Chaire Innovation technologique Liliane Bettencourt

Biomatériaux de demain :
polymères biomimétiques et biohybrides

Sébastien Lecommandoux

Quelle médecine pour demain et après-demain en cancer et neuroscience?

le 17 mars 2025

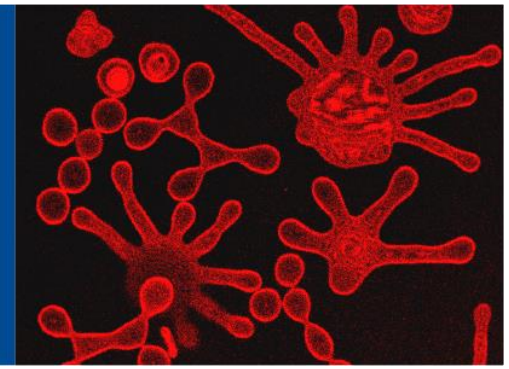
COLLÈGE DE FRANCE
1530

Sébastien LECOMMANDOUX

CHAIRE ANNUELLE INNOVATION TECHNOLOGIQUE
LILIANE BETTENCOURT

Biomatériaux de demain : polymères biomimétiques et biohybrides

27 janv > 31 mars 2025



Cours & séminaire

Amphithéâtre Maurice Halbwachs – Les cours auront lieu les lundis de 10 h à 11 h. Ils seront suivis par le séminaire de 11 h à 12 h.

Les cours, colloques et séminaires sont gratuits, en accès libre, sans inscription préalable.

Lundi 27 janvier 2025

COURS :

Polymères biomimétiques : concept général, design et applications

SÉMINAIRE : **Laurent Billon** (IPREM, UPPA)
Biomimétisme et matériaux bio-inspirés

Lundi 3 février 2025

COURS :

Les polymères à base d'acides aminés : de l'origine de la vie aux médicaments modernes

SÉMINAIRE :

Colin Bonduelle (LCPO, Univ. Bordeaux)
From Proteins to Polymer Synthesis

Hua Lu (Pekin Univ., Chine)
Robust Synthesis and Biomedical Applications of Polypeptides

Lundi 10 février 2025

COURS :

Polymère biohybrides : comment tirer le meilleur du vivant et du synthétique ?

SÉMINAIRE :

Fouzia Boulmedais (ICS, Univ. Strasbourg)
Nanorevêtements de polysaccharides et protéines aux propriétés bioactives pour les biomatériaux

Elisabeth Garanger (LCPO, Univ. Bordeaux)
Polymères inspirés de l'élastine: stratégies de synthèse et applications biomédicales

Lundi 17 février 2025

COURS :

Nanotechnologies biohybrides macromoléculaires et thérapie cancer/immunothérapie

SÉMINAIRE : **Simona Mura** (IGPS, Univ. Paris Saclay)
Particules circulantes comme vecteurs thérapeutiques biomimétiques

Lundi 24 février 2025

COURS :

Des polymersomes aux cellules artificielles : mimer la complexité du vivant pour le comprendre et le soigner

SÉMINAIRE :

Nicolas Martin (CRPP, Univ. Bordeaux)
Coacervats : des gouttelettes dynamiques pour assembler des cellules artificielles

Léa-Lætitia Pontani (LJP, Sorbonne Univ.)
Biomimetic emulsions as a tool to study tissue architecture and mechanics

Lundi 3 mars 2025

COURS :

Assemblages multi-composants et multi-échelles dynamiques : du fondamental à l'application

SÉMINAIRE : **Christophe Tribet** (PASTEUR, ENS-PSL)
Stabiliser, replier, cibler des protéines hors de leur contexte naturel : quelques applications d'assemblages entre protéines solubles ou membranaires et des copolymères synthétiques

Lundi 17 mars 2025

COURS :

Quelle médecine pour demain et après-demain en cancer et neurosciences ?

SÉMINAIRE :

Clémentine Bosch-Bouju (Bordeaux Neurocampus)
Les polymères biomimétiques comme alliés des neurosciences dans le développement des neurotechnologies

Isabel Marey-Semper (DOXANANO)
Repousser les limites de la chimiothérapie conventionnelle grâce à la chimiothérapie activée à distance à l'aide de polymersomes bioinspirés

Lundi 31 mars 2025

COURS :

Biomimétisme, biodégradabilité et (bio)recyclabilité des polymères : enjeux et opportunités

SÉMINAIRE :

Christophe Chassenieux (IMMM, Le Mans Univ.)
Les protéines comme nouvelles sources de matériaux

Daniel Taton (CLPO, Univ. Bordeaux)
Stratégies de déconstruction chimique de plastiques récalcitrants

Image : vésicules polymères (polymersomes) en train de se diviser sous l'action d'une différence de pression osmotique observées en microscopie de fluorescence. Crédit: LCPO - Emmanuel Ibarboure @ Anouk Martin.

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Thomas Römer
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www.college-de-france.fr

Année académique 2024/2025

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Nanomédecine : Nanotechnologie et médecine

Nanotechnologies en médecine

https://www.medicaldevice-network.com/
https://www.biospectrumindia.com/
https://www.azonano.com/
https://medicalfuturist.com/

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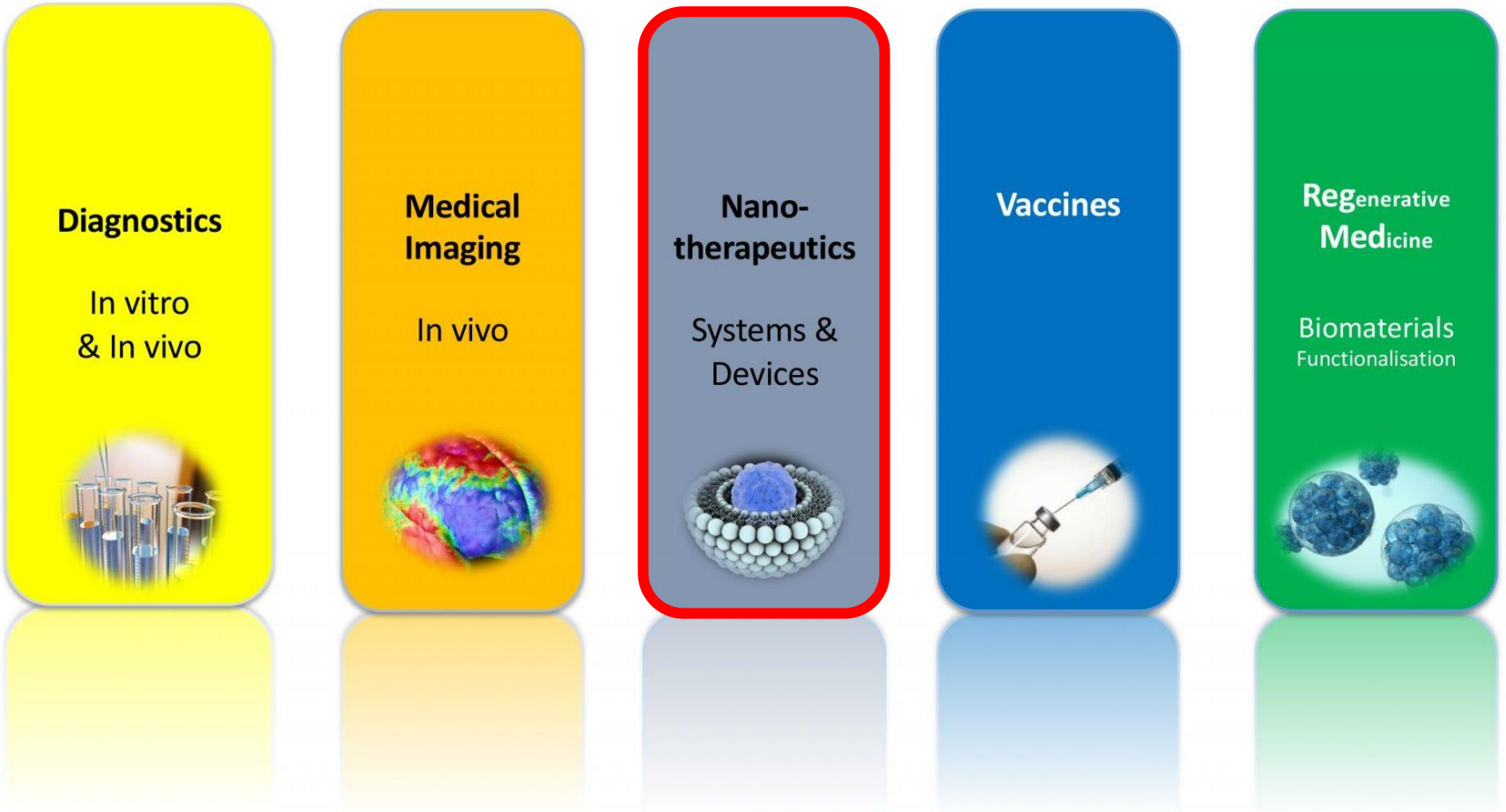
Nanomédecine : Nanotechnologie et médecine

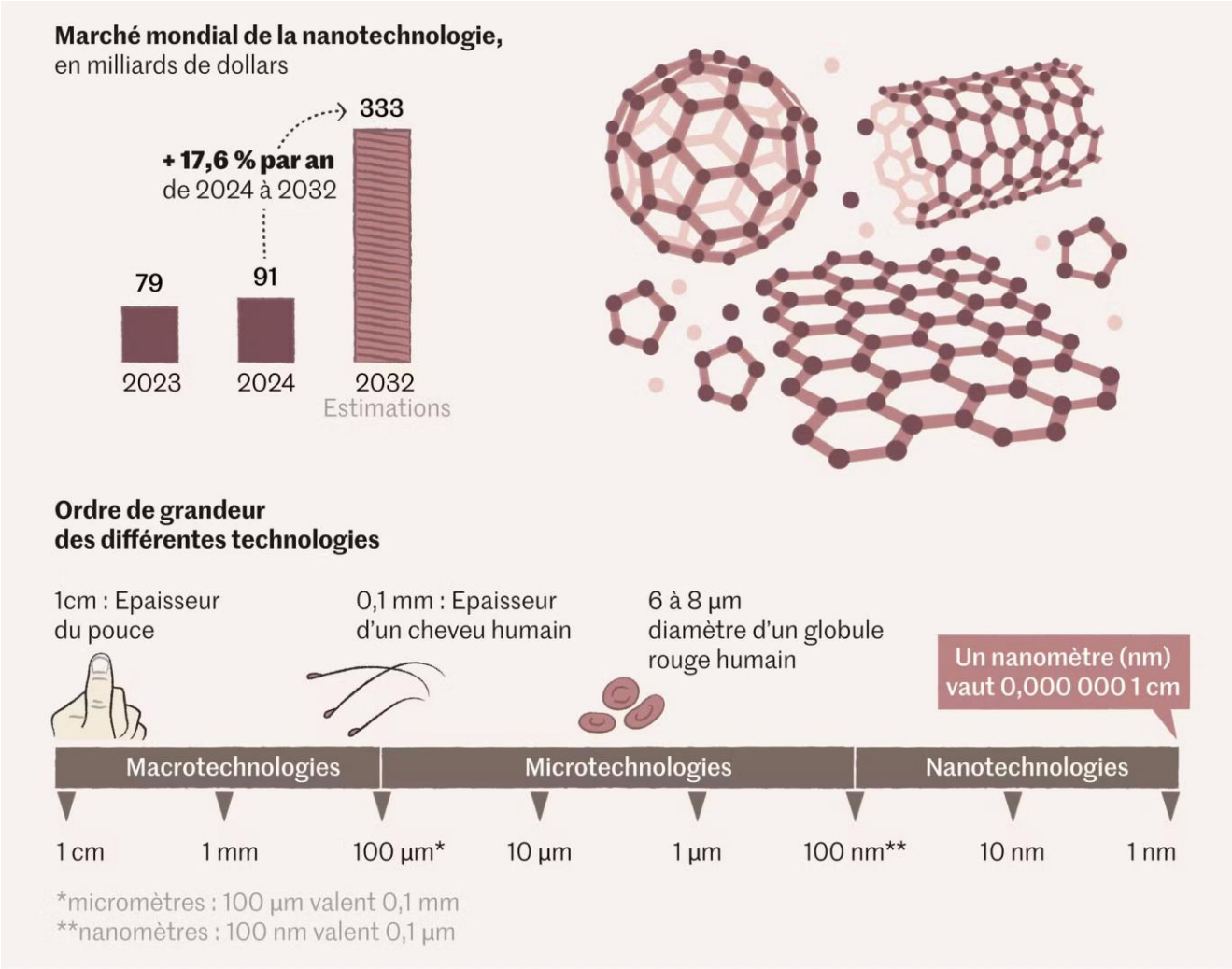
Nanotechnologies en médecine



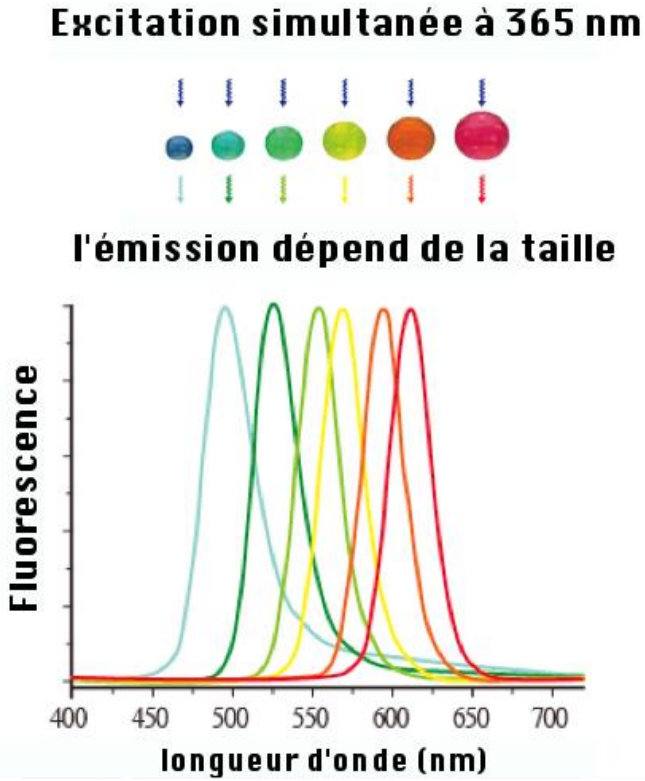
nanomedicine
EUROPEAN TECHNOLOGY PLATFORM

L'importance de la taille

Les Nanotechnologies (en général)



https://www.lemonde.fr/economie/article/2024/09/29/l-essor-discret-des-nanotechnologies-graphene-or-dioxyde-de-titane_6338295_3234.html

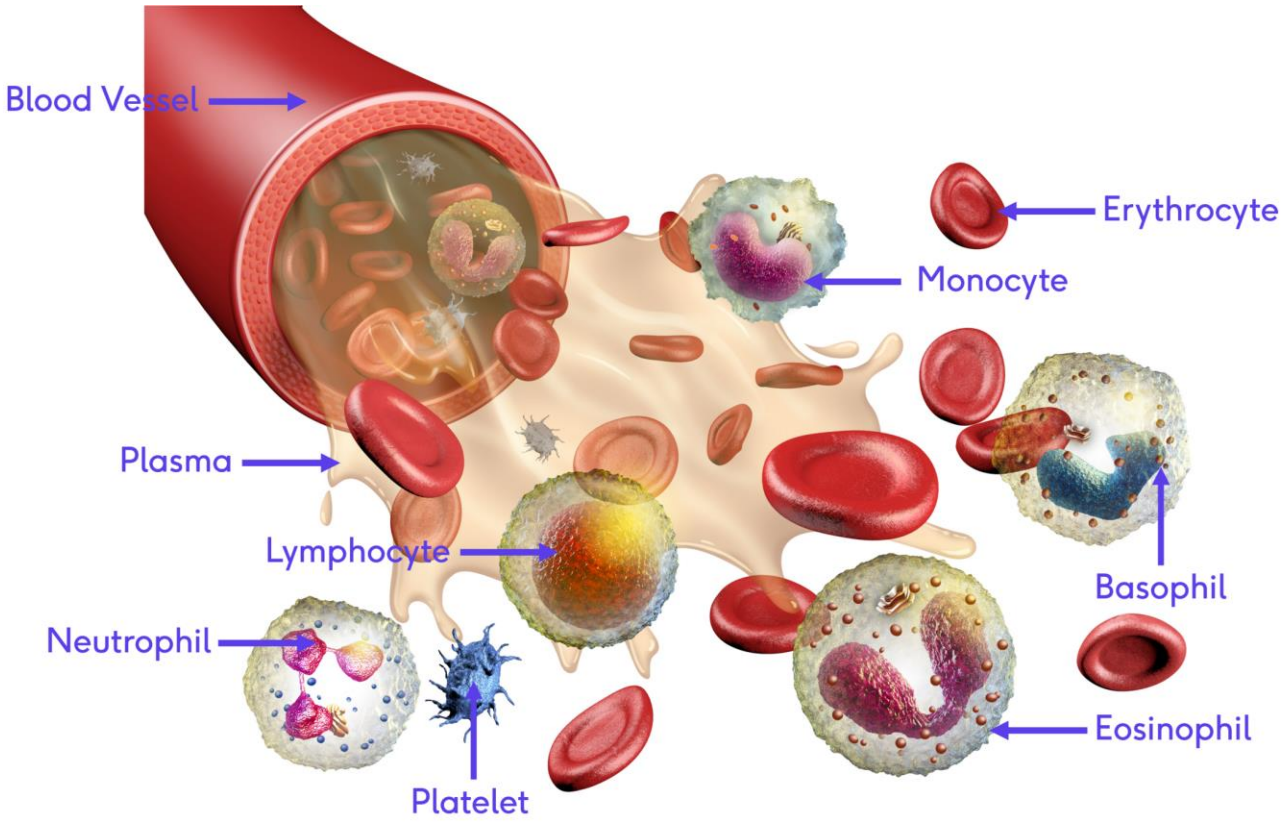


« effets quantiques » en physique

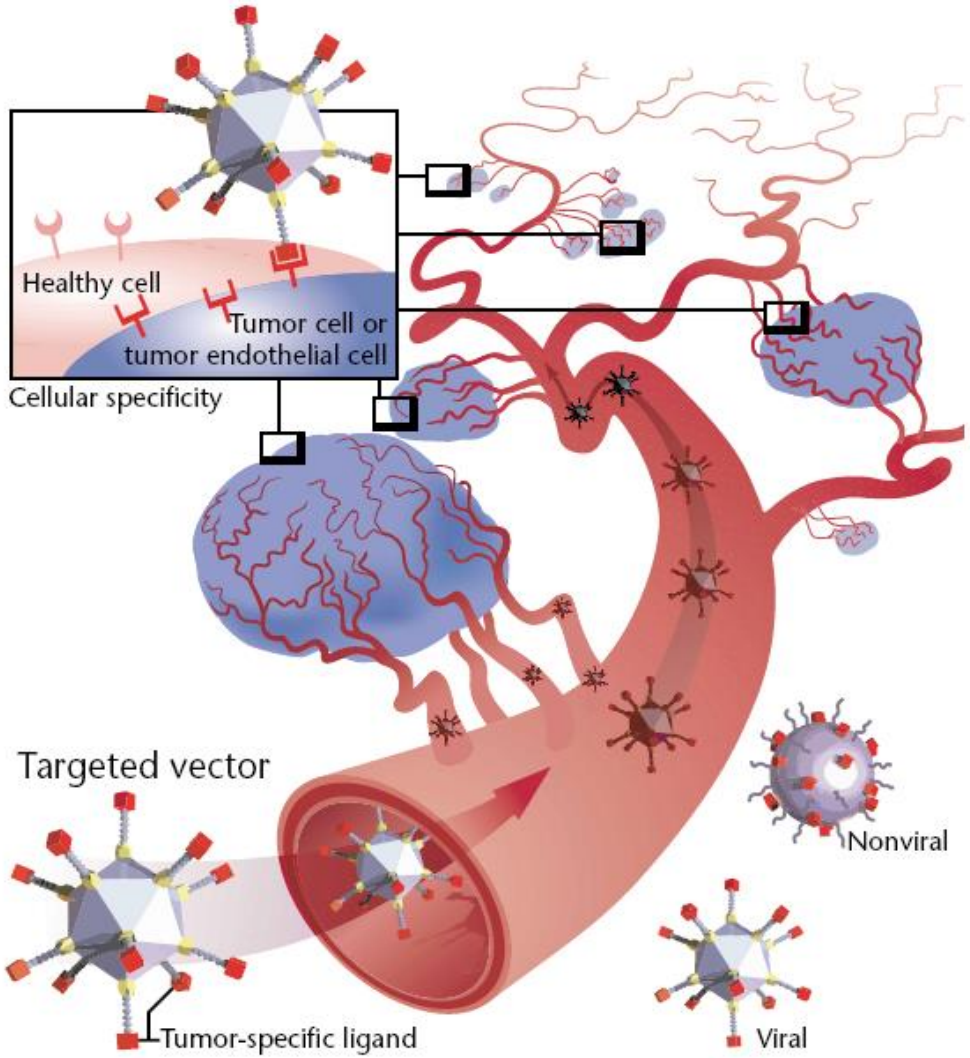
https://culturesciencesphysique.ens-lyon.fr/ressource/nanosciences-Chenevier.xml

L'importance de la taille

La dimension importante: l'échelle 'nano' en biologie



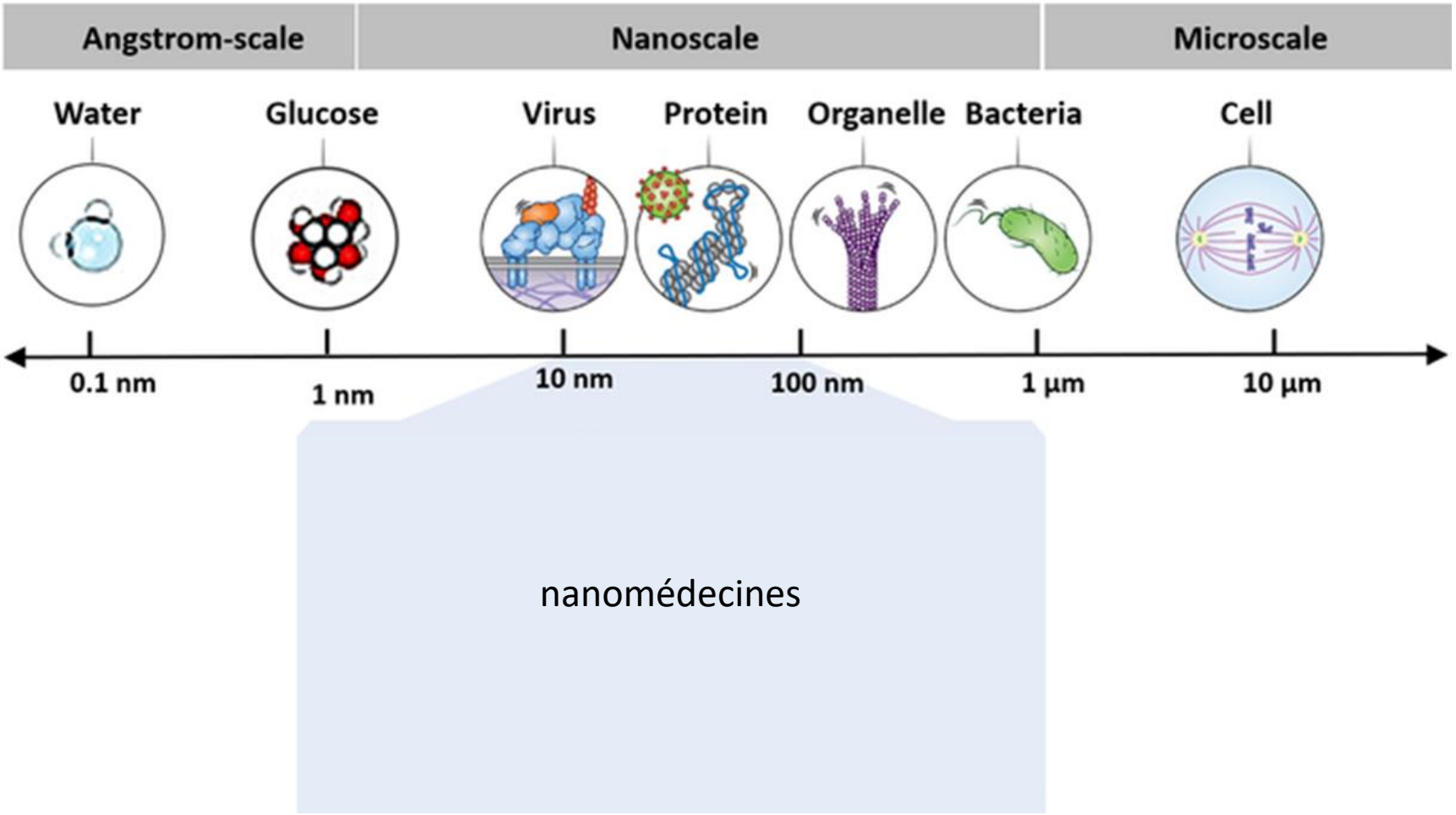
https://www.physio-pedia.com/



T.J. Whickham Nature Medicine 2003, 9, 135

L'importance de la taille

La dimension importante: l'échelle 'nano'

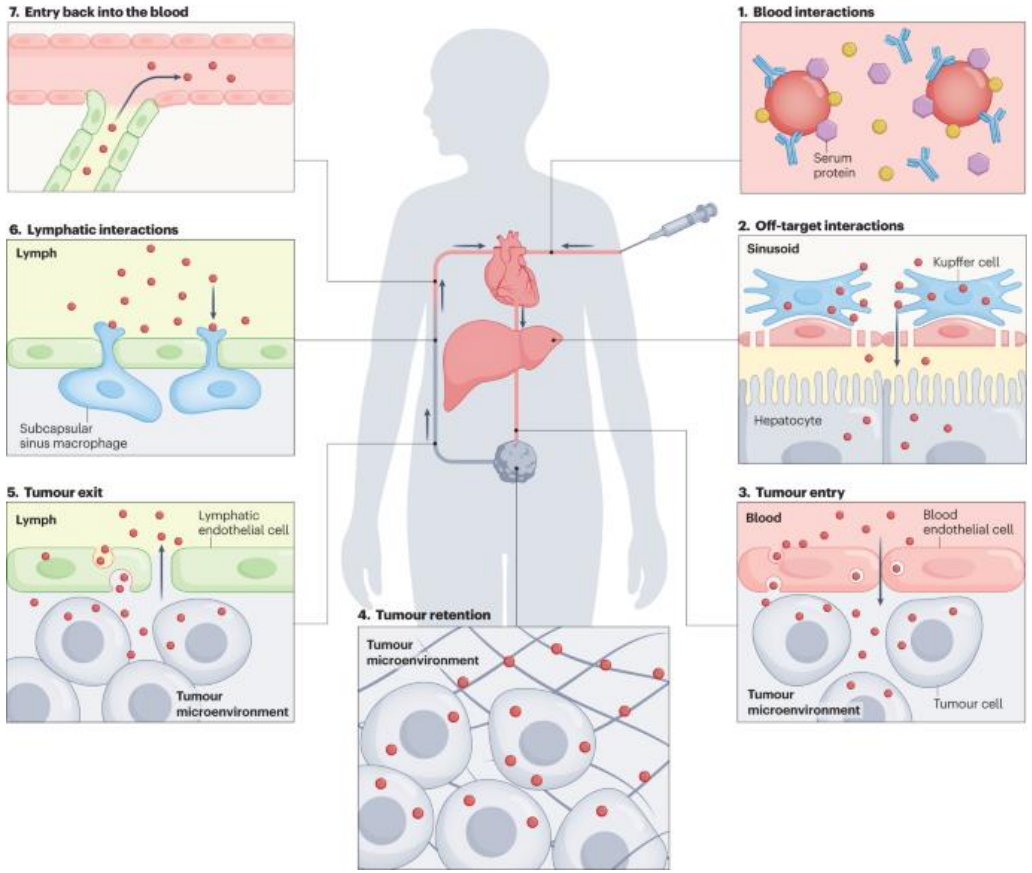


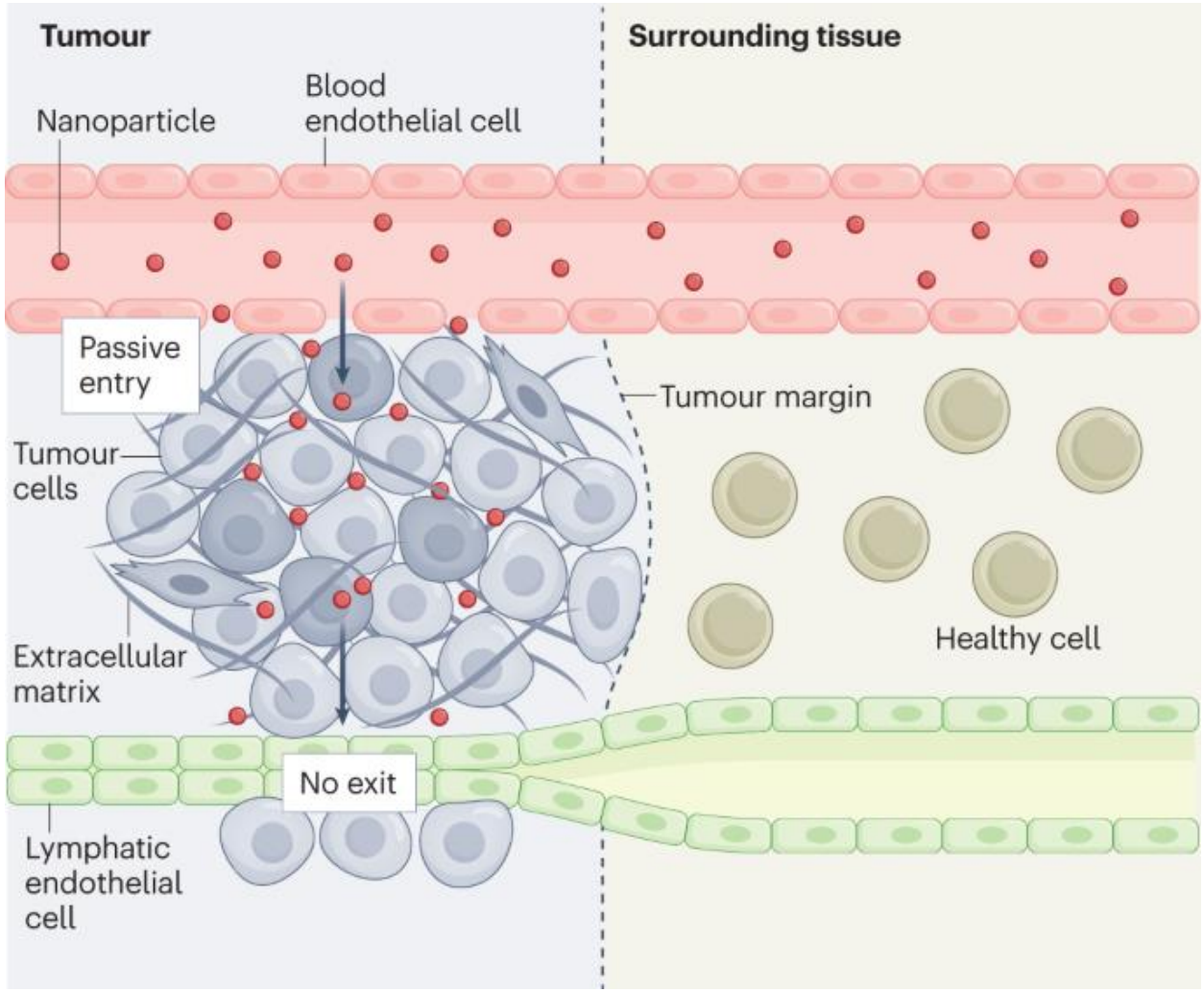
Adapted from Yicong Wu and Hari Shroff, *Histochemistry and Cell Biology*, 2022

L'effet EPR

Enhanced Permeation and Retention effect (EPR)

Matsumura et Maeda. Cancer Res. 1986;46:6387–6392





Nature Rev. Bioeng **2**, 201–213 (2024)

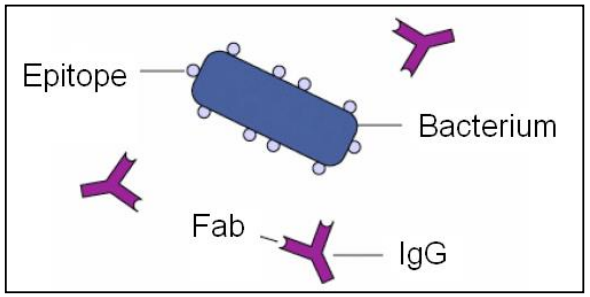
Prérequis pour bénéficier de l'effet EPR

Une longue circulation sanguine

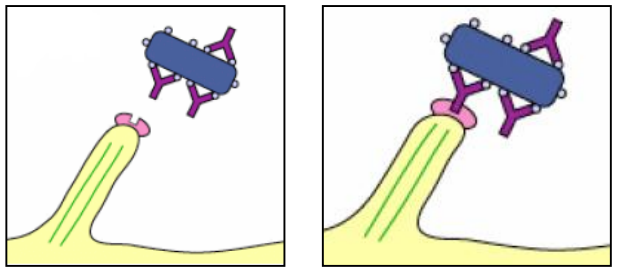
Que se passe t'il lorsqu'on injecte une nanoparticule par voie iv?

1- Opsonisation : reconnaissance et marquage

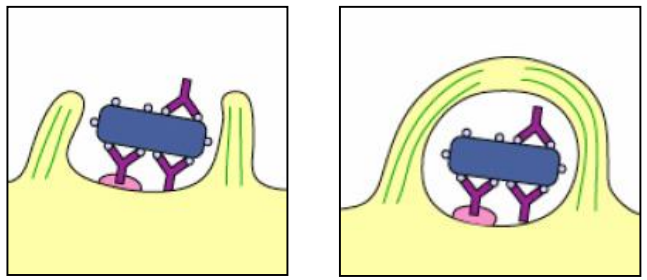
Opsonines (activateur de liaison pour le processus de phagocytose) : anticorps (IgG, IgA) et/ou molécules du complément C3b, C4b…) …



2- Reconnaissance et capture par les macrophages



3- Phagocytose (=endocytose) par les macrophages



4- Digestion et élimination (exocytose)

Si on souhaite éviter l'élimination, il faut ????

Prérequis pour bénéficier de l'effet EPR

Une longue circulation sanguine

Que se passe t'il lorsqu'on injecte une nanoparticule par voie iv?

1- Opsonisation : reconnaissance et marquage

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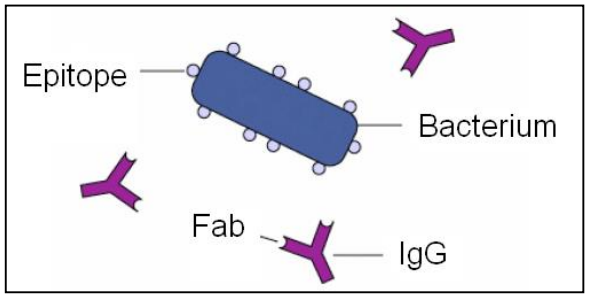

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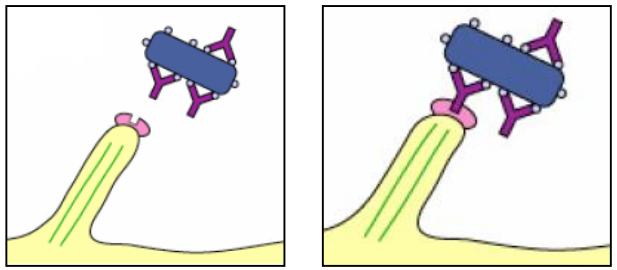

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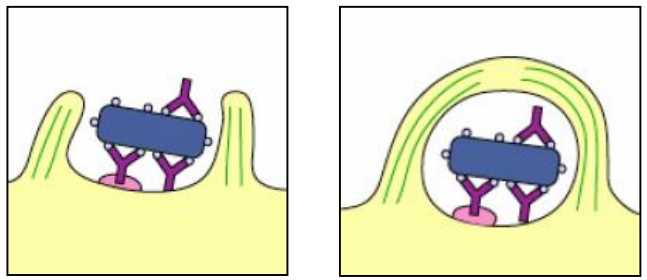
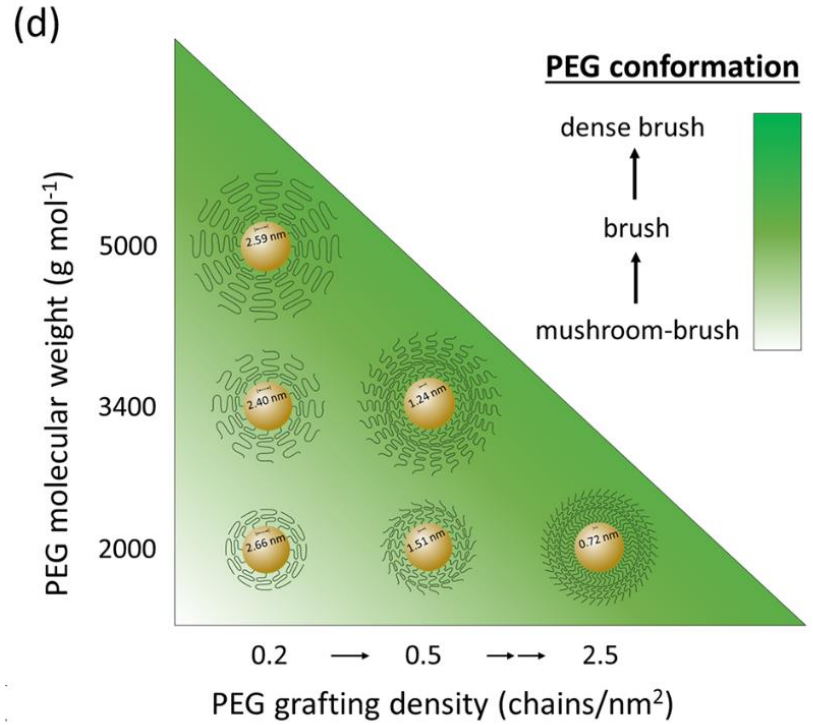


4- Digestion et élimination (exocytose)

Si on souhaite éviter l'élimination, il faut éviter l'opsonisation

Principe physique de la PEGylation



Nano Lett. 2021, 21, 1591−1598

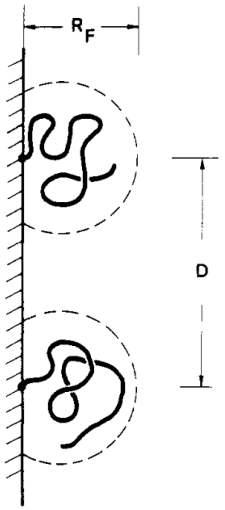
Conformations of Polymers Attached to an Interface

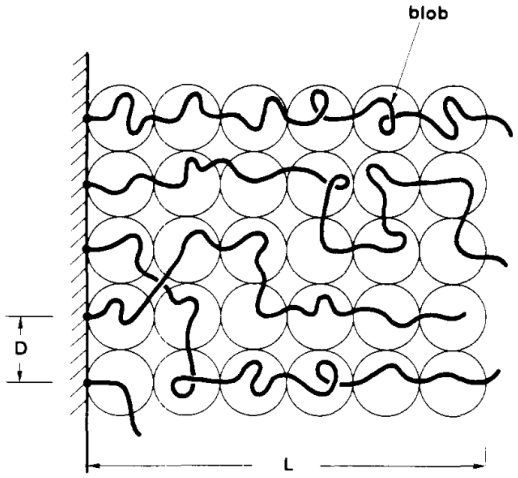
P. G. de Gennes

Collège de France, 75231 Paris Cedex 05, France. *Received April 10, 1980*

ABSTRACT: We discuss the conformations and the concentration profiles for long, flexible chains (N monomers per chain) grafted at one end on a solid surface (fraction of surface sites grafted σ). The chains are immersed either in a pure (good) solvent or in a solution of the same polymer (P monomers per mobile chain, volume fraction ϕ). It is assumed that the polymer does *not* adsorb on the wall surface. The zone occupied by the grafted chain may contain a large fraction of mobile P chains: we call this a mixed case (M), as opposed to the unmixed case (UM). Also the chains may be stretched (S) or unstretched (US). The combination of these two criteria gives four possible regimes. Using scaling laws, we locate the domains of existence of these four regimes in terms of the variables σ and ϕ. High σ values may be hard to reach by grafting but could be obtained with block copolymers at an interface between two immiscible solvents.

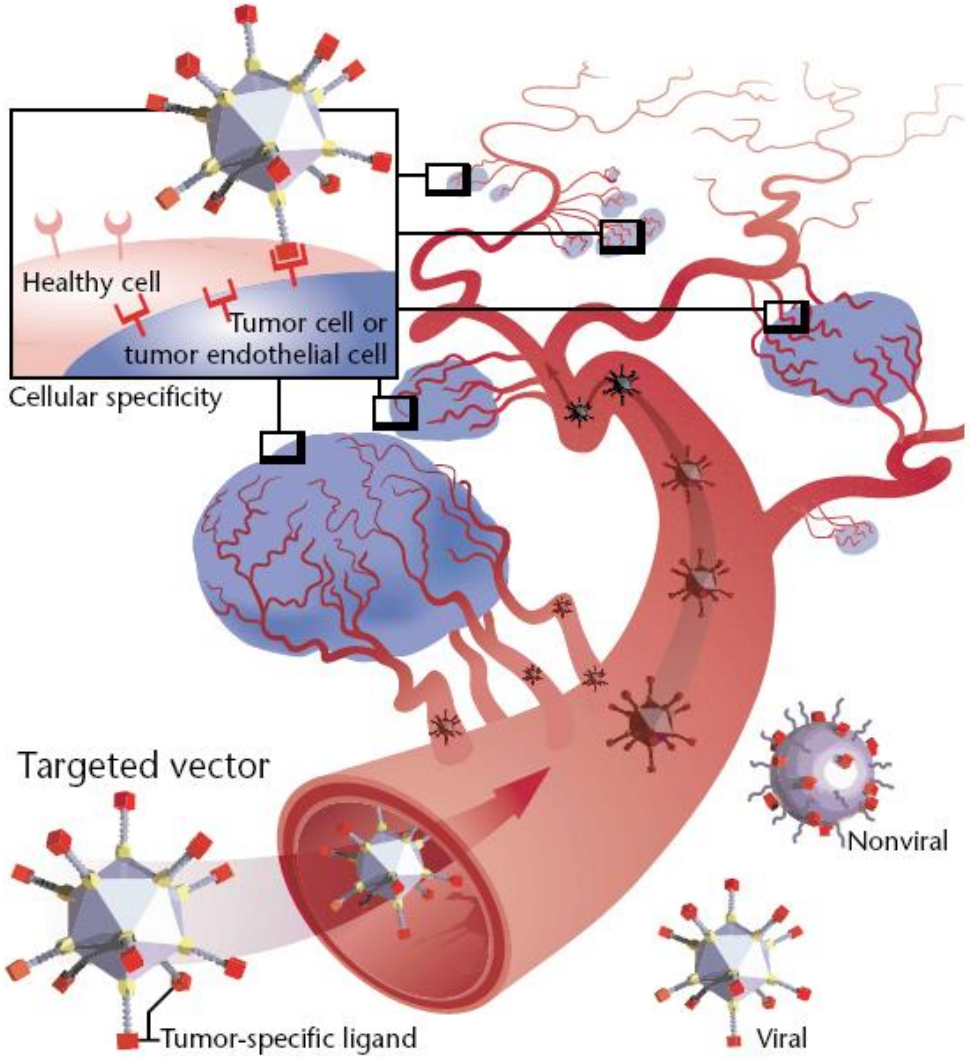
Macromolecules 1980, 13, 1069−1075

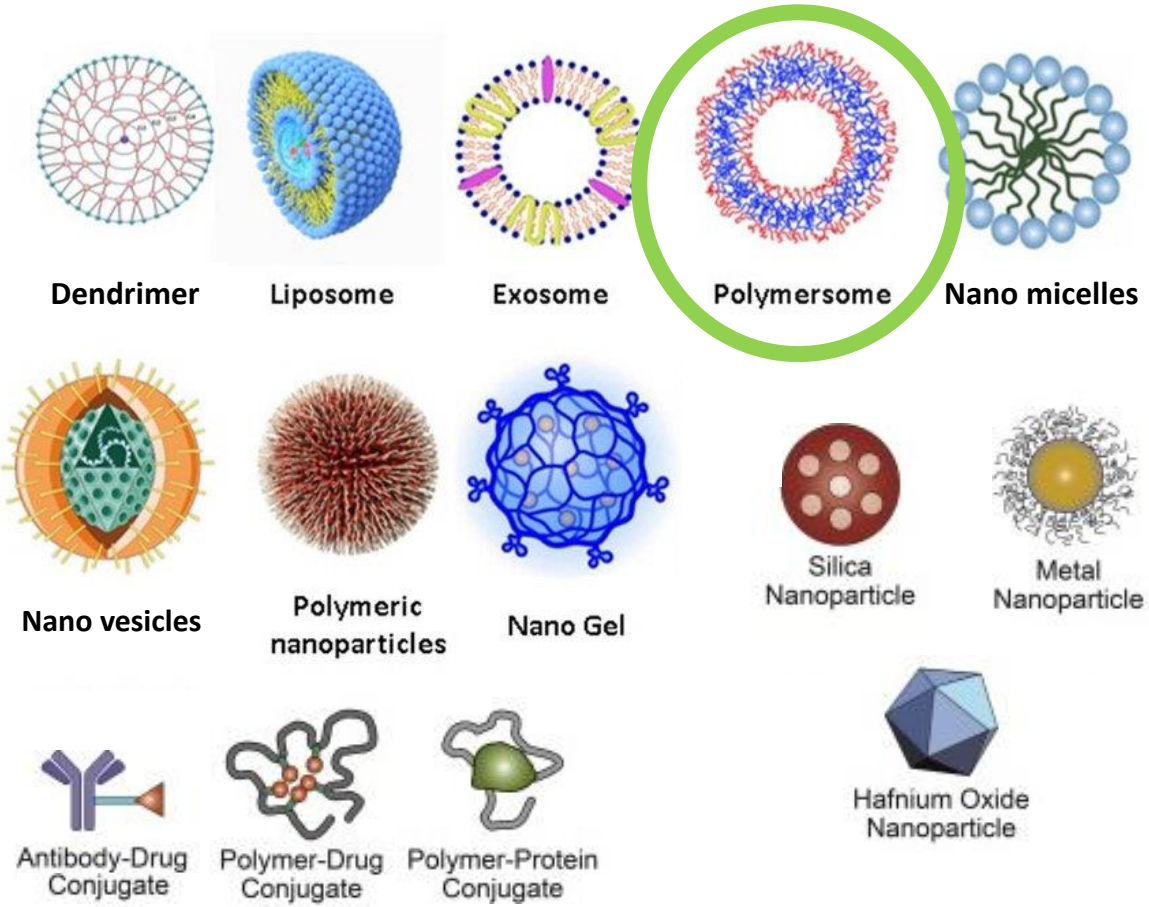




Les principales nanomédecines

Nanotechnologies et systèmes de vectorisation d'actifs thérapeutiques (DDS)



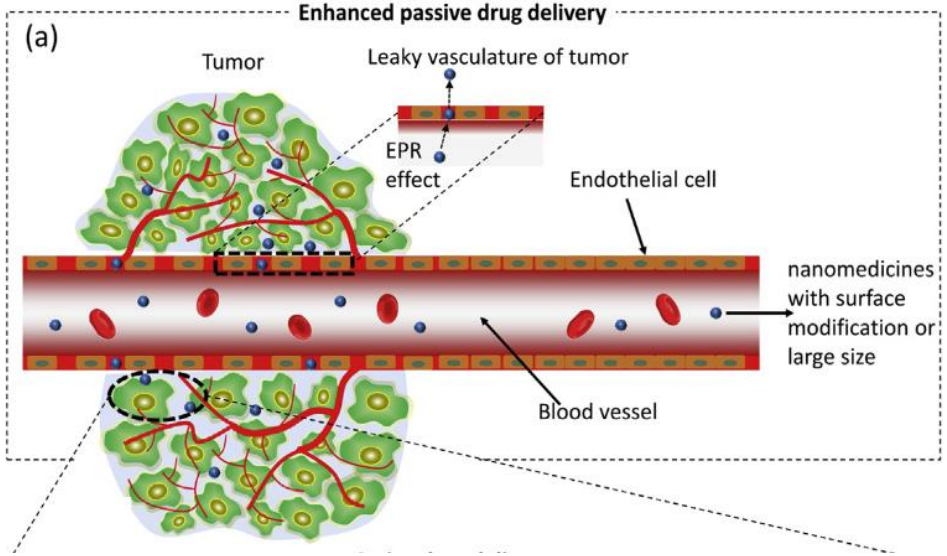


T.J. Whickham Nature Medicine 2003, 9, 135

DOI: 10.1515/gps-2023-0094

‘Design’ avancé des nanomédecines

Vers plus de précision



Nano Today 35 (2020) 101008

Prérequis pour le transfert clinique

GDCh Guest Editorial Angewandte International Edition Chemie

International Edition: DOI: 10.1002/anie.201709002
German Edition: DOI: 10.1002/ange.201709002

Drug Delivery: Too Much Complexity, Not Enough Reproducibility?

*Jean-Christophe Leroux**

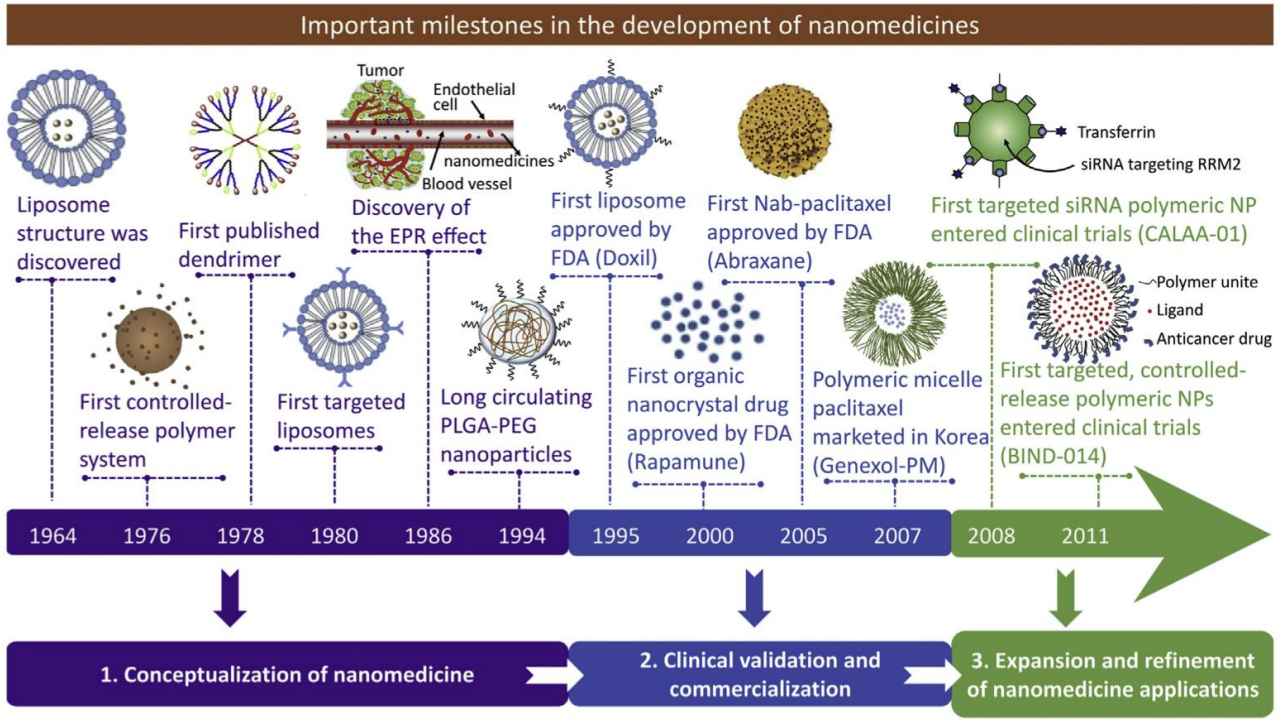
Jean-Christoph Leroux
Professor of Drug Formulation and Delivery, ETH Zurich

Drug formulation and delivery is a part able evolution in scientific practices.

The upsurge in published reports does not correlate with therapeutic advances

Lack of reproducibility is an important issue

Étapes clés des nanomédecines en clinique



Nanotherapeutics in clinical use or in clinical trials. NCT numbers are from clinicaltrials.gov.

Trade name	Active ingredient	Indication(s)	Advantages	Status
Liposome-based nanotherapeutics				
Doxil	Doxorubicin	Karposi's sarcoma, ovarian cancer, multiple myeloma	Enhanced delivery; Reduced systemic toxicity [22]	Approved by FDA (1995)
DaunoXome	Daunorubicin	Karposi's sarcoma	Enhanced delivery; Reduced systemic toxicity [136]	Approved by FDA (1996)
Inflexal V	Virosomal influenza vaccine	Influenza	Better immunogenicity; high safety [137]	Approved in Switzerland (1997)
Visudyne	Verteporfin	Age-related macular degeneration	Photosensitive drug [138]	Approved by FDA (2000)
DepoDur	Morphine sulphate	Analgesia (post-operative)	Extended-release drug [139]	Approved by FDA (2004)
Mepact	Muramyl tripeptide phosphatidyl ethanolamine	Non-metastatic osteosarcoma	Longer half-life; less toxic [140]	Approved in Europe (2009)
Marqibo	Vincristine	Acute lymphoblastic leukemia	Enhanced delivery, increasing maximum tolerated dose [141]	Approved by FDA in 2012
Onivyde	Irinotecan	Pancreatic cancer	Enhanced delivery; Reduced systemic toxicity [142]	Approved by FDA (2015)
MBP-426	Oxaliplatin	Gastric, oesophageal and gastro-oesophageal adenocarcinoma	TfR-targeting liposome [143]	Phase I (Completed; NCT00355888)
ThermoDox	Doxorubicin	Hepatocellular carcinoma	Stimuli-responsive delivery [144]	Phase III (Completed; NCT02112656)
Polymer-based nanotherapeutics				
Pegasys	Interferon alpha-2a	Hepatitis B; Hepatitis C	Increasing the residence time; Improving stability of protein [145]	Approved by FDA (2002)
Genexol-PM	Paclitaxel	Breast cancer and NSCLC	Avoiding toxicities of solvents; Reduced hypersensitivity [146]	Approved in South Korea (2007)
Opaxio	Paclitaxel	Head and neck cancer; Glioblastoma	Responsive release via enzymatic hydrolysis of polyglutamate [147]	Approved by FDA (2012)
Adynovate	PEGylated factor VIII	Hemophilia	Extended half-life [148]	Approved by FDA (2015)
NK012	SN-38	Solid tumor malignancy	Prolonged drug release [149]	Phase II (Completed; NCT00951613; NCT00951054)
NK105	Paclitaxel	Metastatic or recurrent breast cancer	Without solvents; Reduced toxicity [150,151]	Phase III (Completed; NCT01644890)
Protein-based nanotherapeutics				
Ontak	Interleukin-2 receptor and diphtheria toxin	Cutaneous T-Cell lymphoma	Cytokine-targeted fusion protein [154]	Approved by FDA (1999)
Abraxane	Paclitaxel	Breast cancer; NSCLC	Avoiding toxicities of solvents; Enhanced delivery to tumor [109]	Approved by FDA (2005)
Kadcyla	Trastuzumab Emtansine	Metastatic breast cancer	Enhanced delivery [155]	Approved by FDA (2013)
Nab-paclitaxel	paclitaxel	Pancreatic cancer; Cholangiocarcinoma	Expand the approved indications for Abraxane [1]	Phase II (Completed; NCT02077881; NCT02382263; NCT02181634)
Inorganic nanoparticles				
Feridex	Iron oxide NPs	MRI contrast agent	Superparamagnetic character [156]	Approved by FDA (1996)
Feraheme	Iron oxide NPs	Iron deficiency anemia in chronic kidney disease	More stable release, improved safety profile [157]	Approved by FDA (2009)
Nanotherm	Iron oxide	Glioblastoma	Activated by an external magnetic field [129]	Approved in Europe (2010)
NBTXR3	Hafnium oxide NPs	Adult soft tissue sarcoma	Absorption or deposition of a high energy dose [158]	Approved in Europe (2019)
CYT-6091	Tumor necrosis factor	Advanced solid tumors	Reduced toxicity; Improved drug delivery [131]	Phase I (Completed; NCT003569

Nano Today 35 (2020) 101008

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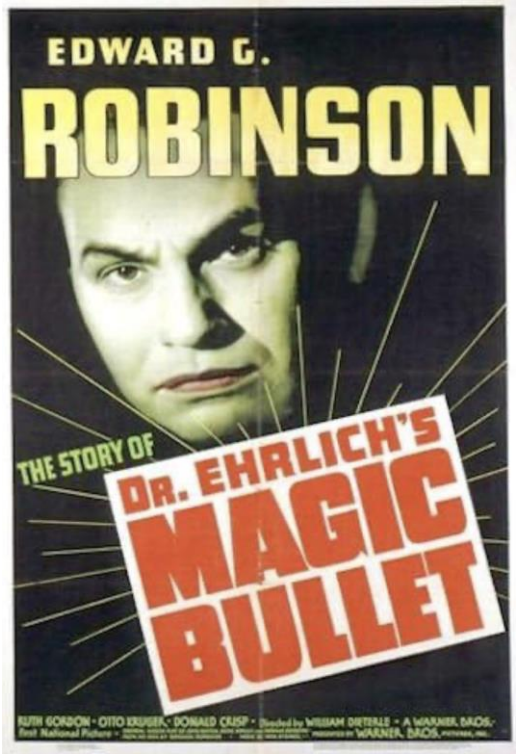
Nanotechnologies et vectorisation de médicaments (DDS)

Des travaux pionniers aux promesses les plus récentes

Les travaux pionniers de la nanomédecine

Le concept de “Magic Bullet” de Paul Ehlrich

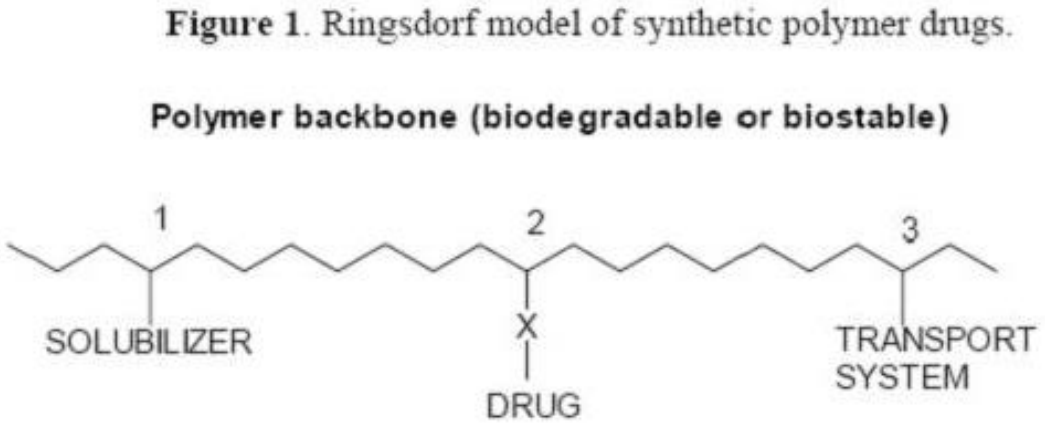
Prix Nobel de Médecine en 1908 « en reconnaissance de ses travaux sur l'immunité »



Les travaux pionniers de la nanomédecine

Origine de l'idée conceptuelle d'utiliser un polymère pour stabiliser, solubiliser, améliorer les propriétés d'un médicament

Dans les années 1970, Ringsdorf a proposé le concept d'un **transporteur polymère pharmacologiquement actif**, capable à la fois de solubiliser et de cibler un médicament. Par la suite, les travaux de Kopeček, Duncan et autres à la fin des années 1970 ont conduit au développement du **premier conjugué polymère-médicament à petite molécule** ayant atteint les essais cliniques, ouvrant la voie à de nombreux autres développements.



Ringsdorf, H. Structure and properties of pharmacologically active polymers. J. Polym. Sci., Symp. 1975, 51, 135-153

Un pionnier de la nanomédecine, Patrick Couvreur

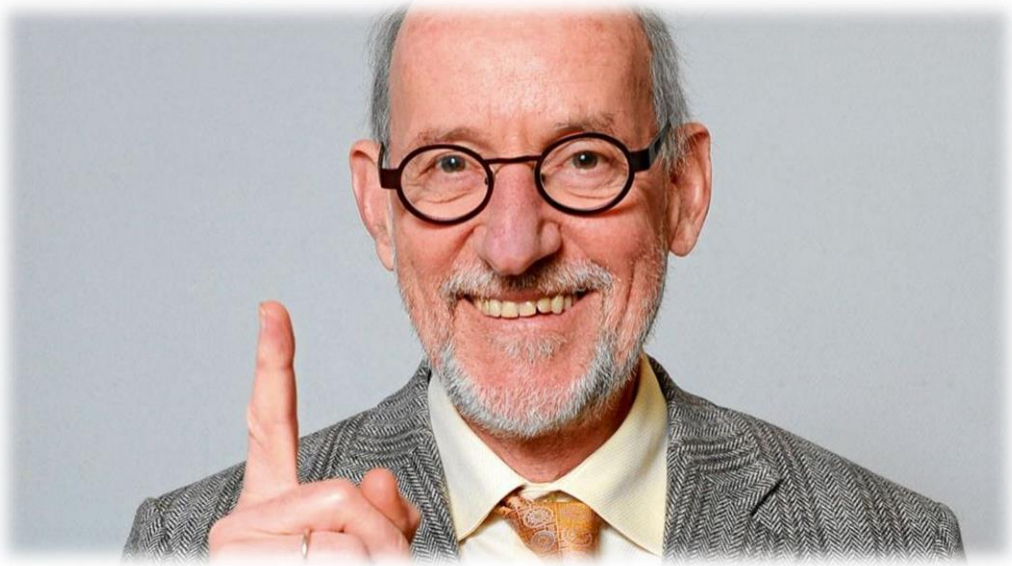
Première démonstration que des particules de taille nanométrique peuvent transporter des médicaments qui ne pénètrent normalement pas spontanément dans les cellules

Volume 84, number 2 FEBS LETTERS December 1977

NANOCAPSULES: A NEW TYPE OF LYSOSOMOTROPIC CARRIER

P. COUVREUR[+], P. TULKENS[‡], M. ROLAND[+], A. TROUET[‡] and P. SPEISER*

[+]*Laboratoire de Pharmacie Galénique, Université Catholique de Louvain, B-1200 Brussels,* [‡]*Laboratoire de Chimie Physiologique, Université Catholique de Louvain, and International Institute of Cellular and Molecular Pathology, B-1200 Brussels, Belgium* and **Pharmazeutische Institut, Eidgenössische Technische Hochschule, Zürich, Switzerland*



Premier article sur les nanoparticules de polyalkylcyanoacrylates

J. Pharm. Pharmacol. 1979, 31: 331

COMMUNICATIONS

Polycyanoacrylate nanocapsules as potential lysosomotropic carriers: preparation, morphological and sorptive properties

P. COUVREUR*§, B. KANTE*, M. ROLAND*, P. GUIOT†, P. BAUDUIN†, P. SPEISER‡, * *Laboratoire de Pharmacie Galénique, Université Catholique de Louvain, B-1200 Bruxelles Belgium.* † *Laboratoire de Chimie Physiologique, Université Catholique de Louvain and International Institute of Cellular and Molecular Pathology, B-1200 Bruxelles, Belgium.* ‡ *Pharmazeutische Institut, Eidgenössische Technische Hochschule, CH-Zürich, Switzerland.*

Les nanomédecines à base de polypeptides

Macromolecular Chemistry and Physics

Article

Adhesion behavior of rat lymphocytes on poly(γ-benzyl L-glutamate) derivatives having hydroxyl groups or poly(ethylene glycol) chains

Takao Nishimura, Yuichi Sato, Masayuki
Kazunori Kataoka, Teruo Okano, Yasuhis

1984

Macromolecular Rapid Communications

Article

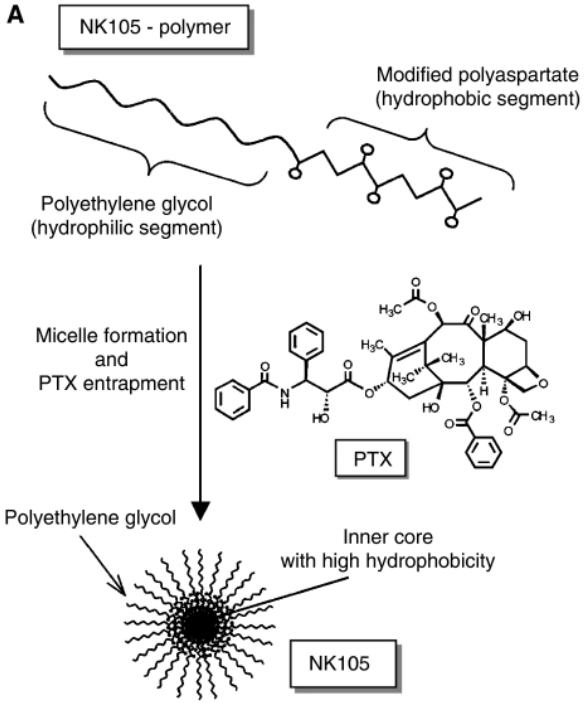
Preparation of adriamycin-conjugated poly(ethylene glycol)-poly(aspartic acid) block copolymer. A new type of polymeric anticancer agent

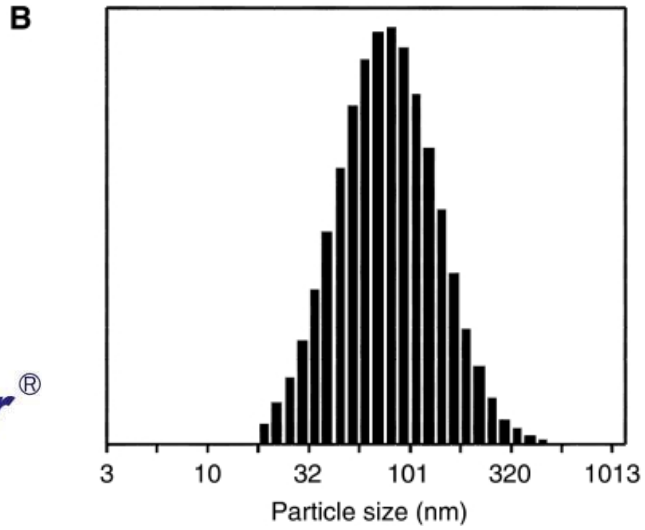
Masayuki Yokoyama, Shohei Inoue, Kazunori Kataoka, Nobuhiko Yui, Yasuhisa Sakurai

1987

Kazunori Kataoka
Tokyo Univ. Japan

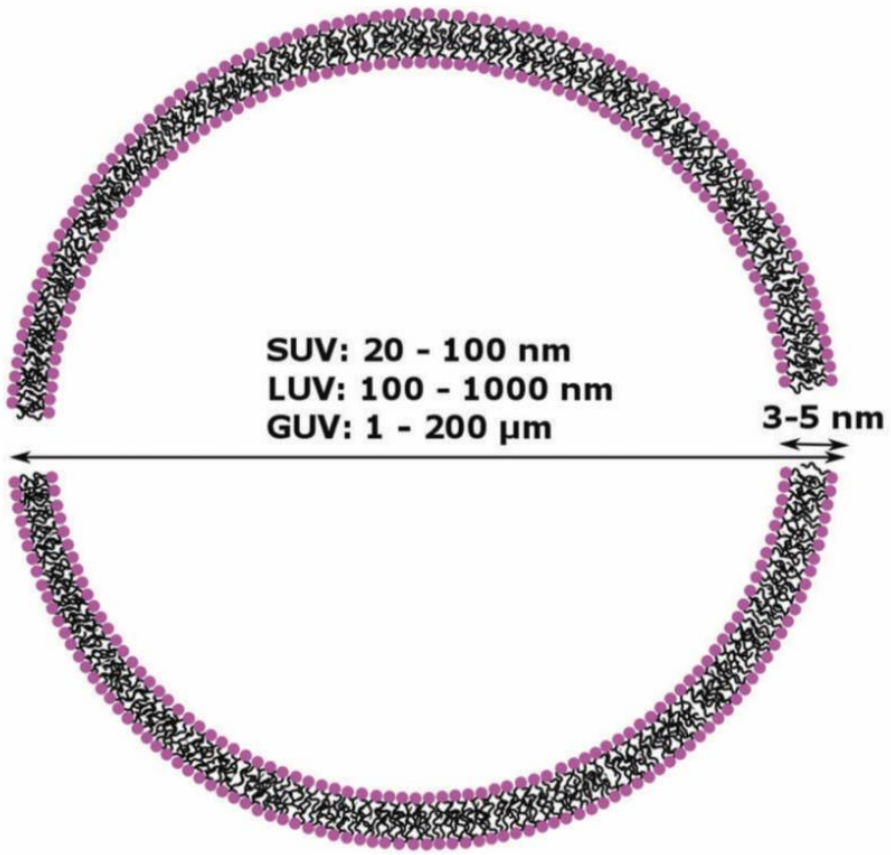
NanoCarrier®





Le cas particulier des « vésicules »

La découverte des liposomes



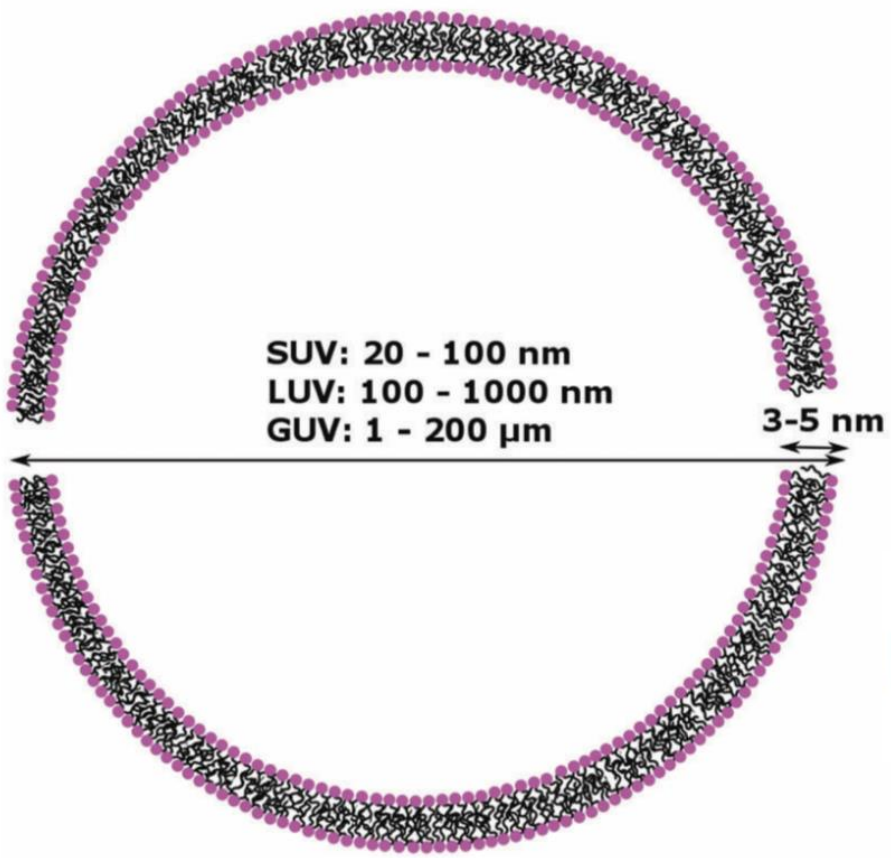
liposome 1965

Alec Bangham et al. J. Mol. Biol. ***1965****, 13, 238–252*

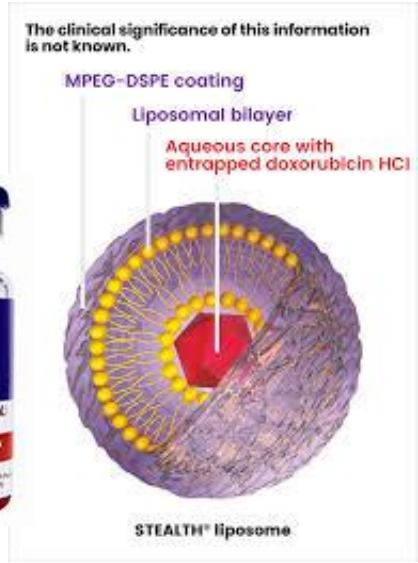
Prof. Alec Bangham (1921-2010)

E. Rideau et al. Chem Soc. Rev 2018

La découverte des liposomes



Approval of Doxil



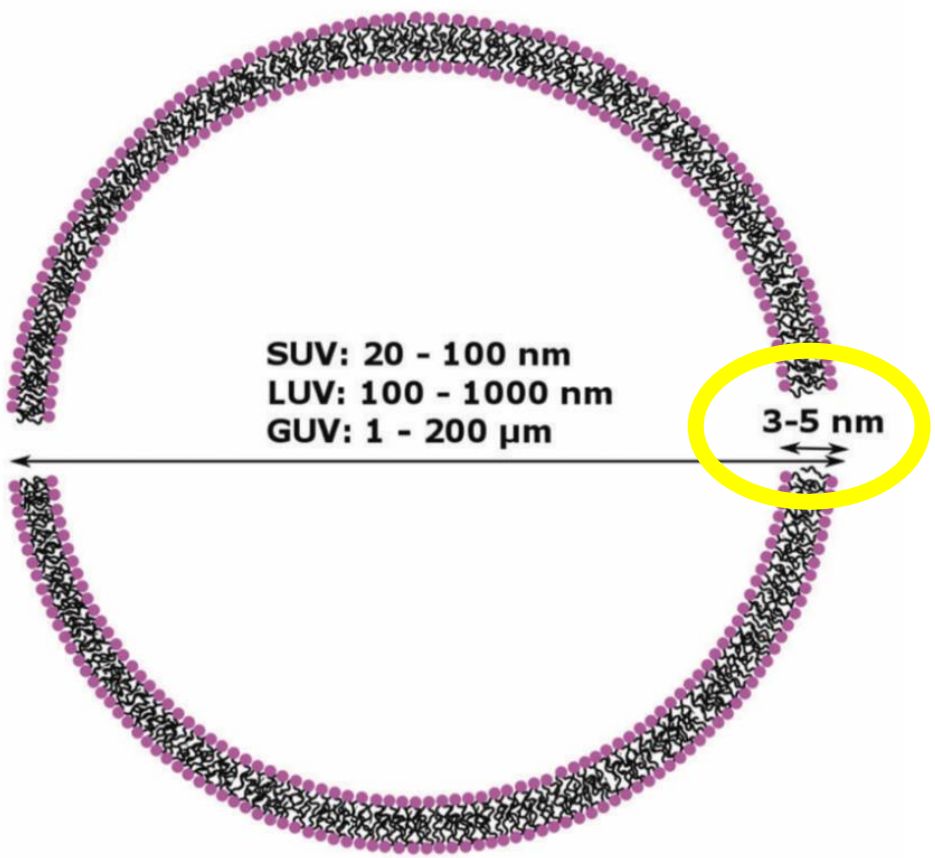
liposome 1965 ----------> **1995**

Alec Bangham et al. J. Mol. Biol. ***1965****, 13, 238–252*

E. Rideau et al. Chem Soc. Rev 2018

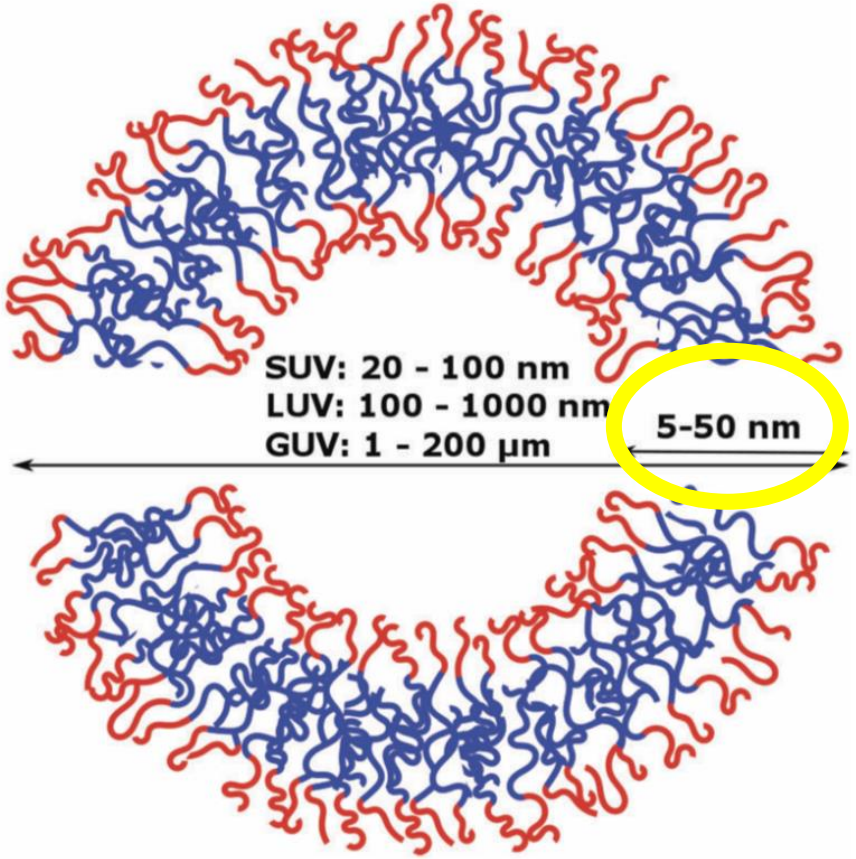
COLLÈGE DE FRANCE 1530

La découverte des liposomes



liposome 1965

Alec Bangham et al. J. Mol. Biol. ***1965****, 13, 238–252*



Polymer vesicle 1995

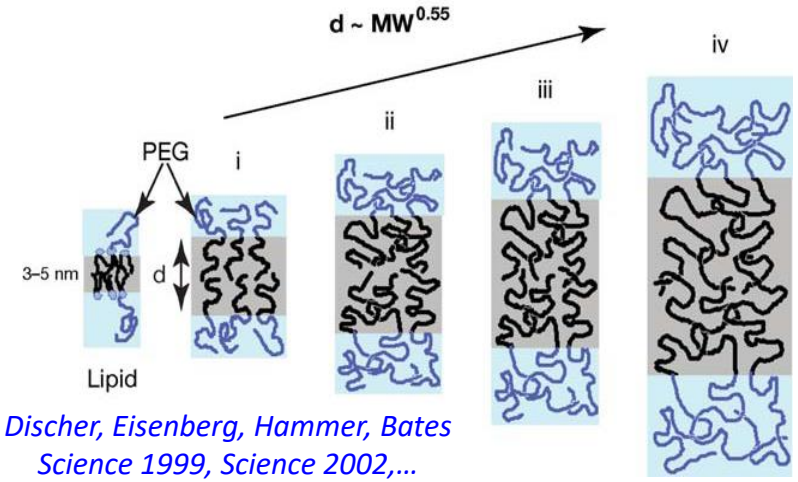
Eisenberg et al. Science ***1995****, 268, 1728-1731*
Meijer et al. Science ***1995****, 268, 1592–1595*

Polymersomes *Discher et al. Science* ***1999****, 284, 1143–1146*

E. Rideau et al. Chem Soc. Rev 2018

L'intérêt spécifique des polymersomes

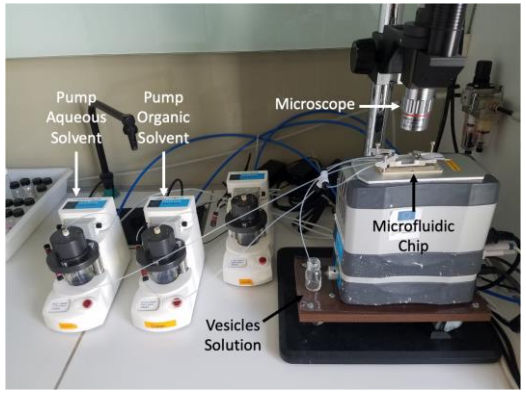
Propriétés contrôlées par l'épaisseur de la membrane

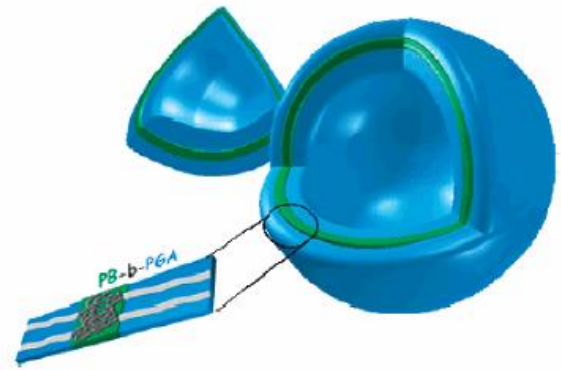


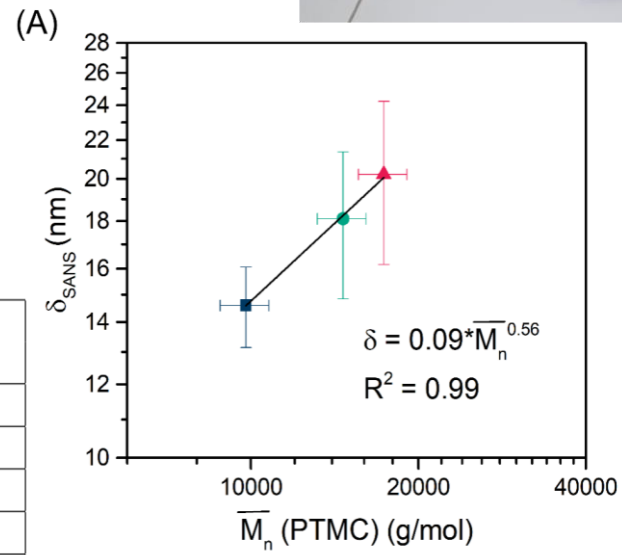
Discher, Eisenberg, Hammer, Bates Science 1999, Science 2002,…

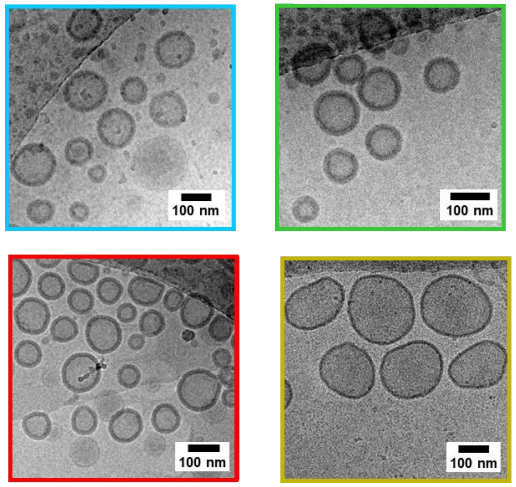
	Scaling with membrane thickness
Bending modulus (kT)	$d^{\sim 2}$ [38]
Stretching modulus (mN/m)	$d^{\sim 0}$ [36]
Lysis strain (%)	$d^{\sim 0.6}$ [36] (for $M < M_c$)
Membrane surface shear viscosity (mN/ms)	-
Membrane thickness (nm)	$M^{\sim 0.55}$ [36,49] or $M^{\sim 0.66}$ [50]
Water permeability (μm/s)	$d^{\sim -1}$ [52]
Lateral diffusion coefficient ($\mu m^2/s$)	Rouse scaling

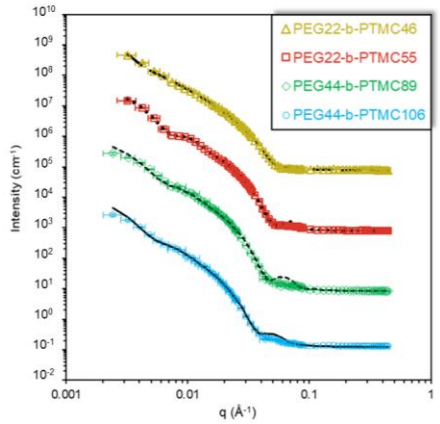
JF Le Meins et al. Eur. Phys. J. E 34, 14 (2011)









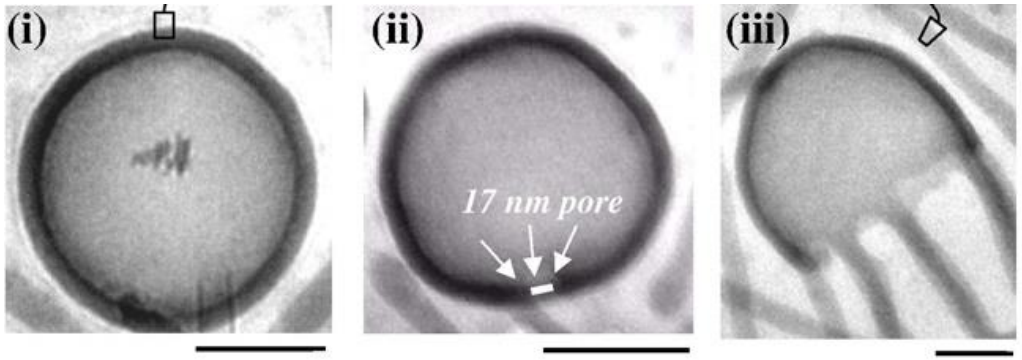


C. Lebleu et al. Langmuir **2019**, *35, 41, 13364-13374*
A. Martin et al. Int. J. Pharm. **2023**, *642, 123157*

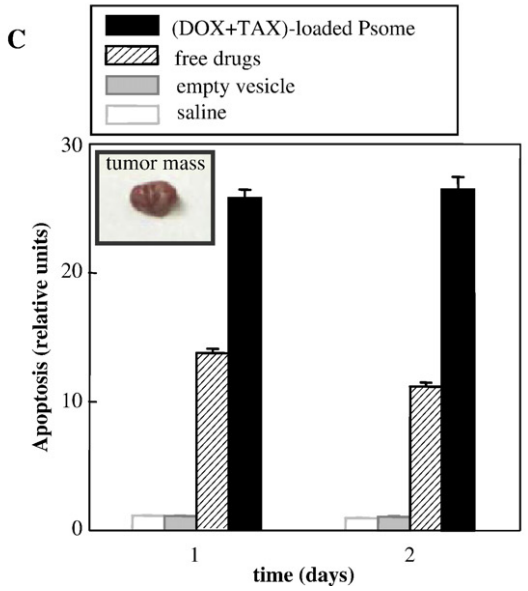
Lois d'échelles de la physique des polymères (générales) + spécificité de la chimie

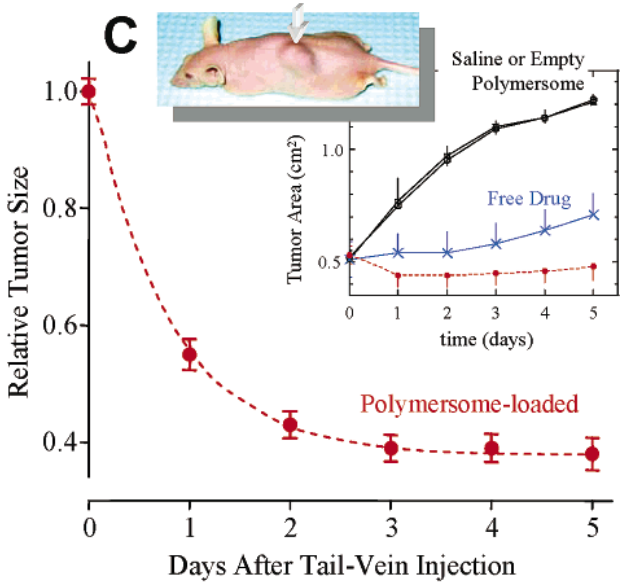
Capacité unique d'encapsulation des polymersomes

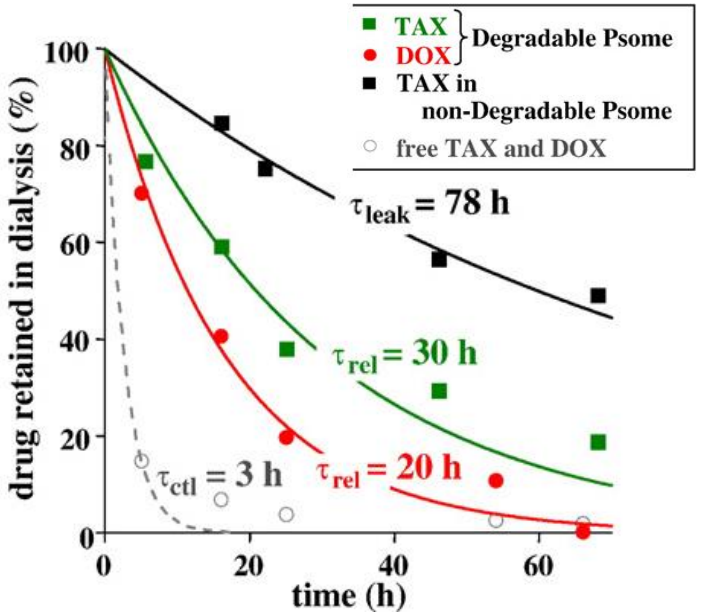
Double encapsulation de doxorubicine (DOX) and de taxol (TAX) dans despolymersomes biodégradables



PLA-*b*-PEG polymersome degradation in neutral buffer (37° C)







"cocktail" thérapeutique

Discher *et al.* Journal of Controlled Release 116 (2006) 150–158

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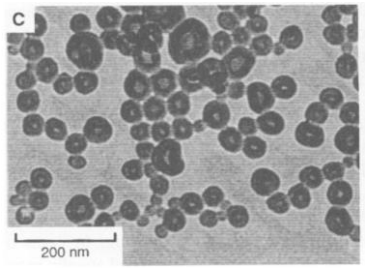
Les polymersomes: une nanotechnologie encore émergente et pleine de promesses

L'histoire des polymersomes



Eisenberg Science 1995
Meijer Science 1995

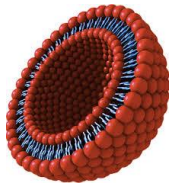
1st polymersome observation

1995

1965

liposomes

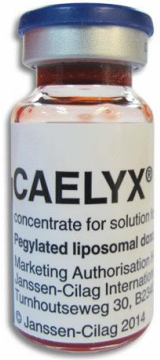
Bangham et al.
J. Mol. Biol. ***1965****, 13, 238–252*



1995

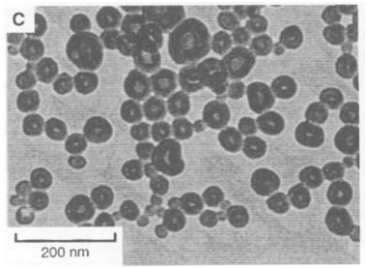
Approval of Doxil

janssen
PHARMACEUTICAL COMPANIES OF Johnson&Johnson



Nowadays, 15 formulations on the market in medicine

L'histoire des polymersomes



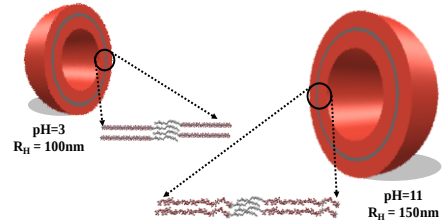
Eisenberg Science 1995
Meijer Science 1995

1st polymersome observation

1995

PB-*b*-PGA dibloc

Lecommandoux
Angew. Chem. 41, 1339 (2002)
Schlaad, JACS 124, 1658 (2002)

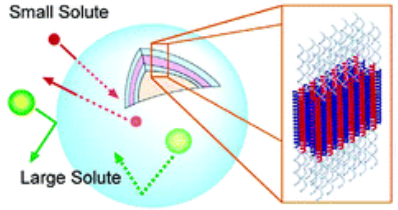


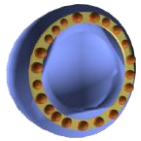
Polypeptide-based pH-responsive

2002

Kataoka
JACS (2006) 128, 5988

PLys-*b*-PEO/PGA-*b*-PEO dibloc





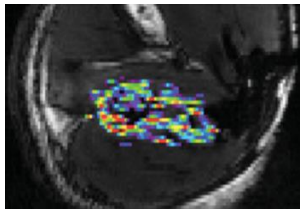
2005

2006

PTMC-*b*-PGA dibloc

Lecommandoux
Advanced Materials 17, 712 (2005)
J. Control. Rel. 147, 428 (2010)
ACS Nano 5, 1122 (2011)

Magnetic & Theranostic



2010

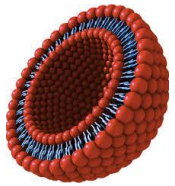
2020

2024

1965

liposomes

Bangham et al.
*J. Mol. Biol. **1965**, 13, 238–252*

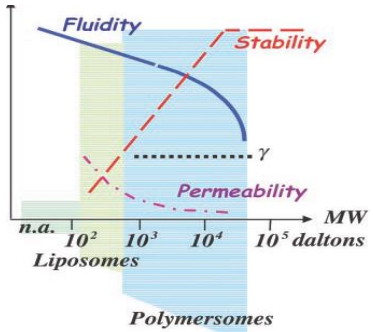


PB-*b*-PEO dibloc

1999 - 2002

Elucidation of scaling laws

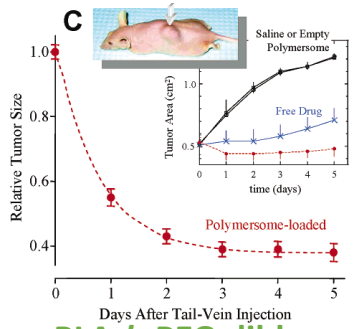
Dischер, Eisenberg, Hammer
Science (1999) 284, 1143
Science (2002) 297, 967



2006

Cocktail therapy

Dischер
J. Control. Rel. 116 (2006) 150–158

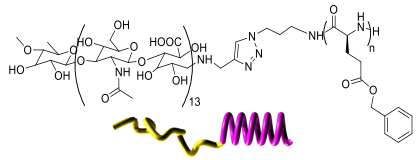


PLA-*b*-PEO dibloc

2009

Glycopeptosome

Lecommandoux
Angew. Chem. (2009) 48, 2572



HA-*b*-PBLG dibloc

ADOCIA
innovative medicine for everyone, everywhere

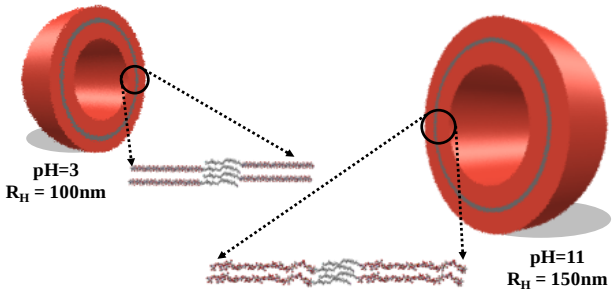
BOOM!

ViaNautis
TARGETED NANOMEDICINES

doxanano
remotely activated chemotherapy

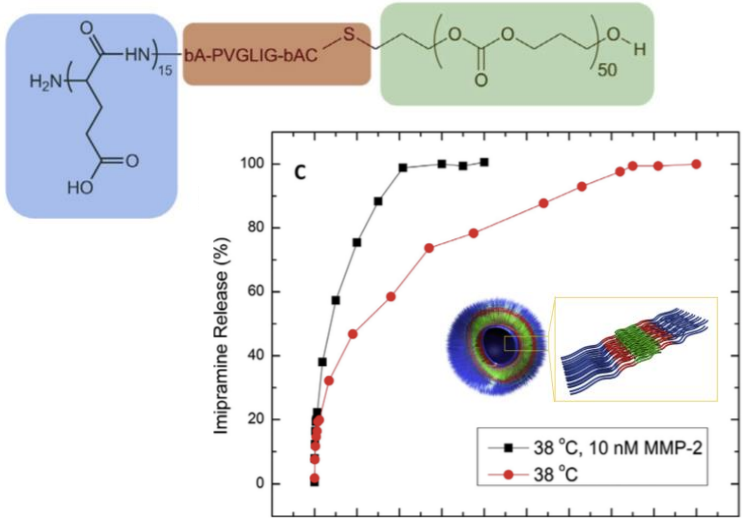
Les polymersomes à base de polypeptides

Les polymersomes à base de polypeptides



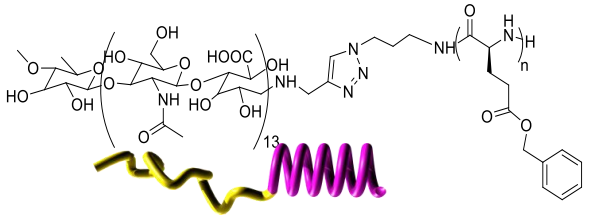
Répondant au pH

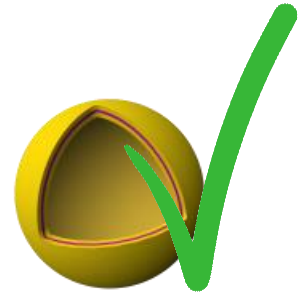
Angew. Chem. 2002



Répondant aux enzymes (MMP2)

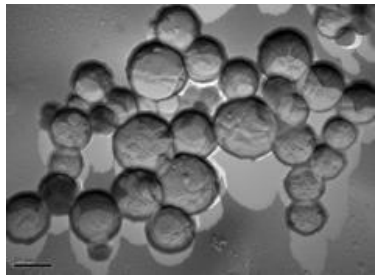
Biomacromolecules 2014; *Eur. Polym. J.* 2015

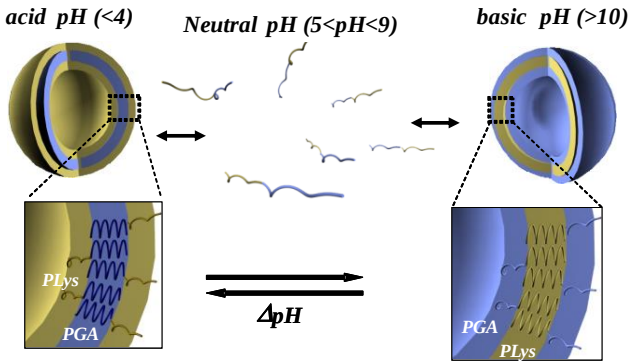




Polymersomes "auto-ciblants"

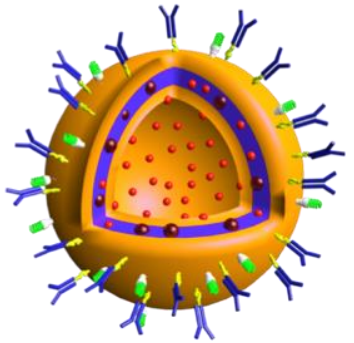
Angew. Chem. 2009
Biomacromolecules 2009
Patent FR 2009/001263
WO 2010/049611 A1

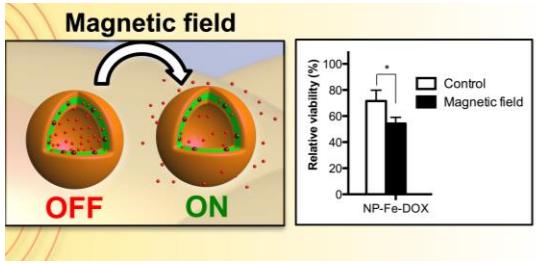




Répondant doublement au pH (Schizophrène)

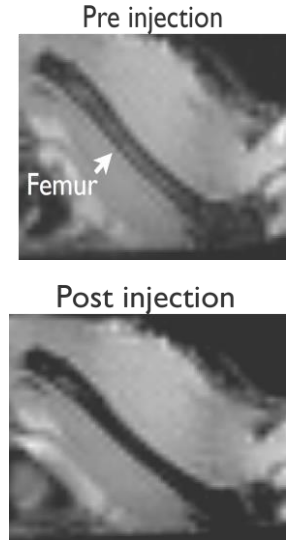
JACS 2005



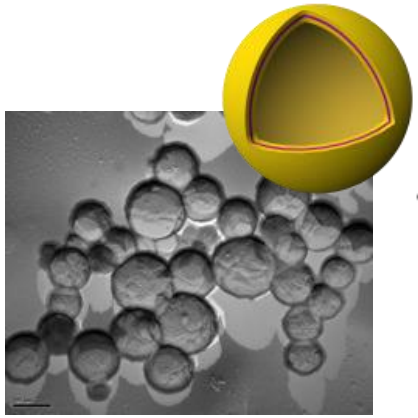


Répondant au champ magnétique et ciblant les tumeurs

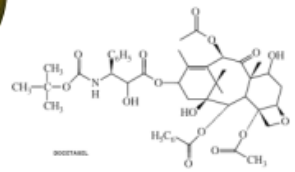
Advanced Materials 2005; ACS Nano 2011; Contr. Rel. 2013; Adv. Health. Mater. 2013



Les polymersomes à base de polypeptides

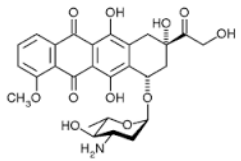


Docetaxel



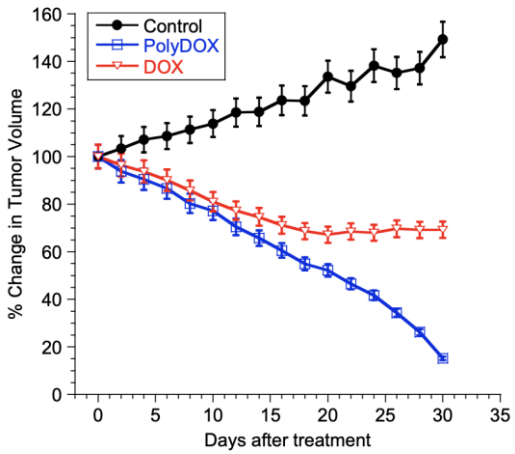
R_H=130nm
loading=11wt%

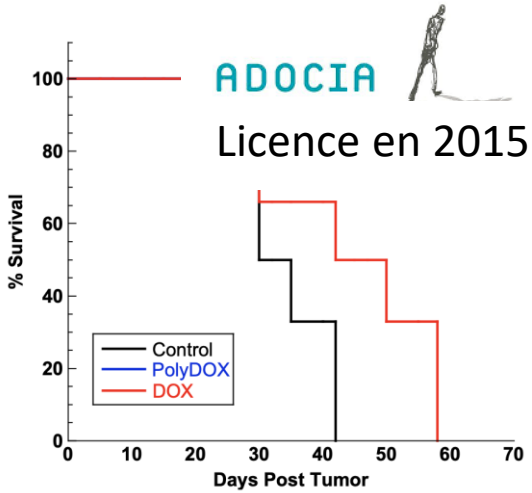
Doxorubicin



R_H=200nm
loading=12wt%

Capacité de double encapsulation

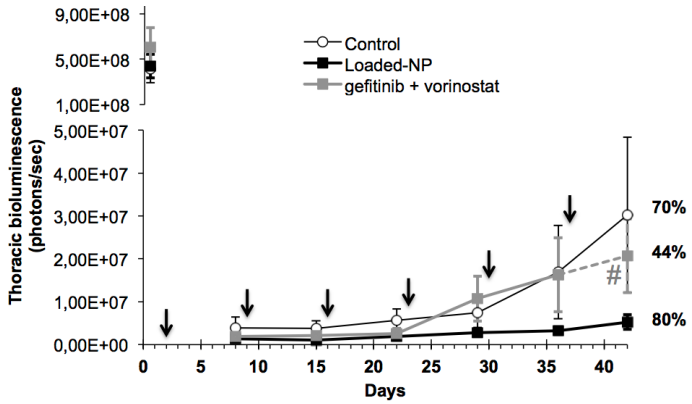




Régression tumorale (sein) et diminution de toxicité

iAB

J.L. Coll
A. Hurbin



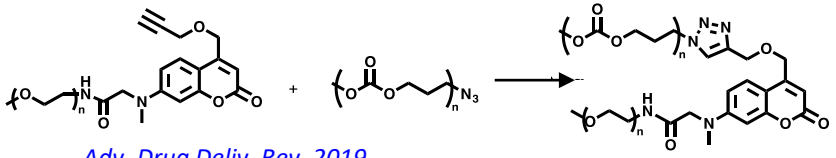
Cocktail thérapeutique et efficacité (poumon)

J. Control. Release 2018

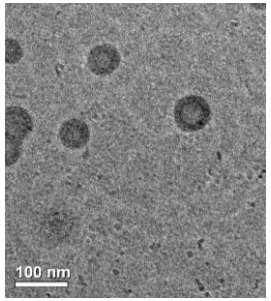
LCPO Laboratoire de Chimie des Polymères Organiques

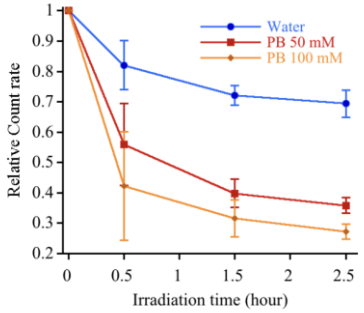
Les polymersomes de seconde génération

Innover plus simplement



Adv. Drug Deliv. Rev. 2019

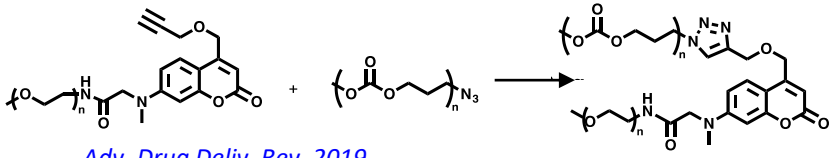




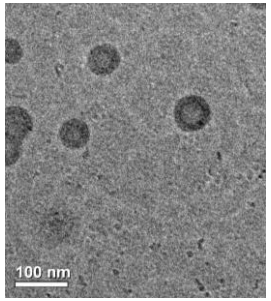
Clivables par la lumière

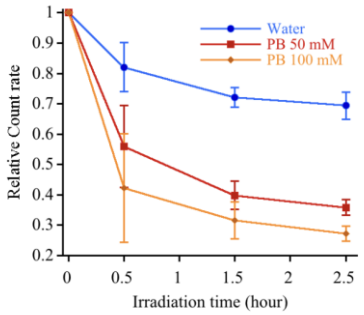
Les polymersomes de seconde génération

Innover plus simplement… avec un control spatio-temporel

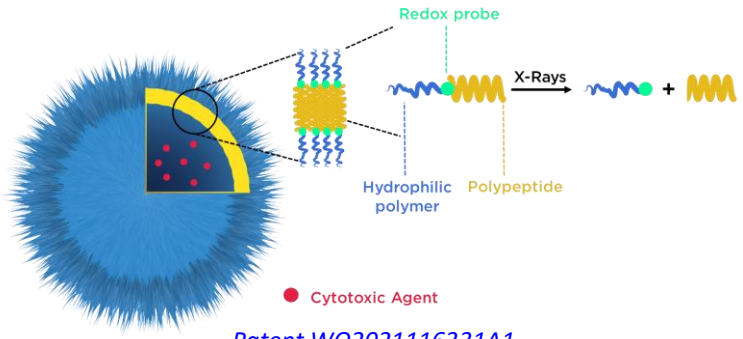


Adv. Drug Deliv. Rev. 2019

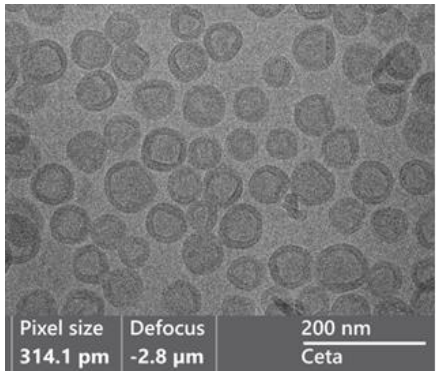




Clivables par la lumière



Patent WO2021116331A1

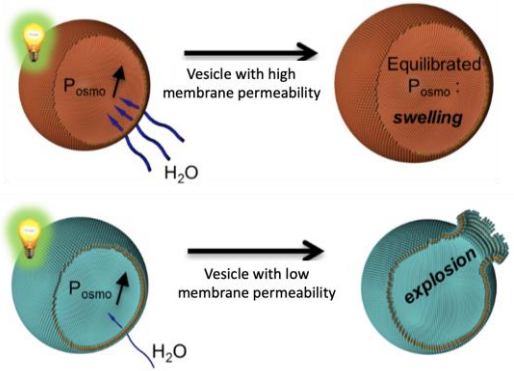


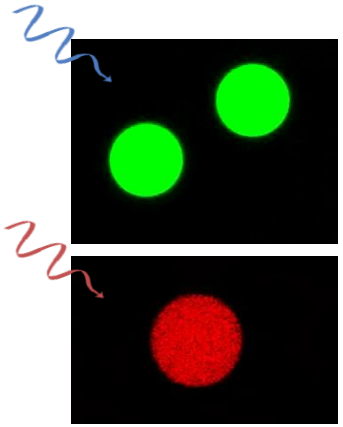
Clivables par les Rayons-X

doxanano
remotely activated chemotherapy

Licence en 2024

Explosion sous lumière





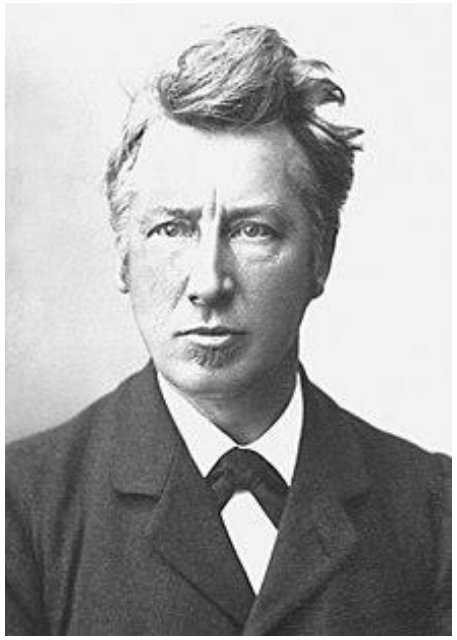
Isabel Marey-Semper

Angew. Chem. 2017; Langmuir 2019

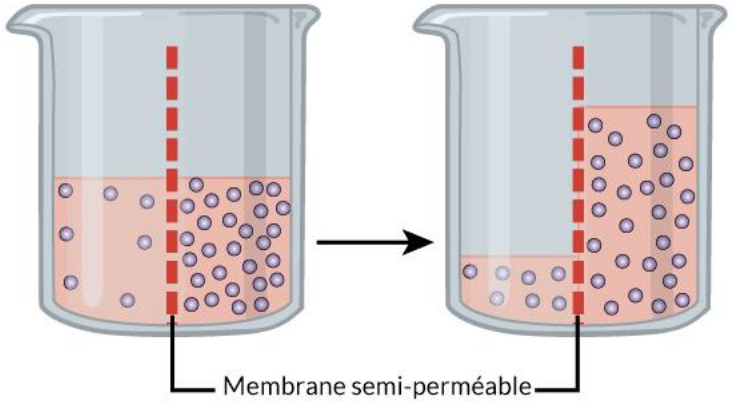
LCPO Laboratoire de Chimie des Polymères Organiques

L'effet de la pression osmotique

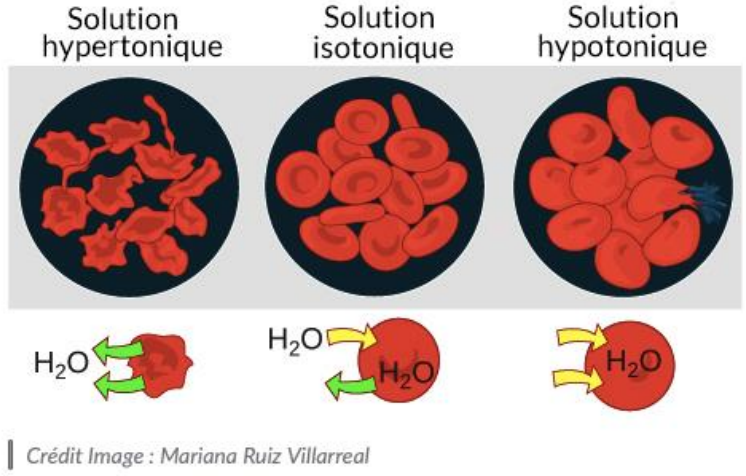
Abbé Nollet (1748)



van 't Hoff, prix Nobel de Chimie en 1901 « pour la dynamique chimie et la pression osmotique »

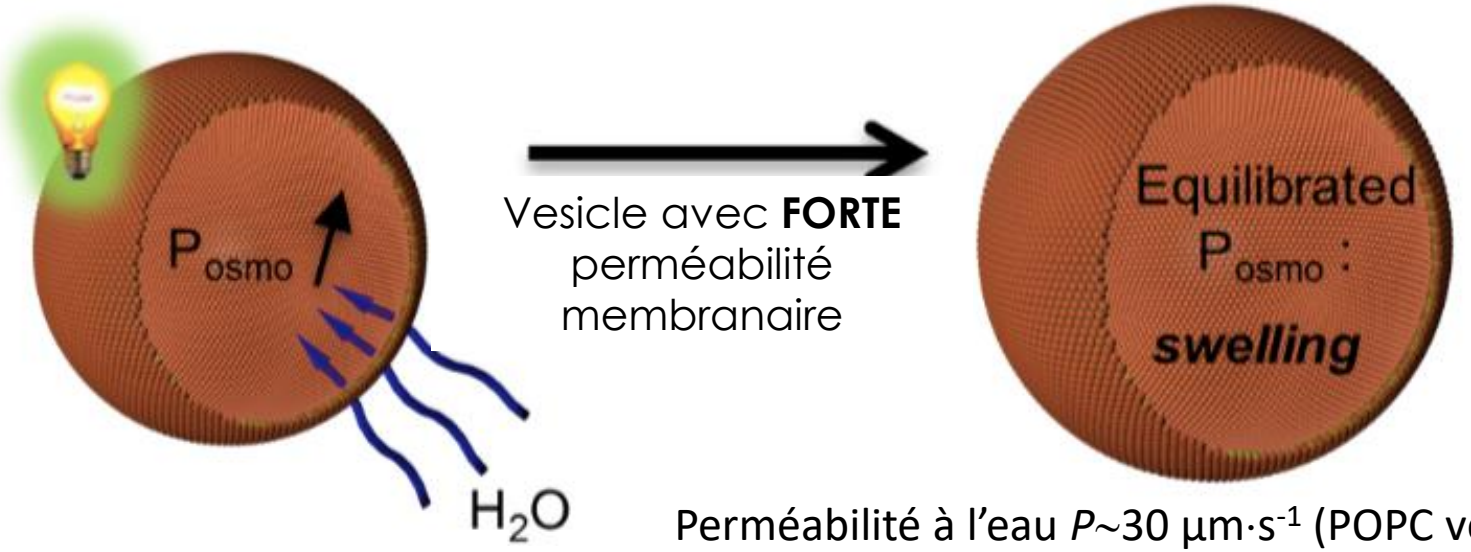


Π = C.R.T (en Pa) C en mol/m^3

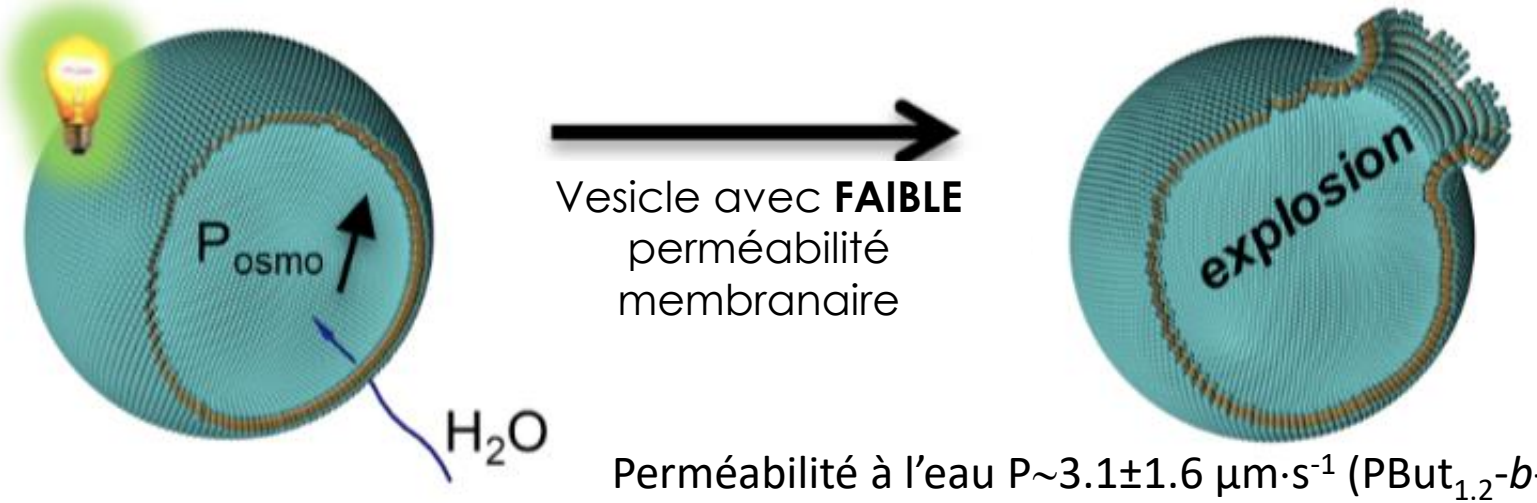


Crédit Image : Mariana Ruiz Villarreal

L'effet de la pression osmotique



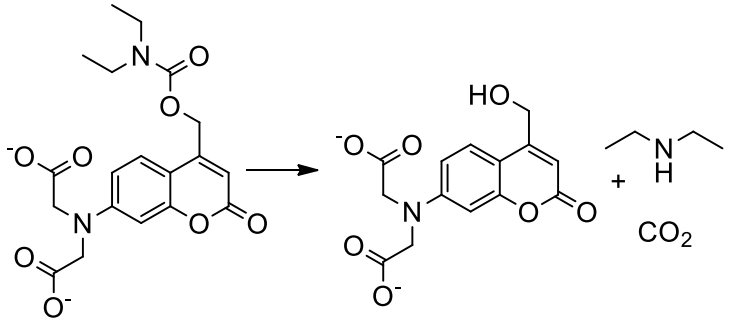
Perméabilité à l'eau P~30 µm·s^{-1} (POPC vesicles)[1]



Perméabilité à l'eau P~3.1±1.6 µm·s^{-1} (PBut$_{1.2}$-*b*-PEO$_{0.6}$)[2]

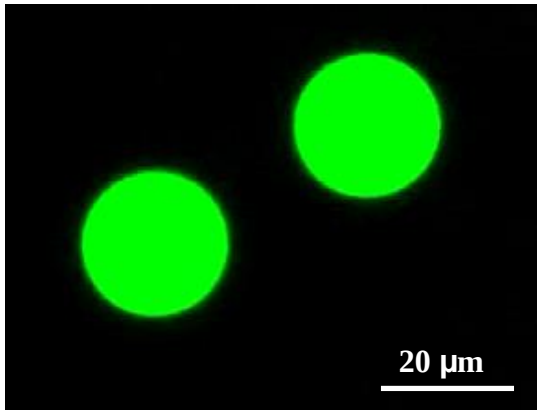
1. Olbrich, K. et al. *Biophys. J.* **79,** 321–327 (2000).
2. Carlsen, A. et al. *Langmuir* **27,** 4884–4890 (2011)

L'effet de la pression osmotique

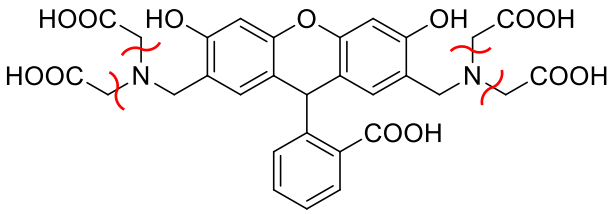


λ_{exc} = 405 nm

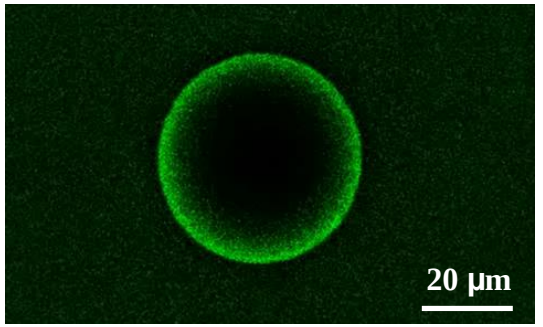
Coumarin derivative



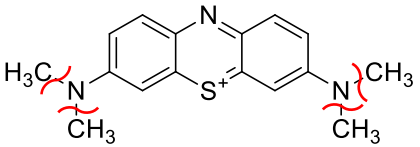
λ_{exc} = 488 nm



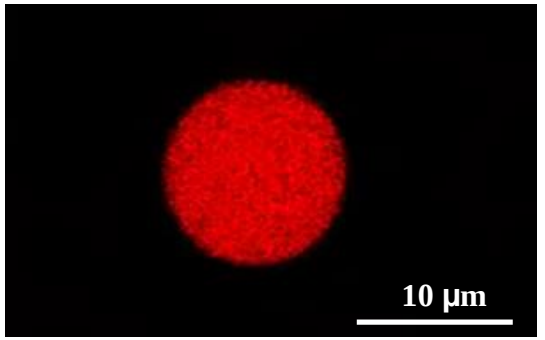
Calcein



λ_{exc} = 633 nm

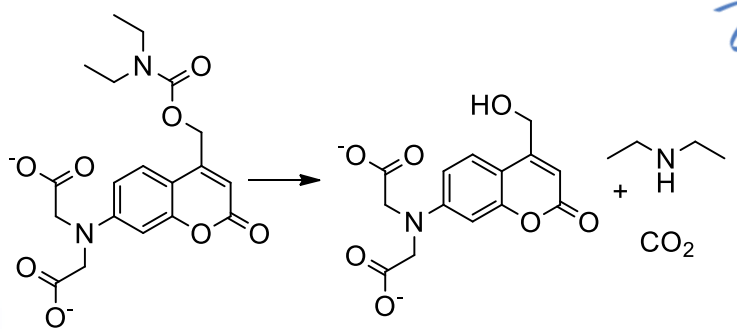


Methylene blue



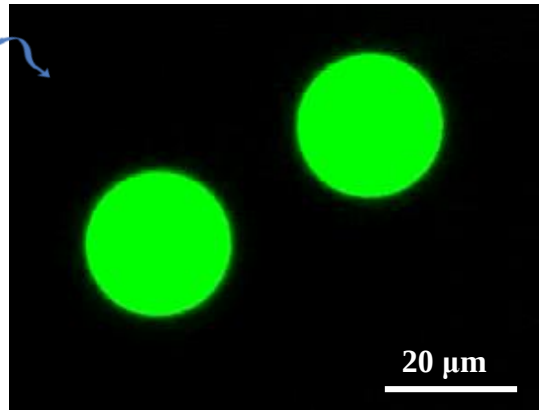
A. Peyret et al. Angew. Chem. Int. Ed. 2017, 56, 1566 –1570

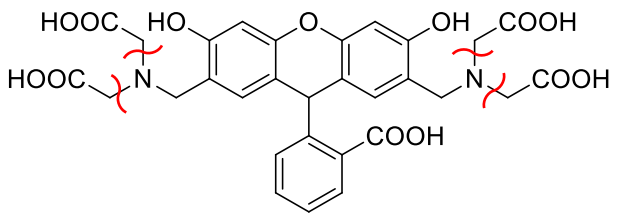
L'effet de la pression osmotique



Coumarin derivative

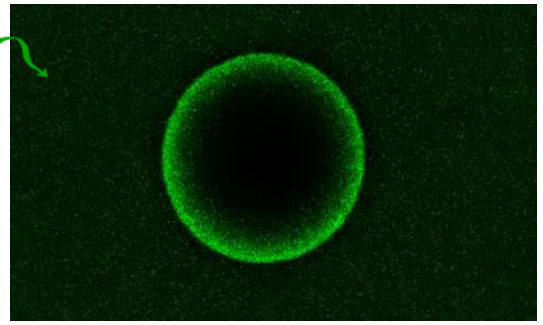
λ_{exc} = 405 nm

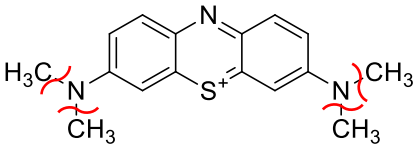




Calcein

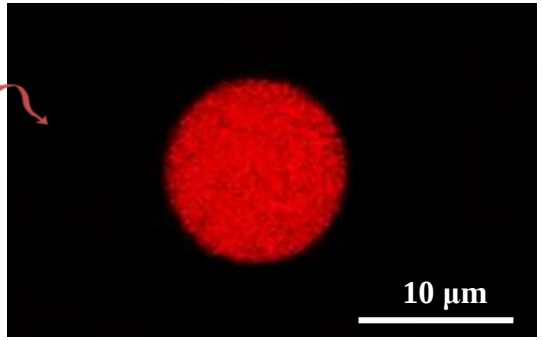
λ_{exc} = 488 nm





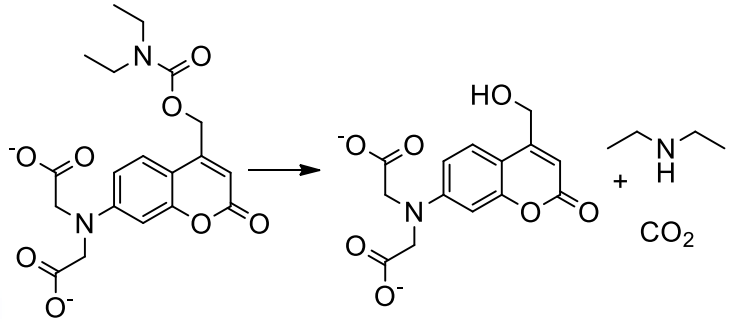
Methylene blue

λ_{exc} = 633 nm



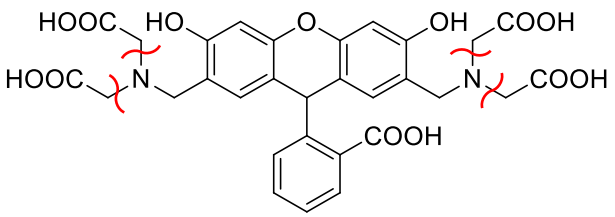
A. Peyret et al. Angew. Chem. Int. Ed. 2017, 56, 1566 –1570

L'effet de la pression osmotique



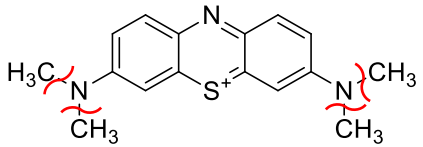
λ_{exc} = 405 nm

Coumarin derivative



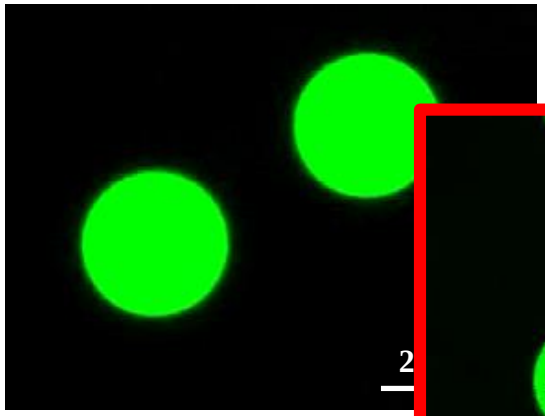
λ_{exc} = 488 nm

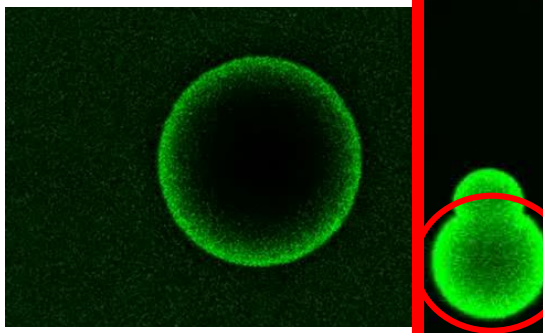
Calcein

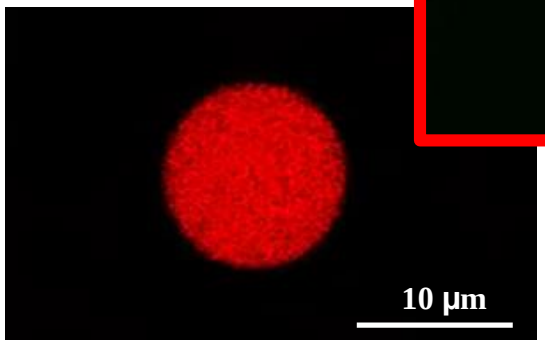


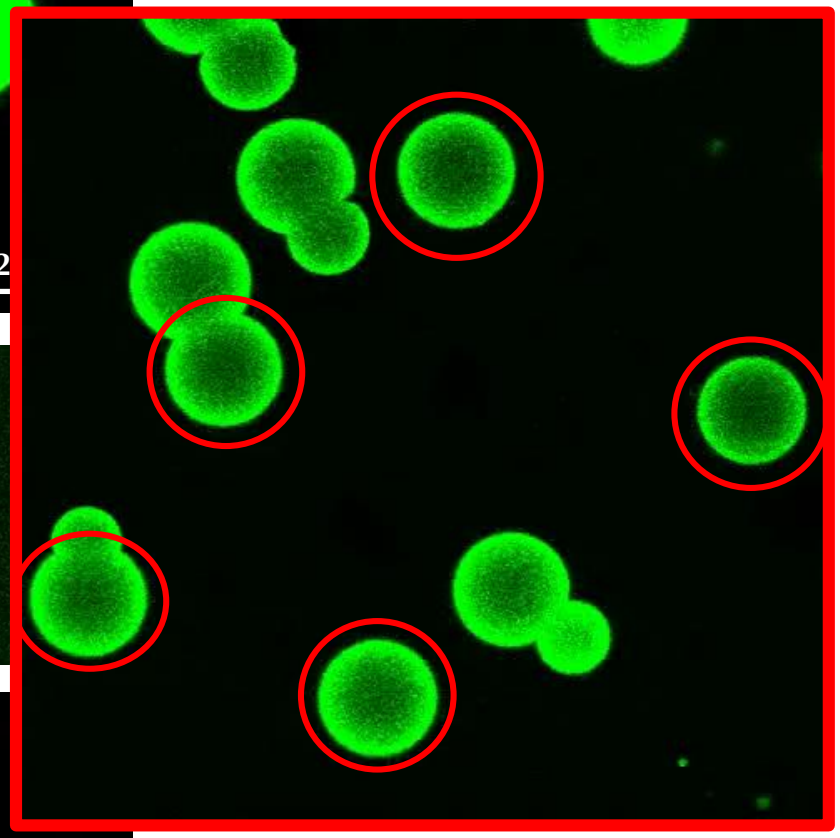
λ_{exc} = 633 nm

Methylene blue





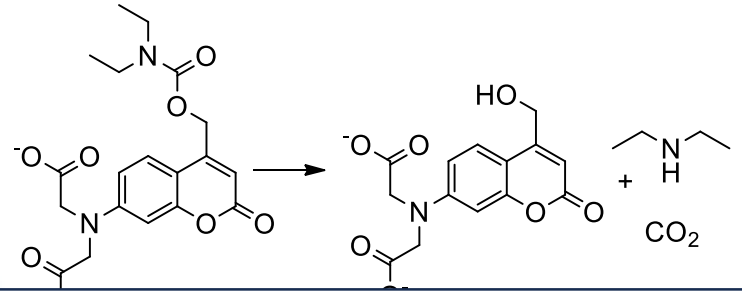


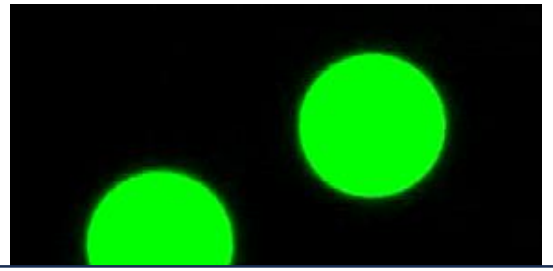


Rupture sélective des vésicules dans le temps, l'espace (et en longueur d'onde)

A. Peyret et al. Angew. Chem. Int. Ed. 2017, 56, 1566 –1570

L'effet de la pression osmotique





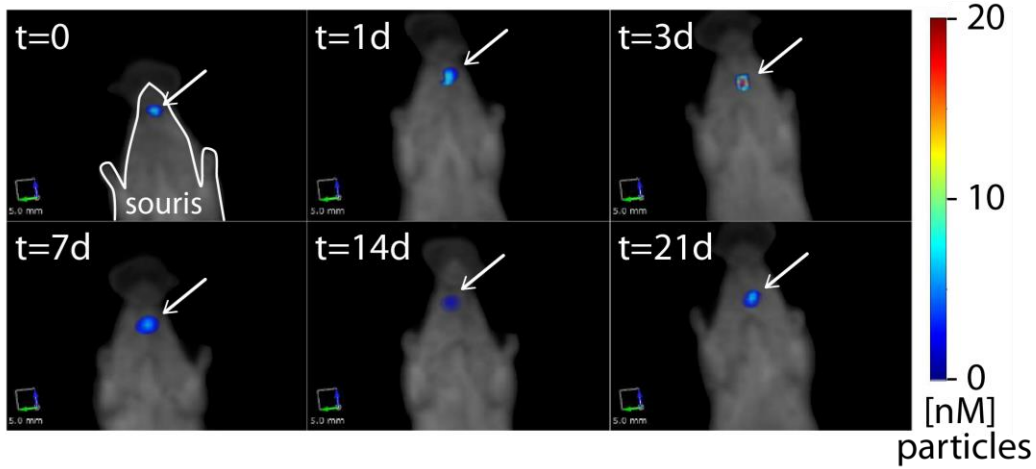
Coumarin	Thiocoumarin	NBD	Calcein	Rhodamine B	Squarine
λ_{max} = 357nm	λ_{max} = 435nm	λ_{max} = 460nm	λ_{max} = 490nm	λ_{max} = 560nm	λ_{max} = 704nm

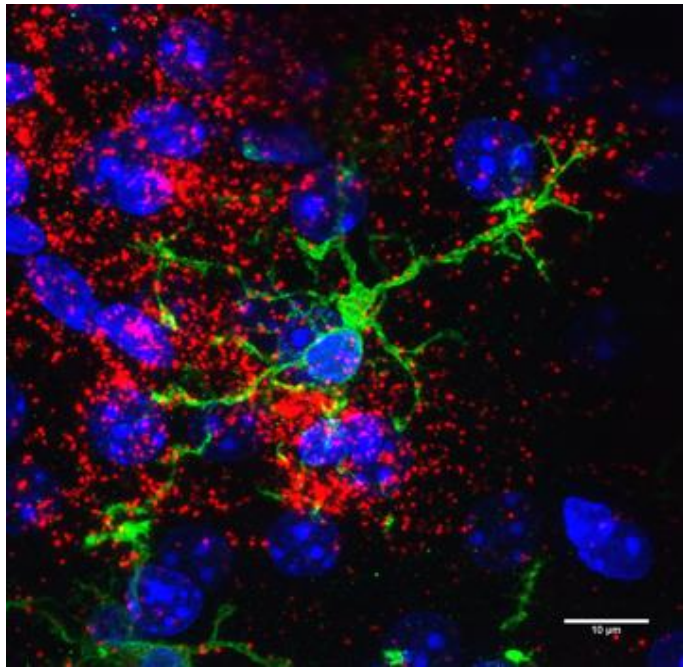
N. McClenaghan
(ISM Bordeaux)

A. Peyret et al. Angew. Chem. Int. Ed. 2017, 56, 1566 –1570

Prochain challenge: activation dans le cerveau

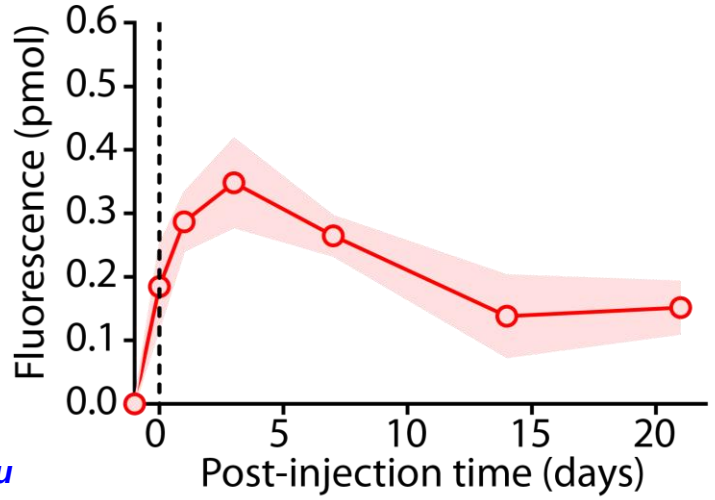
Imagerie *in vivo* imaging des nanoparticules dans le striatum

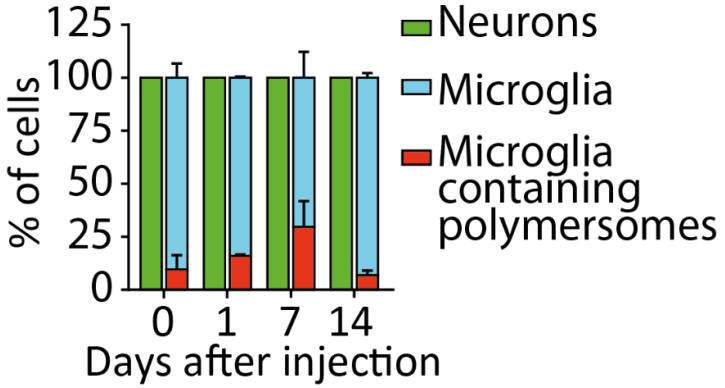




C. Bosch-Bouju (NutriNeuro)

Camille Ruffier





Collaboration with C. Bosch-Bouju (NutriNeuro), Camille Ruffier PhD

Nouvelles opportunités en opto-neurotechnologie

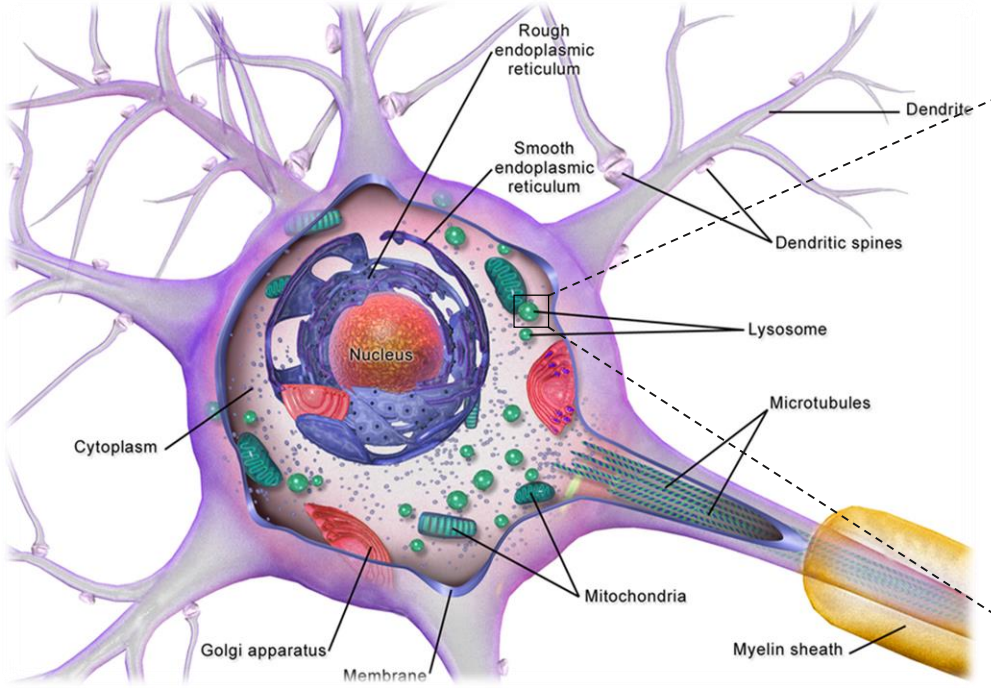
COLLÈGE DE FRANCE 1530

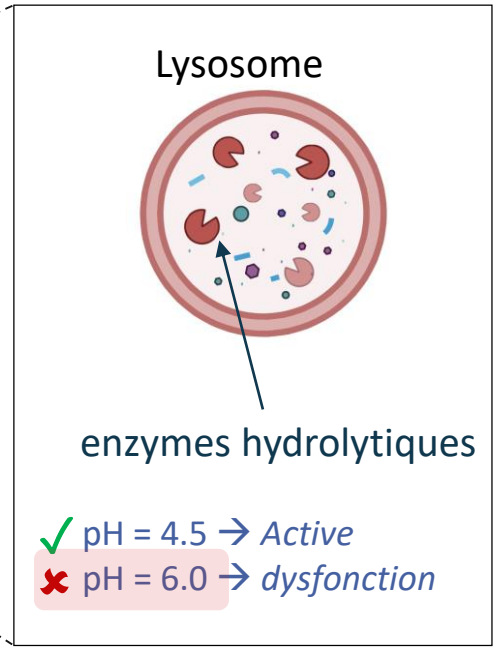
Prochains enjeux des polymersomes en neurosciences

Prochains enjeux des polymersomes en neurosciences

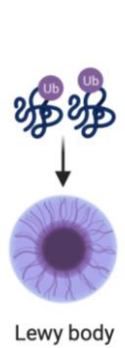
Maladie de Parkinson : maladie neurodégénérative liée à un dérèglement de l'activité des lysosomes

Neurones dopaminergiques





Défaillance de la voie autophagique-lysosomale dans les neurones dopaminergiques



Aggregation des protéines α-synucléines

Neurodégénération

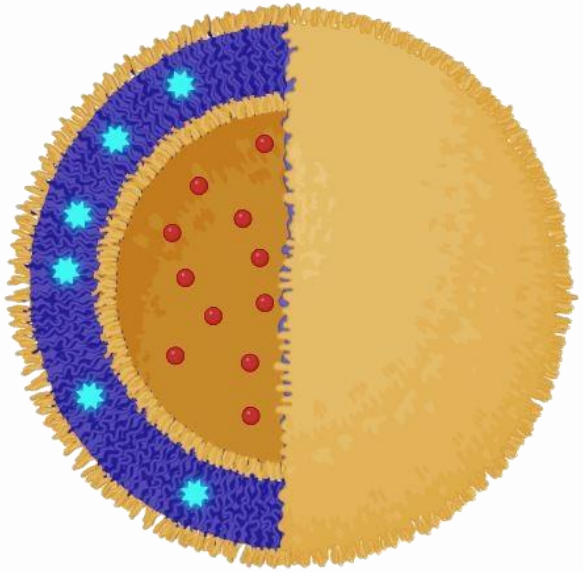
Dehay, B. *et al., The Journal of neuroscience,* **2010**, 30, 12535-12544
Boya, P. *Nature Cell Biology,* **2013**, 15, 713–720

Collaboration équipe de B. Dehay (IMN), thèse R. Kinet

Prochains enjeux des polymersomes en neurosciences

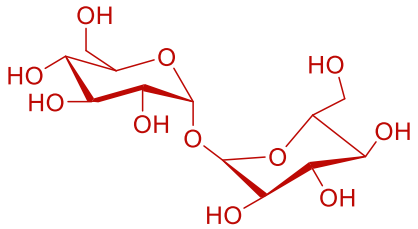
Maladie de Parkinson : maladie neurodégénérative liée à un dérèglement de l'activité des lysosomes

La solution



PEG-*b*-PDLLA or PEG-*b*-PLGA → acidification

Trehalose



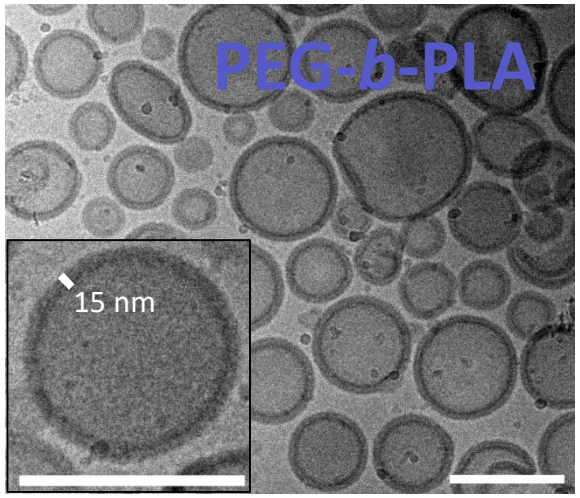
→ Activité Pharmacologique

Cyanine 5.5 → Marqueur fluorescent

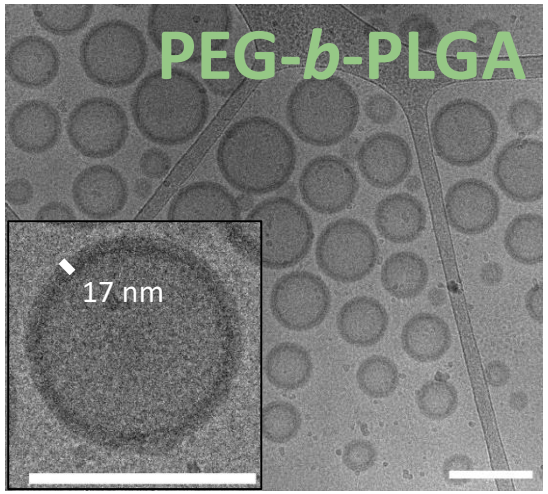
Collaboration équipe de B. Dehay (IMN), thèse R. Kinet

Prochains enjeux des polymersomes en neurosciences

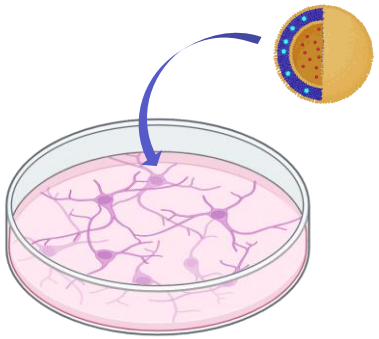
Maladie de Parkinson : maladie neurodégénérative liée à un dérèglement de l'activité des lysosomes

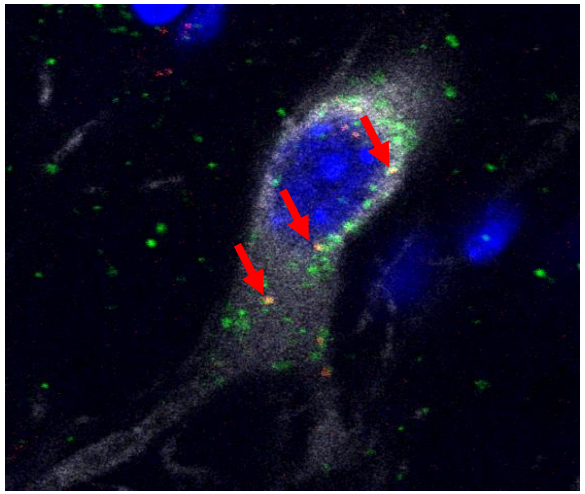


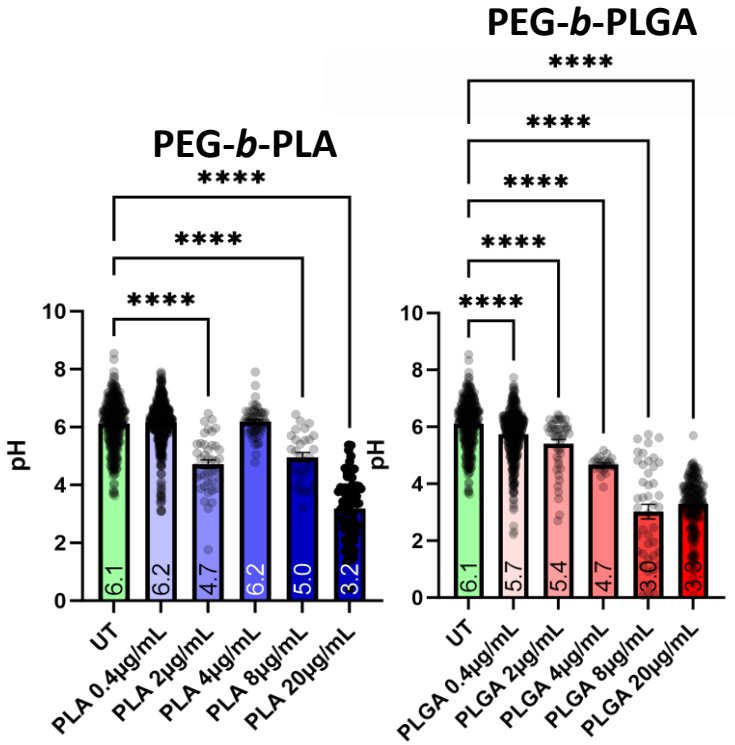
Scale bar 200 nm



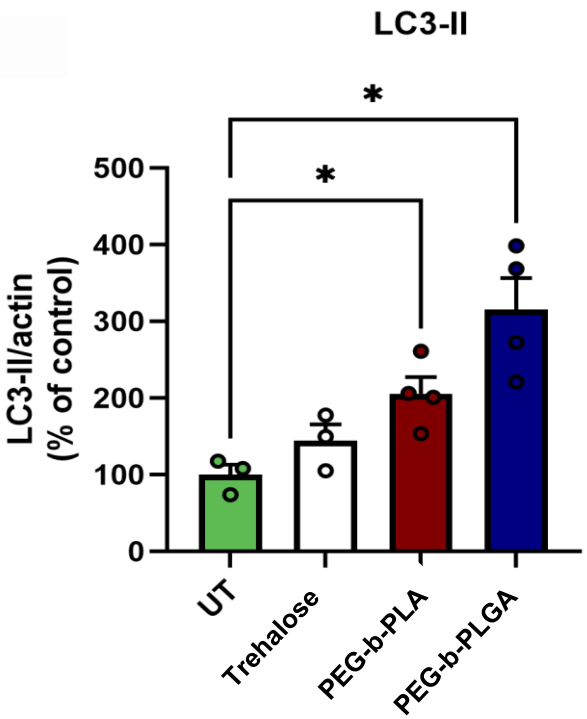
Scale bar 200 nm







acidification



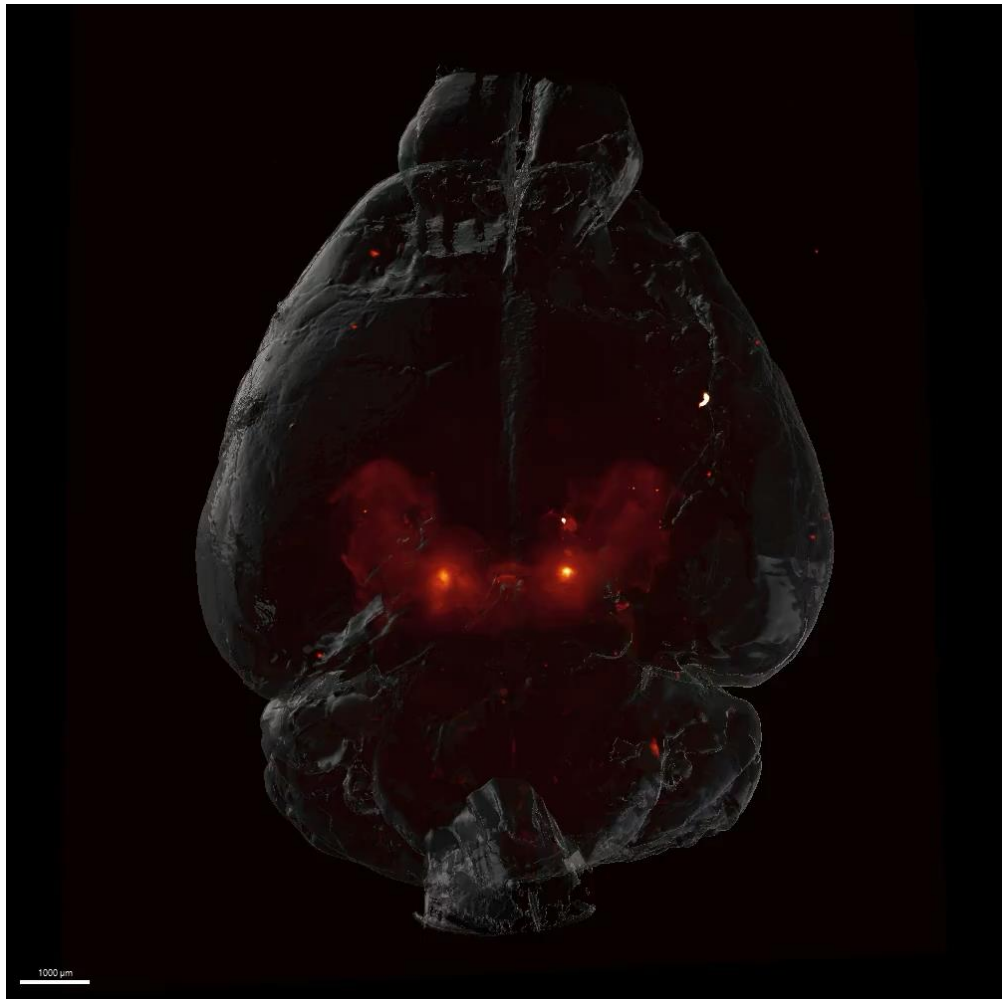
Restauration de l'autophagie

Collaboration équipe de B. Dehay (IMN), thèse R. Kinet

Prochains enjeux des polymersomes en neurosciences

Maladie de Parkinson : maladie neurodégénérative liée à un dérèglement de l'activité des lysosomes

Études in vivo en cours (intracrânien, retro-orbital, intranasal)



Collaboration équipe de B. Dehay (IMN), thèse R. Kinet

Conclusions et messages

Les nanotechnologies ont encore un bel avenir en médecine

progrès en chimie, physique et technologiques ces dernières décennies
meilleur compréhension du vivant
alignement technologie/physiologie

Vers une plus grande précision

ciblage biologique/(bio)chimique
activation physique/physico-chimique

Approches personnalisées et généralisées

Dans ce contexte, les nanotechnologies polymères ont des atouts

lois physiques générales
adaptation des propriétés (par la chimie)
prédictions thermodynamiques
les **polymersomes** et leur versatilité/adaptabilité unique

COLLÈGE DE FRANCE 1530

Intervenantes du jour

Isabel Marey-Semper
(CEO DOXANANO)

doxanano
remotely activated chemotherapy

C. Bosch-Bouju
(Bx-INP, NutriNeuro)

BORDEAUX neurocampus NutriNeuro

MERCI

Lab retreat, May 2024

LCPO
Laboratoire de Chimie des Polymères Organiques

POLY for life
LCPO TEAM 3

INITIATIVE D'EXCELLENCE université de Bordeaux

PROJET FINANCÉ PAR L'ANR · PROJECT FUNDED BY THE ANR

ANR

cnrs

&cnrs 80|Prime

ENM

CHINA SCHOLARSHIP COUNCIL

European Commission

MARIE CURIE ACTIONS

CONTRE LE CANCER LA LIGUE

Fondation pour la Recherche Médicale
Innover pour sauver

L'ORÉAL

MedinCell

MICHELIN

doxanano
remotely activated chemotherapy

COLLÈGE DE FRANCE
1530

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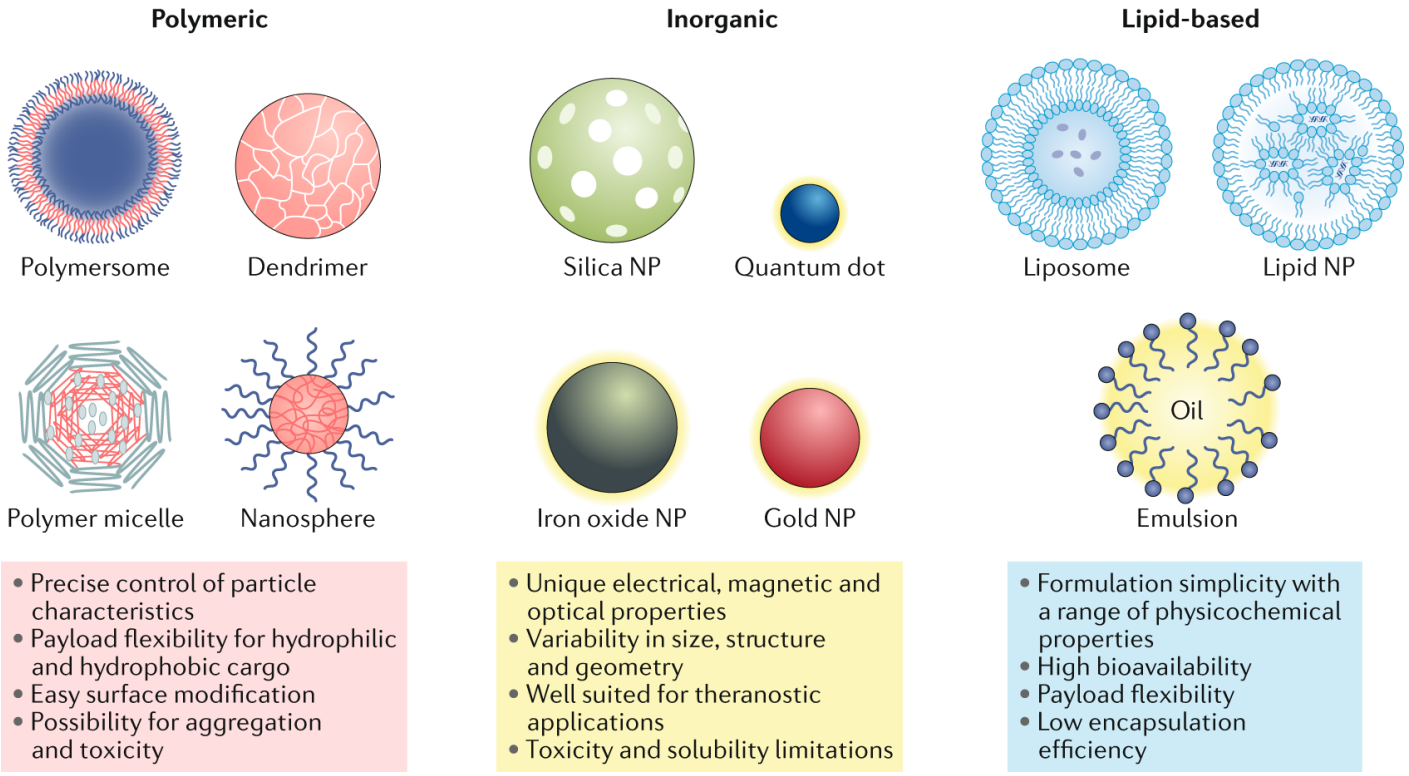
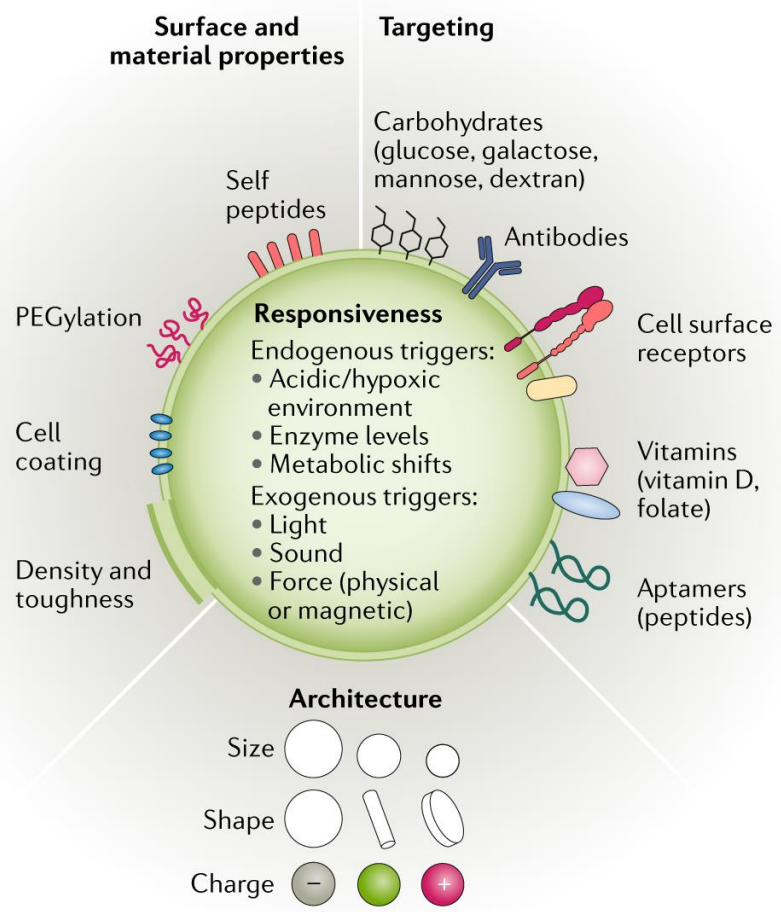
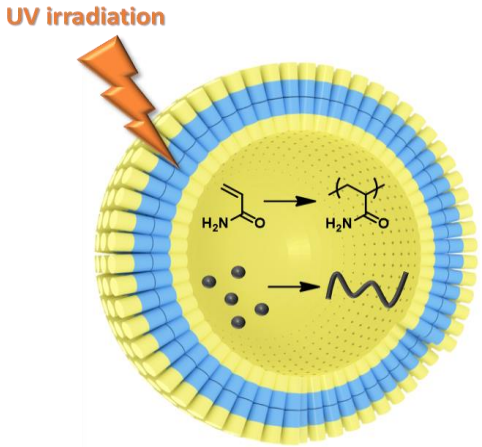
Les principales nanomédecines

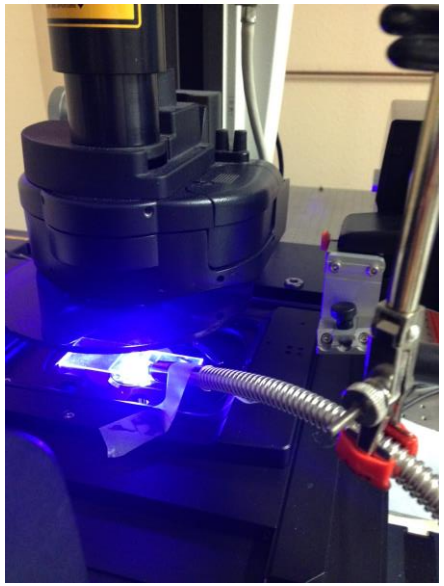


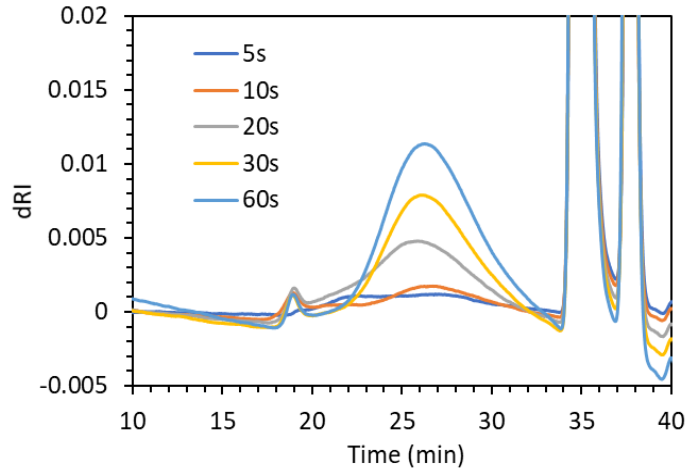


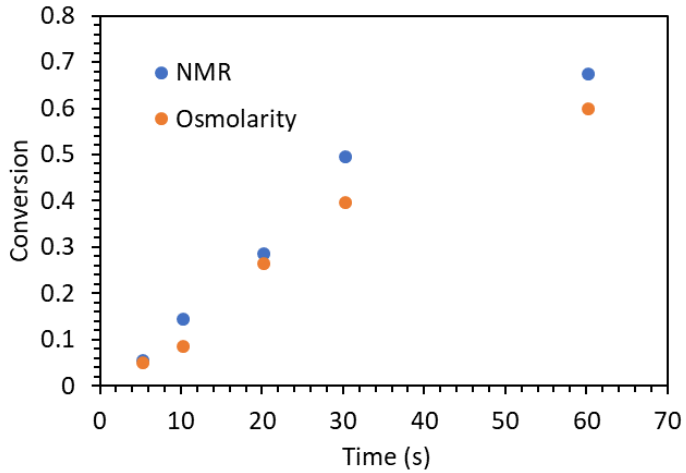
Mitchell, M.J., Billingsley, M.M., Haley, R.M., Wechsler, M.E., Peppas, N.A., Langer, R.
Engineering precision nanoparticles for drug delivery
Nat Rev Drug Discov **20**, 101–124 (2021)

From hypotonic (explosion) to hypertonic (implosion) conditions



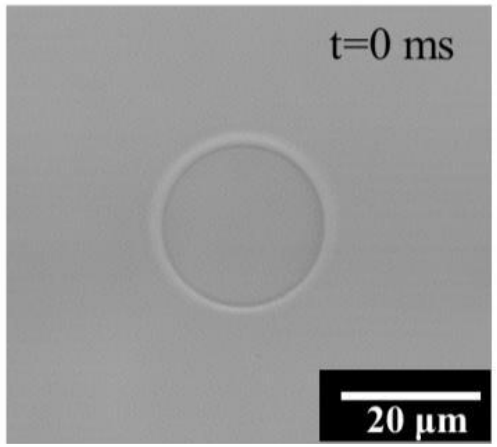


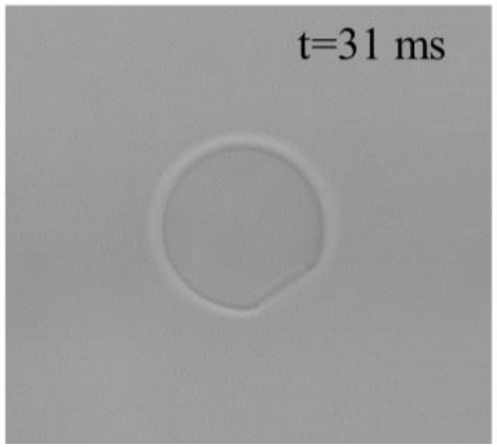


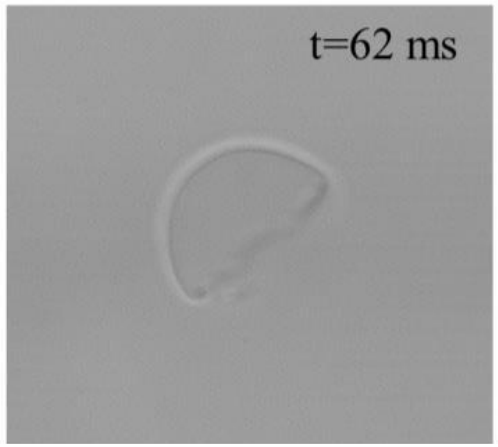


Sophie Larnaudie
Coll. Pierre Nassoy
(LP2N Bordeaux)

Conditions: 0.3 M sucrose, 20 g/L acrylamide, 0.5 wt/v % Irgacure







From explosion to implosion !

S. Larnaudie et al. Langmuir 2019, 35, 8398-8403