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Detecting SARS-CoV-2 in saliva by Small-angle X-ray Scattering

SARS-CoV-2, the causative agent of the COVID-19 pandemic, has speeded its spread across the globe immediately after its emergence in China in December 2019. Since then, a coordinated and tireless race for developing simple, less invasive, cheap, highly accurate, and able to be applied in large-scale tests to supply the huge demand of governments to detect infected persons and plan effective isolation strategies was initiated. Apart from this pandemic, which caused ~6.8 M deaths worldwide, the human population has suffered from many pandemics throughout history. Although in several aspects the worldwide policies to reduce the risk of epidemics have had some success, the International Health Relations (IHR) committee concluded that the world is still not well prepared to respond to a severe pandemic. The IHR has required every country for comprehensive preparedness in developing core capacities to prevent, detect, and respond to public health events. Thereby, here we present an approach based on using small-angle x-ray scattering to analyze saliva specimens combined with an automated pipeline exploiting machine learning to enable massive screening of the population for COVID-19.

The SARS-CoV-2 virus was isolated and by gamma-radiation inactivated at the Bernhard Nocht Institute for Tropical Medicine (BNITM), Hamburg. A serial dilution of the virus into two synthetic salivas (from Sigma Aldrich) was performed: 1:10, 1:100, 1:3000, and 1:20000. Except for the highest concentrated solution, the other concentration solution was chosen to represent the minimum, average, and maximum virus concentration observed in SARS-CoV-2 positive diagnosed patients in a large hospital in Germany.

Synchrotron SAXS data were collected at the P62 beamline (E= 12 keV) at the PETRA III storage ring, in Hamburg, Germany. The X-ray beam (600 x 300 μm2) is focused on the capillary filled up with the samples. The sample-to-detector distance was chosen to obtain a q-range of 0.01 nm-1 to 0.98 nm-1. Five SAXS images were collected for each sample every 1s. These images were summed up to obtain a better signal-to-noise ratio.

A diagnostic model based on principal component analysis of the linear fitting parameter at the q-range between 0.08 and 0.2 nm-1 was developed. Naive Bayes (NB) was used to classify the samples as positive or negative for SARS-CoV-2. The approach was tested by performing it directly on radiation-inactivated viruses in saliva specimens and values of sensitivity, specificity, and accuracy of 87.50%, 100.00%, and 91.67%, respectively, were obtained. Due to no additional sample preparation steps and short acquisition times, significant savings in time and cost can be achieved with the proposed method.

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