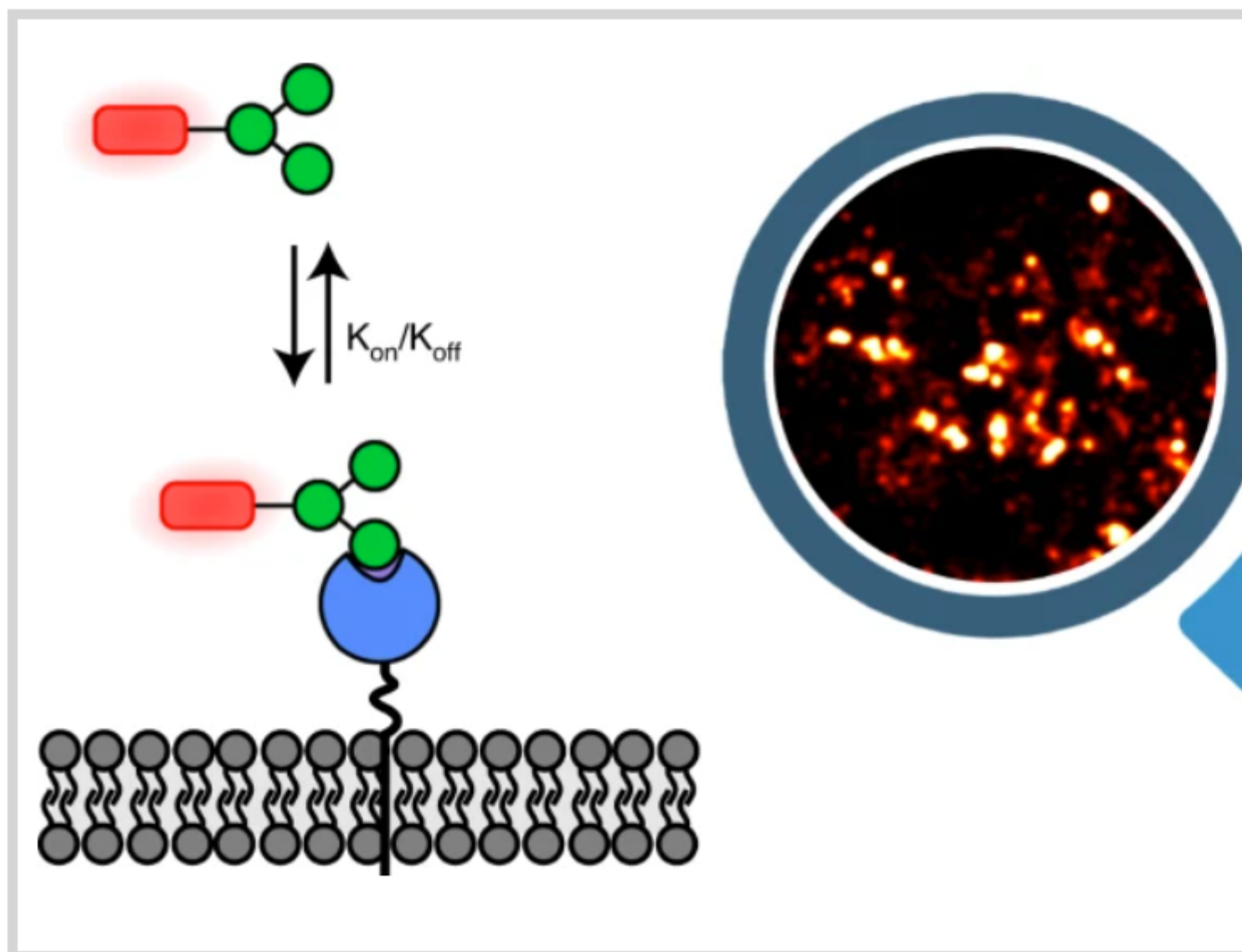


## Single-molecule imaging of glycan–lectin interactions on cells with Glyco-PAINT

### Description

Most lectins bind carbohydrate ligands with relatively low affinity, making the identification of optimal ligands challenging. The authors introduce a point accumulation in nanoscale topography (PAINT) super-resolution microscopy method to capture weak glycan–lectin interactions at the single-molecule level in living cells (Glyco-PAINT). Glyco-PAINT exploits weak and reversible sugar binding to directly achieve single-molecule detection and quantification in cells and is used to establish the relative  $k_{on}$  and  $k_{off}$  rates of a synthesized library of carbohydrate-based probes. The diffusion coefficient of the

receptor–sugar complex is also established.



The uptake of ligands correlates with their binding affinity and residence time to establish the structure–function relations for various synthetic glycans. The authors reveal how sugar multivalency and presentation geometry can be optimized for binding and internalization. Overall, Glyco-PAINT represents a powerful approach to study weak glycan–lectin interactions on the surface of living cells, one that can be potentially extended to a variety of lectin–sugar interactions.

### Category

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