Smart polymersomes: pH-responsive nanocarriers for improved intestinal delivery of immunosuppressants

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CONTROLLED RELEASE SOCIETY
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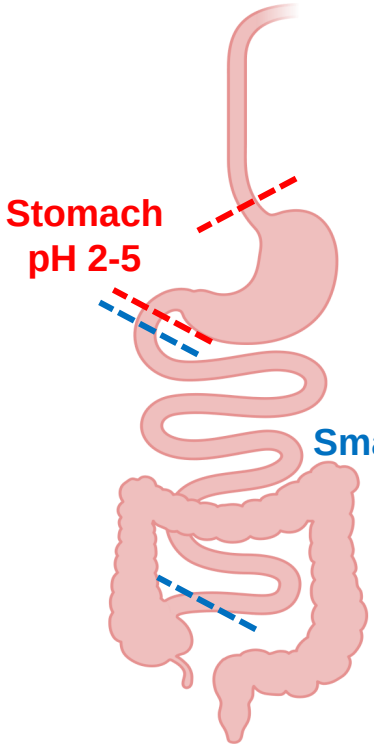
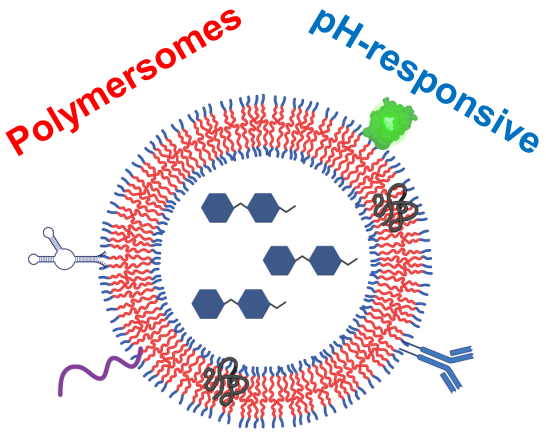
JULY 8-12, 2024 • BOLOGNA, ITALY

INTEGRATING
Delivery Science
ACROSS DISCIPLINES

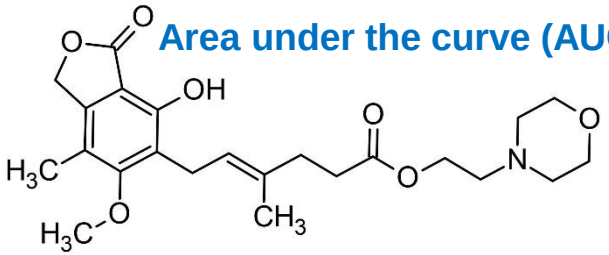
Ingredients



ORAL DRUG DELIVERY

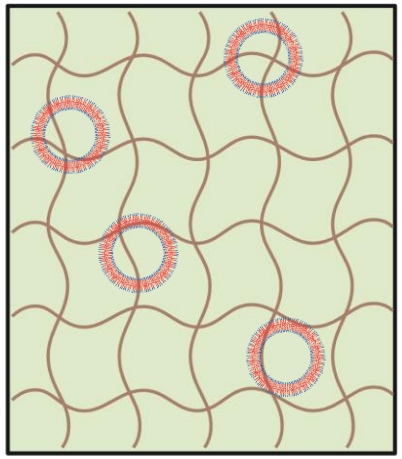


NANOPARTICLES



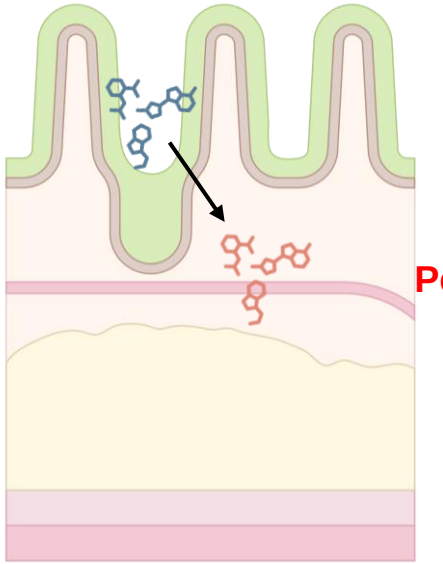
MYCOPHENOLATE MOFETIL
MMF

Increased retention



MUCOADHESION

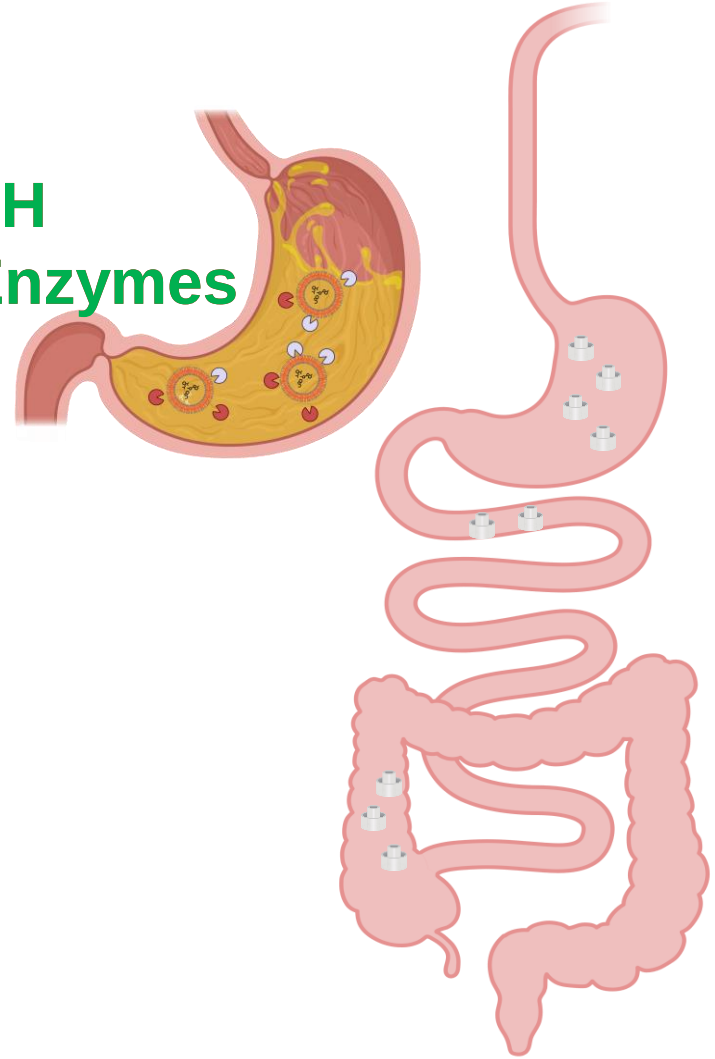
Solubility



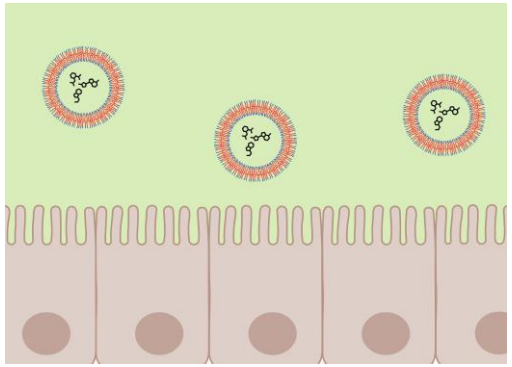
INTESTINAL EPITHELIUM

Oral drug delivery

- pH
- Enzymes



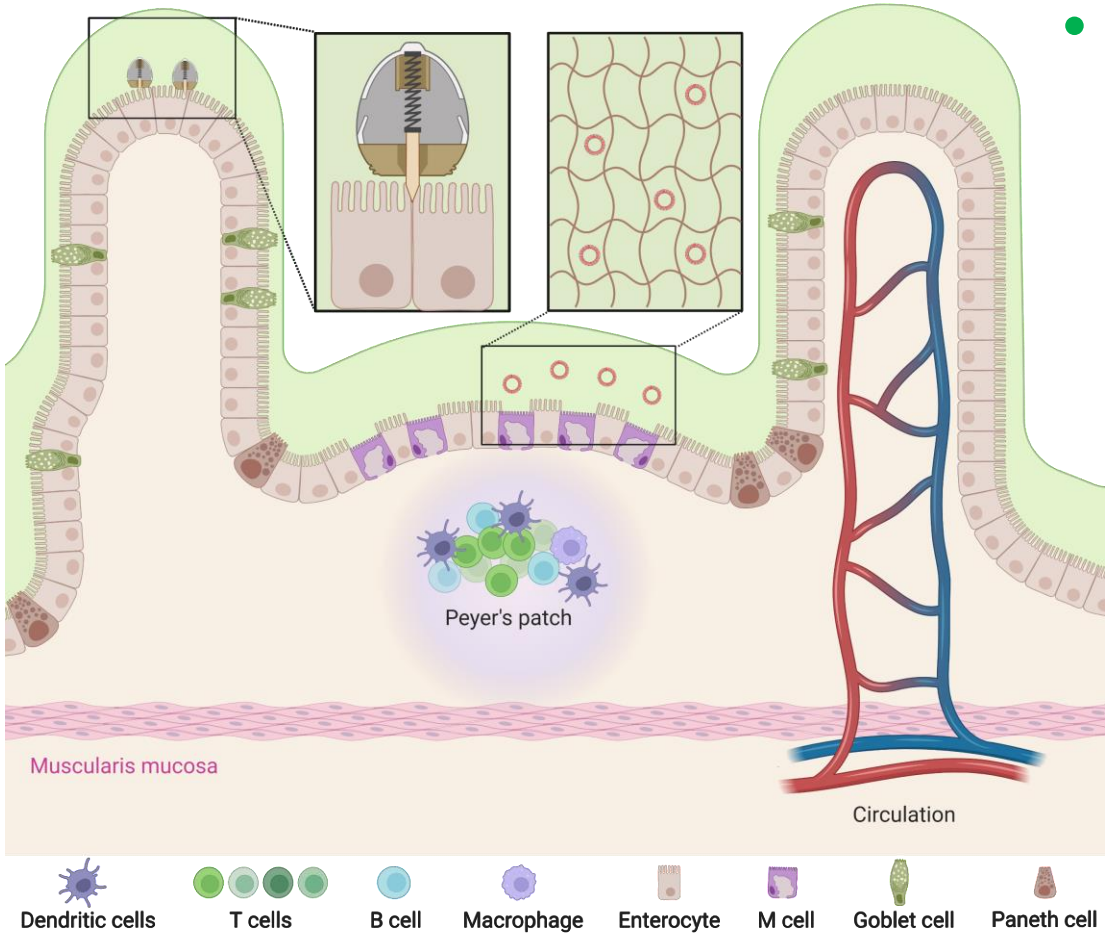
- Retention
- Solubility



Christfort, J., et al. Pharmaceutics 2020, 12(4), 355

Solutions?

- Retention
- Poorly soluble drugs
- Patient compliance

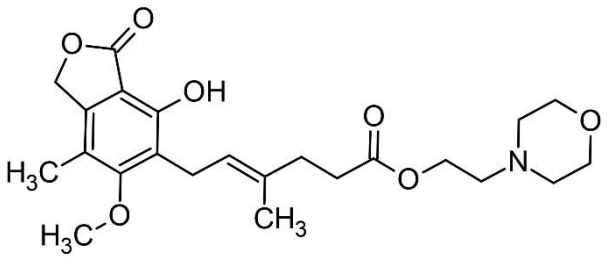


Abramson, A., et al. Science 2019; Vol 363, Issue 6427

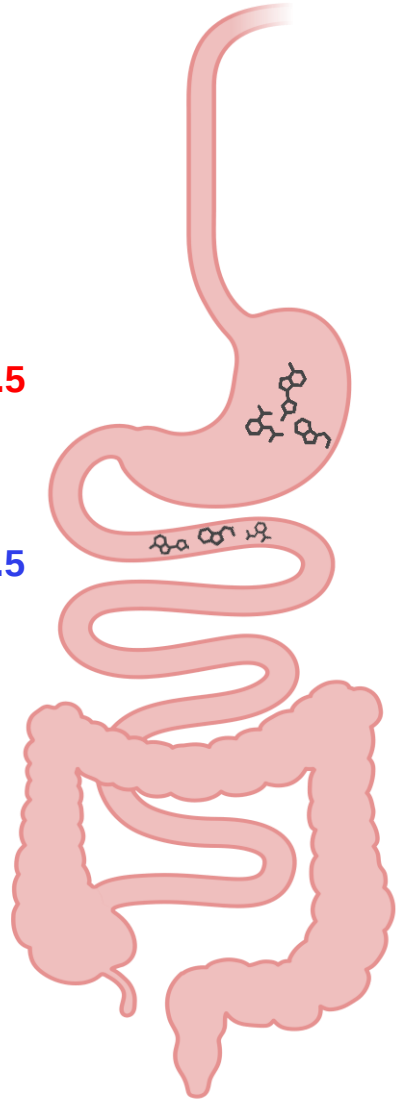
Background

Class I	Class II
High solubility High permeability	Low solubility High permeability
Class III	**Class IV**
High solubility Low permeability	Low solubility Low permeability

Class II

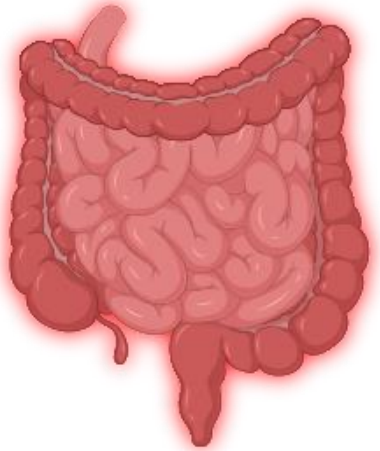


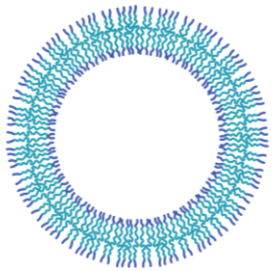
Mycophenolate Mofetil



1. Postpone uptake
2. Keep solubility

Inflammatory Bowel Disease

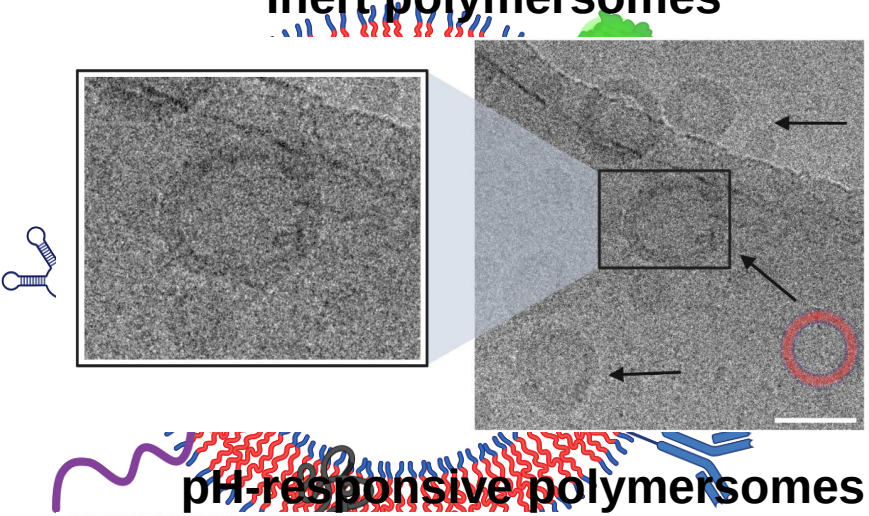




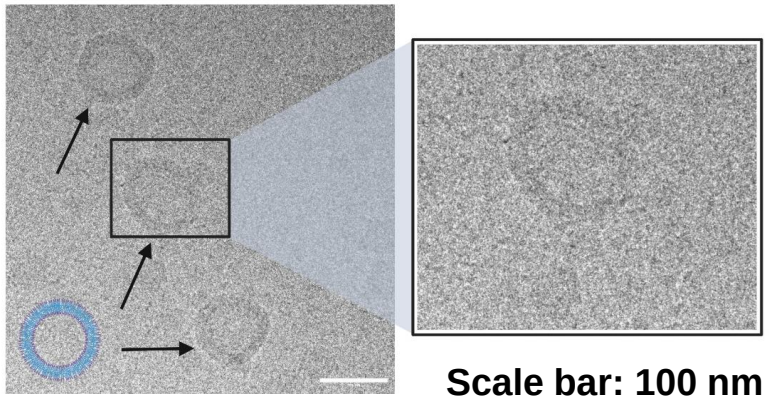
pH > 5.5

Polymersomes

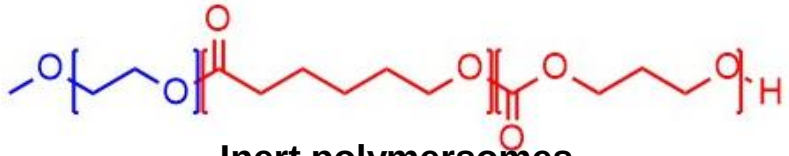
Inert polymersomes



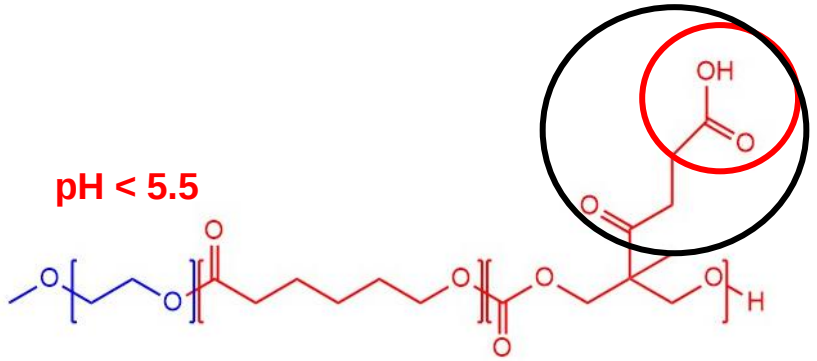
pH-responsive polymersomes



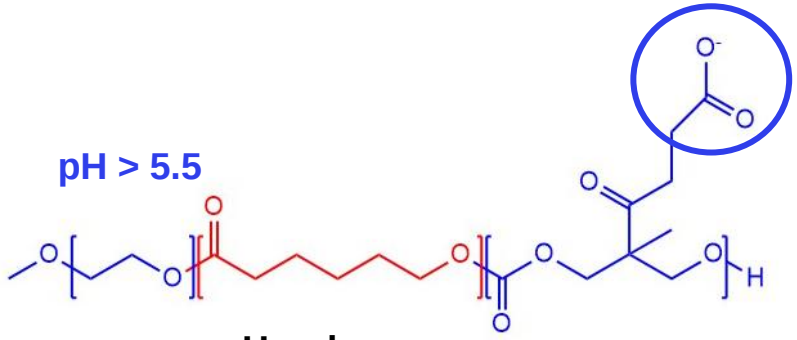
Scale bar: 100 nm



Inert polymersomes
PEG-CL-TMC

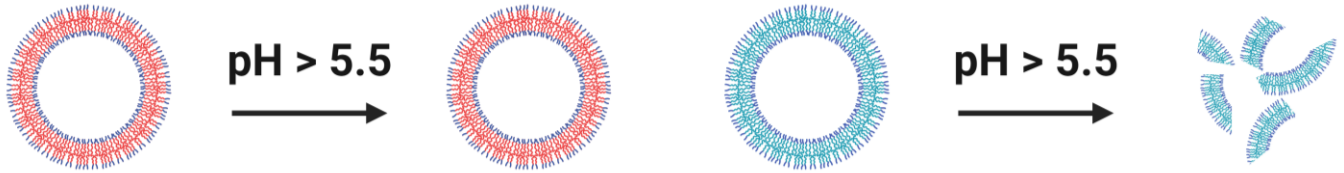


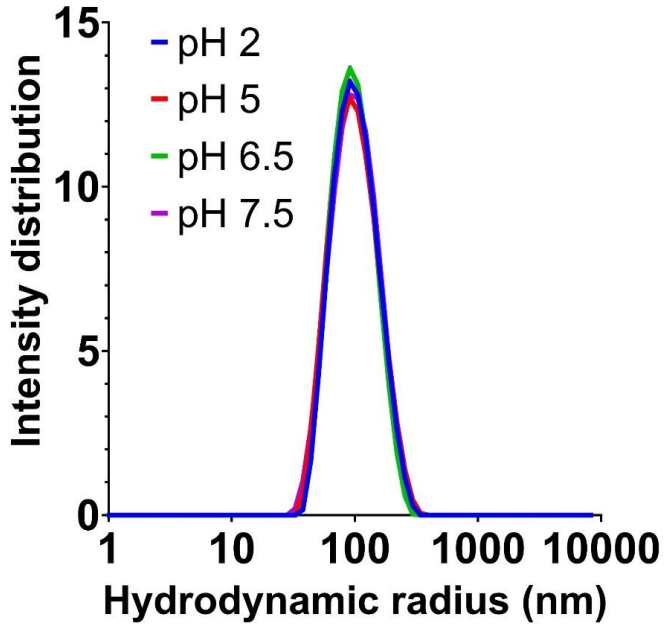
pH-polymersomes
PEG-CL-TMCTBC



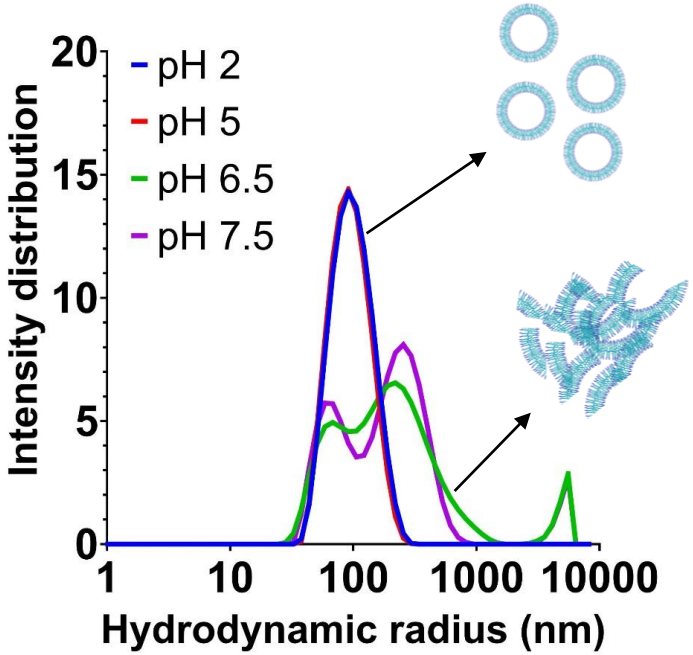
pH-polymersomes
PEG-CL-TMCTBC

Polymersomes' stability



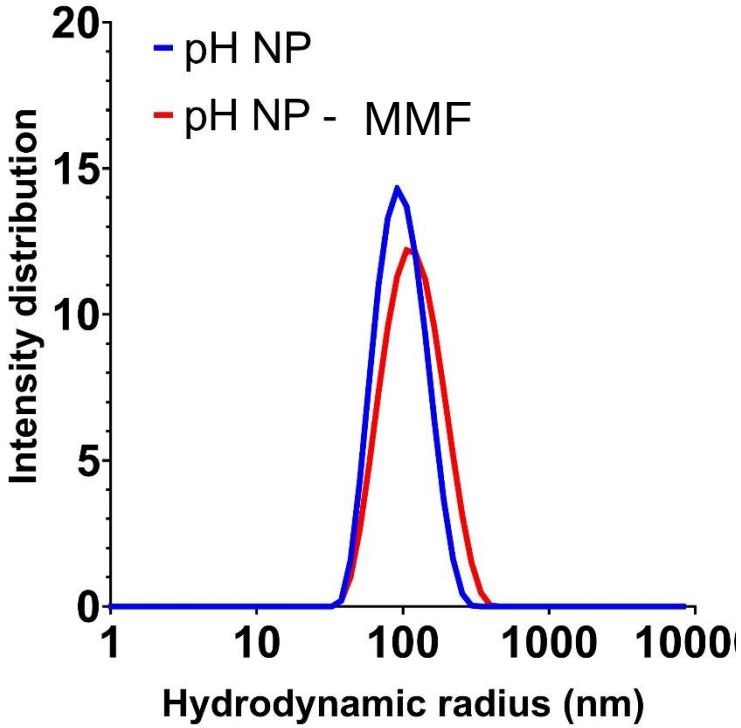


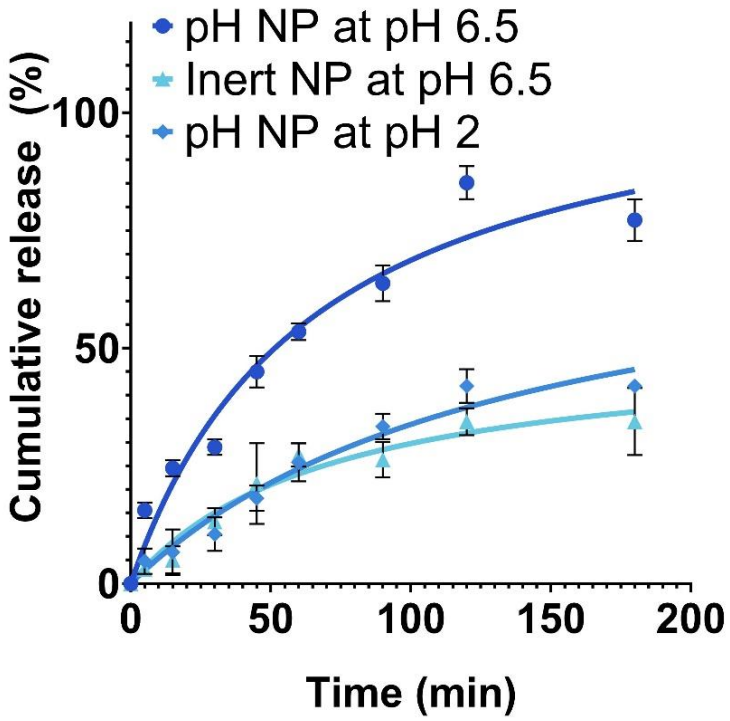
Inert nanoparticles



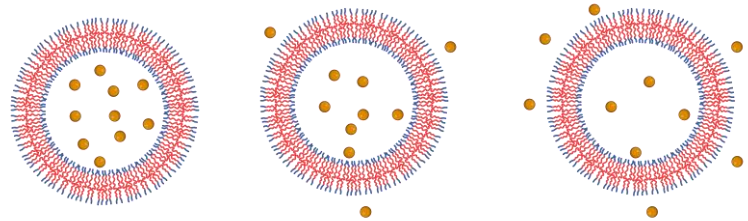
pH-responsive nanoparticles

In vitro release

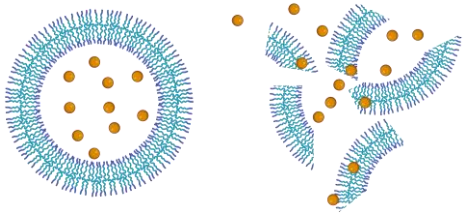




Semi-permeable polymersomes

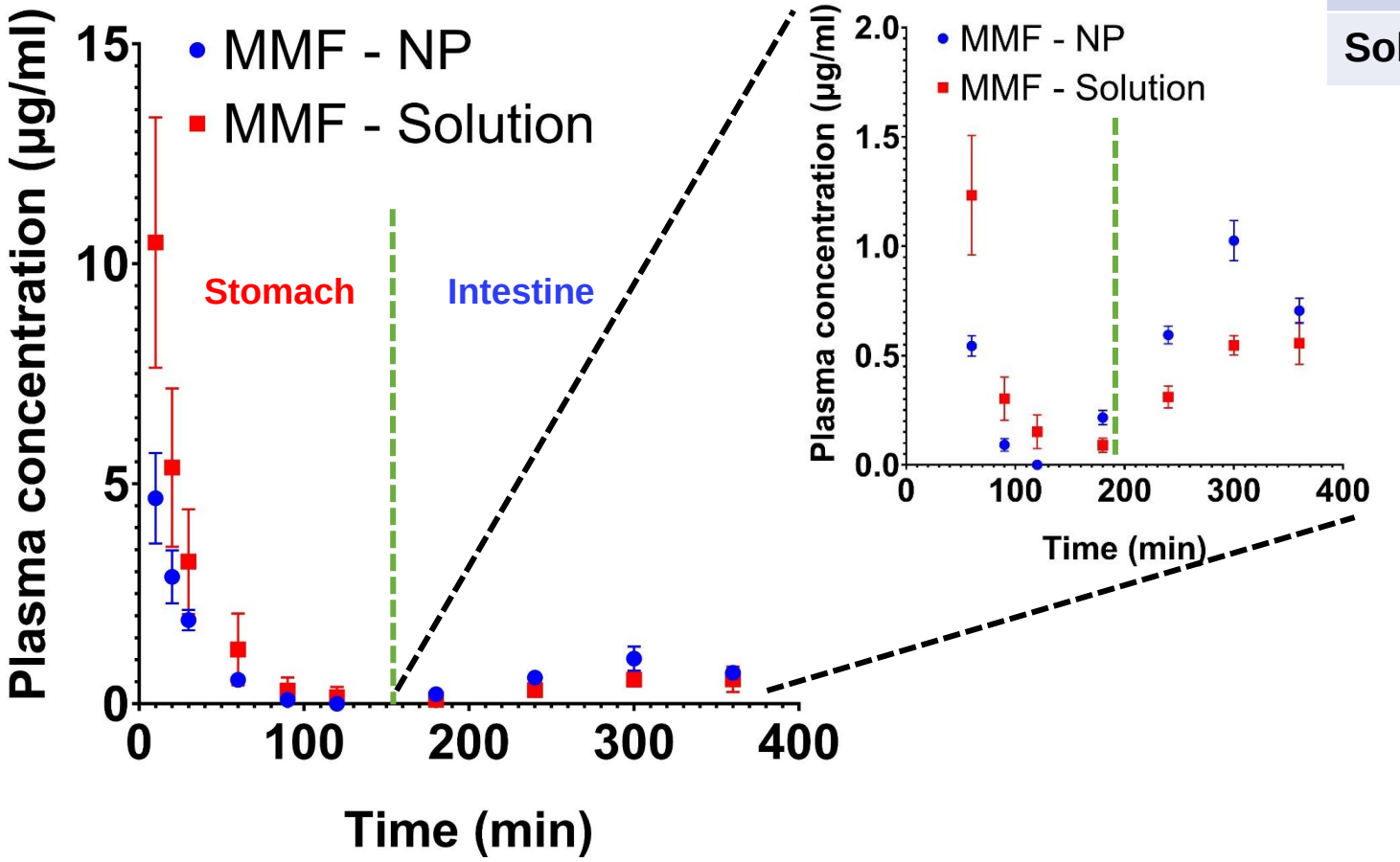


Enhanced release



- **EE: 27%**
- **DLC: 0.3 mg /mg of NP**

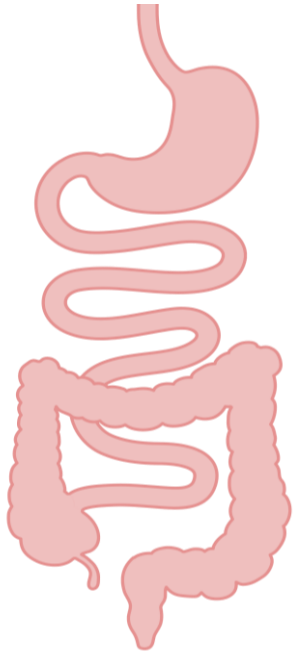
In vivo studies



AUC	Stomach * (ug*h/ml)	Intestine * (ug*h/ml)	Total
NP	1.69 ± 0.07	2.19± 0.14	3.88 ± 0.15
Solution	3.31± 0.47	1.30 ± 0.48	4.61 ± 0.67

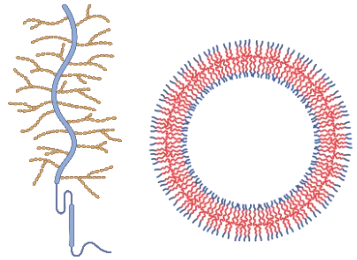
pH < 5.5 — **Reduced 2x**

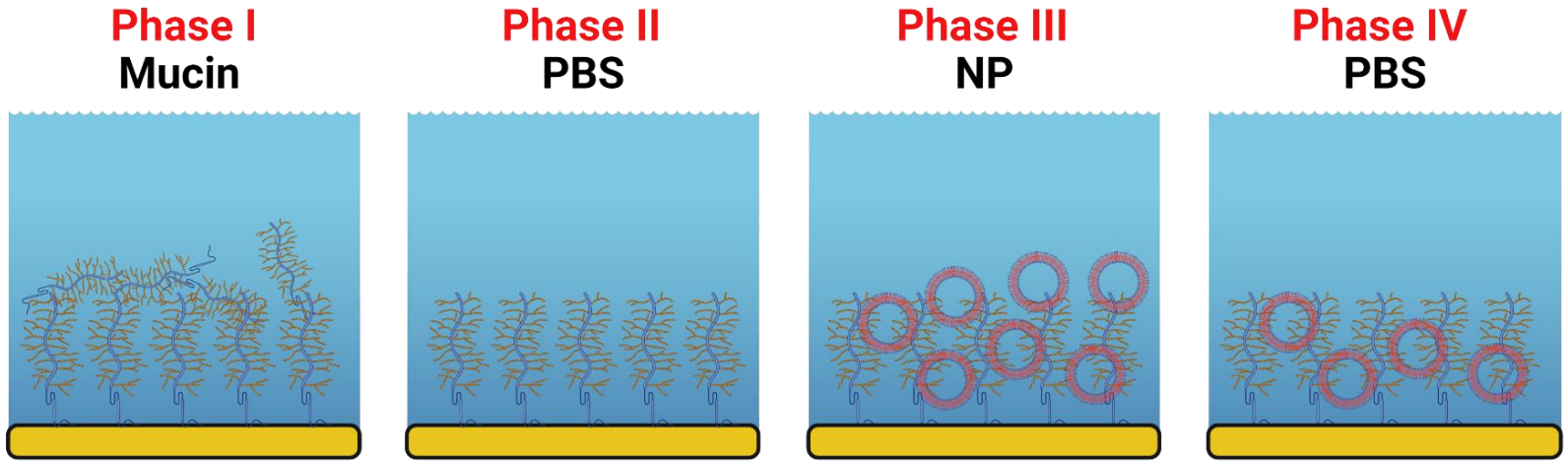
pH > 5.5 — **Increased 2x**

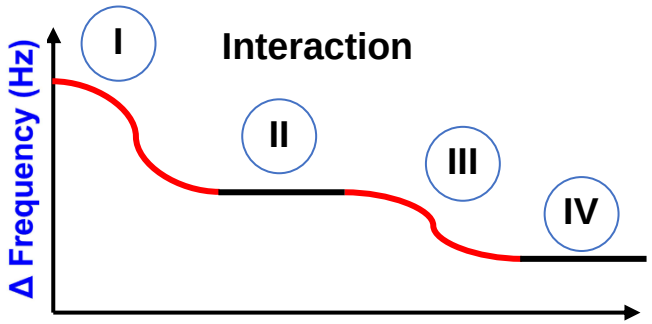


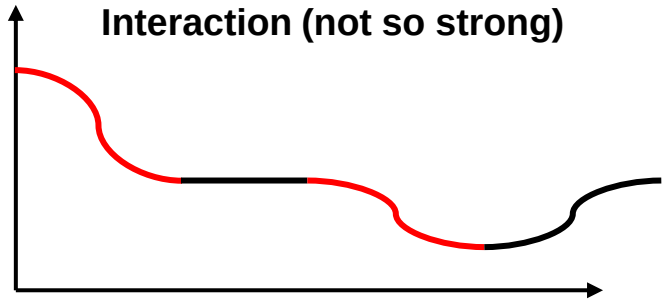
t-test: * $p < 0.05$

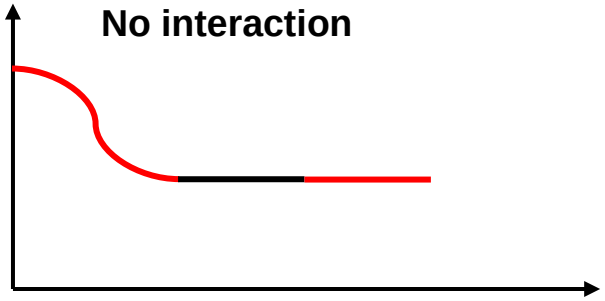
Lost particles? QCM-D



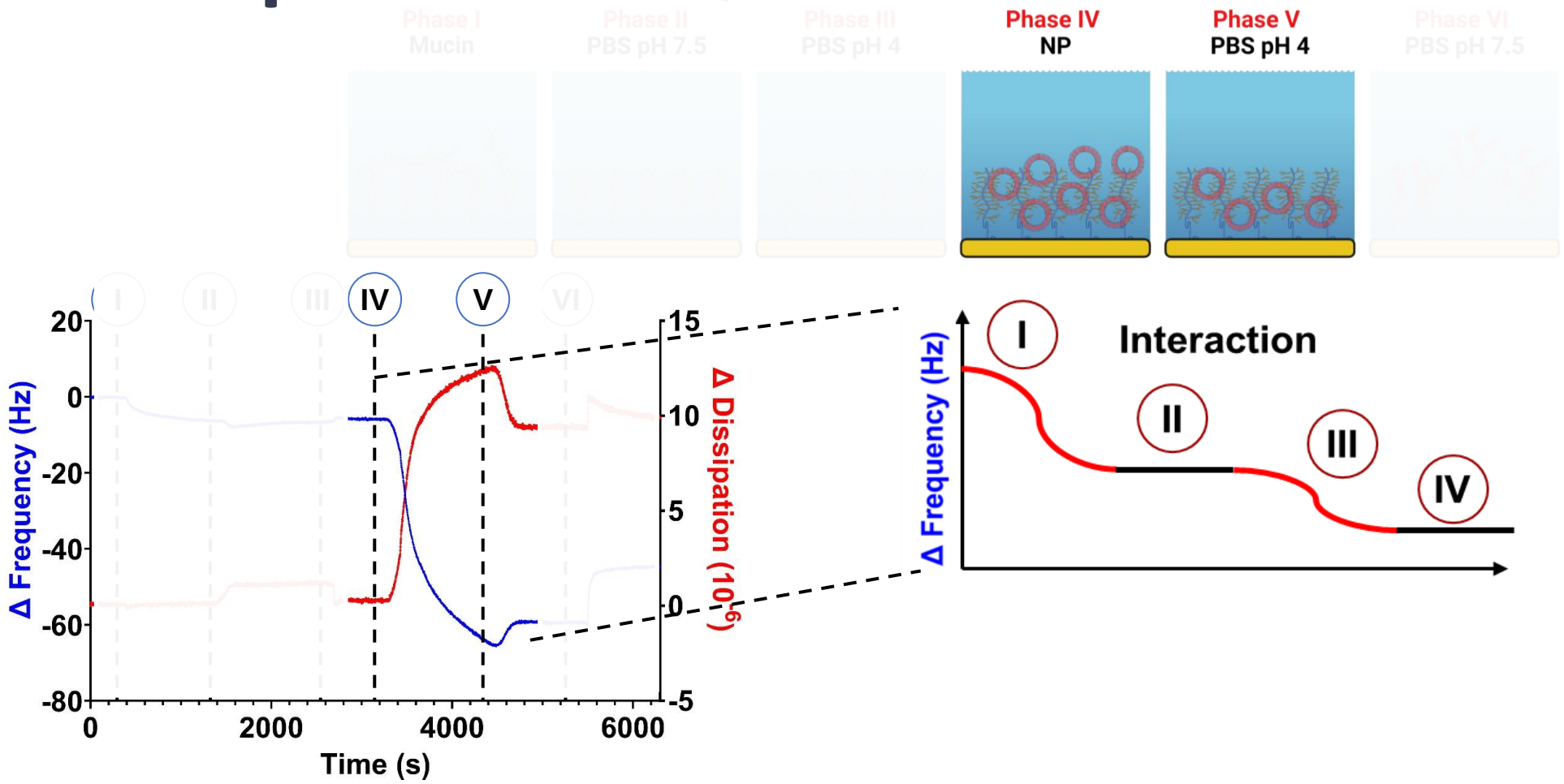


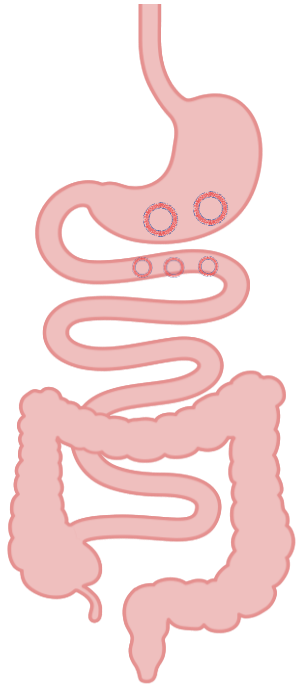




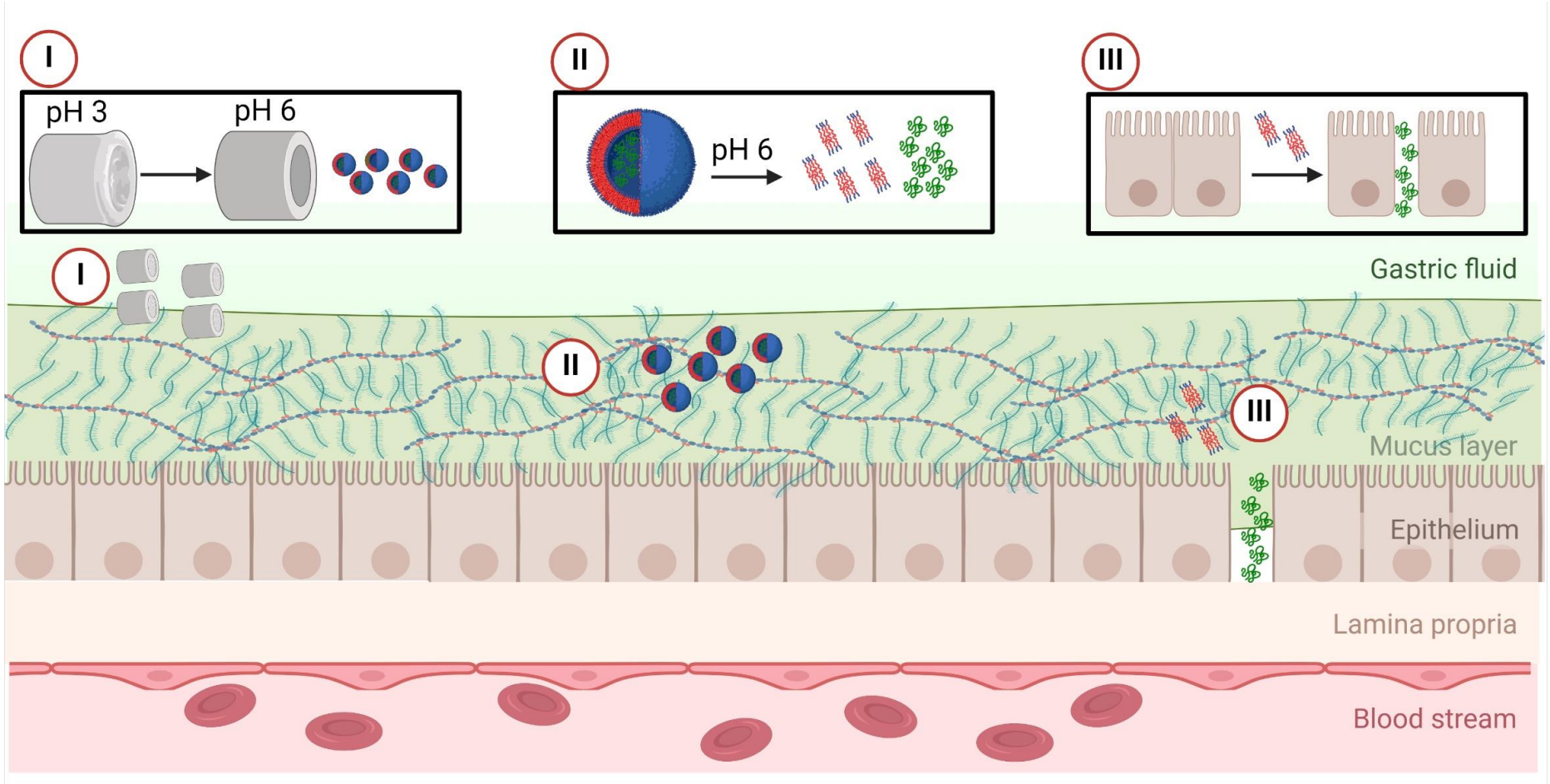


Lost particles? QCM-D





Conclusion & Future outlook



Acknowledgements

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