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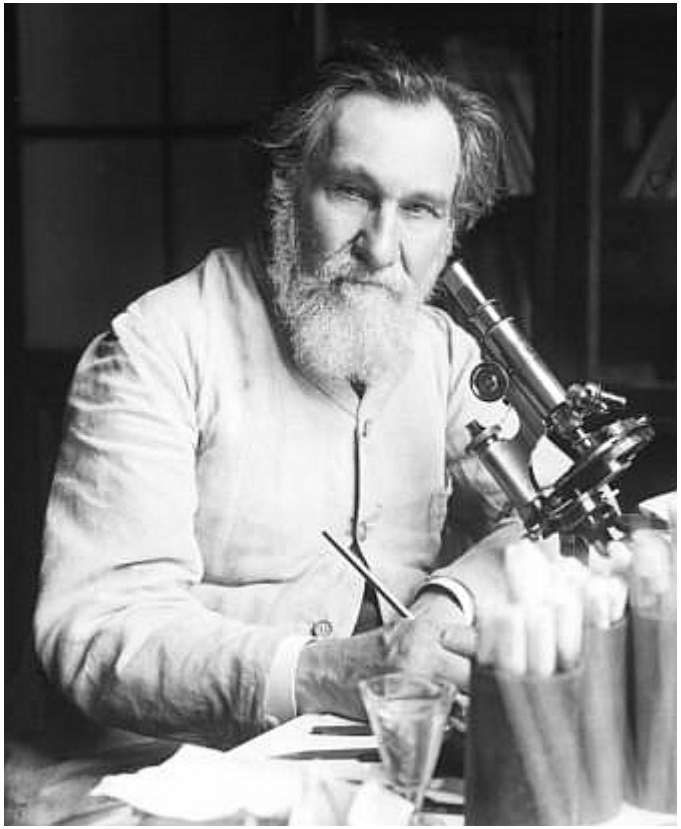
Encapsulation of acid-sensitive probiotic bacteria

Michael Cook, Dimitris Charalampopoulos , George Tzortis, and Vitaliy Khutoryanskiy.

Probiotics

- Very popular nutraceutical
- Show some promising clinical results for treatment of specific conditions, e.g. irritable bowel syndrome[1]
- Attractive due to the safety of oral ingestion and lack of side effects

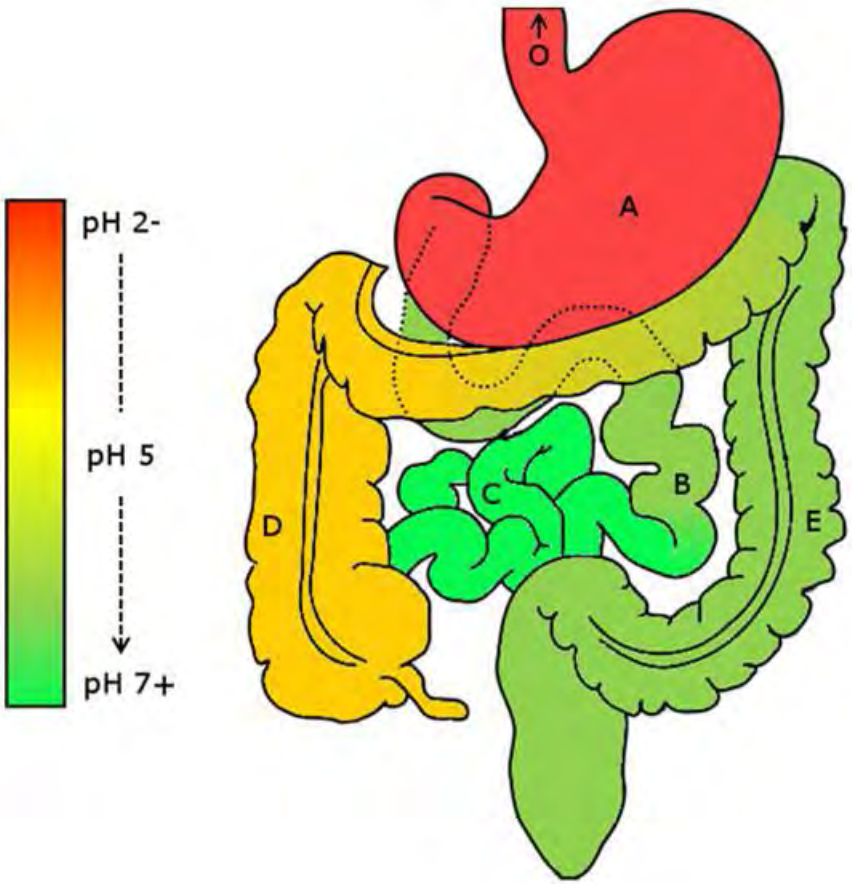


Ilya Metchnikoff

1. Whorwell *et al*; *American Journal of Gastroenterology*; 2006, **101**

Oral administration of probiotics

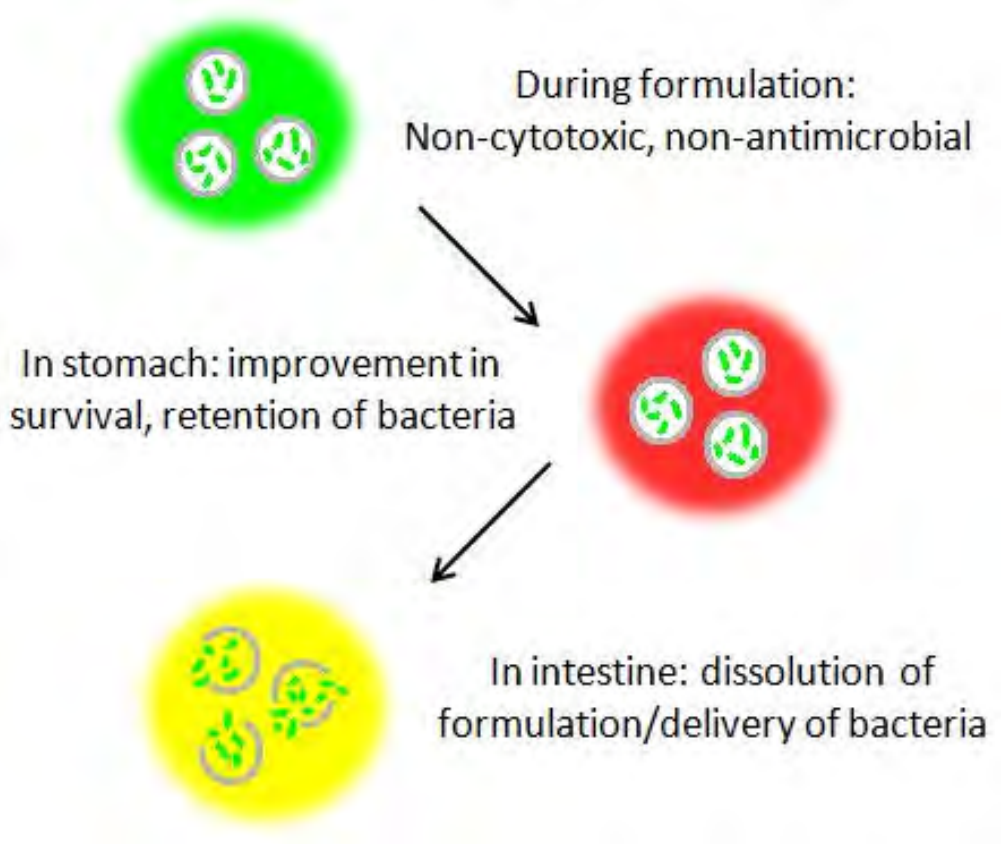
- Loss of viability in the stomach before action in intestine



Letter	Region
O	Oesophagus
A	Stomach
B	Proximal Small Intestine
C	Distal Small Intestine
D	Ascending Colon
E	Descending Colon

Image: Cook et al; *Journal of Controlled Release*, 2012, 162(1), 56-67.

Encapsulation



Encapsulation by extrusion

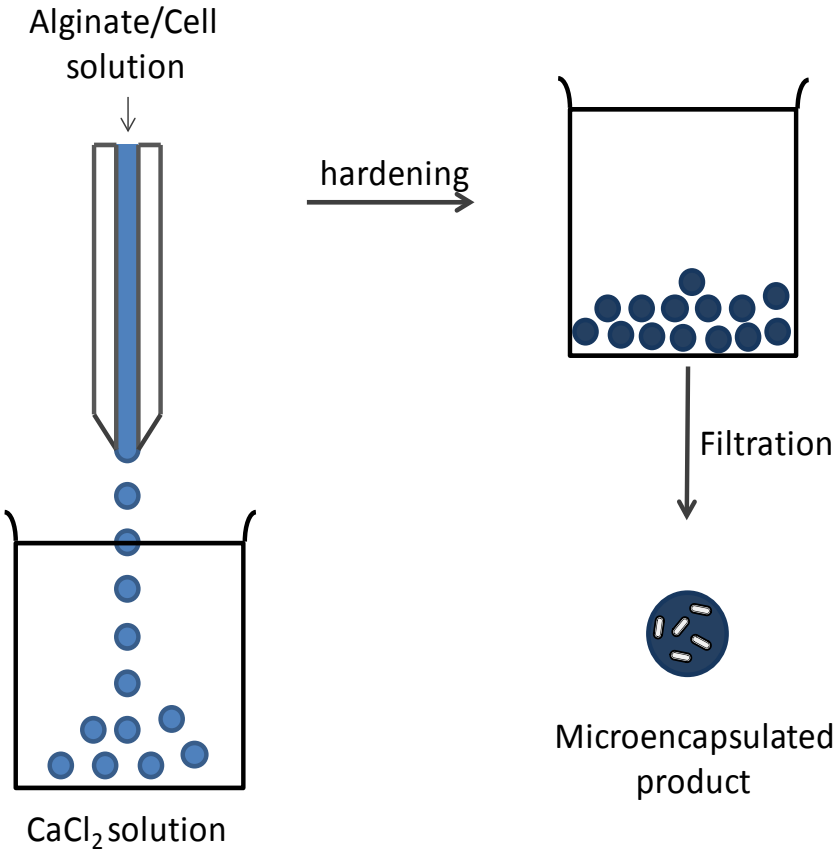
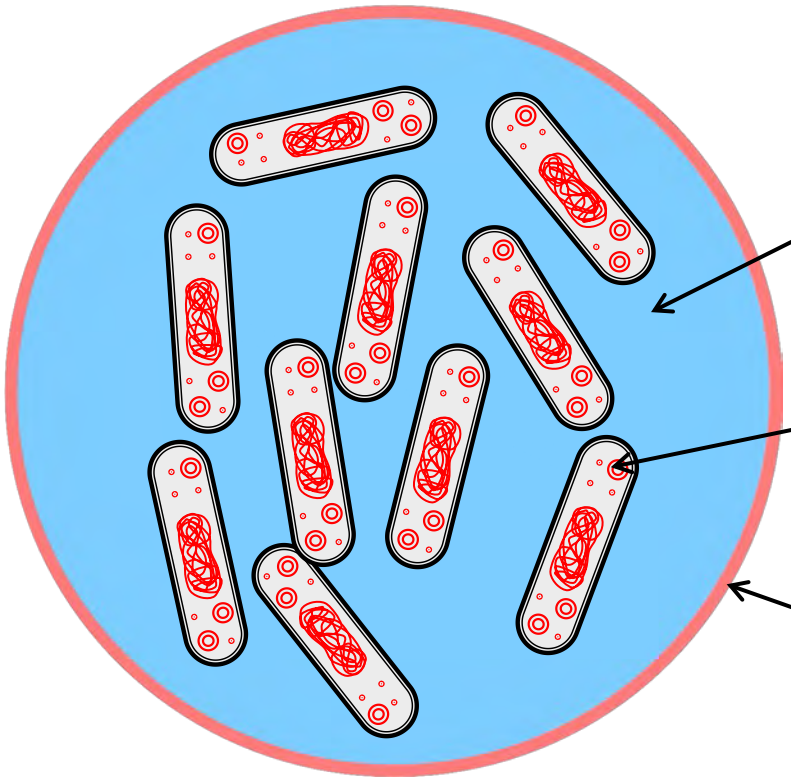
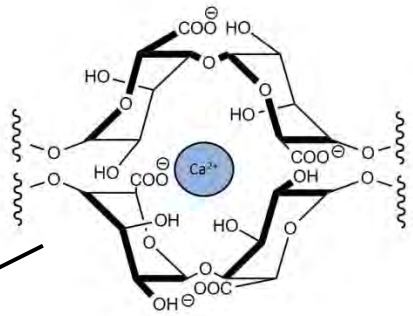


Image: Cook et al ; 2014; Hydrogels in cell-based therapies, RSC publishing, 95-111.

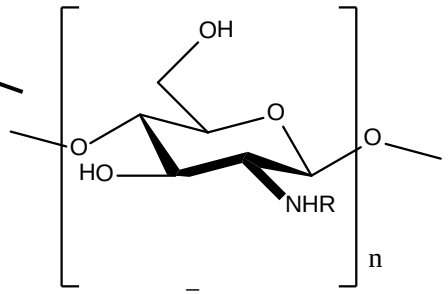
Alginate-chitosan matrices





Ca-alginate

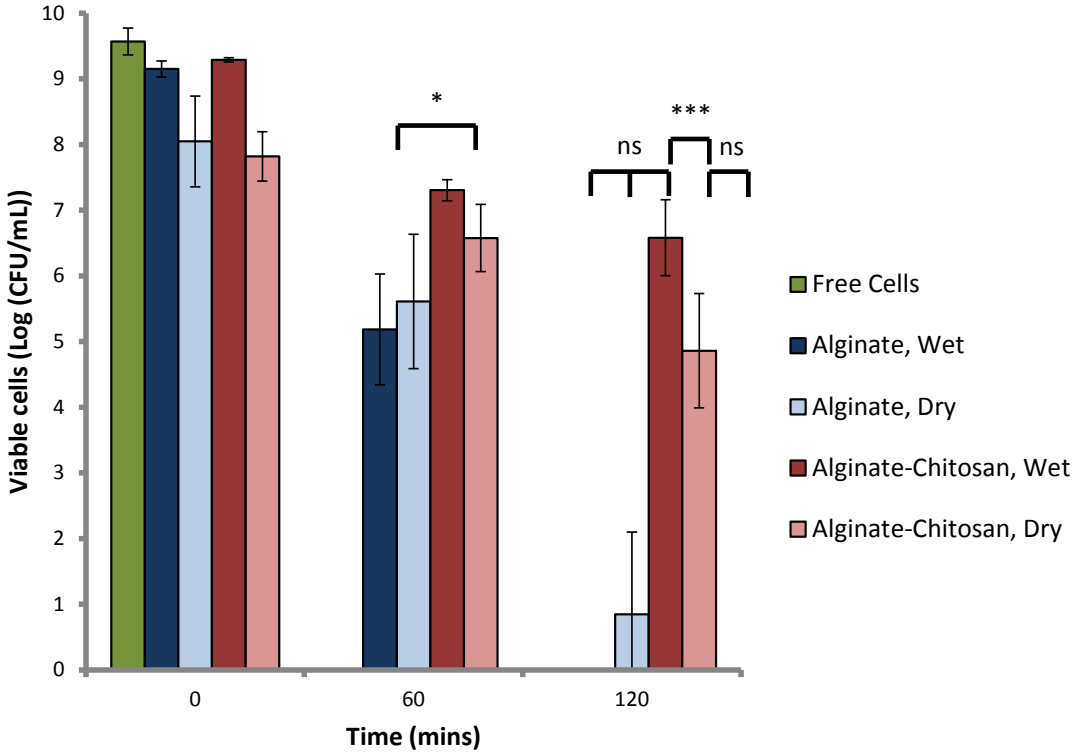
Bifidobacterium breve



R = Ac, H

chitosan

Alginate-chitosan matrices



Cook et al; *Biomacromolecules*; 2011; 12(7), 2834-40.

Lbl-coated matrices

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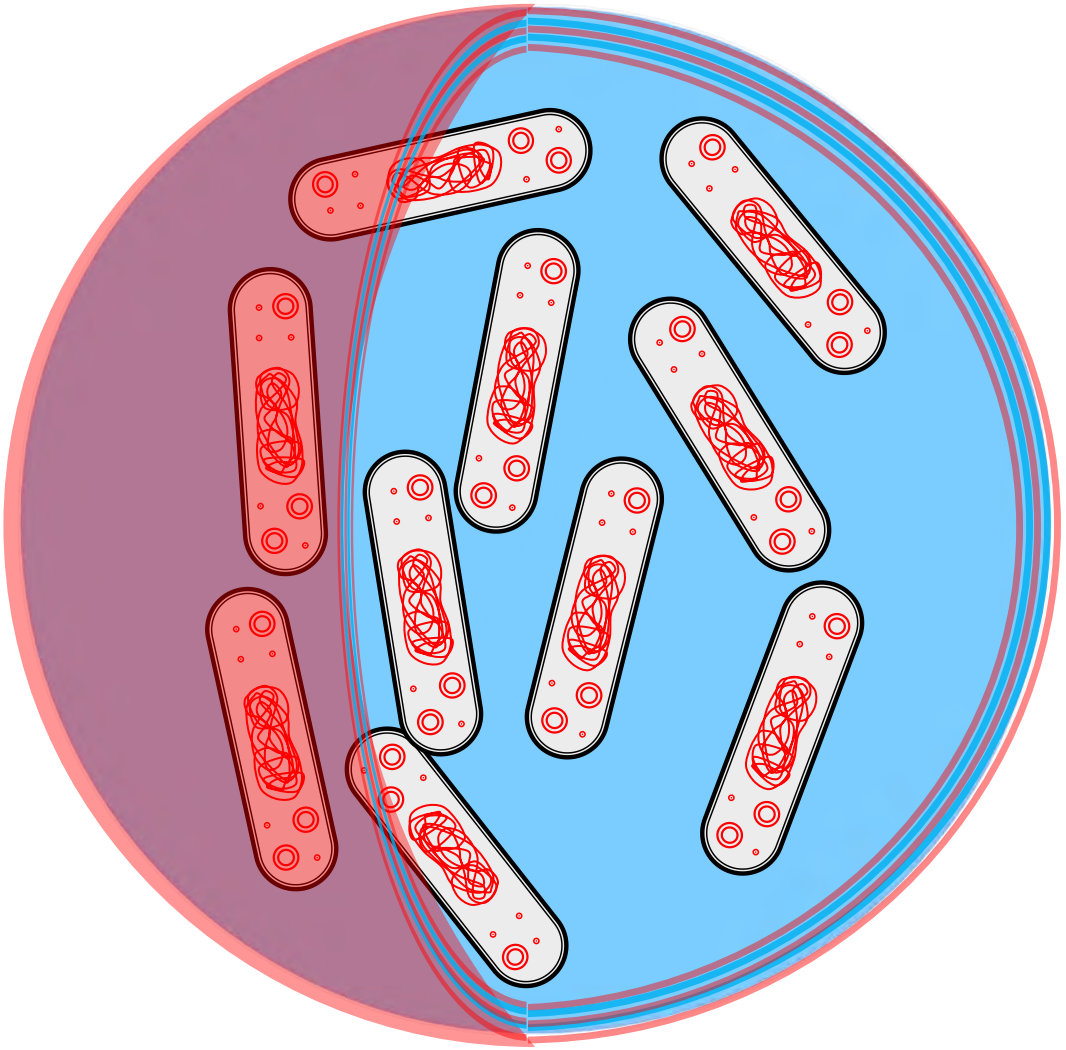
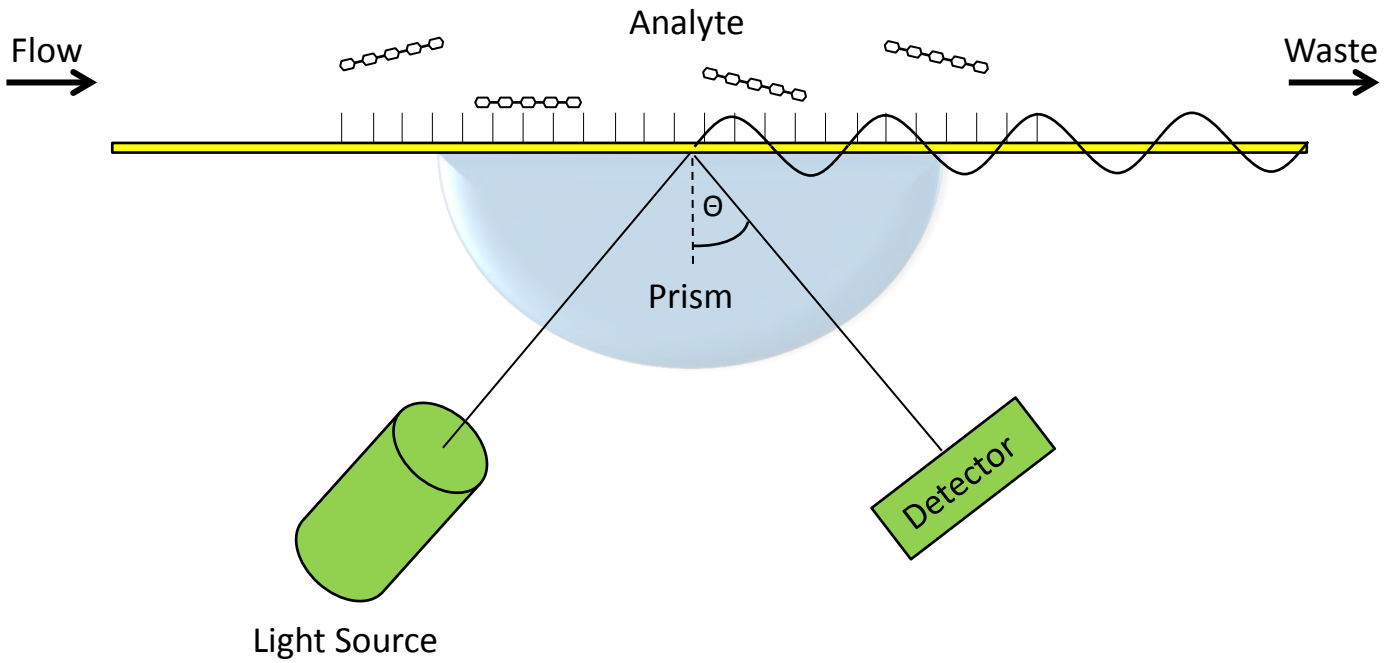
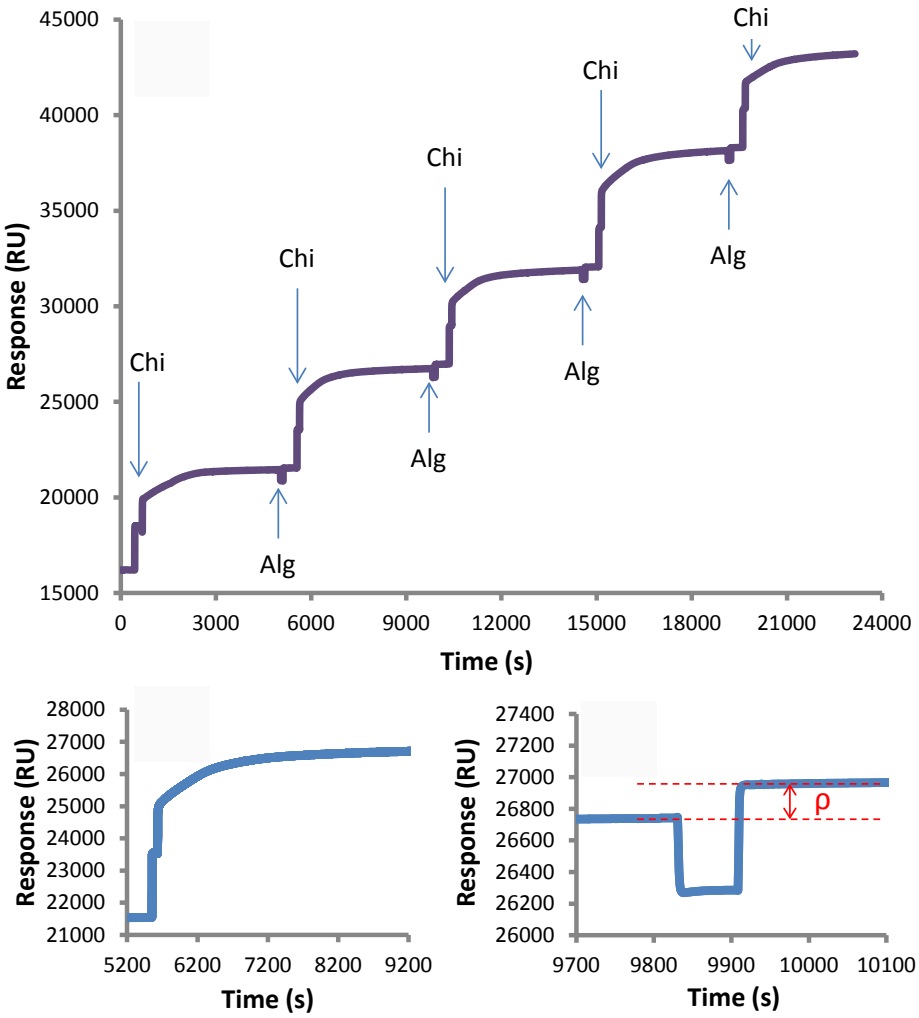


Build up of multilayers

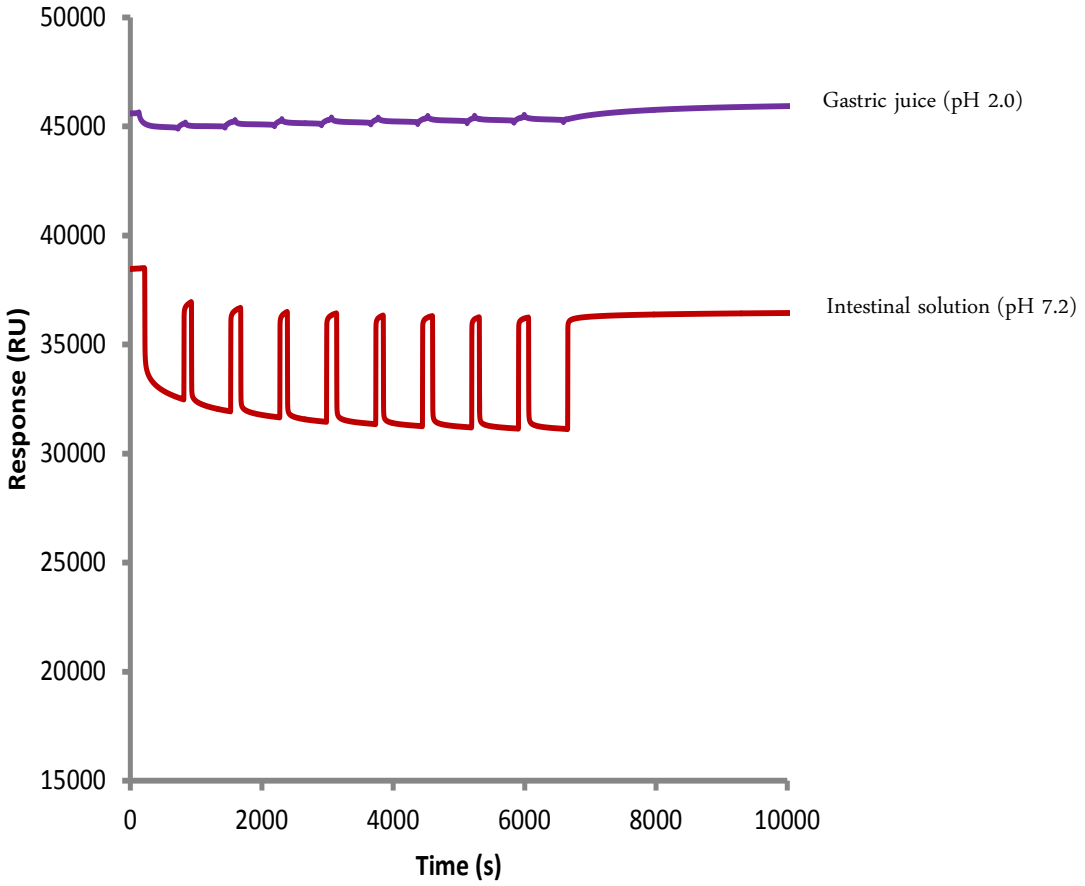
Electrostatic self assembly studied by surface plasmon resonance.



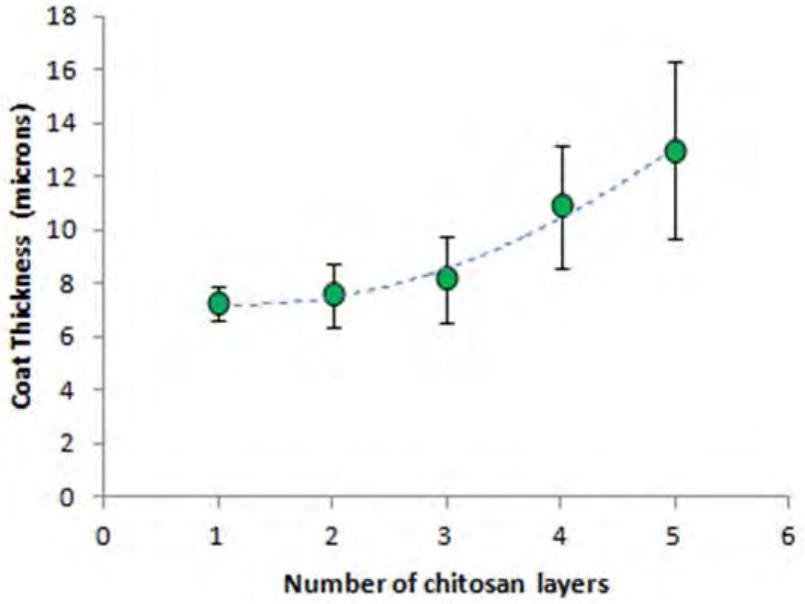
Build up of multilayers

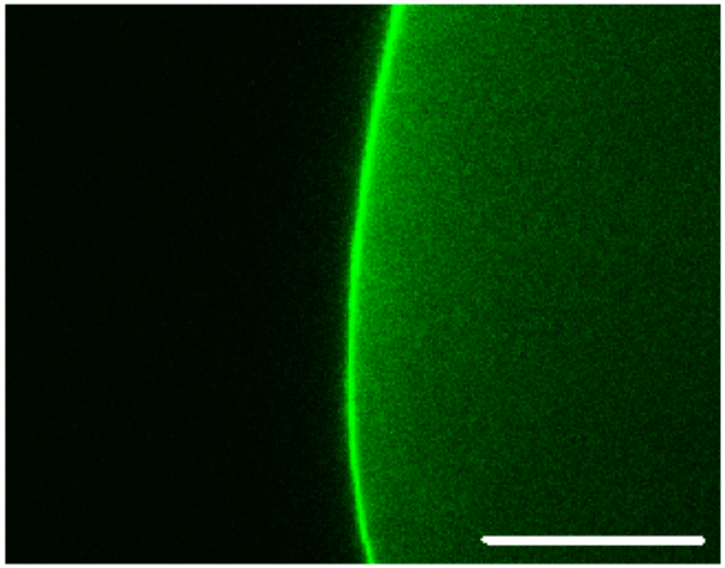


Stability of complexes studied



Coating visualisation by CLSM





Viability of bacteria in simulated gastric conditions

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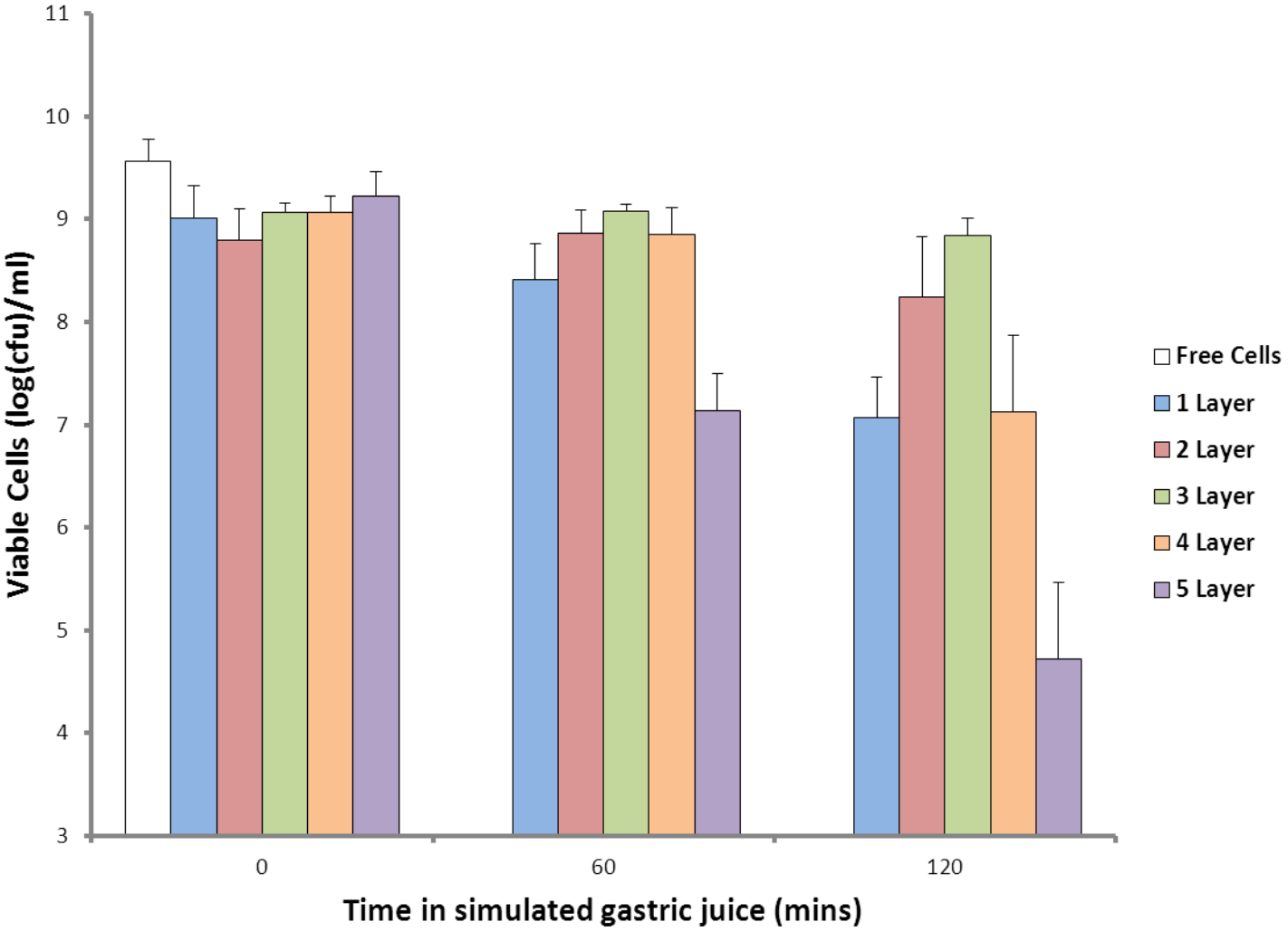
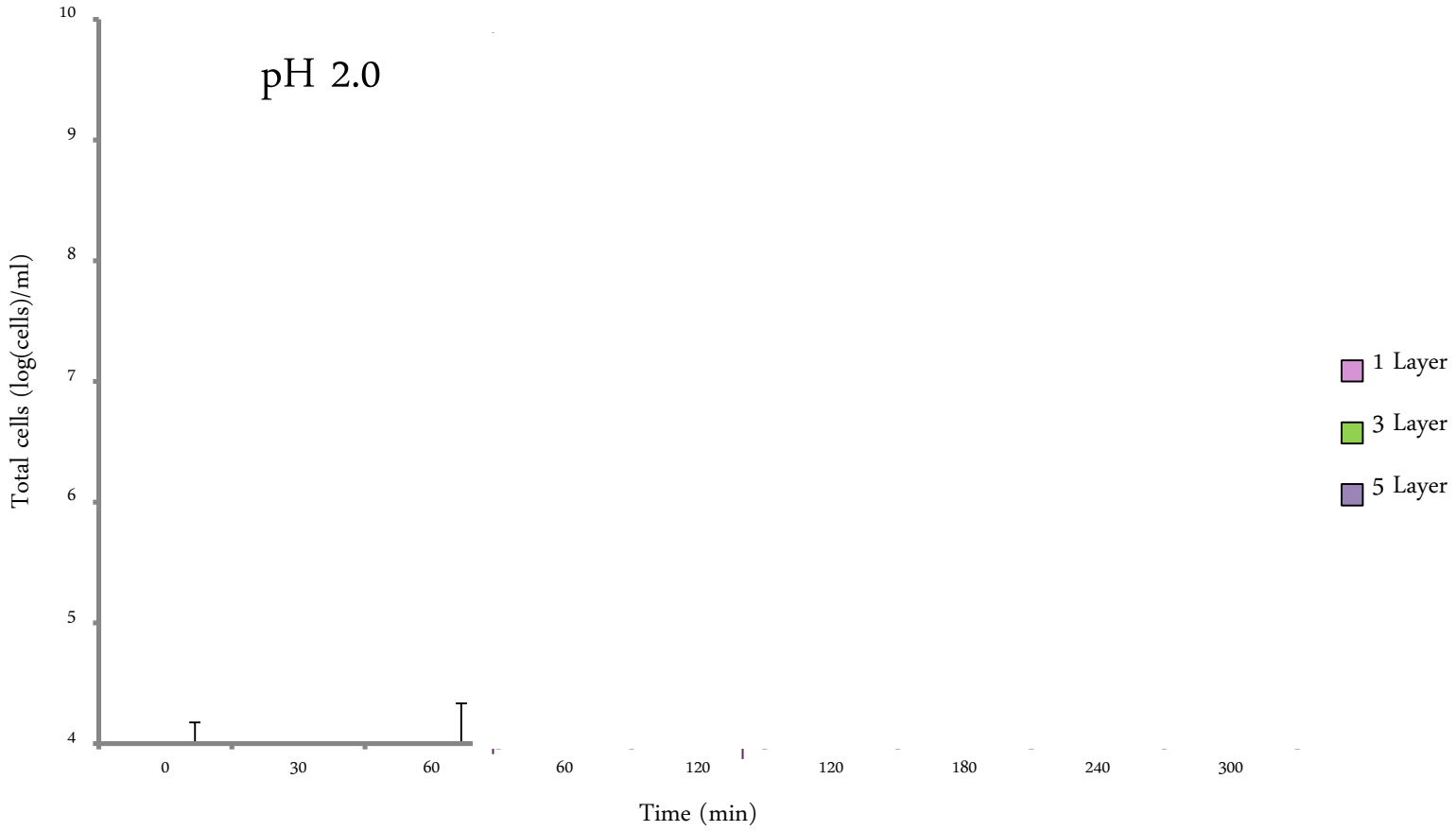


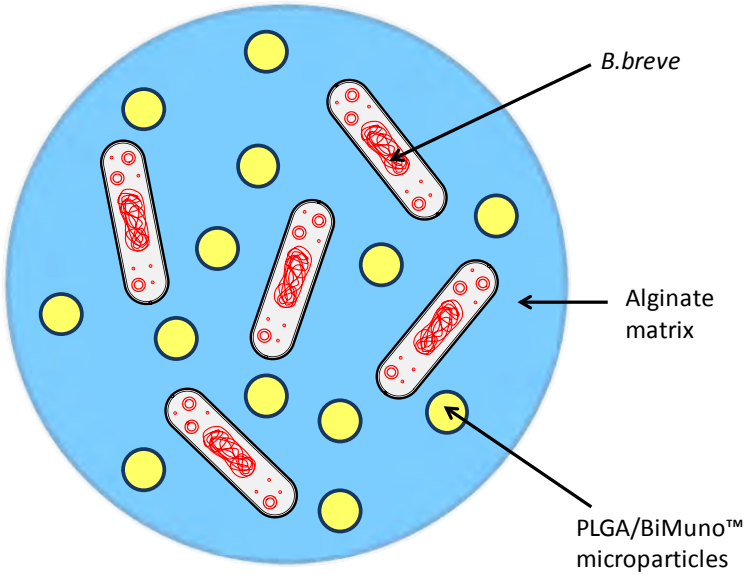
Cook et al; *Journal of Materials Chemistry B*; 2013; 1, 52-60.

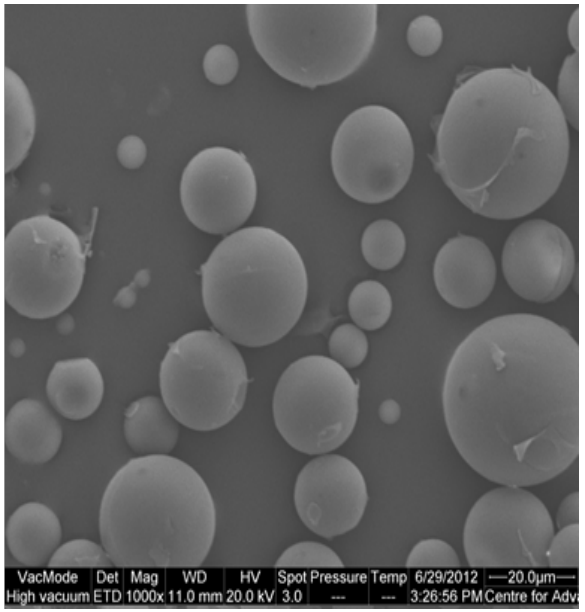
Encapsulation targets release



Encapsulation of Synbiotics

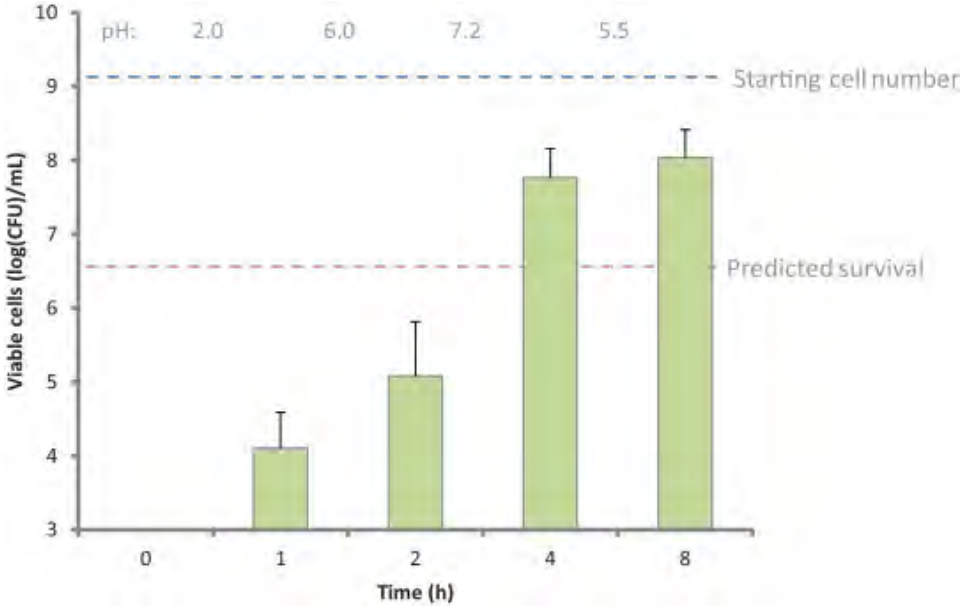
- Galactose-oligosaccharides (GOS) are a "prebiotic"
- Prebiotic + probiotic = "Synbiotic"
- Aim was to form "multiparticulates" so that GOS can be separately formulated

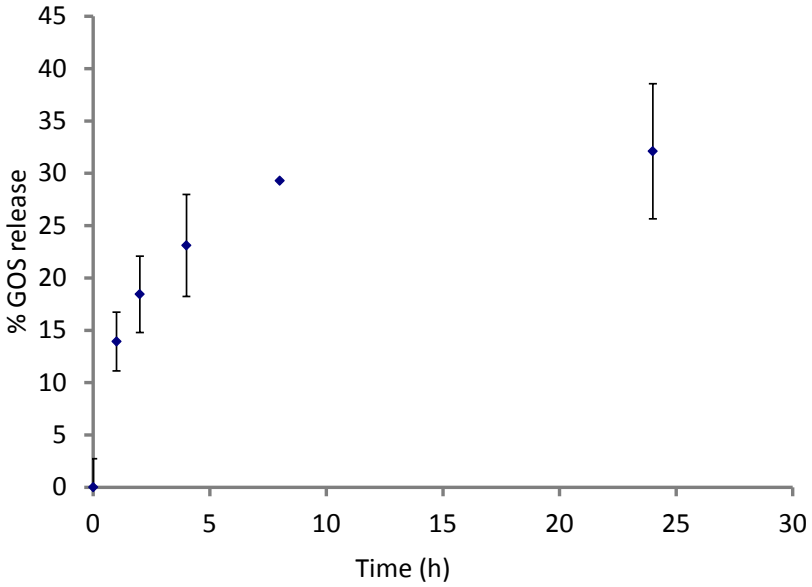




Synbiotic release in GI conditions

- Both prebiotic and probiotic release controlled over duration of simulated GI passage

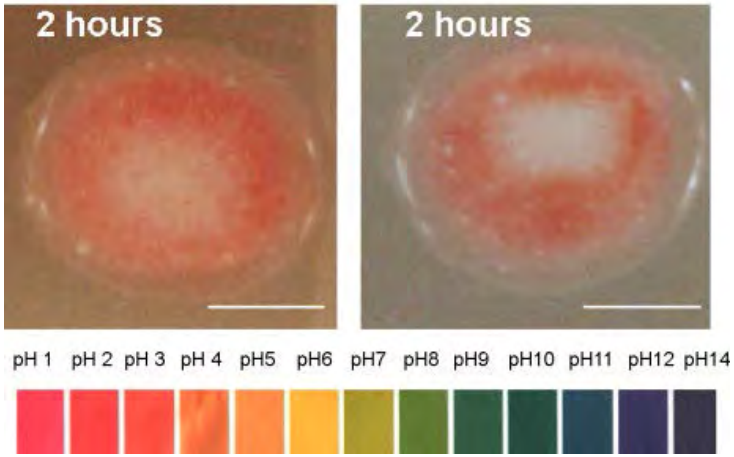




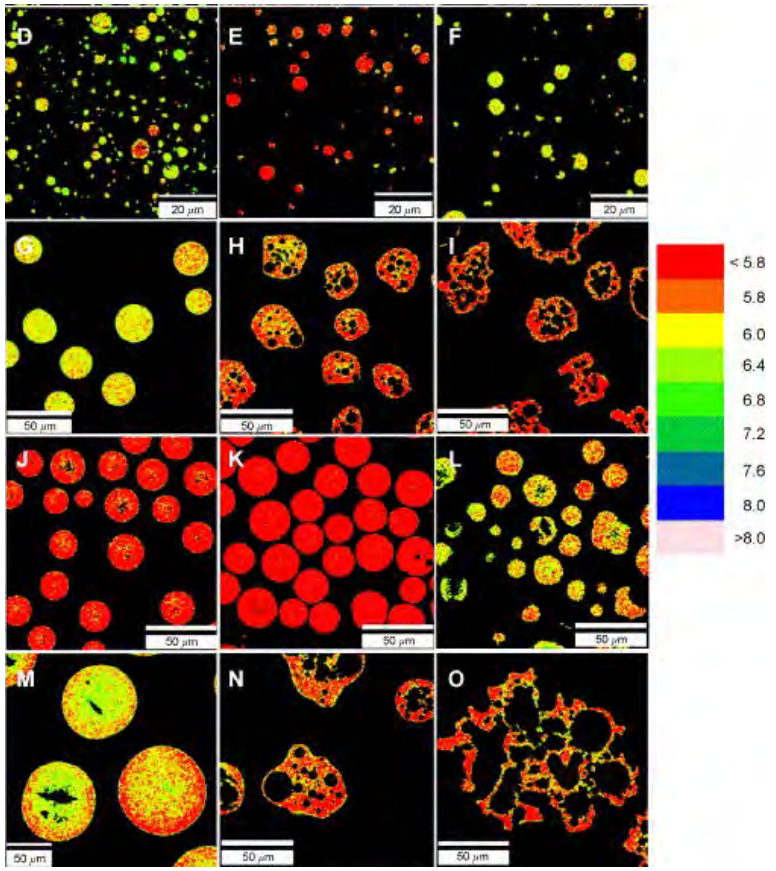
Cook et al; *International Journal of Pharmaceutics*; 2014; 466, 400-408

What's actually happening?

- Literature contains only suggestions of protection mechanism
- We want to 'see' pH inside materials

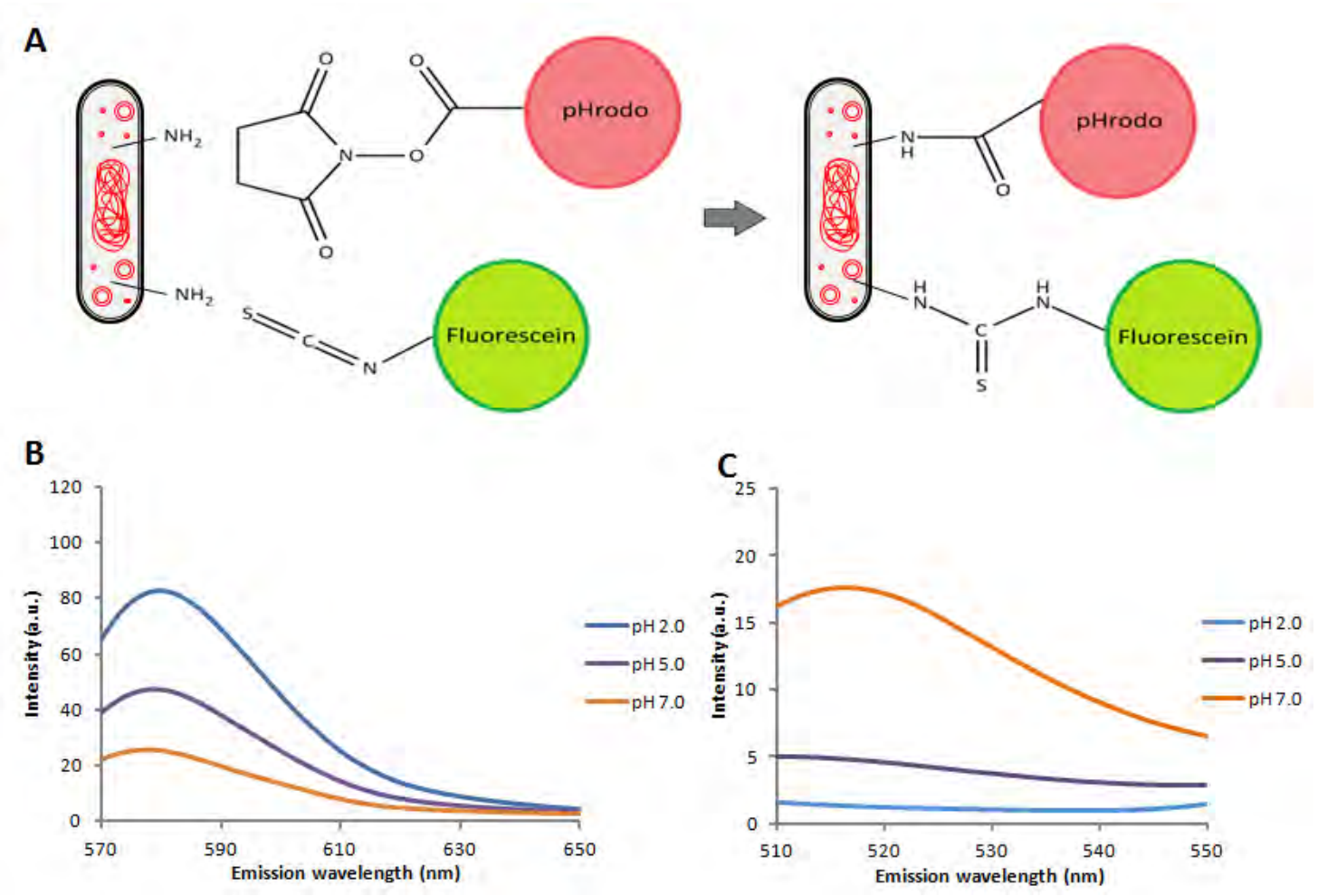


Pygall *et al*; International Journal of Pharmaceutics, 2009. **370**(1-2): p. 110-20



Li and Shwendemann; Journal of Controlled Release, 2005. **101**(1-3): p. 163-173

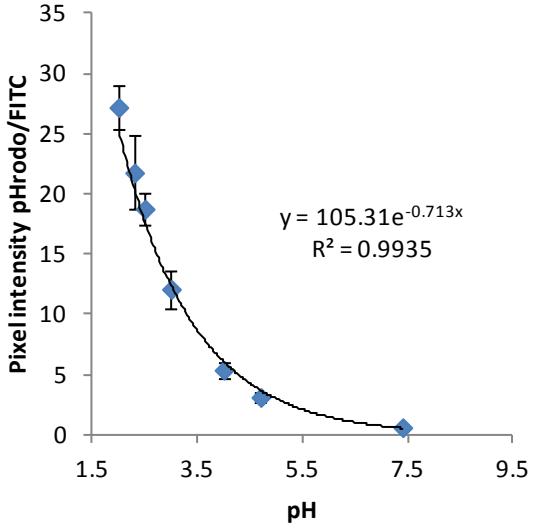
Preparation of pH probes

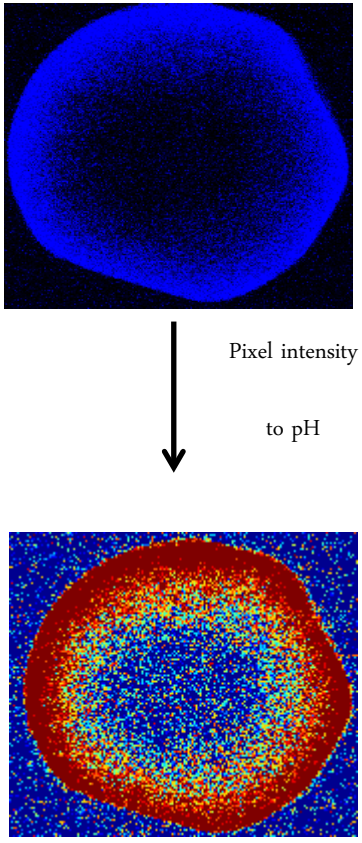


Pixel intensity to pH

Fluorescence intensity

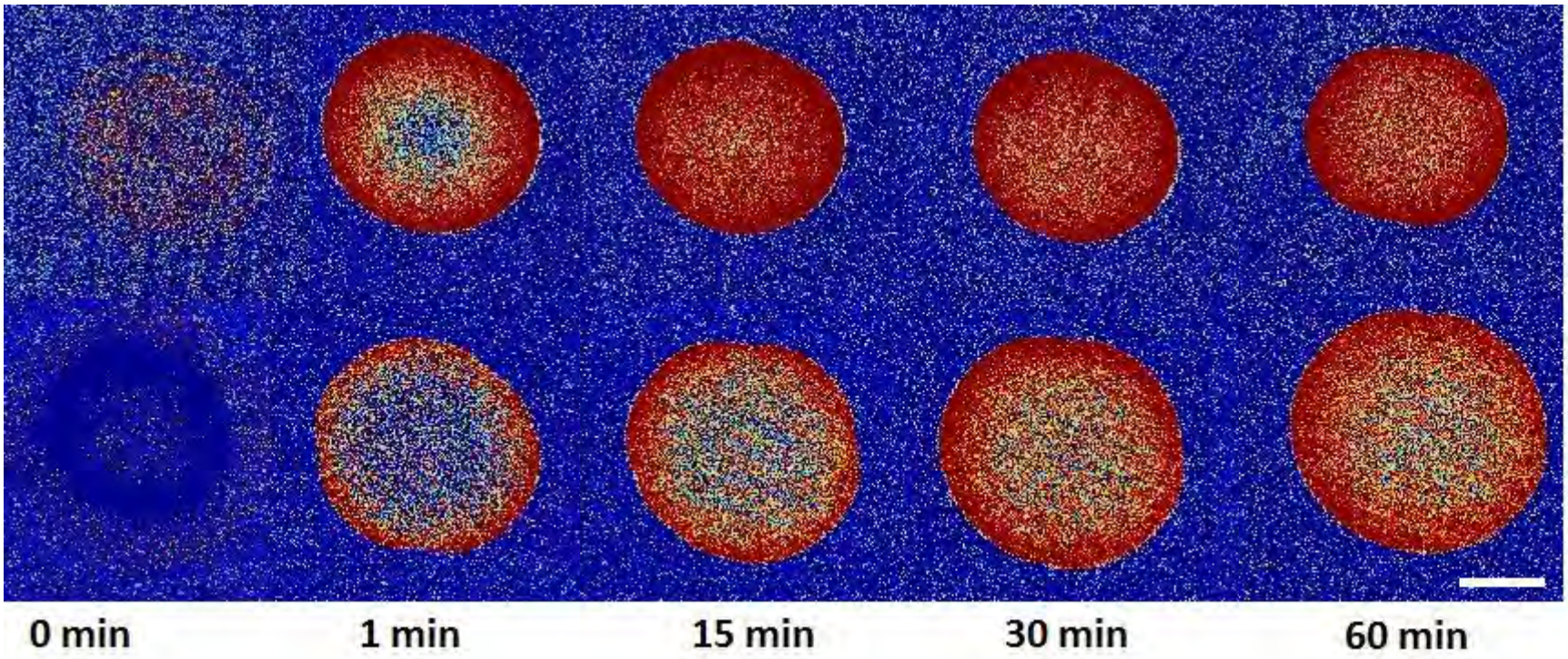
ratio ∝ pH





Cook et al. (2013), Biomacromolecules, 14 (2), 387–393

Why do these work?



To summarise

- Alginate matrices containing probiotic bacteria can be modified in a number of ways to change their properties
- Prebiotic small molecules can also be co-incorporated in multiparticulates
- “pH maps” of capsules can be constructed by labelling the probiotic cells with suitable fluorophores

Acknowledgements

- Dr Dimitris Charalampopoulos and Dr Vitaliy Khutoryanskiy (UoR)
- Dr George Tzortzis (Clasado Ltd)