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pH-Responsive Polymer Nanocapsules for Controlled Uptake, Retention, and Release of Nucleotides

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BACKGROUND

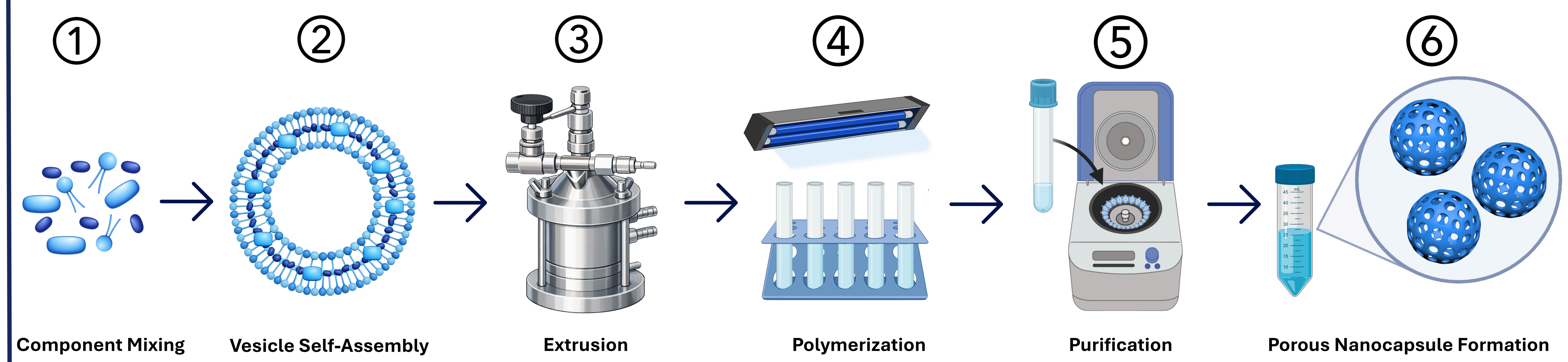
- Controlled drug delivery improves the efficiency, precision, and safety of modern therapeutics, particularly nucleic acid–based drugs, which are often unstable and difficult to deliver.
- Current delivery systems frequently rely on carrier degradation to release cargo, resulting in limited control and potential premature leakage.
- Polymer nanocapsules offer a promising alternative, consisting of hollow structures with nanometer-thin shells and well-defined nanopores that enable selective transport while retaining cargo.
- Their transport properties can be regulated by external stimuli, such as pH, allowing controlled uptake and release without structural degradation of the carrier.
- In this project, pH-responsive nanocapsules are used to regulate the transport of negatively charged nucleotides via electrostatic interactions, enabling loading at low pH, retention at physiological pH, and release under mildly acidic conditions.

HYPOTHESIS & OBJECTIVES

pH-responsive nanocapsules regulate the uptake, retention, and release of negatively charged nucleotides through electrostatic interactions. This behavior enables controlled transport across different physiological pH environments. Uptake occurs at acidic pH (~4), retention at physiological pH (7.4), and release at mildly acidic pH (~5.5).

METHODS

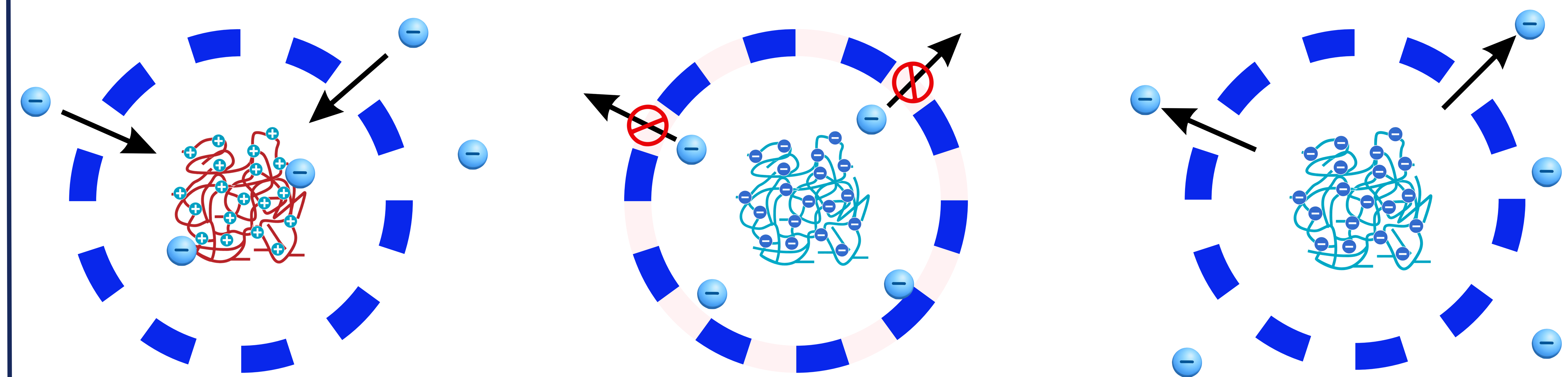
Vesicle-templated synthesis of porous polymer nanocapsules



pH 4.0 — Loading
electrostatic attraction

pH 7.4 — Retention
electrostatic repulsion

pH 5.5 — Release
diffusion through neutral pores



Mechanism of pH-Responsive Transport

pH-dependent electrostatic interactions control the transport of negatively charged nucleotides across nanocapsule membranes. At low pH (4.0), positively charged polyelectrolytes promote uptake through electrostatic attraction. At physiological pH (7.4), negatively charged pores prevent cargo release via electrostatic repulsion. At mildly acidic pH (5.5), neutralization of pore charge enables diffusion-driven release.
Conceptual model based on electrostatic interactions and diffusion.

RESULTS

- Porous polymer nanocapsules containing polyelectrolytes were successfully synthesized and exhibited pH-dependent transport behavior toward negatively charged molecules. Under acidic conditions (pH ≈ 4.0), increased uptake was observed, which is consistent with electrostatic attraction between positively charged polyelectrolytes and anionic cargo.
- At physiological pH (7.4), partial retention of encapsulated molecules was observed; however, measurable release also occurred, suggesting that electrostatic repulsion alone may not fully prevent cargo diffusion. Additionally, release behavior did not consistently align with the expected mechanism, as in some cases, greater release was observed at neutral pH compared to mildly acidic conditions (pH 5.5).
- These observations suggest that factors beyond electrostatic interactions—such as pore size, diffusion, and buffer composition—may influence transport behavior. Variability in capsule structure and particle size may also contribute to incomplete retention and non-ideal release profiles.

REFERENCES

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