Multivalent protein-carbohydrate interactions

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Introduction

Protein-carbohydrate interactions at cell surfaces mediate many important processes in biology from fertilisation to adhesion of viruses, bacteria and their toxins. Individually, protein-sugar interactions are usually very weak, but both affinity and binding selectivity can be enhanced through a phenomenon called multivalency: multiple binding sites on the protein interact simultaneously with multiple copies of the sugar ligand to achieve a high avidity and enhance binding selectivity. The multivalency phenomenon can be reproduced using synthetic molecules that incorporate multiple copies of the carbohydrate ligands.

Some of our recently published research includes developing fluorescent probes based on glycosylated quantum dots for use in understanding the structures of multivalent complexes. Using such tools we have been able to probe the differences in binding selectivity for two very closely related human cell surface lectins (DC-SIGN and DC-SIGNR) which mediate virus invasion. We have been able to show that the different presentation of the binding sites determines whether or not the proteins can form stable interactions with virus-sized glycosylated quantum dots.

We have also developed methods to exploit multivalent protein-carbohydrate interactions for applications in materials science. We have found that single chain polymer nanoparticles bearing many pendant carbohydrate groups can be used to create stable polymer films on functionalised surfaces (Figure 1). The polymer nanoparticles contain hydrazone linkages that can be reversibly formed and broken under mild conditions. We have found that they can reorganise to form extended cross-linked films in a process that is dependent on formation of specific protein-carbohydrate interactions. These methods could be exploited in industrial biotechnology to “shrink-wrap” bacteria for immobilisation in bioreactors or to stabilise virus-based vaccines to give them longer shelf-lives without need for refrigeration process that increase the cost of biopharmaceuticals.

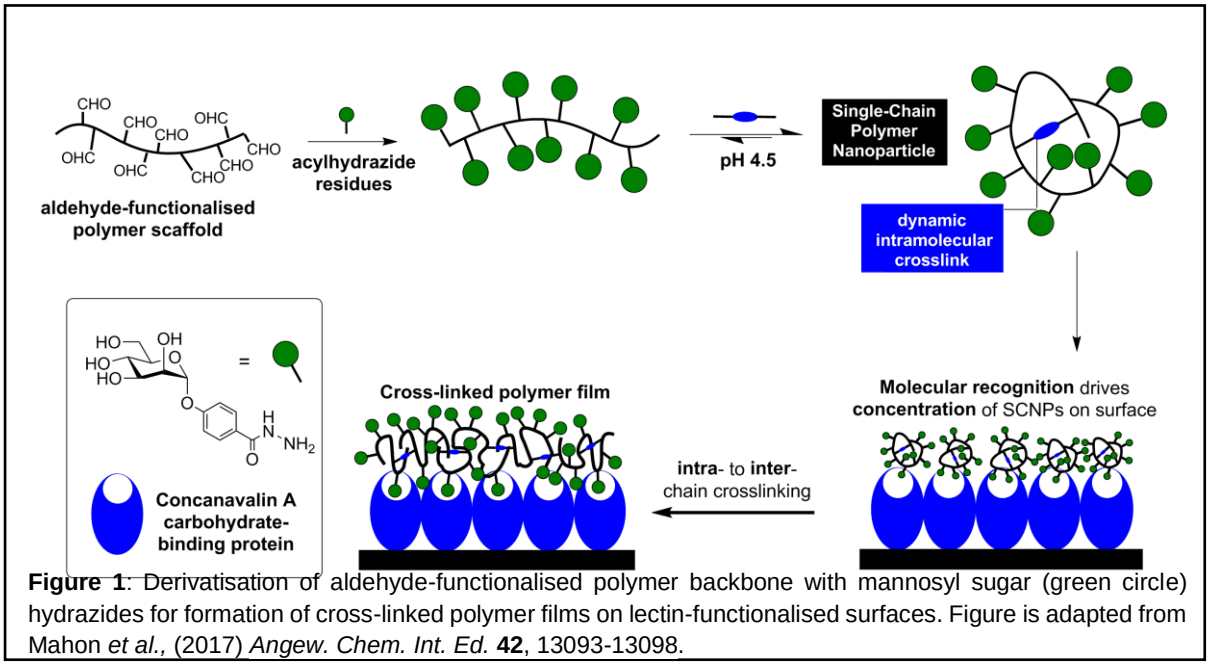

Figure 1: Derivatisation of aldehyde-functionalised polymer backbone with mannosyl sugar (green circle) hydrazides for formation of cross-linked polymer films on lectin-functionalised surfaces. Figure is adapted from Mahon *et al.*, (2017) *Angew. Chem. Int. Ed.* **42**, 13093-13098.

Publications

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Collaborators

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