SARS-CoV-2 Detection using Peptide-functionalized Ring Resonators

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Motivation

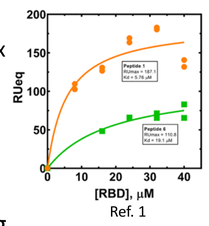
- Rapid and accurate detection of viruses and other species causing infectious diseases is of high clinical importance.
- Current biosensing technology frequently uses antibodies as a capture agent, however peptides as capture agents exhibit some advantages due to their less complex structure.
- In this work, we investigate a newly developed peptide capture agent for the detection of the SARS-CoV-2 virus on a ring resonator optical biosensor platform.

Optical Biosensing using Peptides

Background

- Peptides as capture agents

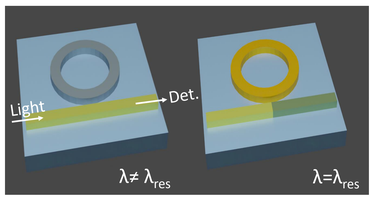
Compared to antibodies, a commonly used capture agent, peptides have a less complex structure. This makes them:
- Easier to modify
- More thermally/biologically stable
- Faster and cheaper to generate



Ref. 1

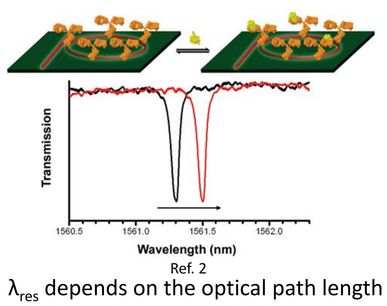
Peptide sequence has good binding affinity for SARS-CoV-2 spike protein RBD (receptor binding domain)

- Ring resonators for optical sensing



When $\lambda \neq \lambda_{res}$, all light is transmitted through the waveguide to the detector.

At λ_{res}, light couples into the ring which gives a dip in transmission.

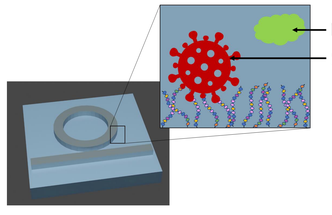


Ref. 2

λ_{res} depends on the optical path length of light in the ring, which changes when molecules are attached to the surface.

Capturing SARS-CoV-2 using Peptide-coated Ring Resonators

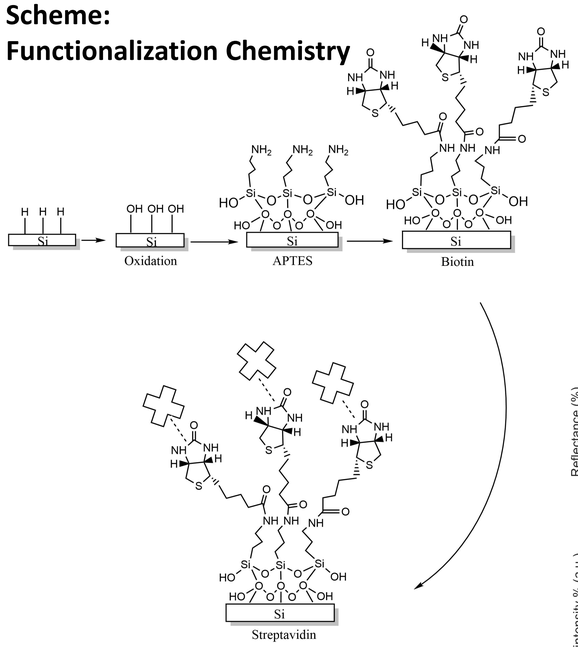
- Specific binding of SARS-CoV-2



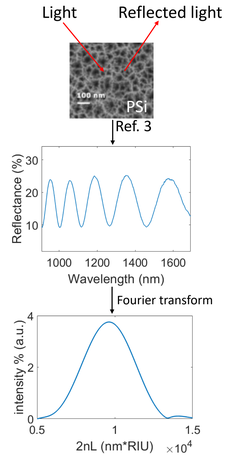
Specific binding prevents false positive diagnostic results by only capturing the desired target analyte.

Functionalization Strategy

Scheme:
Functionalization Chemistry

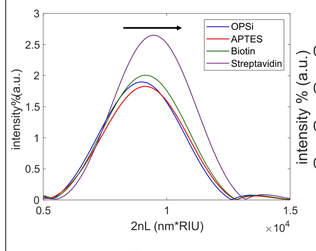


Chemistry validated on porous silicon (PSi) because it is easy to fabricate and molecule attachment can be readily verified by reflectance and ATR-FTIR measurements.

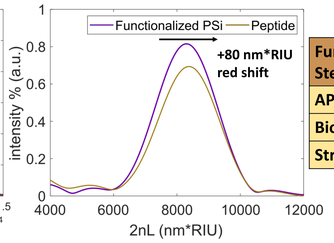


Optical Thickness Change

PSi Functionalization



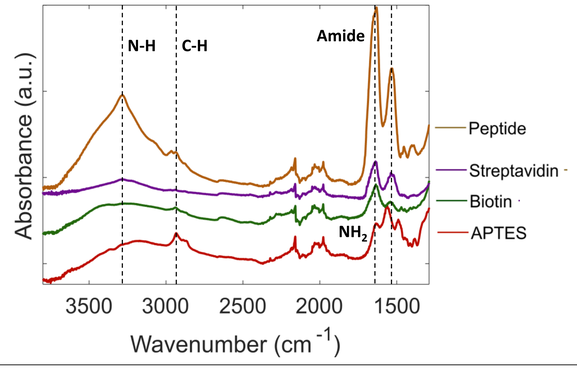
Peptide Attachment



Functionalization Step	Shift (nm*RIU)
APTES	+139.4
Biotin	+20.3
Streptavidin	+322.7

Each subsequent step has a **red shift**, which indicates that material was successfully added during functionalization

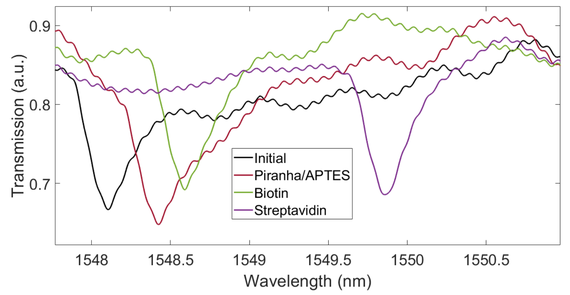
ATR-FTIR Spectra of PSi Functionalization



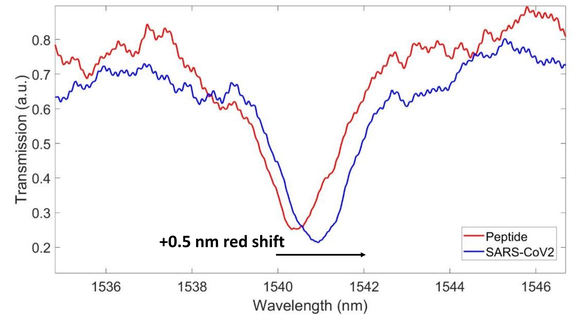
Expected peaks are present in the spectrum after each step, confirming each species was successfully attached to the PSi surface

Ring Resonator Sensor Results

Functionalization and SARS-CoV-2 Virus Exposure



Step	Avg. Shift (nm)	Sd. Dev (nm)
APTES	+0.3	0.07
Biotin	+0.1	0.04
Streptavidin	+0.4	0.11



2h incubation of **SARS-CoV-2 virus, isolate USA-WA1/2020 (Lineage A)** at a 10^3 pfu/μL concentration

Conclusions and Next Steps

- Surface chemistry approach was validated for attaching biotin-functionalized peptides to silicon surfaces
- Ring resonators were functionalized with newly developed peptides for the detection of SARS-CoV-2 virus
- Future work:
  - Assess sensitivity and selectivity of peptide capture agent
  - Compare results to SARS-CoV-2 detection with antibodies

References and Acknowledgements

[Ref. 1] Yang, F., Liu, L., et. al. Phage Display-Derived Peptide for the Specific Binding of SARS-CoV-2. *ACS Omega.* 2022; 7(4):3203-3211.

[Ref. 2] Washburn AL, Gunn LC, Bailey RC. Label-Free Quantitation of a Cancer Biomarker in Complex Media Using Silicon Photonic Microring Resonators. *Analytical Chemistry*. 2009; 81(22):9499-9506.

[Ref. 3] Layouni, R., Cao, T., Coppock, M.B., Laibinis, P.E., Weiss, S.M. Peptide-Based Capture of Chikungunya Virus E2 Protein Using Porous Silicon Biosensor. Sensors. 2021;21(24):8248.

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