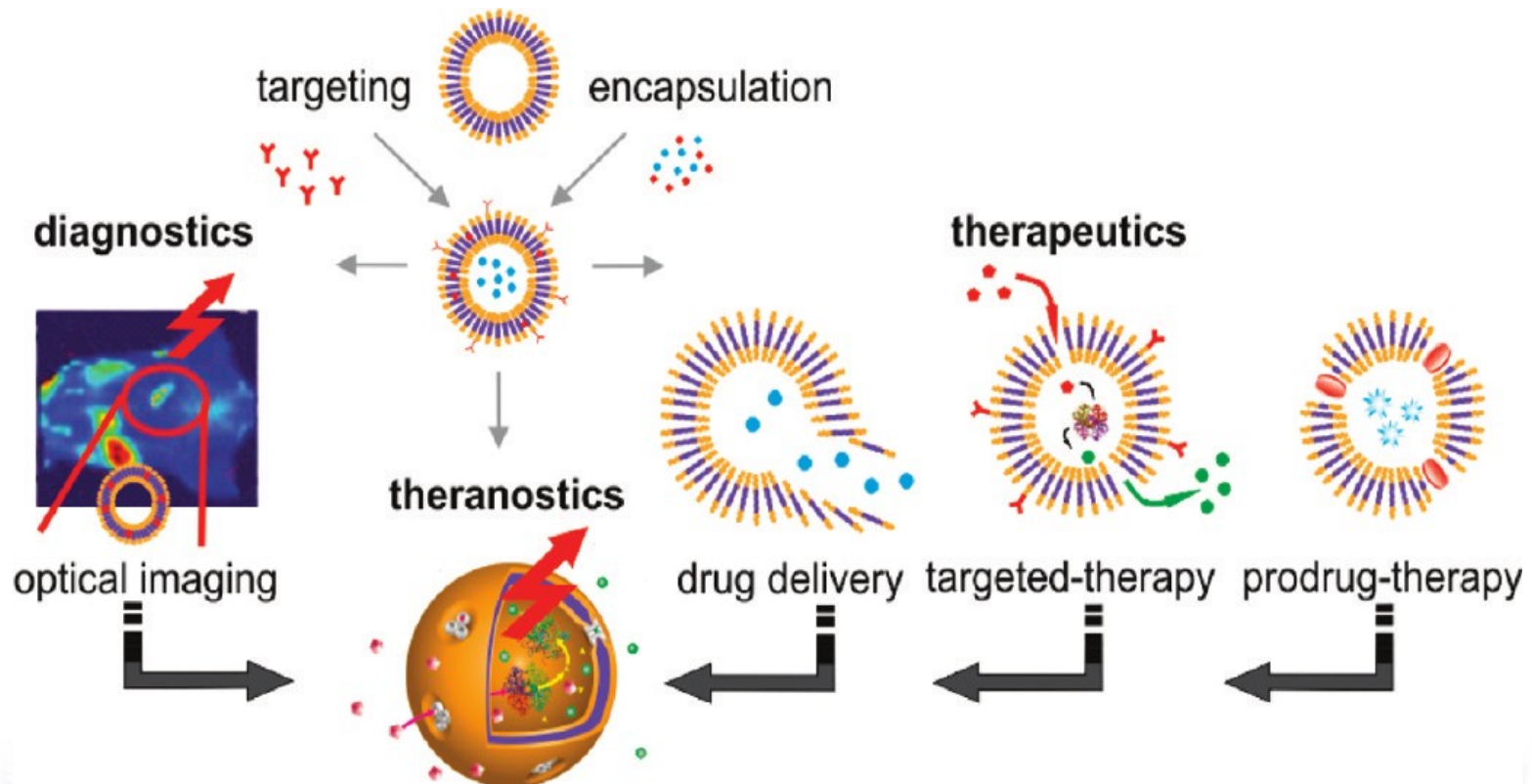


Diseño computacional de polimerosomas óptimos para aplicaciones en Nanomedicina

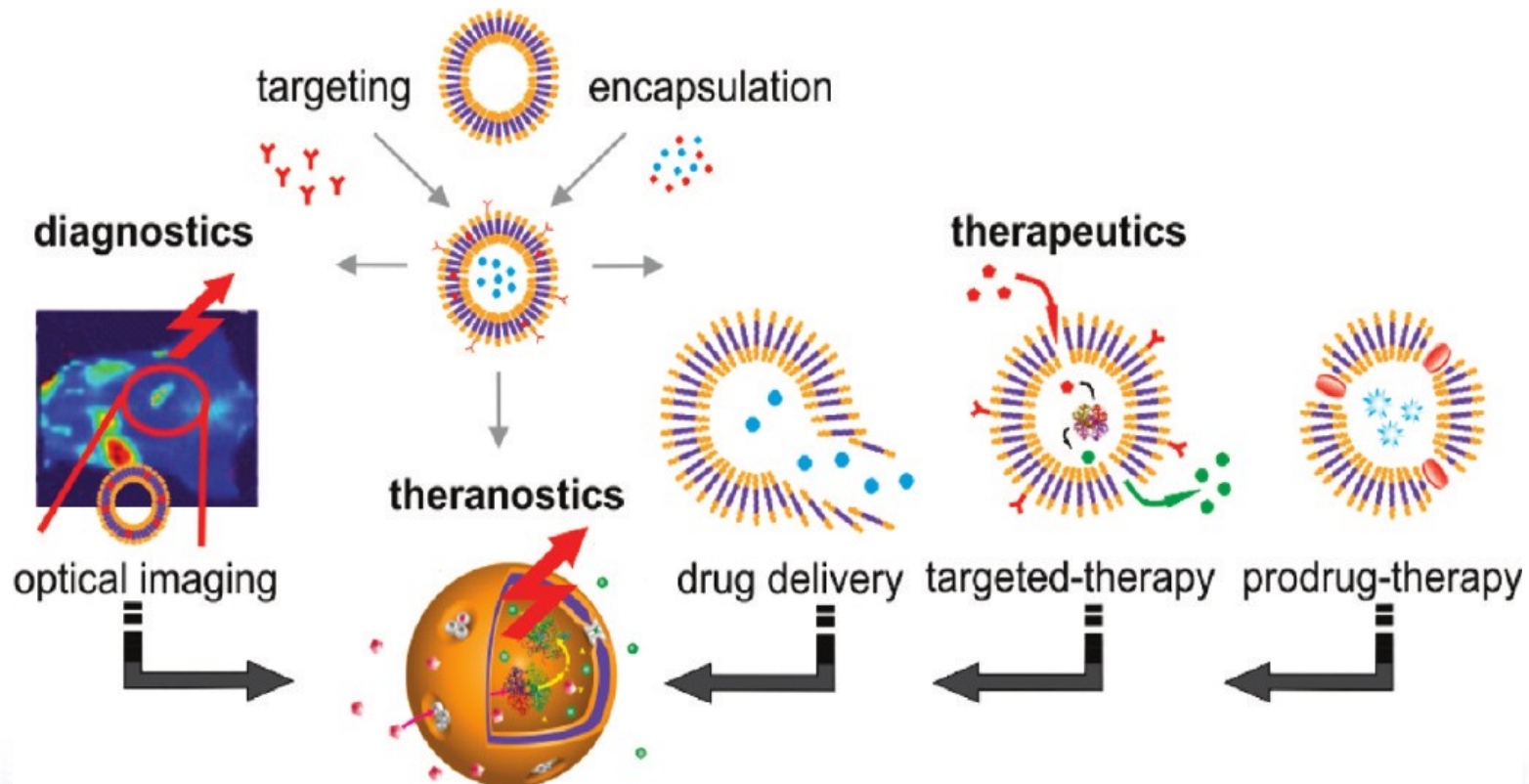
Becario: Damián A. Grillo

Directores: Marta B. Ferraro (DF), Esteban Mocskos (DC)

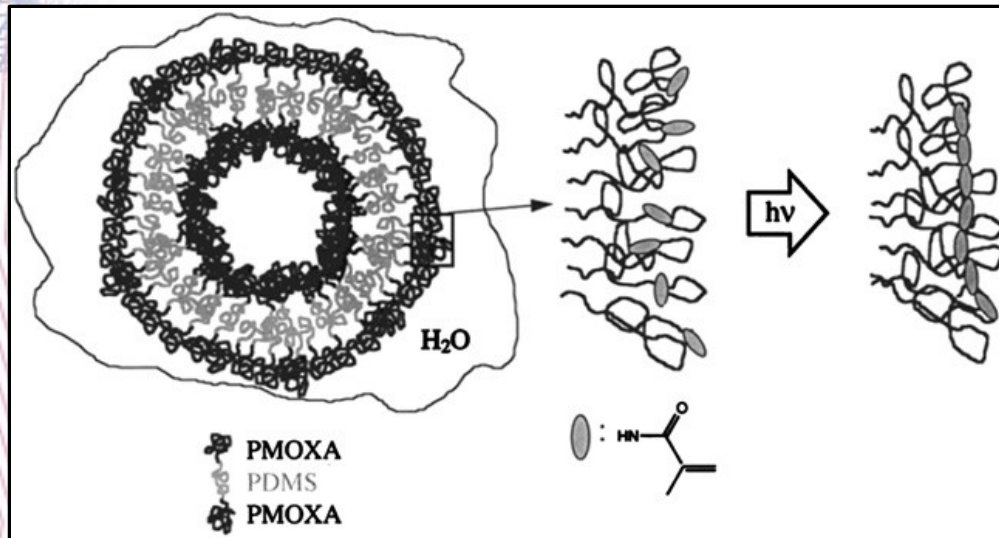


¿Qué son los polimerosomas? ¿Para qué sirven?

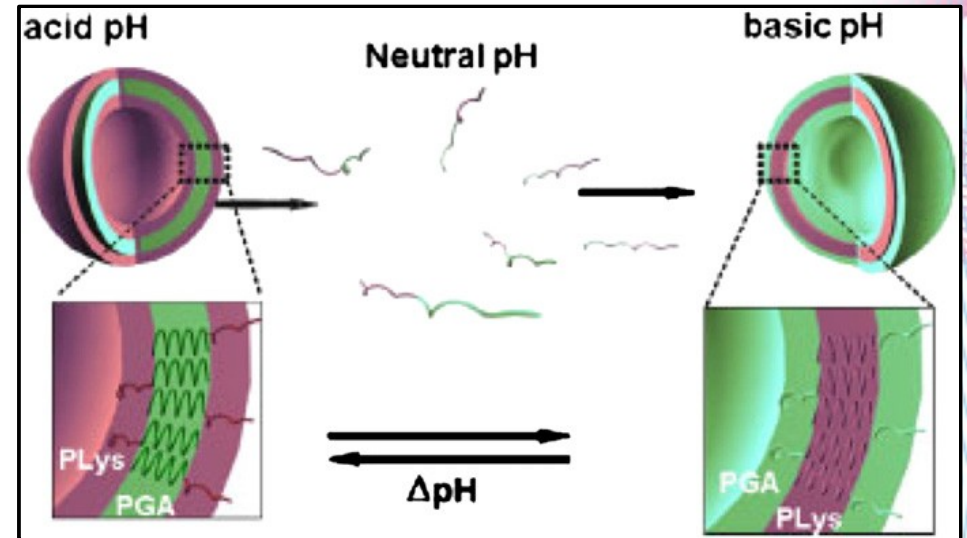
- **Polimerosomas:** Vesículas poliméricas artificiales.
- **Utilidad:** Encapsulamiento y transporte de diversas sustancias (drogas, proteínas, etc).
- **Aplicaciones biomédicas:** Administración de drogas, targeting de sustancias.



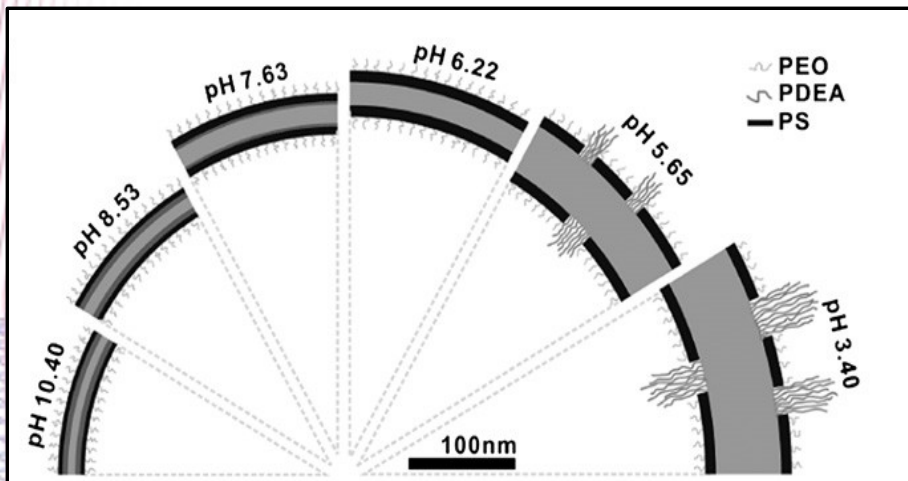
Polimerosomas sensibles a estímulos externos



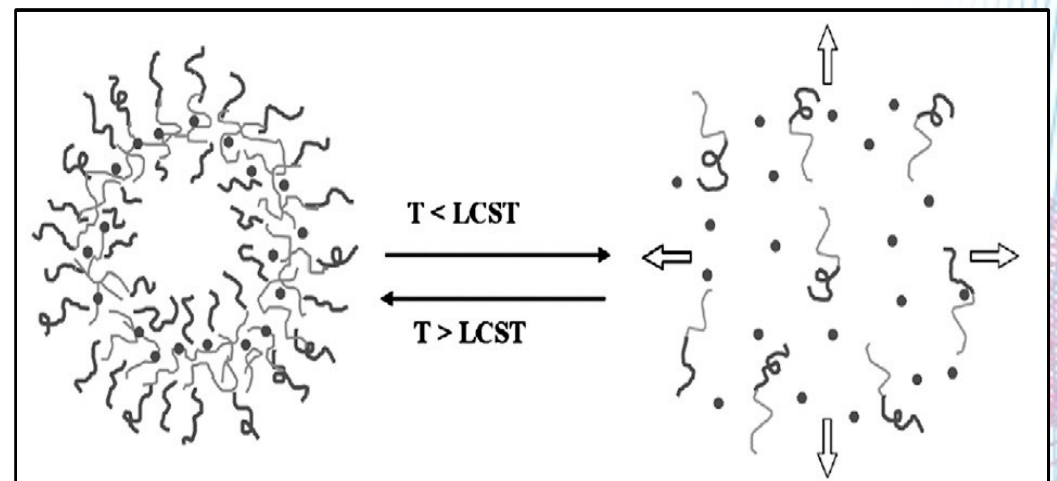
Cambios estructurales por radiación



Estructura dependiente del nivel de pH



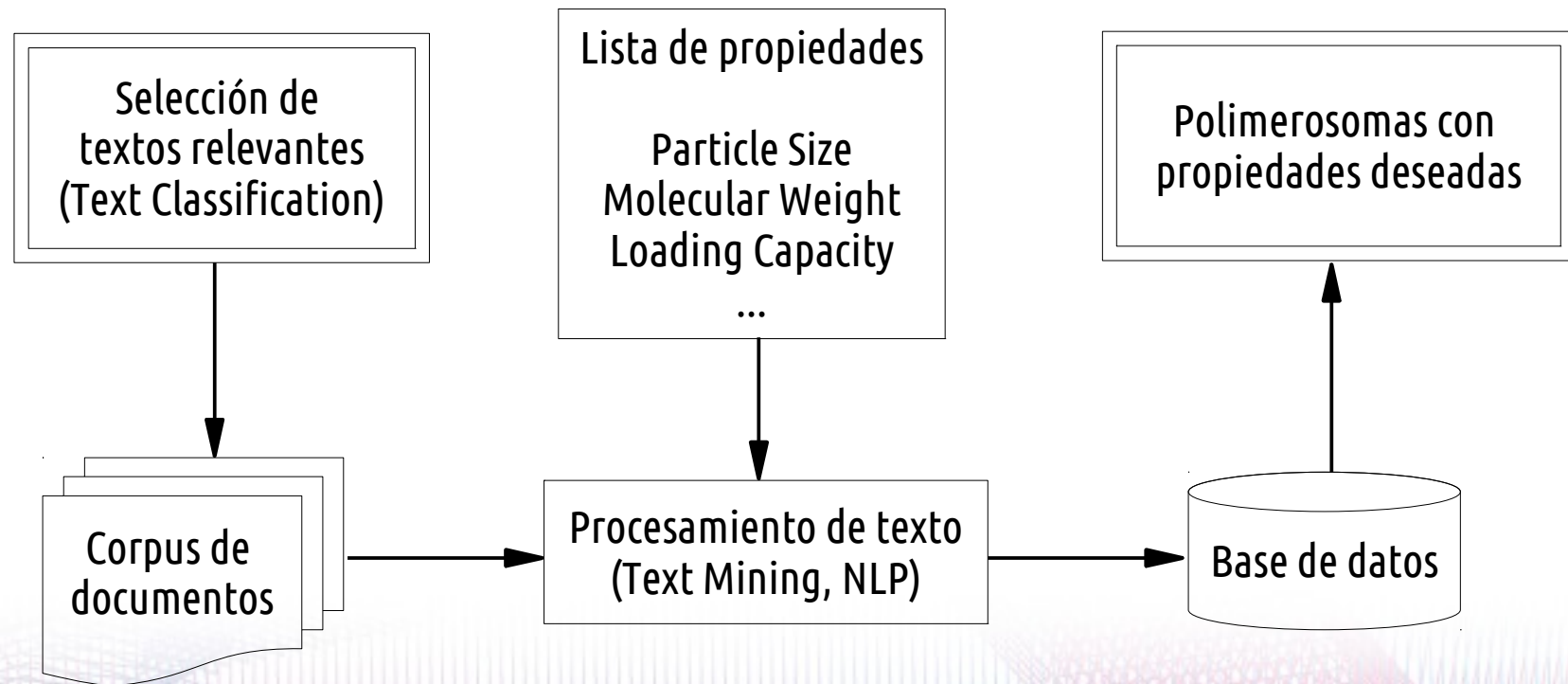
Tamaño dependiente del nivel de pH



Cambios estructurales por temperatura

Resumen del proyecto

- Dada cierta aplicación, ¿Qué sintetizar? ¿Cómo hacerlo? ¿Qué materiales?
- Gran volumen de información disponible. Búsqueda manual ineficiente.
- **Objetivos:** Desarrollar un esquema computacional para diseño eficiente de polimersomas utilizados en aplicaciones biomédicas.
- **Metodología:** Extracción automática de datos relevantes + Simulaciones



Resultados preliminares - GATE

The **critical micelle concentration** of CS-SA micelles with $26.9\% \pm 1.08\%$ amino substitute degree was $65 \mu\text{g/mL}$. The **diameter** and surface potential of synthesized CS-SA micelles in aqueous solution was $22 \pm 0.98 \text{ nm}$ and $36.4 \pm 0.71 \text{ mV}$, respectively. CS-SA micelles presented excellent cellular uptake ability on bEnd.3 cells, the **IC₅₀** of which was $237.6 \pm 6.61 \mu\text{g/mL}$. DOX-loaded micelles exhibited slow drug-release behavior, with a cumulative release up to **72%** within **48** hours in vitro. The **cytotoxicity** of DOX-loaded CS-SA micelles against **C6** was $2.664 \pm 0.036 \mu\text{g/mL}$, compared with $0.181 \pm 0.066 \mu\text{g/mL}$ of DOX · HCl.

CS with an average **molecular weight** of **18 kDa** was obtained by enzymatic degradation from CS (Mw = **450.0 kDa**, **95%** deacetylated degree; Yuhuan Marine Biochemistry, Zhejiang, China). SA was purchased from Chemical Reagent (Shanghai, China). EDC, **2,4,6**-trinitrobenzene sulfonic acid (TNBS), and **3**-(**4**, **5**-dimethylthiazol-**2**-yl)-**2,5**-diphenyl-tetrazolium bromide (MTT) came from Sigma (St Louis, MO).

The **critical micelle concentration** of CS-SA in aqueous medium was estimated by spectroscopy using pyrene as a probe. **18** The fluorescence emission spectrum of pyrene was obtained by a fluorometer (F-**2500**; Hitachi, Tokyo, Japan). The excitation wavelength was **337 nm**, and the slits were set at **2.5 nm** (excitation) and **10 nm** (emission), respectively. The concentrations of CS-SA solution with $5.93 \times 10^{-7} \text{ M}$ pyrene were varied from 5.0×10^{-3} to **1.0 mg/mL**. The intensity ratio of the first peak (I **1**, **374 nm**) to the third peak (I **3**, **385 nm**) in the emission spectra of pyrene was calculated.

The synthesized CS-SA was able to self-assemble to form micelles in aqueous solution. As seen in Table **1**, CS-SA micelles exhibited an average number **diameter** of $22 \pm 0.98 \text{ nm}$, consistent with the TEM observation results (Figure **2**), which showed a regular spherical morphology of CS-SA micelles. The relatively high **zeta potential** of $36.4 \pm 0.71 \text{ mV}$ helped to increase the stability of micelles by repulsion interaction. The concentration of CS-SA plotted against I **1** / I **3** is presented in Figure **2**. The **critical micelle concentration** of CS-SA measured by fluorescence was $65 \mu\text{g/mL}$, which indicated that CS-SA micelles had good self-assembling ability.

The **IC₅₀** of CS-SA against bEnd.3 was $237.6 \pm 6.61 \mu\text{g/mL}$, determined by MTT assay. The **cytotoxicity** of CS-SA/DOX micelles against **C6** was $2.664 \pm 0.036 \mu\text{g/mL}$, compared with $0.302 \pm 0.069 \mu\text{g/mL}$ of DOX · HCl. The relatively lower toxicity of CS-SA/DOX micelles might be relevant with slow release of DOX from micelles.
Characteristics of CS-SA/DOX micelles

DOX was physically entrapped into the hydrophobic core of CS-SA micelles. As seen in Table **1**, the **size** of micelles increased after drug loading, while the surface potential presented no significant change. The EE and DL were determined to be **81.23%** and **10.65%**, respectively. In vitro release profiles of DOX from CS-SA micelles in PBS (pH **7.2**) are shown in Figure **4**. CS-SA/DOX micelles exhibited relatively slow release behavior in vitro. As shown in Figure **4**, the cumulative DOX release percentage was **34.7%** in the first **8** hours and reached **72%** in **48** hours.

Annotations in the text include: NumAnnot (orange), PropAnnot (green), Sentence (pink), SpaceToken (yellow), Split (purple), Token (magenta), UnitAnnot (blue), sub (pink), sup (green), and Original markups (black).