Glycosylated Nanomaterials: Neutralisation and Detection of Bacteria and Toxins

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MultiGlycoNano 2014 – 26th June

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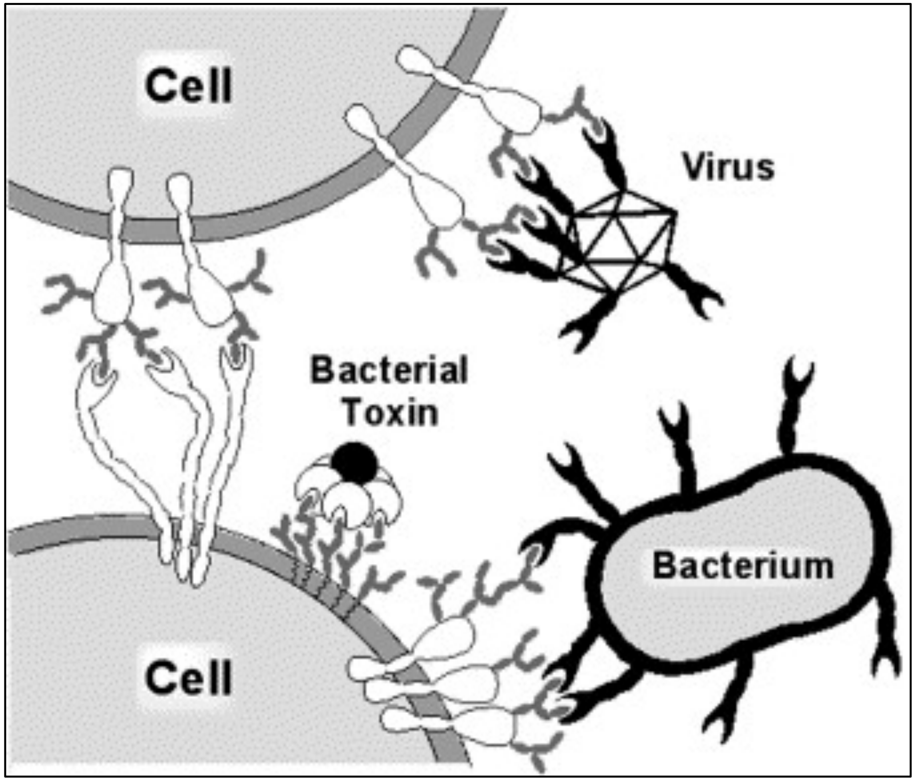
Protein-Carbohydrate Interactions

Cell signalling

Fertilisation

Inflammation



Cellular adhesion of
- Viruses
- Bacteria
- Bacterial toxins

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Miura, *JPOLA,* **2007**, 45, 5031
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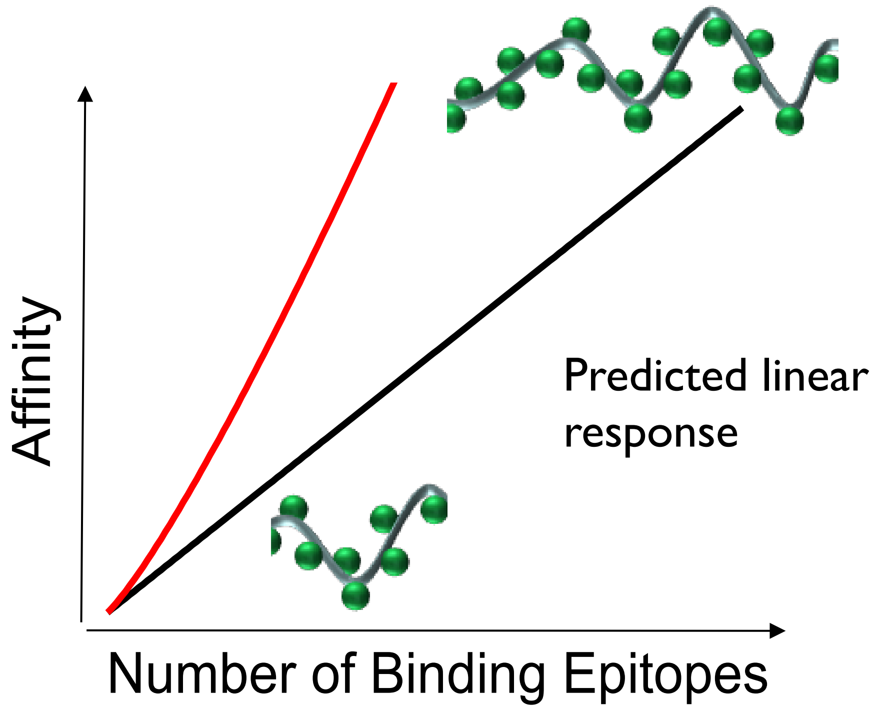
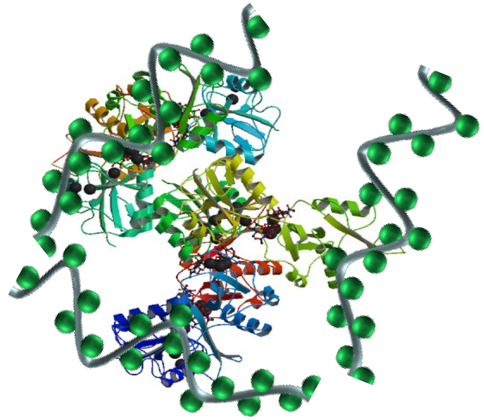
Gamblin, *Chem. Rev*, **2009**, 109, 131
Imberty, *Chem. Eur. J.*, **2008**, 14, 7490
Turnbull, B., *Rev. Mol. Biotech., **2002**, 90, 231*

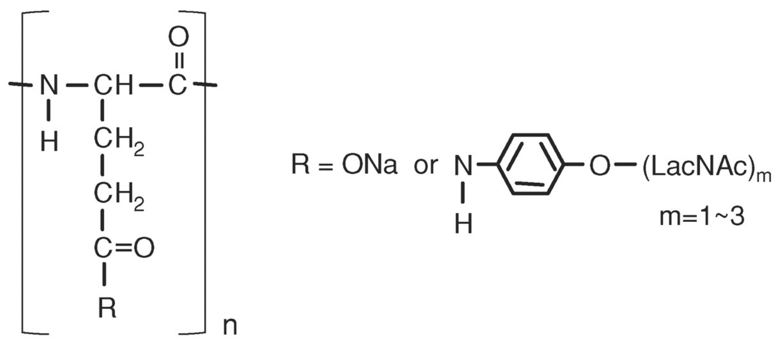
Why Materials?



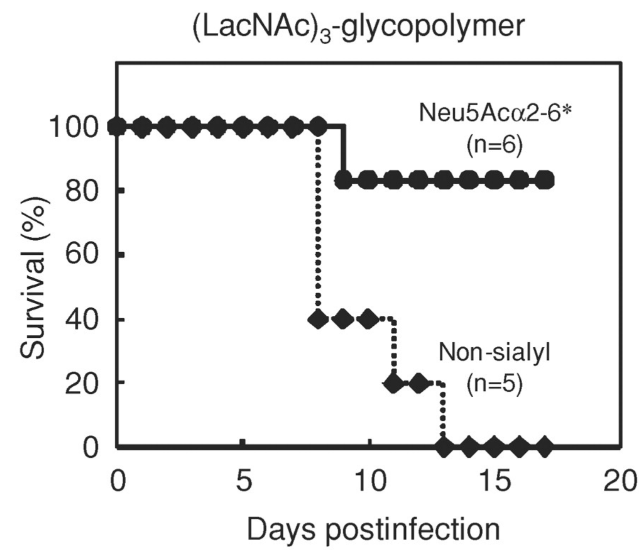
Applications: Anti-adhesion Therapy



Interactions can be inhibited at ***nM*** *of glycopolymers*



α-polyglutamic acid (α-PGA)



Influenza inhibition in mice

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Sharon, N. Biochimica et Biophysica Acta, **2006**, 527–537
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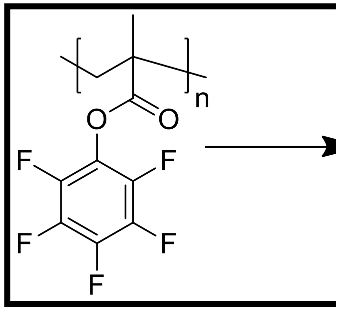
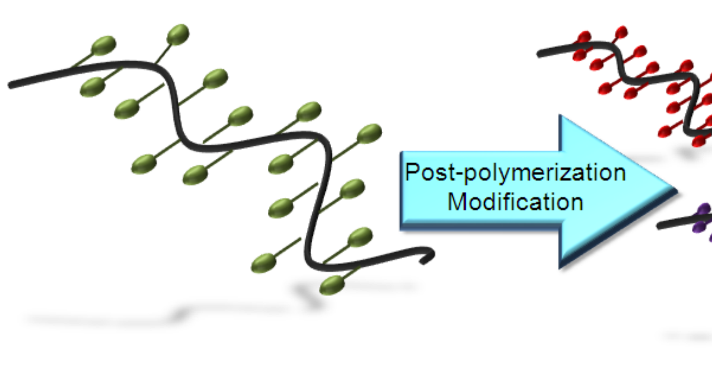
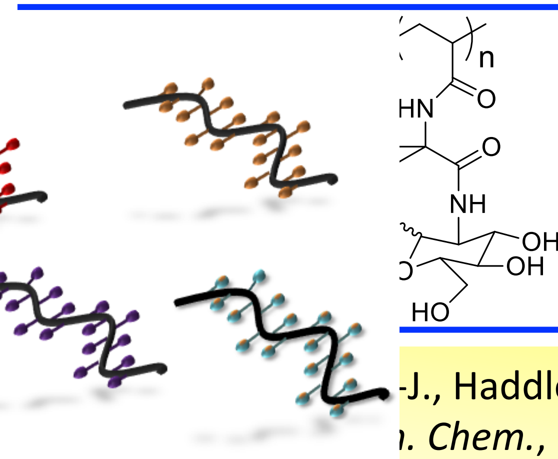
Glycopolymers by Post-Polymerisation Modification







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ı. *Chem.*, **2013**,

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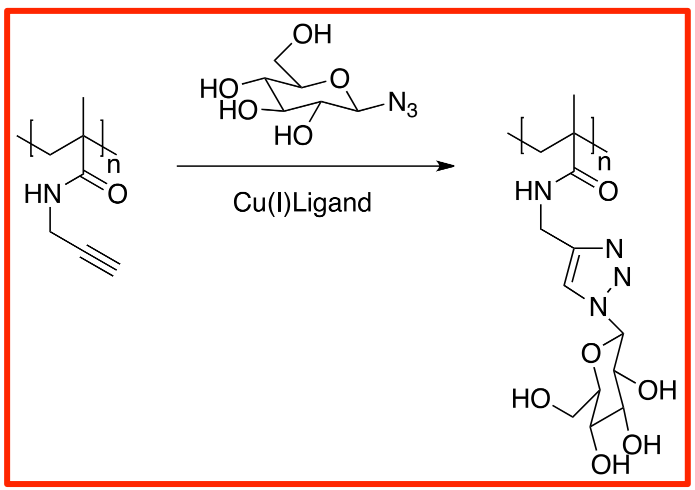
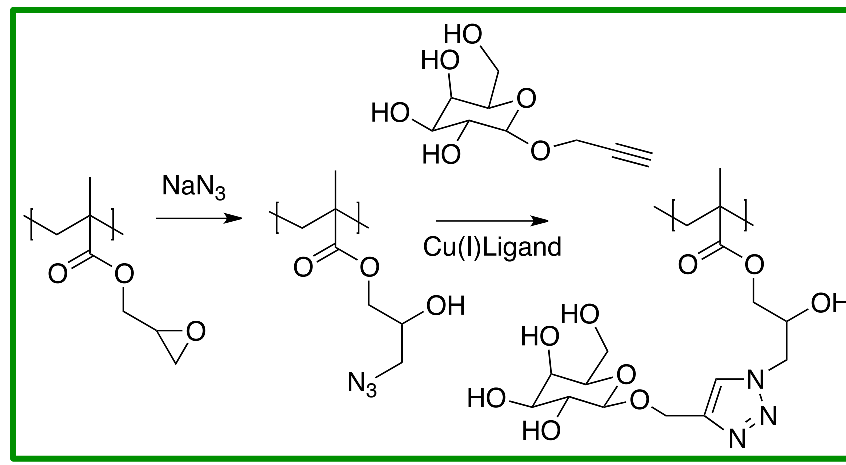
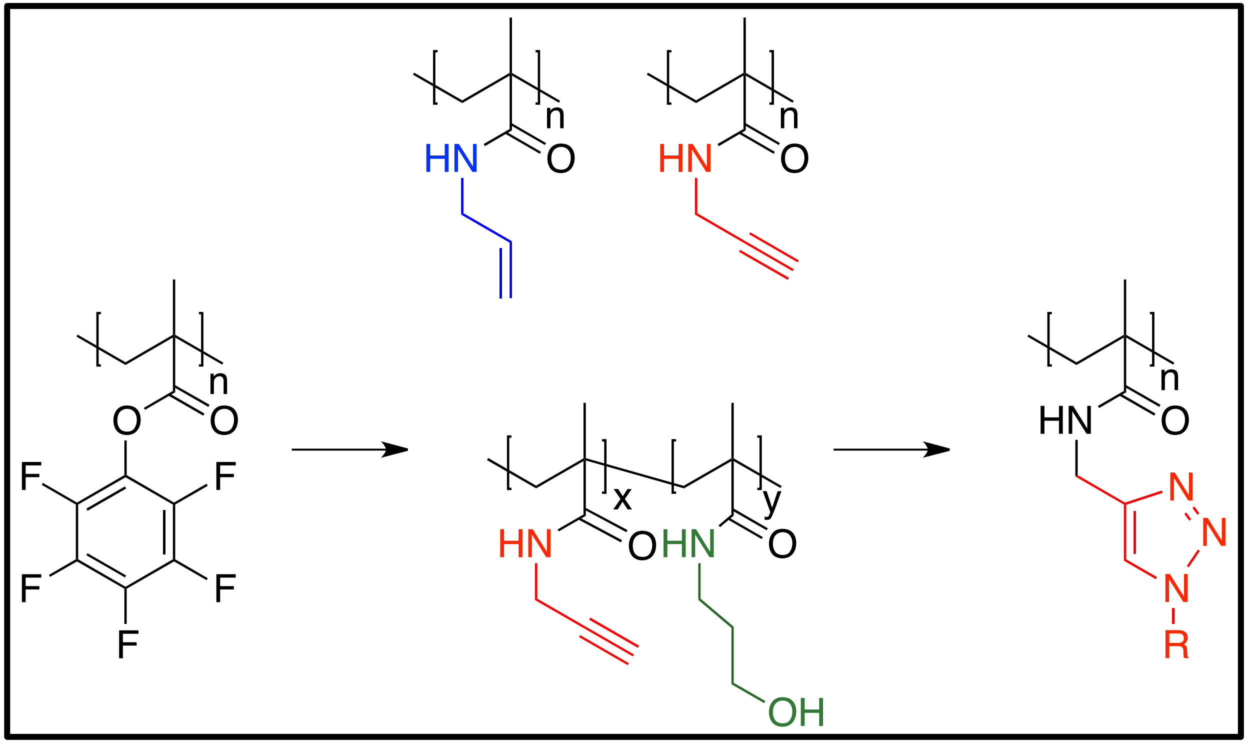




Jones, M. W., L. Otten, Richards, S-J., Lowery, R., Phillips, D. J. Haddleton, D. M. Gibson, M. I.; *Chem. Sci.*, **2014**



- Easy to make 50 gram scale
- 1 column/distillation
- Compatible with RAFT/ ATRP

- Quantitative functionalisation with non-hindered amines
- Density control

- Sequentially modified polymer libraries

Theato, P.; *J. Pol. Sci. A.*, **2008**, 46, 6677

Selective Binding of Cholera-Toxin

Enzymatic domain → Induces toxic effect

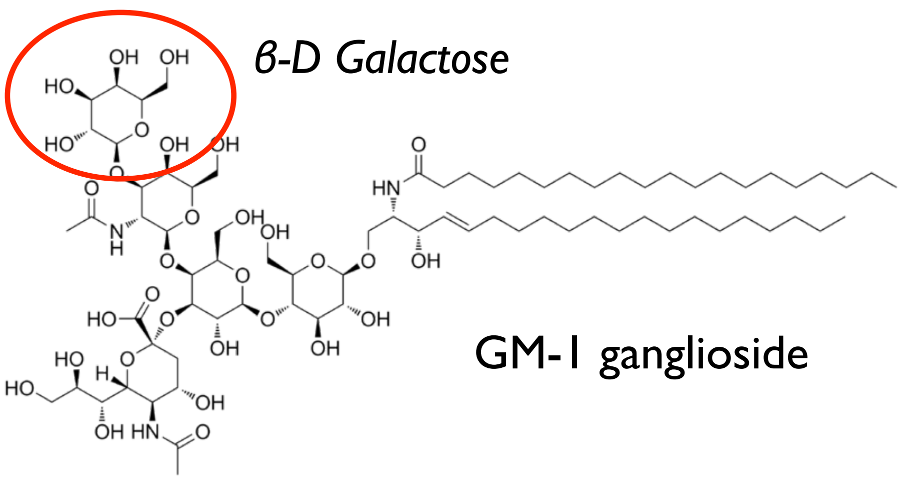
Carbohydrate binding domain → Binds to epithelial cells to promote cell uptake

Anti-adhesion therapy does not target bacteria, so less evolutionary stress

Galectins – at least 13

Sigma-Aldrich – 8 Galactose-'specific' lectins

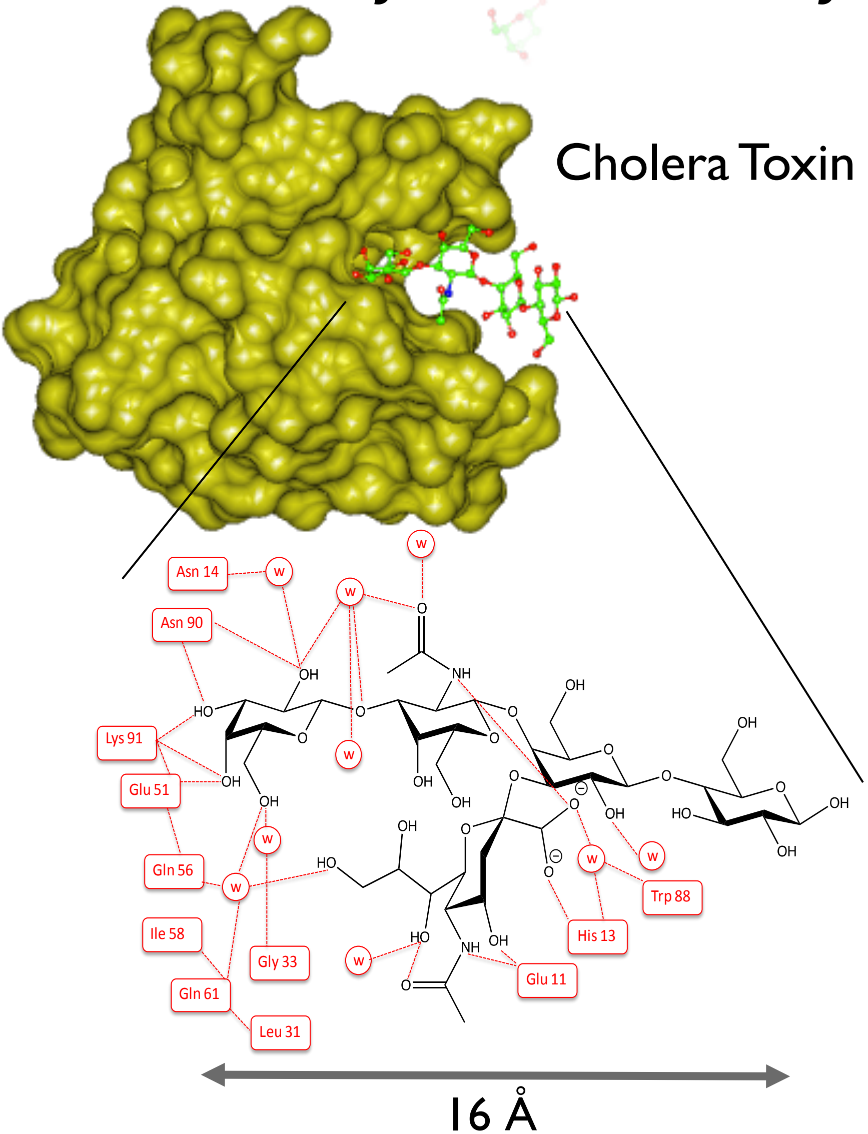
How do we engineer a high-affinity binder for cholera toxin, without total synthesis of complex carbohydrates?

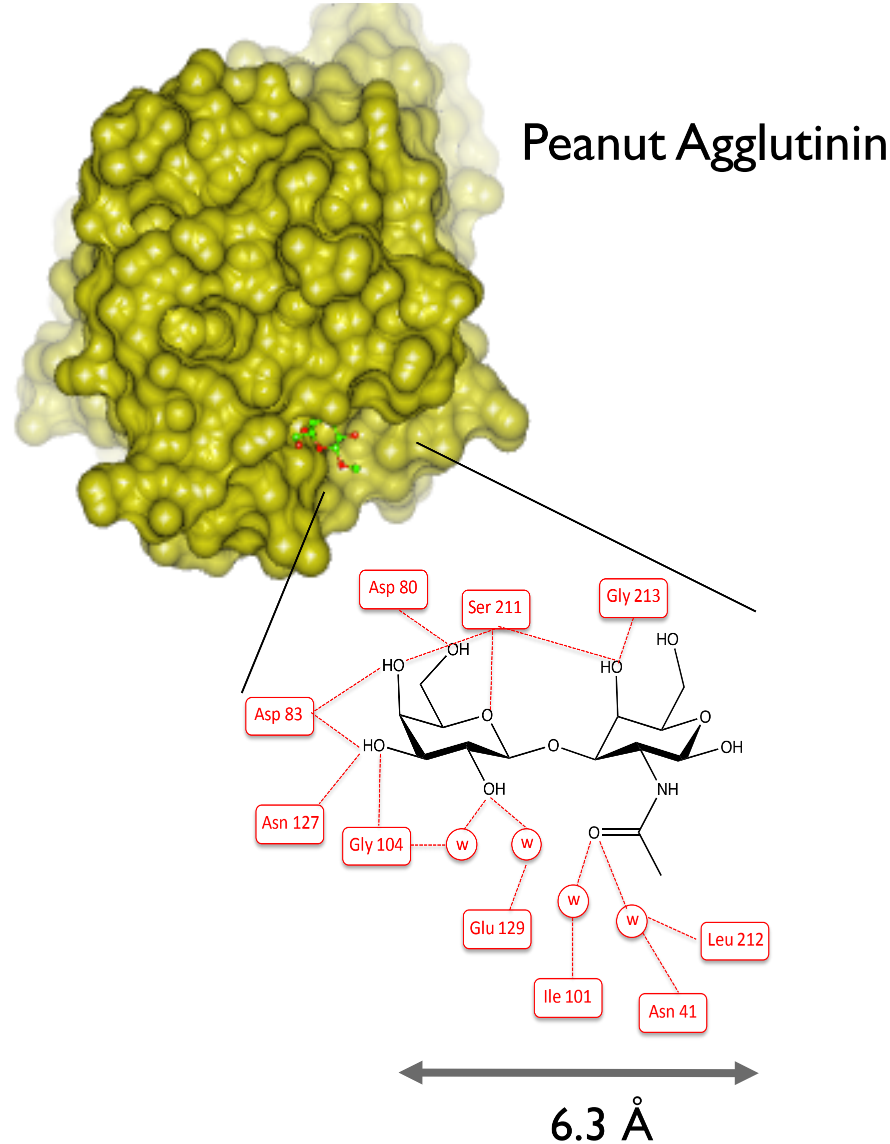


β-D Galactose

GM-1 ganglioside

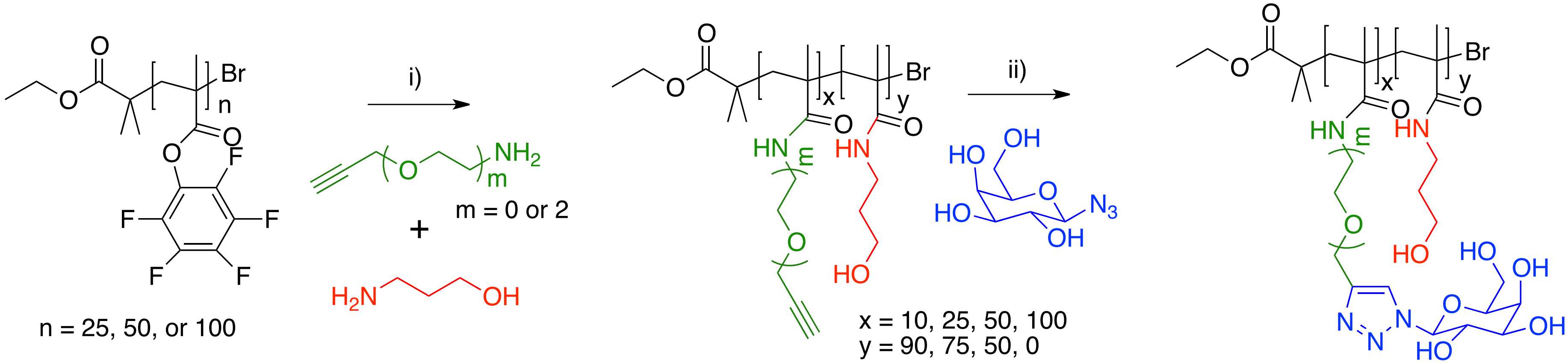
Glycan Accessibility as a Tool for Lectin Specificity

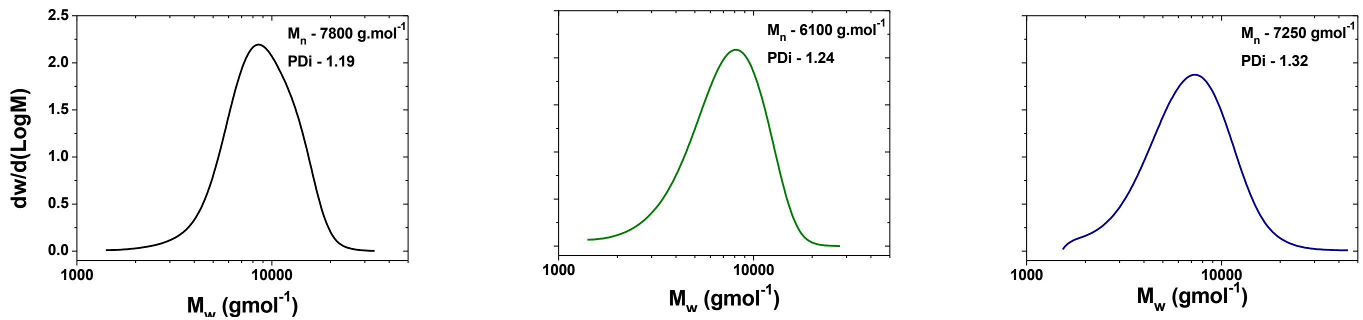


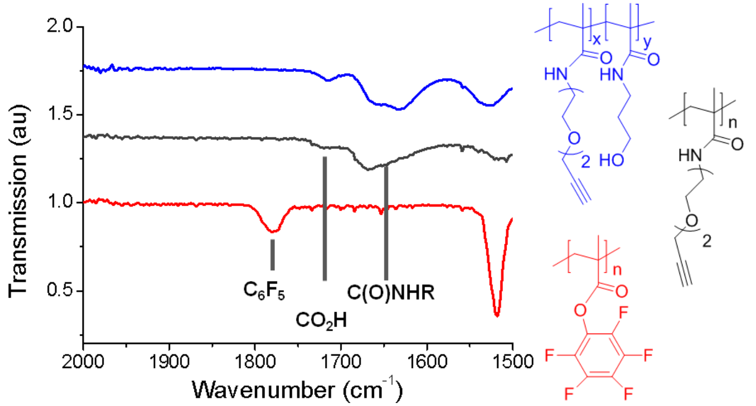


Kiick *et al.*; *Macromol.* **2007**, 40, 7103 and Biomac., **2006**, 7 483

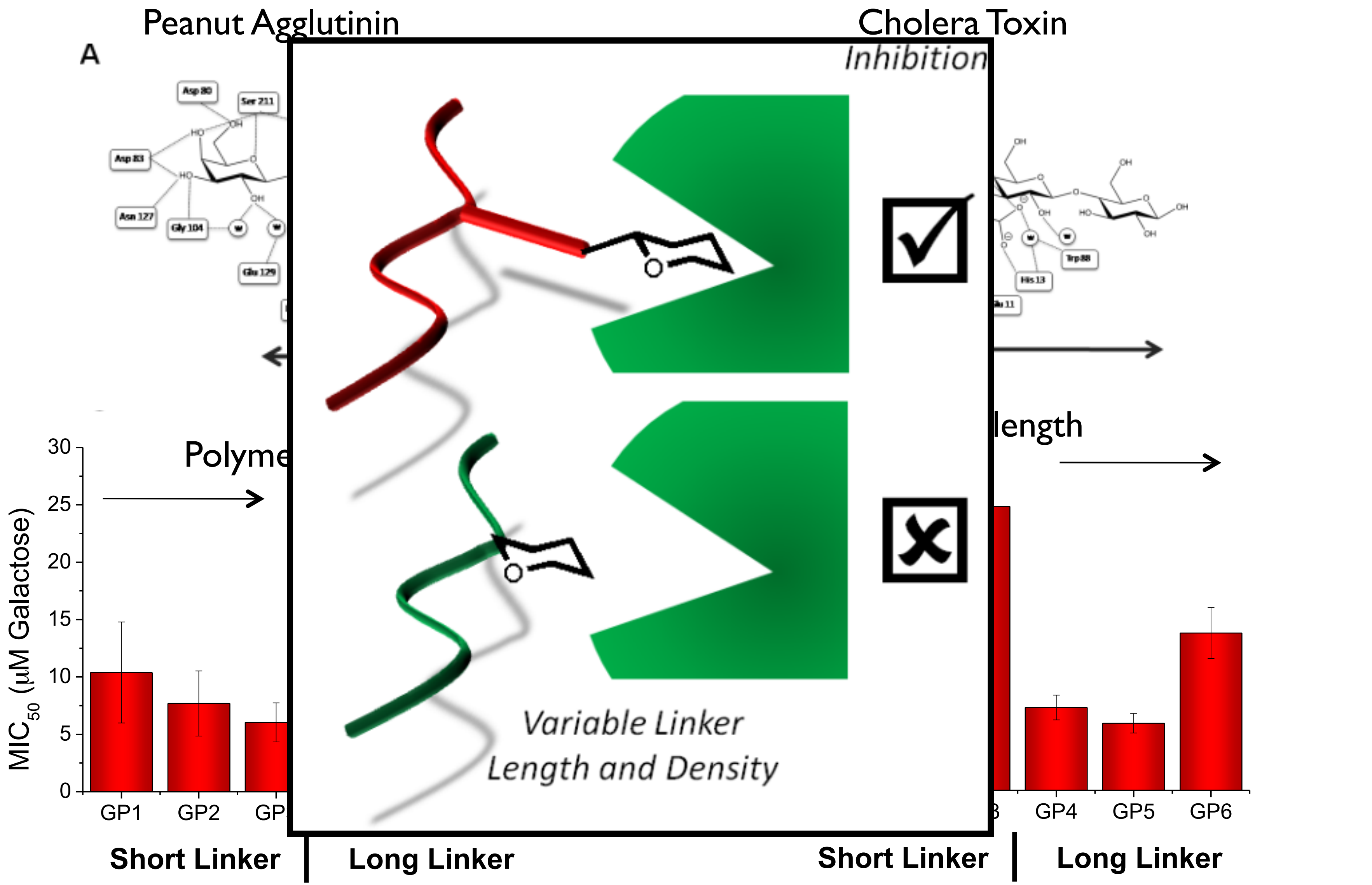
Glycopolymer Library







Polymer	DP[a]	Linker[b]	Density[c]	M_w/M_n[d]
GP1	18	Short	100	1.29
GP2	33	Short	100	1.27
GP3	70	Short	100	1.26
GP4	18	Long	100	1.32
GP5	33	Long	100	1.28
GP6	70	Long	100	1.27
GP7	33	Long	50	1.23
GP8	33	Long	25	1.21
GP9	33	Long	10	1.20



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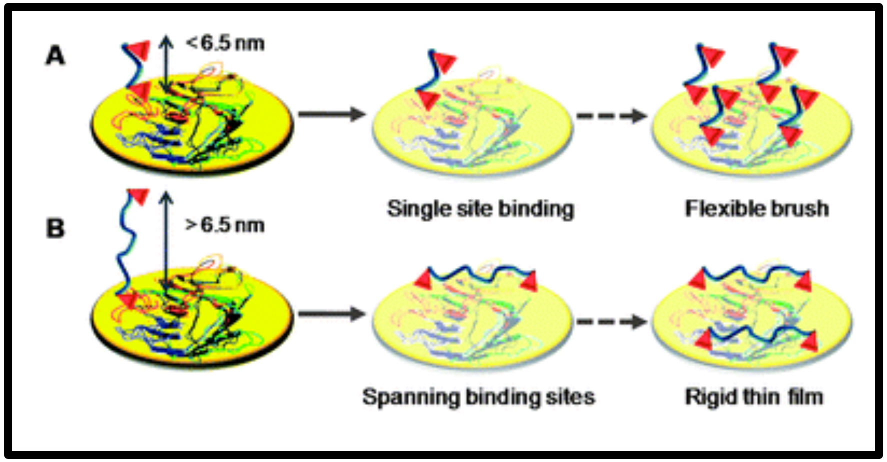

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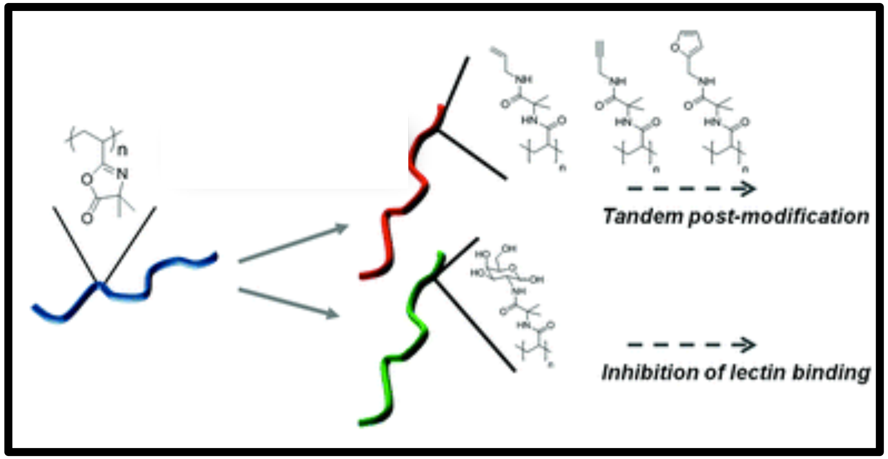
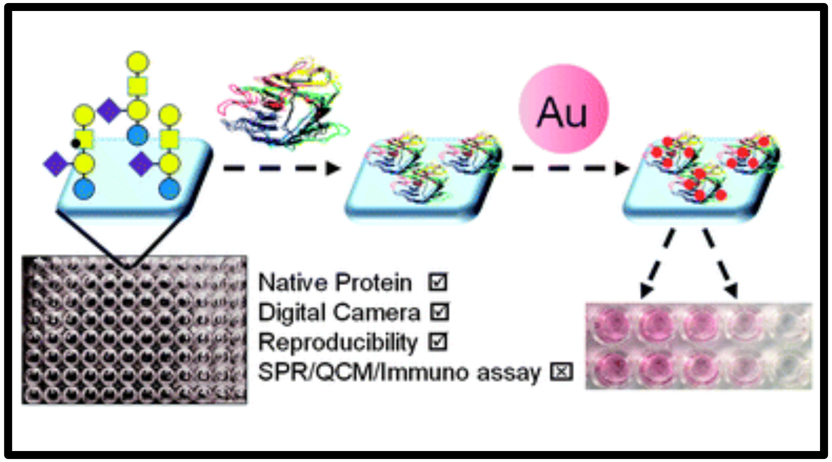
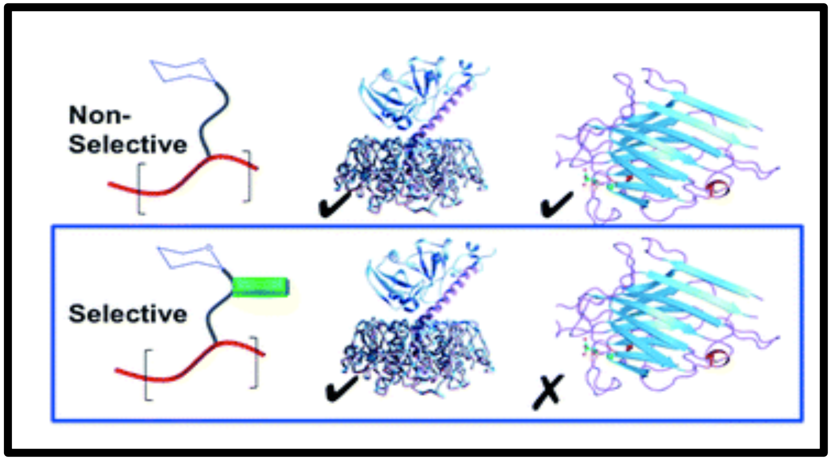


Jones, M. W., Richards, S-J., Haddleton, D. M. Gibson, M. I.; *Polym. Chem.*, **2013**, 4, 717-723



Otten, L., Richards, S-J., Fullam, E., Besra, G. S. Gibson, M. I.; *J. Mater. Chem. B*, **2013**, 1, 2665-2672



Jones, M. W., L. Otten, Richards, S-J., Lowery, R., Phillips, D. J. Haddleton, D. M. Gibson, M. I.; *Chem. Sci.*, **2014**, 5, 1611-1616

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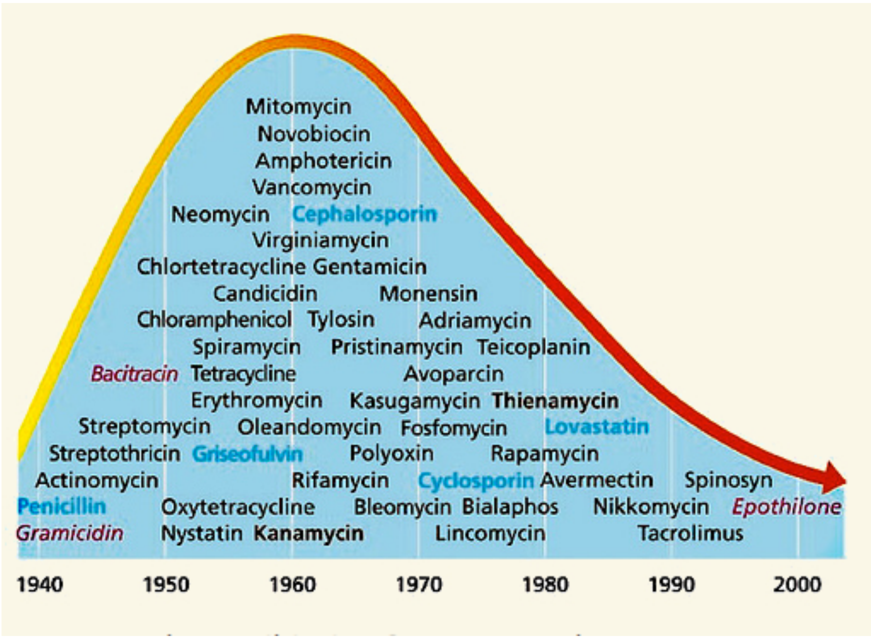
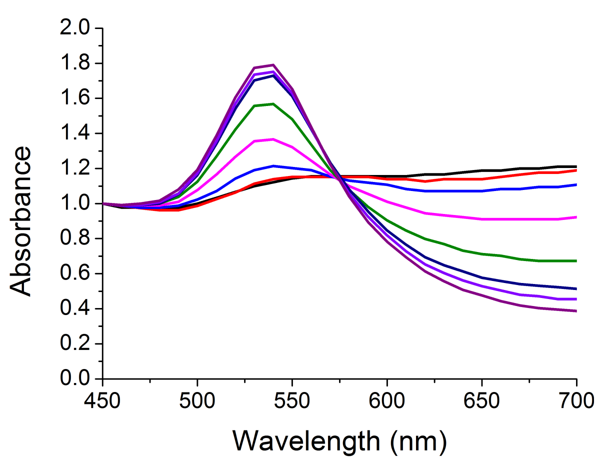
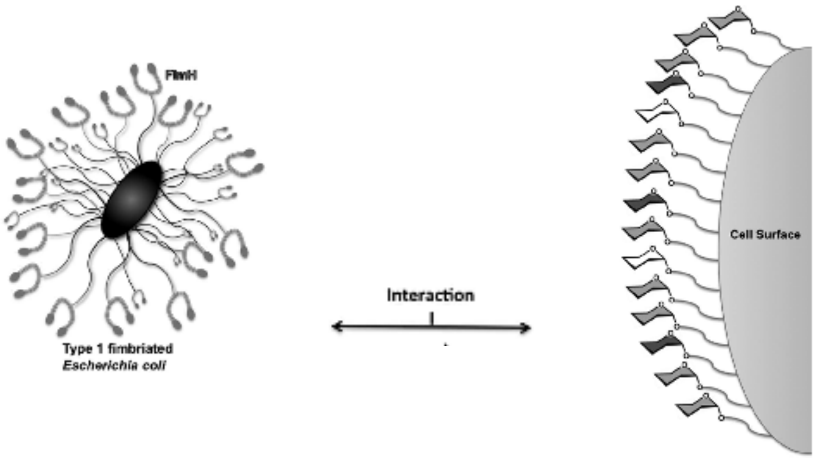
Applications: Detection

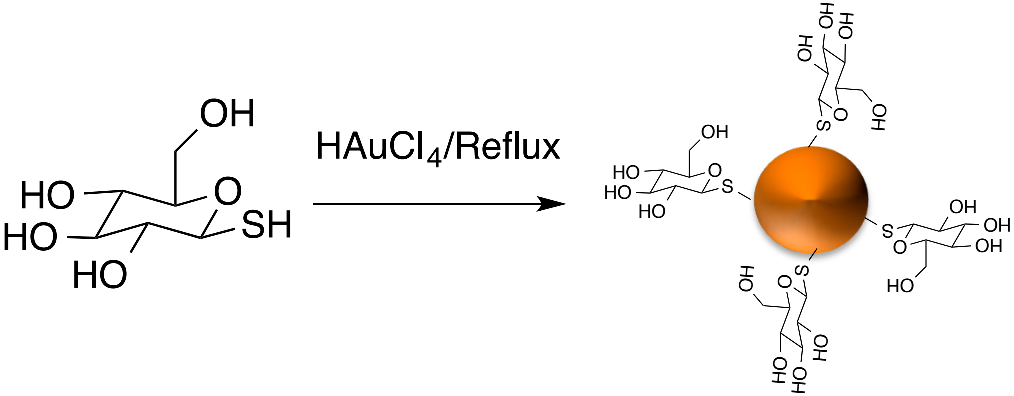


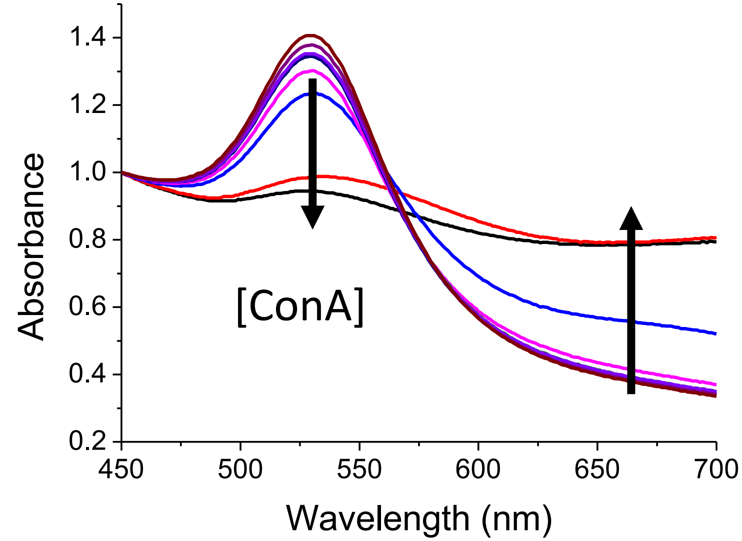
- Direct
- Label-free
- Easy
- Sensitive
- Quantifiable in real-time

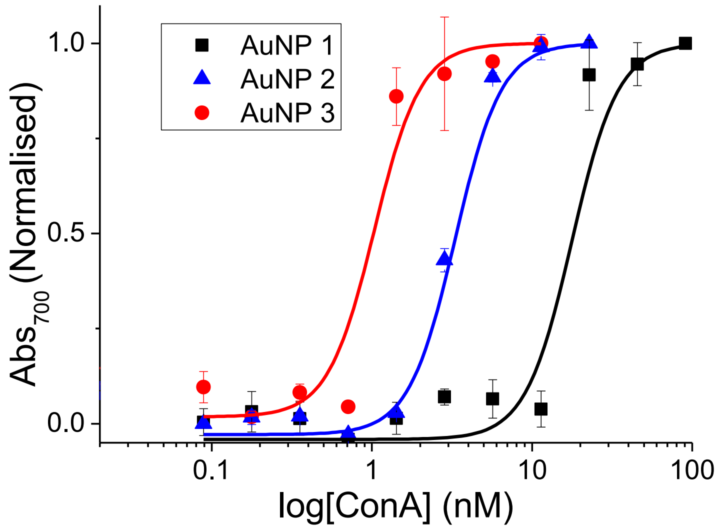


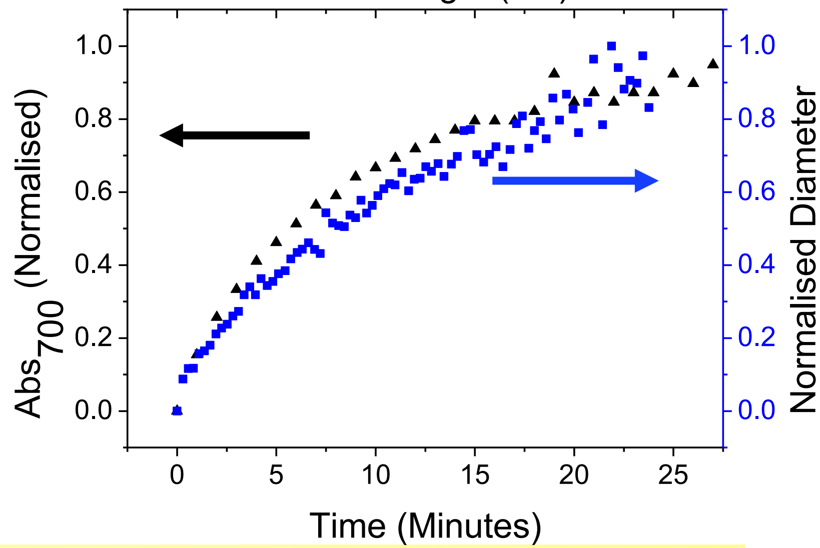


Potential Sensor for Ricin









Richards, S-J., Fullam, E., Besra, G. S. Gibson, M. I.; *J. Mater. Chem. B*, **2014**, 2, 1490-1498

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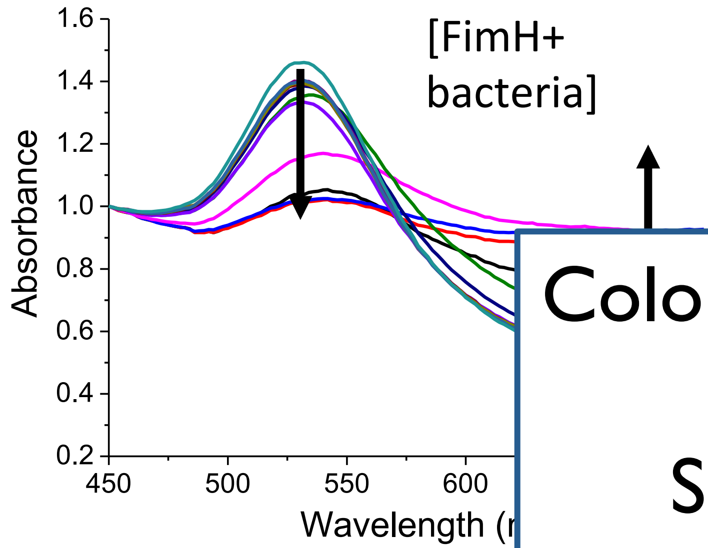
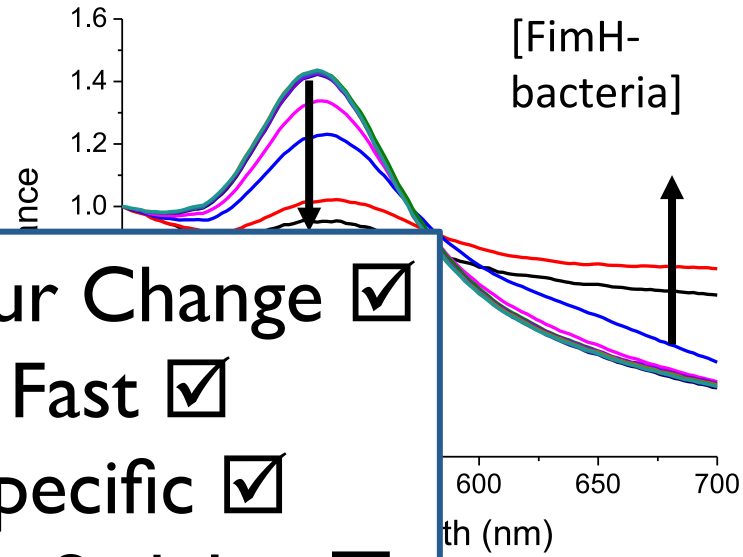


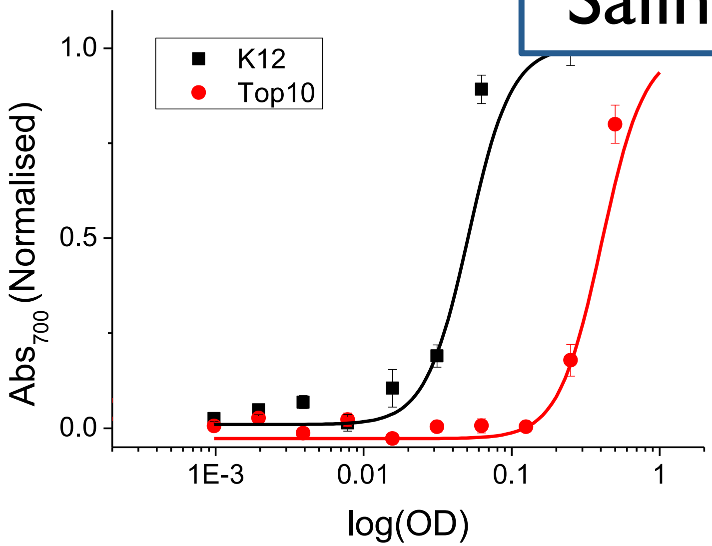


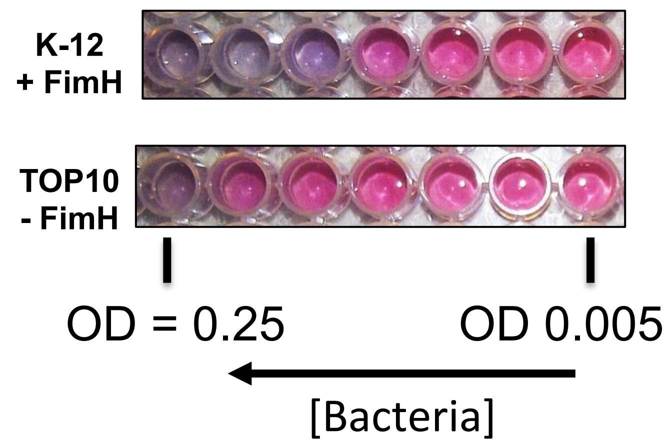
Colour Change ☑

Fast ☑

Specific ☑

Saline Stability ☒





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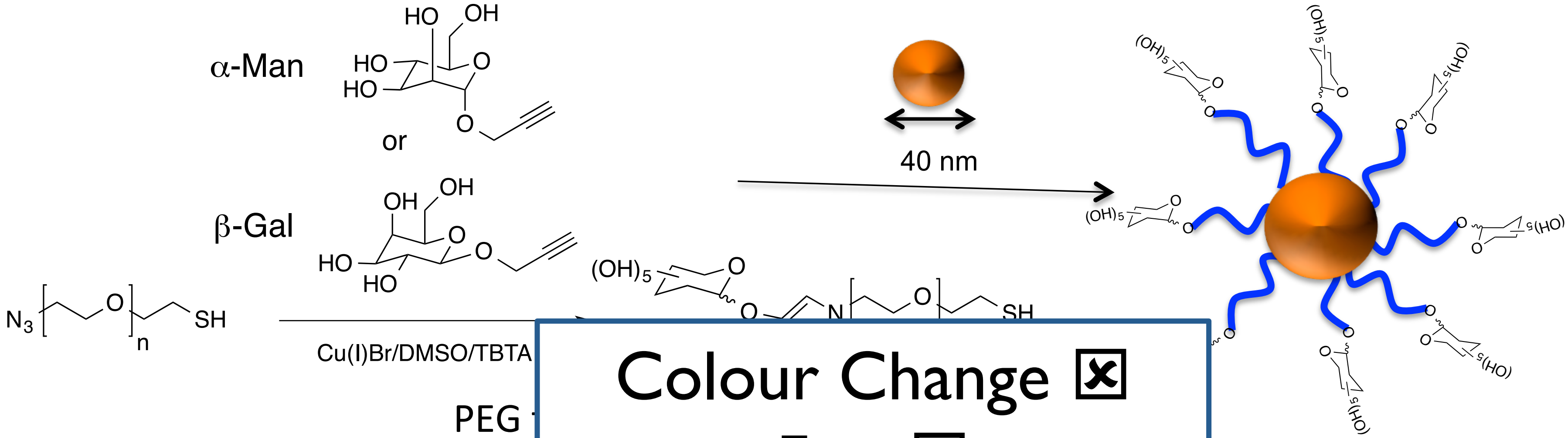
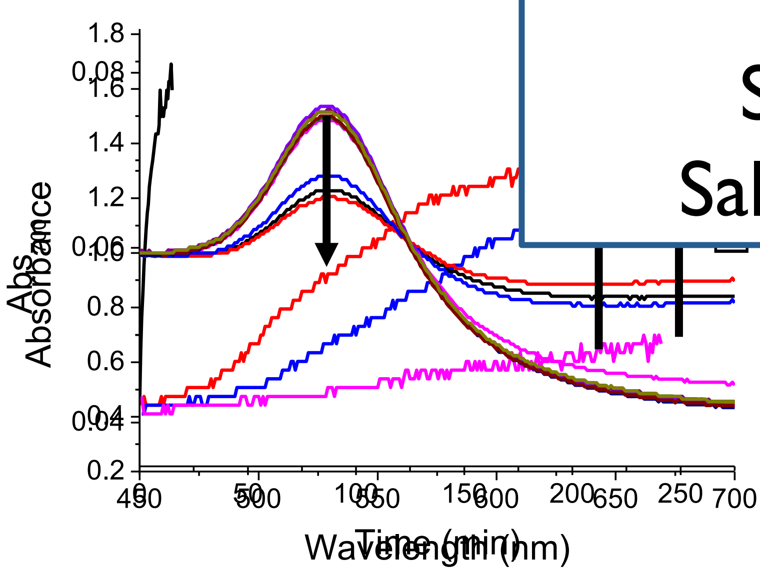
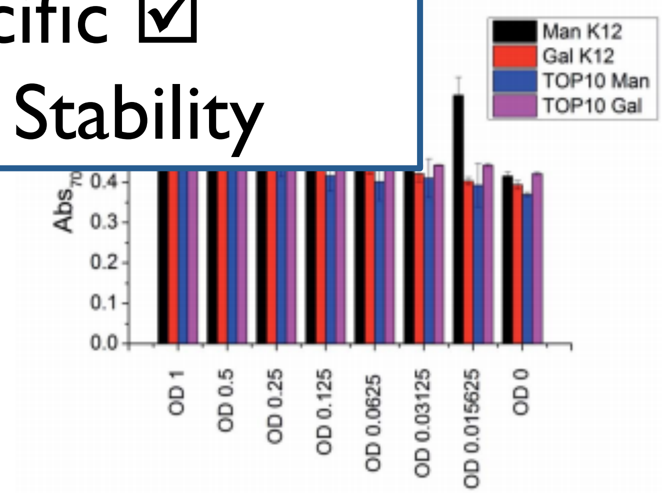


Colour Change ☒
Fast ☒
Specific ☑
Saline Stability





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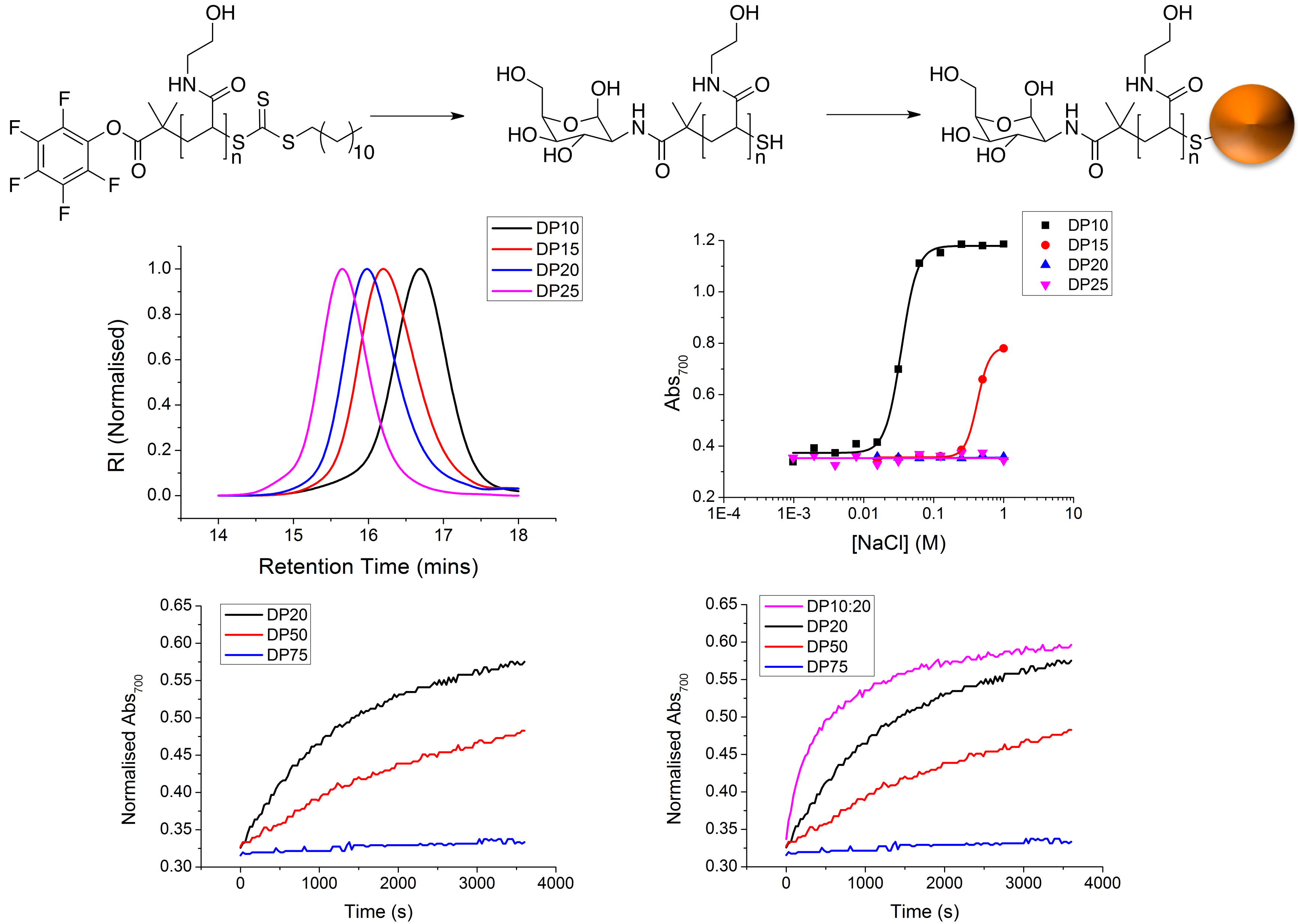
OH
HN
O
S
F
O
S
S
10
n
HO
OH
H
N
SH
Retention Time (mins)
RI (Normalised)
DP10
DP15
DP20
DP25
[NaCl] (M)
Abs700
Time (s)
Normalised Abs700
DP20
DP50
DP75
DP10:20

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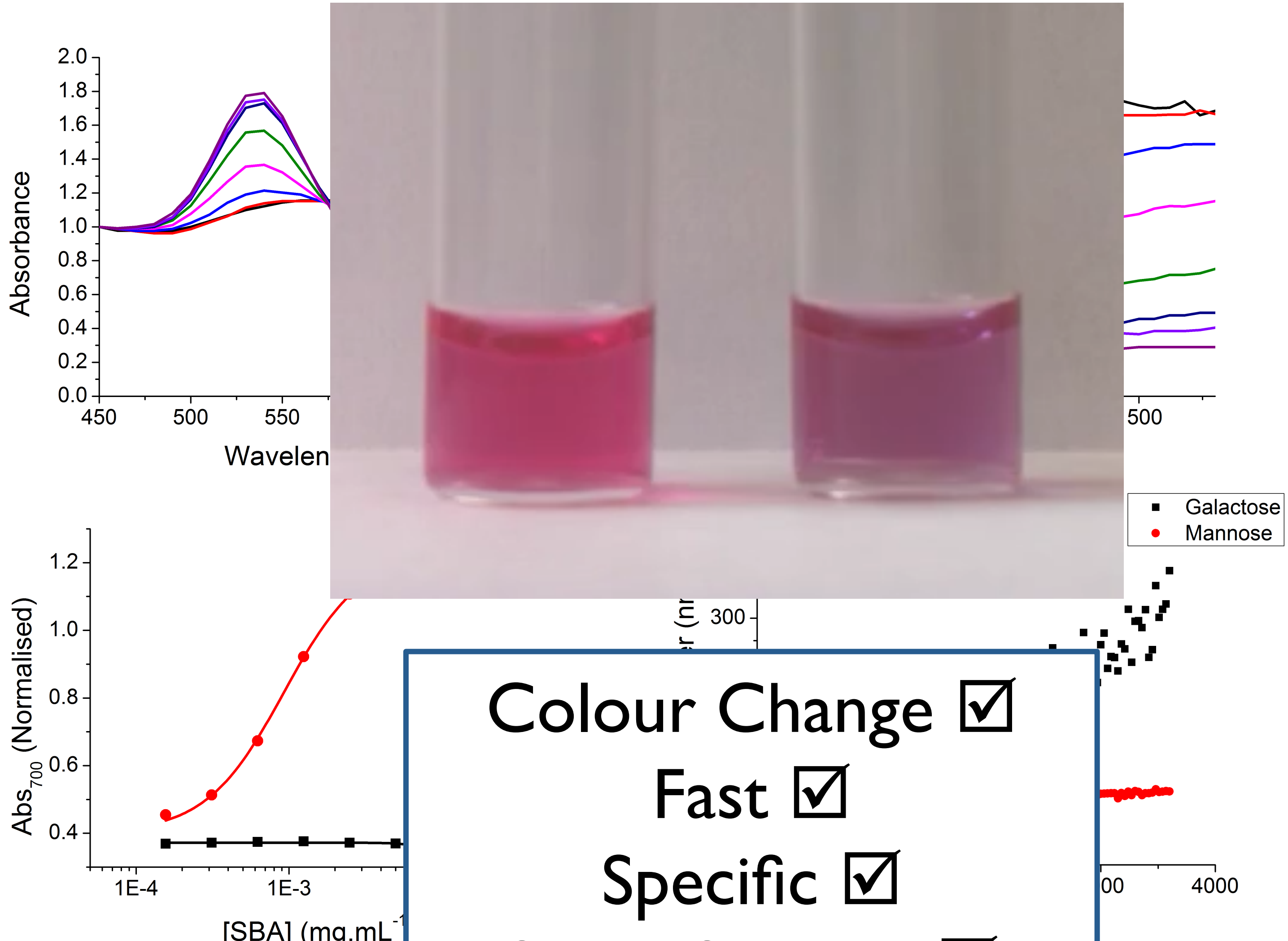

Colour Change ☑

Fast ☑

Specific ☑

Saline Stability ☑

Richards, S-J., Fullam, E., Besra, G. S. Gibson, M. I., In Preparation

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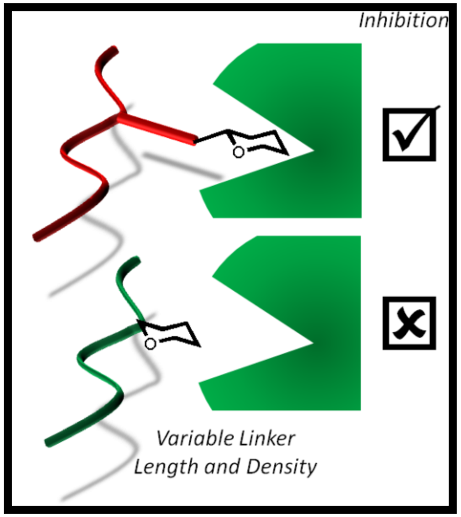
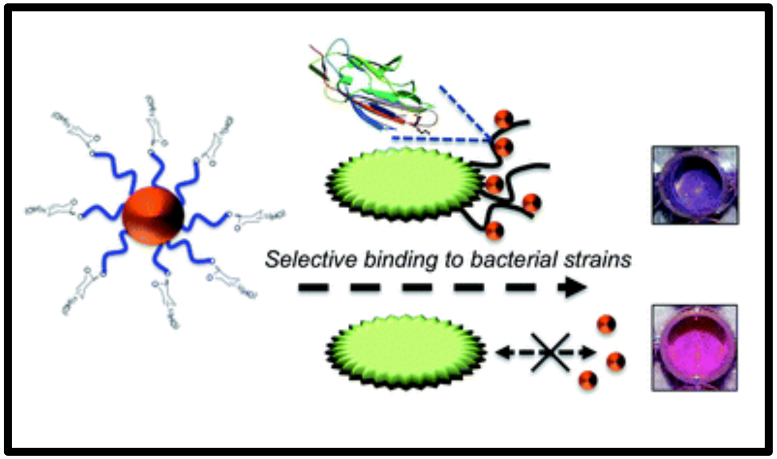
Summary

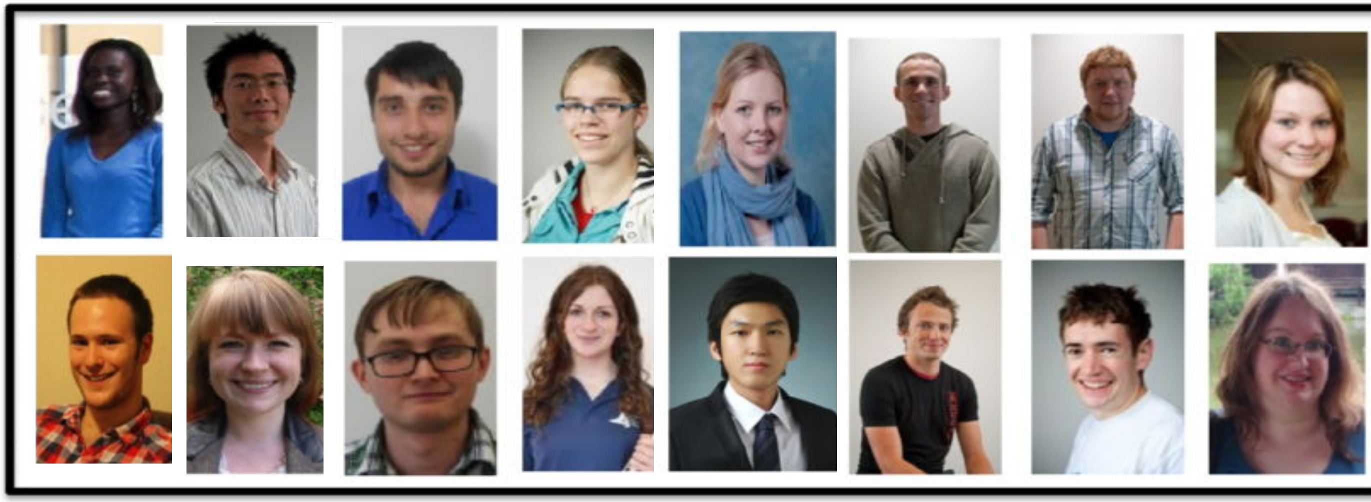


- Tandem Post-Polymerisation Modification
- Multivalent inhibitors that have good affinity AND specificity



- Glycogoldnanoparticles
- Optimised polymer coating for lectin detection

Acknowledgements



Gibson Group Members

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- Daniel Phillips
- Tom Congdon
- Lucienne Otten

- Daniel Mitchell
- Richard Lowery
- Ben Martyn
- Lewis Blackman
- Sang-Ho Won
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- Robert Keogh

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MultiGlycoNano 2014 – 26^{th} June

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