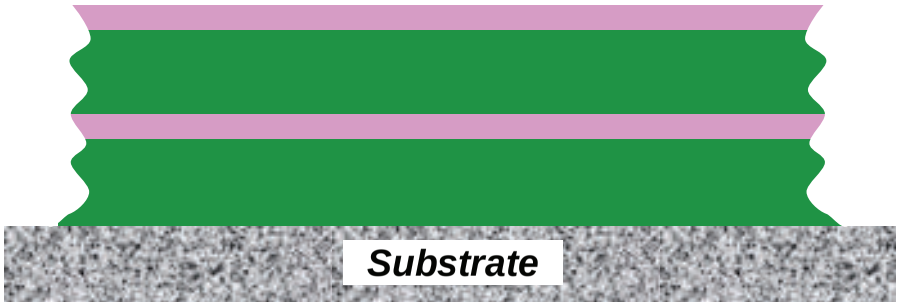
Thin & dense

COMPARTMENTS

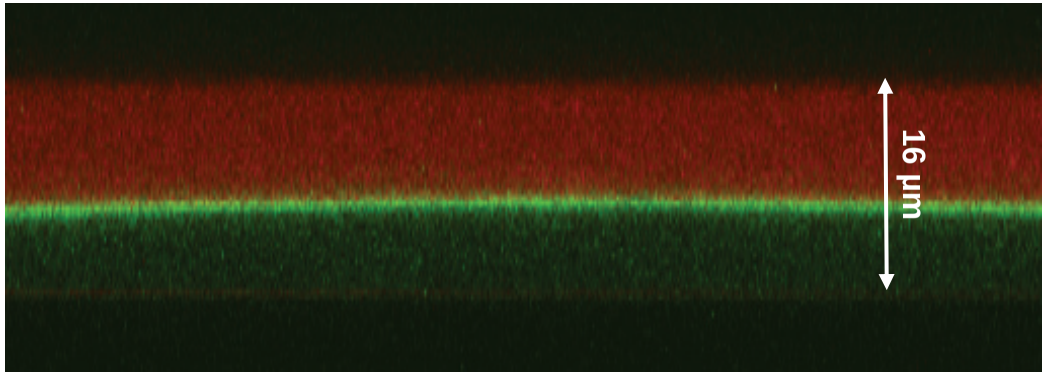
- films with **diffusion** of polymers, peptides, proteins

= *films with exponential growth regime* like (PLL/HA) films

Thick & highly hydrated



PSS / PDADMA as barrier layers



$(PLL/HA)_{30}$ / PLL^{FITC} / (PSS/PDADMA) / HA / $(PLL/HA)_{30}$ / PLL^{Rho}

***Langmuir* 2004**; 20: 7298

***Langmuir* 2005**; 21: 12372

***Macromolecules* 2007**, 40, 316

Adaptative surfaces made of polyelectrolyte multilayers

- ***Polyelectrolyte multilayer films responding to external stimuli***

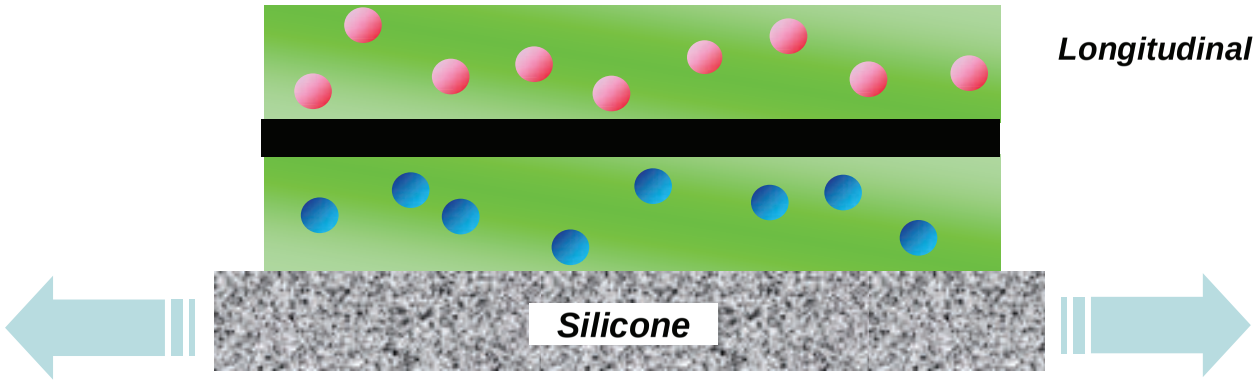
pH
Ionic strength
Temperature

- ***Our objectives :***

To develop coatings responding to *<u>mechanical stimuli</u>*

Applications: Bioactive Patches / Biosensors

Schedule of conditions



Longitudinal stretching

?

- **No breakage of compartments**

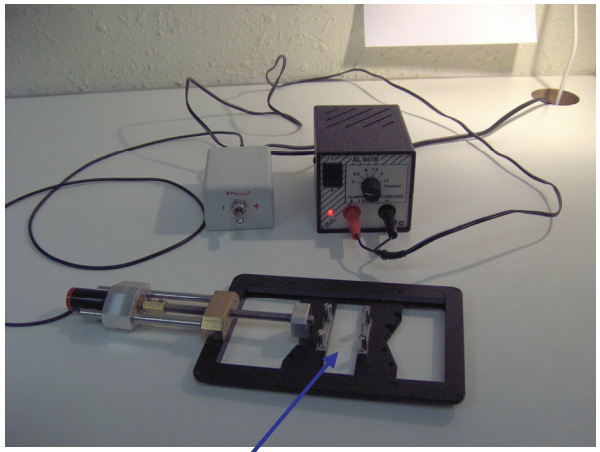
  but opening of the barriers under stretching ?

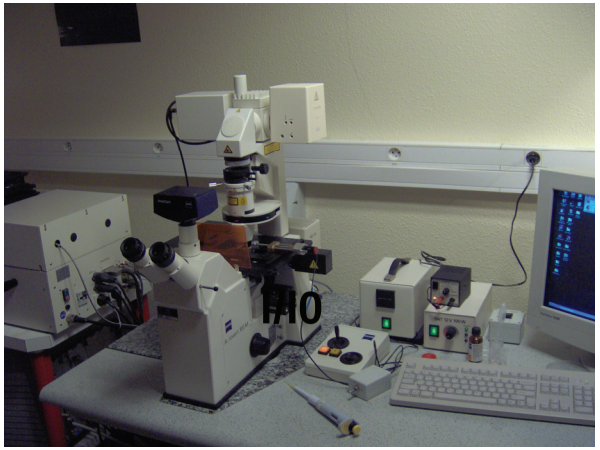
- **Mixing 2 components to trigger enzymatic or chemical reactions,**

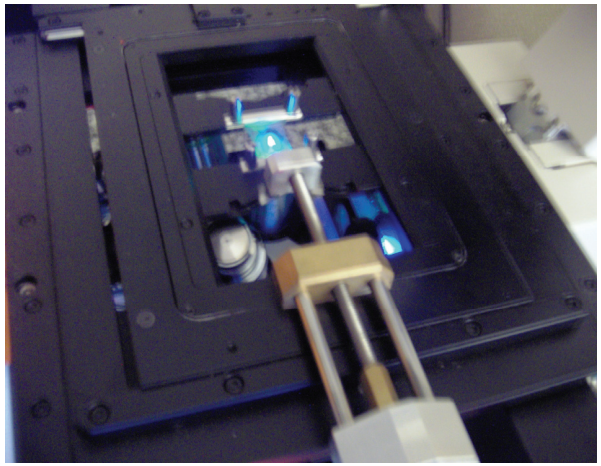
  Release of active compounds under stretching

Methods

Homemade stretching devices adapted to AFM, CLSM… techniques



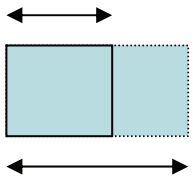




Silicone substrate

Stretching degree is defined by the elongation parameter $\alpha = l/l_0$

l_0 initial length



l stretched length

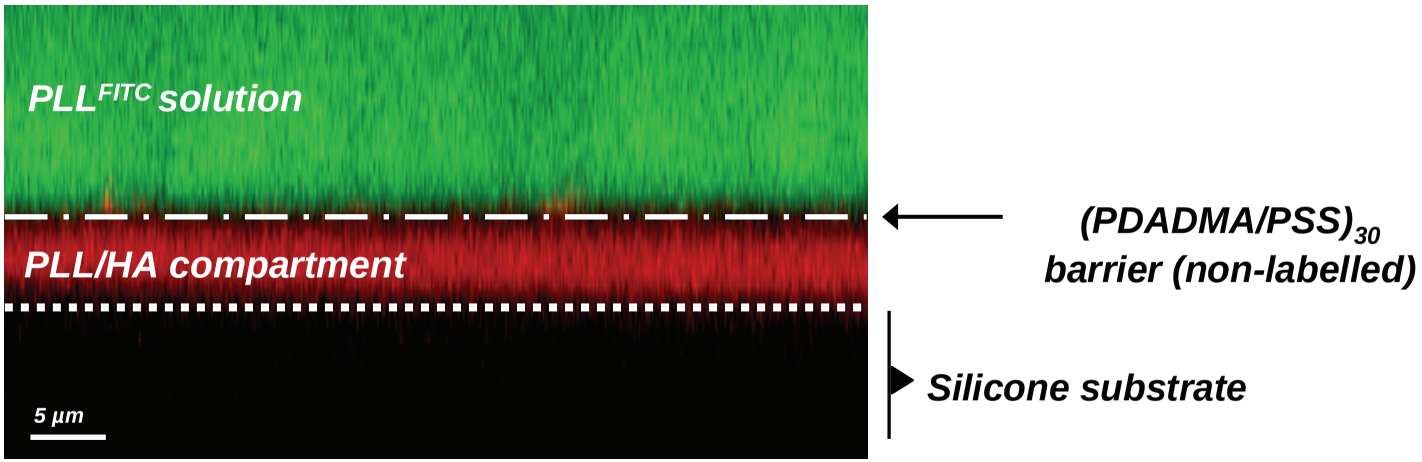
α =1 *No stretching*

α =2 *Elongation of the silicone sheet X2*

Compartment / Barrier systems

$(PLL/HA)_{30}$ labelled in red - $(PDADMA/PSS)_n$ capping
+ PLL^{FITC} green solution at the non-stretched state

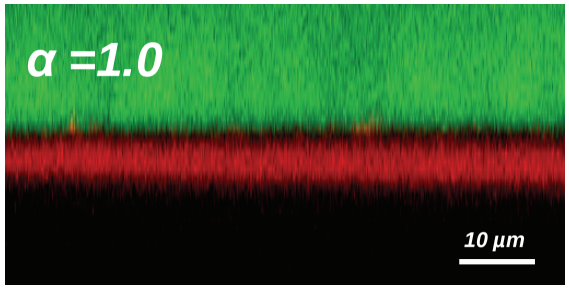
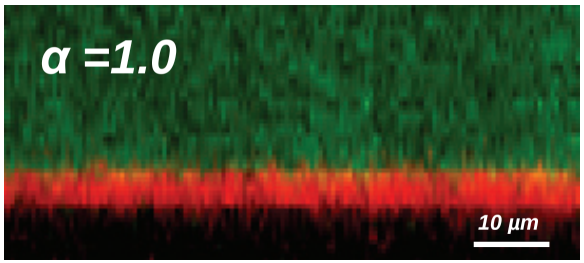
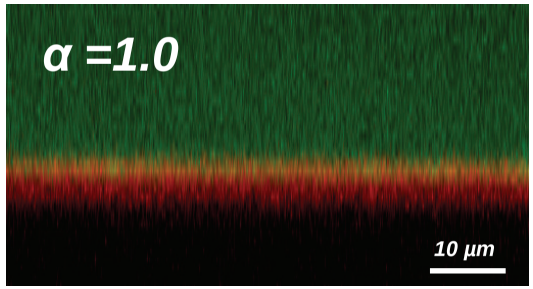
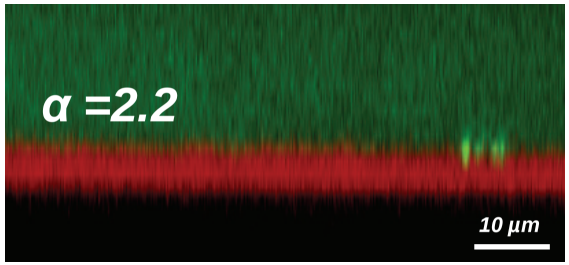
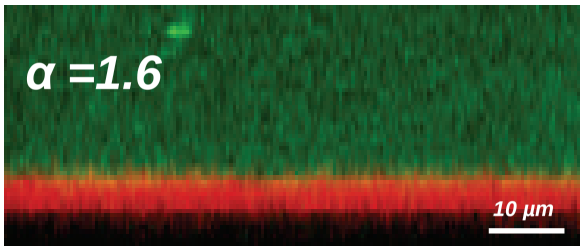
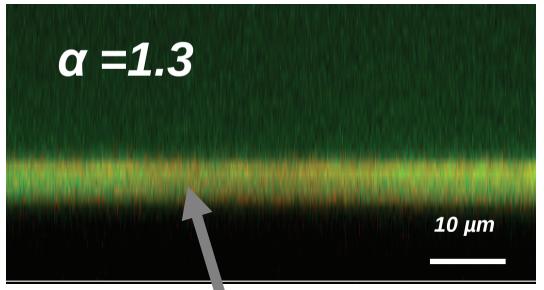
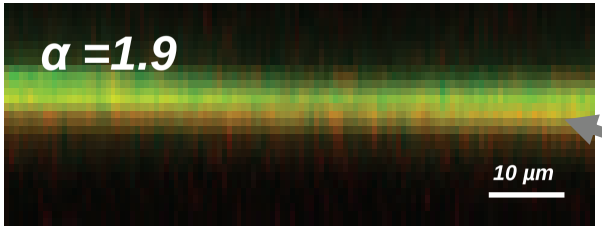
Confocal (x,z) section in liquid condition



No green color detected in the compartment over more than several hours

Compartment / Barrier systems

$(PLL/HA)_{30}$ labelled in red - $(PDADMA/PSS)_n$ capping + PLL^{FITC} solution under stretching

n=30	n=15	n=5
		
		
Confocal x,z sections in liquid conditions	 	***PLL^{FITC} diffusion from the solution to the compartment***

Influence of n upon the critical stretching degree

increasing with n

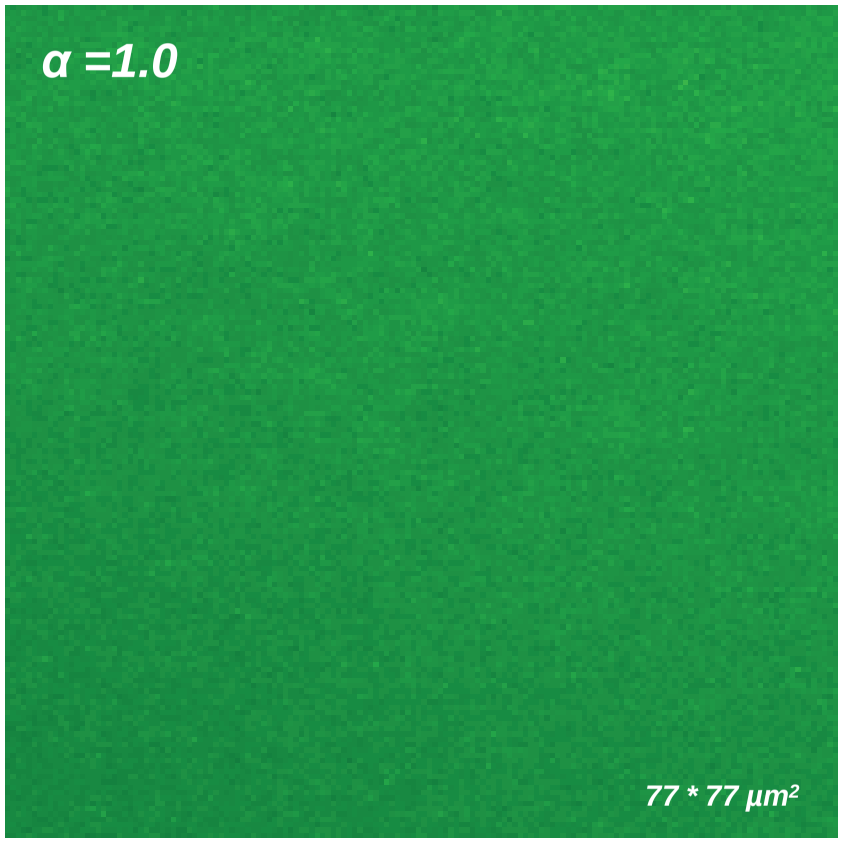
n	*Critical stretching degrees*
2	1.1
5	1.3 – 1.4
15	1.9 – 2.0
30	> 2.2

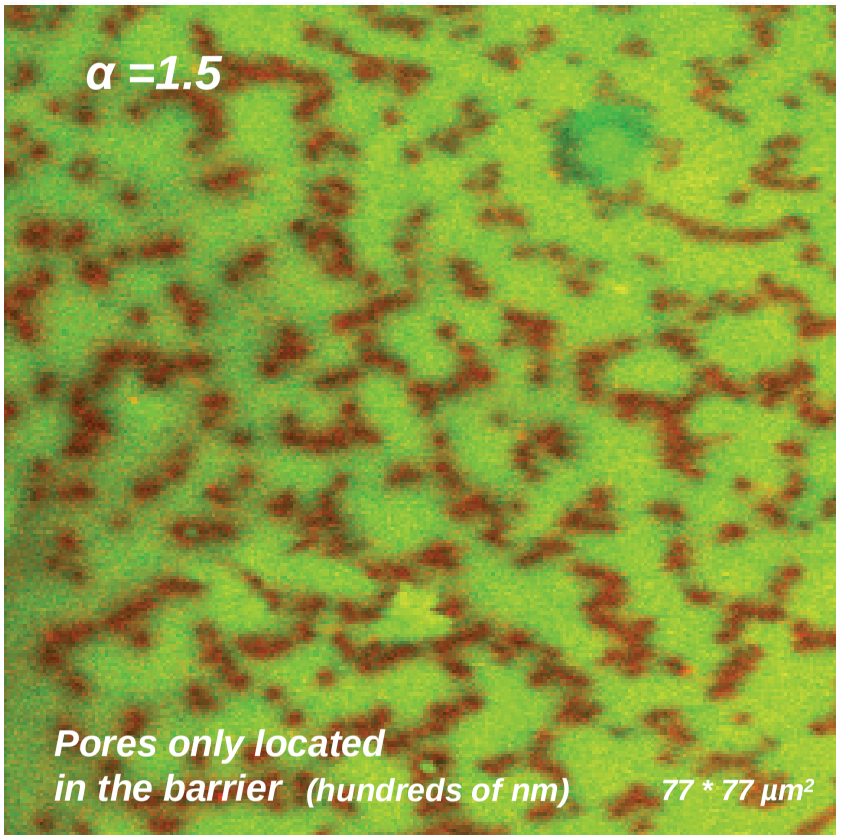
Tune the response by adjusting n

Formation of nanopores in the barrier

CLSM (x,y) images at the film/solution interface

$(PLL/HA)_{30}$ labelled in red - $(PDADMA/PSS)_5$ barrier + PLL^{FITC} solution

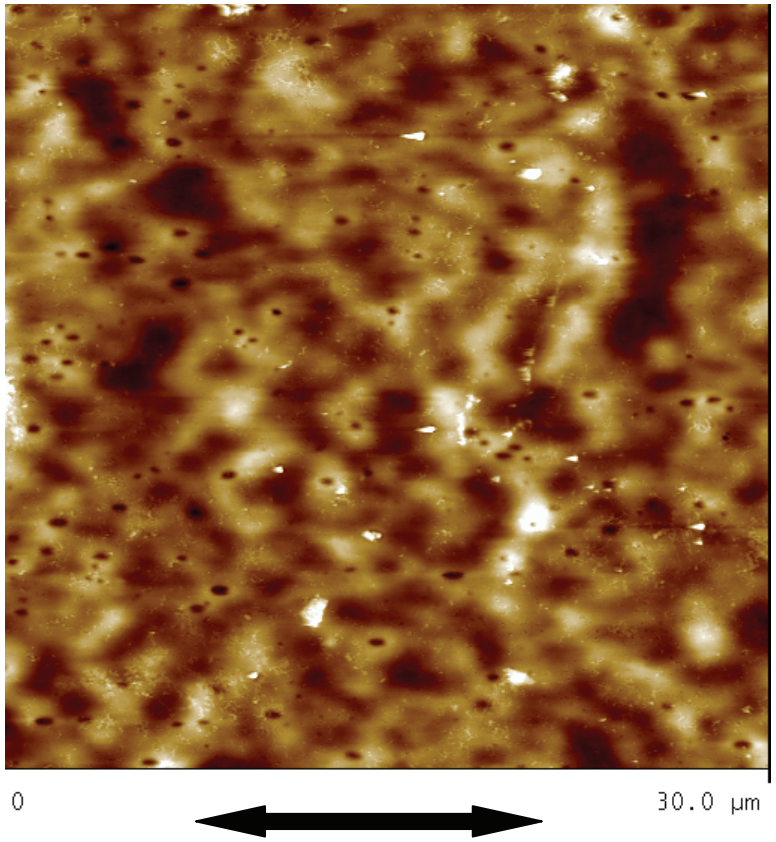


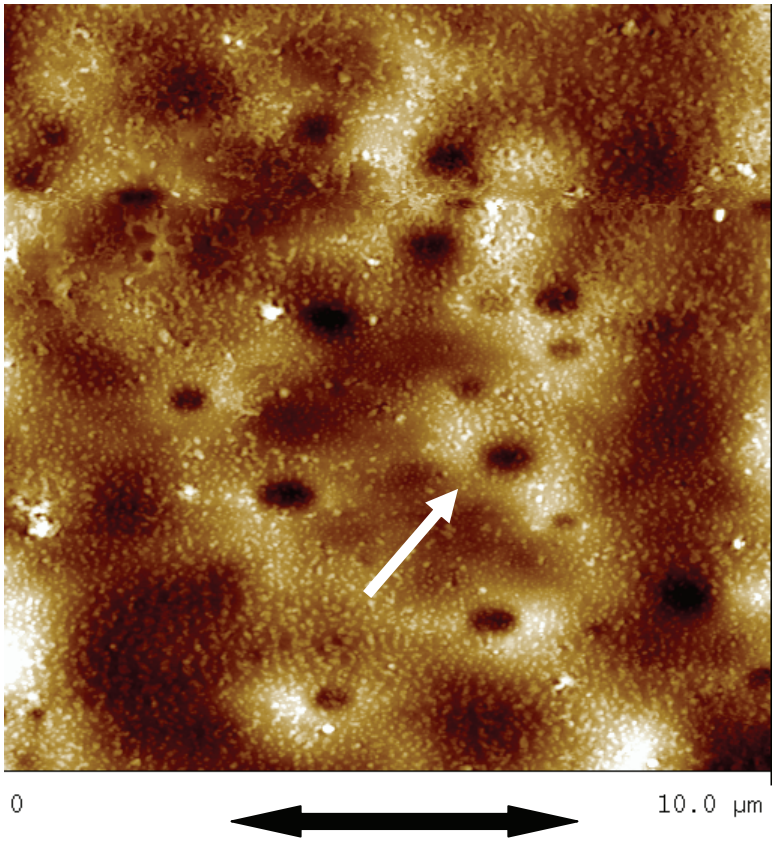


Formation of nanopores in the barrier

AFM images under mechanical stretching at 2.0

$(PLL/HA)_{30}$ compartment - $(PDADMA/PSS)_5$ barrier





Pore sizes in accordance with CLSM measurements

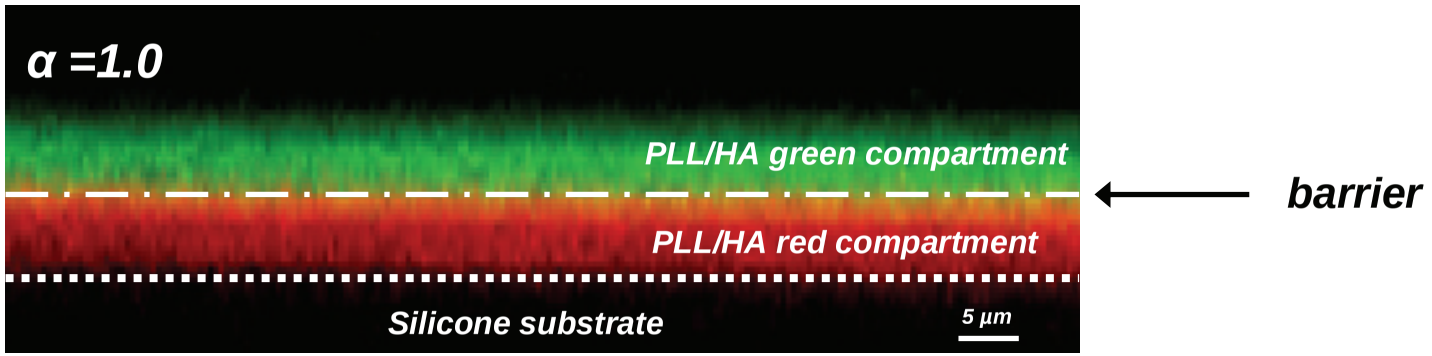
Compartment/Barrier/Compartment systems

n= 5

$(PLL/HA)_{30}$ compartment labelled in red

$(PDADMA/PSS)_5$ barrier

$(PLL/HA)_{30}$ compartment labelled in green

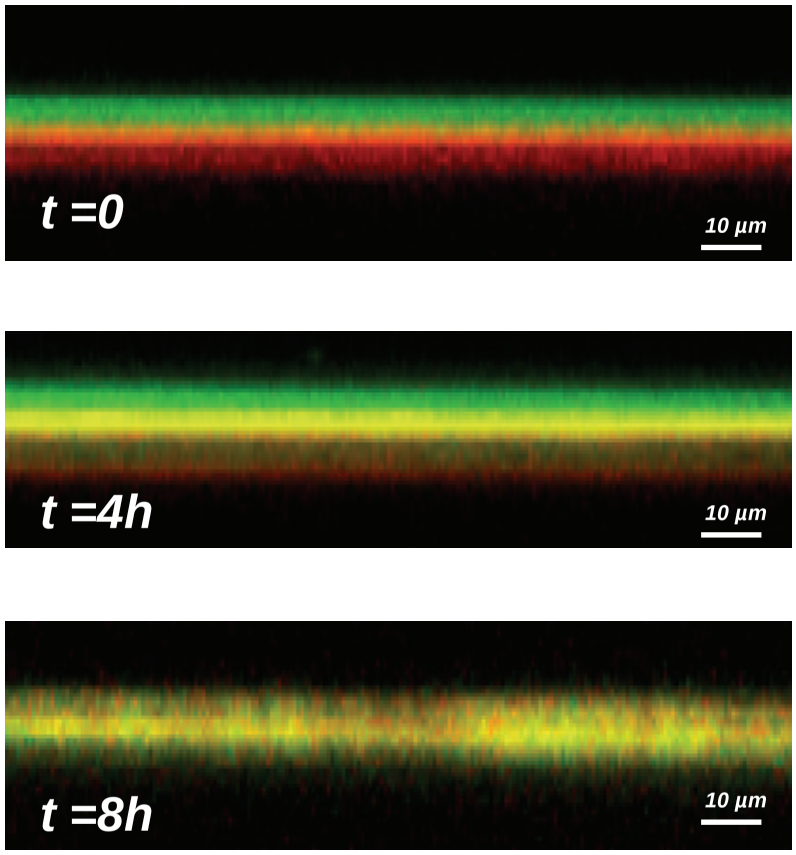


No diffusion of PLL chains through the barrier

Control of PLL mixing by mechanical stretching, α =1.9

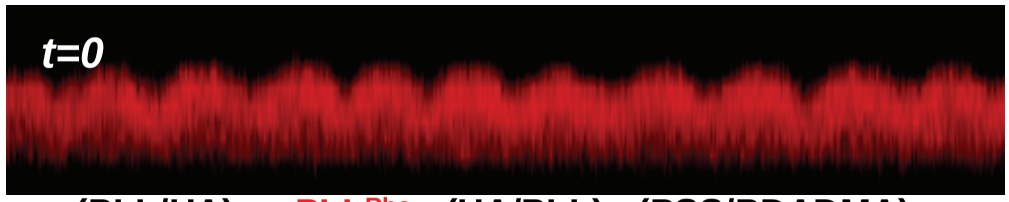
Time evolution under stretching for :

$(PLL/HA)_{30}$ labelled in red - $(PSS/PDADMA)_5$ - $(PLL/HA)_{30}$ labelled in green

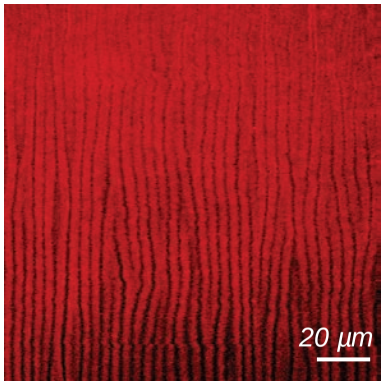


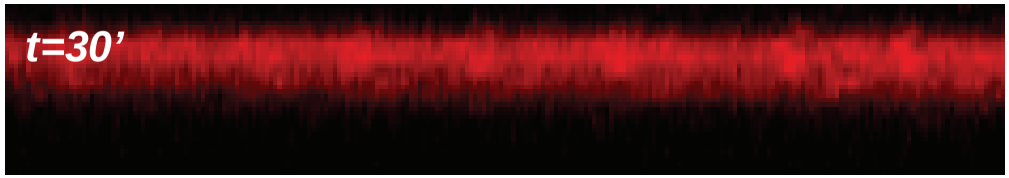
Reversibility of the mechanism : PSS/PDADMA wound healing

Back to α =1.0

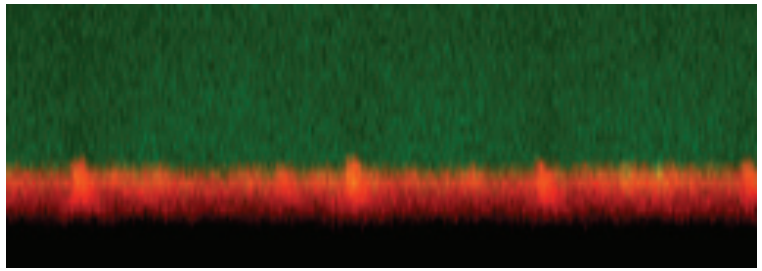


$(PLL/HA)_{30}$ - PLL^{Rho} - (HA/PLL) - $(PSS/PDADMA)_5$



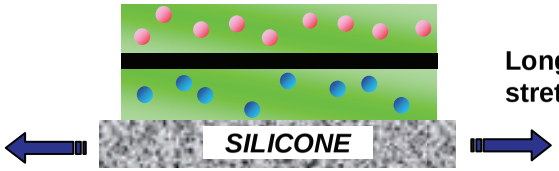


+ PLL^{FITC}



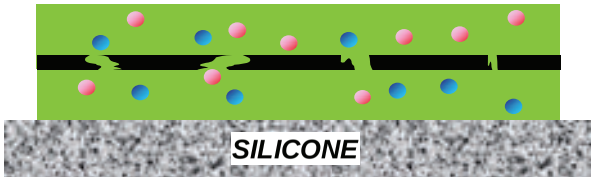
Barrier becomes again efficient and prevents PLL diffusion, pores are closed

Results

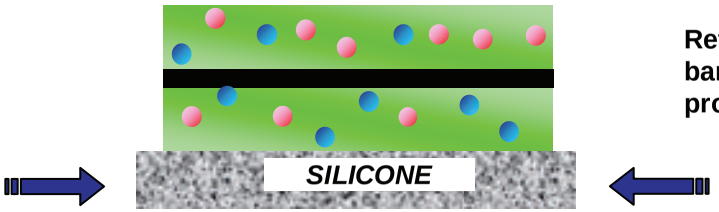


Longitudinal stretching

Multicompartments films under mechanical stretching



Nanopores in the barrier allow a diffusion process



Return to the unstretched state: barrier closing by « healing » process

Pore formation is a reversible process : nanovalves

Potential Applications : ***biocatalytic surfaces with enzymatic activity controlled by mechanical stretching***

Nano Letters, *7, 657,* 2007.

Soft Matter, *3, 1413,* 2007.

Acknowledgements

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