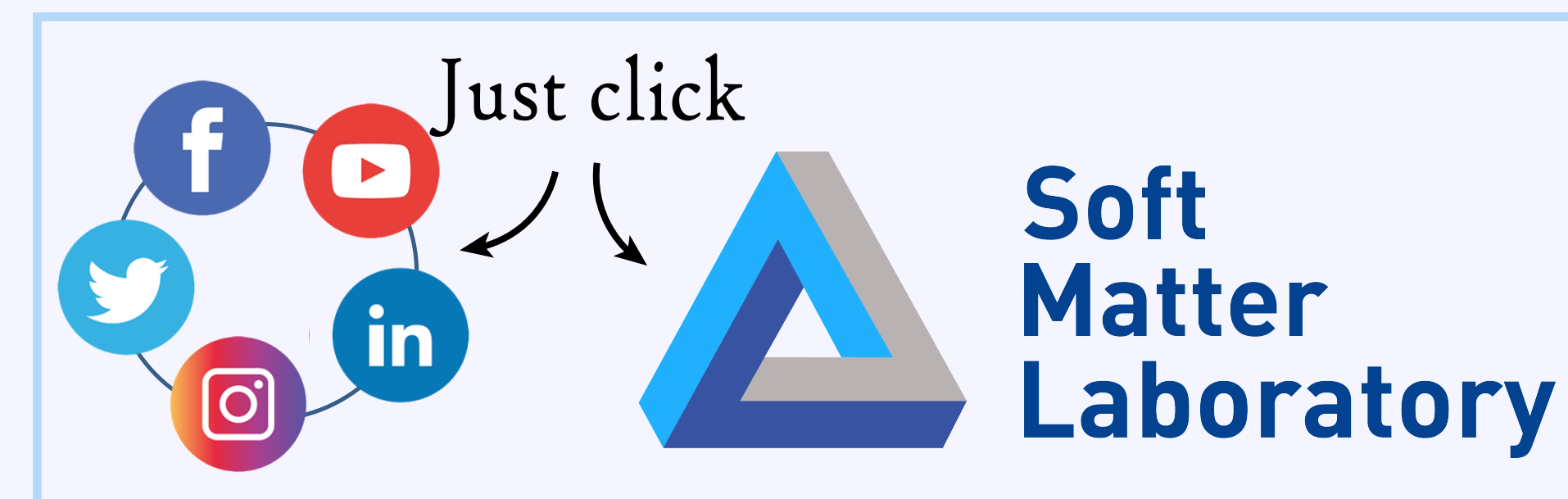


Insulin-delivery from glucose-responsive polyamine-salt aggregates: smart "sense-and-treat" nanocarriers made easy

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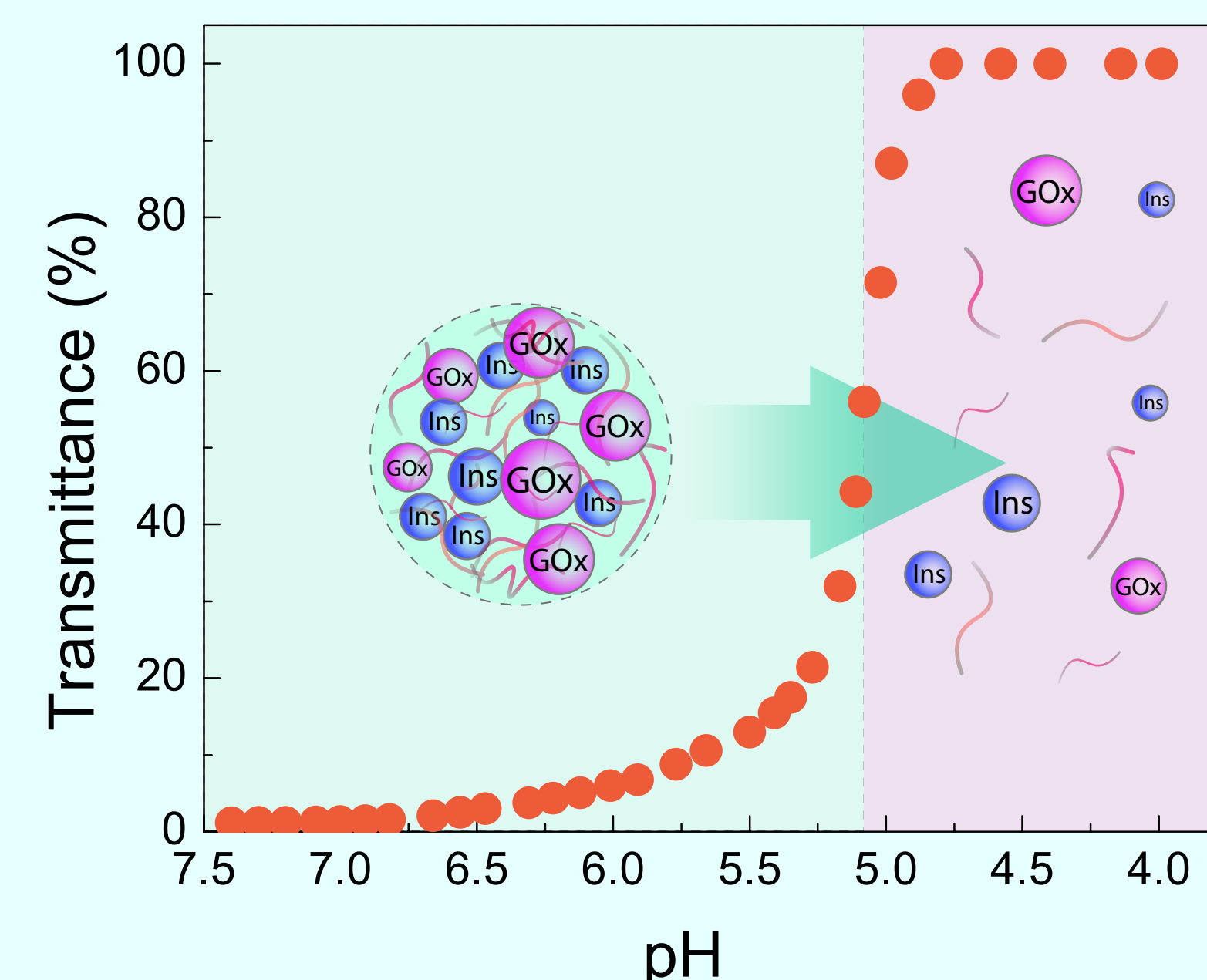
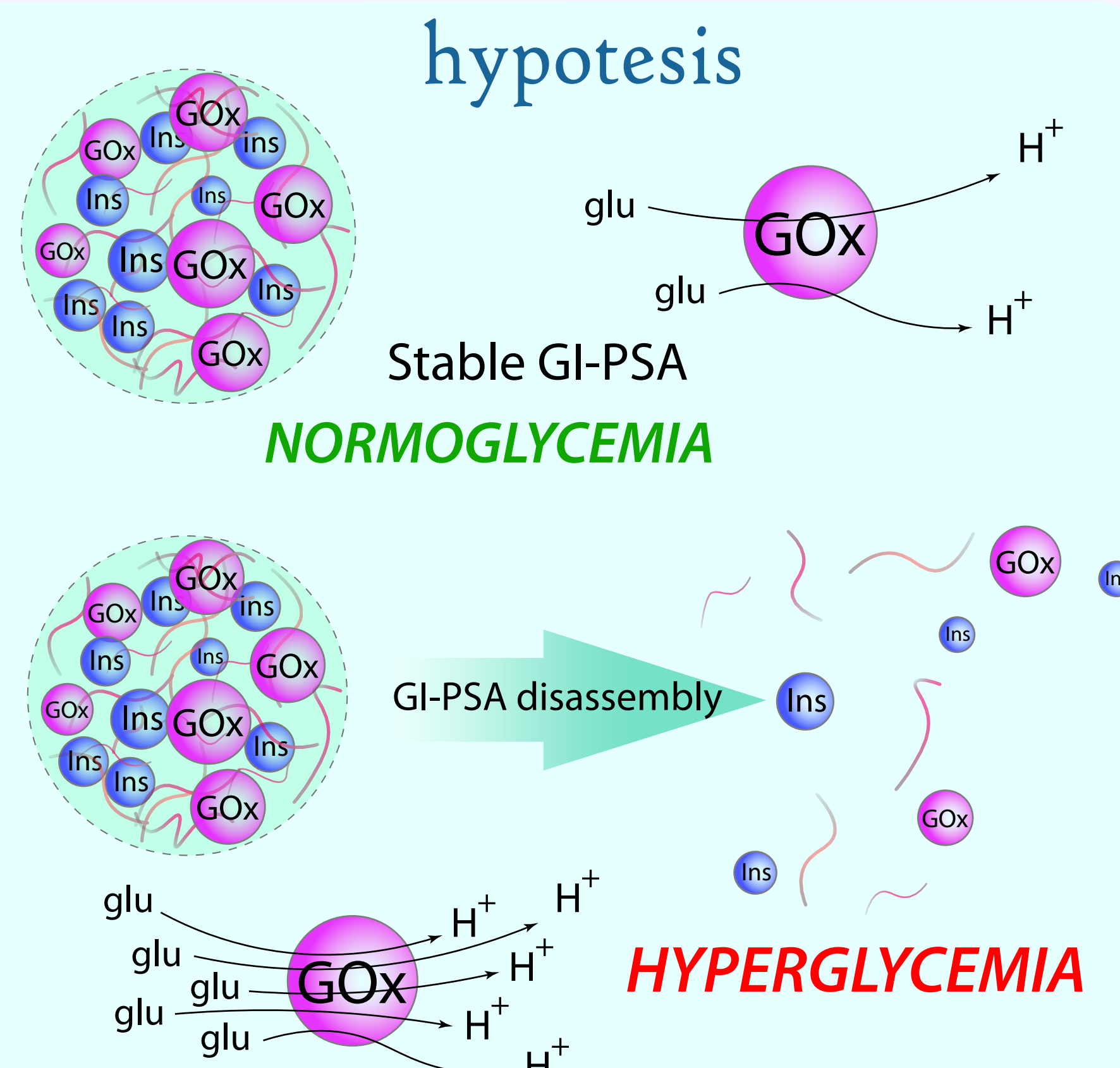
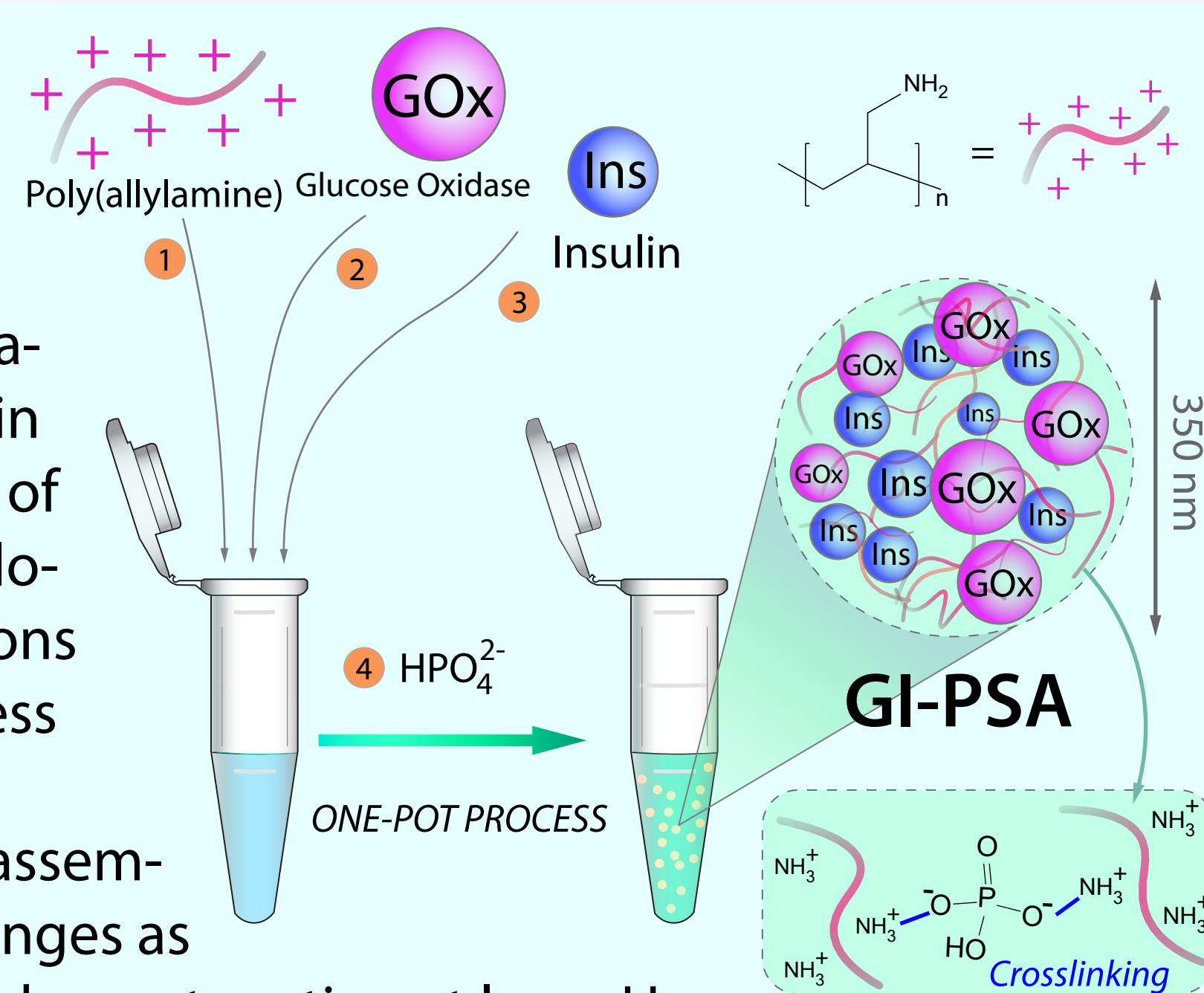


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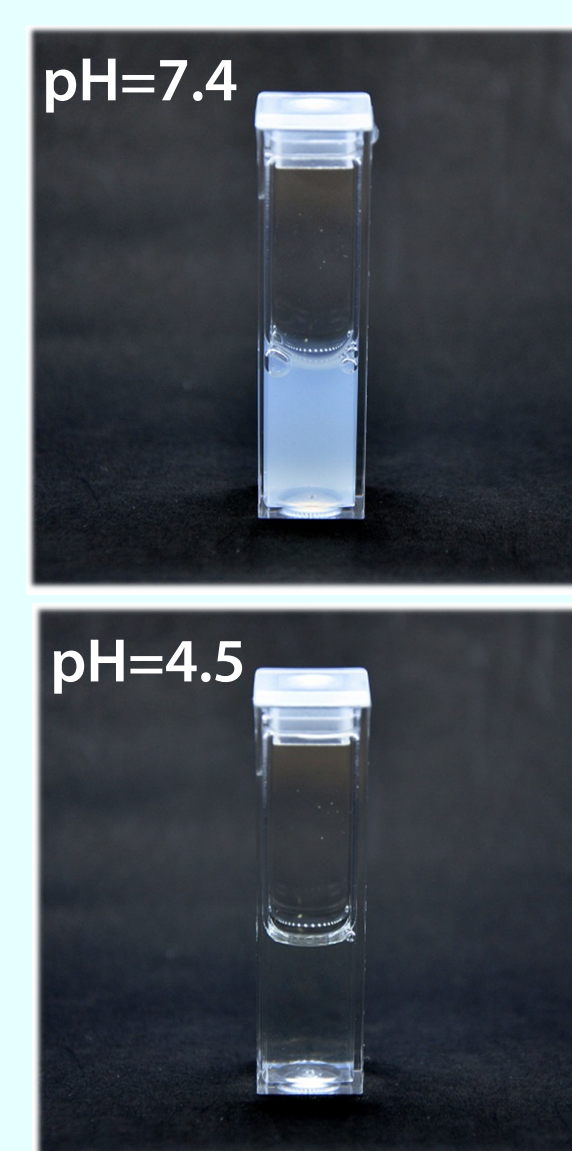


the idea

Insulin and glucose oxidase (GOx) were fixed within a supramolecular matrix of poly(allylamine hydrochloride) and phosphate anions through a one-pot process (ionic gelation method). The integrity of the self-assembly is sensitive to pH changes as phosphates loses charge by protonation at low pH.

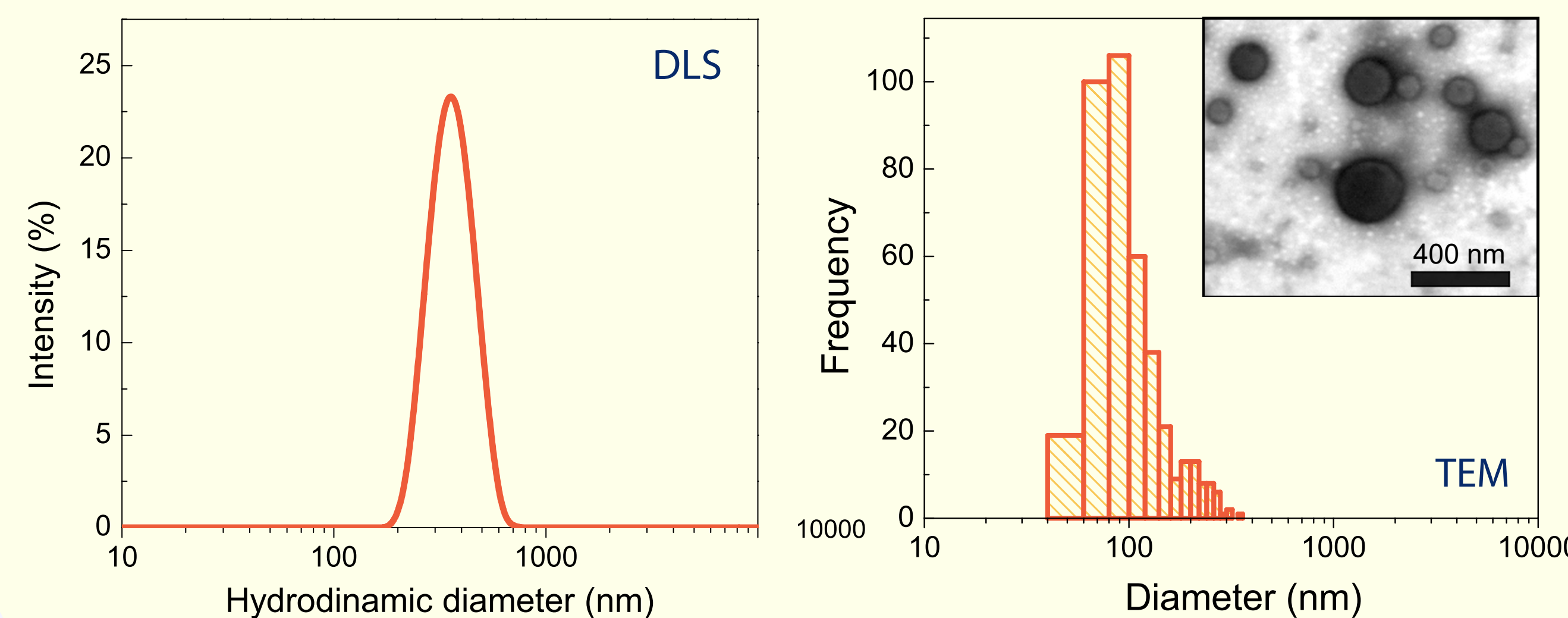


By external titration with HCl we demonstrate that, for pH lower than 5, colloids dissolve completely. Thus, releasing the full insulin content. As GOx catalyzes the oxidation of glucose into glucuronic acid (pKa=3.86), in presence of high levels of glucose the product of the catalytic reaction could trigger the colloid disassembly. Therefore, the presence of glucose could act as an indirect GI-PSA disassembly agent.



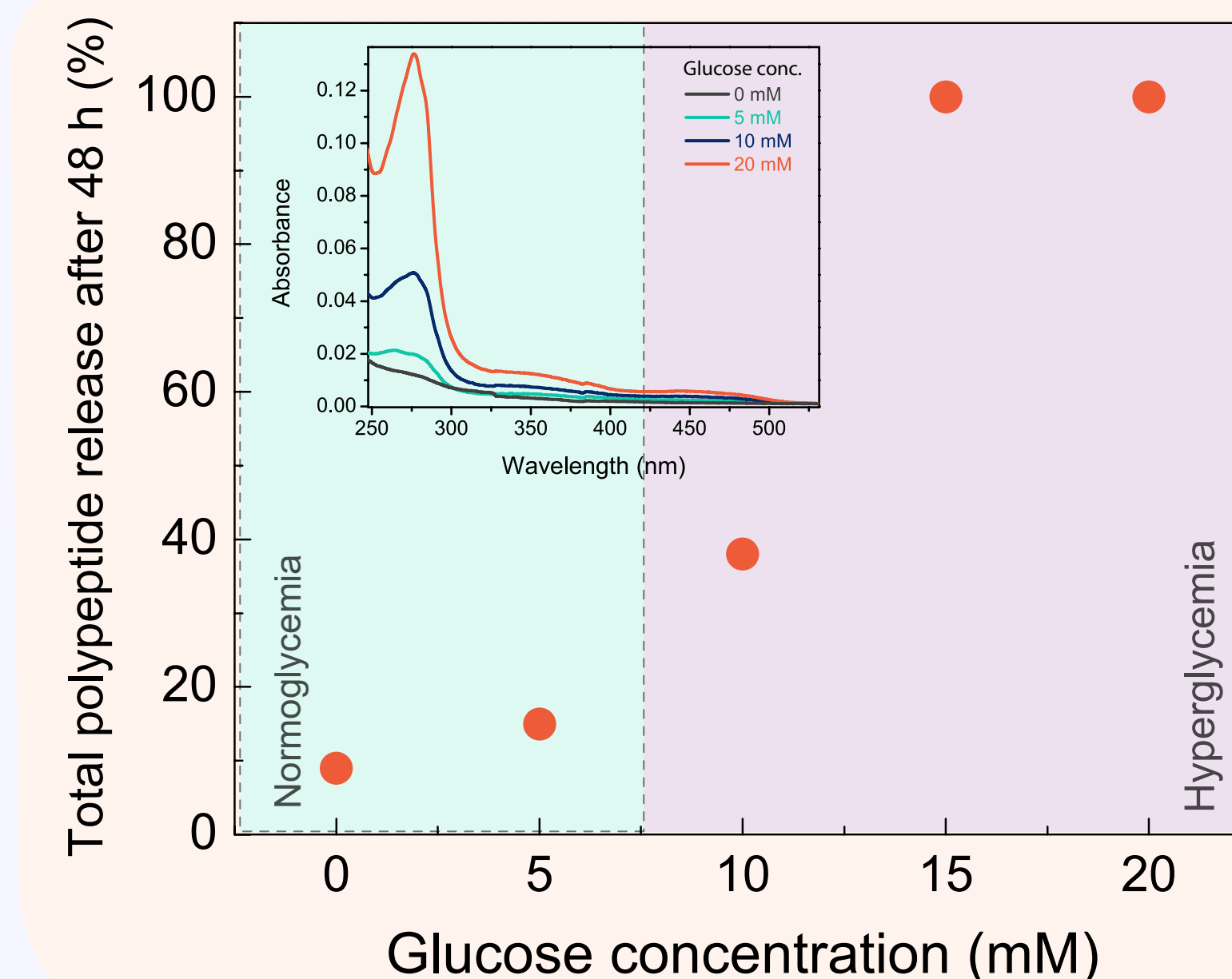
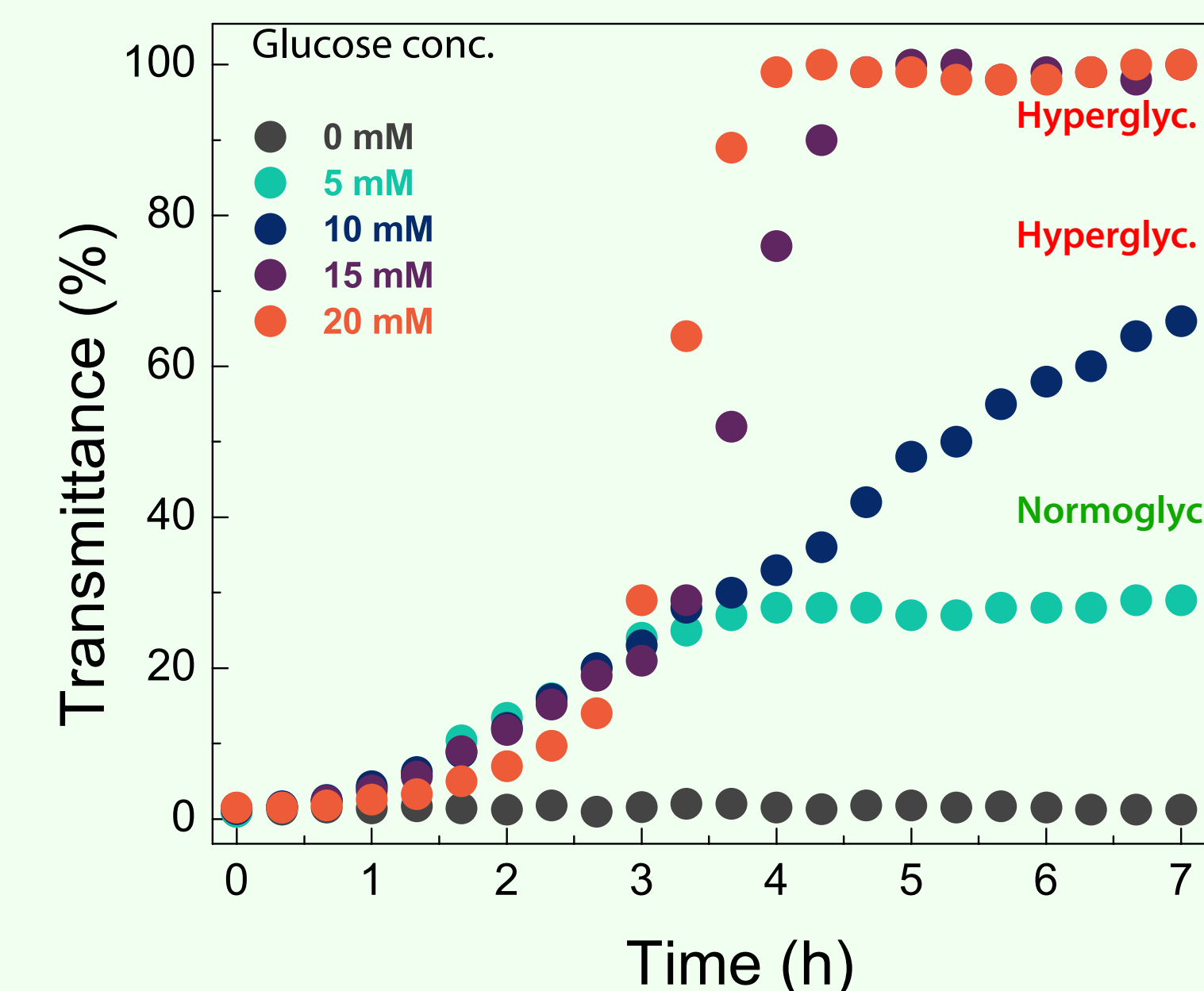
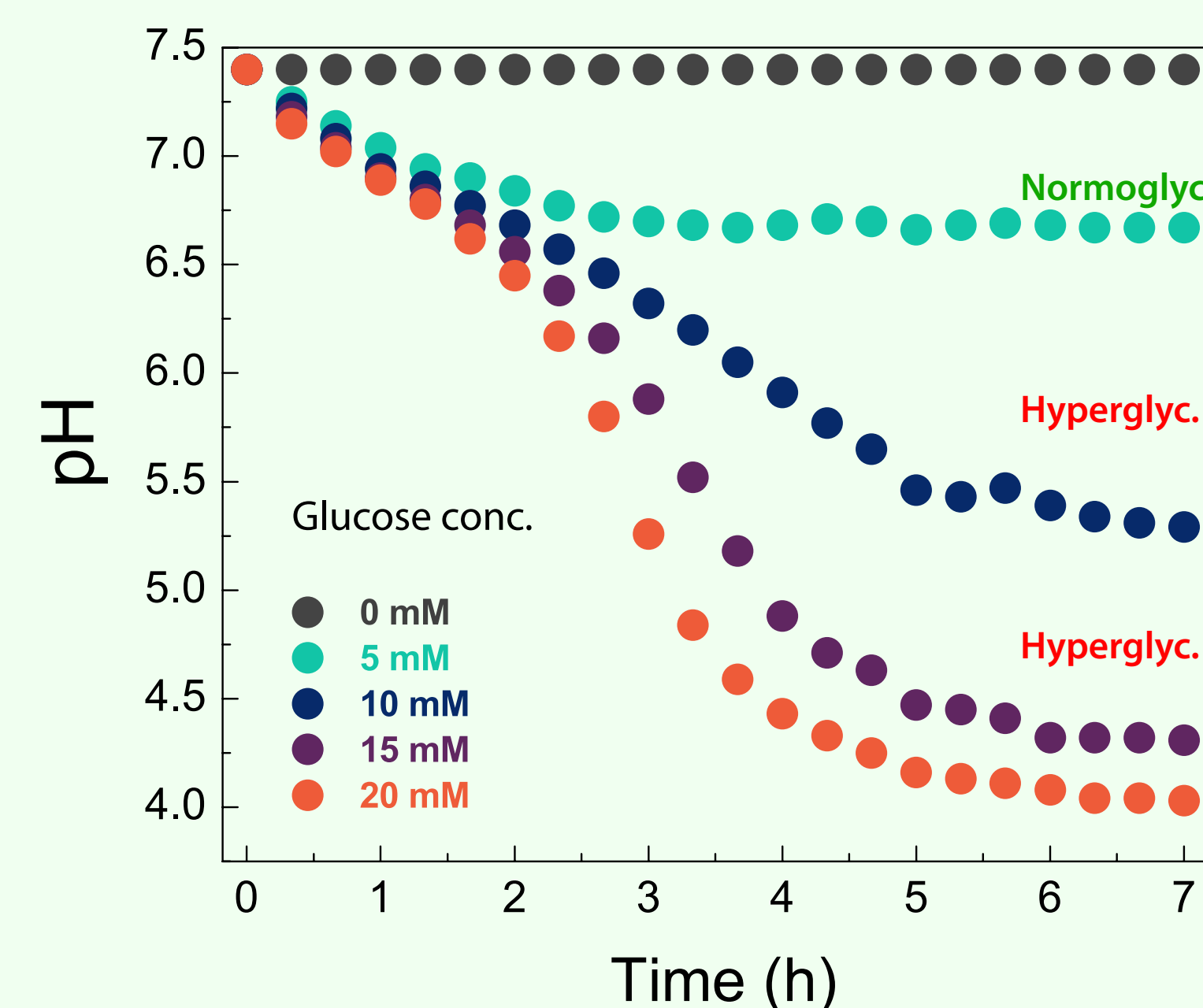
GI-PSA characterization

A single peak centered at 360 nm (DLS) with a polydispersity index of 0.1 indicates a narrow and homogeneous distribution of sizes in the solution phase. This indicates that the crosslinking of PAH occurs concomitantly with the uptake of insulin and GOx. TEM image analysis showed that GI-PSAs have a spherical shape and a wide distribution of particle diameters with a maximum at 90 nm and a tail at larger diameters.



responsivity to glucose

Both the pH and transmittance % at 580 nm (turbidity) were measured over time at 37 °C in HEPES after adding increasing concentrations of glucose. While for hyperglycemic conditions (>10 mM) GI-PSAs were completely dissolved (T=100 %), for normoglycemic conditions (5 mM) GI-PSAs remained stable. The pH time-dependence fits with the hypothesis.



releasing of insulin

The total polypeptide release (GOx + Ins) was obtained by measuring the UV-spectra of the supernatant after 48 h of incubation.

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The article

M. L. Agazzi, S. E. Herrera, M. L. Cortez, W. A. Marmisollé, M. Tagliazucchi and O. Azzaroni, Chem. Eur. J., **2020**, 26, 11, 2456–2463.