’Catching the Flu’:
A Supramolecular View on the Interaction of Viruses at Interfaces

Jurriaan Huskens
Nico Overeem, Erik Hamming, Erhard van der Vries
Department of Molecules & Materials, MESA+ Institute for Nanotechnology, Enschede, The Netherlands
j.huskens@utwente.nl

Multivalency describes the interaction between viruses and cell membranes. The influenza virus binds through multiple sialyl-terminated carbohydrates (SLNs) non-covalently interacting with hemagglutinin coat proteins. This interaction is weakly multivalent in nature, and it is expected to be superselective, explaining the large differences between virus affinities by mutations in the receptor binding domain. A key aspect of the multivalent interaction of viruses at cell membranes is its strong dependence on the receptor density displayed at the surface. Here, we show the use of surface gradients [1] of receptor-modified supported lipid bilayers (SLBs) to visualize and quantify the receptor density dependence in one microscopic image (Figure 1) [2]. The gradients in biotin-functionalized SLBs are visualized by using fluorescently labeled streptavidin, onto which biotinylated SLNs are attached. Images of of dye-labeled influenza viruses binding to these platforms show a steeply, nonlinear dependence of the virus coverage on the SLN density, which is the hallmark of superselective binding. The description of the data by a thermodynamic model allows quantification of the threshold density, comparison of binding selectivities for different virus strains, and a molecular understanding of the supramolecular binding energy landscape. This supramolecular and nanoscopic picture links fundamental molecular aspects of binding to biological processes of antigenic drift and zoonosis.

REFERENCES

[1] J. van Weerd, S. O. Krabbenborg, J. Eijkel, M. Karperien, J. Huskens, P. Jonkheijm, *Journal of the American Chemical Society* **2014**, *136*, 100-103.
[2] N. J. Overeem, P. H. Hamming, O. C. Grant, D. Di Iorio, M. Tieke, M. C. Bertolino, Z. Li, G. Vos, R. P. de Vries, R. J. Woods, N. B. Tito, G.-J. P. H. Boons, E. van der Vries, J. Huskens, *ACS Central Science* **2020**, *6*, 2311-2318.

FIGURES

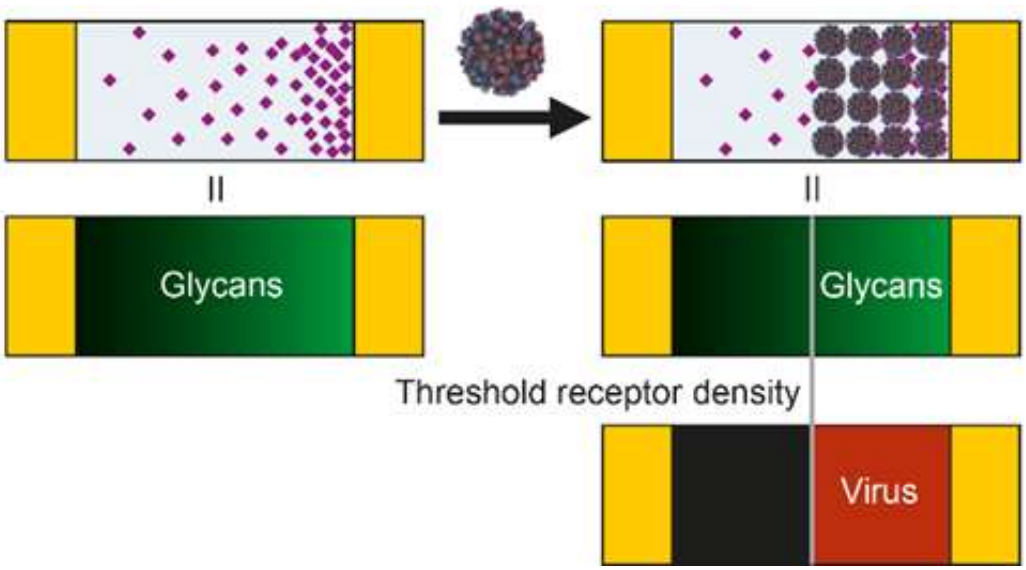

Figure 1: Concept of using receptor-modified surface gradients as a way to detect the threshold receptor density of a virus