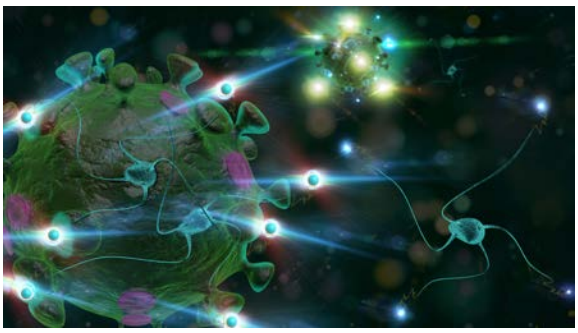
"Non-Conventional" Approaches and Ligands for Virus Detection

Róbert E. Gyurcsányi, István Makra, Zsófia Bognár, László Simon

Department of Inorganic and Analytical Chemistry, Budapest University of Technology and Economics, Szt. Gellért tér 4, Budapest, 1111 Hungary
gyurcsanyi.robert@vbk.bme.hu

Most diagnostic virus detection methods target only a single component of the virus, i.e., characteristic nucleic acids or proteins, even though virus pathogenesis involves whole virus particles. Hence, the measurement of intact virus particles, which is important also for characterizing and standardizing virus formulations, may be considered non-conventional in the current context of virus analytics.

This talk will introduce electrochemical and optical sensing methods that we developed to detect intact viruses, addressing also the challenges of their "calibration-free" quantification even in clinically relevant settings. The main requisite in this respect was the development of devices and theories for single virus particle detection in aqueous solutions. This led to virus counters based on nanopore sensing[1] and fluorescent nanoparticle tracking analysis that enable the high-resolution sizing of virus particles along with their quantification. The sensitivity and selectivity of the detection can be enhanced by tagging characteristic virus proteins with aptamer-based ligands, transforming viruses into fluorescent nanoparticles[2], or by using *in situ* surface-induced metal encapsulation, into metallic nanoparticles to enable their measurement by nanoimpact electrochemistry[3]. The development of multivalent star-shaped aptamers, has made the non-covalent surface tagging of the viruses especially resilient to displacement in complex samples.[4]



The talk will be rounded off by presenting a new class of synthetic ligands for the selective detection of SARS-CoV-2 based on epitope-imprinted polymers.[5] In this respect, we have managed to address the deficiencies of the highly empirical methodologies by implementing a chip-based platform for both high-throughput synthesis and label-free characterization of the synthetic ligands. Even a single chip screening led to polymeric ligands with dissociation constants in the lower nanomolar range for the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein, which exceeds the affinity of RBD for its natural target, angiotensin-converting enzyme 2.

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[4] L. Simon, Z. Szakács, R. E. Gyurcsányi, *Sensors and Actuators B: Chemical* **2025**, *422*, 136520.
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