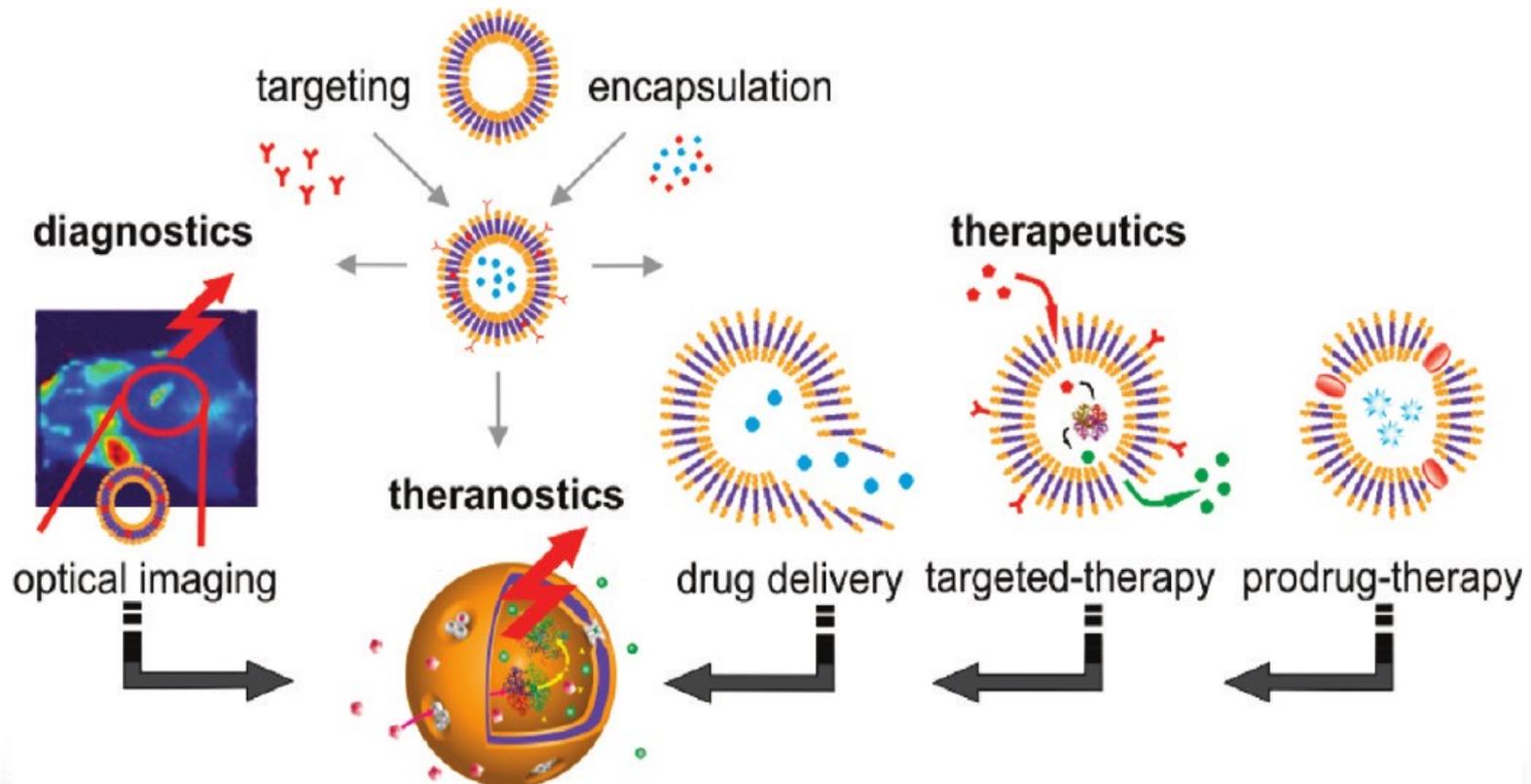


Diseño computacional de polimerosomas óptimos para aplicaciones en Nanomedicina

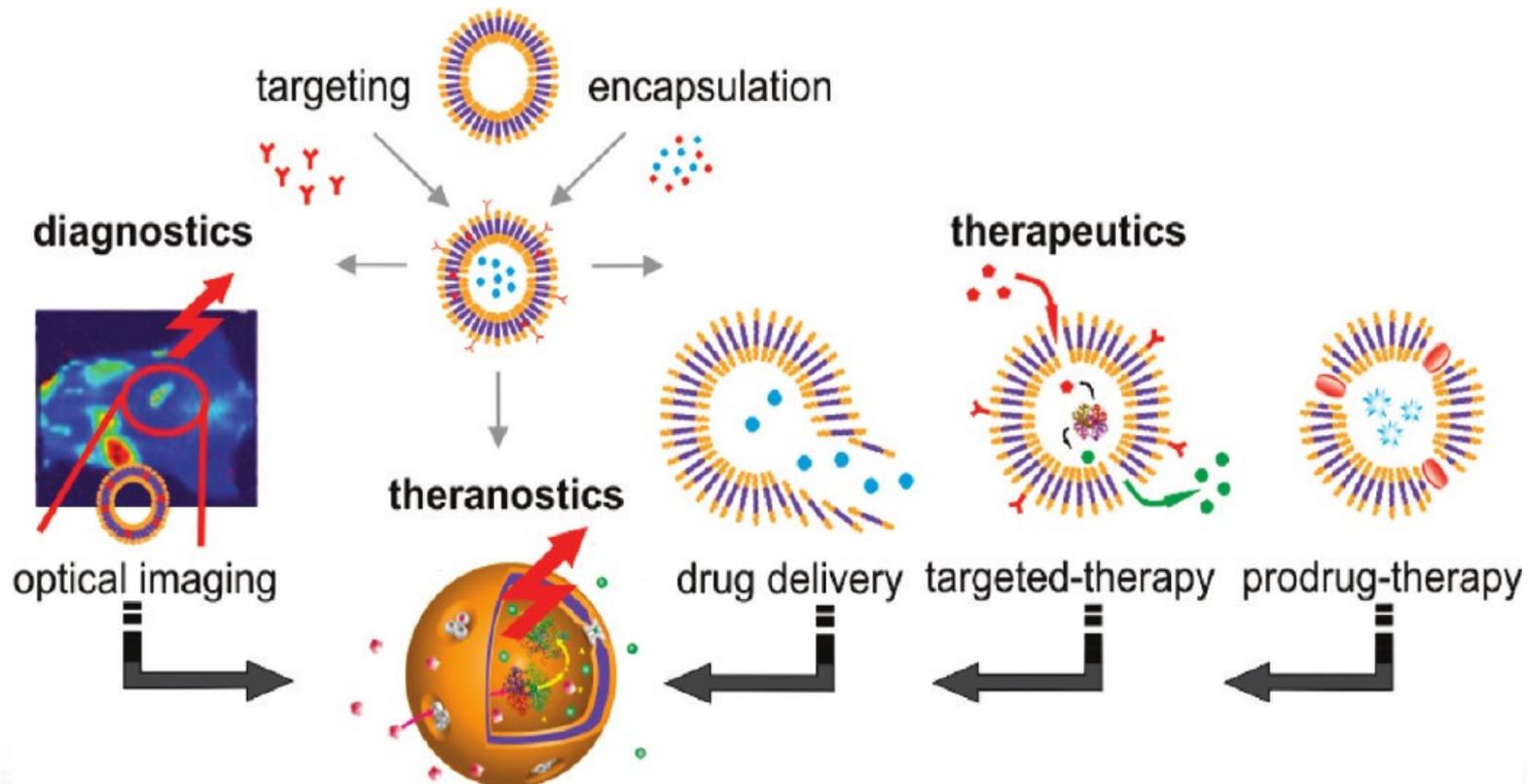
Becario: Damián A. Grillo

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

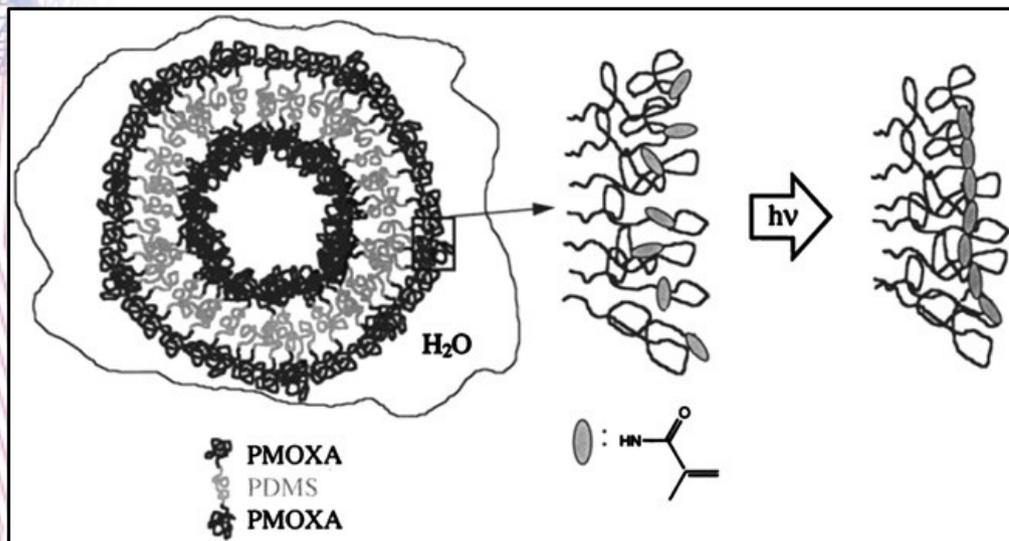


¿Qué son los polimerosomas? ¿Para qué sirven?

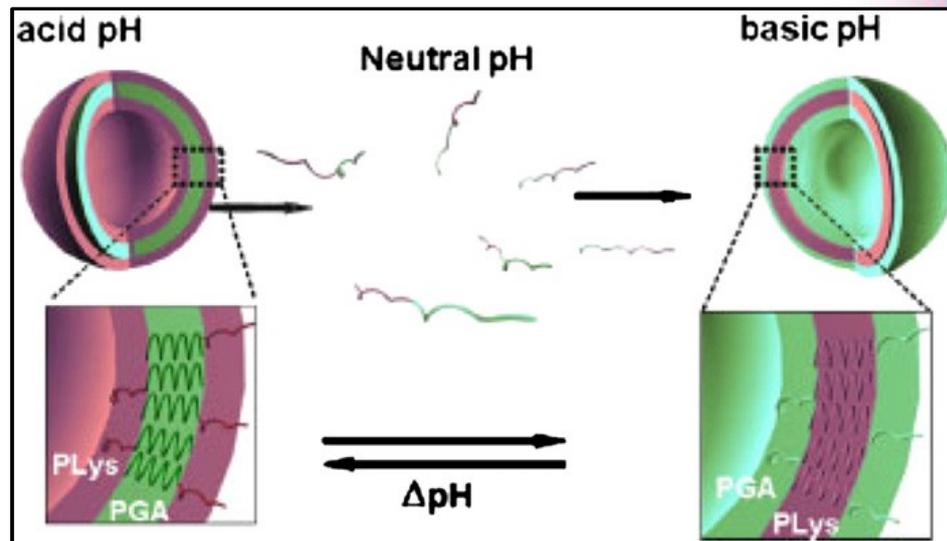
- **Polimerosomas:** Vesículas poliméricas artificiales.
- **Utilidad:** Encapsulamiento y transporte de diversas sustancias (drogas, proteínas, etc).
- **Aplicaciones biomédicas:** Administración de drogas, targeting de sustancias.



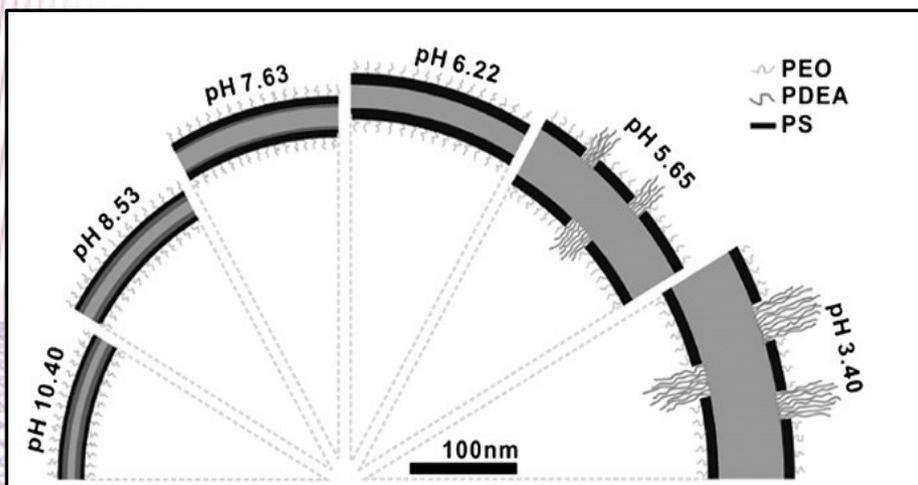
Polimerosomas sensibles a estímulos externos



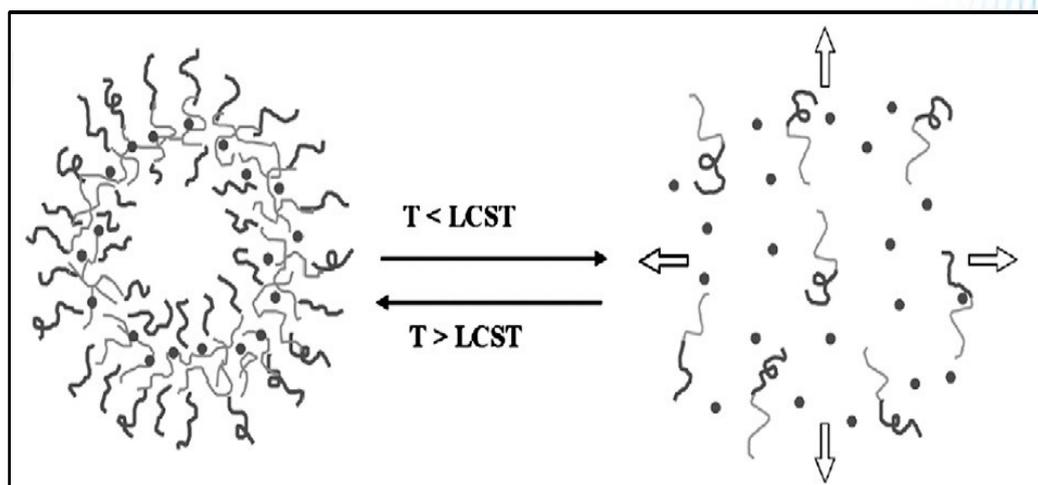
Cambios estructurales por radiación



Estructura dependiente del nivel de pH



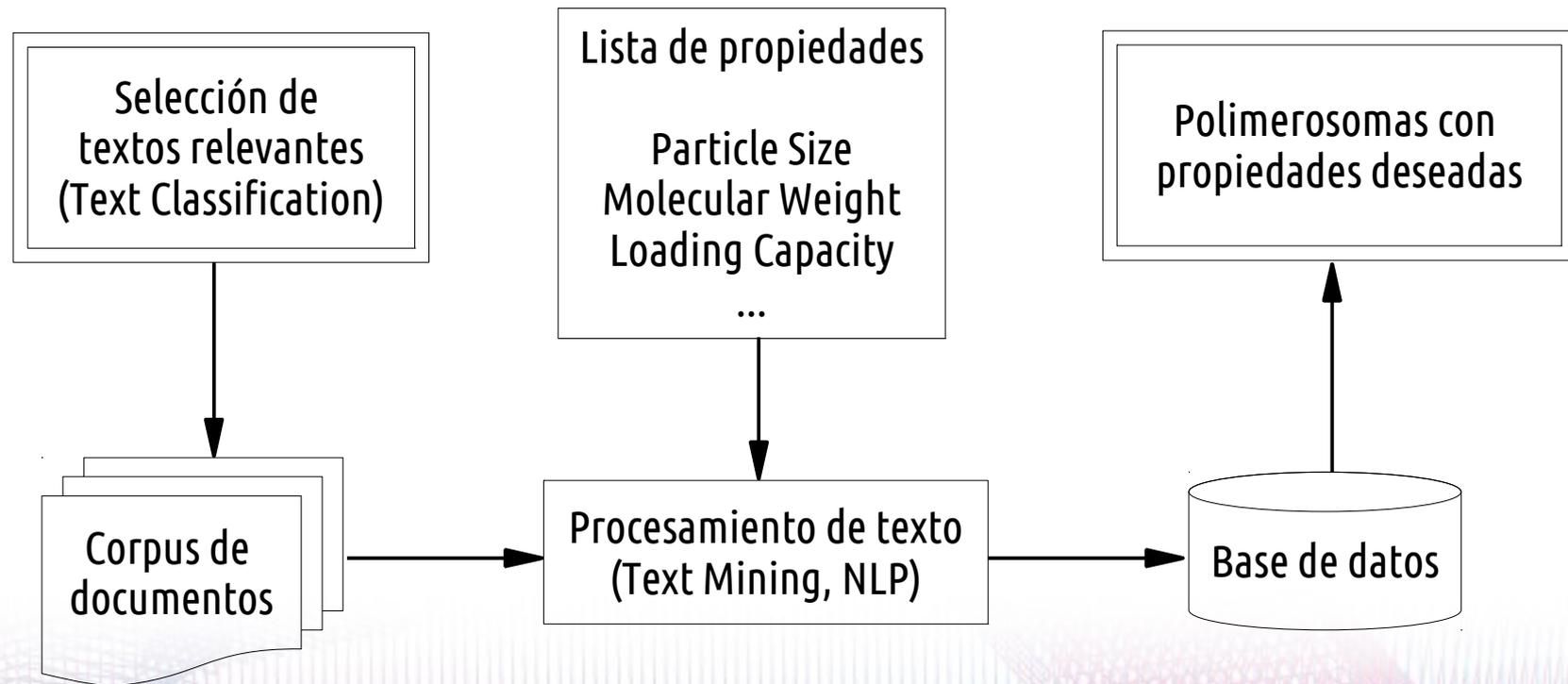
Tamaño dependiente del nivel de pH



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

GATE Developer 7.1 build 4485

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The **critical micelle concentration** of CS-SA micelles with **26.9% ± 1.08%** amino substitute degree was **65 µg/mL**. The **diameter** and surface potential of synthesized CS-SA micelles in aqueous solution was **22 ± 0.98 nm** and **36.4 ± 0.71 mV**, respectively. CS-SA micelles presented excellent cellular uptake ability on bEnd.3 cells, the **IC 50** of which was **237.6 ± 6.61 µg/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 ± 0.036 µg/mL**, compared with **0.181 ± 0.066 µg/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 × 10⁻⁷ 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 ± 0.98 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 ± 0.71 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 µg/mL**, which indicated that CS-SA micelles had good self-assembling ability.

The **IC 50** of CS-SA against bEnd.3 was **237.6 ± 6.61 µg/mL**, determined by MTT assay. The **cytotoxicity** of CS-SA/DOX micelles against **C6** was **2.664 ± 0.036 µg/mL**, compared with **0.302 ± 0.069 µg/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.

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